Prosthetic heart valve and method for making such a valve

The present invention relates to a prosthetic heart valve from biological tissue and to a method of making such a valve.

The human heart has a right side and a left side. The function of the right side of the heart is to collect de-oxygenated blood from the body, in the right atrium, and pump it, via the right ventricle, into the lungs so that carbon dioxide can be dropped off and oxygen picked up. The left side collects oxygenated blood from the lungs into the left atrium. From the left atrium the blood moves to the left ventricle which pumps it out to the body.

Starting in the right atrium, the blood flows through the tricuspid valve to the right ventricle. Here it is pumped out through the pulmonary valve and travels through the pulmonary artery to the lungs. From there, blood flows back through the pulmonary vein to the left atrium. It then travels through the mitral valve to the left ventricle, from where it is pumped through the aortic valve to the aorta. From the aorta, the blood is divided between major arteries which supply the upper and lower body.

The tricuspid valve, pulmonary valve and aortic valve each comprise three leaflets (or cusps). The mitral valve has two leaflets. All heart valves are non-return valves, i.e. they ensure blood flow in only one direction and open under the influence of pressure differences. The mitral valve and tricuspid valve ensure that blood can flow from the atria to the ventricles and not the other way. The pulmonary valve and aortic valve ensure blood flow from the ventricles to the pulmonary vein and aorta respectively.

A malfunctioning heart valve may result in either backward flow (regurgitation) or impeded forward flow (stenosis). Certain heart valve pathologies may necessitate the complete surgical replacement of the natural heart valves with heart valve prostheses.

US 4,441,216 discloses a method for making a replacement heart valve. In this document, the replacement heart valve is made by taking a piece of pericardial tissue, tanning the tissue and cutting three leaflets. The leaflets are then connected to each other and to a stent via stitching.

US 2003/0130729 describes a percutaneously implantable

replacement heart valve device. The replacement heart valve device comprises a stent member and a biological tissue artificial valve means disposed within the inner space of the stent member. The method of making the replacement heart valve device involves taking a rectangular fragment of animal pericardium, treating, drying, folding and rehydrating it in such a way that it forms a two- or three-leaflet valve. At its cylindrical base, two borders are stitched together.

It is an object of the present invention to provide an improved prosthetic heart valve and an improved method of making a prosthetic heart valve. This object is achieved by a method of making a prosthetic valve according to claim 1 and a prosthetic heart valve according to claim 8.

According to one aspect of the invention, the method of making a prosthetic heart valve comprises the steps of placing a piece of biological tissue in or over a mould, and simultaneously tanning said tissue and forming it to an appropriate shape.

Traditionally, biological tissue is tanned in a first step. After tanning, the tissue is cut into several pieces of appropriate shape. These pieces are then sutured back together to form the prosthetic heart valve. Inventors however have found that the biological tissue can be tanned and given the appropriate shape simultaneously by placing it in or over a mould and applying appropriate tension. There is thus no need for cutting tissue into several pieces and then suturing them back together. The result is a heart valve that resembles a human heart valve much better. Since the heart valve is from a single biological tissue (thus also from a single animal), the tissue of the heart valve is more homogeneous. Additionally, no sutures are required. Sutures in a prosthetic heart valve device are problematic for a number of reasons. They cause local stress concentrations and limit the life time of a prosthetic heart valve and are the main cause for leakage occurring in prosthetic heart valves. Also, a prosthetic heart valve aims at being anatomically correct in comparison to a normal heart valve, and sutures are not anatomically correct.

Preferably, in some methods according to the invention, the step of placing the biological tissue in or over a mould comprises using two moulds, a positive mould with substantially the desired shape of the valve and a negative mould with a negative shape of said positive mould. Using two moulds with a

positive and a negative shape is advantageous in the process of shaping the heart valve.

Optionally, said step of placing the biological tissue in or over a mould comprises the steps of placing the tissue over said positive mould and then placing said negative mould over the biological tissue. Another option is that said step of placing the biological tissue in or over a mould comprises the steps of placing the biological tissue in said negative mould and then placing the positive mould within the negative mould.

Optionally, the mould that the tissue is placed over has a bottom ring and said step of placing said biological tissue over a mould includes folding the tissue around said bottom ring. The result of folding the tissue around such a bottom ring is to have a heart valve with a ring which can be fixed to a support structure. When the prosthetic heart valve device (prosthetic heart valve and support structure) is positioned appropriately in a patient's body (e.g. for an aortic heart valve, at the connection of the heart to the aorta), leaks around the outside of the valve may, in certain cases, be avoided. Optionally, said bottom ring may be a conical bottom ring. This shape may be given to further reduce leaks around the valve. Yet another option is that the bottom ring is ridged or undulated, which may also be beneficial in reducing leaks around the valve.

However, the appropriate mould and also whether a plurality of moulds should be used, depends to a large extent on the desired shape of the valve. In this sense, two kinds of valves should be distinguished: "open" valves and "closed" valves. "Open" valves have a substantially open cylindrical shape in a relaxed state. Their leaflets are merely defined by parts of the cylinder that can move inwardly when appropriate pressure conditions are created. "Closed" valves have a partly cylindrical shape which however is closed by three (or two) leaflets at one side. In use, under suitable pressure, these leaflets may move outward to open and let blood pass. Open and closed valves work in the same way, but their default state is different (respectively open and closed). Clearly, the mould to be used for shaping the valve depends on the desired end shape of the valve.

Preferably, the tanning step occurs by subjecting the biological tissue to a glutaraldehyde solution. The tanning step occurs simultaneously with the shaping of the heart valve, with the biological tissue placed in or over

a mould. The goal of the tanning step is to make the tissue biocompatible. Other aldehydes are known in the art and may be used. The best results have been obtained with glutaraldehyde solutions with concentrations between 0.1 and 1%, preferably around 0.65%.

Optionally, in the method according to the invention, said step of forming the tissue to an appropriate shape includes applying tension to the tissue. By applying tension (e.g. by pulling, by using two moulds or by creating a vacuum) in appropriate points at appropriate moments, the tissue takes the desired form of the heart valve.

In some embodiments, the method of making a prosthetic heart valve includes an additional step of cutting the biological tissue to form the leaflets of the valve. The whole process was started with a single piece of biological tissue. After the tissue has been given the appropriate shape to function as a heart valve and has been tanned, in some embodiments, the leaflets are formed by making cuts in the single piece of biological tissue and as such “opening” the tissue. This way no form of suturing is required to form the leaflets. As mentioned before, sutures are a source of inconvenience in prosthetic heart valves. These cuts may be made when the tissue is placed over the mould, using the shape of the mould as a guide in the cutting process. The cuts may also be made after it has been released from the mould and fixed on a support structure, together forming a heart valve device, hereinafter further described. This may be a bit more complicated, but it has the advantage of having the valve in its mounted position when cutting. This avoids possible cutting errors due to the valve being mounted in a support structure slightly differently. It is however also possible to use an additional mould or guide for the cutting process or to cut without any additional guide or tool.

According to a second aspect of the invention, a method of making a prosthetic heart valve device is provided, said method comprising the steps of making a prosthetic heart valve according to the invention and the additional step of attaching the prosthetic heart valve to a support structure. The support structure, in use, has the function of supporting the heart valve, and mostly supporting the leaflets of the heart valve to keep them in their desired shape.

According to another aspect of the invention, a prosthetic heart valve of a single piece of biological tissue is provided, said valve comprising a

substantially cylindrical base and leaflets, characterised in that said cylindrical base and leaflets have a continuous peripheral wall. The single piece of biological tissue ensures a homogeneous heart valve, and the continuous peripheral wall avoids the need of any sutures (which are known to cause problems during the life-time of the heart valve).

Preferably, the heart valve is formed using a method according to the invention. The method of making a prosthetic heart valve described here within is the most advantageous way of providing a heart valve of homogeneous tissue without any sutures.

In an aspect of the invention, the invention provides a prosthetic heart valve of a single piece of biological tissue, said valve being an open valve and having a continuous peripheral wall.

In another aspect according to the invention, a prosthetic heart valve device is provided comprising a prosthetic heart valve of a single piece of biological tissue and a support structure for supporting said valve, said valve comprising a cylindrical base and leaflets, said cylindrical base and leaflets having a continuous peripheral wall. The support structure is provided such that the leaflets in use can maintain their original shape and function properly. Any suitable support structure may be used.

In some embodiments, the support structure of the heart valve device comprises three legs for fixing three leaflets of the valve. The present invention is especially aimed at prosthetic aortic heart valves. Aortic heart valves comprise three leaflets. However, within the scope of the present invention, any suitable support structure may be used such as e.g. balloon expandable or self-expandable stents.

A preferred way of connecting the leaflets to the support structure is through suturing. It is to be noted that these sutures are not sutures for closing or forming the heart valve (the peripheral wall of the heart valve is continuous); the heart valve itself is completely free from sutures and thus has a continuous peripheral wall. The sutures serve merely to attach the valve to the support structure. Another preferred way of fixing the leaflets of the valve to the support structure is by using bendable piercing members (like staples) along the support structure. It is possible to provide the support structure with these piercing members already during its manufacturing. It is also possible to provide them separately. These piercing members can be bent around the

support perforating the tissue of the heart valve, and as such securing the valve in place. Other mechanical means, such as clamps or clips could also be used for fixing the leaflets along the support structure.

In some embodiments, the support structure comprises two annular discs for positioning the prosthetic heart valve in place, said two annular discs interconnected by a cylinder. By using two annular discs interconnected by a cylinder, the support structure can be positioned at the junction of e.g. the left heart ventricle and the aorta, in the place of the original malfunctioning heart valve (if the prosthetic heart valve is an aortic heart valve). Additionally, in combination with the heart valve comprising a bottom ring (if a mould with a bottom ring has been used) it avoids leaks around the prosthetic heart valve device.

Preferably, the support structure of the heart valve device is collapsible. Optionally, the support structure is made from nitinol. Heart valve replacement can occur in open heart surgery, but preferably it occurs percutaneously by using a catheter or in minimally invasive surgery, such as thoracotomy or sternotomy (or similar). To enable this, the support structure needs to be collapsible. One way of giving the support this collapsibility is to manufacture it (or its parts) with nitinol. Nitinol is a shape memory alloy and additionally has the necessary characteristic of biocompatibility. Alternatively, it is possible to use other shape memory alloys. A valve device with a nitinol support structure as such is self-expandable. It can expand to its proper size and shape once delivered in the appropriate position. Alternatively, the valve device may be made with a different support structure which may expand to its desired form using other known conventional means, such as by mechanical means or by a balloon. One known alternative way is e.g. the use of a balloon expandable stent as the support structure. Materials which may be used for the support structure in this case are e.g. stainless steel and cobalt chromium alloys.

The present invention is especially aimed at providing prosthetic heart valves and heart valve devices for replacing aortic and pulmonary heart valves. However, the invention may explicitly also be used to provide a prosthetic tricuspid or mitral valve.

These and further possible embodiments of the invention and their advantages will be explained, only by way of non-limiting example, with reference to the appended figures, in which:

Figure 1(a) is a perspective view of a preferred mould used in the method according to the present invention;

Figure 1(b) is a perspective view of another preferred mould used in the method according to the present invention;

Figure 1(c) is a top view of the mould shown in figure 1(a);

Figure 1(d) is a perspective view of yet another preferred mould used in the method according to the present invention;

Figures 2(a)-2(d) show perspective views of different steps in a preferred method of making a "closed" valve according to the present invention;

Figures 2(e)-2(h) show perspective views of different steps in a preferred method of making an "open" valve according to the present invention;

Figures 3(a)-3(c) show perspective, schematic views of three possible heart valves according to the invention.

Figures 4(a)-4(c) show perspective views of support structures that may be used in heart valve devices according to the present invention;

Figures 5(a) and 5(b) shows in perspective view two steps in a preferred method of making a "closed" heart valve device according to the present invention;

Figure 5(c) shows the top view of the heart valve device shown in 5(a);

Figure 5(d) shows a perspective view of an "open" heart valve device according to an embodiment of the present invention.

Before the heart valve is actually made, suitable tissue needs to be harvested. Preferably, biological tissue is tissue from bovine, equine or porcine pericardium. In principle, other biological tissue may be used as well. Preferably, the whole pericardial sac is harvested and is inspected for defects, such as blood in the tissue, or anatomical defects. Then the fat tissue is removed. Once a clean pericardium has been selected, it is normally put in a clean container in sterile distilled water or similar for cleansing and

transportation. During the cleansing, the distilled water may be refreshed a number of times. The tissue is then transported to the laboratory where the heart valve is going to be made.

From the selected pericardium, the most suitable tissue must now be selected. Positive criteria used for this selection may include: homogeneous colour and texture of tissue, well hydrated, absence of blood, absence of grooves and homogeneous thickness (depending on the application, the desired thickness may be different, e.g. of at least a 100 microns. The invention is not limited in this sense.). A piece of tissue is then cut from the pericardium. This piece of tissue should of course be big enough to be placed over the mould used in the manufacturing process, and the exact dimensions of the selected piece may vary with the desired size of the heart valve and the mould chosen.

With reference to figures 1(a) and (b), two possible moulds (10) which may be used in the method according to the invention are shown. In figure 1(a), the mould includes a bottom ring (11), a cylindrical base (19) for forming a continuous cylindrical base in the resulting heart valve, and a three winged structure at the top for forming three leaflets. In figure 1(b), the mould does not have such a bottom ring, but has the same cylindrical base and the same three winged structure. In another mould that may be used, the bottom ring may be conical in shape (not disclosed in any figure). Yet another option is that the bottom ring (11) of the mould may be ridged or undulated (not disclosed in any figure) such that the resulting heart valve also comprises an undulated or ridged bottom ring. Both figures 1(a) and 1(b) refer to moulds that are suitable for making a “closed” heart valve. “Closed” valves have a partly cylindrical shape which is closed by three (or two) leaflets at one side. In use, under suitable pressure, these leaflets may move outward to open and let blood pass. The moulds shown in figures 1(a) and 1(b) have an appropriate shape with (in this case) three wings (17) for forming the leaflets of the heart valve.

Figure 1(c) shows a top view of the mould shown in figure 1(a). It more clearly shows the three wings (17) of the structure at the top of the mould. The cylindrical base (19) indicated in figure 1(a) may also be more pronounced, i.e. the point where the base transforms into the leaflets may be higher.

Figure 1(d) shows a cylindrical mould, which is suitable for making an "open" valve. "Open" valves have a substantially open cylindrical shape in a relaxed state. Their leaflets are merely defined by parts of the cylinder that can move inwardly when appropriate pressure conditions are created.

Figures 2(a) and 2(b) show the first steps according to the invention. The mould (10) shown in these figures has a substantially flat bottom ring. As has been mentioned before, this ring may also be conical or the mould may not have a ring. The biological tissue (12) has been made available and it is placed over the mould. The tissue placed over the mould is shown as hatched in this figure. The top side of the mould should be covered as completely as possible, in order for the tissue to take the shape of the mould. The goal of the bottom ring of the mould is that by covering the ring with tissue, a ring is formed which may reduce, in certain cases, the leaks around the valve when in use. Tension is applied to the tissue to shape it more accurately.

A negative mould (15), which has the negative shape of the positive mould (such as shown in figure 2(c)) may be placed over the tissue to help shape the tissue. At this point, the tanning process begins. The tissue including the mould (and optionally a second mould) is placed in a tanning solution. Preferably, a glutaraldehyde solution with a concentration between 0.1% and 1%, most preferably around 0.65%, is used. It is important to note that the shaping of the tissue and the tanning of the tissue occur simultaneously. This allows the valve to be formed from a single piece of biological tissue without any sutures.

The order of using the two moulds may also be reversed. The tissue may first be placed in negative mould (15) and then positive mould (10) may be used to help the tissue take the proper shape. In the following, the tanning and shaping process is described in a method using two moulds. It should however be noted that the tanning and shaping may also occur using a single mould.

Steps of an alternative method according to the present invention are illustrated in figures 2(e) - 2(g). Figure 2(e) shows a single piece of biological tissue (12) and a mould (10'). The mould (10') is suitable for making an "open" valve. The biological tissue is placed over the mould (10'), similarly to the steps described before with respect to figures 2(a) and 2(b). Also, when forming an "open" valve, a negative mould (15') may be used. This is illustrated

in figure 2(g). Negative mould (15') has the negative shape of positive mould (10').

The tanning (and shaping) process may pass through various phases. One possibility is that after some 15 minutes, the negative mould is taken away and it is ensured that the tissue takes the desired shape of the mould by forcing it in the appropriate shape. The tissue may extend beyond the borders of the mould, since some form of tension may have been applied to the tissue to give it the appropriate shape. In a next step, the tissue, still on the positive mould, is placed in a fresh glutaraldehyde solution for a few hours, e.g. approximately two hours.

An alternative possibility is that the positive mould is taken away after some 15 minutes and the tissue stays positioned in the negative mould. It is important to also ensure in this case that the tissue assumes the desired shape, i.e. the tissue is manipulated in such a way that it has no folds. Then, the tissue, still in the negative mould, is placed in a glutaraldehyde solution for a few hours, e.g. approximately two hours.

Optionally, the next step may be to cut the tissue along the three wings of the mould to form three leaflets. This is illustrated in figure 2(d). Suitable scissors (13) or other cutting means may be used. The cut may be performed on the top of the union of the leaflets, e.g. by cutting parallel to the vertical plane of the valve. Alternatively, the cut may be performed slightly below the union of the leaflets by cutting in a plane perpendicular to the vertical plane of the valve. Additionally, it is possible to use both cutting methods. In the case of the open valve of figure 2(h), cuts are also made to provide a valve with a cylindrical shape, which is open on both sides. Notice that in this case, no cuts are made to form leaflets of the valve.

After these hours in the glutaraldehyde solution, the remaining mould is removed when it is ensured that the tissue has taken the appropriate shape. Yet another possibility is leaving the valve in or over the mould for a longer time. The benefit of removing the mould after a while is to put the tissue in contact with the glutaraldehyde along its entire surface, which accelerates the tanning process. By keeping the valve in the mould longer, the tanning process may be slower, but the valve will keep its shape better. A way to balance both these advantages and disadvantages can be to provide the mould with a plurality of perforations along its surface or to make the mould out

of a meshed material, such that it is permeable to a certain extent.

The tanning may continue until the desired tanning level has been obtained. At this point, tissue that sticks out beyond the desired shape of the valve may be cut. But this should be done carefully; the final cut is only made after the heart valve has been fixed on a support structure.

At this point, the heart valve is ready to be positioned on a support structure. For reasons of clarity, the tissue is no longer hatched. Figures 3(a) and 3(b) show two possible embodiments of the heart valve (1) according to the invention. Figure 3(a) shows a heart valve (1) comprising three leaflets (2), a cylindrical base (3) and a bottom ring (4). If another mould is used, the resulting heart valve may look differently, as illustrated in figure 3(b). The cylindrical base (3) is much less pronounced and it does not have a bottom ring. Additionally in figure 3(b), the leaflets have already been separated through cuts (5). Both figures 3(a) and 3(b) refer to closed heart valves. Figure 3(c) illustrates an open valve (1'), which may result from the previously described process. In figure 3(c), the cylindrical base (3') cannot be readily be distinguished from the leaflets (2'). The composition of open valve (1') comprising a cylindrical base (3') and leaflets (2') can more clearly be recognized in figure 5(d). Also the open valve according to the present invention has a continuous peripheral wall.

A support structure (20) is shown in figure 4. It comprises a bottom annular disc (21), a top annular disc (23) connected with each other through a cylindrical structure (22). In the case of a prosthetic heart valve device used as a replacement aortic valve, the bottom disc (21) may be regarded as the ventricular disc and the top disc (23) may be regarded as the aortic disc. The top disc (23) preferably comprises three legs (24) for supporting three leaflets of the heart valve. In order to be able to replace a heart valve percutaneously or by minimally invasive surgery (i.e. not through open heart surgery), the support structure has to be made collapsible. A preferred way of making the support structure collapsible is by making it from nitinol. The heart valve device in this case is self-expandable. Alternative collapsible support structures may also be used. Suitable means for expanding the valve device once it has been delivered in the appropriate position may then need to be provided.

Another possible support structure is shown in figure 4(b), which shows a schematic view of a balloon expandable stent. A self-expandable

stent may also be used, such as shown in figure 4(c). Such alternative structures are well known in the art. The invention is not limited to any particular support structure. Instead the heart valve according to the present invention may be used with any suitable support structure.

In a next step, to form a heart valve device ready for implant in the body, the support structure is placed over the heart valve. The legs (24) of the support structure are connected to the three leaflets (2), preferably though suturing or using mechanical means such as bendable piercing members, clips, or clamps. This has been shown, very schematically, in figure 5(a). The valve is also connected to the support along its bottom periphery. Non absorbable polyester may be used for suturing. In a next step, the leaflets (2) may be formed by cutting the tissue along the three dotted lines, indicated in figure 5(b). This way, the three leaflets (2) are formed. It is important to note that even though the legs may be sutured or otherwise attached to the support structure, the valve still has a continuous peripheral wall. As is also schematically indicated in figure 5(b), the remaining extra tissue is cut of along the bottom of the support. As was mentioned before, it is also possible that the three leaflets have already been formed by cutting in an earlier step.

For reasons of clarity, the tissue (12) is not shown as hatched in these figures. In figures 5(a) and 5(b), the tissue (12) that sticks out beyond its desired form has been left out, also for reasons of clarity. In figure 5(c), the top view of a heart valve device is shown and this extra tissue is shown. Part of this tissue may already have been removed in a previous step.

It is also foreseen that with an alternative design of the support structure the valve may be placed over the support structure (instead of the other way around). In this case, the support structure would still have three legs but would not have a top disc. The way of fixing the valve to the support structure is further similar to what was described before.

An open valve mounted on a similar support structure as shown in figures 5(a)-5(c) is shown in figure 5(d). The three leaflets 2' of the heart valve device are formed by the parts of the cylindrical valve which are not attached to the three legs (24) of the support structure. The material in between the legs will move inward and outward in use due to the prevailing pressure conditions. The cylindrical base (3') of the open valve is not visible, since it is covered by the support structure.

Once the prosthetic heart valve device has been made available, it should be inspected to ensure it has the appropriate dimensions and it is well connected to the support structure. If the inspection results are positive, the device should be made sterile before it can be implanted in a patient's body. The sterilization may take place through a chemical process or through radiation. These techniques are well known in the art.

Claims

1. A method of making a prosthetic heart valve (1,1') comprising the steps of placing a piece of biological tissue (12) in or over a mould (10, 10'), and simultaneously tanning said tissue and forming it to an appropriate shape.

2. A method of making a prosthetic heart valve according to claim 1, characterised in that the step of placing the biological tissue in or over a mould comprises using two moulds, a positive mould (10; 10') with substantially the desired shape of the valve and a negative mould (15; 15') with a negative shape of said positive mould (10; 10').

3. A method of making a prosthetic heart valve according to claim 2 and the step of placing the biological tissue in or over a mould comprises the steps of placing the tissue over said positive mould (10; 10') and then placing said negative mould (15; 15') over the biological tissue or comprises the steps of placing the biological tissue in said negative mould and then placing the positive mould within the negative mould.

4. A method of making a prosthetic heart valve according to any previous claim, characterised in that the mould has a bottom ring (11) and said step of placing said biological tissue in or over a mould includes folding the tissue around said bottom ring (11).

5. A method of making a prosthetic heart valve according to any previous claim, characterised in that said step of forming the tissue to an appropriate shape includes applying tension to the tissue.

6. A method of making a prosthetic heart valve according to any previous claim, including the additional step of cutting the biological tissue to form the leaflets (2; 2') of the valve.

7. A method of making a prosthetic heart valve according to any previous claim, characterised in that the prosthetic heart valve is a closed valve.

8. A method of making a prosthetic heart valve according to any of claims 1-5, characterised in that the prosthetic heart valve is an open valve.

9. A method of making a prosthetic heart valve device comprising the steps of claim 1 and the additional step of attaching the prosthetic heart valve to a support structure (20).

10. A prosthetic heart valve (1) of a single piece of biological tissue (12), said valve comprising a cylindrical base (3; 3') and leaflets (2; 2'), characterised in that said cylindrical base and leaflets have a continuous peripheral wall.

11. A prosthetic heart valve according to claim 10, characterised in that is a closed valve.

12. A prosthetic heart valve according to claim 10, characterised in that it is an open valve.

13. A prosthetic heart valve according to any of claims 10-12, characterised in that the heart valve is made by a method according to any of the claims 1-6.

14. A prosthetic heart valve device comprising a prosthetic heart valve according to any of claims 10-13 and a support structure (20; 20'; 20'') for supporting said valve.

15. A prosthetic heart valve device according to claim 14, characterised in that the support structure (20) comprises three legs (24) and the leaflets (2) of the valve are each connected to one of said legs.

16. A prosthetic heart valve device according to claim 14 or 15, characterised in that the support structure comprises two annular discs (21,23) for positioning the prosthetic heart valve in place, said two rings interconnected

by a cylindrical structure (22).

17. A prosthetic heart valve device according to claim 14, characterised in that the support structure is a balloon expandable or a self-expandable stent.

18. A prosthetic heart valve device according to any of claims 14-16, characterised in that the support structure is collapsible.

19. A prosthetic heart valve device according to claim 18, characterised in that, said support structure is made from nitinol.

20. A prosthetic heart valve device according to claim 18, characterised in that, said support structure is made from stainless steel or a cobalt chromium alloy.

21. A prosthetic heart valve device according to any of claims 14-20, characterised in that it is a prosthetic aortic or pulmonary heart valve device.

22. A prosthetic heart valve device according to any of claims 14-21, characterised in that is a percutaneous heart valve device.

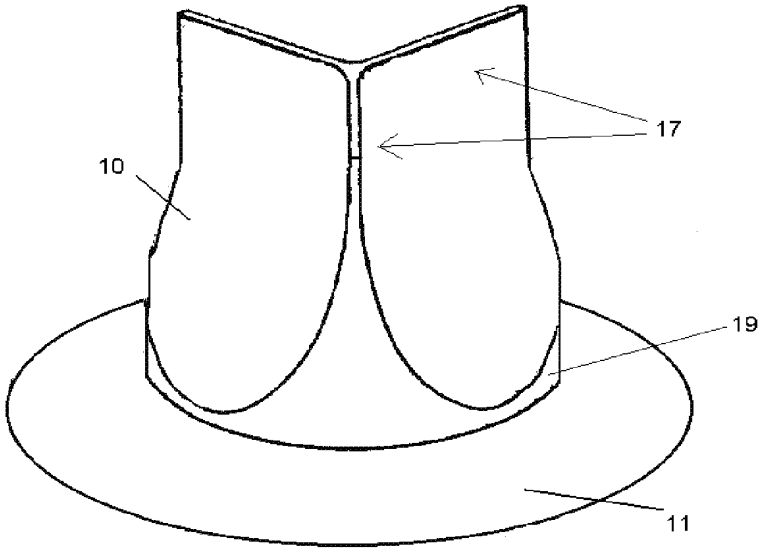
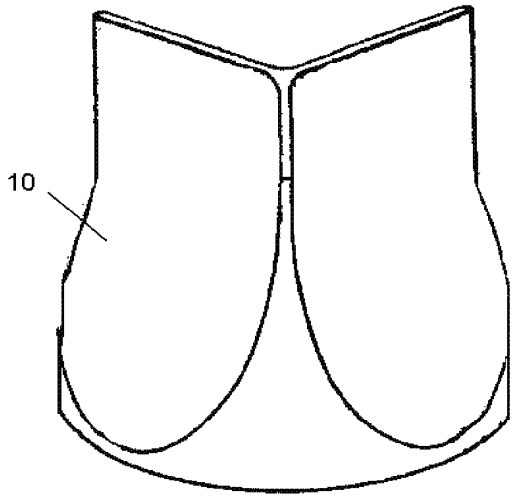


Figure 1(a)



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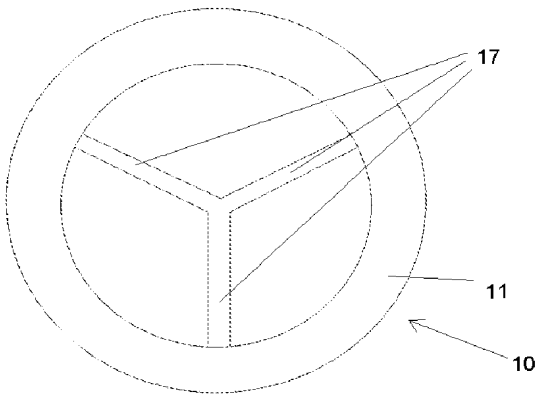


Figure 1(c)

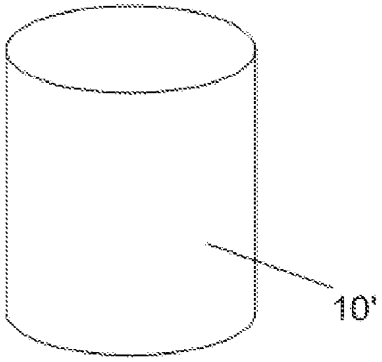


Figure 1 (d)

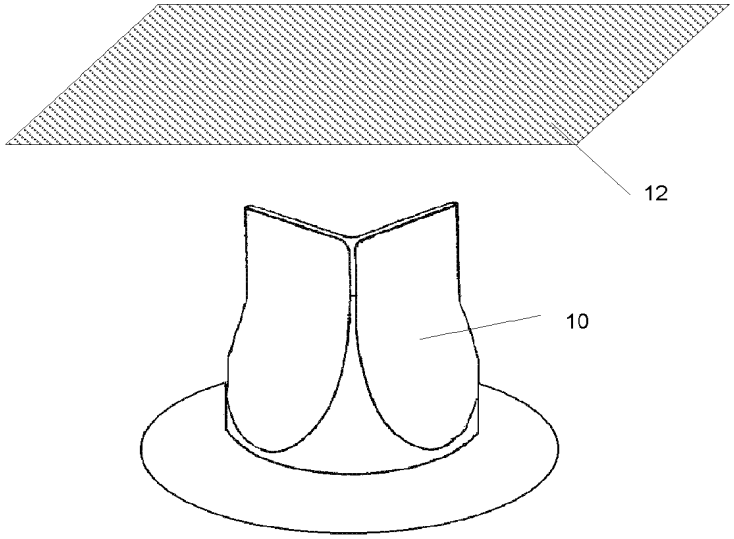


Figure 2(a)

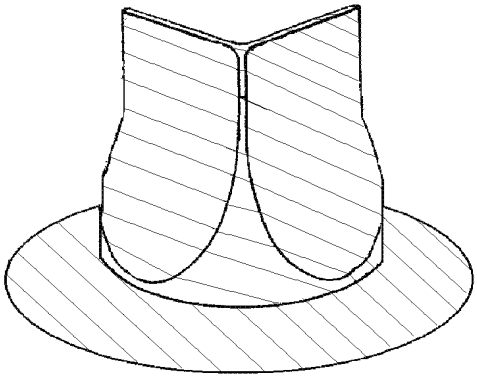
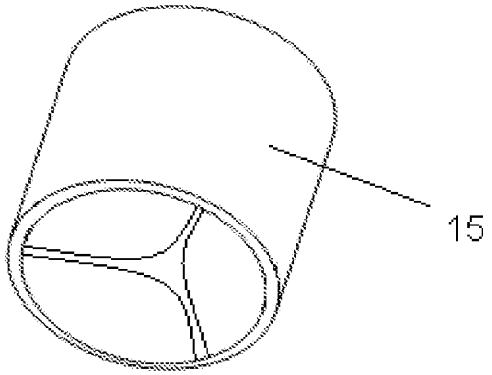


Figure 2(b)



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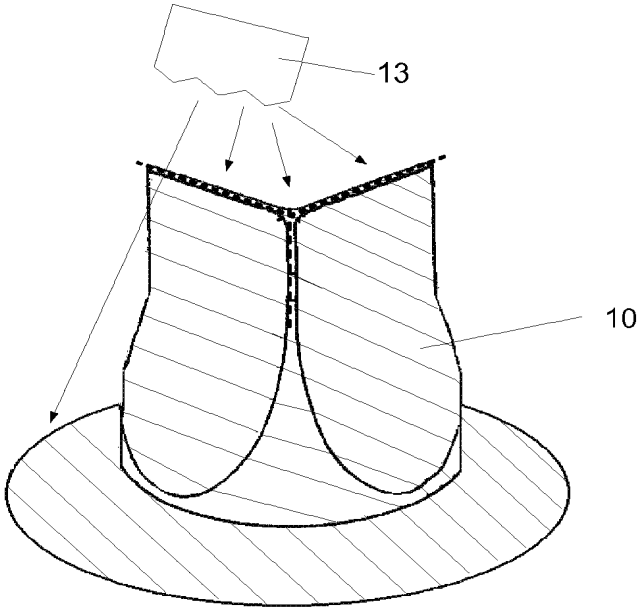

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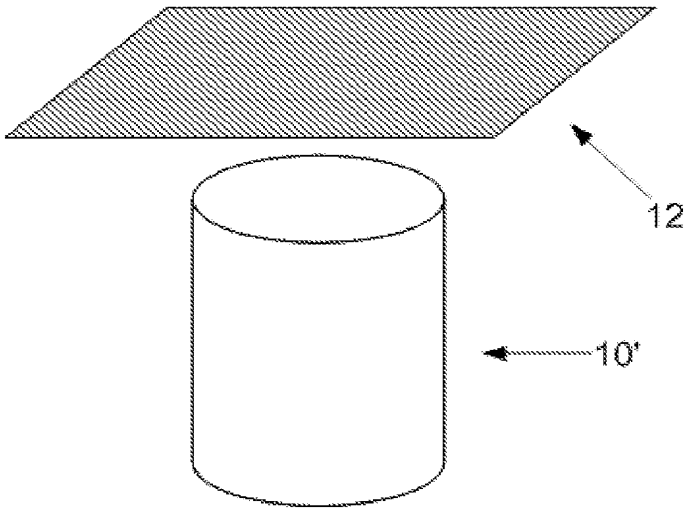

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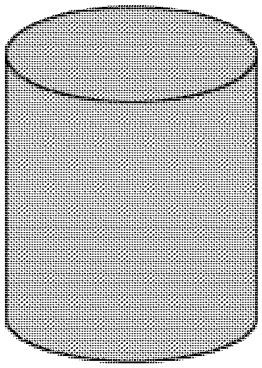

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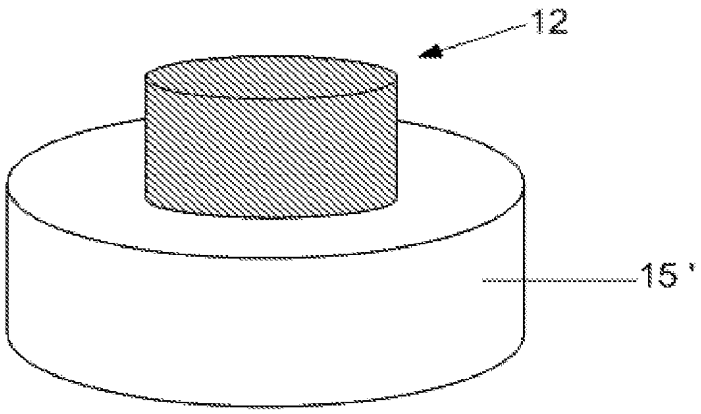

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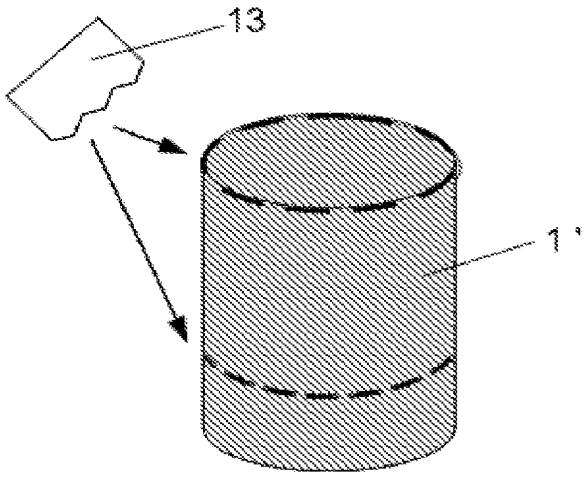

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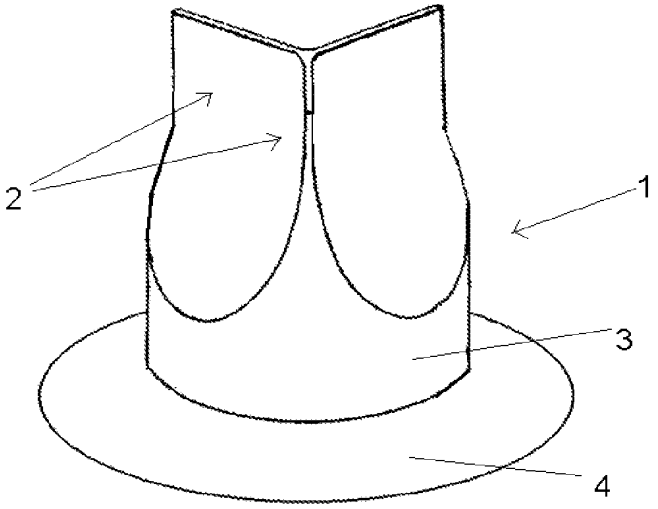
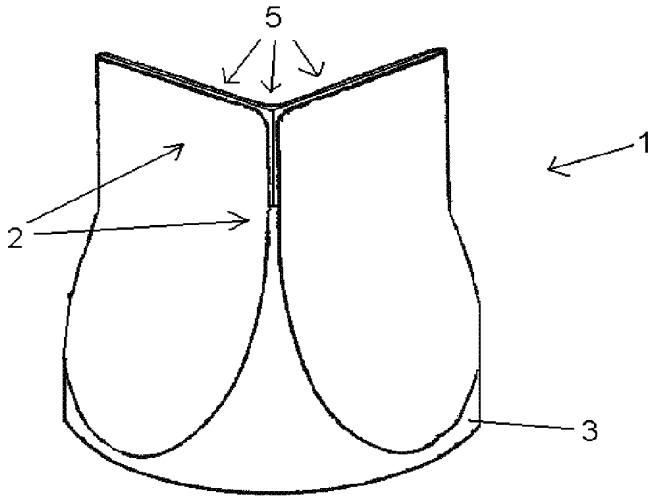


Figure 3(a)



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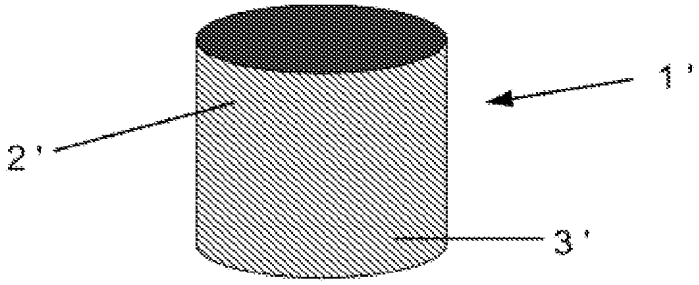

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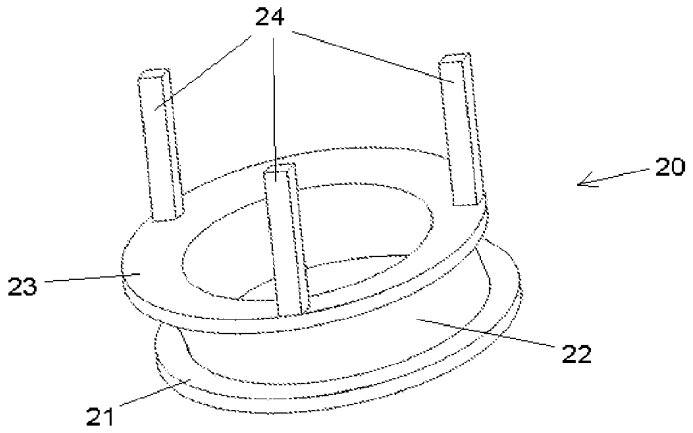
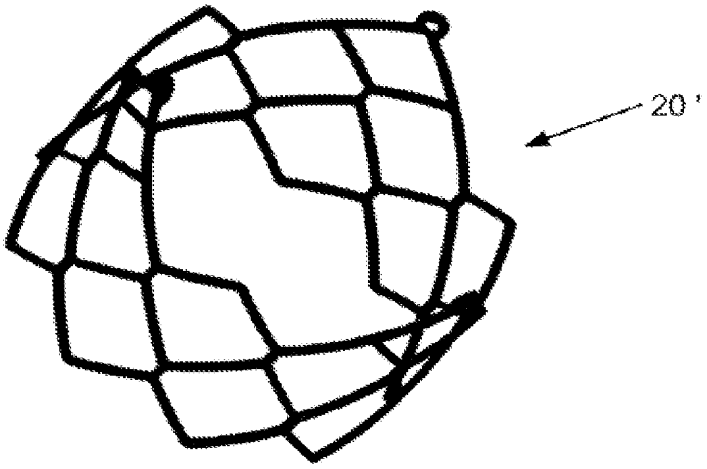


Figure 4 (a)



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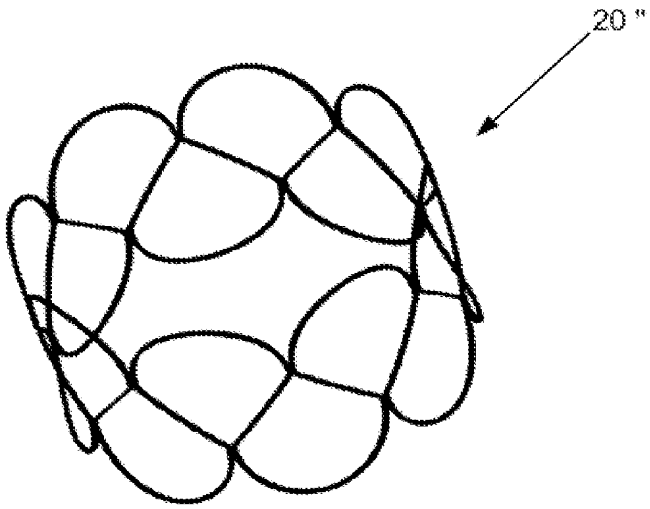

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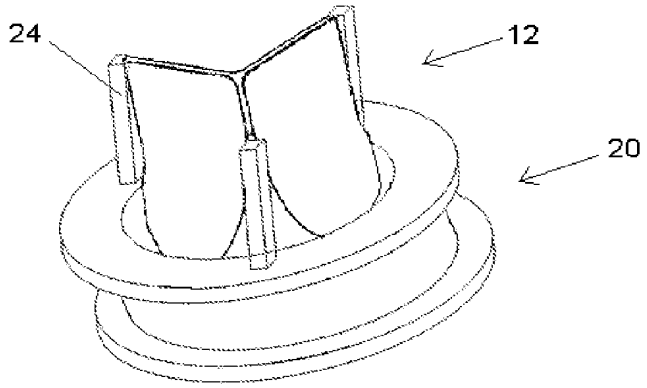
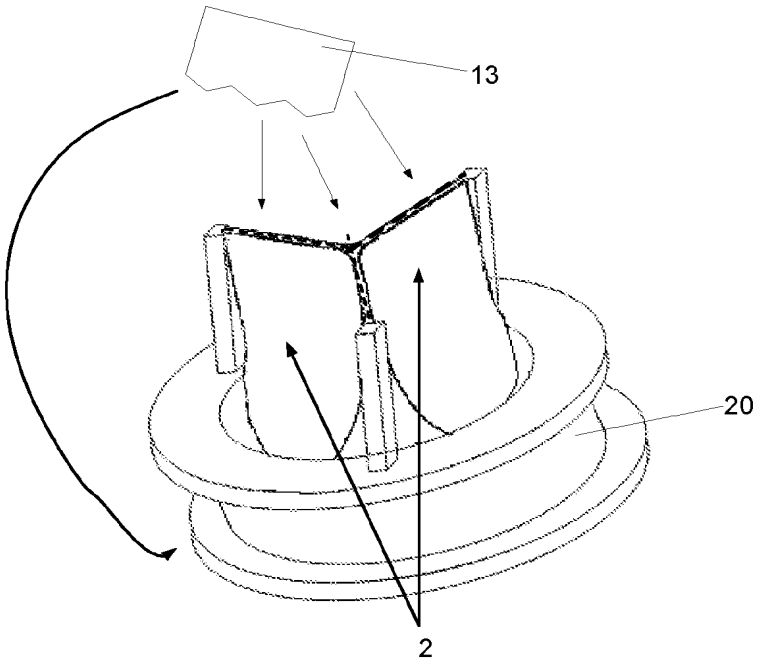


Figure 5(a)



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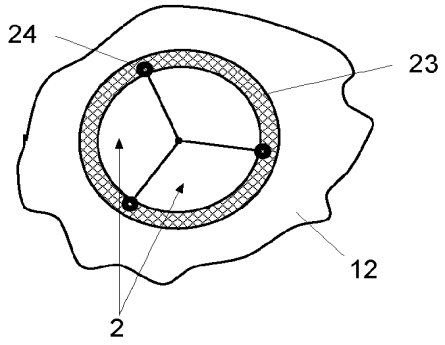

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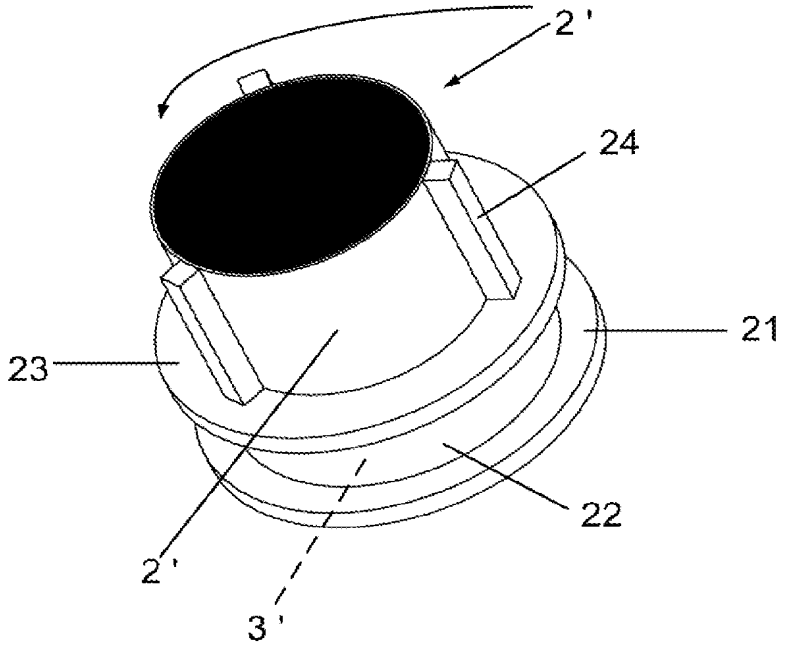

Figure 5(d)

INTERNATIONAL SEARCH REPORT

International application No
PCT/EP2009/057970

A. CLASSIFICATION OF SUBJECT MATTER
INV. A61F2/24

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
A61F

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	GB 2 046 165 A (ROSS D N; BODNAR E) 12 November 1980 (1980-11-12) page 2, line 99 - page 3, line 31 figures 1-3	1-3, 5-15, 17-22
X	US 6 129 758 A (LOVE JACK W [US]) 10 October 2000 (2000-10-10) column 12, lines 55-64 figure 5b	1-3,5-9
X	WO 2007/046000 A (UNIV NANYANG [SG]; YEO JOON HOCK [SG]; LIM KHEE HIANG [SG]; GOETZ WOLF) 26 April 2007 (2007-04-26) paragraph [0040] figures 2,4a,4b	1-3, 5-14, 17-22

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[X] Further documents are listed in the continuation of Box C.

[X] See patent family annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

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"P" document published prior to the international filing date but later than the priority date claimed

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Date of the actual completion of the international search	Date of mailing of the international search report
11 August 2009	19/08/2009

Name and mailing address of the ISA/	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016	Espuch, Antonio

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INTERNATIONAL SEARCH REPORT

International application No
PCT/EP2009/057970

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 01/26587 A (INTERNAT HEART INST OF MONTANA [US]) 19 April 2001 (2001-04-19) page 12, lines 26-28 page 14, lines 18-28 figures 17,18	1-3, 5-14,21, 22

X	EP 1 671 604 A (PURDUE RESEARCH FOUNDATION [US]) 21 June 2006 (2006-06-21) paragraph [0038] figures 6a,6b	10-12, 14-22
A		4

1

Form PCT/ISA/210 (continuation of second sheet) (April 2005)

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/EP2009/057970

Patent document cited in search report		Publication date	Patent family member(s)		Publication date
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EP 1671604	A	21-06-2006	NONE		

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60/980,112 15 October 2007 (15.10.2007) US

(71) Applicant *(for all designated States except US)*: **EDWARDS LIFESCIENCES CORPORATION** [US/US]; One Edwards Way, Irvine, CA 92614 (US).

(72) Inventor; and
(75) Inventor/Applicant *(for US only)*: **ROWE, Stanton** [US/US]; 117 Old Course Drive, Newport Beach, CA 92660 (US).

(74) Agents: **HAUSER, David, L.** et al.; Edwards Lifesciences LLC, One Edwards Way, Irvine, CA 92614 (US).

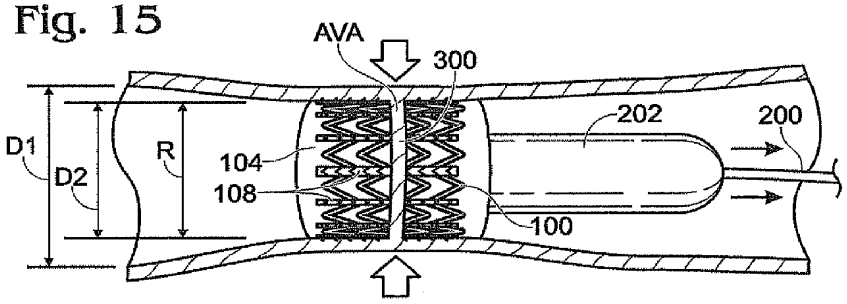
(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(84) Designated States *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, NO, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:
— *with international search report*

(54) **Title:** TRANSCATHETER HEART VALVE WITH MICRO-ANCHORS

Fig. 15



(57) **Abstract:** Various embodiments of methods and apparatus for treating defective heart valve are disclosed herein. In one exemplary embodiment, a transcatheter heart valve is disclosed that includes an expandable shape memory stent and a valve member supported by the stent. A plurality of micro-anchors can be disposed along an outer surface of the stent for engaging native tissue. The transcatheter heart valve can be configured to be advanced into a dilated valve annulus via a balloon catheter. The balloon can be inflated to expand the transcatheter heart valve from a collapsed diameter to an over-expanded diameter such that the micro-anchors engage tissue along the surrounding valve annulus. After engaging the tissue, the balloon can be deflated and the shape memory stent can retract or recoil toward its predetermined recoil diameter. As the stent recoils, the surrounding tissue is pulled inward by the stent such that the diameter of the valve annulus is reduced.

WO 2009/052188 A1

TRANSCATHETER HEART VALVE WITH MICRO-ANCHORS

FIELD

[0001] The disclosed technology relates generally to methods and devices for improving valve function of a heart. For instance, embodiments of the disclosed technology can be used to treat aortic insufficiency in a human heart.

BACKGROUND

[0002] The aortic valve in the human heart is a one-way valve that separates the left ventricle from the aorta. The aorta is a large artery that carries oxygen-rich blood out of the left ventricle to the rest of the body. Aortic insufficiency is a condition in which the aortic valve does not fully close during ventricular diastole, thereby allowing blood to flow backward from the aorta into the left ventricle. This leakage of blood through the aortic valve back into the left ventricle is often referred to as aortic valve regurgitation.

[0003] Aortic insufficiency is typically caused by aortic root dilatation (annuloaortic ectasia), which is idiopathic in over 80% of the cases. Aortic insufficiency may also result from other factors, such as aging and hypertension. In any case, the regurgitation of blood resulting from aortic insufficiency substantially reduces the pumping efficiency of the left ventricle. Therefore, even during periods of rest, the heart must work hard simply to maintain adequate circulation through the body. Over time, this continuous strain on the heart can damage the left ventricle. For example, the additional strain on the heart may result in a thickening of the heart muscle (hypertrophy). When heart-wall thickening occurs due to aortic insufficiency, the geometry of the heart can be adversely affected and the heart can be permanently damaged.

[0004] Although aortic insufficiency is relatively common, the treatment of this condition still represents a substantial clinical challenge for surgeons and cardiologists. For example, because aortic insufficiency has a long latency period, afflicted patients may already be at significant risk for heart failure by the time the symptoms arise. In many cases, when patients are not monitored

well for aortic insufficiency and are left untreated, the patient's left ventricle may become irreversibly damaged before therapy can be delivered. Therefore, even if a defective aortic valve is replaced with a prosthetic valve, the patient may never fully recover and their survival rate may be substantially impaired.

[0005] Existing methods of treating aortic insufficiency suffer from a number of significant disadvantages. For example, open heart surgical valve replacement is often too traumatic for older and/or frail individuals. Replacement of the aortic valve using existing catheterization techniques is also challenging because it is difficult to anchor a prosthetic valve within a soft and dilated annulus. More particularly, when a prosthetic valve is delivered to the site of the aortic valve and expanded, it engages and continuously exerts an outward force against the aortic valve wall. This continuous outward pressure is necessary for anchoring the prosthetic valve within the native valve but may also cause the already-dilated native aortic annulus to become further expanded. The tissue along the annulus of a valve suffering from aortic insufficiency is typically soft and flexible (as opposed to being hard and calcified as with aortic stenosis) and therefore the further expansion of the aortic annulus may lead to dislodgement of the prosthetic valve. Such dislodgement could require delivery of a still larger valve or result in death of the patient. A prosthetic valve with a very large diameter may be delivered via a catheterization technique to reduce the possibility of dislodgement. However, it follows that such a valve would also have a large diameter in its crimped condition. The delivery of such a large-diameter prosthetic valve is much more challenging and dangerous than the delivery of a relatively small prosthetic valve of the type currently used to treat aortic stenosis.

[0006] Therefore, a need exists for new and improved methods and devices for treating aortic insufficiency.

SUMMARY

[0007] Embodiments of the disclosed technology are directed to percutaneous (e.g., catheter-based) and/or minimally invasive surgical (MIS) procedures for

treating aortic insufficiency. These less invasive therapies, which do not require open-heart surgery, provide patients with a more attractive option for early treatment of aortic insufficiency, thus mitigating or even avoiding the risk of damage to the left ventricle. These less invasive therapies also provide an urgently needed treatment option for patients who cannot be treated by open-heart surgery because they are too sick or frail to withstand the treatment. Unfortunately, at the present time, these "high-risk" patients are typically left untreated.

[0008] According to one exemplary embodiment disclosed herein, a system is provided for replacing the native aortic valve using a catheter-based approach. The system includes a transcatheter heart valve (THV), sometimes referred to herein as a "bioprosthesis." The transcatheter heart valve of this embodiment comprises a support structure, such as a stent, formed of, for example, a shape-memory material. The support structure can be configured to be radially compressible into a compressed state, expandable into an over-expanded state having a first diameter, and self-adjustable into a functional state having a second diameter less than the first diameter. The transcatheter heart valve can also include a flexible valve member or membrane, such as a prosthetic one-way valve member, within an interior of the support structure. In particular implementations, one or more grabbing mechanisms such as micro-anchors, are disposed on an outer surface of the support structure, where the grabbing mechanisms can be configured to penetrate or otherwise securably engage the support structure to surrounding native tissue, such as along a valve orifice when the support structure is expanded within the valve orifice.

[0009] In particular implementations, at least one of the one or more grabbing mechanisms comprises a projection having a hook, a sharpened barb, tree-shaped barbs, or an anchor-shaped barb. In some embodiments, at least one of the one or more grabbing mechanisms comprises a strip of projections disposed circumferentially around the support structure. In other implementations, at least one of the one or more grabbing mechanisms comprises a strip of projections disposed along a vertical axis of the support structure. At least one

of the one or more grabbing mechanisms can include a projection that changes shape after a period of time. For example, the projection can be initially held in an undeployed state by a resorbable material.

[0010] The support structure, the one or more grabbing mechanisms, or both the support structure and the one or more grabbing mechanisms can be formed of a shape memory alloy, such as of Nickel-Titanium (Nitinol), in some embodiments. The support structure can be constructed with sufficient radial strength to maintain the native aortic valve in a dilated condition such that the prosthetic valve member can effectively replace the function of the native aortic valve, but is configured such that its diameter is not substantially greater than the native valve's diameter.

[0011] The flexible membrane can be a valve assembly having an inlet side and an outlet side, the valve assembly being configured to allow flow from the inlet side to the outlet side but prevent flow from the outlet side to the inlet side. In some embodiments, the flexible membrane is configured to replace an aortic valve.

[0012] Embodiments of a prosthetic heart valve can comprise an inner and outer support structure that can be delivered separately from one another. For example, one embodiment comprises an outer support structure configured to be radially compressible, expandable into an over-expanded state having a first diameter, and self-adjustable into a functional state having a second diameter less than the first diameter. The prosthetic heart valve can also comprise one or more grabbing mechanisms disposed on an outer surface of the outer support structure, the one or more grabbing mechanisms being configured to penetrate or otherwise securably engage the outer support structure to surrounding native tissue, and an inner support structure configured to be radially compressible and expandable into an expanded state within the interior of the outer support structure, where a flexible valve member can be secured within an interior of the inner support structure.

[0013] As with other embodiments, embodiments comprising an inner and outer support structure can also include at least one grabbing mechanism that

comprises a projection having a hook, a sharpened barb, tree-shaped barbs, or an anchor-shaped barb. One or more of the outer support structure, the inner support structure, or the one or more grabbing mechanisms can be formed of a shape memory alloy. The flexible membrane can be configured to replace an aortic valve. The inner support structure can be configured to securably engage the interior of the outer support structure upon being expanded within the outer support structure.

[0014] In one exemplary method disclosed herein, the transcatheter heart valve can be "over-expanded" within a native aortic valve using a balloon catheter. More particularly, an expandable prosthetic heart valve can be positioned within a patient's aortic valve and expanded, such as by inflating a balloon of a balloon catheter around which the prosthetic heart valve is disposed, to an over-expanded diameter thereby causing one or more projections on an outer surface of the prosthetic heart valve to engage native tissue of the patient's aortic valve. The prosthetic heart valve can be allowed to retract toward a recoil diameter less than the over-expanded diameter (e.g., a "memorized" (if the support structure comprises a shape-memory alloy) or "recoil" diameter), such as by deflating the balloon. As the prosthetic heart valve recoils (reduces in diameter), the one or more projections are engaged with the native tissue of the patient's aortic valve, thereby reducing a diameter of the patient's native aortic valve. This can occur because the projections (*e.g.* micro-anchors) on the support structure are securely engaged with the tissue of the valve annulus. Conventional valves cannot undergo such over-expansion due to materials used and methods of manufacture.

[0015] In some embodiments, the expandable prosthetic heart valve comprises a support structure made of a shape memory alloy that causes the support structure to have the recoil diameter when the support structure is not acted on by any external force. In certain embodiments, the one or more projections include hooks, barbs, or anchors. At least one of the one or more projections changes its shape after penetrating the native tissue of the patient's aortic valve in some embodiments.

[0016] This exemplary method of implanting an over-expanded transcatheter heart valve has a number of advantageous features over known transcatheter heart valves. For example, unlike existing transcatheter heart valves, the over-expanded transcatheter heart valve does not apply an outward radial force on the native valve annulus after implantation. This is advantageous because, as discussed above, a regurgitating valve typically results from a diseased or aging valve annulus that is already substantially dilated. The application of a continuous outward radial force on a weakened and dilated annulus will usually dilate the annulus further. This could result in serious damage to the anatomical structure of the heart and, as the weakened aortic root dilates further, could eventually lead to dislodgement of the transcatheter heart valve.

[0017] By reducing the diameter of the surrounding annulus, it is also possible to replace the native aortic valve using a smaller transcatheter heart valve than would be typically required to treat aortic insufficiency. Due to the recoil of the support structure, the final diameter of the over-expanded transcatheter heart valve is substantially smaller than a conventional THV. A conventional THV must be expanded to a diameter that is capable of being securely maintained in a dilated valve annulus, whereas the over-expanded transcatheter heart valve constricts the annulus and therefore can have a smaller outer diameter. As a result of the smaller final diameter, the over-expanded transcatheter heart valve can also employ a smaller valve member. The smaller valve member allows the over-expanded transcatheter heart valve to be crimped to a much smaller diameter and have a smaller profile during advancement through the patient's vasculature. It will be recognized by those skilled in the art that a smaller diameter facilitates advancement of the transcatheter heart valve through a patient's vasculature.

[0018] Some methods for treating aortic insufficiency can comprise a two-stage delivery. For example, one method comprises positioning an outer stent within a patient's aortic valve, expanding the outer stent to an over-expanded diameter, thereby causing projections on the outer surface of the outer stent to engage tissue of the patient's aortic valve, allowing the outer stent to retract

toward a recoil diameter that is less than the over-expanded diameter while the projections are engaged with the tissue of the patient's aortic valve, thereby causing the diameter of the patient's native aortic valve to be reduced, positioning a prosthetic heart valve within the outer stent, and expanding the prosthetic heart valve while the prosthetic heart valve is positioned within the outer stent.

[0019] In some embodiments, the act of expanding the prosthetic heart valve comprises frictionally securing the prosthetic heart valve within the outer stent, engaging grooves provided within the outer stent with complementary members of the prosthetic heart valve, or engaging a snap mechanism that causes the prosthetic heart valve to be secured within the outer stent, and/or inflating a balloon of a balloon catheter around which the outer stent is disposed. In certain embodiments, the act of allowing the outer stent to retract comprises deflating the balloon of the balloon catheter. In some methods, the outer stent comprises a shape memory alloy. In some methods, the prosthetic heart valve comprises a compressible and expandable inner support structure and a valve membrane secured in an interior of the inner support structure

[0020] The foregoing and other features and advantages of the invention will become more apparent from the following detailed description, which proceeds with reference to the accompanying figures.

BRIEF DESCRIPTION OF THE DRAWINGS

[0021] FIG. 1 is an anatomic anterior view of a human heart, with portions broken away and in section to view the interior heart chambers and adjacent structures.

[0022] FIG. 2 is a perspective view of a transcatheter heart valve formed with a shape-memory stent in accordance with an embodiment of the disclosed technology.

[0023] FIG. 3 is a perspective view of another embodiment of a transcatheter heart valve formed with a shape memory support structure according to the disclosed technology.

[0024] FIG. 4 shows an elevation view of one embodiment of a projection (or micro-anchor) that can be used with embodiments of a transcatheter heart valve.

[0025] FIG. 5 illustrates an elevation view of another embodiment of a projection (or micro-anchor) that can be used with a transcatheter heart valve.

[0026] FIG. 6 illustrates an elevation view of another embodiment of a projection (or micro-anchor) that can be used with a transcatheter heart valve.

[0027] FIG. 7 illustrates an elevation view of another embodiment of a projection (or micro-anchor) that can be used with a transcatheter heart valve.

[0028] FIG. 8 illustrates an elevation view of another embodiment of a projection (or micro-anchor) that can be used with a transcatheter heart valve.

[0029] FIG. 9 illustrates an elevation view of another embodiment of a projection (or micro-anchor) that can be used with a transcatheter heart valve.

[0030] FIG. 10 is a perspective view of a transcatheter heart valve formed with a shape memory support structure in accordance with another embodiment of the disclosed technology.

[0031] FIG. 11 is a simplified side view of a balloon catheter delivery system that is configured to over-expand the shape memory support structure at a target area inside a patient's body in accordance with an embodiment of the disclosed technology.

[0032] FIGS. 12-15 are simplified sectional views of a transcatheter heart valve being deployed in accordance with an embodiment of the disclosed technology.

[0033] FIGS. 16-20 show simplified sectional views of one embodiment of a transcatheter heart valve being deployed in a two-stage process according to an exemplary method of the disclosed technology.

[0034] FIGS. 21-25 show perspective views of additional embodiments of projections (or micro-anchors) that can be used with a transcatheter heart valve.

[0035] FIG. 26 is an elevation view of another embodiment of a transcatheter heart valve according to the disclosed technology. In particular, the embodiment illustrated in FIG. 26 has two attachable sections.

DETAILED DESCRIPTION

[0036] As used in this application and in the claims, the singular forms "a," "an," and "the" include the plural forms unless the context clearly dictates otherwise. Additionally, the term "includes" means "comprises." Although the operations of exemplary embodiments of the disclosed method may be described in a particular, sequential order for convenient presentation, it should be understood that the disclosed embodiments can encompass an order of operations other than the particular, sequential order disclosed. For example, operations described sequentially may in some cases be rearranged or performed concurrently. Further, descriptions and disclosures provided in association with one particular embodiment are not limited to that embodiment, and may be applied to any embodiment disclosed herein. Moreover, for the sake of simplicity, the attached figures may not show the various ways in which the disclosed system, method, and apparatus can be used in combination with other systems, methods, and apparatuses.

[0037] In vertebrate animals, the heart is a hollow muscular organ having four pumping chambers as seen in FIG. 1. The left and right atria 2, 4 and the left and right ventricles 6, 8, are each provided with their own one-way valve. The natural heart valves are identified as the aortic 10, mitral (or bicuspid) 12, tricuspid 14, and pulmonary 16, and are each mounted in an annulus comprising dense fibrous rings attached either directly or indirectly to the atrial and ventricular muscle fibers. Each annulus defines a flow orifice.

[0038] The atria 2, 4 are the blood-receiving chambers, which pump blood into the ventricles 6, 8. The ventricles 6, 8 are the blood-discharging chambers. The synchronous pumping actions of the left and right sides of the heart constitute the cardiac cycle. The cycle begins with a period of ventricular relaxation, called ventricular diastole. The cycle ends with a period of ventricular contraction, called ventricular systole. The four valves 10, 12, 14, 16 ensure that blood does not flow in the wrong direction during the cardiac cycle; that is, to ensure that the blood does not back flow from the ventricles 6, 8 into the corresponding atria 2, 4, or back flow from the arteries into the

corresponding ventricles 6, 8. The mitral valve 12 is between the left atrium 2 and the left ventricle 6, the tricuspid valve 14 between the right atrium 4 and the right ventricle 8, the pulmonary valve 16 is at the opening of the pulmonary artery, and the aortic valve 10 is at the opening of the aorta. As discussed, in aortic insufficiency, the aortic valve 10 can become dilated, thus preventing the valve from fully closing. Embodiments of the present disclosure can be deployed to the aortic valve, specifically to the area of the aortic valve annulus, to treat aortic insufficiency.

[0039] FIG. 2 is a perspective view of an exemplary transcatheter heart valve 100 (also referred to as bioprosthesis 100). Bioprosthesis 100 includes a tubular support structure 102, a flexible membrane 104 (e.g., a valve member), a membrane support 106, and one or more grabbing mechanisms 108 affixed about a circumference of the support structure 102.

[0040] The support structure 102 in FIG. 2 can be formed of a shape memory material, such as Nitinol. In one exemplary embodiment, the support structure 102 can be radially compressed into a compressed state for delivery through the patient's vasculature, but can self expand to a natural, uncompressed or functional state having a preset diameter. In other words, the support structure 102 moves or tends toward a preset diameter when free of external forces. Furthermore, the support structure 102 can be expanded beyond its natural diameter to an over-expanded diameter. After the support structure 102 is in this over-expanded state, the support structure returns toward its preset diameter (or naturally recoils to the preset or recoil diameter).

[0041] The support structure 102 can be generally tubular in shape and has a longitudinal flow path along its structural axis. The support structure 102 can include a grated framework, such as a stent, configured to secure bioprosthesis 100 within or adjacent to the defective valve annulus of the heart. The support structure 102 further provides stability and prevents the bioprosthesis 100 from migrating after it has been implanted.

[0042] In alternative embodiments, the support structure 102 can comprise other shape memory alloys, or other materials capable of providing sufficient

support for the bioprosthesis 100. Such materials can include other metals, metal alloys such as stainless steel or cobalt chromium, and/or polymers. The support structure 102 can have configurations other than that shown in FIG. 2. For example, the support structure 102 can have a different shape, more or fewer vertical support bars, and/or additional structures for added stability. The support structure 102 can comprise a strut mesh and/or sleeve structure.

[0043] The flexible membrane 104 is a valve member that is positionable in the flow path of the support structure 102 and that is configured to permit flow in a first direction but substantially resist flow in a second direction. In certain implementations, the flexible membrane 104 comprises a biological tissue formed into a valve member. The biological tissue which forms the valve member can comprise pericardial tissue harvested from an animal heart, such as porcine, bovine, or equine pericardium. The flexible membrane 104 can also comprise, alternatively or additionally, biocompatible materials including synthetic polymers such as polyglycolic acid, polylactic acid, and polycaprolactone, and/or other materials such as collagen, gelatin, chitin, chitosan, and combinations thereof.

[0044] The membrane support 106 can be positionable in the flow path and affixed to the support structure 102. Membrane support 106 can comprise polyethylene terephthalate (PET) (e.g., Dacron), or any other suitable material. The membrane support 106 can be positioned such that it folds under and around the bottom of the flexible membrane 104. The membrane support 106 can be sutured or otherwise affixed to the flexible membrane 104. In some embodiments, the membrane support 106 can comprise a skirt on the exterior surface of the flexible membrane 104, and a thinner ribbon on the interior surface of the flexible membrane 104, within the flow path. In this embodiment, the ribbon and skirt structures of the membrane support 106 can be sutured together, with a portion of the flexible membrane between them. In some embodiments, the membrane support 106 can be a thin layer of material, such as a layer of PET that can be from about 0.01 mm thick to about 0.2 mm thick. In some embodiments, the thickness of the membrane support 106 can

vary from the center to the edge. For example, in one embodiment, the membrane support 106 can be about 0.07 mm thick at an edge, and about 0.05 mm thick at the center. In another specific embodiment, the membrane support 106 can be about 0.13 mm thick at the edge, and about 0.10 mm thick at the center. Additional details of the support structure 102, the flexible membrane 104, and the membrane support 106 are described in U.S. Patent Nos. 6,730,188 and 6,893,460, both of which are hereby incorporated herein by reference. Furthermore, U.S. Patent Nos. 6,730,188 and 6,893,460 describe additional prosthetic valve that can be modified according to the disclosed technology and used as part of any of the disclosed apparatus or systems or used with any of the disclosed methods or procedures.

[0045] In certain embodiments, grabbing mechanisms 108 are configured as strips of projections or micro-anchors 110. The grabbing mechanisms 108 can vary from implementation to implementation, but in certain implementations comprise any structure capable of at least partially penetrating and engaging the target tissue. For example, the projections 110 can be designed to at least partially penetrate and/or otherwise engage (*e.g.* by clamping or grabbing) the surrounding tissue upon over-expansion and to contract the aortic annulus and surrounding native tissue along with the support structure 102 upon recoil of the support structure 102. In other embodiments, the projections 110 may include barbed projections, umbrella projections, and/or hooks also designed to at least partially penetrate the tissue upon over-expansion and contract the aortic annulus and surrounding tissue upon recoil of the support structure 102.

[0046] As shown in FIG. 2, the grabbing mechanisms 108 can be positioned and coupled to the support structure 102 as vertical, or axial, strips of projections 110. In an alternative embodiment shown in FIG. 3, the grabbing mechanisms 109 can be positioned and coupled to the support structure 102 as one or more horizontal, or circumferential, strips of projections 111. For example, one or more strips of projections 111 can be disposed around the circumference of the support structure 102. Such grabbing mechanisms 109 can extend substantially around the circumference of the support structure 102,

and/or strips of projections 111 can extend only partially around the circumference of the support structure 102, such as horizontal arcs of projections. In some embodiments, projections can be provided in one or more localized areas of the support structure 102, in addition to or instead of being provided in linear strips. In certain embodiments, one or more strips of projections can be provided along one or more struts or wires of the support structure 102, substantially paralleling the angles of the support structure 102. In another embodiment, the strips can be disposed circumferentially around the support structure 102 and located along the commissural supports (e.g. portions of the support structure wherein adjacent prosthetic leaflets meet and attach to the support structure) of support structure 102.

[0047] Some implementations of the bioprosthesis 100 shown in FIGS. 2 and 3 can comprise only one grabbing mechanism 108, 109. Alternative embodiments can comprise two or more grabbing mechanisms 108, 109. Further, the grabbing mechanisms 108, 109 can be manufactured separately from the support structure 102 and attached to the support structure through a suitable means (e.g., sutures, adhesive, weld, snap-fit mechanism, friction, and the like). Alternatively, the grabbing mechanisms 108, 109 can be formed as an integral feature of the support structure. Each grabbing mechanism 108, 109 generally comprises one or more projections or micro-anchors 110, 111. The projections or micro-anchors 110 can have any suitable dimension. For instance, the projections 110 can have a length from approximately 1 mm to approximately 2 mm. Projections 110 can be smaller in some embodiments, such as having a length from about .001 mm to about 1 mm. Alternatively, projections 110 can be larger in some embodiments, such as having a length from about 2 mm to about 6.5 mm or larger. In some embodiments, a grabbing mechanism 108, 109 can include a plurality of projections 110, where at least a first projection can be a different size from a second projection. A single grabbing mechanism can include a plurality of sizes of projections.

[0048] In some embodiments, the projections can be formed of a shape memory material that is configured to change shape. For instance, in one

implementation, the projections can change shape after penetrating the tissue. For example, barbs at the tip of the projections can change in angle or configuration in relation to the projection after penetrating the tissue in order to more securely engage with the tissue. In another embodiment, the projections can change shape after expansion of the support structure 102. For example, the projections 110 can lay flat against the support structure 102 while the bioprosthesis is in its contracted configuration, and the projections can expand and the barbs can change shape to extend laterally outward from the projection to prevent the projection from slipping out of the tissue once the bioprosthesis 100 has been expanded.

[0049] In one variation, one or more projections can be configured with a delayed release mechanism, such that at least a portion of each projection changes shape after a period of time. This may be achieved by incorporating a resorbable material into the projection for temporarily holding the projection in a constrained condition. As the resorbable material is resorbed by the body, the projection becomes free to assume its relaxed condition. As the projection moves to its relaxed condition, its shape can change to more securely engage and hold the surrounding tissue. For example, barbs or hooks associated with the projection can initially be held against the main body portion of the projection until the resorbable material is resorbed. At that time, the barb or hook can extend outwardly from the main body portion, thereby creating a more secure attachment to the tissue in which the projection is inserted.

[0050] FIGS. 4-9 show elevation views of various embodiments of projections 400, 402, 404, 406, 408, 410 that can be used with embodiments of a transcatheter heart valve according to the present disclosure. In general, the projections 400, 402, 404, 406, 408 include a main body portion and one or more barbs. For instance, the illustrated projections include projection 400 with a single sharpened barb 401, projection 402 with a hook-shaped barb 403, projection 404 with an anchor-shaped (arrow head) barb 405, projection 406 with multiple branch-like barbs 407, projection 408 with multiple tree-shaped sharpened barbs 409, and hook-shaped projection 410. Suitable projections

further include spikes, staples, fasteners, tissue connectors, or any other suitable projection capable of engaging with a patient's native tissue. Embodiments of suitable projections 400, 402, 404, 406, 408, 410 can be designed to penetrate the aortic valve annulus and engage or lodge within the thickness of the aortic valve annulus such that when the bioprosthesis retracts toward its natural state, the projections pull the patient's native tissue inward towards the center of the flow path, substantially without dislodging from their engaged positions. The barbs can be formed on the projections 400, 402, 404, 406 408 by laser cutting or other appropriate manufacturing method. Suitable materials for projections include Nitinol, other shape memory alloys, stainless steel, cobalt chromium, titanium, Elgiloy, HDPE, nylon, PTFE, other biocompatible polymers, resorbable materials, and combinations thereof. Other suitable materials are known in the art, and the projections of the present disclosure are not limited to those discussed.

[0051] FIGS. 21-25 illustrate additional possible embodiments of projections 416, 418, 420, 422, 424. FIG. 21 shows a projection 416 that has a square cross-sectional base and a pyramidal pointed tip, wherein a cutout between the base and the tip can facilitate engagement within a patent's native tissue. FIG. 22 shows a pointed projection 418 that can extend at an angle from the surface of a support structure or bioprosthesis. FIG. 23 shows an asparagus tip-like projection 420. FIG. 24 shows a conical projection 422. FIG. 25 shows another embodiment of a tree-like projection 424.

[0052] FIG. 10 is a perspective view of another embodiment of a transcatheter heart valve 100a (also referred to as bioprosthesis 100a) according to the disclosed technology. Bioprosthesis 100a includes a support structure 102a having a tubular or cylindrical base, a flexible membrane 104a (e.g., valve member), a membrane support 106a and at least one grabbing mechanism 108a affixed about a circumference of the support structure 102a. The support structure 102a is expandable from a first reduced diameter to a second enlarged diameter, and has a flow path along a structural axis. The support structure 102a generally can include a tubular framework, such as a stent, which

primarily secures bioprosthesis 100a within or adjacent to the defective valve annulus of the heart. In this embodiment, the support structure 102a is configured to approximate the shape of the flexible membrane 104a such that the upper end of support structure 102a comprises peaks at the commissure supports and valleys (e.g. U-shaped cusps) between the commissure supports.

[0053] FIG. 26 is a perspective view of another embodiment of a transcatheter heart valve having two attachable sections 700, 702 that can be delivered separately. This embodiment can reduce the cross-sectional profile during delivery because each section 700, 702 can have a smaller delivery profile than the entire assembled bioprosthesis. In the illustrated embodiment, outer section 700 comprises an outer stent structure 710, and inner section 702 comprises an inner stent structure 720 and a valve member 722. In this embodiment, the inner stent structure 720 and the valve member 722 together form the expandable prosthetic heart valve. The outer section 700 can optionally include a temporary valve member 712, which can be thinner or less durable than the more permanent valve member 722. The temporary valve member 712 can be mounted on or otherwise secured to the outer stent structure 710 using any suitable mechanism (e.g., sutures, snaps, screws, friction, hooks, barbs, adhesives, and/or a slide structure). Furthermore, the temporary valve member 712 can be configured to have a diameter and flexibility suitable to receive the inner section 702 during valve delivery. The valve member 722 can be any valve as described herein and can be mounted to or otherwise secured to the inner stent structure 720 using any suitable means (e.g., sutures, snaps, screws, a slide structure, friction, hooks, barbs, and/or an adhesive).

[0054] In some embodiments, the outer section 700 can comprise a thin compressible member 712 that can facilitate securing the inner section 702 within the outer section 700. Such a compressible member 712 can create a tight seal between the outer section 700 and the inner section 702 as the inner section presses into the compressible material. Further details regarding a compressible member 712 are disclosed in U.S. Patent Application Publication No. 2008/0208327, which is hereby incorporated herein by reference.

[0055] According to one exemplary delivery procedure, and as more fully explained below in connection with FIGS. 16-20, the outer section 700 is delivered to the aortic valve first. The outer stent structure 710, like embodiments discussed above, can comprise a shape memory alloy such as Nitinol, and can have a predetermined recoil (or natural) diameter. The outer section 700 can be over-expanded to a diameter greater than its recoil diameter. For example, the outer section 700 can be disposed around a balloon catheter and delivered to the interior of the native heart valve. The balloon of the balloon catheter can then be inflated, causing the outer section 700 to expand to a diameter beyond its recoil diameter. In particular implementations, the outer section 700 comprises one or more grabbing mechanisms 708 configured to engage with the native tissue when the outer stent structure 710 is over-expanded. For example, the grabbing mechanisms 708 can be any of the grabbing mechanisms described above. Once the balloon of the balloon catheter is deflated and removed, the outer section 700 will contract to its memorized or recoil diameter. On account of the engagement of the grabbing mechanisms 708 to the surrounding tissue, the contraction of the outer section 700 will cause the size of the aortic annulus to be reduced as well. Inner section 702 can then be delivered and engaged with the outer section 700.

[0056] In an alternative method of delivering the two part bioprosthesis, the outer section 700 can be delivered to the interior of a native heart valve in a crimped state, and allowed to expand to its predetermined natural diameter, once positioned. A balloon can then be inserted within the outer section 700. When the balloon is expanded, the outer section can be over-expanded to a diameter greater than its natural diameter to allow the grabbing mechanisms of the outer section 700 to engage with the native valve tissue. When the balloon is deflated, contraction of the outer section 700 can cause the size of the aortic annulus to be reduced. When compared to the previous method, this can allow for delivering the outer section 700 in a smaller crimped state, because the outer section 700 is not crimped over the balloon for delivery; the balloon is not inserted until after the outer section 700 is first allowed to expand to its natural

diameter. Inner section 702 can then be delivered and engaged with the outer section 700.

[0057] FIG. 11 is a simplified illustration of a balloon catheter 200, which can be used to deliver and deploy a bioprosthesis (such as bioprosthesis 100 shown in FIG. 2 above) into a native heart valve. In one embodiment, the balloon catheter 200 advances the bioprosthesis 100 through an outer sheath of the delivery system over a guide wire 204. The balloon catheter 200 can also be configured to aid in the delivery and positioning of the bioprosthesis 100 within the native valve. For example, as shown in FIG. 11, the balloon catheter 200 can include a tapered nose cone tip 206 at its distal end that allows a balloon portion 202 and bioprosthesis 100 to cross easily into the native valve. The balloon portion 202 can be inflated (*e.g.*, using a controlled volume of saline), causing the bioprosthesis 100 to expand within and engage the native hart valve.

[0058] In one exemplary method, the guide wire 204 is inserted into the femoral artery of a patient, advanced through the aortic arch of a patient, and into the aortic valve. The balloon catheter 202 is advanced through the outer sheath of the delivery system, over the guide wire 204, and into the aortic valve. The bioprosthesis 100 is then positioned and secured within the native valve by inflating the balloon portion 202. FIGS. 12-15, described below, illustrate one exemplary procedure for deploying the bioprosthesis 100 into the native valve. The balloon portion 202 can then be deflated, and the balloon catheter 202 retracted from the patient's aorta and femoral artery. An exemplary delivery system designed to deliver the bioprosthesis 100 is the RETROFLEX II catheter assembly available from Edwards Lifesciences in Irvine, CA. Furthermore, although the operation described above is a percutaneous transfemoral procedure, it should be understood that embodiments of the disclosed technology include the use of a shorter catheter assembly or semi-rigid cannula for deploying a bioprosthesis in a minimally invasive surgical (MIS) procedure, such as a trans-apical procedure. In a transapical procedure, the catheter or cannula is inserted through a gap between the ribs and is advanced through a small incision formed along the apex of the heart. This technique

advantageously provides the surgeon with a direct line of access to the aortic valve. U.S. Patent Application Publication Nos. 2008/0065011, 2007/0005131, and 2007/008843 disclose further details regarding suitable delivery methods, and are hereby incorporated herein by reference.

[0059] FIGS. 12-15 are schematic cross-sectional views of a patient's aorta illustrating delivery of the support structure and valve of FIG. 2. As shown in FIG. 12, in one embodiment, the bioprosthesis 100 may be introduced into the patient's body using a percutaneous delivery technique with the balloon portion 202 of the balloon catheter 200 deflated, and the bioprosthesis 100 operably disposed thereon. The bioprosthesis can be contained in a radially crimped or compressed state. In embodiments using a self-expandable bioprosthesis 100, the bioprosthesis 100 can be held in a compressed state for delivery, by, for example, containing the bioprosthesis within an outer covering or sheath 201. The outer covering 201 can be removed or retracted, or the bioprosthesis 100 pushed through the outer covering 201, to allow the self-expandable bioprosthesis 100 to self-expand. In embodiments having a bioprosthesis that does not self-expand, such an outer covering may not be needed to retain the bioprosthesis in a crimped state, but can nonetheless be used if desired (*e.g.* to reduce friction during delivery).

[0060] In the embodiment illustrated in FIG. 12, the projections 110 of the grabbing mechanisms 108 are disposed around the outside circumference of support structure 102.

[0061] In the illustrated embodiment, the bioprosthesis 100 is introduced and positioned across the native aortic valve annulus (AVA) 300 by being inserted at least partially through native valve leaflets 302 and expanded. Because the AVA of an aortic valve suffering from aortic insufficiency is dilated, diameter D1 of the AVA 300 is expected to be larger than the diameter of a healthy AVA.

[0062] As shown in FIG. 13, outer sheath or covering 201 can be retracted or removed from over the bioprosthesis 100. In embodiments having a bioprosthesis 100 comprising a shape memory alloy, the bioprosthesis can

expand from its crimped or compressed diameter d to a predetermined or memorized diameter R once the sheath 201 is removed.

[0063] As shown in FIG. 14, the balloon portion 202 of the balloon catheter 200 is expanded to increase the diameter of the support structure 102 from its relaxed diameter R (FIG. 13) to an over-expanded diameter OE such that the outer diameter of the bioprosthesis 100 equals or exceeds the original diameter D1 of the AVA 300. In this manner, the AVA 300 may expand beyond the diameter D1 as well. During the expansion, the projections 110 of the grabbing mechanisms 108 are forced to contact and can penetrate or otherwise engage (*e.g.* clamp or grab) the target tissue, which may include the AVA 300 and some of the tissue surrounding the AVA. This causes the bioprosthesis 100 to adhere to the surrounding tissue.

[0064] Next, as shown in FIG. 15, the balloon portion 202 of the balloon catheter 200 can be deflated, and the balloon catheter 200 removed from the AVA 300. In embodiments where the support structure 102 is formed of a shape memory material, removing the expansion force of balloon 202 from support structure 102 allows the support structure 102 to return from an over-expanded diameter OE (FIG. 14) to a recoil or relaxed diameter R. The manufacture of the support structure (*i.e.*, stent) determines what the recoil diameter will be. For example, the recoil diameter of a support structure comprising a shape memory alloy can be the memorized or functional diameter of the support structure. The recoil diameter of a support structure comprising, for example, stainless steel and/or cobalt chromium can be that of the natural or resting diameter of the support structure, once it inherently recoils from being over-expanded by the balloon 202. As the diameter of bioprosthesis 100 decreases to the recoil diameter R, the diameter of the AVA 300 also decreases to a final diameter D2. The AVA 300 can decrease in diameter due to the projections 110 of the support structure 102 pulling the target tissue inward.

[0065] An existing bioprosthesis is generally configured to be radially expanded to a diameter capable of providing secure fixation in a dilated AVA. However, as discussed above, existing bioprostheses are not well suited for

treating aortic insufficiency due to the lack of firm tissue in the aortic annulus. Using existing technology, a larger bioprosthesis could be used to create a more secure fixation; however, a larger bioprosthesis cannot be easily crimped down for delivery via a catheterization technique. In contrast, embodiments of the present bioprosthesis 100 allow for the collapsed diameter of bioprosthesis 100 to be a smaller diameter because bioprosthesis 100 may be assembled with a smaller stent and a smaller valve member. This smaller size is possible because, rather than stretch the AVA, the present bioprosthesis advantageously reduces the diameter of the AVA during implantation. As a result, a smaller overall structure can be achieved which allows the support structure 102 of bioprosthesis 100 to be crimped to the smaller collapsed diameter and thus have a smaller profile for delivery through a patient's vasculature. For example, in some embodiments, bioprosthesis 100 can be crimped to a size of from about 4 French to about 7 French.

[0066] In alternative embodiments, the bioprosthesis 100 need not be operably disposed on the balloon 202 during delivery. For example, the bioprosthesis 100 can be crimped onto the catheter 200 at a different location than the balloon 202. The bioprosthesis can be allowed to self-expand once positioned within a patient's native aortic valve, and the balloon 202 can be positioned inside the self-expanded bioprosthesis 100 and inflated to then over-expand the bioprosthesis 100.

[0067] FIGS. 16-20 show simplified elevation views of one embodiment of a transcatheter heart valve being deployed in a two-stage process according to one method of the present disclosure. The illustrated method can be used, for example, to deliver the transcatheter heart valve assembly shown in FIG. 11. In the method illustrated in FIGS. 16-20, the outer section 700 can be deployed to the aortic valve separately from valve member 702. FIG. 16 shows the outer section 700 on a balloon 202, positioned inside the leaflets 302 of the aortic valve annulus 300. The outer section 700 can be a self-expanding stent, such as a stent comprising a shape memory alloy, or the outer section 700 can be simply balloon expandable, such as a stent comprising stainless steel, cobalt chromium

and/or other suitable biocompatible materials. FIG. 17 shows the balloon 202 in an inflated configuration, which can expand the outer section 700 such that grabbing mechanisms 708 engage with the native tissue of the leaflets 302 and/or the aortic valve annulus 300.

[0068] As shown in FIG. 18, the balloon 202 can be deflated and removed. The outer section 700 can reduce the diameter of the aortic valve annulus 300 as it retracts after the balloon 202 is removed. The outer section 700 can retract to a functional or memorized diameter if it comprises a shape memory alloy, or the outer section 700 can simply naturally recoil or retract due to the ductility of the material. The inner section 702 can be positioned within the outer section 700 using a catheter 200 and a balloon 202, as shown in FIG. 19. As shown in FIG. 20, the balloon 202 can be expanded, thus expanding the crimped inner section 702, allowing it to engage with the outer section 700.

[0069] The outer section 700 and the inner section 702 can be delivered on a single catheter 200 or on separate catheters. For example, a catheter 200 can include two expandable balloons, one distal to the other. A first balloon can be used to expand the outer section 700 then deflated and either guided through the lumen of the expanded outer section 700 or removed back through the lumen. The second balloon and inner section 702 can then be positioned within the outer section 700, and the second balloon can be expanded, allowing for the inner section 702 to engage with the outer section 700. The second balloon can then be deflated, and the catheter 200 removed, thus removing the first and second balloons. In alternative embodiments, separate catheters can be used, such that a first catheter is used to deliver a first balloon and the outer section 700 to the native valve, and a second catheter is used to deliver a second balloon and the inner section 702 to the native valve once the outer section has been deployed and the first catheter has been removed.

[0070] While FIG. 16 illustrates the outer section 700 being delivered while already crimped on the balloon 202, in alternative embodiments, the outer section 700 can be located at a different position on the catheter 200 than the balloon 202. For example, in some embodiments, a crimped outer section 700

can be delivered to a native aortic valve and allowed to self-expand, such as by removing an outer covering. The balloon 202 can then be positioned within the expanded outer section 700 and inflated, thereby over-expanding the outer section 700, allowing the grabbing mechanisms 708 to engage with the native tissue. The balloon can then be deflated and removed, and the inner section 702 can be delivered and engaged with the outer section 700.

[0071] It should be understood that embodiments of bioprosthesis 100 can be deployed using a non-inflatable, mechanical embodiment of delivery catheter 200. Furthermore, bioprosthesis 100 can be delivered using any suitable delivery method, including both transapical and femoral artery delivery methods. Additionally, although the disclosed embodiments concern aortic valve replacement, embodiments of the disclosed technology can be used to replace any dilated heart valve (e.g., a dilated mitral valve). Moreover, although bioprosthesis 100 is used as an exemplary embodiment of the disclosed technology, it should be understood that bioprosthesis 100 and bioprosthesis 100a may be considered interchangeable with one other, or with any other bioprosthesis made or adapted in accordance with the teachings of the disclosed technology.

[0072] Having illustrated and described the principles of the disclosed technology, it will be apparent to those skilled in the art that the disclosed embodiments can be modified in arrangement and detail without departing from such principles. In view of the many possible embodiments to which the principles of the disclosed technologies can be applied, it should be recognized that the illustrated embodiments are only preferred examples of the technologies and should not be taken as limiting the scope of the invention. Rather, the scope of the invention is defined by the following claims and their equivalents. I therefore claim all that comes within the scope and spirit of these claims.

I claim:

1. A prosthetic heart valve comprising:

a support structure configured to be radially compressible into a compressed state, expandable into an over-expanded state having a first diameter, and self-adjustable into a functional state having a second diameter less than the first diameter;

a flexible valve member secured within an interior of the support structure; and

one or more grabbing mechanisms disposed on an outer surface of the support structure, the one or more grabbing mechanisms being configured to penetrate or otherwise securably engage the support structure to surrounding native tissue.

2. The prosthetic heart valve of claim 1, wherein at least one of the one or more grabbing mechanisms comprises a projection having a hook, a sharpened barb, tree-shaped barbs, or an anchor-shaped barb.

3. The prosthetic heart valve of claim 1, wherein the support structure, the one or more grabbing mechanisms, or both the support structure and the one or more grabbing mechanisms are formed of a shape memory alloy.

4. The prosthetic heart valve of claim 1, wherein the flexible membrane is a valve assembly having an inlet side and an outlet side, the valve assembly being configured to allow flow from the inlet side to the outlet side but prevent flow from the outlet side to the inlet side.

5. The prosthetic heart valve of claim 1, wherein the flexible membrane is configured to replace an aortic valve.

6. The prosthetic heart valve of claim 1, wherein at least one of the one or more grabbing mechanisms comprises a strip of projections disposed circumferentially around the support structure.

7. The prosthetic heart valve of claim 1, wherein at least one of the one or more grabbing mechanisms comprises a strip of projections disposed along a vertical axis of the support structure.

8. The prosthetic heart valve of claim 1, wherein at least one of the one or more grabbing mechanisms includes a projection that changes shape after a period of time.

9. The prosthetic heart valve of claim 8, wherein the projection is initially held in an undeployed state by a resorbable material.

10. A prosthetic heart valve comprising:

an outer support structure configured to be radially compressible, expandable into an over-expanded state having a first diameter, and self-adjustable into a functional state having a second diameter less than the first diameter;

one or more grabbing mechanisms disposed on an outer surface of the outer support structure, the one or more grabbing mechanisms being configured to penetrate or otherwise securably engage the outer support structure to surrounding native tissue;

an inner support structure configured to be radially compressible and expandable into an expanded state within the interior of the outer support structure; and

a flexible valve member secured within an interior of the inner support structure.

11. The prosthetic heart valve of claim 10, wherein at least one of the one or more grabbing mechanisms comprises a projection having a hook, a sharpened barb, tree-shaped barbs, or an anchor-shaped barb.

12. The prosthetic heart valve of claim 10, wherein any one or more of the outer support structure, the inner support structure, or the one or more grabbing mechanisms are formed of a shape memory alloy.

13. The prosthetic heart valve of claim 10, wherein the flexible membrane is configured to replace an aortic valve.

14. The prosthetic heart valve of claim 10, wherein the inner support structure is configured to securably engage the interior of the outer support structure upon being expanded within the outer support structure.

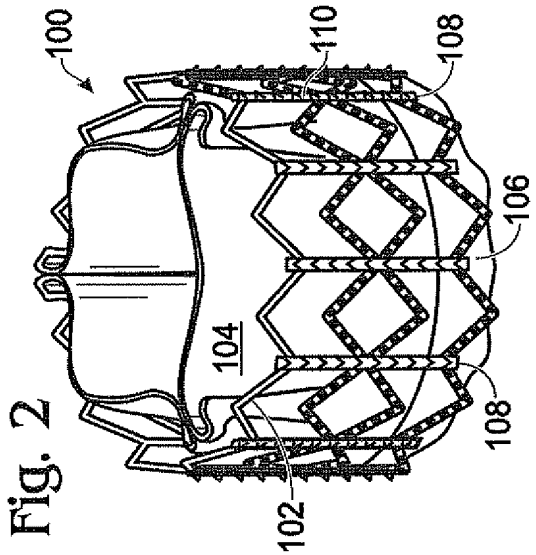


Fig. 2

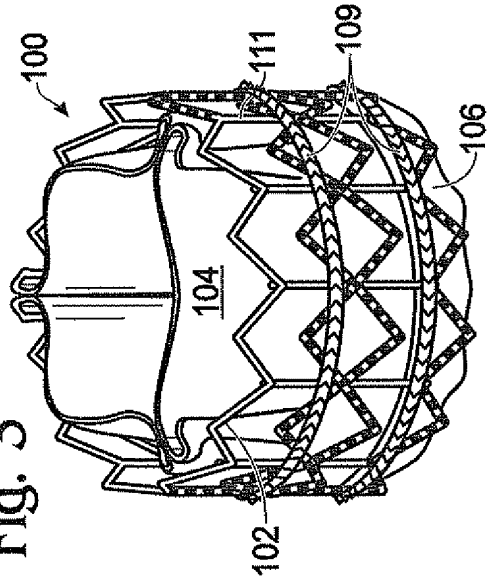


Fig. 3

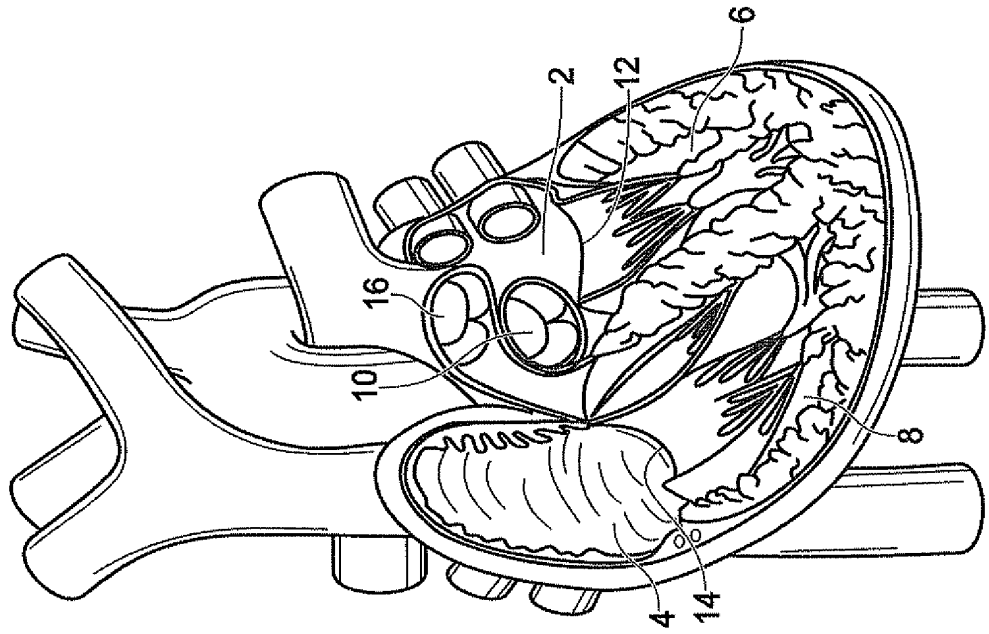


Fig. 1

Fig. 4

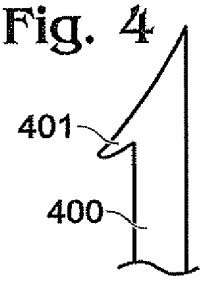


Fig. 5

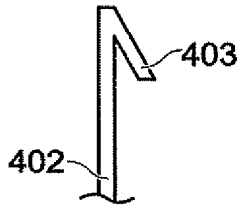


Fig. 6

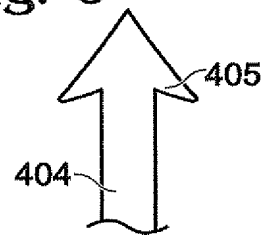


Fig. 7

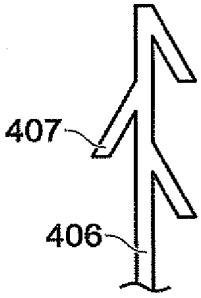


Fig. 8

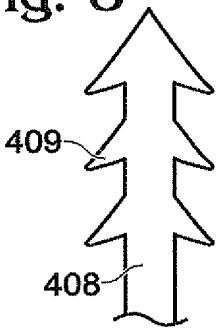


Fig. 9

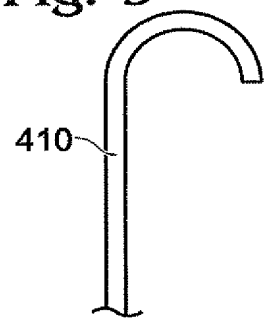


Fig. 10

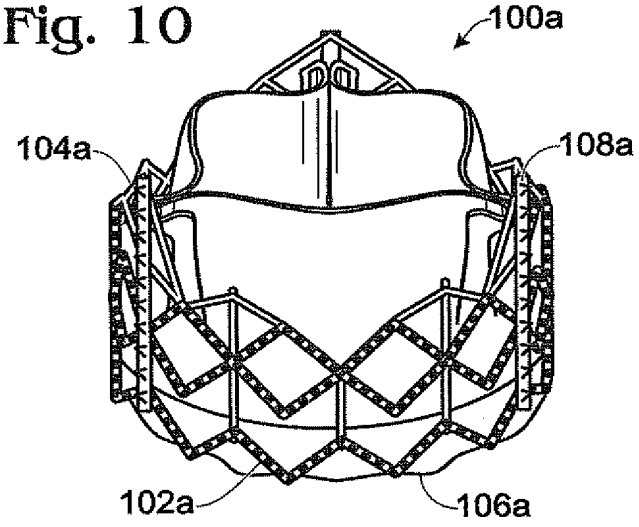


Fig. 11

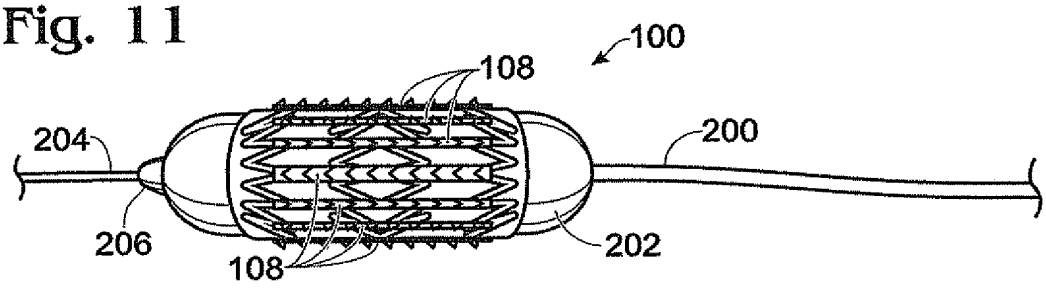


Fig. 12

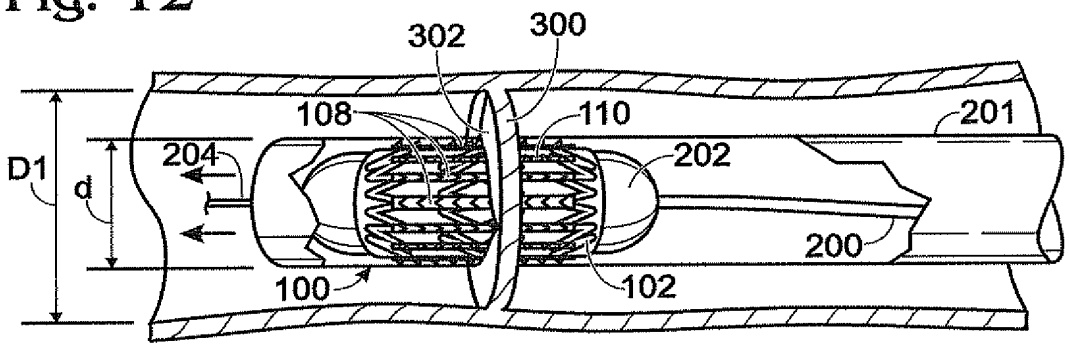


Fig. 13

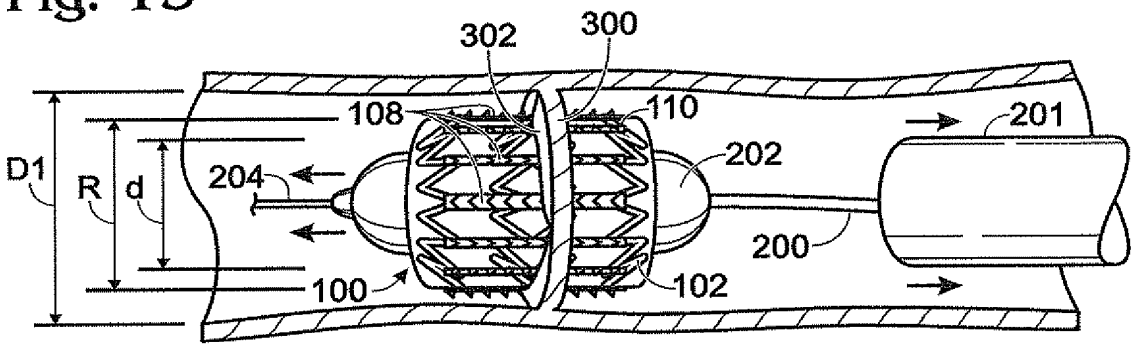


Fig. 14

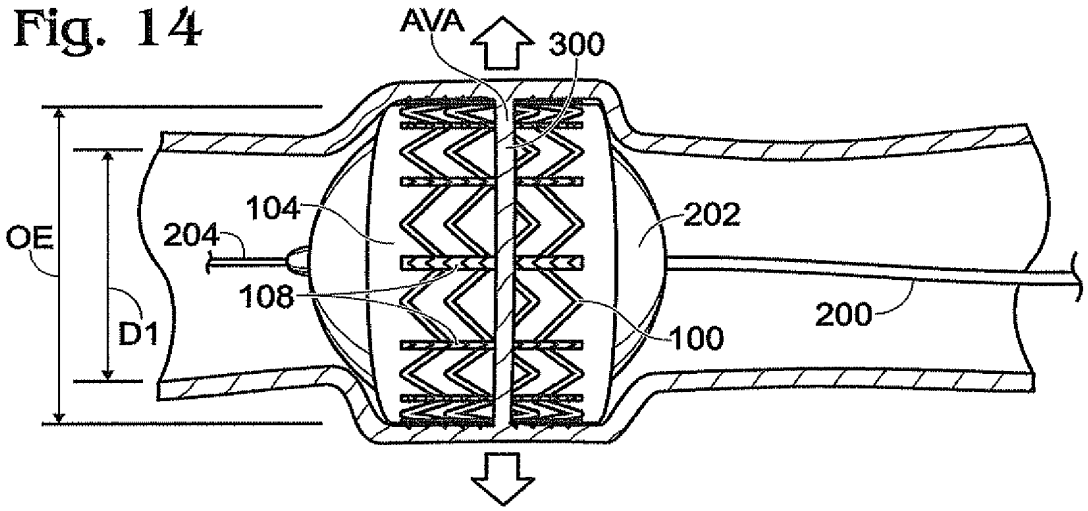


Fig. 15

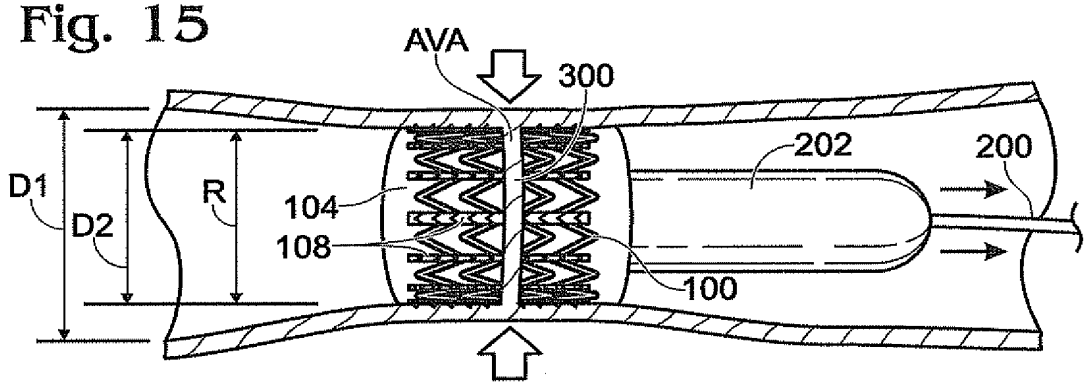


Fig. 16

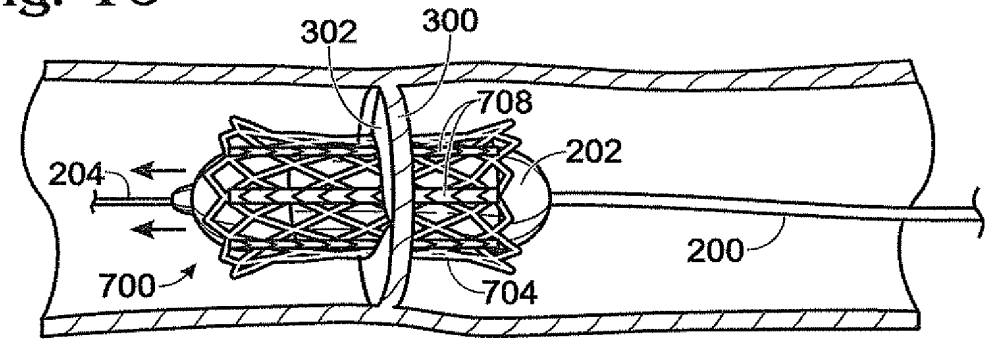


Fig. 17

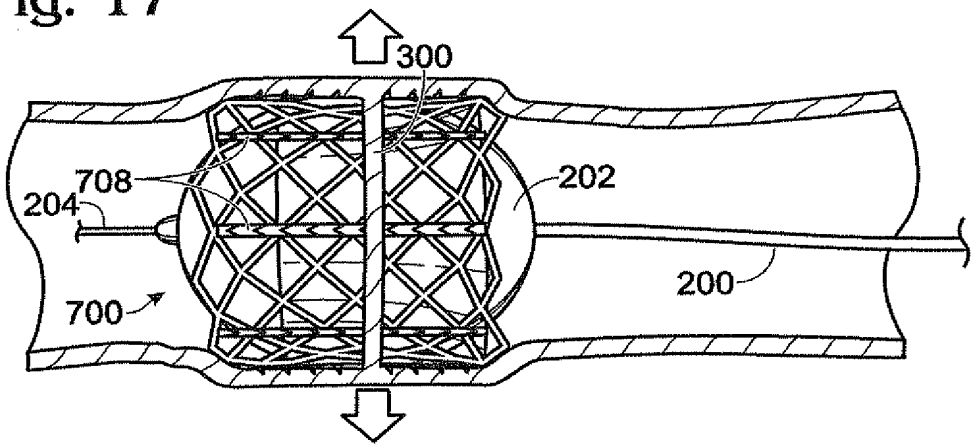


Fig. 18

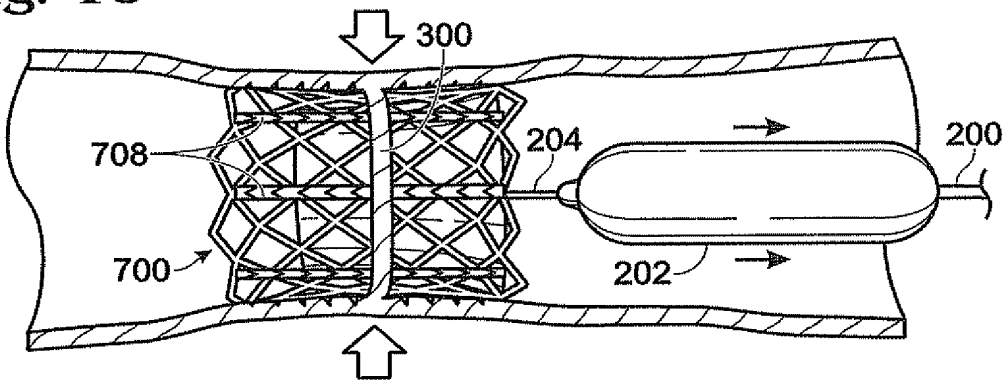


Fig. 19

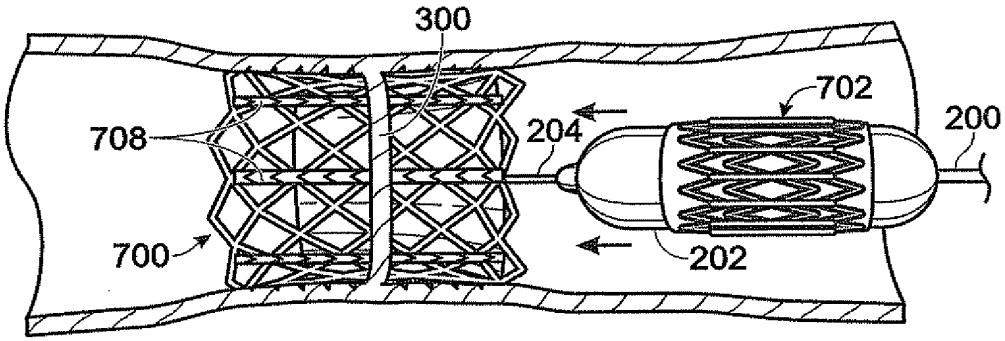


Fig. 20

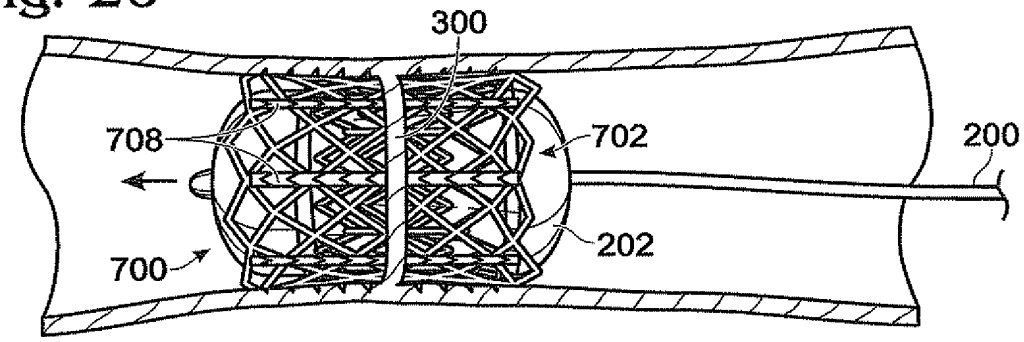


Fig. 21

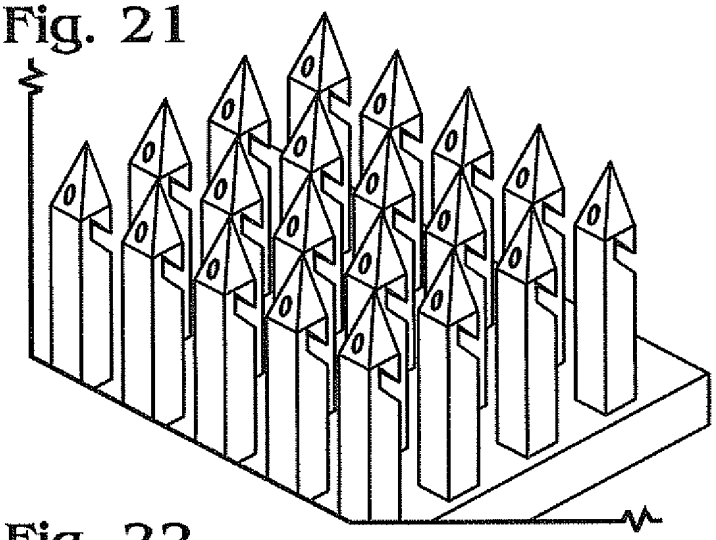


Fig. 22

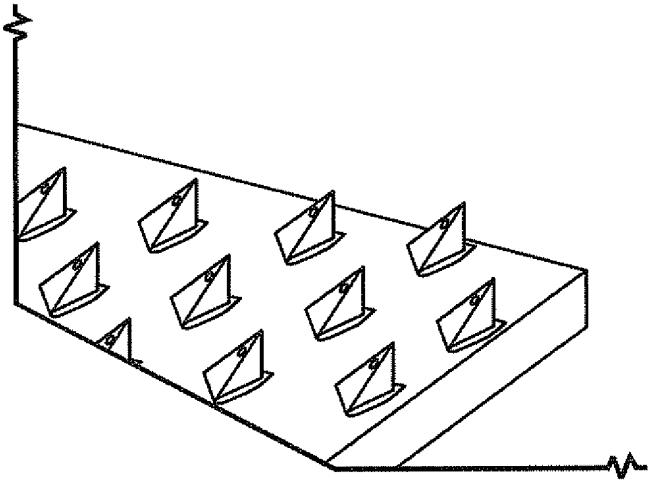


Fig. 23

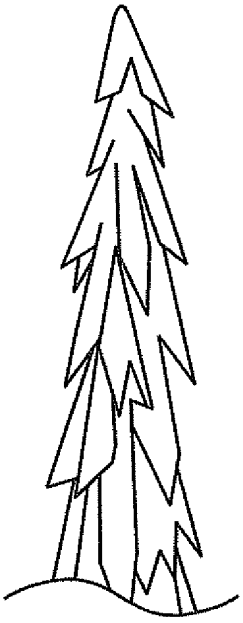


Fig. 24

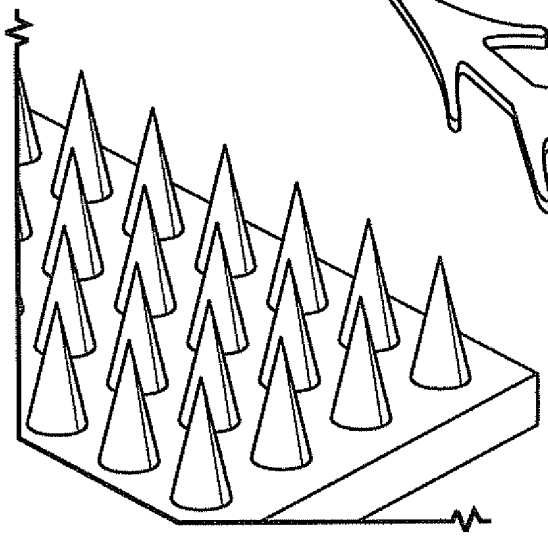


Fig. 25

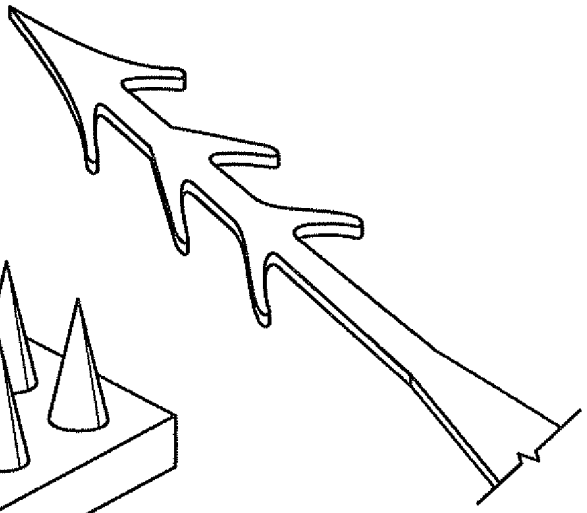
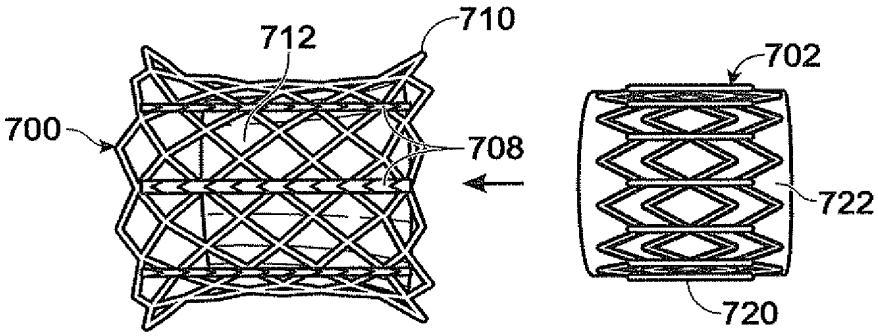


Fig. 26



INTERNATIONAL SEARCH REPORT

International application No
PCT/US2008/080004

A. CLASSIFICATION OF SUBJECT MATTER
INV. A61F2/24

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
A61F

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 2007/053243 A (SADRA MEDICAL INC [US]; SALAHIEH AMR [US]; HILDEBRAND DANIEL [US]; SAU) 10 May 2007 (2007-05-10) paragraphs [0056], [0121]; figures	1-6
Y		7-14
A		10-13
Y	WO 2006/127756 A (EDWARDS LIFESCIENCES CORP [US]; ROWE STANTON J [US]; WOOD LARRY [US];) 30 November 2006 (2006-11-30) paragraphs [0012], [0061], [0062], [0067], [0088] - [0092]; figures	7-9
Y	US 2006/129235 A1 (SEGUIN JACQUES [GB] ET AL SEGUIN JACQUES [GB] ET AL) 15 June 2006 (2006-06-15) paragraph [0081] - paragraph [0082]; figures	10-14

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[X] Further documents are listed in the continuation of Box C.

[X] See patent family annex.

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"P" document published prior to the international filing date but later than the priority date claimed

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Date of the actual completion of the international search	Date of mailing of the international search report
14 January 2009	23/01/2009

Name and mailing address of the ISA/	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016	Neumann, Elisabeth

Form PCT/ISA/210 (second sheet) (April 2005)

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2008/080004

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,X	US 2007/293942 A1 (MIRZAEE DARYUSH [US]) 20 December 2007 (2007-12-20) paragraphs [0034] - [0036], [0039]; figures	1,3-5
P,A		10,12,13
A	WO 2004/103223 A (CLEVELAND CLINIC FOUNDATION [US]) 2 December 2004 (2004-12-02) page 7, line 3 - line 9 page 16, line 6 - line 19 page 20, line 7 - page 21, line 14	1,10

Form PCT/ISA/210 (continuation of second sheet) (April 2005)

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/US2008/080004

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 2007053243 A	10-05-2007	AU 2006309251 A1	10-05-2007
		CA 2623814 A1	10-05-2007
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		CN 101180010 A	14-05-2008
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US 2007293942 A1	20-12-2007	NONE	
WO 2004103223 A	02-12-2004	CA 2526347 A1	02-12-2004
		EP 1626682 A1	22-02-2006

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

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(51) International Patent Classification:
A61B 17/12 (2006.01) *A61B 17/22* (2006.01)
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(21) International Application Number:
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(22) International Filing Date:
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(25) Filing Language: English

(26) Publication Language: English

(71) Applicant *(for all designated States except US)*: **CARDIOKINETIX, INC.** [US/US]; 925 Hamilton Avenue, Menlo Park, CA 94025 (US).

(72) Inventor; and
(75) Inventor/Applicant *(for US only)*: **KHAIRKHAHAN, Alexander** [US/US]; 925 Hamilton Avenue, Menlo Park, CA 94025 (US).

(74) Agents: **SHOOP, Richard, D.** et al.; Shay Glenn LLP, 2755 Campus Drive, Suite 210, San Mateo, CA 94403 (US).

(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(84) Designated States *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE,

[Continued on next page]

(54) Title: RETRIEVABLE CARDIAC DEVICES

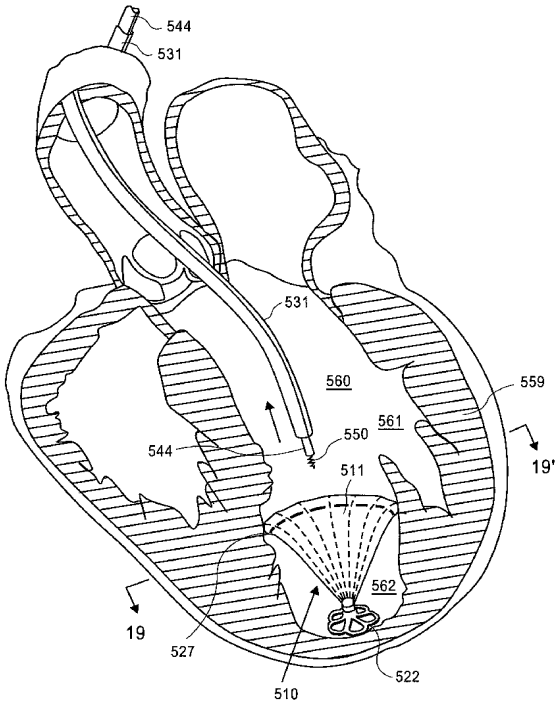

FIG. 18E

(57) Abstract: Removable cardiac implants, applicators for inserting, repositioning and/or removing them, and methods of using them are described. In particular, removable or repositionable ventricular partitioning devices are described. Systems including removable implants and applicators for inserting and/or removing them are also described.

WO 2010/024801 A1

ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, NO, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

— *with international search report (Art. 21(3))*

RETRIEVABLE CARDIAC DEVICES

CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] This application does not claim priority to any other patent application.

[0002] This application may be related to U.S. patent application Serial No. 10/463,959, filed on May 12, 2003 (titled "SYSTEM FOR IMPROVING CARDIAC FUNCTION") which is a continuation-in-part of prior U.S. patent application Ser. No. 09/635,511, filed on Aug. 9, 2000, which claims priority from U.S. provisional patent application No. 60/147,894 filed on Aug. 9,1999. This application is also a continuation-in-part of U.S. patent application Serial No. 11/151,164, filed on June 10, 2005, titled "PERIPHERAL SEAL FOR A VENTRICULAR PARTITIONING DEVICE." Each of these patent applications is herein incorporated by reference in its entirety.

BACKGROUND OF THE INVENTION

[0003] Described herein are systems, methods and devices for improving cardiac function, and may relate generally to the treating heart disease, particularly congestive heart failure, and more specifically, to a systems, methods, and devices for partitioning a patient's heart chamber.

[0004] Congestive heart failure annually leads to millions of hospital visits internationally. Congestive heart failure is the description given to a myriad of symptoms that can be the result of the heart's inability to meet the body's demand for blood flow. In certain pathological conditions, the ventricles of the heart become ineffective in pumping the blood, causing a back-up of pressure in the vascular system behind the ventricle.

[0005] The reduced effectiveness of the heart is usually due an enlargement of the heart. A myocardial ischemia may, for example, cause a portion of a myocardium of the heart to lose its ability to contract. Prolonged ischaemia can lead to infarction of a portion of the myocardium (heart muscle) wherein the heart muscle dies and becomes scar tissue. Once this tissue dies, it no longer functions as a muscle and cannot contribute to the pumping action of the heart. When the heart tissue is no longer pumping effectively, that portion of the myocardium is said to be hypokinetic, meaning that it is less contractile than the uncompromised myocardial tissue. As this situation worsens, the local area of compromised myocardium may in fact bulge out as the heart contracts, further decreasing the heart's ability to move blood forward. When local wall motion moves in this way, it is said to be dyskinetic, or akinetic. The dyskinetic portion of the myocardium may stretch and eventually form an aneurysmic bulge. Certain diseases may cause a

global dilated myopathy, i.e., a general enlargement of the heart when this situation continues for an extended period of time.

[0006] As the heart begins to fail, distilling pressures increase, which stretches the ventricular chamber prior to contraction and greatly increases the pressure in the heart. In response, the heart tissue reforms to accommodate the chronically increased filling pressures, further increasing the work that the now comprised myocardium must perform.

[0007] Patients suffering from congestive heart failure are commonly grouped into four classes, Classes I, II, III and IV. In the early stages, Classes I and II, drug therapy is presently the most common treatment. Drug therapy typically treats the symptoms of the disease and may slow the progression of the disease, but it cannot cure the disease. Presently, the only permanent treatment for congestive heart disease is heart transplantation, but heart transplant procedures are very risky, extremely invasive and expensive and are performed on a small percentage of patients. Many patient's do not qualify for heart transplant for failure to meet any one of a number of qualifying criteria, and, furthermore, there are not enough hearts available for transplant to meet the needs of CHF patients who do qualify.

[0008] Substantial effort has been made to find alternative treatments for congestive heart disease. For example, surgical procedures have been developed to dissect and remove weakened portions of the ventricular wall in order to reduce heart volume. This procedure is highly invasive, risky and expensive and is commonly only done in conjunction with other procedures (such as heart valve replacement or coronary artery by-pass graft). Additionally, the surgical treatment is usually only offered to Class III and IV patients and, accordingly, is not an option for most patients facing ineffective drug treatment. Finally, if the procedure fails, emergency heart transplant is the only presently available option.

[0009] Mechanical assist devices have been developed as intermediate procedures for treating congestive heart disease. Such devices include left ventricular assist devices and total artificial hearts. A left ventricular assist device includes a mechanical pump for increasing blood flow from the left ventricle into the aorta. Total artificial heart devices, such as the Jarvik heart, are usually used only as temporary measures while a patient awaits a donor heart for transplant.

[0010] Other efforts to treat CHF include the use of an elastic support, such as an artificial elastic sock, placed around the heart to prevent further deleterious remodeling. Treatment of the heat by mechanical means typically requires accurate and effective placement of treatment devices. Once a treatment device is implanted, it is often difficult (if not impossible) to correct or adjust placement of a treatment device. Furthermore, removal of a treatment device may require further invasive procedures. Thus, it would be beneficial to

provide device, systems and methods for removal of cardiac treatment devices that may address these problems.

[0011] Described herein are treatment devices that are configured to be removable (or re-positionable), systems for removing and/or repositioning such devices, and methods of removing and/or repositioning treatment devices.

SUMMARY OF THE INVENTION

[0012] Described herein are devices and systems including removable implants, applicators for inserting, repositioning and/or removing them, and methods of removing them. The implants described herein are cardiac implants that may be inserted into a chamber of a patient's heart, particularly the left ventricle. The implant may support the heart wall. In some variations the implant is a ventricular partitioning device for partitioning the ventricle into productive and non-productive regions.

[0013] An implant typically includes a frame comprising a plurality of struts formed of a relatively elastic and biocompatible material. For example, the frame may be formed of a metal or metal alloy. The frame may be formed of a shape memory alloy such as Nitinol. The implant may also include a membrane connected to the frame. The struts of the frame may include a first end that is connected to a hub, and a second end that includes a passive anchor. A passive anchor may be configured to secure the strut to the wall of the heart. For example, the passive anchor may be a sharp tip that is configured to partially penetrate the heart wall. The implant may also include a foot or anchor (including an active anchor) at the distal end.

[0014] In general, an implant may be inserted into a heart chamber using an applicator. An applicator typically includes a proximal end which may include a handle and may also include one or more controls for operating the applicator. The applicator may also include an elongate body extending distally. The distal end of the applicator may be adapted for releasably connecting to an implant. For example, the applicator may include an implant stabilization shaft that can connect and release the implant. The applicator may include one or more collapsing elements for collapsing the implant. For example, the applicator may include a lariat or collapse wire for collapsing the struts of the implant. In some variations the applicator includes a collapse sleeve or umbrella/cone for collapsing an implant. In some variations the applicator includes one or more engagement elements for engaging a collapsing element on the implant. For example, the applicator may include a capture wire, hook or the like that may engage a strand or other collapse element (e.g., collapse sleeve) on the implant that can assist in collapsing the struts of the implant.

[0015] The implant may also be adapted for disengaging from the wall of the heart. For example, the implant may be shortenable or movable so that any anchors on the implant, such as passive anchors on the struts or an active anchor on distal end, can be disengaged prior to removing the implant. In some variations the implant includes a shortenable region on the stem and/or foot that can be shortened to separate the struts from the heart wall by shortening the length of the stem and/or foot region. Since the implant is typically concave relative to the heart wall, foreshortening the implant in this way may cause passive anchors at the ends of the struts to withdraw from the wall of the heart. In some variations the struts themselves are shortenable. For example, the passive anchors may be retracted, allowing the implant to be removed.

[0016] In general, an implant may be removed and/or repositioned after it has been implanted, as described herein. For example, an implant may be positioned at a first location in a heart chamber such as within a cardiac ventricle, the struts forming the implant may be expanded to secure the implant in position. In some variations the implant may partition the chamber (e.g., when a membrane spans the strut regions). In some variations, the implant is disengaged from the applicator prior to repositioning or removal; in other variations, the implant is not disengaged from the applicator prior to repositioning or removal. To remove the implant from the first location in the heart, the implant (e.g., the struts of the implant) is at least partially collapsed. In some variations the implant may first be disengaged from the heart wall. The implant may be collapsed by activating a collapse element on the implant, on the applicator, or both. For example, a strand connected to the struts may be tensioned (e.g., by pulling) to collapse the struts. Thereafter, the implant may be drawn to the applicator. In some variations the implant may be repositioned. In some variations, the implant is withdrawn into a protecting element in the applicator, such as a cannula or sleeve. After repositioning, the implant may be again deployed. Alternatively, the implant may be removed from the patient by withdrawing the implant and actuator from the patient.

[0017] For example, described herein is a method of deploying a ventricular partitioning device comprising advancing a ventricular partitioning device having a membrane into a patient's left ventricle chamber in a contracted configuration, expanding the partitioning device into a deployed configuration at a first left ventricle location, at least partially collapsing the partitioning device into the contracted configuration, and withdrawing the partitioning device from the first left ventricle location. The method may also include the step of repositioning the partitioning device within the left ventricle and expanding the portioning device into the deployed configuration at a second left ventricle location so that the partitioning device partitions the left ventricle chamber into a main productive portion of the left ventricular chamber and a

secondary, non-productive portion of the left ventricular chamber. In some variations, the method also includes the step of removing the partitioning device from the patient.

[0018] The step of expanding the partitioning device may include expanding a frame connected to the membrane. The membrane may be a reinforced membrane.

[0019] The step of expanding the partitioning device may include allowing a frame connected to the reinforced membrane to self-expand. Also, as mentioned above, the step of withdrawing the partitioning device may comprise pulling the device into a retrieval catheter.

[0020] In any of the variations described herein, the implant (e.g., the ventricular partitioning device) may be secured or anchored to the first left ventricle location, and after repositioning, may be anchored to the second location.

[0021] The method may also include a step of disengaging the ventricular partitioning device from the left ventricle in the first location. For example, any anchors on the implant may be collapsed, withdrawn, or otherwise removed. Thereafter, or simultaneously, the step of at least partially collapsing the partitioning device into the contracted position may comprise pulling on at least one strand connected to the partitioning device. In some variations, the step of at least partially collapsing the partitioning device into the contracted position comprises drawing a collapse sheath at least partially over the partitioning device.

[0022] Also described herein are methods of deploying a ventricular partitioning device including the steps of: advancing a ventricular partitioning device having a membrane into a patient's left ventricle chamber in a contracted configuration, expanding the partitioning device into a deployed configuration at a first left ventricle location, pulling on a strand in communication with the partitioning device to at least partially collapse the partitioning device into the contracted configuration after it has been expanded, retrieving the partitioning device into a retrieval catheter; and withdrawing the partitioning device from the first left ventricle location.

[0023] The step of pulling on a strand in communication with the partitioning device may include pulling on an expansive strand extending from the periphery of the reinforced membrane. The step of pulling on the stand in communication with the partitioning device may include pulling on a retrieval wire at least partially surrounding the expanded reinforced membrane.

[0024] Also described herein are devices for partitioning a chamber of a patient's heart into a main functional portion and a secondary non-functional portion. These devices (implants) may include: a membrane having a collapsed configuration for delivery through a delivery catheter and an expanded configuration for deployment within the heart chamber so as to partition the heart chamber into a main functional portion and a secondary non-functional

portion, an expandable frame formed of a plurality of struts having a distal end secured to a hub, wherein the membrane is secured to the expandable frame, a distally extending stem, and a collapse element configured to convert the partitioning component from the expanded configuration to the folded configuration.

[0025] The collapse element may be a collapse sheath, a strand extending around the periphery of the partitioning component and extending therefrom, or the like.

[0026] Also described herein are devices for partitioning a chamber of a patient's heart into a main functional portion and a secondary non-functional portion that include: a membrane having an expanded configuration and a collapsed configuration, wherein the membrane forms a recess when in the expanded configuration, an expandable frame formed of a plurality of struts having a distal end secured to a hub, wherein the reinforced membrane is secured to the expandable frame, a non-traumatic distal tip, configured to engage a region of the ventricular wall; and a strand extending at least partially around the periphery of the membrane at or near the proximal end of the expandable frame, wherein the strand is configured to be tensioned to collapse the device from the expanded configuration to the collapsed configuration.

[0027] Also described herein is a system for partitioning a chamber of a patient's heart into a main functional portion and a secondary non-functional portion, the system comprising an implant configured for deployment into a heart chamber and an elongate applicator configured to insert and retrieve the implant. For example, the implant may include a plurality of struts, wherein the struts are configured to have a collapsed delivery configuration and an expanded deployed configuration, and a strand extending between the struts, wherein the strand may be tensioned to collapse the struts. The elongate applicator configured to insert and retrieve the implant may include a control at the proximal end of the applicator for controlling release of the implant from the applicator, and an elongate body extending from the proximal end to a distal end, wherein the distal end of the elongate body is configured to relaseably secure the implant. The strand extends proximally from the implant along the elongate body of the applicator so that the strand may be manipulated from the proximal end of the applicator.

[0028] The applicator may further comprise a port at the proximal end through which the strand may pass. In some variations, the applicator includes an implant capture element at the distal end of the applicator. The implant capture element may be selected from the group consisting of: an implant capture sleeve and an implant capture umbrella.

[0029] Also described herein are methods of deploying, repositioning and/or removing an implant comprising: advancing an implant into a patient's left ventricle chamber in a contracted configuration, wherein the implant comprises a plurality of struts formed of a shape

memory material, expanding the implant into a deployed configuration at a first left ventricle location, changing the temperature of the implant to at least partially collapse the implant into the contracted configuration, retrieving the implant into a retrieval catheter, and withdrawing the implant from the first left ventricle location. In some variations, the step of changing the temperature of the implant comprises exposing the implant to cooled saline.

[0030] Also described herein are systems for partitioning a patient's ventricle, comprising: an implant configured for deployment into the patient's ventricle, the implant including a plurality of struts, wherein the implant is configured to have a collapsed delivery configuration and an expanded deployed configuration, and an applicator configured to insert and retrieve the implant, comprising a control at the proximal end of the applicator for controlling release of the implant from the applicator, an elongate body extending from the proximal end to a distal end, wherein the distal end of the elongate body is configured to releasably secure the implant, and a capture wire extendable from the applicator's distal end and configured to draw the implant toward the applicator's distal end. The applicator may also include a control at the proximal end for manipulating the capture wire.

[0031] In some variations, the capture wire is configured as a lariat. In some variations, the implant includes a strand that may be tensioned to collapse the implant from the expanded configuration, and the capture wire of the implant is configured as a hook that may engage the strand. The capture wire may be connected to the implant.

[0032] In some variations, the applicator further comprises an inflatable sleeve configured to extend from the distal end of the applicator and collapse the implant. As mentioned above, the applicator may include a capture umbrella configured to extend from the distal end of the applicator and collapse the implant.

[0033] The implant may also include collapse sleeve configured to collapse the struts. Thus, an applicator may include a collapse sleeve pullwire configured to engage the collapse sleeve on the implant.

[0034] Also described herein are systems for partitioning a patient's ventricle, the system comprising: an implant configured for deployment into the patient's ventricle and an elongate applicator configured to insert and retrieve the implant. The implant may include a plurality of struts, wherein the implant is configured to have a collapsed delivery configuration and an expanded deployed configuration, and a strand extending between the struts, wherein the strand may be tensioned to collapse the struts. The elongate applicator configured to insert and retrieve the implant may include a control at the proximal end of the applicator for controlling release of the implant from the applicator, an implant stabilization shaft extending distally from the

proximal end, wherein the implant stabilization shaft is configured to releasably secure to the implant, and a strand capture element extending distally from the proximal end, wherein the strand capture element is configured to engage the strand on the implant and collapse the struts of the implant.

[0035] Also described herein are devices for partitioning a patient's ventricle into a main functional portion and a secondary non-functional portion that include: a membrane having an expanded configuration and a collapsed configuration, an expandable frame formed of a plurality of struts having a distal end secured to a hub, wherein the membrane is secured to the expandable frame, a stem extending distally from the hub, and a collapse sleeve configured to axially slide from the stem and to collapse the expandable frame and membrane into a collapsed configuration. These devices may also include a passive anchor at the ends of each of the struts of the expandable frame.

[0036] In some variations the devices include a non-traumatic foot at the distal end of the device. The devices may also include an attachment mechanism for a collapse sleeve pullwire.

[0037] Also described herein are removable or repositionable implants for partitioning a chamber of a patient's heart into a main functional portion and a secondary non-functional portion, comprising: a membrane, a plurality of struts secured to a hub at a first end, wherein the membrane is secured to the plurality of struts, and the plurality of struts and membrane have a collapsed delivery configuration and an expanded deployed configuration for deployment within a heart chamber, wherein the membrane forms a recess when in the expanded configuration, wherein end of each of the plurality of struts includes a passive anchor configured to secure to the wall of the patient's heart, and a stem extending distally from the hub, wherein the stem comprises a shortenable region configured to be decreased in length and permit the passive anchors to disengage from the wall of the patient's heart.

[0038] In some variations, the implant further includes a trigger configured to shorten the shortenable region of the stem. The trigger comprises a wire or line extending distally through the stem portion.

[0039] The shortenable region may be a collapsible region, or a telescoping region. In some variations, the device includes a lock for locking the shortenable region.

[0040] Also described herein are methods of removing an implant that has been deployed at a first ventricle location, wherein the implant includes a plurality of struts each having a passive anchor at a first end and connected to a hub at a second end and a stem extending from the hub. The method may include the steps of: shortening a shortenable region of the stem to

disengage the passive anchors from the heart wall, at least partially collapsing the plurality of struts, and withdrawing the implant from the first left ventricle location.

[0041] In some variations, the step of shortening the shortenable region comprises applying pulling on a wire or string to shorten the shortenable region. The method may also include the step of unlocking the implant so that the shortenable region may be shortened. The step of at least partially collapsing the implant may include pulling on a strand or collapse line to draw the struts together.

[0042] The method may also include the step of repositioning the implant within the left ventricle and expanding the struts into a deployed configuration at a second left ventricle location. In addition, the method may also include the step of removing the implant from the patient.

INCORPORATION BY REFERENCE

[0043] All publications and patent applications mentioned in this specification are herein incorporated by reference in their entirety as if each individual publication or patent application was specifically and individually indicated to be incorporated by reference.

BRIEF DESCRIPTION OF THE DRAWINGS

[0044] FIG. 1 is a perspective view of one variation of a cardiac treatment device including a hub, a frame, and a stem thereof.

[0045] FIG. 2A is a cross-section of a system including a cardiac device with the cardiac device partially retracted into an applicator (e.g., delivery catheter).

[0046] FIG. 2B is a cross-sectional side view of a portion of FIG. 2A.

[0047] FIG. 3A is a side view of the system of FIG. 2A with the cardiac device further retracted.

[0048] FIG. 3B is a cross-sectional side view of a portion of FIG. 3A.

[0049] FIG. 4A is a side view of the system of FIG. 2A with the cardiac device fully retracted.

[0050] FIG. 4B is a cross-sectional side view of a portion of FIG. 4A.

[0051] FIG. 5A is a cross-sectional side view of a human heart with a portion of an applicator inserted therein.

[0052] FIGS. 5B-5K are cross-sectional side views of the human heart illustrating installation (FIGS. 5B-5E), removal (FIGS. 5E-5H), and subsequent final installation (FIGS. 5I-5K) of a cardiac device.

[0053] FIG. 6A is a perspective view of another variation of a cardiac device.

[0054] FIG. 6B is a cross-sectional side view of the human heart with the cardiac device of FIG. 6A installed.

[0055] FIG. 7A is a perspective view of another variation of a cardiac device.

[0056] FIG. 7B is a cross-sectional top plan view of the cardiac device on 7B-7B' in FIG. 7A.

[0057] FIG. 7C is a cross-sectional side view of the human heart with the cardiac device of FIG. 7A installed.

[0058] FIG. 8 is an elevational view of another variation of a partitioning device in an expanded configuration.

[0059] FIG. 9 is a plan view of the partitioning device shown in FIG. 8 illustrating the upper surface of the device.

[0060] FIG. 10 is bottom view of the partitioning device shown in FIG. 8.

[0061] FIG. 11 is a perspective view of the non-traumatic tip of the distally extending stem of the device shown in FIG. 8.

[0062] FIG. 12 is a partial cross-sectional view of the hub of the partitioning device shown in FIG. 9 taken along the lines 12-12'.

[0063] FIG. 13 is a transverse cross sectional view of the hub shown in FIG. 12 taken along the lines 13-13'.

[0064] FIG. 14 is a longitudinal view, partially in section of a reinforcing strut and membrane at the periphery of the partitioning device shown in FIG. 8.

[0065] FIG. 15 is a schematic elevational view, partially in section, of a delivery system with the partitioning device shown in FIGS. 8 and 9 mounted thereon.

[0066] FIG. 16 is a transverse cross-sectional view of the delivery system shown in FIG. 15 taken along the lines 16-16'.

[0067] FIG. 17 is an elevational view, partially in section, of the hub shown in FIG. 12 being secured to the helical coil of the delivery system shown in FIG. 15.

[0068] FIGS. 18A-18E are schematic views of a patient's left ventricular chamber illustrating the deployment of the partitioning device shown in FIGS. 8 and 9 with the applicator shown in FIG. 15 to partition a patient's heart chamber (left ventricle) into a primary productive portion and a secondary, non-productive portion.

[0069] FIG. 19 is a schematic plan view of the deployed device shown in FIG. 18E within a patient's heart chamber.

[0070] FIG. 20A is a partial schematic view of the partitioning device shown in FIGS. 8 and 9 in a contracted configuration resulting from pulling the free ends of the expansive strand at the periphery of the reinforced membrane.

[0071] FIG. 20B is a schematic view of the contracted device shown in FIG. 20A being pulled into an expanded distal end of an applicator to facilitate withdrawal of the partitioning device.

[0072] FIG. 20C is a schematic view of the contracted device shown in FIG. 20A pulled further into the inner lumen of the receiving applicator.

[0073] FIG. 21 is a schematic view of another variation of an inserter configured to apply and remove and/or reposition an implant.

[0074] FIG. 22A-22F illustrate retrieval of a cardiac implant as (partitioning device) using the applicator of FIG. 21.

[0075] FIG. 23A illustrates another variation of an applicator.

[0076] FIG. 23B shows a cross-section through a region of the applicator of FIG. 23A.

[0077] FIGS. 24A-24F illustrate a method of using the applicator similar to that shown in FIG. 23A to retrieve an implant.

[0078] FIGS. 25A and 25B show another variation of a system including an applicator and an implant in which the implant is secured to the applicator and released from the applicator, respectively.

[0079] FIG. 26A shows another variation of an applicator configured to deliver and reposition and/or remove an implant, and FIGS. 26B-26C illustrate operation of the applicator of FIG. 26A.

[0080] FIGS. 27A-27E illustrate the operation of a system including an implant having a collapse sleeve.

[0081] FIGS. 28A and 28B show front and side views, respectively, of an implant having a collapse sleeve, similar to the implant shown in FIGS. 27A-27E.

[0082] FIG. 29A shows an applicator including a retrieval element configured as a lariat. FIGS. 29B-29E illustrate operation of the applicator of FIG. 29A and an implant.

[0083] FIGS. 30A and 30B show front and side views, respectively, of an implant that may be used with the applicator shown in FIG. 29A and illustrated in FIGS. 29B-29E.

[0084] FIG. 31A shows another variation of a system including an applicator and an implant.

[0085] FIGS. 31B-31D illustrate retrieval of an implant using the system shown in FIG. 31A.

[0086] FIGS. 32A and 32B show another variation of an applicator configured for retrieval of an implant.

[0087] FIG. 33A and FIG. 33C-33H illustrate operation of an applicator similar to that shown in FIGS. 32A and 32B, and FIG. 33B shows a cross-section through a region of the applicator shown in FIGS. 33A and 33C-33H.

[0088] FIG. 34A, 34C and 34E show an implant having a shortenable stem region. FIG. 34C shows the implant of FIG. 34A in which the stem region has been shortened by tensioning an activating element. FIG. 34E shows the implant of FIGS. 34A and 34C during removal of the activating element. FIGS. 34B, 34D and 34F show a slightly enlarged view of the stem regions of the implants of FIGS. 34A, 34C and 34E, respectively.

[0089] FIGS. 35A-35E illustrate the operation of another system for deploying and removing an implant. The system includes an applicator (partially illustrated in FIGS. 35A-35E) and an implant.

[0090] FIG. 36A shows a cross-section of another variation of an implant, and FIGS. 36B-36C illustrate a method of removing an implant such as the one shown in FIG. 36A, in which temperature is changed to induce collapse of an implant so that it can be withdrawn.

DETAILED DESCRIPTION OF THE INVENTION

[0091] Described herein are deployable and retrievable cardiac treatment devices or implants, systems including retrievable devices, and methods of using them. For example, any of the implants described herein may be positioned in a patient's heart (and particularly the patient's ventricle, such as the left ventricle), deployed into the heat by expanding the device, and then, either immediately or after some time period, disengaged from the heart, at least partially collapsed, and repositioned and/or removed. The implants, which may also be referred to as cardiac treatment devices, may be configured to partition the heart (e.g., into a productive and non-productive region), or to support the wall of the heart. Examples of such implants are described herein. Applicators for deploying and/or retrieving any of the implants described herein are also taught, as are systems including the applicators and the implants. Methods of using these implants are also described.

[0092] FIGS. 1, 6A, 7A and 8 show variations of implants (e.g., device 34 in FIG. 1). Any of the implants described herein may also be referred to as cardiac treatment devices or treatment devices. Alternatively, these devices may be referred to as ventricular partitioning devices or partitioning devices. Such partitioning devices may be configured to partition a ventricle into function (or productive) and non-function (or non-productive) regions. FIGS. 2A-

2B, and 3 illustrate this implant (cardiac device 34) in more detail. The cardiac device 34 includes a frame 184 and a stem 186, or flexible body, and has a vertical axis 188. Partitioning devices, including ventricular partitioning devices, are only one class of implants which are described herein and may be used with the device removal or repositioning systems and methods described herein. Other such devices may be support devices that do not include a membrane, or do not partition a heart chamber, but predominantly support the cardiac tissue.

[0093] Referring now to FIG. 1, the frame 184 includes a frame hub 190, a plurality of main segments 192, and a membrane 194. The hub 190 in this example is a ring-shaped body with an outer surface with a diameter of about 5 mm, an inner surface with a diameter of about 4 mm, a thickness of about 3 mm, and a pin extending off-center across the inner surface creating a smaller and a larger gap. The pin has a length of about 3.5 mm and a diameter of about 1 mm and is located in a plane. The frame 184 has a diameter 209 of approximately 75 mm, however, other embodiments may have diameters of between 10 mm and 120 mm. The entire hub 190 in this example is made of nickel titanium.

[0094] In this example, the main segments 192 include first portions, or central segments, 210, second portions, or outer segments, 212, and passive anchors 214. The first portions 210 are connected to the hub 190 at a central portion of the outer surface and extend radially from the hub 190 at an angle away from the plane of the pin to a length of about 8 mm. The second portions 212 of the segments 192 are connected to ends of the first portions 210 and further extend radially from the hub 190 but at an angle towards the plane. The second portions 212 each have a length of 5-50 mm. The passive anchors 214 are formed at an end of each of the second portions 212. The passive anchors 214 have sharp ends that point slightly radially from the hub 190. The segments 192 are made from nickel titanium, which after a prescribed thermal process, allows for the segments 192 to hold their shape as illustrated in FIG. 1. The entire frame 184, or just portions of the frame 184, may also be made of stainless steel, polymers, or biodegradable materal(s).

[0095] In FIG. 1, the membrane 194 is stretched over the first 210 and second 212 portions of the segments 192 to give the frame 184 a disk like shape. The membrane 194 is made of expanded Polytetrafuoroethylene (ePTFE) and has a thickness of about 0.08 mm. Other embodiments may use a mesh membrane, or other appropriate permeable, semi-permiable, or impermeable membranes. While porous ePTFE material may be preferred, the membrane may be formed of suitable biocompatible polymeric material which includes Nylon, PET (polyethylene terephthalate) and polyesters such as Hytrel. The membrane may be foraminous in nature to facilitate tissue ingrowth after deployment within the patient's heart. The applicator

(including delivery catheter and/or a guiding catheter) may be formed of suitable high strength polymeric material such as PEEK (polyetheretherketone), polycarbonate, PET, Nylon, and the like. Braided composite shafts may also be employed.

[0096] The stem 186 may be made of Polytetrafuoroethylene (PTFE) and is thus expandable and flexible. Referring again to FIG. 1, the stem 186 can be compressed or stretched by 30% of its length and can be bent from the vertical axis 188 of the device 34 by 90 degrees in any direction. The first hub 232, second hub 234, and active anchor 236 may be made of nickel titanium. In other embodiments, the hubs may be made of stainless steel.

[0097] FIG. 2A illustrates one variation of a systems including an applicator 30 and an implant 34. The implant shown is the variation described above from FIG. 1. The applicator shown in FIG. 2 includes a handle 44, a deployment member 46, which is partially within a catheter region (catheter tube 38). The proximal end of the deployment member 46 is secured to the handle 44. The handle may include one or more controls for deploying and/or retrieving an implant. For example, the handle may be formed of molded plastic and may include knobs, buttons, or other controls for operating the applicator to deploy or retrieve a device. The distal end of a portion of the applicator (e.g., the deployment member 46) may be adapted to releasably grasp the implant.

[0098] In use, the deployment member 46 may be inserted through the catheter tube 38 so that the distal end 54 of the deployment member 46 may exit the distal end of the tube 38. The deployment member 46 may connect to a cardiac implant device 34 such that a key (not visible) engages the hub 190 of the frame 184 of the implant by passing through the larger gap in the hub 190. The implant may then be secured to the deployment member, and may be deployed by manipulation of a control on the handle, e.g., by rotating the key to disengage the implant from the deployment member.

[0099] As illustrated in FIGS. 2A and 2B, the distal end 54 of the deployment member 46 may be pulled into the distal end of the catheter tube 38. As a proximal section of the frame 184 of the implant enters the catheter tube 38, it may be collapsed by the smaller diameter of the catheter opening of the applicator. For example, in the variation shown in FIG. 2, the first portions 210 of the segments 192 begin to collapse towards the stem 186 when the implant is drawn into the catheter tube. The segments 192 collapse, or fold, against a spring force that is created by the resilient nature of the nickel titanium material from which they are made. At the same time, the second portions 212 fan out radially away from the hub 190.

[00100] FIGS. 3A and 3B show a distal section of the frame 184 and the second portions 212 of the segments 192 beginning to enter the tube 38, so that the second portions have been

bent back to collapse towards the stem 186 similarly to the first portions 210. FIGS. 4A and 4B illustrate this system 30 with the cardiac implant device 34 completely contained within the catheter tube 38.

[00101] FIGS. 5A-5J illustrate a human heart 242 while the implant 34 is being deployed. The heart 242 contains a right ventricle 244 and a left ventricle 246 with papillary muscles 248 and an akinetic (e.g., damaged) portion 250 with an apex 252. The distal end of the catheter 38 has been inserted through the aorta and aortic valve into the left ventricle 246 to a selected position where the ventricular partitioning device 34 can be deployed. The catheter tube 38 is then partially pulled off of the cardiac device 34 exposing the stem 186.

[00102] The active anchor 236 is then deployed. In the implant shown in FIGS. 1-5J, the implant includes an active anchor at the distal end. This anchor may be inserted into the tissue as illustrated in FIG. 5C. In other variations (e.g., described below), the distal end of the implant may be configured with one or more atraumatic feet that does not penetrate the tissue. In FIG. 5C, the active anchor at the distal end may be deployed into the tissue by operating (e.g., rotating) a control (e.g. an anchor knob) on the handle of the device. The active anchor 236 penetrates the myocardium of the heart 242 to secure the cardiac device 34 in the selected position at the apex 252 of the akinetic portion 250 of the left ventricle 246.

[00103] The catheter 38 is then completely removed from the distal end 54 of the deployment member 46, exposing the cardiac device 34. As the cardiac device 34 expands, due to the resilient nature of the segments 192, and the pre-set shape of the frame 184, the passive anchors 214 on the segments 192 penetrate the myocardium in a first direction. The membrane 194 seals a portion of the ventricle 246 and separates the ventricle 246 into two volumes.

[00104] If the cardiac device 34 has not been properly positioned, or if it is of the wrong size or shape for the particular heart, the device 34 may be repositioned or completely removed from the heart 242, as illustrated in FIGS. 5E-5H.

[00105] For example, in variations in which an active anchor at the distal end has been used, the implant may be removed by first releasing the active anchor. If the implant has been completely deployed, e.g., so that the applicator has been separated from the implant (which has been inserted into the tissue), then the implant may re-coupled to the applicator. For example, the distal end of a portion of the applicator, such as the deployment member 46, 54, may be connected to the implant. Thus, in FIG. 5E, the applicator has been re-coupled to the deployment member 46 of the applicator. A control (e.g., knob, etc.) on the handle may be manipulated to engage the applicator to the implant. In this variation a central portion of the implant, such as the hub, is configured to releaseably engage and re-engage the applicator. In

some variations an additional tether or other element may be used to grab and position the deployed implant so that it can be engaged with the applicator. Examples and illustrations of these additional elements are provided in greater detail below.

[00106] Furthermore, the device may be repositioned before disengaging from the applicator.

[00107] After the applicator has been engaged with the implant (or before disengaging the implant), activation of a control on the applicator (e.g., rotation of an anchor knob on the handle of the applicator) may disengage the active anchor 236 from the left ventricle 246. The distal end 54 of the deployment member 46 may be retracted into the catheter 38 to once again fold the cardiac device 34 into the position shown in FIG. 4B, from where it can again be deployed. The passive anchors 214 may be removed from the myocardium in a second direction which is approximately 180 degrees from the first direction so that minimal damage is done to the myocardium. This is illustrated in FIGS. 5F-5H.

[00108] The implant 34 may then be properly re-positioned, as shown in FIG. 5I, and deployed in the new location using the applicator. Once positioned, the applicator may be activated to release the deployment member 46 as previously described. After deploying it as desired, the distal end of the applicator may be separated from the cardiac device 34 to allow removal of the deployment member 46 and removal of the applicator from the heart 242, as shown in FIG. 5J. FIG. 5K illustrates the heart 242 with the cardiac device 34 installed and the deployment mechanism 36 removed from the heart 242.

[00109] In this variation, the shape of the frame 184 allows the device 34 to be retrieved as long as the deployment member 46 is connected to the device 34. When the device 34 is retrieved, the passive anchors 214 withdraw from the myocardium in a direction that is approximately 180 degrees from, or opposite, the first direction to minimize the amount of damage done to the myocardium. The device 34 also provides support for the akinetic region 250, minimizes the bulging of the akinetic region 250, and reduces stress on the working parts of the myocardium. In general, the ePTFE membranes which may be used with the implants is biocompatible, has a non-thrombogenic surface, promotes healing, and accelerates endothelization. These membranes may be used to partition the heart, as previously described.

[00110] FIG. 6A illustrates another variation of a cardiac device 254. The cardiac device includes a hub 256, a frame 258, and a membrane 260. The hub 256 lies at a central portion of the frame 258 and an active anchor 262 is connected to the hub 256 and extends downwards therefrom. The frame 258 includes a plurality of segments 264 which extend radially and

upwardly from the hub 256. A sharp passive anchor 266 lies at the end of each of the segments 264. The membrane 260 is stretched between the segments 264 to form a cone-shaped body.

[00111] FIG. 6B illustrates a sectional view of a human heart with the cardiac device 254 of FIG. 6A having been secured to an akinetic portion thereof.

[00112] FIG. 7A and FIG. 7B illustrate another variation of a cardiac device 268. The cardiac device includes a hub 270, a frame 272, and membrane 274. The hub 270 lies at a central portion of the frame 272 and an active anchor 276 extends downwardly from the hub 270. The frame 272 includes a plurality of segments 278 which extend radially and upwardly from the hub 270. The segments 278 are of different lengths such that an outer edge 280 of the cardiac device 268 is not planar. The device 268 has a vertical axis 282 which intersects a diameter 284 across the outer edge 280 of the device 268 at an angle other than 90 degrees. A sharp passive anchor 286 lies at the end of each of the segments 278. The membrane 274 is stretched between the segments 278 to form a cone-shaped body. Referring specifically to FIG. 7B, a cross-section perpendicular to the vertical axis 282 of the device 268 is circular.

[00113] FIG. 7C illustrates a sectional view of a human heart with the cardiac device 268 of FIG. 7A having been secured to an akinetic portion thereof. The outer edge 280 of the cardiac device 268 defines a non-planar cross-section of an inner surface of the left ventricle. The implant 268 can be sized and shaped for use on a wider variety of heart regions, including a variety of sizes and shapes of akinetic portions in left ventricles.

[00114] In some variations, the implants may include one or more collapsing elements that are configured to help collapse the implant from the expanded (deployed) configuration into the collapsed (or partially collapsed) position. For example, a sleeve or cover may be used to collapse the frame of the implant. In other variations, the implant may include a strand, wire, thread, cable, chain, etc. (which may generally be referred to as a "strand") for collapsing the device. For example, a strand may be included around the perimeter of the ribs or struts (e.g., spaced from the central hub region by any desired spacing). The strand may be a loop (e.g., joined at the ends) or it may have one or both ends free. Pulling on the strand may contract the struts, drawing them together towards the collapsed configuration.

[00115] FIGS. 8-11 illustrate one variation of a cardiac implant device including a strand which may be used to collapse the device. In this variation, the implant (partitioning device)10 includes a partitioning membrane 511, a hub 512, preferably centrally located on the partitioning device, and a radially expandable reinforcing frame 513 that is secured to the proximal or pressure side of the frame 513 as shown in FIG. 8. The struts 514 have distal ends 515 which are secured to the hub 512 and free proximal ends 516 which are configured to curve or flare away

from a center line axis. Radial expansion of the free proximal ends 516 unfurls the membrane 511 secured to the frame 513 so that the membrane presents a pressure receiving surface 517 which defines in part the productive portion of the patient's partitioned heart chamber. The peripheral edge 518 of the membrane 511 may be serrated as shown.

[00116] The variation shown in FIGS. 8-11 also includes a continuous expansive strand 519 that extends around the periphery of the membrane 511 on the pressure side thereof. In operation, this strand may also help apply pressure to the pressure side of the flexible material of the membrane to effectively seal the periphery of the membrane against the wall of the ventricular chamber. The ends 520 and 521 of the expansive strand 519 are shown extending away from the partitioning device in FIGS. 8 and 9. As mentioned, the ends 520 and 521 may be left unattached or may be secured together, e.g. by a suitable adhesive, knot, or the like, or secured to the membrane 511 itself. While not shown in detail, the membrane 511 in this example has a proximal layer secured to the proximal faces of the struts 514 and a distal layer secured to the distal faces of the struts in a manner described in US Patent Application Ser. No. 10/913,608, filed on Aug. 5, 2004, herein incorporated by reference in its entirety.

[00117] The hub 512 shown in FIGS. 10 and 11 may be connected to a non-traumatic support component 522. The support component 522 shown in FIGS. 10 and 11 has a stem 523 a plurality of pods or feet 524 extending radially away from the center line axis and the ends of the feet 524 are secured to struts 525 which extend between adjacent feet. A plane of material (not shown) may extend between adjacent feet 524 in a web-like fashion to provide further support in addition to or in lieu of the struts 525. The inner diameter of the stem 523 is threaded to secure the partitioning device 510 to a delivery catheter as shown in FIGS. 15-17.

[00118] As shown in FIG. 12, the distal ends 515 of the struts 514 are secured within the hub 512 and, as shown in FIG. 13, a transversely disposed connector bar 526 is secured within the hub which is configured to secure the hub 512 to the nontraumatic support component 522.

[00119] In FIGS. 12 and 13, the screw thread inside stem 523 allows the partitioning device 510 to be secured to the non-traumatic support component 522 and to be released from the delivery system within the patient's heart chamber. The distal ends 515 of the reinforcing struts 514 are secured within the hub 512 in a suitable manner or they may be secured to the surface defining the inner lumen or they may be disposed within channels or bores in the wall of the hub 512. The distal end of the struts 514 are preshaped so that when the struts are not constrained, other than by the membrane 511 secured thereto (as shown in FIGS. 8 and 9), the free proximal ends 516 thereof expand to a desired angular displacement away from the centerline axis which is about 20 degrees to about 90 degrees, preferably about 30 degrees to

about 60 degrees. The unconstrained diameter of the partitioning device 510 should be greater than the diameter of the heart chamber at the deployed location of the partitioning device so that an outward force is applied to the wall of the heart chamber by the partially expanded struts 514 during systole and diastole so that the resilient frame 513 augments the heart wall movement.

[00120] FIG. 14 illustrates the curved free proximal ends 516 of struts 514 which are provided with sharp tip elements 527 configured to engage and preferably penetrate into the wall of the heart chamber and hold the partitioning device 510 in a deployed position within the patient's heart chamber so as to partition the ventricular chamber into a productive portion and a non-productive portion.

[00121] FIGS. 15-17 illustrate one variation of an applicator (delivery system) 530 that may be used for delivering the partitioning device 510 shown in FIGS. 8 and 9 into a patient's heart chamber and deploying the partitioning device to partition the heart chamber as shown in FIGS. 18A-18E. The applicator system 530 includes a guide catheter 531 and a delivery catheter 532.

[00122] The guide catheter 531 has an inner lumen 533 extending between the proximal end 534 and distal end 535. A hemostatic valve (not shown) may be provided at the proximal end 534 of the guide catheter 531 to seal about the outer shaft 537 of the delivery catheter 532. A flush port 536 on the proximal end 534 of guide catheter 531 is in fluid communication with the inner lumen 533.

[00123] The delivery catheter 532 in this variation includes an outer shaft 537 with an adapter 538 on the proximal end thereof having a proximal injection port 539 which is in fluid communication with the interior of the outer shaft 537. As shown in more detail in FIG. 16, the outer shaft 537 has an inner shaft 541 which is disposed within the interior thereof and is secured to the inner surface of the outer shaft 537 by webs 543 which extend along a substantial length of the inner shaft. The injection port 539 is in fluid communication with the passageways 542 between the inner and outer shafts 541 and 537 respectively and defined in part by the webs 542. A torque shaft 544, which is preferably formed of hypotubing (e.g. formed of stainless steel or superelastic NiTi), is disposed within the inner lumen 545 of the inner shaft 541 and has a proximal end 546 secured within the adapter 538. Balloon inflation port 547 is in fluid communication with the inner lumen 548 of the torque shaft 544. Torque shaft 544 is rotatably disposed within the inner lumen 545 of the inner shaft 541 and is secured to rotating knob 549. A helical coil screw 550 is secured to the distal end 551 of the torque shaft 544 and rotation of the torque knob 549 on the proximal end 546 of the torque shaft 544 rotates the screw 550 to facilitate deployment of a partitioning device 510. The proximal end 552 of inflatable balloon

553 is sealingly secured by adhesive 554) about the torque shaft 544 proximal to the distal end 551 of the torque shaft. The balloon 553 has an interior 555 in fluid communication with the inner lumen 548 of the torque shaft 544. Inflation fluid may be delivered to the balloon interior 555 through port 547 which is in fluid communication with the inner lumen 548 of the torque shaft 544. The distal end 556 of the balloon 553 is sealingly secured by adhesive 557 to the helical screw 550. The proximal and distal ends 552 and 556 of the balloon 553 are blocked by the adhesive masses 554 and 557 to prevent the loss of inflation fluid delivered to the interior 555 of the balloon 553. Delivery of inflation fluid through a fluid discharge port 558 in the distal end 551 of the torque shaft 544 inflates the balloon 553 which in turn applies pressure to the proximal surface of the partitioning component 510 (or device) to facilitate securing the partitioning component 510 to the wall 559 of heart chamber 560 as shown in FIGS. 18A-18E discussed below.

[00124] As shown in FIG. 18A, the partitioning component 510 is delivered through a delivery system 530 which includes a guide catheter 531 and a delivery catheter 532. The partitioning component 510 is collapsed in a first, delivery configuration which has small enough transverse dimensions to be slidably advanced through the inner lumen 533 of the guide catheter 531. Preferably, the guide catheter 531 has been previously percutaneously introduced and advanced through the patient's vasculature, such as the femoral artery, in a conventional manner to the desired heart chamber 560. The delivery catheter 532 with the partitioning component 510 attached is advanced through the inner lumen 533 of the guide catheter 531 until the partitioning component 510 is ready for deployment from the distal end of the guide catheter 531 into the patient's heart chamber 560 to be partitioned.

[00125] As shown in FIG. 18B-18C, the partitioning component 510 mounted on the screw 550 is urged further out of the inner lumen 533 of the guide catheter 532 until the support component 522 engages the heart wall 559. The guide catheter 531 is withdrawn while the delivery catheter 532 is held in place until the proximal ends 516 of the struts 514 exit the distal end 35 of the guide catheter. As shown in FIG. 18C, the free proximal ends 516 of struts 514 expand outwardly to press the sharp proximal tips 527 of the struts 514 against and preferably into the tissue lining the heart wall 559.

[00126] With the partitioning component 510 deployed within the heart chamber 560 and preferably partially secured therein, inflation fluid is introduced through the inflation port 558 in the distal end 551 torque shaft 544 where it is directed into the balloon interior 555 to inflate the balloon 553. The inflated balloon 553 presses against the pressure receiving surface 517 of the

membrane 511 of the partitioning component 510 to ensure that the sharp proximal tips 527 are pressed well into the tissue lining the heart wall 559 as shown in FIG. 18D.

[00127] With the partitioning device 510 properly positioned within the heart chamber 560, the knob 549 on the torque shaft 544 (as shown in FIG. 15) is rotated counter-clockwise to disengage the helical coil screw 550 of the delivery catheter 532 from the stem 523 secured within hub 512. The counter-clockwise rotation of the torque shaft 544 rotates the helical coil screw 550 which rides on the screw thread inside the stem 523secured within the hub 512. Once the helical coil screw 550 disengages the screw thread inside the stem 523, the delivery system 530, including the guide catheter 531 and the delivery catheter 532, may then be removed from the patient.

[00128] The proximal end 534 of the guide catheter 531 is provided with a flush port 536 to inject fluids such as therapeutic, diagnostic or other fluids through the inner lumen 533 during the procedure. Similarly, the proximal injection port 539 of adapter 538 is in communication with passageways 542 if the delivery catheter 532 for essentially the same purpose.

[00129] The deployment of the partitioning component 510 in the patient's heart chamber 560 as shown in FIG. 18E divides the chamber into a main productive or operational portion 561 and a secondary, essentially non-productive portion 562. The operational portion 561 is smaller than the original heart chamber 560 and provides for an improved ejection fraction and an improvement in blood flow. Over time, the non-productive portion 562 fills first with thrombus and subsequently with cellular growth. Bio-resorbable fillers such as polylactic acid, polyglycolic acid, polycaprolactone and copolymers and blends may be employed to initially fill the non-productive portion 562. Fillers may be suitably supplied in a suitable solvent such as dimethylsulfoxide (DMSO). Other materials which accelerate tissue growth or thrombus may be deployed in the non-productive portion 562 as well as non-reactive fillers.

[00130] FIG. 19 is a top view of the deployed partitioning device shown in FIG. 18E schematically illustrating the sealed periphery of the membrane 511 against the ventricular wall.

[00131] Once the device is deployed, as shown in FIGS. 18E and 19, the device may be removed and/or repositioned. For example, in the implant variation shown in FIGS. 8 and 9, pulling the strand 519 may disengage the anchors or tip element 527 at the ends of the struts 514 from the heart wall. For example, the applicator 530 may be re-engaged with the implant (e.g., the hub region). An element on the applicator may engage the strand so that it can be pulled to collapse the implant. In some variations, one or more ends of the strand remain connected to the applicator during the insertion procedure, so that even when initially disengaged from the applicator, the strand is connected to the applicator until the position is confirmed.

[00132] Examples of applicators including members for grasping and/or manipulating a strand are described in greater detail below.

[00133] FIGS. 20A-20C illustrate the collapse and retrieval of an implant (partitioning device 510) by pulling on the ends 520 and 521 of an expansive strand 519 which extends around the periphery of the membrane 511. Typically, the partitioning device 510 may be secured to the delivery catheter 532, but the delivery catheter is not shown in this example to simplify the drawings. In FIG. 20A the partitioning device 510 is shown in a partially collapsed configuration. In FIG. 20B the partially collapsed partitioning device 510 is shown being withdrawn into the flared distal end 563 of retrieval catheter 564. FIG. 20C illustrates the completely collapsed partitioning device 510 pulled further into the retrieval catheter 564. The partitioning device 510 may be withdrawn by pulling the device through the inner lumen 565 of the retrieval catheter 564. Optionally, the partitioning device 510 and applicator (e.g., retrieval catheter) may be withdrawn from the patient together.

[00134] In this variation the applicator includes a flanged distal end on the catheter, so that the implant may more readily be inserted into the distal end of the applicator. This flanged distal end is optional, and is not necessarily present.

[00135] In general, the implantation, removal and/or repositioning of the impants described herein may be performed under direct or indirect visualization. For example, any of the procedures or methods described herein may be performed under fluoroscopy. To assist in properly locating the device during advancement and placement thereof into a patient's heart chamber, parts, e.g. the distal extremity, of one or more of the struts 14 and/or the hub 12 may be provided with markers at desirable locations that provide enhanced visualization by eye, by ultrasound, by X-ray, or other imaging or visualization means. Radiopaque markers may be made with, for example, stainless steel, platinum, gold, iridium, tantalum, tungsten, silver, rhodium, nickel, bismuth, other radiopaque metals, alloys and oxides of these metals.

[00136] FIG. 21 shows another variation of an applicator configured to apply and retrieve and/or reposition a cardiac implant. In some variations, an applicator such as the one illustrated in FIG. 21 is included as part of a system including an implant. In FIG. 21, the applicator includes a control handle 701 having a plurality of controls for controlling engaging and disengaging from an implant, as well as a flush port 703 and a balloon inflating port 705. In this variation, the applicator also includes an elongate shaft 707 comprising an inner shaft 709 and an outer shaft 711. The distal end of the applicator includes an everting balloon or inflatable sleeve 713 that is inflatable by applying fluid (e.g., air, liquid, etc.) through the inflation port 705. Inflating the everting balloon may cause it to extend, as illustrated in FIGS. 22A-22F. In

addition to the features illustrated in FIG. 21, other elements such as an implant stabilizing shaft and or a strand-grasping hook (not visible in FIG 21) may also be included within the inner shaft, and controlled proximally, e.g., using the handle. For example, the applicator may include a deployment member, as described above. The implant stabilizing shaft may be configured as a deployment member.

[00137] FIGS. 22A-22F illustrate operation of an applicator such as that shown in FIG. 21 to remove an implant (partitioning implant 720). FIG. 22A illustrates a cardiac implant 720 that has been deployed into a patient's heart, as shown. The implant 720 includes a strand, suture 724 that extends around the perimeter of the implant and has two ends 722, 722' which are knotted or otherwise prevented from pulling past the membrane surrounding the device. The strand 724 is threaded around the inner diameter of the implant.

[00138] In FIG. 22B, the applicator shown in FIG. 21 has been inserted into the heart so that the distal end of the applicator is positioned across from the deployed implant. The elongate catheter, including the inflatable distal portion 713 is positioned across from the implant so that an implant stabilizing shaft 726 may be extended from the distal end of the applicator to engage the implant. As previously described, the implant stabilizing shaft 726 (e.g., a deployment member) may engage with the implant at the hub or any other appropriate region (e.g., the foot, etc.). A strand hook 728 may also be extended from the distal end of the applicator as shown in FIG. 22B, so that it can extend from the applicator and engage at least a portion of the strand. In some variations, the strand hook is a grasper, jaw, or other strand-capturing element. As shown in FIG. 22C, the strand can then be drawn proximally by withdrawing the strand hook 728 proximally into the applicator while holding the device in position. Drawing the strand proximally while keeping the device distally positioned will constrict the strand and collapse the struts of the implant. In some variations, the method of collapsing the implant may include a step of pushing the implant distally (away from the applicator) to disengage the ends of the struts from the heart wall. As described in more detail below, the implant (e.g., the foot region) may also be configured to collapse or shorten to facilitate disengaging of the struts from the heart wall.

[00139] After collapse of the implant, as shown in FIG. 22C, the applicator may be extended over the implant. In one variation, illustrated in FIGS. 22D-22E, the inflatable everting balloon or cuff 713is inflated so that it extends and advances over the implant. In some variations, the cuff on the distal end of the applicator is not inflatable, but is otherwise extendable from the distal end to cover the device. For example, the distal end may include a toroidal region that can be "rolled" over the collapsed implant so that the implant is secured

within the central lumen of the toroidal region. Once the implant has been secured within the applicator, it may be removed, along with the applicator, from the patient, or repositioned and deployed again.

[00140] FIG. 23A illustrates another variation of an applicator which may be used to apply and remove and/or reposition an implant. In FIG. 23A, the applicator includes a handle region 801 having one or more controls. In the variation shown in FIG. 23A the handle includes a control, shown as a knob 803 for extending an capture umbrella (described below), and a control for operating a suture hook (suture hook knob 805). The applicator also includes an elongate catheter region 807, and suture capture hook 822 as well as an implant capture umbrella 810.

[00141] FIG. 23B illustrates a cross-sectional view through the catheter region of the applicator shown in FIG. 23A along line A-A'. As shown in FIG. 23B, the applicator include an implant capture umbrella lumen 830 and a suture capture hook lumen 831. In some variations only a single lumen is used to house both the suture capture hook and the implant capture lumen. In some variations an implant stabilizing shaft is also included, similar to that described above in FIG. 21 and 22A-F. For example, an implant stabilizing shaft (not shown in FIGS. 23A-24F) may be positioned concentrically within the shaft connected to the implant capture umbrella. The implant stabilizing shaft may be operated independently of the implant capture umbrella 810.

[00142] FIGS. 24A-24F illustrate operation of an applicator as shown in FIG. 23A to remove an implant that has been deployed in a patient's heart. FIG. 24A shows an implant, similar to the implant shown and described for FIG. 22A, is shown implanted into the hleft ventricle 850 of a patient's heart. The implant 720 also includes a suture or strand 724, having two ends that have been jointed together or knotted 722. The implant may be removed from the deployed position in the heart as illustrated in FIGS. 24B-24. The stand capture hook 822 is extended distally from the applicator to capture or otherwise engage the strand 724 on the implant. In some variations an implant stabilization shaft 726 is also extended from the distal end of the applicator so that it engages the implant, as shown for FIG. 22B, above. After capture of the strand, the stand capture hook 822 is drawn proximally back using the applicator. For example, the applicator handle may be manipulated to draw the strand proximally, e.g., by operating the strand hook knob 805. This results in collapsing the implant, as illustrated in FIG. 24C. Thereafter, the implant capture umbrella 810 of the applicator is extended distally out of the catheter of the applicator. As shown in FIG. 24D, when the implant capture umbrella is extended from the applicator, it expands as it leaves the implant catheter region. For example, the implant capture umbrella may be formed of struts of Nitinol or other materials that are biased

outwards. A membrane or netting may be present between the struts. In some variations, the umbrella does not include a membrane, but comprises only struts. The struts may be coated (e.g., with a polymeric material) to prevent damage to the tissue and/or the implant.

[00143] The implant capture umbrella may be extended over the collapsed device 720, as shown in FIG. 24D. The implant 720 may then be drawn into the applicator by retracting the capture umbrella 810 (and an implant stabilization shaft, if included) into the catheter region of the applicator, as shown in FIG. 24E. In some variations, the implant is only partially withdrawn into the applicator. FIG. 24F illustrates removal of the applicator and implant from the patient.

[00144] Although many of the applicator devices described herein are configured for both insertion and removal of an implant, it should be understood that an applicator can be configured as an implant removal device alone. For example, an implant removal device may otherwise resemble the applicators described above (including FIG. 23A), but may not be configured to release the implant in the patient's heart after it has been captured and removed. In some variations an implant removal device resembles the applicator of FIG. 23A, and does not include an implant stabilization shaft that is configured to release the implant.

[00145] In some variations, the applicator is configured so that the end or ends of the collapse or expansive strand extend proximally in the applicator and can be removed (e.g., withdrawn) from the implant or the applicator after it has been finally positioned. For example, FIG. 25A illustrates one variation of a system including an applicator 901 and an implant 903, in which the implant 903 includes a collapse strand 905 that extends around the perimeter of the implant and can collapse the struts of the implant if tensioned. The ends of the collapse strand 905 extend proximally into the applicator and extend from a port (e.g., on the handle at the proximal end of the applicator) 906, 906'. The applicator variation shown also includes an implant stabilization shaft (catheter) 909 which includes a balloon 907 for helping expand the implant once positioned, and an implant capture umbrella 920, within an outer cannula or guide catheter 915 of the applicator, similar to the applicator shown in FIG. 23A. In this example, the distal region of the applicator also includes a radiopaque marker 913 to aid in visualization. A balloon inflation port 927 is also present on the proximal end of the device. FIG. 25B illustrates the system of FIG. 25A in which the implant 903 has been detached from the applicator 901. In FIG. 25B the collapse strand 905 has been removed from the device. Presumably the device has been positioned in an acceptable position, and further adjustment is unnecessary. Until the strand is removed, the implant may be continuously collapsed and repositioned by pulling on the collapse strand 905, and using the implant capture umbrella 920 as previously described.

[00146] For example, FIGS. 26A-26D illustrate operation of the system of FIG. 25A. FIG. 26A shows a perspective view of the system of FIG. 25A, including an implant 903 that is attached to the distal end of an applicator 901. The very distal end of the implant includes a soft tip of foot 930. The implant may be inserted into the subject's heart (e.g., the left ventricle) as previously described. Once in position, it may be expanded as shown in FIG. 26A. The position or orientation of the implant may be confirmed or checked using visualization such as fluoroscopy. FIGS. 26B-26D illustrate retrieval of the implant after initially deploying it, but before removal of the collapse strand 905.

[00147] The implant 903 shown in FIGS. 25A-26D may be retrieved by pulling the free ends of the collapse wire 905 to collapse the implant, as shown in FIG. 26B. In this example, the passive anchors 935 can thus be disengaged from the heart wall. After at least partially collapsing the implant, the guide catheter 915 may be withdrawn to expose and expand the implant capture umbrella 920, as shown in FIG. 26C. In some variations, as described for FIG. 24C, above, the implant capture wire may be extended distally. Drawing the implant proximally and then pushing the guide catheter forward distally, as shown in FIG. 26D, will then capture the implant within the implant capture umbrella as it closes around the collapsed implant.

[00148] As mentioned briefly above, in some variations, the implant device includes a collapse element, such as the collapse strand described above, or a collapse sleeve. FIGS. 27A-27E illustrate operation of a system including an implant having a collapse sleeve and an applicator configured to operate the collapse sleeve.

[00149] In FIG. 27A, the implant 1001 is shown in an expanded state. For simplicity sake, the struts are not shown. The implant includes a collapse sleeve 1005 that is positioned distally (e.g., over the stem of the implant) when the implant struts and membrane are deployed, as shown in FIG. 27A. In this example, the implant is coupled to an applicator 1000, that includes a handle region having a collapse knob 1013, an active anchor knob 1015, and a detachment knob 1010. The applicator also includes a guide catheter 1007, within which an extendable/retractable collapse sleeve pullwire 1006 and an implant stabilization shaft 1009 reside. FIGS. 27B-27E illustrate use of the applicator to collapse the implant 1005. For example, in FIG. 27B, the collapse knob (or other appropriate control) on the handle may be operated to draw the collapse sleeve 1005 proximally. For example, turning the collapse knob may cause the pull wire to draw the collapse sleeve 1005 over the implant membrane/struts, collapsing it, as illustrate in FIG. 27C. After the implant is collapsed, it may be pulled inside the guide catheter and removed from the patient, or repositioned and redeployed (e.g., by extending the implant from the guide catheter and pushing on the collapse sleeve guidewire to expand the

membrane/struts). The collapse sleeve pullwire may be a wire, a rod, a tube, etc., and may be used for pulling and/or pushing the collapse sleeve.

[00150] The collapse sleeve may be coupled with the collapse sleeve pullwire (or other collapse sleeve control on the applicator), using a configuration such as that illustrated in FIG. 28A and 28B. FIG. 28A shows a front view of an expanded implant including a centrally-located attachment mechanism 1101 for the collapse sleeve. This attachment mechanism can be a cross-bar or wire that extends across the central opening and connects to one or more points on the inner surface of the sleeve. In this example, both the hub region of the implant and the collapsible struts/membrane region include a track or slot along which this cross-bar or wire can move to allow the collapse sleeve to be moved proximally or distally. For example, two opposite struts 1107 shown in FIG. 28A include a slot or track 1105 along which the cross-bar or wire connected to the collapse sleeve may move. The applicator may include a shaft or wire that engages this attachment mechanism and pulls it proximally or pushes it distally. FIG. 28B shows a side view of the implant shown in FIG. 28A, including the collapse sleeve 1110.

[00151] Another variation of an implant delivery system is shown in FIGS. 29A-29E. FIG. 29A shows an applicator including a collapse line or lasso 1201 extending from a side port on an implant stabilizing shaft passing through a guide catheter 1207 on the device. The distal end of the implant stabilizing shaft includes a detachment screw 1205 that may be activated to detach an implant from the device. In this example, the collapse line may be drawn proximally (e.g., towards the handle of the applicator 1211) by manipulating a control on the handle such as a collapse line control knob 1209. The handle may also include one or more controls for detaching the implant 1213, or the like. In some variations the collapse line is connected to an implant prior to deployment of the implant, and may be released from the implant after it has been finally positioned. In other variations, the collapse line is not integral to the implant, but may be connected around the implant after it has been released.

[00152] FIGS. 29B-29E illustrate operation of the implant delivery system including the applicator and implant. For example, in FIG. 28B, the deployed implant is still attached to the applicator, but it is desired to collapse and reposition (or remove) the implant. In this variation the implant includes an implant stem, configured as an atraumatic foot 1220 extending from an expanded implant umbrella region 1222. In FIG. 29C the collapse line or lasso 1201 is contracted to collapse the implant until it is sufficiently collapsed to fit into the guide catheter 1207, as shown in FIG. 29D. Once it has collapsed sufficiently, the guide catheter may be moved distally to enclose the implant, as shown in FIG. 29E. FIGS. 30A and 30B illustrate side and front views, respectively, of an implant which may be used with the applicator shown in

FIG. 29A-29E. The implant is shown connected to a collapse line 1201 (or strand) that passes through two or more skives 1250 on the membrane 1240. The collapse line 1201 includes a push knot 1252. The implant also includes multiple struts 1245.

[00153] FIGS. 35A-35E illustrate another variation of a system for applying and removing a partitioning device (implant) that includes an applicator having a collapse line. For example, FIG. 35A shows a system including an applicator 1700 having a delivery cannula, and an implant 1701 including expandable struts with passive anchors at their ends. The system shown in FIG. 35A is in the undeployed state, and the distal end of the implant (including an atraumatic foot region extending distally). It can be deployed by pushing it from the delivery catheter region so that the struts can expand, as shown in FIG. 35B. In this example, a strand or lariat 1705 is pre-positioned around the device, and passes into a lariat guide tube 1707 that is within the delivery catheter. As the device is deployed, the lariat expands around it, and the lariat guide tube 1707 remains connected. If the position is correct, the lariat (string) may be withdrawn by pulling it from one end to remove it from around the device (not shown), and withdrawing both the lariat and the lariat guide tube with the applicator 1700. FIGS. 35C-35E illustrate one method of repositioning or removing the implant by pulling on one or both ends of the lariat and collapsing the implant (e.g., collapsing the expanded struts, as shown in FIG. 35C), until it can be either repositioned, as shown in FIG. 35D, or withdrawn into the delivery catheter and removed, as shown in FIG. 35E.

[00154] In some variations the implant is retrieved into the applicator after inverting the implant so that the membrane and/or struts may be collapsed as the implant is drawn into a catheter region of the applicator. One variation of this method and a system including this method is shown in FIGS. 31A-31D. For example, in FIG. 31A, the applicator includes a handle region 1401 having one or more controls 1403, 1405, an elongate catheter region 1408 including a guide catheter, and an implant stabilization shaft and a retrieval line 1410 that connects to the distal end (e.g., the foot region 1422) of the implant. FIGS. 31B-31D illustrate removal of a deployed implant using this applicator. Pulling on the retrieval line 1410 after deployment will disengage the implant 1420 from the walls of the left ventricle, as shown in FIG. 31C and invert the implant within the left ventricle (lv) as it is drawn towards the guide catheter in the applicator. In this example, the retrieval line 1410 is attached to a flexible foot region 1422. Withdrawing the inverted implant into the applicator collapses the implant, as shown in FIG. 31D.

[00155] FIGS. 32A and 32B illustrate another variation of an applicator 1500 configured to remove an implant by inverting the implant, and FIGS. 33A-33H illustrate the operation of the

applicator 1500. In FIG. 32A, the system includes a handle region 1501 (control region) having a balloon inflation port 1503, an implant release port 1505, and an implant capture port 1507. The proximal control/handle region is connected to an elongate insertion cannula. An implant stabilization shaft 1509 configured to releaseably secure to an implant and an implant capture wire 1511 extend through the cannula, and are axially movable therein. Thus, the cannula may include one or more internal axial lumen through which these structures may move. The implant stabilization shaft may include a balloon 1515 or other deployment-aiding structure, and/or a screw 1513 that can be used to detach/reattach the implant. FIG. 33B shows the device of claim 33A in partial cross-section, so that the implant stabilization shaft 1509 and implant capture wire 1511 are visible. The proximal end of the implant stabilization shaft 1509 is shown withdrawn so that the implant stabilization shaft is completely within the cannula.

[00156] FIGS. 33A-33H illustrate operation of this system. In FIG. 33A, the applicator 1500 of FIGS. 32A and 32B is shown in partial cross-section with an implant 1520 pre-loaded on the distal end. The implant capture wire 1511 in this variation is pre-loaded through the implant, so that it extend from the implant release port, through the implant, and out of the implant capture port. For convenience, FIG. 33A shows the implant in an expanded (deployed) configuration, although it may also be contracted in a delivery configuration in which the struts and any membrane between them is collapsed and retracted at least partially into the delivery catheter.

[00157] FIG. 33B shows a cross-section through the distal region of the implant, showing a passageway through which the implant capture wire may pass. This passageway may be sized so that a retainer 1530 on the end of the implant capture wire cannot pass through the implant, so that it can be retrieved by pulling on the wire, as illustrated below. If the implant it positioned and deployed as desired, the implant capture wire may be completely withdrawn through the implant. For example, the retainer 1530 on the end of the implant capture wire may be removed or disengaged.

[00158] After deploying the device into a heart, e.g., into the left ventricle of the heart, the device may be withdrawn. For example, to remove the implant from the heart, one end of the implant capture wire 1511 may be withdrawn down the device, as illustrated in FIG. 33C. In this example, the implant capture wire is drawn proximally by pulling on the end of the implant capture wire extending from the implant capture port 1507. The opposite end of the implant capture wire is attached to a retainer 1530. The retainer is sized (or otherwise configured) so that it cannot pass through the implant hub 1533, as shown in FIG. 33D.

[00159] FIG. 33E shows the implant stabilization shaft disengaged from the implant 1520. With the implant stabilization shaft attached, the implant may partially withdrawn from the wall of the heart, to allow it space to move (e.g., within the ventricle) so that it has adequate room to be flipped, as illustrated in FIG. 33F. For example, pulling on the implant capture wire 1511 extending from the implant capture port 1507 will draw the foot (tip) of the implant to be drawn towards the applicator (the distal end of the cannula). In the example shown in FIG. 33F, the distal end of the catheter is marked with a radiopaque marker 1550, so that the position of the applicator can be observed. FIGS. 33G and 33H illustrate the steps of collapsing the implant into, by continuing to secure the implant at the distal end of the applicator (e.g., pulling on the implant capture wire 1511) while sliding a guide catheter, sheath, or collapsing catheter 1539 over the flipped implant. The guide catheter (or sheath, or collapsing catheter) 1539 moves axially over the delivery catheter 1561 to extend distally beyond the end of the guide catheter, and the distal end of the both may include a radiopaque marker 1550. Once collapsed, the implant and applicator may be removed from the patient.

[00160] In any of the variations described herein the implant may be removed after it has been at least partially secured or even anchored to the patient's heart wall. For example, an implant may include passive anchors at the ends of the ribs (struts), which may be pointed or sharp, and configured to partially penetrate the heart wall. Removal or re-positioning of the implant may therefore be simplified by disengaging the implant from the heart wall. In some variations a portion of the implant is axially shortenable (e.g., collapsible, compressable, etc.) after it has been deployed so that it can be disengaged. For example, the hub and/or foot region of the implant may be collapsible, as illustrated in FIGS. 34A-34D. In some variations the shortenable region is a telescoping region. In some variations the shortenable region includes a spring or other biasing element that holds the region is an extended (unshortened) position until it is allowed to compress or otherwise activated. Thus, the shortenable region may be activated by applying force to shorten it. In some variations, the shortenable region is lockable so that it cannot be shortened until the lock is disengaged. A lock may include a pin, a catch, or the like. The lock may be mechanically, electrically or magnetically activated.

[00161] FIG. 34A shows an implant having an elongated hub region 1601 that includes a collapse region 1601. The hub region 1601 of FIG. 34A is shown in more detail in FIG. 34B. In this variation, the collapsible region includes hinged arms. The hub region in this example may be foreshortened by pulling proximally on a string (or strings) 1605 attached distally to the collapse region 1601. This is illustrated in FIG. 34C, and in greater detail in FIG. 34D. In this example, the string passes from the proximal end of the implant (and may pass through or into an

applicator), loops around a hole in the implant, and then back out proximally. After the device position is finalized, the string 1605 may be removed by withdrawing one end of the string while allowing the other end to be pulled through the implant and out again, as illustrated in FIGS. 34E and 34F.

[00162] In other variations, the foreshortening of the implant does not require a string, but may be activated by merely applying pressure or force to the device.

[00163] In addition to the devices and methods for collapsing an implant described above, other methods may also be applied, either separately or in combination with the methods described above. For example, the implant may be collapsed by changing the temperature of the implant. This method is particularly effective when the implant is made (at least partially) of a shape memory material, such as Nitinol. FIG. 36A shows a cross-section through one variation of an implant 3600 in which the device includes a frame (e.g., having struts 3601), and a centrally (and proximally) located tip 3603 that may be grasped by an applicator, as illustrated in FIGS. 36B and 36C, described below. The frame (e.g., struts 3601) may be formed in part from a shape-memory material that may transition between an expanded (Austentite) configuration into a collapsed (Martensite) configuration when exposed to cold.

[00164] FIGS. 36B and 36C illustrate this transition. In FIG. 36B the device 3600 has been inserted in to left ventricle 3612. An applicator 3609 including a pair of grabbing jaws 3615 (although any coupling means for securing the implant to the applicator may be used, including those described above) is brought near the implant, and the jaws 3615 may be secured to the tip 3603 of the implant. The applicator also includes a channel for applying chilled fluid 3621. For example, cooled saline (e.g., between 0 and 10 degrees C) may be applied from the channel 3621 to change the Nitinol of the implant from the austenite phase (expanded) to the martensite phase (collapsed). This is illustrated in FIG. 36C. The implant 3600 is shown in a collapsed configuration, disengaged from the wall. The implant is also shown being drawn into the applicator (which may include a catheter into which the implant may be withdrawn. In this example, the central region of the applicator, including the grasping jaws 3615 can be withdrawn into the outer cannula of the applicator.

[00165] To the extent not otherwise described herein, the various components of the implants, applicators, and delivery systems including any of them may be formed of conventional materials and in a conventional manner as will be appreciated by those skilled in the art.

[00166] While particular forms of the invention have been illustrated and described herein, it will be apparent that various modifications and improvements can be made to the invention.

Moreover, individual features of embodiments of the invention may be shown in some drawings and not in others, but those skilled in the art will recognize that individual features of one embodiment of the invention can be combined with any or all the features of another embodiment. Accordingly, it is not intended that the invention be limited to the specific embodiments illustrated. It is intended that this invention to be defined by the scope of the appended claims as broadly as the prior art will permit.

WHAT IS CLAIMED IS:

1. A method of deploying an implant comprising:

advancing an implant into a patient's left ventricle chamber in a contracted configuration, wherein the implant comprises a plurality of struts formed of a shape memory material;

expanding the implant into a deployed configuration at a first left ventricle location;

changing the temperature of the implant to at least partially collapse the implant into the contracted configuration;

retrieving the implant into a retrieval catheter; and

withdrawing the implant from the first left ventricle location.

2. The method of claim 1, wherein the step of changing the temperature of the implant comprises exposing the implant to cooled saline.

3. A system for partitioning a patient's ventricle, the system comprising:

an implant configured for deployment into the patient's ventricle, the implant including a plurality of struts, wherein the implant is configured to have a collapsed delivery configuration and an expanded deployed configuration; and

an applicator configured to insert and retrieve the implant, comprising

a control at the proximal end of the applicator for controlling release of the implant from the applicator;

an elongate body extending from the proximal end to a distal end, wherein the distal end of the elongate body is configured to relasably secure the implant; and

a capture wire extendable from the applicator's distal end and configured to draw the implant toward the applicator's distal end.

4. The system of claim 3, further wherein the applicator comprises a control at the proximal end for manipulating the capture wire.

5. The system of claim 3, wherein the capture wire is configured as a lariat.

6. The system of claim 3, wherein the implant comprises a strand that may be tensioned to collapse the implant from the expanded configuration, and further wherein the capture wire of the implant is configured as a hook that may engage the strand.

7. The system of claim 3, wherein the capture wire is connected to the implant.

8. The system of claim 3, wherein the applicator further comprises an inflatable sleeve configured to extend from the distal end of the applicator and collapse the implant.

9. The system of claim 3, wherein the applicator further comprises a capture umbrella configured to extend from the distal end of the applicator and collapse the implant.

10. The system of claim 3, wherein the implant further comprises a collapse sleeve configured to collapse the struts, wherein the system further comprises a collapse sleeve pullwire configured to engage the collapse sleeve on the implant.

11. A system for partitioning a patient's ventricle, the system comprising:
an implant configured for deployment into the patient's ventricle, the implant including:
a plurality of struts, wherein the implant is configured to have a collapsed delivery configuration and an expanded deployed configuration, and
a strand extending between the struts, wherein the strand may be tensioned to collapse the struts; and
an elongate applicator configured to insert and retrieve the implant, the applicator including:
a control at the proximal end of the applicator for controlling release of the implant from the applicator,
an implant stabilization shaft extending distally from the proximal end, wherein the implant stabilization shaft is configured to relasably secure to the implant, and
a strand capture element extending distally from the proximal end, wherein the strand capture element is configured to engage the strand on the implant and collapse the struts of the implant.

12. A device for partitioning a patient's ventricle into a main functional portion and a secondary non-functional portion, comprising:

a membrane having an expanded configuration and a collapsed configuration;

an expandable frame formed of a plurality of struts having a distal end secured to a hub, wherein the membrane is secured to the expandable frame;

a stem extending distally from the hub; and

a collapse sleeve configured to axially slide from the stem and to collapse the expandable frame and membrane into a collapsed configuration.

13. The device of claim 12, further comprising a passive anchor at the ends of each of the struts of the expandable frame.

14. The device of claim 12, further comprising a non-traumatic foot at the distal end of the device.

15. The device of claim 12, further comprising an attachment mechanism for a collapse sleeve pullwire.

16. A removable or repositionable implant for partitioning a chamber of a patient's heart into a main functional portion and a secondary non-functional portion, comprising:

a membrane;

a plurality of struts secured to a hub at a first end, wherein the membrane is secured to the plurality of struts, and the plurality of struts and membrane have a collapsed delivery configuration and an expanded deployed configuration for deployment within a heart chamber, wherein the membrane forms a recess when in the expanded configuration;

wherein end of each of the plurality of struts includes a passive anchor configured to secure to the wall of the patient's heart; and

a stem extending distally from the hub, wherein the stem comprises a shortenable region configured to be decreased in length and permit the passive anchors to disengage from the wall of the patient's heart.

17. The implant of claim 16 further comprising a trigger configured to shorten the shortenable region of the stem.

18. The device of claim 17, wherein the trigger comprises a wire or line extending distally through the stem portion.

19. The device of claim 16, wherein the shortenable region is a collapsible region.

20. The device of claim 16, wherein the shortenable region is a telescoping region.

21. The device of claim 16, further comprising a lock for locking the shortenable region.

22. A method of removing an implant that has been deployed at a first ventricle location, wherein the implant includes a plurality of struts each having a passive anchor at a first end and connected to a hub at a second end and a stem extending from the hub, the method comprising:

shortening a shortenable region of the stem to disengage the passive anchors from the heart wall;

at least partially collapsing the plurality of struts; and

withdrawing the implant from the first left ventricle location.

23. The method of claim 22, wherein the step of shortening the shortenable region comprises applying pulling on a wire or string to shorten the shortenable region.

24. The method of claim 22, further comprising unlocking the implant so that the shortenable region may be shortened.

25. The method of claim 22, wherein the step of at least partially collapsing the implant comprises pulling on a strand or collapse line to draw the struts together.

26. The method of claim 22, further comprising repositioning the implant within the left ventricle and expanding the struts into a deployed configuration at a second left ventricle location.

27. The method of claim 22, further comprising removing the implant from the patient.

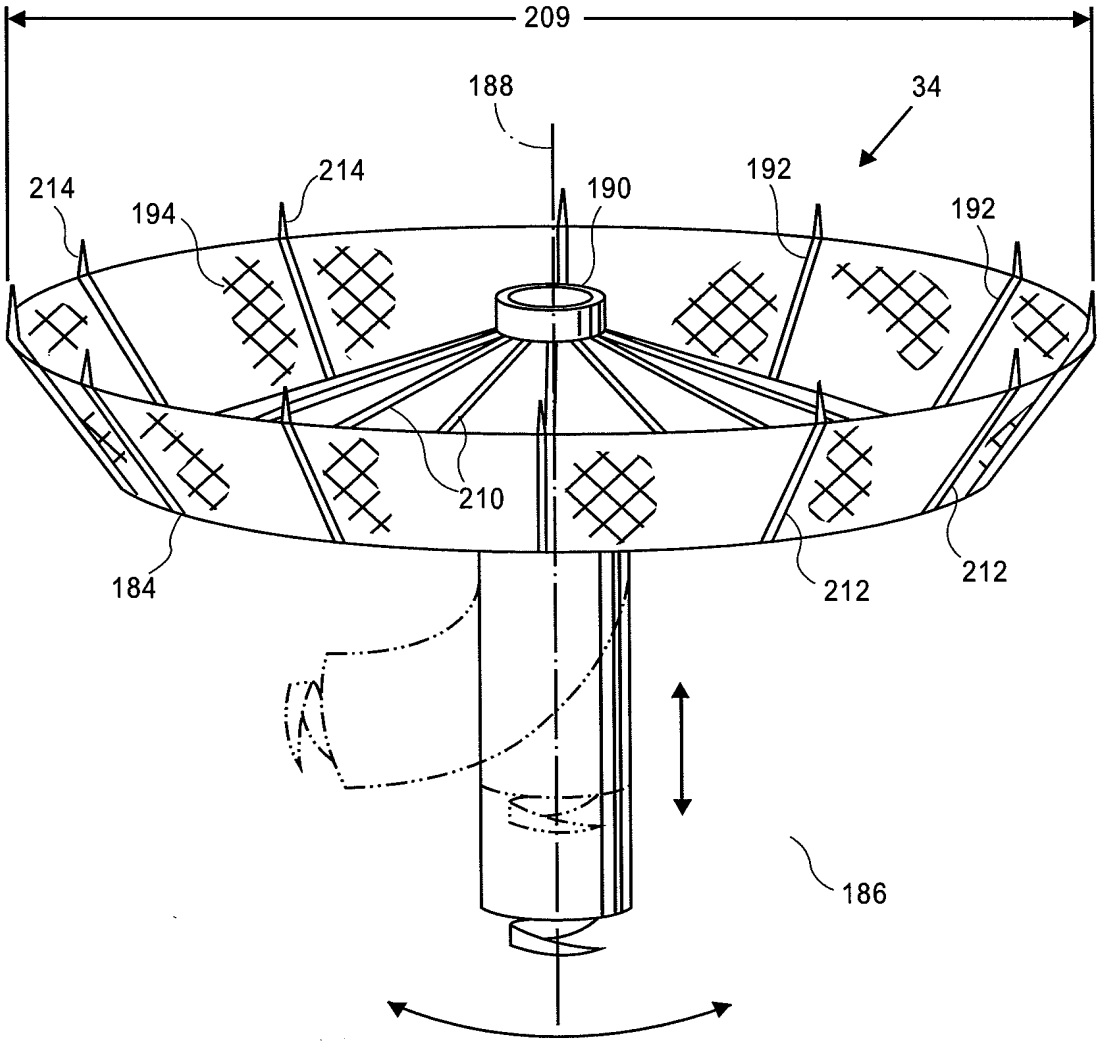

FIG. 1

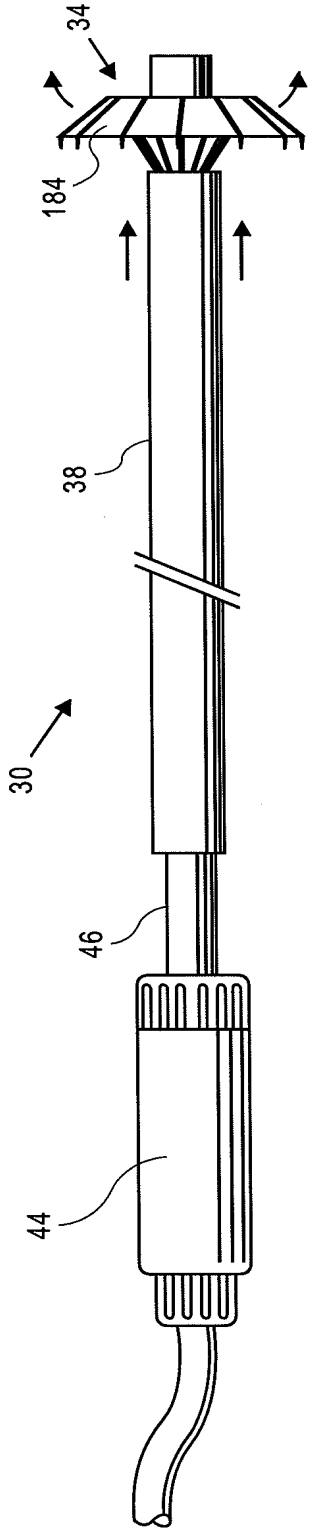

FIG. 2A

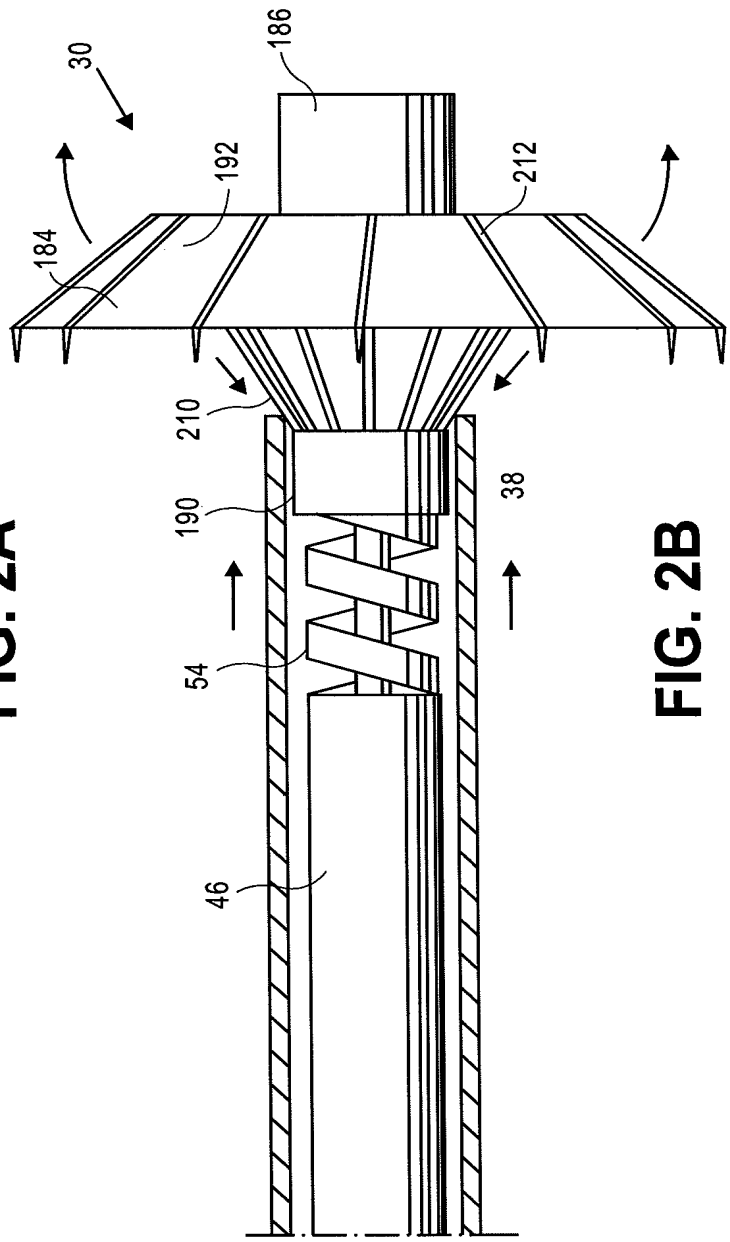

FIG. 2B

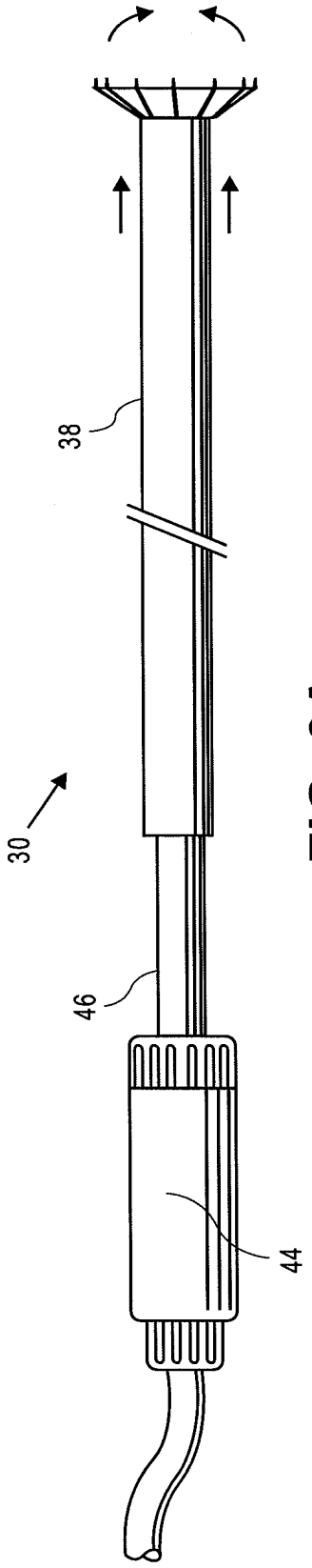

FIG. 3A

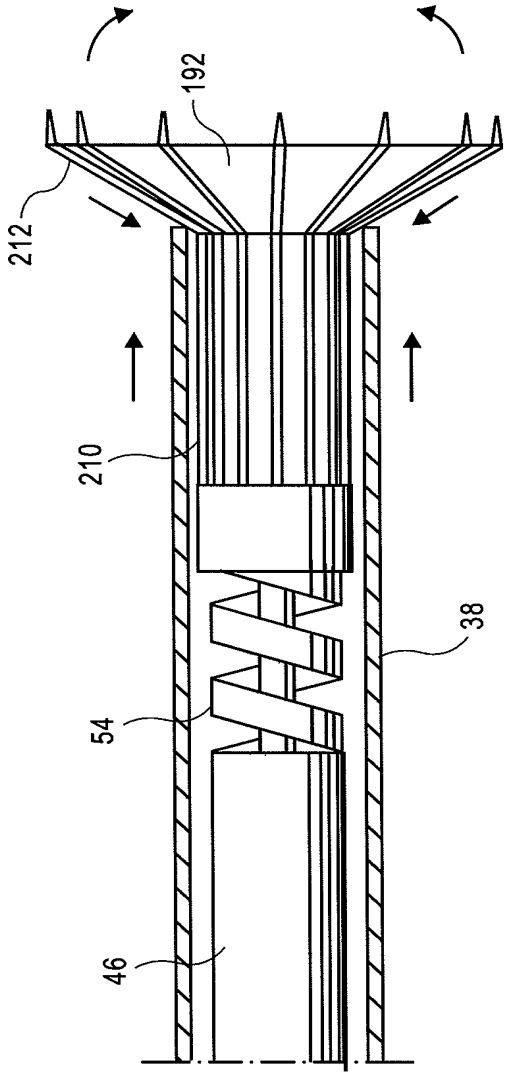

FIG. 3B

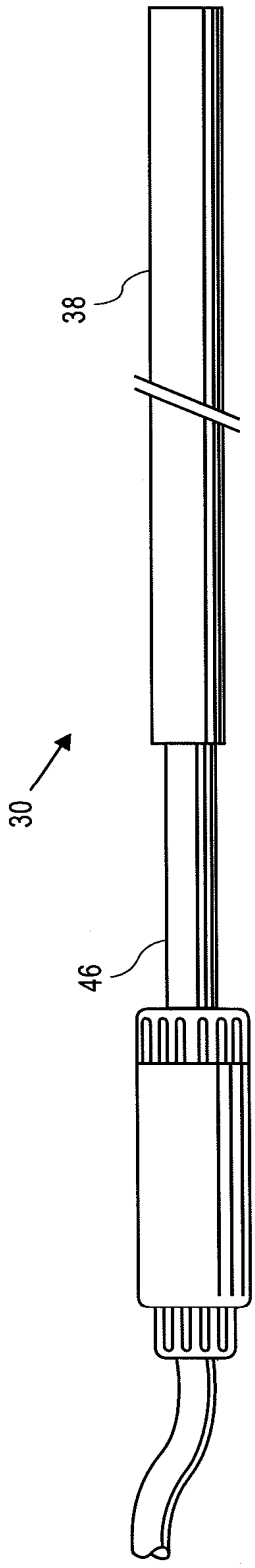

FIG. 4A

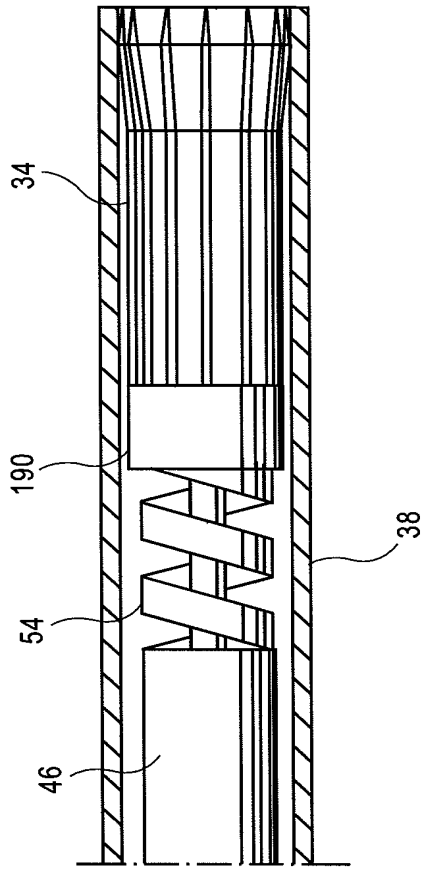

FIG. 4B

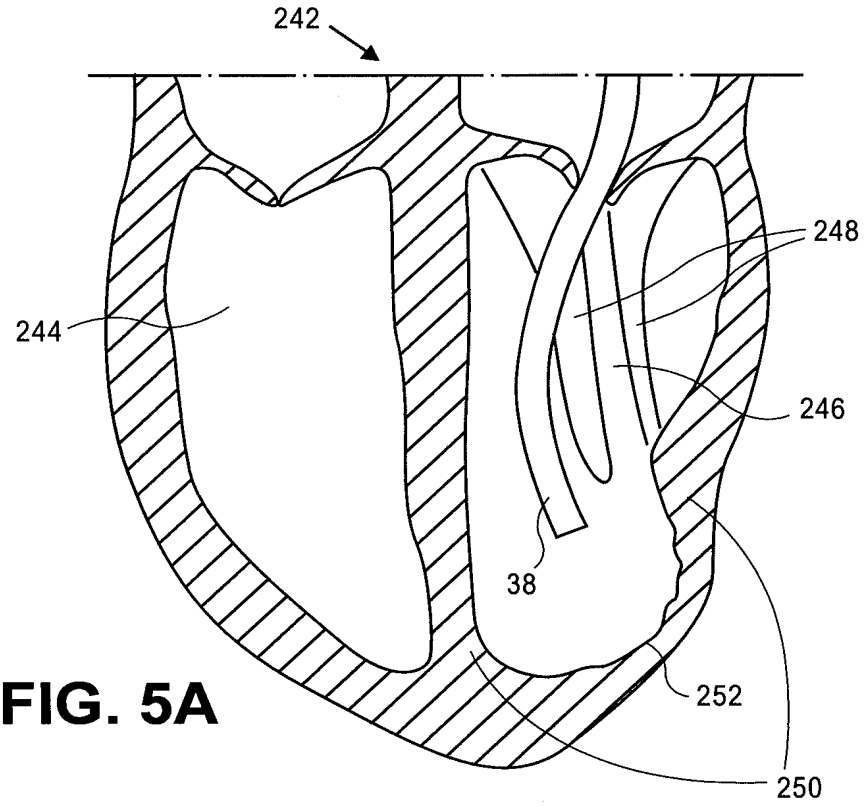

FIG. 5A

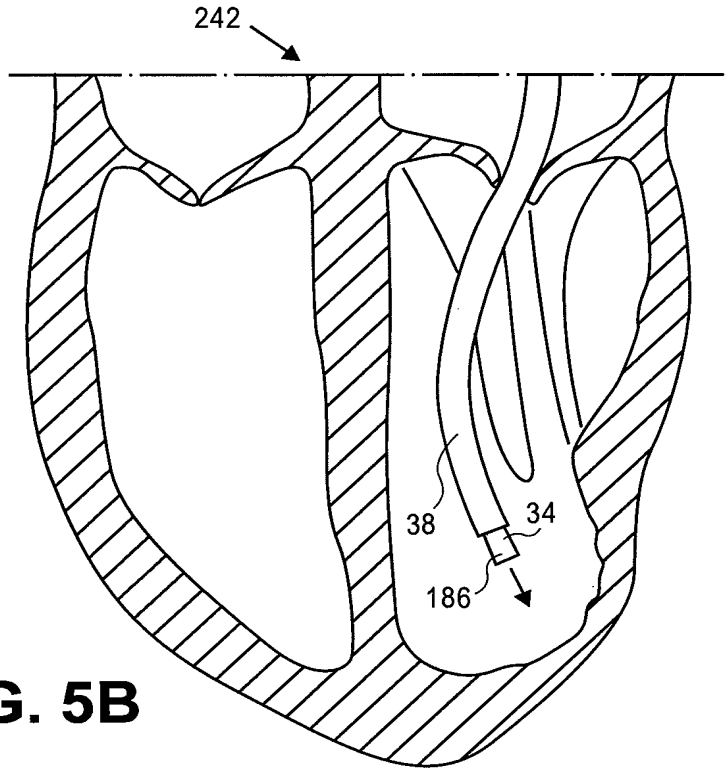

FIG. 5B

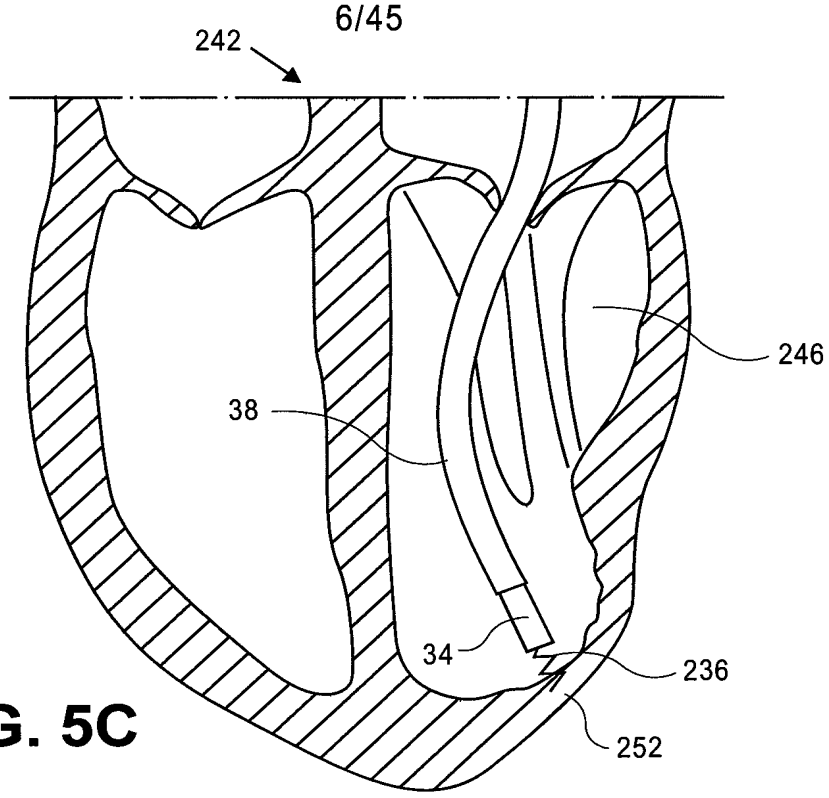

FIG. 5C

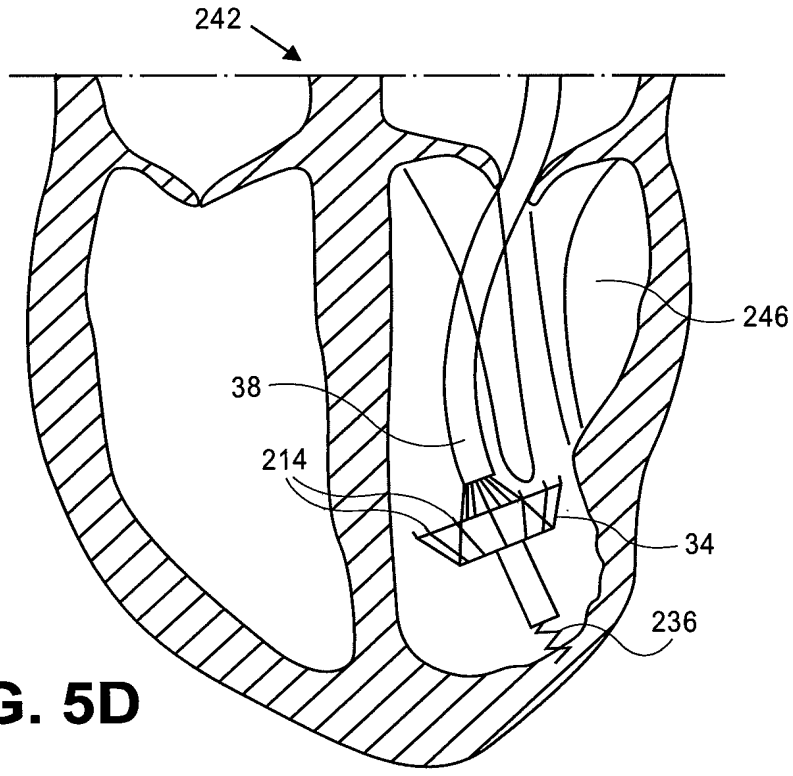

FIG. 5D

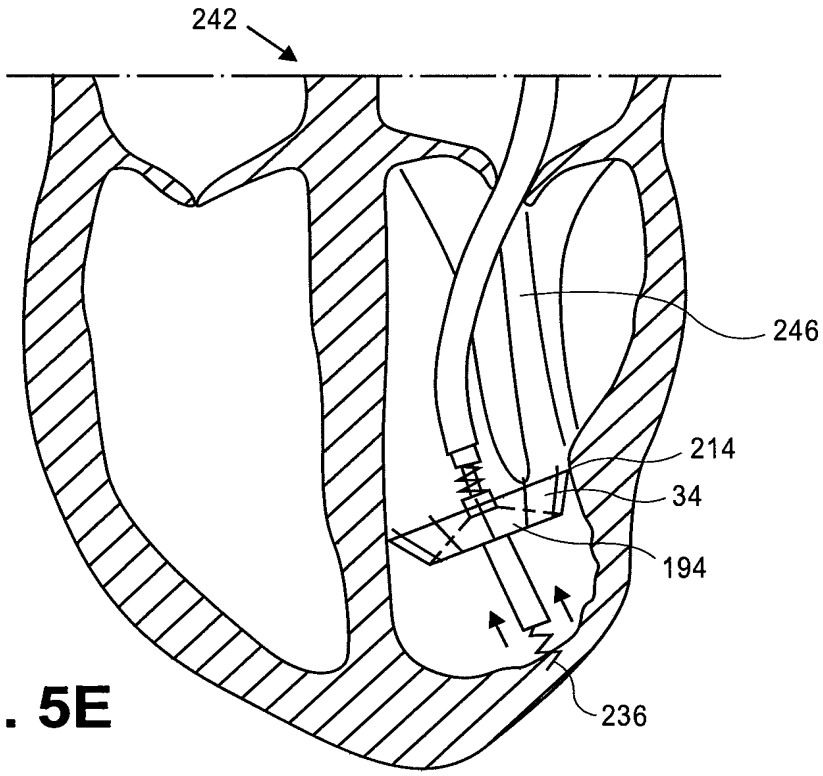

FIG. 5E

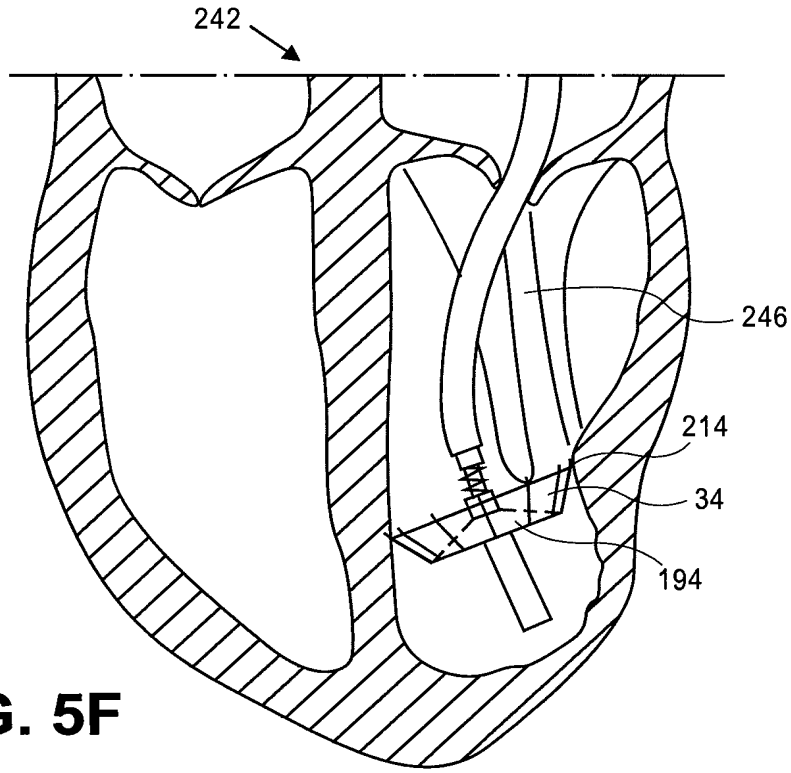

FIG. 5F

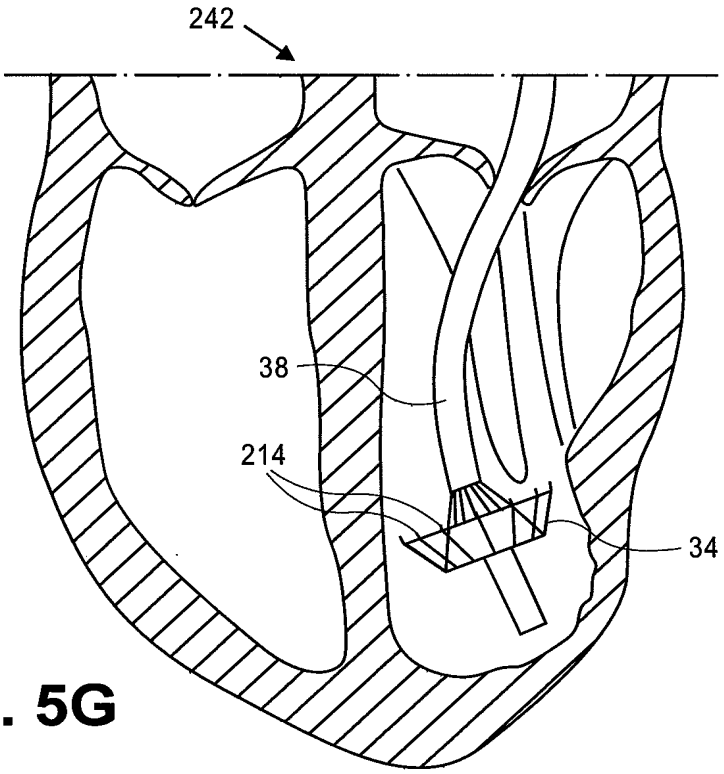

FIG. 5G

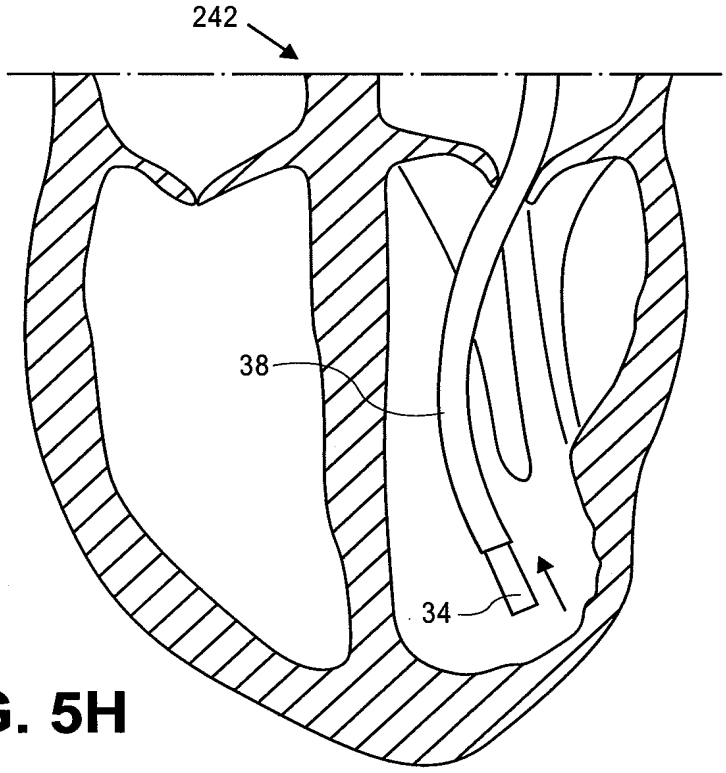

FIG. 5H

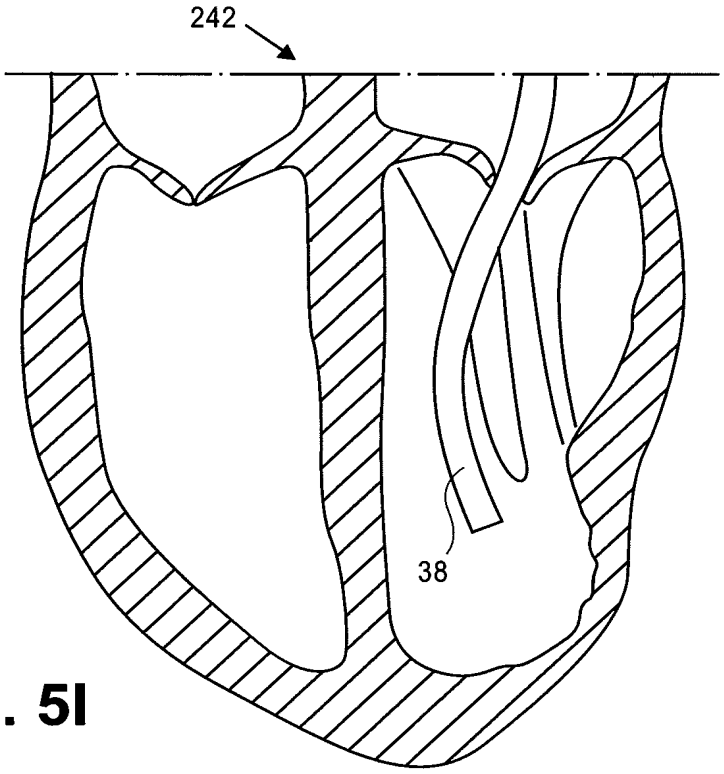

FIG. 5I

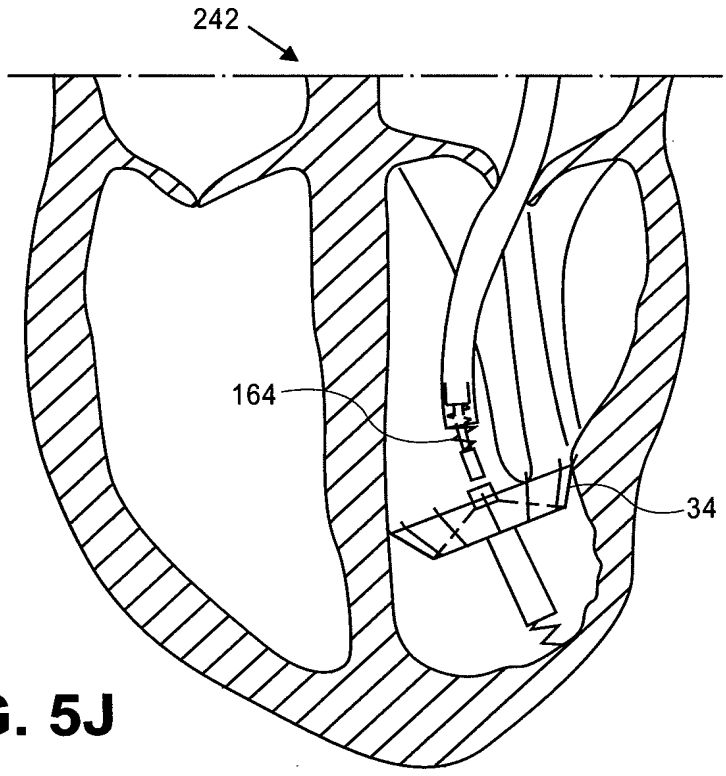

FIG. 5J

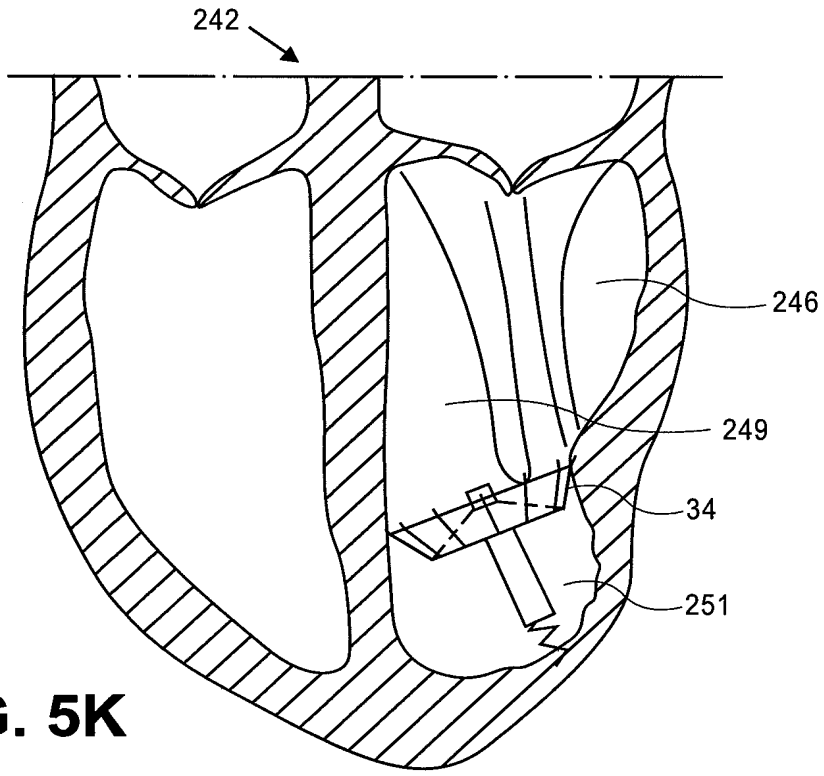

FIG. 5K

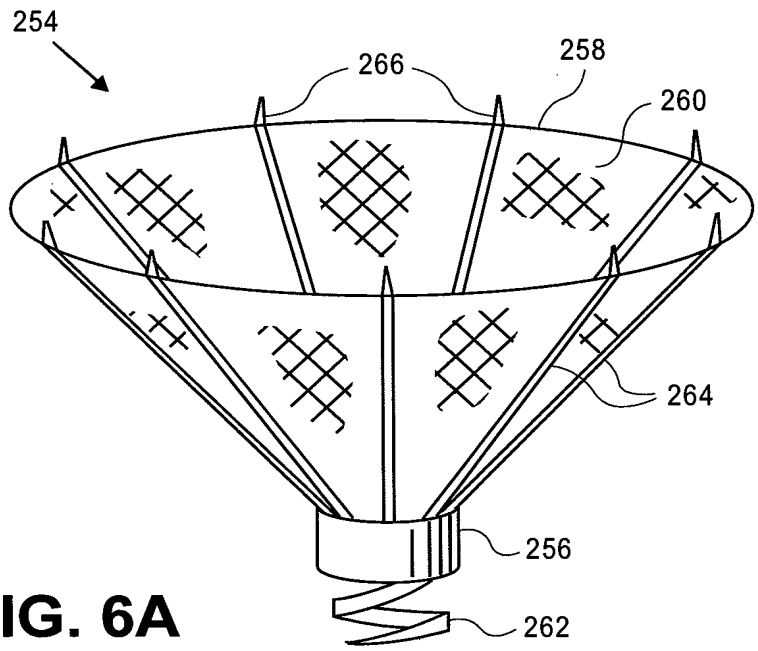

FIG. 6A

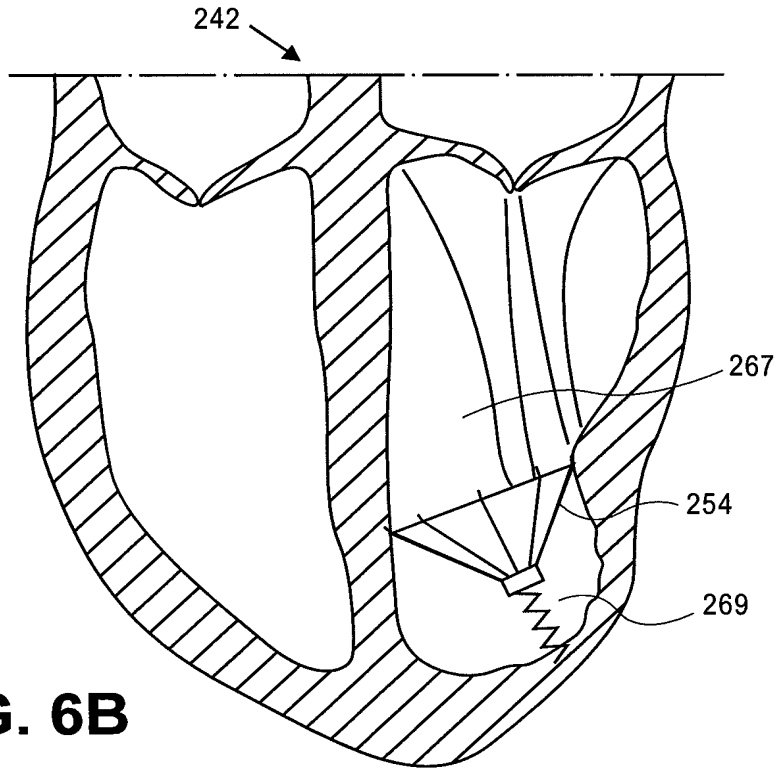

FIG. 6B

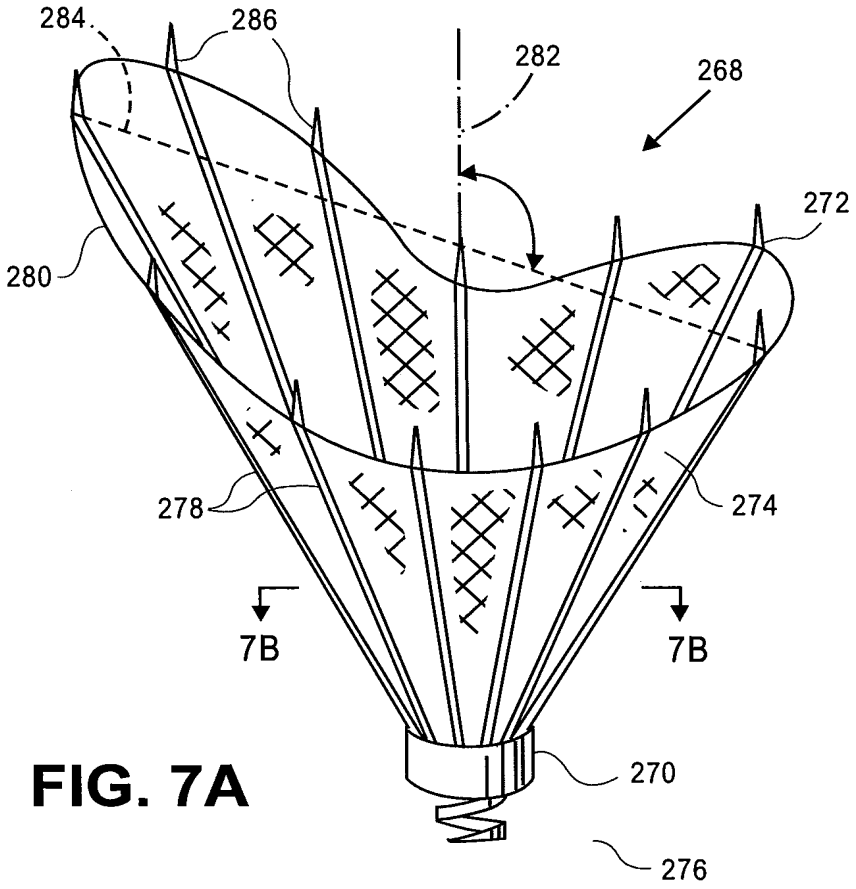

FIG. 7A

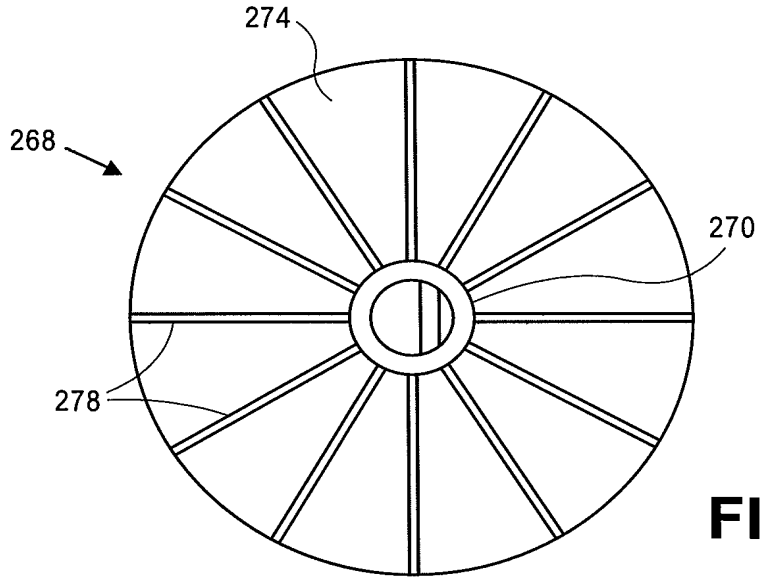

FIG. 7B

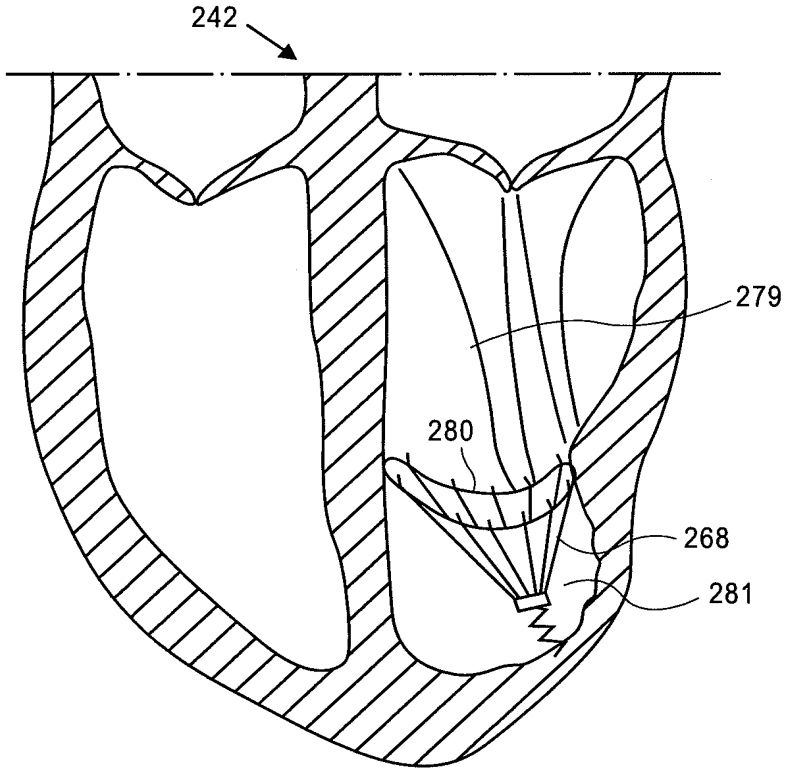

FIG. 7C

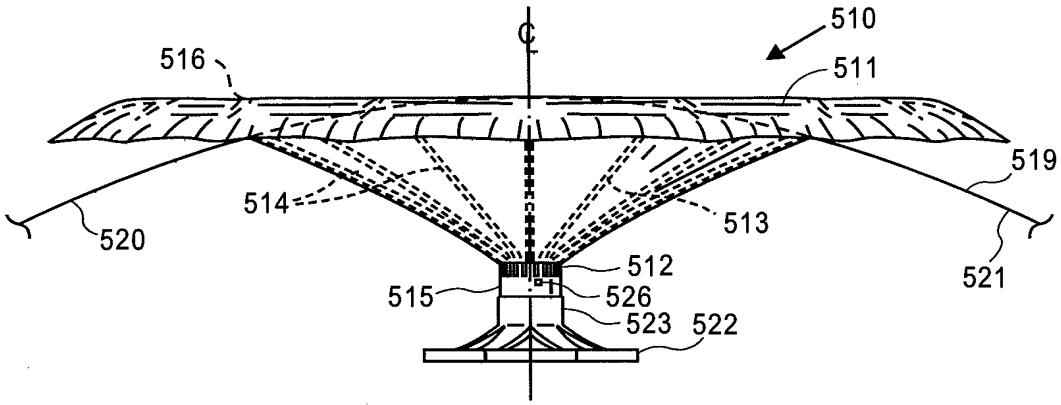
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FIG. 8

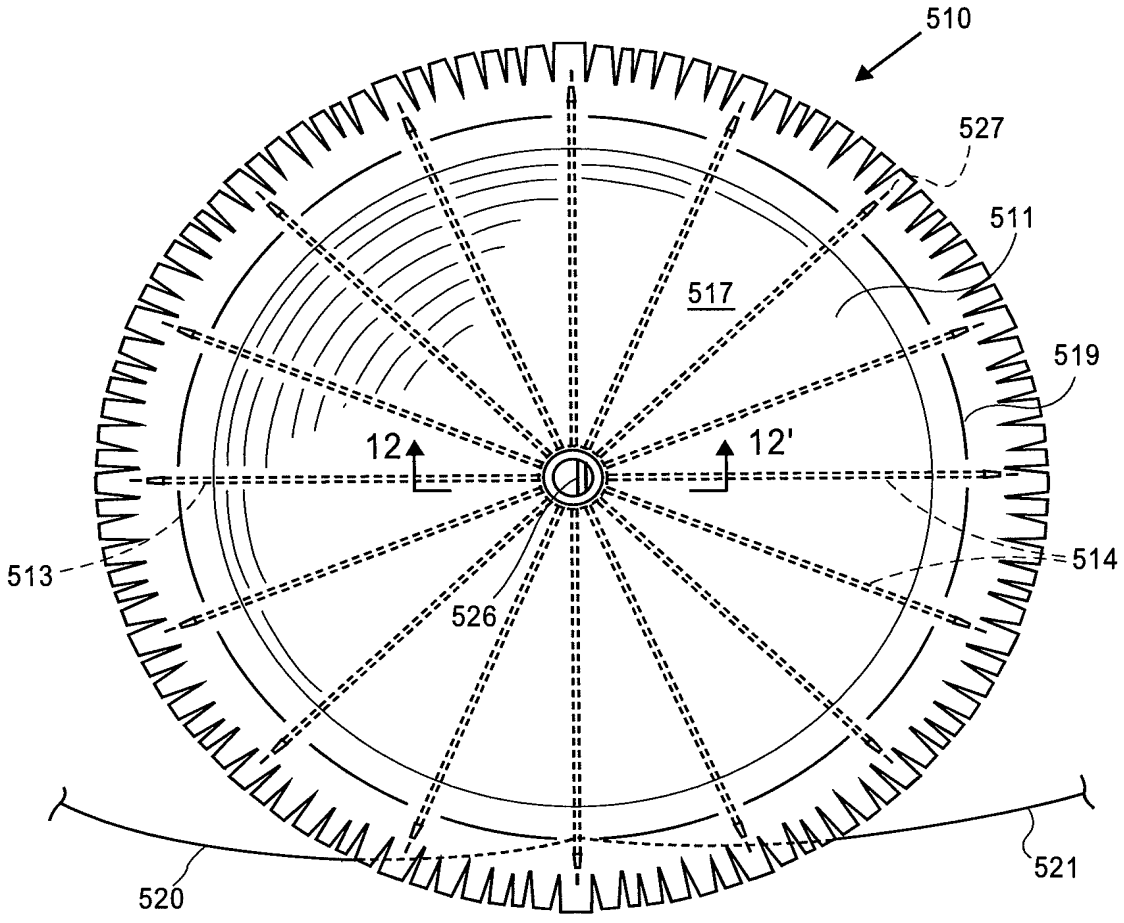
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FIG. 9

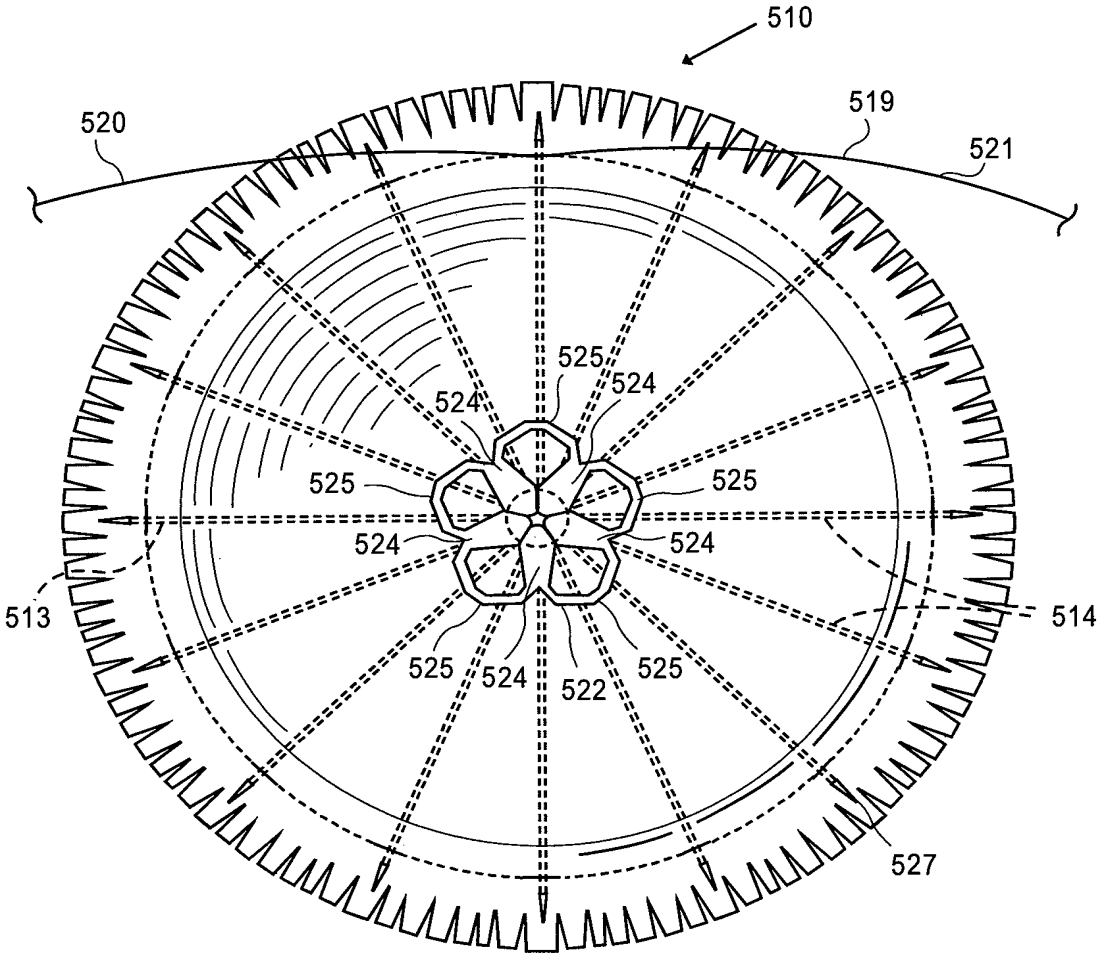
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FIG. 10

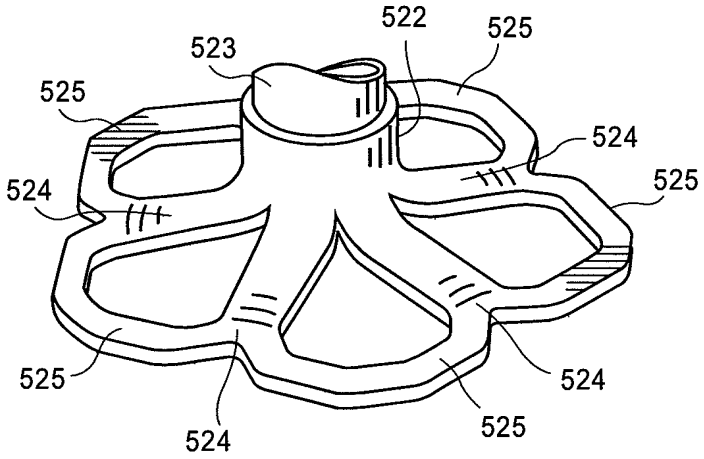
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FIG. 11

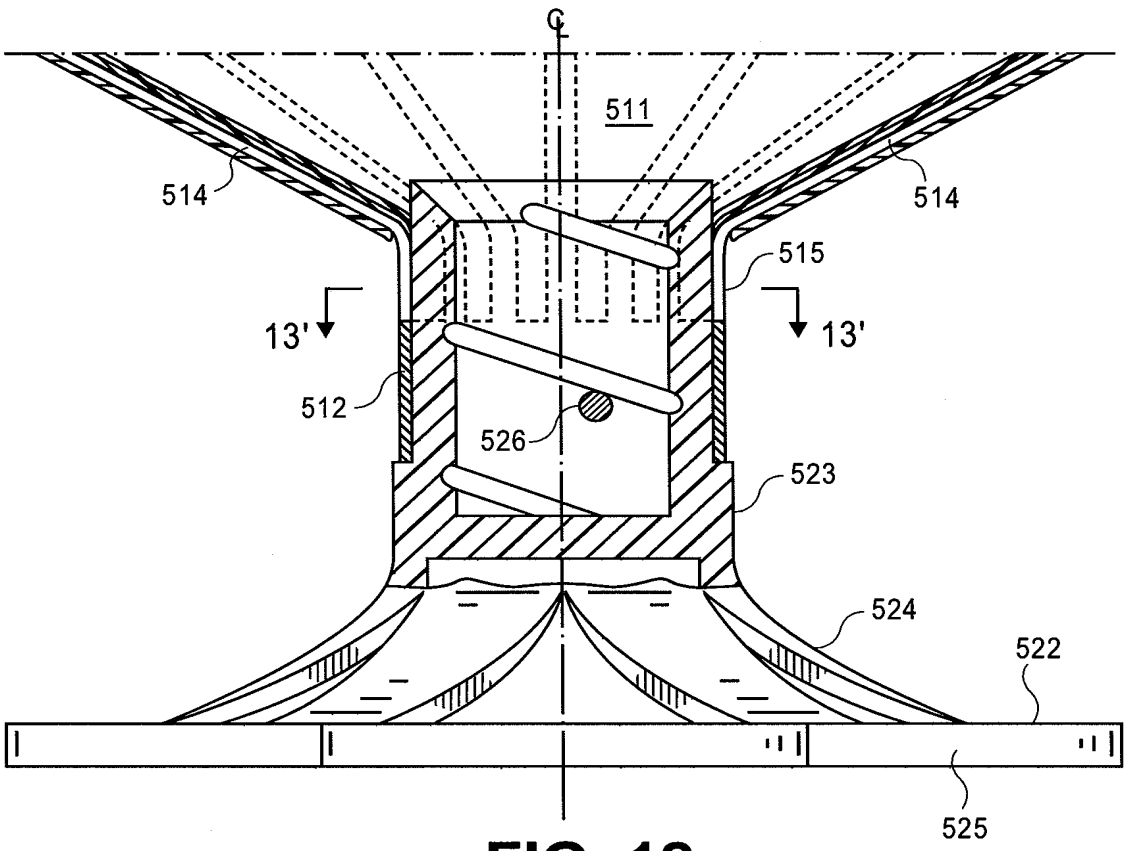

FIG. 12

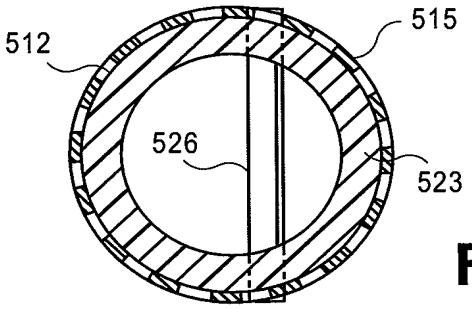

FIG. 13

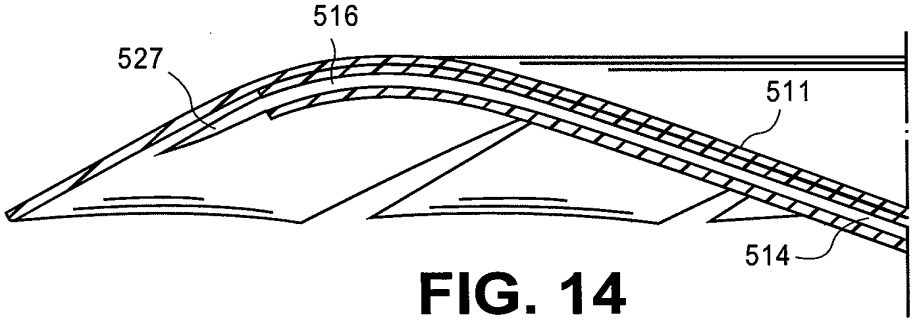

FIG. 14

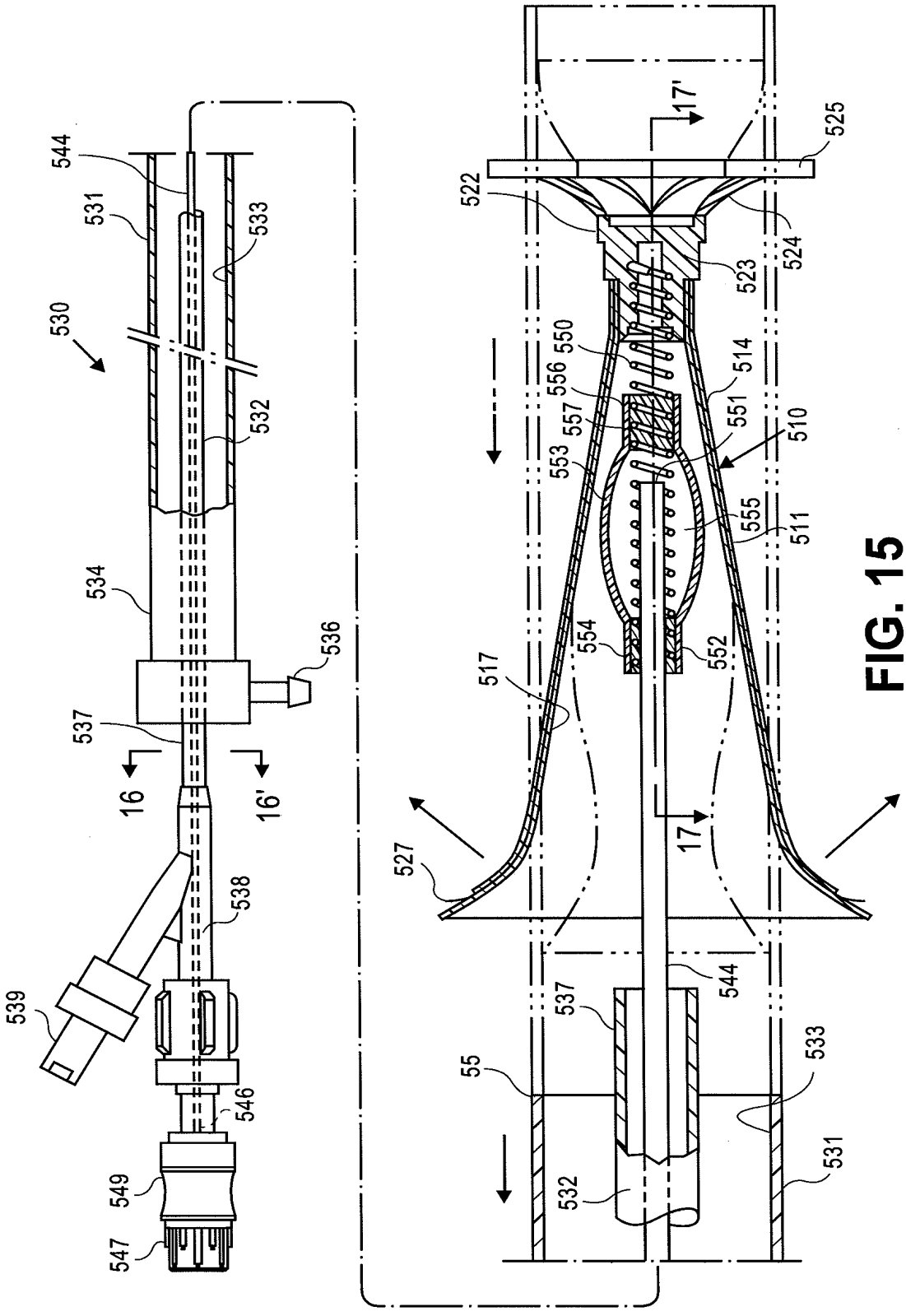
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FIG. 15

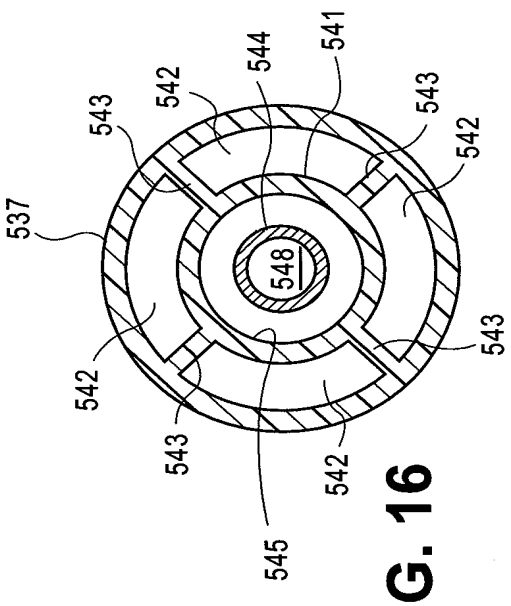
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FIG. 16

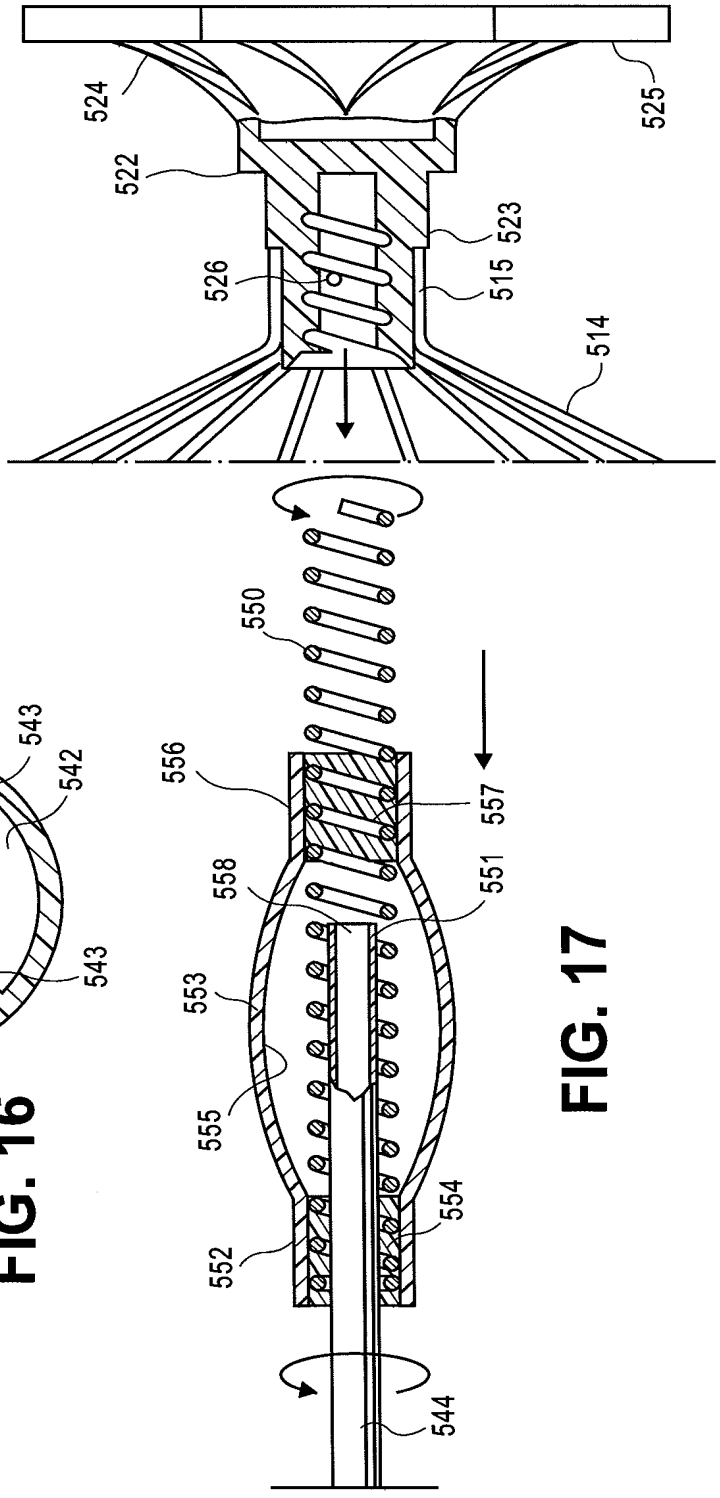
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FIG. 17

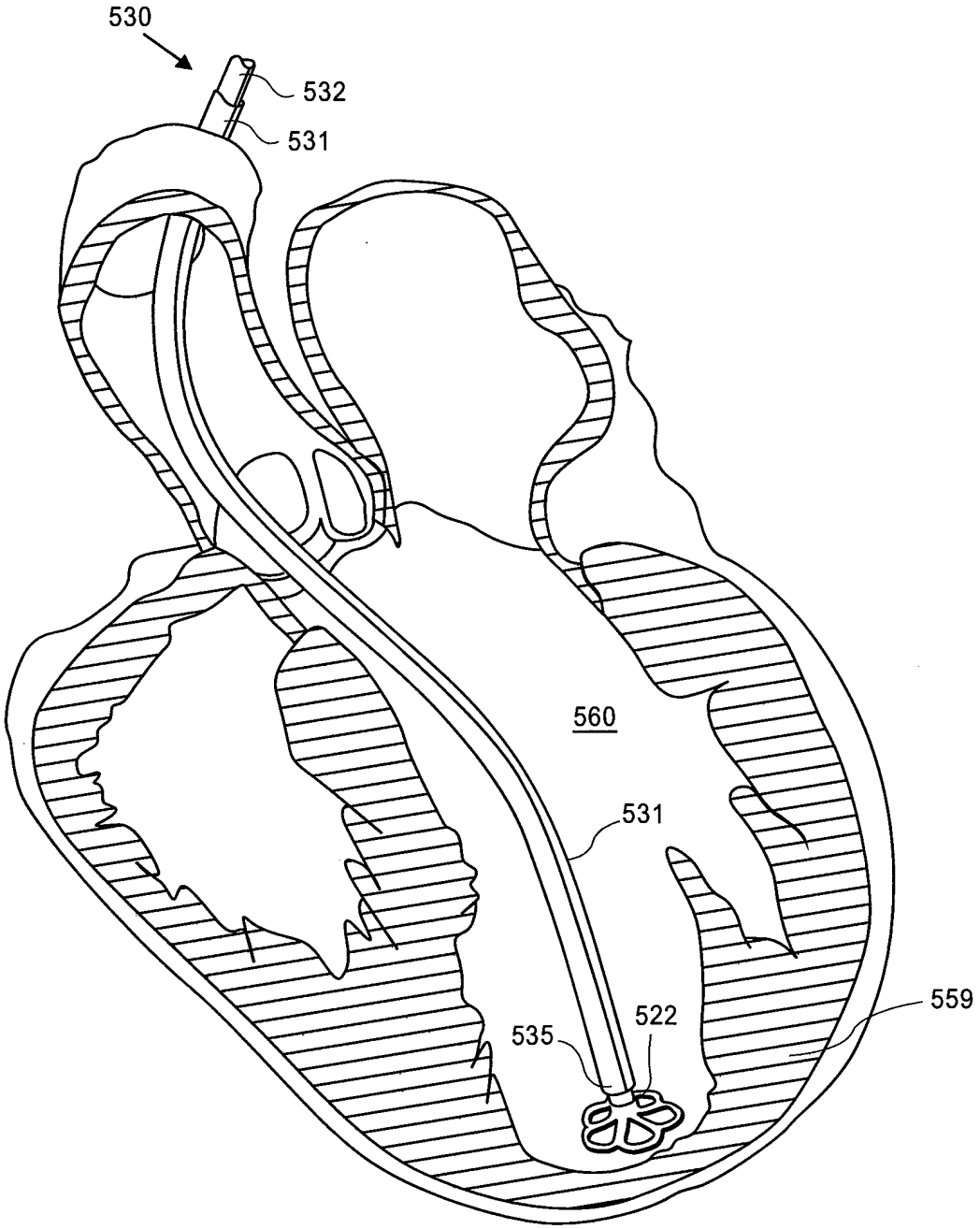


FIG. 18A

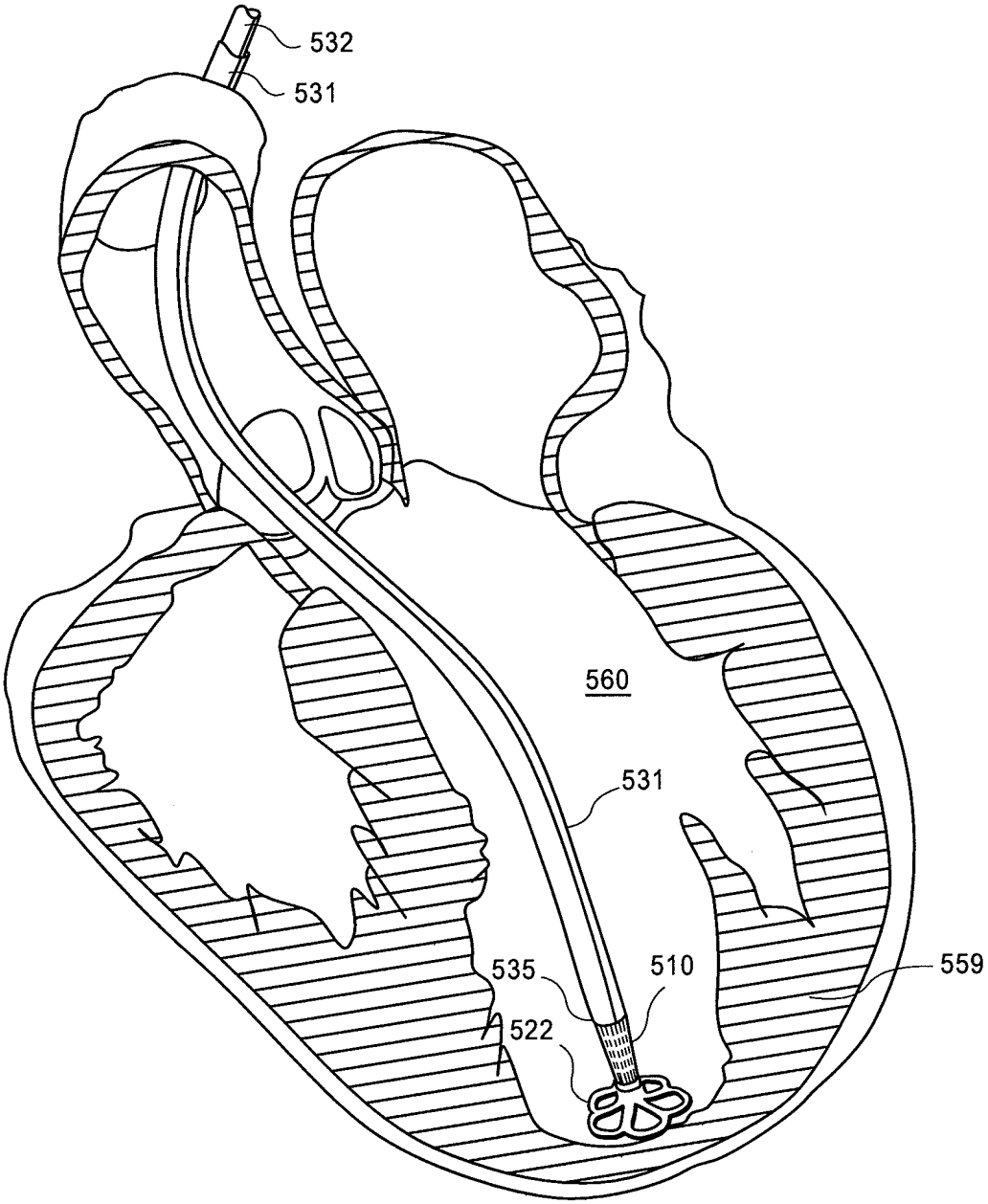


FIG. 18B

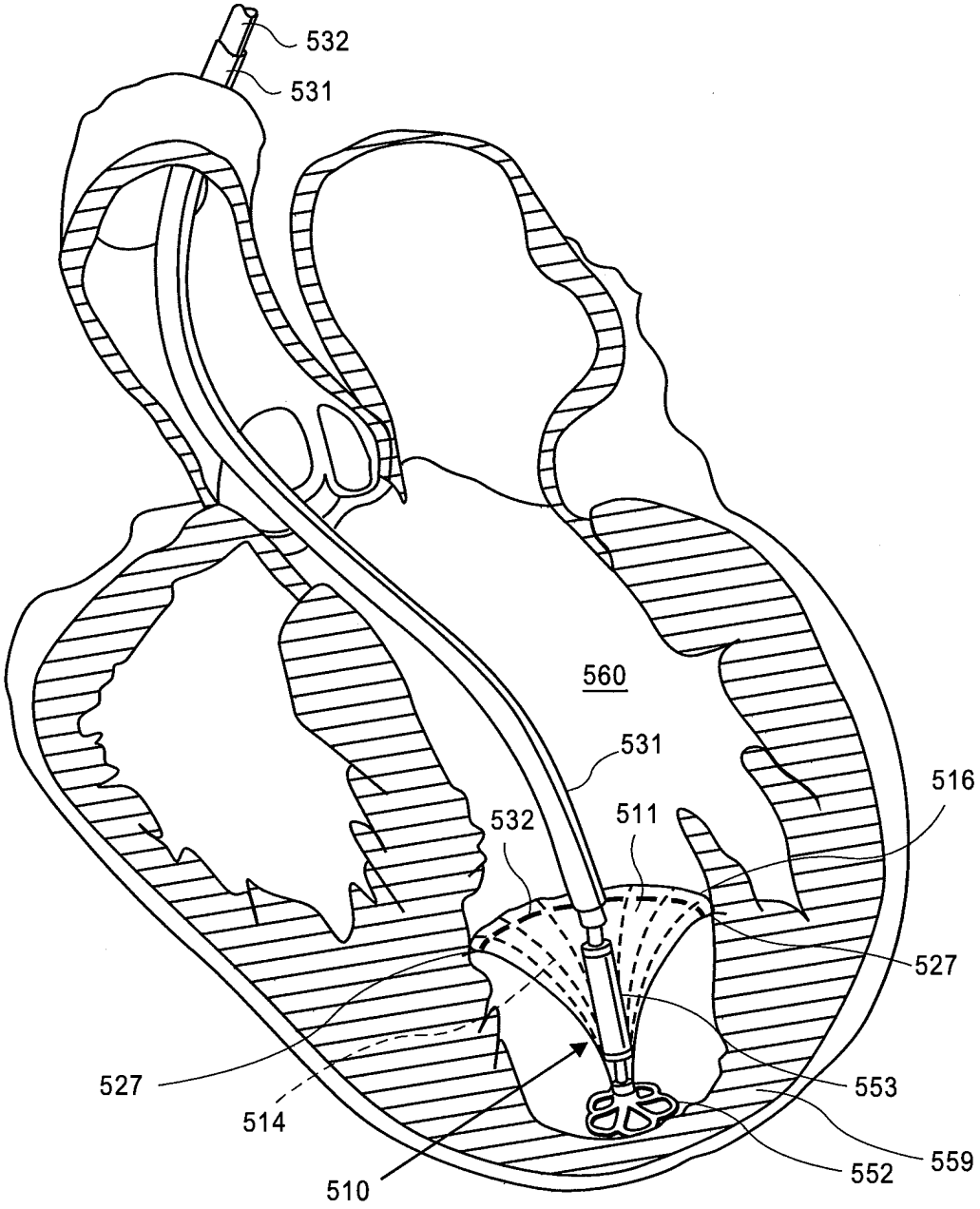


FIG. 18C

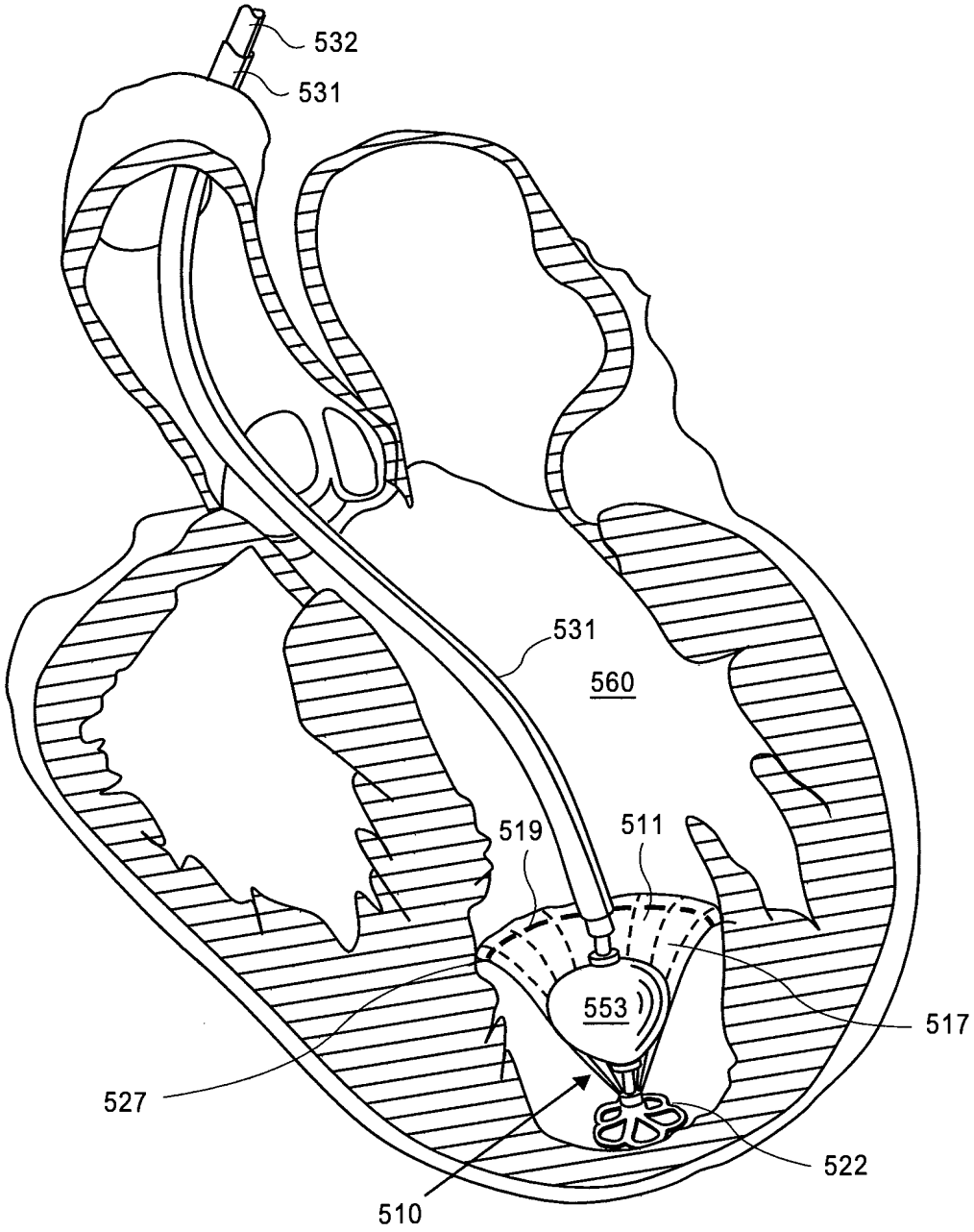


FIG. 18D

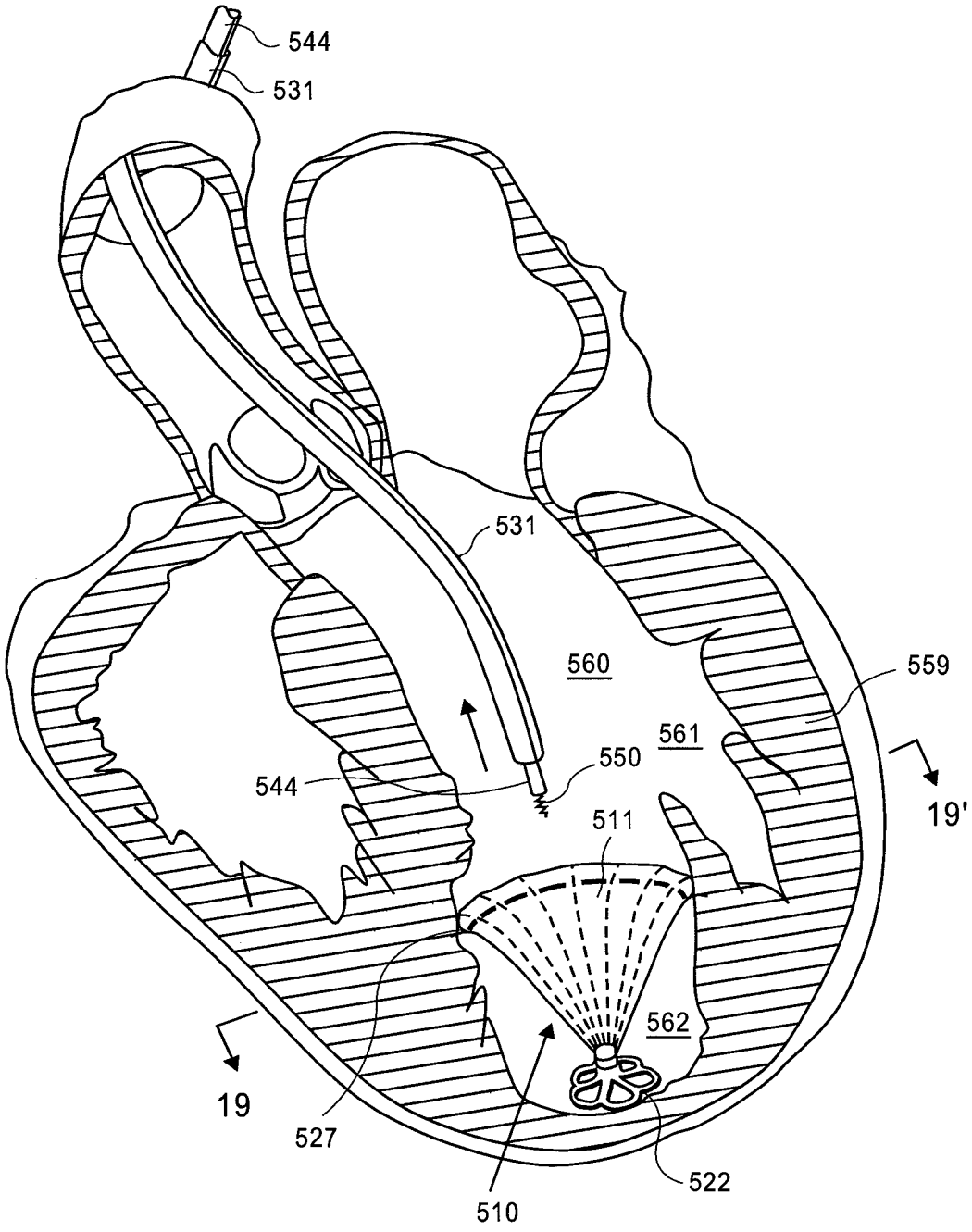


FIG. 18E

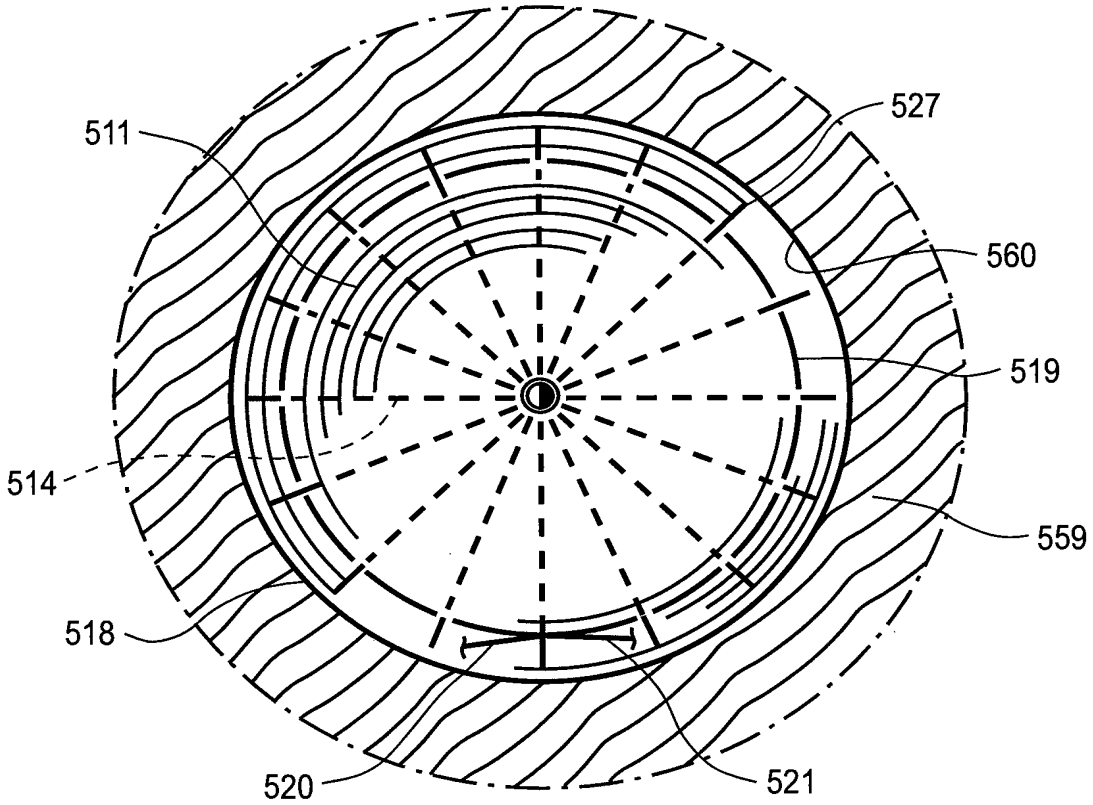


FIG. 19

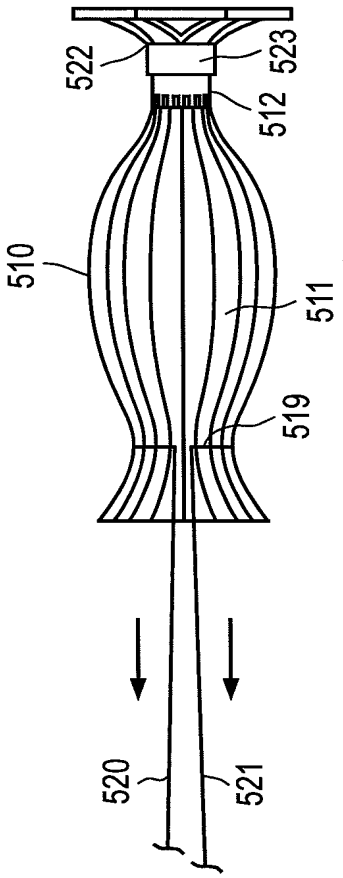


FIG. 20A

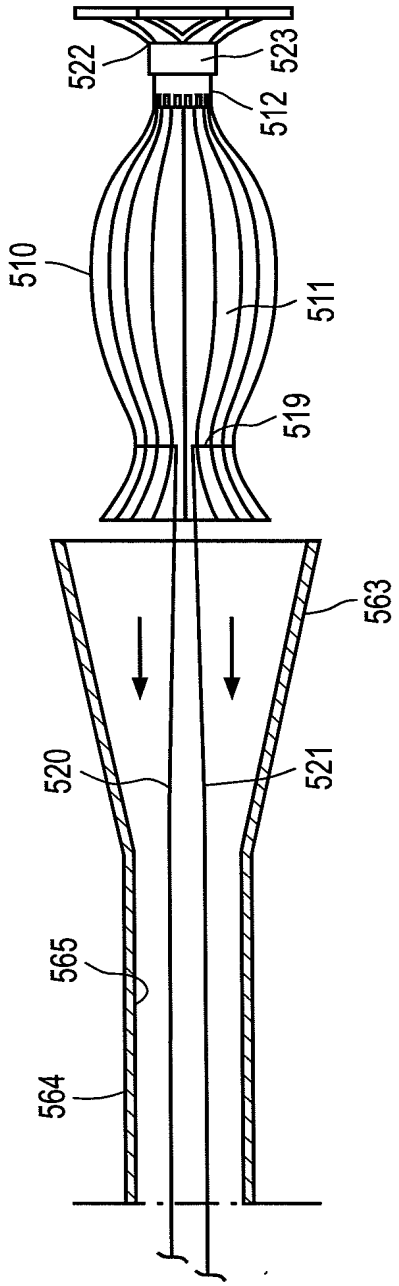


FIG. 20B

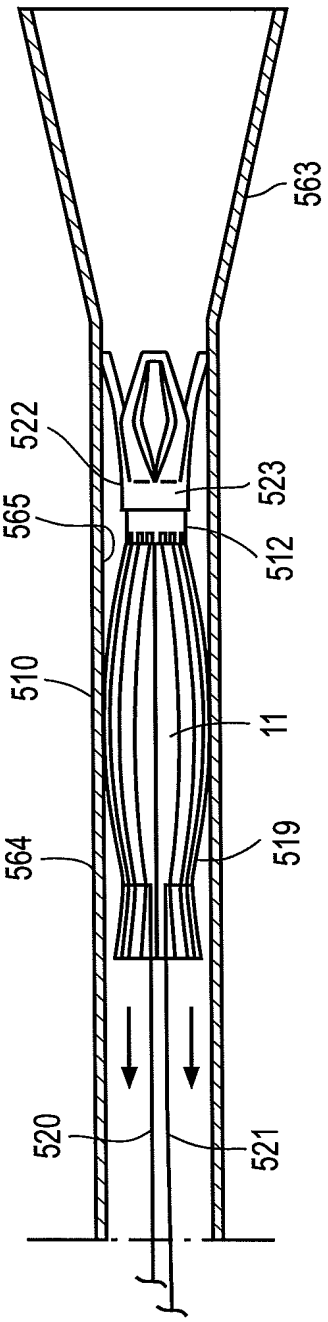


FIG. 20C

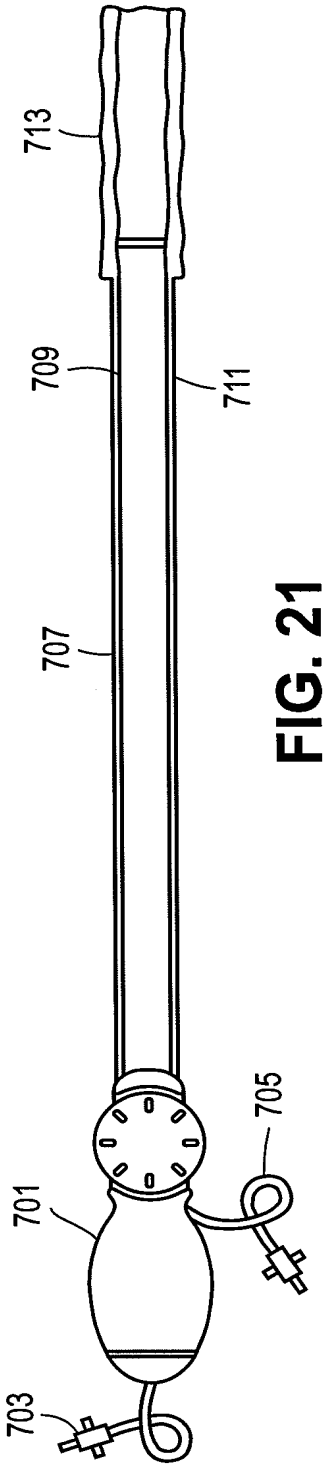


FIG. 21

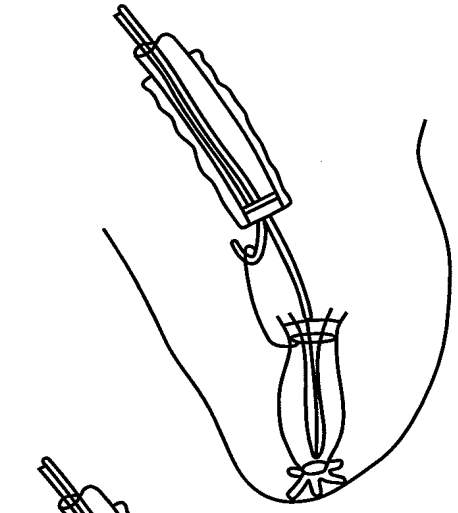


FIG. 22C

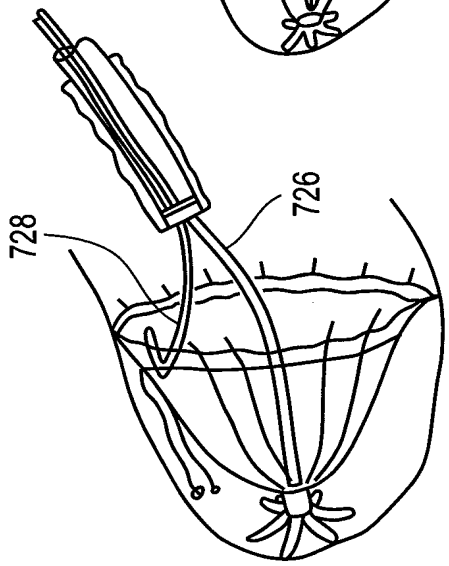


FIG. 22B

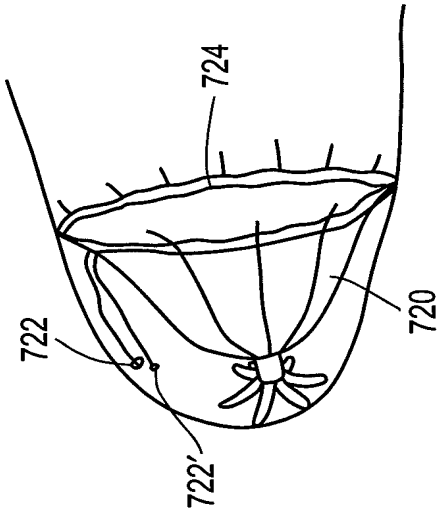


FIG. 22A

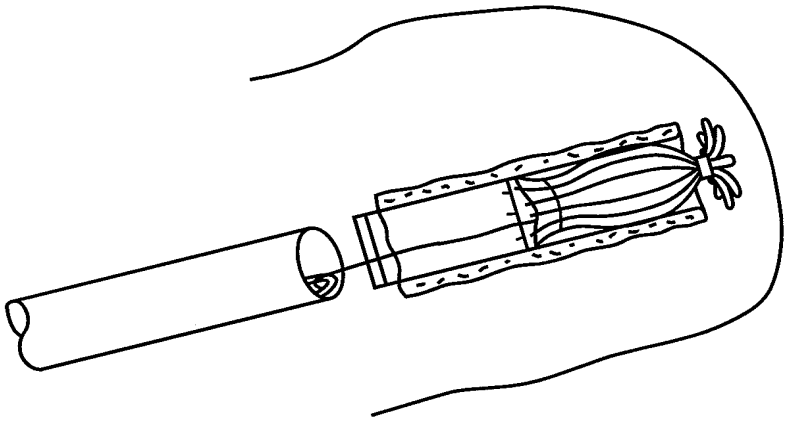


FIG. 22F

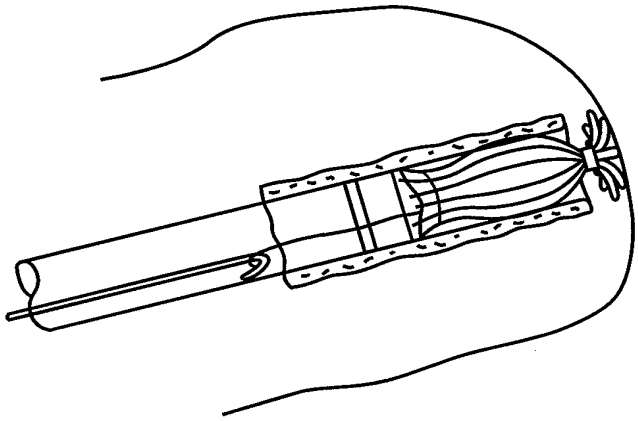


FIG. 22E

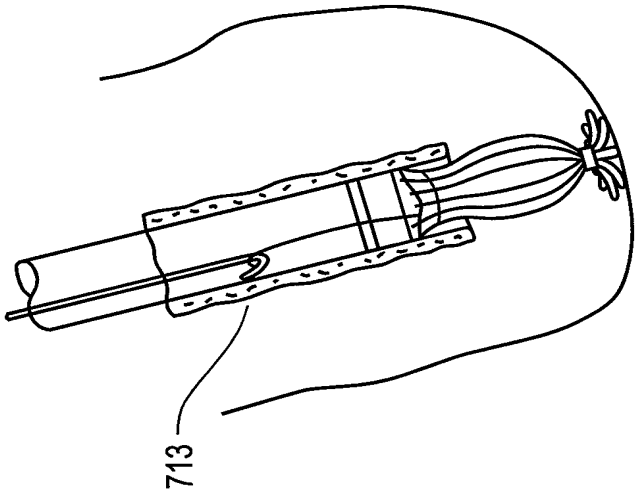


FIG. 22D

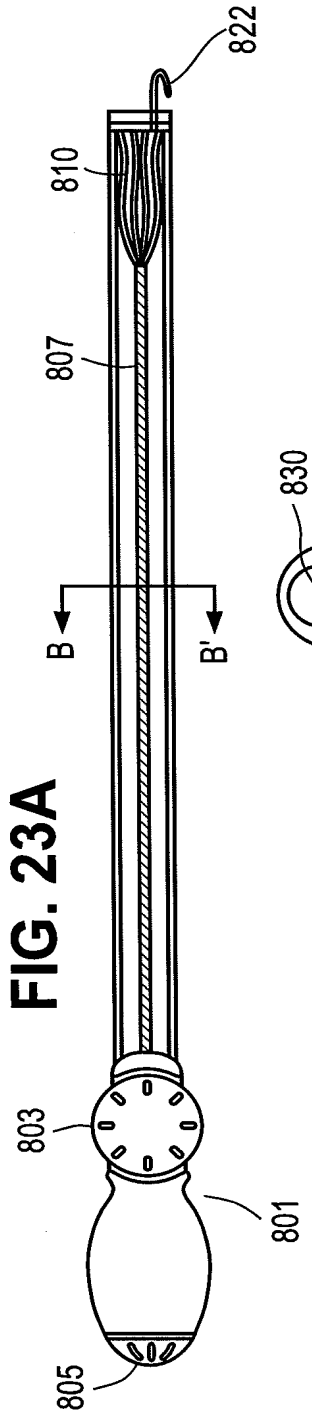


FIG. 23A

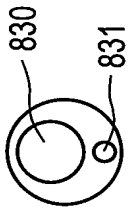


FIG. 23B

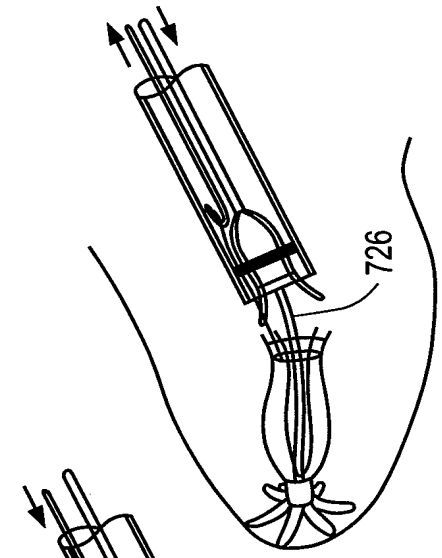


FIG. 24C

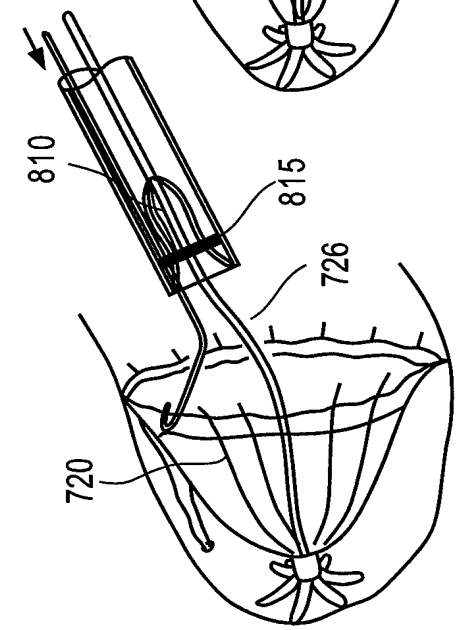


FIG. 24B

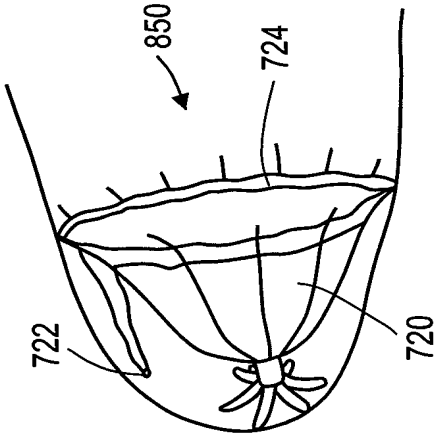


FIG. 24A

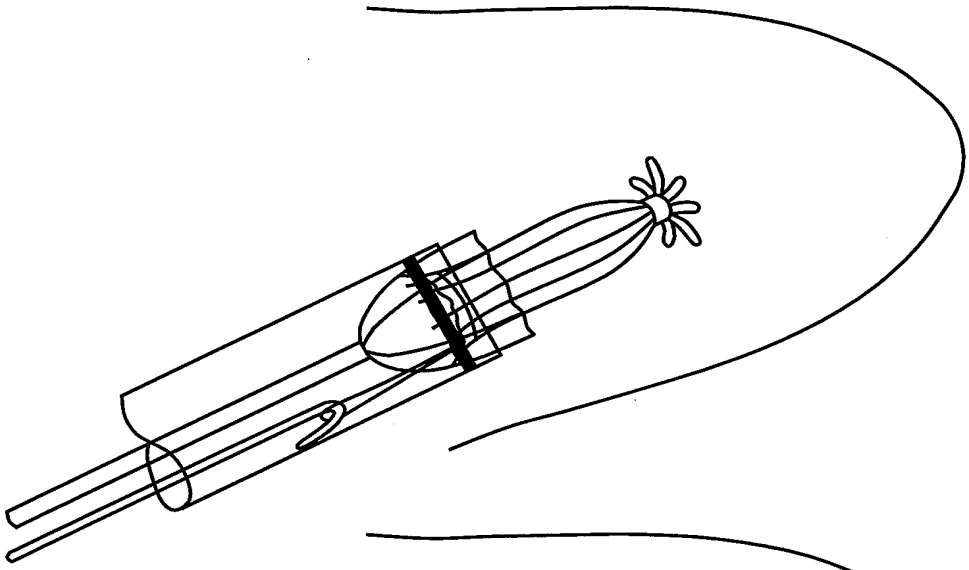


FIG. 24F

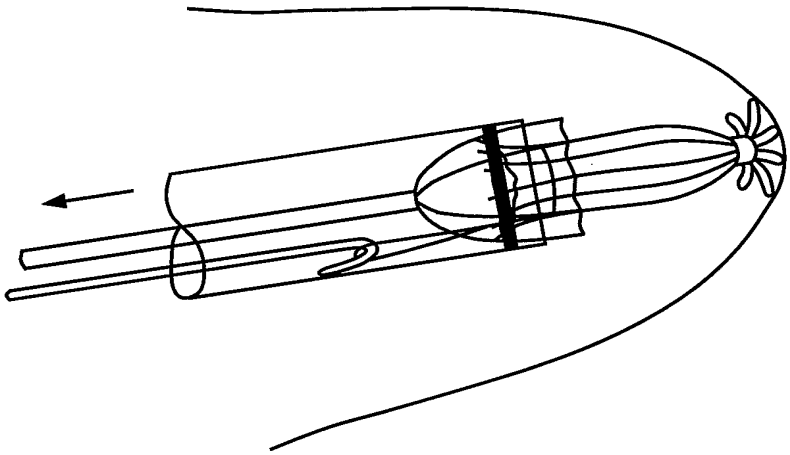


FIG. 24E

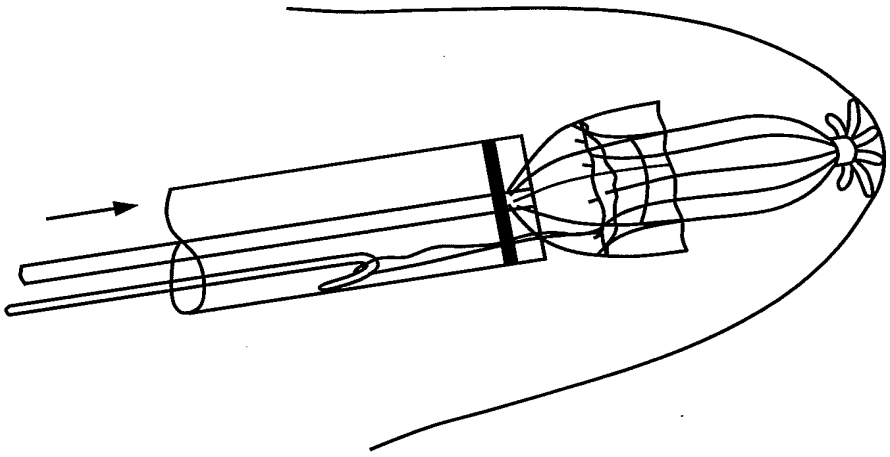


FIG. 24D

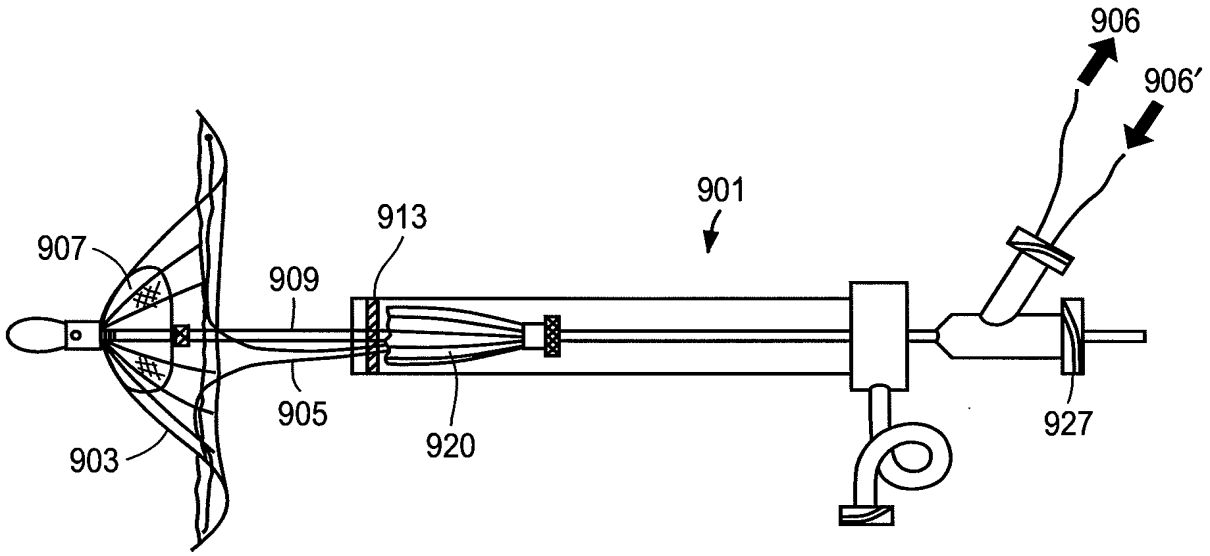


FIG. 25A

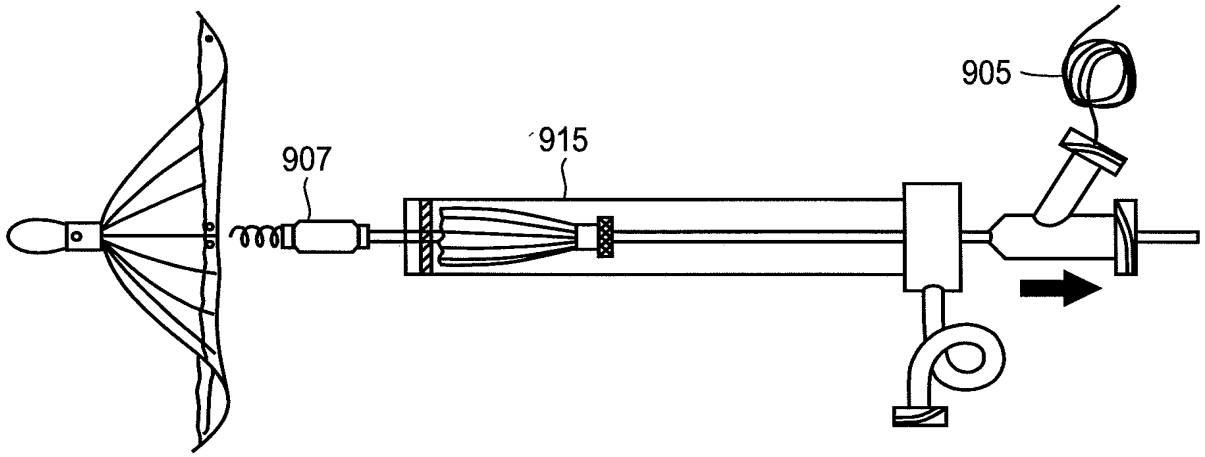


FIG. 25B

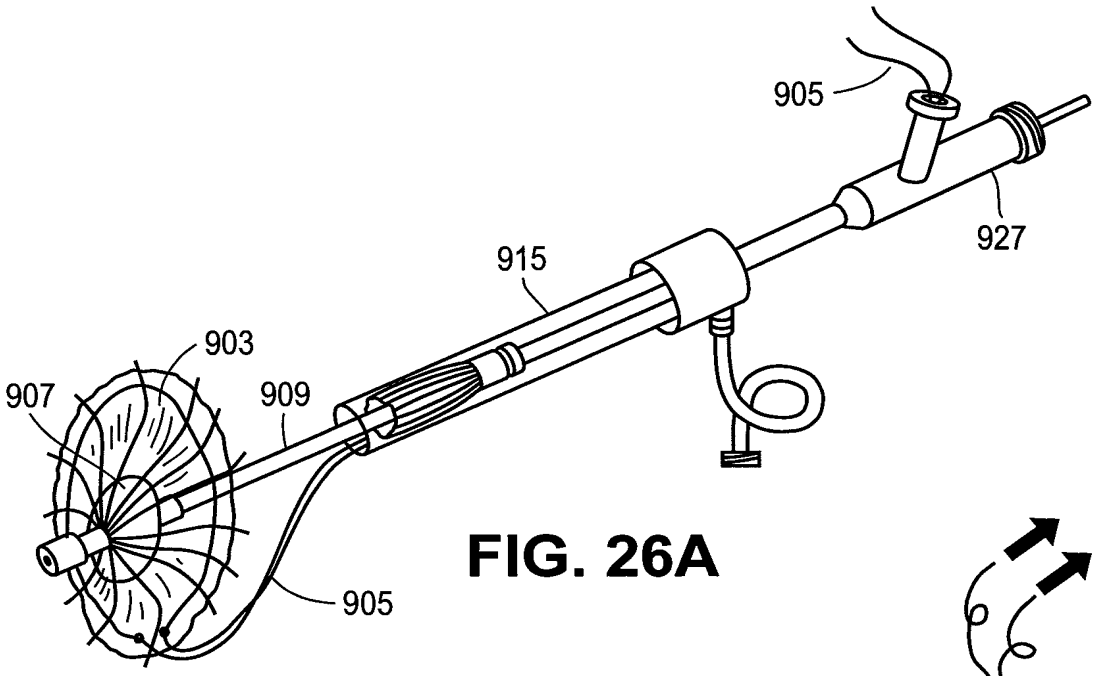


FIG. 26A

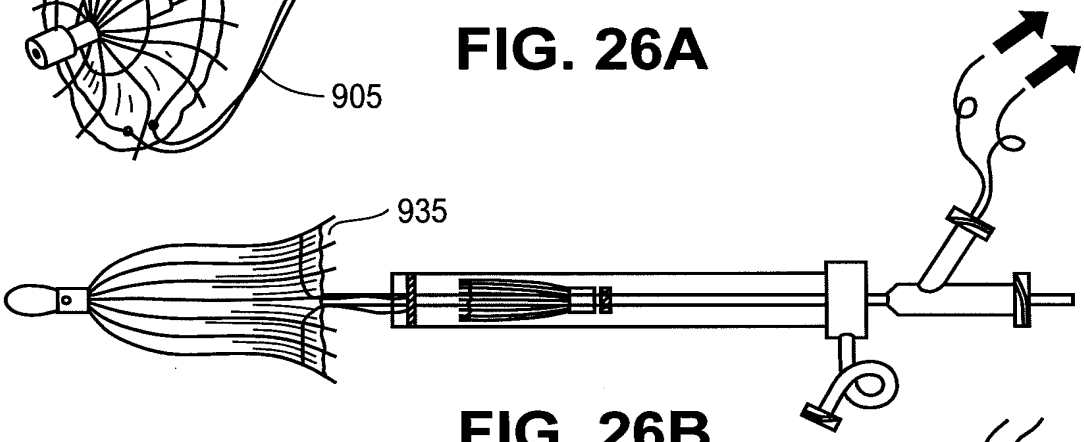


FIG. 26B

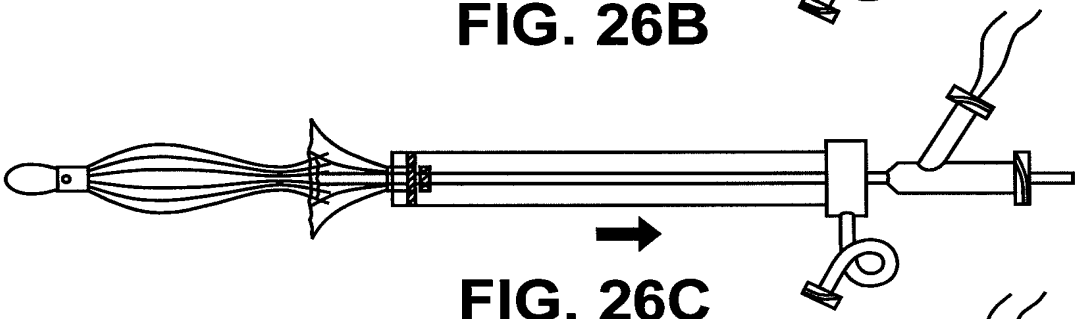


FIG. 26C

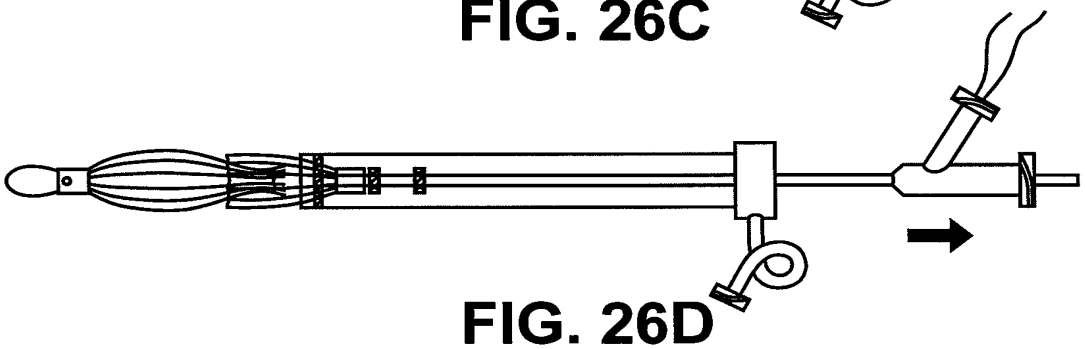


FIG. 26D

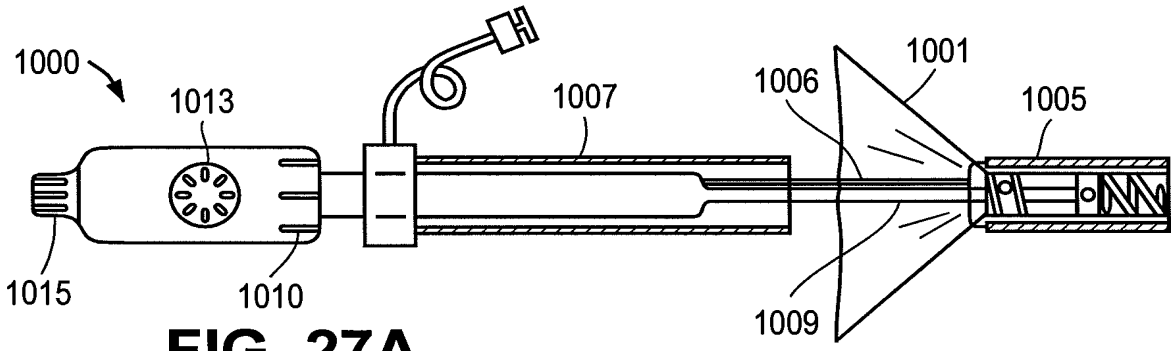


FIG. 27A

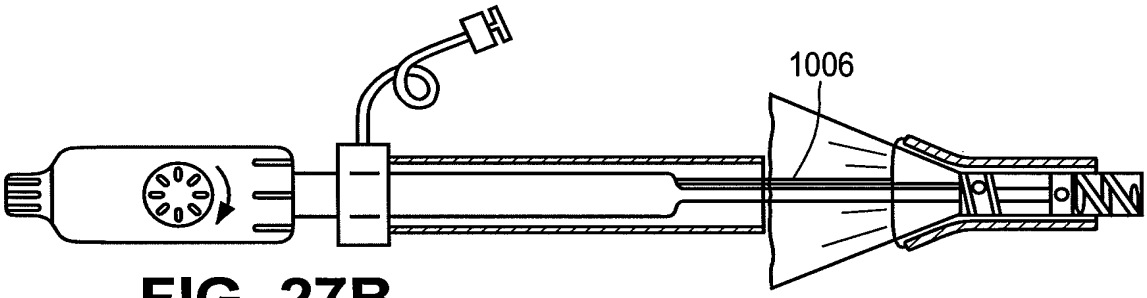


FIG. 27B

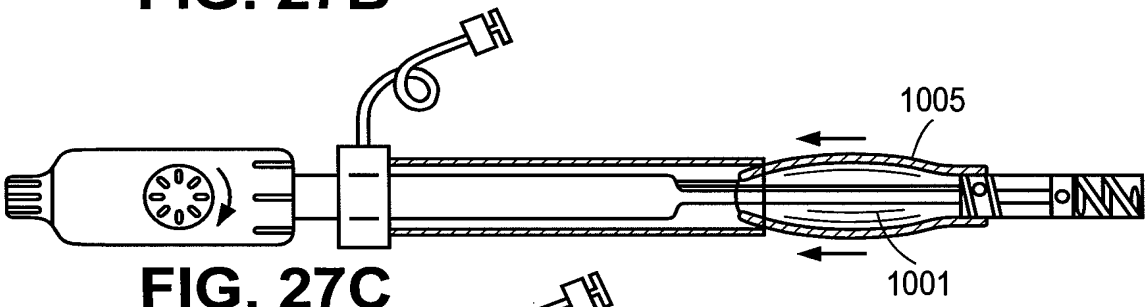


FIG. 27C

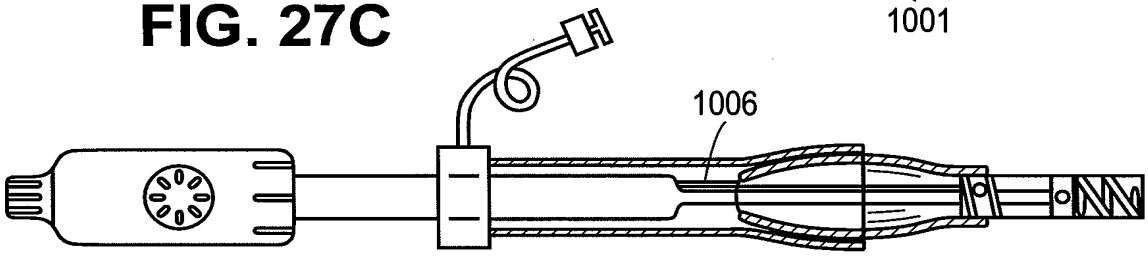


FIG. 27D

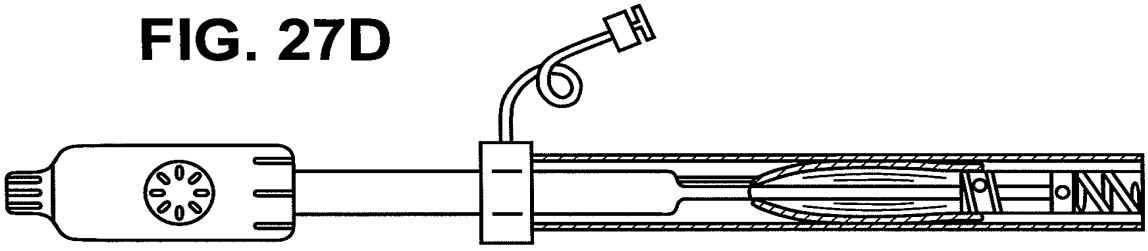


FIG. 27E

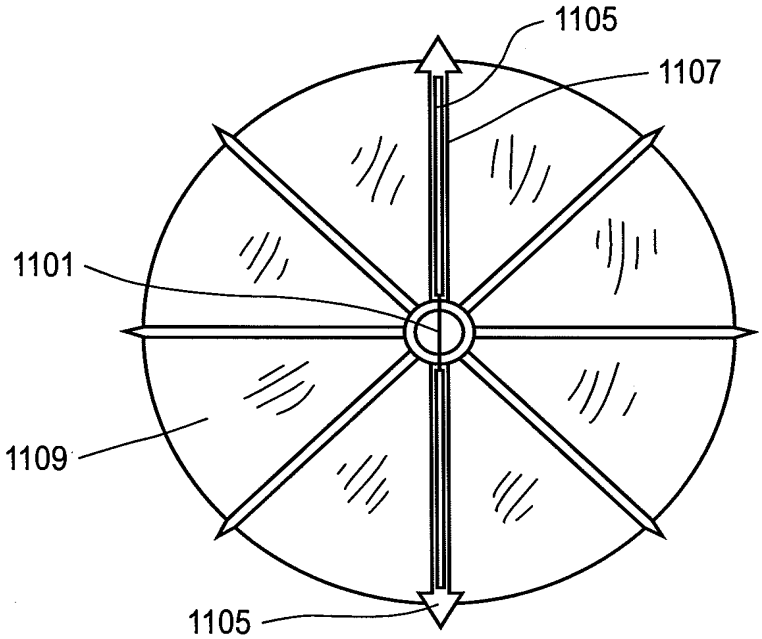


FIG. 28A

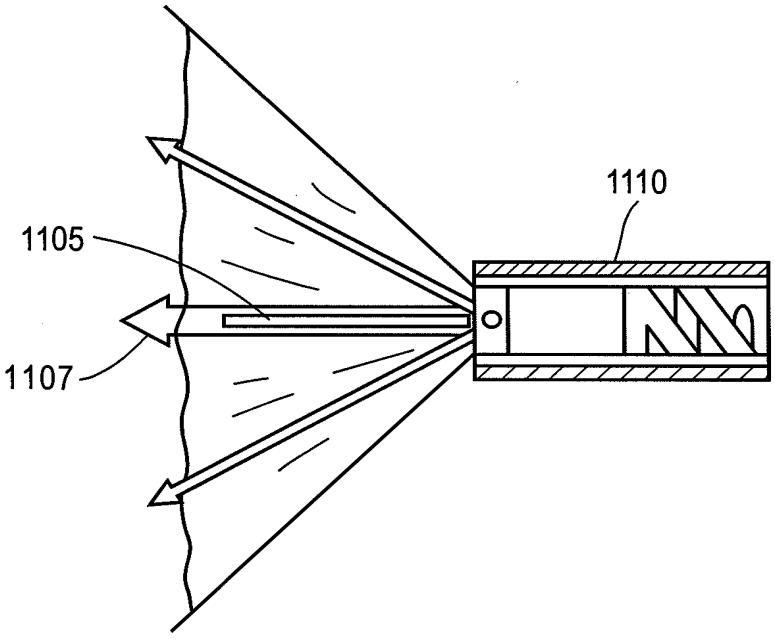


FIG. 28B

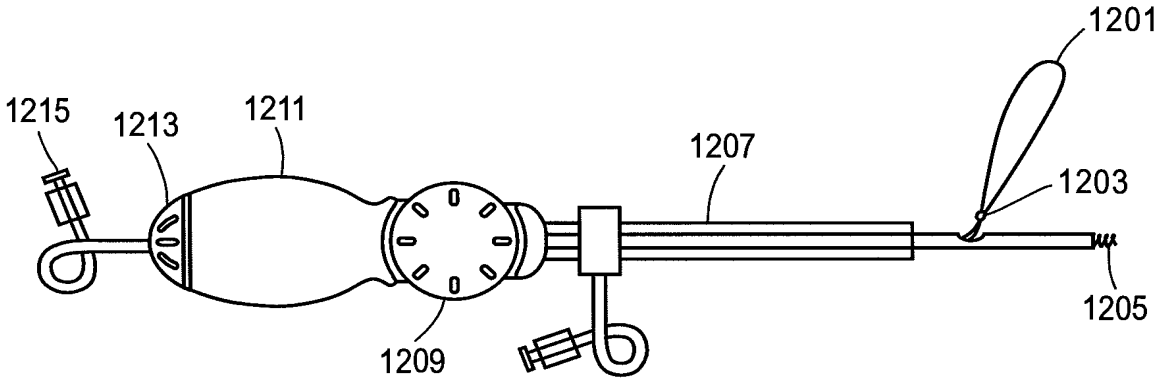


FIG. 29A

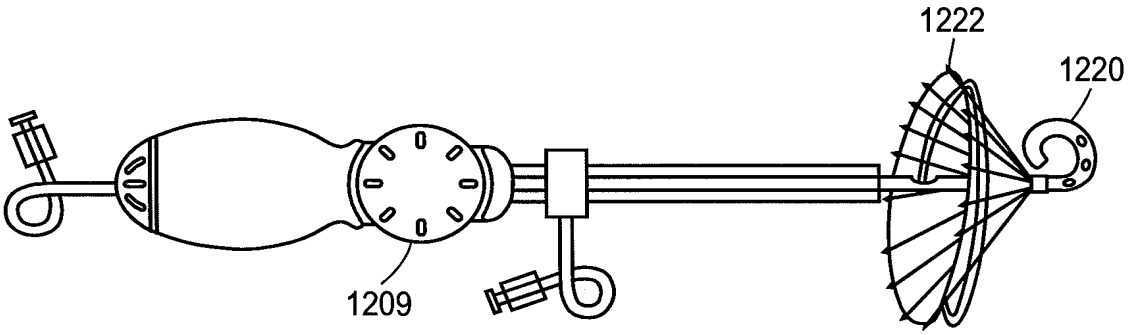


FIG. 29B

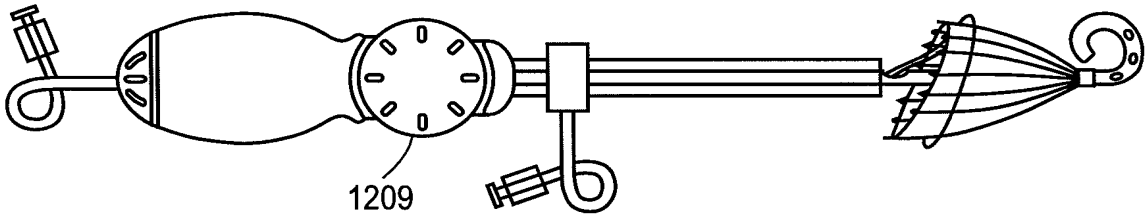


FIG. 29C

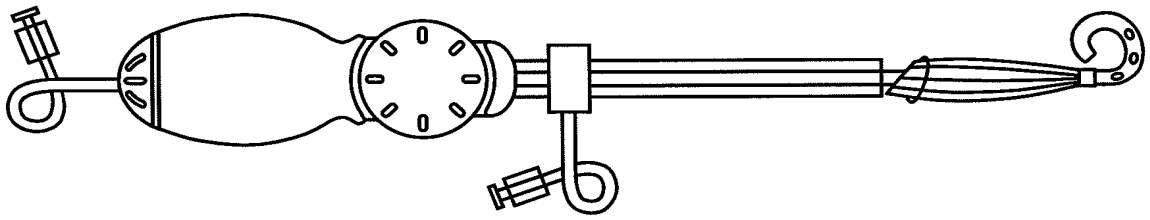


FIG. 29D

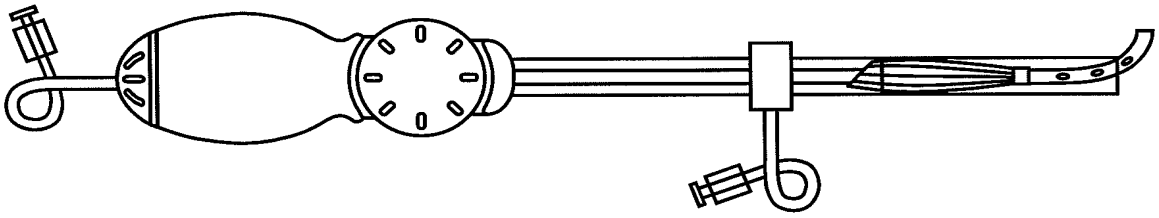


FIG. 29E

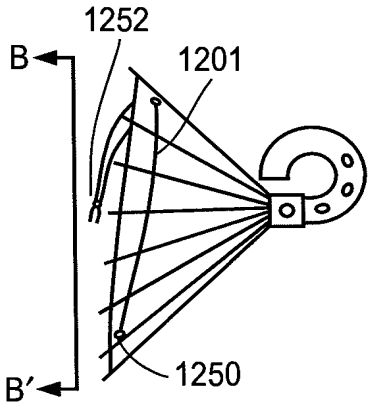
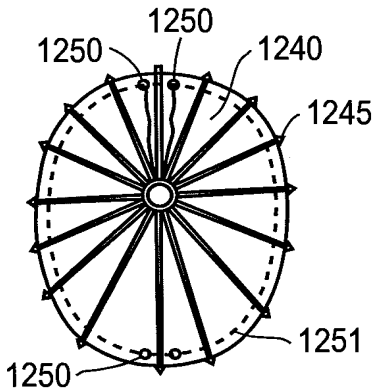


FIG. 30A



Section B – B′

FIG. 30B

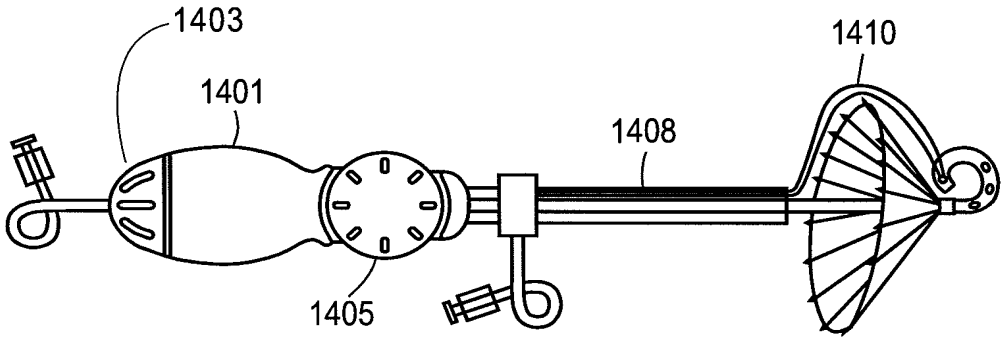


FIG. 31A

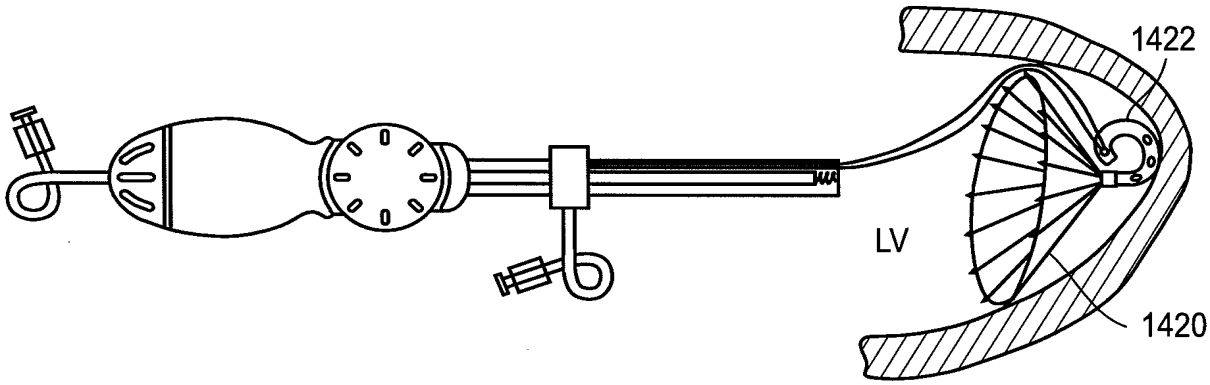


FIG. 31B

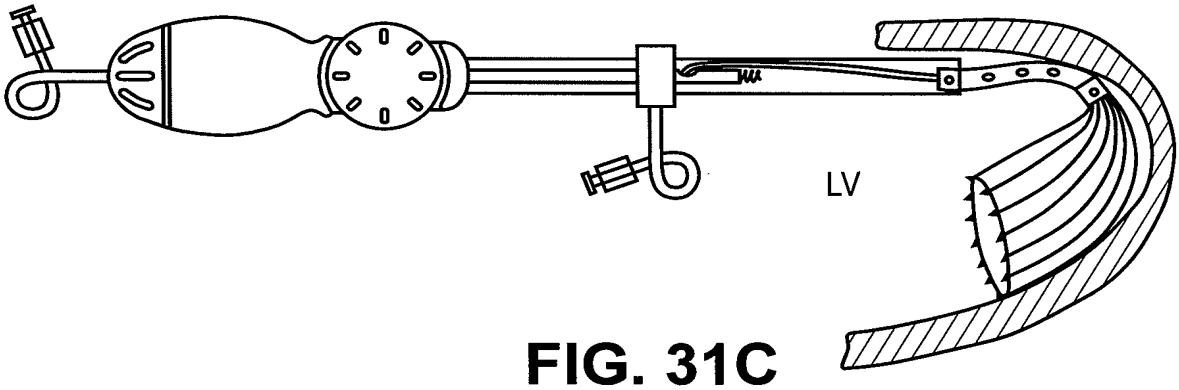


FIG. 31C

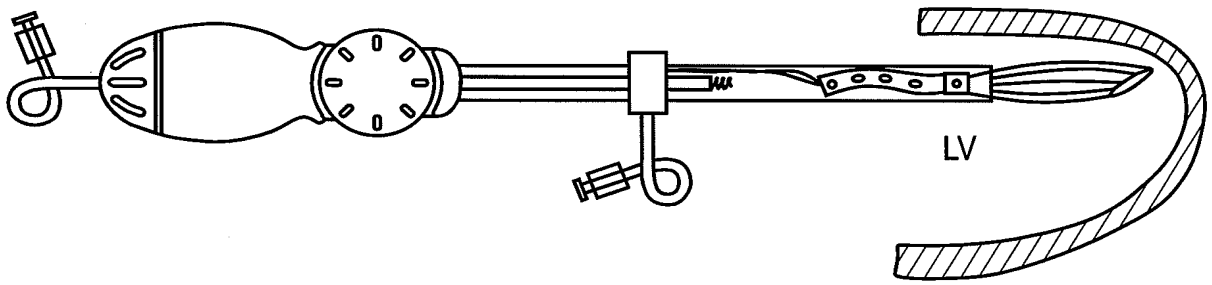


FIG. 31D

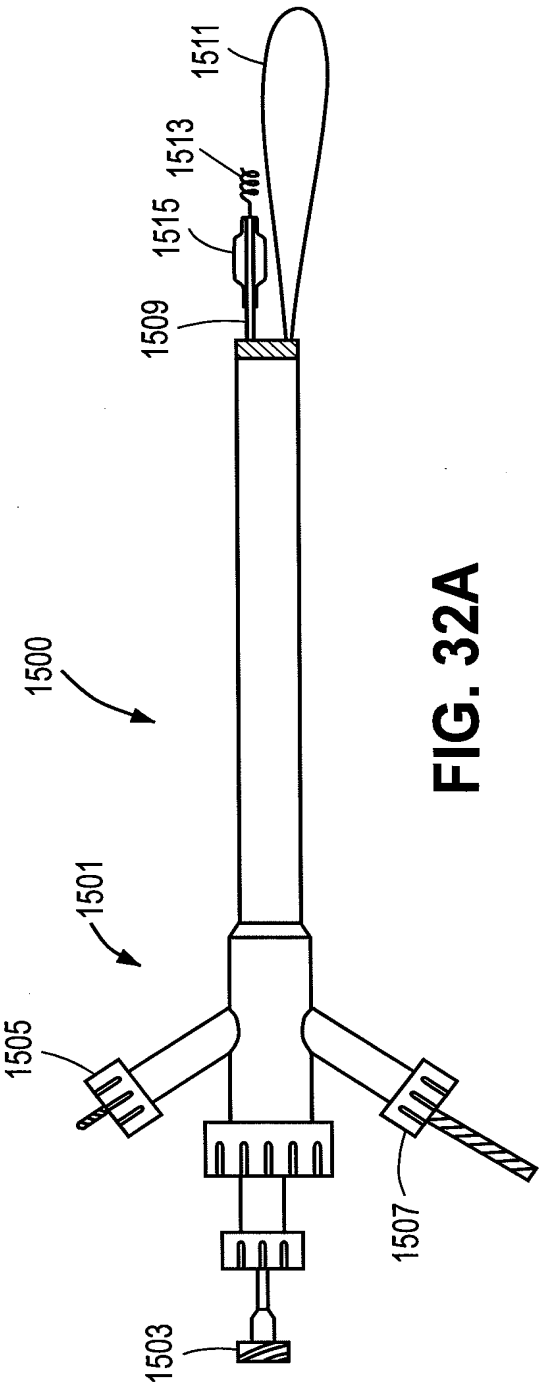


FIG. 32A

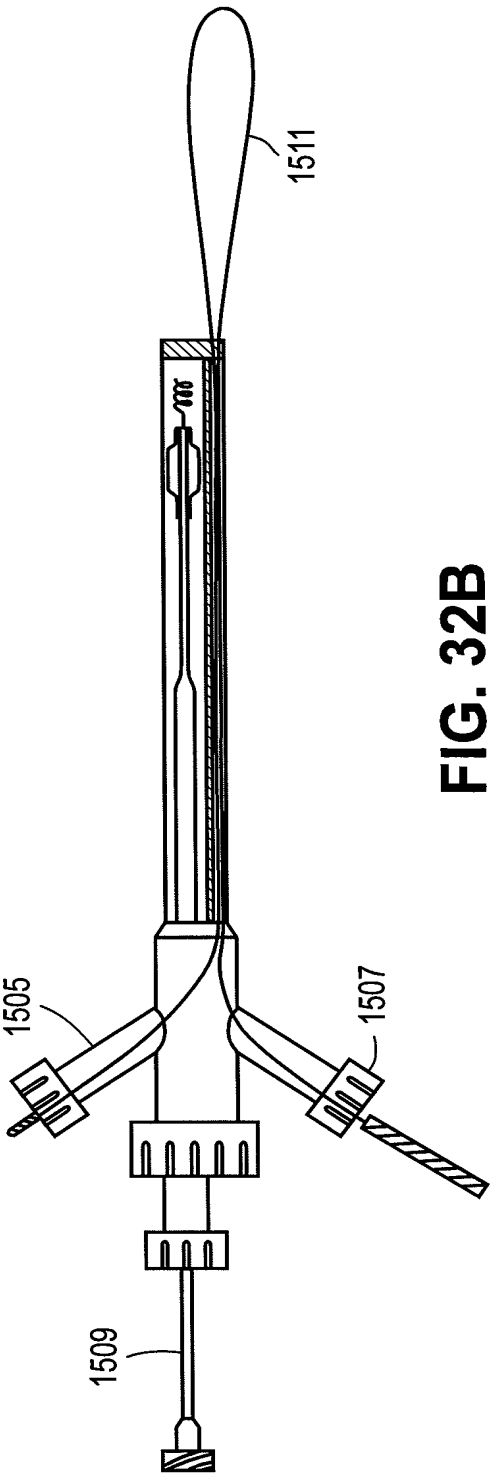


FIG. 32B

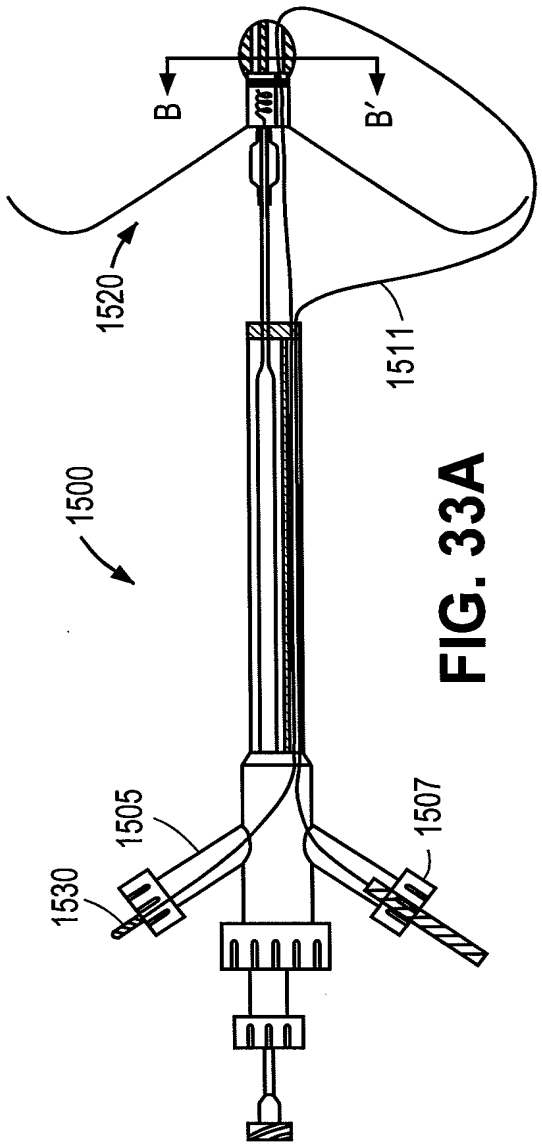


FIG. 33A

FIG. 33B

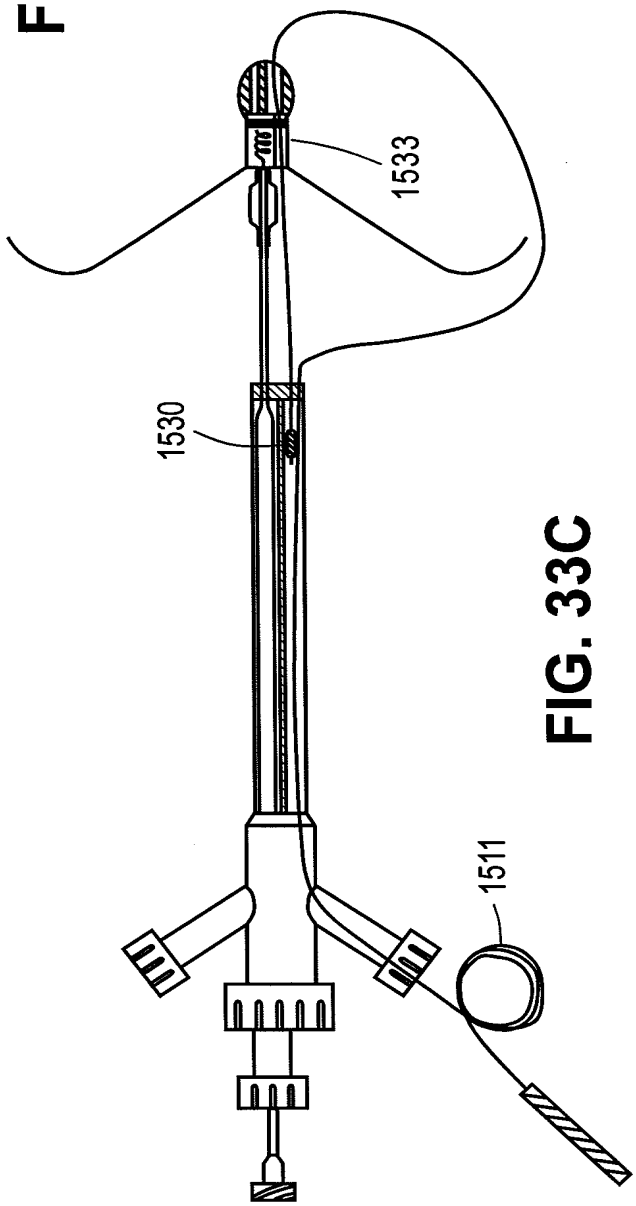


FIG. 33C

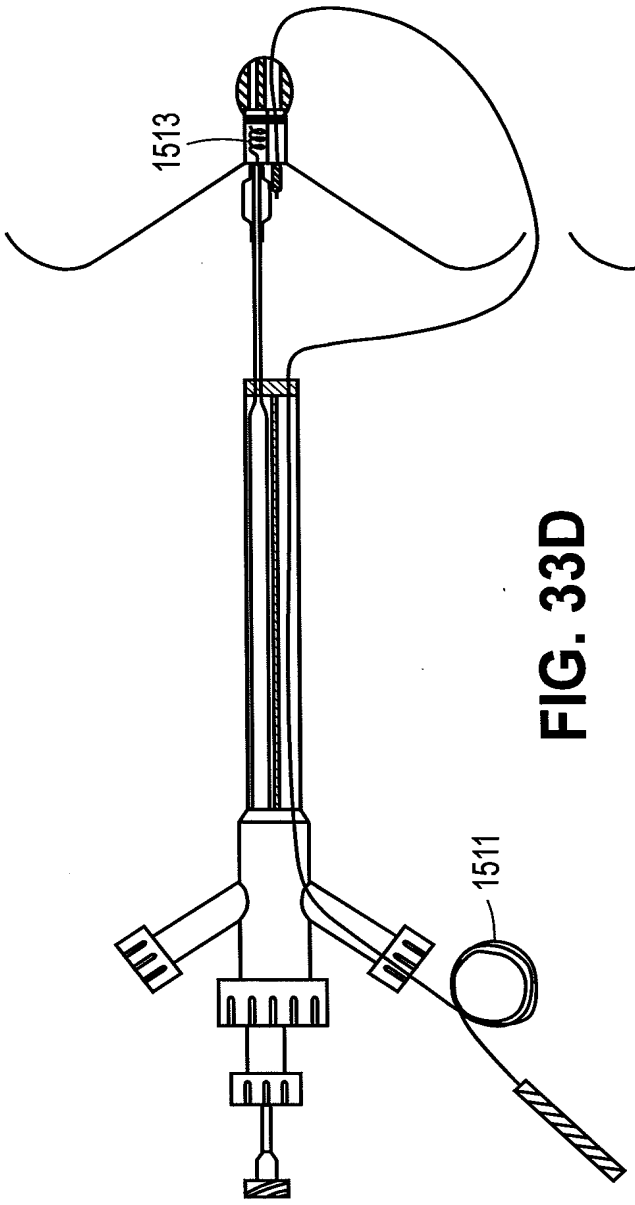


FIG. 33D

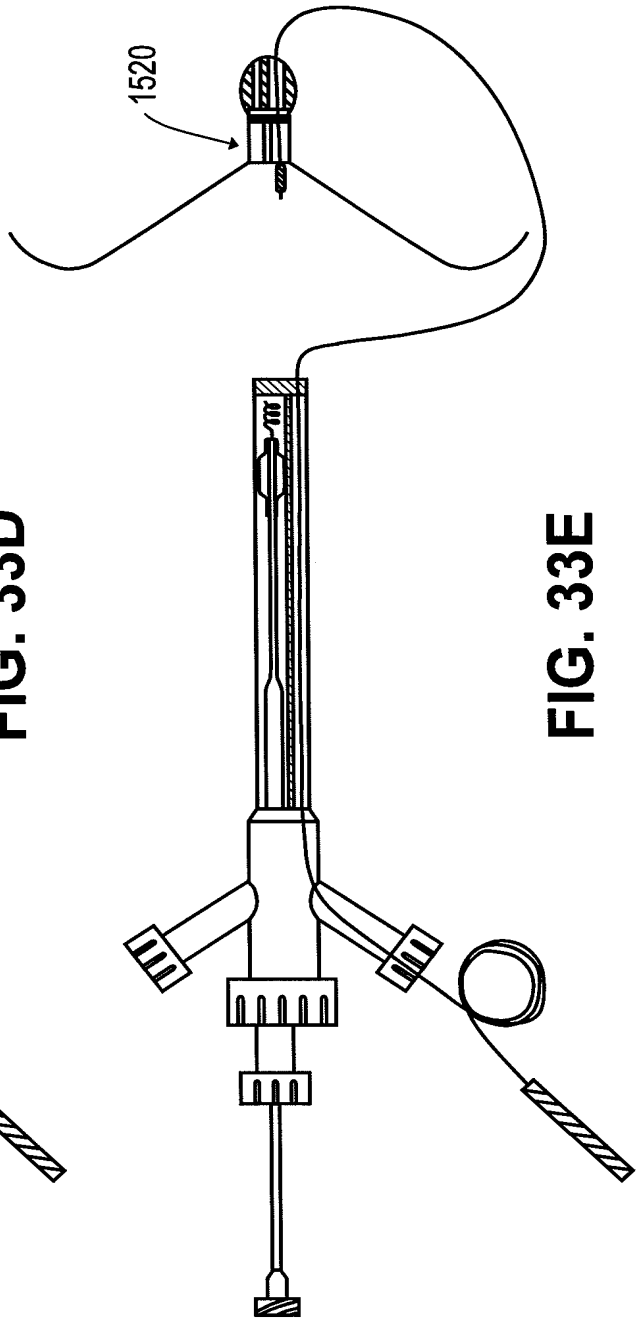


FIG. 33E

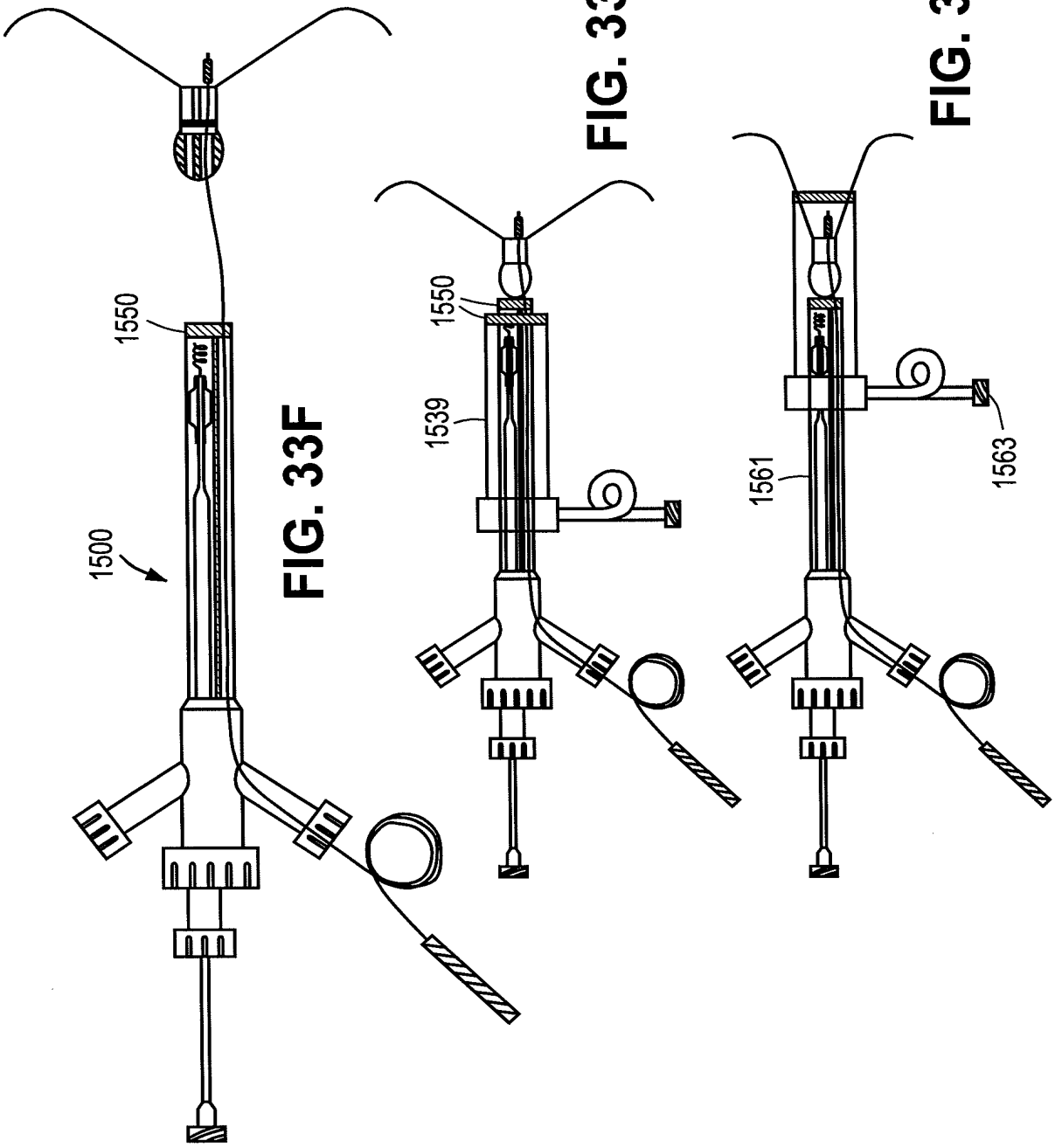


FIG. 33F

FIG. 33G

FIG. 33H

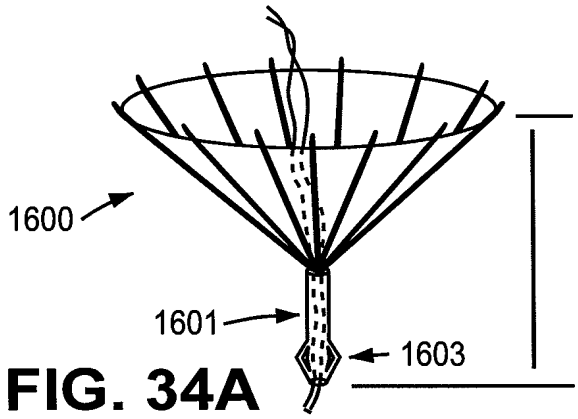


FIG. 34A

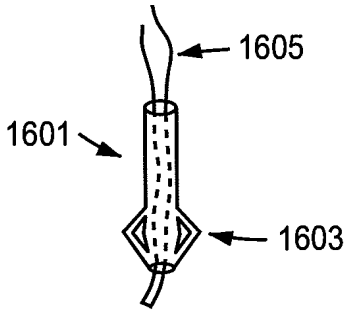


FIG. 34B

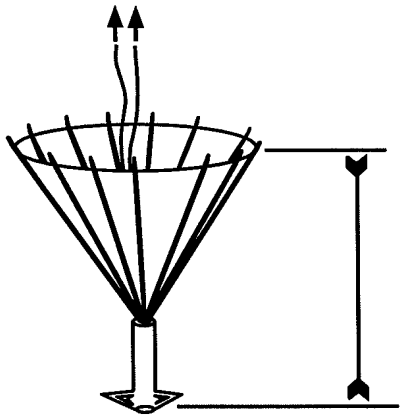


FIG. 34C

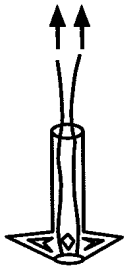


FIG. 34D

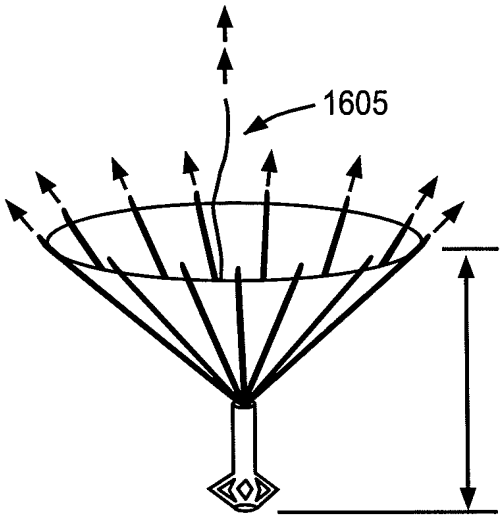


FIG. 34E

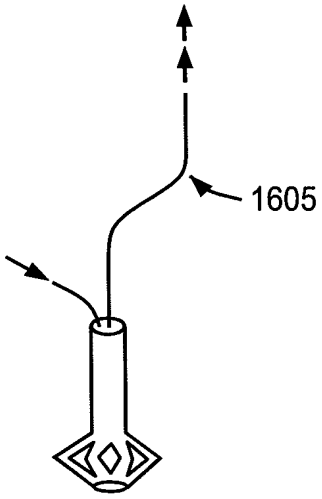


FIG. 34F

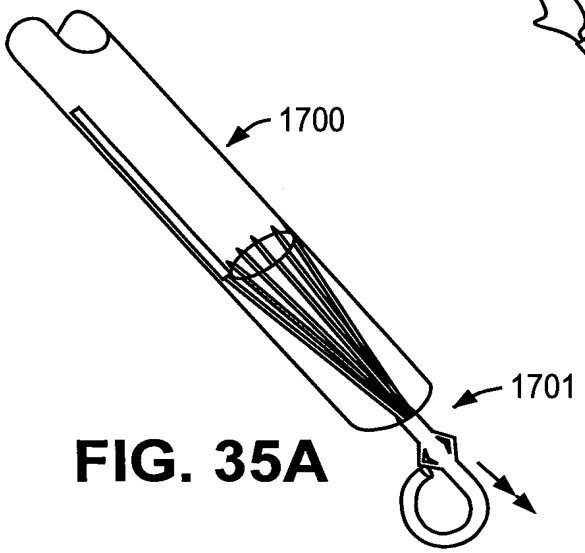


FIG. 35A

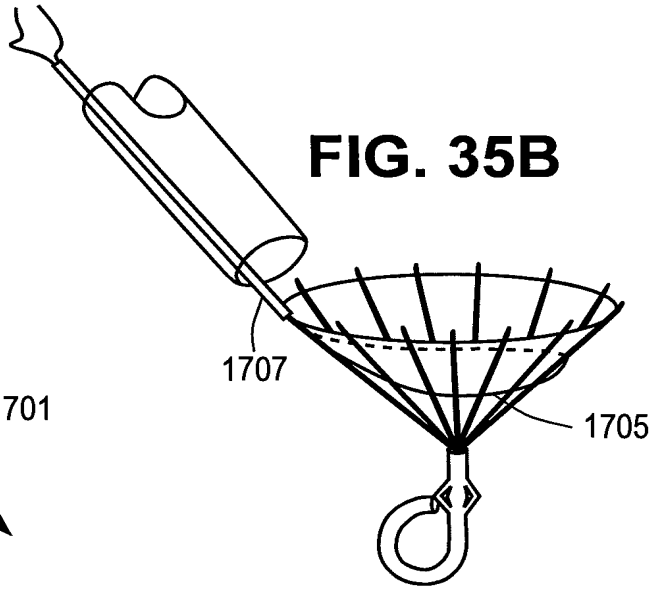


FIG. 35B

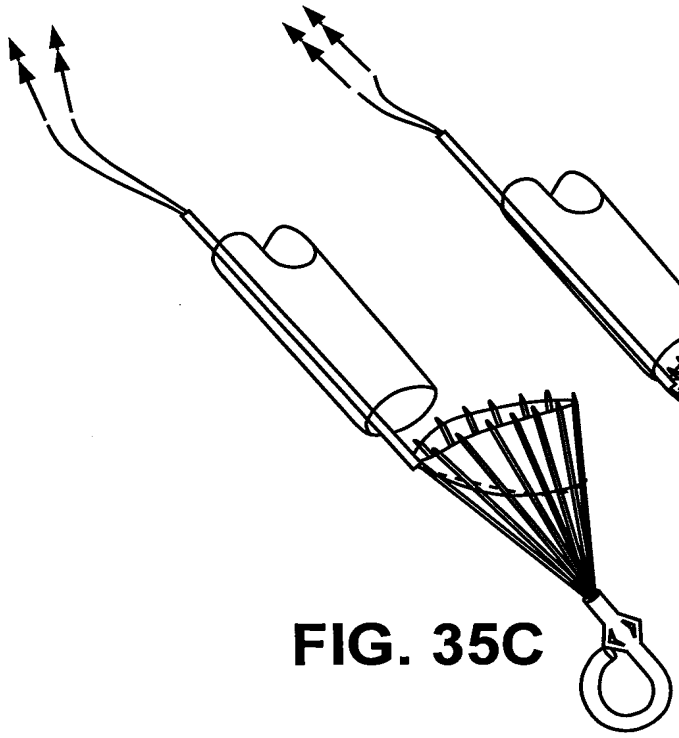


FIG. 35C

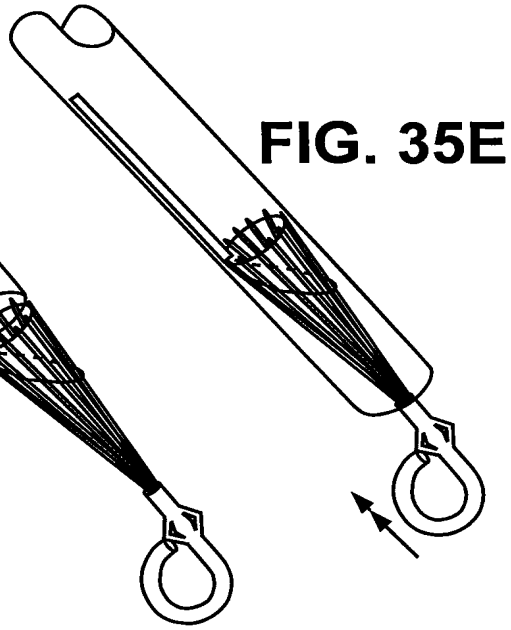


FIG. 35E

FIG. 35D

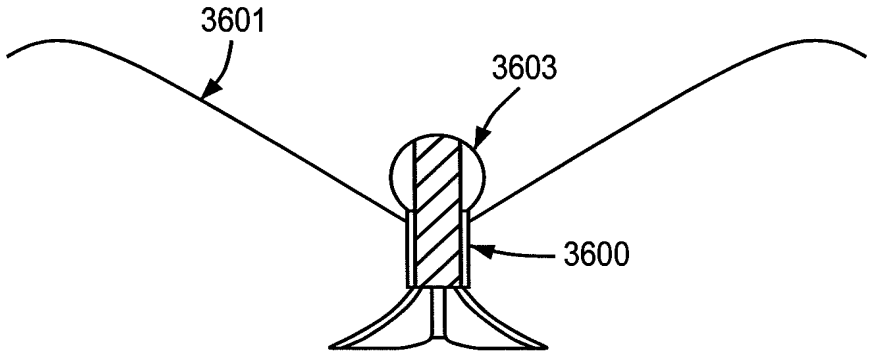


FIG. 36A

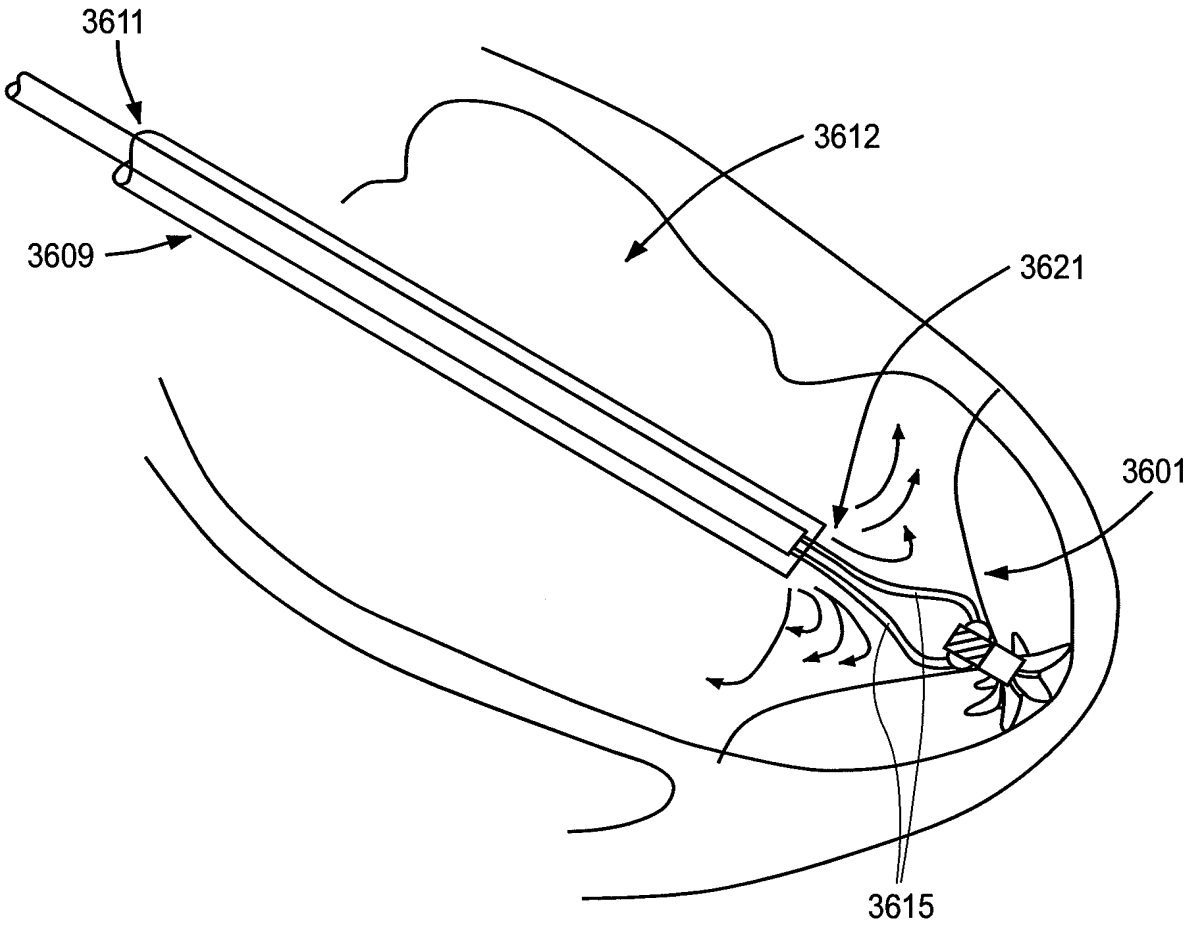


FIG. 36B

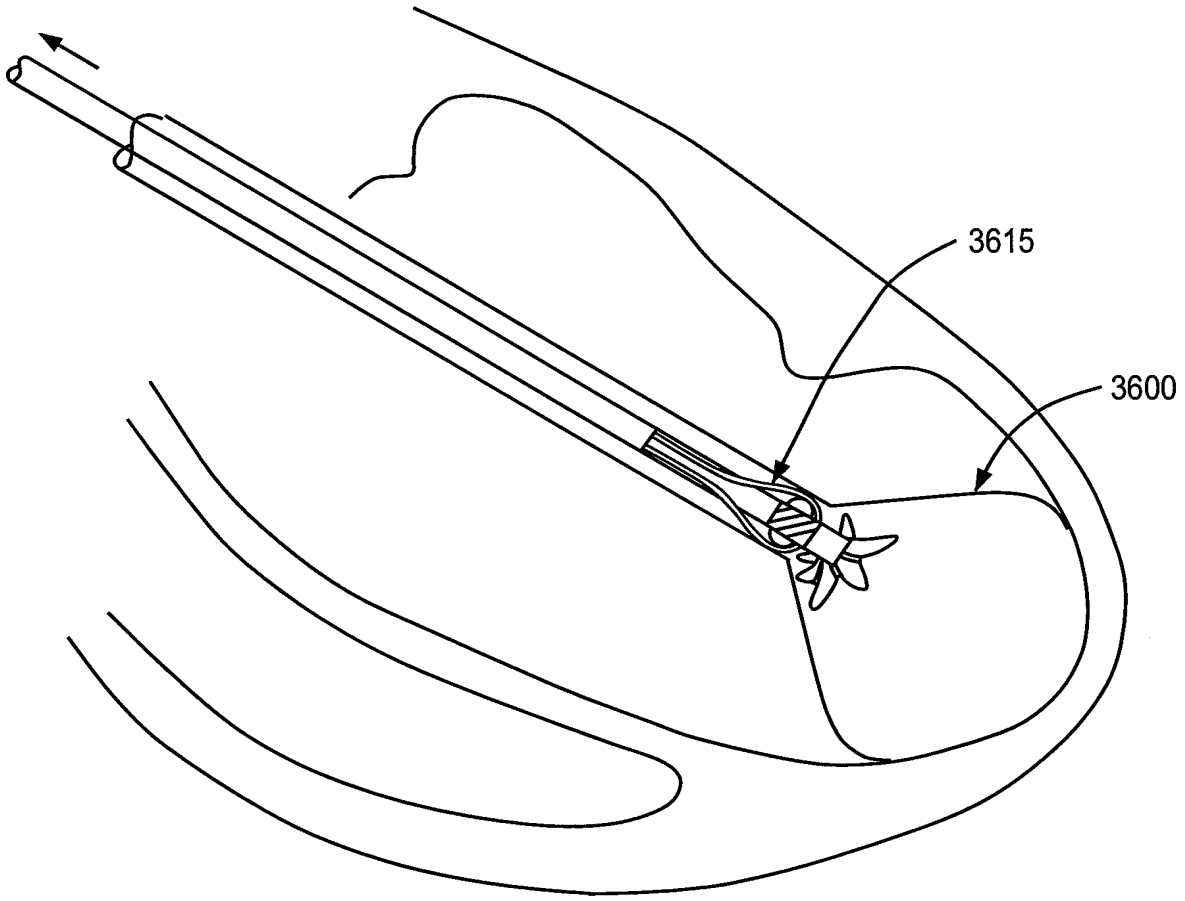


FIG. 36C

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2008/074217

A. CLASSIFICATION OF SUBJECT MATTER
INV. A61B17/12 A61F2/00 A61B17/22

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
A61B A61F

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2006/281965 A1 (KHAIRKHAHAN ET AL.) 14 December 2006 (2006-12-14) abstract; figures 1-4,8,13-13K,14-16 paragraphs [0049] - [0052], [0054], [0058]	3,4,7,11
Y		5,6,8,10
A		16
X	US 2007/129753 A1 (QUINN ET AL.) 7 June 2007 (2007-06-07) abstract; figure 11 paragraphs [0082] - [0088]	3,9
Y	WO 03/073961 A (SALVIAC LIMITED) 12 September 2003 (2003-09-12) abstract; figures 1,8-15,167-171,179-182,219-226,263,264	5,6
	-/--	

[X] Further documents are listed in the continuation of Box C.

[X] See patent family annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

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"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

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Date of the actual completion of the international search	Date of mailing of the international search report
8 July 2009	17/07/2009

Name and mailing address of the ISA/	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016	Giménez Burgos, R

Form PCT/ISA/210 (second sheet) (April 2005)

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2008/074217

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 2005/085826 A1 (NAIR ET AL.) 21 April 2005 (2005-04-21) paragraphs [0040] - [0042]; figures 10-12	8
X	WO 02/071977 A (ATRITECH, INC.) 19 September 2002 (2002-09-19) abstract; figures 3-7 page 17, line 1 - page 19, line 8	12-15
Y		10
A	US 2006/264980 A1 (KHAIRKHAHAN ET AL.) 23 November 2006 (2006-11-23) paragraphs [0125], [0141] - [0144], [0156], [0157]; figures 4,13A-13k	3,11
A	WO 2004/047679 A (CARDIOKINETIX, INC.) 10 June 2004 (2004-06-10) the whole document	3,11
A	US 2008/045778 A1 (LICHTENSTEIN ET AL.) 21 February 2008 (2008-02-21) the whole document	3
A	US 2007/162048 A1 (QUINN ET AL.) 12 July 2007 (2007-07-12) the whole document	3-5,7,10
A	US 2004/172042 A1 (SUON ET AL.) 2 September 2004 (2004-09-02) figures	3

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2008/074217

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. [X] Claims Nos.: 1,2,22-27
because they relate to subject matter not required to be searched by this Authority, namely:

Rule 39.1(iv) PCT - Method for treatment of the human or animal body by surgery

2. [ ] Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. [ ] Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. [X] As all required additional search fees were timely paid by the applicant, this international search report covers allsearchable claims.

2. [ ] As all searchable claims could be searched without effort justifying an additional fees, this Authority did not invite payment of additional fees.

3. [ ] As only some of the required additional search fees were timely paid by the applicant, this international search reportcovers only those claims for which fees were paid, specifically claims Nos.:

4. [ ] No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

[ ] The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.

[ ] The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.

[X] No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 3-11

   An applicator configured to insert and retrieve an implant into a patient's ventricle.

   ---

2. claims: 12-21

   An expandable device for partitioning a patient's ventricle comprising means to facilitate the collapse of the expandable device into its reduced configuration.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/US2008/074217

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 2006281965 A1	14-12-2006	AU 2006257971 A1	21-12-2006
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US 2008045778 A1	21-02-2008	NONE	
US 2007162048 A1	12-07-2007	NONE	
US 2004172042 A1	02-09-2004	NONE	

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International Bureau

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(51) International Patent Classification:
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(21) International Application Number:
PCT/US2008/075504

(22) International Filing Date:
5 September 2008 (05.09.2008)

(25) Filing Language: English

(26) Publication Language: English

(71) Applicant *(for all designated States except US)*: **MERLIN MD PTE LTD** [SG/SG]; 29 Woodlands Industrial Park E1, #04-13/14 Northtech Lobby 3, Singapore 757716 (SG).

(72) Inventor; and
(75) Inventor/Applicant *(for US only)*: **RUDAKOV, Leon** [US/US]; 1797 Playa Vista, San Marcos, CA 92078 (US).

(74) Agent: **HILL, James, W.**; MCDERMOTT WILL & EMERY LLP, 18191 Von Karman, Suite 500, Irvine, CA 92612 (US).

(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(84) Designated States *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, NO, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

— *with international search report (Art. 21(3))*

(54) **Title**: ENDOVASCULAR DEVICE

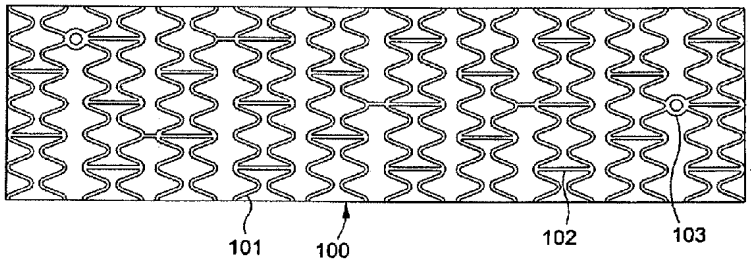

FIG. 1A

(57) **Abstract**: Embodiments of an endovascular device and of methods for treating an aneurysm therewith are described. In certain embodiments, an endovascular device includes a distal assembly coupled to a flow reducing member. In some embodiments, the distal assembly is composed of multiple engagement members that, when deployed within an aneurysm, engage an inner surface of the aneurysm. In certain embodiments, the engagements members are substantially parallel to a central axis of the distal assembly in a first position and shift away from the central axis to a second position, and the distal ends of some engagement members are substantially curled when in the second position. In certain embodiments, the flow-reducing member reduces blood flow from a blood vessel into the aneurysm. In certain embodiments the flow reducing member includes a membrane, which can include a porous section.

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ENDOVASCULAR DEVICE

Field of the Invention

[0001] The invention concerns an endovascular device for insertion into a bodily vessel to treat a diseased, damaged, or weakened portion of a vessel.

Background of the Invention

[0002] Vascular diseases include aneurysms causing hemorrhage, atherosclerosis causing occlusion of blood vessels, vascular malformation, and tumors. Vessel occlusion or rupture of an aneurysm within the brain can result in stroke. Aneurysms fed by intracranial arteries can grow within the brain to a point where their size can also cause a stroke or the symptoms of a stroke, requiring surgery to remove the aneurysm, or other remedial intervention.

[0003] Occlusion of coronary arteries is a common cause of heart attack. Diseased and obstructed coronary arteries result in restricted blood flow in the heart which can lead to ischemia or necrosis. While the exact etiology of sclerotic cardiovascular disease is still in question, the treatment of narrowed coronary arteries is more defined. Surgical construction of coronary artery bypass grafts (CABG) is often the method of choice when there are several diseased segments in one or multiple arteries. Conventional open-heart surgery is of course highly invasive and traumatic for patients undergoing such procedures. Therefore, less invasive procedures that accomplish the same goals are highly desirable.

[0004] One alternative method of treatment involves the use of balloon angioplasty as a way in which to reopen the lumen of an occluded vessel. In this procedure a folded balloon is inserted via a catheter into a stenosed region that is either partially or fully occluding the vessel lumen. Inflation of the balloon physically expands the lumen, reopening the occluded region, and restoring normal or at least significantly improved blood flow through the vessel. Alternatively, occlusive atheromas may be cut from the inner surface, a procedure known as atherectomy. In both methods, a certain incidence of restenosis (resealing) occurs resulting in a loss of the benefit of the procedure, and potentially the need for additional rounds of therapy. Restenosis also results in reversion back to the original occluded condition, such that the vessel no longer

conducts a normal flow volume, which can lead to ischemia or infarct depending on the particular location and function of the vessel in question.

[0005] A recent preferred therapy for repairing vascular occlusions involves placement of an expandable metal wire-frame (i.e. a stent) within the occluded region of a blood vessel in order to keep the lumen of the vessel open. Stents are generally delivered to the desired location within a vascular system by an intraluminal route, usually via a catheter. Advantages of the stent placement method over conventional vascular surgery include obviating the need for surgically exposing, removing, replacing, or by-passing the defective blood vessel, including heart-lung bypass, opening the chest and in some cases general anaesthesia.

[0006] When inserted and deployed in a vessel, duct or tract (all of which can be conveniently referred to as a vessel) of the body, for example, a coronary artery after dilation of the artery by balloon angioplasty, a stent acts as a prosthesis to maintain the vessel in an open state, thus providing a fluid pathway in the previously occluded vessel. The stent usually has an open-ended tubular form with interconnected struts as its sidewall to enable its expansion from a first outside diameter which is sufficiently small to allow the stent to traverse the vessel lumen and be delivered to a site where it is to be deployed, then expanded to a second outside diameter sufficiently large to engage the inner lining of the vessel for retention at that site. The stent may be expanded via the use of a mechanical device, for example a pressurizable balloon, or alternatively the stent may be self-expanding. Self-expanding stents can be manufactured at a to be deployed size, and then compressed to a smaller size to enable delivery, or may be manufactured from shape memory materials that are deformable to a memorized shape in response to an externally applied energy.

[0007] Usually a stent suitable for successful interventional placement should be hypoallergenic, or preferably non-allergenic, have good radio-opacity to permit radiographic visualization, free from distortion during magnetic resonance imaging (MRI), plastically deformable, resistant to vessel recoil, and be as thin as possible to minimize obstruction to blood flow (or other materials or fluids in vessels other than those of the cardiovascular system), and be relatively non-reactive in terms of eliciting thrombogenic responses.

[0008] The typical reaction when a foreign body is implanted in a body vessel is generally negative. Foreign bodies frequently cause an inflammatory response, and in the case of blood vessels, neointimal proliferation which results in narrowing and occlusion of the body vessel, obviating the benefit of the implant. As a result, both selection of the materials from which the stent is composed, as well as the design of the stent, play an important role in influencing the final suitability of the device in practice. Therefore, in addition to the structural requirements for a stent to maintain a previously occluded vessel in a substantially open conformation, stents must also be biologically compatible, and must be chemically stable when exposed to a biological environment.

[0009] A variety of materials have been tested and used in stents to address the issues of biocompatibility and material stability. For example, polyurethanes have been used in long term implants, but are not always suitable for use in endovascular treatments, especially in small blood vessels. Small blood vessels are considered to be those with an inner diameter of 2.0 to 5.0 mm. In addition, many commercially available polymers are with additives, or have impurities, that are surface-active and so reduce their usefulness in some biological applications.

[0010] More recently, polymers have been developed which can be further modified by the covalent attachment of various surface-modifying end groups, these end groups reducing the reactivity of the material with cells and other factors that function in the immune response. End groups can also be useful in providing greater chemical stability to the material, reducing degradation and improving the longevity of the prosthesis. For example, U.S. Patent No. 5,589,563 (Ward & White) discloses a series of biomedical base polymers with covalently attached end groups that give the polymer certain desirable properties. These modified polymers possess surface properties that improve the biocompatibility and overall performance of objects fashioned from them.

[0011] In addition to their biomechanical functionality, implantable medical devices like stents have been utilized for delivery of drugs or bioreagents for different biological applications. U.S. Patent 5,891,108 (Leone *et al.*) discloses a hollow tubular wire stent with holes through which an active substance can be delivered to a site in a vessel. In some cases the drugs or bioreagents can be coated directly onto the surface of the implantable medical devices or mixed with polymeric materials that are then applied

to the surface of the devices. For example, U.S. Patent No. 5,599,352 (Dinh *et al.*) discloses a drug eluting stent comprising a stent body, a layer of a composite of a polymer combined with a therapeutic substance, overlaid by a second layer comprising fibrin.

[0012] However, each of these methods suffers from one or more problems including poor control of release or limitations of the form of drug or other reagent that can be applied. Also, these methods are unsuitable for situations where it would be desirable to maintain the bioactive molecule on the device rather than having it be released, in order to maintain a relatively high local activity of the reagent of interest.

[0013] As a result, in practice, the design and use of stents in the repair of aneurysms or other vessel defects or diseases typically represents a compromise among competing factors. First, the stent must adequately support the diseased or weakened region in order to prevent rupture of the aneurysm or vessel during and after stent placement, either of which could lead to serious complications including death, depending on the size, location and nature of the aneurysm or defect. Second, in the case of stents use in the repair of aneurysms, the stent must permit sufficient blood supply to maintain the patency of both the parent and perforator vessels, while at the same time limiting flow to the aneurysm proper. Generally speaking, flow of material through the framework of a stent is achieved by regulating the porosity of the stent.

[0014] Stent porosity can be managed in a number of ways. The simplest way is to manufacture the stent so that the framework itself defines the porosity of the device. However, in biological applications, regulating movement of materials on cellular or subcellular scale is required, and it is difficult and costly to manufacture stents that have such fine effective pore size. Other approaches have been to cover the stent framework for example with a membrane, where the membrane is either impermeable or porous as desired. U.S. Patent Application No. 2006/0217799 (Mailander *et al.*) discloses a stent comprising a grid or mesh structure in which one or more cells of the grid are covered with a membrane. Similarly, U.S. Patent Application No. 2006/0200230 (Richter) discloses a covering for an endoprosthetic device that comprises a sheath with holes of varying size and varying frequency disposed in different areas of the sheath.

[0015] However, a problem inherent with these designs is that they are not easily adapted for effecting vessel wall repairs where the area of disease, damage or weakness can vary in size. Thus, in order to optimally treat an aneurysm, it would be necessary to tailor the stent and its covering to more or less the precise size of the damaged area, in order to properly occlude the aneurysm site, while maintaining vessel patency in the parent vessel and any perforator vessels. Furthermore, these designs are not optimized such that they will generally provide flow to perforator vessels that are part of the collateral circulation in the area of the diseased, damaged, or weakened vessel, while blocking flow to an aneurysm.

Summary of the Invention

[0016] Some embodiments of the present invention provide an endovascular device, for treating an aneurysm of a body vessel, comprising a distal assembly, movable from a first position to a second position when the distal assembly is at least partially in an aneurysm; and a first flow-reducing member, coupled to the distal assembly, that reduces blood flow from the body vessel into the aneurysm when the distal assembly is in the second position; wherein the distal assembly comprises a plurality of engagement members, each of which extends, from a proximal portion to a distal portion, away from the flow-reducing member, and, when the distal assembly is in the first position, each of the plurality of engagement members is substantially parallel to a central axis of the distal assembly, and, when the distal assembly changes from the first to the second position, the distal portion of each of the plurality of engagement members moves away from the central axis, such that the distal portions of each of the plurality of engagement members: substantially curl; move closer to the first flow-reducing member; and engage an inner surface of the aneurysm.

[0017] In certain embodiments, an endovascular device of the invention comprises a mass and/or a volume less than a mass and/or a volume of known aneurysm "coil" devices, which provides such an endovascular device of the present invention with surprisingly improved properties in regard to aneurismal mass effects, in regard to pressure effects on nerve tissue at or near the aneurysm deployment site, and in regard to allowing for aneurysmal shrinkage over time. In certain embodiments, an endovascular

device of the invention comprises a flow reducing member that resides entirely within the aneurysm and has no impact on branch vessels in a proximity of the aneurysm.

[0018] As used herein, the term "curl" encompasses forming a linear element into a curved two-dimensional or three-dimensional shape, or a curved element into a shape having a different curvature. The term "curl" also includes bending a structure such as a structure having a joint. The "curl" or bend can be at the joint or elsewhere in the structure.

[0019] In some embodiments, at least one of the plurality of engagement members comprises a polymer. In some embodiments, the polymer comprises at least one member selected from the group consisting of polyurethane, polyethylene terephthalate, expanded polytetrafluoroethylene (ePTFE), polyvinylchloride, nylon, polyimide, polyurethane ether, polyurethane ester, polyurethaneurea, polylactide, polyglycolide, poly-orthoester, polyphosphazene, polyanhydride, and polyphosphoester.

[0020] In some embodiments, at least one of the plurality of engagement members comprises a metal. In some embodiments, the metal comprises at least one member selected from the group consisting of NiTi, tungsten, stainless steel, iridium, platinum, alloys and/or joined combinations thereof.

[0021] In some embodiments, a distal end of at least one of the plurality of engagement members is blunt.

[0022] In some embodiments, when the distal assembly is in the second position, a distal end of each of the plurality of engagement members engages the inner surface of the aneurysm.

[0023] In some embodiments, when the distal assembly is in the second position, the first flow-reducing member resides in the body vessel.

[0024] In some embodiments, when the distal assembly is in the second position, the first flow-reducing member resides in the aneurysm.

[0025] In some embodiments, an endovascular device comprises a second flow-reducing member, coupled to the first flow-reducing member or to the distal assembly.

[0026] In some embodiments, the distal assembly is in the second position, the first flow-reducing member resides in the body vessel and the second flow-reducing member resides in the aneurysm.

[0027] In some embodiments, an endovascular device comprises a linking member that couples the second flow-reducing member to the first flow-reducing member or to the distal assembly.

[0028] In some embodiments, at least one of the linking member, the distal assembly, the first flow-reducing member, and the second flow-reducing member comprises a metal.

[0029] In some embodiments, at least one of the linking member, the distal assembly, the first flow-reducing member, and the second flow-reducing member comprises at least one metal selected from the group consisting of NiTi, tungsten, stainless steel, iridium, and platinum.

[0030] In some embodiments, the linking member comprises a wire.

[0031] In some embodiments, each of the linking member, the first flow-reducing member, the second flow-reducing member, and the distal assembly comprises a metal, and wherein a weld couples the linking member to at least one of the distal assembly, the first flow-reducing member, and the second flow-reducing member.

[0032] In some embodiments, the second flow-reducing member comprises a plug that substantially resides within a neck of the aneurysm and substantially inhibits blood flow through the neck.

[0033] In some embodiments, the first flow-reducing member comprises a membrane.

[0034] In some embodiments, when the distal assembly is in the second position within the aneurysm, a thickness of the membrane is between about 5 μm and about 500 μm.

[0035] In some embodiments, the membrane comprises at least one polymer selected from the group consisting of ePTFE, polyurethane, polyethylene terephthalate, polyvinylchloride, nylon, , polyimide, silicone, polyurethane ether, polyurethane ester, polyurethaneura, polylactide, polyglycolide, poly-orthoester, polyphosphazene, polyanhydride, and polyphosphoester.

[0036] In some embodiments, the first flow-reducing member is coupled to the distal assembly by suture or by interweaving.

[0037] In some embodiments, at least a portion of the membrane is non-porous.

[0038] In some embodiments, the membrane comprises a porous section having a porosity over a length extending from a proximal end of the porous section to a distal end of the porous section, wherein a pore spacing and a pore size of the porous section determine the porosity of the porous section, and wherein, when the distal assembly is in the second position, the membrane is effective to reduce blood flow into the aneurysm and to promote thrombosis at or in the aneurysm.

[0039] In some embodiments, a membrane porosity is selected such that, when the distal assembly is in the second position, the porous section of the membrane is effective to enhance endothelial cell migration and tissue growth onto the membrane and to substantially inhibit blood flow from the body vessel into the aneurysm.

[0040] In some embodiments, the pore size is between about 1 μm and about 150 μm. In some embodiments, the pore size is between about 10 μm and about 50 μm.

[0041] In some embodiments, the pore spacing is between about 40 μm and about 100 μm. In some embodiments, the pore spacing is between about 60 μm and about 75 μm.

[0042] In some embodiments, a material ratio of the porous section of the membrane comprises a ratio of a total area of an outer surface of the porous section of the membrane that comprises material to a total area of an outer surface of the porous section that comprises pores.

[0043] In some embodiments, when the distal assembly is in the second position, the material ratio is between about 25% and about 90%. In some embodiments, when the distal assembly is in the second position, the material ratio is between about 70% and about 80%. In some embodiments, when the distal assembly is in the second position within the aneurysm, the material ratio is about 75%.

[0044] In some embodiments, an endovascular device comprises at least one surface-modifying end group that, when the distal assembly is in the second position, promotes healing of the body vessel. In some embodiments, the at least one surface-modifying end group comprises at least one of a fluorocarbon and the combination of polyethylene glycol and silicon.

[0045] In some embodiments, an endovascular device comprises at least one agent, permanently attached to the membrane, that promotes healing of the aneurysm. In

some embodiments, the healing agent comprises at least one of a peptide, a protein, an enzyme regulator, an antibody, a nucleic acid, and a polynucleotide. In some embodiments, an endovascular device comprises an endothelial cell inhibiting agent, such as L-PDMP. In some embodiments, an endovascular device comprises an endothelial cell inducing agent, such as D-PDMP.

[0046] Some embodiments of the present invention provide an endovascular device, for treating an aneurysm of a body vessel, comprising means for engaging an inner surface of an aneurysm, the means for engaging being movable from a first position to a second position when the means for engaging is at least partially within an aneurysm; and a first means for reducing blood flow into the aneurysm, the means for reducing blood flow coupled to the means for engaging such that, when the means for engaging is in the second position, the first means for reducing blood flow is effective to reduce blood flow from the body vessel into the aneurysm; wherein the means for engaging comprises a plurality of engagement members, each of which extends, from a proximal portion to a distal portion, away from the flow-reducing member, and wherein, when the means for engaging is in the first position, each of the plurality of engagement members is substantially parallel to a central axis of the distal assembly, and wherein, when the means for engaging changes from the first to the second position, the distal portion of each of the plurality of engagement members moves away from the central axis, such that the distal portions of each of the plurality of engagement members: substantially curl; move closer to the first flow-reducing member; and engage an inner surface of the aneurysm.

[0047] In some embodiments, an endovascular device comprises a second means for reducing blood flow into the aneurysm, coupled to the first flow-reducing member and effective to reduce blood flow into the aneurysm when the means for engaging is in the second position. In some embodiments, when the means for engaging is in the second position, the first flow-reducing means resides in the body vessel and the second flow-reducing means resides in the aneurysm.

[0048] Some embodiments of the present invention provide a method of treating an aneurysm of a body vessel comprising providing an endovascular device comprising a distal assembly, movable from a first position to a second position when the distal

assembly is at least partially within an aneurysm, the distal assembly comprising a plurality of engagement members, each of which extends, from a proximal portion to a distal portion, away from the flow-reducing member and each of which, when the distal assembly is in the first position, is substantially parallel to a central axis of the distal assembly; and a first flow-reducing member, coupled to the distal assembly, that reduces blood flow from the body vessel into the aneurysm when the distal assembly is in the second position; positioning the distal assembly at least partially within the aneurysm; and changing the distal assembly from the first position to the second position such that the distal portion of each of the plurality of engagement members moves away from the central axis, whereby the distal portions of each of the plurality of engagement members: substantially curl; move closer to the first flow-reducing member; and engage an inner surface of the aneurysm.

[0049] Some embodiments of the present invention provide an endovascular device, for treating an aneurysm of a body vessel, comprising: a distal assembly, comprising an engagement member, the distal assembly being movable from a first position to a second position when the distal assembly is at least partially in the aneurysm; a flow-reducing assembly, coupled to the distal assembly and comprising a first flow-reducing member, the flow-reducing assembly reducing blood flow from the body vessel into the aneurysm when the distal assembly is in the second position; wherein the engagement member is elongate and curvilinear and extends, from a proximal to a distal end of the engagement member, along a path that originates from a point at the flow-reducing assembly and terminates at a point within the aneurysm when the first flow-reducing member resides in the body vessel; wherein the engagement member is coterminous with the path; wherein, when the distal assembly is in the second position in the aneurysm, the first flow-reducing member resides in the body vessel, a first portion of the engagement member engages a first region of an inner surface of the aneurysm, and a second portion of the engagement member engages a second region of the inner surface of the aneurysm; wherein the first and second regions are spaced at least 2 mm apart. In some embodiments, the flow-reducing assembly further comprises a second flow-reducing member; wherein, when the second flow-reducing member resides

at least partially in the aneurysm, and the distal assembly is in the second position, the first flow-reducing member resides in the body vessel.

[0050] In some embodiments, a form of an engagement member comprises a curve. In some embodiments, a form of at least a portion of the engagement member is helical.

[0051] In some embodiments, the first and the second regions of the inner surface of the aneurysm are spaced at least 4 mm apart. In some embodiments, the first and second portions of the engagement member are spaced at least 2 mm apart. In some embodiments, the first portion and the second portion of the engagement member are spaced at least 4 mm apart.

[0052] Some embodiments of the present invention provide an endovascular device for insertion into a body vessel to treat an aneurysmal portion of the body vessel, the endovascular device comprises: an expandable member, expandable from a first position to a second position, said expandable member being expandable radially outwardly to the second position such that an outer surface of said expandable member engages with an inner surface of the vessel so as to maintain a fluid pathway in said vessel through a lumen in the expandable member; a membrane covering at least a portion of an outer surface of said expandable member; a plurality of pores in a porous section of the membrane, the porous section having a substantially uniform porosity over a length extending from a proximal end to a distal end of the porous section, porosity being determined by a pore spacing and a pore size; wherein the proportion of the total area of an outer surface of the porous section that consists of membrane material defines a material ratio; wherein the substantially uniform porosity is selected such that, when the expandable member is positioned in the body vessel, the membrane permits a flow of blood from within the lumen of the expandable member, through at least one of the pores, and into at least one branch vessel that branches off of the body vessel; and wherein the substantially uniform porosity is further selected such that, when the expandable member is positioned in the body vessel, the membrane reduces blood flow to the aneurysmal portion of the vessel, promoting thrombosis at or in the aneurysmal portion.

[0053] In some embodiments, the porosity of the porous section is selected such that it enables enhanced endothelial cell migration and tissue in-growth for

endothelialization of the neck bridge while substantially preventing blood circulation to the diseased, damaged or weakened portion of the vessel wall.

[0054] In some embodiments, an endovascular device of the invention deployed within an aneurysm can be supported in that position by an endovascular device deployed in a body vessel at or near the aneurysm.

[0055] In some embodiments, the pore size is between about 1 μm and about 150 μm.

[0056] In some embodiments, the pore size is between about 10 μm and about 50 μm.

[0057] In some embodiments, the pore spacing is between about 40 μm and about 100 μm.

[0058] In some embodiments, the pore spacing is between about 60 μm and about 75 μm.

[0059] In some embodiments, the material ratio in an as-manufactured state is between about 85% and about 96%.

[0060] In some embodiments, the material ratio in a deployed state is between about 25% and about 90%.

[0061] In some embodiments, the material ratio in the deployed state is between about 70% and about 80%.

[0062] In some embodiments, the material ratio in the deployed state is about 75%.

[0063] In some embodiments, a diameter of the device in the deployed state is between about 2 mm and about 5 mm.

[0064] In some embodiments, a thickness of the membrane is between about 25 μm to about 125 μm.

[0065] In some embodiments, the thickness of the membrane is measured in an as-manufactured state.

[0066] In some embodiments, a thickness of the membrane is between about 5 μm to about 25 μm.

[0067] In some embodiments, the thickness of the membrane is measured in a deployed state.

[0068] In some embodiments, the device further comprises at least one surface-modifying end group that promotes healing of the body vessel after the device is inserted into the body vessel.

[0069] In some embodiments, the surface-modifying end group comprises at least one of a fluorocarbon and the combination of polyethylene glycol and silicon.

[0070] In some embodiments, the device further comprises at least one agent, permanently attached the membrane, that promotes healing of the aneurysm.

[0071] In some embodiments, at least one permanently attached agent comprises at least one of a peptide, a protein, an enzyme regulator, an antibody, a naturally occurring molecule, a synthetic molecule, a nucleic acid, a polynucleotide, L-PDMP, and D-PDMP.

[0072] In some embodiments, each pore has a diameter between about 30 μm and about 40 μm, and a distance between adjacent pores is between about 60 μm and about 70 μm.

[0073] In some embodiments, the aneurysmal portion of the vessel is located at or near at least one of an intracranial aneurysm, a saccular aneurysm, a wide-neck aneurysm, a fusiform aneurysm, a caroticocavernous fistula, an arteriovenous malformation, a carotid artery stenosis, a saphenous vein graft, a small vessel stenosis, and a renal artery repair.

[0074] In some embodiments, the porous section can be divided into n porous regions, and wherein an outer surface area of each of the n porous regions is substantially $1/n$ of a total outer surface area of the porous segment, and wherein each one of the n porous regions has substantially the same porosity as each of the other $n-1$ porous regions.

[0075] In some embodiments, $n = 2$.

[0076] In some embodiments, $n = 3$.

[0077] In some embodiments, $n = 4$.

[0078] In some embodiments, $n = 5$.

[0079] In some embodiments, the pore size is in a range between about 1 μm and about 150 μm, and pore spacing is between about 10 μm and about 50 μm.

[0080] In some embodiments, the pore size is between about 10 μm and about 50 μm, and the pore spacing is between about 60 μm and about 75 μm.

[0081] In some embodiments, an endovascular device system for insertion into a body vessel to treat an aneurysmal portion of the vessel, the endovascular device comprises: an expandable member, expandable from a first position to a second position, said expandable member being expandable radially outwardly to the second position such that an outer surface of said expandable member engages with an inner surface of the vessel so as to maintain a fluid pathway in said vessel through a lumen in the expandable member; a membrane covering at least a portion of an outer surface of said expandable member; a plurality of pores in a porous section of the membrane, the porous section having a substantially uniform porosity over a length extending from a proximal end to a distal end of the porous section, porosity being determined by a pore spacing and a pore size; wherein the proportion of the total area of an outer surface of the porous section that consists of membrane material defines a material ratio; wherein the substantially uniform porosity is selected such that, when the expandable member is positioned in the body vessel, the membrane permits a flow of blood from within the lumen of the expandable member, through at least one of the pores, and into at least one branch vessel that branches off of the body vessel; and wherein the substantially uniform porosity is further selected such that, when the expandable member is positioned in the body vessel, the membrane reduces blood flow to the aneurysmal portion of the vessel, promoting thrombosis at or in the aneurysmal portion; and a delivery device, operable to deliver the expandable member to the aneurysmal portion of the vessel, onto which the expandable member is loaded prior to delivery.

[0082] In some embodiments, the pore size is between about 1 μm and about 150 μm.

[0083] In some embodiments, the pore size is between about 10 μm and about 50 μm.

[0084] In some embodiments, the pore spacing is between about 40 μm and about 100 μm.

[0085] In some embodiments, the pore spacing is between about 60 μm and about 75 μm.

[0086] In some embodiments, the material ratio in an as-manufactured state is between about 85% and about 96%.

[0087] In some embodiments, the material ratio in a deployed state is between about 25% and about 80%.

[0088] In some embodiments, the material ratio in the deployed state is between about 70% and about 80%.

[0089] In some embodiments, the material ratio in the deployed state is about 75%.

[0090] In some embodiments, a diameter of the expandable member in the deployed state is between about 2 mm and about 5 mm

[0091] In some embodiments, a thickness of the membrane is between about 25 μm to about 125 μm.

[0092] In some embodiments, the thickness of the membrane is measured in an as-manufactured state.

[0093] In some embodiments, a thickness of the membrane is between about 5 μm to about 25 μm.

[0094] In some embodiments, the thickness of the membrane is measured in a deployed state.

[0095] In some embodiments, the system further comprises at least one surface-modifying end group that promotes healing of the body vessel after the device is inserted into the body vessel.

[0096] In some embodiments, the at least one surface-modifying end group is at least one of a fluorocarbon and the combination of polyethylene glycol and silicon.

[0097] In some embodiments, the system further comprises at least one permanently attached agent to promote healing of the aneurysmal portion.

[0098] In some embodiments, the at least one permanently attached agent comprises at least one of a peptide, a protein, an enzyme regulator, an antibody, a naturally occurring molecule, a synthetic molecule, a nucleic acid, a polynucleotide, L-PDMP, and D-PDMP.

[0099] In some embodiments, each pore has a diameter between about 10 μm and about 50 μm and the distance between adjacent pores is between about 60 μm and about 75 μm.

[0100] In some embodiments, the aneurysmal portion of the body vessel is located at or near at least one of an intracranial aneurysm, a saccular aneurysm, a wide-neck aneurysm, a fusiform aneurysm, a caroticocavernous fistula, an arteriovenous malformation, a carotid artery stenosis, a saphenous vein graft, a small vessel stenosis, and a renal artery repair.

[0101] In some embodiments, an endovascular device for insertion into a body vessel to treat an aneurysmal portion of a body vessel, the endovascular device comprises: means for maintaining a fluid pathway in the body vessel; means for covering at least part of the means for maintaining, the means for covering having a substantially uniform porosity in a porous segment of the means for covering; and wherein, when the means for maintaining is positioned in a body vessel, the means for covering permits blood flow from the fluid pathway to at least one branch vessel branching off the body vessel, while reducing blood flow to the aneurysmal portion, and the means for maintaining supports the body vessel in the region of the aneurysmal portion and provides a fluid pathway in the body vessel.

[0102] In some embodiments, a method of treating a body vessel having an aneurysmal portion comprises the steps of: providing an endovascular device, comprising: an expandable member, expandable from a first position to a second position, said expandable member being expandable radially outwardly to the second position such that an outer surface of said expandable member engages with an inner surface of the body vessel so as to maintain a fluid pathway in said body vessel through a lumen in the expandable member; a membrane covering at least a portion of an outer surface of said expandable member; a plurality of pores in a porous section of the membrane, the porous section having a substantially uniform porosity over a length extending from a proximal end to a distal end of the porous section, porosity being determined by a pore spacing and a pore size; wherein the proportion of the total area of an outer surface of the porous section that consists of membrane material defines a material ratio; wherein the substantially uniform porosity is selected such that, when the

expandable member is positioned in the body vessel, the membrane permits a flow of blood from within the lumen of the expandable member, through at least one of the pores, and into at least one branch vessel that branches off of the body vessel; and wherein the substantially uniform porosity is further selected such that, when the expandable member is positioned in the body vessel, the membrane reduces blood flow to the aneurysmal portion of the body vessel, promoting thrombosis at or in the aneurysmal portion; and positioning the expandable member in the body vessel.

[0103] In some embodiments, the porosity of the membrane is selected such that it enhances endothelial cell migration and tissue in-growth.

[0104] In some embodiments, the pore size is between about 1 μm and about 150 μm.

[0105] In some embodiments, the pore size is between about 10 μm and about 50 μm.

[0106] In some embodiments, the pore spacing is between about 40 μm and about 100 μm.

[0107] In some embodiments, the pore spacing is between about 60 μm and about 75 μm.

[0108] In some embodiments, the material ratio in an as manufactured state is between about 85% and about 96%.

[0109] In some embodiments, the material ratio in a deployed state is between about 25% and about 80%.

[0110] In some embodiments, the material ratio in the deployed state is between about 70% and about 80%.

[0111] In some embodiments, the material ratio in the deployed state is about 75%.

[0112] In some embodiments, a diameter of the expandable member in the deployed state is between about 2 mm and about 5 mm.

[0113] In some embodiments, a thickness of the membrane is between about 25 μm to about 125 μm in the as-manufactured state.

[0114] In some embodiments, a thickness of the membrane is between about 5 μm to about 25 μm in the deployed state.

[0115] In some embodiments, the method further comprises providing a membrane having at least one surface-modifying end group that encourages healing of the body vessel after the device is inserted.

[0116] In some embodiments, the at least one surface-modifying end group is at least one of a fluorocarbon and the combination of polyethylene glycol and silicon.

[0117] In some embodiments, the membrane further comprises at least one permanently attached agent to promote healing of the aneurysm.

[0118] In some embodiments, the at least one permanently attached agent comprises at least one of a peptide, a protein, an enzyme regulator, an antibody, a naturally occurring molecule, a synthetic molecule, a nucleic acid, a polynucleotide, L-PDMP. and D-PDMP.

[0119] An endovascular device, for treating an aneurysm of a body vessel, comprising: a distal assembly comprising an engagement member, the distal assembly being movable from a first position to a second position when the distal assembly is at least partially in an aneurysm; a flow-reducing assembly comprising a first flow-reducing member and coupled to the distal assembly, the flow-reducing assembly reduces blood flow from the body vessel into the aneurysm when the distal assembly is in the second position; wherein the engagement member comprises an elongate and curvilinear form which follows a path originating from a point on the flow-reducing assembly and terminating at a point within the aneurysm; wherein the engagement member is coterminous with the path; wherein a space exists between the origination and termination points of the path; wherein, when the distal assembly is in the second position in the aneurysm, the first flow-reducing member resides in the body vessel, a first portion of the engagement member engages a first region of an inner surface of the aneurysm, and a second portion of the engagement member engages a second region of the inner surface of the aneurysm; wherein the first and second regions are spaced at least 2 mm apart.

[0120] In some embodiments, the flow-reducing assembly further comprises a second flow-reducing member, the first flow-reducing member resides in the aneurysm, and the second flow-reducing member resides in the body vessel.

[0121] In some embodiments, at least a portion of the form of the engagement member is helical.

[0122] In some embodiments, the first and the second regions of the engagement member are spaced at least 4 mm apart

[0123] In some embodiments, the first and the second portions of the engagement member are spaced at least 2 mm apart.

[0124] In some embodiments, the first portion and the second portions of the engagement member are spaced at least 4 mm apart.

[0125] In certain embodiments, an endovascular device of the invention that is positionable within an aneurysm can be used to treat a bifurcation aneurysm or a trifurcation aneurysm.

[0126] In certain embodiments, an endovascular device positionable within an aneurysm comprises a profile of about 0.018" to about 0.030" and may be delivered by microcatheter as a single unit. Delivery may comprise initial advancement and deployment followed by one or more retraction and repositioning events, if needed. In contrast, known coils are deployed by multiple delivery procedures and lack means for retraction and repositioning after being deployed.

[0127] Brief Description of the Drawings

[0128] Examples of embodiments of the invention will now be described with reference to the following drawings.

[0129] Fig. 1A illustrates an embodiment of a balloon expandable stent.

[0130] Fig. 1B illustrates another embodiment of a balloon expandable stent.

[0131] Fig. 2 illustrates a self-expanding stent.

[0132] Fig. 3 illustrates a delivery system with a stent expanded on a balloon.

[0133] Fig. 4A is a view of a stent disposed in the location of an aneurysm

[0134] Fig. 4B is a second diagrammatic view of a stent disposed in the location of an aneurysm.

[0135] Fig. 5 illustrates a membrane joining two stents for treating a bifurcation aneurysm.

[0136] Fig. 6 illustrates a stent with a membrane having a pattern of pores.

[0137] Fig. 7 illustrates a stent having polymer strips.

[0138] Fig. 8 illustrates a stent with a membrane having a mesh.

[0139] Fig. 9 illustrates a membrane secured to the struts of a stent.

[0140] Fig. 10 illustrates a membrane before the stent is deployed.

[0141] Fig. 11 illustrates a membrane flipping in side the vessel rather than staying close to the vessel wall.

[0142] Fig. 12 illustrates a stent partially covered by a membrane having pockets for release of therapeutically effective agents.

[0143] Fig. 13 illustrates a stent with a membrane secured at three different positions and with three different sizes.

[0144] Fig. 14 illustrates a sleeve as a membrane supported by two ring-like stents.

[0145] Fig. 15 illustrate one embodiments of a membrane showing pore positioning.

[0146] Fig. 16 illustrates equidistantly spaced pores.

[0147] Fig. 17 illustrates a macroporous membrane.

[0148] Fig. 18 illustrates a microporous membrane.

[0149] Fig. 19A is a graphical representation of a membrane as manufactured, (i.e. unexpanded) state.

[0150] Fig. 19B illustrates a membrane in the expanded (i.e. deployed) state.

[0151] Fig. 20 illustrates an experimental model for inducing aneurysms using elastase delivered by a catheter.

[0152] Fig. 21A illustrates a radiographic view of an aneurysm prior to treatment of an experimentally induced aneurysm.

[0153] Fig. 21B illustrates a radiographic view of the same aneurysm, 137 days after the start of treatment with an embodiment of a membrane-covered stent.

[0154] Fig. 21C is a histological section taken at the level of a thrombosed aneurysm.

[0155] Fig. 22 diagrams progressive remodeling of an aneurysm after implantation of a stent.

[0156] Fig. 23 is a graph of the relationship between coverage ratio and stent diameter.

[0157] Fig. 24A is a radiographic view of an aneurysm located in the subclavian artery of a rabbit.

[0158] Fig. 24B is the artery shown in Fig. 25A subsequent to treatment.

[0159] Fig. 25A is an image of a chronic angiograph of iliac arteries showing the patency of vessels implanted with the endovascular device having a solid membrane made from a polyurethane based material with fluorocarbon surface-modifying end groups.

[0160] Fig. 25B is an image of a chronic angiograph of iliac arteries showing the patency of vessels implanted with the endovascular device having a porous membrane made from a polyurethane based material with fluorocarbon surface-modifying end groups.

[0161] Fig. 26 illustrates an embodiment comprising a membrane having permanently attached agents.

[0162] Fig. 27 is a diagrammatic view of a stent with a membrane being used to treat a bifurcation aneurysm in a first example.

[0163] Fig. 28 is a diagrammatic view of a stent with a membrane being used to treat a bifurcation aneurysm in a second example.

[0164] Fig. 29 is a diagrammatic view of a stent with a membrane being used to treat a bifurcation aneurysm in a third example.

[0165] Fig. 30a illustrates an embodiment of a deployed endoprosthetic aneurysm occlusion device comprising a distal assembly, engagement members, and a flow-reducing member residing in a vessel, and a catheter useful for delivering the device to the aneurysm.

[0166] Figure 30b illustrates a cross section view of the embodiment of the device shown in figure 30a.

[0167] Figure 31 illustrates an embodiment of a deployed device comprising a distal assembly, engagement members, a flow-reducing member residing in the vessel, and a linking member.

[0168] Figure 32 illustrates an embodiment of a deployed device comprising a distal assembly, engagement members, a flow-reducing member comprising a membrane

residing in the aneurysm, another flow-reducing member comprising a plug residing in the vessel, and two linking members.

[0169] Figure 33 illustrates an embodiment of a deployed device comprising a distal assembly, an engagement member comprising a curve, a flow-reducing member comprising a membrane, and a linking member.

[0170] Figure 34 illustrates an embodiment of a deployed device comprising a distal assembly, an engagement member comprising a helical shape, and a flow-reducing member residing in the vessel.

[0171] Figure 35 illustrates an embodiment of a deployed device together with certain forces that contribute to the secured positioning of the deployed device.

[0172] Detailed Description of the Invention

[0173] Implantable medical devices include physical structures for delivering drugs or reagents to desired sites within the endovascular system of a human body. These devices may take up diversified shapes and configurations depending upon specific applications. Common implantable medical devices include stents, vena cava filters, grafts and aneurysm coils.

[0174] The endovascular system of a human body includes blood vessels, cerebral circulation system, tracheo-bronchial system, the biliary hepatic system, the esophageal bowel system, and the urinary tract system. Although exemplary stents implantable in blood vessels are described, they are applicable to the remaining endovascular system. Embodiments of the invention, some of which are described herein are readily adaptable for use in the repair of a variety of vessels, including but not limited to, treatment or repair in cases of aneurysm, ischemic stroke, carotid artery stenosis, saphenous vein graft, small vessel stenosis, or renal artery repair.

[0175] Stents are expandable prostheses employed to maintain vascular and endoluminal ducts or tracts of the human body open and unoccluded. For example, stents are now frequently used to maintain the patency of a coronary artery after dilation by a balloon angioplasty procedure. A stent is a typically a tubular meshwork structure having an exterior surface defined by a plurality of interconnected struts and spaces between the struts. The tubular structure is generally expandable from a first position, wherein the stent is sized for intravascular insertion, to a second position, wherein at least a portion of

the exterior surface of the stent contacts and engages the vessel wall where the stent has been placed.

[0176] The expanding of the stent is accommodated by flexing and bending of the interconnected struts throughout the structure. The force for expansion can be applied externally as from a inflated balloon onto which the stent is loaded prior to placement, or the stent itself may be self-expanding. A myriad of strut patterns are known for achieving various design goals such as enhancing strength, maximizing the expansion ratio or coverage area, enhancing longitudinal flexibility or longitudinal stability upon expansion, etc. One pattern may be selected over another in an effort to optimize those parameters that are of particular importance for a particular application.

[0177] Illustrated in Figs. 1A and 1B are two exemplary balloon expandable stent designs. Fig. 1A shows a tubular balloon expandable stent 100, further comprising end markers 103 to increase visibility of the stent 100 when viewed *in situ* using radiologic techniques. In some embodiments, the stent 100 is made of multiple circumstantial rings 101, where the ring connectors 102 connect two or three adjacent rings 101 and hold the rings in place. In Fig. 1A the end marker 103 is shown as a disc-shape. The shape of an end marker 103 is not critical to the function of the stent 100, and will be useful as long as the shape selected is effective to increase the radiographic visibility of the stent 100.

[0178] Fig. 1B illustrates a tubular balloon expandable stent 104, similar to the stent 100 shown in Fig 1A, with the exception that the stent 104 comprises center markers 105, 106. The center markers 105, 106 help to aid in placing the stent over an aneurysm opening during an implantation operation. The center markers 105, 106 can be of the same material and shape as the end markers 103.

[0179] Fig. 2 illustrates a self-expanding stent 107 made of wires or ribbons. While a self-expanding stent may have many designs, the stent 107 shown in Fig. 2 has a typical braided pattern 108 with welded ends 109. The stent 107 is designed to be relatively flexible along its longitudinal axis, to facilitate delivery through tortuous body lumens, but is still stiff and stable enough radially in the expanded state, such that it will serve to maintain the patency of a vessel lumen when implanted, for example in the lumen of an artery.

[0180] Illustrated in Fig. 3 is a delivery system and an expanded tubular stent 112, loaded over an expandable balloon 114. When the tubular stent 112 is fully expanded to its deployed diameter by inflation of the balloon 114, the latticework of struts takes on a shape in which adjacent crests undergo wide separation, and portions of the struts take on a transverse, almost fully lateral orientation relative to the longitudinal axis of the stent. Such lateral orientation of a plurality of the struts enables each fully opened cell to contribute to the firm mechanical support offered by the stent in its fully deployed condition, and insures a rigid structure that is highly resistant to recoil of the vessel wall following stent deployment.

[0181] While a stent 112 may be deployed by radial expansion under outwardly directed radial pressure exerted, for example, by active inflation of a balloon 114 of a balloon catheter on which the stent is mounted, the stent 112 may be self-expandable. In some instances, passive spring characteristics of a preformed elastic (i.e., self-opening) stent serve the purpose, while in others shape memory materials are used, such that upon activation by the appropriate energy source, the stent deforms into a pre-determined memorized shape. Regardless of design, in all cases the stent is expanded to engage the inner lining or inwardly facing surface of the vessel wall with sufficient resilience to allow some contraction, but also with sufficient stiffness to largely resist the natural recoil of the vessel wall following deployment.

[0182] Referring to the delivery system depicted in Fig. 3, there is included a guide wire lumen 110, a balloon inflating lumen 111, a connector 116, a balloon catheter shaft 113, and platinum marker bands 115 on the catheter shaft 113. The guide wire lumen 110 is used for introducing a guide wire in a balloon catheter, and the balloon inflating lumen 111 for inflating the balloon after the stent has been placed at a desired location. The connector 116 is used for separating the guide wire lumen 110 and the balloon inflating lumen 111. The balloon catheter shaft 113 carries the guide wire lumen 110 and the balloon inflating lumen 111 separately, with a typical length of about 135-170 cm. The ring markers 115 on the catheter shaft 113 are used so that the start of balloon tapers and the edges of the stent can be visualized by X-ray.

[0183] In Fig. 3, an expanded stent 112 is shown mounted onto an expanded balloon. Conveniently, the delivery catheter can be a conventional balloon dilation

catheter used for angioplasty procedures. The balloon can be formed of suitable materials such as irradiated polyethylene, polyethylene terephthalate, polyvinylchloride, nylon, and copolymer nylons such as Pebax™. Other polymers may also be used. In order for the stent to remain in place on the balloon during delivery to the desired site within an artery, the stent is typically crimped onto the balloon. However, the precise design choices in delivery systems are not limiting to the scope of the disclosure.

[0184] In some embodiments, the delivery of the stent is accomplished as follows. The stent is first mounted onto an inflatable balloon on the distal extremity of the delivery catheter, and the stent is mechanically crimped onto the exterior of the folded balloon. The catheter/stent assembly is then introduced into the vasculature through a guiding catheter. A guide wire is disposed across the diseased arterial section and then the catheter/stent assembly is advanced over the guide wire that has been placed in the vessel until the stent is substantially located at the site of the diseased or damaged portion of the vessel. At this point, the balloon of the catheter is inflated, expanding the stent against the artery. The expanded stent engages the vessel wall, which serves to hold open the artery after the catheter is withdrawn.

[0185] Due to the formation of the stent from an elongated tube, the undulating component of the cylindrical elements of the stent is relatively flat in transverse cross-section, so that when the stent is expanded, the cylindrical elements are pressed into the wall of the vessel and as a result do not significantly interfere with the blood flow through the lumen. The cylindrical elements of the stent, which are pressed into the wall of the vessel, will eventually be overgrown with a layer of endothelial cells, further minimizing interference with blood flow that could be caused by the presence of the stent in the lumen. The closely spaced cylindrical elements, located at substantially regular intervals, provide uniform support for the wall of the artery, and consequently are well adopted to tack up and hold in place small flaps or dissections that may exists in the vessel wall.

[0186] Resilient or self-expanding prostheses can be deployed without dilation balloons. Self-expanding stents can be pre-selected according to the diameter of the blood vessel or other intended fixation site. While their deployment requires skill in stent positioning, such deployment does not require the additional skill of carefully dilating the

balloon to plastically expand the prosthesis to the appropriate diameter, as the final diameter will be primarily a function of the stent design itself. Further, the size of the self-expanding stent is chosen such that when in place it remains at least slightly elastically compressed, and thus has a restoring force which facilitates acute fixation. By contrast, a plastically expanded stent must rely on the restoring force of deformed tissue, or on hooks, barbs, or other independent fixation elements included as part of the stent structure.

[0187] Self-expanding stents can be fashioned from resilient materials such as stainless steel, and the like, wherein the stent is loaded onto the delivery device in a compressed state, and upon placement at the desired location is allow to naturally elastically expand. Expandable stents can also be fashioned from shape memory materials such as nickel-titanium alloys and the like, wherein the stent is expanded from a first shape to a second shape by activation with an energy source such as heat, magnetic fields or an RF pulse for example.

[0188] The presence of a foreign object in a vessel, like a stent, can promote thrombus formation as blood flows through the vessel, and platelets contact the stent surface. This is a well-recognized problem in other areas of cardiovascular treatment, such as when artificial heart valves are implanted. In serious instances, clot formation can lead to acute blockage of the vessel. In addition, as the outward facing surface of the stent in contact or engagement with the inner lining of the vessel, tissue irritation can lead to an inflammatory reaction, further exacerbating restenosis due to localized hyperplasia. Stent design and use must take into account all these myriad factors.

[0189] In one embodiment, illustrated in Fig. 4A, and 4B, there is provided an intracranial stent 202 and for use in the repair of stenotic lesions and aneurysms 201. Due to the characteristics of intracranial blood vessels, the intracranial stents 202 are designed to be very flexible, low profile (diameter of 0.8 mm or less when crimped onto the delivery catheter) and having a thin wall (less than 0.1 mm). As they are used in small vessels, intracranial stents 202 do not necessarily possess, or need, the highest possible radial strength.

[0190] As shown in Fig. 4A, the intracranial stent 202 is located at the site of an aneurysm 201. A membrane 203 partially covers the stent 202 and is positioned to seal

the neck, thus blocking blood flow to the aneurysm 201. Blocking blood flow is an important function of the stent, as it reduces the risk of aneurysm rupture, which can cause neurological deficit or even death if it occurs intracranially, and promotes the formation of a thrombus and resolution of the aneurysm. Radiopaque markers 204 can be located in the middle of the stent 202 to provide visibility of the stent 202 during operation and post-operation inspection.

[0191] In Fig. 4B, a portion of the stent 202 is shown to include open "cells" 205. This design avoids blocking perforator vessels (sometimes called perforators), small capillary vessels that have important and distinctive blood supply functions. It is possible that tubular stents can block perforators and inhibit important functions of these vessels, which may be related, but not limited the general health of the vessel and surrounding tissue. Moreover, stents covered with non-porous membranes suffer from the disadvantage that the membrane portion of the stent can block the perforators.

[0192] Stents may also be used to treat a number of different types of aneurysms, including bifurcation aneurysm, as shown in Fig. 5. For example, as illustrated, an intracranial aneurysm 201 can be treated with a stent 202 and membrane 203 to effectively prevent ischemic and hemorrhagic stroke. At least 30 to 35% of aneurysms are located at bifurcation sites of intracranial vessels. In this embodiment, the membrane 203 is one-sided and non-circumferential. In some embodiments the membrane may be circumferential and may cover substantially the entire stent. The stents 202 are joined by the membrane 203, which covers the aneurysm neck 201. The same pattern can be applicable to self-expandable (super-elastic) or balloon expandable (stainless steel, CoCr, PtIr alloys) stents. Thus, the intracranial stent 202 coupled with a membrane 203 acts as a scaffold to open clogged arteries, and the membrane provides a cover to prevent blood flow to the aneurysm 201. Obstructing blood supply to the aneurysm 201 isolates the aneurysm 201 from normal blood circulation, eventually resulting in thrombus formation within the aneurysm. Complete obstruction of the aneurysm 201 may not be necessary in order to achieve initiation of an aneurytic thrombus.

[0193] Table 1 provides a table with exemplary dimensions for an intracranial stent 202 designed for use with a membrane 203. The membrane 203 is biocompatible, has good adhesion to stent struts made from a variety of materials including, but not

limited to stainless steel, titanium and nickel alloys and the like. The membrane forms an ultra-thin film that is porous as opposed to being a solid film, having holes or pores included during the process of manufacturing the membrane. In some embodiments, the pore size and material coverage area are selected to prevent blockage of perforator vessels, and while restricting blood flow to the aneurysm.

TABLE 1: Typical Dimensions of Manufactured Stents for Intracranial Use

Dimensions	**As Manufactured**	**Crimped**	**Expanded**
Strut Thickness	0.003" (0.076 mm)		
Outer Diameter	0.080" (2.03 mm)	0.040" (1.02 mm)	0.16" – 0.20" (4.0 – 5.0 mm)
Distance Between Struts	0.031" (0.80 mm)	0.016" (0.40 mm)	0.079" (2.0 mm)

[0194] In some embodiments, the membrane 203 is made from a thin film generally in a range of from about 25 μm to about 125 μm in thickness, measured in the as-manufactured state, and is from about 5 μm to about 25 μm thick, as measured in the deployed state (expanded state). The film has good expandability, and can be expanded up to about 400% using relatively low force. The membrane 203 also has good chemical stability at ambient conditions allowing for extended storage prior to use, and is stable under sterilization conditions (ethanol). Examples of physical properties of the membrane are a hardness of about 75A (measured with a Shore durometer), tensile strength up to about 7500 p.s.i., and elongation of up to about 500%.

[0195] Conveniently, membranes can be made porous, and if desired uniformly porous, by drilling holes into a solid film. In this way a stent 202 covered by a uniformly porous membrane 203 can be provided as illustrated in Fig. 6. The exploded view of Fig. 6 depicts an area of a membrane having uniformly spaced pores. The pore diameter is generally in the range of about 1-150 μm, while the distance between pores is generally less than about 100 μm. Porosity of a stent 202 covered by a membrane can be varied in other ways, including covering the stent 202 with membrane strips as shown in Fig. 7, or by providing a stent 202 covered with a mesh like membrane 203, as in Fig. 8.

Porosity can also be varied by changing pore diameter, or the number of pores per unit area of the membrane.

[0196] Where the stent is covered with membrane strips, as shown in Fig. 7, the strips of membrane 203 can be wrapped laterally around the stent 202. Securing the strips to the stent 202 may be accomplished by interlacing the strips above and below the struts of the stent (not shown). Typically the width of strips would be less than 0.075 mm, and the distance between adjacent strips would be less than about 100 μm.

[0197] Where a mesh or woven membrane is used, a sheet of woven membrane 203 can be wrapped circumferentially around the stent 202, as illustrated in Fig. 8. In one embodiment the mesh size is about 0.025 to 0.05 mm, while the width of the polymer is typically less than about 100 μm.

[0198] In some embodiments, the membrane 203 completely surrounds the stent struts, and forms a stable film between the struts, as shown in Fig. 9A and B. The film between struts can be disposed centrally between struts as in Fig. 9A, or outside struts as shown in Fig. 9B. Fig. 10 illustrates a membrane and stent in the unexpanded state, prior to deployment. Where the film is located outside the struts, as in Fig. 9B, there is a further advantage provided in that the membrane will tend to maintain closer contact with the vessel wall, and will avoid "flipping" toward the inside the vessel, as is depicted in Fig. 11.

[0199] Implantable medical devices can also be used to deliver drugs or reagents to specific locations within the vascular system of a human body. As shown in Fig. 12, a membrane 203 can comprise pockets 208 which serve as reservoirs for drugs or reagents intended for delivery into the region of a vessel wall or lumen. In certain embodiments, the membrane 203 comprises a first layer 206 attached to the outer surface of an implantable medical device such as a stent 202. An intermediate layer is attached to the first layer wherein the intermediate layer comprises at least two circumferential strips being separated from each other and a second layer covering the first layer and the intermediate layer.

[0200] The spaces surrounded by the first layer, and the circumferential strips and the second layer form the pockets 208 that serve as receptacles for drugs or reagents. In other embodiments, the intermediate layer includes at least one opening so that the

pockets can be formed within the openings. The shapes and sizes of the openings can be varied in accordance with specific applications. The stent 202 can be partially covered by a membrane 203 that comprises a first layer 206 and a second layer 207.

[0201] In some embodiments, the membrane 203 can cover the entire stent, or portions of the stent 202 , as is shown in Fig. 13. Thus, the size of the membrane can be varied if desired to particularly suit the location where the stent is to be placed.

[0202] Many polymeric materials are suitable for making the layers of the membrane 203. Typically, one first layer is disposed onto the outer surface of a stent. The first layer has a thickness of about 50-125 μm, with pore sizes of about 20-30 μm as a nominal initial diameter. In certain embodiments, the first layer can serve as an independent membrane 203 to mechanically cover and seal the aneurysm 201. The first and/or second layers can be comprised of biodegradable material, and function as a drug or reagent carrier in order to provide sustained release functionality.

[0203] It is desirable that the intermediate layer be formed of a material which can fuse to the first and second layers or attached to the first layer in a different manner. In certain embodiments, the intermediate layer may be merged with the first layer to form a single layer with recessions within the outer surface of the merged layer. The second and intermediate layers can be made of biodegradable material that include drugs or other reagents for immediate or sustained release. After the biodegradable material is dissipated through the degradation process, the membrane 203 is still intact, providing vessel support. The second layer can also be composed of a polymeric material. In some embodiments, the second layer has a thickness of about 25-50 μm, with pore sizes ranging from about 70-100 μm.

[0204] The polymeric layers may be fashioned from a material selected from the group consisting of fluoropolymers, polyimides, silicones, polyurethanes, polyurethanes ethers, polyurethane esters, polyurethaneureas and mixtures and copolymers thereof. Biodegradable polymers can include polylactide, poly(lactide-co-glycolide), poly-orthoesters, polyphosphazenes, polyanhydrides, or polyphosphoesters. The fusible polymeric layers may be bonded by adhering, laminating, or suturing. The fusion of the polymeric layers may be achieved by various techniques such as heat-sealing, solvent bonding, adhesive bonding or the use of coatings.

[0205] Types of drugs or reagents that may prove beneficial include substances that reduce the thrombogenic, inflammatory or smooth muscle cell proliferation response due to the implanted device. For example, cell proliferation inhibitors can be delivered in order to reduce or inhibit smooth muscle cell proliferation. In intracranial or some other applications fibrin sealants can be used and delivered to seal aneurysm neck and provide fibroblasts and endothelial cells growth. Specific examples of drugs or reagents include heparin, phosporylcholine, albumin, dexamethasone, paclitaxel and vascular endothelial growth factor (VEGF). This list is not exhaustive, and other factors known to regulate inflammatory responses, cellular proliferation, thrombogenesis and other processes related to reaction to foreign bodies are contemplated to be useful within the scope of the disclosure.

[0206] The drug or reagents can be incorporated into the implantable medical devices in various ways. For example the drug or reagent can be injected in the form of a gel, liquid or powder into the pockets. Alternatively the drug or reagent can be supplied in a powder which has been formed into a solid tablet composition, positioned in receptacles placed in the device.

[0207] It is at times desirable to provide a stent that is highly flexible and of small profile in order to effect treat vessels of very small caliber, for example, intracranial vessels with lumen diameters ranging in size from about 1.5 mm to about 5.0 mm. High flexibility allows the stent to be advanced along the anatomy of the intracranial circulation.

[0208] In some embodiments, as illustrated in Fig. 14, a membrane 203 is embodied as a sleeve 301 supported by two ring-like short stents 302 at both ends of a device so that the membrane 203 covers the whole area of the device 302. There is no scaffold support in the middle of the device 302. Radiopaque markers 303 are located at both ends of the stent 302. Depending on the particular application, the rings can be balloon expandable and made from stainless steel or self-expandable and made from NiTi (memory shaped nickel- titanium alloy), and the like.

[0209] The membrane 203 is part of the stent structure and is effective to occlude the aneurysm neck and "recanalize" a diseased, damaged, or weakened vessel, leading to healing of the vessel and elimination of the aneurysm. The use of a stent as

shown in Fig. 14, further obviates the need for coiling procedures, which are at times used in conjunction with stents to treat wide neck aneurysms. The present apparatus and methods are also a preferred treatment solution for cc fistula ruptured in cavernous sinus, pseudoaneurysms, saccular aneurysms.

[0210] In some embodiments, there is provided a porous membrane as part of the device. The membrane 203 has a system of holes or pores 25 with pore diameter 21 on the order of about 1 to 100 μm, and borders 23 between the pores have a width generally less than about 100 μm, as shown in Fig. 15. To provide a membrane of variable porosity, pore spacing and even pore size can be varied in different areas of the membrane.

[0211] It has been further discovered that a membrane having uniform porosity can be effective in blocking blood flow to an aneurysm while maintaining flow to perforator vessels.

[0212] In some embodiments, pore spacing (the distance between adjacent pores) can be in a range of from about 40 to 100 μm. To produce a membrane of uniform porosity, pore diameter 21, and interpore spacing 22, will be generally equidistant, as in Fig. 16, over substantially the entire area of the membrane. Depending on the size and number of pores in the membrane, the membrane can be described as being macroporous or microporous. For example, in a macroporous membrane, an schematic of which is shown in Fig. 17, pores 25, may range in size from about 10 to 100 μm, and are relatively equally spaced within the membrane material 20. Alternatively, in a microporous membrane, pore diameter may be on the order of about 1 to 10 μm, and again are generally equally spaced in a uniformly porous section of a membrane. The pore sizes shown in Fig. 17 and 18 are only examples, and a range of pore sizes are expected to be useful in an implantable device.

[0213] Furthermore, the characterization of a membrane as either macro-or microporous is not limiting to the disclosure. The functionality of the membrane is dependent on pore diameter and pore spacing, which are described in terms of physical measurement units, and how the particular physical dimensions of the membrane pores operate *in situ* to regulate blood flow. In either case, membranes having porous sections of uniform porosity can be fashioned by selecting a desired pore diameter and pore

spacing combination. As is seen in the data presented below, various combinations of pore diameter and pore spacing are effective to provide a membrane of optimal porosity over a range of deployed sizes. Thus, a porous membrane 203 is able to significantly improve hemodynamics around the aneurysm 201, since it has a lower delivery profile and is more flexible, as compared to a stent 202 with a solid membrane.

[0214] One application for a device having a macroporous membrane is to treat aneurysms within close proximity of branches or perforators. Another specific application is the treatment of an intracranial saccular or wide neck aneurysm located above the ophthalmic artery where perforators extend from the parent artery within close proximity of the aneurysm. Microporous devices are suitable for use in areas where perfusion of perforators is of less immediate concern. Thus, the micro-porous device is used for conditions which require total coverage to immediately block blood flow, for example, a caroticocavernous fistula, or where there is little or no risk of blocking perforators, for example, below the ophthalmic artery.

[0215] The device may be used for the treatment of endovascular disease such as aneurysms, arteriovenous malformations (AVM's) and caroticocavernous fistulas. The device may also be useful in other vessel related applications such as treatment or repair in cases of ischemic stroke, carotid artery stenosis, saphenous vein graft, small vessel stenosis, or renal artery repair. The pore patterns are designed with consideration of factors such as specific flow conditions of blood vessels, and the location of the vessel being repaired.

[0216] The design of the porous section of a membrane is therefore initially determined according to the intended application of the device, and three main factors, pore size 21, bridge dimensions 22, 23, and material ratio of the membrane. Pore size 21 can be measured in the "as designed and manufactured" (i.e. unexpanded) and "as deployed" (i.e. expanded) states. Typically, pore size in the unexpanded state is about 1.5 to 2.5 times smaller than pore size after the membrane has been expanded to its deployed size. This is depicted in Fig. 19A and B.

[0217] Bridge dimensions 22, 23 refer to the shortest distance separating one pore 25 from its adjacent pores, as shown in Fig. 15. Each pore 25 may be spaced from adjacent pores at variable distances, or as shown in one embodiment depicted in Fig. 16,

at generally equal distance. In a uniformly porous section of a membrane the pore spacing will be relatively equidistant throughout the membrane. Similar to pore size 21, bridge dimensions 22, 23 can also be measured in two states, as designed and manufactured, or as deployed. The as designed and manufactured bridge dimensions are typically larger than the as deployed bridge dimension 22, 23 by a factor of 1 to 2, since stretching of the membrane during deployment reduces the size of the bridge.

Membrane Porosity

[0218] The relative porosity of a porous section of a membrane will be dictated by the size of individual pores and the number of pores per unit area (i.e. pore density). As used herein, the term "porous section" refers to that area of a membrane that includes substantially all the pores of the membrane. Coverage and porosity can both be described in terms of a relationship between the area of the apparent area of the porous section of the membrane corresponding to membrane material, versus that corresponding to the pores. Thus, the material ratio is the fraction of a membrane area that corresponds to membrane material, or in other terms, total apparent area or the porous section (100%) – pore area (%) = material ratio (%). As used herein, the term "material ratio" refers in particular to the membrane material versus pore area in a porous section of a membrane.

[0219] As indicated, material ratio is conveniently expressed as a percentage. So, for example, a membrane lacking pores has a material ratio = 100%, while in a membrane with 20% of its total area encompassed by pores, the material ratio = 80%. Likewise, porosity can also be expressed as a percentage, where porosity (%) = total area of the porous section of the membrane (100%) – material ratio (%). A membrane having a material ratio of 75% would have a porosity of 25%. Both material ratio and porosity can be described in membranes in the "as manufactured" and "as deployed" stages. In some embodiments, the overall material ratio in the deployed state can range between about 25% to about 80%.

[0220] It has been discovered that a membrane of uniform porosity can be effective to promote healing of an aneurysm if the material ratio of the porous section of the membrane is within a certain range when the membrane is in the deployed state. Thus, in some embodiments the material ratio of the porous section of the membrane is preferably in a range between about 70% to 80%, with the optimal material ratio

considered to be about 75%, when the membrane is deployed. Uniformity is achieved by maintaining the variance in the size of pores, as well as the spacing between pores in a porous section of the membrane, while an optimal material ratio is achieved on the basis of particular pore diameters and spacing.

[0221] The porous section can also be conceptually divided into a number (n) of porous regions, wherein the area of each of the n regions is substantially $1/n$ of the total area of the porous section of the membrane. For example, in some embodiments, there can be 2, 3, 4, 5 or more porous regions, where each of the regions has substantially the same porosity as each of the other porous regions existing with the porous section of the membrane. The porosity of either a region or the porous section as a whole is determined by the combination of pore size and pore spacing.

[0222] While the interpore size variance will be substantially uniform over the area of a porous section within each individual membrane, it is to be recognized that it is possible to provide different membranes with different numbers of pores, or different pore spacing as a way in which to provide a set of membranes of varying porosity. In this way it is possible to have a set of membranes with a range of porosities, any one of which can be chosen based on the requirement in a particular application. Thus depending on a variety of factors, a membrane could be produced with properties that would make it particularly well-suited for use in aiding in the stabilization and repair of a particular vessel, while for another application a membrane of a different porosity might be preferable, and could be fashioned accordingly.

[0223] Porosity of the membrane is considered optimal when the membrane permits blood supply to perforators of main arteries while reducing blood circulation to the diseased, damaged or weakened portion of the vessel wall being repaired. In addition, a further benefit may be realized by selecting a membrane having a porosity that enables enhanced endothelial cell migration and tissue ingrowth for faster endothelialization. The membrane as disclosed may be used in devices designed for a variety of vessel repair applications other than aneurysms. These may include, but are not limited to, use in the treatment of ischemic stroke, carotid artery stenosis, saphenous vein graft, small vessel stenosis, or renal artery repair.

[0224] As indicated above, part of the novelty described in the present disclosure lies in the discovery that a stent having a uniformly porous membrane is capable of supporting a vessel wall at the site of an aneurysm, maintaining the patency of parent and perforator vessels, while restricting blood flow to the aneurysm itself. In prior art devices these functionalities were achieved using membranes with non-uniform porosity, or regions of varying porosity. By providing these features the device promotes more rapid and more effective healing of an aneurysm, while at the same time providing a device that is more universally adaptable for use in a wider variety of *in vivo* locations than previously possible, and simpler to manufacture and use.

[0225] This has been confirmed experimentally in an animal aneurysm model. In this model system, aneurysms are induced by infusion of elastase into the lumen of a vessel by way of a catheter, as diagrammed in Fig. 20 (See: Miskolczi, L. et al., Rapid saccular aneurysm induction by elastase application *in vitro*, Neurosurgery (1997) 41: 220-229; Miskolczi, L. et al., Saccular aneurysm induction by elastase digestion of the arterial wall, Neurosurgery (1997) 43: 595-600). An example aneurysm 200 produced by this method is shown in Fig. 21A.

[0226] In the illustrated experiment, a stent was deployed at the site of the aneurysm shown in Fig. 21A, in order to support the vessel wall and to aid in repair of the damaged area. As can be seen in Fig. 20B, after 137 days blood flow to the aneurysm had ceased, while the patency and flow in the parent vessel 210 and a nearby perforator vessel 220 was maintained. A histological section through the vessel at the site of the aneurysm, shown in Fig. 21C, reveals that a thrombus 240 formed at the site of the aneurysm, indicating that the aneurysm had become substantially occluded. Note that the parent vessel 210 is open and unobstructed. This process of remodeling of the aneurysm is diagrammed in Fig. 22.

[0227] Results from a series of studies like these have suggested that the material ratio of the membrane for optimal efficacy should be about 75%, or at least in the range of about 70-80%. In order to achieve this optimal porosity, several factors are considered. For example, the size as manufactured relative to the deployed size will be important, as the change in pore area occurs at a different rate than does the overall area of the membrane.

[0228] The material ratio has therefore been determined for membranes of varying pore diameter, pore spacing, and degree of expansion from the manufactured size to various deployment sizes, in order to evaluate what pore spacing and pore size can provide a material ratio in the range of about 70-80%, at deployed sizes ranging from 2.5-5.0 mm. In the examples described, material ratio in the unexpanded state ranged from 86-96% depending on the pore size and spacing. To determine the material ratio in the expanded state, membranes were expanded as they would be during deployment, and the pore diameter measured at selected areas. The material ratio was then determined as follows:

A = total area of porous section of membrane; P = total area of pores;

Porosity = (P ÷ A) x 100%; Material Ratio = (1 – (P ÷ A)) x 100%

[0229] In the data shown in Table 2, two membranes having porous sections with different pore size and pore spacing were evaluated. Porous 30/70 (30/70 membrane) refers to a membrane manufactured with 30 μm pores with an interpore spacing of 70 μm in the unexpanded state; likewise, Macroporous 40/60 (40/60 membrane) refers to a membrane with 40 μm pores and an interpore spacing of 60 μm, again, in the unexpanded state.

TABLE 2: Effect of Deployment Size on Material Ratio

Configuration	**Diameter of Stent**				
	2.0 mm (as made)	2.5mm	3.0mm	3.5mm	4.0mm
Macroporous 30/70 Pore Diameter: 30 μm Pore Spacing: 70 μm	92%	87%	80%	75%	69%

Macroporous 40/60 Pore Diameter: 40 μm Pore Spacing: 60 μm	86%	78%	72%	64%	56%

[0230] As the data in Table 2 shows, when a membrane is expanded from its manufactured size (here 2.0 mm) to various deployed sizes, ranging from 2.5 to 4.0 mm, the material ratio decreases. Thus, depending on the initial pore size and density, the optimal material ratio of about 70-80% will be achieved at different degrees of expansion, analogous to the various deployment diameters of the stent being covered by the membrane.

[0231] For example, in a 30/70 membrane, material ratios within the optimal desired range of about 70-80% are substantially achieved at deployment diameters of about 3.0 to about 4.0 mm, when starting with a manufactured size of 2.0 mm. For a 40/60 membrane the optimal material ratio is achieved at a point between 2.0 to 2.5 mm, up to about 3.0 to 3.5 mm.

[0232] By extending this analysis it is possible to determine the number of different stent pore patterns, the pattern being the combination of pore size and interpore spacing, necessary to provide about a 70-80% material ratio over wide range of stent diameters. The goal is to know beforehand, the combination of pore size and spacing that, when the membrane is expanded to its deployed size, will provide a material ratio within the desired range of about 70-80% and preferably about 75%.

[0233] For example, the calculations in Table 3 show that with three different membrane patterns, it is possible to achieve a material ratio in the range of about 70-80% using a stent with a manufactured size of 2.2 mm, expanded to deployment sizes ranging from 2.5-5.0 mm. In these cases, the material ratio of the membrane in the unexpanded state ranges from 86-96%.

TABLE 3: Relationship of Material Ratio and Stent Diameter

Final diameter of patch	Stent size	Pore diameter, μm	Interpore distance, μm	% coverage as	% coverage as manufactured at 2.2mm

				deployed	
2.5, 2.75, 3.0 mm	2.5/3.0mm	40	60	70-80%	86%
3.25, 3.5, 3.75, 4.0mm	3.5/4.0mm	30	70	70-80%	92%
4.25, 4.5, 4.75, 5.0mm	4.5/5.0mm	20	75	70-80%	96%

[0234] These results are further exemplified in Fig. 23, which shows a graphic analysis of the relationship between pore diameter, pore spacing and deployment size for three different pore patterns, and the material ratio that results upon deployment to various diameters. In each case the material ratio of the membrane is plotted as a function of diameter of the stent in the expanded state. In all cases, the stents are manufactured at a size of about 2.2 mm. A surgeon, simply by knowing the size of the vessel to be repaired, can readily select a stent and membrane combination optimized to provide a 70-80% material ratio within a porous section of the membrane when the device is deployed, and achieve effective healing and repair of an aneurysm.

[0235] As shown in Fig. 23, for a 40/60 membrane, deployment sizes ranging from about 2.7 mm to about 3.5 mm will provide a coverage area in the desired range of about 70-80%. For a 30/70 membrane, deployment diameters ranging from about 3.5 mm to about 4.5 mm will result in a coverage area in the desired range of about 70-80%, and for a 20/75 membrane (i.e. 20 μm pore diameter; 75 μm pore spacing) deployment sizes ranging from about 4.2 mm to about 5.4 mm will provide a coverage area in the desired range of about 70-80%. Thus, a material ratio in the range of about 70-80% can be achieved over deployment sizes of 2.7-5.4 mm by selecting the membrane from a set of only three membranes. It is contemplated that by varying pore spacing and pore

diameter, as well as with membranes made from various materials, greater flexibility in obtaining optimum material ratio at the widest variety of deployed sizes is possible.

[0236] In practice, and as shown in Fig. 24A and B, an embodiment of a device 10 effectively reduces blood flow into an aneurysm 50. Reducing flow to the aneurysm induces intra-aneurysmal thrombosis. Fig. 24A shows an aneurysm 50 located in the subclavian artery of a rabbit. In Fig. 24B, the results show that within a few hours deployment of the device 10 in the vessel 5, blood supply to the body of the aneurysm 50 is effectively stopped. Significantly, the pore pattern of the membrane continues to allow an uninterrupted supply of blood through perforator vessels 55 located proximal to the deployed device 10. The device 10 uses the antagonistic relationship between the sufficient reduction of blood supply to disrupt and thus heal an aneurysm 50 and the maintenance of sufficient blood supply vital to keep the perforators 55 patent.

[0237] For example, consider an aneurysm 50 with aneurysm neck diameter of about 6 mm and height of about 10 mm. If the aneurysm neck is covered by a 25% material ratio macro-porous device 10, a reduction of 25% blood flow into the aneurysm sac is possible, with higher material ratios, for example 70-80%, or preferable 75%, even greater inhibition of blood flow to the aneurysm is achieved. It is expected that the percentage reduction in blood flow will exceed the simple percentage material ratio due to the viscosity of blood, as well as further reduction of blood flow due to flow disruption and dispersion. The geometry of the aneurysm can also play a role in the effectiveness and operation of the device.

Chemical Properties of the Membrane

[0238] The membrane is preferably made from biocompatible, highly elastomeric polymer. Polyether urethane (PEU) or polycarbonate urethane (PCU) may be used.

[0239] Trade names for PEU include Tecoflex, Tecothane, Hapflex, Cardiothane, Pellethane, and Biospan. Trade names for PCU include ChronoFlex, Carbothane, and Corethane.

[0240] In some embodiments the membrane is made from BioSpan F, a material developed by Polymer Technology Group (PTG), Berkeley, California, USA. BioSpan F is a polyurethane based material with fluorocarbon surface-modified end

groups. In studies performed both *in vitro* and *in vivo*, this material has been shown to possess excellent compatibility properties matching the environment of small blood vessels. The selection of BioSpan F for the membrane of the device in treating small vessels is preferred due to resistance to thrombogenesis as compared with PET or e-PTFE membranes. Preferably, the membrane fashioned from BioSpan F will include a specific pore pattern as described earlier to obtain better resolution and healing of the aneurysm.

TABLE 4: Summary of Protein Adsorption Test

Test article	Concentration of protein found (μg/ml)	Amount of protein (μg)	Adsorbed protein (μg/cm^2)	Adsorbed protein (μg/g)
BioSpan	5.5	28	1.4	230
BioSpan F	3.5	18	0.88	160
ePTFE	16	80	4.0	4600

[0241] Table 4 shows initial results from *in vitro* biocompatibility tests comparing three materials; BioSpan, BioSpan F, and ePTFE. As can be seen, BioSpan F was the least thrombogenic of the three. The results of animal studies, shown in Fig. 25A and B, confirm the superior biocompatibility of BioSpan F. An endovascular device 76 with a membrane made from BioSpan F was placed in the right iliac artery 78 (left side of Fig. 25A). The angiographic study shows normal patency of the artery after healing of the implant. In contrast, an endovascular device 80, made from a different membrane material, and placed in the left iliac artery 74 of the same animal (right side of Fig. 25A), showed poor biocompatibility, such that after healing the vessel 74 became completely occluded in the region of the device 80.

[0242] Additional animal studies, shown in Fig. 25B, revealed that when BioSpan F was used as the membrane material, a stent covered with a porous membrane 78 had a lower degree of narrowing and thus had better healing properties than the stent covered with a solid membrane 79. With a porous membrane approximately 5% narrowing was observed (left side of Fig. 25B), while with a solid membrane 15-20% narrowing was seen (right side of Fig. 25B).

[0243] In some embodiments, membranes can be fashioned from materials of the BioSpan family using the same surface modifying end group technique, but with

application of different end groups. BioSpan PS, for example, is a surface modified material with PEO and silicon end groups.

Membranes With Permanently-Attached Agents

[0244] In some embodiments, one of which is illustrated in Fig. 26, the device 1010 is a stent comprising struts 1011, covered by an ultra-thin membrane or coating 1015, and where the membrane 1015 is of substantially uniform porosity over its length. The membrane comprises two surfaces, a luminal surface and a vessel wall surface. On the luminal surface, agents 1020, 1021, 1022 are permanently attached to the membrane 1015. On the vessel wall surface, agents 1023, 1024, and 1025 are permanently attached to the membrane. At least one capture agent 1021 is permanently attached to the luminal surface of the membrane 1015 to capture a desired target component 1030 present in the fluid passing through the vessel. At least one signal agent 1022 is permanently attached to the luminal surface of the membrane 1015 to signal the captured target component 1030 to up regulate or down regulate a cell function of the captured target component 1030 to enhance endothelialization and healing.

[0245] The cell function being regulated can include, but is not limited to, proliferation, migration, maturation, and apoptosis. The desired target component 30 can include, but is not limited to, an endothelial progenitor cell, in which case the signal agent 22 could up regulate the rate of endothelialization, and reduce the time for inflammation and thrombosis. Conveniently it is possible to combine a membrane having uniform porosity, with one comprising agents, 1020, 1021, 1022, permanently attached to the membrane. A membrane configured in this way would thus be adapted to substantially prevent blood flow to an aneurysm, while maintaining blood flow to perforators, and in addition could provided various agents that would enhance the process of healing the aneurysm.

[0246] The pharmaceutical agents 1020, 1021. 1002, coated on the lumen side of the membrane 1015, prevent the occlusion of the original patent lumen. In some embodiments, the capture and agent 1021 is arranged in a first conformation of a single arm structure made of an organic linker anchored to the membrane 1015. The organic linker may be a short chain of organic molecules anchored on one end to the membrane 1015, and the other end bound to the agent molecule that captures specific endothelial

cells from the blood to promote endothelialization. The capture and signal agents 1020, 1021, 1022 are arranged in a second conformation of a branched structure made up of an organic linker anchored to the membrane 1015. The capture agent 1021 specifically captures endothelial progenitor cells similar to the other capture agent 1020, while a signal agent 1022 enhances endothelial cell alignment and proliferation. Alternatively, the signal agent 1022 is arranged in a first conformation of a single arm structure made up of an organic linker anchored to the membrane 1015.

[0247] On the vessel wall side of the membrane 1015, a third pharmaceutical agent 1023 is permanently attached to the vessel wall surface of the membrane 1015 to enhance healing of the vessel wall 1005 from injury after the stent 1011 is deployed. Alternatively, the agents on the vessel wall side of the membrane 1015 also encourage proliferation of vessel wall components, for example, intima, elastic lamina, for enhancing the healing of the weakened, damaged or diseased portion of the vessel wall, for example, the aneurysm neck.

[0248] The agents can be effective to reduce, minimize, or prevent, immune reactions to foreign bodies. In some embodiments, agents can be effective to attract and capture endothelial cells, or endothelia progenitor cells, to aid in the formation of a healthy endothelium in the region of the aneurysm being treated. The lumen side of the membrane can be configured to generally discourage factors that are involved in thrombosis.

[0249] The capture and signal agents 1021, 1022, can include, but are not limited to, enzyme regulators tagged with antibodies or peptides, ceramides like L-PDMP, peptides, antibodies, naturally occurring molecules, and synthetic molecules, a nucleic acid, or even a polynucleotide, if desired. Specifically, the signal agent 1022 can be an endothelial cell specific L-PDMP or an smooth muscle cell-specific D-PDMP, that can bind specifically to target molecules on endothelial cells or progenitors. Peptide or antibodies have high binding affinity and specificity for endothelial cells and progenitors. Naturally occurring molecules (pure or synthesized) can mimic part of the basal lamina of the endothelium, so that endothelia cells or progenitors will preferentially bind and orient on the membrane. For example, laminin-mimetic pentapeptide immobilized on the lumen surface can be effective as a capture agent. The choice of capture agent is not

considered to be a limitation of the disclosure. A number of molecules or moieties will be useful in preventing blood flow to an aneurysm, while maintaining flow to perforators, and which will promote healing and/or endothelialization, while reducing the risk of thrombosis or other injury to the vessel being treated are considered to be within the scope of the disclosure.

[0250] The signal agent 1022 can also be an anti-inflammatory agent in order to reduce recruitment and infiltration of white blood cells. Thus, through the choice of various signal agents it is possible to enhance attachment of endothelial cells to the membrane, while minimizing the inflammatory response. The capture agent 1021 and signal agent 1022 thus act cooperatively to increase the rate of endothelialization and decrease the during which thrombosis and restenosis might occur after the stent is expanded.

[0251] As shown in Figs. 27 through 29, in some embodiments the stent 202 can be used to treat a bifurcation or trifurcation aneurysm 201. It should be noted that the use of the device is not limited to those embodiments that are illustrated. The stent 202 is implanted to be partially located in a main artery extending to be partially located in a subordinate artery. For example, in Fig. 27, two vertebral arteries join to the basilar artery. The stent 202 is deployed such that it is located in the basilar artery and in a vertebral artery (right side) where the aneurysm 201 is formed. On the other vertebral artery (left side), blood continues to flow to the basilar artery without any obstruction since the membrane 203 is permeable to blood flow. Preferably, the membrane 203 covers the whole stent 202, and the permeability of the membrane 203 allows blood flow through the left vertebral artery (left side). Conveniently, radio-opaque markers 204 are provided in order to permit more accurate placement of the stent 202.

[0252] In Fig. 28, the middle cerebral artery divides into the superior trunk and the inferior trunk. The stent 202 is deployed such that it is located in the middle cerebral artery and in the inferior trunk. Again, the struts of the stent 202 do not inhibit blood flow to the superior trunk, and blood flows through the stent 202 to the inferior trunk.

[0253] In Fig. 29, the stent 202 is deployed in the vertebral artery. As the aneurysm 201 in this example is located in a middle portion of the vertebral artery, there

is no need for the stent 202 to be located in more than one artery. When implanted, the stent 202 diverts blood flow away from the aneurysm 201. This leads to occlusion of the aneurysm 201 and keeps the arterial branches and the perforators patent. The stent 202 does not require precise positioning because it is uniformly covered with a porous membrane 203. Thus, most of the circumferential surface of the stent 202 is covered by the membrane 203, and thus the vessel wall will be uniformly contacted by the membrane in the area of the stent.

[0254] Due to the particular porosity and dimensions of the membrane 203, blood circulation to the aneurysm 201 is obstructed while blood supply to perforators and microscopic branches of main brain arteries as well as larger arteries is permitted. As described earlier, obstructing blood supply to the aneurysm 201 isolates the aneurysm 201 from normal blood circulation. The aneurysm in effect "dries out." The stent 202 and membrane 203 thus treats the aneurysm 201 by altering the hemodynamics in the aneurysm sac such that intra-aneurysmal thrombosis is initiated. At the same, blood flow into the arteries (branch, main, big or small) are not significantly affected by the implantation of the stent 202 or the membrane 203 due to the special porosity of the membrane 203. Although a bifurcation aneurysm has been described, it is envisaged that the stent 202 may be used to treat a trifurcation aneurysm, or other aneurysms, in a similar manner.

[0255] As used herein, the terms "secured to" and "coupled to" include direct and indirect means to secure and couple elements and/or components of endoprosthetic devices of the invention.

[0256] Fig. 30a illustrates an embodiment of a deployed endoprosthetic device 395. As shown, the distal assembly 400 of device 395 is made up of a plurality of engagement members 405, 410, 415, 420, coupled to flow-reducing member 425. While the embodiment illustrated in Fig. 30a comprises four engagement members 405, 410, 415, 420, some embodiments comprise one or more engagement members. Distal portions of the engagement members 405, 410, 415, 420 are curled and engage inner surfaces of an aneurysm 200. Flow reducing member 425 comprises a membrane 440, resides within the vessel 210, and reduces blood flow from the vessel 210 into the aneurysm 200. Device 395 can be delivered to the aneurysm by catheter 450 over a

guide wire 452, and device 395 can be repositioned at or within the aneurysm 200, or entirely removed from the aneurysm as described herein.

[0257] In some embodiments, the delivery of an aneurysm occlusion device can be accomplished by advancing a guide wire through the vasculature and into the aneurysm, advancing a catheter over the guide wire, and withdrawing the guide wire. At this point, an aneurysm occlusion device can be advanced by a pusher, and pushed through the catheter until the device is positioned at least partially within the aneurysm (e.g. a neck of an aneurysm).

[0258] In some embodiments, the delivery of an aneurysm occlusion device can be achieved by a multilumenal catheter comprising a guide wire lumen and a pusher-device. The guidewire is advanced through the vasculature and into the aneurysm. The catheter is advanced through the vasculature and to the aneurysm by tracking over the guide wire, disposed within the guide wire lumen, with a pusher and a device loaded into the pusher-device lumen of the catheter. Upon deployment, the pusher can be used to advance the device into the aneurysm. In some embodiments, the pusher can be used to retract the initially advanced device so as to reposition the device within the aneurysm. In some embodiments, the device and the pusher can be reversibly coupled, and the device released from the pusher by breaking of a chemical bond and/or an electrical heating process.

[0259] In some embodiments, an aneurysm occlusion device can, alone or coupled with a catheter delivery device, have an outside diameter in a range of from about 0.017" to 0.035." In some embodiments, an aneurysm occlusion device can, alone or coupled with a catheter delivery device, have an outside diameter in a range of from about 0.022" tot 0.030."

[0260] In some embodiments, the device comprises a balloon (e.g. a flow reducing member), which is inflated once the device has been delivered to the aneurysm, thereby expanding the distal assembly of the device. The expanded device is released from the catheter, and the catheter is withdrawn from the vasculature. The expanded device engages an inner surface of the aneurysm, which secures the device at the aneurysm in a position in which the flow reducing member(s) reduces blood flow from the vessel into the aneurysm.

[0261] In some embodiments, the device comprises shape-memory elements that, upon the device being released from the catheter, provide movement to the distal assembly so that it engages an inner surface of the aneurysm, thereby securing the device in a position in which the flow reducing member(s) reduce blood flow from the vessel into the aneurysm.

[0262] In some embodiments, the device comprises one or more forming elements, the manipulation of which provide(s) movement to the distal assembly into a position in which it engages an inner surface reduces blood flow from the vessel into the aneurysm.

[0263] In certain embodiments, the size of device is chosen such that, when in place at the aneurysm, it remains at least slightly elastically compressed, and therefore has a restoring force which facilitates secure positioning. In certain embodiments, a device in place at the aneurysm can rely on the restoring force of deformed tissue for secure positioning, and/or on hooks, barbs, or other independent fixation elements included as part of the device structure.

[0264] In Fig. 30a, Engagement members 405, 410, 415, 420 of device 395 can be made of metals or polymers, such as NiTi, tungsten, stainless steel, iridium, platinum alloy, polyurethane, polyethylene terephthalate, polyvinylchloride, nylon, polyimide, polyurethane ether, polyurethane ester, polyurethaneurea, polylactide, polyglycolide, poly-orthoester, polyposphazene, poly anhydride, and polyphosphoester. The engagement members 405, 410, 415, 420 can have shape-memory properties that enable self expansion from a first, delivery position to the illustrated second, deployment position. Engagement member 405, 410, 415, 420 movement from a first position to the illustrated second position can be accomplished by assisted movement of the engagement members, either in the absence of or in combination with any degree of shape-memory properties that engagement members 405, 410, 415, 420 may have. Assisted engagement member movement can be accomplished by, for instance, inflating a balloon located at a central axis of the distal assembly 400.

[0265] Flow reducing member 425 can comprise a porous or nonporous membrane 440, as described herein, and can be expandable from a first, delivery position to a second, deployed position, in which at least a portion of the membrane 440 of the

flow reducing member 425 is adjacent to an inner surface of the vessel 210. Flow reducing member 425 can comprise a frame, inflatable balloon, and/or thick plug. Frames of flow reducing members can comprise polymers and/or metals, such as such as NiTi, tungsten, stainless steel, iridium, platinum alloy, polyurethane, polyethylene terephthalate, polyvinylchloride, nylon, polyimide, polyurethane ether, polyurethane ester, polyurethaneurea, polylactide, polyglycolide, poly-orthoester, polyposphazene, poly anhydride, and polyphosphoester, and comprise struts. Flow reducing members can be coupled to a distal assembly and/or each other by weld, interweaving, suture, stitch, adhesive, combinations thereof, etc.

[0266] Fig. 30b illustrates a cross sectional view of device 395 shown in Fig. 30.

[0267] Fig. 31 illustrates a device 495 similar to the one shown in Fig. 30, but the engagement members 405, 410, 415, 420 of device 495 illustrated in Fig. 31 are curled in a different manner than those of device 395 of illustrated in Fig. 30. In addition, device 495 illustrated in Fig. 31 comprises a linking member 435, whereas device 395 shown in Fig. 30 does not have a linking member.

[0268] Fig. 32 illustrates a device 595 similar to device 495 shown in Fig. 31, but device 595 illustrated in Fig. 32 comprises three engagement members 405, 410, 415, whereas device 495 shown in Fig. 31 comprises four engagement members 405, 410, 415, 420. Device 495 shown in Fig. 31 has one flow reducing member 425, whereas device 595 illustrated in Fig. 32 further comprises a second flow-reducing member 430 that comprises a balloon, resides in the aneurysm 200, and reduces blood flow from the vessel 210 into the aneurysm 200. In addition, device 595 illustrated in Fig. 32 further comprises two linking members 436 and 437 that couple flow reducing members 425, 430 to each other and to the distal assembly 400, whereas device 495 illustrated in Fig. 31 comprises one linking member. A linking member can couple, directly or indirectly, itself to another linking member, a flow reducing member, and/or a distal assembly.

[0269] Fig. 33 illustrates a device 695 similar to device 495 shown in Fig. 31, but device 695 illustrated in Fig. 33 has one engagement member 505, whereas device 595 shown in Fig. 32 has three engagement members. As can be seen in Fig. 33, first and second portions of engagement member 505 engage first and second regions of the inner

wall of the aneurysm 200, and the first and second portions of the engagement member can be separated by a space of at least 2 mm.

[0270] Fig. 34 illustrates a device 795 that comprises a flow reducing member 425 that comprises a membrane 440, a linking element 435, and a distal assembly 400 that engages an inner surface of an aneurysm in the illustrated, deployed position. The distal assembly is comprised of an engagement member 605 having a helical shape, first and second portions of which engage first and second regions of the inner wall of the aneurysm 200, and the first and second portions of the engagement member can be separated by a space of at least 2 mm.

[0271] Fig. 35 illustrates a device 895 that comprises a flow reducing member 425, positioned in the vessel 210 and comprising a membrane 440. The device 895 also comprises a distal assembly 400, within an aneurysm 200, having four engagement members 405, 407, 410, 415. Linking member 435 couples the flow reducing member 425 to the distal assembly 400. Also illustrated in Figure 35 are some forces that contribute to securing the device 895 in the deployed position within the aneurysm. For example, pull forces (FP) 421, 422, 423, 424 are established by the engagement of engagement members 405, 407, 410, 415 with the inner surfaces of the aneurysm 200. In addition, resistance forces (RF) 426, 427 are established by the interaction between the flow reducing member and blood pressure of the vessel 210. The FPs 421, 422, 423, 424 and the RFs 426, 427 contribute to a secure deployment of the device 895.

[0272] It will be appreciated by persons skilled in the art that certain embodiments of the devices illustrated in Figures 30a-35, and variants of those devices, can be used in combination with knows aneurysm occlusion devices, such as aneurysm coils. In addition, such devices can be useful in the treatment of different types of aneurysms, such as intracranial aneurysms, saccular aneurysms, wide-neck aneurysms, fusiform aneurysms, bifurcation aneurysms, and trifurcation aneurysms.

[0273] It will be also appreciated by persons skilled in the art that numerous variations and/or modifications may be made to the specific embodiments disclosed herein, without departing from the scope or spirit of the disclosure as broadly described. The present embodiments are, therefore, to be considered in all respects illustrative and not restrictive of the invention, which is defined by the claims as presented herein.

What Is Claimed Is:

1. An endovascular device, for treating an aneurysm of a body vessel, comprising:

a distal assembly, movable from a first position to a second position when the distal assembly is at least partially in an aneurysm; and

a first flow-reducing member, coupled to the distal assembly, that reduces blood flow from the body vessel into the aneurysm when the distal assembly is in the second position;

wherein the distal assembly comprises a plurality of engagement members, each of which extends, from a proximal portion to a distal portion, away from the flow-reducing member;

wherein, when the distal assembly is in the first position, each of the plurality of engagement members is substantially parallel to a central axis of the distal assembly;

wherein, when the distal assembly changes from the first to the second position, the distal portion of each of the plurality of engagement members moves away from the central axis, such that the distal portions of each of the plurality of engagement members:

substantially curl;

move closer to the first flow-reducing member; and

engage an inner surface of the aneurysm.

2. The endovascular device of Claim 1, wherein at least one of the plurality of engagement members comprises a polymer selected from the group consisting of ePTFE, polyurethane, polyethylene terephthalate, polyvinylchloride, nylon, polyimide, polyurethane ether, polyurethane ester, polyurethaneurea, polylactide, polyglycolide, poly-orthoester, polyphosphazene, polyanhydride, and polyphosphoester.

3. The endovascular device of Claim 1, wherein at least one of the plurality of engagement members comprises a metal selected from the group consisting of NiTi, tungsten, stainless steel, iridium, and platinum.

4. The endovascular device of Claim 1, wherein a distal end of at least one of the plurality of engagement members is blunt.

5. The endovascular device of Claim 1, wherein, when the distal assembly is in the second position, a distal end of each of the plurality of engagement members engages the inner surface of the aneurysm.

6. The endovascular device of Claim 1, wherein, when the distal assembly is in the second position, the first flow-reducing member resides in the body vessel.

7. The endovascular device of Claim 1, wherein, when the distal assembly is in the second position, the first flow-reducing member resides in the aneurysm.

8. The endovascular device of Claim 1, further comprising a second flow-reducing member, coupled to the first flow-reducing member or to the distal assembly, that reduces blood flow from the body vessel into the aneurysm when the distal assembly is in the second position.

9. The endovascular device of Claim 8, wherein, when the distal assembly is in the second position, the first flow-reducing member resides in the body vessel and the second flow-reducing member resides in the aneurysm.

10. The endovascular device of Claim 8, further comprising a linking member that couples the second flow-reducing member to the first flow-reducing member or to the distal assembly.

11. The endovascular device of Claim 10, wherein at least one of the linking member, the distal assembly, the first flow-reducing member, and the second flow-reducing member comprises at least one metal selected from the group consisting of NiTi, tungsten, stainless steel, iridium, and platinum.

12. The endovascular device of Claim 10, wherein the linking member comprises a wire.

13. The endovascular device of Claim 10, wherein each of the linking member, the first flow-reducing member, the second flow-reducing member, and the distal assembly comprises a metal, and wherein a weld couples the linking member to at least one of the distal assembly, the first flow-reducing member, and the second flow-reducing member.

14. The endovascular device of Claim 10, wherein the second flow-reducing member comprises a plug, and wherein, when the distal assembly is in the second position, the plug substantially resides within a neck of the aneurysm and substantially inhibits blood flow through the neck of the aneurysm.

15. The endovascular device of Claim 14, wherein the plug comprises a balloon.

16. The endovascular device of Claim 8, wherein the first flow-reducing member comprises a membrane.

17. The endovascular device of Claim 16, wherein, when the distal assembly is in the second position, a thickness of the membrane is between about 5 μm and about 500 μm.

18. The endovascular device of Claim 16, wherein the membrane comprises at least one polymer selected from the group consisting of ePTFE, polyurethane, polyethylene terephthalate, polyvinylchloride, nylon, polyimide, silicone, polyurethane ether, polyurethane ester, polyurethaneura, polylactide, polyglycolide, poly-orthoester, polyphosphazene, polyanhydride, and polyphosphoester.

19. The endovascular device of claim 16, wher ein the first flow-reducing member is coupled to the distal assembly by suture or interweaving.

20. The endovascular device of Claim 16, wherein at least a portion of the membrane is non-porous.

21. The endovascular device of Claim 16, wherein the membrane comprises a porous section having a porosity over a length extending from a proximal end of the porous section to a distal end of the porous section;

wherein a pore spacing and a pore size of the porous section determine the porosity of the porous section;

wherein, when the distal assembly is in the second position, the membrane is effective to reduce blood flow into the aneurysm and to promote thrombosis at or in the aneurysm.

22. The endovascular device of Claim 21, wherein the porosity is selected such that, when the distal assembly is in the second position, the porous section of the

membrane is effective to enhance endothelial cell migration and tissue growth onto the membrane and to substantially inhibit blood flow from the body vessel into the aneurysm.

23. The endovascular device of Claim 21, wherein the pore size is between about 1 μm and about 150 μm.

24. The endovascular device of Claim 21, wherein the pore size is between about 10 μm and about 50 μm.

25. The endovascular device of Claim 21, wherein the pore spacing is between about 40 μm and about 100 μm.

26. The endovascular device of Claim 21, wherein the pore spacing is between about 60 μm and about 75 μm.

27. The endovascular device of Claim 21, wherein a material ratio of the porous section of the membrane comprises a ratio of a total area of an outer surface of the porous section of the membrane that comprises material to a total area of an outer surface of the porous section that comprises pores.

28. The endovascular device of Claim 27, wherein, when the distal assembly is in the second position, the material ratio is between about 25% and about 90%.

29. The endovascular device of Claim 16, further comprising at least one agent, permanently attached to the membrane, that, when the distal assembly is in the second position, promotes healing of the aneurysm.

30. The endovascular device of Claim 29, wherein the healing agent comprises at least one of a peptide, a protein, an enzyme regulator, an antibody, a naturally occurring molecule, a synthetic molecule, a nucleic acid, a polynucleotide, L-PDMP, and D-PDMP.

31. An endovascular device, for treating an aneurysm of a body vessel, comprising:

means for engaging an inner surface of an aneurysm, the means for engaging being movable from a first position to a second position when the means for engaging is at least partially within an aneurysm; and

first means for reducing blood flow into the aneurysm, the means for reducing blood flow being coupled to the means for engaging, such that when the

means for engaging is in the second position, the first means for reducing blood flow is effective to reduce blood flow from the body vessel into the aneurysm;

wherein the means for engaging comprises a plurality of engagement members, each of which extends, from a proximal portion to a distal portion, away from the first means for reducing blood flow;

wherein, when the means for engaging is in the first position, each of the plurality of engagement members is substantially parallel to a central axis of the distal assembly;

wherein, when the means for engaging changes from the first to the second position, the distal portion of each of the plurality of engagement members moves away from the central axis, such that the distal portions of each of the plurality of engagement members:

substantially curl;

move closer to the first flow-reducing member; and

engage an inner surface of the aneurysm.

32. The endovascular device of claim 31, further comprising second means for reducing blood flow into the aneurysm, coupled to the first means for reducing blood flow and effective to reduce blood flow into the aneurysm when the means for engaging is in the second position.

33. The endovascular device of Claim 32, wherein, when the means for engaging is in the second position, the first flow-reducing means resides in the body vessel and the second flow-reducing means resides in the aneurysm.

34. A method of treating an aneurysm of a body vessel comprising:

providing an endovascular device comprising:

a distal assembly, movable from a first position to a second position when the distal assembly is at least partially within an aneurysm, the distal assembly comprising a plurality of engagement members, each of which extends, from a proximal portion to a distal portion, away from the flow-reducing member and each of which, when the distal assembly is in the first position, is substantially parallel to a central axis of the distal assembly; and

a first flow-reducing member, coupled to the distal assembly, that reduces blood flow from the body vessel into the aneurysm when the distal assembly is in the second position;

positioning the distal assembly at least partially within the aneurysm; and

changing the distal assembly from the first position to the second position such that the distal portion of each of the plurality of engagement members moves away from the central axis, whereby the distal portions of each of the plurality of engagement members:

substantially curl;

move closer to the first flow-reducing member; and

engage an inner surface of the aneurysm.

35. The method of Claim 34, wherein at least one of the plurality of engagement members comprises a polymer selected from the group consisting of ePTFE polyurethane, polyethylene terephthalate, polyvinylchloride, nylon, polyimide, polyurethane ether, polyurethane ester, polyurethaneurea, polylactide, polyglycolide, poly-orthoester, polyphosphazene, polyanhydride, and polyphosphoester.

36. The method of Claim 34, wherein at least one of the plurality of engagement members comprises at least one metal selected from the group consisting of NiTi, tungsten, stainless steel, iridium, and platinum.

37. The method of Claim 34, wherein a distal end of at least one of the plurality of engagement members is blunt.

38. The method of Claim 34, wherein, when the distal assembly is in the second position, a distal end of each of the plurality engagement members engages the inner surface of the aneurysm.

39. The method of Claim 34, wherein, when the distal assembly is in the second position, the first flow-reducing member resides in the body vessel.

40. The method of Claim 34, wherein, when the distal assembly is in the second position, the first flow-reducing member resides in the aneurysm.

41. The method of Claim 34, wherein the endovascular device further comprises a second flow-reducing member, coupled to the first flow-reducing member or

to the distal assembly, that reduces blood flow from the body vessel into the aneurysm when the distal assembly is in the second position; and further comprising:

positioning the second flow-reducing member at least partially in the aneurysm.

42. The method of Claim 41, wherein, when the distal assembly is in the second position, the first flow-reducing member resides in the body vessel and the second flow-reducing member resides in the aneurysm.

43. The method of Claim 41, wherein the endovascular device further comprises a linking member that couples the second flow-reducing member to the first flow-reducing member or to the distal assembly.

44. The method of Claim 43, wherein the second flow-reducing member comprises a plug, and wherein, when the distal assembly is in the second position, the plug substantially resides within a neck of the aneurysm and substantially inhibits blood flow through the neck of the aneurysm.

45. The method of Claim 34, wherein the first flow-reducing member comprises a membrane.

46. An endovascular device, for treating an aneurysm of a body vessel, comprising:

a distal assembly, comprising an engagement member, the distal assembly being movable from a first position to a second position when the distal assembly is at least partially in the aneurysm;

a flow-reducing assembly, coupled to the distal assembly and comprising a first flow-reducing member, the flow-reducing assembly reducing blood flow from the body vessel into the aneurysm when the distal assembly is in the second position;

wherein the engagement member is elongate and curvilinear and extends, from a proximal to a distal end of the engagement member, along a path that originates from a point at the flow-reducing assembly and terminates at a point within the aneurysm when the first flow-reducing member resides in the body vessel;

wherein the engagement member is coterminous with the path;

wherein, when the distal assembly is in the second position in the aneurysm, the first flow-reducing member resides in the body vessel, a first portion of the engagement member engages a first region of an inner surface of the aneurysm, and a second portion of the engagement member engages a second region of the inner surface of the aneurysm;

wherein the first and second regions are spaced at least 2 mm apart.

47. The endovascular device of Claim 46, wherein the flow-reducing assembly further comprises a second flow-reducing member;

wherein, when the second flow-reducing member resides at least partially in the aneurysm, and the distal assembly is in the second position, the first flow-reducing member resides in the body vessel.

48. The endovascular device of Claim 46, wherein a form of at least a portion of the engagement member is helical.

49. The endovascular device of Claim 46, wherein the first and the second portions of the engagement member are spaced at least 2 mm apart.

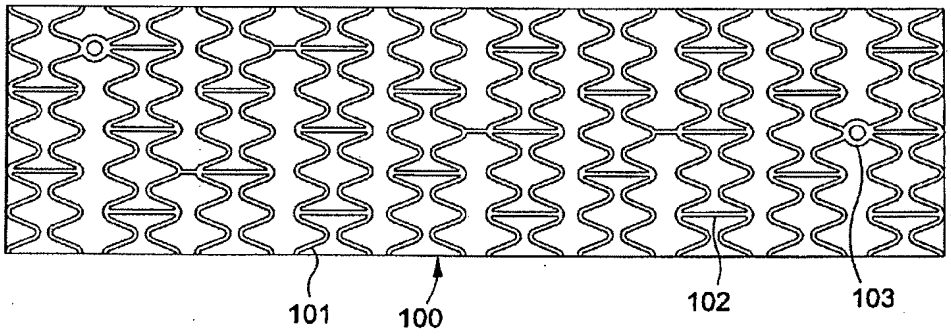


FIG. 1A

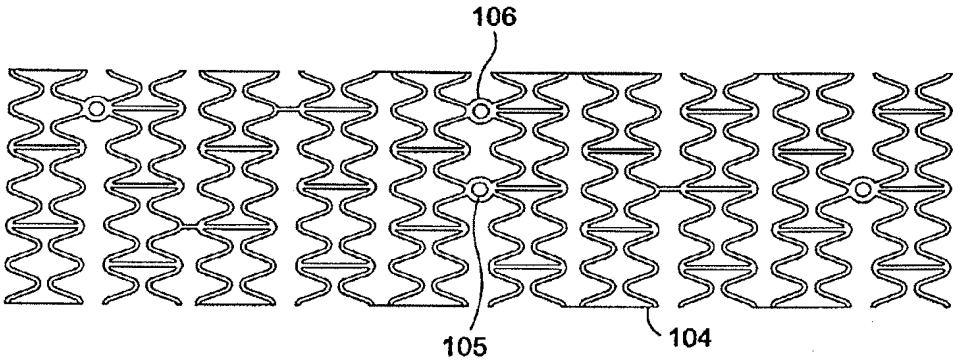


FIG. 1B

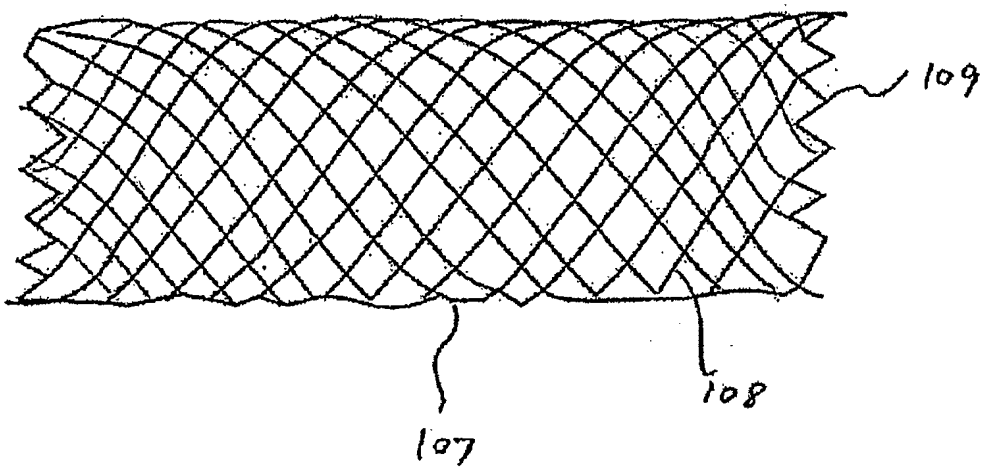


FIGURE 2

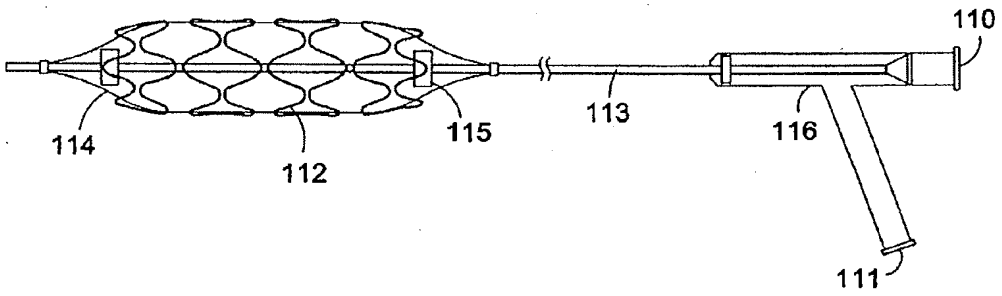


FIG. 3

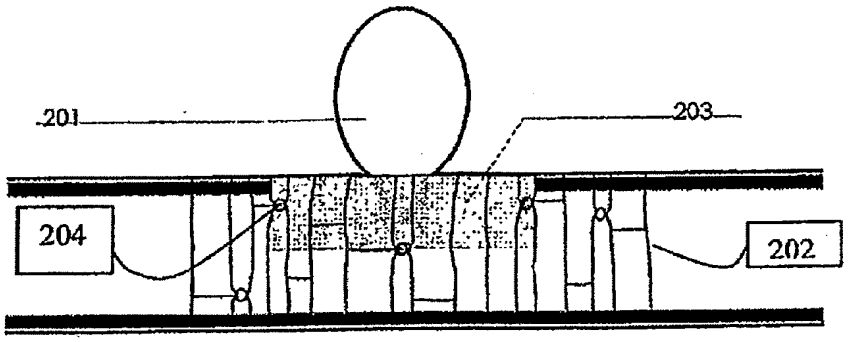


FIGURE 4A

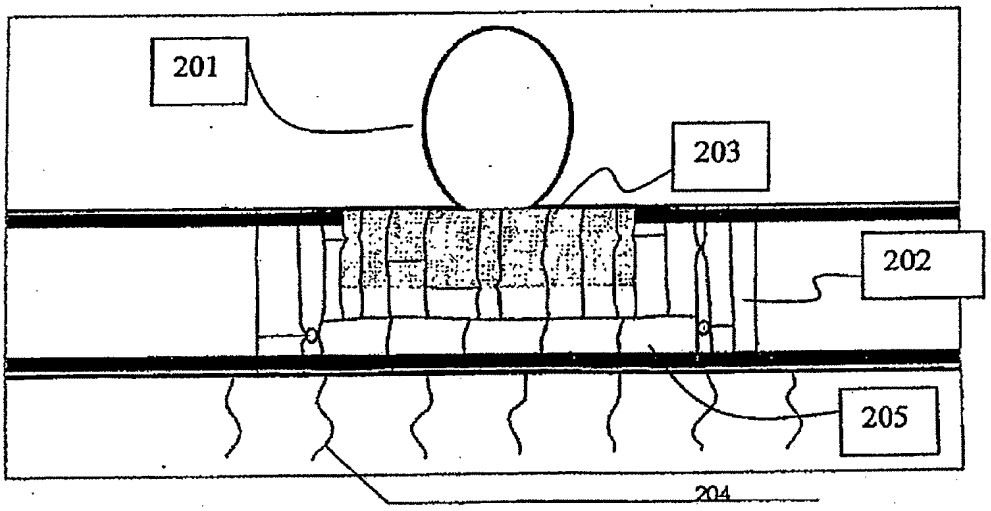


FIGURE 4B

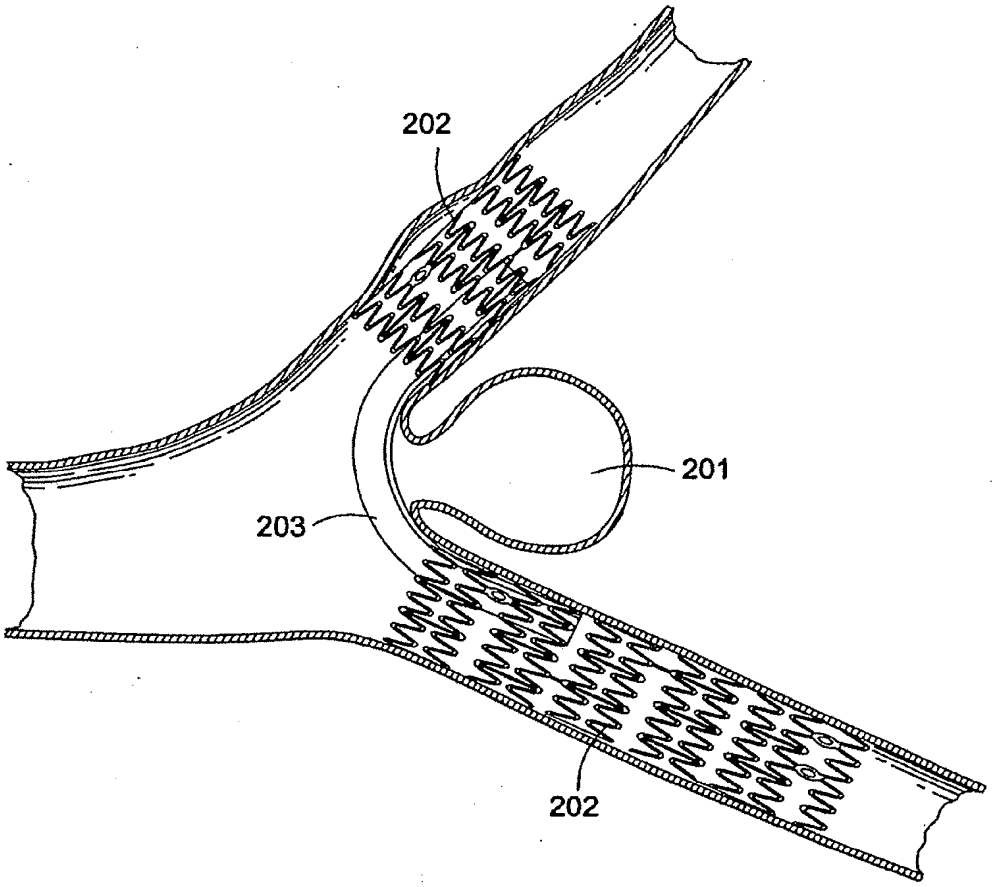


FIG. 5

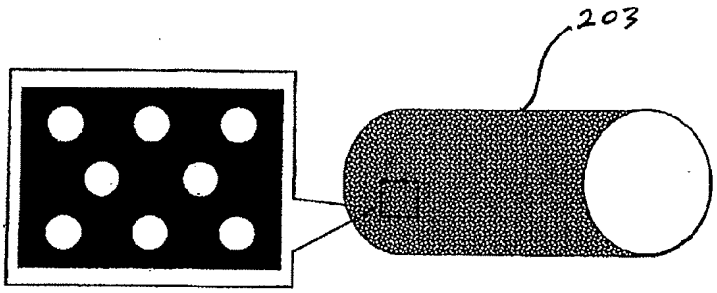


FIGURE 6

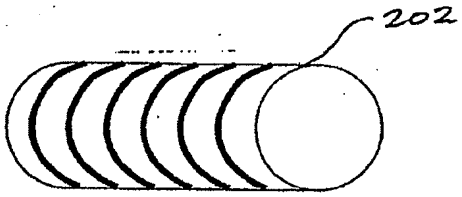


FIGURE 7

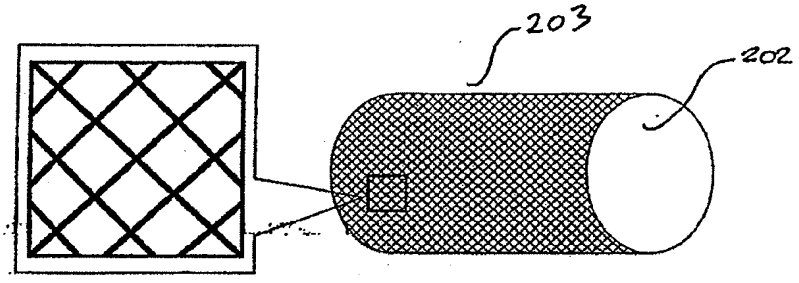


FIGURE 8

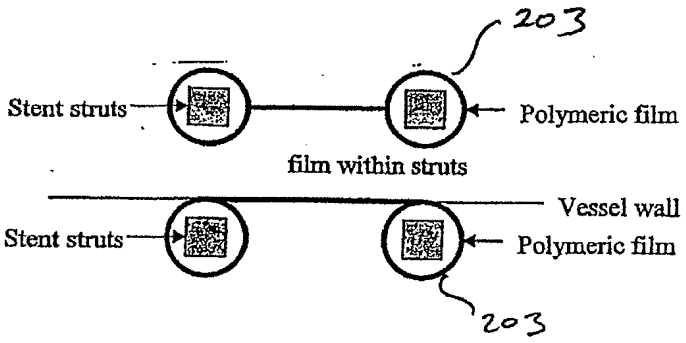


FIGURE 9

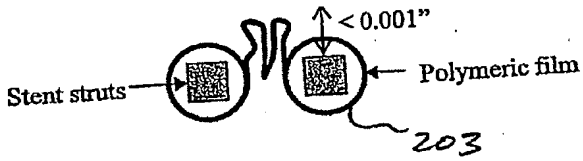


FIGURE 10

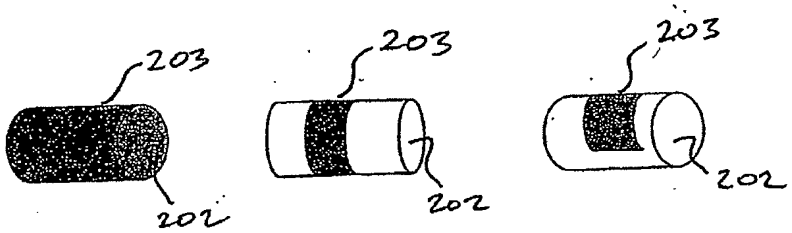


FIGURE 13

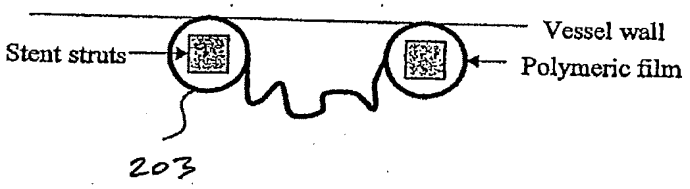


FIGURE 11

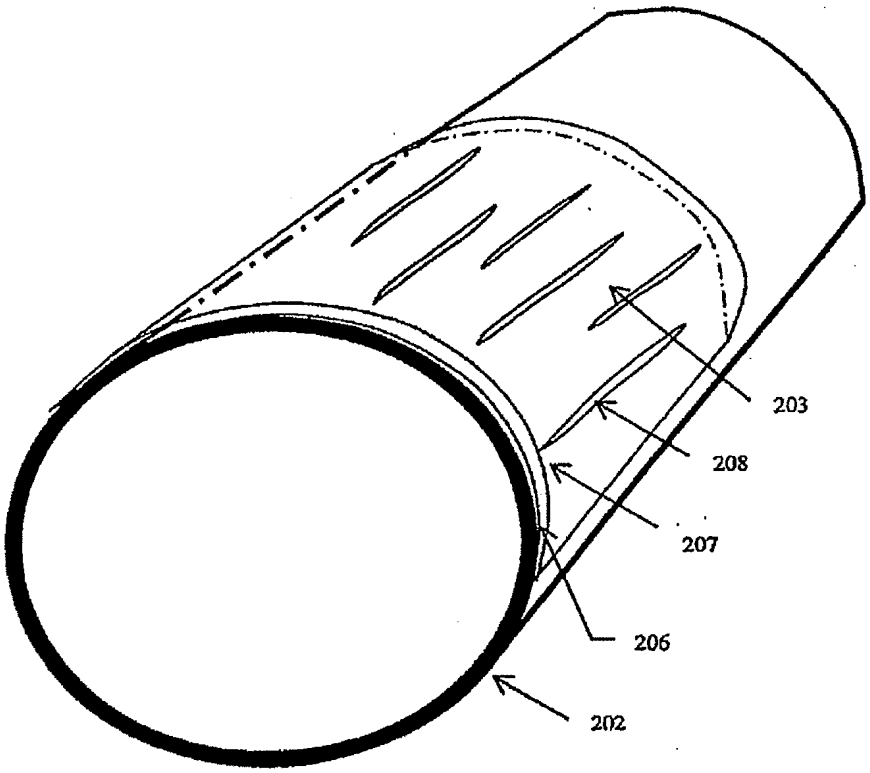


FIGURE 12

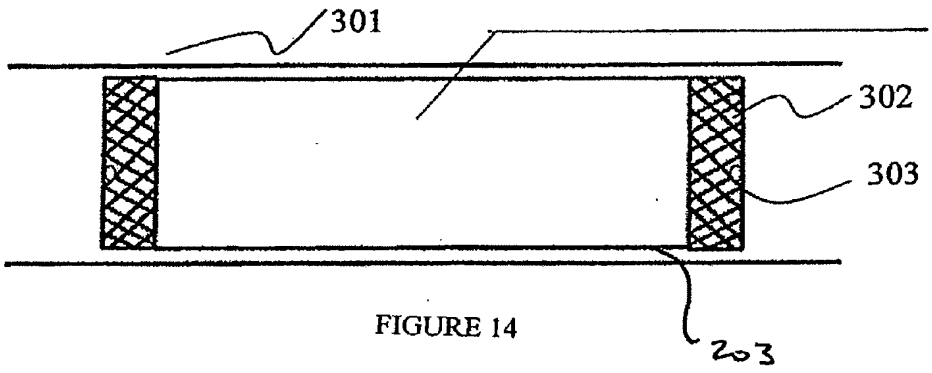


FIGURE 14

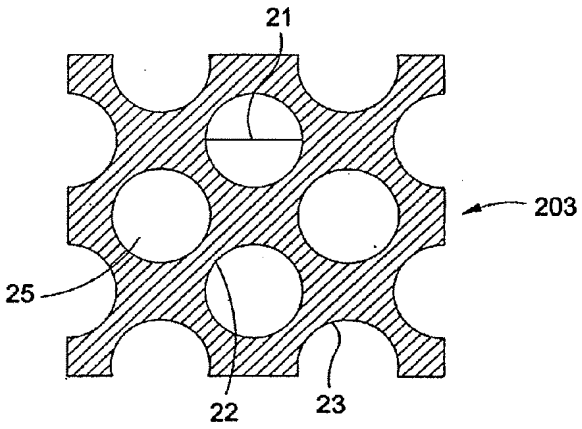


FIG. 15

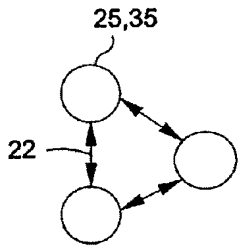


FIG. 16

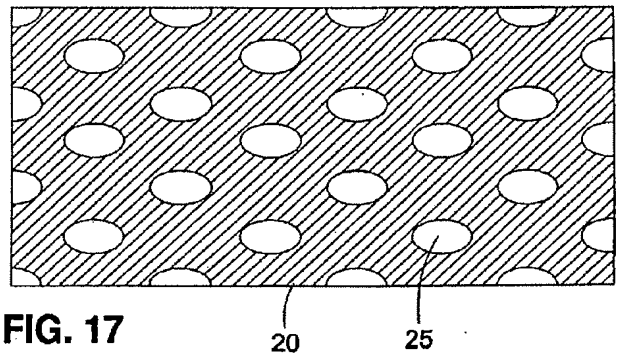


FIG. 17

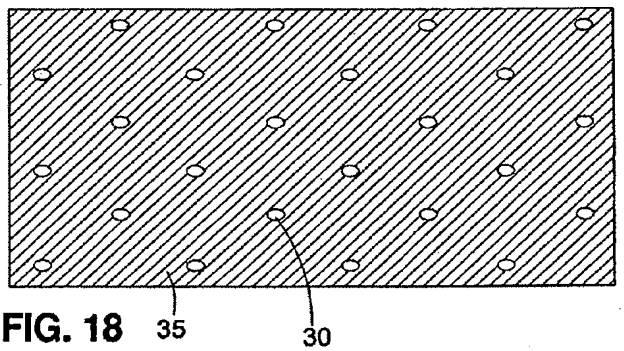


FIG. 18

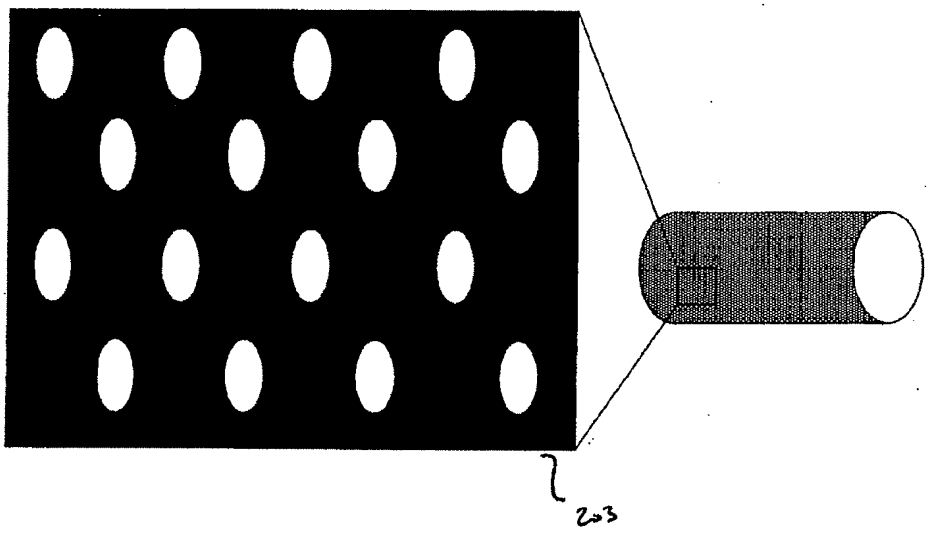


FIGURE 19B

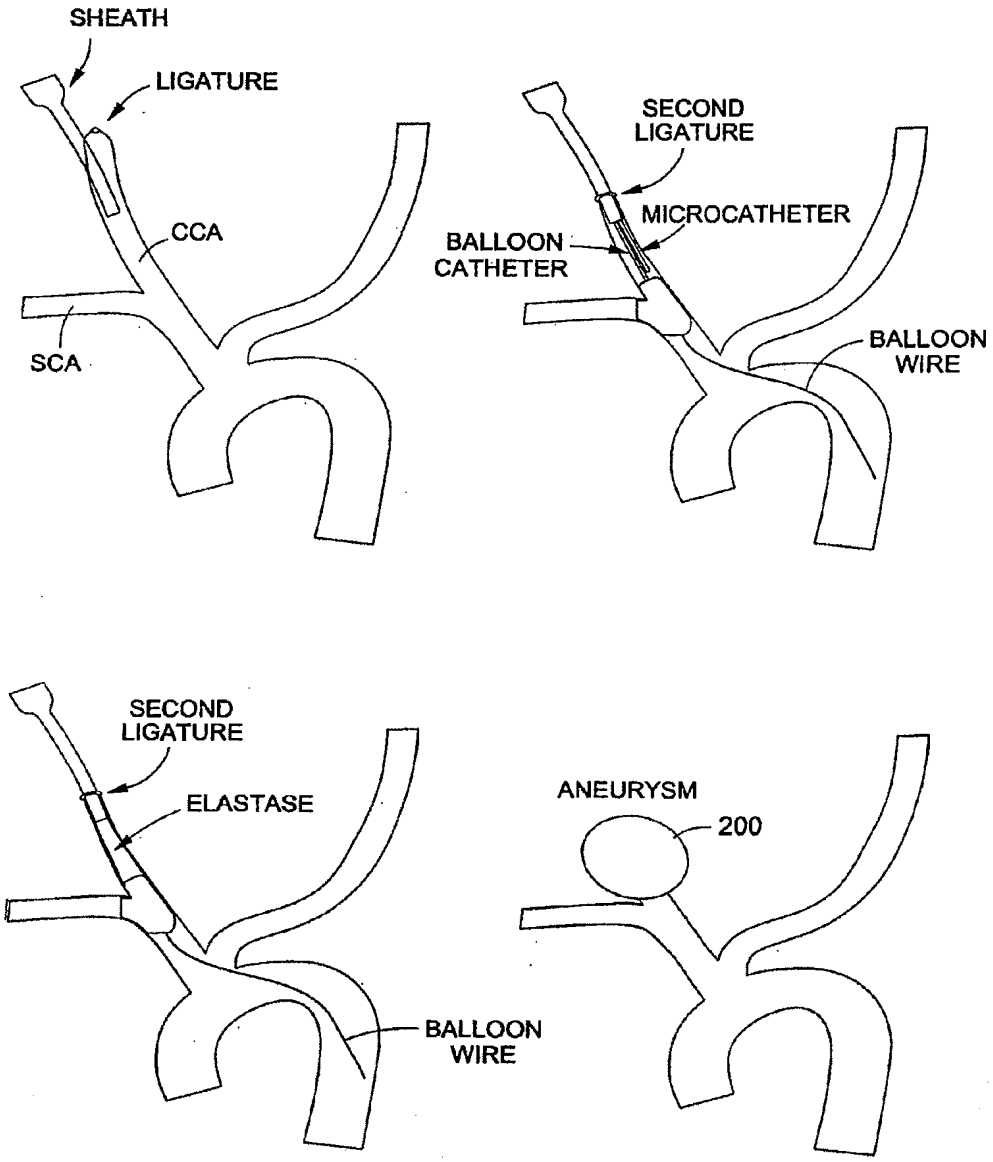

SHEATH
LIGATURE
CCA
SCA
SECOND LIGATURE
MICROCATHETER
BALLOON CATHETER
BALLOON WIRE
SECOND LIGATURE
ELASTASE
BALLOON WIRE
ANEURYSM
200

FIG. 20

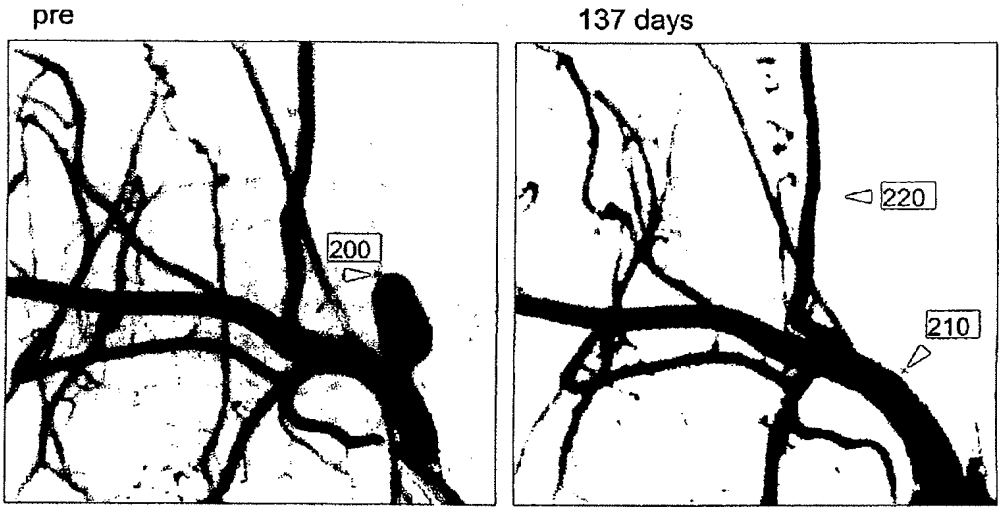


FIG. 21A FIG. 21B

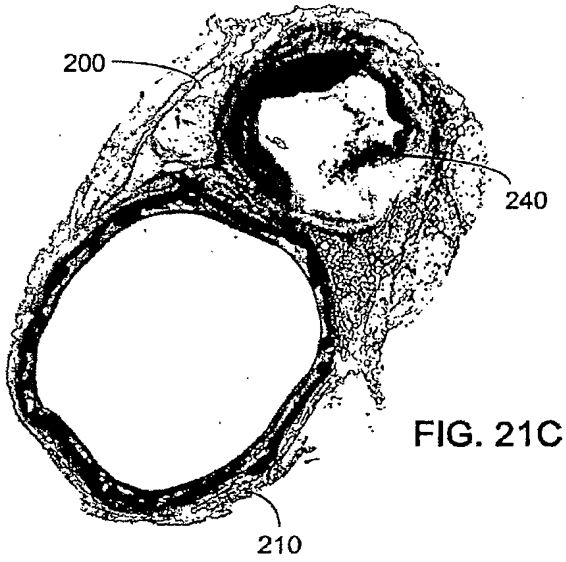


FIG. 21C

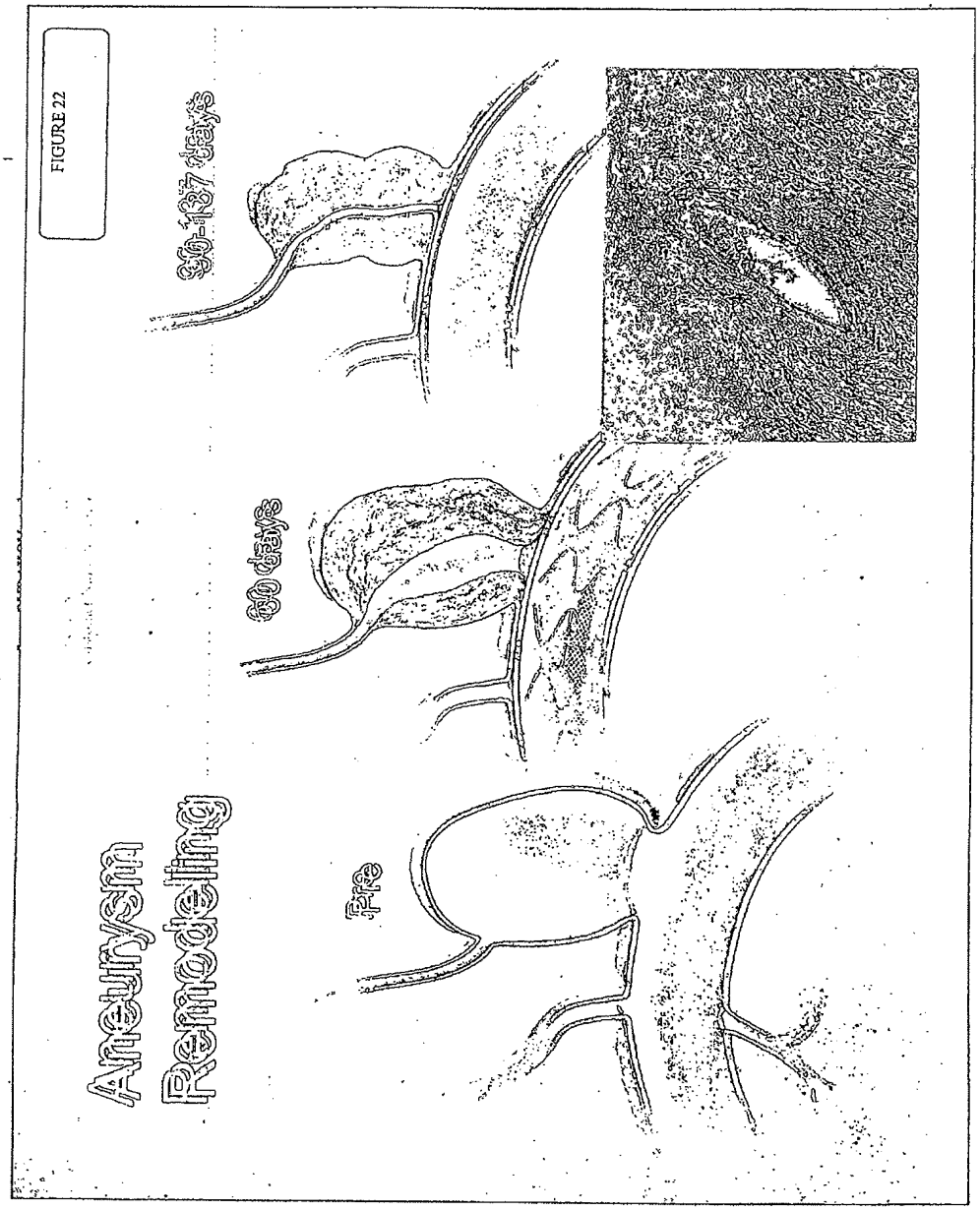


FIGURE 22
Aneurysm Remodeling
Pre
30 days
90-137 days

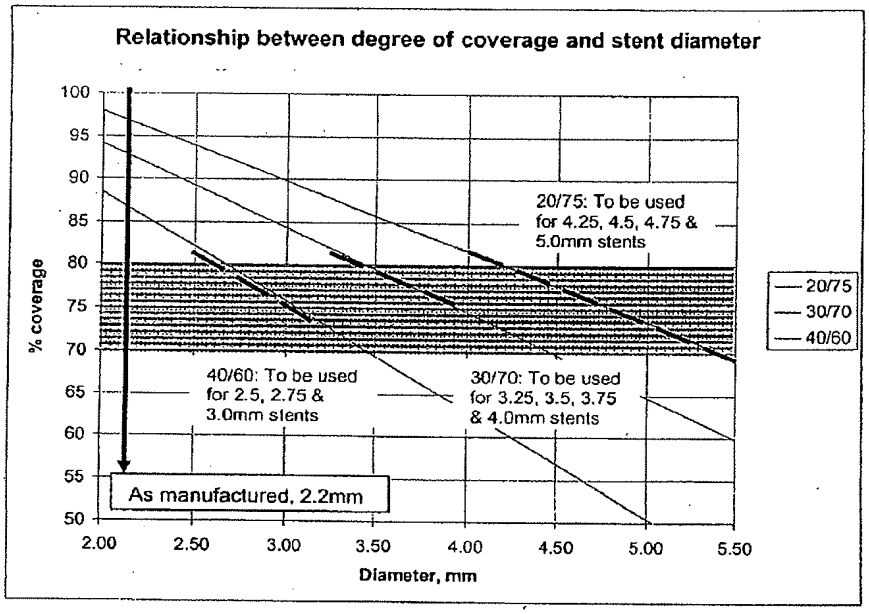


FIGURE 23

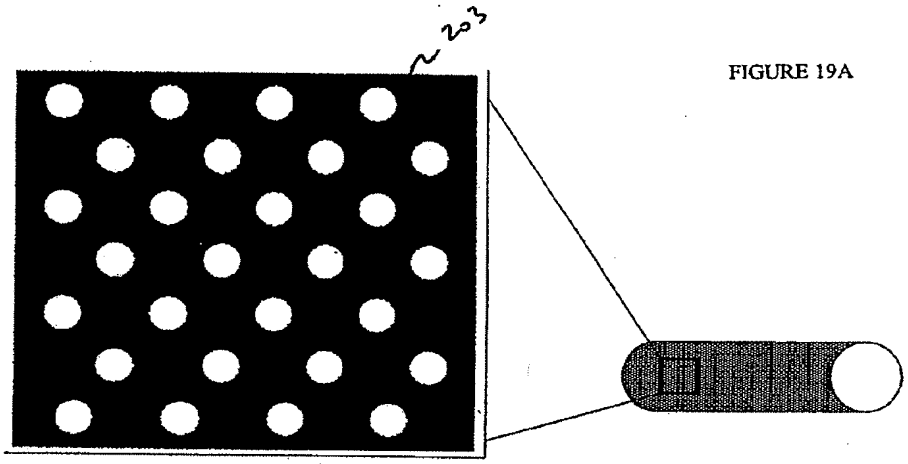


FIGURE 19A

FIGURE 24A

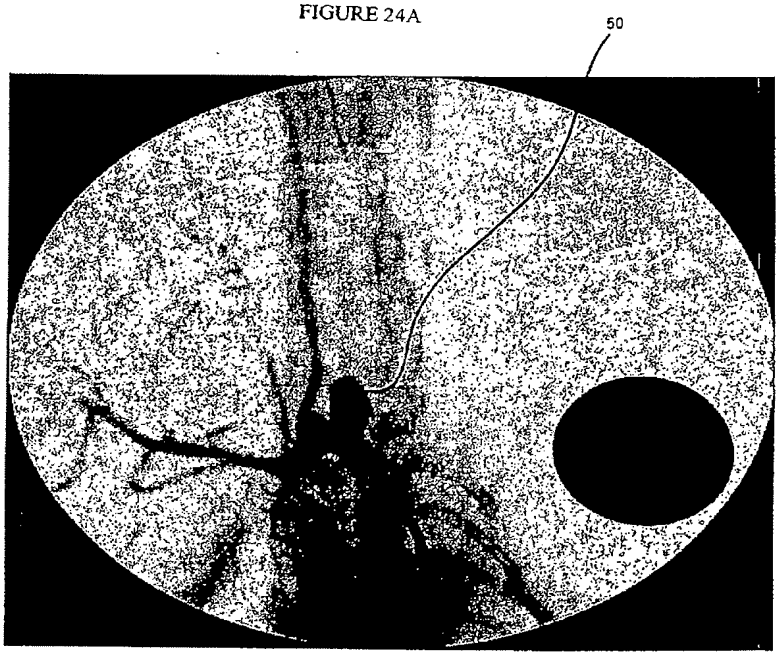


FIGURE 24B

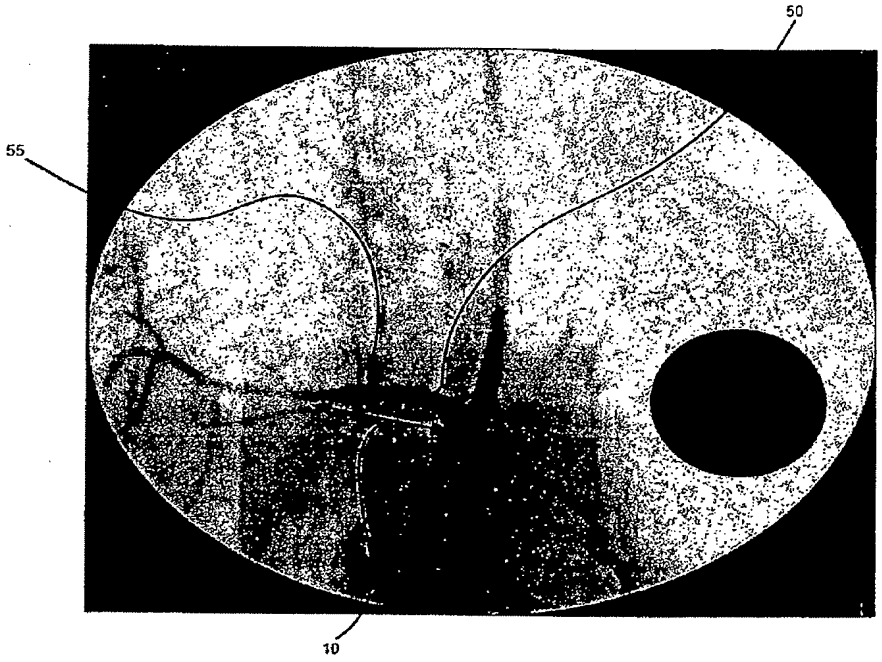


FIGURE 25A

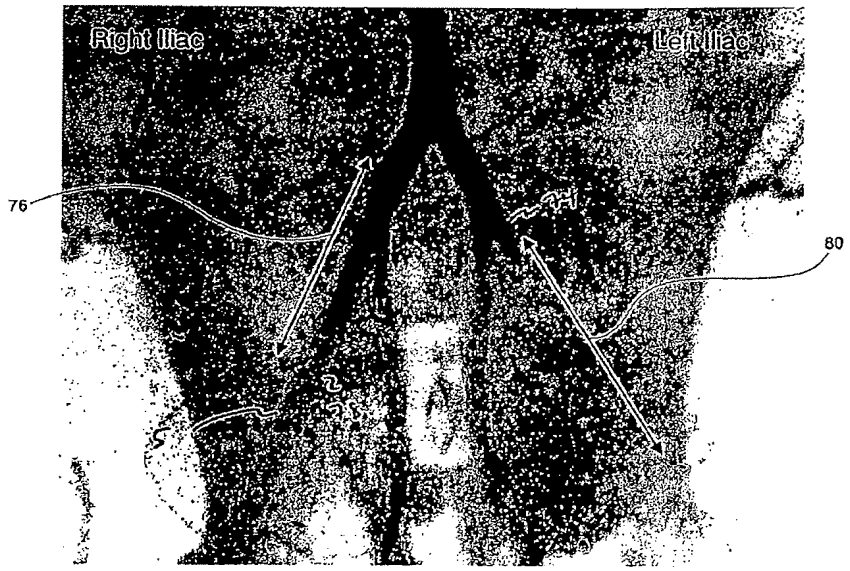


FIGURE 25B

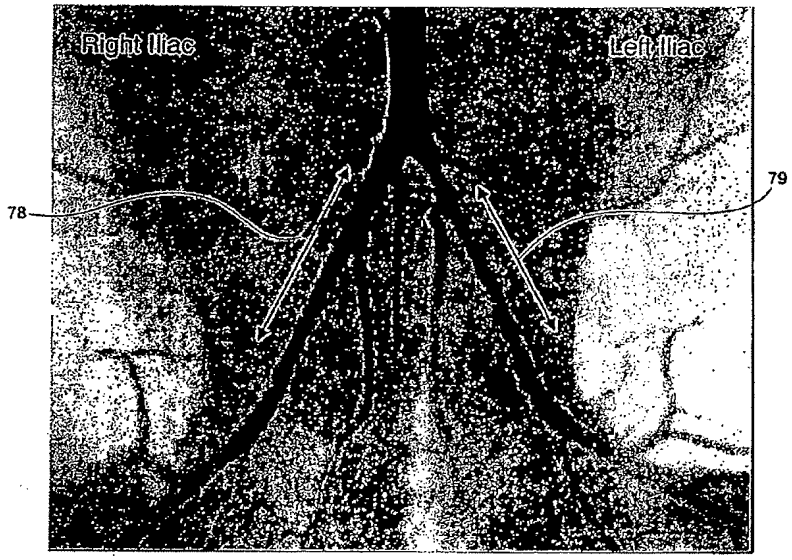


FIGURE 26

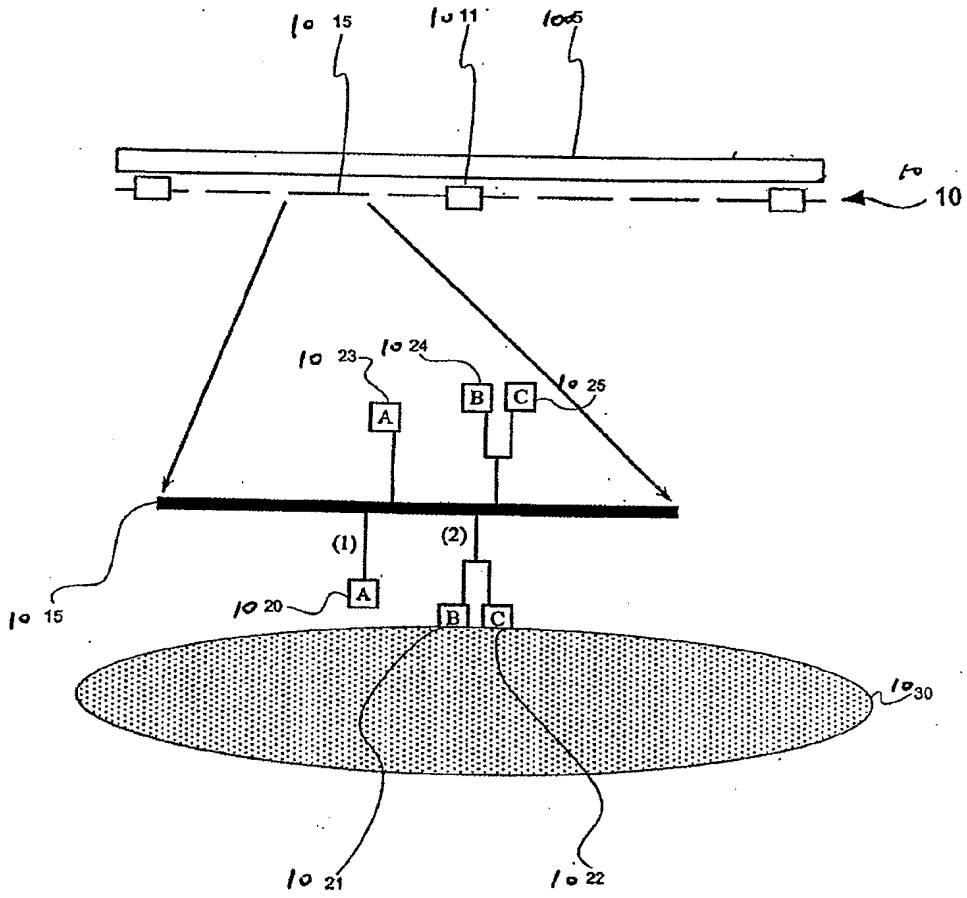

10 15
10 11
10 10
10
10 23
10 24
10 25
A
B
C
(1)
(2)
10 15
10 20
A
B
C
10 30
10 21
10 22

FIGURE 27

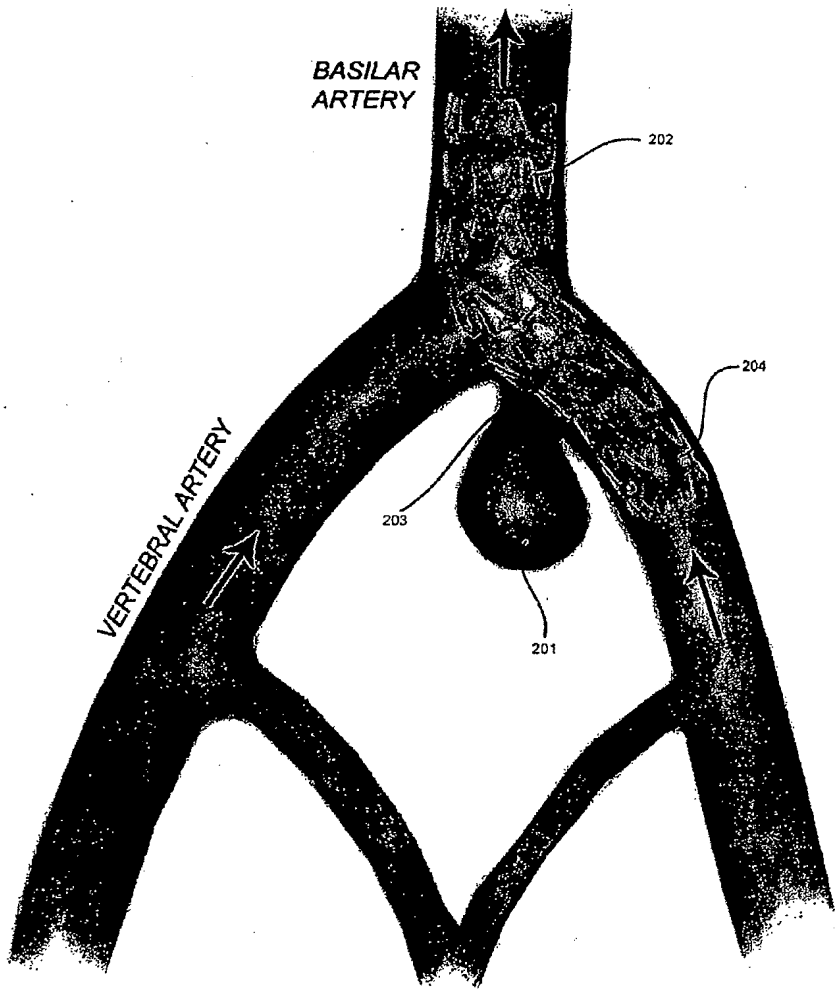


FIGURE 28

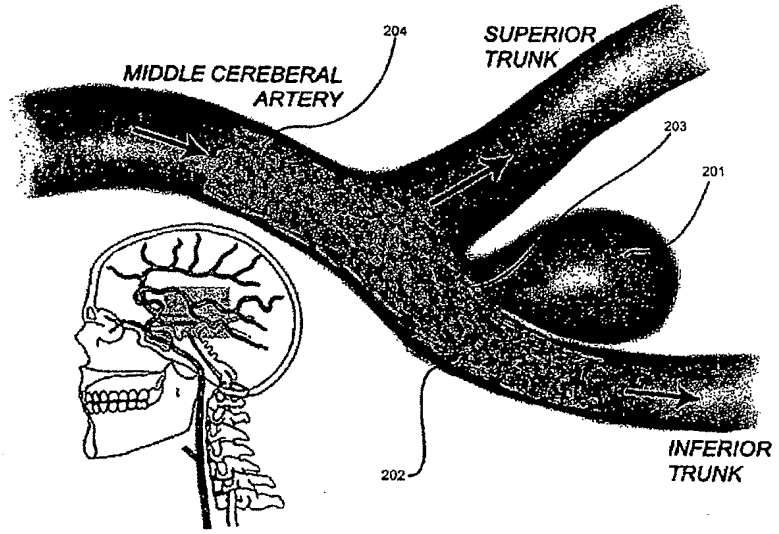
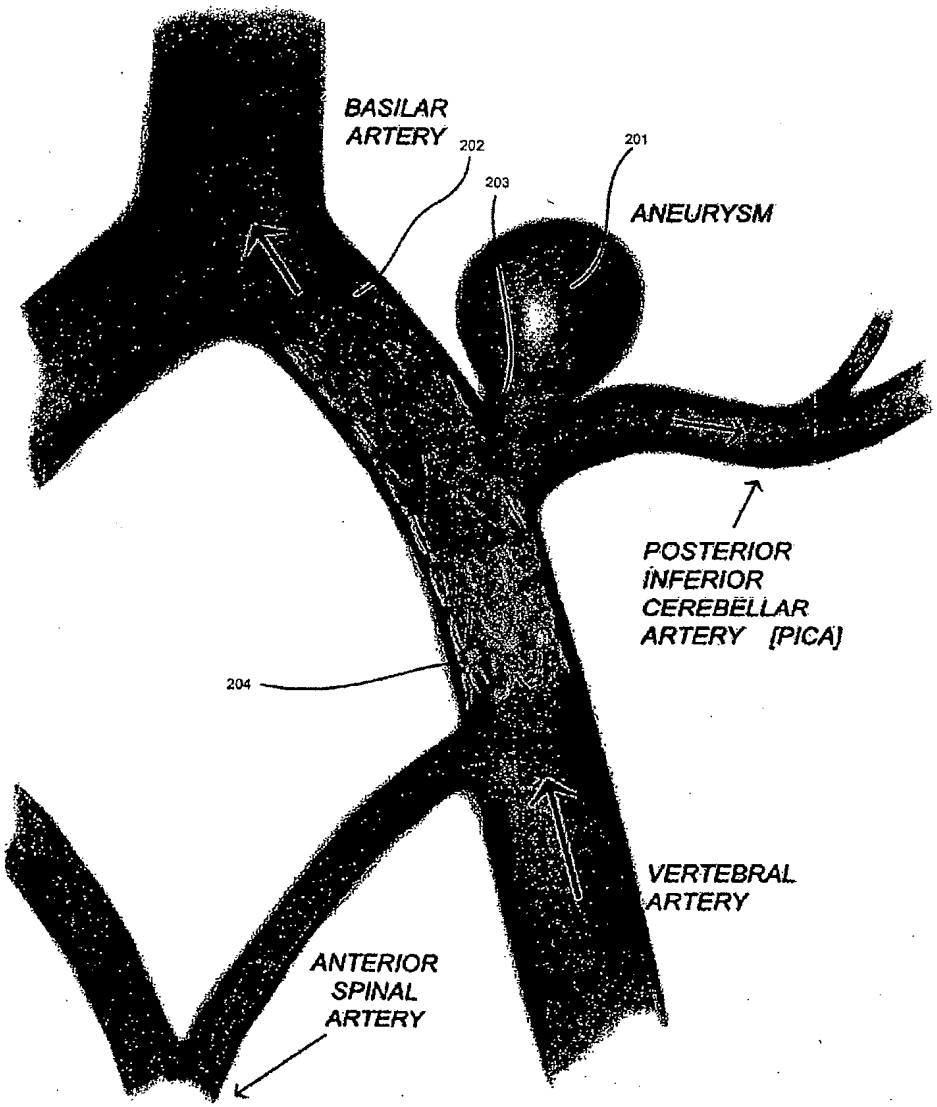

204
SUPERIOR TRUNK
MIDDLE CEREBERAL ARTERY
203
201
202
INFERIOR TRUNK

FIGURE 29


BASILAR ARTERY
202
201
203
ANEURYSM
POSTERIOR INFERIOR CEREBELLAR ARTERY (PICA)
204
VERTEBRAL ARTERY
ANTERIOR SPINAL ARTERY

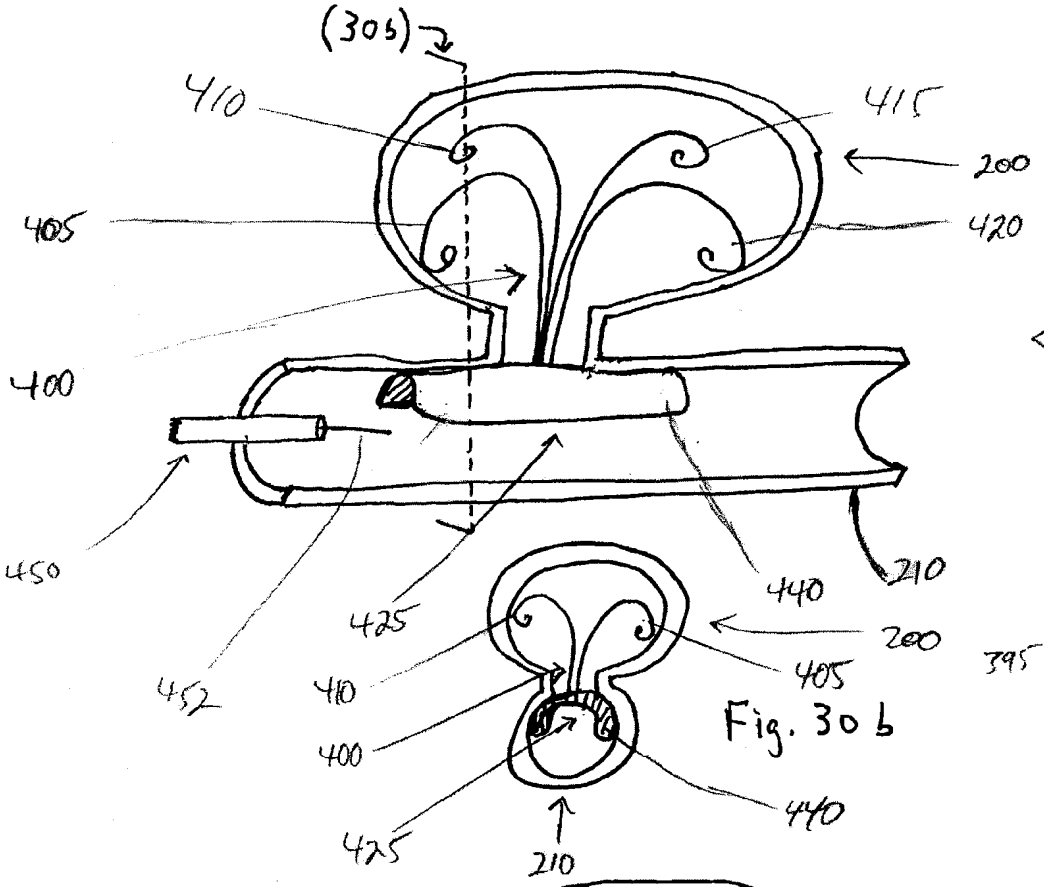


Fig. 30a

Fig. 30b

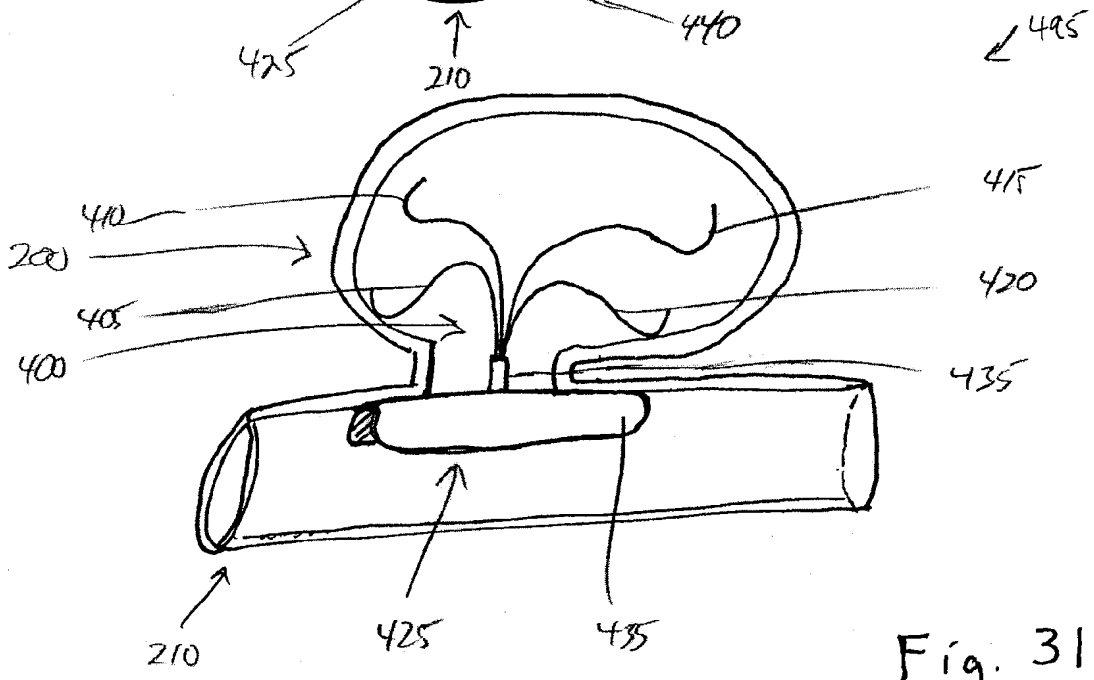


Fig. 31

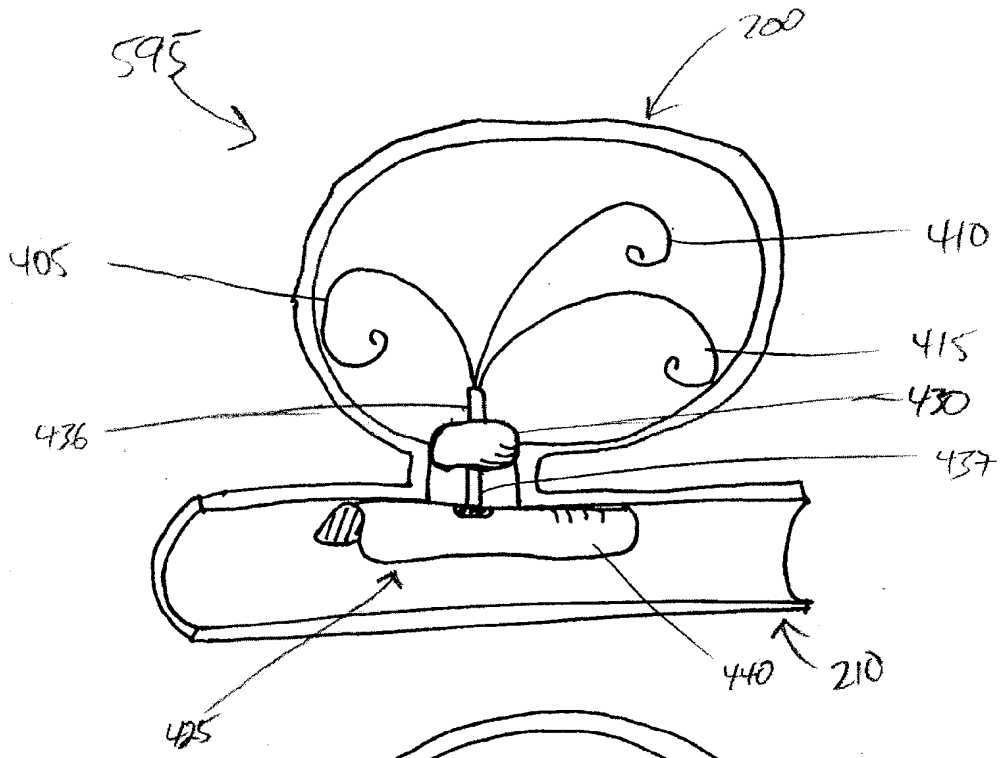

595
200
405
410
415
430
436
437
440
210
425

Fig. 32

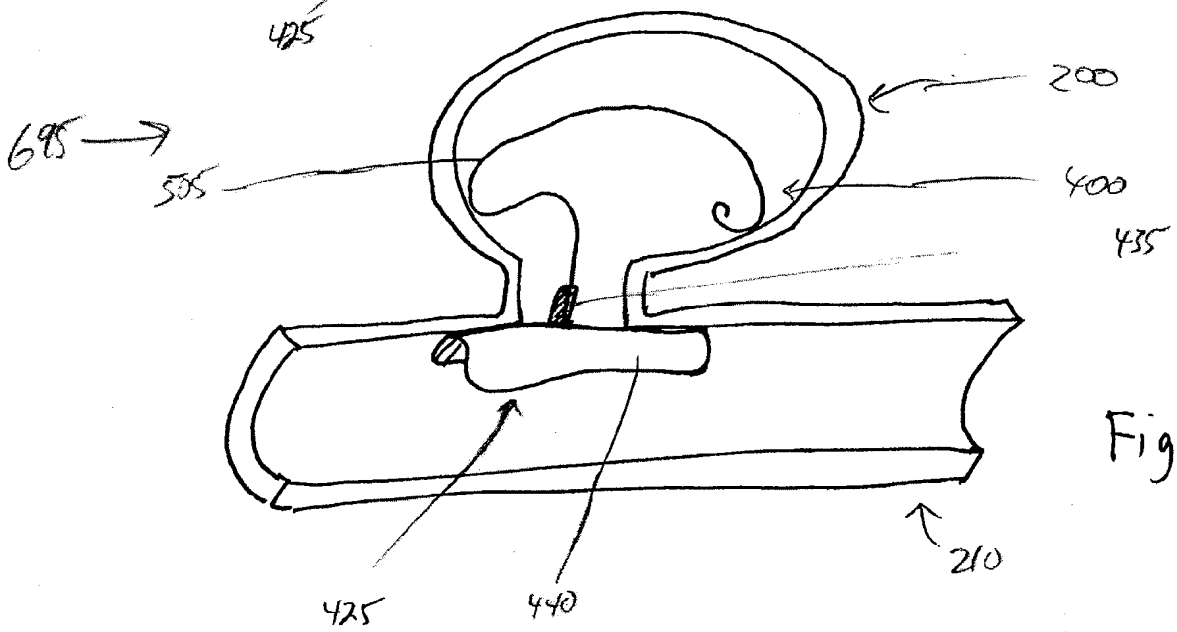

695
200
505
400
435
210
425
440

Fig. 33

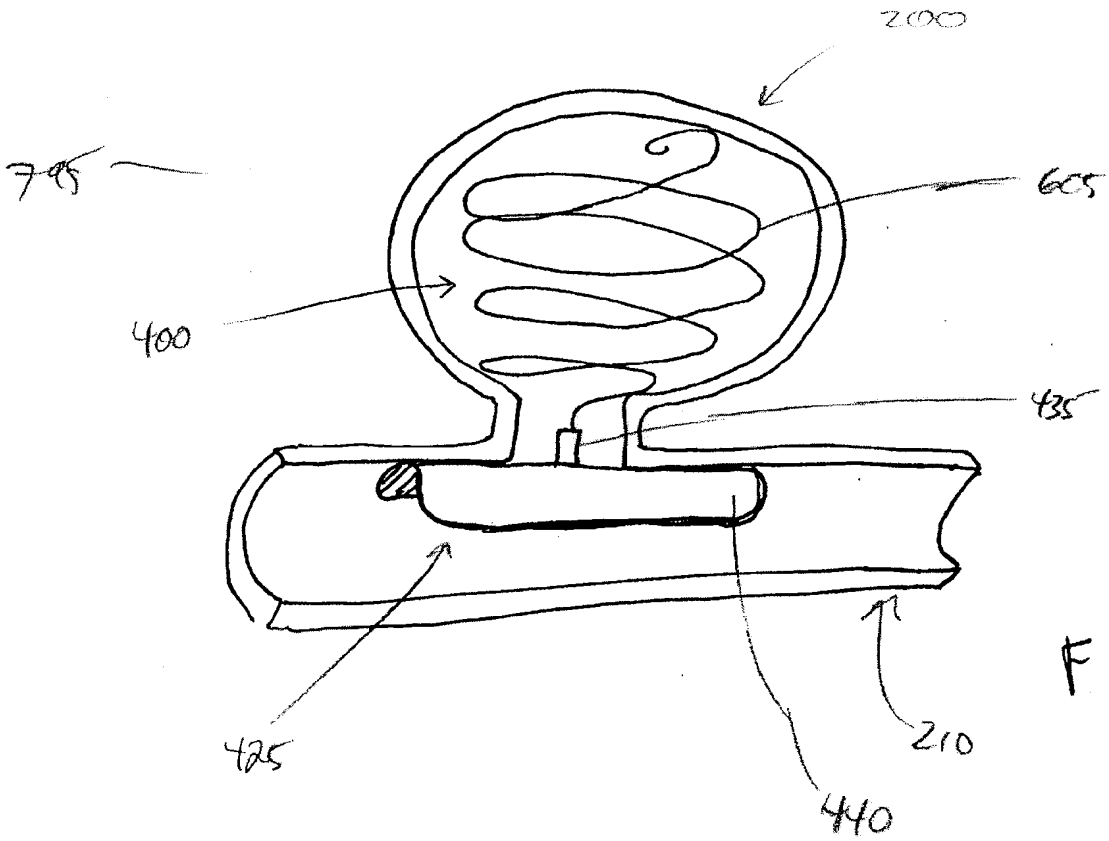


Fig. 34

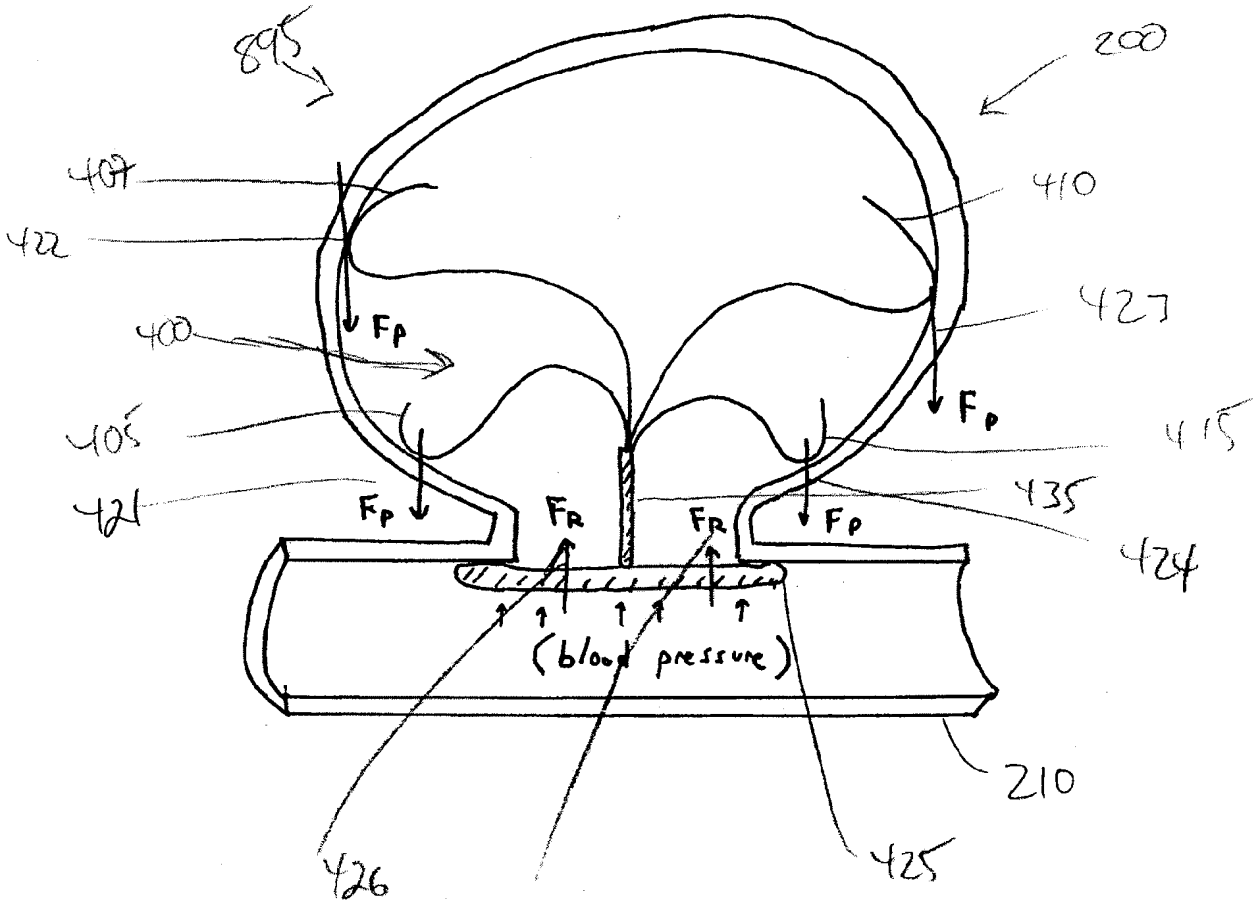

895
200
407
410
422
427
400
F_P
405
415
421
F_P
F_R
F_R
F_P
435
424
(blood pressure)
210
426
425
427

Fig. 35

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 08/75504

A. CLASSIFICATION OF SUBJECT MATTER
IPC(8) - A61F 2/06 (2008.04)
USPC - 623/1
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
USPC 623/1

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
All USPC; USPC 623/1, 623/1.36, 623/1.42, 623/1.46; IPC A61F 2/06

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
PubWEST(USPT,PGPB,EPAB,JPAB); Google: @PD<20080509; aneurysm; engage; anchor; NiTi$; tungsten; stainless steel; iridium; platinum; graft; stent; pore size; pore spacing; non-porous; ePTFE; polyurethane; polyethylene terephthalate; polyvinylchloride; nylon; polyimide; polyurethane ether; polyurethane ester; etc.

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 2007/0083258 A1 (Falotico, et. al.) 12 April 2007 (12.04.2007); para [0194], [0315]-[0320], [0364], [0368]-[0369], [0391], [0397]-[0399], [0404]-[0412], [0415]; Fig 27-29, 35-36	1-49
Y	US 2007/0038288 A1 (Lye, et. al.) 15 February 2007 (15.02.2007); Abstract; para [0012], [0027], [0053], [0072]; Fig 3A, 4A, 5A, 6C, 13, 14	1-49
Y	US 2004/0186562 A1 (Cox) 23 September 2004 (23.09.2004); Abstract; para [0080]-[0081]; Fig 13-15, 22, 23	14, 15, 44, 48
Y	US 5,866,217 A (Stenoien, et. al.) 2 February 1999 (02.02.1999); Abstract; col 3, ln 15-40	21-28

☐ Further documents are listed in the continuation of Box C. ☐

* Special categories of cited documents:
"A" document defining the general state of the art which is not considered to be of particular relevance
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"O" document referring to an oral disclosure, use, exhibition or other means
"P" document published prior to the international filing date but later than the priority date claimed
"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
3 November 2008 (03.11.2008)	13 NOV 2008
Name and mailing address of the ISA/US Mail Stop PCT, Attn: ISA/US, Commissioner for Patents P.O. Box 1450, Alexandria, Virginia 22313-1450 Facsimile No. 571-273-3201	Authorized officer: Lee W. Young PCT Helpdesk: 571-272-4300 PCT OSP: 571-272-7774

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(74) Agents: **YADAV, Rajiv** et al.; Edwards Lifesciences LLC, One Edwards Way, Irvine, CA 92614 (US).

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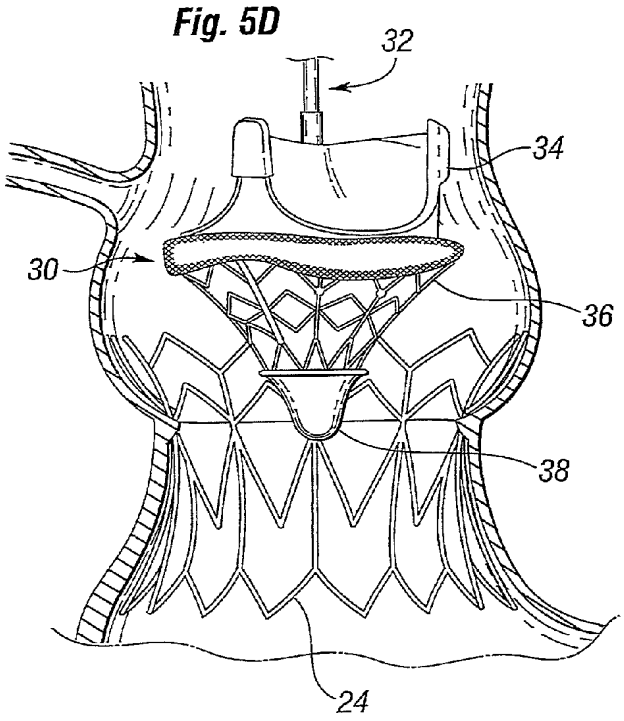
[Continued on next page]

(54) Title: QUIK-CONNECT PROSTHETIC HEART VALVE AND METHODS



(57) Abstract: A heart valve prosthesis that can be quickly and easily implanted during a surgical procedure is provided. The prosthetic valve has a base stent that is deployed at a treatment site, and a valve component configured to quickly connect to the base stent. The base stent may take the form of a self- or balloon-expandable stent that expands outward against the native valve with or without leaflet excision. The valve component has a non-expandable prosthetic valve and a self- or balloon-expandable coupling stent for attachment to the base stent, thereby fixing the position of the valve component relative to the base stent. The prosthetic valve may be a commercially available to valve with a sewing ring and the coupling stent attaches to the sewing ring. The system is particularly suited for rapid deployment of heart valves in a conventional open-heart surgical environment. A catheter-based system and method for deployment is provided.

WO 2010/080594 A2

NO, NZ, OM, PE, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

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Published:

— *without international search report and to be republished upon receipt of that report (Rule 48.2(g))*

QUICK-CONNECT PROSTHETIC HEART VALVE AND METHODS

Field of the Invention

[0001] The present application claims priority under 35 U.S.C. §119(e) to U.S. provisional application number 61/139,398 filed December 19, 2008.

[0002] The present invention generally relates to prosthetic valves for implantation in body channels. More particularly, the present invention relates to prosthetic heart valves configured to be surgically implanted in less time than current valves.

Background of the Invention

[0003] In vertebrate animals, the heart is a hollow muscular organ having four pumping chambers as seen in Figure 1: the left and right atria and the left and right ventricles, each provided with its own one-way valve. The natural heart valves are identified as the aortic, mitral (or bicuspid), tricuspid and pulmonary, and are each mounted in an annulus comprising dense fibrous rings attached either directly or indirectly to the atrial and ventricular muscle fibers. Each annulus defines a flow orifice.

[0004] The atria are the blood-receiving chambers, which pump blood into the ventricles. The ventricles are the blood-discharging chambers. A wall composed of fibrous and muscular parts, called the interatrial septum separates the right and left atria (see Figures 2 to 4). The fibrous interatrial septum is a materially stronger tissue structure compared to the more friable muscle tissue of the heart. An anatomic landmark on the interatrial septum is an oval, thumbprint sized depression called the oval fossa, or fossa ovalis (shown in Figure 4).

[0005] The synchronous pumping actions of the left and right sides of the heart constitute the cardiac cycle. The cycle begins with a period of ventricular relaxation, called ventricular diastole. The cycle ends with a period of ventricular contraction, called ventricular systole. The four valves (see

Figures 2 and 3) ensure that blood does not flow in the wrong direction during the cardiac cycle; that is, to ensure that the blood does not back flow from the ventricles into the corresponding atria, or back flow from the arteries into the corresponding ventricles. The mitral valve is between the left atrium and the left ventricle, the tricuspid valve between the right atrium and the right ventricle, the pulmonary valve is at the opening of the pulmonary artery, and the aortic valve is at the opening of the aorta.

[0006] Figures 2 and 3 show the anterior (A) portion of the mitral valve annulus abutting the non-coronary leaflet of the aortic valve. The mitral valve annulus is in the vicinity of the circumflex branch of the left coronary artery, and the posterior (P) side is near the coronary sinus and its tributaries.

[0007] The mitral and tricuspid valves are defined by fibrous rings of collagen, each called an annulus, which forms a part of the fibrous skeleton of the heart. The annulus provides peripheral attachments for the two cusps or leaflets of the mitral valve (called the anterior and posterior cusps) and the three cusps or leaflets of the tricuspid valve. The free edges of the leaflets connect to chordae tendineae from more than one papillary muscle, as seen in Figure 1. In a healthy heart, these muscles and their tendinous chords support the mitral and tricuspid valves, allowing the leaflets to resist the high pressure developed during contractions (pumping) of the left and right ventricles.

[0008] When the left ventricle contracts after filling with blood from the left atrium, the walls of the ventricle move inward and release some of the tension from the papillary muscle and chords. The blood pushed up against the under-surface of the mitral leaflets causes them to rise toward the annulus plane of the mitral valve. As they progress toward the annulus, the leading edges of the anterior and posterior leaflet come together forming a seal and closing the valve. In the healthy heart, leaflet coaptation occurs near the plane of the mitral annulus. The blood continues to be pressurized in the left ventricle until it is ejected into the aorta. Contraction of the papillary muscles is simultaneous with

the contraction of the ventricle and serves to keep healthy valve leaflets tightly shut at peak contraction pressures exerted by the ventricle.

[0009] Various surgical techniques may be used to repair a diseased or damaged valve. In a valve replacement operation, the damaged leaflets are excised and the annulus sculpted to receive a replacement valve. Due to aortic stenosis and other heart valve diseases, thousands of patients undergo surgery each year wherein the defective native heart valve is replaced by a prosthetic valve, either bioprosthetic or mechanical. Another less drastic method for treating defective valves is through repair or reconstruction, which is typically used on minimally calcified valves. The problem with surgical therapy is the significant insult it imposes on these chronically ill patients with high morbidity and mortality rates associated with surgical repair.

[0010] When the valve is replaced, surgical implantation of the prosthetic valve typically requires an open-chest surgery during which the heart is stopped and patient placed on cardiopulmonary bypass (a so-called "heart-lung machine"). In one common surgical procedure, the diseased native valve leaflets are excised and a prosthetic valve is sutured to the surrounding tissue at the valve annulus. Because of the trauma associated with the procedure and the attendant duration of extracorporeal blood circulation, some patients do not survive the surgical procedure or die shortly thereafter. It is well known that the risk to the patient increases with the amount of time required on extracorporeal circulation. Due to these risks, a substantial number of patients with defective valves are deemed inoperable because their condition is too frail to withstand the procedure. By some estimates, about 30 to 50% of the subjects suffering from aortic stenosis who are older than 80 years cannot be operated on for aortic valve replacement.

[0011] Because of the drawbacks associated with conventional open-heart surgery, percutaneous and minimally-invasive surgical approaches are garnering intense attention. In one technique, a prosthetic valve is configured to be implanted in a much less invasive procedure by way of catheterization. For

instance, U.S. Patent No. 5,411,552 to Andersen et al. describes a collapsible valve percutaneously introduced in a compressed state through a catheter and expanded in the desired position by balloon inflation. Although these remote implantation techniques have shown great promise for treating certain patients, replacing a valve via surgical intervention is still the preferred treatment procedure. One hurdle to the acceptance of remote implantation is resistance from doctors who are understandably anxious about converting from an effective, if imperfect, regimen to a novel approach that promises great outcomes but is relatively foreign. In conjunction with the understandable caution exercised by surgeons in switching to new techniques of heart valve replacement, regulatory bodies around the world are moving slowly as well. Numerous successful clinical trials and follow-up studies are in process, but much more experience with these new technologies will be required before they are completely accepted.

[0012] Accordingly, there is a need for an improved device and associated method of use wherein a prosthetic valve can be surgically implanted in a body channel in a more efficient procedure that reduces the time required on extracorporeal circulation. It is desirable that such a device and method be capable of helping patients with defective valves that are deemed inoperable because their condition is too frail to withstand a lengthy conventional surgical procedure. The present invention addresses these needs and others.

Summary of the Invention

[0013] Various embodiments of the present application provide prosthetic valves and methods of use for replacing a defective native valve in a human heart. Certain embodiments are particularly well adapted for use in a surgical procedure for quickly and easily replacing a heart valve while minimizing time using extracorporeal circulation (i.e., bypass pump).

[0014] In one embodiment, a method for treating a native aortic valve in a human heart to replaces the function of the aortic valve, comprises: 1)

accessing a native valve through an opening in a chest; 2) advancing an expandable base stent to the site of a native aortic valve, the base stent being radially compressed during the advancement; 3) radially expanding the base stent at the site of the native aortic valve; 4) advancing a valve component within a lumen of the base stent; and 5) expanding a coupling stent on the valve component to mechanically couple to the base stent in a quick and efficient manner.

[0015] In one variation, the base stent may comprise a metallic frame. In one embodiment, at least a portion of the metallic frame is made of stainless steel. In another embodiment, at least a portion of the metallic frame is made of a shape memory material. The valve member may take a variety of forms. In one preferred embodiment, the valve component comprises biological tissue. In another variation of this method, the metallic frame is viewed under fluoroscopy during advancement of the prosthetic valve toward the native aortic valve.

[0016] The native valve leaflets may be removed before delivering the prosthetic valve. Alternatively, the native leaflets may be left in place to reduce surgery time and to provide a stable base for fixing the base stent within the native valve. In one advantage of this method, the native leaflets recoil inward to enhance the fixation of the metallic frame in the body channel. When the native leaflets are left in place, a balloon or other expansion member may be used to push the valve leaflets out of the way and thereby dilate the native valve before implantation of the base stent. The native annulus may be dilated between 1.5-5 mm from their initial orifice size to accommodate a larger sized prosthetic valve.

[0017] In accordance with a preferred aspect, a prosthetic heart valve system comprises a base stent adapted to anchor against a heart valve annulus and defining an orifice therein, and a valve component connected to the base stent. The valve component includes a prosthetic valve defining therein a non-expandable, non-collapsible orifice, and an expandable coupling stent extending from an inflow end thereof. The coupling stent has a contracted state for

delivery to an implant position and an expanded state configured for outward connection to the base stent. The base stent may also be expandable with a contracted state for delivery to an implant position adjacent a heart valve annulus and an expanded state sized to contact and anchor against the heart valve annulus. Desirably, the base stent and also the coupling stent are plastically expandable.

[0018] In one embodiment, the prosthetic valve comprises a commercially available valve having a sewing ring, and the coupling stent attaches to the sewing ring. The contracted state of the coupling stent may be conical, tapering down in a distal direction. The coupling stent preferably comprises a plurality of radially expandable struts at least some of which are arranged in rows, wherein the distalmost row has the greatest capacity for expansion from the contracted state to the expanded state. Still further, the strut row farthest from the prosthetic valve has alternating peaks and valleys, wherein the base stent includes apertures into which the peaks of the coupling stent may project to interlock the two stents. The base stent may include a plurality of radially expandable struts between axially-oriented struts, wherein at least some of the axially-oriented struts have upper projections that demark locations around the stent.

[0019] A method of delivery and implant of a prosthetic heart valve system is also disclosed herein, comprising the steps of:

advancing a base stent to an implant position adjacent a heart valve annulus;

anchoring the base stent to the heart valve annulus;

providing a valve component including a prosthetic valve having a non-expandable, non-collapsible orifice, the valve component further including an expandable coupling stent extending from an inflow end thereof, the coupling stent having a contracted state for delivery to an implant position and an expanded state configured for outward connection to the base stent;

advancing the valve component with the coupling stent in its contracted state to an implant position adjacent the base stent; and

expanding the coupling stent to the expanded state in contact with and connected to the base stent.

[0020] The base stent may be plastically expandable, and the method further comprises advancing the expandable base stent in a contracted state to the implant position, and plastically expanding the base stent to an expanded state in contact with and anchored to the heart valve annulus, in the process increasing the orifice size of the heart valve annulus by at least 10%, or by 1.5-5 mm. Desirably, the prosthetic valve of the valve component is selected to have an orifice size that matches the increased orifice size of the heart valve annulus. The method may also include mounting the base stent over a mechanical expander, and deploying the base stent at the heart valve annulus using the mechanical expander.

[0021] One embodiment of the method further includes mounting the valve component on a holder having a proximal hub and lumen therethrough. The holder mounts on the distal end of a handle having a lumen therethrough, and the method including passing a balloon catheter through the lumen of the handle and the holder and within the valve component, and inflating a balloon on the balloon catheter to expand the coupling stent. The valve component mounted on the holder may be packaged separately from the handle and the balloon catheter. Desirably, the contracted state of the coupling stent is conical, and the balloon on the balloon catheter has a larger distal expanded end than its proximal expanded end so as to apply greater expansion deflection to the coupling stent than to the prosthetic valve.

[0022] In the method where the coupling stent is conical, the coupling stent may comprise a plurality of radially expandable struts at least some of which are arranged in rows, wherein the row farthest from the prosthetic valve

has the greatest capacity for expansion from the contracted state to the expanded state.

[0023] The method may employ a coupling stent with a plurality of radially expandable struts, wherein a row farthest from the prosthetic valve has alternating peaks and valleys. The distal end of the coupling stent thus expands more than the rest of the coupling stent so that the peaks in the row farthest from the prosthetic valve project outward into apertures in the base stent. Both the base stent and the coupling stent may have a plurality of radially expandable struts between axially-oriented struts, wherein the method includes orienting the coupling stent so that its axially-oriented struts are out of phase with those of the base stent to increase retention therebetween.

[0024] Another aspect described herein is a system for delivering a valve component including a prosthetic valve having a non-expandable, non-collapsible orifice, and an expandable coupling stent extending from an inflow end thereof, the coupling stent having a contracted state for delivery to an implant position and an expanded state. The delivery system includes a valve holder connected to a proximal end of the valve component, a balloon catheter having a balloon, and a handle configured to attach to a proximal end of the valve holder and having a lumen for passage of the catheter, wherein the balloon extends distally through the handle, past the holder and through the valve component. In the system, the prosthetic valve is preferably a commercially available valve having a sewing ring to which the coupling stent attaches.

[0025] The contracted state of the coupling stent in the delivery system may be conical, tapering down in a distal direction. Furthermore, the balloon catheter further may include a generally conical nose cone on a distal end thereof that extends through the valve component and engages a distal end of the coupling stent in its contracted state. Desirably, the handle comprises a proximal section and a distal section that may be coupled together in series to form a continuous lumen, wherein the distal section is adapted to couple to the

hub of the holder to enable manual manipulation of the valve component using the distal section prior to connection with the proximal handle section. Preferably, the balloon catheter and proximal handle section are packaged together with the balloon within the proximal section lumen.

[0026] The system of claim 21, wherein the valve component mounted on the holder is packaged separately from the handle and the balloon catheter.A further understanding of the nature and advantages of the present invention are set forth in the following description and claims, particularly when considered in conjunction with the accompanying drawings in which like parts bear like reference numerals.

Brief Description of the Drawings

[0027] The invention will now be explained and other advantages and features will appear with reference to the accompanying schematic drawings wherein:

[0028] Figure 1 is an anatomic anterior view of a human heart, with portions broken away and in section to view the interior heart chambers and adjacent structures;

[0029] Figure 2 is an anatomic superior view of a section of the human heart showing the tricuspid valve in the right atrium, the mitral valve in the left atrium, and the aortic valve in between, with the tricuspid and mitral valves open and the aortic and pulmonary valves closed during ventricular diastole (ventricular filling) of the cardiac cycle;

[0030] Figure 3 is an anatomic superior view of a section of the human heart shown in Figure 2, with the tricuspid and mitral valves closed and the aortic and pulmonary valves opened during ventricular systole (ventricular emptying) of the cardiac cycle;

[0031] Figure 4 is an anatomic anterior perspective view of the left and right atria, with portions broken away and in section to show the interior of the

heart chambers and associated structures, such as the fossa ovalis, coronary sinus, and the great cardiac vein;

[0032] Figures 5A-5H are sectional views through an isolated aortic annulus showing a portion of the adjacent left ventricle and aorta, and illustrating a number of steps in deployment of an exemplary prosthetic heart valve system of the present invention;

[0033] Figure 5A shows a deflated balloon catheter having a base stent thereon advanced into position at the aortic annulus;

[0034] Figure 5B shows the balloon on the catheter inflated to expand and deploy the base stent against the aortic annulus;

[0035] Figure 5C shows the deployed base stent in position within the aortic annulus;

[0036] Figure 5D shows a valve component mounted on a balloon catheter advancing into position within the base stent;

[0037] Figure 5E shows the valve component in a desired implant position at the aortic annulus and within the base stent, with the balloon catheter advanced farther to displace a nose cone out of engagement with a coupling stent;

[0038] Figure 5F shows the balloon on the catheter inflated to expand and deploy a valve component coupling stent against the base stent;

[0039] Figure 5G shows the deflated balloon on the catheter along with the nose cone being removed from within the valve component;

[0040] Figure 5H shows the fully deployed prosthetic heart valve of the present invention;

[0041] Figure 6 is an exploded view of an exemplary system for delivering the prosthetic heart valve of the present invention;

[0042] Figure 7 is an assembled view of the delivery system of Figure 6 showing a nose cone extending over a distal end of a valve component coupling stent;

[0043] Figure 8 is a view like Figure 7 but with a balloon catheter displaced distally to disengage the nose cone from the coupling stent;

[0044] Figure 9 is an assembled view of the delivery system similar to that shown in Figure 7 and showing a balloon inflated to expand the valve component coupling stent;

[0045] Figure 10 is an exploded elevational view of several components of the introducing system of Figure 9, without the balloon catheter, valve component and holder;

[0046] Figures 11A and 11B are perspective views of an exemplary valve component assembled on a valve holder of the present invention;

[0047] Figure 11C is a side elevational view of the assembly of Figures 11A and 11B;

[0048] Figures 11D and 11E are top and bottom plan views of the assembly of Figures 11A and 11B;

[0049] Figures 12A-12B illustrate an exemplary coupling stent in both a flat configuration (12A) and a tubular expanded configuration (12B);

[0050] Figures 13A-13B illustrate an alternative coupling stent having a discontinuous upper end in both flat and tubular expanded configurations;

[0051] Figure 14-17 are plan views of a still further alternative coupling stent;

[0052] Figure 18A-18B are flat and tubular views of an exemplary base stent with upper position markers and a phantom coupling stent superimposed thereover;

[0053] Figure 19 is a flat view of an alternative base stent with a coupling stent superimposed thereover;

[0054] Figure 20 is a sectional view of a coupling stent within a base stent illustrating one method of interlocking; and

[0055] Figure 21-23 is a perspective view of a device for delivering and expanding a base stent with mechanical fingers.

Detailed Description of the Preferred Embodiments

[0056] The present invention attempts to overcome drawbacks associated with conventional, open-heart surgery, while also adopting some of the techniques of newer technologies which decrease the duration of the treatment procedure. The prosthetic heart valves of the present invention are primarily intended to be delivered and implanted using conventional surgical techniques, including the aforementioned open-heart surgery. There are a number of approaches in such surgeries, all of which result in the formation of a direct access pathway to the particular heart valve annulus. For clarification, a direct access pathway is one that permits direct (i.e., naked eye) visualization of the heart valve annulus. In addition, it will be recognized that embodiments of the two-stage prosthetic heart valves described herein may also be configured for delivery using percutaneous approaches, and those minimally-invasive surgical approaches that require remote implantation of the valve using indirect visualization.

[0057] One primary aspect of the present invention is a two-stage prosthetic heart valve wherein the tasks of implanting a tissue anchor first and then a valve member are distinct and certain advantages result. The exemplary two-stage prosthetic heart valve of the present invention has an expandable base stent secured to tissue in the appropriate location using a balloon or other expansion technique. A hybrid valve member that has non-expandable and expandable portions then couples to the base stent in a separate or sequential operation. By utilizing an expandable base stent, the duration of the initial anchoring operation is greatly reduced as compared with a conventional sewing procedure utilizing an array of sutures. The expandable base stent may simply be radially expanded outward into contact with the implantation site, or may be provided with additional anchoring means, such as barbs. The operation may be carried out using a conventional open-heart approach and cardiopulmonary bypass. In one advantageous feature, the time on bypass is greatly reduced due to the relative speed of implanting the expandable base stent.

[0058] For definitional purposes, the term "base stent," refers to a structural component of a heart valve that is capable of attaching to tissue of a heart valve annulus. The base stents described herein are most typically tubular stents, or stents having varying shapes or diameters. A stent is normally formed of a biocompatible metal wire frame, such as stainless steel or Nitinol. Other base stents that could be used with valves of the present invention include rigid rings, spirally-wound tubes, and other such tubes that fit tightly within a valve annulus and define an orifice therethrough for the passage of blood, or within which a valve member is mounted. It is entirely conceivable, however, that the base stent could be separate clamps or hooks that do not define a continuous periphery. Although such devices sacrifice some dynamic stability, and speed and ease of deployment, these devices could be configured to work in conjunction with a particular valve member.

[0059] A distinction between self-expanding and balloon-expanding stents exists in the field. A self-expanding stent may be crimped or otherwise compressed into a small tube and possesses sufficient elasticity to spring outward by itself when a restraint such as an outer sheath is removed. In contrast, a balloon-expanding stent is made of a material that is substantially less elastic, and indeed must be plastically expanded from the inside out when converting from a compressed diameter to an expanded. It should be understood that the term balloon-expanding stents encompasses plastically-expandable stents, whether or not a balloon is used to actually expand it. The material of the stent plastically deforms after application of a deformation force such as an inflating balloon or expanding mechanical fingers. Both alternatives will be described below. Consequently, the term "balloon-expandable stent" should be considered to refer to the material or type of the stent as opposed to the specific expansion means.

[0060] The term "valve member" refers to that component of a heart valve that possesses the fluid occluding surfaces to prevent blood flow in one direction while permitting it in another. As mentioned above, various

constructions of valve numbers are available, including those with flexible leaflets and those with rigid leaflets or a ball and cage arrangement. The leaflets may be bioprosthetic, synthetic, or metallic.

[0061] A primary focus of the present invention is a two-stage prosthetic heart valve having a first stage in which a base stent secures to a valve annulus, and a subsequent second stage in which a valve member connects to the base stent. It should be noted that these stages can be done almost simultaneously, such as if the two components were mounted on the same delivery device, or can be done in two separate clinical steps, with the base stent deployed using a first delivery device, and then the valve member using another delivery device. It should also be noted that the term "two-stage" refers to the two primary steps of anchoring structure to the annulus and then connecting a valve member, which does not necessarily limit the valve to just two parts.

[0062] Another potential benefit of a two-stage prosthetic heart valve, including a base stent and a valve member, is that the valve member may be replaced after implantation without replacing the base stent. That is, an easily detachable means for coupling the valve member and base stent may be used that permits a new valve member to be implanted with relative ease. Various configurations for coupling the valve member and base stent are described herein.

[0063] It should be understood, therefore, that certain benefits of the invention are independent of whether the base stent is expandable or not. That is, various embodiments illustrate an expandable base stent coupled to a hybrid valve member that has non-expandable and expandable portions. However, the same coupling structure may be utilized for a non-expandable base stent and hybrid valve member. Therefore, the invention should be interpreted via the appended claims.

[0064] As a point of further definition, the term "expandable" is used herein to refer to a component of the heart valve capable of expanding from a first, delivery diameter to a second, implantation diameter. An expandable

structure, therefore, does not mean one that might undergo slight expansion from a rise in temperature, or other such incidental cause. Conversely, "non-expandable" should not be interpreted to mean completely rigid or a dimensionally stable, as some slight expansion of conventional "non-expandable" heart valves, for example, may be observed.

[0065] In the description that follows, the term "body channel" is used to define a blood conduit or vessel within the body. Of course, the particular application of the prosthetic heart valve determines the body channel at issue. An aortic valve replacement, for example, would be implanted in, or adjacent to, the aortic annulus. Likewise, a mitral valve replacement will be implanted at the mitral annulus. Certain features of the present invention are particularly advantageous for one implantation site or the other. However, unless the combination is structurally impossible, or excluded by claim language, any of the heart valve embodiments described herein could be implanted in any body channel.

[0066] Figures 5A-5H are sectional views through an isolated aortic annulus AA showing a portion of the adjacent left ventricle LV and ascending aorta with sinus cavities S. The two coronary sinuses CS are also shown. The series of views show snapshots of a number of steps in deployment of an exemplary prosthetic heart valve system of the present invention, which comprises a two-component system. A first component is a base stent that is deployed against the native leaflets or, if the leaflets are excised, against the debrided aortic annulus AA. A second valve component fits within the base stent and anchors thereto. Although two-part valves are known in the art, this is believed to be the first that utilizes a stent within a stent in conjunction with a non-expandable valve.

[0067] Figure 5A shows a catheter 20 having a balloon 22 in a deflated state near a distal end with a tubular base stent 24 crimped thereover. The stent 24 is shown in a radially constricted, undeployed configuration. The catheter 20

has been advanced to position the base stent 24 so that it is approximately axially centered at the aortic annulus AA.

[0068] Figure 5B shows the balloon 22 on the catheter 20 inflated to expand and deploy the base stent 24 against the aortic annulus AA, and Figure 5C shows the deployed base stent in position after deflation of the balloon 22 and removal of the catheter 20. The stent 24 provides a base within and against a body lumen (e.g., a valve annulus). Although a stent is described for purposes of illustration, any member capable of anchoring within and against the body lumen and then coupling to the valve component may be used. In a preferred embodiment, the base stent 24 comprises a plastically-expandable cloth-covered stainless-steel tubular stent. One advantage of using a plastically-expandable stent is the ability to expand the native annulus to receive a larger valve size than would otherwise be possible with conventional surgery. Desirably, the left ventricular outflow tract (LVOT) is significantly expanded by at least 10%, or for example by 1.5-5 mm, and the surgeon can select a valve component 30 with a larger orifice diameter relative to an unexpanded annulus. On the other hand, the present invention could also use a self-expanding base stent 24 which is then reinforced by the subsequently implanted valve component 30. Because the valve component 30 has a non-compressible part, the prosthetic valve 34, and desirably a plastically-expandable coupling stent 36, it effectively resists recoil of the self-expanded base stent 24.

[0069] With continued reference to Figure 5B, the stent 24 has a diameter sized to be deployed at the location of the native valve (e.g., along the aortic annulus). A portion of the stent 24 may expand outwardly into the respective cavity adjacent the native valve. For example, in an aortic valve replacement, an upper portion may expand into the area of the sinus cavities just downstream from the aortic annulus. Of course, care should be taken to orient the stent 24 so as not to block the coronary openings. The stent body is preferably configured with sufficient radial strength for pushing aside the native leaflets and holding the native leaflets open in a dilated condition. The native

leaflets provide a stable base for holding the stent, thereby helping to securely anchor the stent in the body. To further secure the stent to the surrounding tissue, the lower portion may be configured with anchoring members, such as, for example, hooks or barbs (not shown).

[0070] As will be described in more detail below, the prosthetic valve system includes a valve component that may be quickly and easily connected to the stent 24. It should be noted here that the base stents described herein can be a variety of designs, including having the diamond/chevron-shaped openings shown or other configurations. The material depends on the mode of delivery (i.e., balloon- or self-expanding), and the stent can be bare strut material or covered to promote ingrowth and/or to reduce paravalvular leakage. For example, a suitable cover that is often used is a sleeve of fabric such as Dacron.

[0071] One primary advantage of the prosthetic heart valve system of the present invention is the speed of deployment. Therefore, the base stent 24 may take a number of different configurations as long as it does not require the time-consuming process of suturing it to the annulus. For instance, another possible configuration for the base stent 24 is one that is not fully expandable like the tubular stent as shown. That is, the base stent 24 may have a non-expandable ring-shaped orifice from which an expandable skirt stent or series of anchoring barbs deploy.

[0072] Figure 5D shows a valve component 30 mounted on a balloon catheter 32 advancing into position within the base stent 24. The valve component 30 comprises a prosthetic valve 34 and a coupling stent 36 attached to and projecting from a distal end thereof. In its radially constricted or undeployed state, the coupling stent 36 assumes a conical inward taper in the distal direction. The catheter 32 extends through the valve component 30 and terminates in a distal nose cone 38 which has a conical or bell-shape and covers the tapered distal end of the coupling stent 36. Although not shown, the catheter 32 extends through an introducing cannula and valve holder.

[0073] When used for aortic valve replacement, the prosthetic valve 34 preferably has three flexible leaflets which provide the fluid occluding surfaces to replace the function of the native valve leaflets. In various preferred embodiments, the valve leaflets may be taken from another human heart (cadaver), a cow (bovine), a pig (porcine valve) or a horse (equine). In other preferred variations, the valve member may comprise mechanical components rather than biological tissue. The three leaflets are supported by three commissural posts. A ring is provided along the base portion of the valve member.

[0074] In a preferred embodiment, the prosthetic valve 34 partly comprises a commercially available, non-expandable prosthetic heart valve, such as the Carpentier-Edwards PERIMOUNT Magna® Aortic Heart Valve available from Edwards Lifesciences of Irvine, California. In this sense, a "commercially available" prosthetic heart valve is an off-the-shelf (i.e., suitable for stand-alone sale and use) prosthetic heart valve defining therein a non-expandable, non-collapsible orifice and having a sewing ring capable of being implanted using sutures through the sewing ring in an open-heart, surgical procedure. The particular approach into the heart used may differ, but in surgical procedures the heart is stopped and opened, in contrast to beating heart procedures where the heart remains functional. To reiterate, the terms "non-expandable" and "non-collapsible" should not be interpreted to mean completely rigid and dimensionally stable, merely that the valve is not expandable/collapsible like some proposed minimally-invasively or percutaneously-delivered valves.

[0075] An implant procedure therefore involves first delivering and expanding the base stent 24 at the aortic annulus, and then coupling the valve component 30 including the valve 34 thereto. Because the valve 34 is non-expandable, the entire procedure is typically done using the conventional open-heart technique. However, because the base stent 24 is delivered and implanted by simple expansion, and then the valve component 30 attached thereto by

expansion, both without suturing, the entire operation takes less time. This hybrid approach will also be much more comfortable to surgeons familiar with the open-heart procedures and commercially available heart valves.

[0076] Moreover, the relatively small change in procedure coupled with the use of proven heart valves should create a much easier regulatory path than strictly expandable, remote procedures. Even if the system must be validated through clinical testing to satisfy the Pre-Market Approval (PMA) process with the FDA (as opposed to a 510k submission), the acceptance of the valve component 30 at least will be greatly streamlined with a commercial heart valve that is already approved, such as the Magna® Aortic Heart Valve.

[0077] The prosthetic valve 34 is provided with an expandable coupling mechanism in the form of the coupling stent 36 for securing the valve to the base stent 24. Although the coupling stent 36 is shown, the coupling mechanism may take a variety of different forms, but eliminates the need for connecting sutures and provides a rapid connection means.

[0078] In Figure 5E the valve component 30 has advanced to a desired implant position at the aortic annulus AA and within the base stent 24. The prosthetic valve 34 may include a suture-permeable ring 42 that desirably abuts the aortic annulus AA. More preferably, the sewing ring 42 is positioned supra-annularly, or above the narrowest point of the aortic annulus AA, so as to allow selection of a larger orifice size than a valve placed intra-annularly. With the aforementioned annulus expansion using the base stent 24, and the supra-annular placement, the surgeon may select a valve having a size one or two increments larger than previously conceivable. As mentioned, the prosthetic valve 34 is desirably a commercially available heart valve having a sewing ring 42. The balloon catheter 32 has advanced relative to the valve component 30 to displace the nose cone 38 out of engagement with the coupling stent 36. A dilatation balloon 40 on the catheter 30 can be seen just beyond the distal end of the coupling stent 36.

[0079] Figure 5F shows the balloon 40 on the catheter 32 inflated to expand and deploy the coupling stent 36 against the base stent 24. The balloon 40 is desirably inflated using controlled, pressurized, sterile physiologic saline. The coupling stent 36 transitions between its conical contracted state and its generally tubular expanded state. Simple interference between the coupling stent 36 and the base stent 24 may be sufficient to anchor the valve component 30 within the base stent, or interacting features such as projections, hooks, barbs, fabric, etc. may be utilized.

[0080] Because the base stent 24 expands before the valve component 30 attaches thereto, a higher strength stent (self-or balloon-expandable) configuration may be used. For instance, a relatively robust base stent 24 may be used to push the native leaflets aside, and the absent valve component 30 is not damaged or otherwise adversely affected during the high-pressure base stent deployment. After the base stent 24 deploys in the body channel, the valve component 30 connects thereto by deploying the coupling stent 36, which may be somewhat more lightweight requiring smaller expansion forces. Also, the balloon 40 may have a larger distal expanded end than its proximal expanded end so as to apply more force to the coupling stent 36 than to the prosthetic valve 34. In this way, the prosthetic valve 34 and flexible leaflets therein are not subject to high expansion forces from the balloon 40. Indeed, although balloon deployment is shown, the coupling stent 36 may also be a self-expanding type of stent. In the latter configuration, the nose cone 38 is adapted to retain the coupling stent 36 in its constricted state prior to position in the valve component 30 within the base stent 24.

[0081] As noted above, the base stents described herein could include barbs or other tissue anchors to further secure the stent to the tissue, or to secure the coupling stent 36 to the base stent 24. Further, the barbs could be deployable (e.g., configured to extend or be pushed radially outward) by the expansion of a balloon. Preferably, the coupling stent 36 is covered to promote

in-growth and/or to reduce paravalvular leakage, such as with a Dacron tube or the like.

[0082] Figure 5G shows the deflated balloon 40 on the catheter 32 along with the nose cone 38 being removed from within the valve component 30. Finally, Figure 5H shows the fully deployed prosthetic heart valve system of the present invention including the valve component 30 coupled to the base stent 24 within the aortic annulus AA.

[0083] Figure 6 is an exploded view, and Figures 7 and 8 are assembled views, of an exemplary system 50 for delivering the prosthetic heart valve of the present invention. Modified components of the delivery system 50 are also shown in Figures 9 and 10. The delivery system 50 includes a balloon catheter 52 having the balloon 40 on its distal end and an obturator 54 on a proximal end. The obturator 54 presents a proximal coupling 56 that receives a luer connector or other such fastener of a Y-fitting 58. The aforementioned nose cone 38 may attach to the distalmost end of the catheter 52, but more preferably attaches to a wire (not shown) inserted through the center lumen of the balloon catheter 52.

[0084] The catheter 52 and the nose cone 38 pass through a hollow handle 60 having a proximal section 62 and a distal section 64. A distal end of the distal handle section 64 firmly attaches to a hub 66 of a valve holder 68, which in turn attaches to the prosthetic heart valve component 30. Details of the valve holder 68 will be given below with reference to Figures 11A-11E.

[0085] The two sections 62, 64 of the handle 60 are desirably formed of a rigid material, such as a molded plastic, and coupled to one another to form a relatively rigid and elongated tube for manipulating the prosthetic valve component 30 attached to its distal end. In particular, the distal section 64 may be easily coupled to the holder hub 66 and therefore provide a convenient tool for managing the valve component 30 during pre-surgical rinsing steps. For this purpose, the distal section 64 features a distal tubular segment 70 that couples to the holder hub 66, and an enlarged proximal segment 72 having an opening on

its proximal end that receives a tubular extension 74 of the proximal handle section 62. Figure 6 shows an O-ring 76 that may be provided on the exterior of the tubular extension 74 for a frictional interference fit to prevent the two sections from disengaging. Although not shown, the distal tubular segment 70 may also have an O-ring for firmly coupling to the holder hub 66, or may be attached with threading or the like. In one preferred embodiment, the balloon 40 on the catheter 52 is packaged within the proximal handle section 62 for protection and ease of handling. Coupling the proximal and distal handle sections 62, 64 therefore "loads" the system 50 such that the balloon catheter 52 may be advanced through the continuous lumen leading to the valve component 30.

[0086] Figures 9 and 10 illustrate a delivery system 50 similar to that shown in Figure 7, but with alternative couplers 77 on both the proximal and distal handle sections 62, 64 in the form of cantilevered teeth that snap into complementary recesses formed in the respective receiving apertures. Likewise, threading on the mating parts could also be used, as well as other similar expedients. Figure 9 shows the balloon 40 inflated to expand the valve component coupling stent 36.

[0087] In a preferred embodiment, the prosthetic valve component 30 incorporates bioprosthetic tissue leaflets and is packaged and stored attached to the holder 68 but separate from the other introduction system 50 components. Typically, bioprosthetic tissue is packaged and stored in a jar with preservative solution for long shelf life, while the other components are packaged and stored dry.

[0088] When assembled as seen in Figures 7-9, an elongated lumen (not numbered) extends from the proximal end of the Y-fitting 58 to the interior of the balloon 40. The Y-fitting 58 desirably includes an internally threaded connector 80 for attachment to an insufflation system, or a side port 82 having a luer fitting 84 or similar expedient may be used for insufflation of the balloon 40.

[0089] Figures 7 and 8 show two longitudinal positions of the catheter 52 and associated structures relative to the handle 60 and its associated structures. In a retracted position shown in Figure 7, the balloon 40 primarily resides within the distal handle section 64. Figure 7 illustrates the delivery configuration of the introduction system 50, in which the surgeon advances the prosthetic valve component 30 from outside the body into a location adjacent the target annulus. The nose cone 38 extends around and protects a distal end of the conical undeployed coupling stent 36. This configuration is also seen in Figure 5D, albeit with the holder 68 removed for clarity. Note the spacing **S** between the proximal coupling 56 and the proximal end of the handle 60.

[0090] As explained above with respect to Figures 5A-5H, the surgeon advances the prosthetic valve component 30 into its desired implantation position at the valve annulus, and then advances the balloon 40 through the valve component and inflates it. To do so, the operator converts the delivery system 50 from the retracted configuration of Figure 7 to the deployment configuration of Figure 8, with the balloon catheter 40 displaced distally as indicated by the arrow 78 to disengage the nose cone 38 from the coupling stent 36. Note that the proximal coupling 56 now contacts the proximal end of the handle 60, eliminating the space **S** indicated in Figure 7.

[0091] It should be understood that the prosthetic valve component 30 may be implanted at the valve annulus with a pre-deployed base stent 24, as explained above, or without. The coupling stent 36 may be robust enough to anchor the valve component 30 directly against the native annulus (with or without leaflet excision) in the absence of the base stent 24. Consequently, the description of the system 50 for introducing the prosthetic heart valve should be understood in the context of operating with or without the pre-deployed base stent 24.

[0092] Prior to a further description of operation of the delivery system 50, a more detailed explanation of the valve component 30 and valve holder 68 is necessary. Figures 11A-11E show a number of perspective and other views

of the exemplary valve component 30 mounted on the delivery holder 68 of the present invention. As mentioned, the valve component 30 comprises the prosthetic valve 34 having the coupling stent 36 attached to an inflow end thereof. In a preferred embodiment, the prosthetic valve 34 comprises a commercially available off-the-shelf non-expandable, non-collapsible commercial prosthetic valve. Any number of prosthetic heart valves can be retrofit to attach the coupling stent 36, and thus be suitable for use in the context of the present invention. For example, the prosthetic valve 34 may be a mechanical valve or a valve with flexible leaflets, either synthetic or bioprosthetic. In a preferred embodiment, however, the prosthetic valve 34 includes bioprosthetic tissue leaflets 86 (Figure 11A). Furthermore, as mentioned above, the prosthetic valve 34 is desirably a Carpentier-Edwards PERIMOUNT Magna® Aortic Heart Valve (e.g., model 3000TFX) available from Edwards Lifesciences of Irvine, California.

[0093] The coupling stent 36 preferably attaches to the ventricular (or inflow) aspect of the valve's sewing ring 42 during the manufacturing process in a way that preserves the integrity of the sewing ring and prevents reduction of the valve's effective orifice area (EOA). Desirably, the coupling stent 36 will be continuously sutured to sewing ring 42 in a manner that maintains the outer contours of the sewing ring. Sutures may be passed through apertures or eyelets in the stent skeleton, or through a cloth covering that in turn is sewn to the skeleton. Other connection solutions include prongs or hooks extending inward from the stent, ties, Velcro, snaps, adhesives, etc. Alternatively, the coupling stent 36 may be more rigidly connected to rigid components within the prosthetic valve 34. During implant, therefore, the surgeon can seat the sewing ring 42 against the annulus in accordance with a conventional surgery. This gives the surgeon familiar tactile feedback to ensure that the proper patient-prosthesis match has been achieved. Moreover, placement of the sewing ring 42 against the outflow side of the annulus helps reduce the probability of migration of the valve component 30 toward the ventricle.

[0094] The coupling stent 36 may be a pre-crimped, tapered, 316L stainless steel balloon-expandable stent, desirably covered by a polyester skirt 88 to help seal against paravalvular leakage and promote tissue ingrowth once implanted within the base stent 24 (see Figure 5F). The coupling stent 36 transitions between the tapered constricted shape of Figures 11A-11E to its flared expanded shape shown in Figure 5F, and also in Figure 10.

[0095] The coupling stent 36 desirably comprises a plurality of sawtooth-shaped or otherwise angled, serpentine or web-like struts 90 connected to three generally axially-extending posts 92. As will be seen below, the posts 92 desirably feature a series of evenly spaced apertures to which sutures holding the polyester skirt 88 in place may be anchored. As seen best in Figure 5F, the stent 36 when expanded flares outward and conforms closely against the inner surface of the base stent 24, and has an axial length substantially the same as the base stent. Anchoring devices such as barbs or other protruberances from the coupling stent 36 may be provided to enhance the frictional hold between the coupling stent and the base stent 24.

[0096] It should be understood that the particular configuration of the coupling stent, whether possessing straight or curvilinear struts 90, may be modified as needed. There are numerous stent designs, as described below with reference to Figures 12-17, any of which potentially may be suitable. Likewise, although the preferred embodiment incorporates a balloon-expandable coupling stent 36, a self-expanding stent could be substituted with certain modifications, primarily to the delivery system. The same flexibility and design of course applies to the base stent 24. In a preferred embodiment, both the base stent 24 and the coupling stent 36 are desirably plastically-expandable to provide a firmer anchor for the valve 34; first to the annulus with or without native leaflets, and then between the two stents. The stents may be expanded using a balloon or mechanical expander as described below.

[0097] Still with reference to Figures 11A-11E, the holder 68 comprises the aforementioned proximal hub 66 and a thinner distal extension 94 thereof

forming a central portion of the holder. Three legs 96a, 96b, 96c circumferentially equidistantly spaced around the central extension 94 and projecting radially outward therefrom comprise inner struts 98 and outer commissure rests 100. The prosthetic valve 34 preferably includes a plurality, typically three, commissures 102 that project in an outflow direction. Although not shown, the commissure rests 100 preferably incorporate depressions into which fit the tips of the commissures 102.

[0098] In one embodiment, the holder 68 is formed of a rigid polymer such as Delrin or polypropylene that is transparent to increase visibility of an implant procedure. As best seen in Figure 11E, the holder 68 exhibits openings between the legs 96a, 96b, 96c to provide a surgeon good visibility of the valve leaflets 86, and the transparency of the legs further facilitates visibility and permits transmission of light therethrough to minimize shadows. Although not described in detail herein, Figure 11E also illustrate a series of through holes in the legs 96a, 96b, 96c permitting connecting sutures to be passed through fabric in the prosthetic valve 34 and across a cutting guide in each leg. As is known in the art, severing a middle length of suture that is connected to the holder 68 and passes through the valve permits the holder to be pulled free from the valve when desired.

[0099] Figures 11C and 11D illustrate a somewhat modified coupling stent 36 from that shown in Figures 11A and 11B, wherein the struts 90 and axially-extending posts 92 are better defined. Specifically, the posts 92 are somewhat wider and more robust than the struts 90, as the latter provide the stent 36 with the ability to expand from the conical shape shown to a more tubular configuration. Also, a generally circular reinforcing ring 104 abuts the valve sewing ring 42. Both the posts 92 and the ring 104 further include a series of through holes 106 that may be used to secure the polyester skirt 88 to the stent 36 using sutures or the like. A number of variants of the coupling stent 36 are also described below.

[0100] Figures 12A-12B illustrate the exemplary coupling stent 36 in both a flat configuration (12A) and a tubular configuration (12B) that is generally the expanded shape. As mentioned, the web-like struts 90 and a reinforcing ring 104 connect three generally axially-extending posts 92. A plurality of evenly spaced apertures 106 provide anchors for holding the polyester skirt 88 (see Figure 11B) in place. In the illustrated embodiment, the web-like struts 90 also include a series of axially-extending struts 108. An upper end of the coupling stent 36 that connects to the sewing ring of the valve and is defined by the reinforcing ring 104 follows an undulating path with alternating arcuate troughs 110 and peaks 112. As seen from Figure 11C, the exemplary prosthetic valve 34 has an undulating sewing ring 42 to which the upper end of the coupling stent 36 conforms. In a preferred embodiment, the geometry of the stent 36 matches that of the undulating sewing ring 42. Of course, if the sewing ring of the prosthetic valve is planar, then the upper end of the coupling stent 36 will also be planar. It should be noted also that the tubular version of Figure 12B is an illustration of an expanded configuration, although the balloon 40 may over-expand the free (lower) end of the stent 36 such that it ends up being slightly conical.

[0101] Figures 13A and 13B show an alternative coupling stent 120, again in flattened and tubular configurations, respectively. As with the first embodiment, the coupling stent 120 includes web-like struts 122 extending between a series of axially-extending struts 124. In this embodiment, all of the axially-extending struts 124 are substantially the same thin cross-sectional size. The upper or connected end of the stent 120 again includes a reinforcing ring 126, although this version is interrupted with a series of short lengths separated by gaps. The upper end defines a plurality of alternating troughs 128 and peaks 130, with lengths of the reinforcing ring 126 defining the peaks. The axially-extending struts 124 are in-phase with the scalloped shape of the upper end of the stent 120, and coincide with the peaks and the middle of the troughs.

[0102] The gaps between the lengths making up the reinforcing ring 126 permit the stent 120 to be matched with a number of different sized prosthetic valves 34. That is, the majority of the stent 120 is expandable having a variable diameter, and providing gaps in the reinforcing ring 126 allows the upper end to also have a variable diameter so that it can be shaped to match the size of the corresponding sewing ring. This reduces manufacturing costs as correspondingly sized stents need not be used for each different sized valve.

[0103] Figure 14 is a plan view of a still further alternative coupling stent 132 that is very similar to the coupling stent 120, including web-like struts 134 connected between a series of axially-extending struts 136, and the upper end is defined by a reinforcing ring 138 formed by a series of short lengths of struts. In contrast to the embodiment of Figures 13A and 13B, the peaks of the undulating upper end have gaps as opposed to struts. Another way to express this is that the axially-extending struts 136 are out-of-phase with the scalloped shape of the upper end of the stent 132, and do not correspond to the peaks and the middle of the troughs.

[0104] Figure 15 illustrates an exemplary coupling stent 140 again having the expandable struts 142 between the axially-extending struts 144, and an upper reinforcing ring 146. The axially-extending struts 144 are in-phase with peaks and troughs of the upper end of the stent. The reinforcing ring 146 is a cross between the earlier-described such rings as it is continuous around its periphery but also has a variable diameter. That is, the ring 146 comprises a series of lengths of struts 148 of fixed length connected by thinner bridge portions 150 of variable length. The bridge portions 150 are each formed with a radius so that they can be either straightened (lengthened) or bent more (compressed). A series of apertures 152 are also formed in an upper end of the stent 142 provide anchor points for sutures or other attachment means when securing the stent to the sewing ring of the corresponding prosthetic valve.

[0105] In Figure 16, an alternative coupling stent 154 is identical to the stent 140 of Figure 15, although the axially-extending struts 156 are out-of-phase with the peaks and troughs of the undulating upper end.

[0106] Figure 17 shows a still further variation on a coupling stent 160, which has a series of expandable struts 162 connecting axially-extending struts 164. As with the version shown in Figures 12A and 12B, the web-like struts 162 also include a series of axially-extending struts 166, although these are thinner than the main axial struts 164. A reinforcing ring 168 is also thicker than the web-like struts 162, and features one or more gaps 170 in each trough such that the ring is discontinuous and expandable. Barbs 172, 174 on the axially extending struts 164, 166 may be utilized to enhance retention between the coupling stent 160 and a base stent with which it cooperates, or with annular tissue in situations where there is no base stent, as explained above.

[0107] As mentioned above, the two-component valve systems described herein utilize an outer or base stent (such as base stent 24) and a valve component having an inner or valve stent (such as coupling stent 36). The valve and its stent advance into the lumen of the pre-anchored outer stent and the valve stent expands to join the two stents and anchor the valve into its implant position. It is important that the inner stent and outer stent be correctly positioned both circumferentially and axially to minimize subsequent relative motion between the stents. Indeed, for the primary application of an aortic valve replacement, the circumferential position of the commissures of the valve relative to the native commissures is very important. A number of variations of coupling stent that attach to the valve component have been shown and described above. Figures 18-20 illustrate exemplary base stents and cooperation between the two stents.

[0108] Figures 18A and 18B show an exemplary embodiment of a base stent 180 comprising a plurality of radially-expandable struts 182 extending between a plurality of generally axially-extending struts 184. In the illustrated embodiment the struts 182 form chevron patterns between the struts 184,

although other configurations such as serpentine or diamond-shaped could also be used. The top and bottom rows of the radially-expandable struts 182 are arranged in apposition so as to form a plurality of triangular peaks 186 and troughs 188. The axial struts 184 are in-phase with the troughs 188.

[0109] The flattened view of Figure 18A shows four axial projections 190 that each extend upward from one of the axial struts 184. Although four projections 190 are shown, the exemplary base stent 180 desirably has three evenly circumferentially spaced projections, as seen around the periphery in the tubular version of Figure 18B, providing location markers for the base stent. These markers thus make it easier for the surgeon to orient the stent 180 such that the markers align with the native commissures. Furthermore, as the valve component advances to within the base stent 180, the visible projections 190 provide reference marks such that the inner stent can be properly oriented within the base stent. In this regard the projections 190 may be differently colored than the rest of the stent 180, or have radiopaque indicators thereon.

[0110] The length of the projections 190 above the upper row of middle struts 182 may also be calibrated to help the surgeon axially position the stent 180. For example, the distance from the tips of the projections 190 to the level of the native annulus could be determined, and the projections 190 located at a particular anatomical landmark such as just below the level of the coronary ostia.

[0111] An undulating dashed line 192 in Figure 18A represents the upper end of the inner or coupling stent 140, which is shown in phantom superimposed over the base stent 180. As such, the dashed line 192 also represents an undulating sewing ring, and it bears repeating that the sewing ring could be planar such that the upper end of the coupling stent is also planar. The coupling stent 140 includes axially-extending struts that are in-phase with the respective peaks and troughs of the scalloped upper end of the stent. In the illustrated combination, the peaks of the scalloped upper end of the coupling stent (dashed line 192) correspond rotationally (are in-phase) with the axial

struts 184 that have the projections 190. Therefore, because the coupling stent 140 axial struts are in-phase with the peaks of the upper end thereof, they are also in-phase with the axial struts 184 of the base stent 180. Conversely, a coupling stent may have axial struts out-of-phase with peaks of the upper end thereof, in which case the respective axial struts of the two stents are also out-of-phase.

[0112] Figure 19 shows an alternative base stent 200 that generally has the same components as the base stent 180 of Figure 18A, but the axial struts 184 extend between the peaks 186 of the outer rows of middle struts 182. In the earlier embodiment, the axial struts 184 extended between the troughs 188. The coupling stent 154 of Figure 16 is shown in phantom superimposed over the base stent 200 to illustrate how the axial struts of the two stents are now out-of-phase to increase interlocking therebetween.

[0113] The stent 200 also exhibits different rows of middle struts 182. Specifically, a first row 202a defines V's having relatively shallow angles, a second row 202b defines V's with medium angles, and a third row 202c defined V's with more acute angles. The different angles formed by the middle struts 182 in these rows helps shape the stent into a conical form when expanded. There is, the struts in the third row 202c which is farthest from the prosthetic valve have the greatest capacity for expansion to accommodate the transition from the collapsed conical shape of the stent to the expanded tubular shape.

[0114] Those of skill in the art will understand that there are many ways to increase retention between the two stents. For example, the peaks and troughs of the web-like expandable struts on the two stents could be oriented out-of-phase or in-phase. In a preferred embodiment the peaks and troughs of the two stents are out of phase so that expansion of the inner stent causes its peaks to deform outwardly into the troughs of the outer stent, and thereby provide interlocking structure therebetween. The variations described above provide a number of permutations of this cooperation.

[0115] Additionally, axial projections on one or both of stents could be bent to provide an interference with the other stent. For example, the lower ends of the axial struts 108 in the stent 36 shown in Figure 12A could be bent outward by expansion of a non-uniform shaped balloon such that they extend in voids within the outer stent. Likewise, the embodiment of Figure 17 illustrates barbs 172, 174 that can be bent outward into interference with the corresponding base stent. Strut ends or barbs that transition from one position to another to increase retention between the two stents can be actuated by mechanical bending, such as with a balloon, or through an automatic shape change upon installation within the body. Namely, some shape memory alloys such as Nitinol can be designed to undergo a shape change upon a temperature change, such that they assume a first shape at room temperature, and a second shape at body temperature.

[0116] Figure 20 illustrates a simplified means for increasing retention between the two stents. An inner valve stent 210 fits within an outer base stent 212 such that a lower end 214 thereof extends below the outer stent. By over-expansion of the balloon within the inner stent 210, the lower end 214 is caused to bend or wrap outward to prevent relative upward movement of the inner stent within the outer stent.

[0117] Figure 21 is a perspective view of a device 220 for delivering and expanding a base stent 222 with a mechanical expander 224. In the illustrated embodiment, the expander 224 includes a plurality of spreadable fingers 226 over which the base stent 22 is crimped. The device 220 includes a syringe-like apparatus including a barrel 230 within which a plunger 232 linearly slides. The fingers 226 are axially fixed but capable of pivoting or flexing with respect to the barrel 230. The distal end of the plunger 232 has an outer diameter that is greater than the diameter circumscribed by the inner surfaces of the spreadable fingers 226. Preferably there is a proximal lead-in ramp on the inside of the fingers 226 such that distal movement of the plunger

232 with respect to the barrel 230 gradually cams the fingers outward. The two positions of the plunger 232 are shown in Figures 21 and 23.

[0118] As an alternative to simple linear movement of the plunger 232, it may also be threadingly received within the barrel 230. Still further, the plunger 232 may be formed in two parts freely rotatable with respect to one another, with a proximal part threadingly received within the barrel 230 while a distal part does not rotate with respect to the barrel and merely cams the fingers 226 outward. Still further, a mechanical linkage may be used instead of a camming action whereby levers hinged together create outward movement of the fingers 226. And even further still, a hybrid version using an inflatable balloon with mechanical parts mounted on the outside of the balloon may be utilized. Those of skill in the art will understand that numerous variants on this mechanism are possible, the point being that balloon expansion is not only vehicle.

[0119] Desirably, the fingers 226 have a contoured exterior profile such that they expand the base stent 222 into a particular shape that better fits the heart valve annulus. For instance, the base stent 222 may be expanded into an hourglass shape with wider upper and lower ends and a smaller midsection, and/or an upper end may be formed with a tri-lobular shape to better fit the aortic sinuses. In the latter case, the tri-lobular shape is useful for orienting the base stent 222 upon implant, and also for orienting the coupling stent of the valve component that is received therewithin.

[0120] In another advantageous feature, the two-component valve system illustrated in the preceding figures provides a device and method that substantially reduces the time of the surgical procedure as compared with replacement valves that are sutured to the tissue after removing the native leaflets. For example, the stent 24 of Figures 5-9 may be deployed quickly and the valve component 30 may also be quickly attached to the stent. This reduces the time required on extracorporeal circulation and thereby substantially reduces the risk to the patient.

[0121] In addition to speeding up the implant process, the present invention having the pre-anchored stent, within which the valve and its stent mount, permits the annulus to be expanded to accommodate a larger valve than otherwise would be possible. In particular, clinical research has shown that the left ventricular outflow tract (LVOT) can be significantly expanded by a balloon-expandable stent and still retain normal functioning. In this context, "significantly expanding" the LVOT means expanding it by at least 10%, more preferably between about 10-30%. In absolute terms, the LVOT may be expanded 1.5-5 mm depending on the nominal orifice size. This expansion of the annulus creates an opportunity to increase the size of a surgically implanted prosthetic valve. The present invention employs a balloon-expandable base stent, and a balloon-expandable valve stent. The combination of these two stents permits expansion of the LVOT at and just below the aortic annulus, at the inflow end of the prosthetic valve. The interference fit created between the outside of the base stent and the LVOT secures the valve without pledgets or sutures taking up space, thereby allowing for placement of the maximum possible valve size. A larger valve size than would otherwise be available with conventional surgery enhances volumetric blood flow and reduces the pressure gradient through the valve.

[0122] It will be appreciated by those skilled in the art that embodiments of the present invention provide important new devices and methods wherein a valve may be securely anchored to a body lumen in a quick and efficient manner. Embodiments of the present invention provide a means for implanting a prosthetic valve in a surgical procedure without requiring the surgeon to suture the valve to the tissue. Accordingly, the surgical procedure time is substantially decreased. Furthermore, in addition to providing a base stent for the valve, the stent may be used to maintain the native valve in a dilated condition. As a result, it is not necessary for the surgeon to remove the native leaflets, thereby further reducing the procedure time.

[0123] It will also be appreciated that the present invention provides an improved system wherein a valve member may be replaced in a more quick and efficient manner. More particularly, it is not necessary to cut any sutures in order to remove the valve. Rather, the valve member may be disconnected from the stent (or other base stent) and a new valve member may be connected in its place. This is an important advantage when using biological tissue valves or other valves having limited design lives.

[0124] While the invention has been described in its preferred embodiments, it is to be understood that the words which have been used are words of description and not of limitation. Therefore, changes may be made within the appended claims without departing from the true scope of the invention.

WHAT IS CLAIMED IS:

1. A prosthetic heart valve system, comprising:

a base stent adapted to anchor against a heart valve annulus and defining an orifice therein; and

a valve component including a prosthetic valve defining therein a non-expandable, non-collapsible orifice, the valve component further including an expandable coupling stent extending from an inflow end thereof, the coupling stent having a contracted state for delivery to an implant position and an expanded state configured for outward connection to the base stent.

2. The system of claim 1, wherein the base stent is expandable and has a contracted state for delivery to an implant position adjacent a heart valve annulus and an expanded state sized to contact and anchor against the heart valve annulus.

3. The system of claim 2, wherein the base stent is plastically expandable.

4. The system of claim 1, wherein the coupling stent is plastically expandable.

5. The system of claim 1, wherein the prosthetic valve comprises a commercially available valve having a sewing ring, and wherein the coupling stent attaches to the sewing ring.

6. The system of claim 1, wherein the contracted state of the coupling stent is conical, tapering down in a distal direction.

7. The system of claim 6, wherein the coupling stent comprises a plurality of radially expandable struts at least some of which are arranged in rows, and wherein the distalmost row has the greatest capacity for expansion from the contracted state to the expanded state.

8. The system of claim 1, wherein the coupling stent comprises a plurality of radially expandable struts, and a row farthest from the prosthetic valve has alternating peaks and valleys, and wherein the base stent includes apertures into which the peaks of the coupling stent may project to interlock the two stents.

9. The system of claim 1, wherein the base stent includes a plurality of radially expandable struts between axially-oriented struts, and at least some of the axially-oriented struts have upper projections that demark locations around the stent.

10. A method of delivery and implant of a prosthetic heart valve system, comprising:

advancing a base stent to an implant position adjacent a heart valve annulus;

anchoring the base stent to the heart valve annulus;

providing a valve component including a prosthetic valve having a non-expandable, non-collapsible orifice, the valve component further including an expandable coupling stent extending from an inflow end thereof, the coupling stent having a contracted state for delivery to an implant position and an expanded state configured for outward connection to the base stent;

advancing the valve component with the coupling stent in its contracted state to an implant position adjacent the base stent; and

expanding the coupling stent to the expanded state in contact with and connected to the base stent.

11. The method of claim 10, wherein the base stent is plastically expandable, and further comprising:

advancing the expandable base stent in a contracted state to the implant position; and

plastically expanding the base stent to an expanded state in contact with and anchored to the heart valve annulus, in the process increasing the orifice size of the heart valve annulus by at least 10%.

12. The method of claim 11, wherein the prosthetic valve of the valve component is selected to have an orifice size that matches the increased orifice size of the heart valve annulus.

13. The method of claim 11, further including mounting the base stent over a mechanical expander, and deploying the base stent at the heart valve annulus using the mechanical expander.

14. The method of claim 10, further including mounting the valve component on a holder having a proximal hub and lumen therethrough, and mounting the holder on the distal end of a handle having a lumen therethrough, the method including passing a balloon catheter through the lumen of the handle and the holder and within the valve component, and inflating a balloon on the balloon catheter to expand the coupling stent.

15. The method of claim 14, further including packaging the valve component mounted on the holder separately from the handle and the balloon catheter.

16. The method of claim 14, wherein the contracted state of the coupling stent is conical, and wherein the balloon on the balloon catheter has a larger distal expanded end than its proximal expanded end so as to apply greater expansion deflection to the coupling stent than to the prosthetic valve.

17. The method of claim 10, wherein the contracted state of the coupling stent is conical, and wherein the coupling stent comprises a plurality of radially expandable struts at least some of which are arranged in rows, and wherein the row farthest from the prosthetic valve has the greatest capacity for expansion from the contracted state to the expanded state.

18. The method of claim 10, wherein the coupling stent comprises a plurality of radially expandable struts, and a row farthest from the prosthetic valve has alternating peaks and valleys, and the method includes expanding the distal end of the coupling stent more than the rest of the coupling stent so that the peaks in the row farthest from the prosthetic valve project outward into apertures in the base stent.

19. The method of claim 10, wherein both the base stent and the coupling stent have a plurality of radially expandable struts between axially-oriented struts, and wherein the method includes orienting the coupling stent so that its axially-oriented struts are out of phase with those of the base stent to increase retention therebetween.

20. The method of claim 10, including increasing the orifice size of the heart valve annulus by 1.5-5 mm by plastically expanding the base stent.

21. A system for delivering a prosthetic heart valve, comprising:

a valve component including a prosthetic valve having a non-expandable, non-collapsible orifice, the valve component further

including an expandable coupling stent extending from an inflow end thereof, the coupling stent having a contracted state for delivery to an implant position and an expanded state;

a valve holder connected to a proximal end of the valve component;

a balloon catheter having a balloon; and

a handle configured to attach to a proximal end of the valve holder and having a lumen for passage of the catheter, the balloon extending distally through the handle, past the holder and through the valve component.

22. The system of claim 21, wherein the prosthetic valve comprises a commercially available valve having a sewing ring, and wherein the coupling stent attaches to the sewing ring.

23. The system of claim 21, wherein the contracted state of the coupling stent is conical, tapering down in a distal direction.

24. The system of claim 21, wherein the contracted state of the coupling stent is conical and tapers down in a distal direction, and wherein the balloon catheter further includes a generally conical nose cone on a distal end thereof that extends through the valve component and engages a distal end of the coupling stent in its contracted state.

25. The system of claim 21, wherein the handle comprises a proximal section and a distal section that may be coupled together in series to form a continuous lumen, and wherein the distal section is adapted to couple to the hub of the holder to enable manual manipulation of the valve component using the distal section prior to connection with the proximal handle section.

26. The system of claim 25, wherein the balloon catheter and proximal handle section are packaged together with the balloon within the proximal section lumen.

27. The system of claim 21, wherein the valve component mounted on the holder is packaged separately from the handle and the balloon catheter.

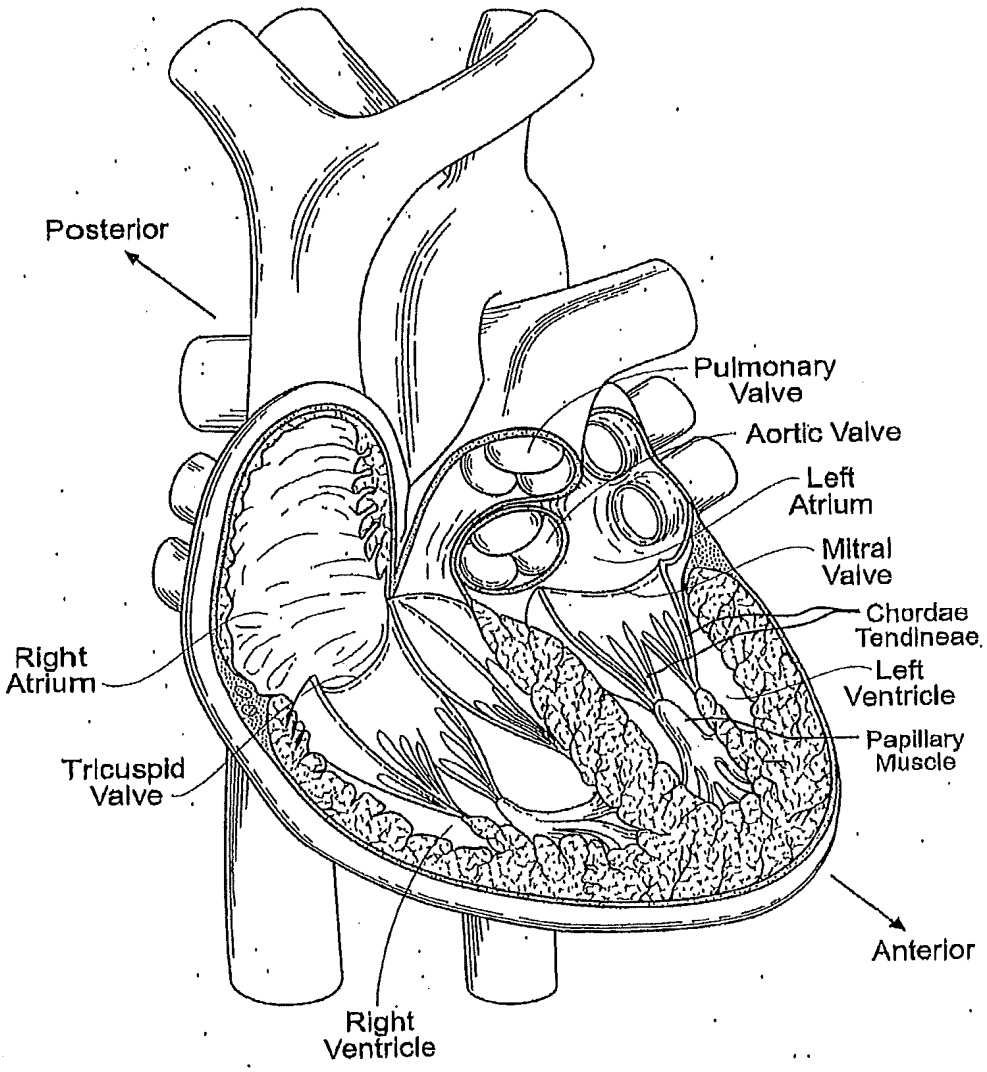

Posterior
Pulmonary Valve
Aortic Valve
Left Atrium
Mitral Valve
Chordae Tendineae
Left Ventricle
Papillary Muscle
Right Atrium
Tricuspid Valve
Anterior
Right Ventricle

Fig. 1

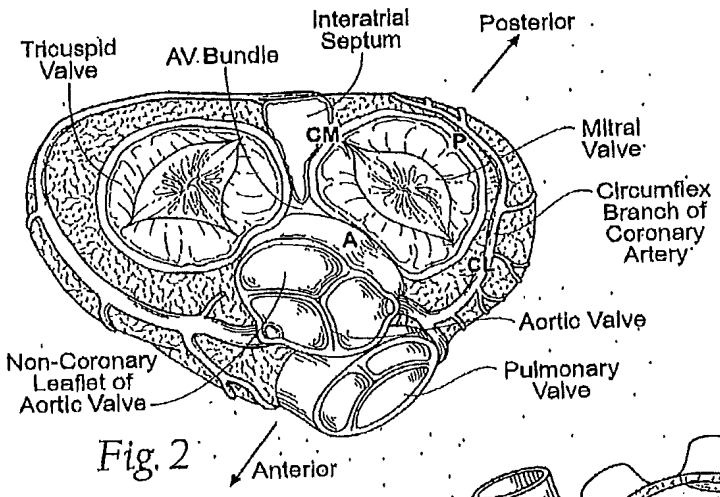


Fig. 2

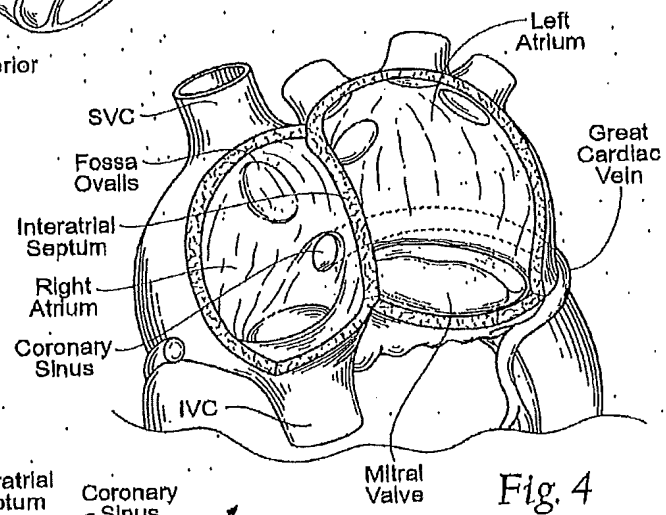


Fig. 4

Fig. 3

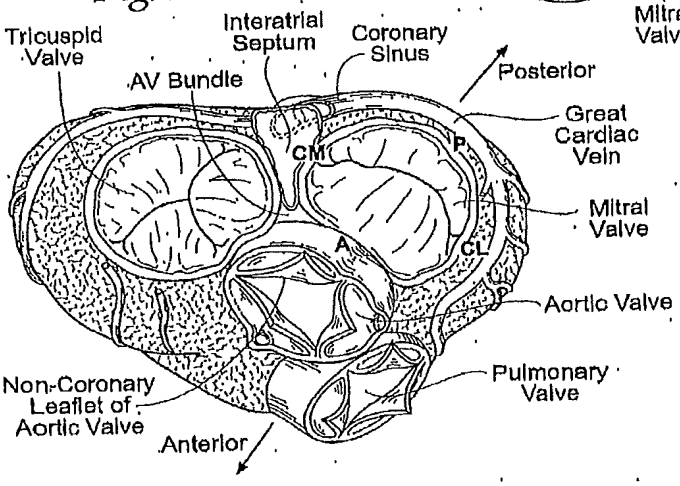


Fig. 5B

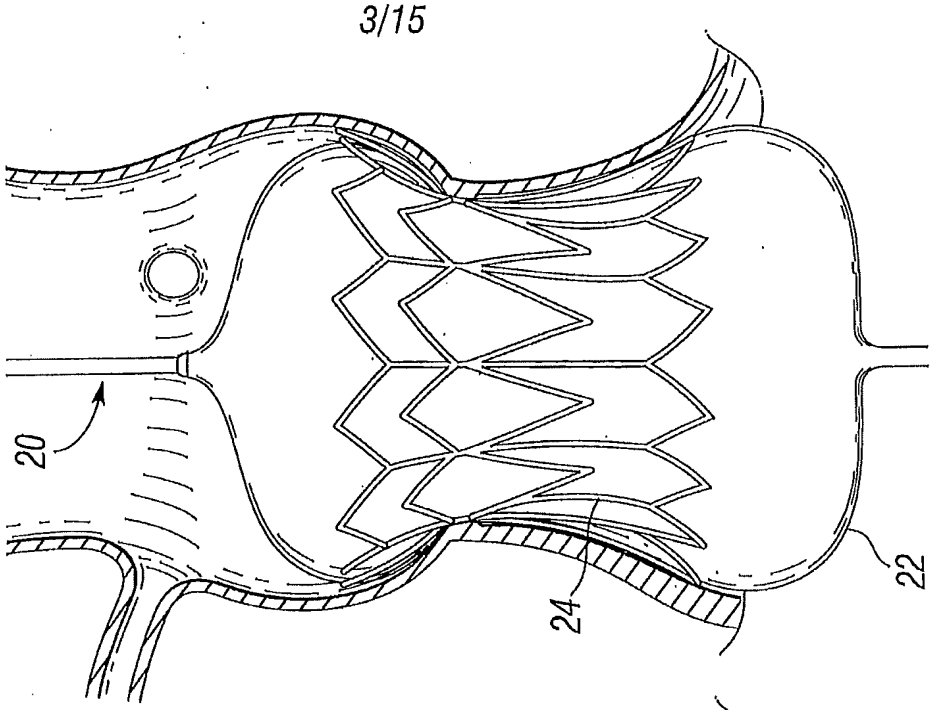
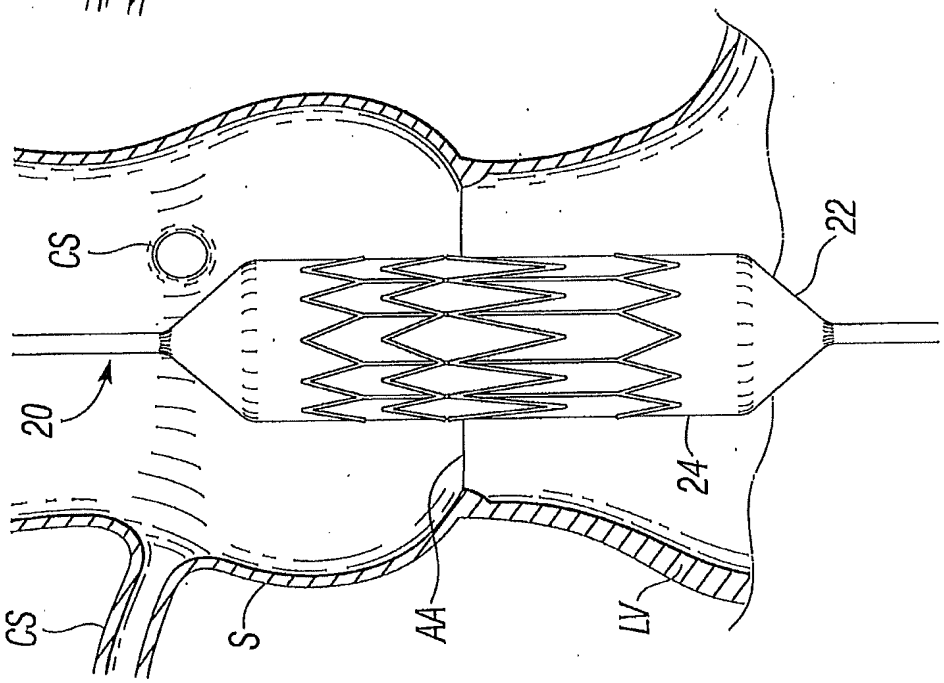


Fig. 5A



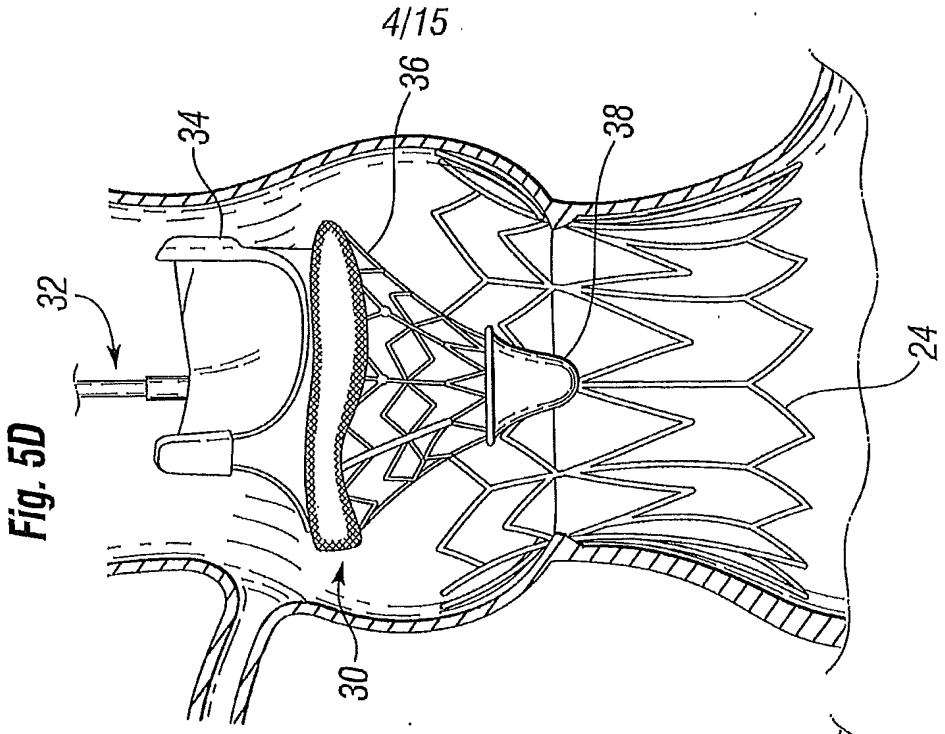


Fig. 5D

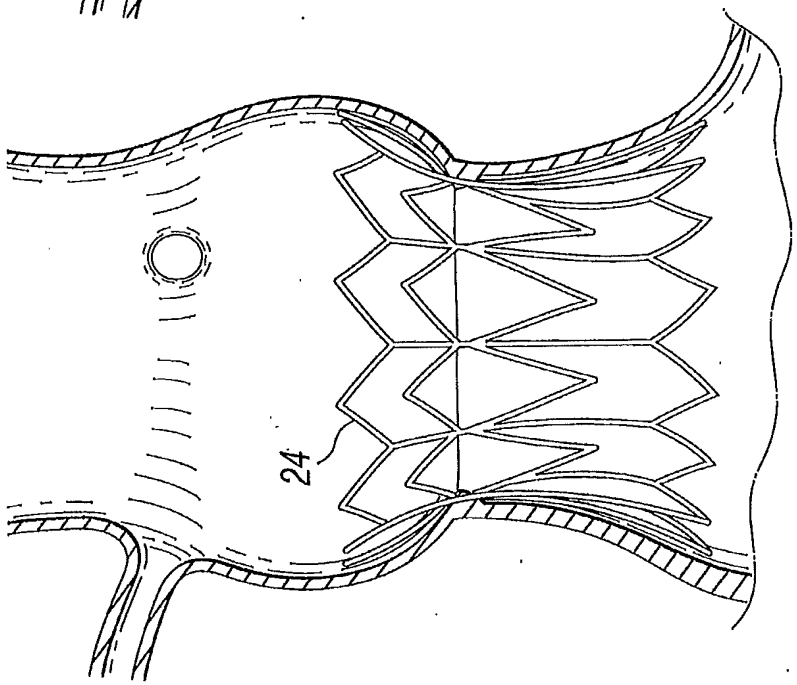


Fig. 5C

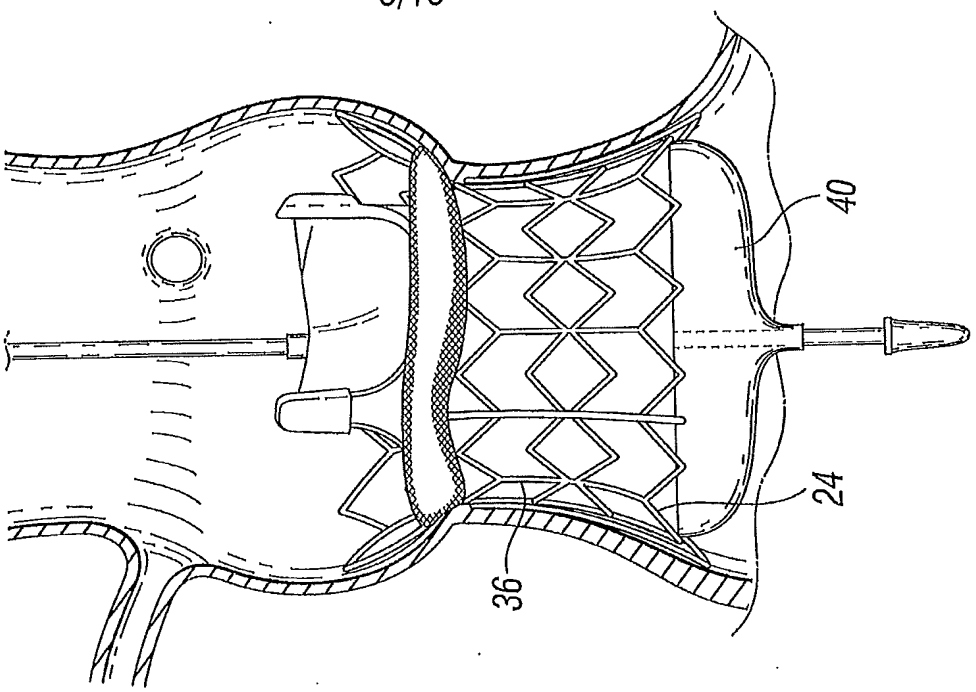


Fig. 5F

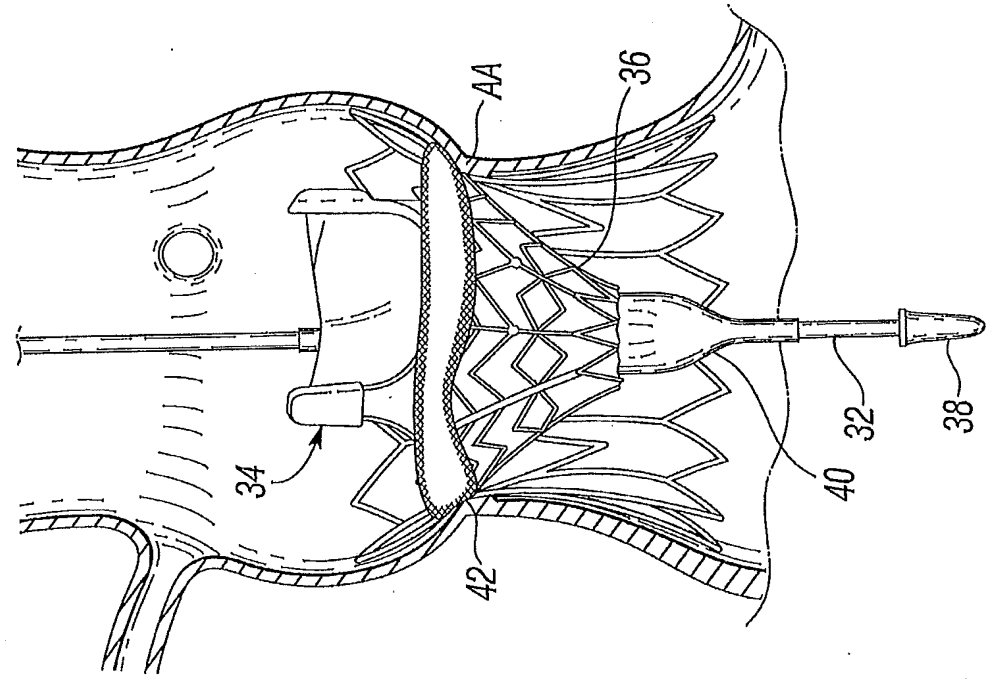


Fig. 5E

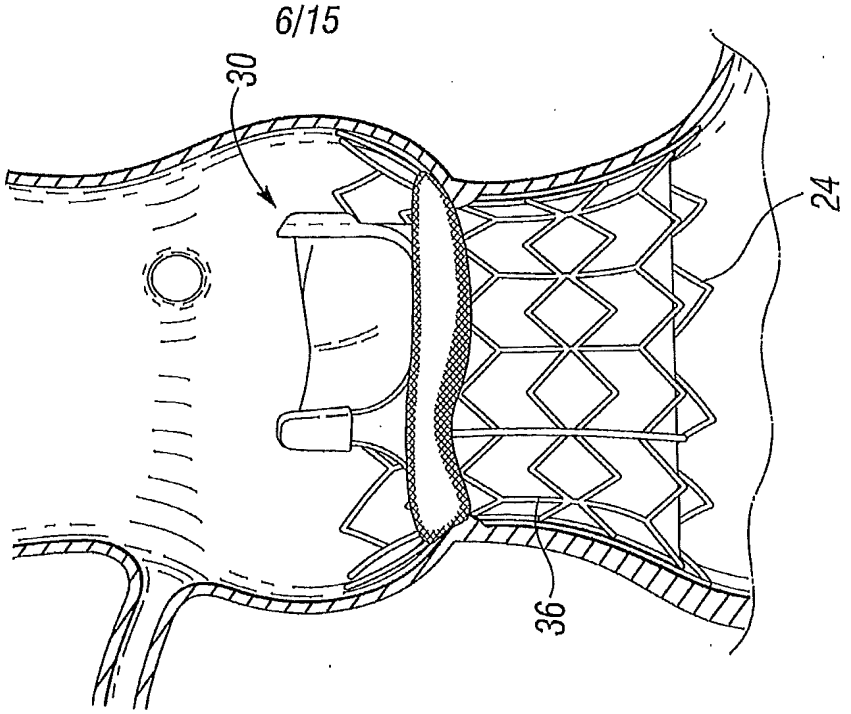


Fig. 5H

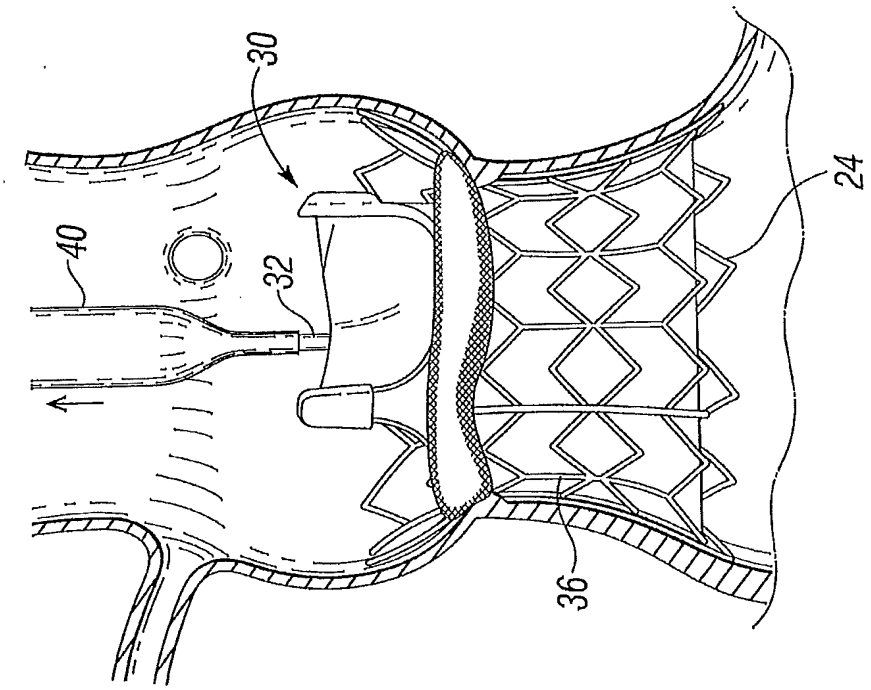


Fig. 5G

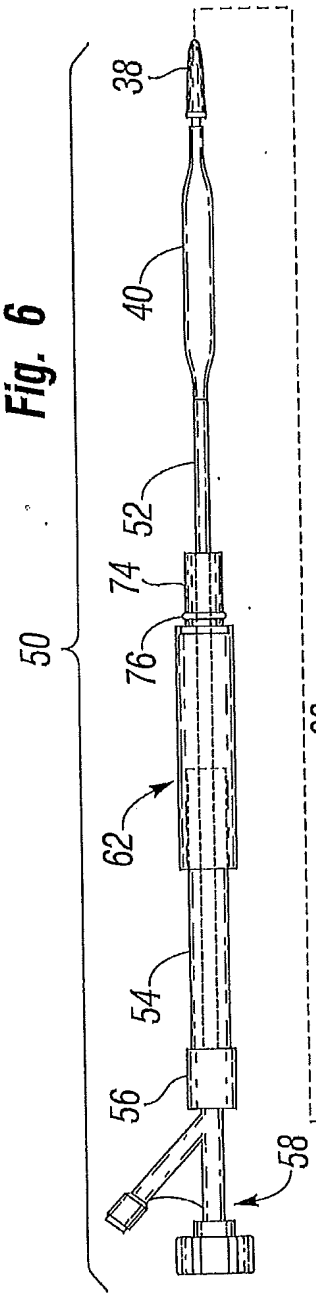


Fig. 6

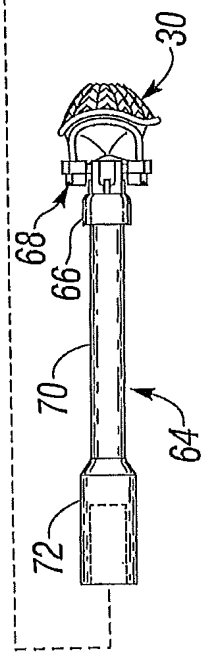


Fig. 7

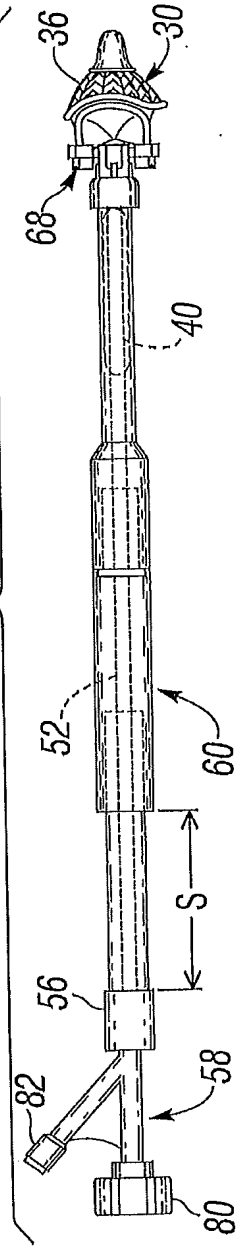
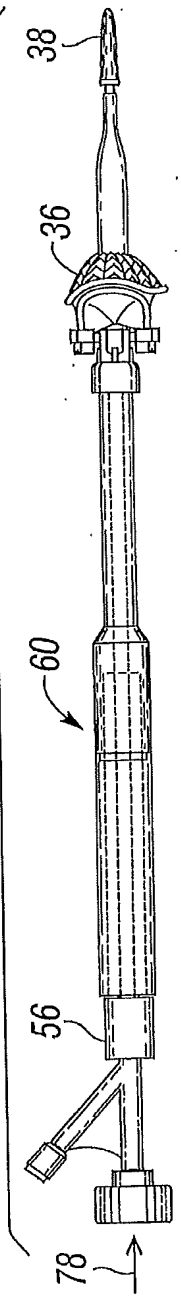


Fig. 8



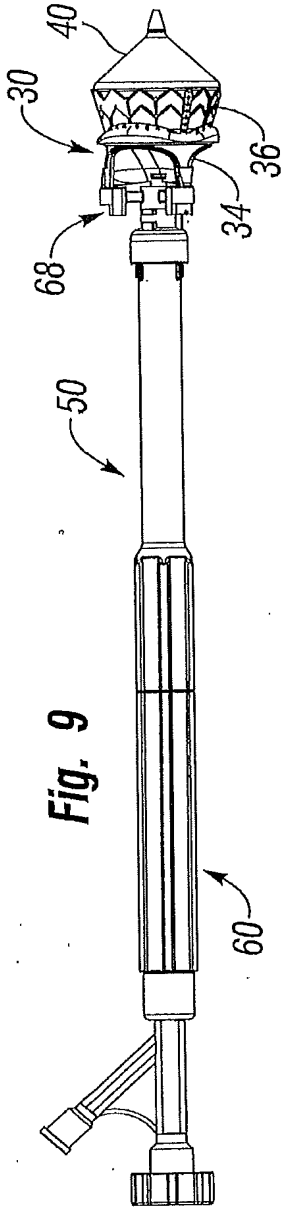


Fig. 9

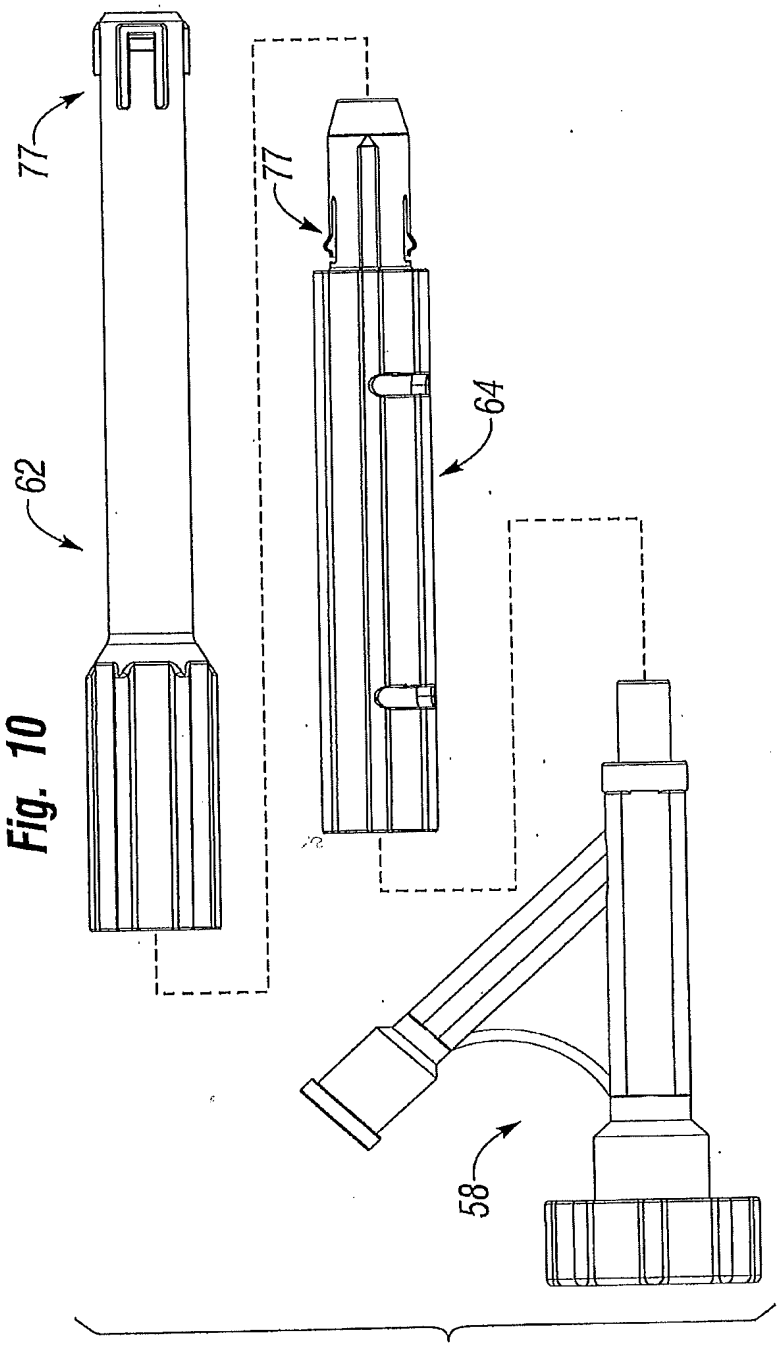


Fig. 10

Fig. 11B

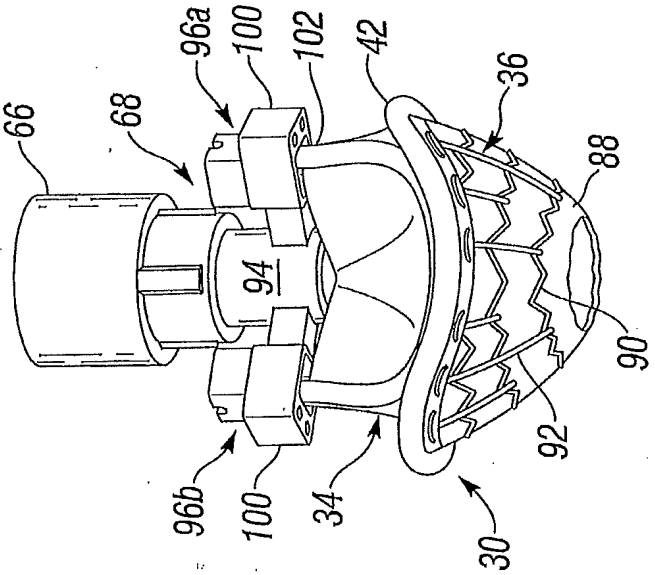


Fig. 11A

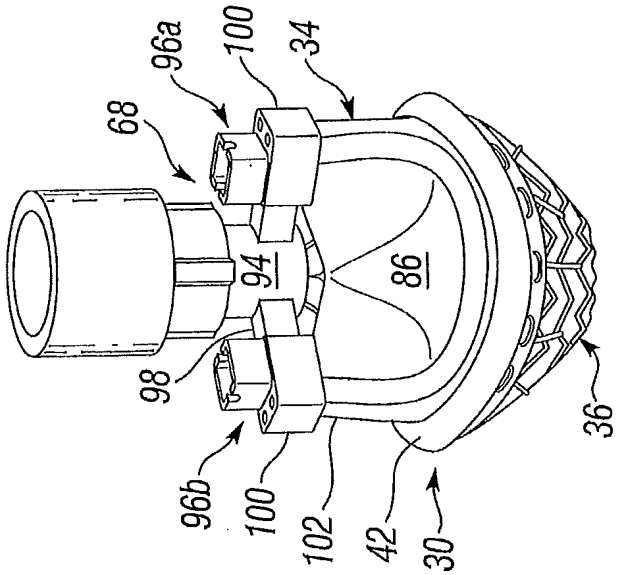


Fig. 11E

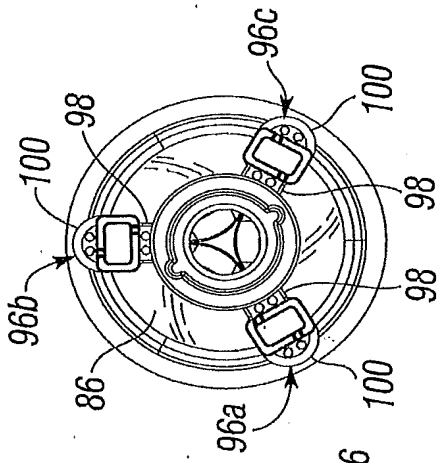


Fig. 11C

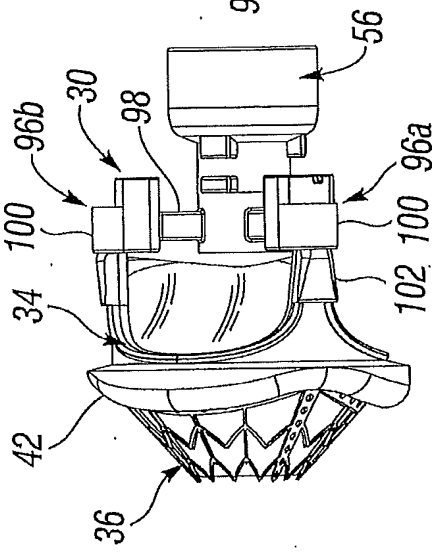


Fig. 11D

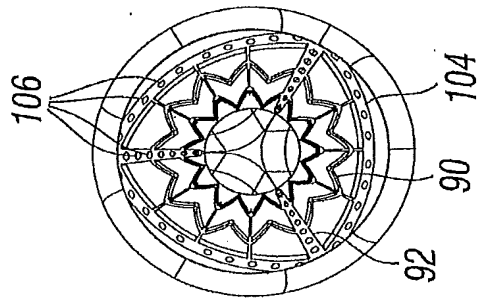


Fig. 12A

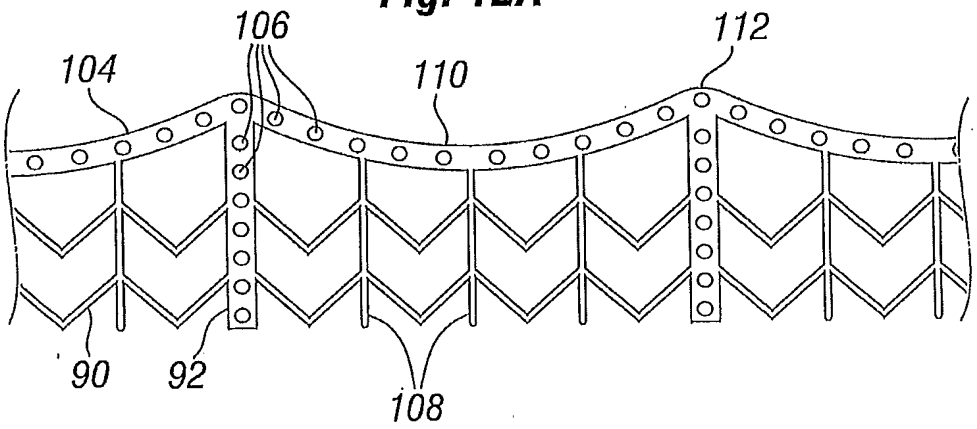


Fig. 12B

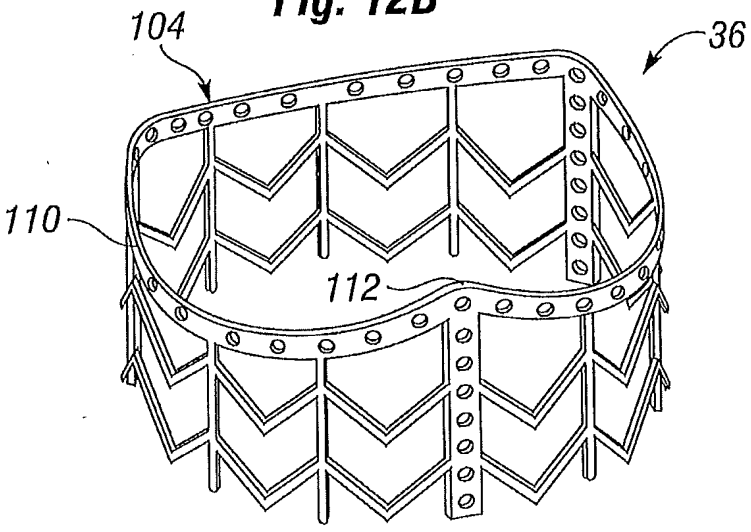


Fig. 13A

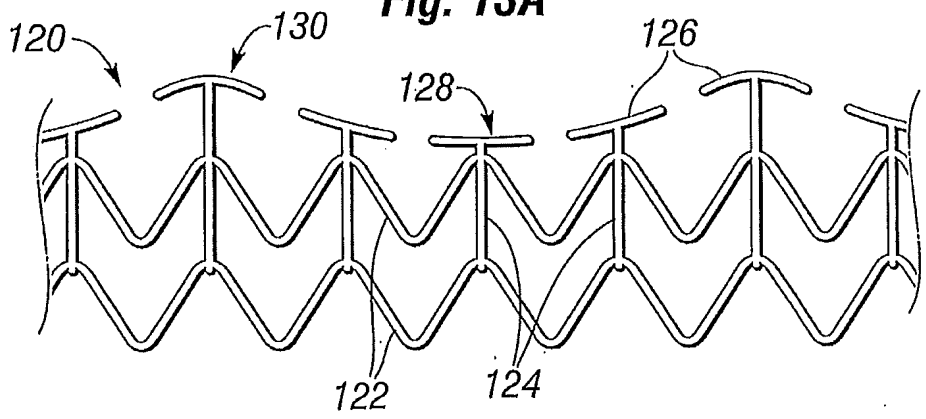


Fig. 13B

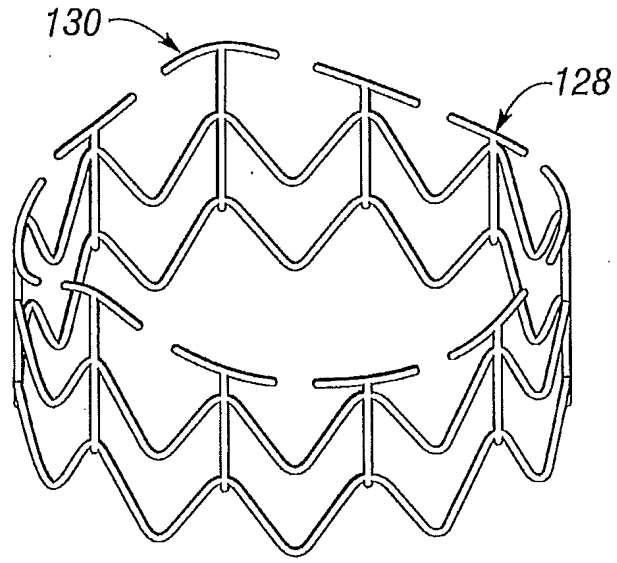


Fig. 14

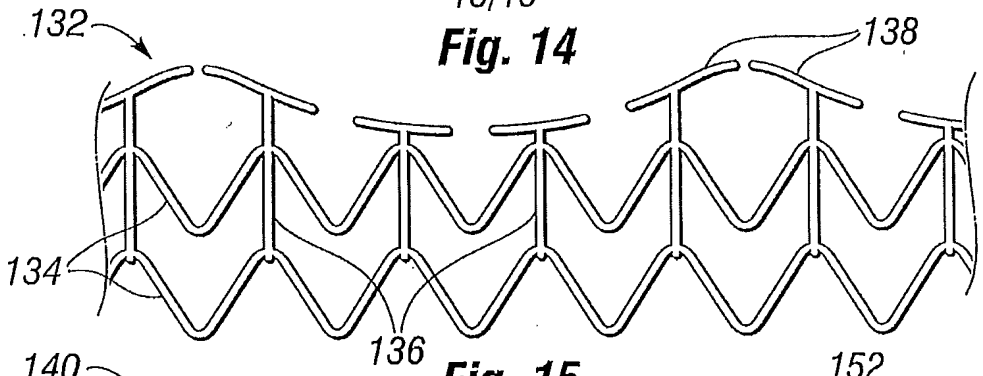


Fig. 15

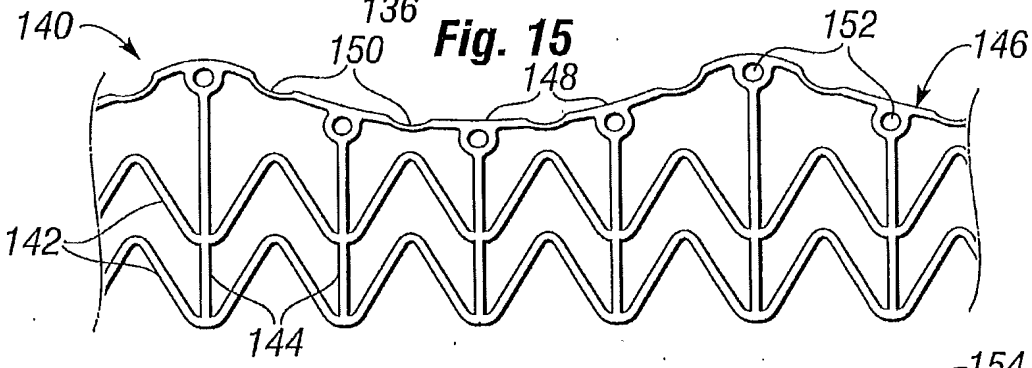


Fig. 16

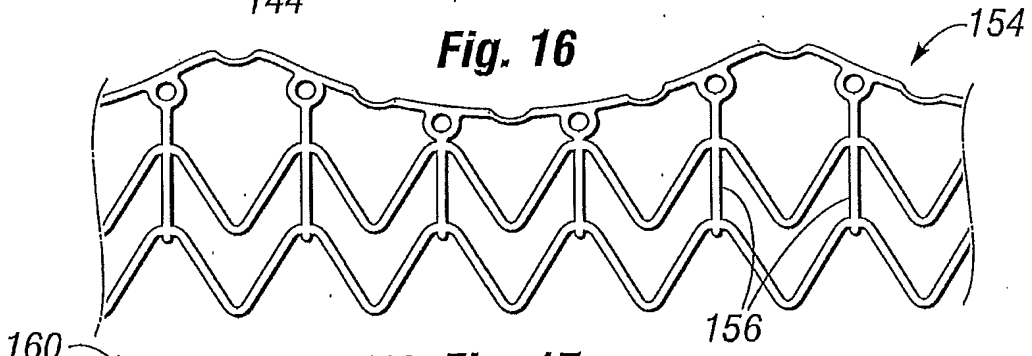
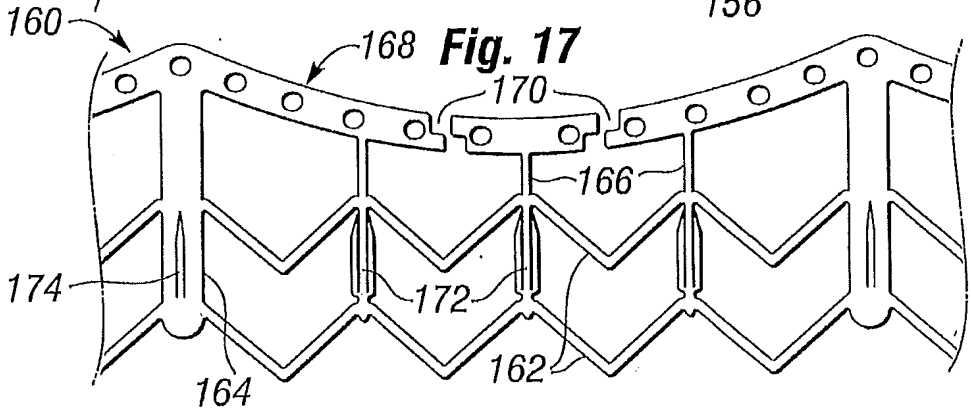


Fig. 17



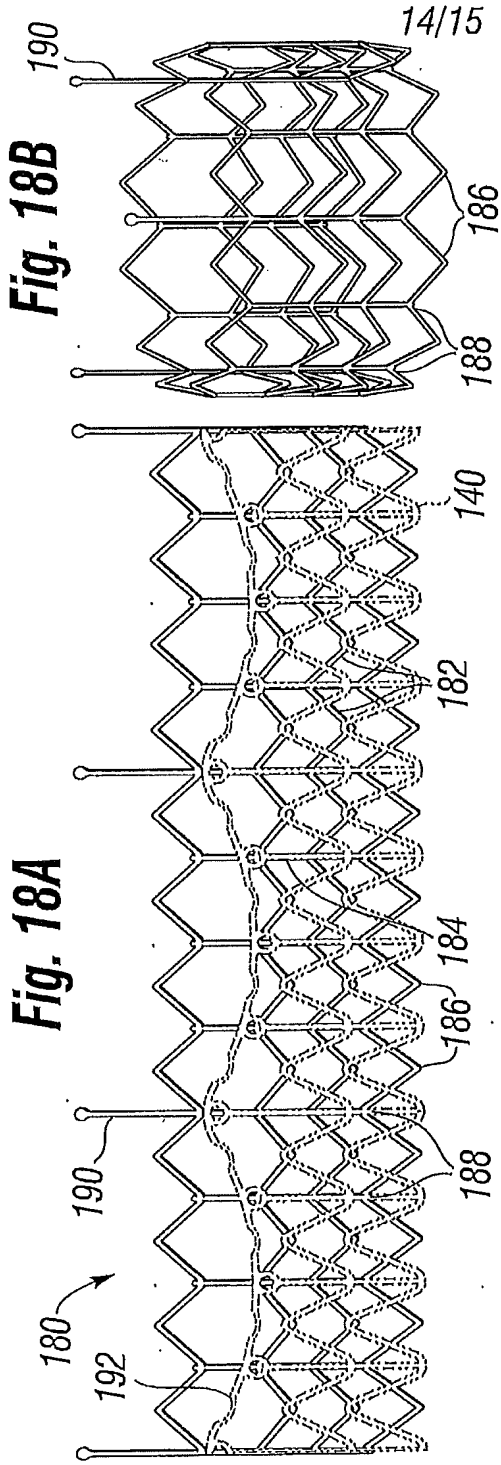


Fig. 18A

Fig. 18B

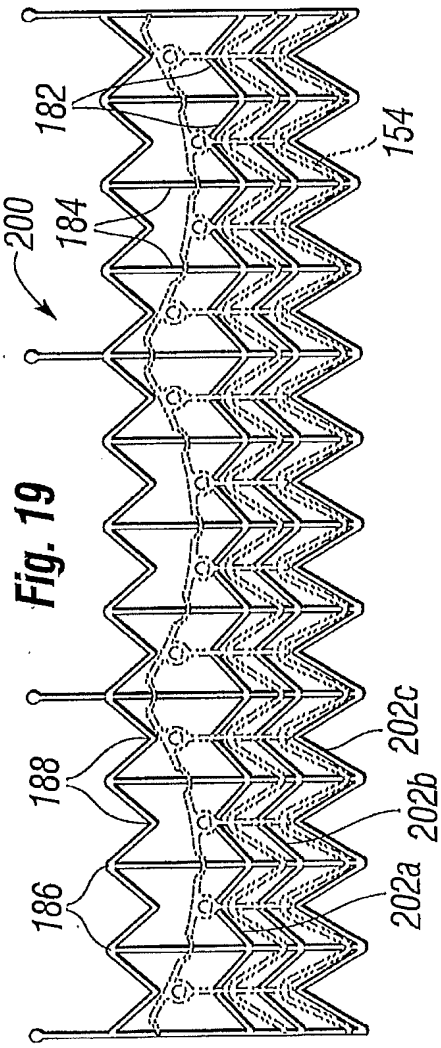


Fig. 19

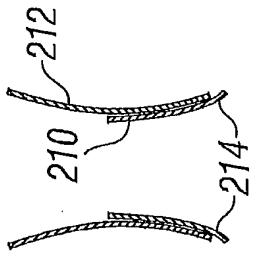


Fig. 20

Fig. 21

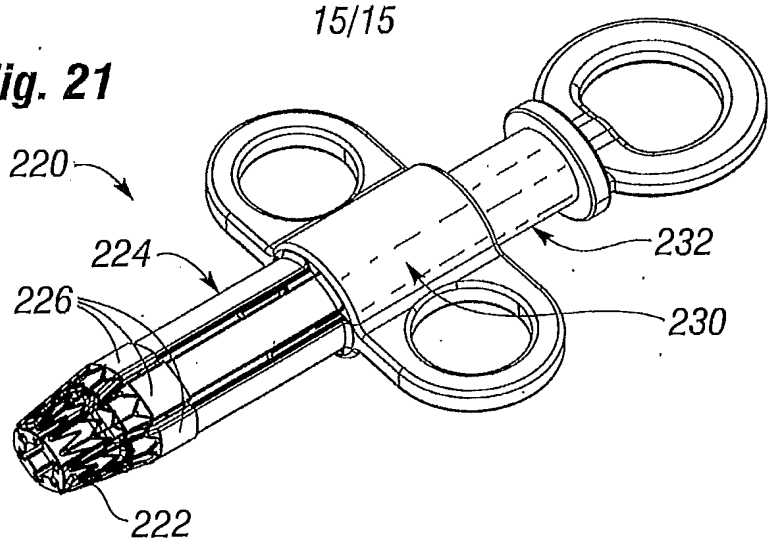


Fig. 22

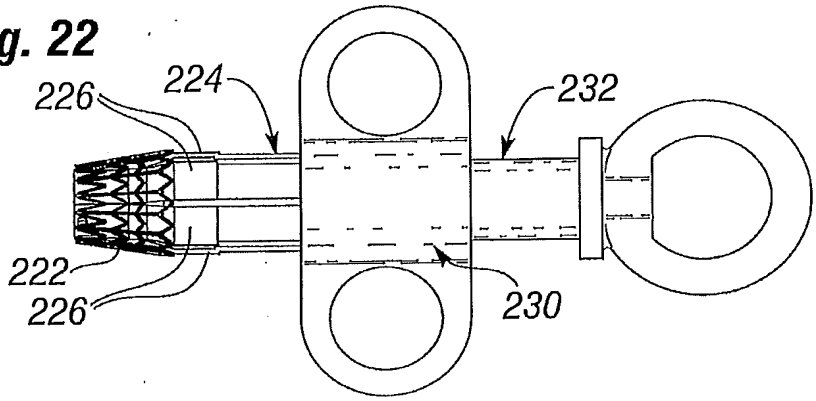
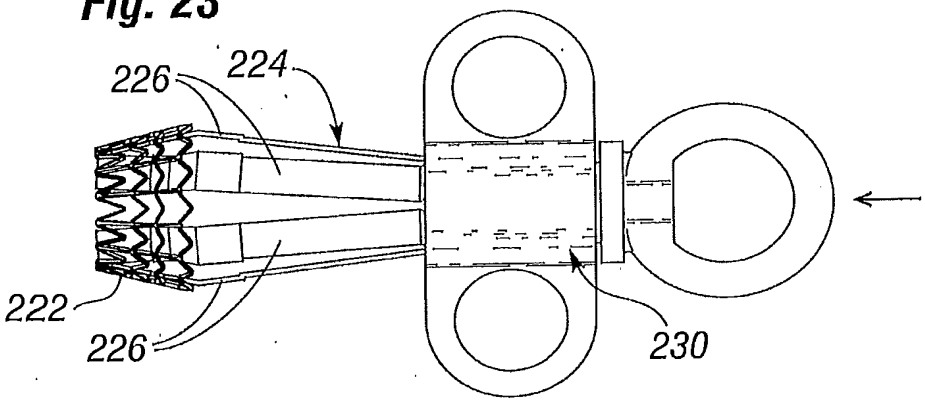


Fig. 23



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(54) **Title**: PACKAGING SYSTEMS FOR PERCUTANEOUSLY DELIVERABLE BIOPROSTHETIC VALVES

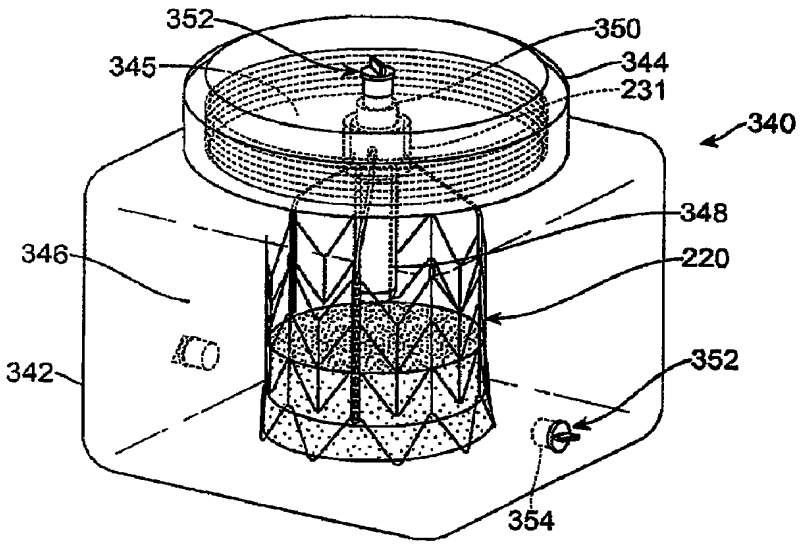

FIG. 3

(57) **Abstract**: A packaging system is disclosed for shipping a prosthetic tissue valve in a storage solution and preparing and loading of the bioprosthetic valve onto a catheter-based delivery system. The packaging system includes a fluid tight container filled with the storage solution attached to a delivery catheter, wherein the container surrounds the prosthetic tissue valve that is in a pre-loaded position on the delivery catheter during shipment and storage. The prosthetic tissue valve may include an attachment mechanism that attaches to the delivery catheter to properly position the tissue valve for loading within the delivery catheter. In another embodiment where the prosthetic tissue valve is not attached to the delivery catheter during shipment, the attachment mechanism may interact with the prosthetic tissue valve shipping container to prevent the bioprosthetic valve from moving during shipment.

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PACKAGING SYSTEMS FOR PERCUTANEOUSLY DELIVERABLE BIOPROSTHETIC VALVES

FIELD OF THE INVENTION

[0001] The invention relates generally to a packaging system for bioprosthetic valves. More specifically, the invention relates to packaging systems designed to protect a percutaneously deliverable bioprosthetic valve during shipping and/or to enable preparation and loading of the bioprosthetic valve onto a delivery catheter.

BACKGROUND OF THE INVENTION

[0002] Bioprosthetic heart valves include valve leaflets formed of flexible biological material. Bioprosthetic valves from human donors are referred to as homografts, whereas such valves from non-human animal donors are referred to as xenografts. These valves as a group are known as tissue valves. The tissue may include donor valve leaflets or other biological materials such as bovine or porcine pericardium, which are formed into the new valve structure. Depending on the method of implantation, the prosthetic valve structure may be sewn directly into place within a patient or attached to a second structure, such as a stent or other prosthesis, for implantation into a patient.

[0003] Conventional implantation of prosthetic tissue valves into the patient's body has been accomplished by invasive surgical procedures. Access to the heart valves (tricuspid, pulmonary, mitral, aortic), for instance, generally includes a thoracotomy or a sternotomy for the patient, and may include placing the patient on heart bypass to continue blood flow to vital organs, such as the brain, during the surgery. Thus, recovery from "open-heart" surgery often requires a great deal of time.

[0004] Recently percutaneous methods using catheter-based delivery mechanisms that traverse the vasculature to a treatment site have been developed allowing for minimally-invasive heart valve replacement and very short patient recovery times. Implantation of a prosthetic tissue valve percutaneously or by implantation using thoracic-microsurgery techniques is a far less invasive act than the surgical operation required for implanting traditional cardiac valve prostheses. Prosthetic tissue valves deliverable by these less invasive methods typically include an anchoring structure for supporting and fixing the valve prosthesis in the implantation position, to which the prosthetic valve leaflets are stably connected.

[0005] As mentioned above, some tissue valves are fashioned from xenografts taken from, for instance, a pig, horse, or cow, and others are fashioned from homografts taken from another human. The natural tissue for the replacement valves may be obtained from, for example, heart valves, aortic roots, aortic walls, aortic leaflets, pericardial tissue such as pericardial patches, bypass grafts, blood vessels, human umbilical tissue and the like. These natural tissues are typically soft tissues, and generally include collagen containing material. The tissue can be living tissue, decellularized tissue or recellularized tissue. The natural tissue can be fixed by crosslinking to provide mechanical stabilization, for example, by preventing enzymatic degradation of the tissue prior to implantation. A solution of glutaraldehyde or formaldehyde is typically used for fixation.

[0006] Preferably, the prosthetic tissue valves will be suspended in the glutaraldehyde storage solution until the surgical or percutaneous procedure is about to begin. As such when used in a catheter-based procedure, the clinician must prepare the fixed prosthetic tissue valve for insertion within the vasculature by removing the prosthetic tissue valve from the glutaraldehyde storage solution and rinsing the prosthetic tissue valve to remove the glutaraldehyde storage solution, followed by loading the prosthetic tissue valve onto or within the catheter-based delivery system. The clinician must take care during the preparation and loading steps not to contaminate or damage the prosthetic tissue valve. Such preparation adds time to the interventional procedure as well as risk that the tissue valve may not be properly loaded onto the catheter-based delivery system, which can lead to serious complications upon implantation of the prosthetic tissue valve at the treatment site. Due to the complexity and criticality of loading the prosthetic tissue valve onto the catheter-based delivery device, some vendors of replacement tissue valves actually provide representatives at the time of implantation to perform this aspect of the interventional procedure.

[0007] One solution to address proper loading concerns would be to "pre-load" the prosthetic tissue valve onto the catheter-based delivery system prior to shipment; however, prosthetic tissue valves heretofore have not been pre-loaded due to the sensitivity of the prosthetic tissue valves to prolonged crimping, as well as the necessity of maintaining the prosthetic tissue valve within a storage solution until just prior to implantation. Thus, there remains a need in the art for bioprosthetic valve packaging that can assure the sterility and integrity of a prosthetic tissue valve

during shipment and ease loading of the prosthetic tissue valve onto a catheter-based delivery system by a clinician prior to performing the interventional procedure.

BRIEF SUMMARY OF THE INVENTION

[0008] Embodiments hereof are directed to a packaging and valve preparation system for shipping and preparing a prosthetic tissue valve having a natural tissue component in a storage solution and easing loading of the bioprosthetic valve onto a catheter-based delivery system. The packaging system includes a fluid tight shipping container or vessel filled with the storage solution, such as a glutaraldehyde solution, sealingly attached to a delivery catheter, wherein the container surrounds the prosthetic tissue valve that is in a pre-loaded position on the delivery catheter during shipment and storage. In an embodiment, the shipping container may be a bladder-type container. The prosthetic tissue valve may include an attachment mechanism that closes, crimps or otherwise attaches to the delivery catheter during shipment to properly position the bioprosthetic valve for loading within the delivery catheter by a clinician.

[0009] In another embodiment, a prosthetic tissue valve with an attachment mechanism may be unattached to the delivery catheter during shipment. In such an embodiment, the prosthetic tissue valve is disposed within a shipping container filled with a storage solution such that the attachment mechanism interacts with the shipping container to prevent the bioprosthetic valve from moving during shipment. In an embodiment, the shipping container may be a jar-like vessel with a threaded cap having a holding tube.

BRIEF DESCRIPTION OF DRAWINGS

[0010] The foregoing and other features and advantages of the invention will be apparent from the following description of embodiments hereof as illustrated in the accompanying drawings. The accompanying drawings, which are incorporated herein and form a part of the specification, further serve to explain the principles of the invention and to enable a person skilled in the pertinent art to make and use the invention. The drawings are not to scale.

[0011] FIG. 1 is a cross-sectional side view of a delivery catheter according to an embodiment hereof.

[0012] FIG. 2 is a side perspective view of a prosthetic tissue valve system according to an embodiment hereof.

[0013] FIG. 3 is a side perspective view of the prosthetic tissue valve system of FIG. 2 in a shipping container according to an embodiment hereof.

[0014] FIG. 4 is a side perspective view of the prosthetic tissue valve system of FIG. 2 being loaded onto the delivery catheter of FIG. 1.

[0015] FIGS 4A and 4B are perspective views of an attachment assembly according to another embodiment hereof.

[0016] FIG. 5 is a cross-sectional side view of the delivery catheter of FIG. 1 with the prosthetic tissue valve system of FIG. 2 in a delivery configuration.

[0017] FIG. 6 is a side view of a delivery catheter attached to a shipping bladder containing the prosthetic tissue valve of FIG. 2 in a shipping/storage configuration in accordance with another embodiment hereof, wherein the bioprosthetic valve is pre-loaded onto the delivery catheter.

[0018] FIG. 7 is a side view of a prosthetic tissue valve delivery system in partial section that is attached to an accordion-like shipping bladder containing the prosthetic tissue valve in a shipping/storage configuration in accordance with another embodiment hereof, wherein the bioprosthetic valve is pre-loaded onto the delivery catheter.

[0019] FIG. 8 is a side view of the delivery system and accordion-like shipping bladder of FIG. 7 with the prosthetic tissue valve collapsed for loading within the delivery catheter.

DETAILED DESCRIPTION OF THE INVENTION

[0020] Specific embodiments are now described with reference to the figures, wherein like reference numbers indicate identical or functionally similar elements. The terms "distal" and "proximal" are used in the following description with respect to a position or direction relative to the treating clinician. "Distal" or "distally" are a position distant from or in a direction away from the clinician. "Proximal" and "proximally" are a position near or in a direction toward the clinician.

[0021] The following detailed description is merely exemplary in nature and is not intended to limit the invention or the application and uses of the invention. Although the description of the invention is in the context of heart valve replacement via blood vessels such as the aorta, coronary, and carotid arteries, embodiments of the present invention may also be used to deliver tissue valves in any other vessel where it is deemed useful. Furthermore, there is no intention to be bound by any

expressed or implied theory presented in the preceding technical field, background, brief summary or the following detailed description.

[0022] FIG. 1 is a cross-sectional side view of a delivery catheter 100 for percutaneously delivering a prosthetic tissue valve according to an embodiment of the present invention. Delivery catheter 100 includes an outer tubular component 102, a middle tubular component 104, and an inner component 106. Outer tubular component 102 defines a first lumen 108 from a proximal end 101 to a distal end 103 thereof through which middle tubular component 104 is slidably disposed, and may alternatively be referred to as a sheath component. Middle tubular component 104 defines a second lumen 110 from a proximal end 105 to a distal end 107 thereof through which inner component 106 is slidably disposed. Inner component 106 has a proximal end 111 and distal tip 112. In the embodiment of FIG. 1, distal tip 112 is a molded polymeric piece attached to a distal end 109 of an elongate shaft portion 114 of inner component 106. In another embodiment, distal end 109 of elongate shaft portion 114 may be coiled to provide a steerable tip, such that distal tip 112 is omitted. During an interventional procedure, proximal ends 101, 105, 111 of outer tubular component 102, middle tubular component 104, and inner component 106, respectively, each extend proximally outside of the patient's body such that they may be manipulated by a clinician and one or more of proximal ends 101, 105, 111 may include a handle or knob (not shown) in order to facilitate securing a longitudinal position or sliding movement thereof.

[0023] Outer and/or middle tubular components 102, 104 may be made from polymeric tubing, such as tubing formed from, for *e.g.*, polyethylene block amide copolymer, polyvinyl chloride, polyethylene, polyethylene terephthalate, polyamide, polyimide, polyetheretherketone (PEEK), nylon or copolymers thereof, as well as from metal tubing formed from stainless steel or nitinol, for example. In an embodiment, outer and/or middle tubular component 102, 104 may include a stainless steel hypotube, such as a hypotube of stainless steel 304 or 316, cut in a spiral or spring-like pattern to have high column strength with flexibility. In various other embodiments hereof, outer and/or middle tubular components 102, 104 may include a reinforced shaft segment, such as a shaft segment of a stainless steel braided polyimide, to provide columnar strength and pushability to delivery catheter 100 and/or multiple shaft components of varying flexibility to provide a gradual transition in flexibility as delivery catheter 100 extends distally. In another

embodiment, outer and/or middle tubular components 102, 104 may be a composite shaft having an outer layer of polytetrafluoroethylene (PTFE) and an inner liner of fluorinated ethylene propylene (FEP). Inner component 106 may be a solid metallic core wire, and, in embodiments hereof, may be tapered at its distal end and/or include one or more core wire sections to provide a stiffness transition. In various other embodiments, inner component 106 may be a hollow polymeric or metallic tube that defines a guidewire lumen therethrough.

[0024] Delivery catheter 100 is depicted in FIG. 1 in a loading configuration with an annular distal stopper 116, which is attached to and surrounds inner component 106, positioned distal of distal ends 103, 107 of outer and middle tubular components 102, 104. In addition, distal tip 107 of middle tubular component 104 is positioned distal of distal end 103 of outer tubular component 102 so that middle tubular component distal end 107 acts as a proximal stopper during loading of a prosthetic valve, such as prosthetic tissue valve 220 depicted in FIG. 2 and described below. The operation of delivery catheter 100 during loading and delivery is also described in detail below. Alternatively, a proximal stopper may be attached to and surround inner component 106 an appropriate length proximal of distal stopper 116.

[0025] With reference to FIG. 2, prosthetic tissue valve system 220 includes a prosthetic tissue valve 221, having a stent-like frame 222 with valve leaflets 224 secured therein, and an attachment assembly 230. Stent-like frame 222 of prosthetic tissue valve 221 is a tubular structure having four sinusoidal rings 226 attached peak-to-peak and valley-to-valley by longitudinal connectors 228 and includes three bands 232, which may be slightly wider than longitudinal connectors 228, longitudinally extending from an outflow end of stent-like frame 222. Sinusoidal rings 226 may be attached to longitudinal connectors 228 and bands 232 by any attachment mechanism known to one of ordinary skill in the art of stent construction or may be formed pre-connected as a unitary structure, such as by laser cutting or etching the entire stent body from a hollow tube or sheet. Bands 232 may each include an eyelet 239, or in an alternate embodiment a broadened paddle-like area, at a proximal end thereof to aid in the releasable engagement of bands 232 with attachment assembly 230, as discussed in more detail below. Stent-like frame 222 is "self-expanding", which as used herein means that stent-like frame 222 has a mechanical memory to return to an expanded or deployed configuration as shown in

FIG. 2. Mechanical memory may be imparted to stent-like frame 222 by thermal treatment to achieve a spring temper in stainless steel, for example, or to set a shape memory in a susceptible metal alloy, such as nitinol. As such in embodiments hereof, sinusoidal rings 226 and longitudinal connectors 228 for producing stent-like frame 222 may be made from stainless steel, a pseudo-elastic metal such as nitinol, or a nickel-based super alloy. It would be understood by one of ordinary skill in the art that other self-expanding stent-like frames, with or without tubular structures having sinusoidal rings and/or connectors, may be utilized in embodiments of the present invention without departing from the scope hereof.

[0026] Valve leaflets 224 of prosthetic tissue valve 221 may be of xenograft or homograft natural tissue and may form a bicuspid, tricuspid, or tube replacement valve. The natural tissue for the replacement valve leaflets may be obtained from, for example, heart valves, aortic roots, aortic walls, aortic leaflets, pericardial tissue, such as pericardial patches, bypass grafts, blood vessels, human umbilical tissue and the like. Valve leaflets 224 may be sutured or otherwise securely attached to stent-like frame 222 as would be known to one of ordinary skill in the art of prosthetic tissue valve construction.

[0027] Attachment assembly 230 includes a locking collar 231 and a holding sleeve 460 (shown in FIG. 4). Locking collar 231 may be formed from a flexible material, such as nylon, polyethylene, polyurethane, silicone or other suitable polymer. In the embodiment of FIG. 2, locking collar 231 is c-shaped having cog-like projections 241 surrounding a distal end thereof with a plurality of slots 233 defined between projections 241. Slots 233 are sized to provide an interference or tight fit with bands 232 of stent-like frame 222 to substantially prevent longitudinal movement between attachment assembly 230 and prosthetic tissue valve 221 with eyelets 239 being wider than slots 233 to prevent bands 232 from sliding free thereof. Locking collar 231 is surrounded by holding sleeve 460 that fits tightly enough around locking collar 231, such as in an interference fit, to prevent radial movement and/or release of bands 232 from slots 233 and thereby secures prosthetic tissue valve 221 to attachment assembly 230.

[0028] In embodiments hereof, holding sleeve 460 is a thin-walled cylinder of a polymeric or elastomeric material that is slidable or stretchable over locking collar 231. In another embodiment, holding sleeve 460 may be of a material that is heat shrinkable around locking collar 231 to radially secure bands 232 therein. In one

such embodiment, holding sleeve 460 may be a short, tubular component made from a thin, stretchable material, such as silicone or polyurethane, having an inner diameter slightly larger than the diameters of catheter tip 112 and outer tubular component 102, wherein the inner diameter may be stretched to a second, larger inner diameter when holding sleeve 460 contains the unlocked or open locking collar 231, such that holding sleeve 460 substantially returns to its reduced, original inner diameter when locking collar 231 is locked or closed onto inner component 106. In an embodiment where holding sleeve 460 is formed from a non-stretchable material, while snapping or closing locking collar 231 in place a clinician may maintain a position of holding sleeve 460 over locking collar 231 to retain band(s) 232 therein until outer tubular component 102 has been distally forward to capture band(s) 232 and retain prosthetic tissue valve 221. In each of the aforementioned embodiments, holding sleeve 460 is removed after the loading of bioprosthetic valve 221 is completed.

[0029] Locking collar 231 includes projections or posts 234 protruding from a first longitudinal end surface 237 thereof that align with and have an interference fit within holes 236 in a second longitudinal end surface 235 thereof. Each post 234 is fit within a respective hole 236 when locking collar 231 is closed or crimped onto delivery catheter 100 to pre-load prosthetic tissue valve 221 thereon, as discussed in more detail below.

[0030] In another embodiment shown in FIGS. 4A and 4B, attachment assembly 430 includes locking collar 431 having interlocking half-ring segments 431a, 431b and holding sleeve 460'. Half-ring segment 431a includes projections or posts 434 that fit or snap within corresponding holes 436 in half-ring segment 431b. Each half-ring segment 431a, 431b includes cog-like projections 441 radially extending from a distal end thereof between which slots 433 are defined for receiving bands 232. In an embodiment, slots 433 are sized to have an interference fit with bands 232 and/or to be narrower than eyelets 239. Locking collar 431 is surrounded by holding sleeve 460', which may be a thin-walled polymeric or elastomeric cylinder/tubular component as described above with reference to the embodiments of holding sleeve 460, that radially secures bands 232 within slots 433 in a manner as previously described with reference to the embodiments of holding sleeve 460. Locking collar 431 may be formed from a flexible material, such as nylon, polyethylene, polyurethane, silicone or other suitable polymer.

[0031] In FIG. 4A, attachment assembly 430 is shown holding prosthetic tissue valve 221 in a pre-loaded configuration over inner component 106 of delivery catheter 100, with unattached half-ring segments 431a, 431b encircling inner component 106 and positioned between distal stopper 116 and distal end 107, *viz.*, proximal stopper, of middle tubular component 104. In FIG. 4B, half-ring segments 431a, 431b have been closed or locked onto inner component 106 such that bands 232 are radially constrained within slots 433 by outer tubular component 102, which is drawn over locking collar 431 concurrent with the removal of holding sleeve 460'. With prosthetic tissue valve 221 secured in this manner to delivery catheter 100, a clinician is ready to load the bioprosthetic valve within the delivery catheter as described in more detail below.

[0032] In various other embodiments, attachment assemblies for securing prosthetic tissue valves to delivery systems in accordance herewith may include hooks, pigtails or cartridge-type connectors, such as those shown and described in patent application publications US 2008/0228254 A1 to Ryan and US 2008/0228263 A1 to Ryan, U.S. Appl. No. 12/357,958 to Bloom *et al.* (Atty. Dkt. No. P0027615.01) and/or U.S. Appl. No. 12/358,489 to Tabor *et al.* (Atty. Dkt. No. P0027615.04), each of which is incorporated by reference herein in its entirety.

[0033] FIG. 3 is a side perspective view of prosthetic tissue valve system 220 of FIG. 2 in a shipping container 340 according to an embodiment of the present invention. Shipping container 340 includes a jar-like vessel 342 having a threadably removable cap 344 for covering and uncovering a mouth 345 of vessel 342. Cap 344 has a centrally disposed holding tube 348 attached thereto that extends through locking collar 231, which is positioned within holding sleeve 460 (shown in FIG. 4), and into an interior of prosthetic tissue valve 221. With holding tube 348 so positioned, prosthetic tissue valve system 220 is prevented from moving during shipment and storage. In an embodiment, an upper or first end of the hollow holding tube 348 is accessible from an outside surface of cap 344 and defines an inflow port 350, which is fitted with a fluid-tight plug 352 during shipment and storage. Two outflow ports 354, which are apertures or holes, are shown in opposing walls of jar-like vessel 342, and are each fitted with a respective fluid-tight plug 352. Shipping container 340 holds prosthetic tissue valve 221 in a storage solution 346, such as a glutaraldehyde solution, during shipment and storage and is fluid-tight when cap 344 is threadably secured to jar-like vessel 342 and plugs 352 are in place within their

respective ports 350, 354. Shipping container 340 may be made of glass or a suitable polymeric material, such as polyethylene, polyethylene terephthalate, polypropylene, acetal or nylon.

[0034] When a clinician is ready to use prosthetic tissue valve 221, plugs 352 are removed from inflow and outflow ports 350, 354 and a saline or other rinsing solution is introduced into jar-like vessel 342 via inflow port 350 to flush storage solution 346 out through outflow ports 352. As shown in FIG. 4, prosthetic tissue valve system 220 is then removed from vessel 342 and slipped/loaded over distal tip 112 of delivery catheter 100 until locking collar 231 surrounded by holding sleeve 460 is positioned around inner component shaft portion 114 between distal stopper 116 and distal end 107 of middle tubular component 104, which as mentioned above acts as a proximal stopper during loading and delivery. In FIG. 4, an optional radiopaque marker band 462 is shown surrounding distal end 103 of outer tubular component 102 to aid in fluoroscopic placement of delivery catheter 100 within a vessel. In order to secure prosthetic tissue valve system 220 to delivery catheter 100, locking collar 231 is crimped or otherwise closed down around inner component shaft portion 114 until male posts 234 are seated/snapped within holes 236, so that prosthetic tissue valve 221 is pre-loaded onto delivery catheter 100.

[0035] Once prosthetic tissue valve system 220 is properly locked onto delivery catheter 100 by snapping locking collar 231 in place, holding sleeve 460 is moved distally a short distance, for *e.g.*, approximately 5 – 10 mm, to expose stent eyelets 239 and locking collar 231 while maintaining stent bands 232 in slots 233 of locking collar 231. Outer tubular component 102 is moved distally to initially capture and cover stent bands/eyelets 232, 239 and locking collar 231 with continued distal movement of outer tubular component 102, relative to middle tubular component 104 and inner component 106, collapses and loads prosthetic tissue valve system 221 into the delivery system 100. Holding sleeve 460 is removed after completion of the loading process and stent bands/eyelets 232, 239 are held within slots 233 of locking collar 231 by outer tubular component 102 so that prosthetic tissue valve 221 remains attached to locking collar 231. In FIG. 5, prosthetic tissue valve 221 is shown fully collapsed and loaded in a delivery configuration within delivery catheter 100. During loading and delivery, proximal and distal stoppers 107, 116 aid in maintaining a longitudinal position of locking collar 231, and thus prosthetic tissue valve system 220, relative to delivery catheter inner component 106. In an alternate

embodiment, proximal and distal stoppers may be omitted and locking collar 231 sized to have an interference or frictional fit with inner component 106 when closed thereon.

[0036] In an embodiment hereof, delivery catheter 100 with prosthetic tissue valve 221 loaded therein may be used in a heart valve replacement procedure, wherein prosthetic tissue valve 221 is to be used to replace an insufficient/incompetent aortic valve. Loaded delivery catheter 100, as shown in FIG. 5, may be introduced into the vasculature either via a percutaneous puncture, a.k.a the Seldinger technique, or via a surgical cut-down, to be positioned at the aortic treatment site via a retrograde approach. Delivery catheter 100 may achieve access to the vasculature through a branch of the femoral artery, a carotid artery, a subclavian artery, or a brachial artery. In another embodiment, access to the heart may be attained via a transapical, transaortic and/or other minimally-invasive surgical approach. Methods and apparatus for accessing the arterial system with catheters and navigating such catheters to the level of the aortic arch are generally known in the art. Once delivery catheter 100 is positioned as desired within the native aortic valve, outer tubular component 102 is proximally retracted relative to middle tubular component 104 and inner component 106 to release prosthetic tissue valve 221 from the collapsed, delivery configuration shown in FIG. 5. When outer tubular component 102 is retracted proximal of locking collar 231, self-expanding prosthetic tissue valve 221 will expand and bands 232 will be released from locking collar 231, which remains with delivery catheter 100 for removal from the patient therewith. In its fully deployed configuration, stent-like frame 222 of prosthetic tissue valve 221 radially displaces the native aortic valve leaflets to conform and seal to the aortic annulus, as would be understood by one of ordinary skill in the art of heart or venous valve replacement.

[0037] FIG. 6 is a side view of delivery catheter 600 attached to a shipping bladder 642 in a shipping/storage configuration in accordance with another embodiment hereof. Prosthetic tissue valve 221 is shown within shipping bladder 642 and attached/pre-loaded onto delivery catheter 600 by attachment assembly 631, which includes a collar component of metal or polymeric tubing having multiple slots around its circumference similar to slots 433 in the embodiment of FIG. 4. Attachment assembly 631 is pre-bonded onto inner tubular component 606, such that during shipment and storage the eyelet proximal ends 239 of stent bands 232

are held or "locked" in place between the collar component of attachment assembly 631 and outer tubular component 602, which is shown in FIG. 6 with a distal end positioned distal of the collar component and stent eyelets 239. In this manner, prosthetic tissue valve 221 is also maintained in a longitudinal position relative to delivery catheter 600 and shipping bladder 642. In addition, prosthetic tissue valve 221 is held in an expanded configuration within shipping bladder 642 and is not crimped or otherwise collapsed onto delivery catheter 600 during shipment, thereby preventing damage to or deformation of valve leaflets 224 that may occur during prolonged crimping. Shipping bladder 642 is a polymeric, fluid-tight vessel or sac-like container, which may or may not be distensible, with a neck portion 664 that is sealing attached around distal end 603 of outer tubular component 602 to contain storage solution 646 and prosthetic tissue valve 221 therein during shipment and storage. In order to prevent storage solution 646 from entering the guidewire lumen of delivery catheter 600, distal tip 612 is capped or otherwise sealed. In various other embodiments, shipping bladder 642 may be temporarily sealed around inner component 606 (not shown), distal tip 612 (not shown) and/or outer tubular component 602 using radial seals to prevent storage solution 646 from entering the lumens of delivery system 600. Shipping bladder 642 includes flushing ports 651, at least one of which is an inflow port 650 and at least one of which is an outflow port 652 that are weakened or thinned areas of shipping bladder 642. Shipping bladder 642 may be made of a suitable polymeric material, for *e.g.*, polyurethane, polypropylene, polyethylene terephthalate, or nylon.

[0038] When a clinician is ready to load prosthetic tissue valve 221 within delivery catheter 600 for delivery within the patient's vasculature, flushing ports 651 are punctured so that a rinsing solution may be introduced into shipping bladder 642 via inflow port(s) 650 to flush storage solution 646 out through outflow port(s) 652. As similarly described with reference to delivery catheter 100 in the embodiment of FIGS. 4 and 5, outer tubular component 602 is advanced distally relative to inner component 606 to thereby collapse prosthetic tissue valve 221 as the prosthetic valve is drawn within outer tubular component 602, wherein in the embodiment of FIG. 6, shipping bladder 642 surrounds and protects tissue valve 221 during the loading process. In another embodiment, a series of funnels may be used to help reduce the diameter of prosthetic tissue valve 221 to aid in retracting the prosthetic valve into delivery system 600. Shipping bladder 642 is then removed so that

delivery catheter 600 with prosthetic tissue valve 221 loaded in a delivery configuration therein is ready for introduction into the patient's vasculature for tracking to a treatment site. In another embodiment, prosthetic tissue valve 221 may be rinsed, shipping bladder 642 removed and then the prosthetic valve may be retracted into or otherwise covered by outer tubular component 602.

[0039] In accordance with another embodiment hereof, FIG. 7 depicts a side view of a prosthetic tissue valve delivery system 700 in partial section that is attached to an accordion-like or pleated shipping bladder 742 containing prosthetic tissue valve 721 pre-loaded thereon in a shipping/storage configuration. Prosthetic tissue valve delivery system 700 includes an elongate outer sheath 702 defining a sheath lumen 708 through which slidably extends a balloon catheter 770. Outer sheath 702 is of a similar construction as outer tubular component 102, which was previously described in detail above. Balloon catheter 770 includes a dilatation balloon 772 along a distal portion of balloon catheter 770 that is connected via an inflation lumen to a source of inflation fluid at a proximal end (not shown) of balloon catheter 770. Balloon catheter 770 is of an over-the-wire construction and as such has a full-length guidewire lumen that extends from the proximal end (not shown) to a distal tip 712 thereof. In another embodiment, balloon catheter 770 may be of a rapid exchange configuration. In various embodiments, balloon catheters manufactured and/or sold by Medtronic Inc. of Minneapolis, MN under the trademarks SPRINTER LEGEND, NC SPRINTER and RELIANT may be adapted for use in embodiments hereof without departing from the scope of the present invention.

[0040] Prosthetic tissue valve 721 includes stent-like frame 722 with valve leaflets 724 secured therein, which are of a similar construction as stent-like frame 222 and valve leaflets 224 described above in detail with reference to prosthetic tissue valve 221. However in the embodiment of FIGS. 7 and 8, stent-like frame 722 is balloon-expandable rather than self-expanding and as such may be constructed of, for *e.g.*, platinum-iridium, cobalt chromium alloys (MP35N), stainless steel, tantalum or other stent materials.

[0041] Accordion-like shipping bladder 742 is a polymeric, fluid-tight vessel or container having a plurality of circumferential fold-lines or creases 775 longitudinally spaced along a length thereof that form pleats or accordion-like folds 776 when shipping bladder 742 is longitudinally compressed, as shown in FIG. 8. Shipping bladder 742 may be made of a suitable polymeric material, for *e.g.*, polyurethane,

polypropylene, polyethylene terephthalate, or nylon. Shipping bladder 742 holds prosthetic tissue valve 721 in a storage solution 746 during shipment and storage and is fluid-tight, having a neck portion (not shown) that is sealed against outer sheath 702 by a sealing ring 774, which may be of silicone, polyurethane, or a medical grade rubber. In order to prevent storage solution 746 from entering balloon catheter 770, distal tip 712 is capped or otherwise sealed. An outer surface of stent-like frame 722 of prosthetic tissue valve 721 contacts an inner surface of shipping bladder 742 by which prosthetic tissue valve 721 is held in an expanded configuration over folded balloon 772 of balloon catheter 770 and otherwise prevented from longitudinal movement during shipment and storage. Shipping bladder 742 includes proximal flushing ports 750 and distal flushing port 752, wherein flushing ports 750, 752 include Luer fittings so that at least one port or ports may be connected to a source of rinsing solution and another port or ports may be connected/directed to a fluid waste receptacle. Flushing ports 750, 752 may be weakened or thinned areas of shipping bladder 742, which are punctured for use, or may be holes/apertures in shipping bladder 742 covered by removable caps, plugs or other covering (not shown).

[0042] When a clinician is ready to load prosthetic tissue valve 721 within delivery system 700 for delivery within the patient's vasculature, one or more flushing ports 750, 752 are uncapped or punctured so that a rinsing solution may be introduced into shipping bladder 742 to flush out storage solution 746. In an embodiment, an inlet flushing port may be connected to a source of sterile saline to properly rinse prosthetic tissue valve 721, wherein the storage solution is initially evacuated from shipping bladder 742 with the sterile saline "rinsing" solution subsequently introduced. In another embodiment, a large diameter syringe or a series of syringes filled with a volume of sterile saline sufficient to replace the volume of the storage solution within shipping bladder 742 may be used to effectively rinse the prosthetic tissue valve 721. Once prosthetic tissue valve 721 is sufficiently rinsed, a distal end 741 of shipping bladder 742 is pushed or slid proximally relative to delivery system 700 to longitudinally compress shipping bladder 742 and thereby form therein accordion-like folds 776 separated by reduced-diameter compression segments or rings 778. As the overall length of shipping bladder 742 is reduced during the compression process, distal tip 712 of balloon catheter 770 exits distal flushing port 752 and compression segments 778 function to collapse/crimp prosthetic tissue

valve 721 onto balloon 772 of balloon catheter 770, as shown in FIG. 8. Although compression segments 778 are shown to have a longitudinal length in the embodiment of FIG. 8, in other embodiments compression segments 778 may be merely the reduced-diameter "valley" between adjacent accordion-like folds 776. Sealing ring 774 and shipping bladder 742 are then removed and delivery system outer sheath 702 is positioned over prosthetic tissue valve 721, such that delivery system 700 with prosthetic tissue valve 721 loaded therein are in a delivery configuration ready for introduction into the patient's vasculature for tracking to a treatment site. In alternate methods of use, outer sheath 702 may be slid over collapsed tissue valve 721 or collapsed tissue valve 721 may be drawn within outer sheath 702 prior to removal of shipping bladder 742 and sealing ring 774.

[0043] In another embodiment, a balloon-expandable prosthetic tissue valve may be used with shipping bladder 642 of FIG. 6 by utilizing an external crimper such that shipping bladder 642 acts as a sterile barrier during the crimping process. Following rinsing and crimping of the prosthetic tissue valve, shipping bladder 642 is removed and the balloon-expandable prosthetic tissue valve may be loaded within the delivery system as previously discussed.

[0044] Similar to prosthetic tissue valve 221 described above, prosthetic tissue valve 721 may be percutaneously or otherwise delivered to replace an insufficient/incompetent aortic valve. However as prosthetic tissue valve 721 is balloon-expandable, once delivery system 700 is positioned as desired within the native aortic valve, outer sheath 702 is proximally retracted and dilatation balloon 772 is expanded to deploy prosthetic tissue valve 721 into apposition with the native aortic valve. Accordingly, in its fully deployed configuration, stent-like frame 722 of prosthetic tissue valve 721 radially displaces the native aortic valve leaflets to conform and seal to the aortic annulus, as would be understood by one of ordinary skill in the art of heart or venous valve replacement.

[0045] It would be understood by one of ordinary skill in the art of prosthetic valve design that known tissue valve prosthesis, such as those disclosed in U.S. Patent No. 6,425,916 to Garrison et al., U.S. Patent Appl. Pub. No. 2006/0178740 to Stacchino et al., U.S. Patent Appl. Pub. No. 2006/0259136 to Nguyen et al., U.S. Patent No. 7,338,520 to Bailey et al., and U.S. Patent No. 7,347,869 to Hojeibane et al., each of which is incorporated by reference herein in its entirety, may be adapted for use in self-expanding and balloon expandable embodiments hereof without

departing from the scope of the present invention. It will also be appreciated by one of ordinary skill in the art that the stent structures shown in the preceding embodiments are merely exemplary in nature and that either self-expanding or balloon-expandable stents of various forms may be adapted for use in accordance with the teaching hereof. Some examples of stent configurations that are suitable for use in embodiments hereof are shown in U.S. Patent No. 4,733,665 to Palmaz, U.S. Patent No. 4,800,882 to Gianturco, U.S. Patent No. 4,886,062 to Wiktor, U.S. Patent No. 5,133,732 to Wiktor, U.S. Patent No. 5,292,331 to Boneau, U.S. Patent No. 5,421,955 to Lau, U.S. Patent No. 5,776,161 to Globerman, U.S. Patent No. 5,935,162 to Dang, U.S. Patent No. 6,090,127 to Globerman, U.S. Patent No. 6,113,627 to Jang, U.S. Patent No. 6,663,661 to Boneau, and U.S. Patent No. 6,730,116 to Wolinsky *et al.*, each of which is incorporated by reference herein in its entirety.

[0046] Additionally it would be understood by one of ordinary skill in the art of medical device packaging that during shipment to the clinician, shipping container 340 and delivery catheter 100, as shown in FIGS. 1 and 3, and the delivery systems shown in FIGS. 6 and 7 would be enclosed within a suitable sterile protective packaging. In another embodiment, the protective packaging with the delivery systems therein may include insulation or be positioned within separate insulative packaging to prevent exposure of the prosthetic valve to extreme temperatures. In addition, temperature alert sensors may be incorporated into the protective packaging to ensure that a prosthetic valve damaged by exposure to extreme temperatures during shipment/storage is not used in an interventional procedure. In another embodiment, the protective packaging may include temperature sensors and/or thermal masses to protect the prosthetic valve by stabilizing its temperature when exposed during shipment/storage to extreme ambient temperatures.

[0047] While various embodiments according to the present invention have been described above, it should be understood that they have been presented by way of illustration and example only, and not limitation. It will be apparent to persons skilled in the relevant art that various changes in form and detail can be made therein without departing from the spirit and scope of the invention. Thus, the breadth and scope of the present invention should not be limited by any of the above-described exemplary embodiments, but should be defined only in accordance with the appended claims and their equivalents. It will also be understood that each feature

of each embodiment discussed herein, and of each reference cited herein, can be used in combination with the features of any other embodiment. All patents and publications discussed herein are incorporated by reference herein in their entirety.

CLAIMS

What is claimed is:

1. A packaging system for a medical device, the system comprising:

a delivery catheter;

a shipping container sealingly attached to the delivery catheter and filled with a storage solution, wherein a component of the delivery catheter extends within the shipping container; and

a prosthetic tissue valve in an expanded configuration disposed in the storage solution within the shipping container and positioned to surround the component of the delivery catheter that extends within the shipping container.

2. The packaging system of claim 1, further comprising:

an attachment assembly for releasably attaching the prosthetic tissue valve to the delivery catheter.

3. The packaging system of claim 2, wherein the delivery catheter further comprises:

an outer tubular component having a distal end to which the shipping container is sealing attached; and

an inner component slidably disposed within the outer tubular component, wherein the component of the delivery catheter that extends within the shipping container is the inner component and the prosthetic tissue valve is secured to the inner component by the attachment assembly.

4. The packaging system of claim 3, wherein upon removal of the storage solution from the shipping container relative longitudinal movement between the inner component and the outer tubular component collapses and loads the prosthetic tissue valve within the outer tubular component.

5. The packaging system of claim 4, wherein upon removal of the shipping container the delivery catheter with the prosthetic tissue valve loaded therein are ready for delivery to a treatment site within the vasculature.

6. The packaging system of claim 1, wherein the shipping container is a bladder of a polymeric material.

7. The packaging system of claim 1, wherein the shipping container includes an inflow port for introducing a rinsing solution into an interior of the shipping container and an outflow port for draining the storage and rinsing solutions from the shipping container.

8. The packaging system of claim 1, wherein an outer surface of the prosthetic tissue valve touches an inner surface of the shipping container to thereby maintain a longitudinal position of the prosthetic tissue valve relative to the delivery catheter.

9. The packaging system of claim 8, wherein the delivery catheter further comprises:

an outer sheath having a distal end to which the shipping container is sealing attached; and

a balloon catheter slidably disposed within the outer sheath and having a dilatation balloon disposed along a distal portion thereof, wherein the component of the delivery catheter that extends within the shipping container includes the dilatation balloon of the balloon catheter such that the prosthetic tissue valve is positioned around the dilatation balloon.

10. The packaging system of claim 9, wherein upon removal of the storage solution from the shipping container longitudinally compressing the shipping container collapses the prosthetic tissue valve onto the dilatation balloon.

11. The packaging system of claim 10, wherein the shipping container forms accordion-like folds when longitudinally compressed and compression rings between the folds contact and collapse the prosthetic tissue valve.

12. The packaging system of claim 9, wherein upon removal of the shipping container the outer sheath is slidable over the prosthetic tissue valve and balloon catheter for delivery to a treatment site within the vasculature.

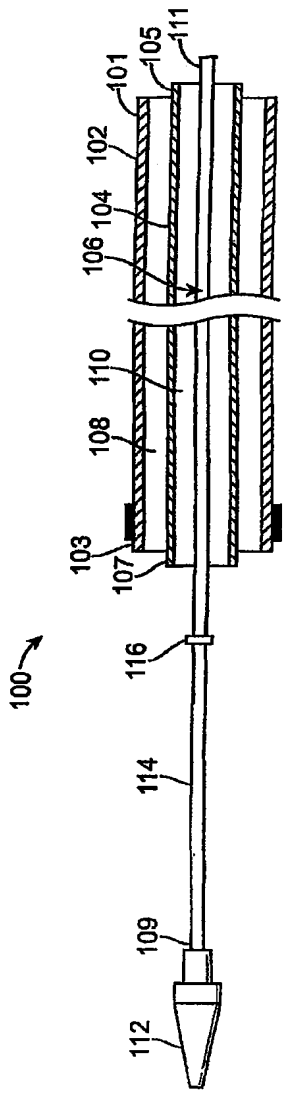
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FIG. 1

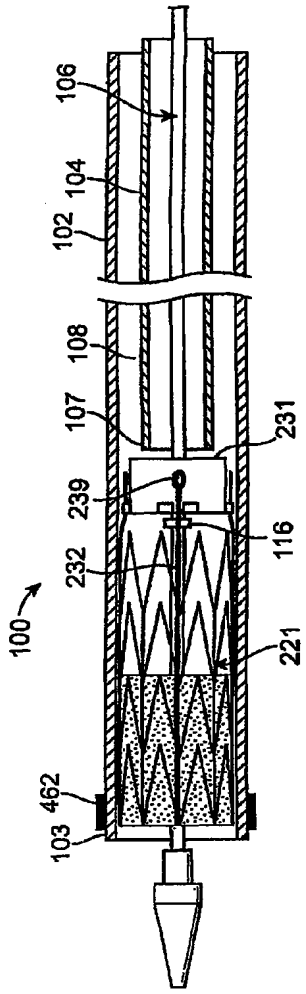
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FIG. 5

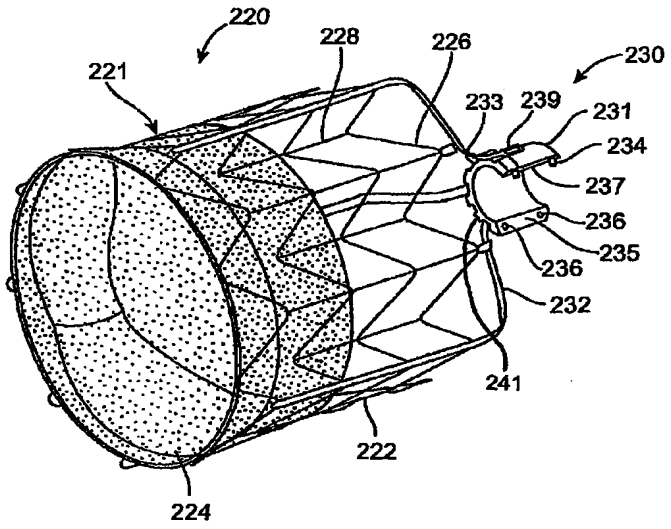
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FIG. 2

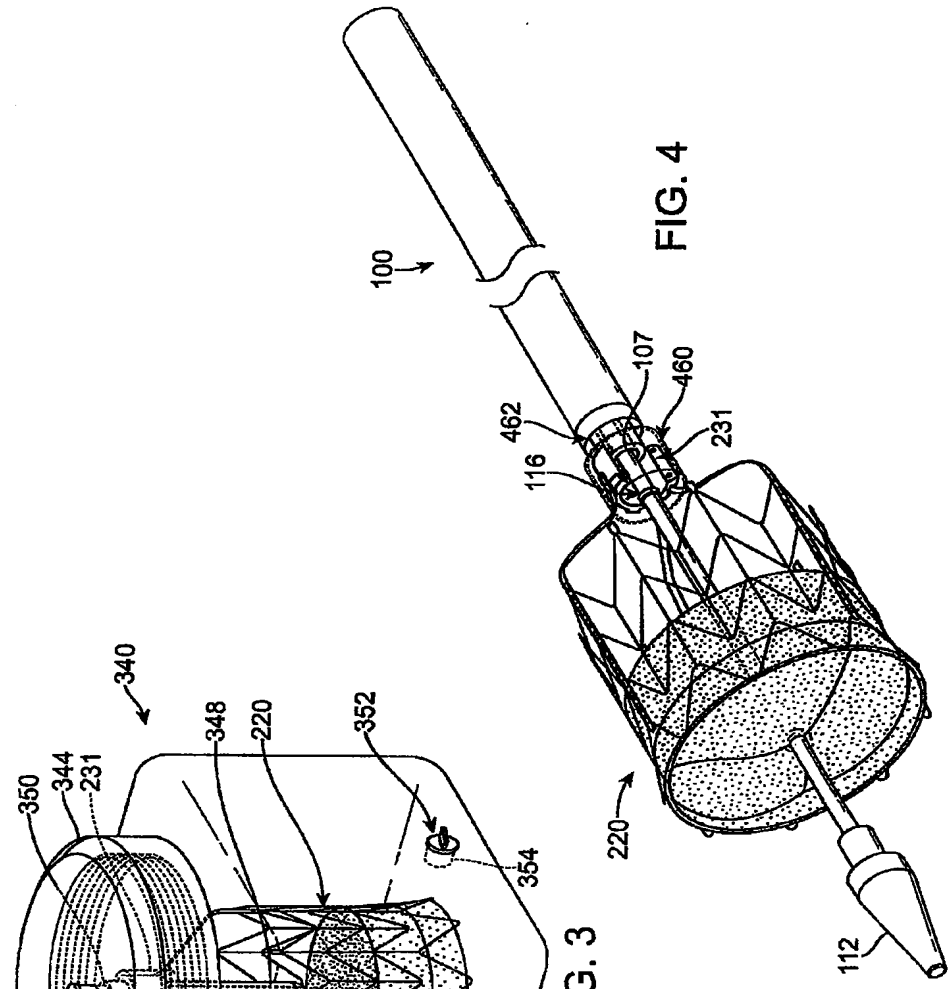
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FIG. 4

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FIG. 3

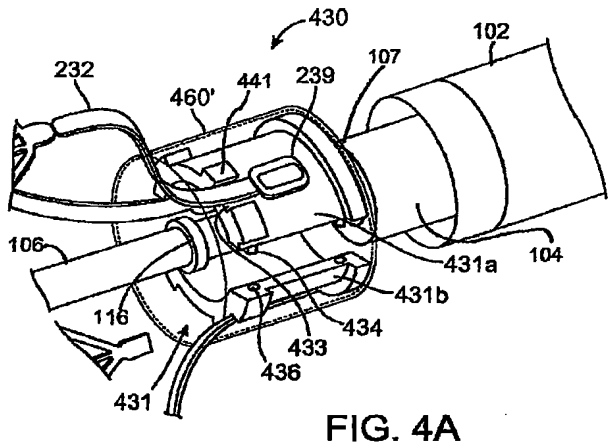
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FIG. 4A

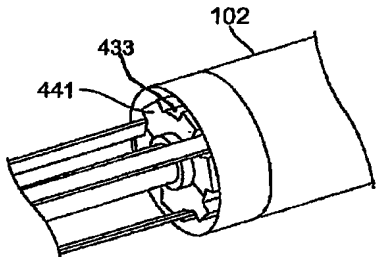
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FIG. 4B

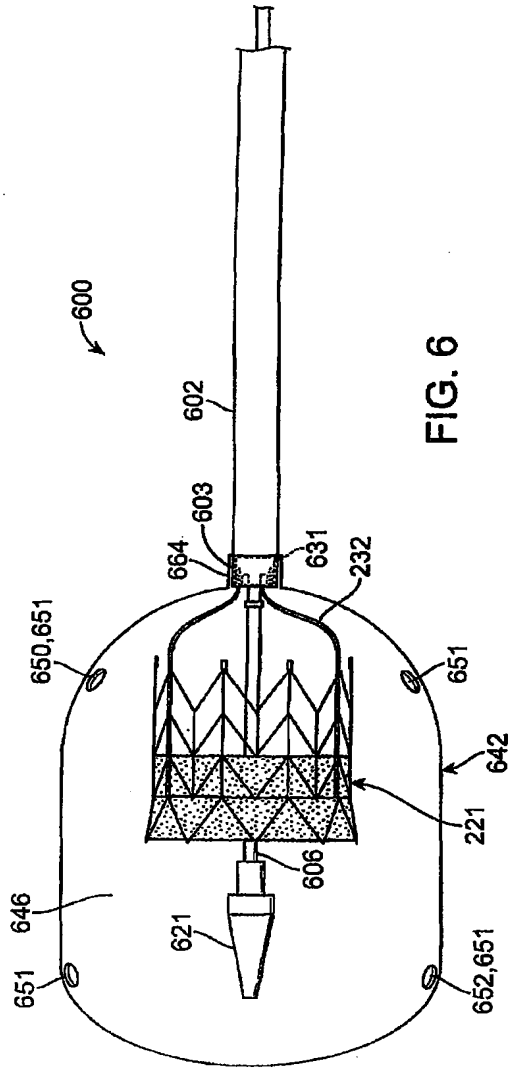
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FIG. 6

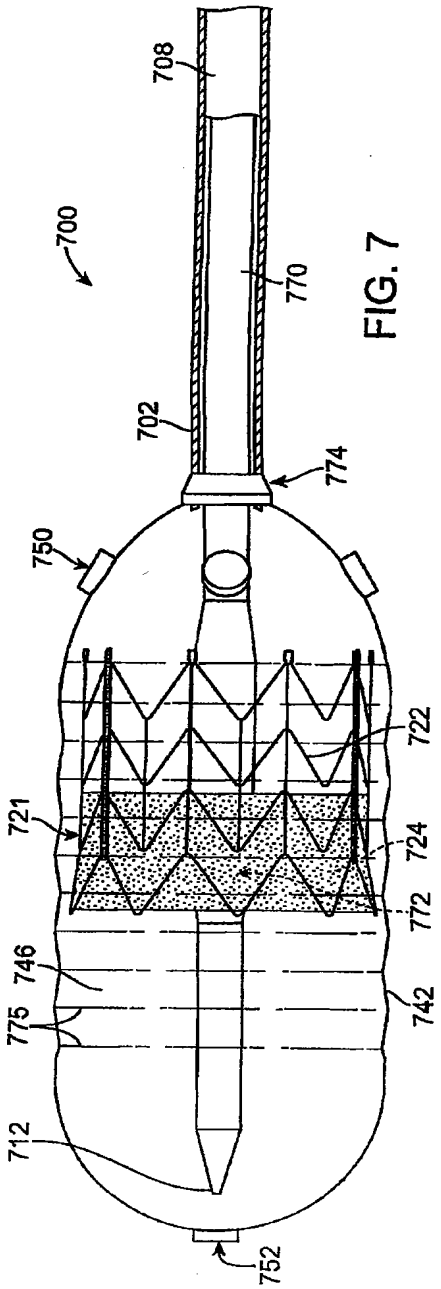
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FIG. 7

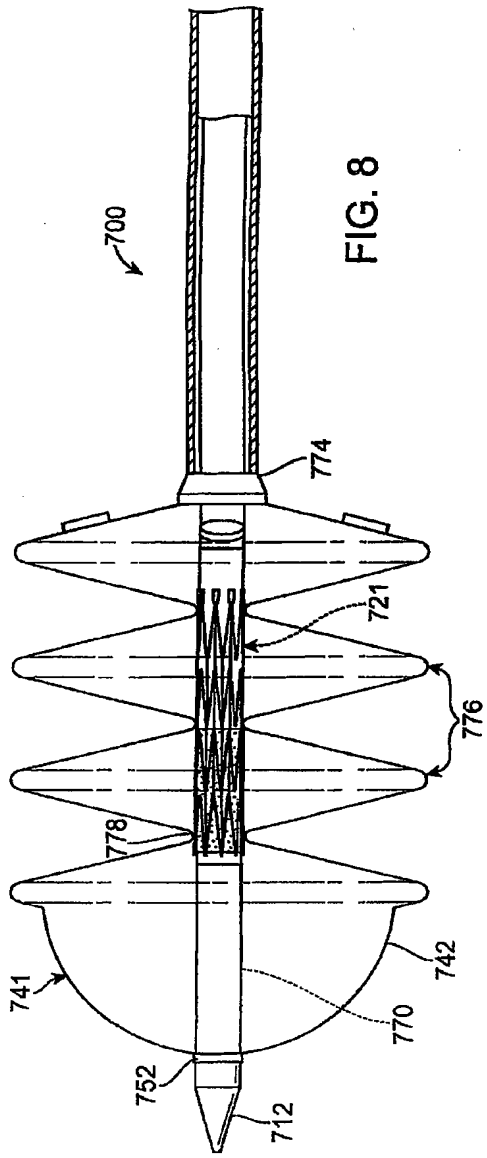
700
774
721
776
778
742
741
770
752
712

FIG. 8

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2010/026942

A. CLASSIFICATION OF SUBJECT MATTER
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According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
A61F

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2007/061008 A1 (SALAHIEH AMR [US] ET AL) 15 March 2007 (2007-03-15) paragraph [0044] - paragraph [0049]; figures	1,2,6-8
A	US 5 560 487 A (STARR STEPHEN [US]) 1 October 1996 (1996-10-01) column 2, line 50 - column 4, line 15; figures	1,2,8
A	WO 01/24730 A1 (EDWARDS LIFESCIENCES CORP [US]) 12 April 2001 (2001-04-12) abstract; figures	1,2,8

☐ Further documents are listed in the continuation of Box C.

☒ See patent family annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

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"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

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"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
19 May 2010	28/05/2010

Name and mailing address of the ISA/	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016	Neumann, Elisabeth

1

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INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/US2010/026942

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
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(54) **Title**: TISSUE FOR PROSTHETIC IMPLANTS AND GRAFTS, AND METHODS ASSOCIATED THEREWITH

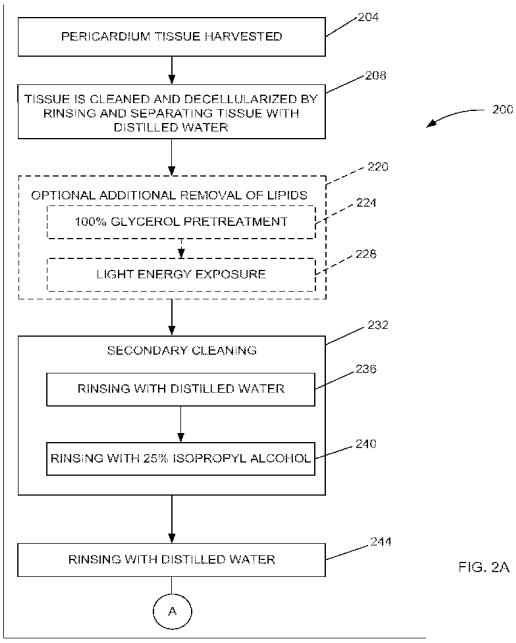

FIG. 2A

(57) **Abstract**: A prepared tissue for medical use with a patient is provided. Methods for preparing such tissue are also provided. Implantable tissue is provided by harvesting a tissue, such as but not limited to a pericardium tissue, and exposing the tissue to various cleaning, rinsing, treatment, separating, and fixation steps. The tissue of at least one embodiment is cleaned with distilled water, rinsed with isopropyl alcohol, and treated with a glutaraldehyde solution. The prepared tissue may be allowed to dry or partially hydrated prior to packaging and shipment. As such, the tissue can be implanted into the receiving patient in either a dry or wet state. The relatively thin yet strong tissue material is adapted for implanting within or grafting to human tissue. By way of example, the tissue may be used in a shunt, a valve, as graft material, as a patch, as a prosthetic tissue in a tendon and/or ligament, and a tissue product for wound management.

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TISSUE FOR PROSTHETIC IMPLANTS AND GRAFTS, AND METHODS ASSOCIATED THEREWITH

FIELD

The present invention relates to the field of tissue engineering, and more particularly, to tissue for prosthetic implants and grafts.

BACKGROUND

Preparing tissue for medical use to treat a patient is common. These tissues are typically used for implanting with or grafting to a human tissue. Prepared tissue is often used in shunts, tissue grafts and patches, as a prosthetic tissue in valves, tendon and/or ligament, and as tissue product for wound management. Many of these medical applications typically employ tissues obtained from mammalian animals and are thus termed xenografts. As with allografts (from human sources), xenograft tissue in the raw state contains immunologically "foreign" proteins and antigenic chemistry provocative of patient host immune responses that would cause destruction of implanted tissue as well as potentially harmful immune-mediated reactions. Thus, tissue for implantation in patients requires a number of preparatory chemical treatments to become biocompatible enough for implantation. For the preparation of xenograft tissue for structural applications, these treatments are typically directed to specific goals to isolate and preserve the structural proteins such as collagen: 1) remove cells within the tissue matrix, 2) remove unwanted chemical constituents, especially lipid components, and 3) chemically fix (i.e., cause thorough cross-linking of) structural proteins. Numerous manipulations of these and other steps in tissue processing have been employed with varying success in the art to achieve durable and biocompatible xenograft tissues for human implant. Nevertheless, conventional tissue materials are plagued by a variety of problems. For example, often in such applications, long-term function and survival of the tissue implants have been compromised by destructive inflammation, loss of structural integrity, and reactive calcification.

When using xenograft tissue membrane for use as formed sheet material, the tissue is usually cleaned and sterilized *ex vivo*, as outlined above. The preparation process itself can deteriorate the strength and biocompatibility characteristics of the tissue, or be the cause of latent host reactions that ultimately cause failure within the body. Often, the prepared tissue must maintain a certain thickness in order to have the desired strength traits. As such, the tissue material may be produced to be relatively thick, which may limit the manner of its application, and may also limit its biocompatibility.

Furthermore, in certain functional forms, such as for prosthetic heart valves, the prepared tissue must be stored in a liquid (usually a preservative) solution, otherwise the tissue will dry out and become brittle and prone to damage. Maintaining the tissue in a "wet" state adds mass and bulk to the tissue product since the moisture content of the tissue is higher and the volume

of the tissue is greater when hydrated. Because the tissue must be stored "wet," packaging must be robust to prevent leaks, the transportation environment must be carefully monitored and controlled, and once at the hospital or medical facility, significant efforts to rinse and prepare the tissue prior to use are needed.

By way of example and not limitation, when a surgeon is ready to use a bioprosthetic tissue heart valve, the valve and attached tissue must be rinsed, and in the case of transcatheter tissue heart valve devices, mounted onto a delivery system. In this example, if the tissue is associated with a percutaneously deliverable heart valve, the prosthetic heart valve is typically mounted to a balloon catheter in a catheterization lab. These steps extend procedure time, require manual manipulation of the tissue, and expose the tissue to harmful contaminants. Moreover, for the example of a percutaneously deliverable heart valve, human errors can be made in mounting and orienting catheters and sheaths.

Because the tissue has a relatively large profile, mass and volume, a surgeon's delivery options are often limited. For example, only patients having large enough vascular systems can use catheter-delivery procedures. Moreover, there is a need for tissue that can be used in a variety of medical indications unrelated to a percutaneously deliverable heart valves.

Accordingly, there is a need to address the shortcomings addressed above.

SUMMARY

It is to be understood that the present invention includes a variety of different versions or embodiments, and this Summary is not meant to be limiting or all-inclusive. This Summary provides some general descriptions of some of the embodiments, but may also include some more specific descriptions of other embodiments.

Embodiments of the one or more present inventions include methods of preparing or treating tissue for medical use, as well as the actual tissue itself. Accordingly, in at least one embodiment, implantable tissue is provided by first harvesting a tissue, and thereafter treating the tissue by: (a) cleaning and decellularizing the tissue by rinsing and separating the tissue with distilled water; (b) optionally treating the tissue to additionally remove lipids by a glycerol pretreatment and exposure to light energy; (c) a secondary cleaning that includes a distilled water rinse, and rinsing with isopropyl alcohol; (d) final rinsing with distilled water; (e) fixation treating for collagen cross-linking by at least one of (I) immersion in formalin, (II) immersion in glycerol, (III) immersion in glutaraldehyde, (IV) immersion in glutaraldehyde filtered to limit oligomeric content, or (V) any of I - IV above with addition to the fixative solution of free amino acids lysine and/or histidine; (f) post-fixation treating by distilled water rinsing then isopropyl alcohol; and (g) final rinsing in distilled water. In at least one embodiment, the implantable tissue is then allowed to dry and thereafter is associated with a package for

shipment. Alternatively, in at least one embodiment, the implantable tissue is then at least partially hydrated and associated with a package for shipment.

As noted above, one or more embodiments described herein are directed to one or more methods of preparing a section of tissue for medical use. By way of example and not limitation, the tissue may be used in a shunt, in a valve, as graft material, as a patch for repair of congenital heart defects, as a prosthetic tissue in tendon and/or ligament replacement, and a tissue product for wound management. Accordingly, a method of preparing a section of tissue for medical use is provided, the method comprising:

(a) cleaning and decellularizing the section of tissue by performing multiple rinses of the section of tissue with distilled water;

(b) rinsing the section of tissue with isopropyl alcohol for a first period of time of not less than about 7 days; and

(c) contacting the section of tissue with one of

(i) a formalin solution, or

(ii) a glutaraldehyde solution

for a second period of time of not less than about 6 days;

wherein step (b) occurs sometime after step (a), and wherein step (c) occurs sometime after step (b).

For the method directly above, in at least one embodiment, for step (c): if the formalin solution is used, then the formalin solution comprises a concentration of about 1-37.5% formalin, and more preferably, about 10% formalin; and if the glutaraldehyde solution is used, then the glutaraldehyde solution comprises a concentration of about 0.1-25% glutaraldehyde, and more preferably, about 0.25% glutaraldehyde.

In at least one embodiment, the method further comprises exposing the section of tissue to light energy for an exposure duration, the exposure duration extending until there is no further visible separation of lipid droplets from an exposed surface of the section of tissue. In at least one embodiment, the light energy is at least equivalent to exposing the section of tissue to a 25-100 watt light source, and more preferably, a 50 watt incandescent light source with a flat radiant face situated at a distance of about 10 centimeters from the exposed surface for about 15 minutes. In at least one embodiment, the method further comprises: (d) rinsing the section of tissue with distilled water and isopropyl alcohol for a post-fixation period of time of not less than about 7 days; wherein step (d) occurs after step (c). In at least one embodiment, the section of tissue comprises an ultimate tensile strength of greater than about 25 MegaPascals. In at least one embodiment, the section of tissue comprises a treated pericardium tissue.

In another embodiment, a method of preparing a tissue for medical use is provided, the method comprising: providing a section of tissue harvested from a mammalian organism; and causing osmotic shocking of the section of tissue by performing multiple rinses of the section of tissue with distilled water. In at least one embodiment, the method further comprises hydrating the section of tissue during a plurality of time intervals using distilled water. In at least one embodiment, the method further comprises not using saline for causing at least one of the osmotic shocking and the hydrating of the tissue. In at least one embodiment, the method further comprises pretreating the section of tissue with glycerol before contacting the section of tissue with one or more of isopropyl alcohol, glutaraldehyde and formalin. In at least one embodiment, the method further comprises contacting the section of tissue with a solution containing formalin after pretreating the section of tissue with glycerol. In at least one embodiment, the method further comprises contacting the section of tissue with a solution containing glutaraldehyde after pretreating the section of tissue with glycerol. In at least one embodiment, the method further comprises pretreating the section of tissue with isopropyl alcohol before contacting the section of tissue with either glutaraldehyde or formalin. In at least one embodiment, the method further comprises contacting the section of tissue with a solution containing formalin after pretreating the section of tissue with isopropyl alcohol. In at least one embodiment, the method further comprises contacting the section of tissue with a solution containing glutaraldehyde after pretreating the section of tissue with isopropyl alcohol. In at least one embodiment, the method further comprises exposing the section of tissue to light energy for a period of time, the period of time extending until there is no further visible separation of lipid droplets from an exposed surface of the section of tissue. In at least one embodiment, the light energy is at least equivalent to exposing the section of tissue to a 50 watt incandescent light source with a flat radiant face situated at a distance of about 10 centimeters from the exposed surface for about 15 minutes. In at least one embodiment, the section of tissue comprises a treated pericardium tissue.

Another embodiment of the one or more present inventions pertains to a method of preparing a section of tissue for medical use, comprising:

(a) contacting the section of tissue with distilled water;

(b) contacting the section of tissue with isopropyl alcohol for a pre-fixation period of time of not less than about 3 days; and

(c) contacting the section of tissue with one of

(i) a formalin solution, or

(ii) a glutaraldehyde solution

for a fixation period of time of not less than about 3 days; and

(d) contacting the section of tissue with isopropyl alcohol for a post-fixation period of time of not less than about 3 days;

wherein step (b) occurs sometime after step (a), wherein step (c) occurs sometime after step (b), and wherein step (d) occurs sometime after step (c).

In at least one embodiment, for step (c): if the formalin solution is used, then the formalin solution comprises a concentration of about 1 - 37.5% formalin; and if the glutaraldehyde solution is used, then the glutaraldehyde solution comprises a concentration of about 0.1 - 25% glutaraldehyde. In at least one embodiment, for step (c): if the formalin solution is used, then the formalin solution comprises a concentration of about 8-12% formalin; and if the glutaraldehyde solution is used, then the glutaraldehyde solution comprises a concentration of about 0.1 - 0.5% glutaraldehyde. In at least one embodiment, the section of tissue comprises a treated pericardium tissue.

As mentioned above, one or more embodiments are directed to a tissue for medical use. Accordingly, a prepared tissue for medical use is provided, comprising: a section of treated tissue harvested from a mammalian organism, the section of tissue including an ultimate tensile strength of greater than about 15 MegaPascals. In at least one embodiment, the section of treated tissue has a thickness of between about 50 to 500 micrometers. In at least one embodiment, the section of treated tissue comprises a water content of less than about 60% by weight of the section of tissue. In at least one embodiment, the section of treated tissue comprises a water content of less than about 50% by weight of the section of treated tissue. In at least one embodiment, the section of treated tissue comprises a water content of less than about 40% by weight of the section of treated tissue. In at least one embodiment, the section of treated tissue is attached to a frame *ex vivo* for at least one of: (a) surgical use; or (b) percutaneous implantation. In at least one embodiment, the section of treated tissue does not include a matrix that has been exposed to a polymer infiltrate. In at least one embodiment, the section of treated tissue is unbraided and uncompounded (as used herein, "unbraided an uncompounded" means the tissue comprises a single layer and is not overlapped or otherwise intertwined). In at least one embodiment, the section of treated tissue comprises an ultimate tensile strength of greater than about 25 MegaPascals. In at least one embodiment, the section of treated tissue has been exposed to isopropyl alcohol before contacting the section of tissue with either glutaraldehyde and formalin. In at least one embodiment, the section of treated tissue has been exposed to a solution containing formalin after pretreatment with isopropyl alcohol. In at least one embodiment, the section of treated tissue has been exposed to a solution containing glutaraldehyde after pretreatment with isopropyl alcohol. In at least one embodiment, the section of treated tissue comprises a pericardium tissue.

In at least one embodiment, a prepared tissue for medical use with a patient is provided, comprising: a section of tissue harvested from a mammalian organism, wherein the section of tissue is prepared *ex vivo* for future grafting or implantation in the patient, the section of tissue including a thickness of about 50 to 500 micrometers and an ultimate tensile strength of greater than about 25 MegaPascals. In at least one embodiment, the section of tissue is unbraided and uncompounded. In at least one embodiment, the section of tissue comprises a water content of less than about 40% by weight of the section of tissue. In at least one embodiment, the section of tissue is attached to a frame *ex vivo* for at least one of: (a) surgical use; or (b) percutaneous implantation in the patient. In at least one embodiment, the section of tissue does not include a matrix that has been exposed to a polymer infiltrate. In at least one embodiment, the section of tissue comprises a treated pericardium tissue.

One or more embodiments described herein are directed to one or more articles comprising a treated tissue. Accordingly, an article is provided, comprising: a section of tissue harvested from an organism, the section of tissue residing within packaging, wherein the section of tissue is adapted for at least one of implanting within or grafting to a human tissue, and wherein the section of tissue comprises a water content of less than about 40% by weight of the section of tissue.

As used herein, the term "dry" (or "substantially dry") when referring to the state of the tissue means a moisture content less than the water moisture content of the tissue when the tissue is allowed to fully rehydrate in the body of a patient. Typically, 70% by weight of the fully hydrated tissue membrane is water. Drying to a constitution of less than 40% by weight of water usefully alters the handling properties for purposes of folding, sewing or otherwise manipulating the tissue. As those skilled in the art will appreciate, the moisture content of the tissue may vary when dry. For example, the moisture content of the tissue when being folded and dry may be different than the moisture content of the tissue when dry and being shipped, for example, in a premounted state within a catheter delivery system.

With regard to delivery characteristics, another significant advantage of a prosthetic implant using a relatively thin tissue component described herein is that the prosthetic implant offers a relatively low packing volume as compared to commercially available prosthetic implants. In accordance with one or more embodiments, a dry tissue membrane has substantially less mass than a wet membrane. By way of example, a substantially dry pericardium tissue prepared by one or more of the present embodiments has approximately 30% of the mass of a wet pericardium tissue, and a marked reduction in profile and packing volume, thereby achieving a relatively low profile and making it suitable for implantation in greater number of patients.

Various components are referred to herein as "operably associated." As used herein, "operably associated" refers to components that are linked together in operable fashion, and encompasses embodiments in which components are linked directly, as well as embodiments in which additional components are placed between the two linked components.

As used herein, "at least one," "one or more," and "and/or" are open-ended expressions that are both conjunctive and disjunctive in operation. For example, each of the expressions "at least one of A, B and C," "at least one of A, B, or C," "one or more of A, B, and C," "one or more of A, B, or C" and "A, B, and/or C" means A alone, B alone, C alone, A and B together, A and C together, B and C together, or A, B and C together.

As used herein, "sometime" means at some indefinite or indeterminate point of time. So for example, as used herein, "sometime after" means following, whether immediately following or at some indefinite or indeterminate point of time following the prior act.

Various embodiments of the present inventions are set forth in the attached figures and in the Detailed Description as provided herein and as embodied by the claims. It should be understood, however, that this Summary does not contain all of the aspects and embodiments of the one or more present inventions, is not meant to be limiting or restrictive in any manner, and that the invention(s) as disclosed herein is/are understood by those of ordinary skill in the art to encompass obvious improvements and modifications thereto.

Additional advantages of the present invention will become readily apparent from the following discussion, particularly when taken together with the accompanying drawings.

BRIEF DESCRIPTION OF THE DRAWINGS

To further clarify the above and other advantages and features of the one or more present inventions, a more particular description of the one or more present inventions is rendered by reference to specific embodiments thereof which are illustrated in the appended drawings. It is appreciated that these drawings depict only typical embodiments of the one or more present inventions and are therefore not to be considered limiting of its scope. The one or more present inventions is described and explained with additional specificity and detail through the use of the accompanying drawings in which:

Fig. 1 is a generalized flow chart illustrating preparation of tissue for use in an implantable construct or for use as a graft material;

Figs. 2A-2B are flow charts illustrating elements of the tissue preparation;

Fig. 3 is a flow chart illustrating elements of the drying and sizing;

Fig. 4 is an elevation view of a piece of tissue; and

Fig. 5 is a graph that shows actual stress-strain test results for five tissue samples prepared in accordance with at least one embodiment.

The drawings are not necessarily to scale.

DETAILED DESCRIPTION

Embodiments of the one or more inventions described herein include tissue for prosthetic implants and/or methods relating to preparation of tissue for prosthetic implants. A prosthetic implant made at least partially from tissue in accordance with at least one embodiment described herein can be surgically implanted or otherwise grafted to a patient. One or more embodiments of the prosthetic implant described herein have application for at least aortic and pulmonary valves, as well as in forming prosthetic ligaments and tendons.

Referring now to Fig. 1, preparation of tissue for use in an implantable construct or as a graft is generally shown in method 100. Method 100 generally includes preparing the tissue at 200 and then, optionally, drying the tissue at 300 in preparation of manipulating the tissue for forming an implantable construct, such as a braided or folded structure. Further detail of the tissue preparation is provided below.

At least one or more embodiments described herein include a relatively thin tissue component. By way of example and not limitation, in at least one embodiment the tissue has a thickness of approximately 50 - 150 μm, and further possesses characteristics of pliability and resistance to calcification after implantation. The relatively thin nature of the tissue used in the implantable prosthetic implant assists with biocompatibility. In addition, the relatively thin tissue component thereby provides for a relatively low mass.

With reference now to Fig. 2A, the process associated with preparation of a biocompatible tissue consistent with the above-noted characteristics is described. In at least one embodiment, pericardium tissue, such as porcine or bovine pericardium tissue, is harvested at 204 and then processed to serve as biocompatible tissue. Accordingly, subsequent to the harvesting at 204, the pericardium tissue is cleaned and decellularized at 208. More particularly, in at least one embodiment the tissue is initially cleaned with distilled water using gentle rubbing and hydrodynamic pressure at 208 in order to remove adherent non-pericardial and non-collagenous tissue. In at least one embodiment, the hydrodynamic pressure at 208 is provided by spraying the tissue with a relatively weak stream of liquid to remove at least some of the non-collagenous material associated with the tissue. The rinsing at 208 is to achieve effective decellularization of the pericardium tissue through osmotic shock. Typically, the thickness of the tissue in the cleaned condition varies from about 50 to 500 micrometers, depending on the source of raw tissue. Cleaning preferably continues until there is no visible adherent non-pericardial or non-collagenous tissue.

With continued reference to Fig. 2A, after the tissue has been cleaned and decellularized at 208, the tissue then undergoes optional additional removal of lipids at 220 to further treat the

tissue for preventing immunologic response and calcification. More particularly, the tissue first optionally undergoes a 100% glycerol pretreatment at 224 while being positioned on a flat surface (e.g., an acrylic plate), after which the tissue becomes nearly transparent.

At 228, the tissue optionally undergoes a "thermophotonic" process. In at least one embodiment, the tissue is optionally exposed to light energy for additional removal of lipids and for initial cross-linking of the collagen. By way of example and not limitation, in at least one embodiment a 25-100 watt incandescent light source, and more preferably, a 50 watt incandescent light source with a flat radiant face is employed at a distance of about 10 centimeters from the tissue surface, typically requiring 15 minutes of exposure before further visible separation of lipid droplets from the tissue stops.

Still referring to Fig. 2A, the tissue is then cleaned again in secondary cleaning at 232. More particularly, at 236 the tissue is again rinsed with distilled water. Thereafter, at 240 the tissue is rinsed with 25% isopropyl alcohol for periods of several hours to several days and weeks, depending on the desired tissue properties of pliability and tensile strength. By way of example, tissue prepared by the methods described herein has been successfully prepared by rinsing with 25% isopropyl alcohol for a period of 7 days, and after the further treatment steps described herein, provided an ultimate tensile strength of greater than 25 MegaPascals. In at least one embodiment where isopropyl alcohol is described as a rinsing agent, ethanol may be used in its place as an alternative, although resulting tissue properties may vary. Referring back to Fig. 2A, after the tissue is rinsed with isopropyl alcohol at 240, the tissue is then rinsed with distilled water at 244 as a final cleaning step and for rehydration.

Referring now to Fig. 2B, following the rinse with distilled water at 244, treatment of the tissue continues. More particularly, fixation for collagen cross-linking at 248 is achieved by performing at least one of the following:

a. At 248a, immersion of the tissue in 1-37.5% formalin, ideally a buffered solution, for between about 3 days to 5 weeks, and more preferably, for between about 3 days to 4 weeks, and more preferably yet, for between about 3 weeks to 4 weeks, at a temperature of between about 4 to 37°C, and more preferably, 10% formalin for 6 days at 20°C; or

b. At 248b, immersion of the tissue in 100% glycerol for up to 6 weeks at between 4 to 37°C, and more preferably, immersion of the tissue in 100% glycerol for about 3 weeks at 20°C; or

c. At 248c, immersion of the tissue in 0.1 - 25% glutaraldehyde for between about 3 days to 5 weeks, and more preferably, for between about 3 days to 4 weeks, and more preferably yet, for between about 3 weeks to 4 weeks, at 0 to 37°C, and more preferably, immersion of the tissue in 0.25% glutaraldehyde for 7 days at 4°C; or

d. At 248d, immersion of the tissue in 0.1 - 25% glutaraldehyde (filtered to limit oligomeric content) for between about 3 days to 5 weeks, and more preferably, for between about 3 days to 4 weeks, and more preferably yet, for between about 3 weeks to 4 weeks, at 0 to 37°C, and more preferably, 0.25% glutaraldehyde for 7 days at 4°C; or

e. At 248e, immersion in the tissue in one of the above formalin, glutaraldehyde, or oligomeric filtered glutaraldehyde solutions together with added amino acids, lysine and/or histidine, wherein the concentration of the amino acids, L-lysine or histidine, used as an additive to the fixative is in the range of about 100 - 1000 milliMolar, with a preferred value of about 684 mM.

In addition to the foregoing, combinations of the processes listed above may be performed, including: step a followed by step b; step a followed by step c; and step a followed by step d.

As those skilled in the art will appreciate, heat-shrink testing may be conducted on tissue samples to correlate the effectiveness of protein cross-linking. Here, results of heat-shrink testing performed on one or more samples of tissue prepared in accordance with at least one embodiment using formalin showed that the tissue had a shrink temperature of 90°C. This compares favorably with samples prepared using glutaraldehyde, wherein the shrink temperature was 80°C. Accordingly, formalin is a suitable variant of fixation. It is noted that formalin was generally abandoned by the field, largely because of material properties that were unfavorable and because of inadequate or unstable protein cross-linking. Such problems have been overcome through the pretreatments described herein, allowing production of tissue with strength, pliability, and durability in a relatively thin membrane. When used in a prosthetic implant, such as a heart valve, the tissue characteristics imparted by the tissue preparation process facilitate formation of a construct having a relatively low-profile, which also thereby facilitates dry packaging of the prosthetic implant. The same advantages are also achieved using the pretreatments when using a glutaraldehyde process.

Referring still to Fig. 2B, after fixation for collagen cross-linking at 248, an alcohol post-fixation treatment at 252 is preferably performed by rinsing the tissue in distilled water at 256, and then at 260 rinsing the tissue in 25% isopropyl alcohol for between about 30 minutes to 14 days or more at between about 0 to 37°C, and more preferably, for at least about 7 days at 20°C. At 264, the tissue undergoes a rinsing with distilled water.

In accordance with at least one embodiment, treatment of the tissue, including from the time of harvest to the time of implantation or grafting, does not include contact and/or exposure to a polymer to infiltrate and/or encapsulate tissue fibers of the tissue.

Referring now to Fig. 3, the drying process at 300 is performed after the tissue preparation at 200. Thus, in accordance with at least one embodiment, the tissue is dried under a load. More particularly, for the tissue drying at 304, the tissue is placed minimally stretched flat (that is, stretched just enough to eliminate visible wrinkles and bubbles) on a flat surface (e.g., a polymer or acrylic sheet) at 308, and held fixed at its edges at 312. Optionally, the joined tissue and underlying sheet are then set in a slight curve. The tension maintains the substantially flat structure of the tissue as it dries, thereby mitigating or preventing excessive shrinkage, wrinkling, and/or curling at the edges, and also making the rate of drying more uniform across the surface of the tissue because of the surface tension between the plate and the tissue. Alternatively, the tissue is dried while compressed between acrylic plates. When drying the tissue, the temperature is held at between about 4 to 37°C, and more preferably, between about 20 to 37°C (i.e., approximately room temperature to normal human body temperature), and more preferably, at about 20°C. At 314, the drying process is performed in substantially dark conditions (i.e., substantially no visible light) for between about 6 hours to 5 days, and more preferably, for about 72 hours. By way of example, the tissue is dried in dark conditions at a temperature of about 20°C for between about 6 hours to 5 days, and more preferably, for about 72 hours. As those skilled in the art will appreciate, drying the tissue while the tissue is compressed between plates requires a longer period of time.

In at least one embodiment, after drying, the tissue lots are inspected at 316, such as by stereomicroscopy, to identify and discard those with defects or discontinuities of the fiber matrix. If desired, the preferential fiber direction for each piece may be identified to determine a particular orientation, for example, to determine the free edge of the pieces that will form valve leaflets for a heart valve. Depending upon the size (i.e., the area) of the tissue being prepared and the size of tissue needed for a given implant, the tissue may be trimmed or otherwise sized in optional sizing at 320, such as by cutting the tissue into an appropriately sized and shaped sheet for implant formation and/or manipulation. Preferably, cutting of the tissue membrane is oriented so that the resulting free edge is parallel to the preferential fiber direction of the tissue membrane. Optionally, the free edge may also be cut with a parabolic or other curved profile to compensate for any attachment angles in order to increase the total contact surface between the tissue membrane and any associated frame or other structure. This approach minimizes weaknesses in the operating margins of the tissue assembly and advantageously distributes the principal loading forces of the operating implant along the long axis of the collagen fibers. As a result, the tissue is resistant to surface fracture and fraying.

As shown in Fig. 3, optional sizing at 320 is performed after the drying at 304 and inspection at 316. A rectangular shaped piece of tissue 400 is shown in Fig. 4. The tissue 400

may be manipulated for use in a variety of prosthetic implants and grafts.

As mentioned above, tissue prepared by the methods described herein has been successfully prepared by rinsing with 25% isopropyl alcohol for a period of 7 days, and after the further treatment steps described herein, provided an ultimate tensile strength of greater than 25 MegaPascals. Here, the combination of tissue pliability and tensile strength is sought for purposes of producing a material having property characteristics suitable for being physically manipulated to form prosthetic implants, such as a tissue leaflet assembly for a heart valve or a ligament, while providing a tissue material that will operate properly once implanted. These techniques are intended to conserve and preserve collagen fibers, minimize damage to the tissue and improve tissue characteristics. The preparation and fixation techniques produce tissue membrane material that may be rendered and used at lesser thicknesses than typically rendered in the prior art. Thinner membranes are more pliable, but with conventional tissue preparation techniques the tensile strength of the tissue is sacrificed. Advantageously, the preparation techniques described herein have produced membranes that have as much as three times the tensile strength of a commercial product of the prior art. This achieved strength is thus desirable for providing a tissue assembly having a low profile with appropriate durability, even in a substantially dry state. More particularly, the tissue possesses a relatively high tensile strength. By way of example and not limitation, testing has shown that embodiments of tissue prepared as described herein provide a tissue having a tensile strength of approximately three times the tensile strength of current pericardial valve tissue, such as on the order of approximately 25 MegaPascals, thereby providing about 2,000 times the physiologic load strength for valve tissue. Moreover, testing of an embodiment of an implantable prosthetic heart valve made with tissue prepared as described herein and under a static load of greater than approximately 250 mmHg showed less than approximately 14% leakage, wherein such results are generally considered superior to surgical tissue valve prostheses.

With reference to Fig. 5, stress-strain curve results for five different tissue samples prepared in accordance with an embodiment are shown. For the testing results shown, the yield stress or ultimate tensile strength was obtained by attaching strips of tissue fixed at the ends in a linear force tester and increasing the length by 0.3 mm/sec while recording resultant force (tension) until the material ruptured or separated entirely; these measurements were then used to calculate the stress-strain curves depicted in Fig. 5. As illustrated in the graph, the yield stress or ultimate tensile strength of the various tissue samples varied from about 30 to about 50 MegaPascals. More particularly, for each curve shown in Fig. 5, the testing procedures were the same. That is, each of the curves shown pertain to separate pieces of tissue that were subjected to the same test. The results show a minimum ultimate tensile strength of 30 MegaPascals, with

a range up to 50 MegaPascals. Accordingly, the illustrated test results demonstrate consistency of the ultimate tensile strength results for the tissue treatment process.

It is to be understood that the tissue generated from one or more of the tissue preparation procedures described herein may be used for a variety of devices or uses, and that use in a prosthetic heart valve is but one possible application for utilizing the tissue. For example, the tissue may be used in a shunt, or as graft material for repair or modification of one or more human organs, including the heart and its blood vessels. By way of further example, the tissue may be used as a pericardial membrane patch for repair of congenital heart defects. The tissue also has application as a prosthetic tissue in tendon and ligament replacement, and as a tissue product for wound management. Moreover, for use in a prosthetic heart valve, the tissue may be configured in a variety of ways and attached to a frame in a variety of ways. In addition, a plurality of separate tissue pieces may each be connected together, such as by suturing, to form a larger composite of treated tissue material. Thereafter, whether the prosthetic implant or graft is made of a folded tissue assembly or a plurality of separate tissue pieces, the resulting prosthetic implant or graft may then be further manipulated for treatment of a patient.

In at least one embodiment, tissue generated from one or more of the tissue preparation procedures described herein may be used to form a prosthetic implant that includes a stent, frame, bone screw or other fastening or anchoring mechanism. In yet other embodiments, tissue generated from one or more of the tissue preparation procedures described herein may be used to form a prosthetic implant or graph that does not include a stent, frame, bone screw or other fastening or anchoring mechanism. Tissue generated from one or more of the tissue preparation procedures described herein may be may be packaged for delivery in a substantially dry, partially hydrated or hydrated ("wet") state. For example, a prosthetic implant utilizing a prepared tissue described herein may be packaged for delivery as a hydrated prosthetic implant. Accordingly, while a portion of the tissue preparation process may include drying the tissue so that it may be manipulated more easily, the tissue may then be hydrated at a later point in time prior to implantation, and it may be maintained in a hydrated condition up to and including packaging, delivery and implantation into a patient. Hydration of the tissue membrane portion occurs rapidly and begins with simple preparatory flushing of the tissue. Those skilled in the art will appreciate that one or more embodiments described herein provide a tissue 400 suitable for implanting in a human, wherein the implantable tissue may be allowed to dry prior to implanting and effectively rehydrated at the time of implanting, such as by flushing of the tissue at the time of implanting using saline or water.

All embodiments described herein are described for use in human patients. However, all embodiments described herein have application for use in veterinary medicine, such as equine

medicine.

The present invention may be embodied in other specific forms without departing from its spirit or essential characteristics. The described embodiments are to be considered in all respects only as illustrative and not restrictive. The scope of the invention is, therefore, indicated by the appended claims rather than by the foregoing description. All changes which come within the meaning and range of equivalency of the claims are to be embraced within their scope.

The one or more present inventions, in various embodiments, include components, methods, processes, systems and/or apparatuses substantially as depicted and described herein, including various embodiments, subcombinations, and subsets thereof. Those of skill in the art will understand how to make and use the present invention after understanding the present disclosure.

The present invention, in various embodiments, includes providing devices and processes in the absence of items not depicted and/or described herein or in various embodiments hereof, including in the absence of such items as may have been used in previous devices or processes (e.g., for improving performance, achieving ease and/or reducing cost of implementation).

The foregoing discussion of the invention has been presented for purposes of illustration and description. The foregoing is not intended to limit the invention to the form or forms disclosed herein. In the foregoing Detailed Description for example, various features of the invention are grouped together in one or more embodiments for the purpose of streamlining the disclosure. This method of disclosure is not to be interpreted as reflecting an intention that the claimed invention requires more features than are expressly recited in each claim. Rather, as the following claims reflect, inventive aspects lie in less than all features of a single foregoing disclosed embodiment. Thus, the following claims are hereby incorporated into this Detailed Description, with each claim standing on its own as a separate preferred embodiment of the invention.

Moreover, though the description of the invention has included descriptions of one or more embodiments and certain variations and modifications, other variations and modifications are within the scope of the invention (e.g., as may be within the skill and knowledge of those in the art, after understanding the present disclosure). It is intended to obtain rights which include alternative embodiments to the extent permitted, including alternate, interchangeable and/or equivalent structures, functions, ranges or acts to those claimed, whether or not such alternate, interchangeable and/or equivalent structures, functions, ranges or acts are disclosed herein, and without intending to publicly dedicate any patentable subject matter.

CLAIMS

What is claimed is:

1. A prepared tissue for medical use, comprising:

a section of treated tissue harvested from a mammalian organism, the section of treated tissue including an ultimate tensile strength of greater than about 15 MegaPascals.

2. The prepared tissue of Claim 1, wherein the section of treated tissue has a thickness of between about 50 to 500 micrometers.

3. The prepared tissue of Claim 1, wherein the section of treated tissue comprises a water content of less than about 60% by weight of the section of treated tissue.

4. The prepared tissue of Claim 1, wherein the section of treated tissue comprises a water content of less than about 50% by weight of the section of treated tissue.

5. The prepared tissue of Claim 1, wherein the section of treated tissue comprises a water content of less than about 40% by weight of the section of treated tissue.

6. The prepared tissue of Claim 1, wherein the section of treated tissue is attached to a frame ex vivo for at least one of: (a) surgical use; or (b) percutaneous implantation.

7. The prepared tissue of Claim 1, wherein the section of treated tissue does not include a matrix that has been exposed to a polymer infiltrate.

8. The prepared tissue of Claim 1, wherein the section of treated tissue is unbraided and uncompounded.

9. The prepared tissue of Claim 1, wherein the section of treated tissue comprises an ultimate tensile strength of greater than about 25 MegaPascals.

10. The prepared tissue of Claim 9, wherein the section of treated tissue is unbraided and uncompounded.

11. The prepared tissue of Claim 1, wherein the section of treated tissue has been exposed to isopropyl alcohol before contacting the section of treated tissue with either glutaraldehyde or formalin.

12. The prepared tissue of Claim 1, wherein the section of treated tissue has been exposed to a solution containing formalin after pretreatment with isopropyl alcohol.

13. The prepared tissue of Claim 1, wherein the section of treated tissue has been exposed to a solution containing glutaraldehyde after pretreatment with isopropyl alcohol.

14. The prepared tissue of Claim 1, wherein the section of treated tissue comprises a pericardium tissue.

15. A prepared tissue for medical use with a patient, comprising:

a section of tissue harvested from a mammalian organism, wherein the section of tissue is prepared ex vivo for future grafting or implantation in the patient, the section of tissue

including a thickness of about 50 to 500 micrometers and an ultimate tensile strength of greater than about 25 MegaPascals.

16. The prepared tissue of Claim 15, wherein the section of tissue is unbraided and uncompounded.

17. The prepared tissue of Claim 15, wherein the section of tissue comprises a water content of less than about 40% by weight of the section of tissue.

18. The prepared tissue of Claim 15, wherein the section of tissue is attached to a frame ex vivo for at least one of: (a) surgical use; or (b) percutaneous implantation in the patient.

19. The prepared tissue of Claim 15, wherein the section of tissue does not include a matrix that has been exposed to a polymer infiltrate.

20. The prepared tissue of Claim 15, wherein the section of tissue comprises a treated pericardium tissue.

21. A method of preparing a tissue for medical use, comprising:

providing a section of tissue harvested from a mammalian organism; and

causing osmotic shocking of the section of tissue by performing multiple rinses of the section of tissue with distilled water.

22. The method of Claim 21, further comprising hydrating the section of tissue during a plurality of time intervals using distilled water.

23. The method of Claim 22, further comprising not using saline for causing at least one of the osmotic shocking and the hydrating of the section of tissue.

24. The method of Claim 21, further comprising pretreating the section of tissue with glycerol before contacting the section of tissue with one or more of isopropyl alcohol, glutaraldehyde and formalin.

25. The method of Claim 24, further comprising contacting the section of tissue with a solution containing formalin after pretreating the section of tissue with glycerol.

26. The method of Claim 24, further comprising contacting the section of tissue with a solution containing glutaraldehyde after pretreating the section of tissue with glycerol.

27. The method of Claim 21, further comprising pretreating the section of tissue with isopropyl alcohol before contacting the section of tissue with either glutaraldehyde or formalin.

28. The method of Claim 27, further comprising contacting the section of tissue with a solution containing formalin after pretreating the section of tissue with isopropyl alcohol.

29. The method of Claim 27, further comprising contacting the section of tissue with a solution containing glutaraldehyde after pretreating the section of tissue with isopropyl alcohol.

30. The method of Claim 21, further comprising exposing the section of tissue to light energy for a period of time, the period of time extending until there is no further visible separation of lipid droplets from an exposed surface of the section of tissue.

31. The method of Claim 30, wherein the light energy is at least equivalent to exposing the section of tissue to a 50 watt incandescent light source with a flat radiant face situated at a distance of about 10 centimeters from the exposed surface for about 15 minutes.

32. The method of Claim 21, wherein the section of tissue comprises a treated pericardium tissue.

33. A method of preparing a section of tissue for medical use, comprising:

(a) cleaning and decellularizing the section of tissue by performing multiple rinses of the section of tissue with distilled water;

(b) rinsing the section of tissue with isopropyl alcohol for a first period of time of not less than about 7 days; and

(c) contacting the section of tissue with one of

(i) a formalin solution, or

(ii) a glutaraldehyde solution

for a second period of time of not less than about 6 days;

wherein step (b) occurs sometime after step (a), and wherein step (c) occurs sometime after step (b).

34. The method of Claim 33, wherein for step (c):

if the formalin solution is used, then the formalin solution comprises a concentration of about 1 - 37.5% formalin; and

if the glutaraldehyde solution is used, then the glutaraldehyde solution comprises a concentration of about 0.1 - 25% glutaraldehyde.

35. The method of Claim 33, further comprising exposing the section of tissue to light energy for an exposure duration, the exposure duration extending until there is no further visible separation of lipid droplets from an exposed surface of the section of tissue.

36. The method of Claim 35, wherein the light energy is at least equivalent to exposing the section of tissue to a 50 watt incandescent light source with a flat radiant face situated at a distance of about 10 centimeters from the exposed surface for about 15 minutes.

37. The method of Claim 33, further comprising:

(d) rinsing the section of tissue with distilled water and isopropyl alcohol for a post-fixation period of time of not less than about 7 days;

wherein step (d) occurs sometime after step (c).

38. The method of Claim 33, wherein the section of tissue comprises an ultimate tensile strength of greater than about 25 MegaPascals.

39. The method of Claim 33, wherein the section of tissue comprises a treated pericardium tissue.

40. A method of preparing a section of tissue for medical use, comprising:

(a) contacting the section of tissue with distilled water;

(b) contacting the section of tissue with isopropyl alcohol for a pre-fixation period of time of not less than about 3 days; and

(c) contacting the section of tissue with one of

(i) a formalin solution, or

(ii) a glutaraldehyde solution

for a fixation period of time of not less than about 3 days; and

(d) contacting the section of tissue with isopropyl alcohol for a post-fixation period of time of not less than about 3 days;

wherein step (b) occurs sometime after step (a), wherein step (c) occurs sometime after step (b), and wherein step (d) occurs sometime after step (c).

41. The method of Claim 40, wherein for step (c):

if the formalin solution is used, then the formalin solution comprises a concentration of about 1 - 37.5% formalin; and

if the glutaraldehyde solution is used, then the glutaraldehyde solution comprises a concentration of about 0.1 - 25% glutaraldehyde.

42. The method of Claim 40, wherein for step (c):

if the formalin solution is used, then the formalin solution comprises a concentration of about 8-12% formalin; and

if the glutaraldehyde solution is used, then the glutaraldehyde solution comprises a concentration of about 0.1-0.5% glutaraldehyde.

43. The method of Claim 40, wherein the section of tissue comprises a treated pericardium tissue.

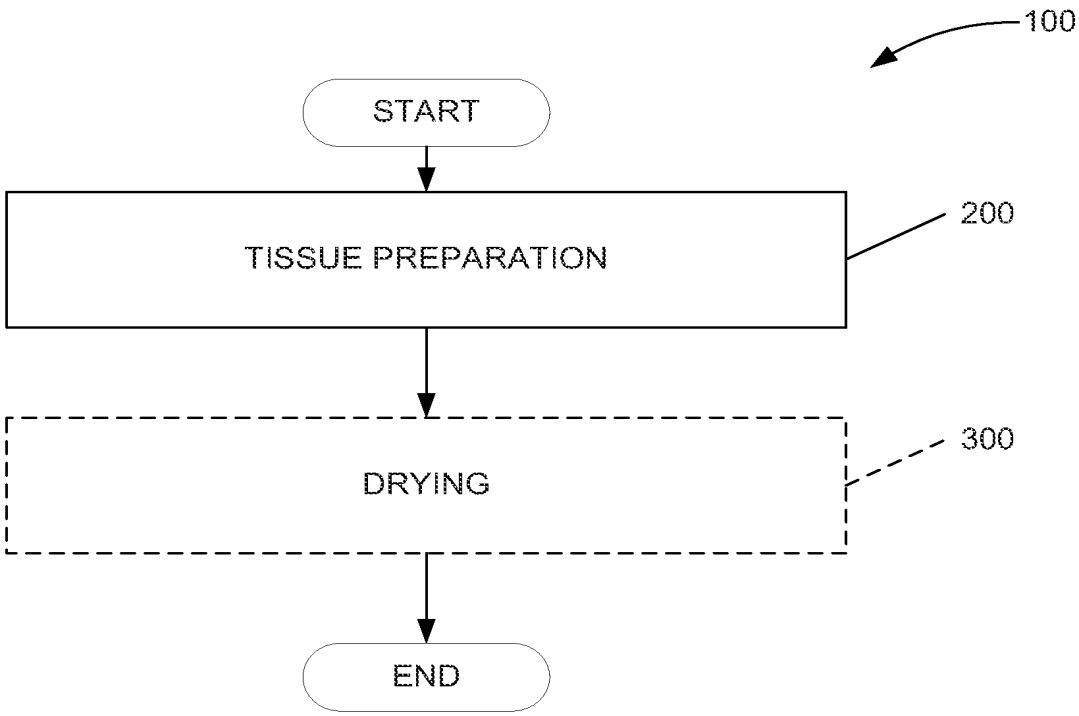


FIG. 1

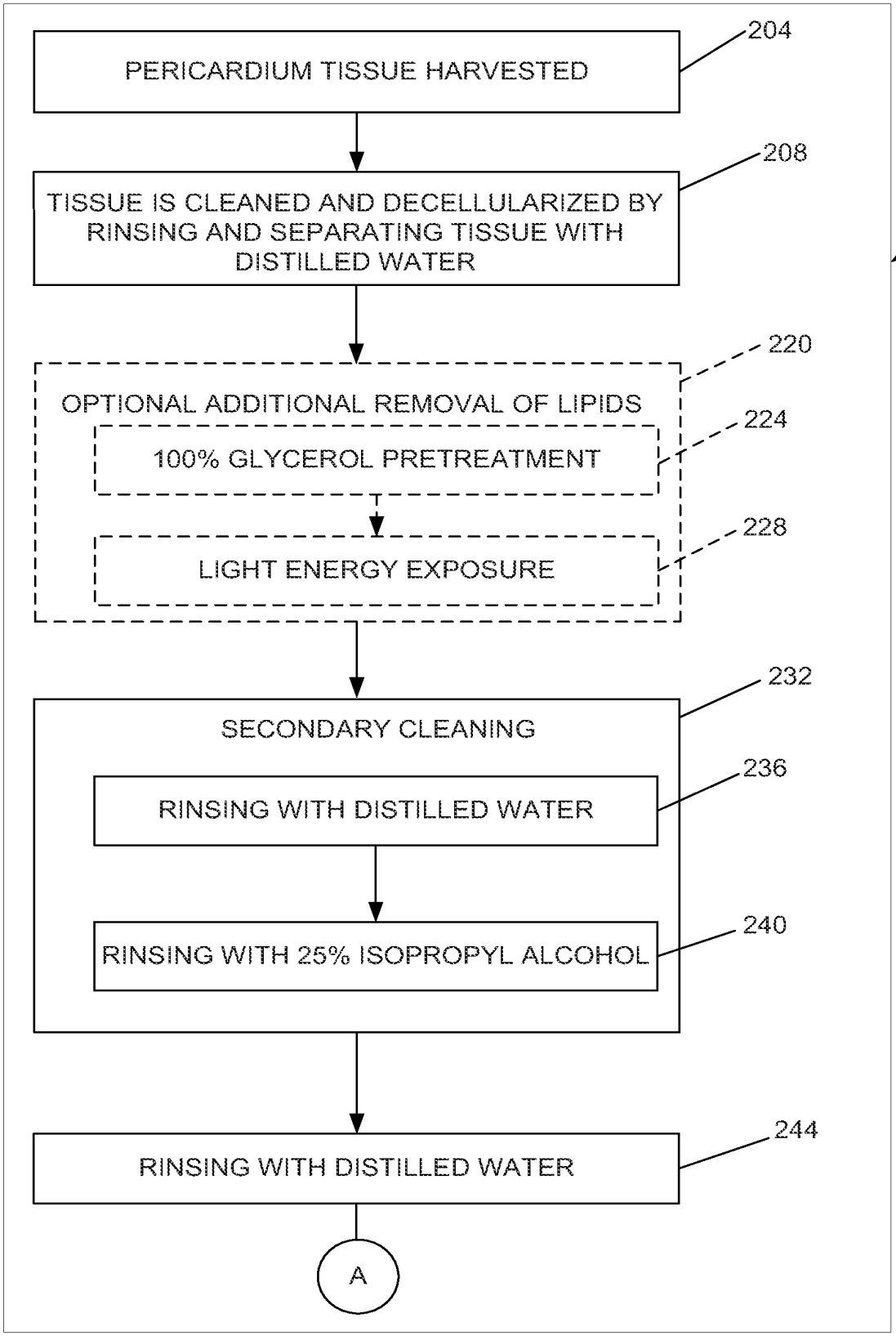

PERICARDIUM TISSUE HARVESTED
204
TISSUE IS CLEANED AND DECELLULARIZED BY RINSING AND SEPARATING TISSUE WITH DISTILLED WATER
208
200
OPTIONAL ADDITIONAL REMOVAL OF LIPIDS
220
100% GLYCEROL PRETREATMENT
224
LIGHT ENERGY EXPOSURE
228
SECONDARY CLEANING
232
RINSING WITH DISTILLED WATER
236
RINSING WITH 25% ISOPROPYL ALCOHOL
240
RINSING WITH DISTILLED WATER
244
A

FIG. 2A

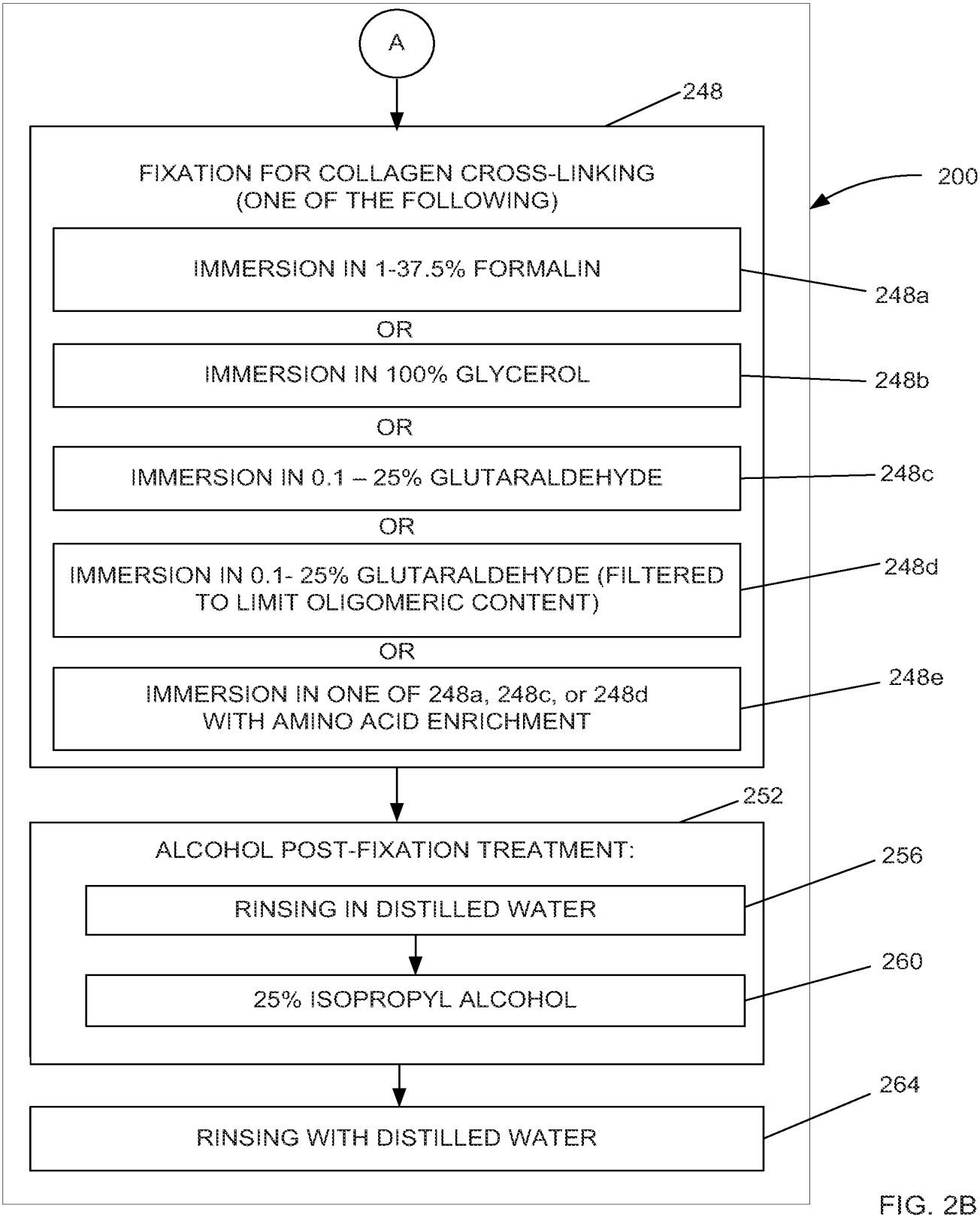

A
248
FIXATION FOR COLLAGEN CROSS-LINKING
(ONE OF THE FOLLOWING)
200
IMMERSION IN 1-37.5% FORMALIN
248a
OR
IMMERSION IN 100% GLYCEROL
248b
OR
IMMERSION IN 0.1 – 25% GLUTARALDEHYDE
248c
OR
IMMERSION IN 0.1- 25% GLUTARALDEHYDE (FILTERED TO LIMIT OLIGOMERIC CONTENT)
248d
OR
IMMERSION IN ONE OF 248a, 248c, or 248d WITH AMINO ACID ENRICHMENT
248e
252
ALCOHOL POST-FIXATION TREATMENT:
256
RINSING IN DISTILLED WATER
260
25% ISOPROPYL ALCOHOL
264
RINSING WITH DISTILLED WATER

FIG. 2B

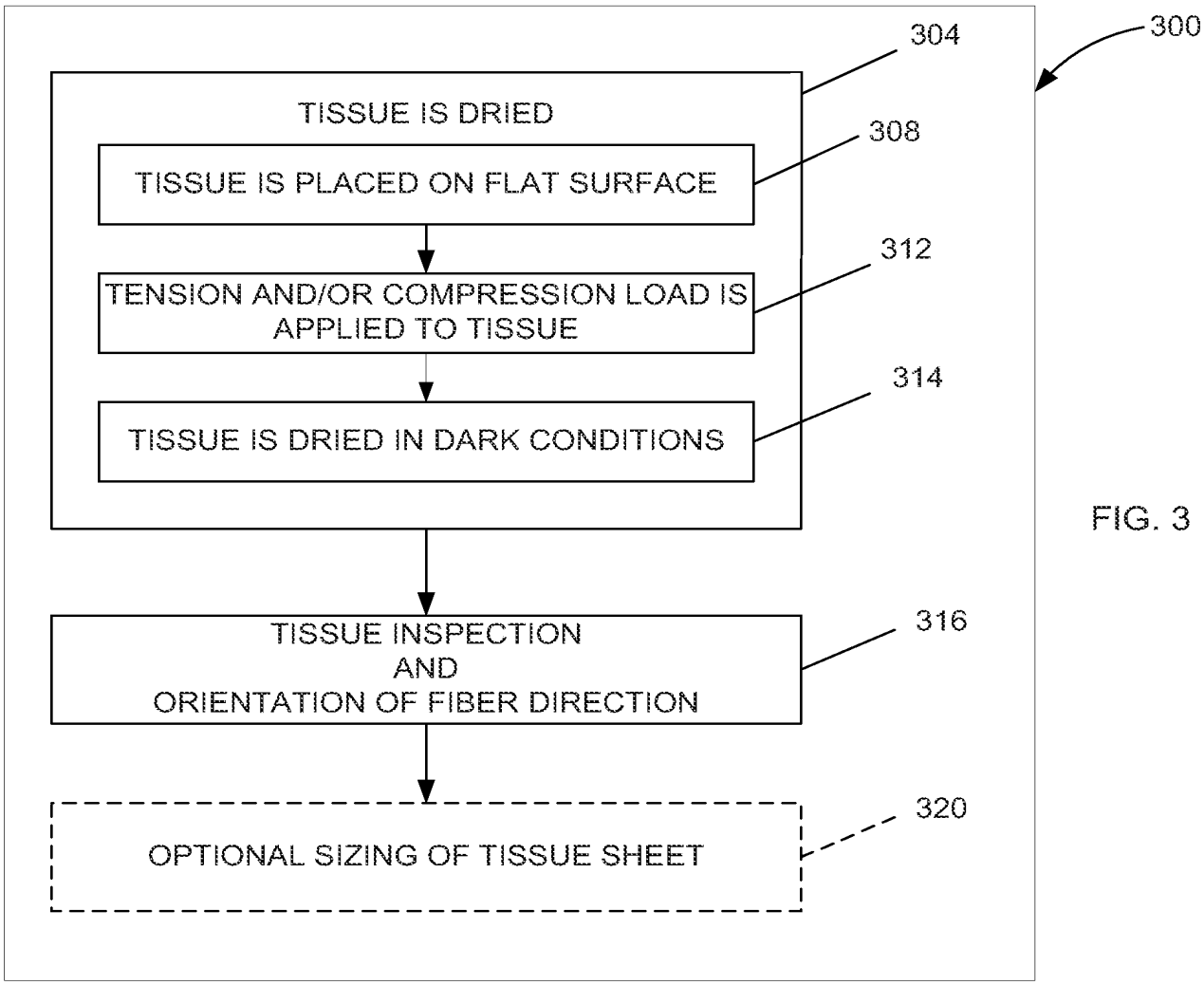

300
304
TISSUE IS DRIED
308
TISSUE IS PLACED ON FLAT SURFACE
312
TENSION AND/OR COMPRESSION LOAD IS APPLIED TO TISSUE
314
TISSUE IS DRIED IN DARK CONDITIONS
316
TISSUE INSPECTION AND ORIENTATION OF FIBER DIRECTION
320
OPTIONAL SIZING OF TISSUE SHEET

FIG. 3

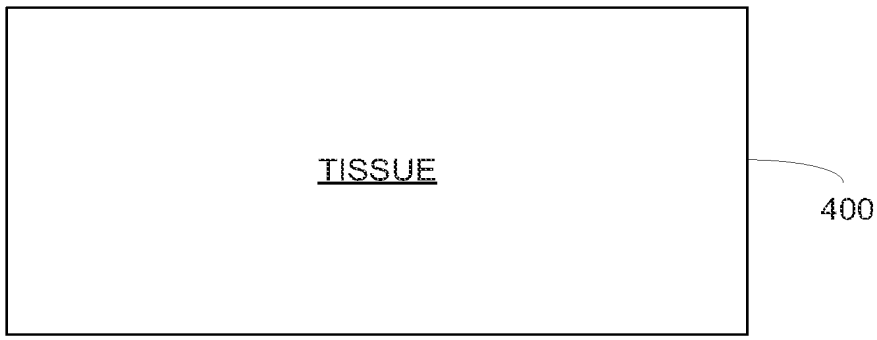
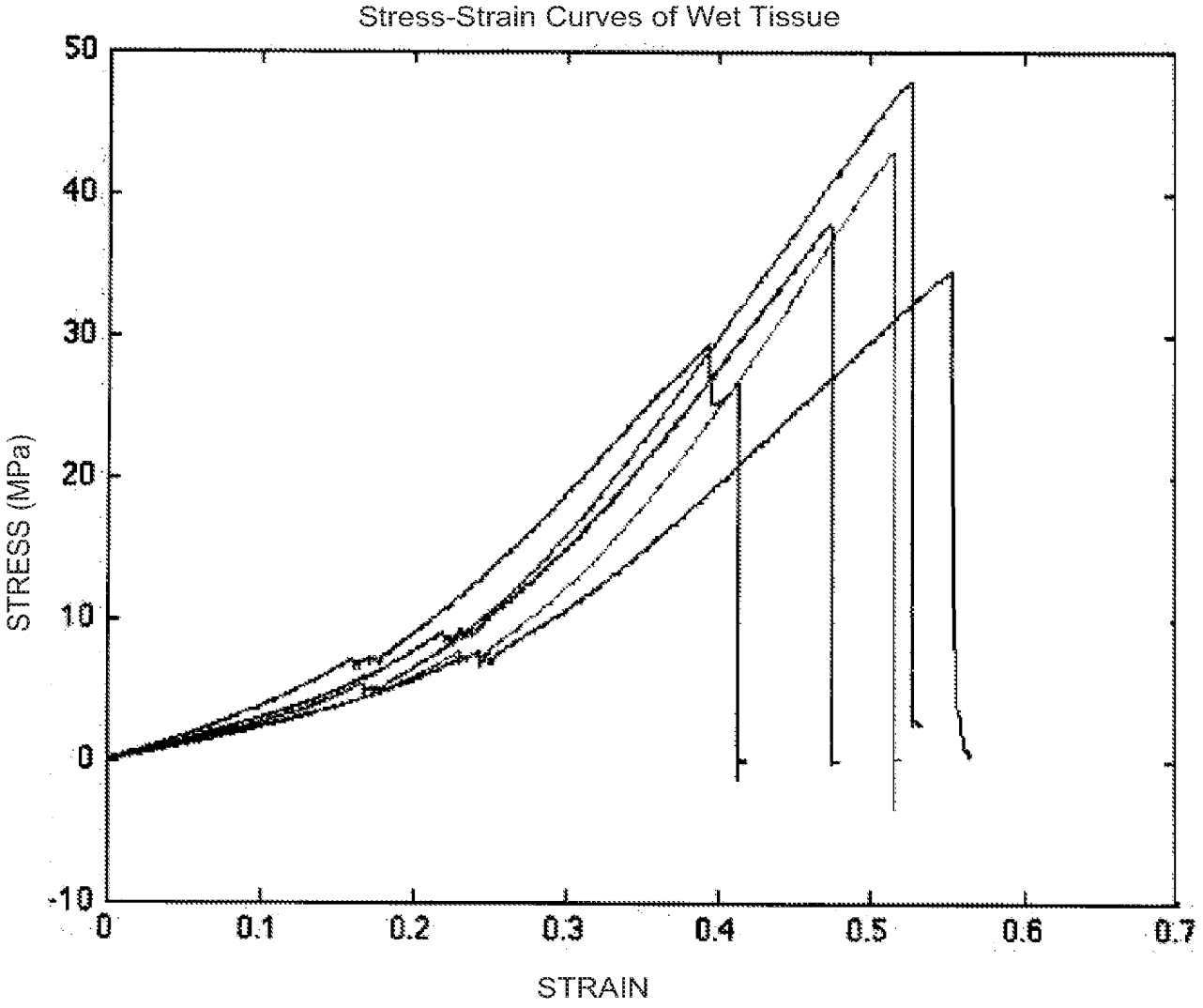

TISSUE
400

FIG.4



Stress-strain curves in wet or hydrated state of five samples. Each curve corresponds to a separate sample.

FIG. 5

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[Continued on next page]

(54) Title: PERCUTANEOUSLY DELIVERABLE HEART VALVE AND METHODS ASSOCIATED THEREWITH

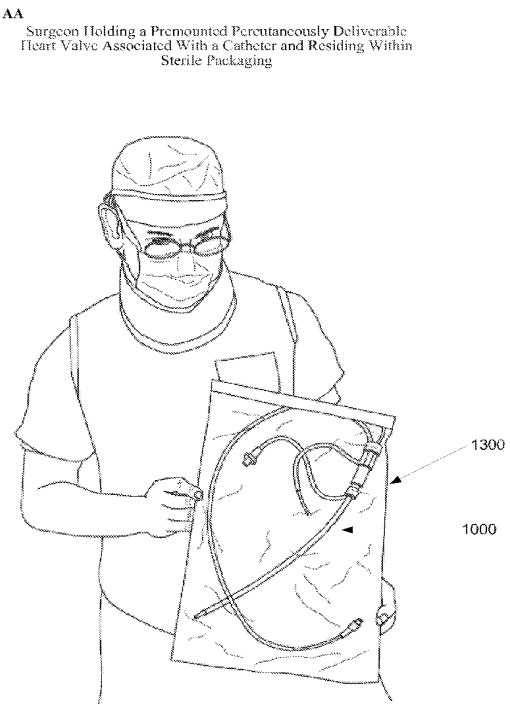

FIG.13

(57) Abstract: A prosthetic heart valve implantable by catheter without surgery includes a substantially "dry" membrane or tissue material. In at least one embodiment, the tissue is folded in a dry state to form a tissue leaflet assembly that is then attached to a frame to form an implantable prosthetic heart valve. Alternatively, one or more tissue leaflets are operatively associated with a frame to form an implantable prosthetic heart valve. The implantable prosthetic heart valve is subsequently pre-mounted on an integrated catheter delivery system. The catheter delivery system that includes the implantable prosthetic heart valve is then packaged and transported while the tissue remains dry. The implantable prosthetic heart valve, while remaining substantially dry, can then be implanted into the receiving patient.

WO 2011/109450 A2

TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

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PERCUTANEOUSLY DELIVERABLE HEART VALVE AND METHODS ASSOCIATED THEREWITH

FIELD

The present invention relates to the field of medical devices, and more particularly, to a percutaneously deliverable heart valve and a method of making a percutaneously deliverable heart valve.

BACKGROUND

Heart valve disease is a common degenerative condition that compromises physiologic function and causes limiting symptoms and threat to life in millions of patients all over the world. There are various underlying causes, but malfunction of heart valves is ultimately expressed as insufficient conduction of blood through the plane of the valve due to narrowing of the anatomic pathway (stenosis), or as incompetent closure that allows blood to return back through the valve again, thereby reducing the effective forward conduction of blood through the valve (insufficiency or regurgitation). These hemodynamic states lead to 1) deficiency of cardiac output and 2) adverse loads on the pumping chambers of the heart, both of which in turn lead to functional compromise of the patient and often premature death unless effectively corrected.

Definitive corrective treatment of heart valve disease is conventionally performed by open-chest surgical techniques, wherein the valve is manipulated, repaired, or replaced with a prosthetic valve under direct vision. Heart valve surgery is performed in hundreds of thousands of cases yearly world-wide, but carries a high burden of cost, morbidity, and mortality, especially in susceptible patients who may be elderly or otherwise physiologically compromised by collateral disease. Further, the costs and resource requirements of the surgical enterprise restrict the availability of heart valve replacement to many more patients all over the world.

In pursuit of alternatives to heart valve surgery, over the last ten years a number of development programs have brought percutaneous, trans-catheter implantation of prosthetic heart valves into commercial use in the European Union (EU) and into pivotal clinical trials in the United States of America. Initial clinical experience in the EU was directed toward patients who had critical aortic valve stenosis, but were deemed to be at unacceptably high risk for open-heart surgical valve replacement. In several thousand such cases, utilizing both balloon-expandable and self-expanding designs in two separate programs, percutaneous heart valve replacement (PHVR) was shown to be feasible and possibly competitive with surgery in selected patients with 12-18 month mortality rates of about 25%. Grube E., et al., *Progress and Current Status of Percutaneous Aortic Valve Replacement: Results of Three Device Generations of the CoreValve Revalving System*, Circ. Cardiovasc Intervent. 2008;1:167-175.

The application of PHVR thus far has been challenged by the technical difficulties of the implantation sequence—especially in the aortic valve position. The technique for available devices is limited by the large caliber of the devices and their delivery catheters; often, if it can be done at all in some smaller arteries, open surgical exposure and management of the femoral artery is required to insert the 18 – 24 French (6 – 8 mm diameter) systems, and their bulkiness inside the central arteries can threaten the safety of the delivery sequence. Further, access site bleeding complications form a significant part of the adverse events of the procedures.

Typically, the current PHV designs comprise a biological membrane forming the operating leaflets of the valve, attached within a metal frame, that is then collapsed onto a delivery catheter or balloon, and then constrained within an outer sheath. After an initial dilation of the diseased valve with a large balloon, this assembly is then advanced to the plane of the valve and deployed by self-expansion or by balloon expansion.

The effective caliber of the valve delivery system is determined by the total bulk of each coaxially mounted component. The bulk of the PHV itself is determined by the diameter of the frame and by the thickness, stiffness, and particular arrangement of the inner membrane forming the operating leaflets of the valve. The characteristic thickness of current PHV membranes is thus a limiting factor in the ultimate delivery profile of the PHV. Such characteristic membrane thickness is, in turn, a result of the methods by which it is processed and ultimately delivered for use. Typically, glutaraldehyde fixation (for protein cross-linking) of animal tissue is employed to produce suitable biological membranes for incorporation. Requirements for strength and durability have determined the most useful ranges for tissue thickness and cross-linking while typically imposing countervailing stiffness and brittleness. Subsequent hydration in suitable solutions improves these characteristics, but the hydrated membrane by this means also gains thickness.

One of the evident requirements for a PHV design is that the valve functions with a high degree of competence immediately on deployment, since the patient's hemodynamic survival depends on it. To this end, in part, like surgical valve prostheses, current PHV designs are completed, transported, and delivered for use in a hydrated state in a jar of solution. In use, commercially available surgical and percutaneously implanted bioprosthetic heart valves are rinsed and prepared before use in a "wet" state. More particularly, commercially available prosthetic heart valves are rinsed, crimped, and mounted in the catheterization lab. Accordingly, problems with current commercially available prosthetic heart valves include the time, cost and variability associated with the necessity to rinse, crimp, and mount the valve in the catheterization lab. That is, current mounting of prosthetic heart valves in the catheterization lab imposes one or more of delay, cost, technical burdens and possible errors. Avoiding one or

more of these problems would be advantageous. In addition, current "wet" valve designs impose additional profile on the collapsed valve. The hydrated membrane, while having desirable and necessary flexibility for reliable operation immediately on deployment, also imposes a large part of the thickness of the assembled and mounted valve that compromises its deliverability.

Expanding on some of the problems described above, the use of current PHVs in the catheter lab requires a number of preparatory acts that are potentially troublesome and can prolong the delivery sequence during a critical phase of the procedure. Since PHVs are delivered for use "wet" in a preservative solution, they have to be treated prior to insertion with a series of cleansing and hydrating solutions. Once this is completed, the PHVs have to be mounted on their delivery catheters. Special crimping and mounting tools are needed in the case of the balloon-expandable Edwards Sapien valve, for example. Accordingly, there is a need to address the shortcomings discussed above.

SUMMARY

It is to be understood that the present invention includes a variety of different versions or embodiments, and this Summary is not meant to be limiting or all-inclusive. This Summary provides some general descriptions of some of the embodiments, but may also include some more specific descriptions of other embodiments.

In at least one embodiment, a substantially "dry" membrane PHV system is provided wherein a tissue material is prepared and folded in a dry state to form a tissue leaflet assembly. Thereafter, the tissue leaflet assembly is attached to a frame to form an implantable prosthetic heart valve that is subsequently pre-mounted in an integrated catheter delivery system. The catheter delivery system that includes the prosthetic heart valve is then packaged and transported while the tissue leaflet assembly remains substantially dry. The prosthetic heart valve is available for use directly out of its package envelope. Accordingly, it can be inserted into the body without need of hydration, crimping or mounting tools, or other preparatory acts. That is, the tissue forming the tissue leaflet assembly of the prosthetic heart valve can be treated and dried, then while remaining dry, folded into a tissue leaflet assembly. Thereafter, the tissue leaflet assembly is at least partially rehydrated and then attached within a frame, such as a stent, to form an implantable prosthetic heart valve. The tissue leaflet assembly of the prosthetic heart valve is then allowed to dry. The prosthetic heart valve can thereafter be subsequently packaged, delivered, and shipped while the tissue leaflet assembly of the prosthetic heart valve remains in a dry condition. The prosthetic heart valve can then be implanted into the receiving patient. Accordingly, the PHV system simplifies arterial insertion, and, as the dry condition also confers lower bulk and profile, procedural manipulation and associated complications may be

reduced if not eliminated. In addition, one or more embodiments of the present invention widen the candidacy of patients with smaller arteries for the PHV procedure. As an added advantage, at least one embodiment of the present invention allows the implantation to take place under shorten elapsed times at the most critical phase of the procedure.

In at least one embodiment, a membrane PHV system is provided wherein a tissue material is prepared and folded in a dry state to form a tissue leaflet assembly, and further wherein the tissue leaflet assembly is thereafter at least partially hydrated and attached to a frame that is subsequently pre-mounted in an integrated catheter delivery system.

In at least one embodiment, a membrane PHV system is provided wherein a tissue material is prepared and folded in a dry state to form a tissue leaflet assembly, and further wherein the tissue leaflet assembly is at least partially hydrated and attached to a frame to form the prosthetic heart valve. Thereafter, the prosthetic heart valve is allowed to dry and subsequently pre-mounted in an integrated catheter delivery system after which the tissue leaflet assembly of the prosthetic heart valve remains dry, and wherein the system is then associated with a package for shipment while the tissue leaflet assembly remains dry.

In at least one embodiment, a membrane PHV system is provided wherein a tissue material is prepared and then folded in a dry state to form a tissue leaflet assembly, and further wherein the tissue leaflet assembly is at least partially hydrated and attached to a frame to form the prosthetic heart valve. Thereafter, the prosthetic heart valve is allowed to dry and subsequently pre-mounted in an integrated catheter delivery system after which the tissue leaflet assembly of the prosthetic heart valve is then at least partially hydrated and associated with a package for shipment.

In at least one embodiment, an article adapted for trans-catheter delivery into a patient is provided, comprising: a prosthetic heart valve further comprising a treated tissue attached to a frame, wherein the treated tissue comprises a thickness of about 50 to 500 micrometers and an ultimate tensile strength of greater than about 15 MegaPascals when at a water content of less than about 50% by weight of the section of treated tissue. Here it is noted that the tensile strength of the treated tissue described herein is higher than the tensile strength of other known prepared tissues, whether hydrated or dry. In at least one embodiment, the water content of the treated tissue is less than about 40% by weight of the treated tissue. In at least one embodiment, the ultimate tensile strength is greater than about 20 MegaPascals. In at least one embodiment, the treated tissue does not include a matrix that has been exposed to a polymer infiltrate. In at least one embodiment the treated tissue comprises a treated pericardium tissue.

In at least one embodiment, the method further comprises exposing the section of tissue to light energy for an exposure duration, the exposure duration extending until there is no further

visible separation of lipid droplets from an exposed surface of the section of tissue. In at least one embodiment, the light energy is at least equivalent to exposing the section of tissue to a 25-100 watt light source, and more preferably, a 50 watt incandescent light source with a flat radiant face situated at a distance of about 10 centimeters from the exposed surface for about 15 minutes. In at least one embodiment, the method further comprises: (d) rinsing the section of tissue with distilled water and isopropyl alcohol for a post-fixation period of time of not less than about 7 days; wherein step (d) occurs after step (c).

In at least one embodiment, an article adapted for implantation in a patient is provided, comprising: a prosthetic heart valve further comprising a treated tissue attached to a frame, wherein the treated tissue comprises a water content of less than about 60% by weight of the treated tissue. In at least one embodiment, the treated tissue comprises a section of pericardium tissue having an ultimate tensile strength of greater than about 12 MegaPascals. In at least one embodiment, the section of treated tissue comprises a thickness of between about 50 to 300 micrometers. In at least one embodiment, the water content of the treated tissue is less than about 40% by weight of the treated tissue.

As used herein, the term "dry" (or "substantially dry") when referring to the state of the tissue that forms the heart valve of the percutaneous heart valve means a moisture content less than the water moisture content of the tissue when the tissue is allowed to fully rehydrate in the body of a patient. Typically, pericardium tissue treated in accordance with one or more embodiments described herein is about 70% by weight water when fully hydrated. Drying to a constitution of less than 40% by weight of water usefully alters the handling properties for purposes of folding and sewing the tissue. As those skilled in the art will appreciate, the moisture content of the tissue may vary when dry. For example, the moisture content of the tissue when being folded and dry may be different than the moisture content of the tissue when dry and being shipped in a premounted state within a catheter delivery system.

Advantageously, at least one embodiment of the one or more present inventions is directed to a prosthetic heart valve that is mounted onto a valve delivery system and stored in a sterile package. Accordingly, in at least one embodiment, an assembly is provided, comprising:

a prosthetic heart valve including:

a frame; and

a tissue leaflet assembly attached to the frame;

a percutaneously insertable valve delivery mechanism, wherein the prosthetic heart valve is releasably mounted onto the percutaneously insertable valve delivery mechanism; and

sterile packaging containing the prosthetic heart valve releasably mounted onto the percutaneously insertable valve delivery mechanism.

In at least one embodiment, the percutaneously insertable valve delivery mechanism comprises a balloon catheter. In at least one embodiment, the balloon catheter is a 12 to 14 French balloon catheter. In at least one embodiment, the balloon catheter is less than about 12 French. In at least one embodiment, the balloon catheter is between about 5 to 12 French. In at least one embodiment, the percutaneously insertable valve delivery mechanism comprises a mandrel. In at least one embodiment, tissue forming the tissue leaflet assembly within the sterile packaging is at least one of hydrated and not substantially dry. In at least one embodiment, tissue forming the tissue leaflet assembly within the sterile packaging is substantially dry. In at least one embodiment, the frame comprises a stent. In at least one embodiment, tissue forming the tissue leaflet assembly comprises treated pericardium tissue.

At least one embodiment of the one or more present inventions includes a prosthetic heart valve for implantation in a patient. Accordingly, a pre-packaged percutaneous, trans-catheter deliverable prosthetic heart valve ready for implantation in a patient is provided, comprising:

a frame; and,

a tissue leaflet assembly attached to the frame, the tissue leaflet assembly comprising a substantially dry tissue.

In at least one embodiment, the substantially dry tissue comprises treated pericardium tissue. In at least one embodiment, the frame and tissue leaflet assembly attached thereto are operably associated with a 12 to 14 French balloon catheter. In at least one embodiment, the frame and tissue leaflet assembly attached thereto are operably associated with a balloon catheter having a size of less than about 12 French. In at least one embodiment, the frame and tissue leaflet assembly attached thereto are operably associated with a balloon catheter having a size of between about 5 to 12 French. In at least one embodiment, the substantially dry tissue comprises a water moisture content of less than about 40% by weight of the substantially dry tissue.

In at least another embodiment, an assembly for use with a patient is provided, comprising:

a sealed sterile package containing a delivery system for percutaneously deploying a heart valve in the patient, the heart valve including:

a frame releasably mounted on the delivery system within the sealed sterile package; and

a tissue leaflet assembly attached to the frame.

In at least one embodiment, the tissue leaflet assembly comprises pericardium tissue.

In at least one embodiment, a method is provided, comprising:

partially compressing and mounting a prosthetic heart valve upon a delivery catheter, the

prosthetic heart valve comprising a tissue;

allowing the tissue to at least partially dry;

further compressing and mounting the prosthetic heart valve upon the delivery catheter; and

sterilizing and packaging the prosthetic heart valve and delivery catheter.

In at least one embodiment, the method further comprises transporting the sterilized and packaged prosthetic heart valve and delivery catheter. In at least one embodiment, the tissue comprises treated pericardium tissue. In at least one embodiment, prior to partially compressing and mounting the prosthetic heart valve upon the delivery catheter, the tissue is at least one of (a) not substantially dry, and (b) at least partially hydrated.

For the various embodiments described herein, the prosthetic heart valve, including the tissue leaflet assembly, comprises membrane tissue other than pericardium tissue.

In at least one embodiment, a method is provided, comprising:

attaching pericardium tissue to a frame;

partially compressing and mounting the frame, with the tissue attached thereto, upon a delivery catheter;

allowing the tissue to at least partially dry;

further compressing and mounting the frame, with the tissue attached thereto, upon the delivery catheter; and

sterilizing and packaging the frame and delivery catheter, with the tissue attached thereto.

In at least one embodiment, prior to partially compressing and mounting the frame, the tissue is at least one of (a) not substantially dry, and (b) at least partially hydrated. In at least one embodiment, the method further comprises transporting the sterilized and packaged frame, with the tissue attached thereto, mounted upon the delivery catheter, to a surgical or medical procedure facility. In at least one embodiment, prior to attaching the tissue to the frame the tissue is folded to form a tissue leaflet assembly. In at least one embodiment, the tissue leaflet assembly comprises at least one cuff and at least one pleat.

In at least one embodiment, a method of preparing a percutaneous, trans-catheter prosthetic heart valve is provided, the method comprising:

providing a membrane tissue from an organism;

treating the membrane tissue with at least one chemical to produce a treated membrane tissue;

drying the treated membrane tissue until it is a substantially dry tissue;

attaching the substantially dry tissue in a frame;

rehydrating the substantially dry tissue that is attached within the frame to form a rehydrated tissue;

collapsing the frame with the rehydrated tissue attached thereto; and

drying the rehydrated tissue within the collapsed frame until it is a substantially dry tissue.

In at least one embodiment the method further comprises compressing and mounting the frame, with the substantially dry tissue attached thereto, upon a delivery catheter. In at least one embodiment the method further comprises sterilizing and packaging the frame, with the substantially dry tissue attached thereto, mounted upon the delivery catheter. In at least one embodiment, the treating comprises sterilizing the frame with the substantially dry tissue attached thereto with exposure to at least one of ethylene oxide, a proton beam, and gamma radiation. In at least one embodiment, the method further comprises shipping the sterilized and packaged frame with the substantially dry tissue attached thereto, mounted upon the delivery catheter, to a surgery or medical procedure facility. In at least one embodiment, prior to the attaching step the dry tissue is not folded to provide a cuff and/or a pleat. In at least one embodiment, prior to the attaching step the dry tissue is folded to form a tissue leaflet assembly. In at least one embodiment, the tissue leaflet assembly comprises at least one cuff and at least one pleat.

In at least one embodiment, the method of preparing a percutaneous, trans-catheter prosthetic heart valve further comprises implanting the frame with the substantially dry tissue attached thereto into a patient. In at least one embodiment, the frame comprises a stent. In at least one embodiment, the method further comprises mounting the frame and the tissue leaflet assembly attached thereto upon a 12 to 14 French balloon catheter. In at least one embodiment, the method further comprises mounting the frame and the tissue leaflet assembly attached thereto upon a balloon catheter having a size of less than about 12 French. In at least one embodiment, the method further comprises mounting the frame and the tissue leaflet assembly attached thereto upon a balloon catheter having a size of between about 5 to 12 French. In at least one embodiment, the method further comprises mounting the frame and the tissue leaflet assembly attached thereto on a mandrel. In at least one embodiment, the method of preparing a percutaneous, trans-catheter prosthetic heart valve further comprises immersion of the membrane tissue in buffered or unbuffered 1-37.5% formalin for between about 3 days to 3 weeks. In at least one embodiment, the method of preparing a percutaneous, trans-catheter prosthetic heart valve further comprises immersion of the membrane tissue in buffered or unbuffered 1-37.5% formalin for between about 3 days to 5 weeks. In at least one embodiment the treating comprises immersion of the membrane tissue in 100% glycerol for greater than 3

weeks. In at least one embodiment the treating comprises immersion of the membrane tissue in 0.1 - 25% glutaraldehyde for between about 3 days to 3 weeks. In at least one embodiment the treating comprises immersion of the membrane tissue in 0.1 - 25% glutaraldehyde for between about 3 days to 5 weeks. In at least one embodiment the treating comprises immersion of the membrane tissue in oligomeric filtered 0.1 - 25% glutaraldehyde for between about 3 days to 3 weeks. In at least one embodiment the treating comprises immersion of the membrane tissue in oligomeric filtered 0.1 - 25% glutaraldehyde for between about 3 days to 5 weeks. In at least one embodiment the treating comprises immersion of the membrane tissue in the aforementioned formalin, glutaraldehyde, or oligomeric filtered glutaraldehyde solutions with the added free amino acids lysine and/or histidine. In at least one embodiment the treating does not include contact and/or exposure to a polymer to infiltrate and/or encapsulate tissue fibers of the tissue.

In at least one embodiment, a method of preparing a percutaneous, trans-catheter prosthetic heart valve is provided, the method comprising:

providing a section of tissue harvested from a mammalian organism; and

causing osmotic shocking of the section of tissue by performing multiple rinses of the section of tissue with distilled water. In at least one embodiment, the method further comprises hydrating the section of tissue during a plurality of time intervals using distilled water. In at least one embodiment the section tissue comprises pericardium tissue. In at least one embodiment, the method further comprises not using saline for causing at least one of the osmotic shocking and the hydrating of the tissue. In at least one embodiment, the method further comprises pretreating the section of tissue with glycerol before contacting the section of tissue with one or more of isopropyl alcohol, glutaraldehyde and formalin. In at least one embodiment, the method further comprises contacting the section of tissue with a solution containing formalin after pretreating the section of tissue with glycerol. In at least one embodiment, the method further comprises contacting the section of tissue with a solution containing glutaraldehyde after pretreating the section of tissue with glycerol. In at least one embodiment, the method further comprises pretreating the section of tissue with isopropyl alcohol before contacting the section of tissue with either glutaraldehyde and formalin. In at least one embodiment, the method further comprises contacting the section of tissue with a solution containing formalin after pretreating the section of tissue with isopropyl alcohol. In at least one embodiment, the method further comprises contacting the section of tissue with a solution containing glutaraldehyde after pretreating the section of tissue with isopropyl alcohol. In at least one embodiment, the method further comprises exposing the section of tissue to light energy for a period time, the period of time extending until there is no further visible separation

of lipid droplets from an exposed surface of the section of tissue. In at least one embodiment, the light energy is at least equivalent to exposing the section of tissue to a 50 watt incandescent light source with a flat radiant face situated at a distance of about 10 centimeters from the exposed surface for about 15 minutes.

With regard to delivery characteristics, another significant advantage of an implantable prosthetic heart valve using a relatively thin tissue component described herein is that the implantable prosthetic heart valve offers a relatively low packing volume as compared to commercially available prosthetic heart valves. As a result, the implantable prosthetic heart valve provides a relatively low catheter delivery profile, thereby enabling implantation in patients possessing relatively small diameter vascular systems.

In accordance with one or more embodiments, a dry tissue membrane has substantially less mass than a wet membrane. By way of example, a substantially dry pericardium tissue prepared by one or more of the present embodiments has approximately 30% of the mass of a wet pericardium tissue, and marked reduction in profile and packing volume, thereby achieving a relatively low profile and making it suitable for implantation in greater number of patients, especially those having small diameter vascular systems. In addition, a dry prosthetic heart valve does not require storage and transport in preservative. A dry prosthetic heart valve can be mounted on a delivery catheter at its location of manufacture, which allows for pre-packaging of an integrated delivery system. Together with a relatively low profile, embodiments of the prosthetic heart valves thereby offer reliability and convenience because the implantable prosthetic heart valve is pre-mounted upon a delivery catheter and forms part of a pre-packaged delivery system. In addition, a dry prosthetic heart valve does not require rinsing, rehydration, or mounting upon a delivery catheter in a catheterization lab. Therefore, a dry prosthetic heart valve can be inserted directly from package into the body at a critical time during the procedure. Advantageously, this avoids procedure time, manipulation, and errors of mounting, crimping, and orienting catheters and sheaths. Once at the surgical facility/location, the dry prosthetic heart valve is inserted and delivered by balloon catheter expansion in the plane of the diseased valve in the standard way and the dry prosthetic heart valve begins to function immediately, even in its dry state or not fully rehydrated state (because some rehydration will occur upon flushing of the catheter with the prosthetic heart valve residing therein), with rehydration of the tissue membrane subsequently completing naturally in the body.

Various components are referred to herein as "operably associated." As used herein, "operably associated" refers to components that are linked together in operable fashion, and encompasses embodiments in which components are linked directly, as well as embodiments in which additional components are placed between the two linked components.

As used herein, "at least one," "one or more," and "and/or" are open-ended expressions that are both conjunctive and disjunctive in operation. For example, each of the expressions "at least one of A, B and C," "at least one of A, B, or C," "one or more of A, B, and C," "one or more of A, B, or C" and "A, B, and/or C" means A alone, B alone, C alone, A and B together, A and C together, B and C together, or A, B and C together.

As used herein, "sometime" means at some indefinite or indeterminate point of time. So for example, as used herein, "sometime after" means following, whether immediately following or at some indefinite or indeterminate point of time following the prior act.

Various embodiments of the present inventions are set forth in the attached figures and in the Detailed Description as provided herein and as embodied by the claims. It should be understood, however, that this Summary does not contain all of the aspects and embodiments of the one or more present inventions, is not meant to be limiting or restrictive in any manner, and that the invention(s) as disclosed herein is/are understood by those of ordinary skill in the art to encompass obvious improvements and modifications thereto.

Additional advantages of the present invention will become readily apparent from the following discussion, particularly when taken together with the accompanying drawings.

BRIEF DESCRIPTION OF THE DRAWINGS

To further clarify the above and other advantages and features of the one or more present inventions, a more particular description of the one or more present inventions is rendered by reference to specific embodiments thereof which are illustrated in the appended drawings. It is appreciated that these drawings depict only typical embodiments of the one or more present inventions and are therefore not to be considered limiting of its scope. The one or more present inventions is described and explained with additional specificity and detail through the use of the accompanying drawings in which:

Fig. 1 is a flow chart of a method associated with at least of one embodiment of the present invention;

Figs. 2A-2B are a flow chart illustrating elements of the tissue preparation;

Fig. 3 is a flow chart illustrating elements of the drying and sizing;

Fig. 4 is a flow chart illustrating elements of the valve construction with attachment of tissue membrane leaflets to a frame;

Fig. 5 is a flow chart illustrating elements of the mounting of the valve into a delivery system;

Fig. 6 is a flow chart illustrating elements of the ensheathing, sterilization, and packaging;

Fig. 7 is a flow chart illustrating elements of the delivery of the valve into a patient;

Fig. 8A is a view of a one-piece section of tissue prior to being folded;

Fig. 8B is a view of two (of three) separate pieces of tissue after folding (detailed below);

Fig. 8C is a view of the two pieces of tissue shown in Fig. 8B after being sutured together at the pleat formed after folding (detailed below);

Fig. 8D is a view of a tissue blank with the line of primary fold shown using a dashed line;

Fig. 8E is a perspective view of the tissue blank being folded along the primary fold line;

Fig. 8F is a 2-part figure showing the pleats fold lines and pleats after folding;

Fig. 8G is a detail perspective view of a single pleat shown in Fig. 8F;

Fig. 8H is a perspective schematic view of a folded and seamed tissue leaflet assembly;

Fig. 8I is a perspective schematic view of a frame;

Fig. 8J is a perspective schematic view of the frame of Fig. 8I with the tissue leaflet assembly of Fig. 8H attached thereto;

Fig. 8K is side elevation schematic view of the device shown in Fig. 8J;

Fig. 8L is an end schematic view of the frame and tissue leaflet assembly attached thereto;

Fig. 9 is a graph that shows actual stress-strain test results for five tissue samples prepared in accordance with at least one embodiment;

Fig. 10 is a schematic of a portion of a catheter with a percutaneously deliverable heart valve mounted thereto;

Fig. 11A is a photo of an implantable prosthetic heart valve, including a tissue leaflet assembly attached within a frame, wherein the tissue is situated in a partially open orientation;

Fig. 11B is a drawing of an implantable prosthetic heart valve, including a tissue leaflet assembly attached within a frame, wherein the tissue is situated in a closed orientation;

Fig. 11C is a side cutaway view of an implantable prosthetic heart valve, including a tissue leaflet assembly attached within a frame, wherein the tissue is situated in a closed orientation;

Fig. 11D is another side cutaway view of an implantable prosthetic heart valve, including a tissue leaflet assembly attached within a frame, wherein the tissue is situated in a closed orientation;

Fig. 12 is a photo of valve tissue after testing through 30,000,000 cycles of pumping used to model human heart conditions, wherein the photo shows a smooth uniform surface;

Fig. 13 is a drawing of a surgeon holding a premounted percutaneously deliverable heart valve associated with a catheter and residing within sterile packaging;

Fig. 14 is a schematic of a simplified cutaway view of a human heart, including heart valves that may be targeted for receiving an embodiment of an implantable prosthetic heart valve;

Fig. 15 is a schematic of a human aorta receiving a catheter with an implantable prosthetic heart valve mounted thereto; and

Fig. 16 is a schematic of a human aorta with the implanted prosthetic heart valve implanted at the site of the original diseased aortic valve.

The drawings are not necessarily to scale.

DETAILED DESCRIPTION

Embodiments of the one or more inventions described herein include one or more devices, assemblies and/or methods related to a prosthetic heart valve. A prosthetic heart valve in accordance with at least one embodiment described herein can be surgically implanted, such as by percutaneous, trans-catheter delivery, to the implantation site within the patient. One or more embodiments of the prosthetic heart valves described herein have application for at least aortic and pulmonary valve positions, including for structural defects and diseased valves.

In at least one embodiment, biocompatible material is attached within a frame to form an implantable prosthetic heart valve, and then at a later time, the implantable prosthetic heart valve is implanted within a patient, such as by way of a percutaneous, trans-catheter delivery mechanism. Once implanted, the prosthetic heart valve serves to regulate the flow of blood associated with the patient's heart by allowing forward blood flow and substantially preventing backflow or valvular regurgitation.

Referring now to Fig. 1, a flow chart illustrates at least one embodiment of a prosthetic heart valve preparation and delivery method 100. The prosthetic heart valve preparation and delivery method 100 generally includes a plurality of procedures to include tissue preparation at 200, drying at 300, tissue leaflet assembly construction and attachment to frame at 400 to form an implantable prosthetic heart valve, mounting of the prosthetic heart valve (that is, the frame with the tissue leaflet assembly) into a delivery system at 500, ensheathing, sterilizing and packaging the delivery system including the prosthetic heart valve at 600, and finally, delivering the prosthetic heart valve into the patient at 700. Further detail of the prosthetic heart valve preparation and delivery method 100 is provided below.

At least one or more embodiments described herein include a relatively thin tissue component. By way of example and not limitation, in at least one embodiment the tissue has a thickness of approximately 50 - 150 μm, and further possesses characteristics of pliability and resistance to calcification after implantation. The relatively thin nature of the tissue used in the implantable prosthetic heart valve assists with biocompatibility. In addition, the relatively thin

tissue component thereby provides for a relatively low mass. As a result, an implantable prosthetic heart valve using the tissue can accelerate to a relatively high heart rate in beats per minute with competent function.

Tissue suitable for use in the one or more prosthetic heart valves and/or one or more assemblies described herein is relatively thin and can generally be considered to be a membrane. Those skilled in the art will appreciate that both natural and synthetic types of materials may be used to form a leaflet assembly of a prosthetic heart valves. Accordingly, it is to be understood that although treated pericardium tissue is described as a suitable material for use in the leaflet assembly of a prosthetic heart valve of one or more embodiments described herein, material other than xenograft tissue membrane can be used, and indeed, xenograft tissue membrane other than pericardium tissue can be used. More specifically, synthetic materials may include, but are not limited to, PTFE, PET, Dacron, and nylon. In addition, other than pericardium tissue, xenograft tissue membrane may include, but is not limited to, membrane material from the intestine, lung and brain. Suitable material may also comprise allograft material, that is, material from human sources. The listing of possible materials is for exemplary purposes and shall not be considered limiting.

With reference now to Fig. 2A, the process associated with preparation of a biocompatible tissue consistent with the above-noted characteristics is described. In at least one embodiment, pericardium tissue, such as porcine or bovine pericardium tissue, is harvested at 204 and then processed to serve as the biocompatible tissue for association with a frame, such as by attaching within a frame. Accordingly, subsequent to the harvesting at 204, the pericardium tissue is cleaned and decellularized at 208. More particularly, in at least one embodiment the tissue is initially cleaned with distilled water using gentle rubbing and hydrodynamic pressure at 208 in order to remove adherent non-pericardial and non-collagenous tissue. In at least one embodiment, the hydrodynamic pressure at 208 is provided by spraying the tissue with a relatively weak stream of liquid to remove at least some of the non-collagenous material associated with the tissue. The rinsing at 208 is to achieve effective decellularization of the pericardium tissue through osmotic shock. Typically, the thickness of the tissue in the cleaned condition varies from about 50 to 500 micrometers, depending on the source of raw tissue. Cleaning preferably continues until there is no visible adherent non-pericardial or non-collagenous tissue.

With continued reference to Fig. 2A, after the tissue has been cleaned and decellularized at 208, the tissue then undergoes optional additional removal of lipids at 220 to further treat the tissue for preventing immunologic response and calcification. More particularly, the tissue first optionally undergoes a 100% glycerol pretreatment at 224 while being positioned on a flat

surface (e.g., an acrylic plate), after which the tissue becomes nearly transparent.

At 228, the tissue optionally undergoes a "thermophotonic" process. In at least one embodiment, the tissue is optionally exposed to light energy for additional removal of lipids and for initial cross-linking of the collagen. By way of example and not limitation, in at least one embodiment a 25-100 watt incandescent light source, and more preferably, a 50 watt incandescent light source with a flat radiant face is employed at a distance of about 10 centimeters from the tissue surface, typically requiring 15 minutes of exposure before further visible separation of lipid droplets from the tissue stops.

Still referring to Fig. 2A, the tissue is then cleaned again in secondary cleaning at 232. More particularly, at 236 the tissue is again rinsed with distilled water. Thereafter, at 240 the tissue is rinsed with 25% isopropyl alcohol for periods of several hours to several days and weeks, depending on the desired tissue properties of pliability and tensile strength. By way of example and not limitation, tissue has been successfully prepared by rinsing with 25% isopropyl alcohol for a period of 7 days, and after further treatment steps described herein, provided an ultimate tensile strength of greater than 25 MegaPascals. Here, the combination of tissue pliability and tensile strength is sought for purposes of producing a material having property characteristics suitable for being physically manipulated to form a tissue leaflet assembly or other configuration appropriate for attaching with a frame, while providing a tissue material that will operate properly once implanted. These techniques are intended to conserve and preserve collagen fibers, minimizing damage to the tissue and improving tissue characteristics. The preparation and fixation techniques produce tissue membrane material that may be rendered and used at lesser thickness than typically rendered in the prior art. Thinner membranes are more pliable, but with conventional preparation techniques the tensile strength of the tissue is sacrificed. Advantageously, the preparation techniques described herein have produced membranes that have as much as three times the tensile strength of a commercial product of the prior art. This achieved strength is thus enabling for providing a tissue leaflet assembly having a low profile with appropriate durability, even in a substantially dry state. More particularly, the tissue possesses a relatively high tensile strength. By way of example and not limitation, testing has shown that embodiments of tissue prepared as described herein provide a tissue with a tensile strength of approximately three times the tensile strength of current pericardial valve tissue, such as on the order of approximately 25 MegaPascals, thereby providing about 2000 times the physiologic load strength for valve tissue. Moreover, testing of an embodiment of an implantable prosthetic heart valve made with tissue prepared as described herein and under a static load of greater than approximately 250 mmHg showed less than approximately 14% leakage, wherein such results are generally considered superior to surgical tissue valve

prostheses.

In at least one embodiment where isopropyl alcohol is described as a rinsing agent, ethanol may be used in its place as an alternative, although resulting tissue properties may vary.

With reference to Fig. 9, stress-strain curve results for five different tissue samples prepared in accordance with an embodiment are shown. For the testing results shown, the yield stress or ultimate tensile strength was obtained by mounting strips of tissue fixed at the ends in a linear force tester and increasing the length by 0.3 mm/sec while recording resultant force (tension) until the material ruptured or separated entirely; these measurements were then used to calculate the stress-strain curves depicted in Fig. 9. As illustrated in the graph, the yield stress or ultimate tensile strength of the various tissue samples varied from about 30 to about 50 MegaPascals. More particularly, for each curve shown in Fig. 9, the testing procedures were the same. That is, each of the curves shown pertain to separate pieces of tissue that were subjected to the same test. The results show a minimum ultimate tensile strength of 30 MegaPascals, with a range up to 50 MegaPascals. Accordingly, the illustrated test results demonstrate consistency of the ultimate tensile strength results for the tissue treatment process.

With reference back to Fig. 2A, the tissue is rinsed with distilled water at 244 as a final cleaning step and for rehydration.

Referring now to Fig. 2B, following the rinse with distilled water at 244, treatment of the tissue continues. More particularly, fixation for collagen cross-linking at 248 is achieved by performing at least one of the following:

a. At 248a, immersion of the tissue in 1-37.5% formalin, ideally a buffered solution, for between about 3 days to 5 weeks, and more preferably, for between about 3 days to 4 weeks, and more preferably yet, for between about 3 weeks to 4 weeks, at a temperature of between about 4 to 37°C, and more preferably, 10% formalin for 6 days at 20°C; or

b. At 248b, immersion of the tissue in 100% glycerol for up to 6 weeks at between 4 to 37°C, and more preferably, immersion of the tissue in 100% glycerol for about 3 weeks at 20°C; or

c. At 248c, immersion of the tissue in 0.1 - 25% glutaraldehyde for between about 3 days to 5 weeks, and more preferably, for between about 3 days to 4 weeks, and more preferably yet, for between about 3 weeks to 4 weeks, at 0 to 37°C, and more preferably, immersion of the tissue in 0.25% glutaraldehyde for 7 days at 4°C; or

d. At 248d, immersion of the tissue in 0.1 - 25% glutaraldehyde (filtered to limit oligomeric content) for between about 3 days to 5 weeks, and more preferably, for between about 3 days to 4 weeks, and more preferably yet, for between about 3 weeks to 4 weeks, at 0 to 37°C, and more preferably, 0.25% glutaraldehyde for 7 days at 4°C; or

e. At 248e, immersion in the tissue in one of the above formalin, glutaraldehyde, or oligomeric filtered glutaraldehyde solutions together with added amino acids, lysine and/or histidine, wherein the concentration of the amino acids, L-lysine or histidine, used as an additive to the fixative is in the range of about 100 - 1000 milliMolar, with a preferred value of about 684 mM.

In addition to the foregoing, combinations of the processes listed above may be performed, including: step a followed by step b; step a followed by step c; and step a followed by step d.

As those skilled in the art will appreciate, heat-shrink testing may be conducted on tissue samples to correlate the effectiveness of protein cross-linking. Here, results of heat-shrink testing performed on one or more samples of tissue prepared in accordance with at least one embodiment using formalin showed that the tissue had a shrink temperature of 90°C. This compares favorably with samples prepared using glutaraldehyde, wherein the shrink temperature was 80°C. Accordingly, formalin is a suitable variant of fixation. It is noted that formalin was generally abandoned by the field, largely because of material properties that were unfavorable and because of inadequate or unstable protein cross-linking. Such problems have been overcome through the pretreatments described herein, allowing production of tissue with strength, pliability, and durability in a relatively thin membrane. When used in a percutaneous deliverable heart valve (also referred to herein as "prosthetic heart valve"), the tissue characteristics imparted by the tissue preparation process facilitate formation of a construct having a relatively low-profile, which also thereby facilitates dry packaging of the prosthetic heart valve. The same advantages are also achieved using the pretreatments when using a glutaraldehyde process.

Referring still to Fig. 2B, after fixation for collagen cross-linking at 248, an alcohol post-fixation treatment at 252 is preferably performed by rinsing the tissue in distilled water at 256, and then at 260 rinsing the tissue in 25% isopropyl alcohol for between about 30 minutes to 14 days or more at between about 0 to 37°C, and more preferably, for at least about 7 days at 20°C. At 264, the tissue undergoes a rinsing with distilled water.

In accordance with at least one embodiment, treatment of the tissue, including from the time of harvest to the time of implantation or grafting, does not include contact and/or exposure to a polymer to infiltrate and/or encapsulate tissue fibers of the tissue.

Referring now to Figs. 1 and 3, the drying process at 300 is performed after the tissue preparation at 200. Thus, in accordance with at least one embodiment, the tissue is dried under a load. More particularly, for the tissue drying at 304, the tissue is placed minimally stretched flat (that is, stretched just enough to eliminate visible wrinkles and bubbles) on a flat surface (e.g., a polymer or acrylic sheet) at 308, and held fixed at its edges at 312. Optionally, the joined tissue

and underlying sheet are then set in a slight curve. The tension maintains the substantially flat structure of the tissue as it dries, thereby mitigating or preventing excessive shrinkage, wrinkling, and/or curling at the edges, and also making the rate of drying more uniform across the surface of the tissue because of the surface tension between the plate and the tissue. Alternatively, the tissue is dried while compressed between acrylic plates. When drying the tissue, the temperature is held at between about 4 to 37°C, and more preferably, between about 20 to 37°C (i.e., approximately room temperature to normal human body temperature), and more preferably, at about 20°C. At 314, the drying process is performed in substantially dark conditions (i.e., substantially no visible light) for between about 6 hours to 5 days, and more preferably, for about 72 hours. By way of example, the tissue is dried in dark conditions at a temperature of about 20°C for between about 6 hours to 5 days, and more preferably, for about 72 hours. As those skilled in the art will appreciate, drying the tissue while the tissue is compressed between plates requires a longer period of time.

In at least one embodiment, after drying, the tissue lots are inspected at 316, such as by stereomicroscopy, to identify and discard those with defects or discontinuities of the fiber matrix. In addition, the preferential fiber direction for each piece is identified to determine the necessary orientation of the free edge of the pieces that will form the valve leaflets. Depending upon the size (i.e., the area) of the tissue being prepared and the size of tissue needed for a given valve, the tissue may be trimmed or otherwise sized in optional sizing at 320, such as by cutting the tissue into an appropriately sized and shaped sheet for valve formation. Preferably, cutting of the tissue membrane is oriented so that the resulting free edge of the leaflet is parallel to the preferential fiber direction of the tissue membrane. Optionally, the free edge of the leaflets may also be cut with a parabolic or other curved profile to compensate for the downward angle from the commissural leaflet attachment point to the central coaptation point and to increase the total contact surface between the coapting leaflets. This approach minimizes focal weaknesses in the operating margins of the leaflet assembly and advantageously distributes the principal loading forces of the operating valve along the long axis of the collagen fibers. As a result, the tissue is resistant to surface fracture and fraying. As shown in Fig. 3, optional sizing at 320 is performed after the drying at 304 and inspection at 316.

With reference now to Fig. 4, an embodiment associated with forming a tissue leaflet assembly and attachment to a frame to form a prosthetic heart valve at 400 is further described. It is to be understood that the tissue generated from one or more of the tissue preparation procedures described herein may be used for a variety of devices or uses, and that use in a prosthetic heart valve is but one possible application for utilizing the tissue. For example, the tissue may be used in a shunt, or as graft material for repair or modification of one or more

human organs, including the heart and its blood vessels. By way of further example, the tissue may be used as a pericardial membrane patch for repair of congenital heart defects. The tissue also has application as a prosthetic tissue in tendon and ligament replacement, and as a tissue product for wound management. Moreover, for use in a prosthetic heart valve, the tissue may be configured in a variety of ways and attached to a frame in a variety of ways. By way of example and not limitation, in at least one embodiment, the prepared tissue is formed into a tissue leaflet assembly at 404 by folding the tissue at 408, preferably while the tissue is in a dry state, to form at least a portion of the tissue leaflet assembly. Here, those skilled in the art will appreciate that a completed tissue leaflet assembly may be formed of a single monolithic piece of tissue 800, such as that shown in Fig. 8A, or alternatively, as shown in Figs. 8B and 8C, it may be formed of a plurality of tissue pieces 802 that are operatively connected, such as by gluing or sewing the tissue pieces together along seams 804. As seen in Fig. 8C, the seams 804 are preferably situated at overlapping portions of pleats 832 of the plurality of tissue pieces 802.

As those skilled in the art will further appreciate, a single monolithic piece of tissue 800 or a plurality of tissue pieces 802 may be used to form a prosthetic heart valve, wherein the tissue leaflet assembly is not a folded construct. By way of example and not limitation, a plurality of separate tissue pieces may each be attached to a frame (such as by suturing) to form a prosthetic heart valve. Thereafter, whether the prosthetic heart valve is made of a folded tissue leaflet assembly or a plurality of separate tissue pieces attached to a frame, the resulting prosthetic heart valve may then be further manipulated for delivery as a dry prosthetic heart valve.

In an alternative embodiment, tissue generated from one or more of the tissue preparation procedures described herein may be used to form a prosthetic heart valve that includes a frame, and that may be implanted by a "trans-apical" approach in which the prosthetic heart valve is surgically inserted through the chest wall and the apex of the heart.

In yet another alternative embodiment, tissue generated from one or more of the tissue preparation procedures described herein may be used to form a prosthetic heart valve that does not include a frame, and is not delivered via a catheter, but rather, is implanted via a surgical opening through the patient's chest. In such a case, the prosthetic heart valve may be packaged for delivery as a dry prosthetic heart valve.

In still yet another alternative embodiment, tissue generated from one or more of the tissue preparation procedures described herein may be used to form a prosthetic heart valve that includes a frame, but that is not delivered via a catheter, but rather, is implanted via a surgical opening through the patient's chest. In such a case, the prosthetic heart valve may be packaged for delivery as a dry prosthetic heart valve.

As a further alternative to the embodiments described herein, tissue may be implanted in a "wet" or hydrated state. For example, a prosthetic heart valve utilizing a prepared tissue described herein may be packaged for delivery as a hydrated prosthetic heart valve. Accordingly, while a portion of the tissue preparation process may include drying the tissue so that it may be manipulated more easily, the tissue may then be hydrated at a later point in time prior to implantation, and it may be maintained in a hydrated condition up to and including packaging, delivery and implantation into a patient. Advantages associated with using a folded tissue leaflet assembly include that a folded structure allows a relatively thin membrane to be used by avoiding suture lines in loaded, dynamically active surfaces. Accordingly, a sutureless leaflet assembly preserves long-term integrity. However, it is to be understood that a prosthetic heart valve that does not include a folded tissue leaflet assembly is encompassed by one or more embodiments described herein.

With reference now to Figs. 8D-8L, and in accordance with at least one embodiment, for a prosthetic heart valve that includes a tissue leaflet assembly formed of a folded tissue membrane, the folding sequence for the tissue is shown for configuring the tissue into a completed tissue leaflet assembly. More particularly, a tissue blank 808 is shown in Fig. 8D, wherein the tissue blank 808 is a single monolithic piece of tissue 800. Depending upon the size requirements for a given tissue leaflet assembly, a line of primary fold or fold line 812 (shown as a dashed line) is visualized for the tissue blank 808. As shown in Fig. 8D, the primary fold 814 is achieved along the fold line 812 by folding the bottom edge 816 of the tissue blank 808 toward the top edge 820, but leaving a cuff portion 824 along the upper portion 828 of the tissue blank 808. Here, it is noted that the direction of top and bottom are relative to each other and are used as a convenience for describing the folding sequence, wherein such directions correspond to the orientation of the page illustrating the drawings. Advantageously, the folding geometry of Figs. 8D-8L forms cuffs 824 that are continuous with the leaflets, thereby reducing the risk of aortic insufficiency or leakage.

With reference now to Fig. 8F, after folding the tissue blank 808 along fold line 812 to form primary fold 814, pleats are formed by folding the tissue along its length. For the embodiment shown in Fig. 8F, three pleats 832a, 832b, and 832c are shown. Fig 8G illustrates a detail drawing of a single pleat 832 representative of one of pleats 832a-c. In Fig. 8G, the inner leaflet layer free edge 836 is shown, as is the valve sinus 840 and the commissure folds 844.

Referring again to Fig. 4 as well as Fig. 8H, at 412 the folded tissue is seamed to form a folded tissue leaflet assembly. More particularly, Fig. 8H shows a schematic perspective drawing of tissue leaflet assembly 848, wherein the pleated tissue construct shown in the bottom half of Fig. 8F is seamed, such as along seam 850, to form a substantially tubular construct. At

416, the folded tissue leaflet assembly 848 is maintained dry or is partially hydrated prior to mounting the tissue leaflet assembly in a frame. At 420, the tissue leaflet assembly 848 is then attached within a frame, such as frame 852 shown in Fig. 8I. The tissue leaflet assembly 848 attached within a frame 852 forms an implantable prosthetic heart valve 860, such as that shown in the schematic perspective drawing of Fig. 8J, side elevation view Fig. 8K, as well as that shown in the photo of Fig. 11A, and drawing of Fig. 11B. Fig. 8K illustrates possible suture points 864 where the tissue leaflet assembly 848 can be sutured to the frame 852. That is, the tissue leaflet assembly 848 may be attached within the frame 852, such as by suturing the outer layer of the tissue leaflet assembly 848 to the frame. In the foregoing sentence, and as used herein, it is noted that the term "attached" means that the tissue leaflet assembly 848 is secured to the frame 852, although the inner leaflet layer free edges 836 are able to readily move during operation of the prosthetic heart valve 860.

Referring now to Fig. 11C, a cutaway side elevation view of a prosthetic heart valve 860 that includes a frame 852 with a tissue leaflet assembly 848 attached therein is shown. The tissue membrane leaflet assembly 848 is disposed coaxially within the frame 852. As shown in Fig. 11C, the valve 860 is illustrated in the closed position with the leaflet free edges 836 in at least partial contact with each other. An arc 1112 of the leaflet free edges 836 (out of plane of the cutaway view) is continuous with pleats 832 at the radial edge of the tissue leaflet assembly 848, and may be seen in the alternate view shown in Fig. 8L. The tissue membrane leaflet assembly 848 is attached to the frame 852 along the axially oriented membrane pleats 832, as illustrated again in Fig. 8L. The extended cuff layer is attached circumferentially at the distal edge 1104 of the frame 852. By way of example and not limitation, continuous suture attachment 1108 may be used to attach the extended cuff layer to the distal edge 1104.

Referring now to Fig. 11D, an embodiment is shown wherein the cuff layer is not extended distally to the distal edge 1104 of the frame 852. As shown in Fig. 11D, the distal edge of the cuff layer is attached circumferentially to an inner aspect of the frame 852, such as along those possible suture points 864 illustrated in Fig. 8K. As a result, a distal portion 1116 of the frame 852 does not include any portion of the tissue leaflet assembly 848, such as the cuff layer. However, with the valve 860 in the closed position the leaflet free edges 836 still at least partially contact each other.

With reference now to Fig. 8L, an end view of the prosthetic heart valve is shown. As depicted in Fig. 8L, the pleats 832 are used as the portion of the tissue leaflet assembly 848 to attach to the frame 852. As can be seen in Fig. 8L, the outer cuff layer is attached to the frame members of frame 852. When the prosthetic heart valve 860 is closed, the cusps 868 formed by the inner leaflet layer are generally situated as depicted in Fig. 8L. Fig. 12 is a photo of the

tissue leaflets of a prosthetic heart valve after 30,000,000 cycles of testing to model performance if associated with a human heart. In testing, the prosthetic heart valve 860 has demonstrated a natural opening gradient of approximately 5 mmHg.

It will be appreciated by one of ordinary skill in the art that the tissue leaflet assembly 848 described and shown herein is but one possible construct for forming a flow control mechanism that can be attached to a frame to regulate the flow of blood in a patient's vascular system upon deployment. That is, the illustrated tissue leaflet assembly 848 is provided by way of example and not limitation, and in no way should be interpreted to limit the geometries of membrane leaflet assemblies that can be used to regulate fluid flow. Accordingly, other leaflet configurations and constructs are considered encompassed by claims directed to or otherwise including premounted percutaneously deliverable valves.

As those skilled in the art will appreciate, the frame 852 may be a stent or a structure having similarities to a stent. The frame 852 essentially serves as a holding mechanism for the tissue leaflet assembly 848 that can then be inserted percutaneously into a patient, wherein the frame 852 serves as a way to anchor the folded tissue leaflet assembly 848 to a vascular portion (e.g., *in situ* arterial tissue) of the patient. Thus, at 424 the tissue leaflet assembly 848 is inserted into a frame 852. More particularly, at 424a the frame 852 may comprise a balloon-expandable frame, or alternatively, at 424b a self-expanding frame may be used. After the tissue leaflet assembly is inserted into the frame, at 428 the folded tissue leaflet assembly 848 is attached to the frame 852, such as by suturing the tissue leaflet assembly 848 to the frame 852 to form an implantable prosthetic heart valve 860, such as that shown in Fig. 8L. In at least one embodiment, after attaching the tissue leaflet assembly 848 within the frame 852 and connecting the tissue leaflet assembly 848 to the frame 852 to form an implantable prosthetic heart valve 860, at 432 the prosthetic heart valve 860 is fully hydrated for inspection and testing. Thereafter, the fully constructed implantable prosthetic heart valve 860 may be dried and maintained in a substantially dry condition. Accordingly, as those skilled in the art will appreciate, one or more embodiments described herein provide a tissue 800 suitable for implanting in a human, wherein the implantable tissue may be allowed to dry prior to implanting, or it may be hydrated prior to implanting. In addition, the tissue 800 is suitable for use in forming a tissue leaflet assembly 848 for use in a prosthetic heart valve, including an implantable prosthetic heart valve 860 that can be implanted with its tissue leaflet assembly in a dry state, or with its tissue leaflet assembly in a partially or fully hydrated state.

One or more of the embodiments of the tissue leaflet assemblies described herein may be implanted into the patient using a balloon-expandable frame or a self-expanding frame. Expandable frames are generally conveyed to the site of the target valve on balloon catheters.

For insertion, the expandable frame is positioned in a compressed configuration along the delivery device, for example crimped onto the balloon of a balloon catheter that is part of the delivery device intended for coaxial mounting on a guidewire. After the expandable frame is positioned across the plane of the valve, the expandable frame is expanded by the delivery device. For a self-expanding frame, commonly a sheath is retracted, allowing expansion of the self-expanding frame.

In at least one embodiment, the frame comprises a metal alloy frame possessing a high strain design tolerance that is compressible to a relatively small diameter. By providing a device with a low profile, the implantable prosthetic heart valve 860 allows standard retrograde arterial aortic delivery via femoral artery insertion, without surgical cutdown or general anesthesia. This is achieved by providing the prosthetic heart valve on a premounted delivery system with the tissue leaflet assembly or tissue membrane construct in a substantially dry condition.

In accordance with one or more embodiments, a dry tissue membrane has substantially less mass than a wet membrane. By way of example, a substantially dry pericardium tissue prepared by one or more of the present embodiments has approximately 30% of the mass of a wet pericardium tissue, and marked reduction in profile and packing volume, thereby achieving a relatively low profile and making it suitable for implantation in greater number of patients, especially those having small diameter vascular systems. In addition, a dry prosthetic heart valve does not require storage and transport in preservative. A dry prosthetic heart valve can be mounted on a delivery catheter at its location of manufacture, which allows for pre-packaging of an integrated delivery system. In the foregoing sentence, it is noted that the term "mounted" means that the prosthetic heart valve 860 is temporarily associated with the delivery catheter. Together with a relatively low profile, embodiments of the prosthetic heart valve thereby offer reliability and convenience because the implantable prosthetic heart valve 860 is pre-mounted upon its delivery catheter and forms part of a pre-packaged delivery system. In addition, a dry prosthetic heart valve does not require rinsing, rehydration, or mounting in a catheterization lab. Therefore, a dry prosthetic heart valve can be inserted directly from package into the patient's body at a critical time during the procedure. Advantageously, this avoids procedure time, manipulation, and errors of mounting, crimping, and orienting catheters and sheaths. Once at the surgical facility/location, the dry prosthetic heart valve is inserted and delivered by balloon catheter expansion in the plane of the target valve in the standard way and the dry prosthetic heart valve begins to function immediately, even without specific steps to rehydrate the tissue membrane portion of the heart valve from its dry state, with hydration of the tissue membrane subsequently occurring rapidly and naturally in the body. More particularly, hydration of the tissue membrane portion occurs rapidly and begins with simple preparatory flushing of catheter

lumens with saline. Thereafter, hydration continues with device insertion and dwelling into the central blood vessels, and completes naturally after deployment in the patient's body.

The low profile of the implantable prosthetic valve is particularly advantageous for patient's having relatively small diameter vascular systems. Table 1 provides aortic and pulmonary valve prosthesis sizing.

Table 1: Aortic and Pulmonary Valve Prosthesis Sizing

Aorta/Pulmonary Valve Diameter	**Collapsed Implantable Prosthetic Heart Valve Size (French)**	**Collapsed Implantable Prosthetic Heart Valve Diameter**
19 - 21 mm	12 French	4.0 mm
22 - 26 mm	14 French	4.7 mm
27 - 30 mm	16 French	5.3 mm

For most human patients, the femoral artery has a diameter of between about 5-8 mm. Accordingly, it is apparent that embodiments of the collapsed implantable prosthetic heart valves 860 described herein offer a low profile that enables a larger group of patients to qualify for receiving an implantable prosthetic heart valve 860. As a result of the sizing advantages offered by one or more embodiments of implantable prosthetic heart valves 860 described herein, virtually no candidate patients would be excluded from treatment with an implantable prosthetic heart valve 860 without open heart surgery and without general anesthesia on the basis of inadequate femoral blood vessel access caliber. In addition, one or more embodiments of the implantable prosthetic heart valve 860 described herein feature a scalable construct, wherein the implantable prosthetic heart valves 860 can be produced to accommodate target valve diameters ranging between 6 - 35 mm, and wherein the implantable prosthetic heart valves 860 offer consistent function using fundamentally a single design.

Referring now to Fig. 5, the mounting of the implantable prosthetic heart valve 860 into a delivery system at 500 is further described. More particularly, at 504 an implantable prosthetic heart valve 860 (also referred to herein as a percutaneously deliverable heart valve) is collapsed. The initial phase of collapsing the percutaneously deliverable heart valve is executed with the tissue membrane in a hydrated condition. That is, since the percutaneously deliverable heart valve 860 includes the frame 852 with the tissue leaflet assembly 848 attached within the frame 852, the percutaneously deliverable heart valve 860 is collapsed down as an integral unit. If a balloon-expandable frame is used, then an axial puller may be utilized to collapse down the frame 852 of the percutaneously deliverable heart valve 860 without the application of force directly to the sides of the frame 852. This procedure offers the advantage of preserving the cell structure of the frame 852 while also maintaining the orientation of the leaflets of the tissue leaflet assembly 848 as the percutaneously deliverable heart valve 860 is compressed. The

proper orientation and disposition of the leaflets is facilitated by the hydrated state of the leaflets. This assists in preventing tissue prolapse or bulging of the tissue 800 or 802 through the frame 852. In addition, this technique reduces recompression strain on the metal frame 852 (e.g., a stent) that can tend to compromise fatigue life of the frame 852. This technique also tends to promote the circumferentially uniform collapsing of cells in the frame 852, thereby mitigating bunching of the tissue that forms the tissue leaflet assembly 848 of the percutaneously deliverable heart valve 860. For a self-expanding frame, the sides are forced to collapse by providing a radial compression force to the frame and may be assisted by axial traction force.

With further reference to Fig. 5, the percutaneously deliverable heart valve 860 (i.e., the frame 852 with the tissue leaflet assembly 848 attached thereto) is collapsed in an initially hydrated state. At 508 the delivery mandrel or balloon is inserted into a delivery sheath, and the mounting segment is then extended out the end of the sheath. Thereafter, at 512 the sheath and frame are coaxially mounted and then compressed with initial crimping onto the mounting segment with the tissue leaflet assembly 848 still in a hydrated state. At 516, the tissue leaflet assembly 848 of the percutaneously deliverable heart valve 860 is then allowed to dry, which further reduces the volume and profile of the tissue membrane leaflets, permitting further compression by radial force. Accordingly, in the final compression step, the percutaneously deliverable heart valve 860 is then further crimped with a circumferential crimping tool at 520 to finally mount the compressed valve/frame onto the delivery mandrel or balloon catheter.

Referring now to Fig. 6, the ensheathing, sterilization and packaging at 600 is described. More particularly, once the percutaneously deliverable heart valve 860 is coaxially mounted and crimped on a delivery mandrel or balloon catheter as described above and shown in Fig. 5, the assembly is then inserted at 604 into a distal end of a delivery sheath, such as by "backloading" the assembly into position with a distal end of the percutaneously deliverable heart valve 860 contained within the delivery sheath proximate the end of the sheath. Reference here is made to Fig. 10 that schematically illustrates catheter 1000 with an implantable prosthetic heart valve 860 mounted thereto.

With further reference to Fig. 6, at 608 the percutaneously deliverable heart valve 860 and delivery catheters are sterilized, such as by using by one or more of ethylene oxide, proton beam, or gamma radiation. At 612, the assembly is then optionally packaged in a sterile package. Additional elements are optionally shipped with the assembly, wherein, by way of example, such elements may include any necessary delivery tools and documentation. In at least one embodiment, the package may optionally contain a device to control the water vapor content

within the sealed volume of the package. Fig. 13 depicts a surgeon holding a sterile package 1300 containing a premounted percutaneously implantable prosthetic heart valve.

Referring now to Fig. 7, a flow chart illustrating the general procedure associated with implantation of the percutaneously deliverable heart valve 860 is provided. More particularly, at 704, catheter access is gained to the patient's femoral artery and a guidewire is placed through the plane of the diseased valve that is targeted to receive the implant. Fig. 14 is a schematic of a simplified cutaway view of a human heart, including heart valves that may be targeted for receiving an embodiment of an implantable prosthetic heart valve. Fig. 15 illustrates the aorta with the guidewire placed through the diseased aortic valve. At 708, the percutaneously deliverable heart valve 860 in the form of a prepackaged assembled dry prosthetic heart valve is removed from the sterile packaging. The dry prosthetic heart valve assembly, including its lumens, are preferably flushed and prepared in the usual fashion for standard balloons and catheters that do not contain a biocompatible tissue. Advantageously, implantation of the dry prosthetic heart valve assembly can be conducted without specific maneuvers for rehydration of the tissue leaflet assembly 848 of the percutaneously deliverable heart valve 860. Some rehydration of the tissue leaflets may occur as a consequence of the routine flushing of the catheter lumens in preparation for use as with any other catheters. Additionally, implantation of the dry prosthetic heart valve assembly can proceed without additional cleaning steps, such as by having to use alcohol or water rinsing solutions. In addition, further mounting of the dry tissue leaflet assembly 848 that resides in the frame 852 of the percutaneously deliverable heart valve 860 is not needed, thereby obviating the need for another mounting step. Accordingly, the percutaneously deliverable heart valve 860 can essentially be implanted percutaneously in its dry state. At 712, the carrier catheter or balloon catheter is then coaxially mounted and advanced over the guidewire, such as under fluoroscopic vision initially to the level of the great vessel where it can be inspected under fluoroscopy. At 716, and after the nominal position and configuration is confirmed, the delivery system is advanced through the plane of the diseased valve under fluoroscopy, and the covering sheath is withdrawn, either at this point or during the advance prior to it, thus exposing the mounted implantable prosthetic heart valve 860 in place. At 720, in the case of a balloon expandable frame, and assuming the delivery approach involving the pre-mounting of the percutaneously deliverable heart valve 860 on the expansion balloon, the balloon is then inflated, deploying the percutaneously deliverable heart valve 860 in the plane of the valve. At 724, the leaflets of the percutaneously deliverable heart valve 860 operate immediately. The deployed prosthetic heart valve 860 is shown in Fig. 16, wherein the tissue leaflet assembly 848 serves to properly control the flow blood.

The present invention may be embodied in other specific forms without departing from

its spirit or essential characteristics. The described embodiments are to be considered in all respects only as illustrative and not restrictive. The scope of the invention is, therefore, indicated by the appended claims rather than by the foregoing description. All changes which come within the meaning and range of equivalency of the claims are to be embraced within their scope.

The one or more present inventions, in various embodiments, include components, methods, processes, systems and/or apparatus substantially as depicted and described herein, including various embodiments, subcombinations, and subsets thereof. Those of skill in the art will understand how to make and use the present invention after understanding the present disclosure.

The present invention, in various embodiments, includes providing devices and processes in the absence of items not depicted and/or described herein or in various embodiments hereof, including in the absence of such items as may have been used in previous devices or processes (e.g., for improving performance, achieving ease and/or reducing cost of implementation).

The foregoing discussion of the invention has been presented for purposes of illustration and description. The foregoing is not intended to limit the invention to the form or forms disclosed herein. In the foregoing Detailed Description for example, various features of the invention are grouped together in one or more embodiments for the purpose of streamlining the disclosure. This method of disclosure is not to be interpreted as reflecting an intention that the claimed invention requires more features than are expressly recited in each claim. Rather, as the following claims reflect, inventive aspects lie in less than all features of a single foregoing disclosed embodiment. Thus, the following claims are hereby incorporated into this Detailed Description, with each claim standing on its own as a separate preferred embodiment of the invention.

Moreover, though the description of the invention has included description of one or more embodiments and certain variations and modifications, other variations and modifications are within the scope of the invention (e.g., as may be within the skill and knowledge of those in the art, after understanding the present disclosure). It is intended to obtain rights which include alternative embodiments to the extent permitted, including alternate, interchangeable and/or equivalent structures, functions, ranges or acts to those claimed, whether or not such alternate, interchangeable and/or equivalent structures, functions, ranges or acts are disclosed herein, and without intending to publicly dedicate any patentable subject matter.

CLAIMS

What is claimed is:

1. An assembly, comprising:

a prosthetic heart valve including:

a frame; and

a tissue leaflet assembly attached to the frame;

a percutaneously insertable valve delivery mechanism, wherein the prosthetic heart valve is releasably mounted onto the percutaneously insertable valve delivery mechanism; and

sterile packaging containing the prosthetic heart valve releasably mounted onto the percutaneously insertable valve delivery mechanism.

2. The assembly of Claim 1, wherein the percutaneously insertable valve delivery mechanism comprises a balloon catheter.

3. The assembly of Claim 2, wherein the balloon catheter is a 12 to 14 French balloon catheter.

4. The assembly of Claim 2, wherein the balloon catheter is less than about 12 French.

5. The assembly of Claim 2, wherein the balloon catheter is between about 5 to 12 French.

6. The assembly of Claim 1, wherein the percutaneously insertable valve delivery mechanism comprises a mandrel.

7. The assembly of Claim 1, wherein tissue forming the tissue leaflet assembly within the sterile packaging is at least one of hydrated and not substantially dry.

8. The assembly of Claim 1, wherein tissue forming the tissue leaflet assembly within the sterile packaging is substantially dry.

9. The assembly of Claim 1, wherein the frame comprises a stent.

10. The assembly of Claim 1, wherein tissue forming the tissue leaflet assembly comprises treated pericardium tissue.

11. A pre-packaged percutaneous, trans-catheter deliverable prosthetic heart valve ready for implantation in a patient, comprising:

a frame; and

a tissue leaflet assembly attached to the frame, the tissue leaflet assembly comprising a substantially dry tissue.

12. The pre-packaged percutaneous, trans-catheter deliverable prosthetic heart valve of Claim 11, wherein the substantially dry tissue comprises treated pericardium tissue.

13. The pre-packaged percutaneous, trans-catheter deliverable prosthetic heart valve of Claim 11, wherein the substantially dry tissue comprises a water moisture content of less than about 40% by weight of the substantially dry tissue.

14. The pre-packaged percutaneous, trans-catheter deliverable prosthetic heart valve of Claim 11, wherein the frame and the tissue leaflet assembly attached thereto are operably associated with a 12 to 14 French balloon catheter.

15. The pre-packaged percutaneous, trans-catheter deliverable prosthetic heart valve of Claim 11, wherein the frame and the tissue leaflet assembly attached thereto are operably associated with a balloon catheter having a size of less than about 12 French.

16. The pre-packaged percutaneous, trans-catheter deliverable prosthetic heart valve of Claim 11, wherein the frame and the tissue leaflet assembly attached thereto are operably associated with a balloon catheter having a size of between about 5 to 12 French.

17. An assembly for use with a patient, comprising:

a sealed sterile package containing a delivery system for percutaneously deploying a heart valve in the patient, the heart valve including:

a frame releasably mounted on the delivery system within the sealed sterile package; and

a tissue leaflet assembly attached to the frame.

18. The assembly of Claim 17, wherein the tissue leaflet assembly comprises a treated pericardium tissue.

19. The assembly of Claim 17, wherein the delivery system includes a percutaneously insertable balloon catheter.

20. The assembly of Claim 19, wherein the balloon catheter is a 12 to 14 French balloon catheter.

21. The assembly of Claim 19, wherein the balloon catheter is less than about 12 French.

22. The assembly of Claim 19, wherein the balloon catheter is between about 5 to 12 French.

23. The assembly of Claim 17, wherein the delivery system includes a percutaneously insertable mandrel.

24. The assembly of Claim 17, wherein the tissue leaflet assembly within the sealed sterile package is at least one of partially hydrated and not substantially dry.

25. The assembly of Claim 17, wherein the tissue leaflet assembly within the sealed sterile package is substantially dry.

26. The assembly of Claim 17, wherein the frame comprises a stent.

27. An article adapted for implantation in a patient, comprising:

a prosthetic heart valve further comprising a treated tissue attached to a frame, wherein the treated tissue comprises a water content of less than about 60% by weight of the treated tissue.

28. The article of Claim 27, wherein the treated tissue comprises a section of treated pericardium tissue having an ultimate tensile strength of greater than about 12 MegaPascals.

29. The article of Claim 28, wherein the section of pericardium tissue comprises a thickness of between about 50 to 300 micrometers.

30. The article of Claim 27, wherein the water content of the treated tissue is less than about 40% by weight of the treated tissue.

31. An article adapted for trans-catheter delivery into a patient, comprising:

a prosthetic heart valve further comprising a treated tissue attached to a frame, wherein the treated tissue comprises a thickness of about 50 to 500 micrometers and an ultimate tensile strength of greater than about 15 MegaPascals when at a water content of less than about 50% by weight of the treated tissue.

32. The article of Claim 31, wherein the treated tissue comprises a treated pericardium tissue.

33. The article of Claim 31, wherein the water content of the treated tissue is less than about 40% by weight of the treated tissue.

34. The article of Claim 31, wherein the ultimate tensile strength is greater than about 20 MegaPascals.

35. The article of Claim 31, wherein the treated tissue does not include a matrix that has been exposed to a polymer infiltrate.

36. A method, comprising:

partially compressing and mounting a prosthetic heart valve upon a delivery catheter, the prosthetic heart valve comprising a tissue;

allowing the tissue to at least partially dry;

further compressing and mounting the prosthetic heart valve upon the delivery catheter; and

sterilizing and packaging the prosthetic heart valve and delivery catheter.

37. The method of Claim 36, further comprising transporting the sterilized and packaged prosthetic heart valve and delivery catheter.

38. The method of Claim 36, wherein the tissue comprises a treated pericardium tissue.

39. The method of Claim 36, wherein prior to partially compressing and mounting the prosthetic heart valve upon the delivery catheter, the tissue is at least one of (a) not substantially dry, and (b) at least partially hydrated.

40. A method, comprising:

attaching a tissue to a frame;

partially compressing and mounting the frame, with the tissue attached thereto, upon a delivery catheter;

allowing the tissue to at least partially dry;

further compressing and mounting the frame, with the tissue attached thereto, upon the delivery catheter; and

sterilizing and packaging the frame and delivery catheter, with the tissue attached thereto.

41. The method of Claim 40, wherein prior to partially compressing and mounting the frame, the tissue is at least one of (a) not substantially dry, and (b) at least partially hydrated.

42. The method of Claim 40, further comprising transporting the sterilized and packaged frame, with the tissue attached thereto, mounted upon the delivery catheter, to a surgical or medical procedure facility.

43. The method of Claim 40, wherein prior to attaching the tissue to the frame the tissue is folded to form a tissue leaflet assembly.

44. The method of Claim 43, wherein the tissue leaflet assembly comprises at least one cuff and at least one pleat.

45. The method of Claim 40, wherein the tissue comprises a treated pericardium tissue.

46. A method of preparing a percutaneous, trans-catheter prosthetic heart valve, comprising:

providing a membrane tissue from an organism;

treating the membrane tissue with at least one chemical to produce a treated membrane tissue;

drying the treated membrane tissue until it is a substantially dry tissue;

attaching the substantially dry tissue to a frame;

rehydrating the substantially dry tissue that is attached to the frame to form a rehydrated tissue;

collapsing the frame with the rehydrated tissue attached thereto; and

drying the rehydrated tissue attached to the collapsed frame until it is a substantially dry tissue.

47. The method of preparing a percutaneous, trans-catheter prosthetic heart valve of Claim 46, further comprising compressing and mounting the frame, with the tissue attached thereto, upon a delivery catheter.

48. The method of preparing a percutaneous, trans-catheter prosthetic heart valve of Claim 47, further comprising sterilizing and packaging the frame, with the substantially dry tissue attached thereto, mounted upon the delivery catheter.

49. The method of preparing a percutaneous, trans-catheter prosthetic heart valve of Claim 48, further comprising at least one of transporting and shipping the sterilized and packaged frame with the substantially dry tissue attached thereto, mounted upon the delivery catheter, to a surgical or medical procedure facility.

50. The method of preparing a percutaneous, trans-catheter prosthetic heart valve of Claim 49, further comprising implanting the frame with the substantially dry tissue attached thereto into a patient.

51. The method of preparing a percutaneous, trans-catheter prosthetic heart valve of Claim 46, wherein the frame comprises a stent.

52. The method of preparing a percutaneous, trans-catheter prosthetic heart valve of Claim 46, wherein prior to the attaching step the dry tissue is not folded with a cuff and a pleat.

53. The method of preparing a percutaneous, trans-catheter prosthetic heart valve of Claim 46, wherein prior to the attaching step the dry tissue is folded to form a tissue leaflet assembly.

54. The method of preparing a percutaneous, trans-catheter prosthetic heart valve of Claim 53, wherein the tissue leaflet assembly comprises at least one cuff and at least one pleat.

55. The method of preparing a percutaneous, trans-catheter prosthetic heart valve of Claim 53, further comprising mounting the frame and the tissue leaflet assembly attached thereto upon a 12 to 14 French balloon catheter.

56. The method of preparing a percutaneous, trans-catheter prosthetic heart valve of Claim 53, further comprising mounting the frame and the tissue leaflet assembly attached thereto upon a balloon catheter having a size of less than about 12 French.

57. The method of preparing a percutaneous, trans-catheter prosthetic heart valve of Claim 53, further comprising mounting the frame and the tissue leaflet assembly attached thereto upon a balloon catheter having a size of between about 5 to 12 French.

58. The method of preparing a percutaneous, trans-catheter prosthetic heart valve of Claim 53, further comprising mounting the frame and the tissue leaflet assembly attached thereto on a mandrel.

59. The method of preparing a percutaneous, trans-catheter prosthetic heart valve of Claim 46, further comprising sterilizing the frame with the substantially dry tissue attached thereto with exposure to at least one of ethylene oxide, a proton beam, and gamma radiation.

60. The method of preparing a percutaneous, trans-catheter prosthetic heart valve of Claim 46, wherein said treating comprises immersion of the membrane tissue in a buffered or unbuffered 1 – 37.5% formalin solution for between about 3 days to 3 weeks.

61. The method of preparing a percutaneous, trans-catheter prosthetic heart valve of Claim 46, wherein said treating comprises immersion of the membrane tissue in a buffered or unbuffered 1 – 37.5% formalin solution for between about 3 days to 5 weeks.

62. The method of preparing a percutaneous, trans-catheter prosthetic heart valve of Claim 46, wherein said treating comprises immersion of the membrane tissue in a buffered or unbuffered 1 - 37.5% formalin solution containing at least one of free amino acids (a) lysine and (b) histidine, for between about 3 days to 3 weeks.

63. The method of preparing a percutaneous, trans-catheter prosthetic heart valve of Claim 46, wherein said treating comprises immersion of the membrane tissue in a buffered or unbuffered 1 - 37.5% formalin solution containing at least one of free amino acids (a) lysine and (b) histidine, for between about 3 days to 5 weeks.

64. The method of preparing a percutaneous, trans-catheter prosthetic heart valve of Claim 46, wherein said treating comprises immersion of the membrane tissue in 100% glycerol for greater than about 3 weeks.

65. The method of preparing a percutaneous, trans-catheter prosthetic heart valve of Claim 46, wherein said treating comprises immersion of the membrane tissue in a 0.1 - 25% glutaraldehyde solution for between about 3 days to 3 weeks.

66. The method of preparing a percutaneous, trans-catheter prosthetic heart valve of Claim 46, wherein said treating comprises immersion of the membrane tissue in a 0.1 - 25% glutaraldehyde solution for between about 3 days to 5 weeks.

67. The method of preparing a percutaneous, trans-catheter prosthetic heart valve of Claim 46, wherein said treating comprises immersion of the membrane tissue in a 0.1 - 25% glutaraldehyde solution containing at least one of free amino acids (a) lysine and (b) histidine, for between about 3 days to 3 weeks.

68. The method of preparing a percutaneous, trans-catheter prosthetic heart valve of Claim 46, wherein said treating comprises immersion of the membrane tissue in a 0.1 - 25% glutaraldehyde solution containing at least one of free amino acids (a) lysine and (b) histidine, for between about 3 days to 5 weeks.

69. The met ous, trans-catheter prosthetic heart valve of Claim 46, wherein said treating comprises immersion of the membrane tissue in an oligomeric filtered 0.1 - 25% glutaraldehyde solution for between about 3 days to 3 weeks.

70. The method of preparing a percutaneous, trans-catheter prosthetic heart valve of Claim 46, wherein said treating comprises immersion of the membrane tissue in an oligomeric filtered 0.1 - 25% glutaraldehyde solution for between about 3 days to 5 weeks.

71. The method of preparing a percutaneous, trans-catheter prosthetic heart valve of Claim 46, wherein said treating comprises immersion of the membrane tissue in an oligomeric filtered 0.1 - 25% glutaraldehyde solution containing at least one of free amino acids (a) lysine and (b) histidine, for between about 3 days to 3 weeks.

72. The method of preparing a percutaneous, trans-catheter prosthetic heart valve of Claim 46, wherein said treating comprises immersion of the membrane tissue in an oligomeric filtered 0.1 - 25% glutaraldehyde solution containing at least one of free amino acids (a) lysine and (b) histidine, for between about 3 days to 5 weeks.

73. The method of preparing a percutaneous, trans-catheter prosthetic heart valve of Claim 46, wherein the membrane tissue comprises a treated pericardium tissue.

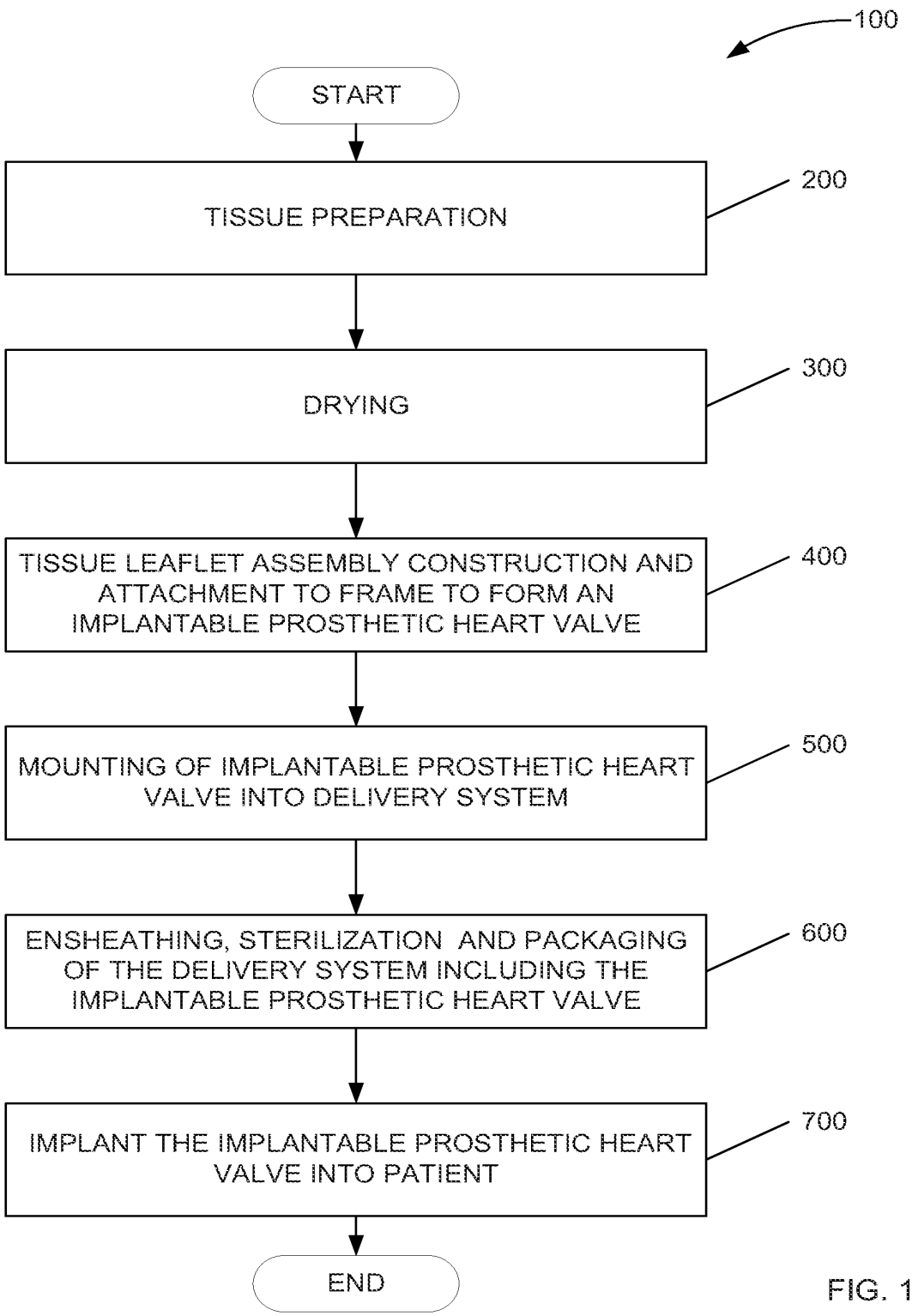


FIG. 1

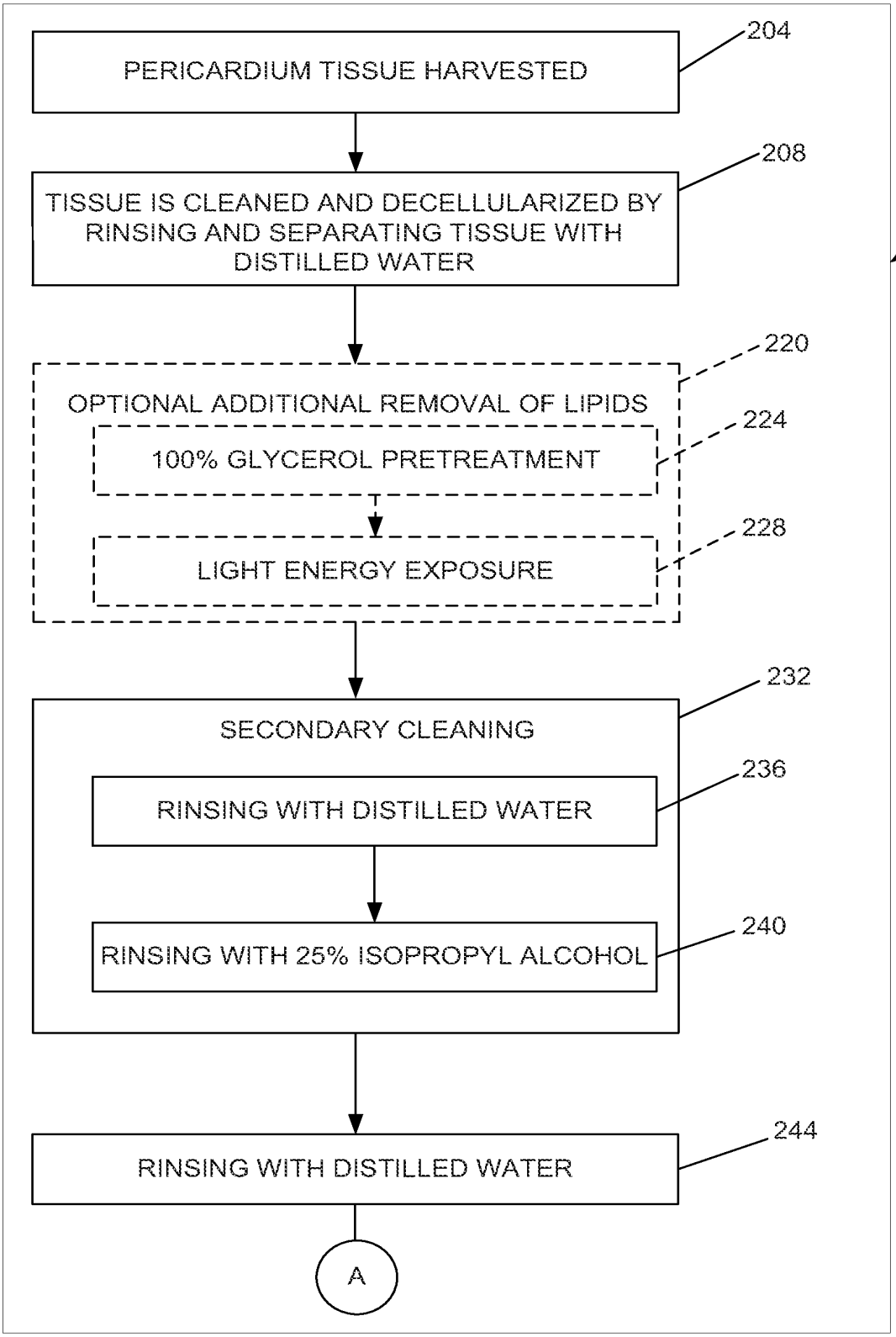


FIG. 2A

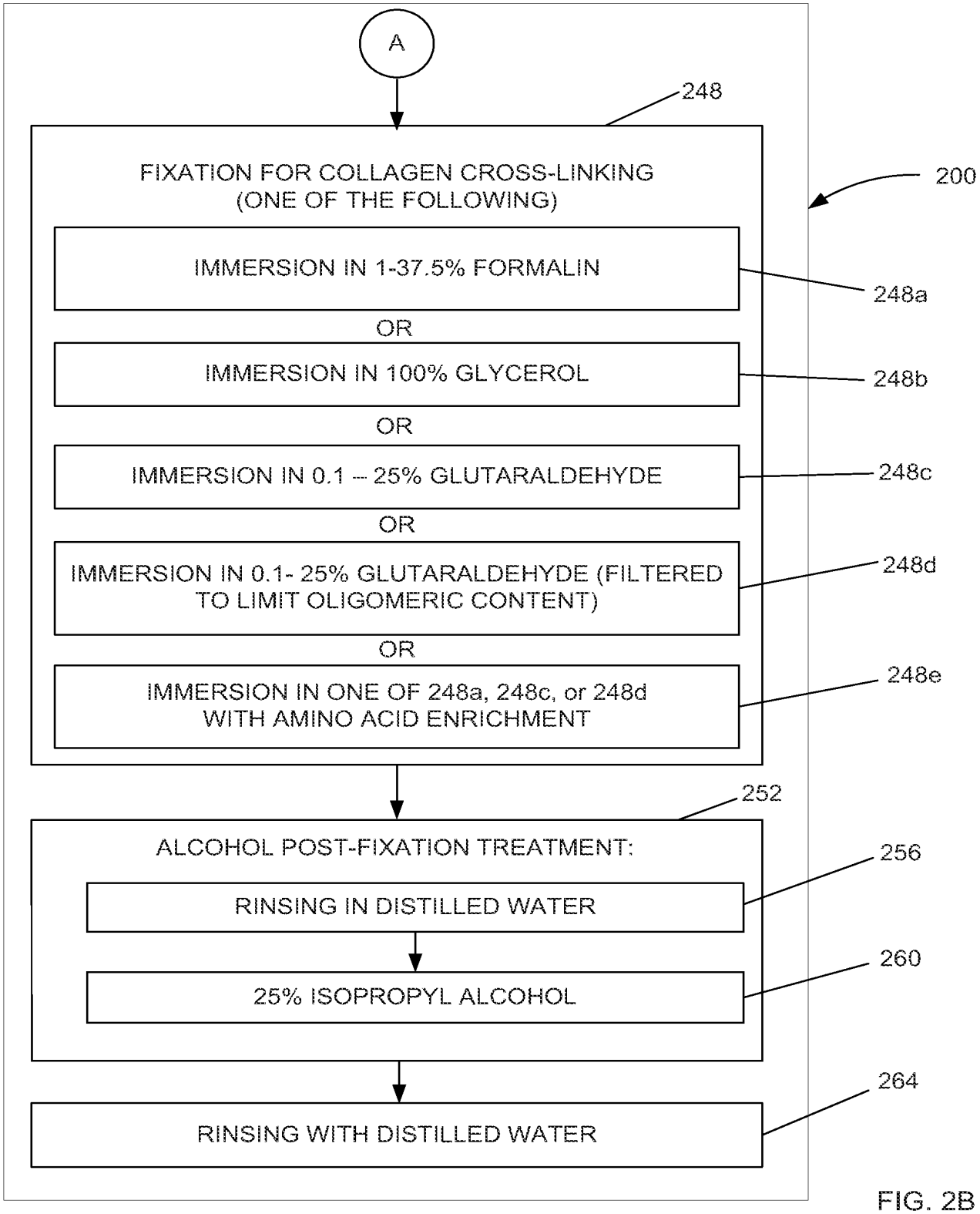

A
248
FIXATION FOR COLLAGEN CROSS-LINKING
(ONE OF THE FOLLOWING)
200
IMMERSION IN 1-37.5% FORMALIN
248a
OR
IMMERSION IN 100% GLYCEROL
248b
OR
IMMERSION IN 0.1 – 25% GLUTARALDEHYDE
248c
OR
IMMERSION IN 0.1- 25% GLUTARALDEHYDE (FILTERED TO LIMIT OLIGOMERIC CONTENT)
248d
OR
IMMERSION IN ONE OF 248a, 248c, or 248d WITH AMINO ACID ENRICHMENT
248e
252
ALCOHOL POST-FIXATION TREATMENT:
256
RINSING IN DISTILLED WATER
260
25% ISOPROPYL ALCOHOL
264
RINSING WITH DISTILLED WATER

FIG. 2B

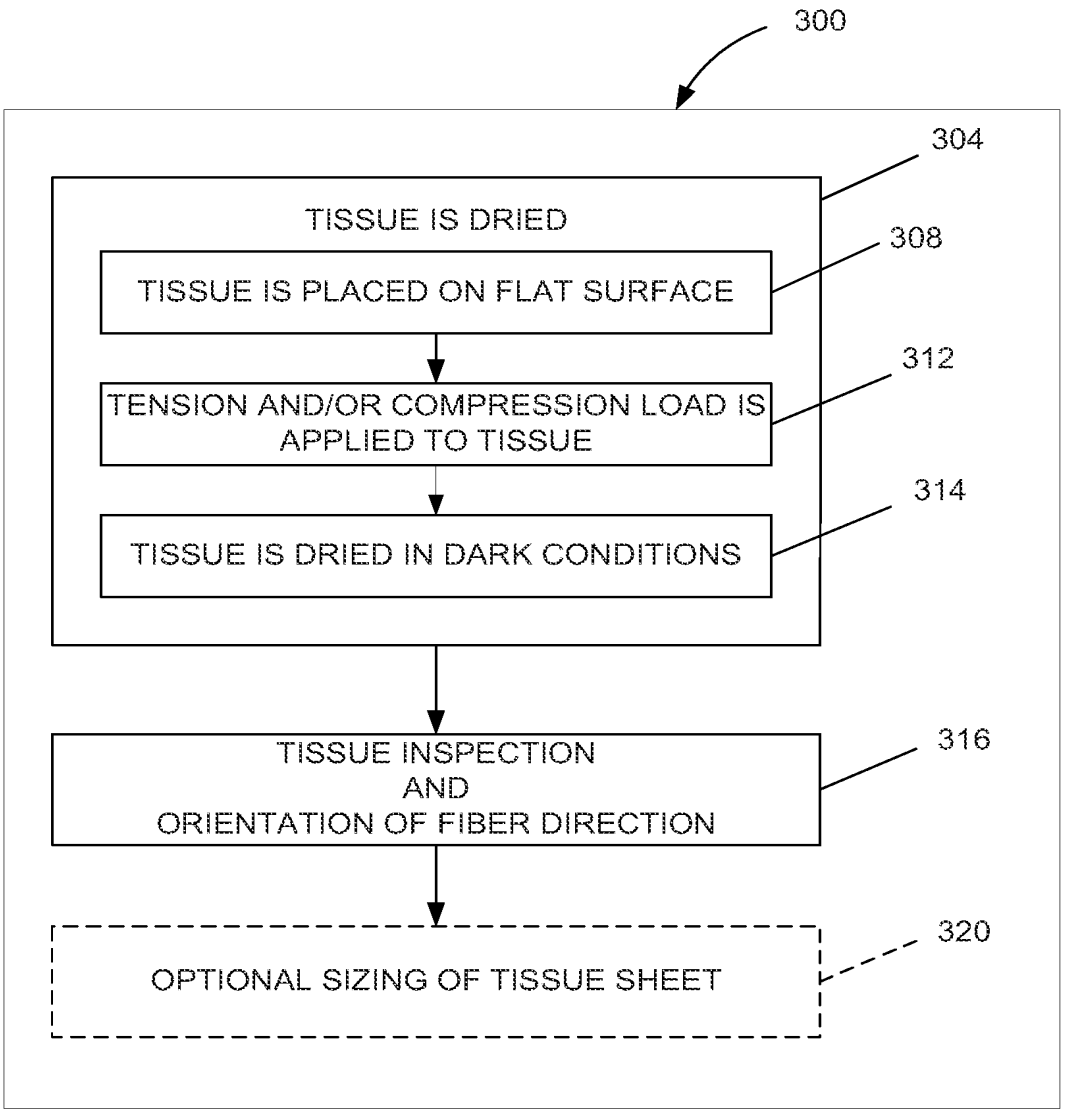


FIG. 3

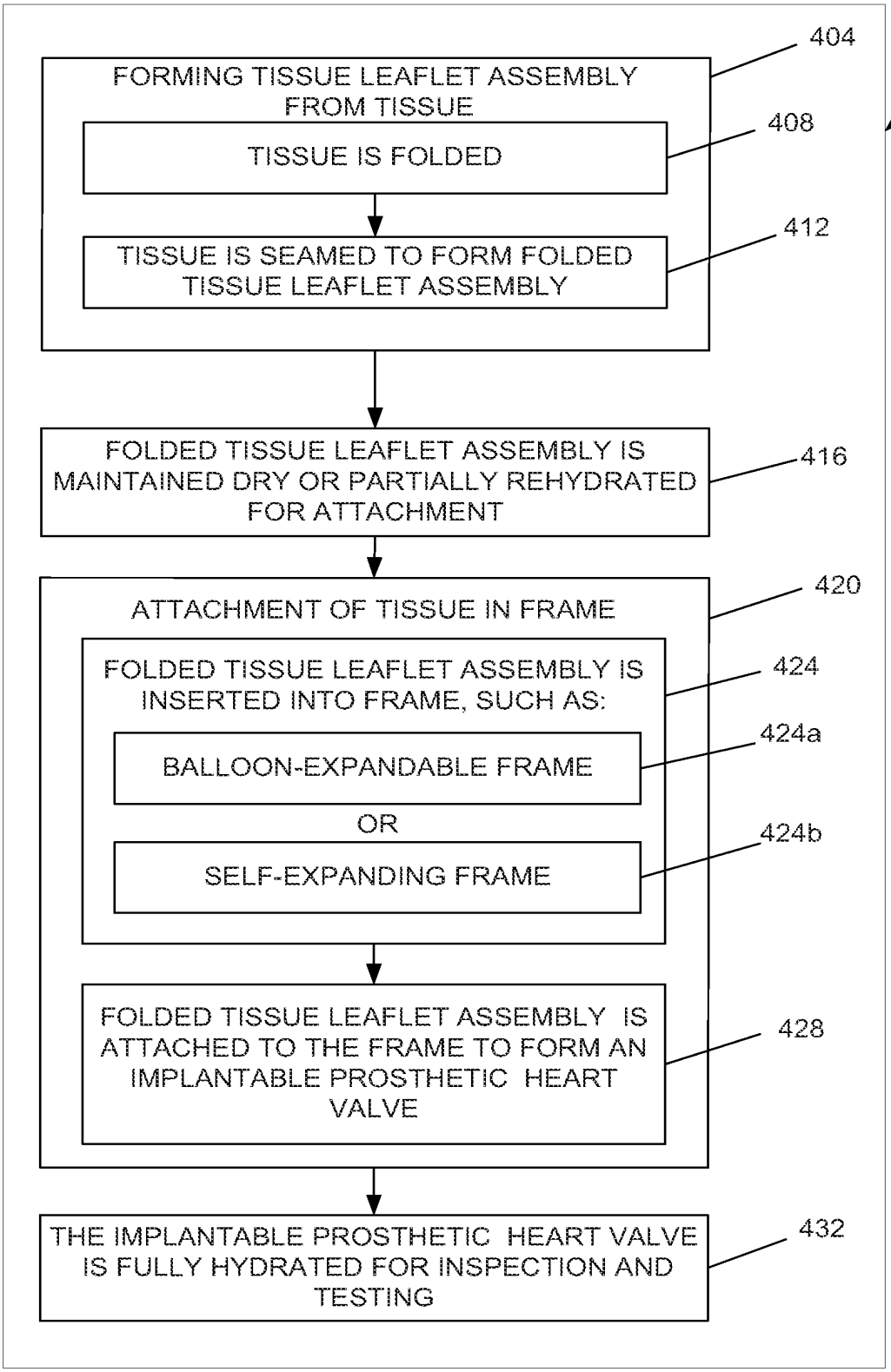


FIG. 4

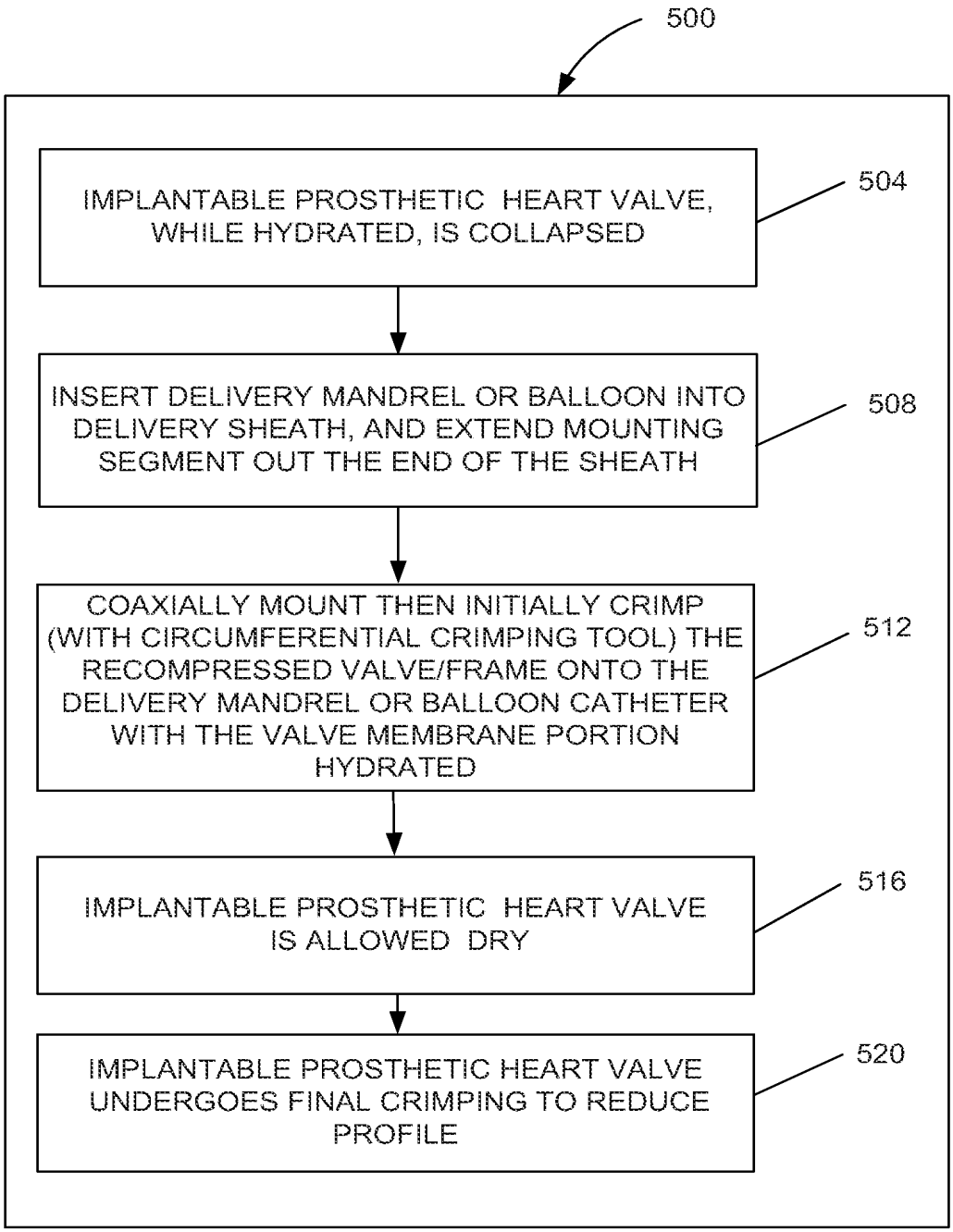

500
IMPLANTABLE PROSTHETIC HEART VALVE, WHILE HYDRATED, IS COLLAPSED
504
INSERT DELIVERY MANDREL OR BALLOON INTO DELIVERY SHEATH, AND EXTEND MOUNTING SEGMENT OUT THE END OF THE SHEATH
508
COAXIALLY MOUNT THEN INITIALLY CRIMP (WITH CIRCUMFERENTIAL CRIMPING TOOL) THE RECOMPRESSED VALVE/FRAME ONTO THE DELIVERY MANDREL OR BALLOON CATHETER WITH THE VALVE MEMBRANE PORTION HYDRATED
512
IMPLANTABLE PROSTHETIC HEART VALVE IS ALLOWED DRY
516
IMPLANTABLE PROSTHETIC HEART VALVE UNDERGOES FINAL CRIMPING TO REDUCE PROFILE
520

FIG. 5

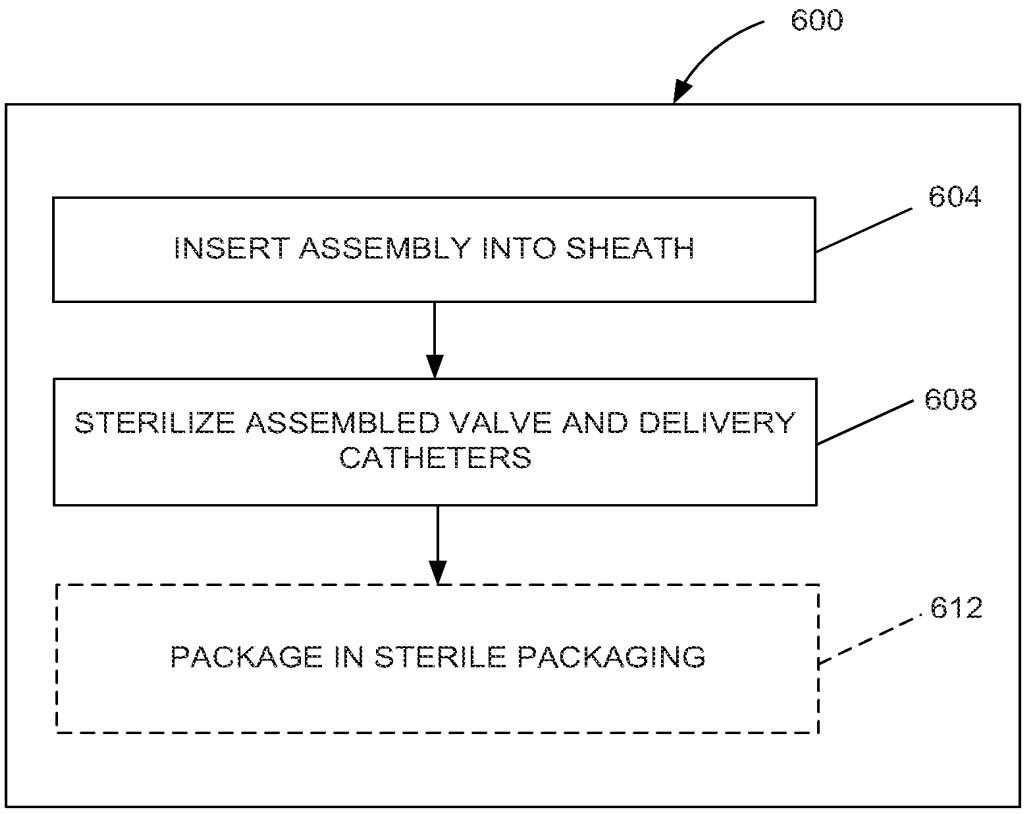


FIG. 6

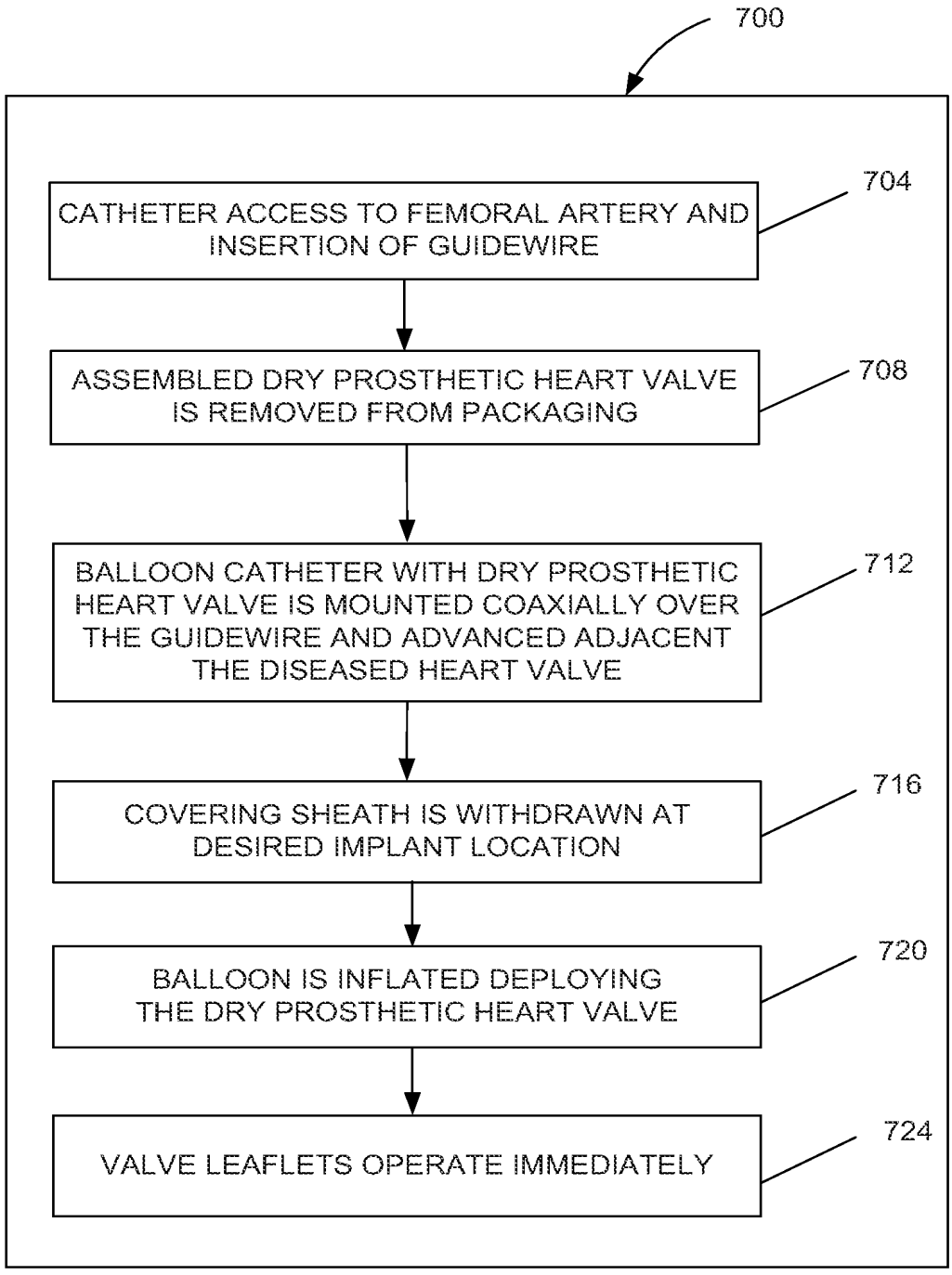


FIG.7

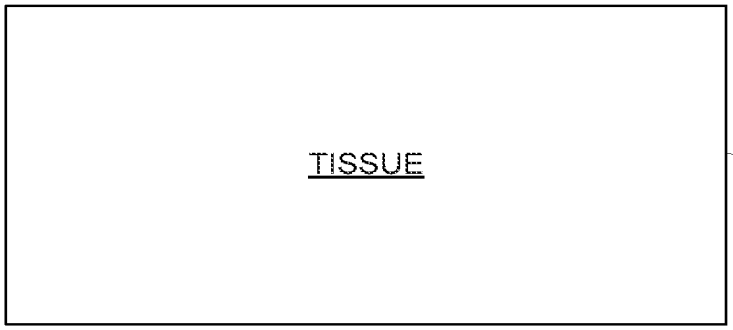


FIG.8A

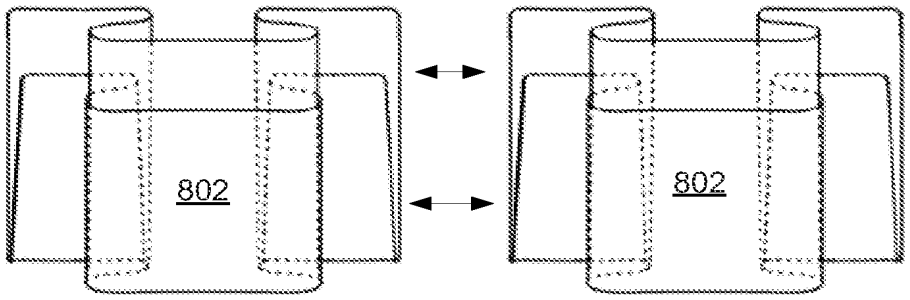


FIG.8B

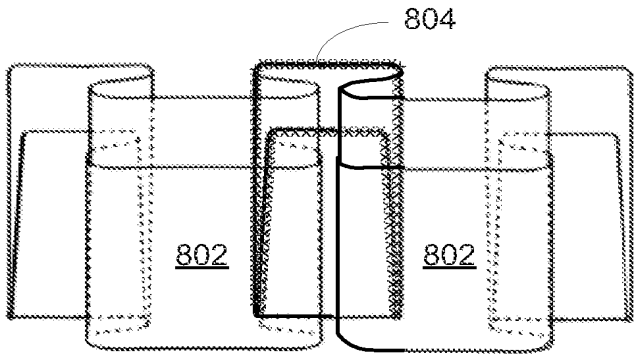


FIG.8C

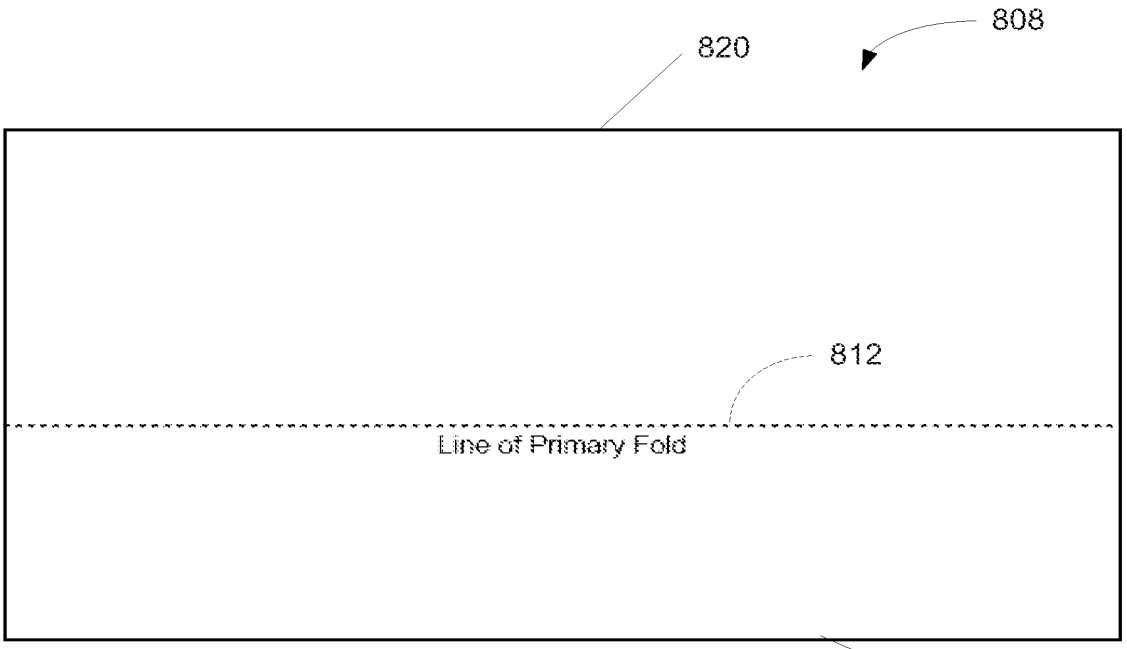

808
820
812
Line of Primary Fold
816

FIG.8D

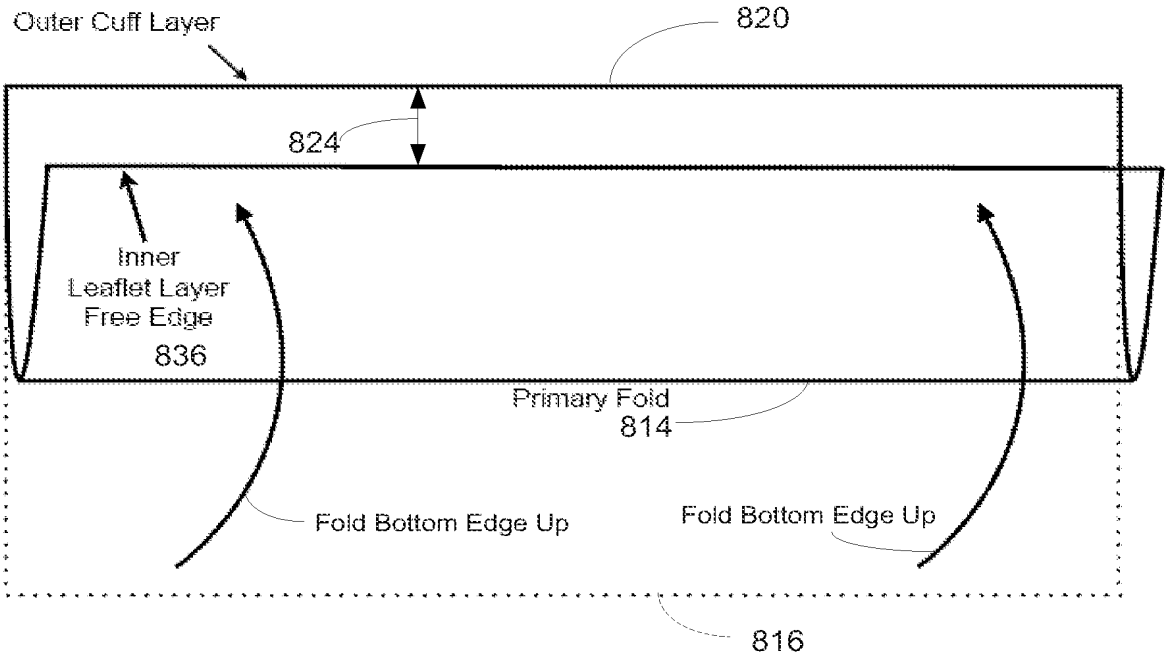

Outer Cuff Layer
820
824
Inner
Leaflet Layer
Free Edge
836
Primary Fold
814
Fold Bottom Edge Up
Fold Bottom Edge Up
816

FIG.8E

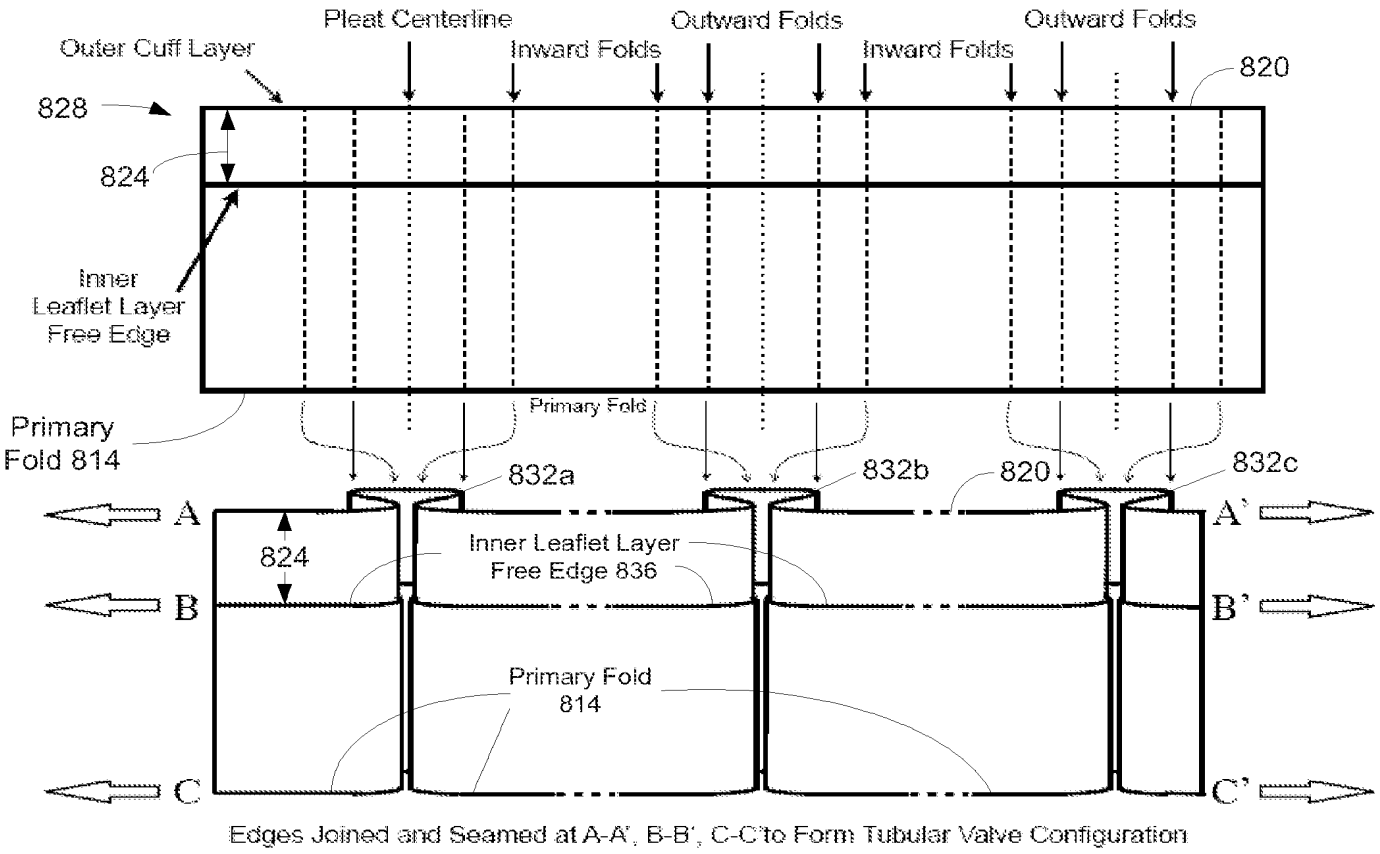

Pleat Centerline
Outward Folds
Outward Folds
Outer Cuff Layer
Inward Folds
Inward Folds
820
828
824
Inner
Leaflet Layer
Free Edge
Primary Fold
Primary
Fold 814
832a
832b
820
832c
A
A'
824
Inner Leaflet Layer
Free Edge 836
B
B'
Primary Fold
814
C
C'
Edges Joined and Seamed at A-A', B-B', C-C'to Form Tubular Valve Configuration

FIG.8F

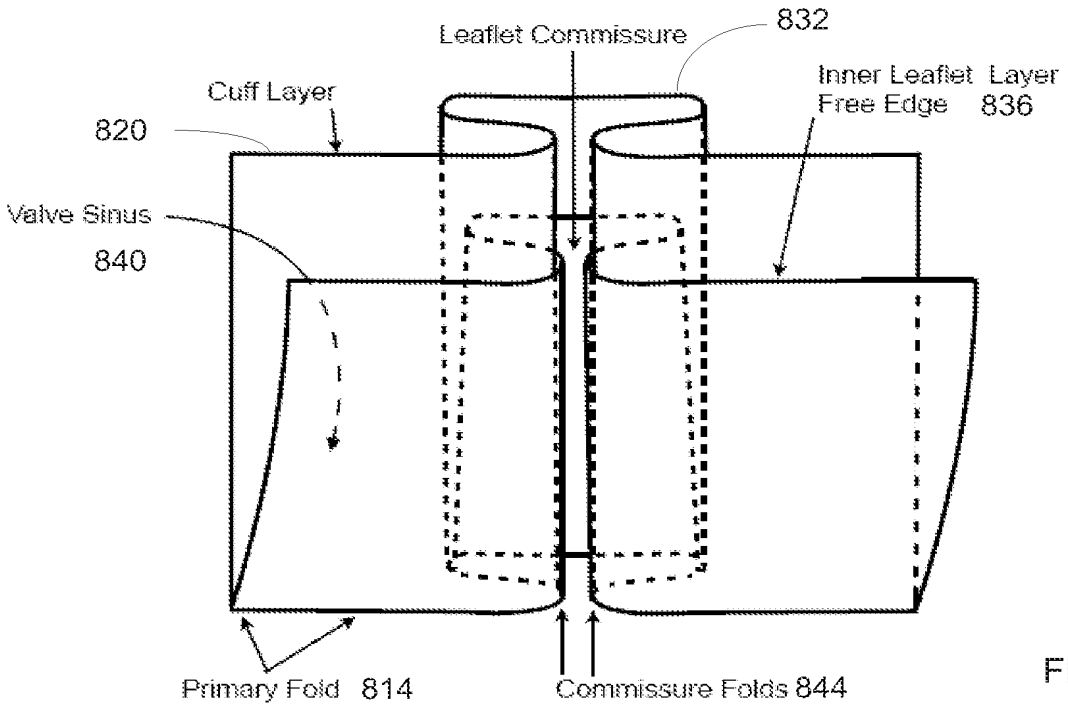
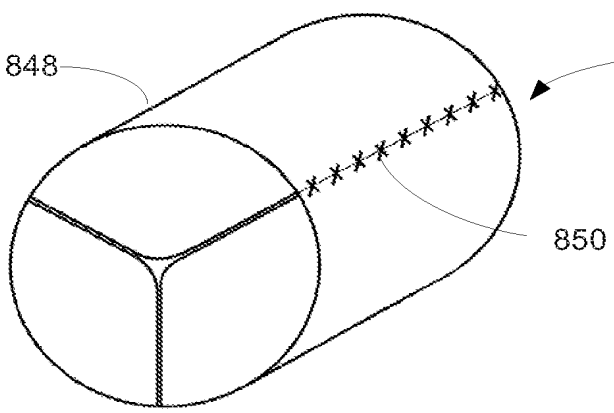


FIG.8G



TISSUE LEAFLET ASSEMBLY
(PLEATS NOT SHOWN, SEE FIG. 8L)

FIG.8H

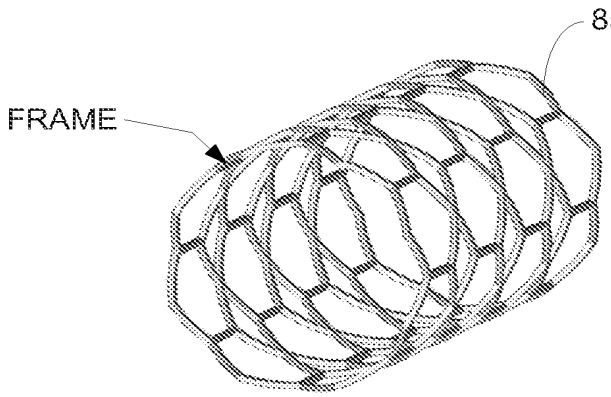


FIG.8I

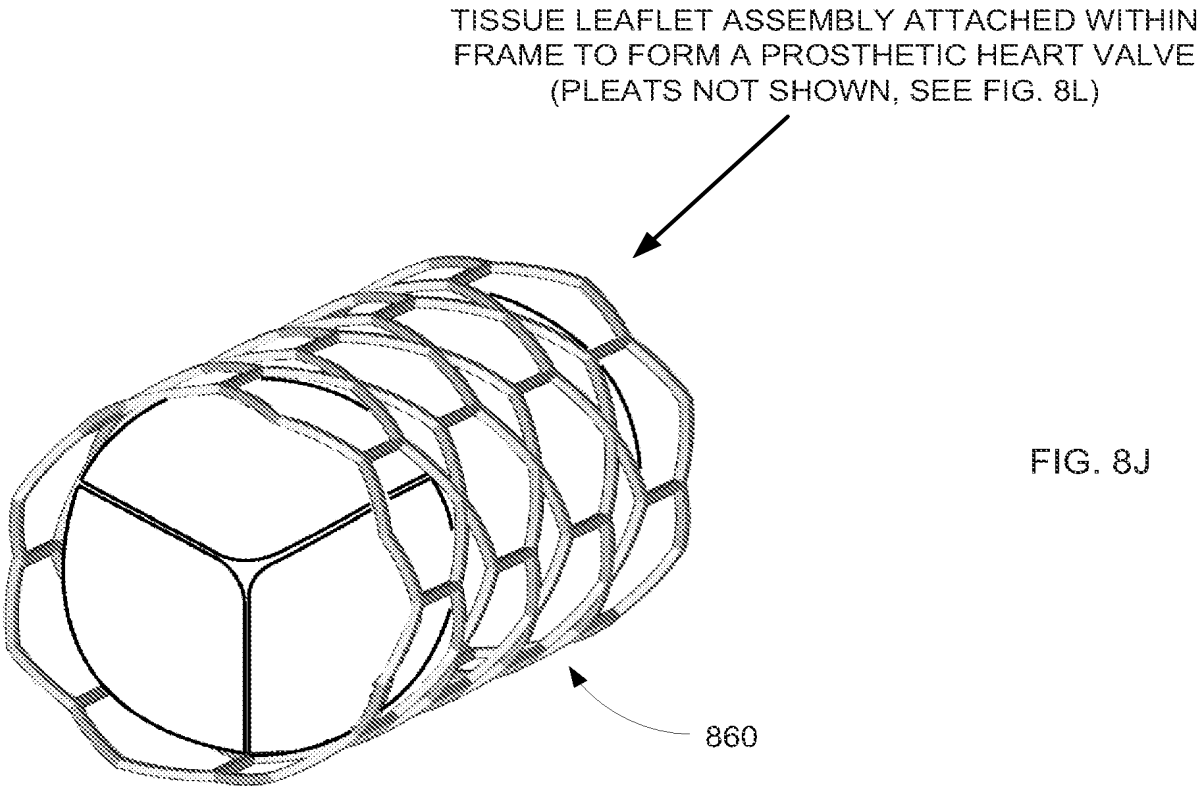


FIG. 8J

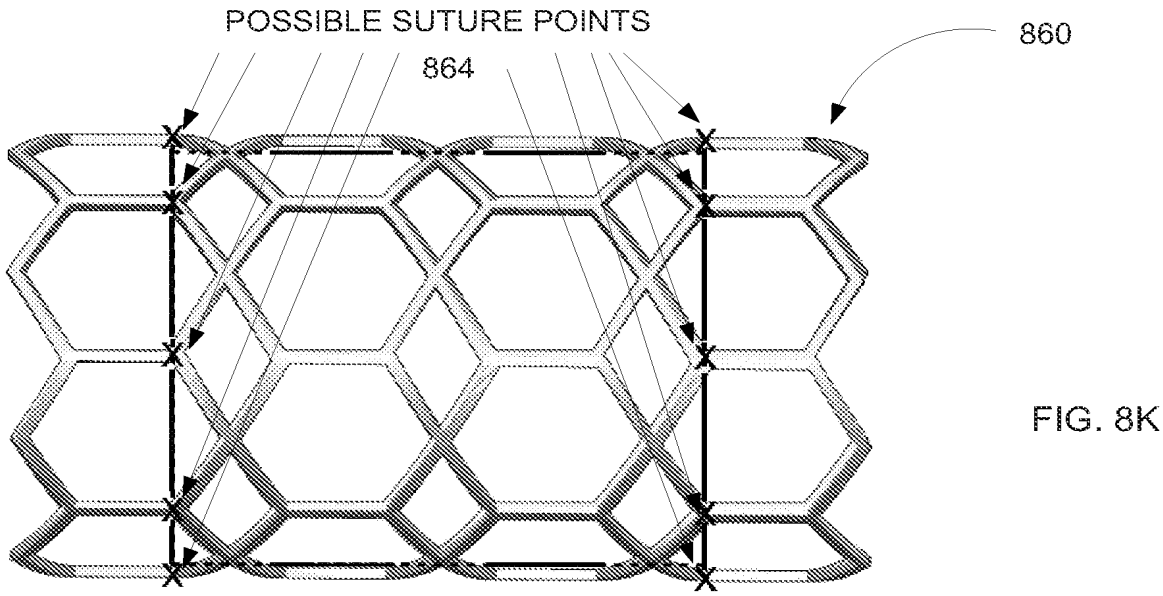


FIG. 8K

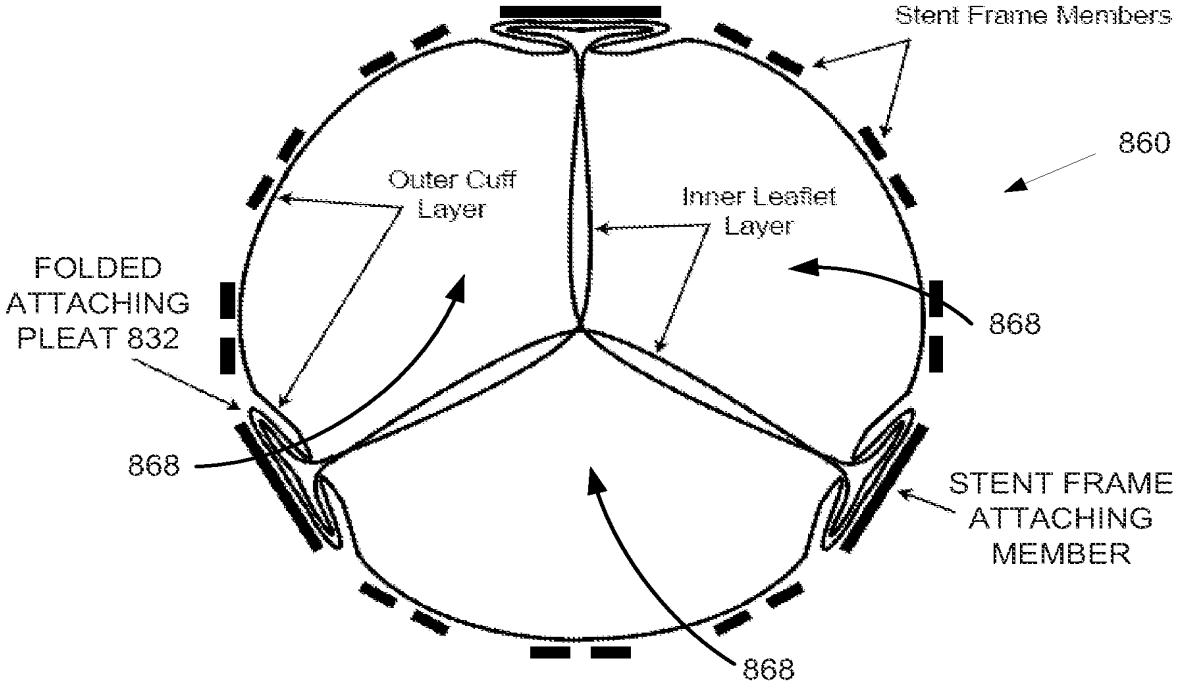
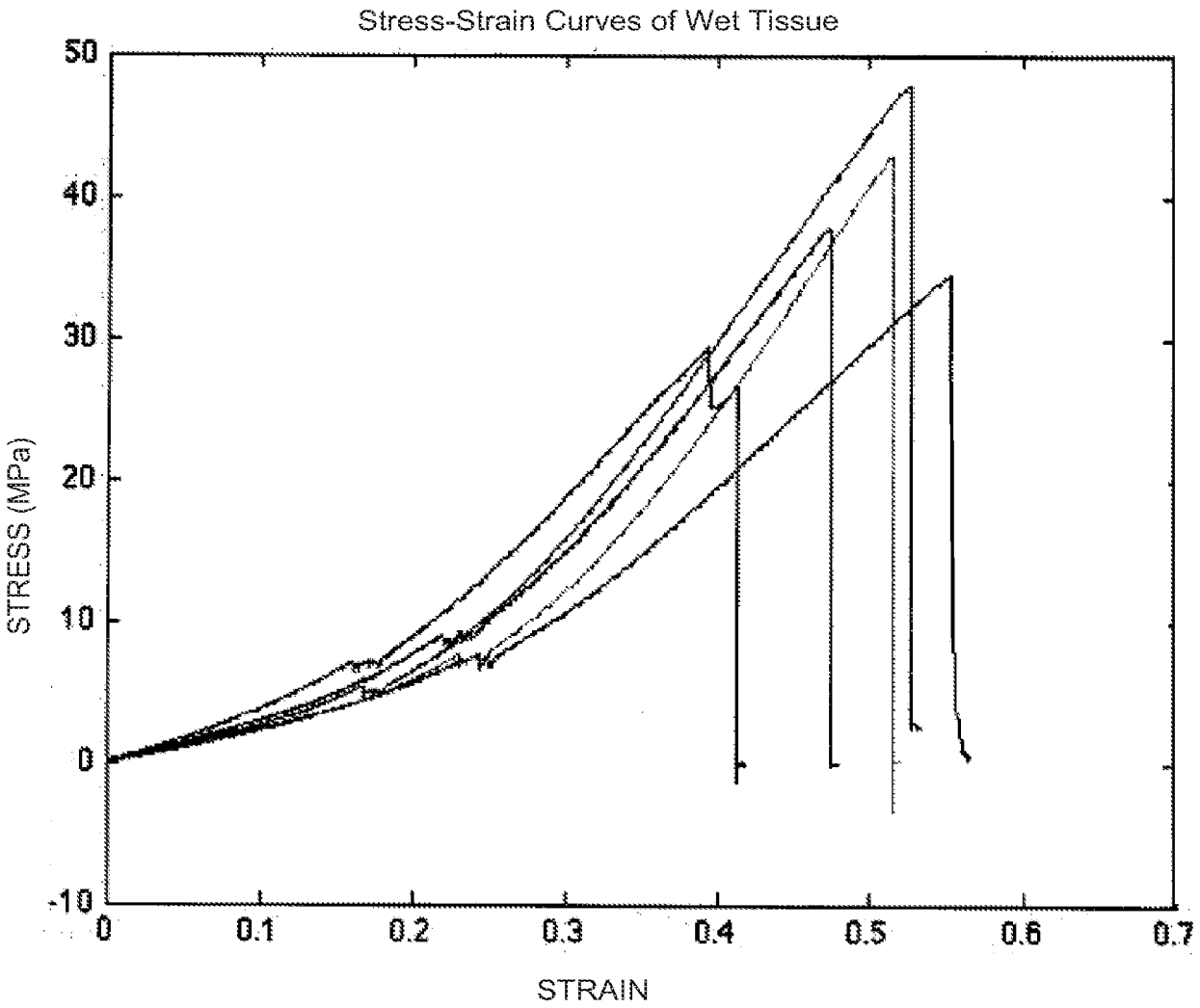

Stent Frame Members
860
Outer Cuff Layer
Inner Leaflet Layer
FOLDED ATTACHING PLEAT 832
868
868
STENT FRAME ATTACHING MEMBER
868

FIG.8L



Stress-strain curves in wet or hydrated state of five samples. Each curve corresponds to a separate sample.

FIG. 9

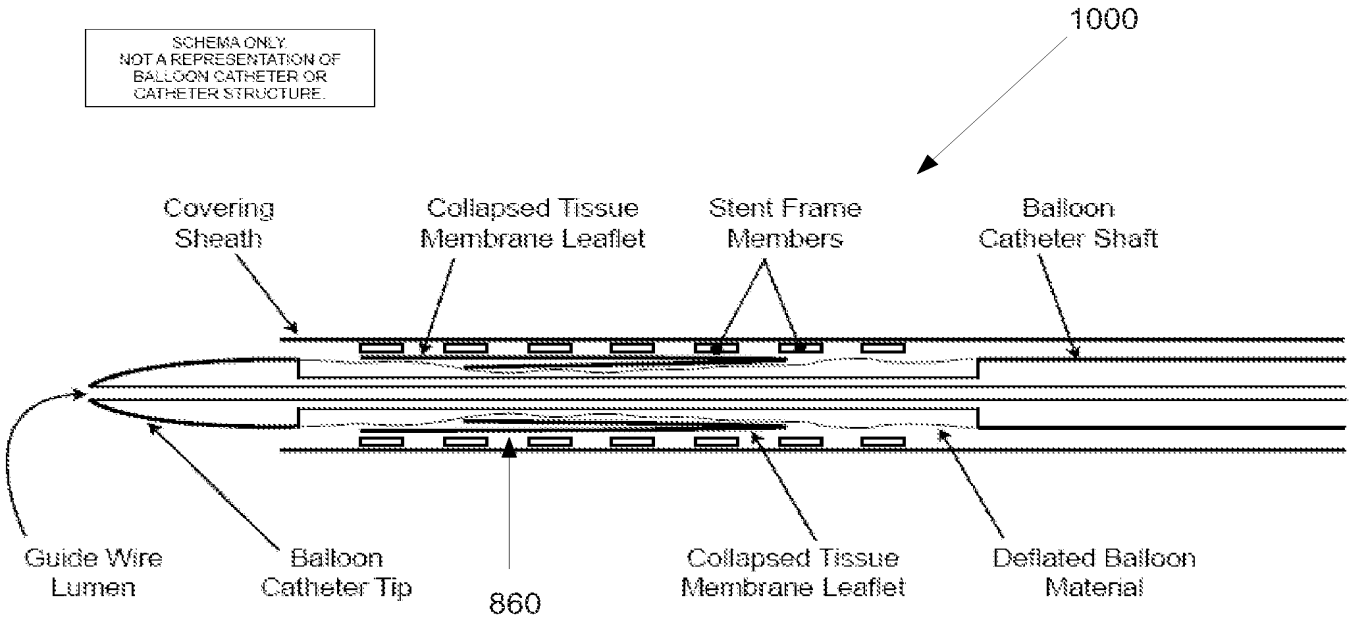

SCHEMA ONLY
NOT A REPRESENTATION OF
BALLOON CATHETER OR
CATHETER STRUCTURE.
1000
Covering Sheath
Collapsed Tissue Membrane Leaflet
Stent Frame Members
Balloon Catheter Shaft
Guide Wire Lumen
Balloon Catheter Tip
860
Collapsed Tissue Membrane Leaflet
Deflated Balloon Material

FIG.10

Photo of Tissue Leaflet Assembly Attached in Frame to Form Implantable Prosthetic Heart Valve

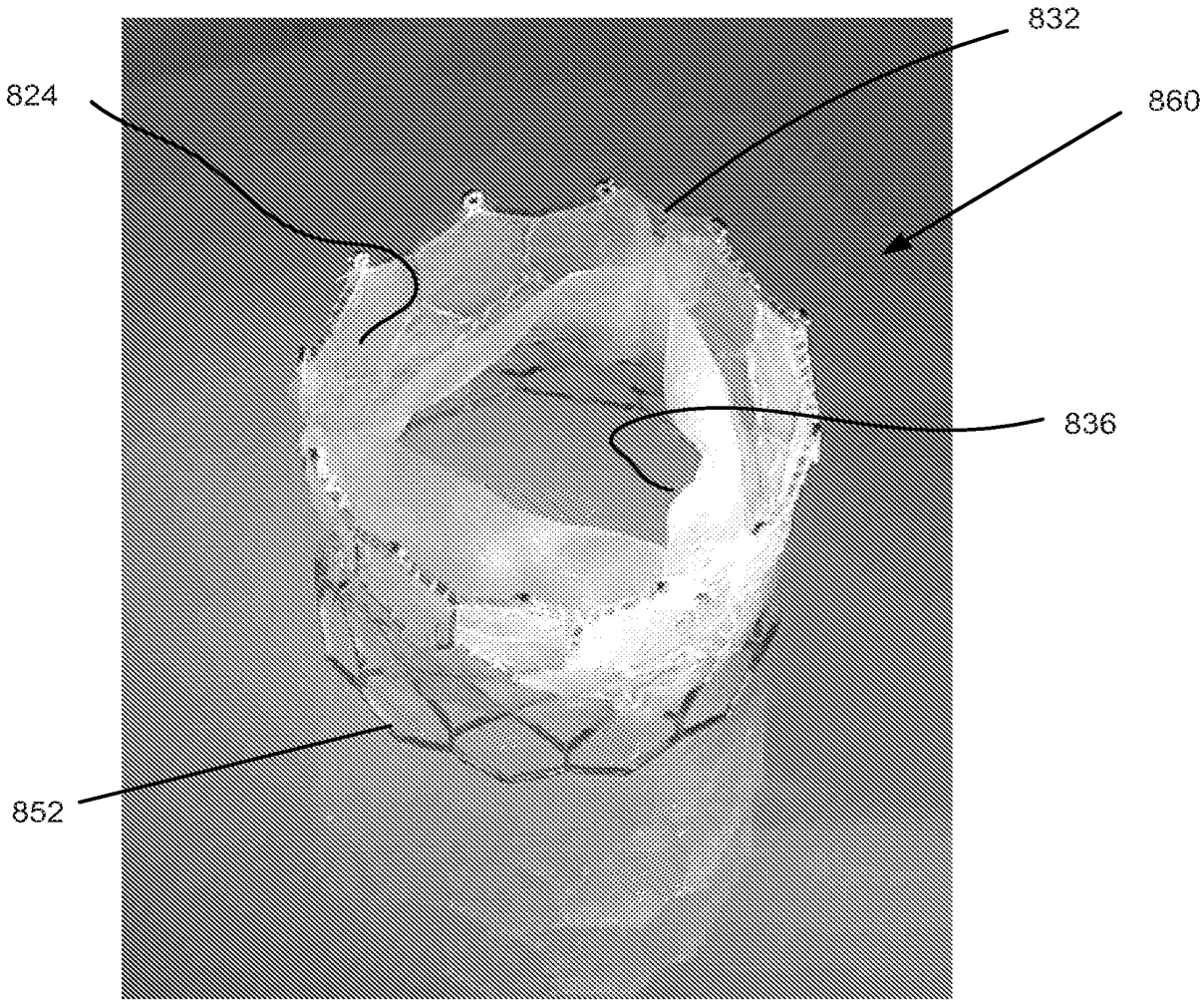


FIG.11A

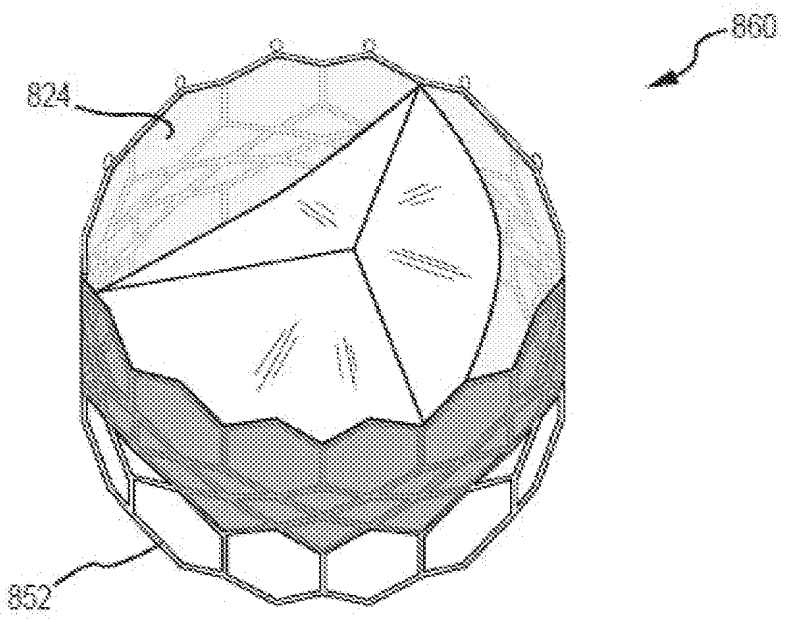


FIG. 11B

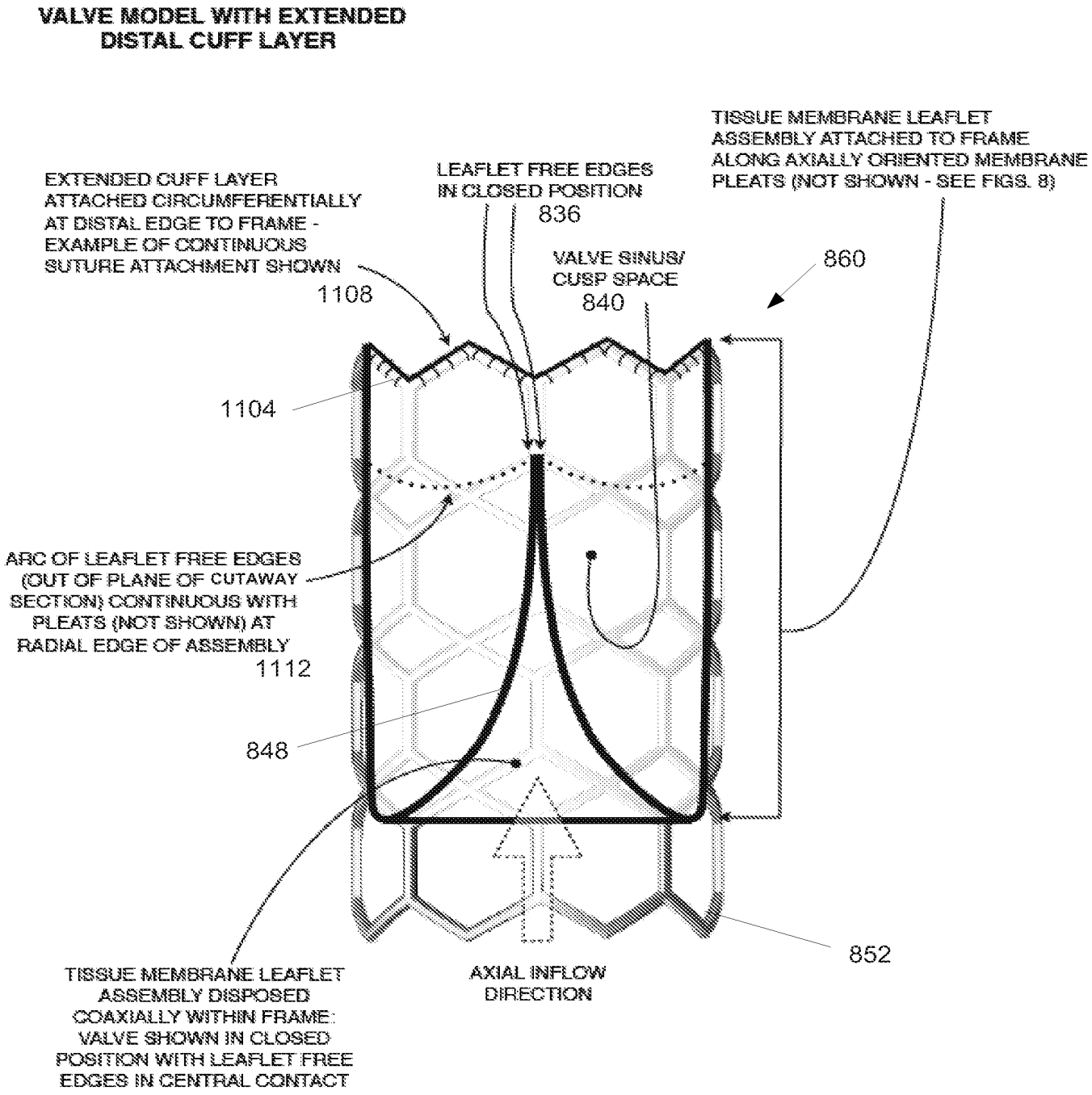

VALVE MODEL WITH EXTENDED DISTAL CUFF LAYER
TISSUE MEMBRANE LEAFLET ASSEMBLY ATTACHED TO FRAME ALONG AXIALLY ORIENTED MEMBRANE PLEATS (NOT SHOWN - SEE FIGS. 8)
EXTENDED CUFF LAYER ATTACHED CIRCUMFERENTIALLY AT DISTAL EDGE TO FRAME - EXAMPLE OF CONTINUOUS SUTURE ATTACHMENT SHOWN
1108
LEAFLET FREE EDGES IN CLOSED POSITION
836
VALVE SINUS/ CUSP SPACE
840
860
1104
ARC OF LEAFLET FREE EDGES (OUT OF PLANE OF CUTAWAY SECTION) CONTINUOUS WITH PLEATS (NOT SHOWN) AT RADIAL EDGE OF ASSEMBLY
1112
848
852
TISSUE MEMBRANE LEAFLET ASSEMBLY DISPOSED COAXIALLY WITHIN FRAME: VALVE SHOWN IN CLOSED POSITION WITH LEAFLET FREE EDGES IN CENTRAL CONTACT
AXIAL INFLOW DIRECTION

FIG. 11C

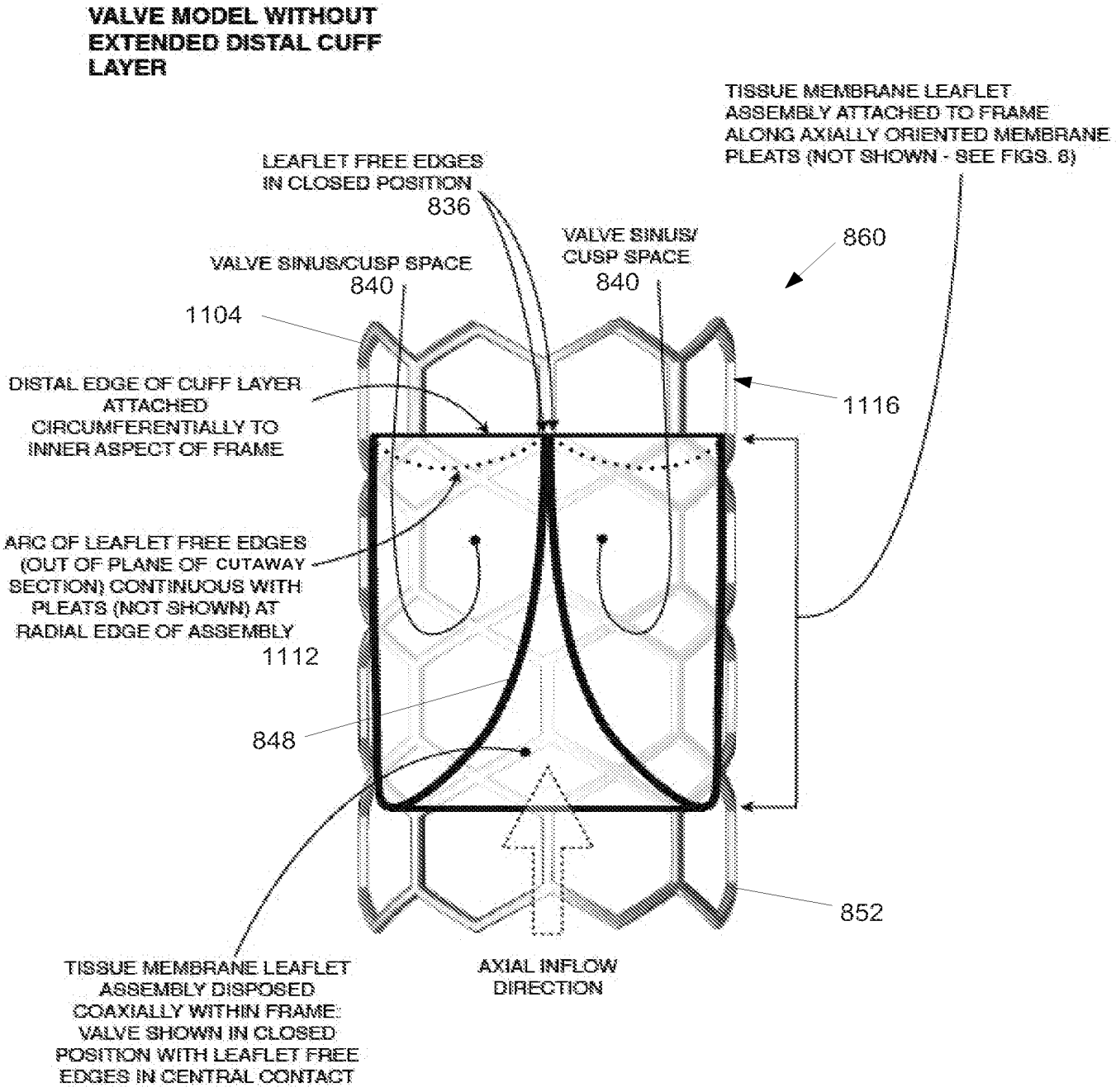

VALVE MODEL WITHOUT EXTENDED DISTAL CUFF LAYER
TISSUE MEMBRANE LEAFLET ASSEMBLY ATTACHED TO FRAME ALONG AXIALLY ORIENTED MEMBRANE PLEATS (NOT SHOWN - SEE FIGS. 8)
LEAFLET FREE EDGES IN CLOSED POSITION
836
VALVE SINUS/CUSP SPACE
840
VALVE SINUS/ CUSP SPACE
840
860
1104
DISTAL EDGE OF CUFF LAYER ATTACHED CIRCUMFERENTIALLY TO INNER ASPECT OF FRAME
1116
ARC OF LEAFLET FREE EDGES (OUT OF PLANE OF CUTAWAY SECTION) CONTINUOUS WITH PLEATS (NOT SHOWN) AT RADIAL EDGE OF ASSEMBLY
1112
848
852
TISSUE MEMBRANE LEAFLET ASSEMBLY DISPOSED COAXIALLY WITHIN FRAME: VALVE SHOWN IN CLOSED POSITION WITH LEAFLET FREE EDGES IN CENTRAL CONTACT
AXIAL INFLOW DIRECTION

FIG. 11D

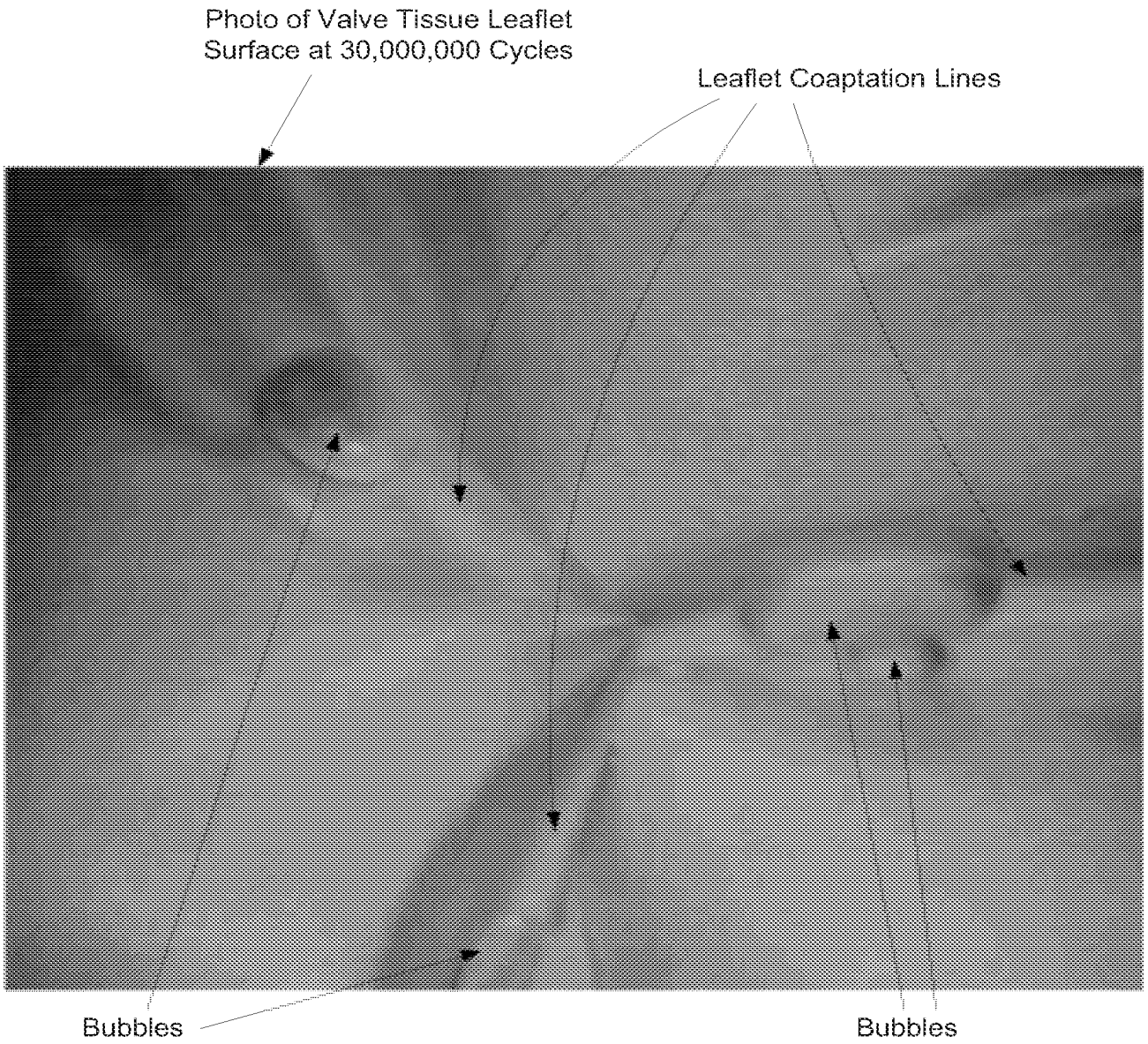


FIG.12

Surgeon Holding a Premounted Percutaneously Deliverable Heart Valve Associated With a Catheter and Residing Within Sterile Packaging

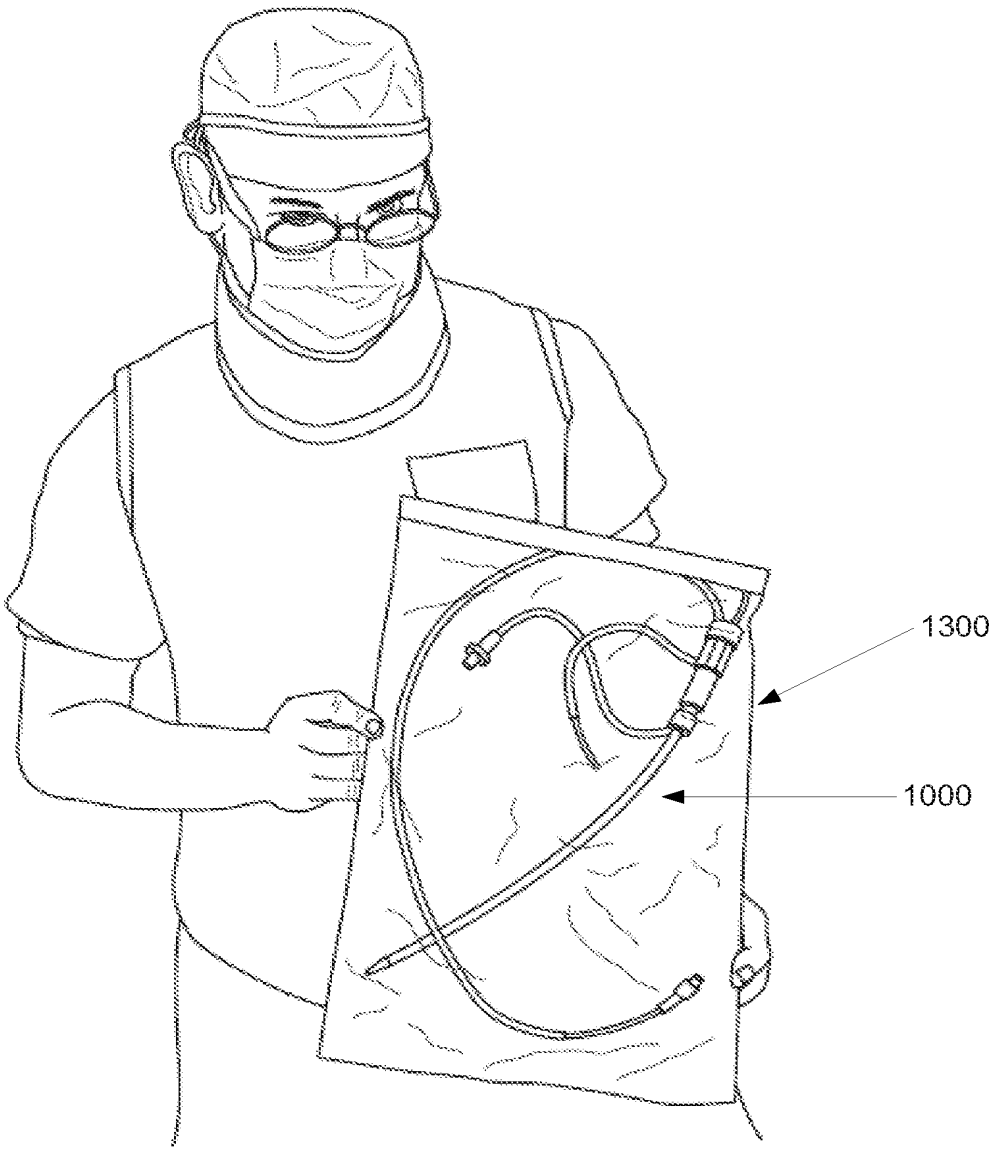


FIG.13

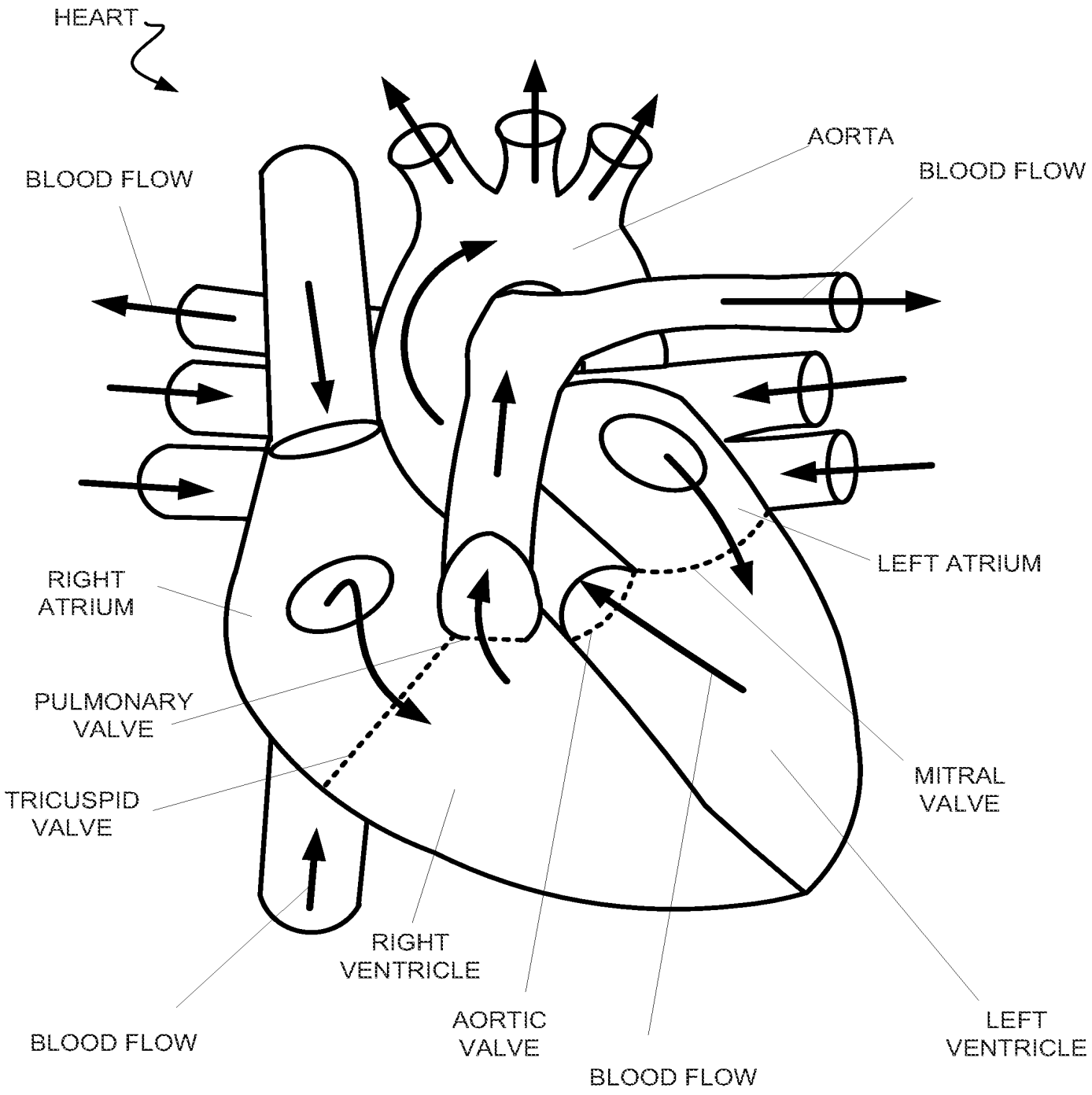

HEART
BLOOD FLOW
AORTA
BLOOD FLOW
LEFT ATRIUM
RIGHT ATRIUM
PULMONARY VALVE
TRICUSPID VALVE
MITRAL VALVE
RIGHT VENTRICLE
BLOOD FLOW
AORTIC VALVE
BLOOD FLOW
LEFT VENTRICLE

FIG.14

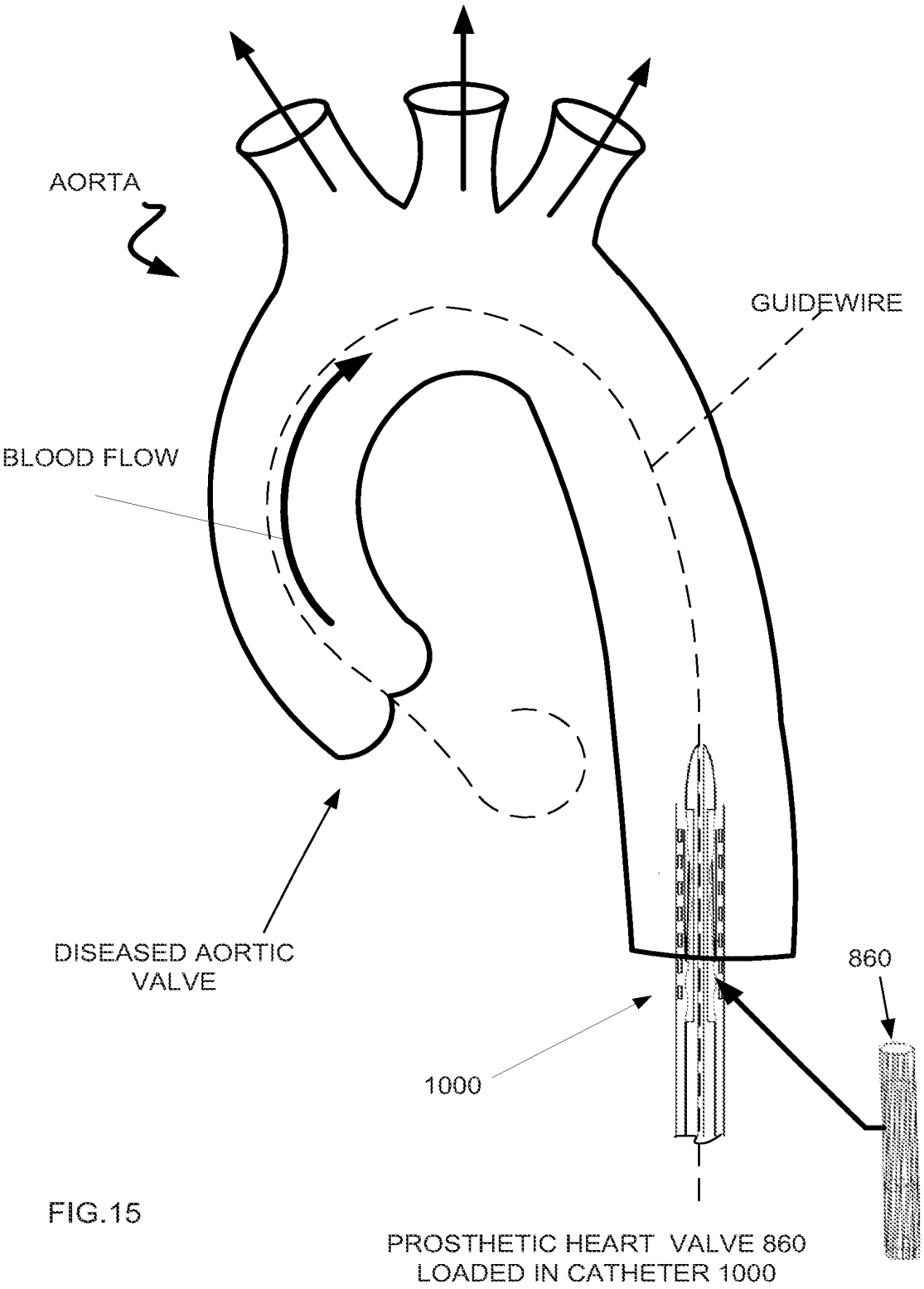

AORTA
GUIDEWIRE
BLOOD FLOW
DISEASED AORTIC VALVE
860
1000
PROSTHETIC HEART VALVE 860 LOADED IN CATHETER 1000

FIG.15

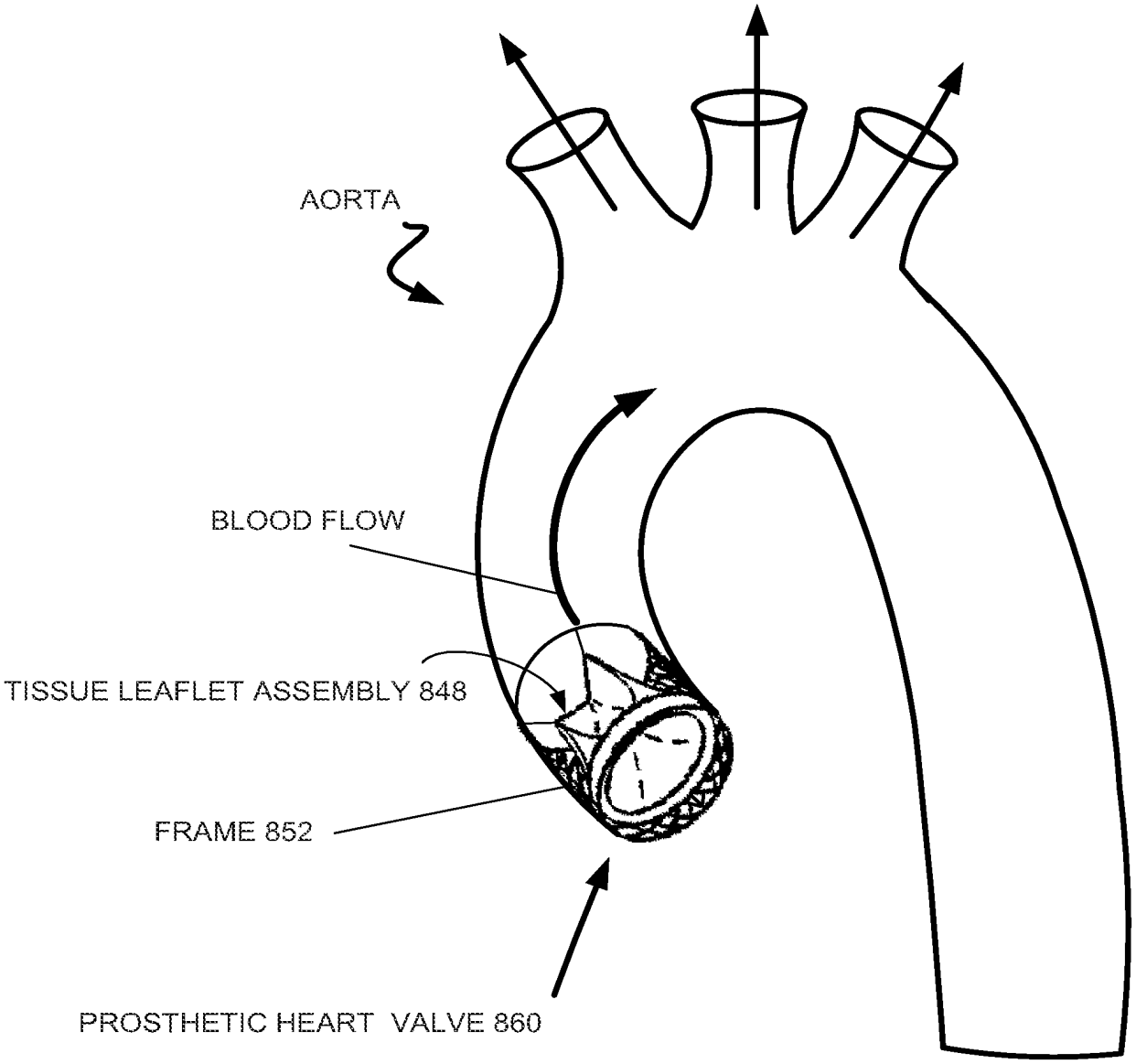


FIG. 16

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(54) **Title**: METHOD AND APPARATUS FOR THE ENDOLUMINAL DELIVERY OF INTRAVASCULAR DEVICES

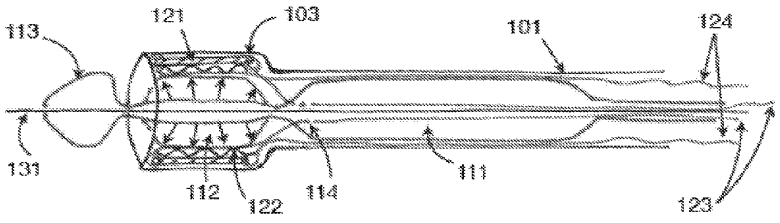


FIG. 4B

(57) **Abstract**: A dual-balloon delivery catheter system includes a carrier segment that is a lead/carrier balloon or mandrel at a distal portion of a catheter. The carrier segment is sequentially arrayed with a more proximally positioned delivery segment, wherein the delivery segment is a delivery balloon or mandrel. The first carrier segment expands the stent-valve a sufficient amount to receive the delivery segment after the carrier segment is moved away from the sent-valve. The delivery segment is then positioned at the target site and the stent-valve is then deployed.

WO 2012/006124 A2

METHOD AND APPARATUS FOR THE ENDOLUMINAL DELIVERY OF INTRAVASCULAR DEVICES

FIELD

Embodiments of the one or more present inventions relate to surgical methods and apparatus in general, and more particularly to surgical methods and apparatus for the endoluminal delivery of intravascular devices to a site within the body.

For the purposes of illustration but not limitation, embodiments of the one or more present inventions will hereinafter be discussed in the context of delivering a percutaneous heart valve to a valve seat located within the heart; however, it should be appreciated that at least one embodiment of the one or more present inventions is also applicable to other endoluminal delivery applications.

BACKGROUND

Percutaneous aortic valves, such as those available from Edwards Lifesciences LLC (Irvine, CA) under the tradename SAPIEN® typically utilize an expandable frame having valve leaflets attached thereto. This expandable frame essentially comprises a stent, with the valve leaflets (preferably in the form of tissue membrane) attached to a portion thereof. For this reason, these percutaneous aortic valves are commonly referred to as "stent-valves". Typically, the percutaneous aortic stent-valve is compressed down upon a deflated balloon catheter, the combined assembly is then inserted into the femoral artery through a covering sheath, and then the combined assembly is delivered endoluminally through the iliac artery and aorta to the valve seat. At the valve seat, the balloon is used to expand the stent so that the stent-valve is set at the valve seat, then the balloon is deflated, and finally the balloon catheter is withdrawn, whereupon the leaflets of the stent-valve act in place of the natural leaflets of the diseased aortic valve.

Percutaneous heart valves of the sort described above currently show great promise, particularly for elderly and/or otherwise infirm patients who cannot tolerate the trauma of conventional open heart valve replacement procedures.

Unfortunately, current percutaneous heart valve systems require the use of relatively large delivery/deployment apparatus. More particularly, since the internal balloon must be capable of expanding the stent portion of the stent-valve to the full size of the natural valve seat, and since the deflated size of a balloon having this full-expansion capability is relatively large, and since the stent-valve must be disposed circumferentially outboard of the balloon, the overall size of the delivery/deployment apparatus is necessarily large. By way of example but not limitation, the Edwards SAPIEN® delivery/deployment apparatus is typically approximately 7 to 8 mm in diameter.

Clinically, this can present a significant problem for the surgeon, since the preferred access to the vascular system of the patient is via the femoral artery, with subsequent delivery to the aortic valve seat via the iliac artery and aorta. However, the femoral artery is typically only about 5 to 8 mm in diameter, and this 5-8 mm range is for the general population as a whole - elderly female patients, who are expected to make up a substantial percentage of the candidate population for percutaneous aortic valve replacement, are on the smaller end of this range (e.g., perhaps 5-6 mm in diameter). Thus, it can be difficult or even impossible to pass the 7-8 mm (diameter) SAPIEN® device through the 5-6 mm (diameter) femoral artery of an elderly female patient, particularly where the femoral artery is tortuous, stenotic and/or occluded. Surgical incision has sometimes been required in order to gain access to a higher level of the ilio-femoral artery (e.g., within the pelvis) that is large enough to accommodate the stent-valve assembly. However, this approach is generally more invasive, and often leads to complications such as substantial bleeding and artery obstruction.

Referring now to Fig. 1, a schematic side view of a catheter-deliverable device, or stent-valve, known in the prior art is shown. The stent-valve may have an expanded diameter of approximately 25 mm. However, the stent-valve can be compressed to approximately 4 mm in diameter. As shown in Fig. 2, to achieve expansion of the stent-valve, it may be mounted on a typical prior art large-diameter delivery balloon catheter that is inflatable to a diameter of 25 mm. However, the combined diameter of the stent-valve mounted on to the large-diameter delivery balloon catheter is perhaps 18 Fr or 6 mm, which is too large to insert into some patient's femoral artery.

For the foregoing reasons, there is a substantial need for a new and improved method and apparatus for the endoluminal delivery of intravascular devices to a site within the body.

SUMMARY

It is to be understood that embodiments of the one or more present inventions include a variety of different versions or embodiments, and this Summary is not meant to be limiting or all-inclusive. This Summary provides some general descriptions of some of the embodiments, but may also include some more specific descriptions of other embodiments.

When first considered, a solution associated with the difficulty of placing a stent-valve in a relatively small femoral artery appears to be use of a small delivery device. Accordingly, a small-diameter delivery balloon initially appears to address the problem. However, and with reference now to Fig. 3, if a small diameter delivery balloon catheter is used, then while the stent-valve can be compressed to a relatively small diameter, the small-diameter delivery balloon is incapable of fully expanding the stent-valve to 25 mm; that is, a small diameter

delivery balloon may only be capable of expanding the stent-valve to approximately 10 mm in diameter, for example.

At least one embodiment of the one or more present inventions addresses the aforementioned problems associated with the prior art by providing a novel method and apparatus for the endoluminal delivery of intravascular devices to a site within the body, at least one embodiment of the one or more present inventions takes advantage of the principle of dividing the volume of the stent-valve delivery apparatus into smaller diameter parts for separate insertion into the vascular system of a patient (e.g., into a relatively small diameter access vessel such as the femoral artery) and then re-assembling those parts within another portion of the vascular system of the patient (e.g., in a larger diameter vessel such as the aorta) which can accommodate the full size of the assembled components. By dividing the balloon expansion task into two serially-deployed balloons, activated in a staged fashion, the stent-valve can be delivered with a smaller profile, yet full stent-valve expansion at the valve seat can be ensured. Accordingly, novel devices and methods are proposed that involve transfer of a deliverable device, such as a stent-valve, after insertion into the body from its "carrier segment" to another "delivery segment" which may reside on the same or separate catheters, and deployment of the stent-valve from that "delivery segment" that is capable of expansion to suitable diameter for the stent-valve.

In at least one embodiment of the one or more present inventions, the stent-valve can be pre-mounted within a packaged pre-assembled delivery system for ready transport and clinical use.

In a first preferred form of the one or more present inventions, the first "carrier" balloon and second "delivery" balloon are mounted on separate inserter elements for independent delivery to the larger blood vessel, such as the aorta, where the second "delivery" balloon is united with the then-partially-expanded stent-valve – in this form, each balloon is independently advanced to the aorta via its own inserter element.

In a second preferred form of the one or more present inventions, the first and second balloons are serially disposed on a single inserter element, with the first "carrier" balloon being mounted to the inserter element distal to (or, optionally, more proximal to) the second "delivery" balloon – in this form, a single inserter element is used to sequentially position the first "carrier" balloon and second "delivery" balloon relative to the stent-valve.

In a third preferred form of the one or more present inventions, the first "carrier" balloon and second "delivery" balloon are mounted on separate inserter elements, but these inserter elements are arranged in a co-axial fashion so as to permit a telescoping action between the two inserter elements (and hence a telescoping action between the first "carrier" balloon and the

second "delivery" balloon). In this form, the first "carrier" balloon shaft, being coaxially mounted upon a leading guide wire, can act as something of a firmer guidewire for the second "delivery" balloon.

In addition to the foregoing, after initial expansion of the stent-valve via the first "carrier" balloon, the first "carrier" balloon catheter can be removed and replaced by a shaped catheter element in order to provide guidance and assistance in traversing the central arteries and crossing the plane of (and, optionally, preparing) the native valve seat. This shaped catheter element can be disposed on an inserter element distal to the second "delivery" balloon or to the first carrier balloon, if desired.

If desired, the first "carrier" balloon can alternatively be another expandable device, e.g., the first "carrier" balloon (which constitutes the mounting segment for the stent-valve) can be an expandable mandrel. Alternatively, the stent-valve may be initially mounted on a non-expanding element, that is, simply a low-profile mandrel or other segment of the delivery catheter.

It should be appreciated that while at least one embodiment of the one or more present inventions has sometimes been discussed in the context of delivering a stent-valve to the aortic valve seat, it may also be used to deliver other valves to other valve seats, and/or for delivering other intravascular devices to other sites within the body.

It should also be appreciated that while at least one embodiment of the one or more present inventions is sometimes discussed in the context of advancing the stent-valve through the arterial system of the body, it may also be used to advance the stent-valve through the venous system of the body, or to endoluminally advance a device through some other luminal system of the body.

In at least one embodiment of the one or more present inventions, the covering sheath (through which the various components are advanced into the blood vessel) can be flexible and expandable so as to allow initial expansion of the stent-valve, and the exchange of the first "carrier" balloon and the second "delivery" balloon within the covering sheath, so that the apparatus is continuously protected.

It will be seen that at least one embodiment of the one or more present inventions provides a novel method and apparatus for the endoluminal delivery of an intravascular device to a site within the body.

Accordingly, at least one embodiment described herein is directed to a stent-valve and delivery system that is inserted separately into the femoral artery, then assembled inside the aorta, and thereafter advanced for deployment at the valve plane. This means that the limiting size of the artery (or vein, for the pulmonary valve) access diameter is determined by the largest

single piece of the system - effectively the stent/valve itself. When the stent/valve is compressed without the balloon catheter, it is possible to deliver a valve into the circulation in as small as 14 French sheath rather than an 18 to 24 French, as has previously been achieved.

In at least one embodiment, an in-line dual-balloon delivery catheter system includes a carrier segment that is a lead/carrier balloon or mandrel at the distal portion of a catheter with the carrier segment arrayed in-line on a catheter shaft with a more proximally positioned delivery segment together at the distal portion of the catheter shaft. In essence, since the first "carrier" balloon only needs to expand the stent-valve a sufficient amount to receive the deflated second "delivery" balloon, the first "carrier" balloon can be quite small in its deflated condition. Moreover, the stent-valve, unrestricted by the traditional need for mounting on a single, relatively large deployment balloon, can be compressed to its minimum structural diameter for mounting on the relatively small first "carrier" balloon. As a result, the combined assembly (i.e., of carrier balloon catheter and stent-valve) can be much smaller in diameter than previous delivery devices at the time of accessing the vascular system of the patient. At the same time, by thereafter uniting the stent-valve with the second, larger "delivery" balloon, sufficient stent expansion can be provided to ensure secure valve seating.

In at least one embodiment, a woven wire "stent" with or without sheath investment is provided wherein its length is coupled to diameter. Nitinol or another alloy wire is formed in an expanded sheath shape and compressed by traction on trailing wire ends. At the point of the procedure requiring distal sheath expansion, the traction is released to allow expansion to a mechanically biased open position. Alternatively, traction wires may be attached to a distal end of the wire weave within the sheath and a traction force, there applied, causes simultaneous expansion and shortening of the distal end of the sheath, thereby advantageously releasing the underlying mounted stent-valve and exposing it for deployment.

In at least one embodiment a mechanism is provided for retaining a stent-valve frame on a delivery balloon by magnetic or electromagnetic means. The frame is preferably constituted of or contains ferrous metal elements. By such means, a stent-valve can be securely advanced through the vascular system without need for a covering sheath, thereby simplifying the delivery procedure and the system. The stent-valve is retained on the balloon segment by magnetic force.

In at least one embodiment, a device that utilizes magnetic force to deploy and, if desired, later retrieve a stent-valve is provided, the device using a magnetic force set at a level to permit ready balloon expansion of a stent-valve at a plane of the diseased native valve. As the frame of the stent-valve is pushed away from the magnet, retention force weakens, thereby allowing unimpeded final device expansion. A stronger magnet/electromagnet mounted on a separate catheter can be used to retrieve or reposition the stent-valve. In addition, a strong

magnet mounted on a retrieval catheter can be used to retract the stent-valve frame from the native valve seat.

For the purposes of illustration but not limitation, embodiments of the one or more present inventions are hereinafter discussed in the context of delivering a prosthetic stent-valve to the aortic valve seat; however, it should be appreciated that at least one embodiment of the one or more present inventions is also applicable to other endoluminal delivery applications.

Accordingly, in at least one embodiment, a system for providing endoluminal delivery of a deliverable device through vasculature of a patient to a delivery site within the patient is provided, the system comprising:

an outer delivery sheath including a distal section, wherein at least a portion of the outer delivery sheath is sized for insertion into the vasculature of the patient;

a carrier segment located at a distal portion of a catheter shaft, the carrier segment having an outer surface sized to temporarily hold the deliverable device in the distal section of the outer delivery sheath, wherein at least a portion of the catheter shaft is located within and coaxial to the outer delivery sheath; and

a delivery segment located coaxial to the outer delivery sheath, the delivery segment having an outer surface sized to radially fit within the deliverable device after detaching the deliverable device from the carrier segment when the deliverable device resides within the distal section of the outer delivery sheath, wherein the delivery segment is configured to deploy the deliverable device at the delivery site.

In addition to the foregoing, in at least one embodiment at least a portion of the distal section of the outer delivery sheath is expandable. In at least one embodiment, the at least a portion of the distal section of the outer delivery sheath comprises one or more electrically activated elements. In at least one embodiment, the at least a portion of the distal section of the outer delivery sheath comprises one or more piezo-ceramic elements. In at least one embodiment, the at least a portion of the distal section of the outer delivery sheath comprises a passively expandable material that is expandable upon application of an outward radial force applied by at least one of the carrier segment and the delivery segment. In at least one embodiment, the at least a portion of the distal section of the outer delivery sheath expands upon application of a tensile force to the at least a portion of the distal section.

In at least one embodiment, the distal section includes at least one of an internal projection and a narrowed area extending radially inward from an interior surface of the distal section.

In at least one embodiment, a portion of an internal surface of the outer delivery sheath further comprises a guide for retaining at least a portion of a longitudinally extending element

configured to selectively manipulate at least a part of the outer delivery sheath or a structure coaxial to the outer delivery sheath. In at least one embodiment, a portion of an internal surface of the outer delivery sheath further comprises a guide, the guide comprising at least one of:

(a) a lumen; and

(b) a grommet;

wherein the guide retains at least one control line for selective retention of the deliverable device.

In at least one embodiment, the carrier segment and the delivery segment are both situated upon the catheter shaft. In at least one embodiment, the carrier segment is situated upon the catheter shaft, and wherein the delivery segment is associated with a delivery segment shaft that is coaxial to the catheter shaft and axially moveable relative to the catheter shaft. In at least one embodiment, the carrier segment is an expandable balloon having an expanded diameter smaller than an expanded diameter for the delivery segment. In at least one embodiment, the delivery segment is an expandable balloon having an expanded diameter larger than an expanded diameter for the carrier segment. In at least one embodiment, at least one of the carrier segment and the delivery segment is a mandrel. In at least one embodiment, the mandrel is expandable by mechanical or electromechanical means. In at least one embodiment, the mandrel is not expandable.

In at least one embodiment, the delivery segment is located axially proximal to the carrier segment. In at least one embodiment, the delivery segment is located axially distal to the carrier segment.

In at least one embodiment, one or both of the carrier segment and the delivery segment include at least one magnet or electromagnet to aid manipulation of the deliverable device.

In at least one embodiment an assembly for intravascular delivery of a deliverable device to a delivery site within a patient is provided, comprising:

a first catheter including a first catheter shaft;

a carrier segment situated along the first catheter shaft, the carrier segment configured to receive the deliverable device prior to inserting the first catheter within the patient; and

a delivery segment sequentially positioned in an axial orientation relative to the carrier segment, wherein the delivery segment is configured to engage the deliverable device within the patient while the deliverable device is coaxial to at least a portion of the first catheter, and wherein the delivery segment is configured to thereafter deploy the deliverable device at the delivery site.

[0037] In at least one embodiment, the delivery segment is also situated along the first catheter. In at least one embodiment, the delivery segment is situated along a second catheter, the second catheter comprising a coaxial lumen through which passes the first catheter. In at least one embodiment, at least one of the first catheter and the second catheter comprise a curved distal portion.

One or more embodiments of the one or more present inventions also pertain to methods of delivering a device, such as a stent-valve, within a patient. Accordingly, in at least one embodiment, a method of delivering a deliverable device through vasculature of a patient to a target site within the patient is provided, comprising:

mounting the deliverable device on a selectively expandable carrier segment located along a catheter shaft, wherein at least a portion of the catheter shaft is located within and coaxial to an outer delivery sheath;

inserting the outer delivery sheath and catheter shaft into the patient;

moving the outer delivery sheath within the patient to position the selectively expandable carrier segment and the deliverable device near the target site;

partially expanding the deliverable device using the selectively expandable carrier segment while the deliverable device remains at least partially within the outer delivery sheath;

positioning a delivery segment radially within the deliverable device and partially expanding the delivery segment to facilitate engagement of the delivery segment with the deliverable device;

moving the delivery segment and deliverable device to the target site; and

deploying the deliverable device at the target site by further expanding the delivery segment.

Various components are referred to herein as "operably associated." As used herein, "operably associated" refers to components that are linked together in operable fashion, and encompasses embodiments in which components are linked directly, as well as embodiments in which additional components are placed between the two linked components.

As used herein, "at least one," "one or more," and "and/or" are open-ended expressions that are both conjunctive and disjunctive in operation. For example, each of the expressions "at least one of A, B and C," "at least one of A, B, or C," "one or more of A, B, and C," "one or more of A, B, or C" and "A, B, and/or C" means A alone, B alone, C alone, A and B together, A and C together, B and C together, or A, B and C together.

Various embodiments of the present inventions are set forth in the attached figures and in the Detailed Description as provided herein and as embodied by the claims. It should be

understood, however, that this Summary does not contain all of the aspects and embodiments of the one or more present inventions, is not meant to be limiting or restrictive in any manner, and that the invention(s) as disclosed herein is/are understood by those of ordinary skill in the art to encompass obvious improvements and modifications thereto.

Additional advantages of at least one embodiment of the one or more present inventions will become readily apparent from the following discussion, particularly when taken together with the accompanying drawings.

BRIEF DESCRIPTION OF THE DRAWINGS

To further clarify the above and other advantages and features of the one or more present inventions, a more particular description of the one or more present inventions is rendered by reference to specific embodiments thereof which are illustrated in the appended drawings. It should be appreciated that these drawings depict only typical embodiments of the one or more present inventions and are therefore not to be considered limiting of its scope. The one or more present inventions are described and explained with additional specificity and detail through the use of the accompanying drawings in which:

Fig. 1 is a schematic side view of a catheter-deliverable device frame (or stent-valve) known in the prior art;

Fig. 2 is a schematic side view of a typical prior art large-diameter delivery balloon catheter in a deflated state;

Fig. 3 is a schematic side view of a small-diameter delivery balloon catheter in a deflated state;

Fig. 4A is a side view of an in-line dual balloon delivery system in accordance with at least one embodiment of the one or more present inventions;

Fig. 4B is a side view of the system shown in Fig. 4A, wherein the carrier balloon is dilated to partially expand a stent-valve to accommodate the larger delivery balloon (catheter inflation ports, lumens, wire lumens not shown for clarity);

Fig. 4C is a side view of the system shown in Fig. 4B, wherein the deflated carrier balloon is advanced out of the partially expanded valve device as the delivery balloon is advanced into the stent-valve to "capture" or "dock" with the stent-valve;

Fig. 4D is a side view of the system shown in Fig. 4C, wherein the carrier balloon is optionally inflated to facilitate crossing the plane of the diseased heart valve with the delivery system, and wherein the delivery balloon is positioned astride the stent-valve to capture and subsequently deploy the stent-valve;

Fig. 4E is a side view of the system shown in Fig. 4D, wherein after the stent-valve is positioned in the plane of the heart valve, the sheath is withdrawn to expose the stent-valve in place at the heart valve seat and to allow for deployment if the stent-valve by expansion;

Fig. 4F is a side view of the system shown in Fig. 4E, wherein with the stent-valve is positioned at the valve seat and the sheath withdrawn, and wherein the delivery balloon then expanded to deploy the stent-valve;

Fig. 5A is a side view of a catheter delivery system in accordance with another embodiment of the one or more present inventions, wherein a carrier balloon shaft passes through a central coaxial lumen of a delivery balloon (wherein the wall of central lumen is omitted for clarity);

Fig. 5B is a side view of the system shown in Fig. 5A, wherein partial inflation of the leading carrier balloon may be used as a "nose cone" to facilitate insertion of the delivery catheter into a patient's artery;

Fig. 5C is a side view of the system shown in Fig. 5B, wherein full inflation of the leading carrier balloon partially expands the stent-valve within an expandable sheath segment;

Fig. 5D is a side view of the system shown in Fig. 5C, wherein at "(1)" the leading carrier balloon is deflated and advanced out of the stent-valve, and wherein at "(2)" the delivery balloon is advanced into position within stent-valve to "dock" with or "capture" the stent-valve;

Fig. 5E is a side view of the system shown in Fig. 5D, wherein the leading carrier balloon and guidewire are first advanced into the left ventricle (in the case of implantation in the native aortic valve seat), and wherein the leading carrier balloon shaft then acts as a guide rail for delivery of the balloon catheter;

Fig. 6A is a side view of an embodiment of a sheath, wherein traction elongates the sheath weave and reduces its diameter, and wherein release of the traction shortens/retracts the sheath weave and expands its diameter;

Fig. 6B is a side view of an embodiment of a cut shape memory alloy stent (nitinol) within a sheath wall investment that expands as a contained balloon and/or stent-valve (omitted for clarity) is expanded therein and self-contracts as the balloon is deflated;

Fig. 6C is a side view of an embodiment of a plastic material sheath that passively expands;

Fig. 6D is a side view of an embodiment of electrically actuated piezo-ceramic (p-c) elements sealed within an elastic sheath wall, wherein each p-c element is connected by a conductor pair to a voltage controlled power source, wherein a switch engages a power source, and wherein p-c elements expand the sheath when electrically energized;

Fig. 6E is a perspective view of an embodiment of actuator elements that utilize differential alloy laminates, wherein an application of current induces bend in the actuator;

Fig. 7 is a side view of an embodiment of a device for retaining a stent-valve on a delivery balloon by magnetic or electromagnetic means (for Figs. 7-8B, conductors and a power source for electromagnet are not shown; the valve membrane or other valve mechanism is not shown; the balloon inflation lumen and optional control lines/harness are omitted for clarity);

Fig. 8A is a side view of an embodiment of a retrieval catheter device that utilizes magnetic force to retrieve a stent-valve;

Fig. 8B is a side view of a stent-valve wherein the stent-valve is contracted by magnetic force and thereafter can be retracted from the native valve seat by optional control lines or a harness;

Fig. 8C is a side perspective view of an embodiment of a multipolar magnetic retrieval catheter system; and

Fig. 8D is an end view of the system shown in Fig. 8C positioned radially within a stent-valve.

For the figures presented herein, balloons in a collapsed state are depicted as partially expanded to emphasize the difference in sizes. In addition, balloon catheter wire lumen and inflation lumens are omitted for clarity.

The drawings are not necessarily to scale.

DETAILED DESCRIPTION

Overview

In general, at least one embodiment of the one or more present inventions uses a serial approach for delivering and deploying the percutaneous aortic valve at the valve seat. This serial approach allows various components of the combined assembly (i.e., the various components of the balloon catheter and the stent-valve) to be separately introduced into the vascular system of the patient, each with its own minimized profile, so as to facilitate a low-profile endoluminal delivery of the system components into the large central blood vessels (e.g. the aorta) where, in a preferred sequence, these components are co-axially re-assembled prior to advancement to the target valve seat. As a result, at least one embodiment of the one or more present inventions facilitates femoral artery access to the aortic valve seat, even with patients having small femoral artery diameters (e.g., elderly female patients). In other words, since the various components of the system are not fully assembled at the time of insertion into the vascular system of the patient, and are only fully assembled at some point subsequent to insertion (e.g., within a larger diameter blood vessel upstream (farther inward) of the insertion site), a relatively large access vessel is no longer necessary - thereby making percutaneous heart

valve therapy available for a larger patient population and with a lower risk of access site and blood vessel complications. By way of example but not limitation, where the intravascular device comprises an aortic stent-valve, the various components of the system can be easily introduced into a relatively narrow femoral artery and thereafter assembled in a larger upstream (farther inward) vessel (e.g., in the relatively wide aorta) before being advanced to and seated at the native aortic valve seat.

More particularly, at least one embodiment of the one or more present inventions preferably utilizes two separate balloons for a staged deployment of the stent-valve: a first, smaller-diameter "carrier" balloon for initial stent expansion (e.g., for preliminarily expanding the stent while the stent-valve is disposed in the descending aorta), and a second, larger-diameter "delivery" balloon for ultimate stent seating at the native valve seat. In one preferred form of at least one embodiment of the one or more present inventions, the stent-valve is mounted on the deflated first, smaller-diameter "carrier" balloon, then this relatively small assembly is introduced (within a covering sheath) into the relatively small femoral artery, advanced through the femoral artery, up through the iliac artery, and then into the relatively large descending aorta. The first, smaller-diameter "carrier" balloon is then inflated so as to expand the stent-valve to an intermediate diameter configuration that is large enough in diameter to receive the deflated second, larger-diameter "delivery" balloon. The first "carrier" balloon is then deflated, the first "carrier" balloon is withdrawn and replaced by the deflated second "delivery" balloon which, by partial inflation or other means, captures the stent-valve, and the assembly is then advanced up the descending aorta, ascending aorta, etc. to the native valve seat. The second "delivery" balloon is then inflated so as to set the stent-valve at the valve seat. Finally, the second "delivery" balloon is deflated and withdrawn from the surgical site.

In-line Dual-Balloon Catheter Delivery System

With reference now to Figs. 4A-4F, a stent-valve 120 may be advanced upon a first, smaller-diameter "carrier" balloon to the aorta and initially deployed (using the first, smaller-diameter "carrier" balloon) to an intermediate size, followed by co-axial exchange for the second, larger-diameter "delivery" balloon for advancement to the valve seat, and then further expansion of the stent-valve 120 at the valve seat. Alternatively, the stent-valve 120 may be advanced upon the carrier balloon all the way to the target valve seat and initially deployed before coaxial exchange for the delivery balloon and subsequent final expansion.

Referring now to Fig. 4A, an integrated system is shown in the form of an in-line dual-balloon delivery catheter system 100 that features an in-line dual-balloon catheter configuration. The configuration shown in Fig. 4A illustrates the in-line dual-balloon delivery catheter system 100 as it is being translated through the patient's body toward the target valve seat, such as the

aortic valve. For the in-line dual-balloon delivery catheter system 100 described herein, the carrier segment 112 is a lead/carrier balloon or mandrel at the distal portion of a catheter with the carrier segment 112 arrayed in-line on a catheter shaft with a more proximally positioned delivery segment 111 together at the distal portion of the catheter shaft. Alternatively, the delivery segment may be positioned distal to the carrier segment. The carrier segment 112 and delivery segment 111 are, for the case of the balloon-expandable stent-valve 120 example in this discussion, expandable balloons, for example, but may also be mandrels or expandable mandrels.

Here, it is noted that, in at least one embodiment (including both the in-line dual-balloon delivery catheter system 100 and the telescoping delivery system 200), a delivery segment comprising a delivery mandrel can be non-expanding. By way of example and not limitation, the means by which the delivery segment retains the stent-valve may vary. For example, in addition to friction, the delivery segment may retain the stent-valve by use of magnetic force. For such an assembly, if the stent-valve (or other deliverable device) is self-expanding or actuated to expansion and retained on the delivery segment for release by some other means (electronic, heat, e.g.), then the delivery mandrel can be non-expanding.

For the configuration shown in Fig. 4A, an outer delivery sheath 101 having, for example, a lengthwise body 104 that is 14 French inside diameter, is coaxially situated over a guidewire 131, for example, a 0.035 inch diameter wire, whereupon the integrated pair of expandable balloons reside. It is noted that all sizes and material types presented herein are exemplary and are not intended to be limiting, nor should they be interpreted as limiting, unless otherwise claimed. Although not required, an optional nose cone 113 may be positioned distally of the carrier segment 112 to assist with insertion of the catheter into the artery and subsequent traverse through it. In the embodiment wherein the delivery segment is disposed distal to the carrier segment, said nose cone is positioned immediately distal to the delivery segment and approximated to the tip of the sheath. The carrier segment 112 is used to hold the stent-valve 120 in place within the outer delivery sheath 101 and provide initial expansion of the stent-valve 120. Thereafter, the delivery segment 111 is used to provide final expansion of the stent-valve 120 for deployment of the stent-valve 120 at the valve seat.

The in-line dual-balloon delivery catheter system 100 is assembled external to the body by passing the delivery catheter with its linearly arrayed carrier segment 112 and delivery segment 111 within the central coaxial lumen of the delivery sheath 101 such that the carrier segment 112 of the catheter extends and is fully exposed beyond the distal terminal opening of the delivery sheath 101. The catheter-deliverable device, such as the stent-valve 120 in this example, is then coaxially mounted upon the carrier segment 112 by collapsing and compressing

it onto the carrier segment 112 such that friction between the two retains the device 120 upon the carrier segment 112. The carrier segment 112 with the catheter-deliverable device (stent-valve 120) mounted upon it is then retracted back (proximally) into the distal portion of the delivery sheath 101 so that the device is completely covered within the sheath 101. In some cases the tip of the carrier segment 112 may be extended beyond the end of the sheath. In such a case, partial expansion of the leading tip 113 of the carrier segment 112 (balloon or expandable mandrel) may be used to form the tapered "nose cone" as noted above, to facilitate advancement or insertion of the delivery system into the blood vessel. Alternatively, the carrier segment may be fabricated with a soft plastic tapered tip for this purpose.

In the example of retrograde (in relation to blood flow) passage of the delivery system carrying the catheter-deliverable device, initial guidance for passage of the delivery system is established by advancement of the guidewire 131 across the heart valve seat 141 into the upstream anatomic chamber, such as the left ventricle, there acting as a guiding rail for the coaxial advancement of the delivery system catheters. Then, at a point external to the body, by inserting the guide wire 131 into the distal tip of the carrier segment 112 of the delivery catheter, the assembled in-line dual-balloon delivery catheter system 100 with sheath 101 is then advanced into the body coaxially over the guidewire 131 to a position proximate to but short of the target anatomic site--in this case, the diseased heart valve seat 141.

Referring now to Fig. 4B, when in the aorta, the leading carrier segment 112 is expanded as by balloon inflation, thus partially expanding the catheter-deliverable device (stent-valve 120) within the expandable distal segment 103 of the delivery sheath 101. That is, the carrier segment 112 is used to pre-dilate the stent-valve 120 so that the diameter of the stent-valve 120 is sufficient to accept the delivery segment 111 when the delivery segment 111 is at least partially deflated or not fully expanded. The outer delivery sheath may include an expandable and flexible distal segment to accommodate the partially expanded stent-valve 120 and hold the partially expanded stent-valve 120 in place. The carrier segment 112 is then contracted as by balloon deflation and advanced by advancing the delivery catheter out of the catheter-deliverable device (stent-valve 120) that is retained within the expanded distal segment 103 of the sheath 101. Optional shallow flanges 102 on the internal surface of the sheath 101 immediately proximal and/or distal to the mounted position of the device 120 can be used to assist in retention of the device during movement relating to the exchange of the carrier segment 112 for the delivery segment 111 with the advance of the delivery catheter. Alternatively, retention or control lines 123, 124 of wire or suture material may be attached to the device 120, as on the frame 121 of the stent-valve 120. Other forms of retaining force may be advantageously

applied, such as by incorporating magnetic or electromagnetic elements within the delivery catheter shaft or within the sheath wall.

Referring now to Fig. 4C, as the delivery catheter 110 is thus advanced, the delivery segment 111 integrated thereupon thus is also advanced within the sheath 101 to a position astride the catheter-deliverable device (stent-valve 120) within the delivery sheath 101, with the tip of the delivery catheter extended beyond the tip of the delivery sheath 101. More particularly, the delivery segment 111 is advanced axially to a position radially interior to the stent-valve 120. The delivery segment 111 is then partially expanded to contact the stent-valve 120.

Referring to Fig. 4D, with the delivery segment 111 positioned within the stent-valve 120, in at least one embodiment the carrier segment 112 is positioned at the valve seat and may be further expanded to facilitate advancement of the stent-valve 120 within the plane of the aortic valve. That is, if deemed desirable by the surgeon, the carrier segment 112 is temporarily expanded and then contracted or deflated within the plane of the valve seat to facilitate subsequent axial advancement of the delivery segment 111 that carries the stent-valve 120.

With the projected tip of the delivery segment, and beyond that the carrier segment leading, the delivery catheter, catheter-deliverable device (stent-valve 120), and delivery sheath 101 are advanced together as a unit across the target anatomic plane (native heart valve seat 141, for example) to a position astride the target plane deemed suitable for deployment of the catheter-deliverable device (stent-valve 120). In the embodiment wherein the carrier segment is disposed proximal to the delivery segment this advancement occurs with the tip of the delivery segment leading the catheter assembly, and the carrier segment further proximal within the sheath. Referring now to Fig. 4E, after the delivery segment 111 is positioned in the plane of the target valve seat, the outer delivery sheath of the delivery system is withdrawn (as shown by the arrows in Fig. 4E) to expose the stent-valve 120; however, the stent-valve 120 remains undeployed because it continues to remain attached to the delivery segment 111. That is, the delivery sheath 101 is coaxially retracted with the delivery catheter held in place so as to expose the catheter-deliverable device (stent-valve 120) retained upon the delivery segment 111 at the site of deployment. The catheter-deliverable device (stent-valve 120) is then deployed by expansion of the delivery segment 111, such as by balloon inflation. Accordingly, and referring now to Fig. 4F, after the stent-valve 120 is exposed at the plane of the aortic valve, the delivery segment 111 is expanded to deploy the stent-valve 120. With full expansion and deployment of the catheter-deliverable device (stent-valve 120) the device is retained within the target anatomic plane (native heart valve seat 141). The delivery segment 111 is then contracted as by balloon deflation, function of the deployed device is confirmed, and the delivery catheter, delivery

sheath 101, and guidewire 131 are retracted from the anatomic target area and removed from the body to complete the procedure.

In at least one embodiment, optional retention/control lines 123, 124 are released from valve frame 121 after successful deployment of stent-valve 120 is confirmed. Then balloon catheter 110 and guidewire 131 are removed from the valve seat 141 and withdrawn into sheath 101 for removal from the body.

In at least one embodiment, the carrier segment 112 is located axially proximal to the delivery segment 111. For such a configuration, the delivery segment 111 is advanced outside the sheath 101 and leads the assembly until the point the exchange is made. Then after the stent-valve 120 is partially expanded by the carrier segment 112, the delivery segment 111 is pulled back into the sheath 101 where the stent-valve 120 is retained, and the delivery segment 111 then captures the stent-valve 120. In this case, the tip of the delivery segment 111 at the tip of the sheath 101 will lead the further advance while the carrier segment 112 is sequestered more proximally in the sheath 101.

Telescoping Catheter Delivery System

Referring now to Figs. 5A-5E, in an alternative embodiment, a telescoping delivery system 200 for a stent-valve 120 is provided wherein a delivery balloon catheter 210 is co-axially situated or "threaded" over a carrier balloon catheter shaft 224 associated with a carrier segment 221. Accordingly, the carrier segment 221 can be advanced axially independent of the axial position of the delivery balloon 211. As a result, the carrier segment shaft 224 acts as a guide rail for the delivery balloon catheter 210 and the stent-valve 120 that is then radially positioned exterior to the delivery balloon 211. Step-by-step illustrations are provided in the drawings and are described in the following paragraphs.

Referring now to Fig. 5A, an outer delivery sheath 101 having, for example, a proximal shaft body with a 14 French inside diameter, is coaxially situated over a guidewire 131, whereupon a carrier segment shaft 224 and a delivery balloon shaft 214 are also co-axially situated. For the embodiment of the telescoping delivery system 200 described, the carrier segment 221 is a carrier balloon or mandrel at a distal portion of a carrier catheter 220 that is passed within the central lumen of a larger delivery catheter 210 that has a delivery segment 211 at its distal portion. By way of example and not limitation, the carrier segment shaft has a 0.035 inch outer diameter and is connected to the carrier segment 221 that is expandable to between 5-10 mm in diameter. The delivery segment 211 is, for the case of the balloon-expandable stent-valve 120 example, an expandable delivery balloon, for example. Accordingly, the delivery balloon may have an outside diameter of, for example, approximately 12-14 French when

uninflated, and, in separate embodiments, is located axially either proximal or distal to the carrier segment 221.

The system is assembled external to the body by passing the carrier catheter 220 within the central coaxial lumen of the larger delivery catheter 210 such that the carrier segment 221 extends and is fully exposed beyond the tip 212 of the delivery catheter. These two catheters thus joined are then passed together through the delivery sheath 101 such that the carrier segment 221 of the carrier catheter 220 again extends and is fully exposed beyond the tip of the delivery sheath 101. The catheter-deliverable device, such as the stent-valve 120 in this example, is then coaxially mounted upon the carrier segment 221 by collapsing and compressing it onto the carrier segment 221 such that friction between the two retains the device 120 upon the carrier segment 221. The carrier segment 221 with the catheter-deliverable device (stent-valve 120) mounted upon it is then retracted back (proximally) into the delivery sheath 101 so that the device is completely covered within the sheath 101.

Referring now to Fig. 5B, the lead carrier segment balloon 221 optionally may be partially expanded to hold the stent-valve 120 within the outer delivery sheath 101. In addition, in some cases the tip 222 of the carrier catheter and carrier segment 221 may be extended beyond the end of the sheath 101. In such a case, partial expansion of the leading tip 223 of the carrier segment 221 (balloon or expandable mandrel) may be used to form a tapered "nose cone" to facilitate advancement or insertion of the delivery system into the blood vessel. Alternatively, and as previously noted for the in-line dual-balloon delivery catheter system 100, the carrier catheter 220 for the telescoping delivery system 200 may be fabricated with a soft plastic tapered tip for this purpose.

In the example of retrograde (in relation to blood flow) passage of the delivery system carrying the catheter-deliverable device, initial guidance for passage of the delivery system is established by advancement of the guidewire 131 across the heart valve seat 141 into the upstream anatomic chamber, such as the left ventricle, there acting as a guiding rail for the coaxial advancement of the delivery system catheters. Then, at a point external to the body, by inserting the guide wire 131 into the distal tip of the carrier catheter 220, the assembled delivery catheter system 200 with carrier catheter 220, delivery catheter 210 and sheath 101 is then advanced into the body coaxially over the guidewire 131 to a position proximate to but short of the target anatomic site--in this case, the diseased heart valve seat 141.

Referring now to Fig. 5C, in at least one embodiment, when in the aorta the carrier segment 221 is further expanded to effect expansion of the stent-valve 120 within the outer delivery sheath so that the delivery balloon can be advanced axially and positioned radially to the interior of the stent-valve 120. That is, when in the aorta, the leading carrier segment 221 is

expanded, such as by balloon inflation, thus partially expanding the catheter-deliverable device (stent-valve 120) within the expandable distal segment 103 of the delivery sheath 101. In at least one embodiment, the outer delivery sheath 101 includes an expandable, flexible distal segment 103 that allows partial expansion of the stent-valve 120 within the outer delivery sheath, such as to a sufficient diameter to receive the unexpanded delivery balloon 211. Although the distal segment of the outer delivery sheath may be expandable, the outer delivery sheath shaft 104 located axially proximal to the carrier segment 221 preferably remains relatively small in diameter, that is, at its original unexpanded diameter, such as having a 14 French inside diameter at the entry point of the body and blood vessel.

With reference now to Fig. 5D, after partial expansion of the stent-valve 120 within the distal portion 103 of the outer delivery sheath 101, the carrier segment 221 is contracted as by balloon deflation and is then advanced axially beyond the outer delivery sheath 101 and out of the catheter-deliverable device (stent-valve 120) leaving it retained within the expanded distal segment 103 of the sheath 101.

The delivery segment balloon 211 is then axially advanced to a position radially to the interior of the stent-valve 120. With the delivery segment 211 of the delivery catheter 210 then coaxially advanced over the shaft 224 of the carrier catheter to a position astride the catheter-deliverable device (stent-valve 120) within the delivery sheath 101, the delivery segment balloon 211 is then partially expanded to dock or capture the stent-valve 120.

Referring now to Fig. 5E, the leading carrier segment balloon 221 of the carrier catheter 220 is then advanced across the target anatomic plane (native heart valve seat 141) coaxially following the guide wire 131 there in place, where it then provides additional mechanical guidance and support for the further coaxial advancement of the larger delivery catheter 210 upon the shaft 224 of the carrier catheter 220. Alternatively, the carrier catheter 220 may be coaxially withdrawn from the system and the body leaving the guide wire in place , then a shaped catheter (one with specifically designed terminal curves, such as “pig tail” or Amplatz type curves commonly found on angiographic catheters, to facilitate its being properly situated relative to the anatomy) may then be advanced over the guide wire to the upstream anatomic chamber, its shaft then substituting for the shaft 224 of the carrier catheter. Accordingly, Fig. 5E illustrates the guidewire 131 and carrier segment 221 as having passed the aortic valve such that the guidewire and carrier segment reside within the patient’s left ventricle. Axial advancement of the carrier segment 221 and the carrier catheter shaft 224 can be done independent of the location of the delivery balloon 211. Thereafter, the delivery segment balloon 211 and the delivery catheter shaft 214 are axially advanced co-axially over the carrier catheter shaft 224 that acts as a guide rail for the delivery segment balloon 211. More

particularly, with the projected tip 212 of the delivery catheter 211 leading beyond the tip of the sheath, the delivery segment 211, catheter-deliverable device (stent-valve 120), and delivery sheath 101 are advanced together as a unit across the target anatomic plane (native heart valve seat 141, for example) to a position astride the target plane deemed suitable for deployment of the catheter-deliverable device (stent-valve 120).

Once positioned at the plane of the valve seat of the patient's aortic valve, the delivery sheath 101 is coaxially retracted with the delivery catheter held in place so as to expose the catheter-deliverable device (stent-valve 120) retained upon the delivery segment 211 at the site of deployment. Thereafter, the final delivery balloon is expanded to deploy the stent-valve 120.

With full expansion and deployment of the catheter-deliverable device (stent-valve 120) the device is retained within the target anatomic plane (native heart valve seat 141). The delivery segment 211 is then contracted as by balloon deflation, function of the deployed device is confirmed, and the delivery catheter, carrier catheter, delivery sheath 101, and guide wire 131 are retracted from the anatomic target area and removed from the body to complete the procedure.

Expandable Outer Delivery Sheath

As described herein, at least one embodiment of the endoluminal delivery system includes an outer delivery sheath that further comprises a distal segment that is expandable. Several different ways of providing an expandable distal segment are described in the following paragraphs.

Referring now to Fig. 6A, the distal segment of the outer delivery sheath 310 may comprise a woven alloy wire portion 311. By way of example and not limitation, the distal segment may be similar in design to the IDEV TECHNOLOGIES SUPERA® stent that includes woven nitinol wire. Alternatively, in at least one embodiment, the woven wire portion 311 may further comprise a flexible plastic investment; that is, a configuration wherein the woven wire portion resides within a flexible plastic matrix forming a tubular portion of the outer delivery sheath. In typical operation, the wire weave is formed in expanded configuration and elongated by longitudinal traction force on the wire elements with resulting contraction of the tubular form to a decreased diameter. Thereafter, the release of traction force effects self-expansion of the weave. In at least one embodiment, a distal portion of the distal segment of the outer delivery sheath 310 may be widened by using control lines to pull on control ends of the woven wire portion of the distal segment.

Referring now to Fig. 6B, in an alternative embodiment, the distal segment of the outer delivery sheath 320 includes a cut nitinol stent 321 residing within the sheath investment. More particularly, the distal segment of the outer delivery sheath includes a nitinol stent 321

embedded within the distal segment, wherein the nitinol stent 321 provides shape-memory functionality for the distal segment. As a result, when the balloon catheter is inflated within the distal segment with the stent-valve 120 mounted on it, the distal segment expands to accommodate the inflated balloon catheter and stent-valve. Thereafter, when the balloon catheter is pushed out of the outer delivery sheath 320, the distal segment then retracts because of the shape-memory functionality associated with the nitinol stent 321 residing with the distal segment.

Referring now to Fig. 6C, in at least one embodiment the distal segment of the outer delivery sheath 330 comprises an elastic material that can passively expand and optionally retract. That is, when a balloon catheter is expanded within the distal segment, the elastic material accommodates the expansion. Thereafter, with deflation of the balloon catheter the elastic material forming the distal segment retracts. Alternatively, the sheath material, such as PTFE (polytetrafluoroethylene) may expand but not contract. In such case, the thin-walled sheath material folds inward along longitudinal lines when retracted through a proximally disposed entry sheath or the vascular entry point itself, permitting ready removal from the body, even in a persistently expanded condition.

Referring now to Fig. 6D, in an alternative embodiment, the distal segment of the outer delivery sheath 340 includes a plurality of electrically actuated piezo-ceramic elements 341. Electrical wiring or conductors 342 extend to the proximal end of the outer delivery sheath 340 to facilitate application of an electrical current to the piezo-ceramic elements 341. When desired, the surgeon closes a circuit to engage a power source 343 and apply the electrical current to the piezo-ceramic elements 341 via the electrical wiring or conductors 342. Upon being energized, the piezo-ceramic elements 341 expand the distal segment of the outer delivery sheath 340. Contraction of the distal segment is achieved by terminating the electrical current to the piezo-ceramic elements 341. Further reference here is made to U.S. Patent No. 5,415,633, the content of which is incorporated by reference in its entirety.

Referring now to Fig. 6E, a variation of the use of electrically charged elements comprises the use of active elements featuring differential alloy sandwiches or laminates 344 that bend when a current is applied. The bending of the active elements causes the distal segment to expand. As with the piezo-ceramic elements 341 described above, contraction of the distal segment is achieved by terminating the application of electrical current to the differential alloy sandwiches or laminates 344.

In another alternative embodiment, a magnetic or electromagnetic force is used to retain a stent-valve 120 on a delivery segment balloon for advancement to the target valve plane and subsequent deployment. More particularly, and with reference now to Fig. 7, an alternative

endoluminal magnetic delivery system 400 is shown that utilizes a magnetic or electromagnetic force to maintain the position of the stent-valve 120 on the delivery segment balloon 411, wherein the delivery segment balloon 411 is located at or near the distal portion of a delivery catheter shaft 414. The magnet or electromagnet 416 are preferably incorporated into the balloon catheter shaft 414 co-axial to and axially centered along the delivery segment balloon 411 so as to align with the axial position of the mounted stent-valve. As one of skill in the art will appreciate, the stent-valve 120 must incorporate a material susceptible to magnetism in a sufficient quantity and distribution to facilitate attraction of the stent-valve 120 to the magnet or electromagnet 416 incorporated into the balloon catheter shaft 414. A guidewire 131 serves to guide the co-axially situated delivery balloon catheter 410. The delivery balloon may be partially expanded to: (a) provide a nose cone for facilitating insertion of the delivery system into, and traverse through the patient's blood vessel; and/or (b) to provide further frictional force for securing the stent-valve 120. Since the stent-valve 120 is held in place by a magnetic or electromagnetic force as well as any further frictional force due to partial expansion of the delivery balloon, the stent-valve 120 can be securely advanced through the patient's vascular system without need of an outer delivery sheath, thereby simplifying and reducing the profile of the delivery system. Once the target valve plane is reached, the delivery balloon 411 is expanded, thereby overcoming the magnetic or electromagnetic force (of course, an electromagnetic force may be terminated by stopping current to the electromagnet), to deploy the stent-valve 120 at the plane of the diseased native valve. Similarly, the magnet of the magnetic delivery catheter 410 may be incorporated into the delivery segment balloons of the in-line dual balloon system 100 and/or the telescoping catheter delivery system 200 in a similar manner to facilitate capture and retention of the stent-valve upon the delivery segment balloon in its traverse through the anatomic structures.

In addition to endoluminal delivery of a stent-valve 120, at least one embodiment of the one or more present inventions is directed to a retrieval and/or repositioning system 500 that can be used to remove a deployed stent-valve 120 from a patient, or otherwise reposition the stent-valve 120 within the patient. With reference now to Figs. 8A and 8B, an embodiment of a retrieval and/or repositioning system 500 is shown. The retrieval and/or repositioning system comprises a retrieval catheter 510 on a distal portion of which is integrated a magnet 511, and more preferably, an electromagnet of sufficient strength to at least partially collapse and secure a previously deployed stent-valve 120. With reference to Fig. 8B, the partially collapsed valve is then either withdrawn (that is, retrieved from the patient), for example as by traction on optional control lines 124 as shown, or repositioned and then redeployed.

Referring now to Figs. 8C and 8D, in a separate embodiment, a multipolar magnetic retrieval catheter system 520 is provided in which multiple magnetic elements 522 are circumferentially arrayed and disposed at a distal portion of a retrieval catheter 521 in a manner that allows the radially outward movement of the magnets 522, and the portions of the underlying catheter elements 523 to which they are attached, into contact with the radially interior surface of the deployed stent-valve 120. In at least one embodiment, the underlying portions 523 of the catheter to which the magnets 522 are attached are longitudinally separate from each other so that they are free to move independently from each other as the attached magnets 522 move radially outward. In at least one embodiment, the magnets 522 are of like polarity and are initially restrained into proximity with each other by an overlying sheath mechanism. When said sheath 524 is retracted the distal catheter portions 523 with their attached magnets 522 move radially outward under repulsive magnetic force into contact with the stent-valve 120. The close proximity if not complete contact of the magnets 522 to the stent-valve frame 121 advantageously maximizes the retention force facilitating the traction force applied in the removal of the device from the valve plane. The sheath 524 may be re-advanced over the magnetic distal portions 523 of the catheter, thus applying radially inward force on the device frame that serves to contract it and facilitate its removal under axial traction.

Shaped Catheter

The various sheath and catheter shafts described herein for the various embodiments may include a "shaped" distal portion. More particularly, a "shaped" catheter may be used to assist in crossing anatomic resistance or provide guidance for recrossing the valve plane in the event the guide wire is displaced from the ventricle. This problem occurs when the stent-valve and the delivery system are advanced around the aorta. In such a situation, the traction forces, not uncommonly, will pull the guide wire out of the ventricle. If this happens—with the delivery system already in the aorta—it requires the delivery system be removed from the patient's body and the sequence started over from the beginning. Advantageously, one or more embodiments described herein can assist with avoiding this problem. That is, a catheter can be used that includes a distal portion with one or more curved shapes, such as "pig tail" or Amplatz type curves commonly found on angiographic catheters, and including a central coaxial lumen through which is passed the guidewire. The shaped catheter is used to "steer" the guide wire across the very narrowed valve orifice. Thus, in one embodiment, a "shaped" catheter is passed within the central lumen of the delivery catheter. In such a configuration, the guide wire can be re-crossed through the valve plane more readily, and the shaped catheter—advantageously, a relatively firm catheter—can be advanced to the ventricle and left to act as an enhanced support rail for the delivery catheter.

To assist in the understanding of the present invention the following list of components and associated numbering found in the drawings is provided herein:

Number	Component
100	In-Line Dual Balloon Catheter Delivery System
101	Delivery Sheath
102	Optional Flange Of Internal Sheath
103	Expandable, Flexible Sheath Segment
104	Sheath Body
110	Dual In-Line Balloon Catheter Assembly
111	Delivery Segment Is Delivery Balloon
112	Carrier Segment Is In-Line Leading Carrier Balloon
113	Optional Nose Cone
114	Exit Of Distal Control Lines From Catheter Shaft
120	Stent-Valve Assembly
121	Valve Frame
122	Collapsed Valve Membrane
123	Optional Control Lines Attached To Distal End Of Valve Frame (Passed Within Catheter Shaft)
124	Optional Control Lines Attached To Proximal End Of Valve Frame
130	Guide Wire Assembly
131	Guide Wire
140	Native Heart Valve
141	Native Heart Valve Seat
200	Telescoping Balloon Catheter Delivery System
210	Delivery Balloon Catheter Assembly
211	Delivery Segment Is Delivery Balloon
212	Tip Of Delivery Segment Balloon
213	Partially Inflated Leading Tip Of Delivery Segment Balloon
214	Delivery Balloon Catheter Shaft
220	Carrier Balloon Catheter Assembly
221	Carrier Segment Is Leading Balloon That Coaxially Telescopes Within Central Lumen Of Delivery Segment Balloon
222	Tip Of Carrier Segment Balloon
223	Inflated Leading Tip Of Carrier Segment Balloon
224	Shaft Of Carrier Catheter

300 Expandable Sheath System
310 Woven Wire Sheath
320 Sheath With Embedded Nitinol Stent
321 Nitinol Stent
330 Flexible Plastic Sheath
340 Electronically Actuated Sheath
341 Piezo-Ceramic Elements
342 Conductors
343 Power Source
344 Alloy Laminates
400 Magnetic Balloon Catheter Delivery System
410 Magnetic Balloon Delivery Catheter
411 Delivery Balloon
412 Tip Of Magnetic Balloon Delivery Catheter
413 Partially Inflated Tip Of Delivery Balloon
414 Shaft Of Magnetic Balloon Delivery Catheter
415 Guide Wire Lumen Of Magnetic Balloon Delivery Catheter
416 Magnet Or Electromagnet
500 Magnetic Retrieval Catheter System
510 Magnetic Retrieval Catheter Assembly
511 Magnet Or Electromagnet
520 Multipolar Magnetic Retrieval Catheter Assembly
521 Multipolar Magnetic Retrieval Catheter
522 Magnets – Circumferentially Arrayed
523 Distal Mobile Catheter Elements Attaching To Magnets
524 Sheath

The one or more present inventions may be embodied in other specific forms without departing from its spirit or essential characteristics. The described embodiments are to be considered in all respects only as illustrative and not restrictive. The scope of the one or more present inventions is, therefore, indicated by the appended claims rather than by the foregoing description. All changes which come within the meaning and range of equivalency of the claims are to be embraced within their scope.

The one or more present inventions, in various embodiments, includes components, methods, processes, systems and apparatus substantially as depicted and described herein, including various embodiments, subcombinations, and subsets thereof. Those of skill in the art

will understand how to make and use the one or more present inventions after understanding the present disclosure.

The one or more present inventions, in various embodiments, includes providing devices and processes in the absence of items not depicted and/or described herein or in various embodiments hereof, including in the absence of such items as may have been used in previous devices or processes (e.g., for improving performance, achieving ease and/or reducing cost of implementation).

The foregoing discussion of the one or more present inventions has been presented for purposes of illustration and description. The foregoing is not intended to limit the one or more present inventions to the form or forms disclosed herein. In the foregoing Detailed Description for example, various features of the one or more present inventions are grouped together in one or more embodiments for the purpose of streamlining the disclosure. This method of disclosure is not to be interpreted as reflecting an intention that the claimed one or more present inventions requires more features than are expressly recited in each claim. Rather, as the following claims reflect, inventive aspects lie in less than all features of a single foregoing disclosed embodiment. Thus, the following claims are hereby incorporated into this Detailed Description, with each claim standing on its own as a separate preferred embodiment of the one or more present inventions.

Moreover, though the description of the one or more present inventions has included description of one or more embodiments and certain variations and modifications, other variations and modifications are within the scope of the one or more present inventions (e.g., as may be within the skill and knowledge of those in the art, after understanding the present disclosure). It will be understood that many changes in the details, materials, steps and arrangements of elements, which have been herein described and illustrated in order to explain the nature of the invention, may be made by those skilled in the art without departing from the scope of embodiments of the one or more present inventions. It is intended to obtain rights which include alternative embodiments to the extent permitted, including alternate, interchangeable and/or equivalent structures, functions, ranges or steps to those claimed, whether or not such alternate, interchangeable and/or equivalent structures, functions, ranges or steps are disclosed herein, and without intending to publicly dedicate any patentable subject matter.

CLAIMS

What Is Claimed Is:

1. A system for providing endoluminal delivery of a deliverable device through vasculature of a patient to a delivery site within the patient, comprising:

an outer delivery sheath including a distal section, wherein at least a portion of the outer delivery sheath is sized for insertion into the vasculature of the patient;

a carrier segment located at a distal portion of a catheter shaft, the carrier segment having an outer surface sized to temporarily hold the deliverable device in the distal section of the outer delivery sheath, wherein at least a portion of the catheter shaft is located within and coaxial to the outer delivery sheath; and

a delivery segment located coaxial to the outer delivery sheath, the delivery segment having an outer surface sized to radially fit within the deliverable device after detaching the deliverable device from the carrier segment when the deliverable device resides within the distal section of the outer delivery sheath, wherein the delivery segment is configured to deploy the deliverable device at the delivery site.

2. The system of Claim 1, wherein at least a portion of the distal section of the outer delivery sheath is expandable.

3. The system of Claim 2, wherein the at least a portion of the distal section of the outer delivery sheath comprises one or more electrically activated elements.

4. The system of Claim 2, wherein the at least a portion of the distal section of the outer delivery sheath comprises one or more piezo-ceramic elements.

5. The system of Claim 2, wherein the at least a portion of the distal section of the outer delivery sheath comprises a passively expandable material that is expandable upon application of an outward radial force applied by at least one of the carrier segment and the delivery segment.

6. The system of Claim 2, wherein the at least a portion of the distal section of the outer delivery sheath expands upon application of a tensile force to the at least a portion of the distal section.

7. The system of Claim 1, wherein the distal section includes at least one of an internal projection and a narrowed area extending radially inward from an interior surface of the distal section.

8. The system of Claim 1, wherein a portion of an internal surface of the outer delivery sheath further comprises a guide for retaining at least a portion of a longitudinally extending element configured to selectively manipulate at least a part of the outer delivery sheath or a structure coaxial to the outer delivery sheath.

9. The system of Claim 1, wherein a portion of an internal surface of the outer delivery sheath further comprises a guide, the guide comprising at least one of:

(a) a lumen; and

(b) a grommet;

wherein the guide retains at least one control line for selective retention of the deliverable device.

10. The system of Claim 1, wherein the carrier segment and the delivery segment are both situated upon the catheter shaft.

11. The system of Claim 1, wherein the carrier segment is situated upon the catheter shaft, and wherein the delivery segment is associated with a delivery segment shaft that is coaxial to the catheter shaft and axially moveable relative to the catheter shaft.

12. The system of Claim 1, wherein the carrier segment is an expandable balloon having an expanded diameter smaller than an expanded diameter for the delivery segment.

13. The system of Claim 1, wherein the delivery segment is an expandable balloon having an expanded diameter larger than an expanded diameter for the carrier segment.

14. The system of Claim 1, wherein at least one of the carrier segment and the delivery segment is a mandrel.

15. The system of Claim 14, wherein the mandrel is expandable by mechanical or electromechanical means.

16. The system of Claim 14, wherein the mandrel is not expandable.

17. The system of Claim 1, wherein the delivery segment is located axially proximal to the carrier segment.

18. The system of Claim 1, wherein the delivery segment is located axially distal to the carrier segment.

19. The system of Claim 1, wherein the delivery segment includes a magnet to aid in capture and retention of the deliverable device on the delivery segment.

20. An assembly for intravascular delivery of a deliverable device to a delivery site within a patient, comprising:

a first catheter including a first catheter shaft;

a carrier segment situated along the first catheter shaft, the carrier segment configured to receive the deliverable device prior to inserting the first catheter within the patient; and

a delivery segment sequentially positioned in an axial orientation relative to the carrier segment, wherein the delivery segment is configured to engage the deliverable device within the patient while the deliverable device is coaxial to at least a portion of

the first catheter, and wherein the delivery segment is configured to thereafter deploy the deliverable device at the delivery site.

21. The assembly of Claim 20, wherein the delivery segment is also situated along the first catheter.

22. The assembly of Claim 20, wherein the delivery segment is situated along a second catheter, the second catheter comprising a coaxial lumen through which passes the first catheter.

23. The assembly of Claim 22, wherein at least one of the first catheter and the second catheter comprise a curved distal portion.

24. The assembly of Claim 20, wherein the carrier segment is an expandable balloon.

25. The assembly of Claim 20, wherein the carrier segment is a mandrel.

26. The assembly of Claim 25, wherein the mandrel is expandable by mechanical or electromechanical means.

27. The assembly of Claim 25, wherein the mandrel is non-expandable.

28. The assembly of Claim 20, wherein the delivery segment is an expandable balloon.

29. The assembly of Claim 20, wherein the delivery segment is a mandrel.

30. The assembly of Claim 29, wherein the mandrel is expandable by mechanical or electromechanical means.

31. The assembly of Claim 29, wherein the mandrel is non-expandable.

32. The assembly of Claim 20, wherein the delivery segment includes a magnet to aid in capture and retention of the deliverable device on the delivery segment.

33. The assembly of Claim 20, wherein the delivery segment includes an electromagnet to aid in capture and retention of the deliverable device on the delivery segment.

34. A method of delivering a deliverable device through vasculature of a patient to a target site within the patient, comprising:

mounting the deliverable device on a selectively expandable carrier segment located along a catheter shaft, wherein at least a portion of the catheter shaft is located within and coaxial to an outer delivery sheath;

inserting the outer delivery sheath and catheter shaft into the patient;

moving the outer delivery sheath within the patient to position the selectively expandable carrier segment and the deliverable device near the target site;

partially expanding the deliverable device using the selectively expandable carrier segment while the deliverable device remains at least partially within the outer delivery sheath;

positioning a delivery segment radially within the deliverable device and partially expanding the delivery segment to facilitate engagement of the delivery segment with the deliverable device;

moving the delivery segment and deliverable device to the target site; and

deploying the deliverable device at the target site by further expanding the delivery segment.

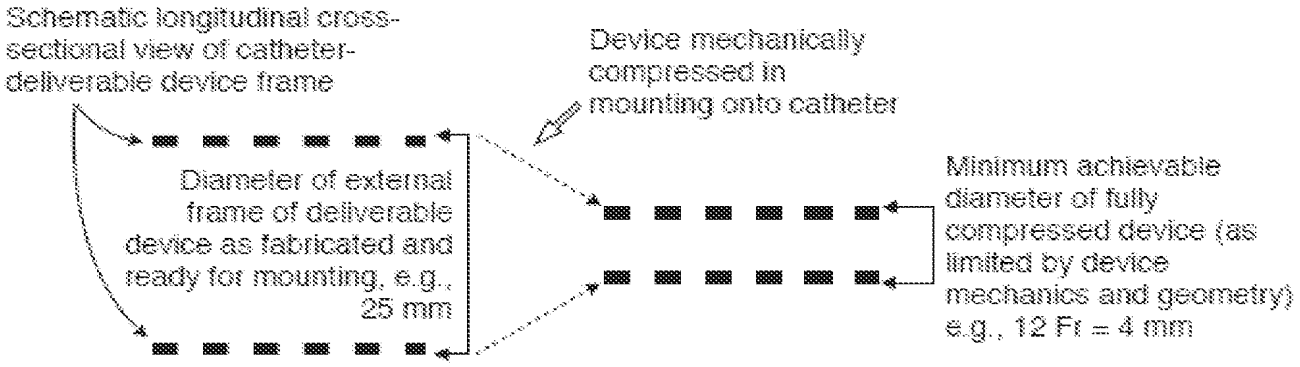


FIG. 1
(PRIOR ART)

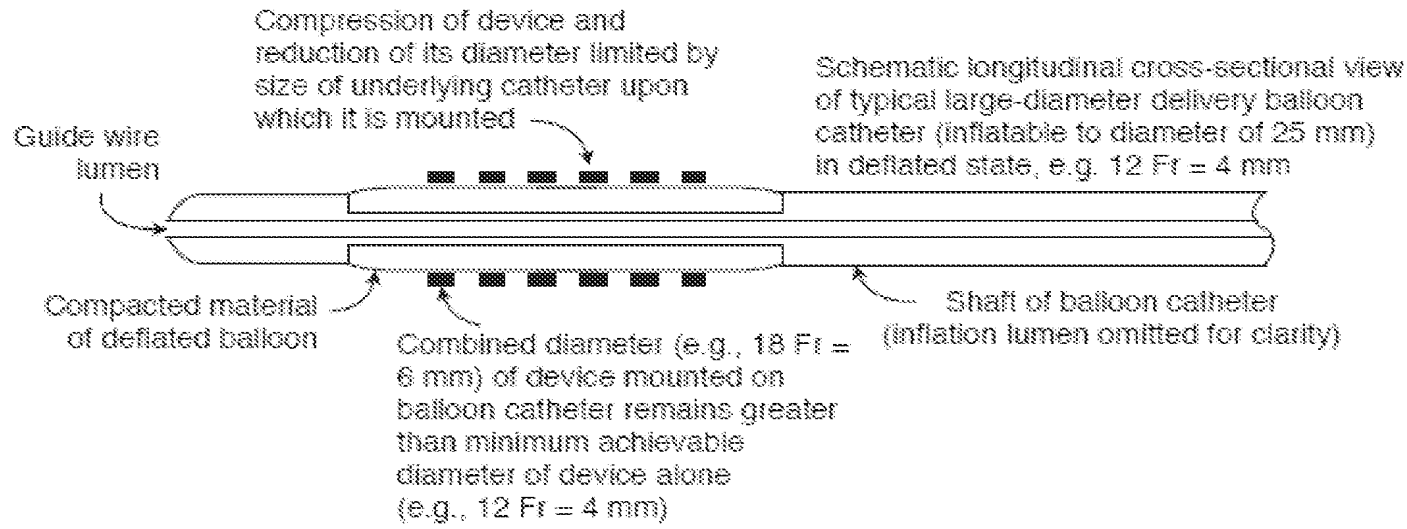


FIG. 2
(PRIOR ART)

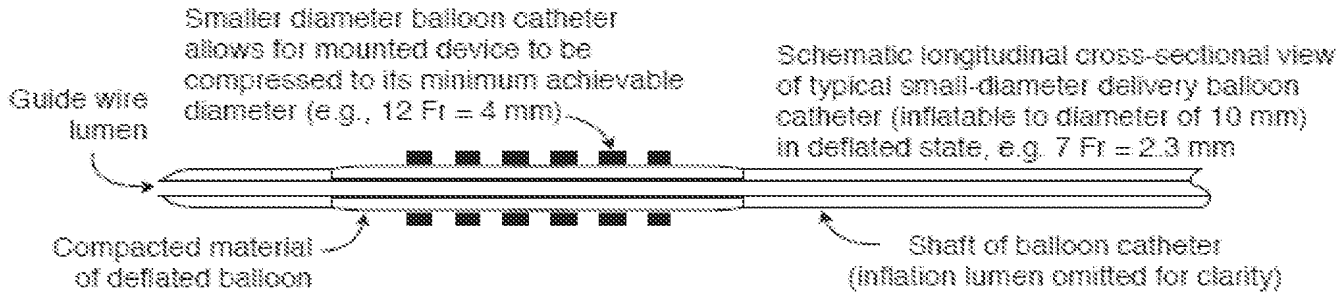
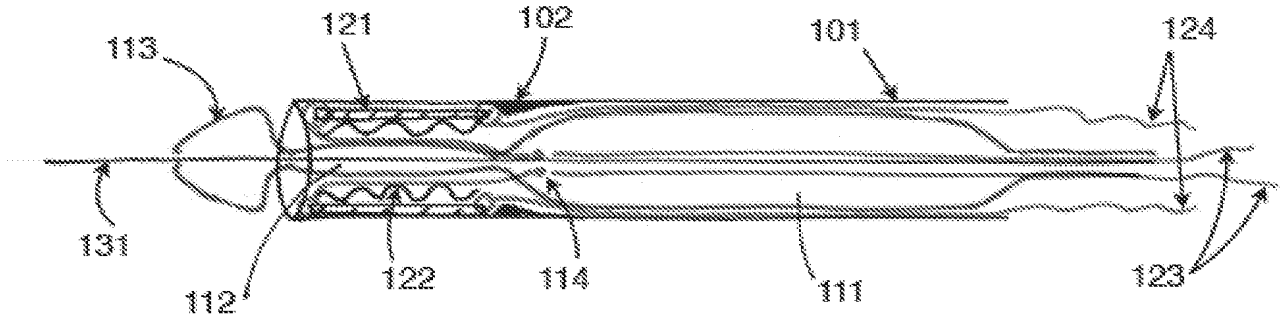

Smaller diameter balloon catheter allows for mounted device to be compressed to its minimum achievable diameter (e.g., 12 Fr = 4 mm)
Guide wire lumen
Schematic longitudinal cross-sectional view of typical small-diameter delivery balloon catheter (inflatable to diameter of 10 mm) in deflated state, e.g. 7 Fr = 2.3 mm
Compacted material of deflated balloon
Shaft of balloon catheter (inflation lumen omitted for clarity)

FIG. 3

FIG. 4A



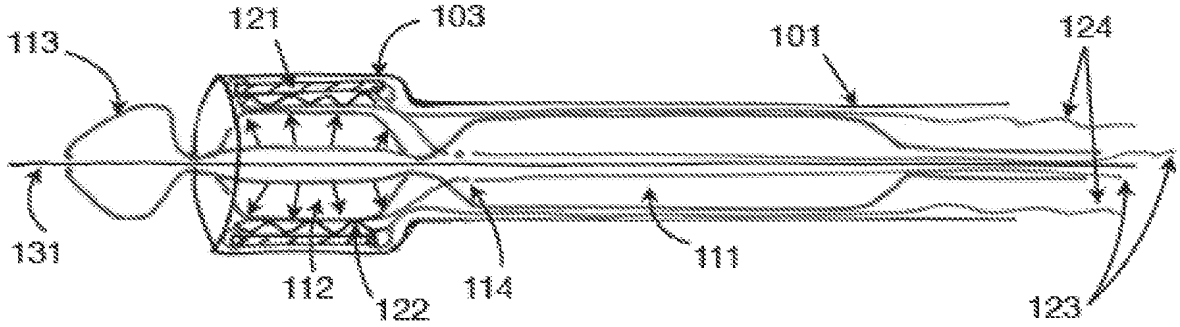


FIG. 4B

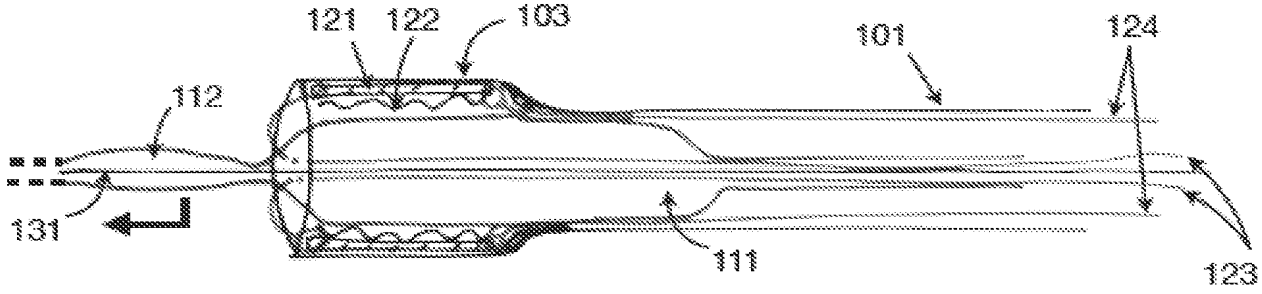
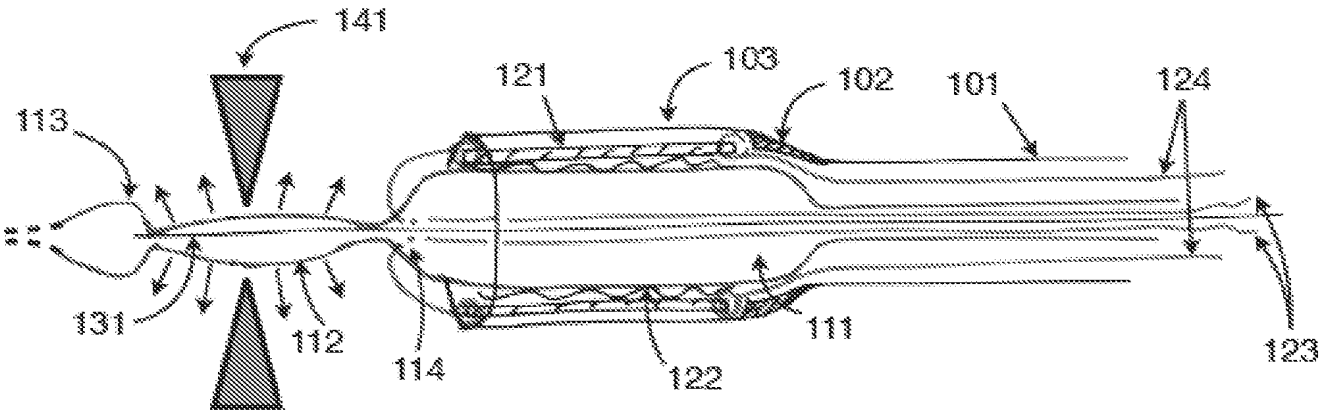


FIG. 4C

FIG. 4D



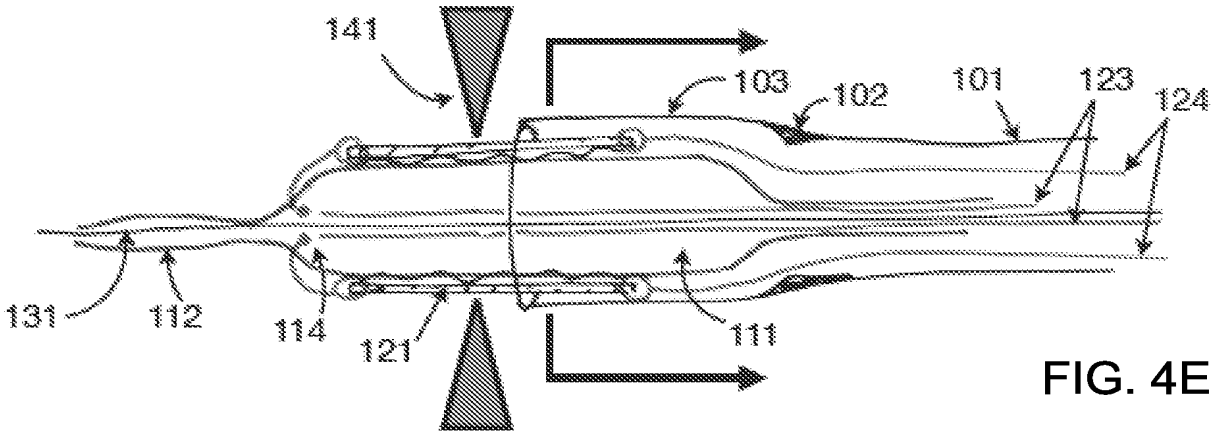


FIG. 4E

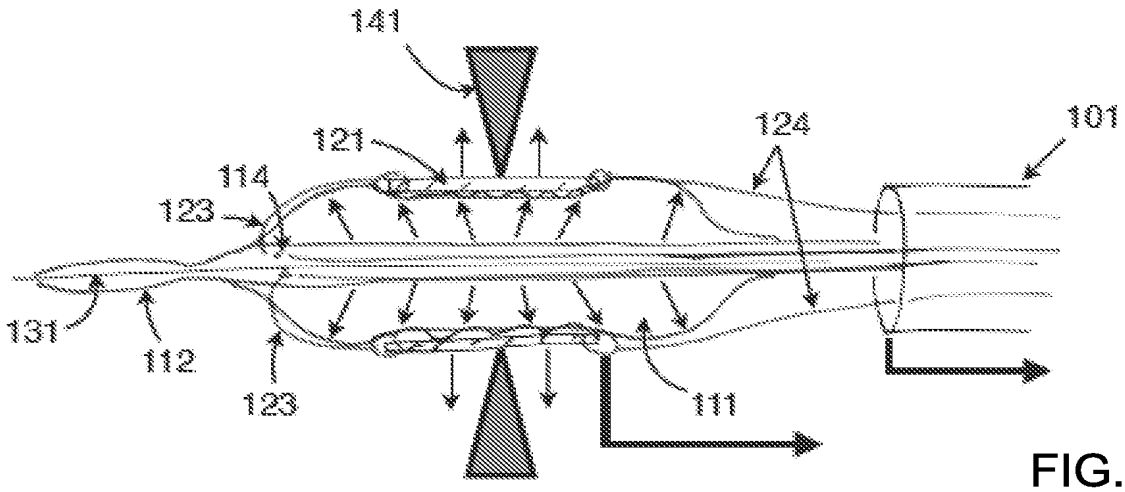


FIG. 4F

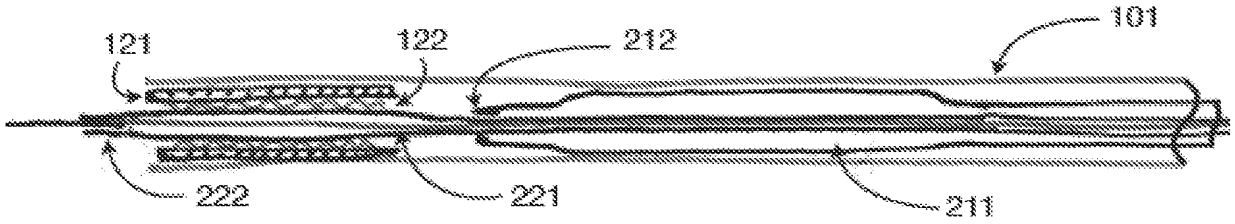


FIG. 5A

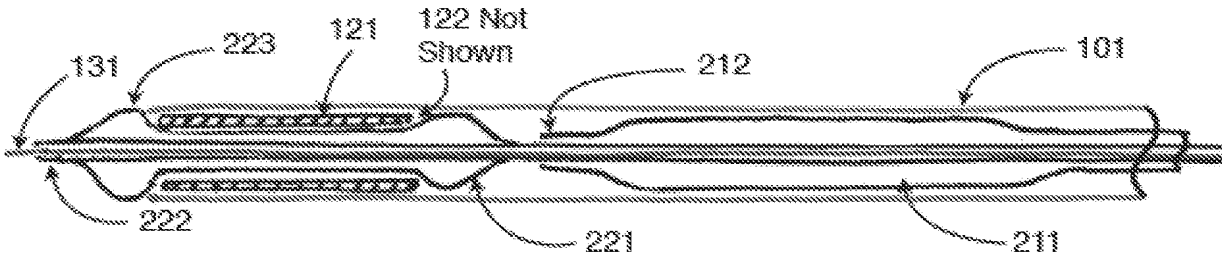


FIG. 5B

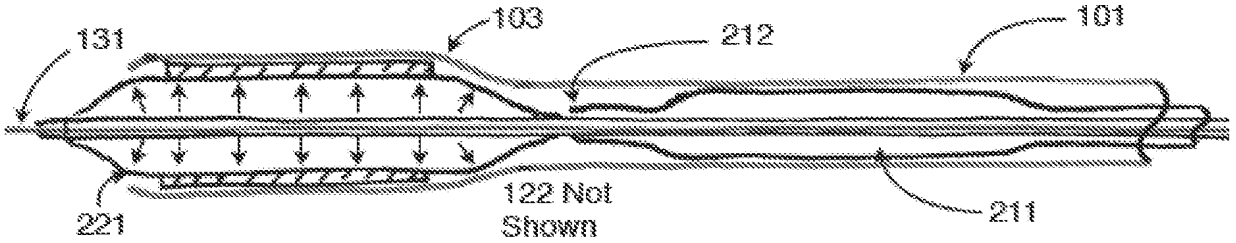


FIG. 5C

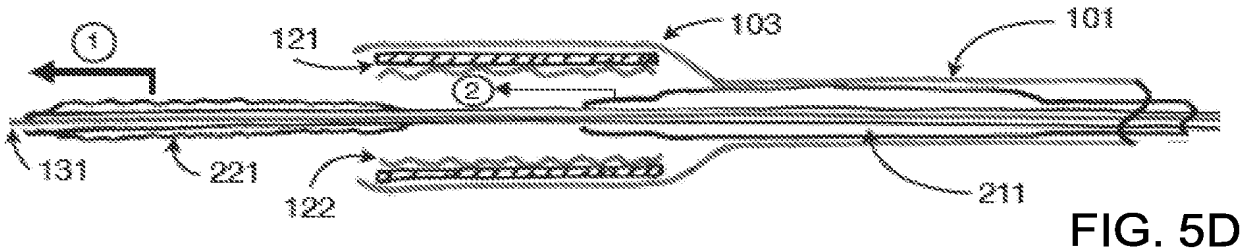


FIG. 5D

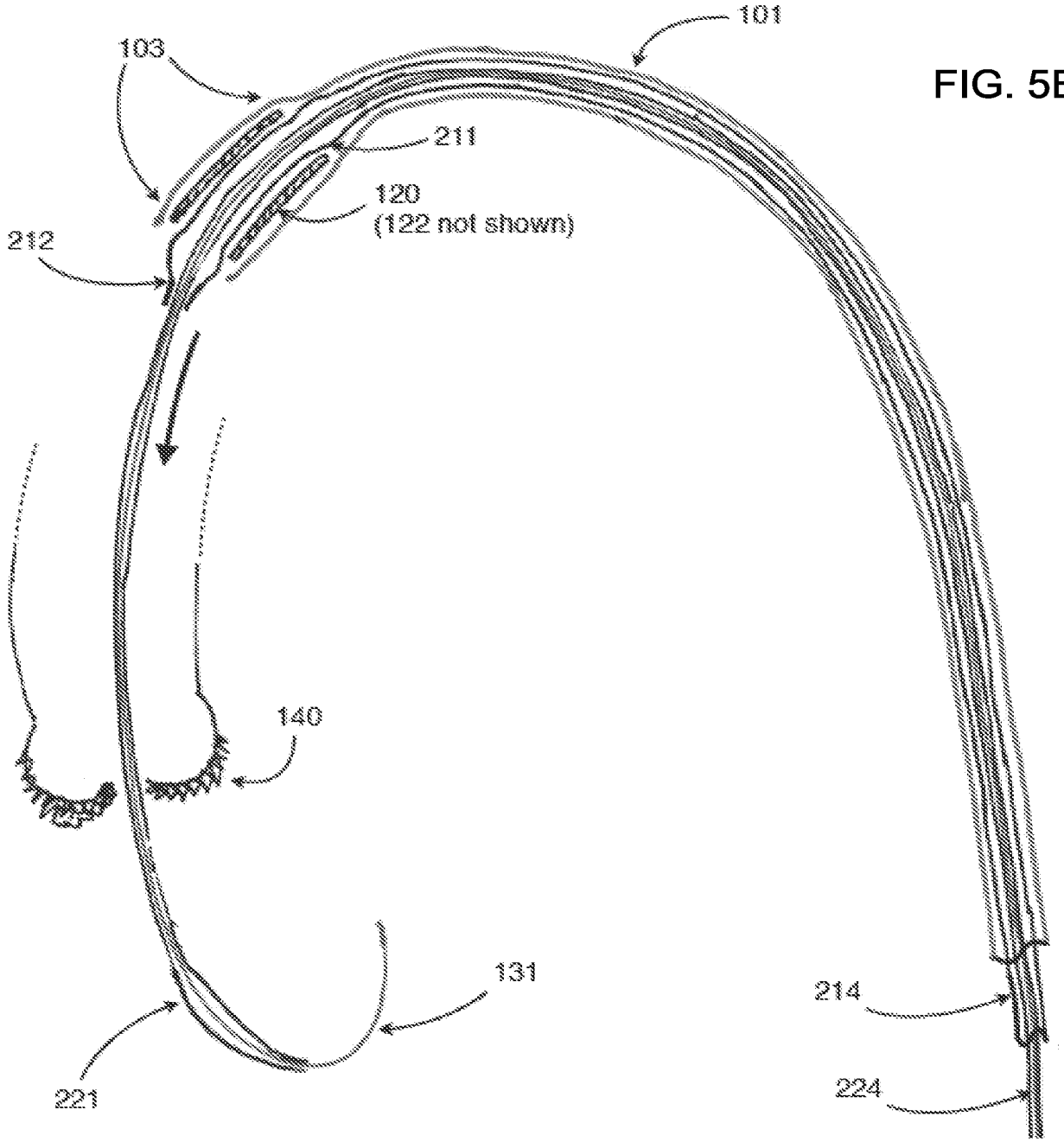
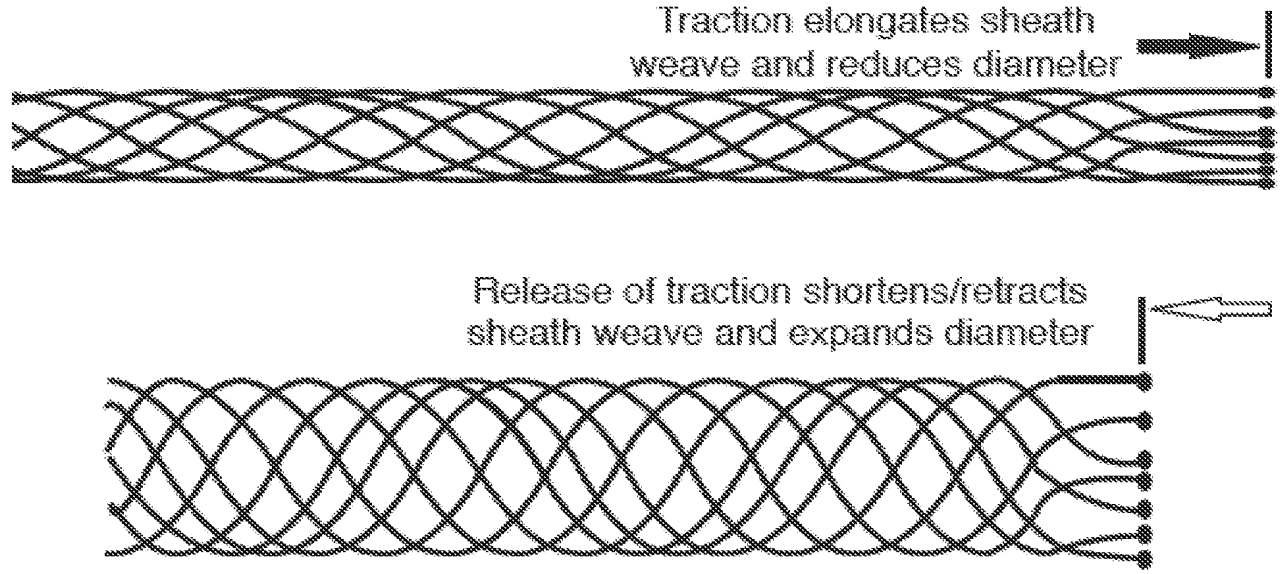

101
103
211
120
(122 not shown)
212
140
131
214
221
224
Proximal catheter ports
and hubs not shown

FIG. 5E

FIG. 6A



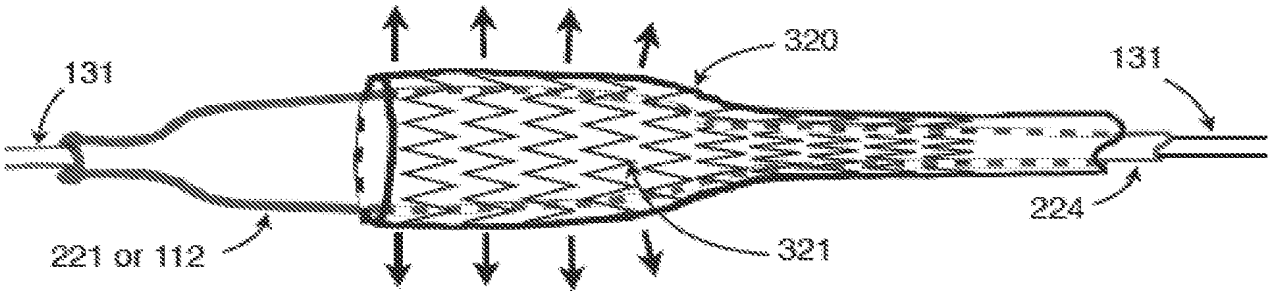


FIG. 6B

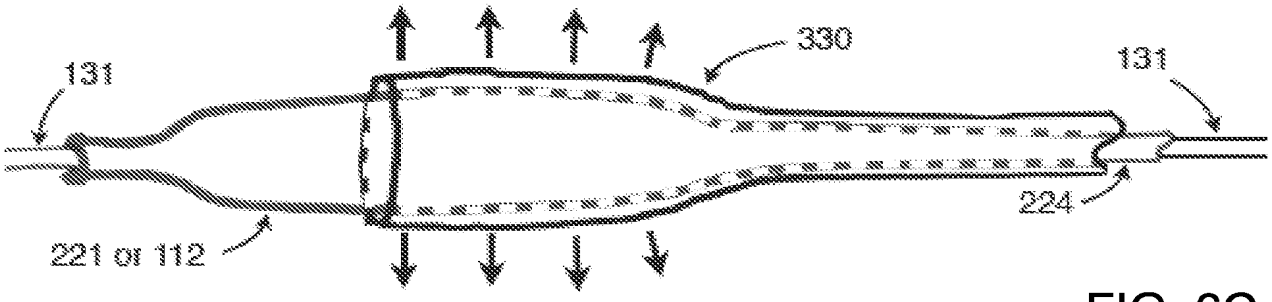
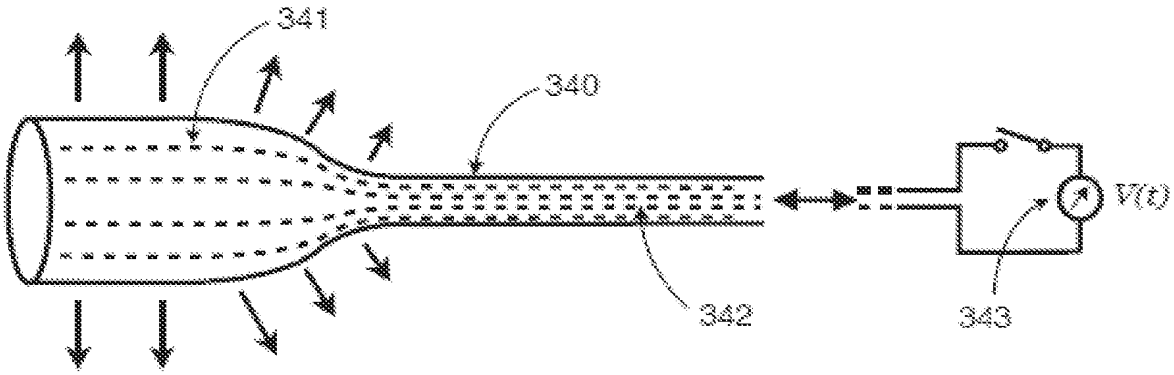


FIG. 6C

FIG. 6D



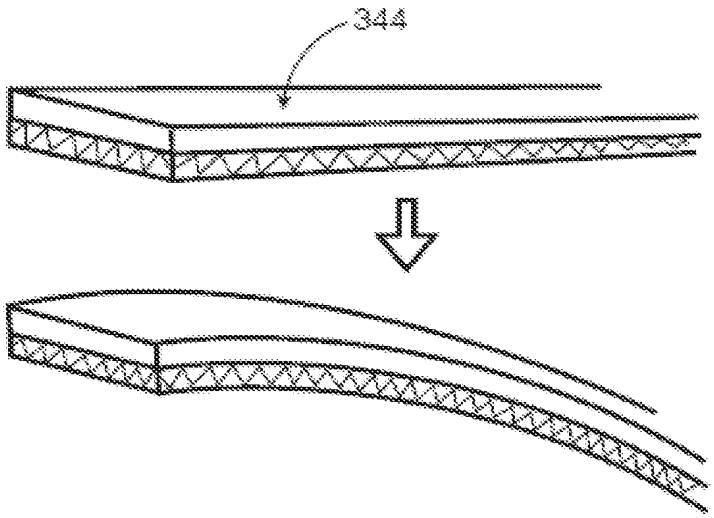


FIG. 6E

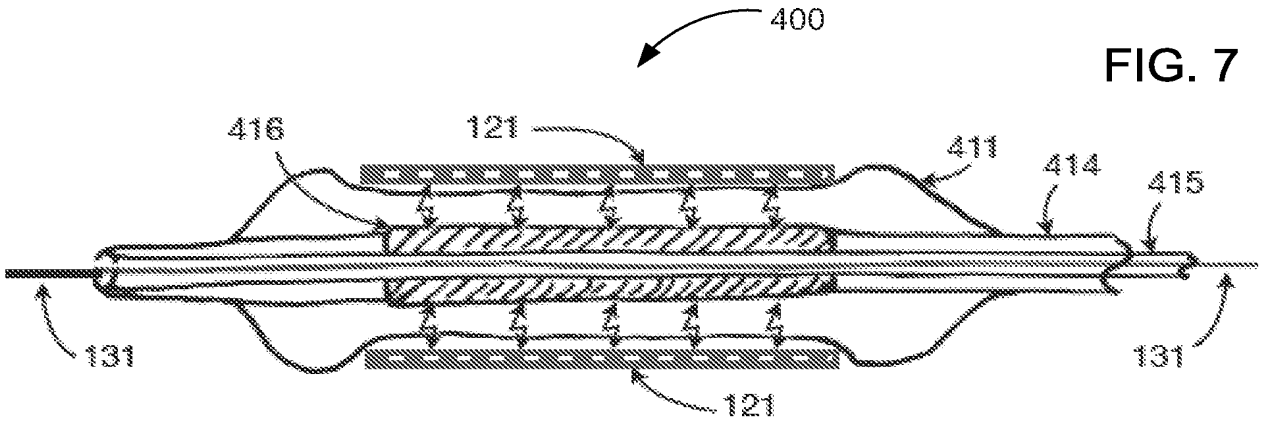


FIG. 7

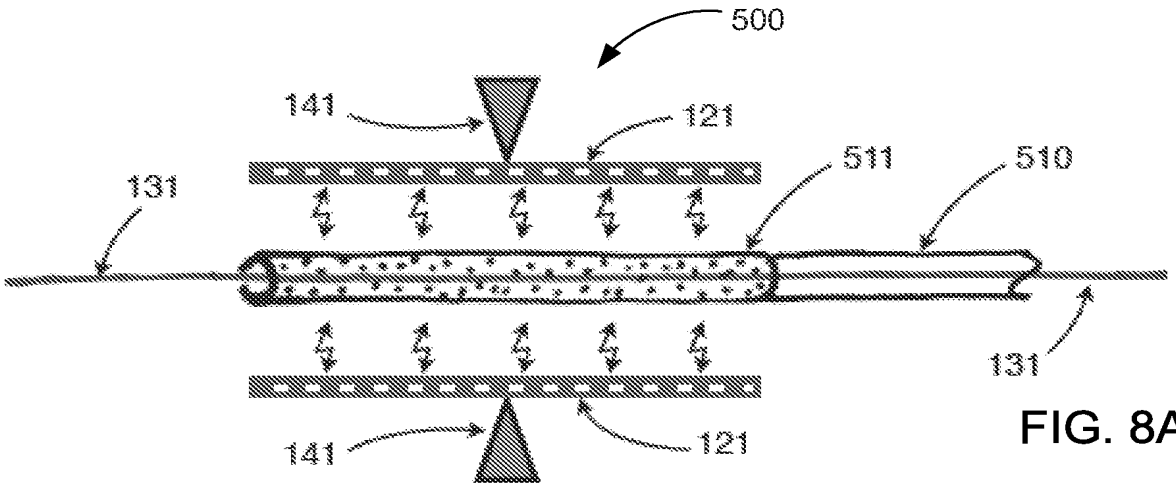


FIG. 8A

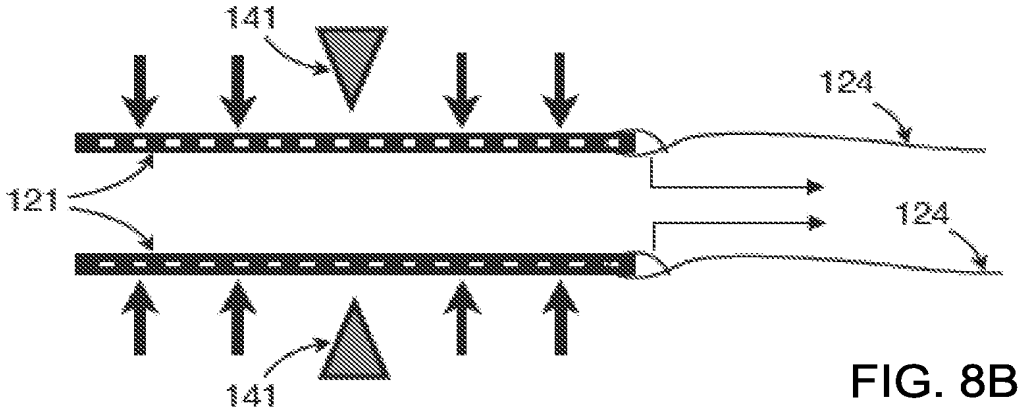


FIG. 8B

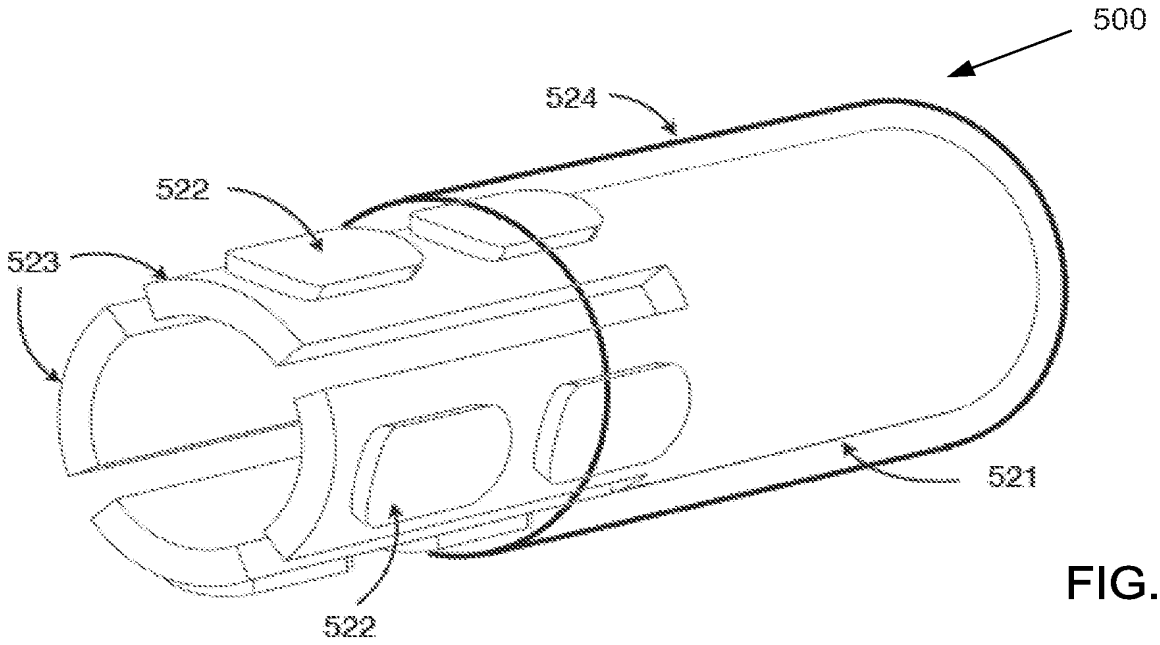

500
524
522
523
521
522

FIG. 8C

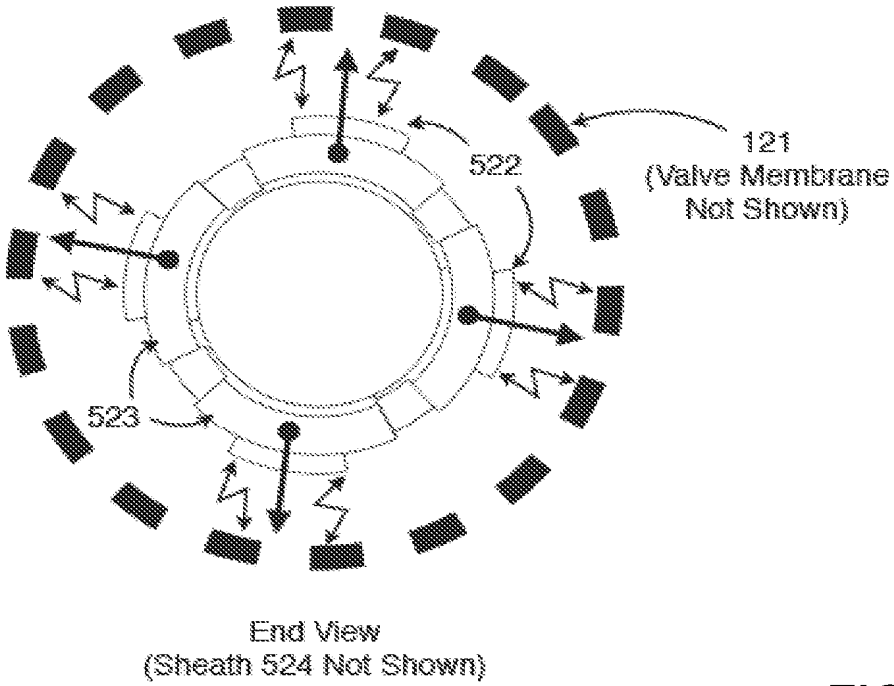

121
(Valve Membrane
Not Shown)
522
523
End View
(Sheath 524 Not Shown)

FIG. 8D

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(54) Title: PERCUTANEOUSLY DELIVERABLE HEART OR BLOOD VESSEL VALVE WITH FRAME HAVING ABLUMINALLY SITUATED TISSUE MEMBRANE

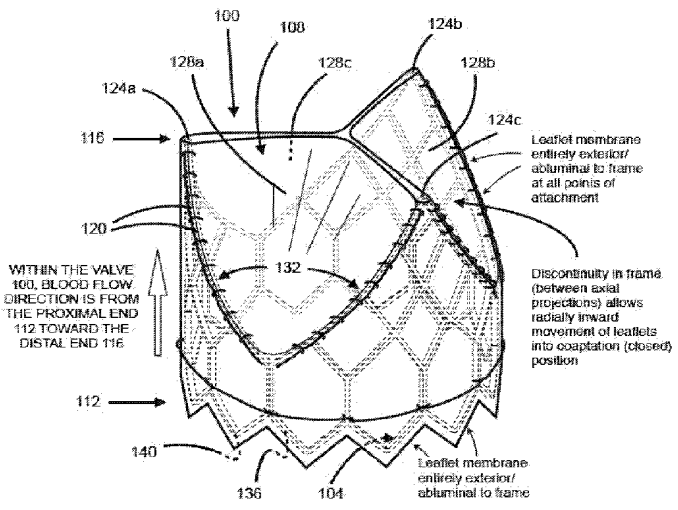

Figure 1A

(57) Abstract: A prosthetic valve implantable by catheter without surgery includes a frame with an abluminal surface extending between a proximal end of the frame and a distal end of the frame, and a single layer of a biocompatible membrane material mounted to the abluminal surface of the frame. The single layer of biocompatible membrane is located such that an interior surface of the membrane sheet extends between the proximal end of the frame and the distal end of the frame, and resides radially exterior the abluminal surface of the frame. In at least one embodiment, the disposition of membrane sheet at all points of attachment is entirely exterior/ab luminal to the frame, such that no part of the abluminal surface of the membrane sheet contacts the frame.

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PERCUTANEOUSLY DELIVERABLE HEART OR BLOOD VESSEL VALVE WITH FRAME HAVING ABLUMINALLY SITUATED TISSUE MEMBRANE

FIELD

The present invention relates to the field of medical devices, and more particularly, to a percutaneously deliverable heart valve and to a percutaneously deliverable blood vessel valve.

BACKGROUND

Heart valve disease is a common degenerative condition that compromises physiologic function and causes limiting symptoms and threat to life in millions of patients all over the world. There are various underlying causes, but malfunction of heart valves is ultimately expressed as insufficient conduction of blood through the plane of the valve due to narrowing of the anatomic pathway (stenosis), or as incompetent closure that allows blood to return back through the valve again, thereby reducing the effective forward conduction of blood through the valve (insufficiency or regurgitation). These hemodynamic states lead to 1) deficiency of cardiac output and 2) adverse loads on the pumping chambers of the heart, both of which in turn lead to functional compromise of the patient and often premature death unless effectively corrected.

Definitive corrective treatment of heart valve disease is conventionally performed by open-chest surgical techniques, wherein the valve is manipulated, repaired, or replaced with a prosthetic valve under direct vision. Heart valve surgery is performed in hundreds of thousands of cases yearly world-wide, but carries a high burden of cost, morbidity, and mortality, especially in susceptible patients who may be elderly or otherwise physiologically compromised by collateral disease. Further, the costs and resource requirements of the surgical enterprise restrict the availability of heart valve replacement to many more patients all over the world.

In pursuit of alternatives to heart valve surgery, over the last ten years a number of development programs have brought percutaneous, trans-catheter implantation of prosthetic heart valves into commercial use in the European Union (EU) and into pivotal clinical trials in the United States of America. Initial clinical experience in the EU was directed toward patients who had critical aortic valve stenosis, but were deemed to be at unacceptably high risk for open-heart surgical valve replacement. In several thousand such cases, utilizing both balloon-expandable and self-expanding designs in two separate programs, percutaneous heart valve replacement (PHVR) was shown to be feasible and possibly competitive with surgery in selected patients with 12-18 month mortality rates of about 25%. Grube E., et al., *Progress and Current Status of Percutaneous Aortic Valve Replacement: Results of Three Device Generations of the CoreValve Revalving System*, Circ. Cardiovasc Intervent. 2008;1:167-175.

Typically, the current percutaneous heart valve (PHV) designs, including the commercialized Medtronic CoreValve and the Edwards Lifesciences Sapien valves, comprise a biological membrane forming the operating leaflets of the valve, mounted within the interior of a metal frame, that is then collapsed onto a delivery catheter or balloon, and then constrained within an outer sheath. After an initial dilation of the diseased valve with a large balloon, this assembly is then advanced to the plane of the valve and deployed by self-expansion or by balloon expansion.

PHV designs are confronted by several central challenges. More particularly, the functioning valve leaflets are typically constructed of flexible and compressible tissue membrane valve members attached by sutures to a surrounding stent frame that together must be durable, yet of sufficiently low mass to allow for passage in collapsed form into the patient's body through an anatomic pathway—a peripheral artery, for example—of limited diameter, leading to the implantation site within the central circulation system. This condition favors simple, yet robust design geometries.

Secondly, the PHV in its implanted operating configuration must emulate both the opening mechanics and the closing mechanics of the native heart valve—two differing geometries and mechanical forms afforded by the native anatomy of the aortic valve, for example, but with the limitation that the PHV must effectively embody both within its physical and operational envelope without the benefit of the grossly different anatomical forms native to the aortic valve.

As a practical matter, the measures of effective function are simple—the pressure gradient during forward passage of blood across the valve must be as low as possible, typically 5 - 10 mmHg or less. While achieving this, the "success" of operation in the closed configuration, wherein the leaflets are pressed together along lines of apposition by the pressure of the blood pumped beyond the valve, would also appear to be simply measured by the amount of retrograde blood passage back into the pumping chamber—the "regurgitation" or "leakage."

However, since this closed phase of valve function is the phase in which the principal force loads are applied to the valve membrane leaflets, and since the manner in which the design of the valve distributes these forces determines the durability of the valve, the real measure of the valve's closing function is best understood by how well the design minimizes and distributes the force loads on the valve leaflets. To date, this problem has not been sufficiently addressed.

In the field of blood vessel diseases certain conditions may be advantageously treated by insertion of valves into an affected patient's blood vessels. Currently no such valve devices are available, though investigation of this approach has suggested potential clinical utility for blood vessel valves, and in particular for valves to be inserted into the vein system for particular

conditions. In the first example, insufficiency of the inlet (atrioventricular) tricuspid valve to the right ventricle of the heart results in regurgitation of blood back into the right atrium, which, serving to receive blood flow returning in the veins from the entire body, then results in turn in suffusion and swelling (edema) of all the organs, most notably in the abdomen and extremities, insufficient forward conduction of blood flow from the right ventricle into the lungs causing compromise of pulmonary function, and ultimately pump failure of the right heart. Collectively these conditions are termed right heart failure, a condition that leads to incapacity and possibly to death if progressive and uncorrected. Often, the remedy is surgical repair or replacement of the tricuspid valve, but results are uncertain, damage to the right ventricle being often irreversible, and progressive heart failure may supervene despite technically successful valve surgery.

In a yet a further example, insufficiency of vein function due to the incompetence or destruction of intrinsic valves within the vein system leads to acute then chronic swelling of the veins and their dependent lymphatics and tissues. This condition can affect the deep veins of the body, commonly the lower extremities or pelvis, or the superficial veins of the lower extremities in particular, leading to progressive expansion of the veins and further valvular incompetence, a condition known as varicose veins. Millions of people worldwide suffer from these conditions and enormous funds are expended on procedures to destroy or remove these dilated incompetent veins. It has long been hoped that some form of implantable valve for the vein system could alleviate these conditions.

Several references of interest have been reviewed in preparation of the present disclosure. The applicants do not admit that the any one or more of the following references constitute citable prior art.

U.S. Patent No. 7,758,632 to Hojeibane discloses a valve construct wherein all embodiments include stent portions that act as proximal and distal anchors that are interconnected by connecting members, and further include a "cantilever valve strut" that acts as a biasing arm to "facilitate the opening and closing of the membrane assembly." Such structures may disrupt the flow channel and potentially interfere with membrane integrity when crimping the valve to mount it on an expandable balloon. In addition, at the point of engagement of the tissue against the connecting members, there is relatively intense focal stress along the straight connecting member – especially at the free edge of the leaflet. Hojeibane further utilizes flaps 403 and cusps 404 that may be independent components attached to the tubular membrane to form the membrane assembly 102. Accordingly, Hojeibane does not appear to use a flat sheet of membrane.

U.S. Patent No. 7,025,780 to Gabbay discloses two separate uses of a device referred to as a "stent." The first use is that of the stent in a surgical valve wherein it is a supportive structure to give shape and mechanical support to the tissue leaflets formed upon it. This device in Gabbay is like a surgical tissue valve. As shown in Figs. 5 and 6 of Gabbay, the stent is disposed outside of at least an inner tissue leaflet layer. In the second use, as shown in Figs. 1 and 2 of Gabbay, a tissue valve of some type is disposed within an outer frame of the vascular stent type. In this case, the tissue layer is not disposed upon the abluminal surface of the outer stent frame. The reader is directed to column 1, lines 61-63 of Gabbay that state "The prosthesis includes a valve apparatus located within a stent apparatus to form a stented valve." Gabbay further references only a "valve apparatus comprising an animal pulmonic heart valve." Accordingly, Gabbay fails to disclose a valve formed of flat tissue membrane wherein the tissue membrane is attached to the abluminal surface of a frame.

U.S. Patent Application Publication No. 2006/0190074 to Hill is directed to venous valves, and as such, the structural embodiments shown in Hill do not appear robust enough for application as prosthetic heart valves, such as in the aortic valve position. The valve material is referred to as a "cover" comprising a matrix and "integrated flexible support members 124" — essentially a reinforcing layer applied to the matrix. While tissue sources of "extracellular membrane" are cited as possible sources for the matrix, the use of a single layer tissue membrane for the leaflets is not disclosed in Hill.

With further reference to U.S. Patent Application Publication No. 2006/0190074, Hill also does not describe how the cover material is attached to the frame to achieve a sufficiently robust construct for utilization as a prosthetic heart valve. That is, while Hill generally discusses attachment of the cover to the frame at Paragraph [0072] using a variety of possible fasteners, none are shown and described relative to the frame. Of particular relevance is that while Hill mentions coupling the cover 108 to the frame 102 at connection regions 132 and 134, there is no mention of coupling the cover 108 to the arcuate portions of the frame members 126 that lead to the connection regions 132 and 134.

Accordingly, there is a need to address the shortcomings discussed above.

SUMMARY

It is to be understood that the present invention includes a variety of different versions or embodiments, and this Summary is not meant to be limiting or all-inclusive. This Summary provides some general descriptions of some of the embodiments, but may also include some more specific descriptions of other embodiments.

As noted above, the real measure of the valve's closing function is best understood by how well the design minimizes and distributes the force loads on the valve leaflets. This

condition favors design geometries in which closing apposition of the leaflet surfaces is achieved with a minimum of traction force on the valve attachment points to the frame. To this end the inventive valve achieves this and other operational advantages by situating the operating tissue membrane to the exterior/abluminal surface of the valve frame rather than the interior/luminal space of the frame and by distributing the operating force loads of the valve along the curved edges forming the distal (downstream to flow direction) end of the frame. No other known percutaneously implantable or even surgical valve bioprosthesis utilizes this configuration with the tissue membrane mounted entirely upon the abluminal aspect of the device frame which carries the closed valve force loads along the distal formed edge of the frame corresponding to the lines of attachment of the leaflet membrane.

Accordingly, in at least one embodiment, an implantable prosthetic valve is provided that includes a frame and tissue membrane. Advantageously, the tissue membrane resides to the exterior of the frame along an axial length of the frame in the flow direction of the implantable prosthetic valve when implanted. That is, the membrane sheet resides entirely exterior or abluminal to the frame when the valve is in the fully open condition and at least at all attachment points when the valve is partly or completely closed. The attachment points may comprise a plurality of sutures that are used to attach the membrane sheet to the frame at a variety of locations, such as at one or more intersections of the frame.

The descriptions of the inventive valve are focused for the purpose of technical specification upon the replacement heart valve application, but will apply as well to the blood vessel valve device. By way of example, in addition to use of the valves described herein to replace heart valves, methods and devices described herein also provide for transcatheter implantation of a valve into the inferior vena cava (the principal conduit vein from the lower body inserting into the right heart) to act as an upstream substitute in part for the tricuspid valve. Such a valve device would be advantageously designed to be low in mass with large effective orifice. The inventive valve device is proposed as suitable to this purpose. Alternatively, the condition of right heart failure may be treated in part by interposing valves into the vein system farther upstream in the venous return flow, such as in the subclavian or principal iliac veins.

Accordingly, in at least one embodiment, an implantable prosthetic valve is provided for controlling, at least in part, a flow of blood, comprising:

a frame having an abluminal frame surface, a proximal end, and a distal end, wherein the proximal end is situated at an inlet end of the frame relative to the flow of blood when implanted, and wherein the distal end is situated at an outlet end of the frame relative to the flow of blood when implanted, the frame having a tubular flow path through its interior; and

a tissue membrane attached to the frame, the tissue membrane having an interior surface and an exterior surface;

wherein the interior surface of the tissue membrane is situated exterior the abluminal frame surface of the frame between the proximal end and distal end of the frame, when the valve is in the fully open position, the interior surface of the tissue membrane intersecting the tubular flow path of the frame when the tissue membrane is located in a closed position.

A percutaneous, trans-catheter prosthetic valve for implantation in a patient is provided, comprising:

a frame including an abluminal surface extending between a proximal end of the frame and a distal end of the frame, wherein the frame is collapsible and expandable and adapted for trans-catheter delivery; and

a biocompatible tissue material mounted to the abluminal surface of the frame to form a plurality of valve leaflets, wherein an entire interior surface of the biocompatible tissue material between the proximal end of the frame and the distal end of the frame resides radially exterior to the abluminal surface of the frame:

(a) at all points of attachment; and

(b) when the plurality of valve leaflets are in an operationally fully open position.

In at least one embodiment the frame comprises a metal alloy substantially configured as tubular stent member. In at least one embodiment a proximal portion of the frame includes a ring. In at least one embodiment a proximal portion of the frame comprises a circumferential zig-zag of wire. In at least one embodiment a proximal portion of the frame includes a lattice. In at least one embodiment the lattice is circumferentially continuous. In at least one embodiment the lattice is circumferentially discontinuous. In at least one embodiment a distal end of the frame includes two or more areas of axial continuity with the proximal end, wherein the two or more areas of axial continuity comprise axially oriented projections. In at least one embodiment the frame further comprises a distally positioned stabilization framework comprising at least one of circumferential or radial continuity with the axially oriented projections. In at least one embodiment the frame includes two or more regions of circumferential discontinuity through which operating leaflets of the biocompatible tissue material move radially inward and outward in closing and opening operation, respectively. In at least one embodiment the biocompatible tissue material between the proximal end of the frame and the distal end of the frame resides substantially adjacent the abluminal surface of the frame. In at least one embodiment the biocompatible tissue material does not contact a luminal surface of the frame. In at least one embodiment an exterior surface of the biocompatible tissue material does not contact a luminal surface of the frame.

In accordance with at least one embodiment, the frame can be a closed cell lattice type construct of circumferentially corrugated/sinusoidal/zig-zag rings. In accordance with at least one embodiment, the frame can be a wire loop with axial loops forming a support for each commissure. In at least one embodiment, the frame includes a proximal portion, wherein at least some of the abluminal surface of the proximal portion includes a tissue sheet attached thereto.

In at least one embodiment, a prosthetic valve for implantation in a patient is provided, comprising:

a frame including an abluminal surface extending between a proximal edge of the frame and a distal edge of the frame, the distal edge undulating axially to define at least two areas of circumferential discontinuity in the frame, wherein the frame is collapsible and expandable and adapted for trans-catheter delivery; and

a single layer of a biocompatible membrane material mounted to the abluminal surface of the frame to form leaflet portions, wherein the leaflet portions are collocated with the at least two areas of circumferential discontinuity in the frame.

In at least one embodiment the leaflet portions are attached to the frame at least along curved frame members formed by the distal edge of the frame and corresponding to the radially outward boundaries of the leaflet cusps.

In at least one embodiment, no portion of the biocompatible membrane material is mounted to an interior surface of the frame. In at least one embodiment, the frame comprises a metal alloy substantially configured as tubular stent member. In at least one embodiment, a proximal portion of the frame includes a lattice to which the biocompatible membrane material is circumferentially mounted entirely upon the abluminal aspect of the tubular stent member. In at least one embodiment, at least some proximal portion of the frame does not include biocompatible membrane material mounted to its luminal or abluminal surfaces. In at least one embodiment, the biocompatible membrane material extends between the proximal edge and the distal edge of the frame. In at least one embodiment, a distal portion of the frame further includes a distally extending stabilizing framework comprising a plurality of axially oriented support members that each extend from a distally extending frame projection situated adjacent the at least two areas of circumferential discontinuity in the frame. In at least one embodiment, the prosthetic valve further comprises a plurality of radial support members interconnecting the axially oriented support members. In at least one embodiment, the prosthetic valve further comprises a wire guide, wherein the wire guide is coaxially aligned with an axis of the valve, and wherein the wire guide is configured to allow for a coaxial passage of a guide wire such that coaxial alignment of the distally extending stabilizing framework may be facilitated during valve

deployment. In at least one embodiment, the wire guide comprises at least one of a ring and a tube.

A method of preparing a percutaneous, trans-catheter prosthetic valve is also provided, the method comprising mounting a single layer of a biocompatible tissue material to an abluminal surface of a trans-catheter deliverable frame such that an interior surface of the biocompatible tissue material between a proximal end of the trans-catheter deliverable frame and a distal end of the trans-catheter deliverable frame resides radially exterior to and substantially adjacent the abluminal surface of the trans-catheter deliverable frame. In at least one embodiment the method further comprises compressing and crimping the trans-catheter deliverable frame, with the biocompatible tissue material mounted thereto, upon a delivery catheter. In at least one embodiment the method further comprises implanting the trans-catheter deliverable frame with the biocompatible tissue material mounted thereto into a patient. In at least one embodiment the trans-catheter deliverable frame comprises a stent. In at least one embodiment the method further comprises mounting the trans-catheter deliverable frame and the biocompatible tissue material mounted thereto on a mandrel.

In accordance with at least one embodiment, a method of constructing a prosthetic valve is provided, the method, comprising attaching a biocompatible membrane material to a collapsible and expandable frame to form a trans-catheter deliverable prosthetic valve, wherein an entire interior surface of the biocompatible membrane material is located exterior of the abluminal surface of the collapsible and expandable frame when leaflet portions of the biocompatible membrane material are in the valve's operationally open position. In at least one embodiment, the method further comprises associating the biocompatible prosthetic valve with a catheter.

In at least one embodiment, a prosthetic trans-catheter deliverable valve is provided that does not include one or more biasing members within the inner flow channel of the valve. That is, with the exception of the membrane during closure of the valve (when the flow cycle is not antegrade from proximal to distal through the valve), the inner flow channel is devoid of flow channel obstructions.

In at least one embodiment, a prosthetic trans-catheter valve includes a flat membrane sheet interconnected to a frame. In at least one embodiment, a flat membrane sheet is interconnected to the abluminal surface of a frame using a plurality of sutures, wherein at least some of the sutures are applied in a buttonhole suture pattern.

Various components are referred to herein as "operably associated." As used herein, "operably associated" refers to components that are linked together in operable fashion, and

encompasses embodiments in which components are linked directly, as well as embodiments in which additional components are placed between the two linked components.

As used herein, "at least one," "one or more," and "and/or" are open-ended expressions that are both conjunctive and disjunctive in operation. For example, each of the expressions "at least one of A, B and C," "at least one of A, B, or C," "one or more of A, B, and C," "one or more of A, B, or C" and "A, B, and/or C" means A alone, B alone, C alone, A and B together, A and C together, B and C together, or A, B and C together.

As used herein, "sometime" means at some indefinite or indeterminate point of time. So for example, as used herein, "sometime after" means following, whether immediately following or at some indefinite or indeterminate point of time following the prior act.

Various embodiments of the present inventions are set forth in the attached figures and in the Detailed Description as provided herein and as embodied by the claims. It should be understood, however, that this Summary does not contain all of the aspects and embodiments of the one or more present inventions, is not meant to be limiting or restrictive in any manner, and that the invention(s) as disclosed herein is/are understood by those of ordinary skill in the art to encompass obvious improvements and modifications thereto.

Additional advantages of the present invention will become readily apparent from the following discussion, particularly when taken together with the accompanying drawings.

BRIEF DESCRIPTION OF THE DRAWINGS

To further clarify the above and other advantages of various embodiments and features of the one or more present inventions, a more particular description of the one or more present inventions is rendered by reference to specific embodiments thereof which are illustrated in the appended drawings. It should be appreciated that these drawings depict only typical embodiments of the one or more present inventions and are therefore not to be considered limiting in scope. The one or more present inventions are described and explained with additional specificity and detail through the use of the accompanying drawings in which:

Fig. 1A is a side perspective view of an embodiment of a percutaneously deliverable valve with the valve membrane illustrated in a closed position;

Fig. 1B is a side elevation view of the frame suited to balloon expansion shown in Fig. 1A;

Fig. 1C is a top plan view of the frame shown in Fig. 1B;

Fig. 1D is a side perspective view of the frame shown in Fig. 1B;

Fig. 1E is a bottom perspective view of the frame shown in Fig. 1B;

Fig. 1F is a side elevation view of the frame shown in Fig. 1B, wherein the cylindrical frame is depicted in an "unrolled" or flat projection to illustrate the geometry of the frame members;

Fig. 1G is a side elevation view of another embodiment of a frame suited to self-expansion, wherein the cylindrical frame is depicted in an "unrolled" or flat projection to illustrate the geometry of the frame members;

Fig. 1H is a side elevation view of the frame shown in Fig. 1G;

Fig. 1I is a top plan view of the frame shown in Fig. 1H;

Fig. 1J is a side perspective view of the frame shown in Fig. 1H;

Fig. 1K is a bottom perspective view of the frame shown in Fig. 1H;

Fig. 1L is a side perspective view of an embodiment of a membrane sheet and its attachment to a frame in accordance with at least one embodiment described herein;

Fig. 2 is a simplified distal end view of an embodiment of a frame illustrating relative locations of the distal ends of two distally positioned frame projections located approximately 180 degrees apart;

Fig. 3 is a simplified distal end view of an embodiment of a frame illustrating relative locations of the distal ends of four distally positioned frame projections located approximately 90 degrees apart;

Fig. 4 is a perspective view of an embodiment of a schematic of a frame having optional stabilization framework with circumferential supports;

Fig. 5 is a perspective view of an embodiment of a schematic of a frame having optional stabilization framework with radial supports;

Fig. 6 is a flow chart of a method of constructing an embodiment of a prosthetic heart valve as described herein;

Fig. 7 is flow chart of a method of deploying an embodiment of a prosthetic heart valve as described herein; and

Fig. 8 is a schematic of a heart showing an embodiment of a heart valve as described herein implanted within a heart.

The drawings are not necessarily to scale.

DETAILED DESCRIPTION

Embodiments of the one or more inventions described herein include one or more devices, assemblies and/or methods related to prosthetic heart valves and to prosthetic blood vessel valves. A prosthetic heart valve in accordance with at least one embodiment described herein can be surgically implanted, such as by percutaneous, trans-catheter delivery, to the implantation site within the patient. One or more embodiments of the prosthetic heart valves

described herein have application for at least aortic and pulmonary valve positions, including for structural defects and diseased valves. Other embodiments have application to the vascular system and in particular to the vein system. When reduced in scale they have particular application to the branch veins of the body and the extremities. The descriptions for these devices are effectively provided in the descriptions and specifications provided for the inventive percutaneously implantable heart valve device.

In at least one embodiment, biocompatible material is mounted to a frame to form an implantable prosthetic heart valve, and then at a later time, the implantable prosthetic heart valve is implanted within a patient, such as by way of a percutaneous, trans-catheter delivery mechanism. The percutaneously implantable heart valve is suitable for implantation into a native (orthotopic or ectopic) valve seat of a patient. Once implanted, the prosthetic heart valve serves to regulate the flow of blood associated with the patient's heart by allowing forward blood flow and substantially preventing backflow or valvular regurgitation.

Referring now to Fig. 1A, and in accordance with at least one embodiment, an implantable prosthetic heart valve 100 is shown that includes a frame 104 and a single layer membrane sheet 108, such as a biocompatible tissue membrane sheet. All or substantially all of the membrane sheet 108 is located on the exterior or abluminal side of the frame 104 between the proximal end 112 and the distal end 116 of the frame 104 when the valve leaflets are in the operationally fully open position and in any case at all points of attachment. The implantable prosthetic heart valve 100 includes a proximal (upstream) portion/margin of membrane sheet 108 that is circumferentially attached to and residing entirely upon the abluminal surface of the frame 104. In at least one embodiment, the membrane sheet 108 is connected to the frame 104 by a plurality of sutures 120. In at least one embodiment, the plurality of sutures comprise curved lines of attachment, axially concave to the distal end 116 of the frame, along the frame members at the frame's distal edge interconnecting the distally extending frame projections 124a-c. It is to be understood that alternate ways of attaching the membrane sheet 108 to the frame 104 may be used, such as staples, an adhesive, an anchoring ring, one or more bands, clips or combinations of the foregoing.

By whatever technique of attachment, the lines of attachment by which the arcuate proximal basal margin of each leaflet is anchored to the arcuate distal edge of the frame act to distribute the force loads acting on the leaflets along these lines while in the operationally closed position. The securement of the leaflets in this manner is advantageous in a high-pressure application such as the aortic valve position. Moreover, these lines of attachment also act to seal the proximal basal margin of each cusp to the frame and are critical in the case of aortic valve implantation, because some portion of these arcuate cusp margins are likely to be disposed

"above" (downstream) of the aortic valve annulus and without anatomic luminal contact to the outer aspect of the valve at this level. As such, those portions that are disposed in the "suprannular" position after implantation can be subject to high pressure blood being injected between the leaflet layer and the frame which can in turn lead to acute and chronic compromise of valve function. The specific form of leaflet attachment provided in the inventive valve addresses this problem that arises as a consequence of the abluminal/exterior position of the leaflet membrane in relation to the frame.

In at least one embodiment, the plurality of sutures 120 attaching the leaflet membrane to the distal arcuate portions of the distal edge of the frame comprise, for each arcuate segment 144, a continuous series of "buttonhole"-technique sutures 120 wherein the segments of suture interconnecting the knots are disposed to the outer/abluminal surface of the membrane. This suture configuration advantageously imposes a small biasing effect upon the leaflet towards the operationally closed position.

With regard to particular material types that may be used to form the membrane sheet, in at least one embodiment the membrane sheet 108 forming the cusp or leaflet portions includes a one-piece, single layer sheet of biocompatible membrane, such as fixed mammalian pericardium tissue or synthetic biocompatible material such as ePTFE. In at least one embodiment, the membrane sheet is made from a tissue preparation process that yields a leaflet material of suitable strength and durability for use in a prosthetic trans-catheter deliverable heart valve. The content of WO 2011/109450A2 published on September 9, 2011, is incorporated herein by reference. Although not preferred, one or more embodiments may alternatively comprise a plurality of sections of membrane sheet connected to form a contiguous sheet.

In at least one embodiment, the membrane sheet is a single layer of a substantially homogenous material. In at least one embodiment, the membrane sheet is an unlaminated single layer of material. In at least one embodiment, the membrane sheet is a single layer of material that does not include any reinforcement, such as reinforcing fibers. In at least one embodiment, the membrane sheet is a single layer of treated pericardium tissue. In at least one embodiment, the membrane sheet is a single layer of a synthetic film.

The frame 104 may include a balloon expandable material. Alternatively, the frame 104 may include one or more of a self expanding alloy such as nitinol, stainless steel, cobalt chromium, bioabsorbable metal, and non-elastic bioabsorbable plastic, such as polylactides, polyglycolides, their co-polymers, or polydioxanones. As further seen in Figs. 1A-1F, in at least one embodiment the geometry of the frame 104 at the distal end 116 may include three distally extending frame projections 124a, 124b and 124c. This configuration is described for exemplary purposes. Accordingly, alternate configurations may be used, including collapsible

and expandable percutaneously deliverable frames that include two, four, five or any multiple number of distally extending frame projections, provided the configuration in combination with the abluminally situated single layer membrane sheet 108 accommodates inward closure of the membrane sheet 108 sufficiently to facilitate operational closure of the valve after being implanted. Thus, those skilled in the art will appreciate that configurations shown and described herein are for purposes of enablement, and therefore, alternate configurations from those shown are encompassed by the claims. Consistent with the foregoing, the distally extending frame projections 124a-c are spaced apart around the circumference of the frame 104 as appropriate to facilitate closure of the membrane sheet 108 when the flow cycle is not antegrade from proximal to distal through the valve.

Referring still to Figs. 1A-1F, in at least one embodiment, the frame 104 has three distally positioned inverted "v" members also referred to herein as distally extending frame projections 124a-c located at substantially equal angular distances apart from each other at the distal end 116 of the frame 104. Alternatively, each of these distally extending frame projections may take other forms such as a single projecting beam or an extending loop formed of a continuous loop of wire. Accordingly, in at least one embodiment, each inverted "v" member or distally extending frame projection 124a-c is about 120 degrees (at the point or apex of the inverted "v" members) away on either side from the other two inverted "v" members at the distal end 116 of the frame 104. In at least one embodiment, the inverted "v" members serve as attachment locations for the membrane sheet 108. In at least one embodiment, the "v" members are integral parts of a generally arcuate configuration of frame members spanning the distal frame edge between the distally extending frame projections 124a-c such that each arcuate span forms: 1) the radially outermost margin of a leaflet cusp; and 2) the line of attachment of each leaflet membrane to the distal edge of the frame. In at least one embodiment, the proximal end 112 of the frame 104 includes a continuous framework, although minor axially oriented recessions 136 in the framework are situated between the proximal-most portions 140 of the frame 104.

With further reference to Figs. 1B-1F, in at least one embodiment, the struts 126 forming the inverted "v" members are located between approximately 40 to 90 degrees apart, and more preferably, at between approximately 50 to 70 degrees apart. By way of example and not limitation, as shown in the example depicted in Fig. 1F, the struts 126 forming distally extending frame projection 124a are about 50 degrees apart. The angular values provided herein are given for purposes of enablement and for exemplary purposes, and are not intended to be limiting. Other values are possible, and such other values are within the scope of the one or more present inventions.

Referring again to Fig. 1A, cusp or leaflet portions 128a, 128b, and 128c reside between the spaced apart distally extending frame projections 124a-c. More particularly, circumferential discontinuities 132 in the frame 104 substantially correspond to the location of leaflet portions 128a-c in the membrane sheet 108. That is, since the membrane sheet 108 is situated exterior of the frame 104, including at the frame projections 124a-c, the absence of framework, internal struts or other types of support for a portion of the distally located membrane sheet 108 allows the abluminally positioned membrane sheet 108 to occupy an area within the flow path of the valve 100 when the flow cycle is not antegrade from proximal to distal through the valve. Therefore, when flow conditions are not antegrade, the leaflet portions 128a-c operate to close the valve 100 because of the absence of framework circumferentially between the distally extending frame projections 124a-c allows the leaflet portions 128a-c of the membrane sheet 108 to close radially inward.

Referring again to Fig. 1A, in the closed position, the leaflet portions 128a-c reside within the interior flow channel or lumen of the valve 100. Accordingly, the valve 100 includes a biocompatible membrane with a distal (downstream) portion/margin that is attached to the abluminal/exterior aspect of the frame 104 at at least two or more points (at or near the apices of the distally extending frame projections 124a-c) corresponding to two or more valve leaflet commissures, wherein the free edge of the membrane sheet 108 between the points of attachment constitutes the free edge of the valve leaflets or leaflet portions 128a-c that are free to move radially inward into a closed position contacting the other leaflet or leaflets, and radially outward into an open position.

In at least one embodiment, when the leaflets 128a-c are in their open position, the membrane sheet 108 at the distal end 116 resides entirely to the radial exterior of the frame 104 including at the distally extending frame projections 124a-c. Accordingly, when flow conditions are antegrade, the leaflets 128a-c extend radially outward from the lumen of valve 100.

In at least one embodiment, the membrane sheet 108, including the material constituting the operating leaflets portions 128a-c, is exterior/abluminal to the frame 104 and may be continuous from the leaflet portions 128a-c to the proximal end 112 of the frame 108. Alternatively, the membrane sheet 108 does not have to extend abluminally along the entire axial length of the frame 104 from the distal end 116 to the proximal end 112. More particularly, with limited proximal coverage, the membrane sheet 108 may only cover a portion of the abluminal surface of the frame 104 and reside at the distal end 116 and extend axially along the abluminal surface sufficiently to provide leaflet portions 128a-c such that there is enough membrane sheet 108 to cover the discontinuities in the frame 104 and thus function as leaflet portions 128a-c by moving radially inward and outward through the frame discontinuities

132. For such a configuration the membrane sheet 108 needs to extend proximally from the distal end 116 a sufficient proximal distance so as to provide a sufficient seal against leakage/regurgitation through the frame 104. Simply stated, the membrane sheet 108 needs to extend axially only a limited distance axially in the proximal direction, that being to slightly beyond the annular intersection or the valve seat formed between the abluminal surface of the membrane sheet 108 situated against the native tissue. Therefore, the proximal extent of the membrane tissue 108 beyond the intersection of the valve 100 against the native tissue may vary.

In at least one embodiment, the membrane sheet 108 may wrap around the proximal edge 136 of the frame 104 so as to make a continuous inner/luminal layer within the proximal end 112 of the frame 104. In contrast, leaving a portion of the proximal end 112 uncovered by the membrane sheet 108 permits the frame to provide additional structure. By way of example, the proximal end 112 can incorporate other structural elements including flared or hooked frame projections for effective securement of the implanted valve. Such configurations have applicability to providing advantageous structure for certain valve implantation sites, such as the mitral valve.

In at least one embodiment, the membrane sheet 108 may wrap around the proximal edge of the frame 104 so as to make a continuous inner/luminal layer within the proximal end 112 of the frame 104. That is, the valve 100 does not require the membrane sheet 108 to extend proximally to the proximal edge 136 of the frame 108, however, the membrane sheet 108 may extend proximally including to the proximal end 112, and indeed, the membrane sheet 108 may wrap around the proximal edge 136 to the luminal side of the frame 104.

With reference to Fig. 1F, a side elevation view of the cylindrical frame 104 is depicted in "unrolled" flat projection to illustrate the geometry of the frame members. The structural differences of the frame 104 at the proximal end 112 and distal end 116 are readily apparent, with the areas of circumferential discontinuities 132 observable between the distally extending frame projections 124a-c. Each circumferential discontinuity 132 includes a pair of generally arcuate side portions 144 that, in at least one embodiment, include a concave (in relation to the distal end of the frame) shape relative to the circumferential discontinuity 132. These arcuate spanning side portions 144 form: 1) lines of attachment of the leaflet membrane to the frame; and 2) the proximal/radially outermost margin of the leaflet cusp, along which are borne the forces exerted upon the closed leaflets. While the leaflets are attached to the arcuate side portions 144 as by suturing, the mobile leaflet portions and the cuff portion of the membrane are preferably continuous, formed of a single sheet of biocompatible membrane disposed around and upon the abluminal aspect of the frame. As noted above, to attach the single layer

membrane sheet 108 to the arcuate side portions 144, sutures may be applied using a continuous series of "buttonhole"-technique sutures 120 wherein the segments of suture interconnecting the knots are disposed to the outer/abluminal surface of the membrane. This suture configuration advantageously imposes a small biasing effect upon the leaflet towards the operationally closed position.

Referring now to Figs. 1G-1K, an alternative embodiment comprising a frame 104′ suited to self-expansion is shown is shown. When comparing frame 104 to frame 104′, differences in the frame structure are apparent. However, both frames 104 and 104′ have circumferential discontinuities 132 that substantially correspond to the location of leaflet portions 128a-c in the membrane sheet 108. Again, since the membrane sheet 108 is situated exterior of the frame 104′, including at the frame projections 124a-c, the absence of framework, internal struts or other types of support for a portion of the distally located membrane sheet 108 allows the abluminally positioned membrane sheet 108 to occupy an area within the flow path of the valve 100 when the flow cycle is not antegrade from proximal to distal through the valve. Similar to frame 104, the location of the circumferential discontinuities 132 in frame 104′ allow the leaflet portions 128a-c operate to close the valve 100 because of the absence of framework circumferentially between the distally extending frame projections 124a-c in frame 104′ allows the leaflet portions 128a-c of the membrane sheet 108 to close radially inward. Also similar to frame 104, each circumferential discontinuity 132 includes a pair of generally arcuate side portions 144 that, in at least one embodiment, include a concave (in relation to the distal end of the frame) shape relative to the circumferential discontinuity 132. These arcuate spanning side portions 144 form: 1) lines of attachment of the leaflet membrane to the frame; and 2) the proximal/radially outermost margin of the leaflet cusp, along which are born the forces exerted upon the closed leaflets.

As noted above, although the embodiment shown in Fig. 1A illustrates a frame 104 including three distally extending frame projections 124a-c, an alternative number of distally extending frame projections may be used, thereby yielding an implantable prosthetic heart valve with fewer or greater than three cusps. By way of example, and with reference now to Fig. 2, for a frame having two distally extending frame projections 124 that are positioned at substantially diametrically opposite sides of the frame's circumference, then two cusps would be provided. Similarly, and with reference now to Fig. 3, for a frame having four distally extending frame projections 124 that are positioned with substantially 90 degrees of separation from one another around the frame's circumference, then four cusps would be provided.

Referring now to Fig. 1L, a frame 104 is shown relative to a single layer membrane sheet 108. The illustrated single layer membrane sheet 108 includes substantially straight edges.

However, in at least one embodiment, the distal free edge of each membrane leaflet portion has a non-linear shape. Preferentially when the leaflet free edge is not linear, it is cut in the shape of a parabola with central axis of curvature aligned to the center of the free edge of the leaflet. This effectively extends the coaptation margin and area of the leaflet free edge for a given leaflet radius, reduces the pressure on the contacting leaflet areas when the valve is closed and improves the effectiveness of orifice sealing in closure. Accordingly, free edge shapes for the leaflets are cut from the corresponding edge of the flat sheet membrane before wrapping and mounting of the membrane upon the frame.

Alternatively, in at least one embodiment, the circumference of the membrane exceeds the outer circumference of the frame. The membrane is then gathered in folds or pleats and attached at the proximal (inlet) end of the frame so as to reduce the effective circumference of the membrane at the proximal end of the frame to equal that of the frame at this level. While the proximal end of the encircling membrane sheet is then directly apposed to the abluminal aspect of the frame for secure attachment, the leaflet free edge of the membrane at the distal (outlet) end of the valve remains at the original larger circumference. This has the effect of increasing the length of each leaflet free edge and the area of each leaflet for a given radius of frame, and is useful to improve valve function, especially for large valve diameters. It will be understood that various curved and polygonal membrane shapes may be used to achieve various three dimensional leaflet shapes in a similar manner. Accordingly, in at least one embodiment, a prosthetic trans-catheter deliverable valve is provided that includes a membrane sheet formed into a tubular shape, wherein a circumference of the tubular shape is greater than a circumference of a radially adjacent portion of the frame. In at least one embodiment, a circumference of the tubular shape is between about 5 to 25% greater than a circumference of a radially adjacent portion of the frame. More preferably, a circumference of the tubular shape is between about 7 to 20% greater than a circumference of a radially adjacent portion of the frame. More preferably yet, a circumference of the tubular shape is between about 10 to 15% greater than a circumference of a radially adjacent portion of the frame. The difference in the circumference of the membrane sheet as compared to the radially adjacent portion of the frame provides leaflet portions that extend within the lumen along lines of apposition with improved sealing characteristics relative to a membrane sheet having a circumference that is substantially the same as the circumference of a radially adjacent portion of the frame.

Referring now to Fig. 4, and in accordance with a separate embodiment, the frame 104 may optionally include a distally extending stabilizing framework 400 that includes axially oriented support members 404 extending from the distally extending frame projections 124a-c. In at least one embodiment, a distally-positioned circumferential ring, or alternatively, a

circumferentially segmented lattice 408 interconnects the axially oriented support members 404. The stabilization framework is located distally of the membrane sheet 108 that is attached to the frame 104.

Referring now to Fig. 5, and in accordance with yet a separate embodiment, an alternative to the stabilization framework of Fig. 4 is shown. More particularly, similar to the distally extending stabilizing framework 400, distally extending stabilizing framework 500 includes a plurality of axially oriented support members 404 that extend from the distally extending frame projections 124a-c; however, a plurality of radial support members 504 are used to interconnect the axially oriented support members 404, thereby providing additional stability to the distal end 116 of the frame 104. In addition, at the central point of intersection of the radial support members, a small ring or short tube coaxially aligned with the central axis of the valve and frame may be provided in order to allow for the coaxial passage of a guide wire such that coaxial alignment of the distal support framework may be facilitated during valve deployment.

With reference now to Fig. 6, and in accordance with at least one embodiment, a method 600 of constructing a prosthetic heart valve or a prosthetic vascular valve is provided. At 604, the method includes attaching a biocompatible membrane material to a frame to form a prosthetic heart valve, wherein an entire interior surface of the biocompatible membrane material is located exterior of the abluminal surface of the frame when leaflet portions of the biocompatible membrane material are in the operationally open position. As described above, a number of different ways of attaching the membrane sheet to the frame may be used, such as by suturing the membrane sheet to the exterior of the frame. At 608, the method includes associating the biocompatible prosthetic heart valve or prosthetic vascular valve with a catheter. The 604 step of associating may be preformed at a different location than the step 608 of attaching.

Referring now to Fig. 7, a flow chart illustrating the general procedure associated with implantation of the percutaneously deliverable heart valve 100 is provided. However, those skilled in the art will understand that with appropriate modification (e.g., changing the vascular entry location) the methodology also has application to a percutaneously deliverable blood vessel valve.

At 704, catheter access is gained to the patient's femoral artery and a guidewire is placed through the plane of the diseased valve that is targeted to receive the implant. Thereafter, the percutaneously deliverable heart valve 100 is removed from its packaging. If the valve was not mounted upon or otherwise associated with a delivery catheter at manufacture, then the valve is cleaned and rinsed and radially compressed upon the delivery catheter and constrained within a

covering sheath coaxial to the delivery catheter. The prosthetic heart valve assembly, including its lumens, is preferably flushed and prepared in the usual fashion for standard balloons and catheters that do not contain a biocompatible tissue. At 708, the carrier catheter or balloon catheter is then coaxially mounted and advanced over the guidewire, such as under fluoroscopic vision initially to the level of the great vessel where it can be inspected under fluoroscopy. At 712, and after the nominal position and configuration is confirmed, the delivery system is advanced through the plane of the diseased valve under fluoroscopy, and the covering sheath is withdrawn, either at this point or during the advance prior to it, thus exposing the mounted implantable prosthetic heart valve 100 in place. At 716, in the case of a balloon expandable frame, the balloon is then inflated, deploying the percutaneously deliverable heart valve 100 in the plane of the valve. The deployed prosthetic heart valve 100 is shown in Fig. 8, wherein the percutaneously deliverable heart valve 100 serves to properly control the flow blood.

One or more of the embodiments of the percutaneously deliverable heart valve described herein may be implanted into the patient using a balloon-expandable frame or a self-expanding frame. Expandable frames are generally conveyed to the site of the target valve on balloon catheters. For insertion, the expandable frame is positioned in a compressed configuration along the delivery device, for example crimped onto the balloon of a balloon catheter that is part of the delivery device intended for coaxial mounting on a guidewire. After the expandable frame is positioned across the plane of the valve, the expandable frame is expanded by the delivery device. For a self-expanding frame, commonly a sheath is retracted, allowing expansion of the self-expanding frame.

In at least one embodiment, the frame comprises a metal alloy frame possessing a high strain design tolerance that is compressible to a relatively small diameter. By providing a device with a low profile, the implantable prosthetic heart valve allows standard retrograde arterial aortic delivery via femoral artery insertion, without surgical cutdown or general anesthesia.

The present invention may be embodied in other specific forms without departing from its spirit or essential characteristics. The described embodiments are to be considered in all respects only as illustrative and not restrictive. The scope of the invention is, therefore, indicated by the appended claims rather than by the foregoing description. All changes which come within the meaning and range of equivalency of the claims are to be embraced within their scope.

The one or more present inventions, in various embodiments, include components, methods, processes, systems and/or apparatus substantially as depicted and described herein, including various embodiments, subcombinations, and subsets thereof. Those of skill in the art

will understand how to make and use the present invention after understanding the present disclosure.

The present invention, in various embodiments, includes providing devices and processes in the absence of items not depicted and/or described herein or in various embodiments hereof, including in the absence of such items as may have been used in previous devices or processes (e.g., for improving performance, achieving ease and/or reducing cost of implementation).

The foregoing discussion of the invention has been presented for purposes of illustration and description. The foregoing is not intended to limit the invention to the form or forms disclosed herein. In the foregoing Detailed Description for example, various features of the invention are grouped together in one or more embodiments for the purpose of streamlining the disclosure. This method of disclosure is not to be interpreted as reflecting an intention that the claimed invention requires more features than are expressly recited in each claim. Rather, as the following claims reflect, inventive aspects lie in less than all features of a single foregoing disclosed embodiment. Thus, the following claims are hereby incorporated into this Detailed Description, with each claim standing on its own as a separate preferred embodiment of the invention.

Moreover, though the description of the invention has included description of one or more embodiments and certain variations and modifications, other variations and modifications are within the scope of the invention (e.g., as may be within the skill and knowledge of those in the art, after understanding the present disclosure). It is intended to obtain rights which include alternative embodiments to the extent permitted, including alternate, interchangeable and/or equivalent structures, functions, ranges or acts to those claimed, whether or not such alternate, interchangeable and/or equivalent structures, functions, ranges or acts are disclosed herein, and without intending to publicly dedicate any patentable subject matter.

CLAIMS

What is claimed is:

1. A percutaneous, trans-catheter prosthetic valve for implantation in a patient, comprising:

a frame including an abluminal surface extending between a proximal end of the frame and a distal end of the frame, wherein the frame is collapsible and expandable and adapted for trans-catheter delivery; and

a biocompatible tissue material mounted to the abluminal surface of the frame to form a plurality of valve leaflets, wherein an entire interior surface of the biocompatible tissue material between the proximal end of the frame and the distal end of the frame resides radially exterior to the abluminal surface of the frame:

(a) at all points of attachment; and

(b) when the plurality of valve leaflets are in an operationally fully open position.

2. The percutaneous, trans-catheter prosthetic valve of Claim 1, wherein the frame comprises a metal alloy substantially configured as tubular stent member.

3. The percutaneous, trans-catheter prosthetic valve of Claim 2, wherein a proximal portion of the frame includes a ring.

4. The percutaneous, trans-catheter prosthetic valve of Claim 2, wherein a proximal portion of the frame comprises a circumferential zig-zag of wire.

5. The percutaneous, trans-catheter prosthetic valve of Claim 2, wherein a proximal portion of the frame includes a lattice.

6. The percutaneous, trans-catheter prosthetic valve of Claim 5, wherein the lattice is circumferentially continuous.

7. The percutaneous, trans-catheter prosthetic valve of Claim 5, wherein the lattice is circumferentially discontinuous.

8. The percutaneous, trans-catheter prosthetic valve of Claim 1, wherein a distal end of the frame includes two or more areas of axial continuity with the proximal end, and wherein the two or more areas of axial continuity comprise axially oriented projections.

9. The percutaneous, trans-catheter prosthetic valve of Claim 8, further comprising a distally positioned stabilization framework comprising at least one of circumferential or radial continuity with the axially oriented projections.

10. The percutaneous, trans-catheter prosthetic valve of Claim 8, wherein the frame includes two or more regions of circumferential discontinuity through which the plurality of valve leaflets of the biocompatible tissue material move radially inward and outward in closing and opening operation, respectively.

11. The percutaneous, trans-catheter prosthetic valve of Claim 1, wherein the biocompatible tissue material between the proximal end of the frame and the distal end of the frame resides substantially adjacent the abluminal surface of the frame.

12. The percutaneous, trans-catheter prosthetic valve of Claim 1, wherein the biocompatible tissue material does not contact a luminal surface of the frame.

13. The percutaneous, trans-catheter prosthetic valve of Claim 1, wherein an exterior surface of the biocompatible tissue material does not contact a luminal surface of the frame.

14. A prosthetic valve for implantation in a patient, comprising:

a frame including an abluminal surface extending between a proximal edge of the frame and a distal edge of the frame, the distal edge undulating axially to define at least two areas of circumferential discontinuity in the frame, wherein the frame is collapsible and expandable and adapted for trans-catheter delivery; and

a single layer of a biocompatible membrane material mounted to the abluminal surface of the frame to form leaflet portions, wherein the leaflet portions are collocated with the at least two areas of circumferential discontinuity in the frame.

15. The prosthetic valve of Claim 14, wherein no portion of the biocompatible membrane material is mounted to an interior surface of the frame.

16. The prosthetic valve of Claim 14, wherein the frame comprises a metal alloy substantially configured as tubular stent member.

17. The prosthetic valve of Claim 16, wherein a proximal portion of the frame includes a lattice to which the biocompatible membrane material is circumferentially mounted entirely upon the abluminal surface of the tubular stent member.

18. The prosthetic valve of Claim 17, wherein the lattice is circumferentially continuous.

19. The prosthetic valve of Claim 17, wherein the lattice is circumferentially discontinuous.

20. The prosthetic valve of Claim 14, wherein a proximal portion of the frame comprises a circumferential zig-zag of wire.

21. The prosthetic valve of Claim 14, wherein the biocompatible membrane material extends between the proximal edge and the distal edge of the frame.

22. The prosthetic valve of Claim 14, wherein at least some proximal portion of the frame does not include biocompatible membrane material mounted to its luminal or abluminal surfaces.

23. The prosthetic valve of Claim 14, wherein a distal portion of the frame further includes a distally extending stabilizing framework comprising a plurality of axially oriented

support members that each extend from a distally extending frame projection situated adjacent the at least two areas of circumferential discontinuity in the frame.

24. The prosthetic valve of Claim 23, further comprising a plurality of radial support members interconnecting the plurality of axially oriented support members.

25. The prosthetic valve of Claim 24, further comprising a wire guide, wherein the wire guide is coaxially aligned with an axis of the prosthetic valve, and wherein the wire guide is configured to allow for a coaxial passage of a guide wire such that coaxial alignment of the distally extending stabilizing framework may be facilitated during valve deployment.

26. The prosthetic valve of Claim 25, wherein the wire guide comprises at least one of a ring and a tube.

27. The prosthetic valve of Claim 14, wherein a circumference of the biocompatible membrane material is between about 5 to 25% greater than a circumference of a radially adjacent portion of the frame.

28. A method of preparing a percutaneous, trans-catheter prosthetic valve, comprising:

mounting a single layer of a biocompatible tissue material to an abluminal surface of a trans-catheter deliverable frame such that an interior surface of the biocompatible tissue material between a proximal end of the trans-catheter deliverable frame and a distal end of the trans-catheter deliverable frame resides radially exterior to and substantially adjacent the abluminal surface of the trans-catheter deliverable frame at all points of attachment and in entirety when a plurality of leaflets of the biocompatible tissue material are in a fully open position.

29. The method of preparing a percutaneous, trans-catheter prosthetic valve of Claim 28, further comprising compressing and crimping the trans-catheter deliverable frame, with the biocompatible tissue material mounted thereto, upon a delivery catheter.

30. The method of preparing a percutaneous, trans-catheter prosthetic valve of Claim 29, further comprising implanting the trans-catheter deliverable frame with the biocompatible tissue material mounted thereto into a patient.

31. The method of preparing a percutaneous, trans-catheter prosthetic valve of Claim 28, wherein the trans-catheter deliverable frame comprises a stent.

32. The method of preparing a percutaneous, trans-catheter prosthetic valve of Claim 28, further comprising mounting the trans-catheter deliverable frame and the biocompatible tissue material mounted thereto on a mandrel.

33. A method, comprising:

attaching a biocompatible membrane material to a collapsible and expandable frame to form a trans-catheter deliverable prosthetic valve, wherein an entire interior surface of the

biocompatible membrane material is located exterior of an abluminal surface of the collapsible and expandable frame when leaflet portions of the biocompatible membrane material are in a fully open position.

34. The method of Claim 33, wherein the attaching includes suturing the biocompatible membrane material to a distal edge of the collapsible and expandable frame that undulates in an axial direction around the collapsible and expandable frame.

35. The method of Claim 33, further comprising associating the trans-catheter deliverable prosthetic valve with a catheter.

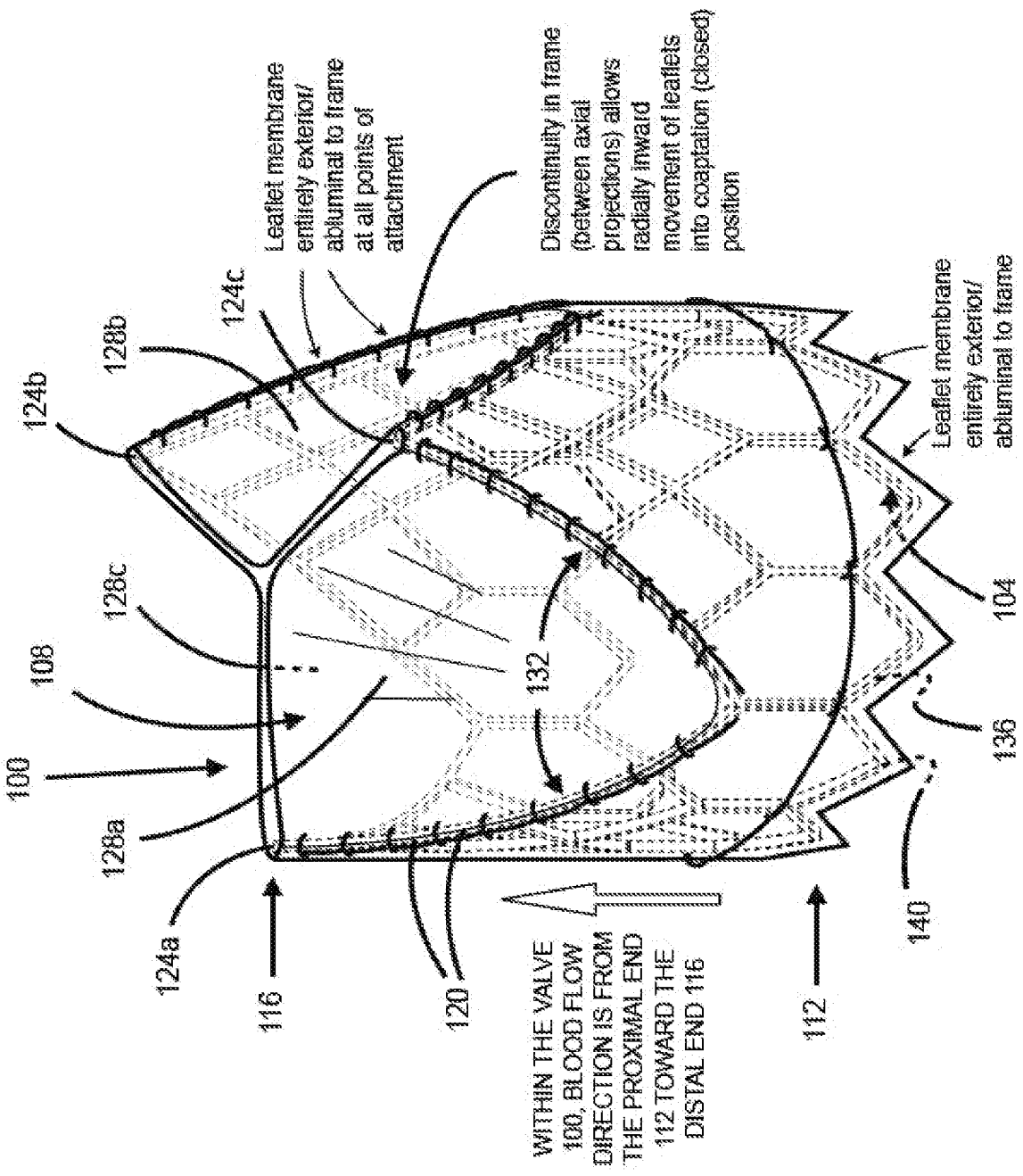

100
108
128a
128b
128c
124a
124b
124c
116
120
132
112
136
140
104
Leaflet membrane entirely exterior/ abluminal to frame at all points of attachment
Discontinuity in frame (between axial projections) allows radially inward movement of leaflets into coaptation (closed) position
Leaflet membrane entirely exterior/ abluminal to frame
WITHIN THE VALVE 100, BLOOD FLOW DIRECTION IS FROM THE PROXIMAL END 112 TOWARD THE DISTAL END 116

Figure 1A

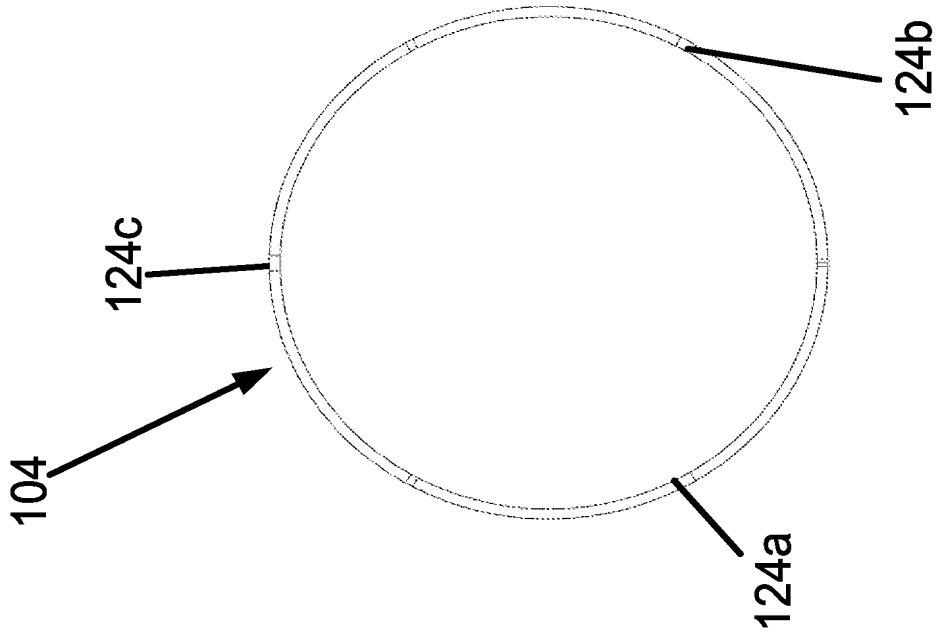


FIG. 1C

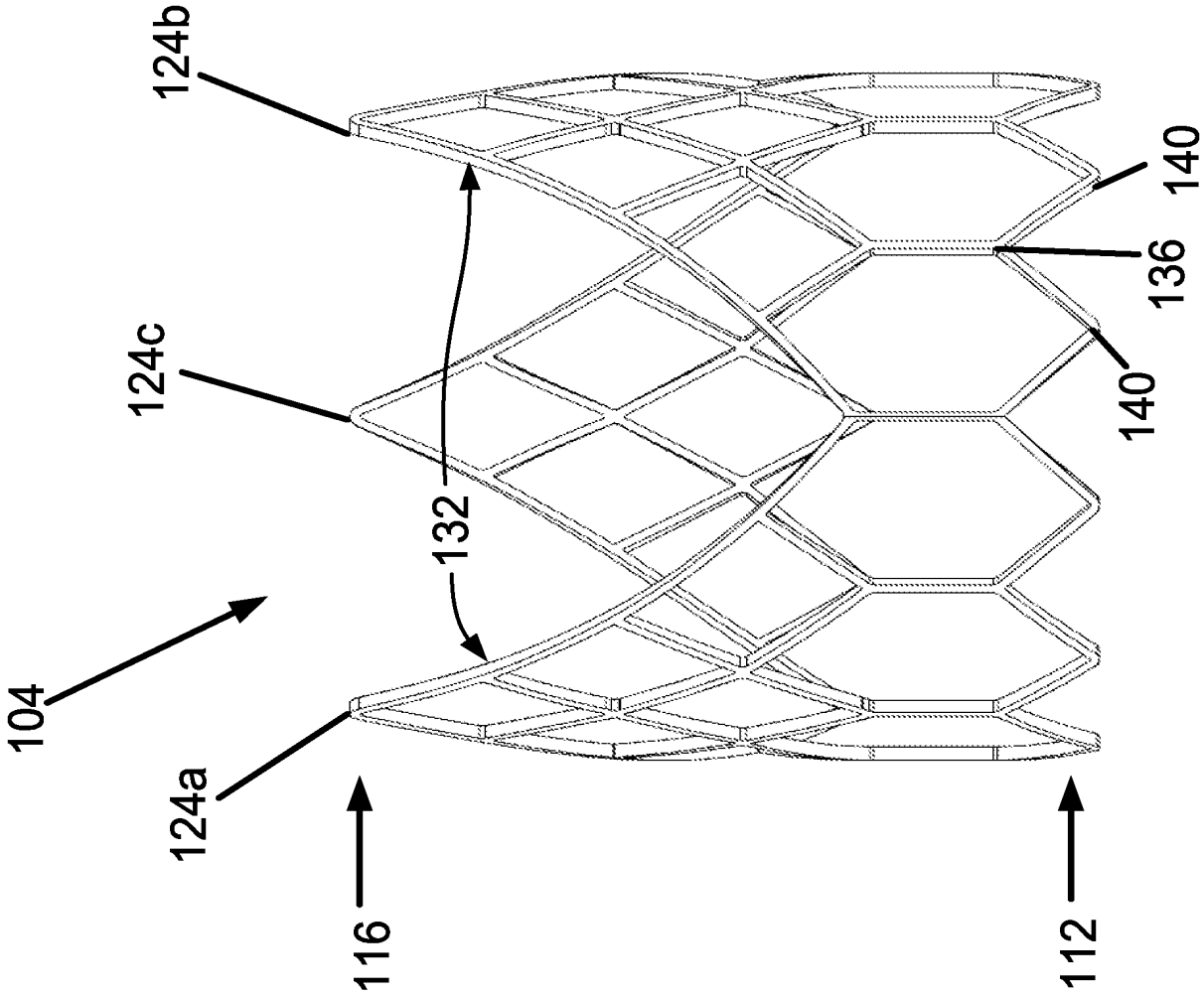
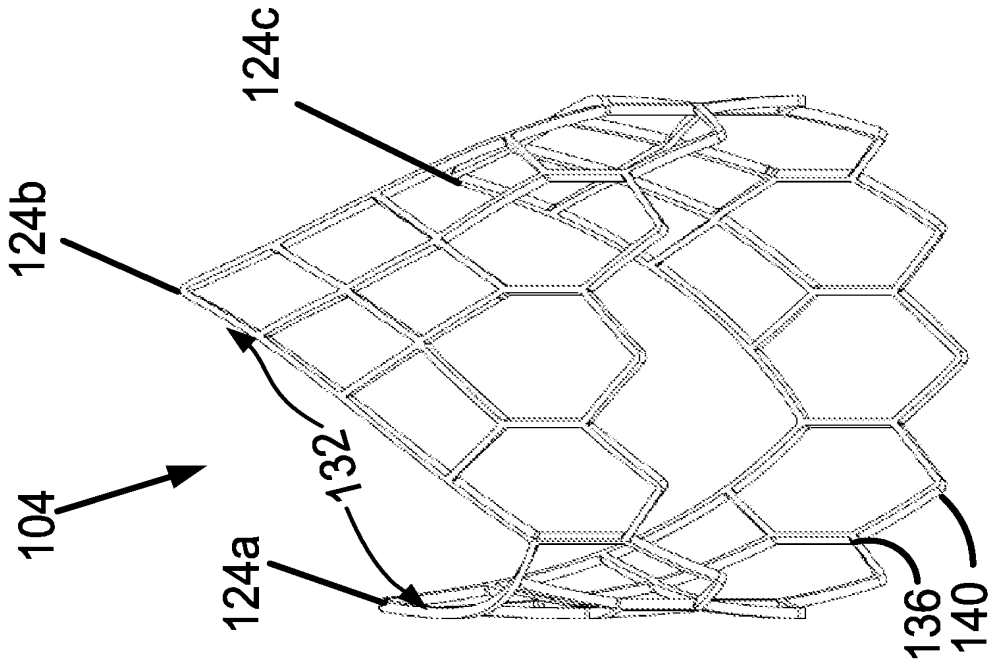


FIG. 1B

FIG. 1E


124c
124b
104
132
124a
136
140

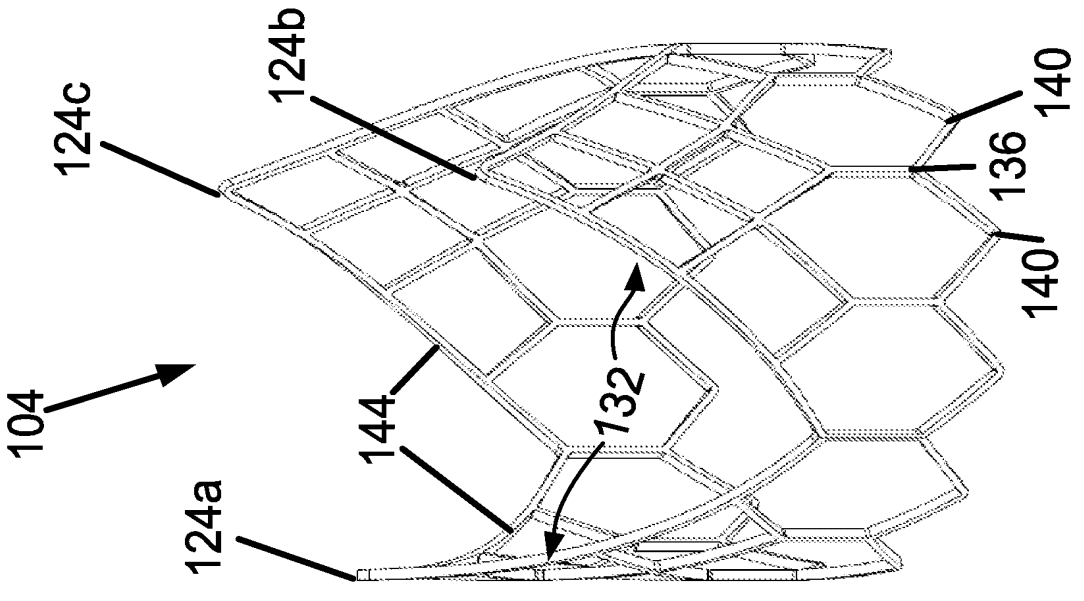

124c
124b
140
136
140
104
144
132
124a

FIG. 1D

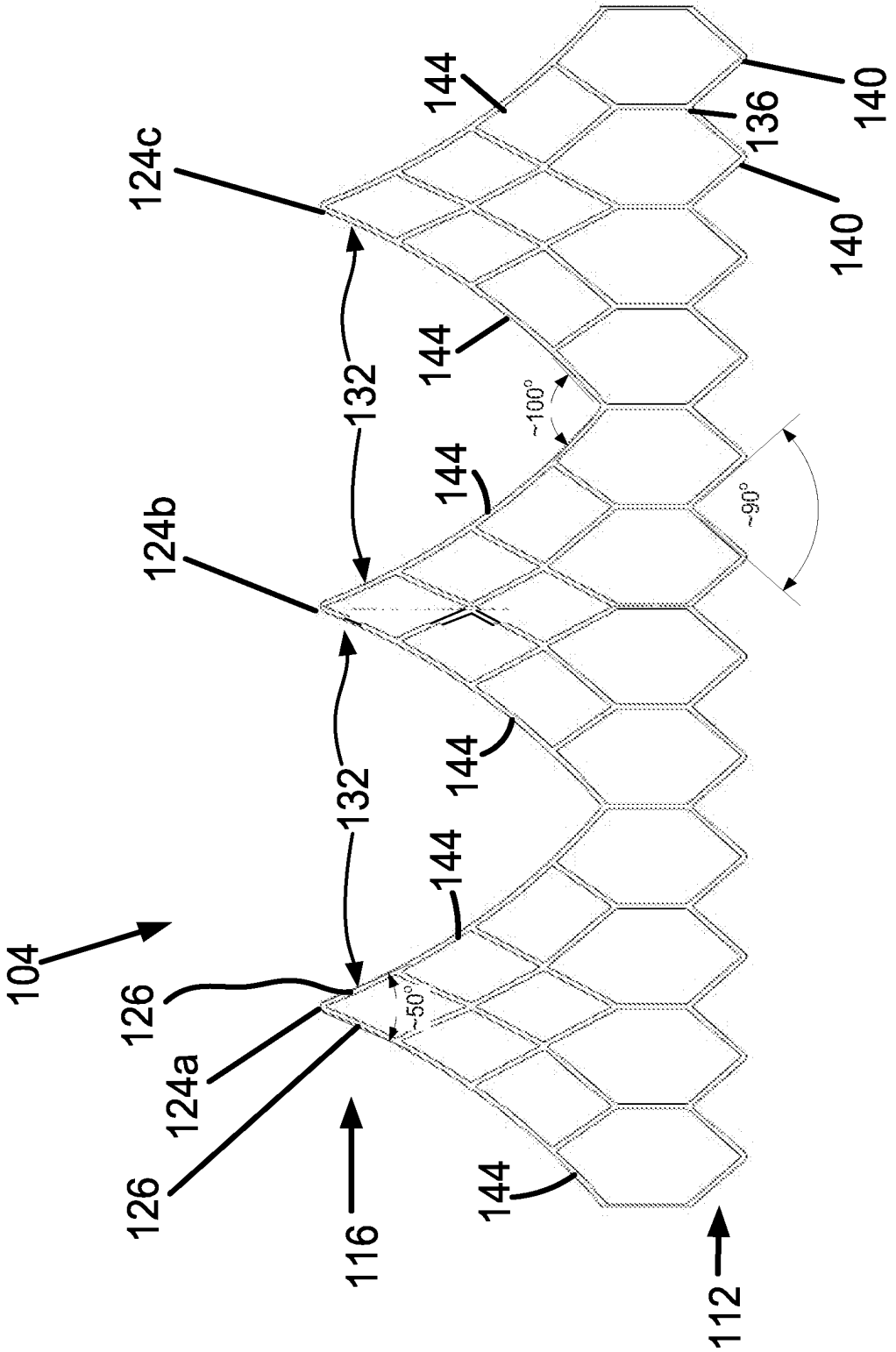

104
126
124a
126
116
112
124b
124c
132
132
144
144
144
144
144
144
140
140
136
~50°
~100°
~90°

FIG. 1F

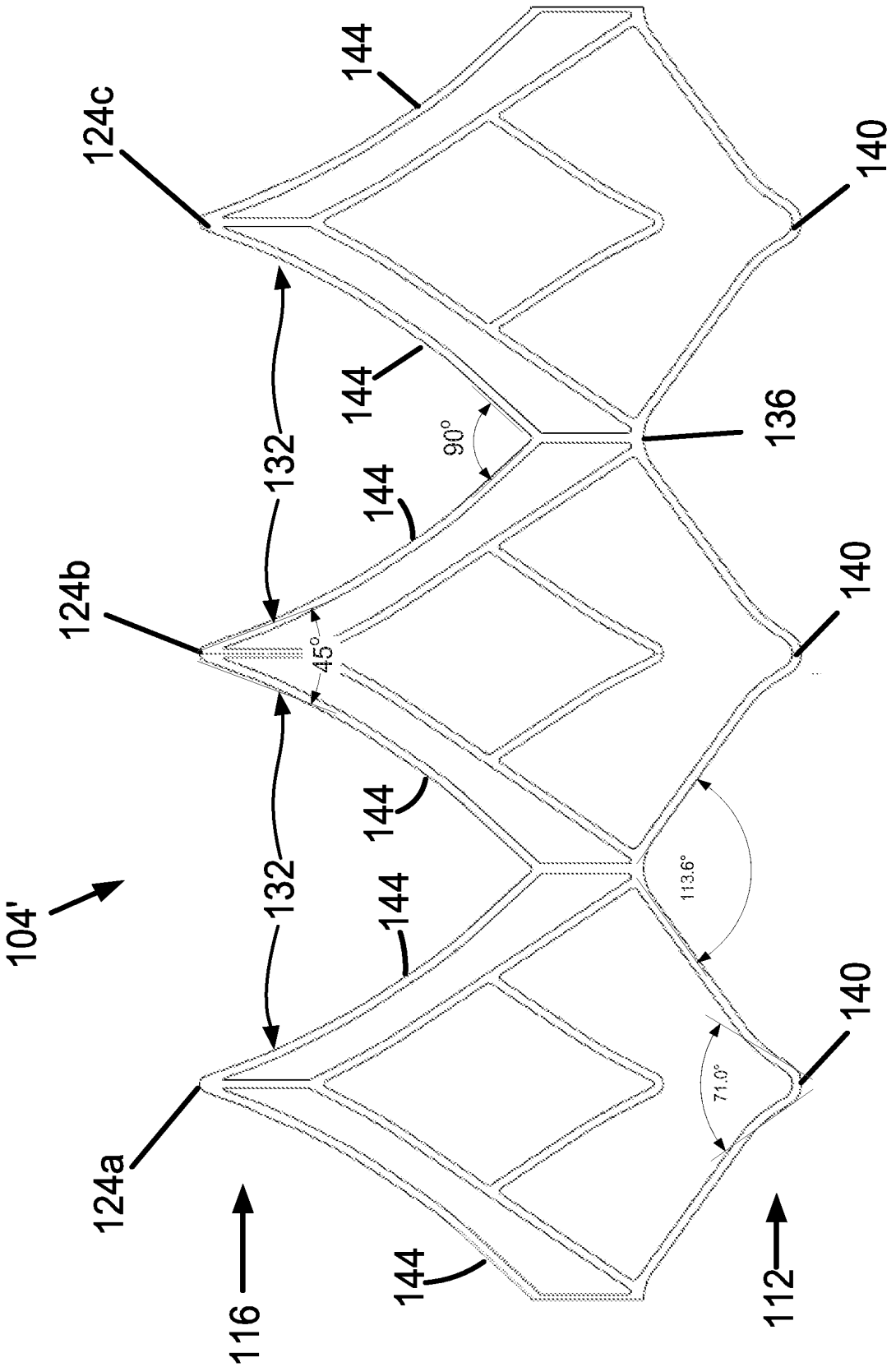

104'
124a
124b
124c
116
112
132
132
144
144
144
144
144
144
140
140
140
136
90°
45°
113.6°
71.0°

FIG. 1G

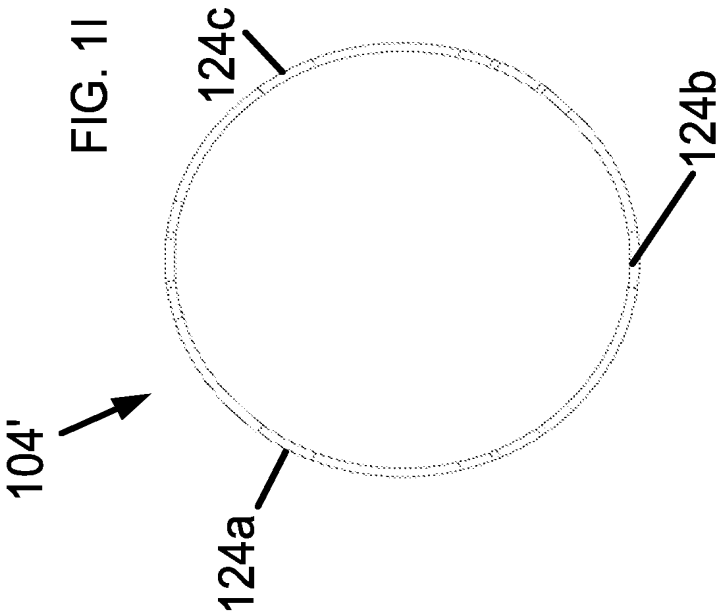

124c
124b
104'
124a

FIG. 1I

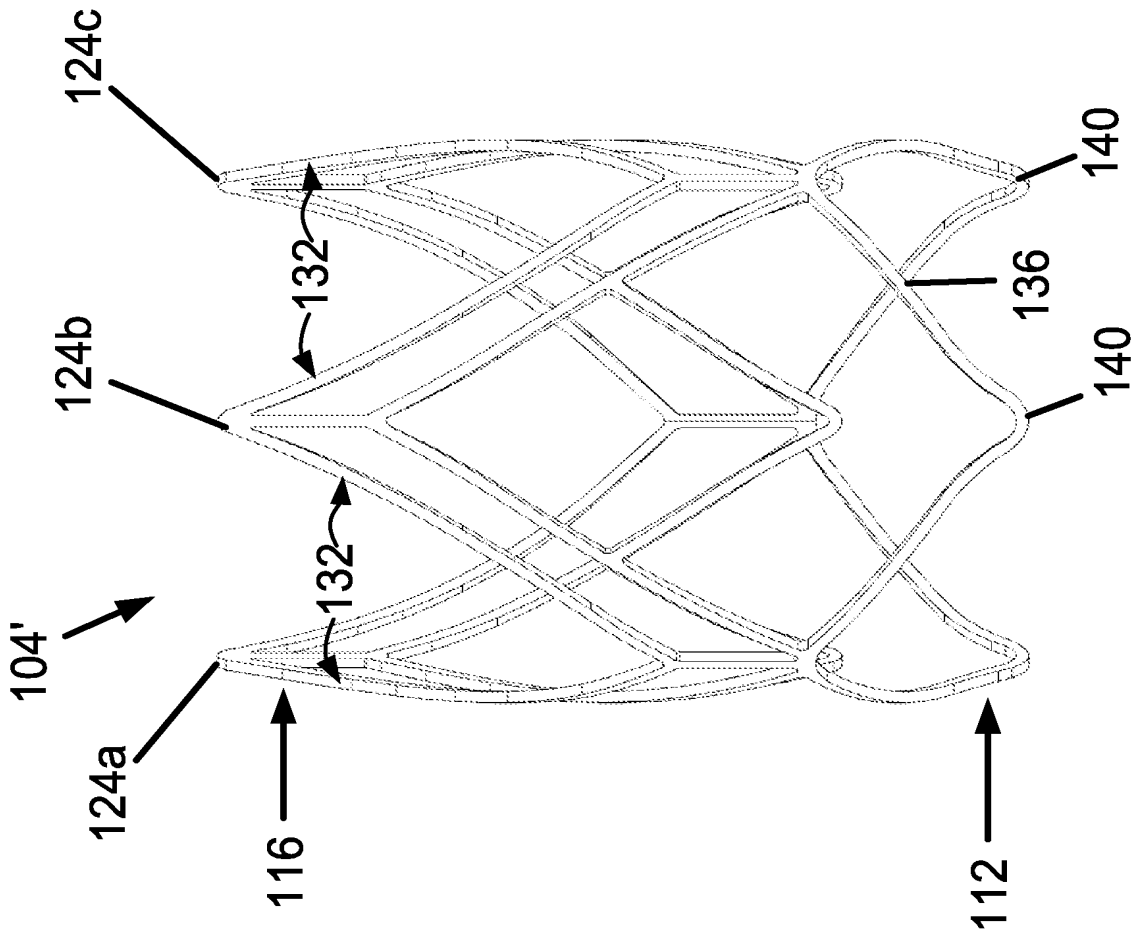

124c
132
140
124b
136
140
132
104'
124a
116
112

FIG. 1H

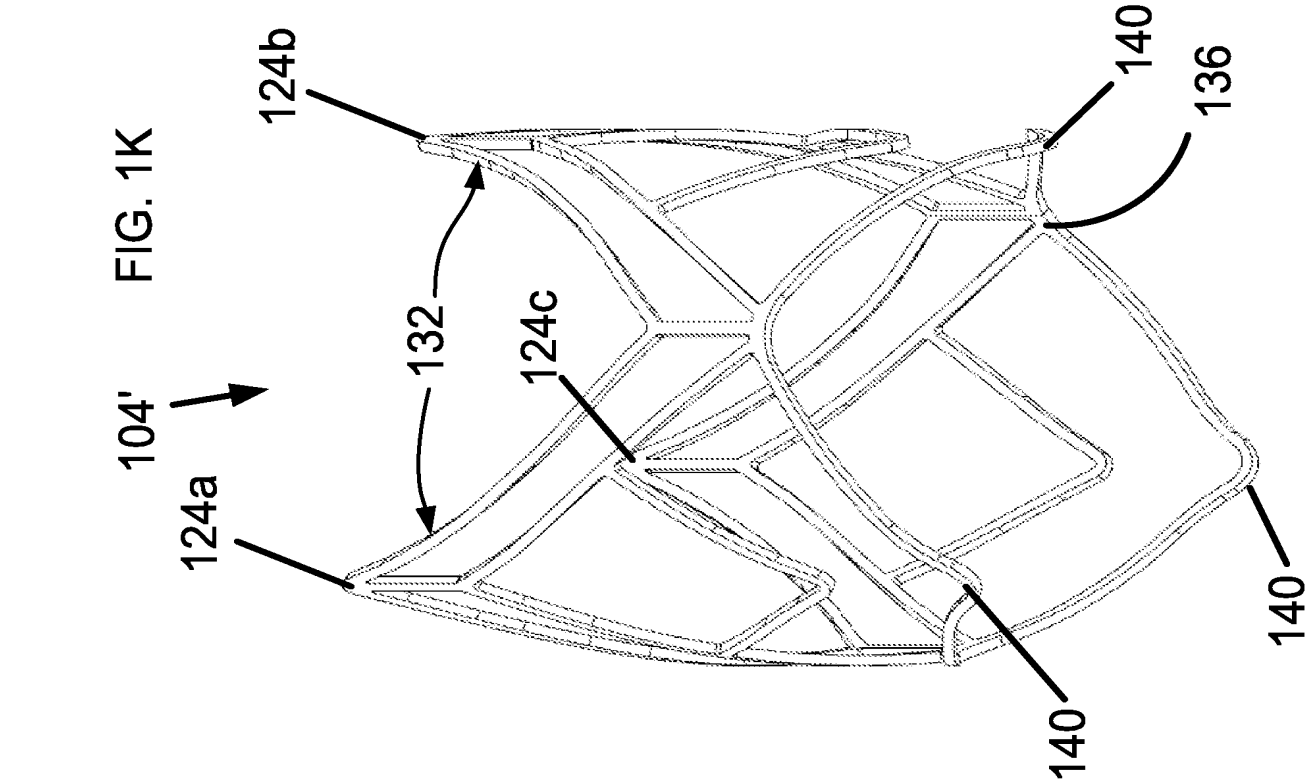

124b
140
136
132
124c
104'
124a
140
140

FIG. 1K

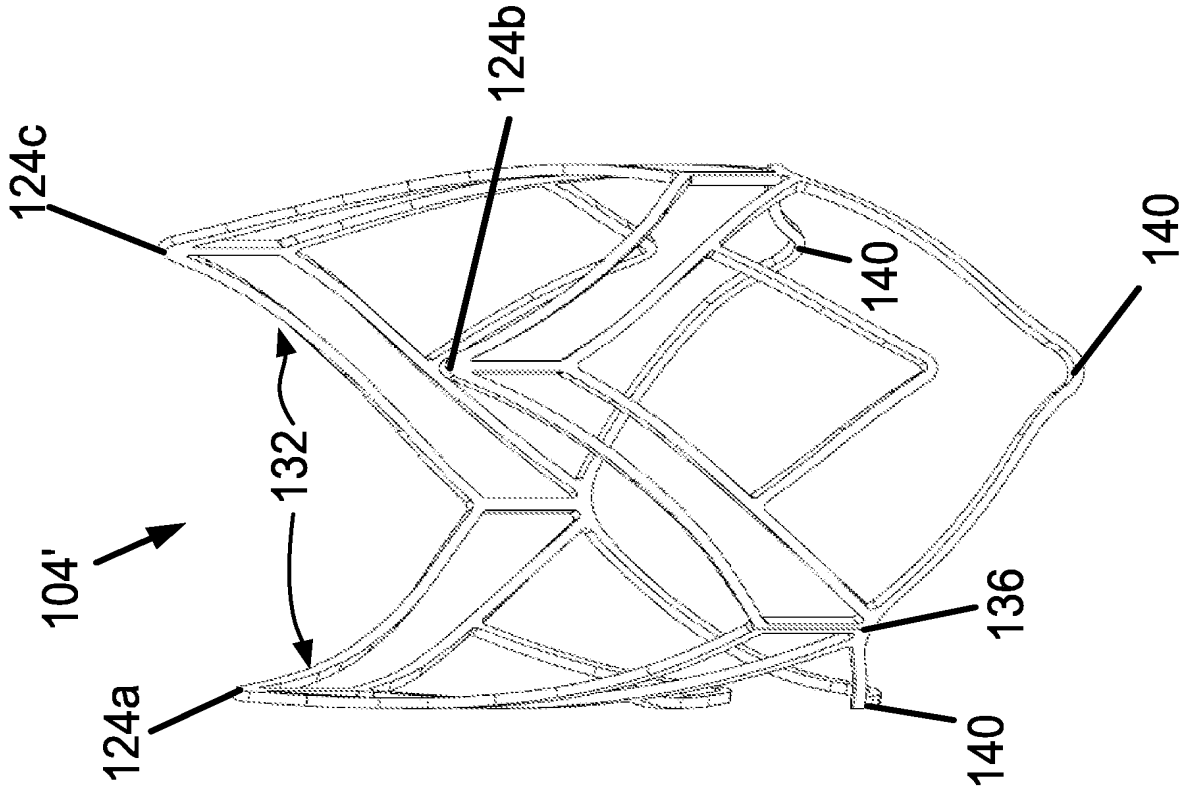

124c
124b
140
140
132
104'
136
124a
140

FIG. 1J

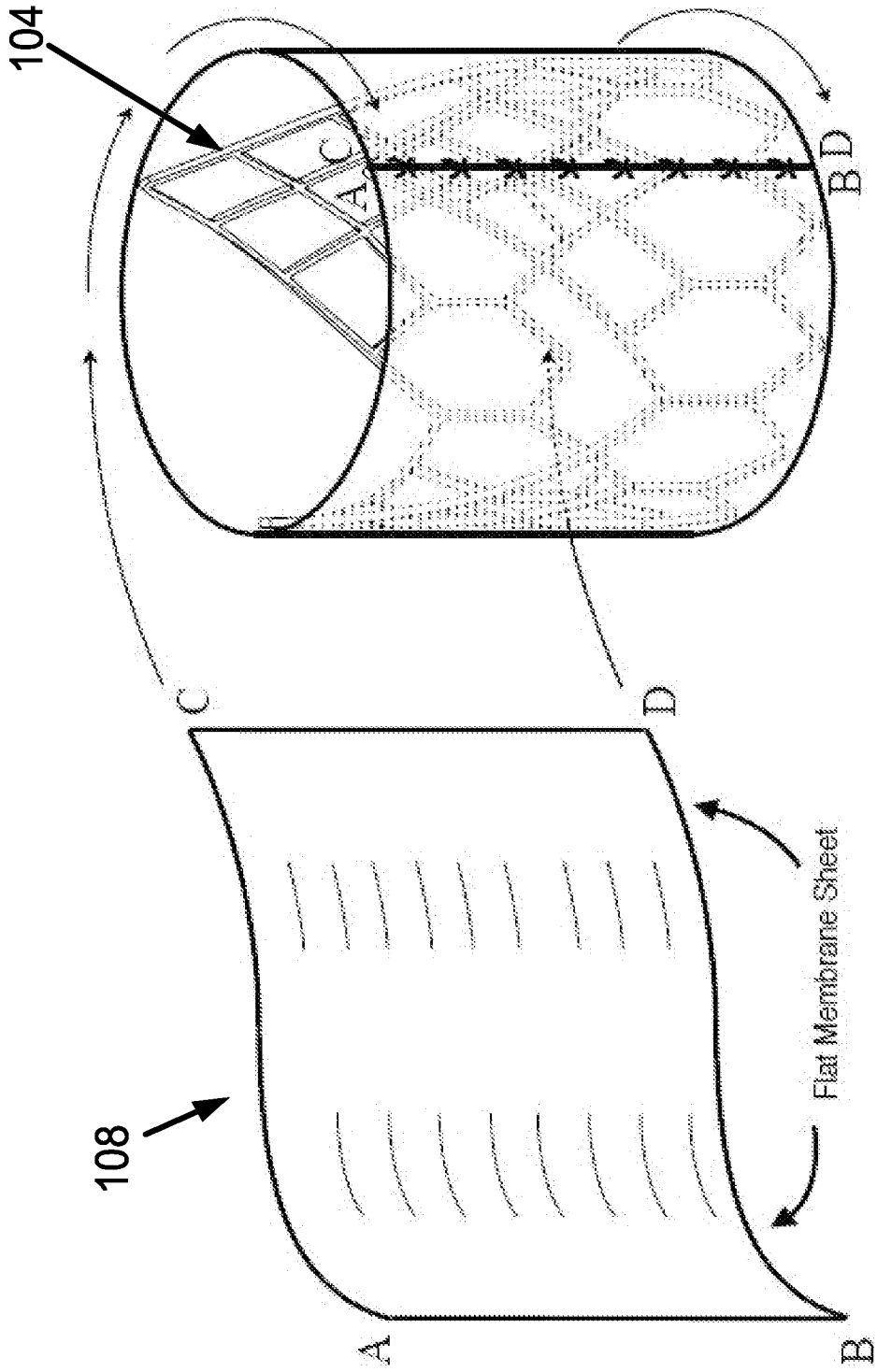

104
108
A
B
C
D
Flat Membrane Sheet
Flat membrane sheet is wrapped around outside/abluminal aspect of cylindrical frame and is secured in closed form by attaching membrane free edges A-B to C-D as by suturing. Membrane is subsequently attached to underlying frame.

FIG. 1L

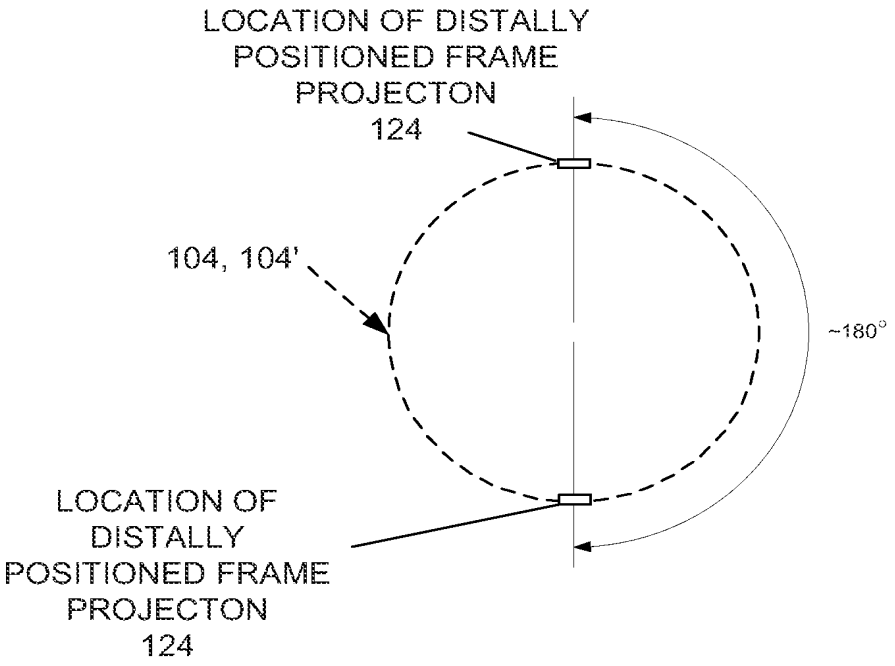

LOCATION OF DISTALLY POSITIONED FRAME PROJECTON 124
104, 104'
~180°
LOCATION OF DISTALLY POSITIONED FRAME PROJECTON 124

Fig. 2

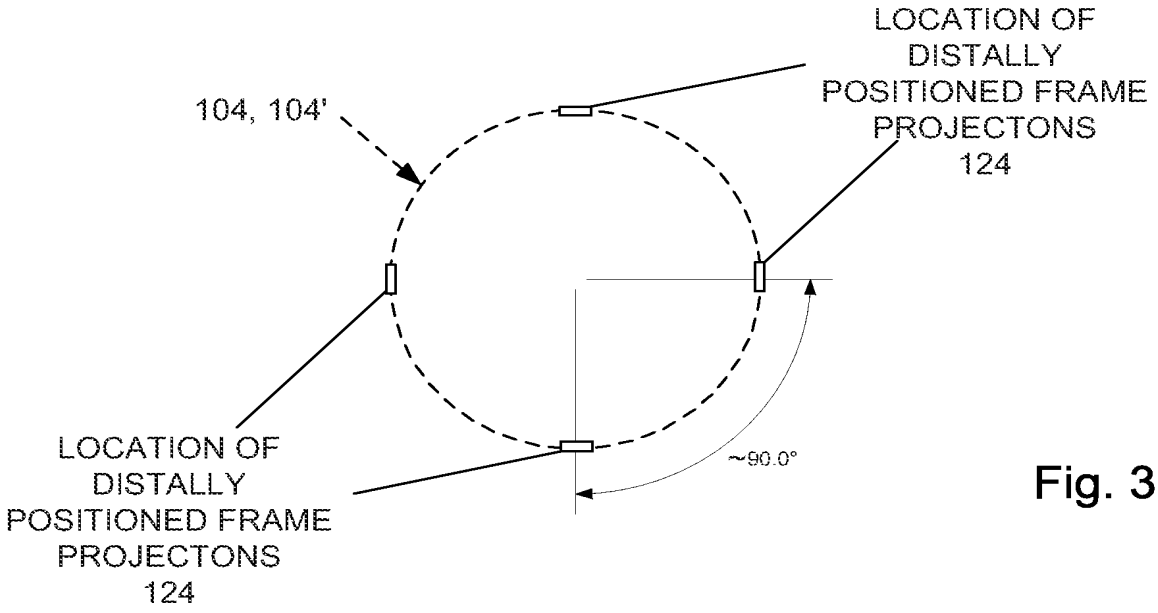

LOCATION OF DISTALLY POSITIONED FRAME PROJECTONS 124
104, 104'
~90.0°
LOCATION OF DISTALLY POSITIONED FRAME PROJECTONS 124

Fig. 3

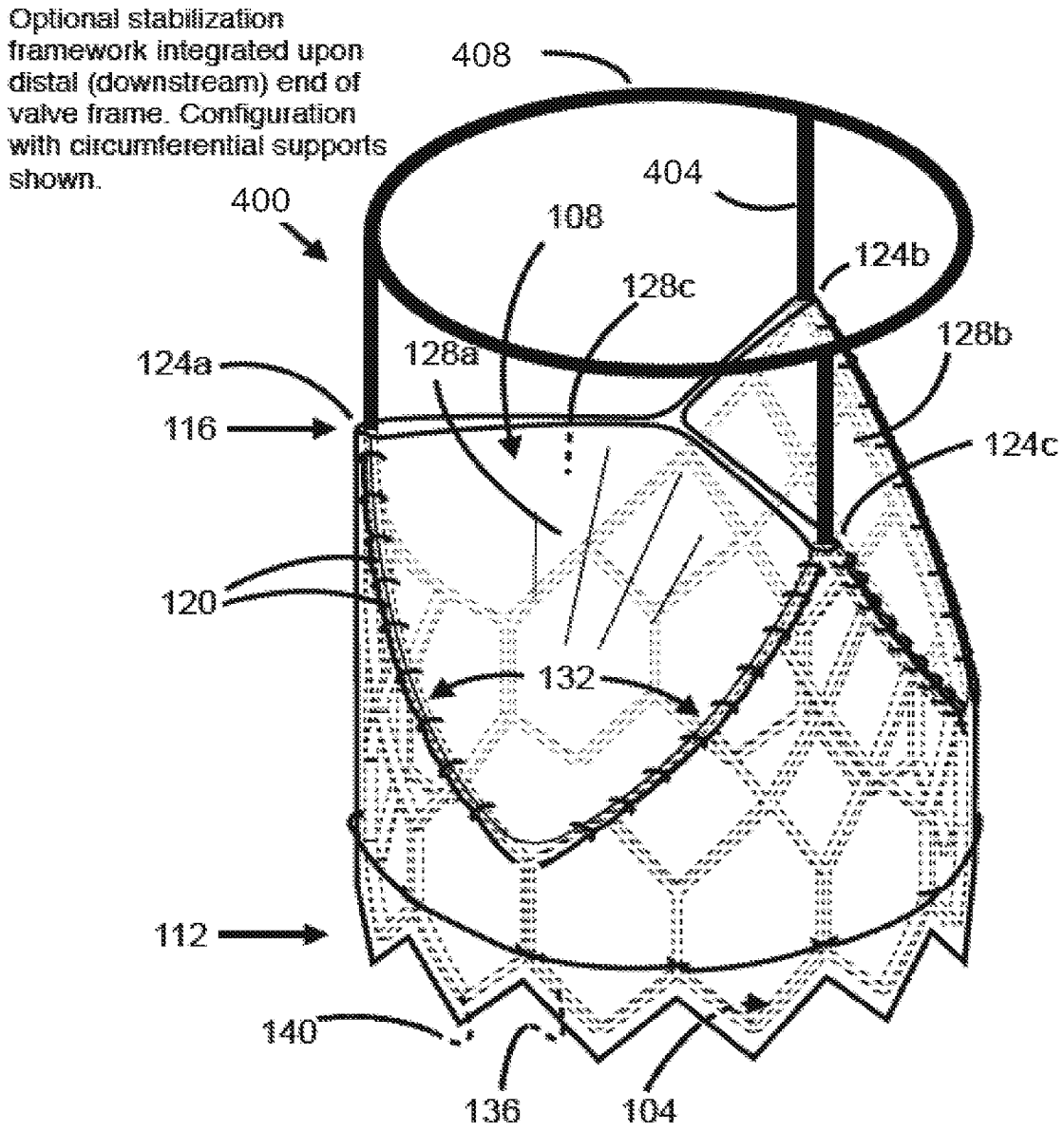

Optional stabilization framework integrated upon distal (downstream) end of valve frame. Configuration with circumferential supports shown.
408
404
400
108
124b
128c
128b
124a
128a
116
124c
120
132
112
140
136
104

Fig. 4

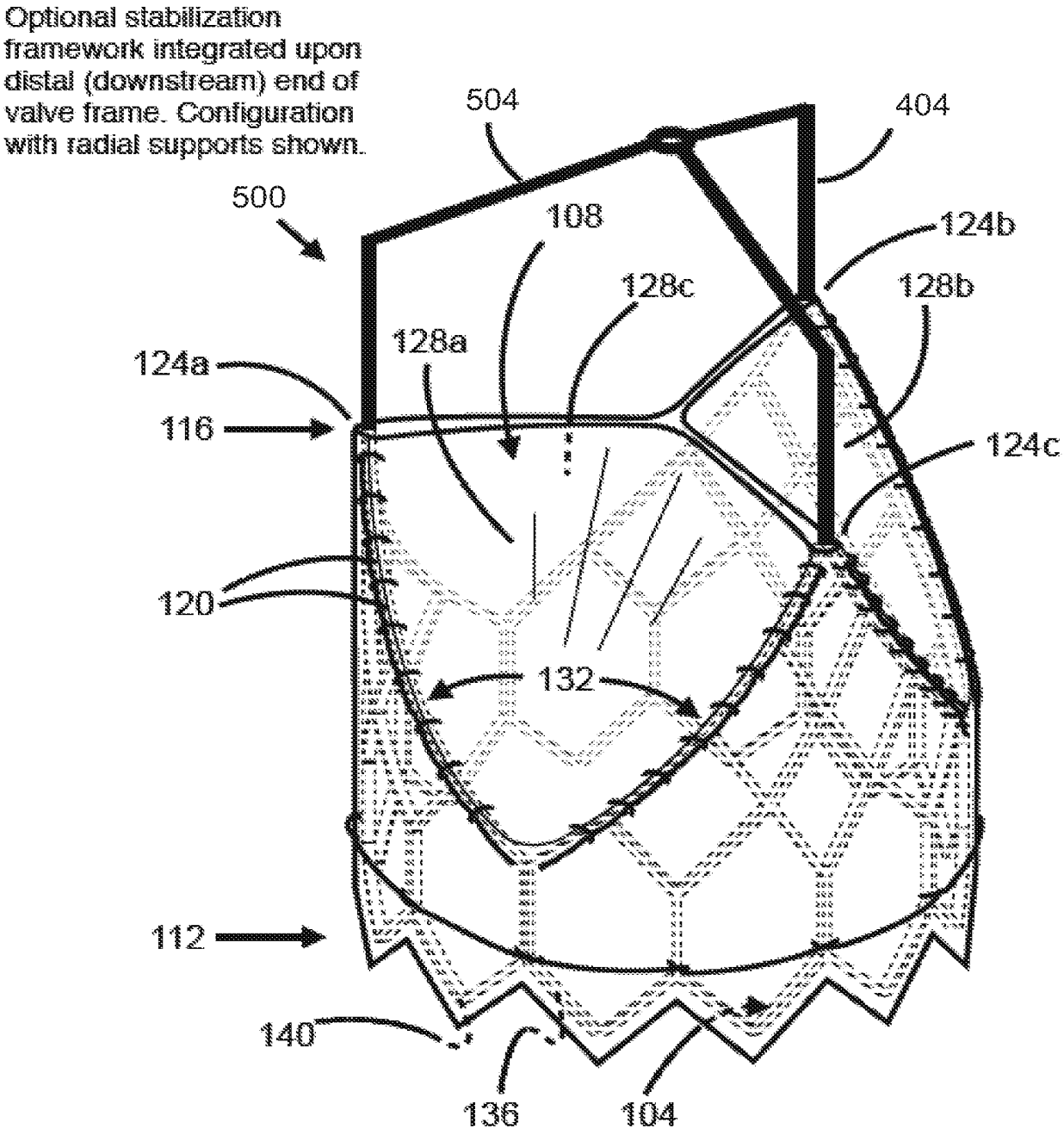

Optional stabilization framework integrated upon distal (downstream) end of valve frame. Configuration with radial supports shown.
504
404
500
108
124b
128c
128b
128a
124a
116
124c
120
132
112
140
136
104

Fig. 5

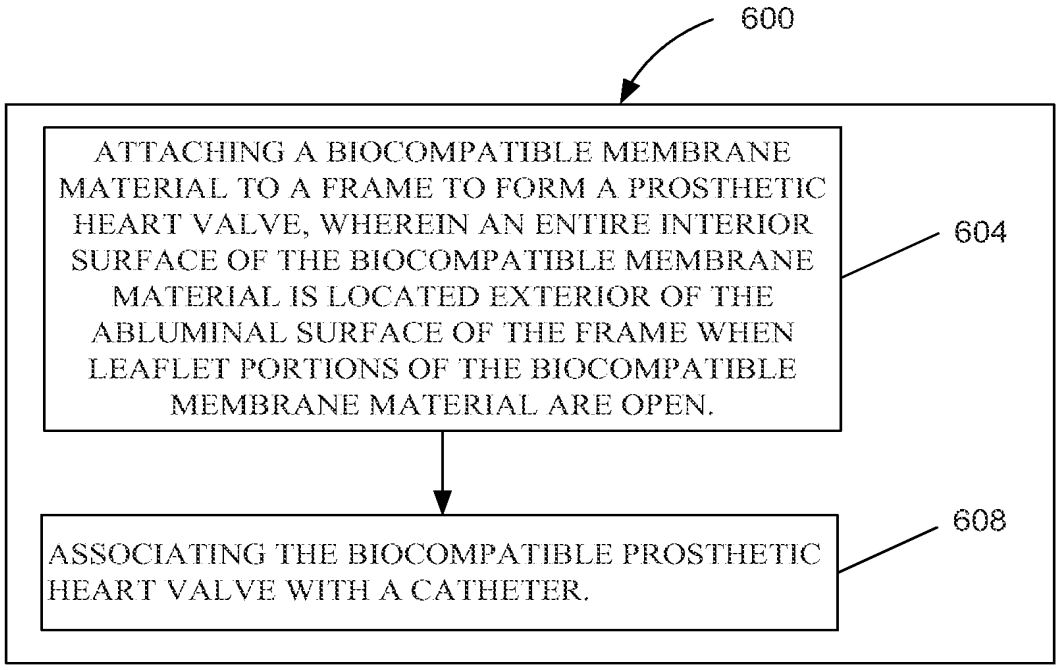

600
ATTACHING A BIOCOMPATIBLE MEMBRANE MATERIAL TO A FRAME TO FORM A PROSTHETIC HEART VALVE, WHEREIN AN ENTIRE INTERIOR SURFACE OF THE BIOCOMPATIBLE MEMBRANE MATERIAL IS LOCATED EXTERIOR OF THE ABLUMINAL SURFACE OF THE FRAME WHEN LEAFLET PORTIONS OF THE BIOCOMPATIBLE MEMBRANE MATERIAL ARE OPEN.
604
ASSOCIATING THE BIOCOMPATIBLE PROSTHETIC HEART VALVE WITH A CATHETER.
608

FIG. 6

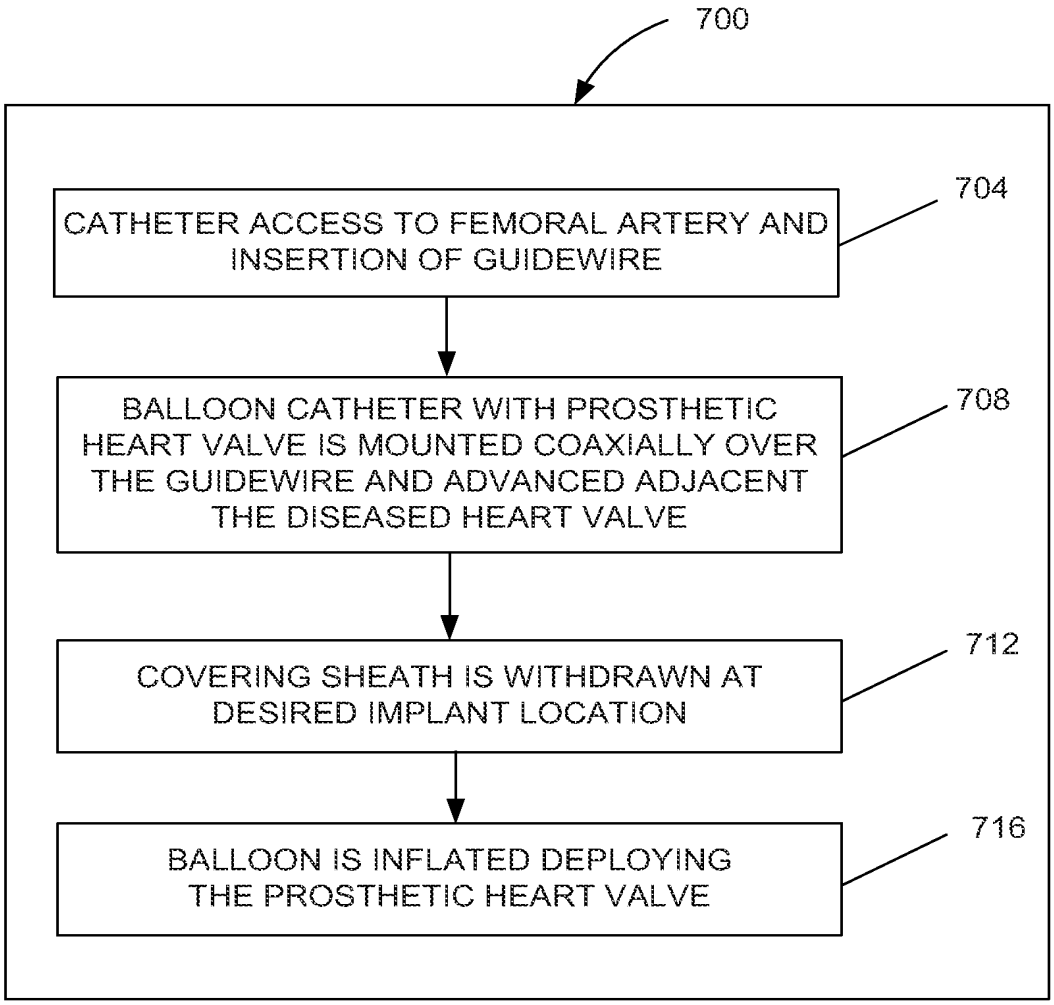

700
CATHETER ACCESS TO FEMORAL ARTERY AND INSERTION OF GUIDEWIRE
704
BALLOON CATHETER WITH PROSTHETIC HEART VALVE IS MOUNTED COAXIALLY OVER THE GUIDEWIRE AND ADVANCED ADJACENT THE DISEASED HEART VALVE
708
COVERING SHEATH IS WITHDRAWN AT DESIRED IMPLANT LOCATION
712
BALLOON IS INFLATED DEPLOYING THE PROSTHETIC HEART VALVE
716

FIG.7

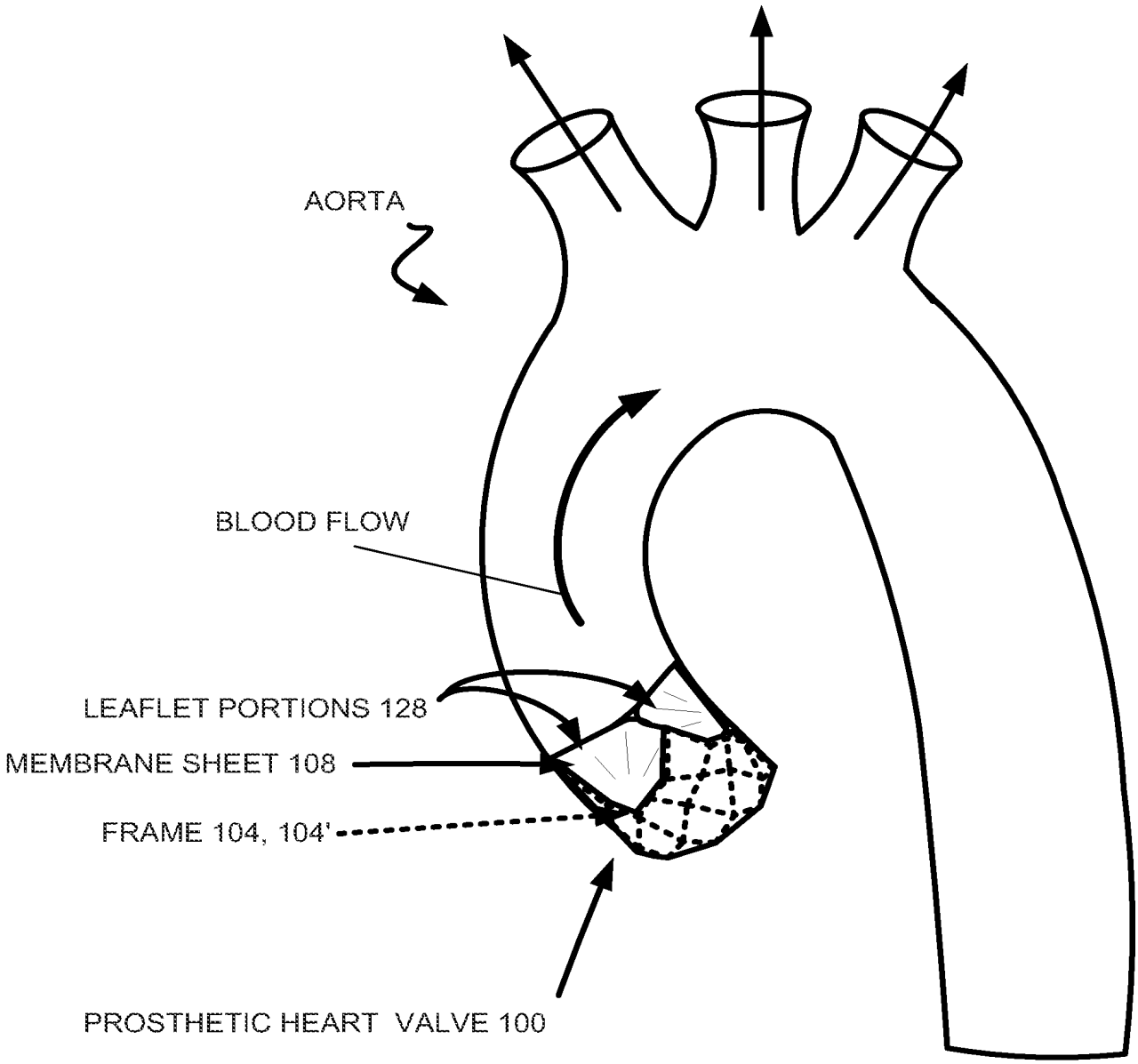

AORTA
BLOOD FLOW
LEAFLET PORTIONS 128
MEMBRANE SHEET 108
FRAME 104, 104'
PROSTHETIC HEART VALVE 100

FIG. 8

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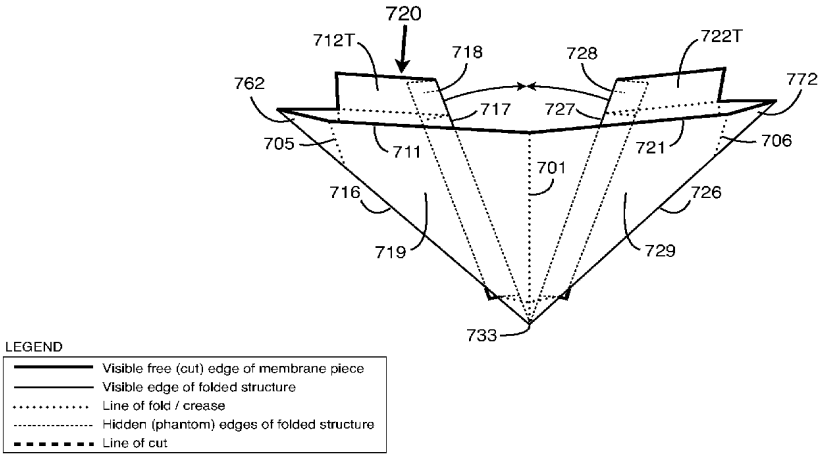
(54) **Title**: PERCUTANEOUSLY DELIVERABLE HEART VALVE INCLUDING FOLDED MEMBRANE CUSPS WITH INTEGRAL LEAFLETS

Figure 7D



(57) **Abstract**: A transcatheter, percutaneously implantable, prosthetic heart valve is provided that comprises a lattice frame and two or more integrated cusp and leaflet folded structures attached to the lattice frame. The two or more integrated cusp and leaflet folded structures each comprise a flat sheet of biocompatible membrane that is folded to include a substantially conical shape according to a flat folding pattern. The substantially conical shape is further formed by joining apposing sides of the substantially conical shape along a seam. The two or more integrated cusp and leaflet folded structures are each attached along their respective seams to the lattice frame in a direction substantially parallel to an axis of the lattice frame. Embodiments of valves described herein have application within the entire vascular system.

WO 2012/082952 A2

PERCUTANEOUSLY DELIVERABLE HEART VALVE INCLUDING FOLDED MEMBRANE CUSPS WITH INTEGRAL LEAFLETS

FIELD

The present invention relates to the field of medical devices, and more particularly, to percutaneously deliverable heart valves.

BACKGROUND

The native heart valves, and in particular, the aortic valve, has a complex geometry that endows both ideal opening and closing geometries through an anatomic joining of a tubular inflow structure of the left ventricular outflow tract and an expansion of the valve sinuses above the hinging point of the valve leaflets defined by the aortic valve annular ring, part of the fibrous "skeleton" of the heart.

For the purposes of discussion and definition in the ensuing descriptions, the "upper", downstream outlet structure of the native aortic valve above its hinging point contains three valve "cusps" of a generally spherical contour with central mobile portions termed "leaflets" that are induced by fluid pressure gradients to meet centrally to close and to move radially outward to open in valve operation. The cusps are further continuous with downstream curved tissue walls meeting the tubular great vessel, the aorta, at the "sino-tubular junction". Each cusp and its upper, downstream extension above the level of leaflet closure ("coaptation") are a continuous structure of a generally spherical contour and together define the envelope of the "sinus of Valsalva. Typically, surgical prosthetic valves are implanted by excision of the diseased native valve leaflets at the level of the annular ring, and suturing of the prosthetic valve at this point, thus replacing only the opening geometry of the valve and leaving the outer structures of the cusps and the sinuses of Valsalva, the anatomy that confers proper closing geometry, generally intact.

Surgical valve prostheses are generally constructed as analogs to this central portion of the native valve geometry involved in the opening phase of the valve cycle. This approach to modeling the replacement valve prosthesis is enabled by the nature of the surgical technique: the replacement valve is sutured into the valve seat under direct vision. In contrast, a percutaneous stent-mounted heart valve ("PHV") is typically a construct in which the operating valve membrane leaflets are mounted and confined within the tubular envelope of a collapsible frame for effective transvascular delivery.

Further, in order to preclude valve regurgitation, the base of each leaflet must lie in exact apposition to the valve seat to form a seal, a condition that is difficult to satisfy without implantation under direct vision. Even then, since the diseased native valve would not be removed and its axial geometry is often distorted, it may not be possible to seat a PHV exactly

under any circumstances. Thus, a cylindrical cuff layer, interior or exterior to the frame, is usually employed that acts as a seal and provides some latitude in the positioning and alignment of the PHV along the axis of flow, allowing for reliable and effective PHV implantation and minimizing the risk of significant valve regurgitation. Finally, the diseased native valve leaflets, when pushed outward by the deployed PHV frame, may themselves form a barrier separating the sinuses of Valsalva from the leaflets of the PHV, then disrupting the native closing geometry of the valve so that the sinuses are no longer continuous with the pressurized space above the PHV leaflets.

These issues illustrate some of the challenges to the formation of a PHV; that is, how to confine operating leaflets within a partially sealed tubular structure while preserving ideal opening and closing valve behavior without the benefit of the natural mechanism of the sinuses of Valsalva in a single valve and leaflet geometry, such as the separate and distinct upper and lower geometries of the native valve. As such, there is a need for additional devices, systems and/or methods that address one or more of the problems or shortcomings noted above.

SUMMARY

It is to be understood that the present invention includes a variety of different versions or embodiments, and this Summary is not meant to be limiting or all-inclusive. This Summary provides some general descriptions of some of the embodiments, but may also include some more specific descriptions of other embodiments.

Two goals of at least some embodiments of the present inventions are: (1) to maximize effective orifice area and minimize opening pressure gradients through geometry that mimics the natural form of inflow into the valve — the tubular outflow tract of the heart pumping chamber; and (2) to minimize the inward tension on the leaflet commissures in the closed position through geometry that mimics the natural effect of the sinuses of Valsalva - an effect that prevents downward displacement of the leaflet free edges under closing pressure, thus distributing force along the lines of leaflet apposition rather than focusing it at the points of leaflet attachment to the frame.

The first of these goals dictates that the inflow to the valve, similar to that of the natural aortic valve, encounters then outwardly displaces the most central portion of the leaflets first, with opening moving progressively outward along the surface of the leaflets. The second suggests that the cross-sectional profile of the valve sinus/cusp formed in its central portion by the free edge of the leaflets, like that of the natural aortic valve, should be approximately elliptical, and that the cross-sectional diameter of each cusp should progressively decrease below the plane of leaflet apposition, like that of the natural valve cusps. One or more embodiments of the one or more present inventions answer the configuration ideals with a robust balance of

functional geometries for valve opening and closing.

The spherical geometry of the native aortic valve leaflets is difficult to replicate in a transcatheter valve. First, while this shape is functionally robust in vivo, even if reproduced in some form it is not suited to efficient radial compression typically required for collapse into a small diameter delivery catheter used in transcatheter valve delivery systems, and discontinuities would develop in the leaflet surface that would resolve into irregular folds with at least some circumferential component, thereby threatening the restitution of the geometry on reopening at deployment. Second, tissue bioprosthetic valve leaflets, if not actually constituted of the animal valve itself, are typically constructed of flat sheet tissue membrane from which rendering of cusps with leaflets of a spherical contour would be difficult if not impossible without the use of traction force on the material, or extensive cutting and suturing of the leaflet cusp portion — an impractical approach, and a threat to the material integrity of the thin tissue membrane.

At least one embodiment of the one or more present inventions answers these challenges by employing conical rather than spherical cusp geometry, thereby reproducing some benefits of the latter with near-elliptical leaflet cross-section that progressively decreases moving proximal to the plane of leaflet apposition while being readily conformed on outward radial compression in the valve opening phase into a substantially flat folded construct against the interior tubular walls of the containing frame. This favorable resolution of the conical geometry in opening phase expresses the opening efficiency of this valve design with a large effective orifice area and low transvalvular energy losses. In the closed position, the free edges of the separate leaflets of the conical cusps meet in apposition, each cone acting as an independent valve; pressure load-bearing is enhanced by the material continuity of the cone structure with the inner apposing wall and outer wall of each cone being part of a single continuous membrane structure. Further, the conical cusps are particularly suited for compression and containment within a collapsible frame for transcatheter delivery.

In at least one embodiment, a transcatheter, percutaneously implantable, bioprosthetic heart valve having a lattice frame comprising a substantially tubular alloy metal mesh, and two or more valve cusps with leaflets mounted to the lattice frame, is provided. Further, the cusps include a flat sheet of processed mammalian tissue membrane that is folded into a substantially conical shape according to a flat folding pattern, the substantially conical shape is further formed by joining opposing sides of the substantially conical shape along a seam that is oriented along a longitudinal axis of the substantially conical shape. In at least one embodiment, the two or more cusps are attached along their seams (which may or may not include the apexes of the cusps), such as, by way of example and not limitation, along the axial centerline of the outer circumference of the cone, to an interior portion of the lattice frame along an axial flow direction

of the valve and are further attached along the distal, downstream, edge of the substantially conical shape along at least an outer half of the substantially conical shape's edge. When the membrane valve leaflet is attached to the frame, its principal line of securement along the axial centerline of the outer circumference of the cone is attached at a non-commissural seam or edge, effecting a coaxial (to the flow axis) line of attachment at an area of the structure that advantageously bears load, thereby relieving the commissural attachment of loads associated with the securement of the cusp structures to the frame. As such, the leaflet commissure attachments, thus located at points where the leaflet membrane is continuous and uncut, advantageously need only bear the centripetal loads associated with the radially inward movement and operation of the free edges of the leaflets.

In at least one embodiment, a transcatheter, percutaneously implantable, bioprosthetic heart valve is provided wherein two distal, downstream, vertices of the flattened cusp and leaflet structure are folded over in a radially outward direction and fixed to the frame such that the vertex folds of neighboring leaflets are adjacent and define an extent of leaflet apposition at the points corresponding to leaflet commissures.

In at least one embodiment, a transcatheter, percutaneously implantable, bioprosthetic heart valve is provided wherein a vertex forming a proximal, upstream, apex of the substantially conical shape is folded over in a radially outward direction and affixed to an inner portion of the frame.

In at least one embodiment, a transcatheter, percutaneously implantable, bioprosthetic heart valve is provided wherein the flat folding pattern is polygonal and includes extending portions that, when the leaflet is mounted, extend circumferentially outward from an axial line of attachment of the leaflet to the frame so as to form, when joined and attached to corresponding extending portions of neighboring leaflets, an integral, inner, luminal, circumferentially partial or complete sealing cuff.

In at least one embodiment, a transcatheter, percutaneously implantable, bioprosthetic heart valve is provided wherein a separate tubular sealing cuff of tissue membrane is attached to an outer, abluminal surface of the frame to form a sealing cuff. In at least one embodiment, the membrane sheet is a single layer of a substantially homogenous material. In at least one embodiment, the membrane sheet is an unlaminated single layer of material. In at least one embodiment, the membrane sheet is a single layer of material that does not include any reinforcement, such as reinforcing fibers. In at least one embodiment, the membrane sheet is a single layer of treated pericardium tissue. In at least one embodiment, the membrane sheet is a single layer of a synthetic film.

Therefore, in accordance with at least one embodiment, a transcatheter, percutaneously implantable, prosthetic heart valve is provided, comprising:

a lattice frame; and

two or more integrated cusp and leaflet folded structures attached to the lattice frame, the two or more integrated cusp and leaflet folded structures each comprising a flat sheet of biocompatible membrane that is folded to include a mobile leaflet layer and a cusp wall layer, wherein the cusp wall layer located radially outside of the mobile leaflet layer, and wherein the cusp wall layer is further formed by joining apposing sides of the cusp wall layer along a seam. In accordance with at least one embodiment, the two or more integrated cusp and leaflet folded structures are each attached along their respective seams to the lattice frame. In accordance with at least one embodiment, the seams are oriented in a direction substantially parallel to an axis of the lattice frame. In accordance with at least one embodiment, the flat sheet of biocompatible membrane forming at least one integrated cusp and leaflet folded structure of the two or more integrated cusp and leaflet folded structures comprises two or more pieces of biocompatible membrane material.

In accordance with at least one embodiment, a transcatheter, percutaneously implantable, prosthetic heart valve is provided, comprising:

a lattice frame; and

two or more integrated cusp and leaflet folded structures attached to the lattice frame, the two or more integrated cusp and leaflet folded structures each comprising a flat sheet of a biocompatible membrane that is folded to include a valve cusp according to a flat folding pattern, wherein the valve cusp is further formed by joining apposing sides of the valve cusp along a seam, and wherein the two or more integrated cusp and leaflet folded structures are each attached along their respective seams to the lattice frame in a direction substantially parallel to an axis of the lattice frame. In accordance with at least one embodiment, two distal, downstream, vertices of the integrated cusp and leaflet folded structure are folded over as vertex folds in a radially outward direction and fixed to the lattice frame such that the vertex folds of circumferentially adjacent leaflets are adjacent and define a degree of leaflet apposition at the points corresponding to leaflet commissures. In accordance with at least one embodiment, the two distal, downstream, vertices are fixed to the lattice frame by attachment not along an alignment with the vertex folds. In accordance with at least one embodiment, a vertex forming a proximal, upstream, tip of the substantially conical shape is folded over in a radially outward direction and attached to an inner portion of the lattice frame. In accordance with at least one embodiment, the flat folding pattern is polygonal and includes extending portions that, when the cusp is mounted, extend circumferentially outward from an axial line of attachment of the cusp

to the frame so as to form, when joined and attached to corresponding extending portions of neighboring cusps, an integral, inner, luminal, circumferentially complete sealing cuff. In accordance with at least one embodiment, the flat folding pattern is polygonal and includes extending portions that, when the two or more cusps are mounted, extend circumferentially outward from an axial line of attachment of the cusp to the lattice frame so as to form a circumferentially incomplete sealing cuff portion associated with each cusp. In accordance with at least one embodiment, a separate tubular sealing cuff of biocompatible membrane is attached to an outer, abluminal surface of the lattice frame to form a sealing cuff. In accordance with at least one embodiment, the lattice frame is collapsible and expandable and comprises a metal alloy substantially configured as tubular stent member. In accordance with at least one embodiment, the biocompatible membrane comprises processed mammalian pericardium tissue. In accordance with at least one embodiment, the biocompatible membrane does not comprise a treated tissue. In accordance with at least one embodiment, the biocompatible membrane comprises a synthetic material. In accordance with at least one embodiment, the seams of the two or more integrated cusp and leaflet folded structures are each oriented along an axis of flow of the valve. In accordance with at least one embodiment, the two or more integrated cusp and leaflet folded structures are each further attached to a circumferential portion of the lattice frame along at least a portion of their distal downstream edges. In accordance with at least one embodiment, the two or more integrated cusp and leaflet folded structures are attached to the lattice frame at least at a non-commissural seam aligned with an axial flow direction of the valve.

In accordance with at least one embodiment, a transcatheter, percutaneously implantable, prosthetic heart valve is provided, comprising:

a lattice frame; and

two or more integrated cusp and leaflet structures attached to the lattice frame, the two or more integrated cusp and leaflet structures each comprising a flat sheet of biocompatible membrane that is folded to include a mobile leaflet layer and a cusp wall layer, wherein with the mobile leaflet layer in a closed position a transverse cross-sectional area of a cusp-sinus space decreases monotonically from a distal end to a proximal end of the mobile leaflet layer. In accordance with at least one embodiment, the cusp wall layer is located radially outside of the mobile leaflet layer. In accordance with at least one embodiment, the cusp wall layer is further formed by joining apposing sides of the cusp wall layer along a seam. In accordance with at least one embodiment, the mobile leaflet layer in the closed position a transverse cross-sectional length of the mobile leaflet layer decreases monotonically from a distal end to a proximal end of the mobile leaflet layer. In accordance with at least one embodiment, the mobile leaflet layer and

the cusp wall layer of each integrated cusp and leaflet structure are a single continuous piece of biocompatible membrane.

At least one invention of the one or more present inventions is a novel integrated cusp and leaflet structure that has application for a variety uses, including implantable valves other than prosthetic heart valves. Accordingly, in at least one embodiment, and in subcombination, an integrated cusp and leaflet structure for attachment to a lattice frame to form a valve configured for implantation in a vascular system of a patient is provided, the integrated cusp and leaflet structure comprising:

a flat sheet of biocompatible membrane that is folded to include a mobile leaflet layer and a cusp wall layer, wherein the cusp wall layer is divided along a seam, and wherein the mobile leaflet layer is continuous and apposes the cusp wall layer when the integrated cusp and leaflet structure is pressed substantially flat. In accordance with at least one embodiment, the mobile leaflet layer and the cusp wall layer of the integrated cusp and leaflet structure are a single continuous piece of biocompatible membrane. In accordance with at least one embodiment, the biocompatible membrane comprises a synthetic material. In accordance with at least one embodiment, the integrated cusp and leaflet structure further comprises at least one commissure tab. In accordance with at least one embodiment, the at least one commissure tab is configured for engaging a slot within a member of the lattice frame.

One or more embodiments of the one or more present inventions are also directed to methods for forming the inventive valves described herein, as well as its component elements. Accordingly, a method of forming an integrated cusp and leaflet folded structure for use in an implantable valve having an axial flow direction is provided, comprising: folding a flat sheet of biocompatible membrane to form an integrated cusp and leaflet folded structure according to a flat folding pattern, wherein said folding includes making two diagonal folds in the flat sheet of biocompatible membrane, the two diagonal folds separating a mobile leaflet layer from a cusp wall layer of the integrated cusp and leaflet folded structure. In accordance with at least one embodiment, the two diagonal folds are angled at between about 10 to 80 degrees from the axial flow direction. In accordance with at least one embodiment, the method further comprises forming first and second cusp wall folds, wherein the cusp wall layer is further formed by joining apposing membrane portions adjacent the first and second cusp wall folds along a seam that is oriented substantially parallel with the axial flow direction.

In addition to the foregoing, in accordance with at least one embodiment, a method of forming a transcatheter, percutaneously implantable, prosthetic heart valve is provided, comprising: folding a plurality of integrated cusp and leaflet folded structures, each integrated cusp and leaflet folded structure of the plurality of integrated cusp and leaflet folded structures

comprising a flat sheet of biocompatible membrane that is folded to form a cusp according to a flat folding pattern, wherein the cusp is further formed by joining apposing sides of the cusp along a seam; and attaching each integrated cusp and leaflet folded structure of the plurality of integrated cusp and leaflet folded structures to a lattice frame, wherein the two or more integrated cusp and leaflet folded structures are each attached along their respective seams to the lattice frame in a direction substantially parallel to an axis of the lattice frame.

Various components are referred to herein as "operably associated." As used herein, "operably associated" refers to components that are linked together in operable fashion, and encompasses embodiments in which components are linked directly, as well as embodiments in which additional components are placed between the two linked components.

As used herein, "at least one," "one or more," and "and/or" are open-ended expressions that are both conjunctive and disjunctive in operation. For example, each of the expressions "at least one of A, B and C," "at least one of A, B, or C," "one or more of A, B, and C," "one or more of A, B, or C" and "A, B, and/or C" means A alone, B alone, C alone, A and B together, A and C together, B and C together, or A, B and C together.

Various embodiments of the present inventions are set forth in the attached figures and in the Detailed Description as provided herein and as embodied by the claims. It should be understood, however, that this Summary does not contain all of the aspects and embodiments of the one or more present inventions, is not meant to be limiting or restrictive in any manner, and that the invention(s) as disclosed herein is/are understood by those of ordinary skill in the art to encompass obvious improvements and modifications thereto.

Additional advantages of the present invention will become readily apparent from the following discussion, particularly when taken together with the accompanying drawings.

BRIEF DESCRIPTION OF THE DRAWINGS

To further clarify the above and other advantages and features of the one or more present inventions, a more particular description of the one or more present inventions is rendered by reference to specific embodiments thereof which are illustrated in the appended drawings. It should be appreciated that these drawings depict only typical embodiments of the one or more present inventions and are therefore not to be considered limiting of its scope. The one or more present inventions are described and explained with additional specificity and detail through the use of the accompanying drawings in which:

Fig. 1A is a plan view of a flat sheet membrane template for the formation of an integrated cusp and leaflet folded structure in accordance with at least one embodiment of the one or more present inventions;

Fig. 1B is an oblique axial top (distal) perspective view directed downward (proximal) and radially outward of a folded membrane sheet after execution of the template foldings illustrated in Fig. 1A, thereby yielding a completed integrated cusp and leaflet folded structure;

Fig. 1C is a side perspective view directed radially outward of the inner aspect of an initially folded version of the integrated cusp and leaflet template shown in Fig. 1A;

Fig. 1D is an oblique axial top (distal) perspective view directed downward (proximal) and radially outward of a further partially folded version of the integrated cusp and leaflet folded structure shown in Fig. 1C;

Fig. 1E is an another oblique axial top (distal) perspective view directed downward (proximal) and radially outward of a further partially folded version of the integrated cusp and leaflet folded structure shown in Fig. 1D;

Fig. 1F is a modified version of the integrated cusp and leaflet folded structure shown in Fig. 1E;

Fig. 1G is same structure and view shown in Fig. 1E, along with a top (distal) cross-section schematic view of the distal end of a three-leaflet valve in a closed operating position;

Fig. 2 is a plan view of another flat sheet membrane template for the formation of an integrated cusp and leaflet folded structure in accordance with at least one embodiment of the one or more present inventions;

Fig. 3 is a plan view of yet another flat sheet membrane template for the formation of an integrated cusp and leaflet folded structure in accordance with at least one embodiment of the one or more present inventions;

Fig. 4 is a plan view of still yet another flat sheet membrane template for the formation of an integrated cusp and leaflet folded structure in accordance with at least one embodiment of the one or more present inventions;

Fig. 5A is a plan view of another flat sheet membrane template for the formation of an integrated cusp and leaflet folded structure in accordance with at least one embodiment of the one or more present inventions;

Fig. 5B is an oblique axial top (distal) perspective view directed downward (proximal) and radially outward of a partially folded version of an integrated cusp and leaflet folded structure prepared in accordance with the template shown in Fig. 5A;

Fig. 5C is an oblique axial top (distal) perspective view directed downward (proximal) and radially outward of a further partially folded version of the integrated cusp and leaflet folded structure shown in Fig. 5B;

Fig. 5D is plan view of the inner (luminal) aspect of a completely folded version of the structure of Fig. 5C, thereby yielding a completed integrated cusp and leaflet folded structure

prepared in accordance with the template shown in Fig. 5A (with the exception of unfolded commissure tabs);

Fig. 5E shows a detail perspective view of a folded commissure tab;

Fig. 5F shows a perspective view of the outer (abluminal) aspect of the device shown in Fig. 5D;

Fig. 6 is a plan view of yet another flat sheet membrane template for the formation of an integrated cusp and leaflet folded structure in accordance with at least one embodiment of the one or more present inventions;

Fig. 7A is a plan view of still yet another flat sheet membrane template for the formation of an integrated cusp and leaflet folded structure in accordance with at least one embodiment of the one or more present inventions;

Fig. 7B is an oblique axial top (distal) perspective view directed downward (proximal) and radially outward of a partially folded version of an integrated cusp and leaflet folded structure prepared in accordance with the template shown in Fig. 7A;

Fig. 7C is an oblique axial top (distal) perspective view directed downward (proximal) and radially outward of a further partially folded version of the integrated cusp and leaflet folded structure shown in Fig. 7B;

Fig. 7D is an oblique axial top (distal) perspective view directed downward (proximal) and radially outward of yet a further partially folded version of the integrated cusp and leaflet folded structure shown in Fig. 7C;

Fig. 7E shows a shallow oblique top perspective view of the outer (abluminal) aspect of the partially folded cusp and leaflet structure of Fig. 7D;

Fig. 7F is a plan view of the inner (luminal) aspect of a completely folded version of the structure of Fig. 7D yielding an integrated cusp and leaflet folded structure prepared in accordance with the template shown in Fig. 7A (excepting that the commissure tabs and apex are not yet folded outward);

Fig. 7G is a side perspective view of the outer (abluminal) aspect of the structure of Fig. 7F showing a completely folded version of an integrated cusp and leaflet folded structure prepared in accordance with the template shown in Fig. 7A (excepting that the commissure tabs and apex are not yet folded outward);

Fig. 7H is a plan view of the inner (luminal) aspect of a completely folded version of an integrated cusp and leaflet folded structure prepared in accordance with the template shown in Fig. 7A;

Fig. 7I is a plan view of the outer (abluminal) aspect of a completely folded version of an integrated cusp and leaflet folded structure prepared in accordance with the template shown in Fig. 7A;

Fig. 7J is an oblique top (distal) perspective view of a completely folded version of an integrated cusp and leaflet folded structure prepared in accordance with the template shown in Fig. 7A;

Fig. 7K is a top perspective view directed downward (proximal) into the cusp space of an integrated cusp and leaflet folded structure prepared in accordance with the template shown in Fig. 7A;

Fig. 8A is an oblique top (distal) perspective view of an embodiment of a lattice frame for mounting three of the single-piece folded integrated cusp and leaflet structures as described herein;

Fig. 8B is a side elevation view of the lattice frame shown in Fig. 8A;

Fig. 8C is a side elevation view of the lattice frame of Fig. 8A with a superimposed plan view of the radially outer aspect of the completely folded integrated cusp and leaflet structure of Fig. 7I;

Fig. 8D is an oblique axial (top/distal) perspective view of an assembled three-leaflet valve in accordance with at least one embodiment;

Figs. 9A and 9B are two different oblique axial (top/distal) perspective views of another embodiment of a lattice frame for mounting three of the single-piece folded integrated cusp and leaflet structures that include commissure tabs;

Fig. 9C is a side perspective view of the lattice frame shown in Figs. 9A and 9B with a superimposed plan view of the outer aspect of the completely folded integrated cusp and leaflet structure of Fig. 7I;

Fig. 9D is a side view of the lattice frame shown in Figs. 9A and 9B with superimposed views of the outer aspect of two circumferentially adjacent completely folded integrated cusp and leaflet structures; and

Fig. 9E is an oblique axial (top/distal) perspective view of an assembled three-leaflet valve comprising the lattice frame shown in Figs. 9A and 9B and three identical folded integrated cusp and leaflet structures.

The drawings are not necessarily to scale.

DETAILED DESCRIPTION

One or more embodiments of the one or more inventions described herein include an implantable prosthetic heart valve having a frame and two or more cusp and leaflet structures mounted to the frame. The frame preferably comprises a lattice of substantially tubular alloy

metal mesh. The cusp and leaflet structures include a membrane operable to open and close, thereby providing a functioning valve when mounted within a frame. In at least one embodiment, the membrane preferably comprises a flat sheet of processed mammalian tissue membrane that is folded into a substantially conical shape according to a flat folding pattern.

In the ensuing descriptions and referenced figures it will be seen that, when applied to a dry sheet membrane, the folding initially results in a cusp shape of an inverted pyramid with a rhomboid base. On relaxation of the folds as occurs naturally with a flexible and pliable membrane, especially when the membrane is hydrated, the cusp shape becomes substantially conical in shape and will be described as such in the ensuing descriptions as it more closely represents the embodiment of the cusp in operation of the valve.

Formation of a valve construct as described herein provides a percutaneously deliverable heart valve with a relatively small diameter for transcatheter placement. That is, the substantially conical shape associated with the flat folding patterns used to form leaflets as described herein allow for construction of a valve that can be compressed prior to introduction to a catheter to an advantageously small diameter, thereby facilitating transcatheter percutaneous delivery of the valve within a patient. The substantially conical shape is further formed by joining two axially oriented sides of the substantially conical shape along a seam that is oriented along a longitudinal axis of the substantially conical shape. The two or more integrated cusp and leaflet structures are affixed to an interior portion of the lattice frame along an axial flow direction of the valve and are further affixed along the distal, downstream, edge of the substantially conical shape along at least an outer half of the substantially conical shape's edge.

One or more of the various embodiments described herein have a number of different features and characteristics as compared to other commercially available prosthetic heart valves. For example, at least one embodiment of a transcatheter, percutaneously implantable, prosthetic heart valve described below comprises a flat polygonal sheet membrane having more than four sides and which forms an integrated cusp and leaflet structure.

In addition, at least one embodiment of a transcatheter, percutaneously implantable, prosthetic heart valve described below comprises integrated cusp and leaflet structures that are attached to a lattice frame at the circumferential perimeter locations corresponding to the commissures. At such locations, the length of the seam that forms the common line of attachment of the cusp and integral leaflet to the frame is less than one-half to two-thirds of the axial length of the membrane portion of the valve.

In at least one embodiment of a transcatheter, percutaneously implantable, prosthetic heart valve, when the valve is in the open position, the mobile leaflet layer apposes or is geometrically free to appose its full outward surface completely to the immediately radially

located outward structure, such as at least one of the cusp wall layer or interior surface of the lattice frame. In at least one embodiment, in the closed position the transverse cross-sectional length of the mobile leaflet layer and the cross-sectional area of the cusp/sinus space decreases monotonically from the distal end to proximal end of the membrane portion of the valve. (That is, generally the property of a cone as well as an inverted pyramid.)

In at least one embodiment, the mobile leaflet layer and the immediately outward structure for the full axial length of the leaflet (cusp wall layer, frame, or other) are a single continuous piece of material.

In at least one embodiment, at the base of each cusp (that is, at the most proximal extent of the leaflet), the circumferential extent of attachment of the membrane to the frame is less than the circumferential extent of attachment of the membrane to the frame at the distal end of the cusp. In addition, at the base of each cusp, the circumferential extent of transverse (that is, on a line or on the plane of a circumferential single-plane curve of folding that is generally perpendicular to the flow axis of the valve) folding of the membrane to the frame is less than the circumferential extent of transverse folding at the distal end of the cusp.

At least one embodiment, a prosthetic valve described herein comprises an integrated cusp and leaflet structure wherein the apposing sides of the cusp are joined at one or more axially oriented seams. In at least one embodiment, all folds and seams are located on line segments.

At least one embodiment of the one or more present inventions does not include frame elements, such as support members, spanning the interior of the valve luminal to support one or more portions of the membrane sheet. Moreover, at least one embodiment of the one or more present inventions does not include any hardware shaping form inward of or attached to any portion of the mobile leaflet portion of the membrane.

In addition, at least one embodiment of the one or more present inventions does not utilize attachment of the leaflet layer to the frame along the substantially complete circumferential distance separating the commissures at any point below (more proximal than) the commissure tabs.

At least one embodiment of the one or more present inventions does not include a transverse fold or reflection of the leaflet layer along the substantially complete circumferential distance separating the commissures at any point below (more proximal than) the commissure tabs.

Nomenclature

For all embodiments presented herein it is to be understood that a "membrane" includes suitable materials for forming the cusps and leaflets. Accordingly, with regard to particular

material types that may be used to form the membrane sheet, in at least one embodiment the membrane sheet forming the cusp or leaflet portions includes a one-piece, single layer sheet of biocompatible membrane, such as fixed mammalian pericardium tissue or synthetic biocompatible material, such as ePTFE. In at least one embodiment, the membrane sheet is made from a tissue preparation process that yields a leaflet material of suitable strength and durability for use in a prosthetic transcatheter deliverable heart valve. The content of WO 2011/109450A2 published on September 9, 2011, is incorporated herein by reference. Although the membrane sheet is preferably a single piece of material, a membrane sheet formed of a plurality of pieces of material may be used, such as two to fifty or more pieces of material that are connected.

As used herein "proximal" means situated near or closer to the upstream or flow inlet end of the valve, and "distal" means situated near or closer to the downstream or flow outlet end of the valve. This convention is further applied in the description of the various folded structure elements (membrane sections, edge segments and fold lines) that are termed "proximal" or "distal" if the final position or orientation of said element within the completed folded structure satisfies the above definitions. Likewise, one of said elements is termed, "axial", "transverse" or "circumferential" to describe its position and orientation in the completed valve.

As used herein, a "cusp" means that structural portion of a valve related to a single leaflet that encompasses a space closed toward the lower (proximal) direction and open to the upper (distal) direction, formed by the joined and/or continuous structures of the mobile leaflet portion on the radially inner side and the cusp wall portion on the radially outer side. The "cusp" in the present invention is that structure described as having a substantially conical shape.

As used herein, the "mobile leaflet layer" or "leaflet" means that radially inward portion of the cusp that moves during operation of the valve. For example, when the valve is closing the mobile leaflet layer moves radially inward toward the central axis of the valve lumen. When the valve is opening, the mobile leaflet layer moves radially outward and away from the central axis of the valve lumen.

As used herein, the "cusp wall layer" means a portion of the cusp that resides radially outward of the mobile leaflet layer. In some embodiments, a portion of the cusp wall layer moves during operation of the valve. In other embodiments, the cusp wall layer remains substantially immobile during operation of the valve.

As used herein, the "cuff wall layer" means a portion of the folded membrane structure that resides radially outward of both the cusp wall layer and the mobile leaflet layer, and where present, is radially closest to the frame of the three layers comprising the mobile leaflet layer, the cusp wall layer, and the cuff wall layer. The cuff wall layer remains substantially immobile

during operation of the valve.

A "frame" as used herein means a substantially tubular member that holds a plurality of cusps and/or leaflets. By way of example, the frame may be a wire lattice or a lattice cut from a single tubular piece of metal alloy, that is both collapsible and expandable.

A "valve" as used herein means a frame with a plurality of cusps and/or leaflets attached thereto. In the present invention each of said leaflets is an integral part of a folded membrane cusp structure. If a frame is used that is a metal lattice that is both collapsible and expandable, such a construct may be delivered through a catheter percutaneously to a target site within a patient, such as the aortic valve.

As used herein, "cone" or "conical" means resembling a cone or portion thereof at some point in the practical use of the structure.

As used herein "substantially conical" means resembling a cone or a portion thereof at some point in the practical use of the structure with the specific property that the transverse (that is, on a plane of section generally perpendicular to the axis of flow of the valve) cross-sectional perimeter or area of said structure in the operationally closed position decreases monotonically moving from the level of the leaflet apposition to the proximal end of the valve.

As used herein, "two or more leaflets," "two or more valve leaflets," "a plurality of leaflets" or a similar term means two, three, four, or more valve leaflets. Accordingly, "a valve with two or more leaflets" includes a valve with two leaflets, a valve with three leaflets, a valve with four leaflets, and a valve with more than four leaflets.

As used herein, a "folding" means the partition of a flat sheet section of material along a sharp line of folding or crease into subsections each lying on separate planes, but without interruption of material continuity.

As used herein, a "complete folding" means folding (as above) wherein the angular change of the planar axis at the line of folding is approximately 180 degrees, such that the subsections lie on approximately parallel planes and the subsections are in approximate overlying contact with each other at least at some point.

As used herein, a "cuff" means that portion of a valve structure that lies radially outward of the cusp wall portion that in some part circumferentially encompasses at least a portion of the cusp structure and acts to limit flow that may pass retrograde around the cusp.

As used herein, "commissure" means the site of union or junction between adjacent cusps and/or leaflets, and by extension, collectively those portions of the adjacent integrated cusp and leaflet structures that are coincident at the union or junction in the completed valve structure.

As used herein, an "integrated cusp and leaflet folded structure" means a membrane folded in accordance with one of the patterns described herein.

Folded Valve Integrated Cusp and Leaflet - Folding Pattern No. 1

Referring generally to Figs. 1A-7K, each cusp embodiment of an integrated cusp and leaflet structure described herein is a substantially flattened cone collapsed along an axis substantially perpendicular to its longitudinal axis. In one or more embodiments, the integrated cusp and leaflet structure, when being formed from a piece of membrane, is readily realized by folding a flat sheet of membrane from a closed polygon pattern. The pattern folding results in apposing seam lines aligned along their axial length. These are joined to close the cusp in the general shape of a cone with the joined seam forming the "spine" along which the cusp meets the inner aspect of the tubular frame. It can be seen that, when formed of a dry sheet membrane, the pattern results initially in a cusp shape that is an inverted pyramid with a rhomboid base that, with a flexible, pliable membrane, is congruent to a substantially conical shape. On relaxation of the folds in practical use a substantially conical cusp is realized wherein the inner mobile operating portions of the leaflet are continuous with the outer portion that forms the integral wall of the cusp sinus or pocket.

Referring now to Fig. 1A, a plan view of a rectangular flat sheet membrane template 100 is shown for the formation of a single-piece folded valve integrated cusp and leaflet. The plan view is shown with a view of that leaflet surface that faces radially inward once folded and mounted within a frame. Reference is also made to Fig. 1G, wherein a schematic of a valve in distal axial view is shown, and wherein three cusps with integral leaflets are shown within the frame that collectively form the valve. As described and illustrated in the present application, alternate polygons and other closed shapes may be employed with alternate folding patterns to generate alternate shapes and functional features of the valve cusp and leaflet, and complete valve.

Referring again to Fig. 1A, and in accordance with at least one embodiment of the one or more present inventions, dotted lines 101, 116, 117, 126 and 127 represent the position of folds or creases applied to a piece of membrane to form a leaflet structure 130. More particularly, folding at lines 116, 126 and 101 is initiated inward (with convexity of the surface disposed radially inward toward the central axis of the valve lumen) while folds 117 and 127 are folded initially outward (with convexity of surface disposed radially outward away from the central axis of the valve lumen). Since folding causes re-orientation of the various sections of the sheet template in relation to each other and to the valve geometry, final orientation of the fold lines within the structure on mounting and operation of the leaflets will not necessarily retain the same orientations as on initiation of the folds. The "inward" and "outward" conventions by this

definition will be followed throughout the descriptions of the various folded geometries presented herein.

Referring again to Fig. 1A, a line of division by cutting is indicated at 102. Cutting at 102 results in opposing edges 115 and 125 that will be separated by folding. The other free edges of the structure are labeled as their position and orientation changes through the folding steps. Fold 101 defines the central axis of symmetry of the leaflet pattern, with the concave side of fold 101 facing radially outward toward the frame and away from the central axis of the valve lumen. Fold 101 assists in the maintenance of axial symmetry of the folded construct, but is not necessary to leaflet function and is not retained in the final operational form of the valve. (See Fig. 7A.)

Referring now to Fig. 1B, an oblique axial top (distal) perspective view of a substantially completed folded leaflet structure 130 is shown. (Three completed folded cusp and leaflet structures 130 are typically mounted to a frame to form an operating heart valve.)

The view of Fig. 1B is directed downward (proximally) and radially outward, with such view illustrating a substantially completed folded leaflet and cusp structure 130 that depicts the reoriented segments and sections of Fig. 1A after execution of the template foldings. Segments 111 and 121 form the left and right halves of the distal free edge of the mobile operating portion of the leaflet. Inward folding at 116 and 126 forms a second layer of membrane outward of the first, with segments 112 and 122 forming the distal free margin of the outer wall of the integrated cusp. In radially flatted form of the integrated cusp and leaflet structure (that is, approximating the open operating position of the leaflet), the segment 111 will appose to 112, and 121 will appose to 122.

The left cusp wall section 161 is bounded by folds 116 and 117 and edge segment 112. The right cusp wall section 171 is bounded by folds 126 and 127 and edge segment 122.

The left cuff wall section 118 is bounded by fold 117 and edge segments 113, 114 and 115. The right cuff wall section 128 is bounded by fold 127 and edge segments 123, 124 and 125. Inward folding at 117 and 127 cause these cuff wall sections 118 and 128 to position outward of the cusp wall sections 161 and 171, respectively. In radially flatted form of the completed folded structure (again, approximating the open operating position of the leaflet), the edge segment 113 will appose to 112, and edge segment 123 will appose to 122.

Folded Valve Folding Sequence

Referring now to Figs. 1C and 1D, oblique axial top (distal) perspective views of a partially completed folded leaflet and cusp are shown. The views provided by Figs. 1C and 1D are directed downward (proximally) and radially outward, with such views depicting the reoriented segments and sections of Fig. 1A after partial execution of the template foldings.

Fig. 1C shows a perspective view of the inner aspect of the template 100 after initiation of the foldings and cutting at 102 resulting in left and right cuff wall sections 118 and 128, respectively. The cut free edges 115 and 125 are separated along with the left and right cuff wall sections 118 and 128 by outward folding at 117 and 127, respectively. Completed folding at 117 and 127 results in the cuff wall sections 118 and 128, respectively. Distally situated (with respect to the blood flow direction) edge segments 113 and 123 of the cuff wall sections 118 and 128, as well as proximally situated edge segments 115 and 125 of the cuff wall sections 118 and 128, are positioned transverse, and in at least one embodiment, substantially perpendicular, to the central axis of the valve.

Fig. 1D shows the cusp and leaflet structure 120 with the folds 116, 126, 117 and 127 at an intermediate stage of completion. Triangular left and right mobile leaflet sections 119 and 129 respectively are bounded by folds 101 and 116 and free edge segment 111 on the left, and folds 101 and 126 and free edge segment 121 on the right. Folds 117 and 127 are then brought into apposition on the outward aspect of the integrated cusp and leaflet along a seam line 132 where the folds will be joined and attached to a frame to close the shape of the single-piece continuous conical integrated cusp and leaflet.

Referring now to Figs. 1E and 1F, oblique axial top (distal) perspective views of a substantially completed folded cusp and leaflet are shown. The views provided by Figs. 1E and 1F are directed downward (proximally) and radially outward, with such views depicting the reoriented segments and sections of Fig. 1A after execution of the template foldings.

Fig. 1E shows the cusp and leaflet folding substantially completed forming the structure 130 with the seam 132 formed by the apposition of folds 117 and 127, thus forming a generally conical cusp and sinus space 131. The triangular corners formed at the distal ends of folds 116 and 126 are apposed to and attached to the cuff wall sections 118 and 128, respectively. Between adjacent cusp and leaflet structures in a multi-leaflet valve, the folded corners form the junction joining the adjacent free edges (121 of leaflet A to 111 of leaflet B, for example) of the mobile leaflet portions. When further attached to the circumferential valve frame, these corners tether the free edges of the mobile leaflet portions to the circumferential inner boundary of the generally cylindrical valve frame, thus forming valve leaflet commissures at each similar join.

Referring now to Fig. 1F, a structure similar to that of Fig. 1E is depicted, but with the cuff wall sections 118B and 128B reduced in circumferential extent from that of leaflet structure 130 shown in Fig. 1E. More particularly, depending on the clinical application of the valve, a fully circumferential cuff wall may be unnecessary, and a valve with a limited cuff wall with less tissue membrane mass may offer functional advantages. Alternatively, an additional piece

of membrane may be placed circumferentially around the outer abluminal surface of the valve frame to act as a sealing cuff to form a barrier against valvular regurgitation.

Referring again to Fig. 1E, the apex 133 (proximal tip) of the conical cusp and leaflet forms the lower (proximal) end of the seam 132. In at least one embodiment, the apex 133 is also attached to the circumferential boundary of the valve and valve frame.

Referring now to Fig. 1G, for ease of reference the structure of Fig. 1E is again shown in Fig. 1G at the top of the page, along with a top (distal) cross-section view of the distal end of a three-leaflet valve in the closed operating position. The three cusps with leaflets are shown residing within a lattice frame in order to indicate the configuration of elements between the folded integrated cusp and leaflet structure 130 and its disposition within a three-leaflet frame-mounted valve. Suture attachments are omitted for clarity.

For each folded integrated cusp and leaflet structure, the outer axial seam 132 is aligned with one or more frame members 141 in a manner to permit the attachment of the folds 117 to 127, and to the coincident frame member by the same attachment, for example, by a single knot or line of suture. Advantageously for this purpose, the frame may preferentially contain axially oriented members that align to the seam 132 for part or all of the full axial extent of the valve. Further, said axially oriented members may advantageously contain holes or notches for securing and tying suture.

In Fig. 1G at point A, an illustrated loop symbolizing a suture knot is shown to demonstrate that a single knot may advantageously pass through or engage the frame member and the six layers; that is, the mobile leaflet section, the cusp wall section, and the cuff wall section of each adjoining cusp and leaflet structure that are coincident at this site of the commissure.

Referring still to Fig. 1G, it can be seen that the folded integrated cusp and leaflet structure, when mounted within the lattice frame and placed in the closed operating position, manifests the following configurations: (1) the left leaflet free edge segment 111 is in each case apposed to the right leaflet free edge segment 121 of the adjacent leaflet; (2) the portions of the leaflets just proximal to the free edges, thus, are also apposed to form the contact seal that enables effective closing operation, thereby preventing valvular regurgitation; and (3) the distal edges 112 and 122 of the cusp wall sections are apposed to the distal edges of the cuff wall sections 113 and 123, respectively.

Folded Valve Pattern Variation No. 2

Referring now to Fig. 2, and in accordance with at least one embodiment, a plan view of a flat sheet membrane template 200 that is polygonal rather than rectangular is shown. Template 200 contains folds 201, 216, 226, 217 and 227 that correspond to folds 101, 116, 126, 117 and

127, respectively, and are disposed in like manner in folding execution, as are the segments enumerated. The folding pattern is designed to form a longer cone of the same diameter, which achieves a more distally disposed central point of valve leaflet coaptation, the mechanics of which are more tolerant of pressure loads. The pattern dimensions may be altered to suit the particular clinical application of the valve. The template examples disclosed herein are for enablement purposes and shall not be interpreted as limiting the scope of the claims. The example is shown for a cusp cone wall disposed at about a 60 degree angle to the horizontal (short axis) of the generally cylindrical valve geometry, whereas that angle for the rectangular pattern of Figs. 1A-1G was about 45 degrees.

Folded Valve Pattern Variation No. 3

Referring now to Fig. 3, and in accordance with at least one embodiment, a plan view of template 300 is shown for a flat sheet membrane that contains the pattern 200 of Fig. 2 with added sections that extend the distal contour of the structure when completed in folding. More particularly, the free edge of the mobile leaflet section is extended distally with a section having a polygonal or curved free edge in order to increase the contacting area of leaflet apposition in valve closing operation. Additionally, the distal contour of the cusp wall sections and cuff wall sections 318 and 328 are extended by "tab" sections 318T and 328T, respectively. These added "tab" extensions allow for increased area by which to mount the outer wall of the cusp and leaflet assembly to the frame and for elevating the cuff wall "above" (more distal to) the plane of leaflet apposition, thereby also increasing the effective volume of the cusp in closing operation. These "tab" extensions, being distally disposed after completion of folding and initial mounting within the lattice frame, or a distal portion of them may optionally be folded radially outward along 312-313 and 322-323, for example, to wrap around the distal edge of the frame such that the "tab" extension areas 318T and 328T lie on the outer, abluminal aspect of the frame where, when attached to the frame, they potentially increase the strength of the cusp attachment.

Referring still to Fig. 3, template 300 contains folds 301, 316, 326, 317 and 327 that correspond to folds 101, 116, 126, 117 and 127, respectively, and are disposed in like manner in folding execution, as are the edge segments similarly enumerated. In addition to the tab features discussed in the preceding paragraph, as with template 200, template 300 is designed to form a longer cone of the same diameter, which achieves a more distally disposed central point of valve leaflet coaptation. Again, the pattern dimensions may be altered to suit the particular clinical application of the valve. The example is shown for a cusp cone wall disposed at about a 60 degree angle to the horizontal (short axis) of the generally cylindrical valve geometry.

Folded Valve Pattern Variation No. 4

Referring now to Fig. 4, and in accordance with at least one embodiment, a plan view of pattern 400 is shown for a flat sheet membrane similar to pattern 300, except that the extension "tab" sections 412T and 422T are distal extensions of the cusp wall sections only. This limitation reduces the double layer of membrane extension at the distal end of the completely folded integrated cusp and leaflet structure to a single layer, thereby reducing the mass of membrane in the heart valve which might otherwise disadvantageously limit the efficiency of collapsing and compressing the valve for use in the percutaneous/transcatheter delivery application.

In addition, at the lower (proximal) apex 433 of the cusp cone pattern the lower (proximal) extent of the cuff wall sections 418 and 428 is limited so as to "expose" the apex of the cone in the pattern. This feature allows, on the completely folded integrated cusp and leaflet structure, the transverse, radially outward folding of the tip of the cone-shaped cusp at line 403 between points U and V. (See figures 7.) The folding of the apex reduces the overall axial length of the cusp and leaflet structure, allowing for increased cusp/sinus volume for a given valve diameter and frame length.

The template 400 contains folds 401, 416, 426, 417 and 427 that correspond to folds 101, 116, 126, 117 and 127, respectively, and are disposed in like manner in folding execution, as are the edge segments similarly enumerated. Similar to templates 200 and 300 described above, template 400 dimensions may be altered to suit the particular clinical application of the valve. The example is shown for a cusp cone wall disposed at about a 60 degree angle to the horizontal (short axis) of the generally cylindrical valve geometry.

Folded Valve Pattern Variation No. 5

Referring now to Figs. 5A-5F, yet another embodiment of a template pattern is illustrated. Referring specifically now to Fig. 5A, a plan view of template 500 is shown for a flat sheet membrane. The template 500 contains folds 501, 516, 526, 517 and 527 that correspond to folds 101, 116, 126, 117 and 127, respectively, and are disposed in like manner in folding execution, as are the edge segments similarly enumerated.

Template 500 illustrates a flat sheet membrane that is basically rectangular and is similar to the upper (distal) portion of template 100 of Figs. 1A-1G, except that (a) the distal extension areas 512T and 522T are added at the left and right margins of the template 500, and (b) the lower quadrants forming the cuff wall sections of the template 100 are truncated in template 500 to narrow cuff wall sections 518 and 528, the extent of which is defined by the length of cut 502. These limited interior cuff sections are still used for frame attachment along the central seam 532 of the cusp and leaflet cone, and the distal extension sections 512T and 522T are still used for attachment of the outer cusp wall to the distal edge of the frame.

Referring still to Figs. 5A-5F, corner folds 505 and 506 are now described. For template 500, after folds 516 and 526 are executed by complete folding, segments 512 and 522 are apposed and aligned to segments 511 and 521, respectively, and overlapping layers (mobile leaflet layer and cusp wall layer) form triangular corner sections at 562 and 572. Radially outward folding of these corner sections at 505 and 506 define the axial extent of the leaflet commissures such that joining the corner sections of adjacent leaflet structures along corner folds 505 and 506 causes the leaflet apposition to be at least the length of 505 in axial extent at the radial margin of the leaflet. (See Fig. 9E that illustrates an embodiment of a valve comprising a frame 920 with a plurality of integral cusp and leaflet structures 730 attached to the frame, wherein the structures 730 include corner sections 762 and 772 corresponding to the corner sections 562 and 572 of template 500.) Additionally, these double-layer triangular corner sections 562 and 572 are used for attachment of the commissures to the frame. The stent frame may optionally contain a slot at this point of attachment through which this triangular "tab" section may be inserted and attached on the abluminal surface of the frame. (Again, see Fig. 9E.)

With specific reference now to Fig. 5B, a perspective view of the inner aspect (that is, a view directed radially outward) of an initially folded structure 510 folded according to template 500 is shown. The central folding along 501 is initiated after cut 502 is executed as shown. Foldings along 501, 516, and 526 are depicted as initiated radially inward (out of the page) and foldings along 517 and 527 are depicted as initiated radially outward (into the page).

Figure 5C shows a steeply oblique perspective view of the folded integrated cusp and leaflet 520 at an intermediate stage of completion of the foldings. The view is directed from the central axis outward and obliquely downward into the cusp space showing the formation of the outer wall of the structure, that is, the cusp wall layer of the subject cusp. Folding along 517 and 527 acts to position the extension sections 518 and 528 outward of the cusp wall sections 561 and 571, respectively. Completion of folding then will position folds 517 and 527 in an axially aligned orientation in apposition to each other along their length. Folding along 516 and 526 acts to position the cusp wall sections 561 and 571 outward of the mobile leaflet sections 519 and 529, respectively. Completion of folding, which radially collapses the folded flattened structure, positions the cusp wall sections 561 and 571 in apposition to the mobile leaflet sections 519 and 529, respectively. In the final folded configuration the structure embodies the integrated cusp and leaflet in the open operating position.

In addition, completed folding at 516 and 526 also forms triangular two-layer sections, 562 and 572, respectively, that are designated as "commissure tabs". These commissure tabs are bounded by the corner folds 505 and 506, folds 516 and 526, and the free edges 511 and 521 of

the mobile leaflet sections 519 and 529, respectively. With further reference to Figs. 5D and 5E, these commissure tabs will be folded at 505 and 506 so as to position both layers of the tabs outward of the cusp wall sections 561 and 571, respectively, with the folds 505 and 506 oriented parallel to the central axis of the valve. With regard to a multi-leaflet valve, when the cusp and leaflet structure is mounted within the frame, this folded commissure tab is aligned along fold 505 in apposition to fold 506 of an adjacent complementary commissure tab of an adjacent integrated cusp and leaflet structure. Thus mounted, the commissure tabs join the mobile leaflet layers and the cusp wall layers of adjacent folded cusp and leaflet structures along a line coincident to both 505 and 506 that forms a common seam for attachment, such as by suturing of the commissure tabs to each other and to the frame forming the circumferential margin of the membrane portion of the folded cusp and leaflet structure.

Fig. 5D shows a plan view of the inner (luminal) aspect of the folded integrated cusp and leaflet structure 530 of template pattern 500. Structure 530 is depicted in a completed state of folding, excepting that the commissure tabs 562 and 572 are not yet folded outward along fold lines 505 and 506, respectively. The radially flattened form shown gives the general configuration and orientation of the membrane segments and sections for the open operating position of the valve cusp and leaflet.

Still referring to Fig. 5D, at the uppermost (distal) portion of the cusp wall layer, the extension tabs 512T and 522T are projected above (or distal to) the lines 512 and 522 (shown in figures 5A and 5B), respectively, that lie in apposition and alignment to the free edges 511 and 521, respectively, of the mobile leaflet layer. A portion or all of these tabs 512T and 522T may be optionally folded outward along 512 and 522, respectively, around the distal edge of the frame to lie upon the outer (abluminal) surface of the frame where they may be attached to both the frame and to the cusp wall sections (where the cusp wall sections are apposed to the inner surface of the frame) through the interstices of the frame. This optional configuration provides for increased strength of attachment for bearing downward (proximally directed) operational loads associated with the valve closing.

Completing the folding associated with template pattern 500 places folds 517 and 527 into axial alignment. Once in axial alignment, apposing folds 517 and 527 are joined along their axial length to form the seam 532 that closes the generally conical cusp structure with the extension sections 518 and 528 situated outward of the cusp wall sections 561 and 571, respectively. The cusp wall sections 561 and 571 are thus disposed outward of the mobile leaflet sections 519 and 529, respectively, with the cusp wall sections axially and circumferentially apposed to the inner surfaces of the generally cylindrical frame. Advantageously, for each valve cusp and leaflet to be mounted within, the frame may contain an

element or elements that are axially oriented and span a significant portion of the axial length of the frame, so as to align with the seam 532 for attachment, such as by suturing to the frame.

Referring now to Fig. 5E, a partial detail perspective view is shown of the commissure tab 572 configuration of the completely folded integrated cusp and leaflet structure 530, indicating radially outward folding of the commissure tab 572 along fold line 506.

With reference now to Fig. 5F, a perspective view is shown of the outer (abluminal) aspect of the completely folded cusp and leaflet structure 530 (except that the triangular commissure tabs are not yet folded) of template 500 in substantially flattened form. This view is complementary to Fig. 5D that shows the inner aspect of the same structure 530. The central seam 532 is seen on the outer face of the cusp wall sections 561 and 571 and is depicted for purposes of illustration as partly separated with the extension sections 518 and 528 incompletely flattened and folds 517 and 527 in close, but not in the complete apposition and alignment that will form the final seam line 532 for attachment to the axially oriented frame members. The slight separation depicted between folds 517 and 527 exposes the centerpoint of the mobile leaflet free edge where the mobile leaflet free edge segments 511 and 521 meet as depicted behind the cusp wall sections 561 and 571, respectively, in this view.

Folded Valve Pattern Variation No. 6

In accordance with at least one embodiment, Fig. 6 shows a plan view of another template 600 that is similar to template 500 except that the cusp cone wall angle α exceeds the 45 degrees of the generally rectangular template 500, and that the mobile leaflet sections are extended by a polygonal or curved extension section 604 of the free edge.

The change in cusp cone wall angle α also results in changes in the angle relating the lower (proximal) margins of the template and fold lines 617 and 627 to the center line of the template in order that when folding is completely executed, the fold lines 617 and 627 and the seam between them will be parallel to the central axis of the assembled valve. Likewise, the further geometry of the cusp cone wall angle will result in fold lines (optional) 613 and 623 and the long axes of extension tabs 612T and 622T being parallel to the transverse axis of the assembled valve.

The template 600 contains folds 601, 616, 626, 617, 627, optional folds 612 and 622, corner folds 605 and 606, and cut line 602 that correspond to folds 501, 516, 526, 517, 527, optional folds 512 and 522, corner folds 505 and 506, and cut line 502, respectively, of template pattern 500 and are disposed in like manner in folding execution, as are the template sections and edge segments similarly enumerated.

Folded Valve Pattern Variation No. 7

Referring now to Figs. 7A-7F, still yet another embodiment of a template pattern is illustrated. Referring specifically now to Fig. 7A, a plan view of another template 700 is shown that is similar to template 600, but with a section of the lower (proximal) midline portion of the template cut away so as to expose the apex 733 of the triangular sections that, when folded, will form the apex of the cone-shaped cusp. Effectively, the midline portions of the extension sections 718 and 728 are removed in relation to template 600 to an extent determined by the desired length of the line segment U-V, which in turn determines the extent to which the apex of the cone-shaped cusp may be truncated by folding at U-V.

After the cusp and leaflet cone is formed by folding, the apex is folded radially outward at line U-V (703) to truncate the cone to reduce the overall length of the cusp and leaflet structure, allowing for increased cusp/sinus volume for a given valve diameter and frame length.

The template 700 contains folds 701, 716, 726, 717, 727, optional folds 712 and 722, and corner folds 705 and 706, that correspond to folds 601, 616, 626, 617, 627, optional folds 612 and 622, and corner folds 605 and 606, respectively, of template 600 and are disposed in like manner in folding execution, as are the template sections and edge segments similarly enumerated.

Fig. 7B shows a perspective view of the inner (luminal) aspect of the initially folded cusp and leaflet structure 710 of template 700 after initiation of the principal folds 716, 726, 717, 727 and 701. Inward folding along 701 assists in aligning the left and right sections of the structure, but is not necessary to the formation of the integrated cusp and leaflet folded structure or to the operation of the valve. The disposition of the folds that converge at the apex 733 of the cusp can be appreciated as later forming an overlapping two-layer triangular apex as the cusp wall sections 761 and 771 are folded outward along lines 716 and 726, respectively, so as to position the cusp wall sections 761 and 771 outward of, and in apposition to, the mobile leaflet sections 719 and 729, respectively.

Fig. 7C shows a steeply oblique perspective view of the folded integrated cusp and leaflet 720 at an intermediate stage of completion of the foldings. The view is directed from the central axis outward and obliquely downward into the cusp space showing the formation of the outer wall of the structure. Folding along 717 and 727 acts to position the extension sections 718 and 728 outward of the cusp wall sections 761 and 771, respectively. Completion of folding then will position folds 717 and 727 in an axially aligned orientation in apposition to each other along their length. Folding along 716 and 726 acts to position the cusp wall sections 761 and 771 outward of the mobile leaflet sections 719 and 729, respectively. Completion of folding, which radially collapses the folded flattened structure, positions the cusp wall sections 761 and 771 in apposition to the mobile leaflet sections 719 and 729, respectively. In the final folded

configuration, the structure embodies the integrated cusp and leaflet in the open operating position.

With reference to Fig. 7D, completed folding at 716 and 726 also forms triangular two-layer sections, 762 and 772, respectively, that are designated as "commissure tabs." These commissure tabs are bounded by the corner folds 705 and 706, folds 716 and 726, and the free edges 711 and 721 of the mobile leaflet sections 719 and 729, respectively. With further reference to Figs. 7D and 7E, these commissure tabs will be folded at 705 and 706 so as to position both layers of the tabs outward of the cusp wall sections 761 and 771, respectively, with the folds 705 and 706 oriented parallel to the central axis of the valve. When the integrated cusp and leaflet structure is mounted within the frame, this folded commissure tab is aligned along fold 705 in apposition to fold 706 of an adjacent complementary commissure tab of an adjacent integrated cusp and leaflet structure of a multi-leaflet valve. Thus mounted, the commissure tabs join the mobile leaflet layers and the cusp wall layers of adjacent folded cusp and leaflet structures along a line coincident to both 705 and 706 that forms a common seam for attachment, such as by suturing of the commissure tabs to each other and to the frame forming the circumferential margin of the membrane portion of the folded cusp and leaflet strucutre.

Fig. 7D shows a perspective view of the inner (luminal) aspect of the partially folded integrated cusp and valve structure 720 of template 700. Integrated cusp and leaflet structure 720 is depicted in nearly completed state of folding, except that the commissure tabs 762 and 772, as well as the cusp apex 733 are not yet folded outward along fold lines 705, 706 and 703, respectively, and that the axial seam 732 is not yet formed by the apposition of the folds 717 and 727.

At the uppermost (distal) portion of the cusp wall layer, the extension tabs 712T and 722T are projected above (or distal to) the lines 712 and 722 (shown in Figs. 7A and 7B). All or a portion of these tabs 712T and 722T may be optionally folded outward along 712 and 722, respectively, around the distal edge of the frame to lie upon the outer (abluminal) surface of the frame where they may be attached to both the frame and to the cusp wall sections (apposed to the inner surface of the frame) through the interstices of the frame. This optional configuration provides for increased strength of attachment for bearing downward (proximally directed) operational loads associated with the valve closing.

Completing the folding associated with template pattern 700 places folds 717 and 727 into axial alignment. Once in axial alignment, apposing folds 717 and 727 are joined along their axial length to form the seam 732 that closes the generally conical cusp structure with the extension sections 718 and 728 situated outward of the cusp wall sections 761 and 771, respectively. The cusp wall sections 761 and 771 then are disposed outward of the mobile

leaflet sections 719 and 729, respectively, with the cusp wall sections axially and circumferentially apposed to the inner surfaces of the generally cylindrical frame. Advantageously, for each integrated cusp and folded leaflet structure to be mounted within, the frame may contain an element or elements that are axially oriented and span a significant portion of the axial length of the frame, so as to align with the seam 732 for attachment as by suturing to the frame.

Fig. 7E shows a shallow oblique top perspective view of the outer (abluminal) aspect of the partially folded cusp and leaflet structure 720 of template 700 (except that the triangular commissure tabs 762 and 772 and apex 733 are not yet folded and that the axial seam 732 is not yet joined). This view is complementary to Fig. 7D that shows the inner aspect of the same structure 720. The central seam 732 will be formed on the outer face of the cusp wall sections 761 and 771 as folds 717 and 727 are brought together into apposition along the midline, with the extension sections 718 and 728 thus also aligned. The outward (abluminal) face of the mobile leaflet sections 719 and 729 are shown between the yet separated folds 717 and 727 before closure of the generally conical cusp along the outer seam 732.

Fig. 7F shows a plan view of the inner (luminal) aspect of the folded integrated cusp and leaflet structure 720 of template pattern 700. Structure 720 is depicted in a completed state of folding, excepting that the commissure tabs 762 and 772 are not yet folded outward along fold lines 705 and 706, respectively. In addition, the apex 733 is not folded outward. The radially flattened form shown gives the general configuration and orientation of the membrane line segments and areal sections for the open operating position of the valve cusp and leaflet.

At the uppermost (distal) portion of the cusp wall layer, the extension tabs 712T and 722T are projected above (distal to) the lines 712 and 722 (shown in Figs. 7A, 7B and 7G), respectively, below (proximal to) which the cusp wall sections 761 and 771 lie in radial apposition to the mobile leaflet sections 719 and 729, respectively, of the mobile leaflet layer. These tabs 712T and 722T may be optionally folded outward along 712 and 722, respectively, around the distal edge of the frame to lie upon the outer (abluminal) surface of the frame where they may be attached to both the frame and to the cusp wall sections (apposed to the inner surface of the frame) through the interstices of the frame. This optional configuration provides for increased strength of attachment for bearing downward (proximally directed) loads of valve closing.

Folding of the template positions folds 717 and 727 into axial alignment, joined along their axial length to form the seam that closes the generally conical cusp structure with the extension sections 718 and 728 reflected outward of the cusp wall sections 761 and 771, respectively. The cusp wall sections 761 and 771 then are disposed outward of the mobile leaflet

sections 719 and 729, respectively, with the cusp wall sections 761 and 771 axially and circumferentially apposed to the inner surfaces of the generally cylindrical frame. Advantageously, for each valve cusp and leaflet folded structure to be mounted within, the frame may contain an element or elements that are axially oriented and span a significant portion of the axial length of the frame, so as to align with the seam 732 for attachment as by suturing to the frame.

Fig. 7G shows a perspective view of the outer (abluminal) aspect of the completely folded cusp and leaflet structure 720 (except that the triangular commissure tabs 762 and 772 and apex 733 are not yet folded) of template 700, in nearly flattened form. This view is complementary to Fig. 7F that shows the inner aspect of the same structure 720. The central seam 732 is seen on the outer face of the cusp wall sections 761 and 771 and is depicted for purposes of illustration as minimally separated with the extension sections 718 and 728 incompletely flattened and folds 717 and 727 in effectively complete apposition and alignment that forms the final seam line 732 for attachment to the axially oriented frame members. The slight separation depicted between folds 717 and 727 exposes the centerpoint between the mobile leaflet free edge segments 711 and 721 depicted behind the cusp wall sections 761 and 771, respectively, in this view.

Fig. 7H shows a plan view of the inner aspect of the completely folded integrated cusp and leaflet structure 730 of template 700. This view is substantially that of Fig. 7F except that the triangular commissure tabs 762 and 772 are folded radially outward of the cusp wall sections 761 and 771 along corner folds 705 and 706, respectively. Additionally, the apex (most proximal) portion of the cone-shaped cusp is folded radially outward along the fold line 703 (between points U and V) to the position radially outward of the joined extension sections 718 and 728 such that the apex point 733 then lies upon the seam line 732.

Fig. 7I shows a plan view of the radially outer aspect of the completely folded integrated cusp and leaflet structure 730 of template 700. The outwardly folded position of the triangular commissure tabs 762 and 772 can be seen so that they lie in apposition to the outer surface of the cusp wall sections 761 and 771, respectively. While they may attached in this position to the underlying cusp wall layer and to the frame, alternatively, the commissure tabs 762 and 772 may be positioned to point radially outward (out of the page in this view) to pass through a slot or space in the frame to be secured and attached to the outer (abluminal) surface of the frame.

Additionally, the apex (most proximal) portion of the cone-shaped cusp is folded radially outward along the fold line 703 (between points U and V) to the position radially outward of the joined extension sections 718 and 728 such that the apex point 733 then lies upon the seam line 732.

The apex portion of the cone-shaped cusp thus configured is to be attached in this position as by suturing and may be similarly attached into this position in the act of attaching or suturing this portion of the folded cusp and leaflet structure to the frame.

Fig. 7J shows an oblique top perspective view of the completely folded and formed cusp and leaflet structure 730 with the view directed radially outward and downward (proximal). The cusp and leaflet structure is shown with the free edge of the mobile leaflet layer in the inward central position corresponding to the substantially closed operating position of the valve leaflet.

The commissure tabs 762 and 772 are depicted in radially aligned positions directed outward as would be required for passing them through slots or spaces in a suitably designed frame.

Fig. 7K shows a top perspective view of the single-piece completely folded and formed cusp and leaflet structure 730 with the view directed downward (proximal) into the cusp space. The cusp and leaflet structure is shown with the free edge of the mobile leaflet layer sections 719 and 729 in the intermediate inward position corresponding to the partially closed operating position of the valve leaflet.

The membrane structure is depicted with the free edges in a relaxed state corresponding to the typical behavior of tissue membranes when hydrated as when implanted in the body.

The commissure tabs 762 and 772 are depicted in radially aligned positions directed outward as would be required for passing them through slots or spaces in a suitably designed frame.

Metal Lattice Frame

Fig. 8A is an oblique top perspective view of a metal lattice frame 910 for mounting three of the single-piece folded integrated cusp and leaflet structures of the ensuing description in order to form a three-leaflet valve. The frame comprises a plurality of strut members 911 and three axially oriented mounting bars 912 each with holes and/or slots for passing suture and/or portions of the folded membrane structure. Each mounting bar 912 is to align with and attach to the axial outer seam of one single-piece completely folded and formed cusp and leaflet structure 730. The diameter D of the open frame, e.g., 19 – 35 mm naturally defines the deployed and operating diameter of the valve assembly after implantation in the body. The strut members 911 are of specific length and orientation to permit radial collapse and compression of the frame to a small diameter, e.g., 3-7 mm. The mounting bars 912 are near to equally spaced around the circumferential course of the frame and the length L of the arc from the center of the mounting bar 912 to the center of the closest mounting bar 912 is approximately equal to (pi x D)/3. Thus defined, L also defines the transverse circumferential distance between folds 705 and 706 , approximating the circumferential extent of the portions of the joined cusp wall sections 761 and

771 extending between 705 and 706 of the folded cusp and leaflet structure of appropriate size when mounted within the frame 910.

Fig. 8B shows a side perspective view of the frame 910 with the view centered on the axial mounting bar 912. The axial bars are shown with holes and/or slots for passing suture and/or portions of the folded membrane structure to enable secure mounting of the folded cusp and leaflet structure within the frame.

Fig. 8C shows a side view of the frame of Fig. 8B with a superimposed plan view of the radially outer aspect of the completely folded integrated cusp and leaflet structure as depicted in Fig. 7I. The cusp wall seam 732 is aligned upon the inner surface of the mounting bar of the frame and attached by sutures in this example. (Example suture locations are shown in Figs. 8C, 9C and 9D shown with an "x"; however, it is to be understood that the locations shown are exemplary and not limiting.) As those skilled in the art will appreciate, means other than sutures for attaching folded integrated cusp and leaflet structure to the frame can be used.

The commissure tabs 762 and 772 are folded flat against the outer surface of the cusp wall layer along corner folds 705 and 706 for mounting entirely within the frame 910. Each fold 705 then forms an axially oriented seam along its length with the complementary fold 706 of the adjacent folded cusp and leaflet structure 730. (Adjacent complementary commissure tabs omitted for clarity.) Said seam is closed and attached by suture, for example, while also attaching to the radially overlying strut member 911 of the frame 910, and thereby affixes the distal margins of the cusp wall sections 761 and 771 and the mobile leaflet sections (obverse of this view) to the frame 910. The other suture points depicted attach only the cusp wall layer 761+771 to the overlying frame strut members 911. At no point within the interior operating volume of the valve is the mobile leaflet layer 719+729 penetrated by suture. This uninterrupted continuity of the operating leaflet material afforded by the folded design of the integrated cusp and leaflet structure endows the valve and its leaflets with strength, durability and resistance to stress damage at suture holes.

Fig. 8D shows an oblique axial (top/distal) perspective view of the assembled three-leaflet valve comprising the frame 910 and three identical folded integrated cusp and leaflet structures 730A, 730B and 730C attached within the frame with the view centered on an axial mounting bar 912A. The suture attachments are omitted for clarity. The cusp and leaflet structure 730A nearest in view is seen within the frame 910, with the outer aspect of the seam 732A, cuff wall extension sections 718A and 728A, and cusp wall sections 761A and 771A viewed through the interspaces of the frame 910. The seam 732A is aligned to the overlying axial mounting bar 912A to which it is attached along its length. The inner (luminal) aspect of the seams 732B and 732C and the cusp wall sections 761B, 771B, 761C and 771C of the other

two folded cusp and leaflet structures 730B and 730C, respectively are seen on the far side of the view. The adjoined folded edges of the membrane portions of the commissure tabs 772B and 762C are shown in the far view in position opposite to the axial mounting bar 912A in the near view. The radially outward surface of the mobile leaflet sections 719A and 729A of the folded cusp and leaflet structure 730A is shown in the near view. The distal free edges of all three mobile leaflets are shown in the centrally apposed (coapted) position corresponding to the closed operating position of the valve. Fig. 8D also shows in that aspect interior to the cusps, folds 726B of cusp and leaflet structure 730B and 716C of cusp and leaflet structure 730C as they form the lower (proximal) boundary of the valve cusps.

Slotted Lattice Frame

Fig. 9A shows an oblique axial (top/distal) perspective view of a frame 920 of a design to receive the commissure tabs 762 and 772 through slots 924 in slotted members 923 in order that the tabs are secured and attached to the outer (abluminal) aspect of the frame. This approach to mounting and attaching the commissure tabs enables the loading forces on the leaflet commissures during valve operation to be advantageously distributed upon the frame slotted members 923 along their length rather than upon suture that directly tethers the leaflets, thus greatly reducing the risk of tearing of the material at points of suture penetration. The frame further comprises axial mounting bars 922 for mounting the central seams 732 joining the cusp wall sections 761 and 771 along folds 717 and 727. The frame further comprises a plurality of strut members 921 that otherwise form the metal lattice of the frame.

Each mounting bar 922 is to align with and attach to the axial outer seam of one single-piece completely folded and formed cusp and leaflet structure 730. The inner diameter D of the open frame, e.g., 19 – 35 mm naturally defines the deployed and operating diameter of the valve assembly after implantation in the body. The strut members 921 are of specific length and orientation to permit radial collapse and compression of the frame to a small diameter, e.g., 3-7 mm. The mounting bars 922 are near to equally spaced around the inner circumferential course of the frame. The length L of the arc along the inner circumference of the frame from the center of the mounting bar 922 to the center of the closest mounting bar 922 is approximately equal to (pi x D)/3. Thus defined, L also defines the transverse circumferential distance between folds 705 and 706 , approximating the circumferential extent of the portions of the joined cusp wall sections 761 and 771 extending between 705 and 706 of the folded cusp and leaflet structure of appropriate size when mounted within the frame 920.

The axial mounting bars 922 optionally contain holes and/or slots to facilitate suture attachment of the folded integrated cusp and leaflet structures 730. The frame is depicted in Figs. 9A-9E as having axial mounting bars 922 each with a hole near the proximal end to

facilitate suture attachment of the apical (most proximal) portion of the folded cusp and leaflet structure.

Fig. 9B shows the metal lattice frame of Fig. 9A in the same perspective, but with the view centered on the slotted frame member 923.

Fig. 9C shows a side perspective view of the frame 920 centered on the axial mounting bar 922 with a superimposed plan view of the outer aspect of the completely folded integrated cusp and leaflet structure 730 (of Fig. 7I) as mounted within the frame 920 to demonstrate the relationships between the two. An example suture pattern for attachment is shown. The cusp wall seam 732 is aligned upon the inner surface of the mounting bar 922 of the frame 920 and attached by sutures in this example.

The commissure tabs 762 and 772 are to be understood as having been passed through the frame slots 924 from within the central space of the frame to the outer (abluminal) side and folded along 705 and 706, respectively onto the outer surface of the cusp and leaflet structure where they are attached along their common length both to the frame members 923 and, through the interspaces of the frame 920, to the radially underlying outer aspect of the cusp wall sections 761 and 771, respectively. The adjacent cusp and leaflet structures of the three-leaflet valve are not shown for clarity. The joining of adjacent commissure tabs at the slotted members 923 is demonstrated in Fig. 9D.

At the apical (most proximal) extent of the completely folded integrated cusp and leaflet structure 730, the apical portion folded radially outward along fold 703 is attached to the lower (most proximal) end of the axial mounting bar 922. When present, a hole near the end of the axial mounting bar 922 facilitates suture attachment at this point.

Fig. 9D shows a side perspective view of the frame 920 centered on the slotted frame member 923AB with a superimposed perspective view of the outer aspect of two circumferentially adjacent completely folded integrated cusp and leaflet structures 730A and 730B (of Fig. 7I) to demonstrate their relationships as mounted within the frame 920. An example suture pattern for attachment is shown. Suture attachment of the commissure folds 705 and 706 at the level of the slot is notably absent. Rather, attachment of the bodies of the commissure tabs 762A and 772B to the outer aspect of the frame at points removed from the free edges and folds of the material avoids suture penetration along the lines of traction in the slot and enhances the resistance of the structure to tearing at such suture attachments. The cusp wall seams 732A and 732B are aligned upon the inner surface of the mounting bars 922A and 922B, respectively of the frame 920 and attached by sutures in this example.

The commissure tabs 762A and 772B are to be understood as having been passed through the frame slot 924 from within the central space of the frame to the outer (abluminal)

side and folded along 705A and 706B, respectively onto the outer surface of the cusp and leaflet structure where they are attached along their common length both to the frame member 923AB and, through the interspaces of the frame 920, to the radially underlying outer aspect of the cusp wall sections 761A and 771B, respectively.

Fig. 9E shows an oblique axial (top/distal) perspective view of the assembled three-leaflet valve comprising the frame 920 and three identical folded integrated cusp and leaflet structures 730A, 730B and 730C attached principally within the central space of the frame, but with the commissure tabs passed in complementary adjacent left-right pairs, 762A-772B, 762B-772C and 762C-772A, through the slots 924AB, 924BC and 924CA, of slotted frame members 923AB, 923BC, and 923CA, respectively. The view is centered on slotted member 923AB. The suture attachments are omitted for clarity.

The cusp and leaflet structure 730C farthest in view is seen within the frame 920, with the inner aspect of the seam 732C and cusp wall sections 761C and 771C in the far view. The cuff wall extension sections 718C and 728C are depicted as folded onto the outer aspect of the cusp wall sections 761C and 771C, respectively, but within the central space of the frame 920 and apposed to the inner surface of the frame. The inner (luminal) aspect of the seam 732C is shown aligned to the outwardly overlying axial mounting bar 922C to which it is attached along its length. The outer (abluminal) aspect of the top (most distal) portions of the seams 732A and 732B and the cusp wall sections 761A and 771B, of the other two folded cusp and leaflet structures 730A and 730B are also shown through the interspaces of the frame on either side of the near view.

The commissure tabs 762A and 772B, aligned and apposed along folds 705A and 706B, respectively are shown centered in the near view in position opposite to the axial mounting bar 922C and cusp wall seam 732C in the far view. The key mounting configuration of the valve commissures to the slotted frame members is here demonstrated. The triangular commissure tabs are formed as a result of the folding of the membrane template along folds 716 and 726, and are comprised of overlapping layers of the cusp wall section and the mobile leaflet section. Thus, with passage of the commissure tabs from within the interior space of the frame through the frame slots, both the cusp wall layer and the mobile leaflet layer are carried together to the outer aspect of the frame where they are attached. In addition, the interior aspect of the commissure folds 706A of cusp and leaflet structure 730A and 705B of cusp and leaflet structure 730B are shown where they mark the segment at which the commissure tabs 772A and 762B are passed through the frame slots 924CA and 924BC of slotted members 923CA and 923BC, respectively, and are tethered thereto.

The radially outward surface of the mobile leaflet sections 719A, 729A of the folded cusp and leaflet structure 730A and sections 719B, 729B of the folded cusp and leaflet structure 730B are shown on the left and right sides, respectively of the near view. (These labels omitted for clarity.)

The distal free edges of all three mobile leaflets are shown in the centrally apposed (coapted) position corresponding to the closed operating position of the valve. Fig. 9E also shows in that aspect interior to the cusps, a portion of folds 726A of cusp and leaflet structure 730A and 716B of cusp and leaflet structure 730B as they form the lower (proximal) boundary of the valve cusps.

The template examples disclosed herein are provided for enablement purposes and shall not be interpreted as limiting the scope of the claims. For example, angular values shown and/or described herein are not to be interpreted as limiting the scope of a claim unless included in a given claim.

As those skilled in the art will appreciate, circumference length varies with the diameter circumscribed therein. Accordingly, refinements in the valve manufacturing process may address adjusting the length of the leaflet free edge to be slightly less than the edge length of the cusp wall, i.e., less than the circumferential arc length between the commissures. This adjustment depends upon the dimensions of a given valve in production, as well as the dimensions of the given valve's component elements.

In still other embodiments of the one or more present inventions, the percutaneously deliverable heart valve may include various other configurations by using different variations of the polygon pattern, so as to include, for example, an inner sealing cuff for the valve that is continuous and integral with the leaflet structure itself. In yet other embodiments, the percutaneously deliverable heart valve may include different configurations by adjusting the pattern and folding technique, such as the angle of the cone and its surface area, or the extent of apposition between the leaflets may also be specified.

The present invention may be embodied in other specific forms without departing from its spirit or essential characteristics. The described embodiments are to be considered in all respects only as illustrative and not restrictive. The scope of the invention is, therefore, indicated by the appended claims rather than by the foregoing description. All changes which come within the meaning and range of equivalency of the claims are to be embraced within their scope.

The one or more present inventions, in various embodiments, include components, methods, processes, systems and/or apparatus substantially as depicted and described herein, including various embodiments, subcombinations, and subsets thereof. Those of skill in the art

will understand how to make and use the present invention after understanding the present disclosure.

The present invention, in various embodiments, includes providing devices and processes in the absence of items not depicted and/or described herein or in various embodiments hereof, including in the absence of such items as may have been used in previous devices or processes (e.g., for improving performance, achieving ease and/or reducing cost of implementation).

The foregoing discussion of the invention has been presented for purposes of illustration and description. The foregoing is not intended to limit the invention to the form or forms disclosed herein. In the foregoing Detailed Description for example, various features of the invention are grouped together in one or more embodiments for the purpose of streamlining the disclosure. This method of disclosure is not to be interpreted as reflecting an intention that the claimed invention requires more features than are expressly recited in each claim. Rather, as the following claims reflect, inventive aspects lie in less than all features of a single foregoing disclosed embodiment. Thus, the following claims are hereby incorporated into this Detailed Description, with each claim standing on its own as a separate preferred embodiment of the invention.

Moreover, though the description of the invention has included description of one or more embodiments and certain variations and modifications, other variations and modifications are within the scope of the invention (e.g., as may be within the skill and knowledge of those in the art, after understanding the present disclosure). It is intended to obtain rights which include alternative embodiments to the extent permitted, including alternate, interchangeable and/or equivalent structures, functions, ranges or steps to those claimed, whether or not such alternate, interchangeable and/or equivalent structures, functions, ranges or steps are disclosed herein, and without intending to publicly dedicate any patentable subject matter.

CLAIMS

What is claimed is:

1. A transcatheter, percutaneously implantable, prosthetic heart valve, comprising:

a lattice frame; and

two or more integrated cusp and leaflet folded structures attached to the lattice frame, the two or more integrated cusp and leaflet folded structures each comprising a flat sheet of biocompatible membrane that is folded to include a mobile leaflet layer and a cusp wall layer, wherein the cusp wall layer located radially outside of the mobile leaflet layer, and wherein the cusp wall layer is further formed by joining apposing sides of the cusp wall layer along a seam.

2. The transcatheter, percutaneously implantable, prosthetic heart valve of Claim 1, wherein the two or more integrated cusp and leaflet folded structures are each attached along their respective seams to the lattice frame.

3. The transcatheter, percutaneously implantable, prosthetic heart valve of Claim 2, wherein the seams are oriented in a direction substantially parallel to an axis of the lattice frame.

4. The transcatheter, percutaneously implantable, prosthetic heart valve of Claim 1, wherein the flat sheet of biocompatible membrane forming at least one integrated cusp and leaflet folded structure of the two or more integrated cusp and leaflet folded structures comprises two or more pieces of biocompatible membrane material.

5. A transcatheter, percutaneously implantable, prosthetic heart valve, comprising:

a lattice frame; and

two or more integrated cusp and leaflet folded structures attached to the lattice frame, the two or more integrated cusp and leaflet folded structures each comprising a flat sheet of a biocompatible membrane that is folded to include a valve cusp according to a flat folding pattern, wherein the valve cusp is further formed by joining apposing sides of the valve cusp along a seam, and wherein the two or more integrated cusp and leaflet folded structures are each attached along their respective cusp seams to the lattice frame in a direction substantially parallel to an axis of the lattice frame.

6. The transcatheter, percutaneously implantable, prosthetic heart valve of Claim 5, wherein two distal, downstream, vertices of each of the two or more integrated cusp and leaflet folded structures are folded over as vertex folds in a radially outward direction and fixed to the lattice frame such that the vertex folds of circumferentially adjacent leaflets are adjacent and define a degree of leaflet apposition at points corresponding to leaflet commissures.

7. The transcatheter, percutaneously implantable, prosthetic heart valve of Claim 6, wherein the two distal, downstream, vertices are fixed to the lattice frame by attachment not along an alignment with the vertex folds.

8. The transcatheter, percutaneously implantable, prosthetic heart valve of Claim 5, wherein a vertex forming a proximal, upstream, tip of the valve cusp is folded over in a radially outward direction and attached to an inner portion of the lattice frame.

9. The transcatheter, percutaneously implantable, prosthetic heart valve of Claim 5, wherein the flat folding pattern is polygonal and includes extending portions that, when the cusp is mounted, extend circumferentially outward from an axial line of attachment of the cusp to the lattice frame so as to form, when joined and attached to corresponding extending portions of neighboring cusps, an integral, inner, luminal, circumferentially complete sealing cuff.

10. The transcatheter, percutaneously implantable, prosthetic heart valve of Claim 5, wherein the flat folding pattern is polygonal and includes extending portions that, when the two or more integrated cusp and leaflet folded structures are mounted, extend circumferentially outward from an axial line of attachment of the cusp to the lattice frame so as to form a circumferentially incomplete sealing cuff portion associated with each cusp.

11. The transcatheter, percutaneously implantable, prosthetic heart valve of Claim 5, wherein a separate tubular cuff of biocompatible membrane is attached to an outer, abluminal surface of the lattice frame to form a sealing cuff.

12. The transcatheter, percutaneously implantable, prosthetic heart valve of Claim 5, wherein the lattice frame is collapsible and expandable and comprises a metal alloy substantially configured as tubular stent member.

13. The transcatheter, percutaneously implantable, prosthetic heart valve of Claim 5, wherein the biocompatible membrane comprises processed mammalian pericardium tissue.

14. The transcatheter, percutaneously implantable, prosthetic heart valve of Claim 5, wherein the biocompatible membrane does not comprise a treated tissue.

15. The transcatheter, percutaneously implantable, prosthetic heart valve of Claim 5, wherein the biocompatible membrane comprises a synthetic material.

16. The transcatheter, percutaneously implantable, prosthetic heart valve of Claim 5, wherein the cusp seams of the two or more integrated cusp and leaflet folded structures are each oriented along an axis of flow of the valve.

17. The transcatheter, percutaneously implantable, prosthetic heart valve of Claim 5, wherein the two or more integrated cusp and leaflet folded structures are each further attached to a circumferential portion of the lattice frame along at least a portion of their distal downstream edges.

18. The transcatheter, percutaneously implantable, prosthetic heart valve of Claim 5, wherein the two or more integrated cusp and leaflet folded structures are attached to the lattice frame at least at a non-commissural seam aligned with an axial flow direction of the valve.

19. A transcatheter, percutaneously implantable, prosthetic heart valve, comprising:

a lattice frame; and

two or more integrated cusp and leaflet structures attached to the lattice frame, the two or more integrated cusp and leaflet structures each comprising a flat sheet of biocompatible membrane that is folded to include a mobile leaflet layer and a cusp wall layer, wherein with the mobile leaflet layer in a position corresponding to a closed operating configuration of the valve a transverse cross-sectional area of a cusp-sinus space decreases monotonically from a distal end to a proximal end of the mobile leaflet layer.

20. The transcatheter, percutaneously implantable, prosthetic heart valve of Claim 19, wherein the cusp wall layer is located radially outside of the mobile leaflet layer.

21. The transcatheter, percutaneously implantable, prosthetic heart valve of Claim 19, wherein the cusp wall layer is further formed by joining apposing sides of the cusp wall layer along a seam.

22. The transcatheter, percutaneously implantable, prosthetic heart valve of Claim 19, wherein with the mobile leaflet layer in a position corresponding to a closed operating configuration of the valve a transverse cross-sectional length of the mobile leaflet layer decreases monotonically from a distal end to a proximal end of the mobile leaflet layer.

23. The transcatheter, percutaneously implantable, prosthetic heart valve of Claim 19, wherein the mobile leaflet layer and the cusp wall layer of each integrated cusp and leaflet structure are a single continuous piece of biocompatible membrane.

24. In subcombination, an integrated cusp and leaflet structure for attachment to a lattice frame to form a valve configured for implantation in a vascular system of a patient, the integrated cusp and leaflet structure comprising:

a flat sheet of a biocompatible membrane that is folded to include a mobile leaflet layer and a cusp wall layer, wherein the cusp wall layer is divided along a seam, and wherein the mobile leaflet layer is continuous and apposes the cusp wall layer when the integrated cusp and leaflet structure is pressed substantially flat.

25. The subcombination of Claim 24, wherein the mobile leaflet layer and the cusp wall layer of the integrated cusp and leaflet structure are a single continuous piece of biocompatible membrane.

26. The subcombination of Claim 24, wherein the biocompatible membrane comprises processed mammalian pericardium tissue.

27. The subcombination of Claim 24, wherein the biocompatible membrane does not comprise a treated tissue.

28. The subcombination of Claim 24, wherein the biocompatible membrane

comprises a synthetic material.

29. The subcombination of Claim 24, wherein the integrated cusp and leaflet structure further comprises at least one commissure tab.

30. The subcombination of Claim 29, wherein the at least one commissure tab is configured for engaging a slot within a member of the lattice frame.

31. A method of forming an integrated cusp and leaflet folded structure for use in an implantable valve having an axial flow direction, comprising:

folding a flat sheet of biocompatible membrane to form an integrated cusp and leaflet folded structure according to a flat folding pattern, wherein said folding includes making two diagonal folds in the flat sheet of biocompatible membrane, the two diagonal folds separating a mobile leaflet layer from a cusp wall layer of the integrated cusp and leaflet folded structure.

32. The method of forming the integrated cusp and leaflet folded structure of Claim 31, wherein said two diagonal folds are angled at between 10 to 80 degrees from the axial flow direction.

33. The method of forming an integrated cusp and leaflet folded structure of Claim 31, further comprising forming first and second cusp wall folds, wherein the cusp wall layer is further formed by joining apposing membrane portions adjacent the first and second cusp wall folds along a seam that is oriented substantially parallel with the axial flow direction.

34. A method of forming a transcatheter, percutaneously implantable, prosthetic heart valve, comprising:

folding a plurality of integrated cusp and leaflet folded structures, each integrated cusp and leaflet folded structure of the plurality of integrated cusp and leaflet folded structures comprising a flat sheet of biocompatible membrane that is folded to form a cusp according to a flat folding pattern, wherein the cusp is further formed by joining apposing sides of the cusp along a seam; and

attaching each integrated cusp and leaflet folded structure of the plurality of integrated cusp and leaflet folded structures to a lattice frame, wherein the two or more integrated cusp and leaflet folded structures are each attached along their respective seams to the lattice frame in a direction substantially parallel to an axis of the lattice frame.

Figure 1A

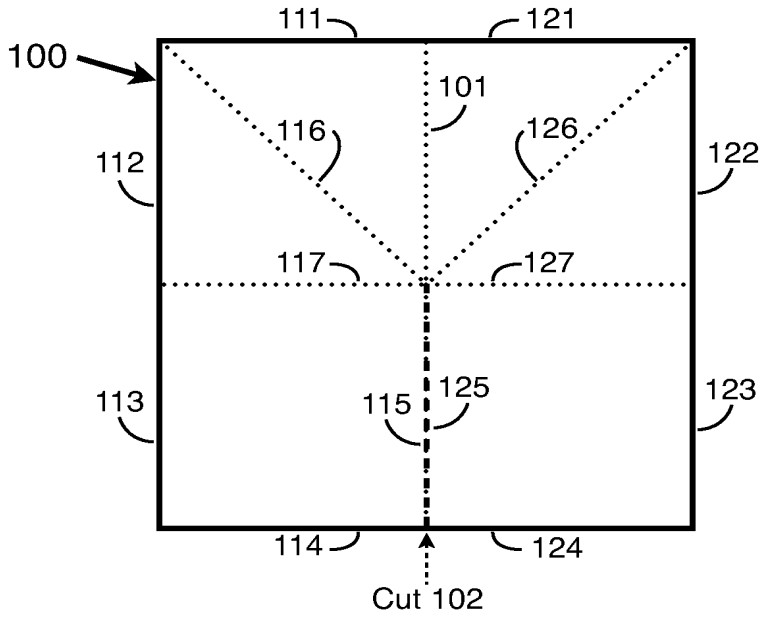
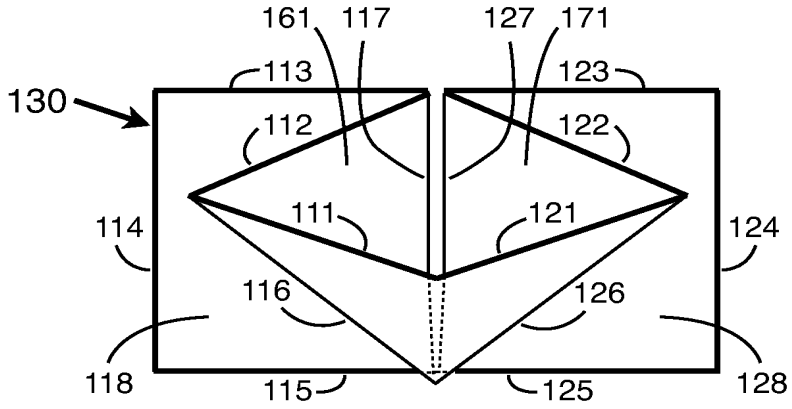


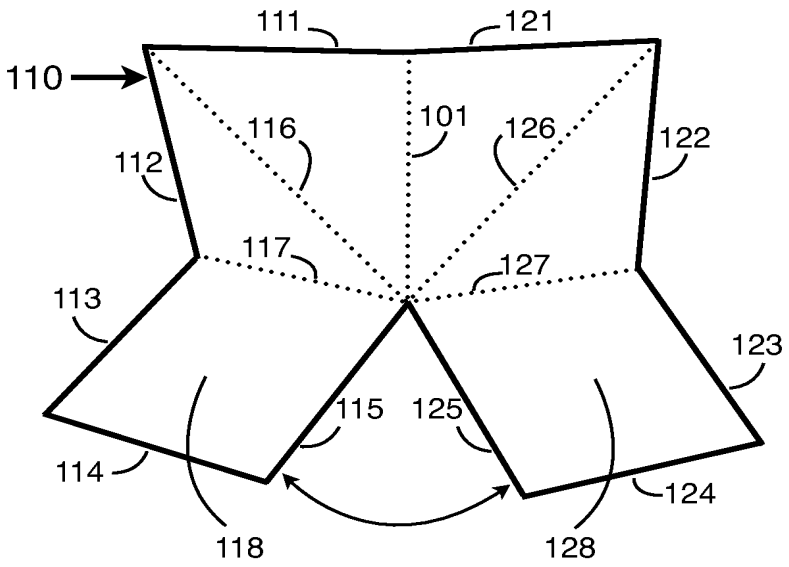
Figure 1B



LEGEND

———	Visible free (cut) edge of membrane piece
———	Visible edge of folded structure
·····	Line of fold / crease
- - - - -	Hidden (phantom) edges of folded structure
- - - - -	Line of cut

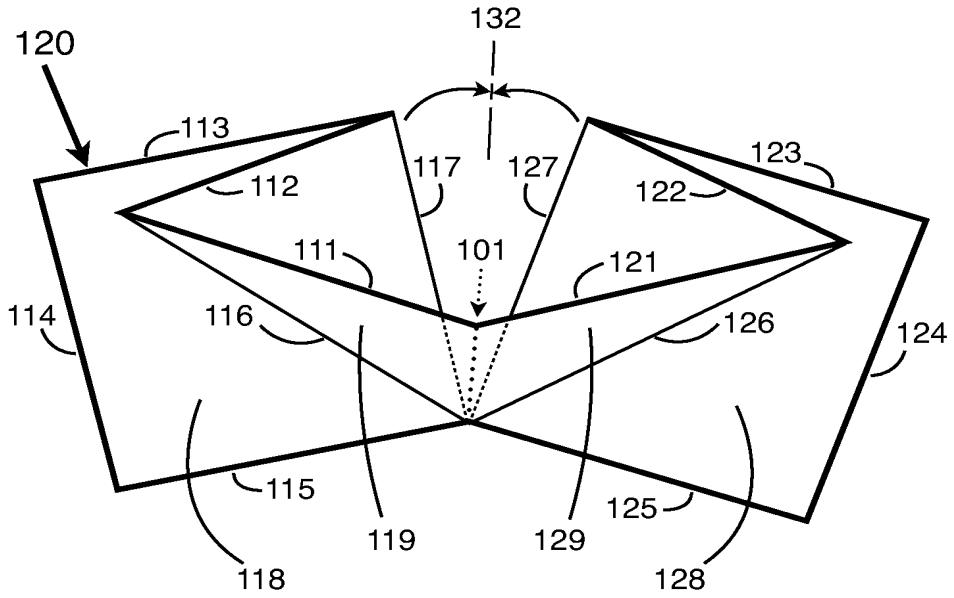
Figure 1C



LEGEND

———	Visible free (cut) edge of membrane piece
———	Visible edge of folded structure
.....	Line of fold / crease
- - - - -	Hidden (phantom) edges of folded structure
- - - - - - -	Line of cut

Figure 1D



LEGEND

———	Visible free (cut) edge of membrane piece
———	Visible edge of folded structure
. . . . .	Line of fold / crease
- - - - -	Hidden (phantom) edges of folded structure
- - - - -	Line of cut

Figure 1E

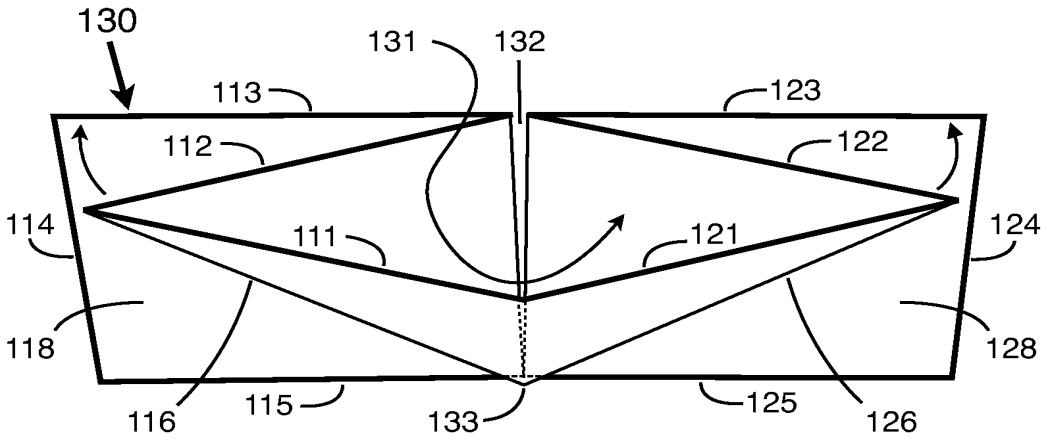
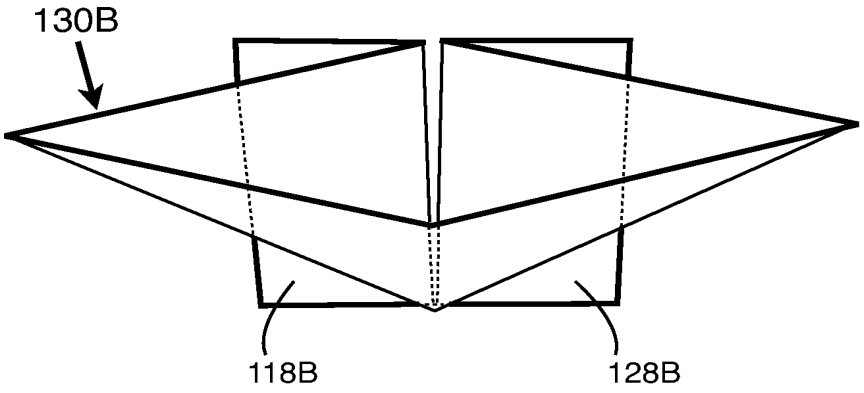


Figure 1F



LEGEND

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———	Visible edge of folded structure
.....	Line of fold / crease
- - - - -	Hidden (phantom) edges of folded structure
- - - - - - -	Line of cut

Figure 1G

Suture attachments omitted for clarity.

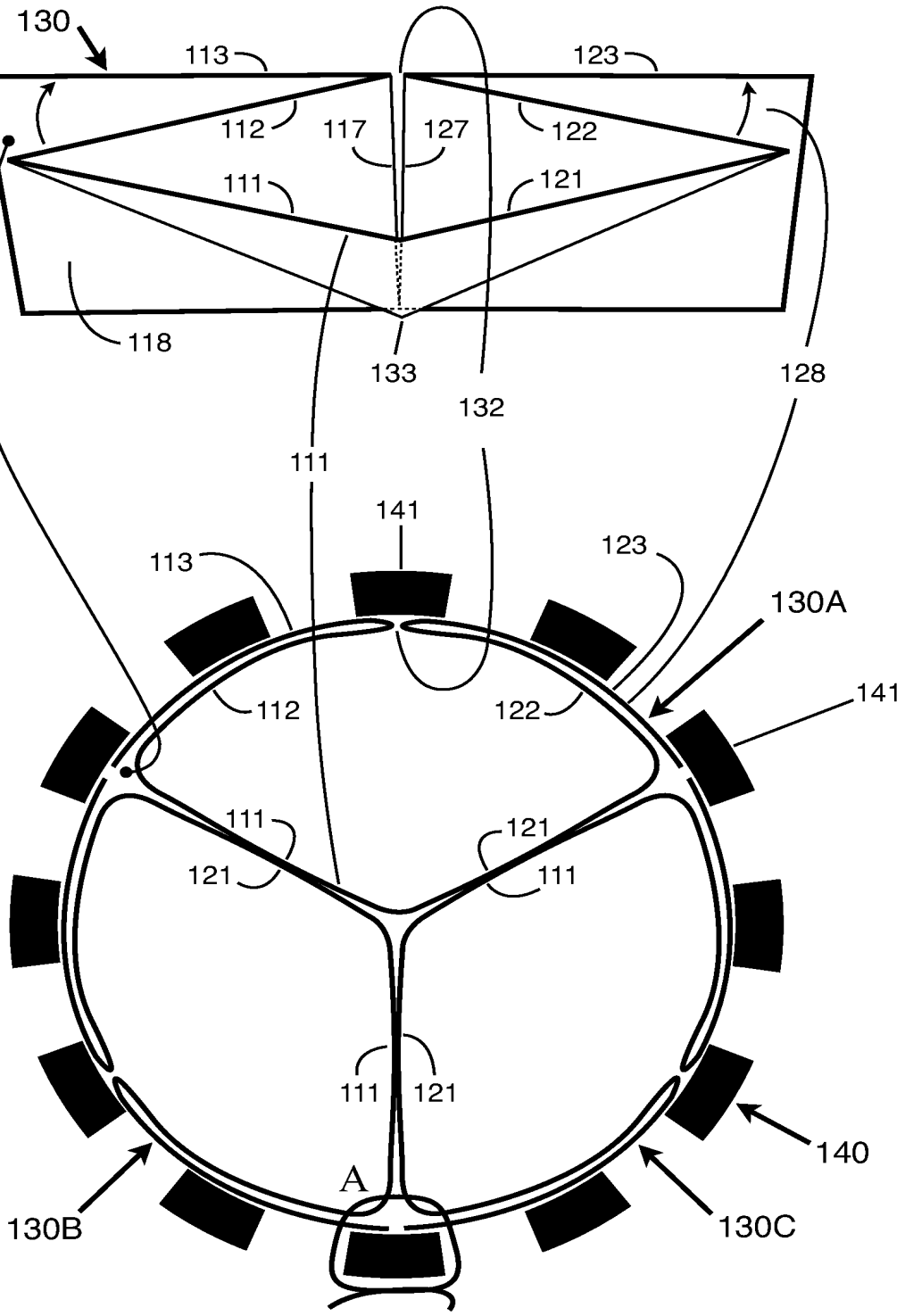
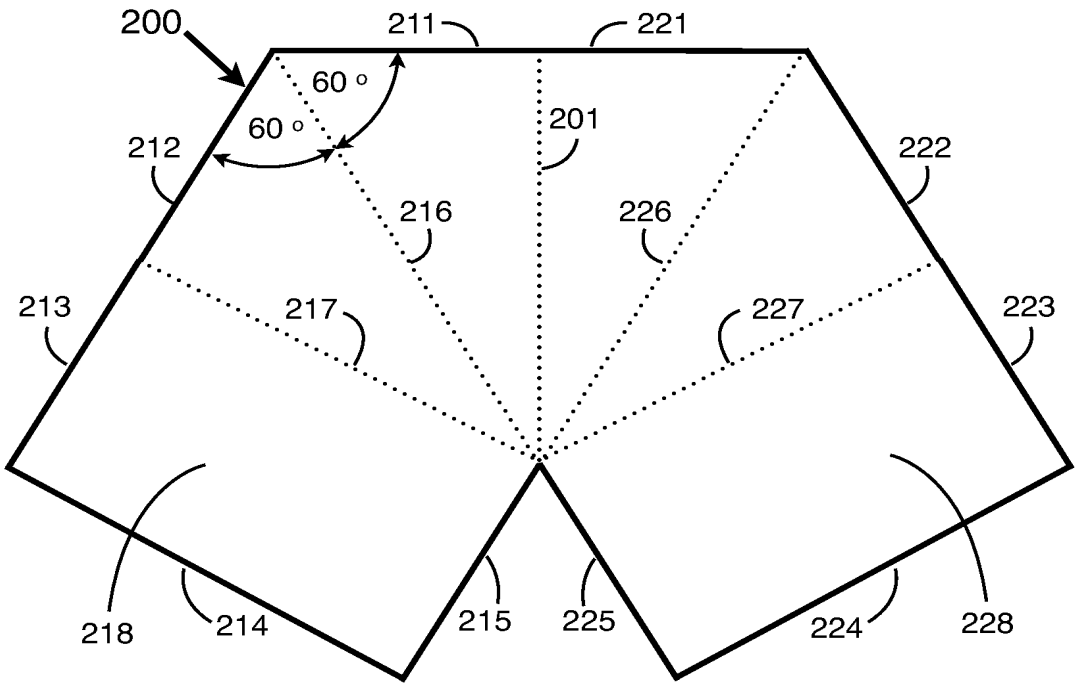


Figure 2



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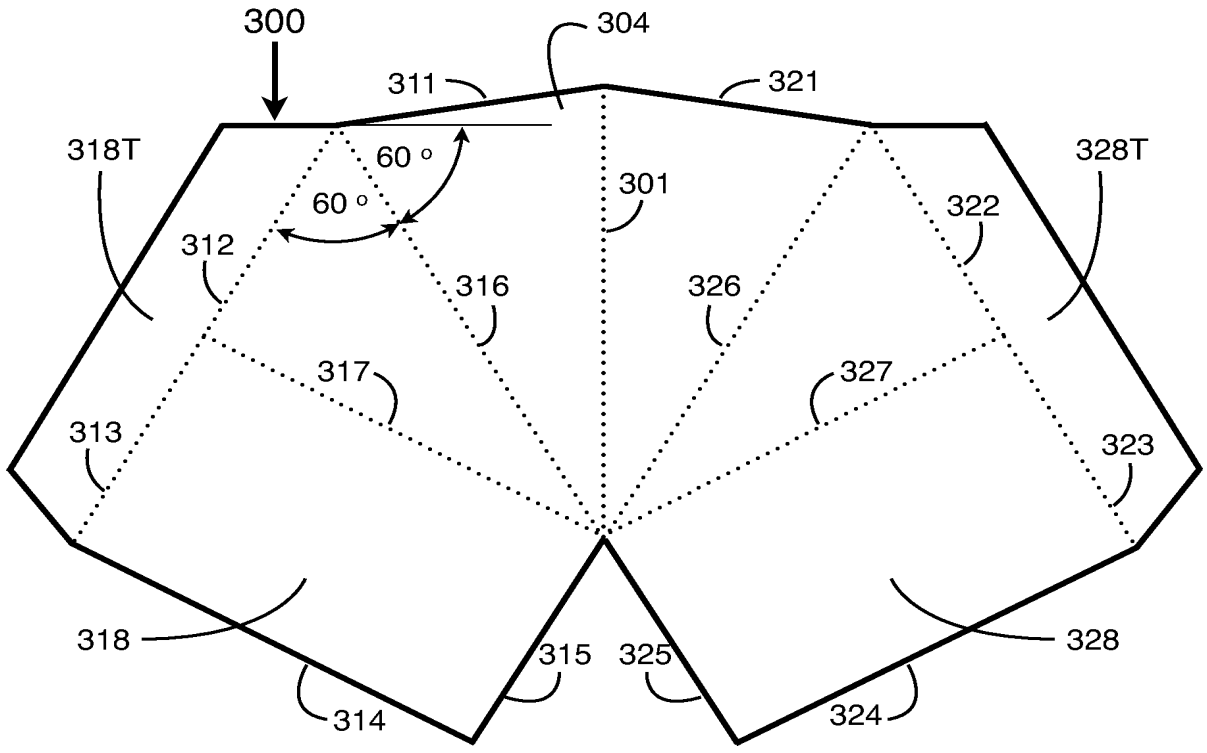
———	Visible edge of folded structure
·····	Line of fold / crease
- - - - -	Hidden (phantom) edges of folded structure
- - - - -	Line of cut

Figure 3



LEGEND

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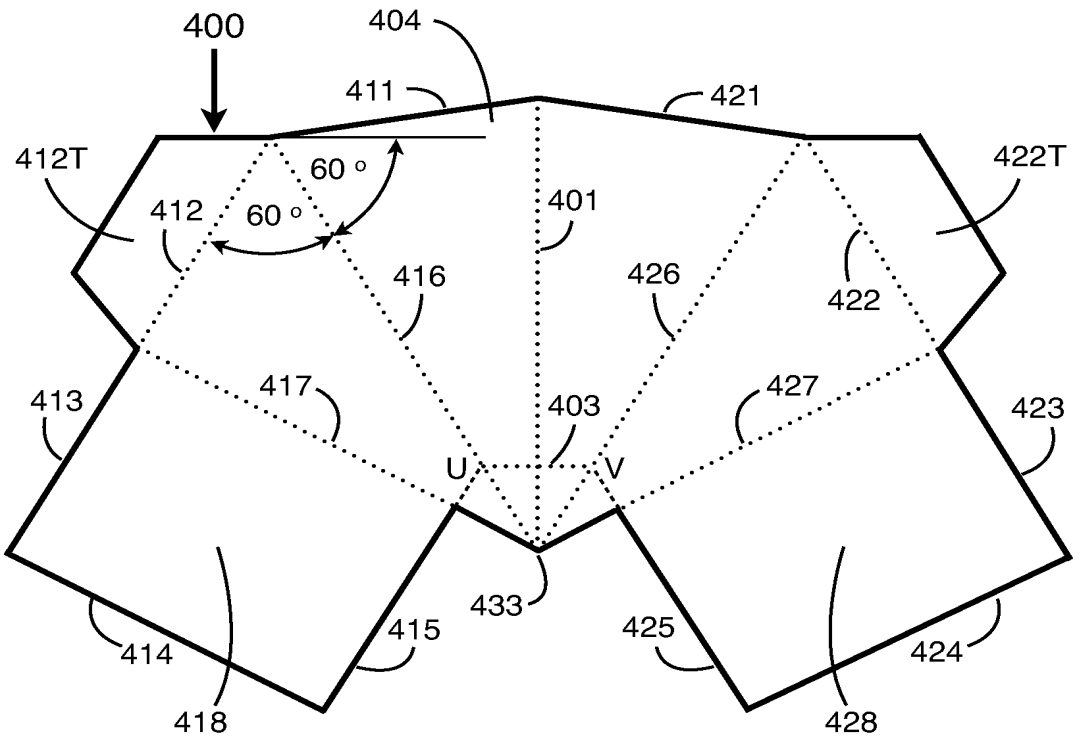
———	Visible edge of folded structure
·····	Line of fold / crease
- - - - -	Hidden (phantom) edges of folded structure
- - - - -	Line of cut

Figure 4



LEGEND

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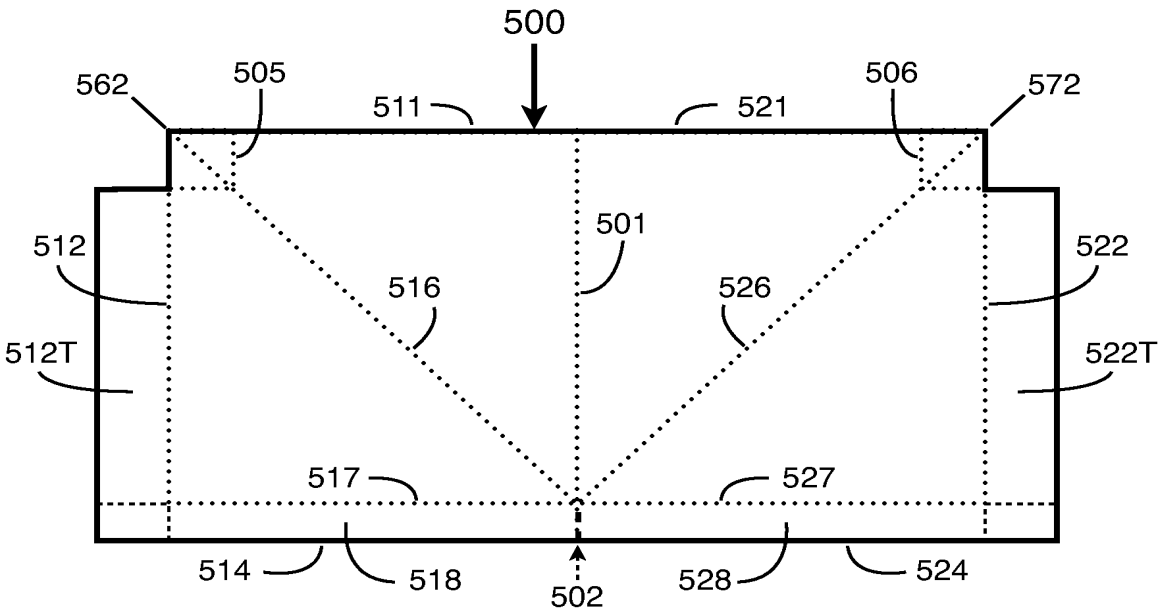
·····	Line of fold / crease
- - - - -	Hidden (phantom) edges of folded structure
- - - - -	Line of cut

Figure 5A



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———	Visible edge of folded structure
·····	Line of fold / crease
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- - - - -	Line of cut

Figure 5B

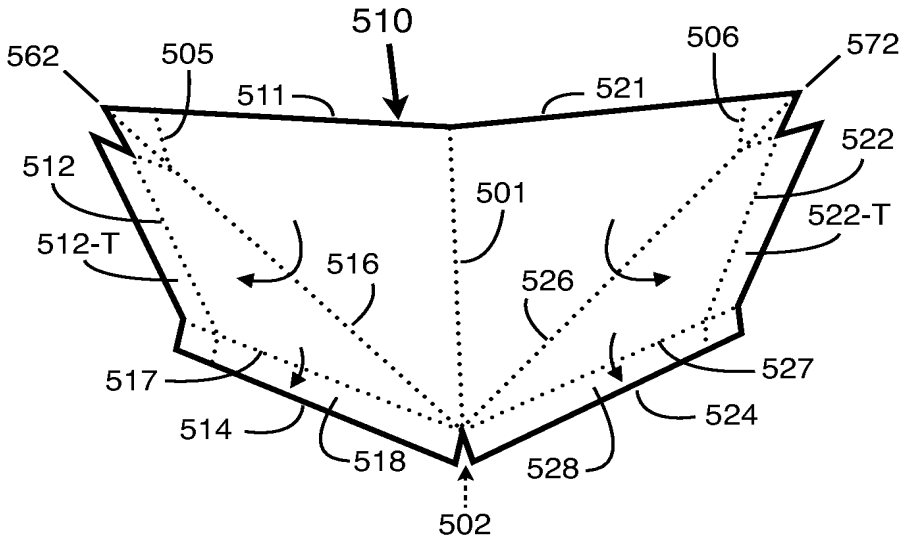
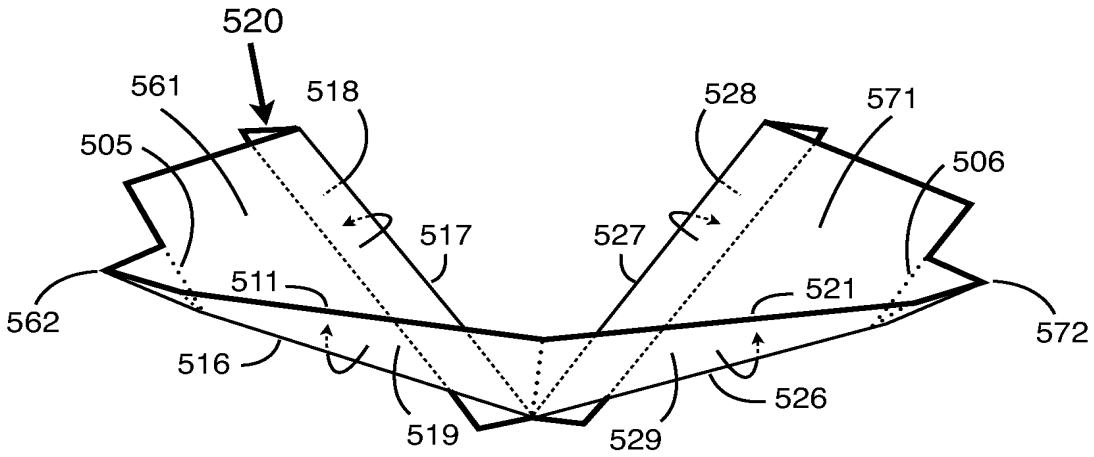


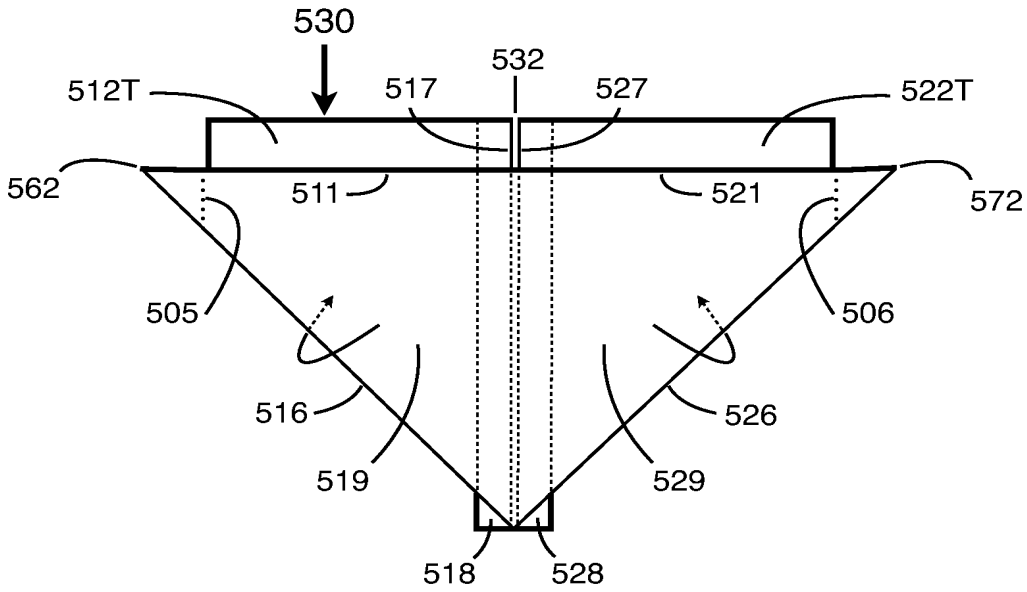
Figure 5C



LEGEND

———	Visible free (cut) edge of membrane piece
———	Visible edge of folded structure
·····	Line of fold / crease
- - - - -	Hidden (phantom) edges of folded structure
- - - - - - -	Line of cut

Figure 5D



LEGEND

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———	Visible edge of folded structure
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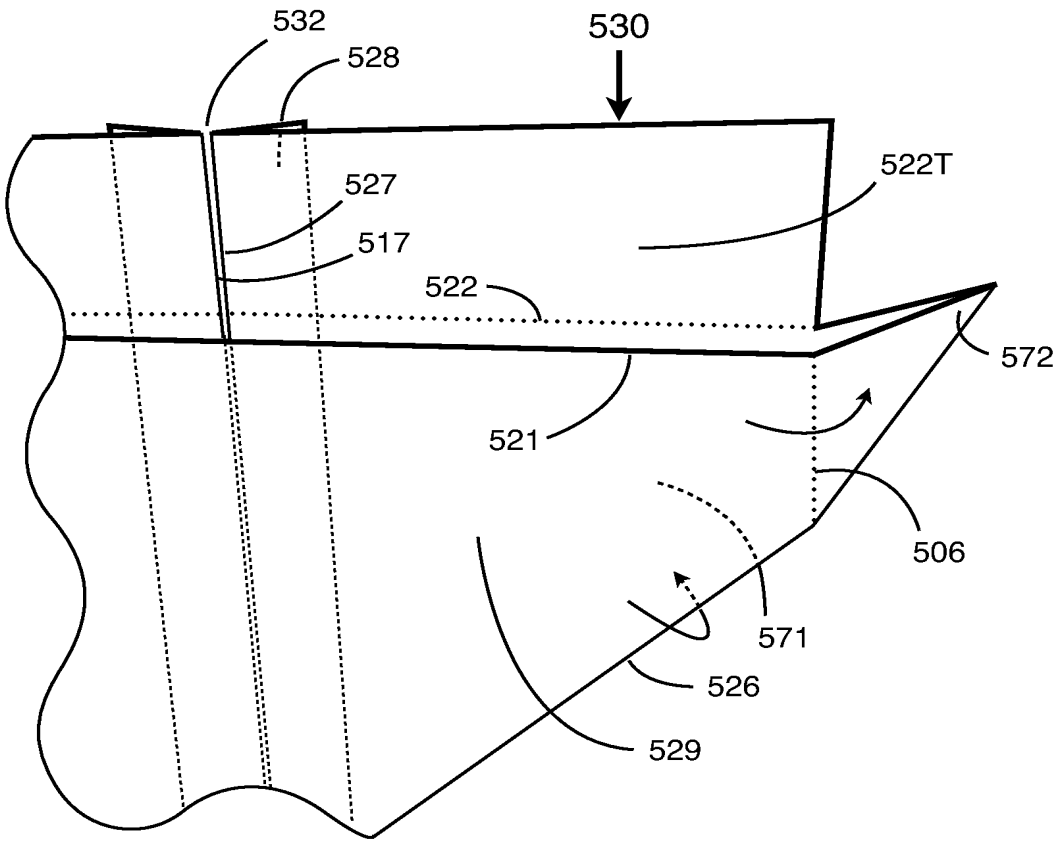
- - - - -	Line of cut

Figure 5E



LEGEND

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———	Visible edge of folded structure
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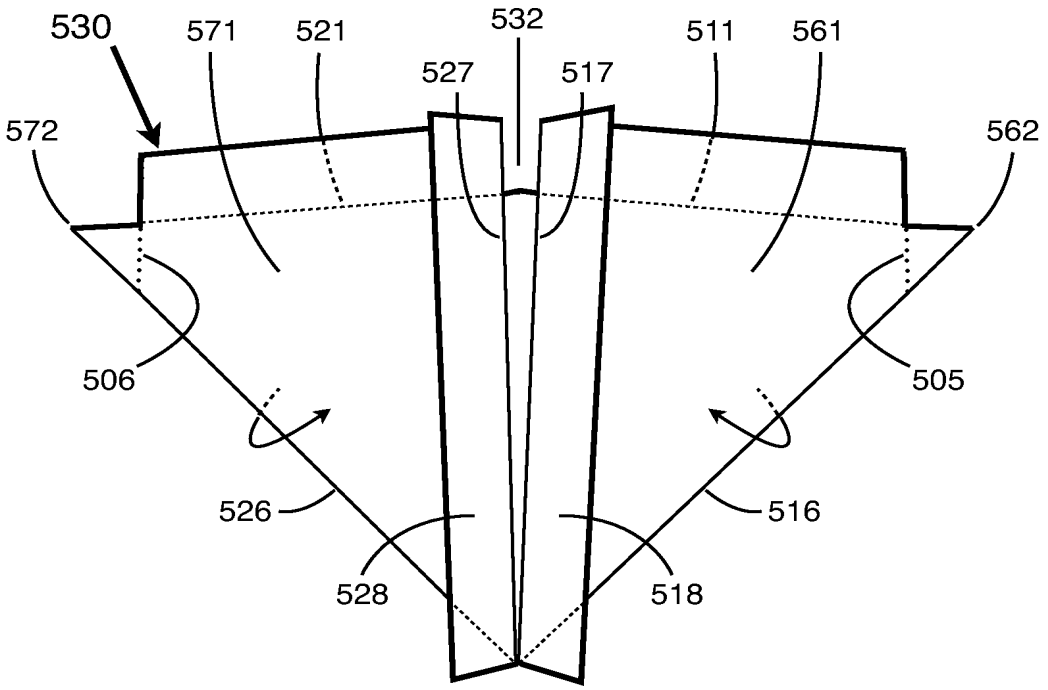
- - - - -	Line of cut

Figure 5F



LEGEND

———	Visible free (cut) edge of membrane piece
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.....	Line of fold / crease
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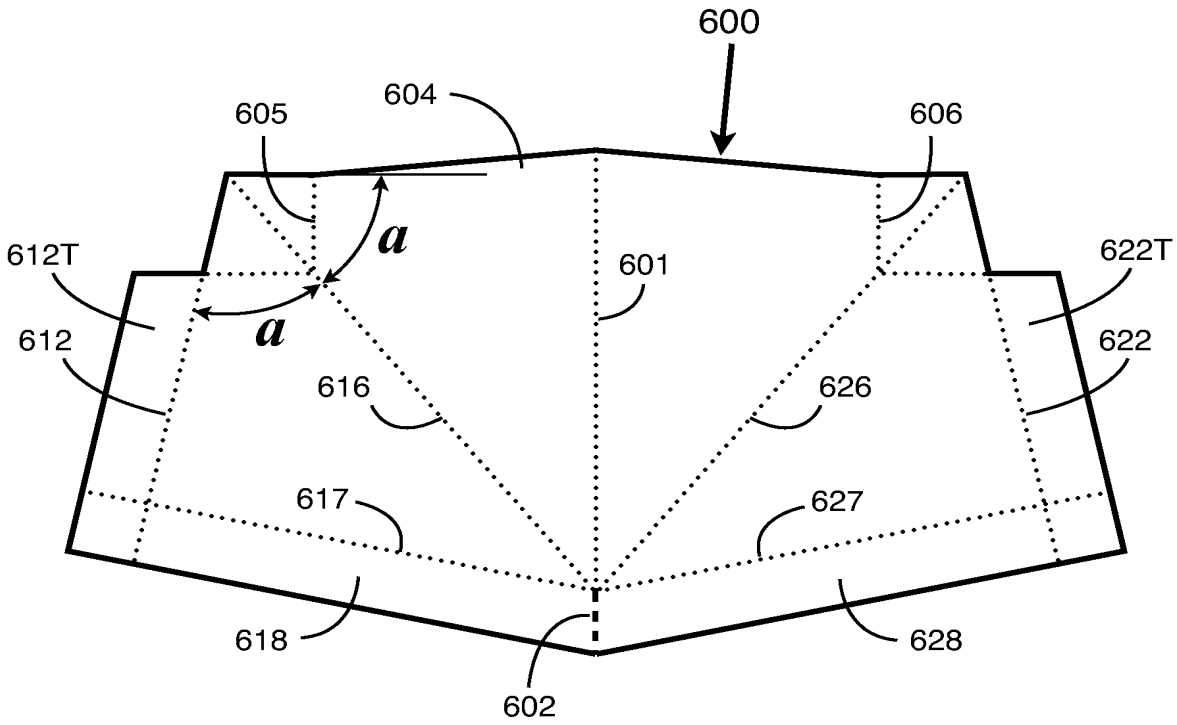
- - - - -	Line of cut

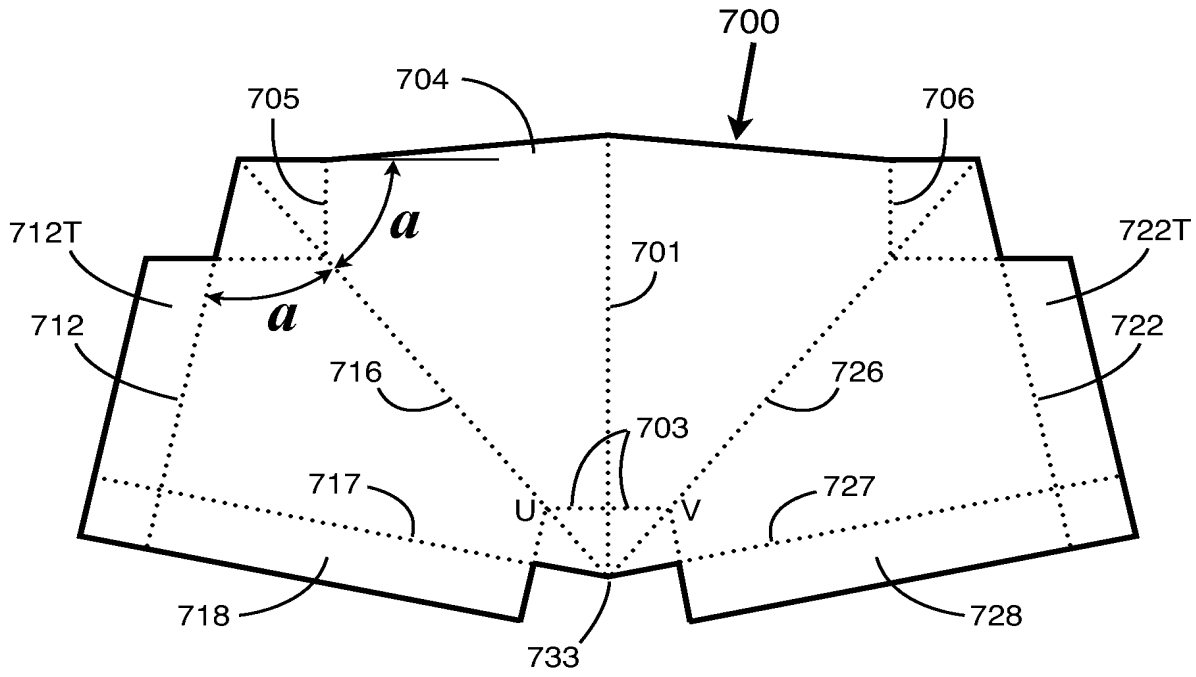
Figure 6



LEGEND

———	Visible free (cut) edge of membrane piece
———	Visible edge of folded structure
·····	Line of fold / crease
- - - - -	Hidden (phantom) edges of folded structure
- - - - -	Line of cut

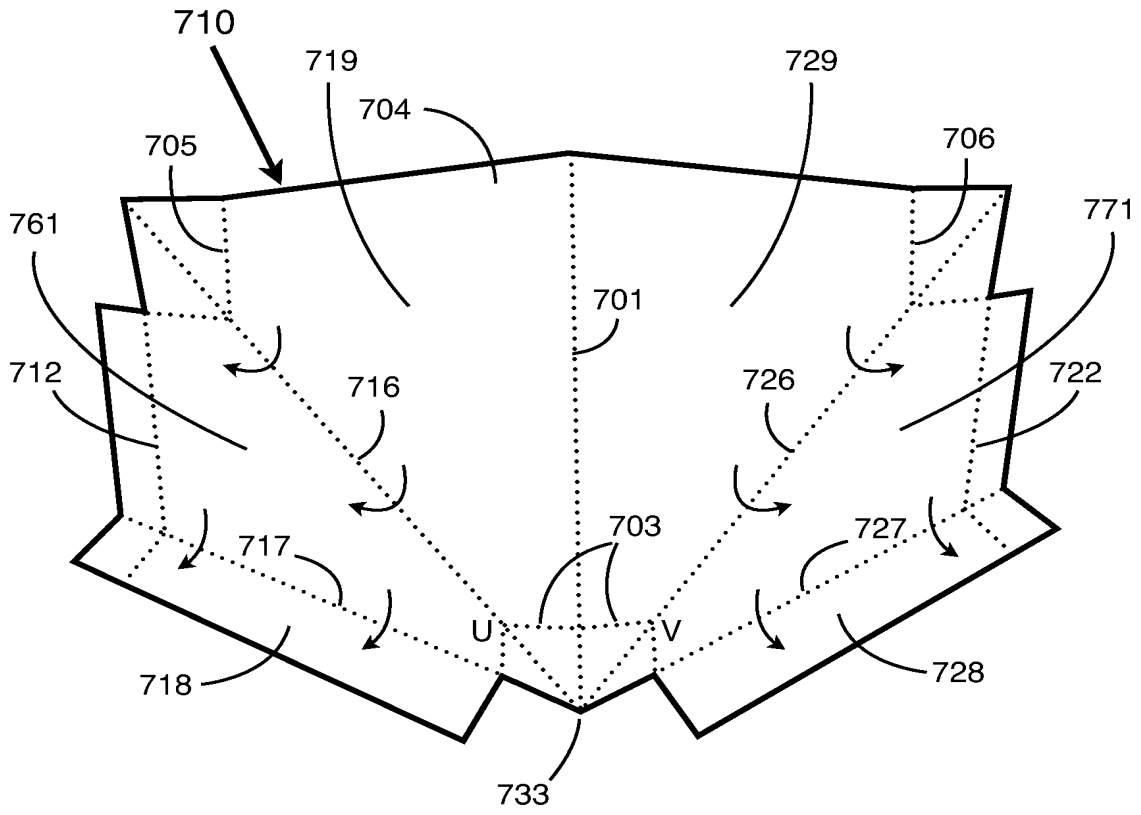
Figure 7A



LEGEND

- Visible free (cut) edge of membrane piece
- Visible edge of folded structure
- Line of fold / crease
- Hidden (phantom) edges of folded structure
- Line of cut

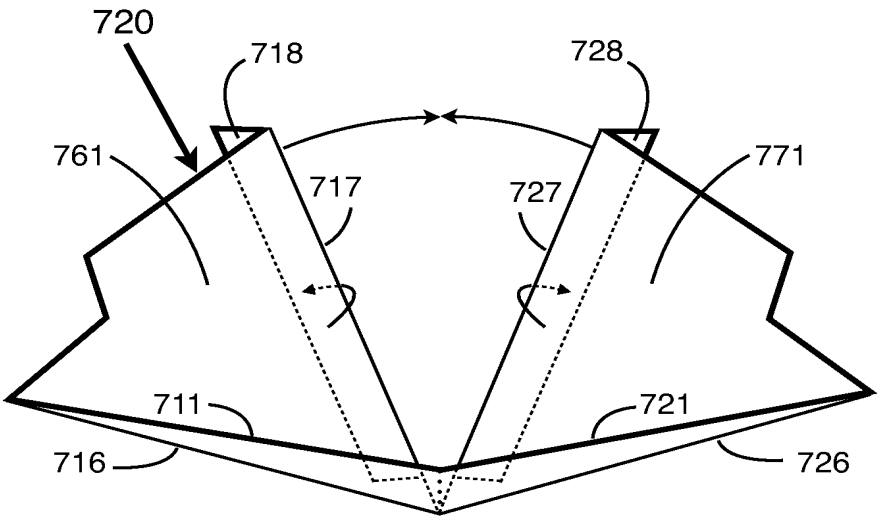
Figure 7B



LEGEND

———	Visible free (cut) edge of membrane piece
———	Visible edge of folded structure
·····	Line of fold / crease
- - - - -	Hidden (phantom) edges of folded structure
- - - - -	Line of cut

Figure 7C



LEGEND

———	Visible free (cut) edge of membrane piece
———	Visible edge of folded structure
.....	Line of fold / crease
-----	Hidden (phantom) edges of folded structure
- - - - -	Line of cut

Figure 7D

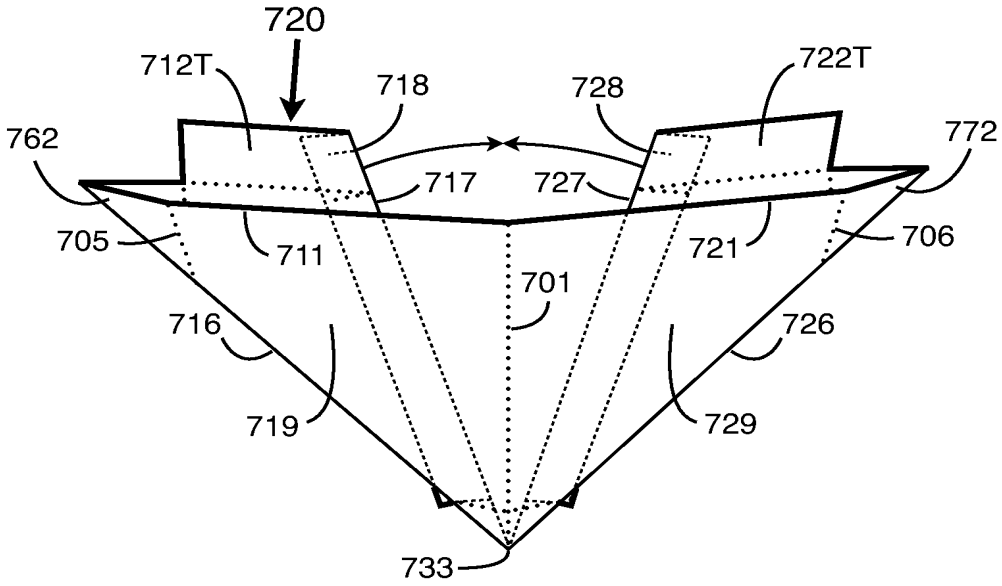
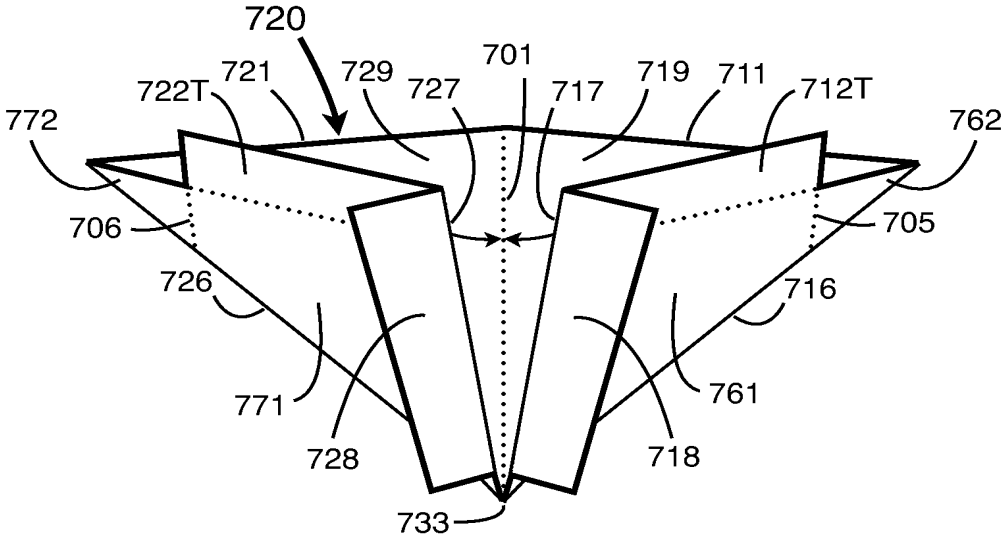


Figure 7E



LEGEND

———	Visible free (cut) edge of membrane piece
———	Visible edge of folded structure
·····	Line of fold / crease
- - - - -	Hidden (phantom) edges of folded structure
- - - - - - -	Line of cut

Figure 7F

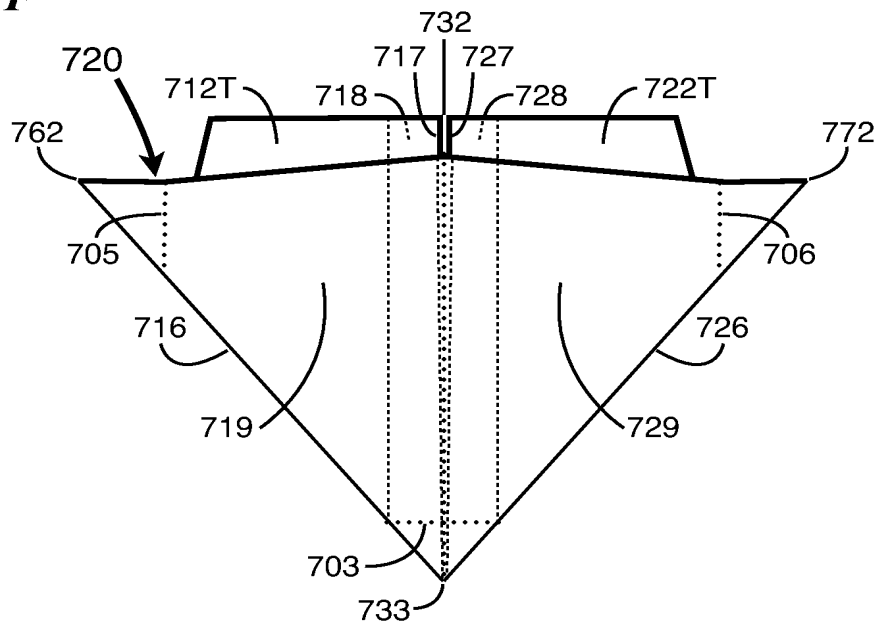
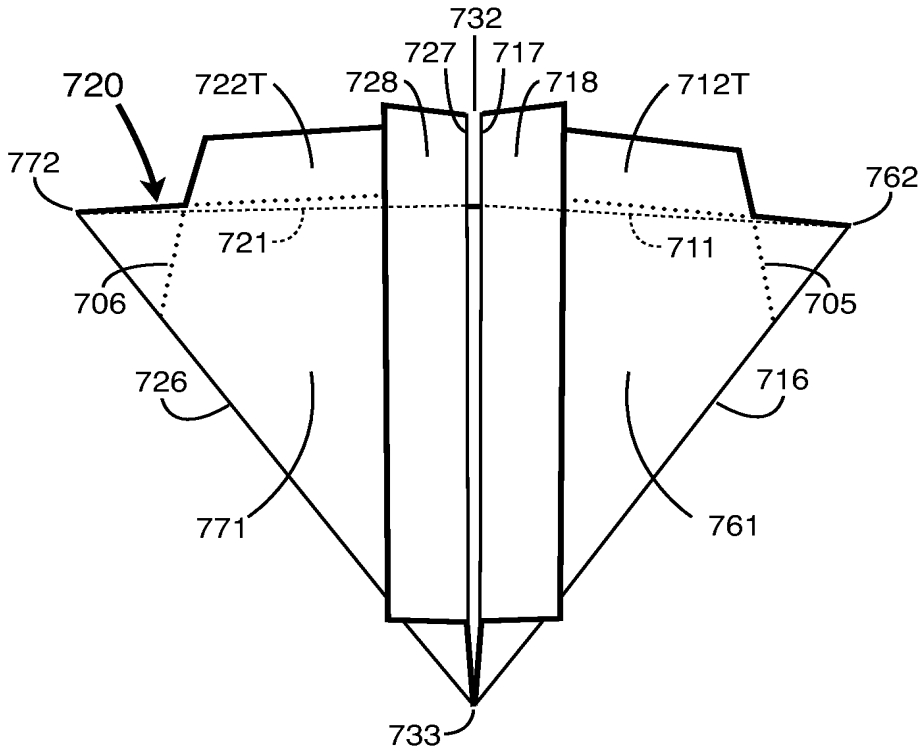


Figure 7G



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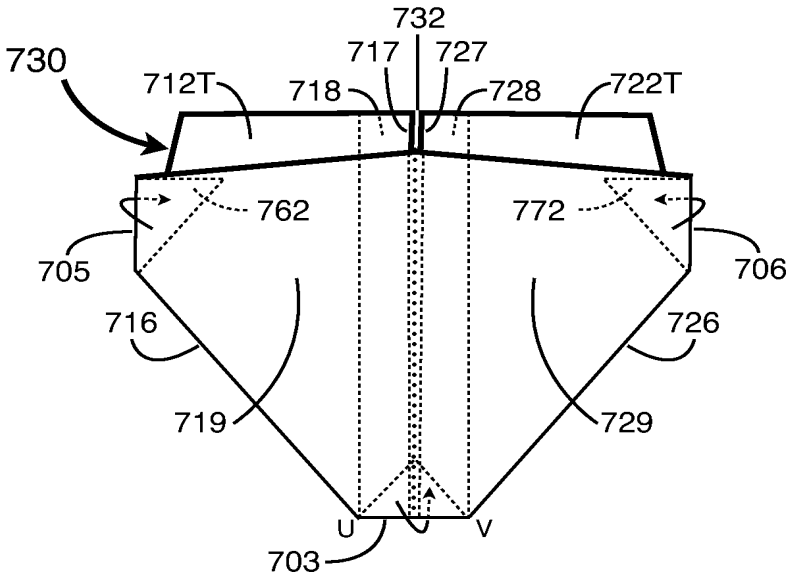


Figure 7I

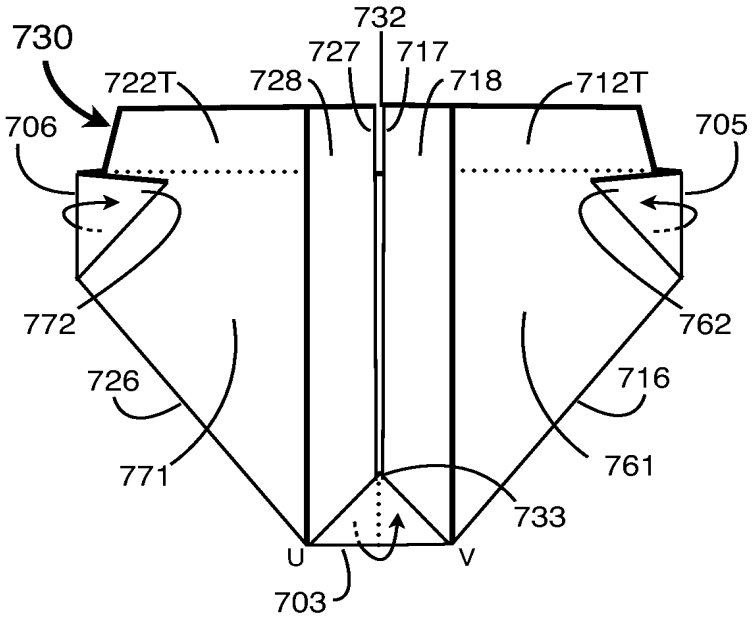
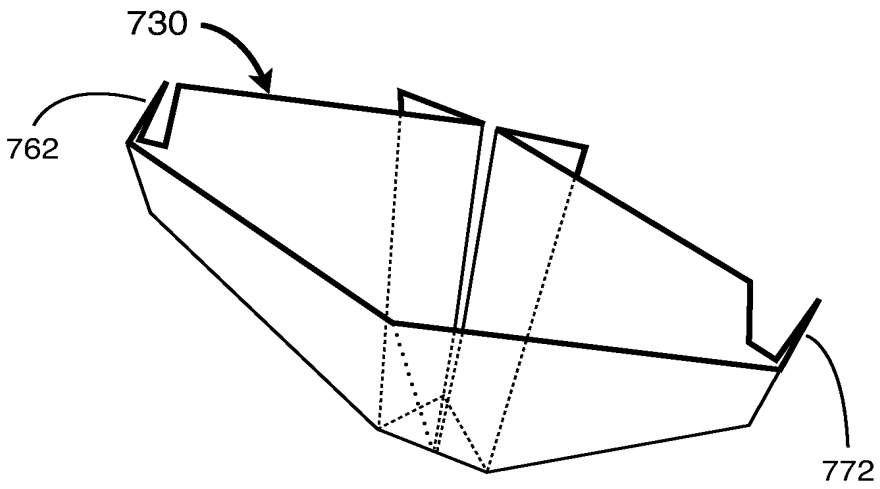


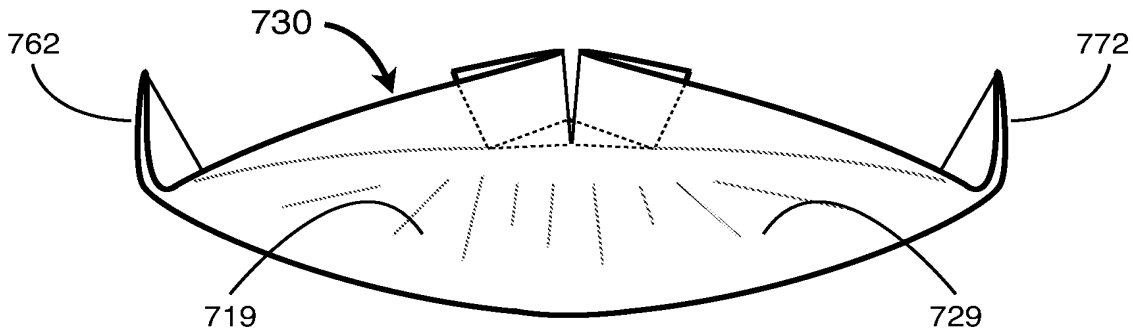
Figure 7J



LEGEND

———	Visible free (cut) edge of membrane piece
———	Visible edge of folded structure
.....	Line of fold / crease
- - - - -	Hidden (phantom) edges of folded structure
- - - - - -	Line of cut

Figure 7K



LEGEND

———	Visible free (cut) edge of membrane piece
———	Visible edge of folded structure
.....	Line of fold / crease
-----	Hidden (phantom) edges of folded structure
- - - - - -	Line of cut

Figure 8A

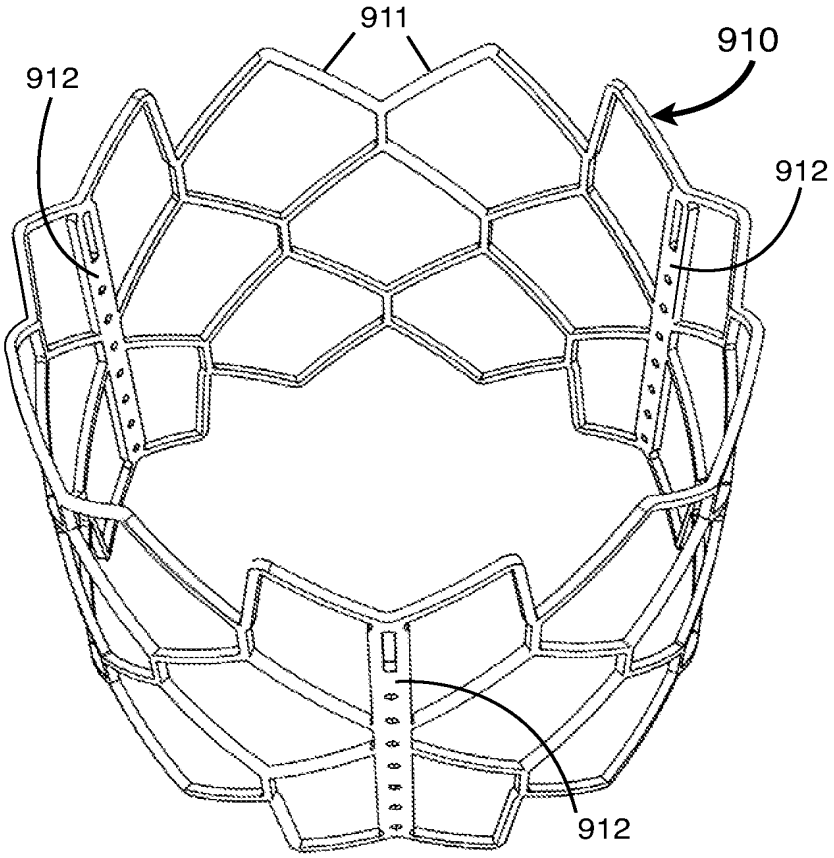


Figure 8B

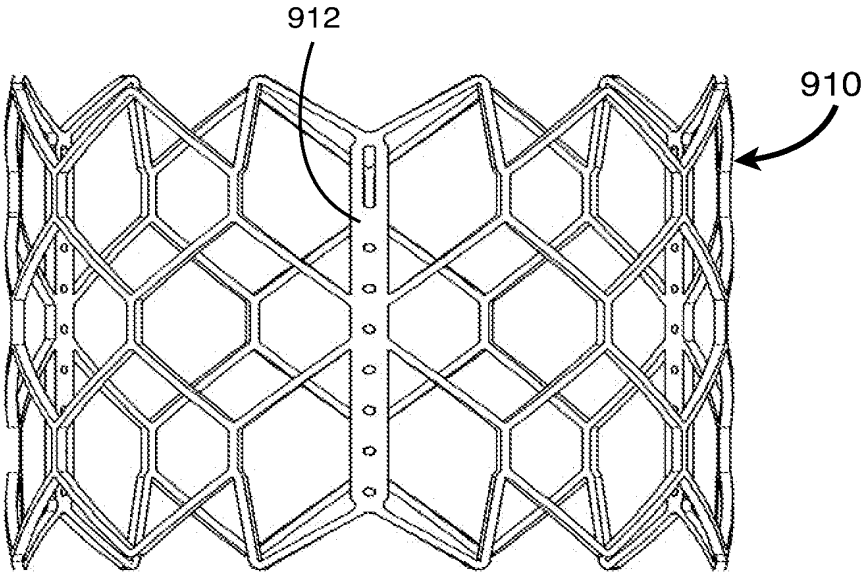
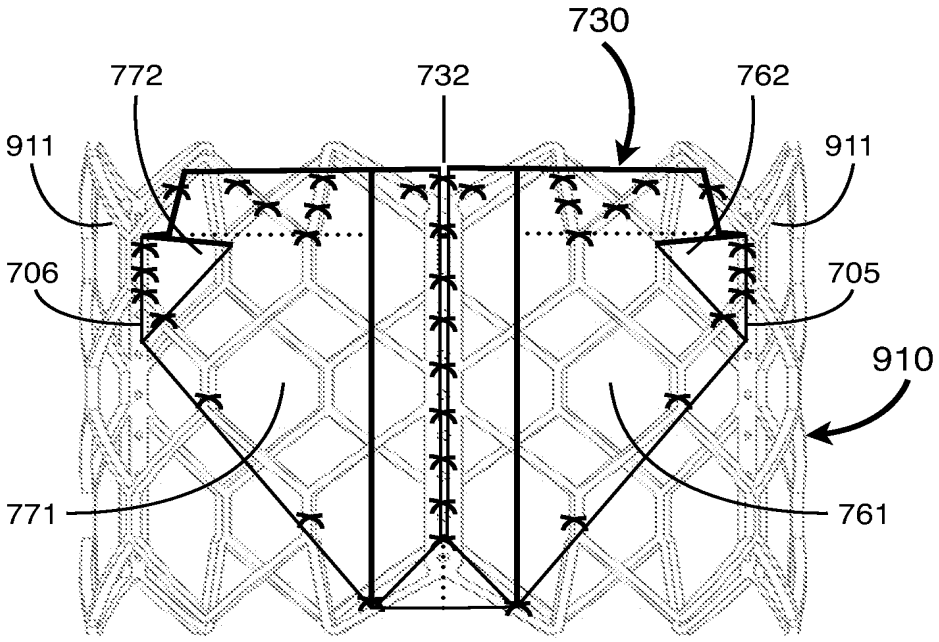


Figure 8C



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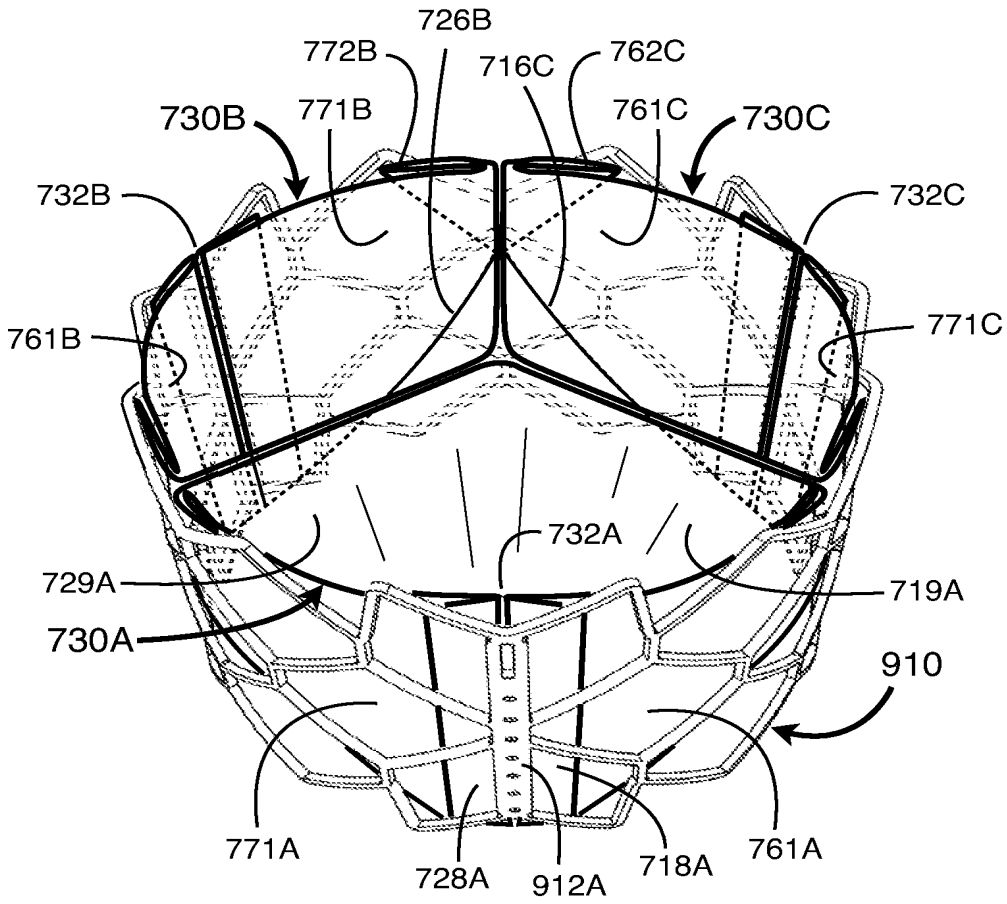
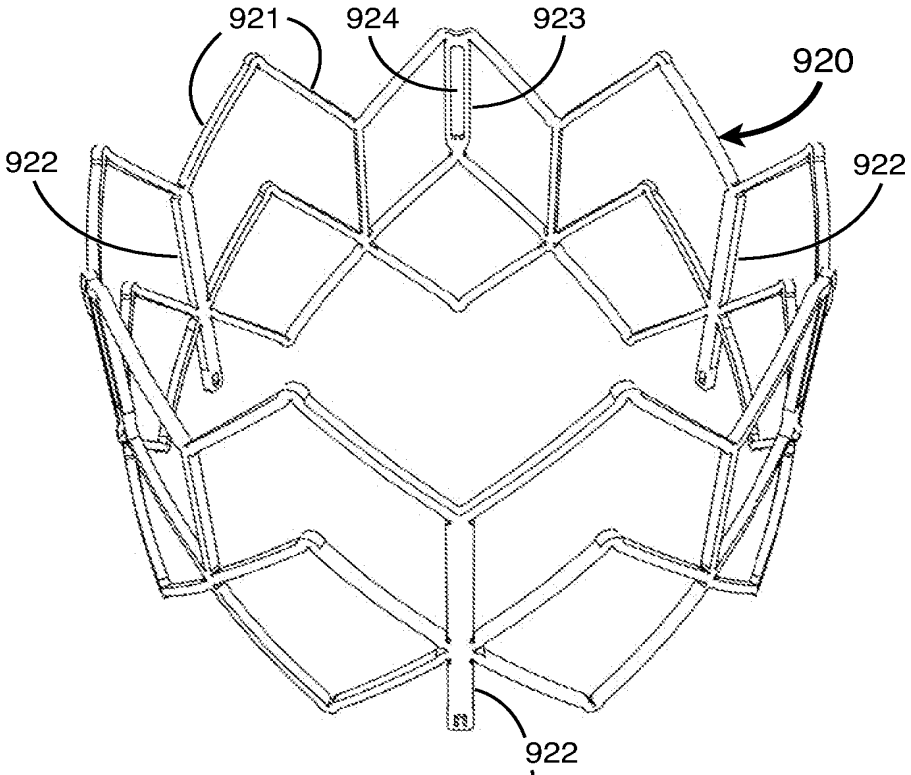


Suture attachments omitted for clarity

Figure 9A



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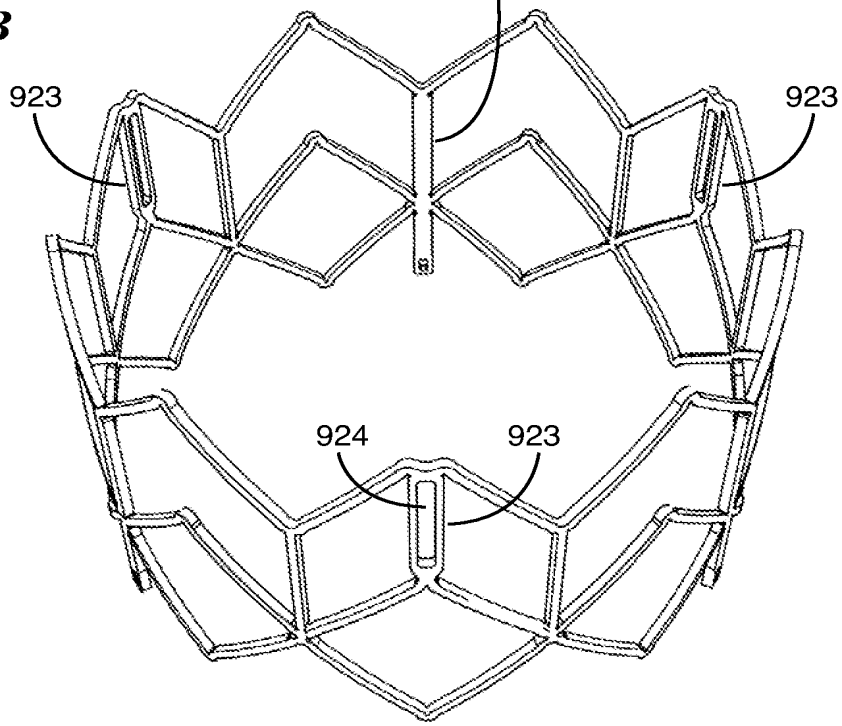
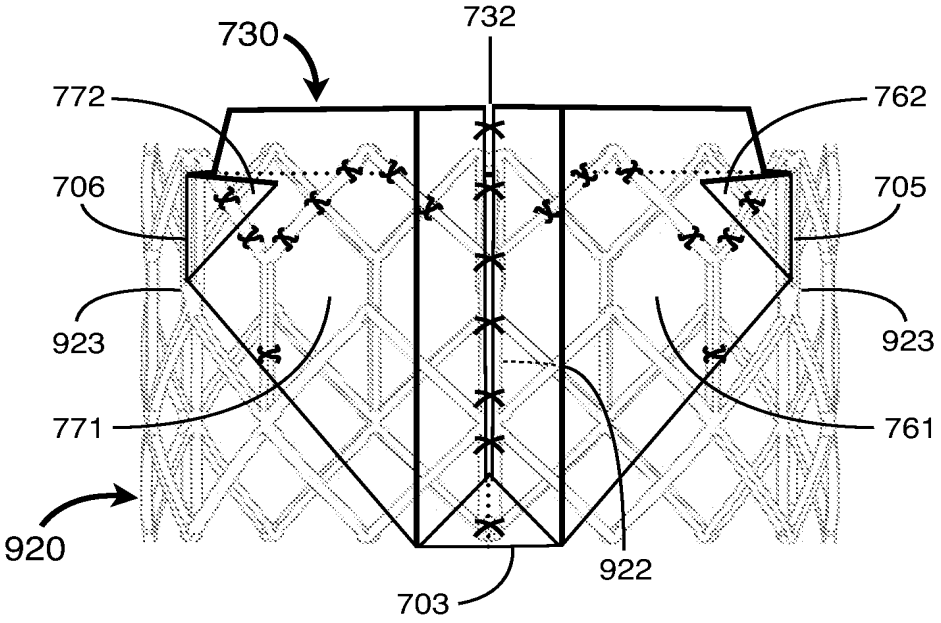


Figure 9C



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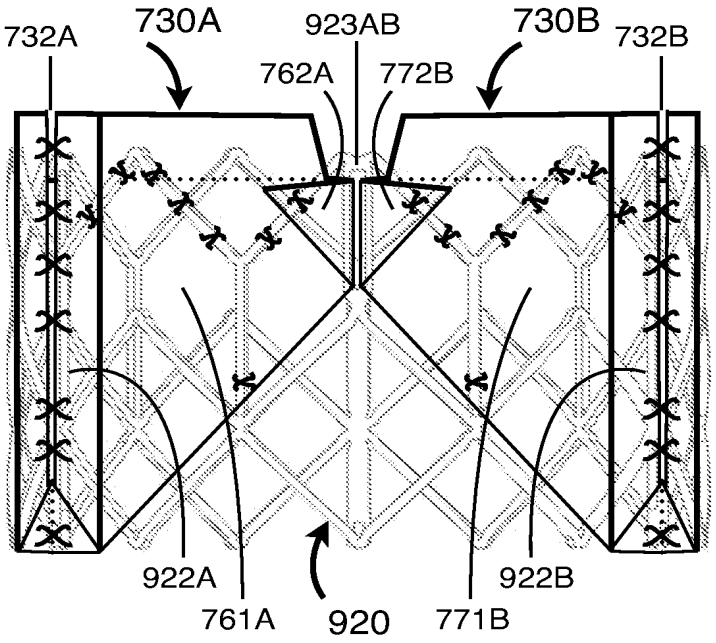
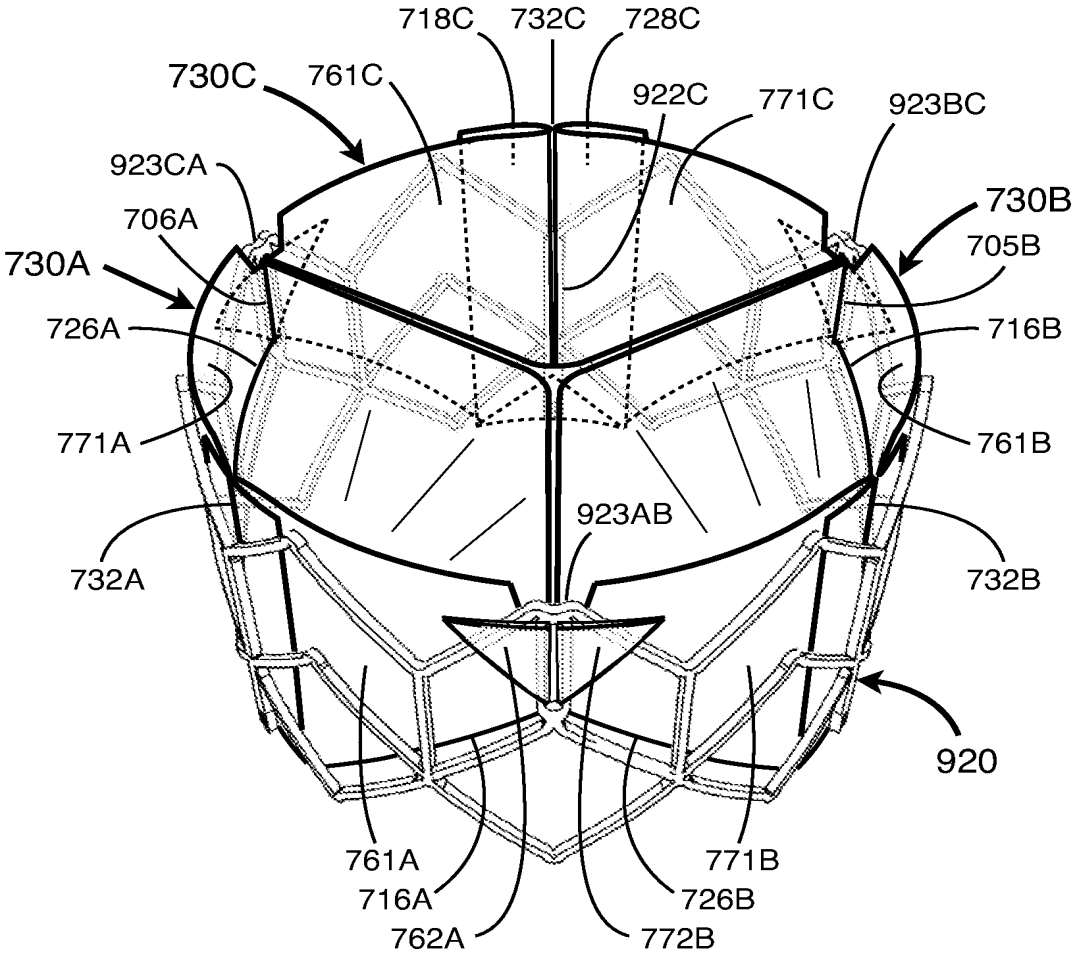


Figure 9E



Suture attachments omitted for clarity

Electronic Acknowledgement Receipt

EFS ID:	16893403
Application Number:	13675665
International Application Number:	
Confirmation Number:	1995
Title of Invention:	PERCUTANEOUSLY IMPLANTABLE REPLACEMENT HEART VALVE DEVICE AND METHOD OF MAKING SAME
First Named Inventor/Applicant Name:	David Paniagua
Customer Number:	29880
Filer:	Mark Lauren Yaskanin/Carol Donahue
Filer Authorized By:	Mark Lauren Yaskanin
Attorney Docket Number:	109978.10101
Receipt Date:	23-SEP-2013
Filing Date:	13-NOV-2012
Time Stamp:	16:22:12
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	no

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New Applications Under 35 U.S.C. 111

If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

National Stage of an International Application under 35 U.S.C. 371

If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office

If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

Electronic Acknowledgement Receipt

EFS ID:	16893738
Application Number:	13675665
International Application Number:	
Confirmation Number:	1995
Title of Invention:	PERCUTANEOUSLY IMPLANTABLE REPLACEMENT HEART VALVE DEVICE AND METHOD OF MAKING SAME
First Named Inventor/Applicant Name:	David Paniagua
Customer Number:	29880
Filer:	Mark Lauren Yaskanin/Carol Donahue
Filer Authorized By:	Mark Lauren Yaskanin
Attorney Docket Number:	109978.10101
Receipt Date:	23-SEP-2013
Filing Date:	13-NOV-2012
Time Stamp:	16:24:53
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	no

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Non Patent Literature	HUFNAGEL_In_The_Beginning_Surgical_Correction.PDF	2912346 f930646f4f11f982b64d1b7c802bd2fd28c280c5	no	2
Warnings:					
Information:					

2	Non Patent Literature	HUFNAGEL_Late_Follow-up_ARTICLE.PDF	2603453 ec63db0d8c53130e6491c126a313f65853ee3579	no	10
Warnings:					
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3	Non Patent Literature	HUFNAGEL_Surgical_Correction_ARTICLE.PDF	13046267 3b9e3c15930877d2e2732e02c0c88b8ce4d40ce7	no	11
Warnings:					
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4	Non Patent Literature	Hufnagel_Vessels_and_Valves.PDF	1988054 ad47ed6f9b9d4b844cd80820b663cdf7b823be74	no	15
Warnings:					
Information:					
5	Non Patent Literature	Introduction_to_Stereomicroscopy.PDF	1264551 c5090da82548abcf3be66d126936b55eddc2214d	no	14
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6	Non Patent Literature	IOPatch_Tutoplact_Description.PDF	148782 3770718a1f2231e34d7d789f8ef34ab3dd88fd8a	no	2
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Information:					
7	Non Patent Literature	Knudsen_catheter-implanted.PDF	8219060 ca8b200b129c12a44cb5460a5851c542bd241a47	no	10
Warnings:					
Information:					
8	Non Patent Literature	Lax_Estimation_of_Ejection_Fraction.PDF	465199 3dc7e34ea659168378c5229ac44957bc9c21e4de	no	8
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Information:					
9	Non Patent Literature	Liao_Molecular_Orientation_ARTICLE.PDF	654708 ea622a62d87b5faf1dc5e5b2a3fe09df2145079d	no	10
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Information:					
10	Non Patent Literature	Liao_Two-dimensional_mechanical.PDF	216352 b348140fc6c53d8cbab7f78df6753ef311e72ba9	no	3
Warnings:					
Information:					

11	Non Patent Literature	Yu_New_Polyurethane_Valves.PDF	8941586 758c058c11671afd5929b70f47c8ac9e63171415	no	7
Warnings:					
Information:					
12	Non Patent Literature	Mirnajafi_The_Effects_of_Collagen_Fiber_ARTICLE.PDF	356222 d09d6fc75240a18c54c294f815e2b7a8e449b7eb	no	10
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13	Non Patent Literature	Mirzaie_A_New_Storage_Solution.PDF	4664571 b75369b4cce58ddfc464a681473750f5c4c6f596	no	8
Warnings:					
Information:					
14	Non Patent Literature	Moazami_Transluminal_Aortic_Valve.PDF	388780 eceb0d75974b1f7ceacdc3f4d0ffdf05dba5cc75	no	5
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15	Non Patent Literature	Nienaber_Nonsurgical_Reconstruction.PDF	159419 278d7a3bcdec3d53b2a1531c31e3a2cc5e3b0eae	no	7
Warnings:					
Information:					
16	Non Patent Literature	Noorlander_Quantitative_Method.PDF	685471 0113df2fae6c4bef20a4ca0d41a9b935af4fa7e1	no	6
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17	Non Patent Literature	Nunn_Structural_Failure.PDF	455905 fae81b3dbe91e1def2e6254d7bd477cf1501051d	no	9
Warnings:					
Information:					
18	Non Patent Literature	Optical_Microscope_Wilipedia.PDF	753293 dbf282ac3626a46bd9134797fa7c10d14dbf2edb	no	9
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Information:					
19	Non Patent Literature	Orthogonality_Wikipedia.PDF	303738 5e60b7beef40f21b1cbb6d5d57897ac69576ad80	no	5
Warnings:					
Information:					

20	Non Patent Literature	Paniagua_Percutaneous_Heart_Valve_Chronic_In_Vitro_Testing_Model.PDF	207888 0d707e39d7d5b43a6349b4ca066f8b70d65a9139	no	3
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21	Non Patent Literature	Paniagua_First_Human_Case.PDF	672008 9789a295ded2878c0c7302016ae722bb1a7314f9	no	6
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Information:					
22	Non Patent Literature	Paniagua_Percutaneous_Implantation_Amer_Heart_Assoc_2009.PDF	73221 bf2806f21f232a3294912a45ad33701789b288d8	no	2
Warnings:					
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23	Non Patent Literature	Pathak_Treatment_of_Bioprosthetic_Heart.PDF	209469 902ff931f93e7ab58ac7cdc437497d005339e008	no	5
Warnings:					
Information:					
24	Non Patent Literature	Pavenik_Development_and_Init_Experimental.PDF	488049 1ea2e4de27d43722ad1c6ee6e28497943ac9e59a	no	4
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Information:					
25	Non Patent Literature	Pick_blog.PDF	310856 86a845a7f2080703f7c385eaaa5486b773205637	no	4
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Information:					
26	Non Patent Literature	Pohl_In_Vitro_Testing.PDF	7954857 602e8becafcece58fe6f018a62f44a81872aa787	no	10
Warnings:					
Information:					
27	Non Patent Literature	Purinya_Biomechanical_and_Structural_Properties_ARTICLE.PDF	9033310 34aac3a58f859b89ab2505a0489222a61754299d	no	13
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28	Non Patent Literature	Sacks_Collagen_Fiber_Architecture_Bovine_ARTICLE.PDF	3761051 d5119914f47d53a9c34858576778a44e30e20548	no	6
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29	Non Patent Literature	Sacks_Small_Angle_Light_Scattering_ARTICLE.PDF	3345039 9495edf3aa353514978a28f514f45a073d734f7d	no	12
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30	Non Patent Literature	Sacks_Experimentally-Derived_Fiber_Orientation.PDF	215108 4a1341505cd9ca7fc67a01b8f0ce670140a61ccd	no	8
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31	Non Patent Literature	Sacks_Quantification_of_FIber_Architecture.PDF	471676 b05631f1bd34303fd453c8a24ec6a296c8fd4cef	no	10
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32	Non Patent Literature	Samouillan_Comparison_of_Chemical_Treatments.PDF	664621 8d558e2571de81927599cae4fc48dccb952c6598	no	9
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33	Non Patent Literature	Schoen_Tissue_heart_valves.PDF	2069247 d9a1b496e3eb0d61558e84906fc402190a9158e1	no	27
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34	Non Patent Literature	Sellaro_Effects_of_Collagen_Fiber_Medium_term_Fatigue.PDF	1073715 cd287a8777b23026c4a7be5a5777467a974dc692	no	12
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35	Non Patent Literature	Sellaro_Effects_of_Collagen_Fiber.PDF	4016322 1b0154df51d6b35c01174b4e32a1c80a2ce71ce6	no	93
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36	Non Patent Literature	Shandas_Method_for_Determining.PDF	618161 a9868be0708de5efc8515492c3281a8649ba164d	no	8
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37	Non Patent Literature	Shen_Effect_of_Ethanol_and_Ether.PDF	121067 d574ba13fcd303eea8cbba5d95977defdacb2c3c	no	4
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Information:					

38	Non Patent Literature	Shen_Protein_adsorption.PDF	242606 2b5fa6df708fe69b690844cc07eb391e74b66a91	no	4
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39	Non Patent Literature	Simionescu_Mapping_Glutaraldehyde-treated_ARTICLE.PDF	12862309 46f0ddd8d9e9a9dcf7c4c0d5534d96a246963cb4	no	8
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40	Non Patent Literature	Sun_Response_of_heterograft.PDF	378209 0ee8524826d07372cd39b222a4becefefdc5b28a	no	12
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41	Non Patent Literature	Topol_Textbook_of_Interventional_Cardiology.PDF	4225303 511d60021cec8bae1413a3eaca66792d91c043bc	no	40
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Information:					
42	Non Patent Literature	Vyavahare_Mechanics_of_Bioprosthetic.PDF	603983 d9140785f6c37c4ebc0c6c67ddddc5b833f9dce5	no	7
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43	Non Patent Literature	Vyavahare_Prevention_of_Glutaraldehyde-Fixed.PDF	1056189 68ce64403862d585c8638804460a3994147fe882	no	6
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44	Non Patent Literature	Wiegner_Mechanical_and_structural_Correlates.PDF	2297229 96e7a6cc92ff1c1b3608d71dbf41f07420727836	no	9
Warnings:					
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45	Non Patent Literature	Yasui_Determination_Collagen_Fiber_Orientation.PDF	725024 3eab612e51d5d59166ecb0dd25c2475a7750b877	no	7
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46	Non Patent Literature	Zioupos_Anisotropic_Elasticity.PDF	15680386 f08432932351a38c9e402937644f10ff8ac832cc	no	9
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47	Non Patent Literature	Zioupos_Mechanical_Optical_Anisotropy_ARTICLE.PDF	1726194 bffabe81bf8ec916e9e9564a18b972c126949fd8	no	7
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48	Non Patent Literature	10100_US_10-887688_Office_Action_2007-11-28.pdf	298533 4e1a45e526a9809e3b1daa5b288452b8fef6e39a	no	7
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49	Non Patent Literature	10100_US_10-887688_Final_Office_Action_2008-07-15.pdf	300122 42d0ed78e24f18c3aceff2930efc6c1a247da450	no	8
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50	Non Patent Literature	10100_US_10-887688_Office_Action_2009-03-16.pdf	466502 46114e18c58b1e61a58e34408e03bd083204767b	no	12
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51	Non Patent Literature	10100_US_10-887688_Examiner_Interview_Summary_2009-06-12.pdf	176346 7b6caf69e2177226a6a149d3a9451e4825355a3a	no	4
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52	Non Patent Literature	10100_US_10-887688_Final_Office_Action_2010-03-02.pdf	633907 daae3008a0a10457e705d8fc6b2dd604c0bd5a69	no	15
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53	Non Patent Literature	10100_US_10-887688_Declaration_of_Inventors_2009-09-14.pdf	5008347 c391469d79fd4897bdd9a67dfad10d4ee0482c1e	no	128
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54	Non Patent Literature	10100_US_10-887688_Declaration_of_Inventors_2008-02-28.pdf	3870953 657ad588a4b50407c16834948af838827e65db3b	no	85
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55	Non Patent Literature	10100_US_10-887688_Declaration_of_Inventors_2008-12-15.pdf	1899083 359d55c2c06023369ab2c36187e7f03b2a9d5982	no	46
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56	Non Patent Literature	10100_US_10-887688_Examiner_Interview_Summary_2010-07-26.pdf	187781 3287a1e03afacd01db7c7c1bfd60e9db8223977f	no	4
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57	Non Patent Literature	10100_US_10-887688_Office_Action_2012-02-16.pdf	385115 edd156e8dd690f32a2d5eaf862602e7b5972d9c2	no	10
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58	Non Patent Literature	10110_US_12-228192_Office_Action_2010-09-29.pdf	303920 70c49a9433dd0acbff8507779bf833421e8acdb1	no	9
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59	Non Patent Literature	10110_US_12-228192_Examiner_Interview_Summary_2011-04-05.pdf	161803 8cd2ca6493510b177d8cfa48b7db348f7fb1ef65	no	3
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60	Non Patent Literature	10110_US_12-228192_Final_Office_Action_2011-07-14.pdf	12085622 48467f8222486a3724a21d8328047ae8fd63e4b7	no	14
Warnings:					
Information:					
		Total Files Size (in bytes):	149108888		

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New International Application Filed with the USPTO as a Receiving Office

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PATENT APPLICATION FEE DETERMINATION RECORD

Substitute for Form PTO-875

Application or Docket Number: 13/675,665

APPLICATION AS FILED - PART I

FOR	(Column 1) NUMBER FILED	(Column 2) NUMBER EXTRA	SMALL ENTITY RATE($)	SMALL ENTITY FEE($)	OR	OTHER THAN SMALL ENTITY RATE($)	OTHER THAN SMALL ENTITY FEE($)
BASIC FEE (37 CFR 1.16(a), (b), or (c))	N/A	N/A	N/A	70		N/A	
SEARCH FEE (37 CFR 1.16(k), (i), or (m))	N/A	N/A	N/A	300		N/A	
EXAMINATION FEE (37 CFR 1.16(o), (p), or (q))	N/A	N/A	N/A	360		N/A	
TOTAL CLAIMS (37 CFR 1.16(i))	14 minus 20 =	*	x 40 =	0.00	OR		
INDEPENDENT CLAIMS (37 CFR 1.16(h))	3 minus 3 =	*	x 210 =	0.00			
APPLICATION SIZE FEE (37 CFR 1.16(s))	If the specification and drawings exceed 100 sheets of paper, the application size fee due is $310 ($155 for small entity) for each additional 50 sheets or fraction thereof. See 35 U.S.C. 41(a)(1)(G) and 37 CFR 1.16(s).			0.00			
MULTIPLE DEPENDENT CLAIM PRESENT (37 CFR 1.16(j))				0.00			
* If the difference in column 1 is less than zero, enter "0" in column 2.			TOTAL	730		TOTAL	

APPLICATION AS AMENDED - PART II

		(Column 1) CLAIMS REMAINING AFTER AMENDMENT		(Column 2) HIGHEST NUMBER PREVIOUSLY PAID FOR	(Column 3) PRESENT EXTRA	SMALL ENTITY RATE($)	SMALL ENTITY ADDITIONAL FEE($)	OR	OTHER THAN SMALL ENTITY RATE($)	OTHER THAN SMALL ENTITY ADDITIONAL FEE($)
AMENDMENT A	Total (37 CFR 1.16(i))	*	Minus	**	=	x =		OR	x =	
	Independent (37 CFR 1.16(h))	*	Minus	***	=	x =		OR	x =	
	Application Size Fee (37 CFR 1.16(s))									
	FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))							OR		
						TOTAL ADD'L FEE		OR	TOTAL ADD'L FEE	

		(Column 1) CLAIMS REMAINING AFTER AMENDMENT		(Column 2) HIGHEST NUMBER PREVIOUSLY PAID FOR	(Column 3) PRESENT EXTRA	RATE($)	ADDITIONAL FEE($)		RATE($)	ADDITIONAL FEE($)
AMENDMENT B	Total (37 CFR 1.16(i))	*	Minus	**	=	x =		OR	x =	
	Independent (37 CFR 1.16(h))	*	Minus	***	=	x =		OR	x =	
	Application Size Fee (37 CFR 1.16(s))									
	FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))							OR		
						TOTAL ADD'L FEE		OR	TOTAL ADD'L FEE	

* If the entry in column 1 is less than the entry in column 2, write "0" in column 3.
** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 20, enter "20".
*** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 3, enter "3".
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APPLICATION NUMBER	FILING OR 371(C) DATE	FIRST NAMED APPLICANT	ATTY. DOCKET NO./TITLE
13/675,665		David Paniagua	109978.10101

CONFIRMATION NO. 1995

29880
FOX ROTHSCHILD LLP
PRINCETON PIKE CORPORATE CENTER
997 LENOX DRIVE
BLDG. #3
LAWRENCEVILLE, NJ 08648

WITHDRAWAL NOTICE

OC000000063948807

Date Mailed: 09/26/2013

Letter Regarding a New Notice and/or the Status of the Application

If a new notice or Filing Receipt is enclosed, applicant may disregard the previous notice mailed on 07/19/2013. The time period for reply runs from the mail date of the new notice. Within the time period for reply, applicant is required to file a reply in compliance with the requirements set forth in the new notice to avoid abandonment of the application.

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/ktesfaye/

Office of Data Management, Application Assistance Unit (571) 272-4000, or (571) 272-4200, or 1-888-786-0101

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APPLICATION NUMBER	FILING or 371(c) DATE	GRP ART UNIT	FIL FEE REC'D	ATTY.DOCKET.NO	TOT CLAIMS	IND CLAIMS
13/675,665	11/13/2012	3738	800	109978.10101	14	3

CONFIRMATION NO. 1995

UPDATED FILING RECEIPT

29880
FOX ROTHSCHILD LLP
PRINCETON PIKE CORPORATE CENTER
997 LENOX DRIVE
BLDG. #3
LAWRENCEVILLE, NJ 08648

OC000000063948880

Date Mailed: 09/26/2013

Receipt is acknowledged of this non-provisional patent application. The application will be taken up for examination in due course. Applicant will be notified as to the results of the examination. Any correspondence concerning the application must include the following identification information: the U.S. APPLICATION NUMBER, FILING DATE, NAME OF APPLICANT, and TITLE OF INVENTION. Fees transmitted by check or draft are subject to collection. Please verify the accuracy of the data presented on this receipt. **If an error is noted on this Filing Receipt, please submit a written request for a Filing Receipt Correction. Please provide a copy of this Filing Receipt with the changes noted thereon. If you received a "Notice to File Missing Parts" for this application, please submit any corrections to this Filing Receipt with your reply to the Notice. When the USPTO processes the reply to the Notice, the USPTO will generate another Filing Receipt incorporating the requested corrections**

Inventor(s)

David Paniagua, Houston, TX;
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Carlos Meija, Houston, TX;
Fransisco Lopez-Jimenez, Rochester, MN;

Applicant(s)

COLIBRI HEART VALVE LLC, Broomfield, CO

Power of Attorney: None

Domestic Priority data as claimed by applicant

This application is a CON of 10/887,688 07/10/2004 PAT 8308797 *
which is a CIP of 10/037,266 01/04/2002 ABN
(*)Data provided by applicant is not consistent with PTO records.

Foreign Applications for which priority is claimed (You may be eligible to benefit from the **Patent Prosecution Highway** program at the USPTO. Please see http://www.uspto.gov for more information.) - None.
Foreign application information must be provided in an Application Data Sheet in order to constitute a claim to foreign priority. See 37 CFR 1.55 and 1.76.

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The country code and number of your priority application, to be used for filing abroad under the Paris Convention, is **US 13/675,665**

Projected Publication Date: 01/02/2014

Non-Publication Request: No

Early Publication Request: No
**** SMALL ENTITY ****
Title

PERCUTANEOUSLY IMPLANTABLE REPLACEMENT HEART VALVE DEVICE AND METHOD OF MAKING SAME

Preliminary Class

623

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PTO/AIA/80 (07-12)
Approved for use through 11/30/2014. OMB 0651-0035
U.S. Patent and Trademark Office; U.S DEPARTMENT OF COMMERCE

POWER OF ATTORNEY TO PROSECUTE APPLICATIONS BEFORE THE USPTO

I hereby revoke all previous powers of attorney given in the application identified in the attached statement under 37 CFR 3.73(c).

I hereby appoint:

■ Practitioners associated with Customer Number: 29880

OR

☐ Practitioner(s) named below (if more than ten patent practitioners are to be named, then a customer number must be used):

Name	Registration Number	Name	Registration Number

As attorney(s) or agent(s) to represent the undersigned before the United States Patent and Trademark Office (USPTO) in connection with any and all patent applications assigned only to the undersigned according to the USPTO assignment records or assignments documents attached to this form in accordance with 37 CFR 3.73(c).

Please change the correspondence address for the application identified in the attached statement under 37 CFR 3.73(c) to:

■ The address associated with Customer Number: 29880

OR

☐	Firm or Individual Name		
	Address		
	City	State	Zip
	Country		
	Telephone	Email	

Assignee Name and Address: Colibri Heart Valve LLC
2150 W. 6th Ave., Suite M
Broomfield, Colorado 80020

A copy of this form, together with a statement under 37 CFR 3.73(c) (Form PTO/AIA/96 or equivalent) is required to be Filed in each application in which this form is used. The statement under 37 CFR 3.73(c) may be completed by one of The practitioners appointed in this form, and must identify the application in which this Power of Attorney is to be filed.

SIGNATURE of Assignee of Record
The individual whose signature and title is supplied below is authorized to act on behalf of the assignee

Signature	Joseph B Horn	Date	1-17-2013
Name	Joseph B. Horn	Telephone	303 460 8667
Title	President and CEO for Colibri Heart Valve LLC		

PTO/AIA/96 (08-12)
Approved for use through 01/31/2013. OMB 0651-0031
U.S. Patent and Trademark Office;U.S. DEPARTMENT OF COMMERCE

STATEMENT UNDER 37 CFR 3.73(c)

Applicant/Patent Owner: Colibri Heart Valve LLC

Application No./Patent No.: 13/675,665 Filed/Issue Date: November 13, 2012

Titled: Percutaneously Implantable Replacement Heart Valve Device and Method of Making Same

Colibri Heart Valve LLC, a limited liability company

(Name of Assignee) (Type of Assignee, e.g., corporation, partnership, university, government agency, etc.)

states that, for the patent application/patent identified above, it is (choose **one** of options 1, 2, 3 or 4 below):

1. ☑ The assignee of the entire right, title, and interest.

2. ☐ An assignee of less than the entire right, title, and interest (check applicable box):

   ☐ The extent (by percentage) of its ownership interest is _____%. Additional Statement(s) by the owners holding the balance of the interest must be submitted to account for 100% of the ownership interest.

   ☐ There are unspecified percentages of ownership. The other parties, including inventors, who together own the entire right, title and interest are:

   Additional Statement(s) by the owner(s) holding the balance of the interest must be submitted to account for the entire right, title, and interest.

3. ☐ The assignee of an undivided interest in the entirety (a complete assignment from one of the joint inventors was made). The other parties, including inventors, who together own the entire right, title, and interest are:

   Additional Statement(s) by the owner(s) holding the balance of the interest must be submitted to account for the entire right, title, and interest.

4. ☐ The recipient, via a court proceeding or the like (*e.g.*, bankruptcy, probate), of an undivided interest in the entirety (a complete transfer of ownership interest was made). The certified document(s) showing the transfer is attached.

The interest identified in option 1, 2 or 3 above (not option 4) is evidenced by either (choose **one** of options A or B below):

A. ☐ An assignment from the inventor(s) of the patent application/patent identified above. The assignment was recorded in the United States Patent and Trademark Office at Reel _____, Frame _____, or for which a copy thereof is attached.

B. ☑ A chain of title from the inventor(s), of the patent application/patent identified above, to the current assignee as follows:

1. From: Inventors Paniagua, Induni, Mejia and Lopez To: Endoluminal Technology Research, LLC

   The document was recorded in the United States Patent and Trademark Office at
   Reel 031280, Frame 0839, or for which a copy thereof is attached.

2. From: Endoluminal Technology Research, LLC To: Endoluminal Technology LLC

   The document was recorded in the United States Patent and Trademark Office at
   Reel 031280, Frame 0877, or for which a copy thereof is attached.

PTO/AIA/96 (08-12)
Approved for use through 01/31/2013. OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

STATEMENT UNDER 37 CFR 3.73(c)

3. From: Inventor R. David Fish To: Endoluminal Technology LLC

The document was recorded in the United States Patent and Trademark Office at
Reel 031280, Frame 0917, or for which a copy thereof is attached.

4. From: Endoluminal Technology LLC To: Vela Biosystems LLC

The document was recorded in the United States Patent and Trademark Office at
Reel 031280, Frame 0930, or for which a copy thereof is attached.

5. From: Vela Biosystems LLC To: R. David Fish and David Paniagua

The document was recorded in the United States Patent and Trademark Office at
Reel 031280, Frame 0942, or for which a copy thereof is attached.

6. From: R. David Fish and David Paniagua To: Colibri Heart Valve LLC

The document was recorded in the United States Patent and Trademark Office at
Reel 031280, Frame 0946, or for which a copy thereof is attached.

☐ Additional documents in the chain of title are listed on a supplemental sheet(s).

☑ As required by 37 CFR 3.73(c)(1)(i), the documentary evidence of the chain of title from the original owner to the assignee was, or concurrently is being, submitted for recordation pursuant to 37 CFR 3.11.

[NOTE: A separate copy (i.e., a true copy of the original assignment document(s)) must be submitted to Assignment Division in accordance with 37 CFR Part 3, to record the assignment in the records of the USPTO. See MPEP 302.08]

The undersigned (whose title is supplied below) is authorized to act on behalf of the assignee.

/ Mark L. Yaskanin /	2013-09-30
Signature	Date
Mark L. Yaskanin	Reg. No. 45,246
Printed or Typed Name	Title or Registration Number

Privacy Act Statement

The **Privacy Act of 1974 (P.L. 93-579)** requires that yoube given certain informationin connection with your submission of the attached form related to a patent application or patent. Accordingly, pursuant to the requirements of the Act, pleasebe advised that: (1) the general authority forthe collection of thisinformation is 35 U.S.C. 2(b)(2); (2) furnishing of the information solicited is voluntary; and(3) the principal purpose forwhich the information isused by the U.S. Patent and Trademark Office is to process and/or examine your submission related to a patent applicationor patent. If you do not furnish the requested information,the U.S. Patent and Trademark Office may not be able to process and/or examineyour submission,which may result in termination of proceedings or abandonment of the applicationor expiration of the patent.

The informationprovided by you in this form will be subject to the following routine uses:

1. The information on this form will be treated confidentially to the extent allowed under the Freedom of Information Act (5 U.S.C. 552) and the Privacy Act (5 U.S.C 552a). Records from this system of records may be disclosed to the Department of Justice to determine whether disclosure of these records is required by the Freedom of Information Act.
2. A record from this system of records may be disclosed, as a routine use, in the course of presenting evidence to a court, magistrate, or administrative tribunal, including disclosures to opposing counsel in the course of settlement negotiations.
3. A record in this system of records may be disclosed, as a routine use, to a Member of Congress submitting a request involving an individual, to whom the record pertains, when the individual has requested assistance from the Member with respect to the subject matter of the record.
4. A record in this system of records may be disclosed, as a routine use, to a contractor of the Agency having need for the informationin order to perform a contract. Recipients of information shall be required to comply with the requirements of the Privacy Act of 1974, as amended, pursuant to 5 U.S.C. 552a(m).
5. A record related to an InternationalApplication filed under the Patent Cooperation Treaty in this system of records may be disclosed, as a routine use, to the International Bureau of the World Intellectual Property Organization, pursuant to the Patent Cooperation Treaty.
6. A record in this system of records may be disclosed, as a routine use, to another federal agency for purposes of National Security review (35 U.S.C. 181) and for review pursuant to the Atomic Energy Act (42 U.S.C. 218(c)).
7. A record from this system of records may be disclosed, as a routine use, to the Administrator, General Services, or his/her designee, during an inspection of records conducted by GSA as part of that agency's responsibility to recommend improvements in records management practices and programs, under authority of 44 U.S.C. 2904 and 2906. Such disclosure shall be made in accordance with the GSA regulations governing inspection of records for this purpose, and any other relevant (*i.e.*, GSA or Commerce) directive. Such disclosure shall not be used to make determinations about individuals.
8. A record from this system of records may be disclosed, as a routine use, to the public after either publication of the application pursuant to 35 U.S.C. 122(b) or issuance of a patent pursuant to 35 U.S.C. 151. Further, arecord may be disclosed, subject to the limitations of 37 CFR 1.14, as a routine use, to the public if the record was filed in an application which became abandoned or in which the proceedings were terminated and which application is referenced by either a published application, an application open to public inspection or an issued patent.
9. A record from thissystem of records may be disclosed, as a routine use, to a Federal, State, or local law enforcement agency, if the USPTO becomes aware of a violation or potential violation of law or regulation.

Electronic Acknowledgement Receipt

EFS ID:	16998851
Application Number:	13675665
International Application Number:	
Confirmation Number:	1995
Title of Invention:	PERCUTANEOUSLY IMPLANTABLE REPLACEMENT HEART VALVE DEVICE AND METHOD OF MAKING SAME
First Named Inventor/Applicant Name:	David Paniagua
Customer Number:	29880
Filer:	Mark Lauren Yaskanin/Carol Donahue
Filer Authorized By:	Mark Lauren Yaskanin
Attorney Docket Number:	109978.10101
Receipt Date:	30-SEP-2013
Filing Date:	13-NOV-2012
Time Stamp:	17:57:40
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	no

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Power of Attorney	Colibri_10101_POA.pdf	71715 67933793860a8b56e380f0c1746c90bece5e0bd5	no	1

Warnings:	
Information:	

2	Assignee showing of ownership per 37 CFR 3.73.	Colibri_10101_3-73_Statement.pdf	124747 22c8dc939435f1b387101875fdaa05b03ef4f3bb	no	3

Warnings:	
Information:	
Total Files Size (in bytes):	196462

This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

New Applications Under 35 U.S.C. 111

If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

National Stage of an International Application under 35 U.S.C. 371

If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office

If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NUMBER	FILING OR 371(C) DATE	FIRST NAMED APPLICANT	ATTY. DOCKET NO./TITLE
13/675,665	11/13/2012	David Paniagua	109978.10101

CONFIRMATION NO. 1995

POA ACCEPTANCE LETTER

29880
FOX ROTHSCHILD LLP
PRINCETON PIKE CORPORATE CENTER
997 LENOX DRIVE
BLDG. #3
LAWRENCEVILLE, NJ 08648

OC000000064151977

Date Mailed: 10/04/2013

NOTICE OF ACCEPTANCE OF POWER OF ATTORNEY

This is in response to the Power of Attorney filed 09/30/2013.

The Power of Attorney in this application is accepted. Correspondence in this application will be mailed to the above address as provided by 37 CFR 1.33.

/ttkim/

Office of Data Management, Application Assistance Unit (571) 272-4000, or (571) 272-4200, or 1-888-786-0101

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
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13/675,665	11/13/2012	David Paniagua	109978.10101

CONFIRMATION NO. 1995

29880
FOX ROTHSCHILD LLP
PRINCETON PIKE CORPORATE CENTER
997 LENOX DRIVE
BLDG. #3
LAWRENCEVILLE, NJ 08648

PUBLICATION NOTICE

Title:PERCUTANEOUSLY IMPLANTABLE REPLACEMENT HEART VALVE DEVICE AND METHOD OF MAKING SAME

Publication No.US-2014-0005766-A1
Publication Date:01/02/2014

NOTICE OF PUBLICATION OF APPLICATION

The above-identified application will be electronically published as a patent application publication pursuant to 37 CFR 1.211, et seq. The patent application publication number and publication date are set forth above.

The publication may be accessed through the USPTO's publically available Searchable Databases via the Internet at www.uspto.gov. The direct link to access the publication is currently http://www.uspto.gov/patft/.

The publication process established by the Office does not provide for mailing a copy of the publication to applicant. A copy of the publication may be obtained from the Office upon payment of the appropriate fee set forth in 37 CFR 1.19(a)(1). Orders for copies of patent application publications are handled by the USPTO's Office of Public Records. The Office of Public Records can be reached by telephone at (703) 308-9726 or (800) 972-6382, by facsimile at (703) 305-8759, by mail addressed to the United States Patent and Trademark Office, Office of Public Records, Alexandria, VA 22313-1450 or via the Internet.

In addition, information on the status of the application, including the mailing date of Office actions and the dates of receipt of correspondence filed in the Office, may also be accessed via the Internet through the Patent Electronic Business Center at www.uspto.gov using the public side of the Patent Application Information and Retrieval (PAIR) system. The direct link to access this status information is currently http://pair.uspto.gov/. Prior to publication, such status information is confidential and may only be obtained by applicant using the private side of PAIR.

Further assistance in electronically accessing the publication, or about PAIR, is available by calling the Patent Electronic Business Center at 1-866-217-9197.

Office of Data Managment, Application Assistance Unit (571) 272-4000, or (571) 272-4200, or 1-888-786-0101

PTO/SB/08a (01-10)
Approved for use through 07/31/2012. OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(Not for submission under 37 CFR 1.99)

Application Number	13675665
Filing Date	2012-11-13
First Named Inventor	David PANIAGUA
Art Unit	3738
Examiner Name	Cheryl L. Miller
Attorney Docket Number	109978.10101

U.S.PATENTS						Remove
Examiner Initial*	Cite No	Patent Number	Kind Code[1]	Issue Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
	1	4011947		1977-03-15	Sawyer	
	2	4657133		1987-04-14	Komatsu et al.	
	3	4743231		1988-05-10	Kay et al.	
	4	6124523		2000-09-26	Banas et al.	
	5	6245102		2001-06-12	Jayaraman	
	6	6540782		2003-04-01	Snyders	
	7	6821297		2004-11-23	Snyders	
	8	6830584		2004-12-14	Seguin	

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	13675665
	Filing Date	2012-11-13
	First Named Inventor	David PANIAGUA
	Art Unit	3738
	Examiner Name	Cheryl L. Miller
	Attorney Docket Number	109978.10101

	9	7018406		2006-03-28	Seguin et al.	
	10	8512401		2013-08-20	Murray et al.	
	11	8512403		2013-08-20	Navia et al.	

If you wish to add additional U.S. Patent citation information please click the Add button. Add

U.S.PATENT APPLICATION PUBLICATIONS Remove

Examiner Initial*	Cite No	Publication Number	Kind Code[1]	Publication Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
	1	20020151970		2002-10-17	Garrison et al.	
	2	20030149477		2003-08-07	Gabbay	
	3	20040039442		2004-02-26	St. Goar	
	4	20040158321		2004-08-12	Reuter et al.	
	5	20040230285		2004-11-18	Gifford, III et al.	
	6	20050241981		2005-11-03	Gupta et al.	

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
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	Filing Date	2012-11-13
	First Named Inventor	David PANIAGUA
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	Examiner Name	Cheryl L. Miller
	Attorney Docket Number	109978.10101

	7	20070104395		2007-05-10	Kinigakis et al.	
	8	20070203575		2007-08-30	Forster et al.	
	9	20070276461		2007-11-29	Andreas et al.	
	10	20090005857		2009-01-01	Ischinger	
	11	20090054969		2009-02-26	Salahieh	
	12	20100241069		2010-09-23	Hatten	
	13	20110240511		2011-10-06	Bolton et al.	
	14	20130304201		2013-11-14	Navia et al.	
	15	20140039613		2014-02-06	Navia et al.	

If you wish to add additional U.S. Published Application citation information please click the Add button. Add

FOREIGN PATENT DOCUMENTS Remove

Examiner Initial*	Cite No	Foreign Document Number[3]	Country Code[2] i	Kind Code[4]	Publication Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear	T[5]

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	13675665
	Filing Date	2012-11-13
	First Named Inventor	David PANIAGUA
	Art Unit	3738
	Examiner Name	Cheryl L. Miller
	Attorney Docket Number	109978.10101

	1	2004/082527	WO		2004-09-30	Edwards Lifesciences Corp.		☐

If you wish to add additional Foreign Patent Document citation information please click the Add button Add

NON-PATENT LITERATURE DOCUMENTS Remove

Examiner Initials*	Cite No	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc), date, pages(s), volume-issue number(s), publisher, city and/or country where published.	T[5]
	1	MENDELSON, Karen et al., "Heart Valve Tissue Engineering: Concepts, Approaches, Progress, and Challenges" Ann Biomed Eng, 2006 Dec; 34(12); pp. 1799-1819; published online 2006 October 12 doi:10.1007/s/10439-006-9163-z	☐
	2	SCHMIDT, Dorthe et al., "Tissue engineering of heart valves using decellularized xenogeneic of polymeric starter matrices" Philos Trans R Soc Lond B Bio Sci., Aug 29, 2007, 362(1484); 1505-1512; published online June 22, 2007, doi: 10.1098/rstb.2007.2131	☐
	3	WERNER, S. et al., "Testing the Hydrodynamic properties of heart valve prostheses with a new test apparatus", Biomed Tech (Berl) 1994 Sep; 30(9); pp. 204-210 (Abstract only)	☐
	4	Office Action issued in U.S. Application No. 14/136,516, dated March 10, 2014 (109978.10102)	☐
	5	Notice of Allowance issued in U.S. Application No. 14/136,516, dated March 31, 2014 (109978.10102)	☐
	6	Cross-reference is made to U.S. Application No. 14/253,650 filed on April 15, 2014, and its associated Preliminary Amendment (109978.10104)	☐
	7	Cross-reference is made to U.S. Application No. 14/253,656 filed on April 15, 2014, and its associated Preliminary Amendment (109978.10113)	☐
	8	Cross-reference is made to U.S. Application No. 14/268,184 filed on May 2, 2014, and its associated Preliminary Amendment (109978.10114)	☐

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	13675665
	Filing Date	2012-11-13
	First Named Inventor	David PANIAGUA
	Art Unit	3738
	Examiner Name	Cheryl L. Miller
	Attorney Docket Number	109978.10101

	9	Cross-reference is made to U.S. Application No. 14/268,190 filed on May 2, 2014, and its associated Preliminary Amendment (109978.10115)	☐
	10	Cross-reference is made to U.S. Application No. 14/284,049 filed on May 21, 2014, and its associated Preliminary Amendment (109978.10116)	☐
	11	Cross-reference is made to U.S. Application No. 14/284,063 filed on May 21, 2014, and its associated Preliminary Amendment (109978.10117)	☐

If you wish to add additional non-patent literature document citation information please click the Add button Add

EXAMINER SIGNATURE

Examiner Signature		Date Considered	

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through a citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

[1] See Kind Codes of USPTO Patent Documents at www.USPTO.GOV or MPEP 901.04. [2] Enter office that issued the document, by the two-letter code (WIPO Standard ST.3). [3] For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. [4] Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. [5] Applicant is to place a check mark here if English language translation is attached.

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(Not for submission under 37 CFR 1.99)

Application Number	13675665
Filing Date	2012-11-13
First Named Inventor	David PANIAGUA
Art Unit	3738
Examiner Name	Cheryl L. Miller
Attorney Docket Number	109978.10101

CERTIFICATION STATEMENT

Please see 37 CFR 1.97 and 1.98 to make the appropriate selection(s):

☐ That each item of information contained in the information disclosure statement was first cited in any communication from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e)(1).

OR

☐ That no item of information contained in the information disclosure statement was cited in a communication from a foreign patent office in a counterpart foreign application, and, to the knowledge of the person signing the certification after making reasonable inquiry, no item of information contained in the information disclosure statement was known to any individual designated in 37 CFR 1.56(c) more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e)(2).

☐ See attached certification statement.

☐ The fee set forth in 37 CFR 1.17 (p) has been submitted herewith.

☒ A certification statement is not submitted herewith.

SIGNATURE

A signature of the applicant or representative is required in accordance with CFR 1.33, 10.18. Please see CFR 1.4(d) for the form of the signature.

Signature	/ Mark L. Yaskanin /	Date (YYYY-MM-DD)	2014-05-23
Name/Print	Mark L. Yaskanin	Registration Number	45246

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 1 hour to complete, including gathering, preparing and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

Privacy Act Statement

The Privacy Act of 1974 (P.L. 93-579) requires that you be given certain information in connection with your submission of the attached form related to a patent application or patent. Accordingly, pursuant to the requirements of the Act, please be advised that: (1) the general authority for the collection of this information is 35 U.S.C. 2(b)(2); (2) furnishing of the information solicited is voluntary; and (3) the principal purpose for which the information is used by the U.S. Patent and Trademark Office is to process and/or examine your submission related to a patent application or patent. If you do not furnish the requested information, the U.S. Patent and Trademark Office may not be able to process and/or examine your submission, which may result in termination of proceedings or abandonment of the application or expiration of the patent.

The information provided by you in this form will be subject to the following routine uses:

1. The information on this form will be treated confidentially to the extent allowed under the Freedom of Information Act (5 U.S.C. 552) and the Privacy Act (5 U.S.C. 552a). Records from this system of records may be disclosed to the Department of Justice to determine whether the Freedom of Information Act requires disclosure of these record s.

2. A record from this system of records may be disclosed, as a routine use, in the course of presenting evidence to a court, magistrate, or administrative tribunal, including disclosures to opposing counsel in the course of settlement negotiations.

3. A record in this system of records may be disclosed, as a routine use, to a Member of Congress submitting a request involving an individual, to whom the record pertains, when the individual has requested assistance from the Member with respect to the subject matter of the record.

4. A record in this system of records may be disclosed, as a routine use, to a contractor of the Agency having need for the information in order to perform a contract. Recipients of information shall be required to comply with the requirements of the Privacy Act of 1974, as amended, pursuant to 5 U.S.C. 552a(m).

5. A record related to an International Application filed under the Patent Cooperation Treaty in this system of records may be disclosed, as a routine use, to the International Bureau of the World Intellectual Property Organization, pursuant to the Patent Cooperation Treaty.

6. A record in this system of records may be disclosed, as a routine use, to another federal agency for purposes of National Security review (35 U.S.C. 181) and for review pursuant to the Atomic Energy Act (42 U.S.C. 218(c)).

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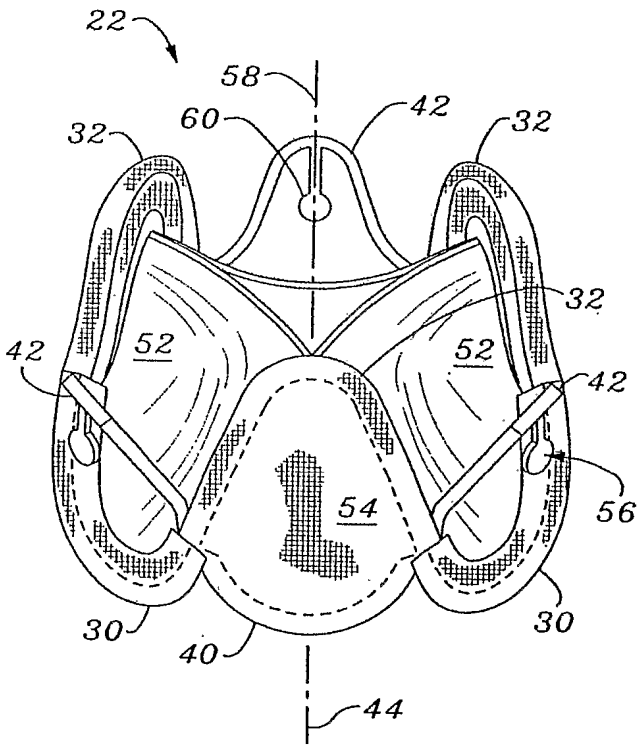

(57) Abstract: A prosthetic heart valve having an internal support frame with a continuous, undulating leaflet frame defined therein. The leaflet frame has three cusp regions positioned at an inflow end intermediate three commissure regions positioned at an outflow end thereof. The leaflet frame may be cloth covered and flexible leaflets attached thereto form occluding surfaces of the valve. The support frame further includes three cusp positioners rigidly fixed with respect to the leaflet frame and located at the outflow end of the support frame intermediate each pair of adjacent commissure regions. The valve is desirably compressible so as to be delivered in a minimally invasive manner through a catheter to the site of implantation. Upon expulsion from catheter, the valve expands into contact with the surrounding native valve annulus and is anchored in place without the use of sutures. In the aortic valve position, the cusp positioners angle outward into contact with the sinus cavities, and compress the native leaflets if they are not excised, or the aortic wall if they are. The support frame may be formed from a flat sheet of Nitinol that is bent into a threedimensional configuration and heat set. A holder having spring-like arms connected to inflow projections of the valve may be used to deliver, reposition and re-collapse the valve, if necessary.

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MINIMALLY-INVASIVE HEART VALVE WITH CUSP POSITIONERS

Field of the Invention

[0001] The present invention relates generally to medical implants, and more particularly to minimally-invasive or collapsible/expandable heart valves and methods of delivering and implanting such valves.

Background of the Invention

[0002] Prosthetic heart valves are used to replace damaged or diseased heart valves. In vertebrate animals, the heart is a hollow muscular organ having four pumping chambers: the left and right atria and the left and right ventricles, each provided with its own one-way valve. The natural heart valves are identified as the aortic, mitral (or bicuspid), tricuspid and pulmonary valves. Prosthetic heart valves can be used to replace any of these naturally occurring valves, although repair or replacement of the aortic or mitral valves is most common because they reside in the left side of the heart where pressures are the greatest.

[0003] Where replacement of a heart valve is indicated, the dysfunctional valve is typically cut out and replaced with either a mechanical valve, or a tissue or bioprosthetic-type valve. Bioprosthetic-type valves are often preferred over mechanical valves because they typically do not require long-term treatment with anticoagulants. The most common bioprosthetic-type valves are constructed with whole porcine (pig) valves, or with separate leaflets cut from bovine (cow) pericardium.

[0004] Although so-called stentless valves, comprising a section of xenograft (e.g., porcine) aorta and valve, are available, the most widely used valves include some form of artificial leaflet support. One such support is an elastic "support frame," sometimes called a "wireform" or "stent," which has a

plurality (typically three) of large radius U-shaped cusps supporting the cusp region of the leaflets of the bioprosthetic tissue (i.e., either a whole valve or three separate leaflets). The free ends of each two adjacent cusps converge somewhat asymptotically to form upstanding commissures that terminate in U-shaped tips, each being curved in the opposite direction as the cusps, and having a relatively smaller radius. The support frame typically describes a conical tube with the commissure tips at the small diameter end. This provides an undulating reference shape to which a fixed edge of each leaflet attaches (via components such as fabric and sutures) much like the natural fibrous skeleton in the aortic annulus. Therefore, the alternating cusps and commissures mimic the natural contour of leaflet attachment. Importantly, the wireform provides continuous support for each leaflet along the cusp region so as to better simulate the natural support structure.

[0005] The support frame is typically a non-ferromagnetic metal such as ELGILOY (a Co-Cr alloy) that possesses substantial elasticity. A common method of forming metallic support frames is to bend a wire into a flat (two-dimensional) undulating pattern of the alternating cusps and commissures, and then roll the flat pattern into a tube using a cylindrical roller. The free ends of the resulting three-dimensional shape, typically in the asymptotic region of the cusps, are then fastened together using a tubular splice that is plastically crimped around the ends. See Figs. 3 and 4 of U.S. Patent No. 6,296,662 for a support frame that is crimped together at a cusp midpoint.

[0006] Some valves include polymeric "support frames" rather than metallic, for various reasons. For example, U.S. Patent No. 5,895,420 discloses a plastic support frame that degrades in the body over time. Despite some favorable attributes of polymeric support frames, for example the ability to mold the complex support frame shape, conventional metallic support frames are generally preferred for their elastic properties, and have a proven track record in highly successfully heart valves. For example, the CARPENTIER-EDWARDS

Porcine Heart Valve and PERIMOUNT Pericardial Heart Valve available from Edwards Lifesciences LLC both have ELGILOY support frames and have together enjoyed the leading worldwide market position since 1976.

[0007] A conventional heart valve replacement surgery involves accessing the heart in the patient's thoracic cavity through a longitudinal incision in the chest. For example, a median sternotomy requires cutting through the sternum and forcing the two opposing halves of the rib cage to be spread apart, allowing access to the thoracic cavity and heart within. The patient is then placed on cardiopulmonary bypass which involves stopping the heart to permit access to the internal chambers. Such open heart surgery is particularly invasive and involves a lengthy and difficult recovery period.

[0008] Some attempts have been made to enable less traumatic delivery and implantation of prosthetic heart valves. For instance, U.S. Patent No. 4,056,854 to Boretos discloses a radially collapsible heart valve secured to a circular spring stent that can be compressed for delivery and expanded for securing in a valve position. Also, U.S. Patent No. 4,994,077 to Dobbin describes a disk-shaped heart valve that is connected to a radially collapsible stent for minimally invasive implantation.

[0009] Recently, a great amount of research has been done to reduce the trauma and risk associated with conventional open heart valve replacement surgery. In particular, the field of minimally invasive surgery (MIS) has exploded since the early to mid-1990s, with devices now being available to enable valve replacements without opening the chest cavity. MIS heart valve replacement surgery still typically requires bypass, but the excision of the native valve and implantation of the prosthetic valve are accomplished via elongated tubes or cannulas, with the help of endoscopes and other such visualization techniques.

[0010] Some examples of more recent MIS heart valves are shown in U.S. Patent No. 5,411,552 to Anderson, et al., U.S. Patent No. 5,980,570 to

Simpson, U.S. Patent No. 5,984,959 to Robertson, et al., U.S. Patent No. 6,425,916 to Garrison, et al., and PCT Publication No. WO 99/334142 to Vesely.

[0011] Although these and other such devices provide various ways for collapsing, delivering, and then expanding a "heart valve" per se, none of them disclose much structural detail of the valve itself. For instance, the publication to Vesely shows a tissue leaflet structure of the prior art in Fig. 1, and an expandable inner frame of the invention having stent posts in Figs. 3A-3C. The leaflets are "mounted to the stent posts 22 in a manner similar to that shown in Fig. 1." Likewise, Anderson describes mounting a porcine valve inside of an expandable stent "by means of a suitable number of sutures to form the cardiac valve prosthesis 9 shown in Fig. 2." Such general disclosures stop short of explaining how to construct a valve in a manner that maximizes long-term efficacy. In particular, the particular means of attaching the leaflets to the MIS stent is critical to ensure the integrity and durability of the valve once implanted. All of the prior art MIS valves are inadequate in this regard. Furthermore, use of conventional support stents or wireforms is difficult in MIS valves because of the need to compress the valve into a relatively small diameter delivery package, which creates material challenges.

[0012] Some MIS valves of the prior art are intended to be used without removing the natural valve leaflets. Sometimes the natural leaflets are heavily calcified, and their removal entails some risk of plaque particles being released into the bloodstream. Therefore, some of the MIS valves are designed to expand outward within the annulus and native leaflets, and compress the leaflets against the annulus. The relatively uneven surface of the calcified annulus and leaflets creates sizing problems and may complicate the delivery and placement steps. Prior art MIS valves are essentially tubular stents embellished with a native xenograft valve. The implant methodology is simply the conventional balloon expansion technique or pushing a self-expanding version from the end

of a catheter. Minimal control over the placement of the valve is provided or contemplated.

[0013] Despite some advances in MIS valve design, there remains a need for an MIS valve that is durable and which has a more flexible delivery and implantation methodology.

Summary of the Invention

[0014] The present invention provides improved prosthetic heart valves that can be implanted in a minimally-invasive manner, but which also has aspects that make it useful for conventional surgeries. The valves and implant tools and methods described herein provide a highly adaptive and simple to use endovascular delivery option for cardiac surgeons or cardiologists because of features that facilitate implantation. The valve is designed to be expelled from a delivery tube in an implant area and then expanded and/or positioned to contact the surrounding tissue without additional anchoring structures. Further, the valve and implant tools permit repositioning and even recollapse of the valve if needed.

[0015] In accordance with a first aspect of the invention, a prosthetic heart valve support frame comprises a leaflet frame and three cusp positioners. The leaflet frame has a continuous, undulating shape that mimics the natural fibrous structure of an aortic valve. The leaflet frame has three cusp regions alternating with and intermediate three commissure regions, the three cusp regions being positioned at an inflow end of the support frame and circumferentially about a flow axis defined within the support frame. The three commissure regions are positioned at an outflow end of the support frame and circumferentially about the flow axis. The three cusp positioners are rigidly fixed with respect to the leaflet frame and are disposed circumferentially about the flow axis. Each cusp positioner is located at the outflow end of the support frame and intermediate two of the commissure regions of the leaflet frame.

[0016] The leaflet frame and the cusp positioners may be formed integrally as a single piece. Desirably, the support frame is formed by a process comprising providing a two-dimensional blank of the support frame, and forming the two-dimensional blank into the three-dimensional heart valve support frame. The leaflet frame and the cusp positioners may be made of Nitinol, preferably with a martensitic transition temperature of less than about 5° C and an austenitic transition temperature of more than about 20° C.

[0017] Each cusp positioner of the heart valve support frame desirably has a U-shape with an apex of the U-shape pointing toward the outflow end of the support frame and two legs of the U-shape pointing toward the inflow end. Each of the two legs of each U-shaped cusp positioner may be rigidly fixed to the continuous leaflet frame at a location approximately midway between a cusp region and a commissure region thereof. An anti-migration member such as an elongated section terminating in an enlarged and rounded head can be rigidly fixed to each cusp positioner to project therefrom. The cusp positioners may flare outwardly from the rest of the support frame to better contact surrounding tissue.

[0018] The support frame further may include three cusp connectors rigidly fixed with respect to the leaflet frame and disposed circumferentially about the flow axis. Each cusp connector is located at the inflow end of the support frame and intermediate two of the cusp regions of the leaflet frame. Each cusp connector desirably has a U-shape with an apex of the U-shape pointing toward the inflow end of the support frame and two legs of the U-shape pointing toward the outflow end. In a preferred embodiment, the leaflet frame, cusp positioners, and cusp connectors are formed integrally as a single piece, and the three cusp positioners and three cusp connectors define a continuous, undulating shape that generally mimics the shape of the leaflet frame but is rotated 60° about the flow axis therefrom.

[0019] Another aspect of the invention is a collapsible prosthetic heart valve that has a collapsible leaflet frame, three separate, flexible leaflets attached to the leaflet frame, and three cusp positioners rigidly fixed with respect to the leaflet frame. The leaflet frame has three cusp regions intermediate three commissure regions, the three cusp regions being positioned at an inflow end of the leaflet frame and circumferentially about a flow axis defined within the support frame. The three commissure regions are positioned at an outflow end of the leaflet frame and circumferentially about the flow axis. Each flexible leaflet has an arcuate cusp edge opposite a free edge and a pair of commissure edges therebetween. The leaflets attach around the leaflet frame with the cusp edge of each leaflet extending along one of the cusp regions, and a commissure edge of each leaflet meeting a commissure edge of an adjacent leaflet at one of the commissure regions. The three cusp positioners are rigidly fixed with respect to the leaflet frame and are disposed circumferentially about the flow axis, each cusp positioner being located at the outflow end of the leaflet frame and intermediate two of the commissure regions of the leaflet frame.

[0020] The heart valve may incorporate the aforementioned features of the support frame, for example a leaflet frame with a continuous, undulating shape that mimics the natural fibrous structure of an aortic valve, cusp connectors, and anti-migration members on each cusp positoiner. Desirably, an inflow periphery of the heart valve is defined along alternating and rigidly fixed cusp regions and cusp connectors. The inflow periphery may have an external fabric covering, and the heart valve may further includes a fabric panel defining an exterior surface of the heart valve between each pair of cusp positioner and cusp connector. Preferably, the leaflet frame has a fabric covering along substantially its entire length, the fabric covering defining a flange, and wherein the arcuate cusp edges of the flexible leaflets attach to the fabric covering flange. The fabric covering flange may project generally outward from the leaflet frame such that the cusp edges of the flexible leaflets extend radially

outward past and underneath the leaflet frame to be sewn to the fabric covering flange. Each flexible leaflet may have a pair of tabs extending on either side of its free edge, wherein two tabs of adjacent flexible leaflets meet and pass together to the outside of the adjacent commissure region of the leaflet frame and are attached thereto using sutures through the tabs.

[0021] In accordance with a still further aspect of the invention, a collapsible prosthetic heart valve comprises:

a continuous, collapsible leaflet frame having three U-shaped cusp regions intermediate three U-shaped commissure regions, the three cusp regions being positioned at an inflow end of the leaflet frame and circumferentially about a flow axis defined within the leaflet frame, the three commissure regions being positioned at an outflow end of the leaflet frame and circumferentially about the flow axis;

a cloth covering extending around the leaflet frame; and

three separate, flexible leaflets attached to the leaflet frame, each leaflet having an arcuate cusp edge opposite a free edge and a pair of commissure edges therebetween, the leaflets being attached around the leaflet frame with the cusp edge of each leaflet extending along one of the cusp regions, and a commissure edge of each leaflet meeting a commissure edge of an adjacent leaflet at one of the commissure regions, the commissure edges of each leaflet further including a tab, wherein the tabs of two adjacent leaflets extend through the U-shape commissure region, diverge on the outside of commissure region, and are attached to the leaflet frame on the outside of the commissure region.

[0022] The present invention also encompasses a method of implanting a prosthetic aortic heart valve with a first step of providing a collapsible prosthetic heart valve having a collapsible leaflet frame defined by three cusp regions on an inflow end of the valve intermediate three commissure regions on an outflow end of the valve. The valve includes three cusp positioners on the

outflow end and intermediate the three commissure regions. The method includes collapsing the prosthetic heart valve within a delivery tube, advancing the prosthetic heart valve within the delivery tube to an aortic annulus, expelling the prosthetic heart valve from the delivery tube by relative movement therebetween, expanding the prosthetic heart valve, and positioning the prosthetic heart valve such that the cusp positioners contact the two coronary and one non-coronary sinuses of the ascending aorta without blocking the coronary ostia.

[0023] The method preferably includes the step of connecting a holder having flexible members to the commissure regions of the prosthetic heart valve and utilizing the flexible members to perform the step of positioning the prosthetic heart valve. Flexible members of the holder may also be connected to the cusp positioners and utilized to perform the step of positioning the prosthetic heart valve, or to rotate the prosthetic heart valve during the step of positioning. Advantageously, the flexible members may be used to re-collapse the prosthetic heart valve after the step of expanding. The prosthetic heart valve is desirably expanded in a location that is inferior to a final implant position such that the cusp positioners contact the surrounding aortic annulus, and the step of positioning comprises displacing the valve in a superior direction to a final implant position. The cusp positioners may be flared outward to define a circle about a flow axis of the valve greater than a circle about the flow axis defined by the three commissure regions, such that the step of displacing the valve in a superior direction causes the outwardly flared cusp positioners to be channeled into perspective coronary sinuses.

[0024] In accordance with a preferred method, the collapsible leaflet frame is formed of a shape memory alloy having a martensitic transition temperature less than room temperature and an austenitic transition temperature less than body temperature, and the step of collapsing is done with the material of the leaflet frame at a temperature less than its martensitic transition

temperature. For example, the step of collapsing may be done in conjunction with immersing the prosthetic heart valve in an ice bath to reduce the temperature of the material of leaflet frame to below its martensitic transition temperature. In another aspect, the collapsible leaflet frame may be formed of a shape memory alloy having a memory condition in its expanded state, and wherein the step of expanding the prosthetic heart valve comprises both permitting self-expansion of the valve to an intermediate diameter and then using a physical expander to increase the diameter of the valve to the memory condition of the leaflet frame.

[0025] A further method of implanting a collapsible prosthetic heart valve provided by the present invention comprises first providing a self-expanding valve comprised of a material displaying hysteresis in the elastic or superelastic region. The valve is permitted to self-expand to a first diameter, and then the valve is assisted with a physical expander such as a balloon to further expand to a second diameter.

[0026] The prosthetic heart valve may includes a collapsible leaflet frame formed of a shape memory alloy having a martensitic transition temperature less than room temperature and an austenitic transition temperature less than body temperature, and the method may further include a step of collapsing the valve with the material of the leaflet frame at a temperature less than its martensitic transition temperature. Fir example, the step of collapsing may be done in conjunction with immersing the prosthetic heart valve in an ice bath to reduce the temperature of the material of leaflet frame to below its martensitic transition temperature.

[0027] The prosthetic heart valve may have a collapsible leaflet frame defined by three cusp regions on an inflow end of the valve intermediate three commissure regions on an outflow end of the valve, and three cusp positioners on the outflow end and intermediate the three commissure regions. In this case, the method may further include:

collapsing the prosthetic heart valve within a delivery tube;

advancing the prosthetic heart valve within the delivery tube to an aortic annulus;

expelling the prosthetic heart valve from the delivery tube by relative movement therebetween;

expanding the prosthetic heart valve by the steps of permitting self-expansion and assisting further expansion; and

positioning the prosthetic heart valve such that the cusp positioners contact the two coronary and one non-coronary sinuses of the ascending aorta without blocking the coronary ostia.

Brief Description of the Drawings

[0028] Fig. 1 is a partial view of a patient's heart generally vertically section through the left ventricle and associated heart valves, and illustrating the implantation approach of a catheter-based prosthetic valve of the present invention;

[0029] Fig. 2A is a vertical sectional view through an aortic annulus and an exemplary prosthetic heart valve of the present invention implanted therein;

[0030] Fig. 2B is a top plan view of the implanted prosthetic heart valve of Fig. 2A;

[0031] Figs. 3A-3C are perspective, top plan, and bottom plan views, respectively, of the prosthetic heart valve of Fig. 2A;

[0032] Fig. 4 is a plan view of a prosthetic heart valve support frame of the present invention in a two-dimensional blank form prior to conversion to three-dimensional final form;

[0033] Fig. 5 is a perspective view of the prosthetic heart valve support frame of Fig. 4 in its three-dimensional final form with a leaflet frame and cusp positioners;

[0034] Figs. 5A and 5B are views of a portion of the three-dimensional heart valve support frame of Fig. 5 showing alternative cusp positioner configurations;

[0035] Fig. 6A is an elevational view of a partially assembled prosthetic heart valve as in Figs. 3A-3C;

[0036] Fig. 6B is an elevational view of the prosthetic heart valve of Fig. 6A fully assembled;

[0037] Fig. 7 is a plan view of an exemplary leaflet used in the prosthetic heart valves of the present invention;

[0038] Fig. 8 is a partial sectional view of a commissure region of the exemplary prosthetic heart valve taken along line 8-8 of Fig. 3B;

[0039] Fig. 9 is a sectional view through a portion of the support frame of the exemplary prosthetic heart valve, taken along line 9-9 of Fig. 8;

[0040] Fig. 10 is a sectional view through a commissure tip region of the exemplary prosthetic heart valve, taken along line 10-10 of Fig. 8;

[0041] Fig. 11 is a schematic perspective view of a prosthetic heart valve support frame of the present invention being loaded into a delivery catheter;

[0042] Fig. 12 is a perspective view of the support frame after having been loaded into a delivery catheter;

[0043] Figs. 13A-13B are perspective and elevational views of an exemplary compressible/expandable heart valve holder attached to a prosthetic heart valve of the present invention;

[0044] Fig. 14 is a perspective view of the expulsion of an assembled prosthetic heart valve and holder as in Figs. 13A and 13B from the distal end of a delivery catheter;

[0045] Fig. 15 is a bottom plan view of an exemplary compressible/expandable heart valve holder of the present invention;

[0046] Fig. 16 is a plan view of a multi-armed flexible portion of the holder of Fig. 15; and

[0047] Figs. 17A-17B are two views of a rigid portion of the holder of Fig. 15.

Description of the Preferred Embodiments

[0048] The present invention provides an improved minimally invasive (MIS) valve support frame, MIS valve, and methods of construction and delivery as described herein and shown in the accompanying drawings.

[0049] The invention pertains primarily to flexible leaflet heart valves and internal support frames, which are also referred to in the art as stents or wireforms. As mentioned above, the flexible leaflets can be formed from biological (e.g., bovine pericardium) or synthetic material. In this context, a "support frame" for a flexible leaflet heart valve provides the primary internal structural support for the leaflets, and substantially mimics the natural fibrous skeleton of the respective valve annulus. More specifically, each of the leaflets has an outer edge that is coupled to a portion of the support frame such that its inner edge is free to move within the orifice area of the valve, thus providing the opening and closing surfaces thereof. A biological xenograft valve can be used to provide the flexible leaflets in the valves of the present invention, though the internal support frame is particularly suited to receive individual leaflets.

[0050] The leaflet frames of the present invention have a continuous, undulating shape with three arcuate or U-shaped cusp regions on the inflow end separated by three upstanding and generally axially-oriented arcuate or U-shaped commissure regions on the outflow end. Around the circumference of the leaflet frame, the shape has an alternating structure of cusp-commissure-cusp-commissure-cusp-commissure, and generally describes a conical surface of revolution with the three commissures on the outflow end of the valve being closer together than the three cusps. Some support frames may alternatively describe a tubular surface of revolution about an axis. The cusp regions and

commissure regions are evenly distributed about a flow axis through the support frame, and therefore the three cusp regions are 120° apart from each other, and each of the three commissure regions is 120° apart from the next and 60° from the adjacent cusp regions.

[0051] The term "continuous" to describe the heart valve leaflet frame means that a single continuous and closed-shape line (i.e., loop) can be drawn following the sequential cusp and commissure regions, and "undulating" refers to the serpentine or alternating sinusoidal character of the line. More generally, a continuous, undulating heart valve leaflet frame approximates the shape of the natural fibrous tissue around the aortic valve annulus so as to mimic that natural support structure for optimum functionality of the prosthetic leaflets.

[0052] The present invention primarily pertains to prosthetic heart valves suitable for minimally invasive delivery and implantation. Such minimally invasive valves are capable of being compressed or collapsed into a small profile and delivered through a catheter or cannula (a tube) to the site of implantation for remote expansion and anchoring thereto. It should be understood, however, that certain aspects of the invention described herein are beneficial for prosthetic heart valves in general, and thus not all of the claims should be construed to require a minimally invasive valve.

[0053] Fig. 1 depicts a portion of a heart of a patient with the left ventricle LV, aortic valve AV, mitral valve MV, and ascending aorta AA shown in section. A delivery catheter or tube 20 is seen in position just prior to complete expulsion and expansion of a prosthetic heart valve 22 from a distal end thereof for implant at the aortic valve AV annulus. The aortic valve AV leaflets L may first be excised prior to implant of the valve 22, or more preferably the leaflets L remain in place and are expanded outward and compressed against the lumen of the aortic valve AV annulus upon expansion of the valve. The distal end of the delivery tube 20 may optionally be stabilized by a balloon 24 (shown in phantom) inflated against the lumen of the ascending

aorta AA, or through other means. The delivery tube 20 is preferably inserted in the vasculature of the patient using a larger diameter introducer 26 through a peripheral vessel such as the femoral artery or femoral vein. Alternatively, the peripheral vessel may be the internal jugular vein, the subclavian artery, the axillary artery, the abdominal aorta, the descending aorta, or any other suitable blood vessel. The introducer 26 may be inserted by surgical cut down or percutaneously using the Seldinger technique.

[0054] Figs. 2A and 2B illustrate the prosthetic heart valve 22 implanted at the aortic valve AV annulus. The heart valve 22 includes three cusps 30 on an inflow end (one of which is not visible) and three commissures 32 on an outflow end. The direction of blood flow BF is indicated with an arrow in the ascending aorta AA. The natural leaflets are desirably compressed against the lumen of the aortic valve annulus by the prosthetic heart valve 22, as seen in Fig. 2B. The valve 22 is oriented about a flow axis such that the commissures 32 are generally aligned with the native commissures C, while the cusps (not shown but intermediate the commissures 32) are generally aligned with the natural cusps/leaflets L. The heart valve 22 contacts the lumen wall of the aortic valve AV annulus and desirably retains its position due to friction therebetween. In this regard, the heart valve 22 expands from its delivery configuration shown in Fig. 1 to the expanded configuration in Figs. 2A and 2B.

[0055] The valve 32 contacts the lumen wall around the entire periphery of the inflow end thereof and in certain areas adjacent to the inflow periphery, as will be explained below. The inflow periphery is defined by the lower ends of the cusps 30 as well as by the lower ends of three cusps connectors 40 that extend between and fill the gaps between the cusps 30. Additionally, the heart valve 22 includes three cusp positioners 42, two of which are visible in Fig. 2A, that are rigidly fixed with respect to an internal valve support frame and are each located generally at the outflow end of the valve intermediate two of the commissures 32. With reference to Fig. 2B, the cusp positioners 42 are evenly

distributed about a central flow axis 44, and when implanted align with the native leaflets L. The cusp positioners 42 preferably extend radially farther outward than the commissures 32 and compress the leaflets L against the natural sinus cavities formed just above the aortic valve AV annulus. Coronary ostia CO open from two of the three sinus cavities, as seen in Fig. 2A, and the cusp positioners 42 are sized and placed by the operator to avoid occluding flow through the coronary ostia CO. The advantageous structure and function of these cusp positioners 42 will be more fully explained below.

[0056] With reference now to Figs. 3A-3C, the exemplary prosthetic heart valve 22 will be more fully described. The shape of an internal support frame 50 seen in Fig. 5 generally governs the shape of the valve 22. As mentioned, the valve 22 includes the aforementioned cusps 30 and commissures 32 evenly distributed about a flow axis 44. The cusps 30 and cusp connectors 40 define a scalloped inflow periphery of the valve 22, while the outflow periphery is defined by the three commissures 32 and the three cusp positioners 42. The entire internal support frame 50 except for the cusp positioners 42 is covered over with one or more layers of material, the exterior layer of which is typically a fabric as shown (but not numbered). The use of a fabric such as polyethylene terephthalate provides a matrix into which surrounding tissue can grow to help anchor the valve in place.

[0057] Three flexible leaflets 52 mount to the valve 22 in a trifoil configuration with free edges 53 thereof arranged to meet or coapt in the middle of the valve and provide one-way occlusion. An outer edge of each leaflet 52 attaches to the valve 22 between two of the commissures 32 and around one of the cusps 30. An exemplary structural attachment of the leaflets 52 to the internal support frame 50 will be described below.

[0058] As mentioned, each cusp connector 40 extends between two of the cusps 30. A panel of fabric or other material 54 covers an area between the inflow or lower edge of each cusp connector 40 and the corresponding

commissures 32. Some of this panel of fabric 54 desirably contacts the lumen wall of the aortic valve AV annulus to help prevent leakage around the valve.

[0059] The exemplary cusp positioners 42 each have an inverted U-shape with an apex pointed toward the outflow end of the valve 22 and two legs extending generally toward the inflow end and connecting with the remainder of the valve. The term "U-shape" is intended to cover all configurations that have two legs and an apex therebetween. Other figurative descriptions such as V-shaped, bell-shaped, sinusoidal, arcuate, or the like are therefore encompassed by the term "U-shape". It is contemplated, however, that the cusp positioners 42 could assume other forms, such as a generally linear, cantilevered arm extending upward from the midpoint of each cusp 30. In whatever form, the cusp positioners 42 provide the valve 22 with three points of contact with the surrounding tissue that is midway between the three commissures 32 so as to help stabilize and anchor the valve in its implant position. Moreover, the cusp positioners 42 desirably perform the function of compressing the native leaflets L outward against the sinus cavities, at least in those procedures where the leaflets L are not excised.

[0060] The leaflets L in a diseased valve may be less than flexible, and indeed may be highly calcified. It is often considered preferable to avoid removing the leaflets L so as to avoid disturbing the calcification or other stenotic material that has built up around the leaflets. Therefore, the present invention desirably provides structure to compress the native leaflets L outward against the aortic wall sinus cavities and hold the leaflets in that position so as to avoid flapping and potentially interfering with blood flow through the prosthetic valve. The inverted U-shape of the cusp positioners 42 is believed to provide effective structure to both anchor the valve in the aortic valve AV annulus and also control, or corral, if you will, the obsolete native leaflets L. At the same time, the cusp positioners 42 are relatively minimal in total area so as to avoid unduly interfering with back flow of blood on the outflow side of each of the

leaflets 52, or to the coronary ostia CO. Therefore, the cusp positioners 42 are desirably defined by relatively thin members, as shown, as opposed to walls or panels, or the like. Multiple cusp positioners 42 per valve cusp 30 are conceivable, though the total solid volume taken up by the cusp positioners should be kept to a minimum so as to minimize the risk of occluding the coronary ostia CO.

[0061] The axial height of the cusp positioners 42 relative to the commissures 32 is seen best in Fig. 2A (and in Fig. 6B). Preferably, the commissures 32 are slightly taller than the cusp positioners 42, although such an arrangement is not considered mandatory. The main consideration in the size of the cusp positioners 42 is to avoid occluding the coronary ostia CO. Therefore, as seen in Fig. 2A, the cusp positioners 42 contact the surrounding aortic valve AV lumen wall just below the coronary ostia CO. Of course, the anatomy of each patient differs slightly from the next, and the precise position of the coronary ostia CO cannot be predicted with absolute certainty. Furthermore, the final location of the cusp positioners 42 is dependent on the skill of the cardiac surgeon or cardiologist. In the ideal situation, however, the cusp positioners 42 are positioned just below and aligned circumferentially with the coronary ostia CO as seen in Figs. 2A and 2B.

[0062] Figs. 2B and 3B-3C illustrate the relative outward radial position of the cusp positioners 42 with respect to the commissures 32 therebetween, and with respect to the cusp connectors 40. As seen in the isolated view of the heart valve support frame 50 in Fig. 5, the cusp positioners 42 are angled or flared outward from the remainder of the support frame. This outward flaring helps ensure good contact between the apex of the cusp positioners 42 and the surrounding walls of the aortic valve AV sinus cavities. In this regard, the outer configuration of the heart valve 22 is designed to maximize contact with the aortic valve AV lumen wall both in the annulus and for a short distance into each sinus cavity. This extensive surface contact between the prosthetic valve

22 and the surrounding tissue may obviate the need for sutures, staples, sharp barbs or other such anchoring structure, although such structure could be used in conjunction with the valve. The valve 22 is merely expelled from the end of the delivery tube 20 (Fig. 1), expanded with or without assistance of a balloon, and held in place by frictional contact between the inflow periphery against the annulus, and between the cusp positioners 42 and the sinus cavities (or intervening native leaflets).

[0063] Each cusp positioner 42 further includes at least one anti-migration member 56 rigidly fixed thereto and designed to help anchor the support frame 50 to the surrounding tissue. In the illustrated embodiment, the anti-migration members 56 each preferably includes an elongated section 58 terminating in an enlarged and rounded head 60, the configuration thus somewhat resembling a spoon. The anti-migration member 56 desirably projects out of the plane defined by the associated cusp positioner 42, and may extend generally axially in the inflow direction from the apex thereof, as seen in Fig. 3A. When the valve 22 is implanted, the anti-migration members 56 are designed to contact and become somewhat entrapped in the native leaflets. Therefore, the anti-migration members 56 act as a rounded barb of sorts to maintain the valve 22 in its implant position. The members 56 also may help prevent flapping of the native leaflets in the swirling blood flow. Numerous other configurations are contemplated, the general idea being that the anti-migration member 56 enhances the ability of the associated cusp positioner 42 to anchor to the surrounding tissue. In this regard, the term "anti-migration member" is meant to include any structure that enhances such anchoring, including both blunt and sharp structures (i.e., barbs).

[0064] Various procedures and apparatuses for converting a two-dimensional blank such as shown in Fig. 4 to the three-dimensional form of Fig. 5 are described in more detail in co-pending U.S. Patent Application Serial No. 10/251,651, filed September 20, 2002, and entitled continuous heart valve

support frame and method of manufacture. In short, the process involves bending the two-dimensional blank 70 around a cylindrical or conical mandrel and altering the material so as to retain its three-dimensional shape. For example, various nickel-titanium alloys (Nitinol) may be easily bent around a mandrel and then set into that shape using heat treatments.

[0065] In an exemplary embodiment of the present invention, the internal support frame 50 of the valve 22 is made of a material that is highly flexible so as to permit maximum relative movement between the valve cusps and commissures, and in some cases to permit constriction into a small profile diameter for minimally invasive delivery to an implantation site. At the same time the support frame must possess a minimum amount of stiffness to provide the desired support to the leaflets. Therefore, there is a balance obtained between the requisite flexibility and stiffness.

[0066] The material for the internal support frame is desirably "elastic," which means that it has the capacity to rebound from imposed strain. Various NITINOL alloys are especially suitable for making the internal support frame of the present invention as in certain circumstances they are considered to be "superelastic." Other materials that may be used include ELGILOY, titanium, stainless-steel, even polymers, and similar expedients. These latter materials do not display superelasticity but are still elastic. Other materials may fit within this definition but they must be suitable for long-term implantation in the body.

[0067] The term "superelastic" (sometimes "pseudoelastic") refers to that property of some materials to undergo extreme strains (up to 8%) without reaching their failure stress limit. Some so-called shape memory alloys (SMAs) are known to display a superelastic phenomena or rubber-like behavior in which a strain attained beyond the elastic limit of the SMA material during loading is recovered during unloading. This superelastic phenomenon occurs when load is applied to an austenitic SMA article which first deforms elastically up to the yield point of the SMA material (sometimes referred to as the critical stress).

Upon the further imposition of load, the SMA material begins to transform into stress-induced martensite or "SIM." This transformation takes place at essentially constant stress, up to the point where the SMA material is completely transformed into martensite. When the stress is removed, the SMA material will revert back into austenite and the article will return to its original, pre-programmed programmed or memorized shape.

[0068] The support frame 50 is desirably constructed of a material that exhibits hysteresis in the elastic and/or superelastic region. "Hysteresis" indicates that when the material is strained beyond the "memory condition" (defined as unconstrained geometry) it produces a stress-strain curve that is different and higher than the stress-strain curve produced as the material attempts to return to its memory condition. An example of a material that exhibits such a hysteresis is NITINOL. The presence of this hysteresis implies that it requires a greater force to displace the material form its memory condition than the material exerts as it recovers to its memory condition.

[0069] When using NITINOL the shape set is done at a particular temperature for a period of time designed to ensure certain properties in the material. Namely, the martensitic transition temperature is desirably less than room temperature and the austenitic transition temperature is desirably less than body temperature. For instance, the temperature below which the material is in martensitic form is around 0-5° C, while the temperature above which the material is in austenitic form is around 20-25° C. When the material is shape set in this way, the heart valve 22 can be cooled, such as in an ice bath, just prior to implant to change the crystalline structure of the support frame 50 to martensite and create high flexibility so as to enable compaction thereof into a small diameter delivery profile. After implant and expansion, the temperature rises from body heat above the austenitic transition temperature and thus the support frame 50 possesses the desired degree of stiffness to properly support the leaflets.

[0070] The support frame 50 (and blank 70) includes a leaflet frame 72 defined by three cusp regions 74 intermediate three commissure regions 76. In Fig. 4 the leaflet frame 72 in the blank 70 exhibits a three-leaf clover shape, while in Fig. 5 the leaflet frame 72 has a continuous, undulating shape as described above. A second three-leaf clover shape can be seen in Fig. 4 formed by the three cusp connectors 40 and three cusp positioners 42. When bent into the three-dimensional configuration of Fig. 5, two continuous, undulating shapes can be seen oriented 60° with respect to one another about the central flow axis. Each cusp connector 40 includes an apex 80 and a pair of legs 82 that rigidly attach to the leaflet frame 72 at junction points 84. Likewise, each cusp positioner 42 includes an apex 90 and a pair of legs 92 that rigidly attach to the leaflet frame 72 at junction points 94. In the preferred and illustrated embodiment, the junction points 84 and 94 are coincident.

[0071] Figs. 5A and 5B show alternative cusp positioner configurations for the three-dimensional heart valve support frame 50 of Fig. 5. As mentioned above, the anti-migration members facilitate anchoring of the support frame 50 to the surrounding anatomy, and prevent axial and rotational movement of the valve 22. The anti-migration members 56 shown in Fig. 5 project generally axially in the inflow direction from the apex 90 of each cusp positioner 42. In Fig. 5A, a second anti-migration member 57 projects generally axially in the outflow direction from the apex 90 of each cusp positioner 42. In Fig. 5B, there are multiple anti-migration members 56 extending generally axially in the inflow direction. Various combinations, placements and orientations of these examples are contemplated, and the examples should not be considered limiting.

[0072] Fig. 6A shows the valve 22 almost completely assembled, but without the aforementioned cloth covers 54 that are seen in the fully assembled valve of Fig. 6B. The covers 54 help prevent leakage of blood around the implanted valve 22, and specifically in the areas between the each pair of cusps 30.

[0073] Fig. 7 illustrates an exemplary leaflet 52 in plan view. The free edge 50 is shown as linear, but may also be arcuate, angled, trapezoidal, or other configuration. Each leaflet includes a pair of opposed generally rectangular tabs 100 at either end of the free edge 53. An arcuate cusp edge 102 extends between the tabs 100 and opposite the free edge 53. The tabs 100 and arcuate cusp edge 102 are secured to the valve 22, and specifically along the contours of the leaflet frame 72 seen in Fig. 5.

[0074] Fig. 8 is an enlarged cutaway view of one of the commissures 32 of the valve 22 taken along line 8-8 of Fig. 3B and showing the internal construction thereof. The commissure region 76 of the leaflet frame 72 tapers down in the outflow direction to a closed tip 104. Attachment flanges 106 are formed adjacent the tip 104 and desirably include a plurality of assembly holes 108 sized to permit passage of sutures therethrough. The adjacent leaflets 52 come together in the commissure regions 76 and the tabs 100 thereof are folded away from each other on the exterior of the flanges 106.

[0075] As seen in Fig. 9, the cusp edge 102 of each leaflet 52 attaches with sutures 110 to a cloth flange 112 of a tubular fabric cover 114 around the leaflet frame 72. This configuration causes tensile forces imparted by the leaflets 52 to be transferred as much as possible to the frame 72 rather than being primarily borne by the attachment sutures 110.

[0076] Fig. 10 shows the attachment structure at the commissure tip 104, and specifically illustrates sutures 120 passing through the fabric cover 114, through the assembly holes 108, and through the folded leaflet tabs 100. A second suture 122 passes through the cloth flange 112, the leaflet tab 100, and cloth covers 54 (also shown in Fig. 6B). Because each of the leaflets 52 includes the tab 100 that extends to the outside of the leaflet frame 72, high forces that are seen with closing of the valve are less likely to pull the sutures 120 through the tabs. That is, the construction shown in Fig. 10 causes tensile

forces imparted by the leaflets 52 to be transferred as much as possible from the sutures 120, 122 to the frame 72, thus helping to prevent tearing of the flexible leaflets and rendering the valve 22 more durable.

[0077] Figs. 11 and 12 schematically illustrate a technique for loading a prosthetic heart valve of the present invention into a delivery tube. For the sake of clarity, only the support frame 50 is shown being loaded into the delivery tube 20. A plurality of sutures or other such flexible members or filaments 130 are shown looped through each of the commissure regions 76 of the support frame 50. These filaments 130 extend into the distal end of the delivery tube 20 and through its lumen to a proximal end (not shown) where they are connected to a tensioning device. In actual use, the filaments 130 would be threaded through the commissures 32 of the valve 22, avoiding the flexible leaflets. A loading adapter 132 couples to the distal end of the delivery tube 20. The adapter 132 includes an inner funnel-shaped opening 134. Tension on the filaments 130 pulls the commissures 32 of the valve into the funnel-shaped opening 134 which gradually compresses the valve into a diameter smaller than the lumen of the delivery tube 20. Once the valve 22 is positioned fully within the delivery tube 20, as seen in Fig. 12, the filaments 130 and adapter 132 are removed.

[0078] Figs. 13-17 illustrate a minimally invasive holder for use with the prosthetic heart valves of the present invention. Figs. 13A and 13B show the holder 150 attach to the heart valve 22 as described above. The holder 150 includes a multi-armed flexible portion 152 and a rigid portion 154 (seen in Figs. 17A-17B). The flexible portion 152 includes a plurality, at least three, but preferably six flexible members or arms 156 extending outward from a central circular disk 158. Each of the arms 156 terminates in a rounded end having an attachment aperture 160. The arms 156 are distributed evenly about the

circumference of the circular disk 158, and are arrayed to attach to each of the commissures 32 and cusp positioners 42 of the valve 22. Releasable sutures 162 or other such attachment structure are used for this purpose.

[0079] Fig. 14 shows the assembled holder 150 and valve 22 emerging from the distal end of a delivery tube 20. Prior to this stage, the flexible members or arms 156 are oriented generally axially within the tube 20 with the valve 22 also collapsed and having its outflow prongs coupled to the distal ends of the arms 156. The arms 156 of the holder 150 are sufficiently flexible to be compressed into the small profile required for delivery through the delivery tube 20. In this regard, the flexible portion 152 is desirably made of Nitinol. A handle 170 which may be flexible or rigid attaches to the holder 150 for manipulation thereof. Displacing the handle 170 in a distal direction with respect to the tube 20 therefore expels the valve/holder combination and the resiliency of the valve 22 and holder arms 156 causes them to spring outward. It should be understood that other designs of the holder 150 may be utilized, such as replacing the spring-like arms 156 with rigid members that are hinged and spring-biased.

[0080] Figs. 15-17 illustrate specifics of the exemplary flexible portion 152 and rigid portion 154. In a relaxed configuration, the flexible portion 152 is planar, and may be cut from a sheet of Nitinol. The rigid portion 154 includes a proximal face 180 that is sized approximately the same as the circular disk 158, and small enough to fit within the delivery tube 20. A central threaded bore 182 opens to the proximal face 180 for receiving the handle 170. Fig. 15 illustrates a number of sutures 162 threaded through the holder 150 and used to couple the holder to the six outflow prongs of the prosthetic heart valve 22. Desirably, these sutures 162 are anchored with respect to the holder and each one passes over a cutting guide in the holder such that the suture may be severed along its midpoint resulting in two free ends that can be pulled free of the valve.

[0081] The holder 150 is sufficiently flexible to be compressed into a

small profile and passed through the delivery tube 20. At the same time, the flexible portion 152 and multiple flexible arms 156 have a sufficient degree of torsional strength to permit the operator to rotate the valve 22 during the implant procedure. Furthermore, the arms 156 are shaped to contact the distal mouth of the delivery tube 20 when the assembly is pulled toward the tube which, due to their radial stiffness, causes the arms to bend back toward their axial orientation within the tube. Since the distal ends of the arms are coupled to at least three of the outflow prongs of the prosthetic heart valve 22, the valve constricts accordingly. Constriction of the valve 22 after having been fully expelled from the end of the delivery tube and expanded permits repositioning of the valve 22. That is, the cusp positioners 42 are designed to contact the sinuses cavities or aortic wall after the valve 22 expands, and the retraction/constriction option afforded by the holder 150 may be necessary to disengage the cusp positioners from the surrounding tissue to reposition or re-orient the valve. Furthermore, the valve 22 can be completely collapsed and retracted back into the delivery tube to permit removal in case the surgeon or cardiologist deems the valve unsuitable for whatever reason.

Method of Use

[0082] Prior to implant, the cardiac surgeon or cardiologist measures the aortic valve AV annulus using appropriate sizers, minimally invasive or not as the case may be, a number of which are available and which will not be further described herein. The correctly sized valve is then selected and compressed into the delivery catheter or tube 20, such as with the use of the loading adapter 132 having the inner funnel-shaped opening 134 as seen in Fig. 11. To facilitate this loading step, the inner support frame 50 of the valve 20 must be able to withstand high stresses without failure. One method is to form the support frame 50 from a material that has superelastic properties, for instance a Nitinol that has a martensitic transition temperature of less than about 5° C can be immersed in an ice bath to change its crystalline structure to

martensite, which is a superelastic phase. Once loaded into the delivery tube 20, the support frame 50 will not revert back to its original shape upon a temperature rise and thus does not exert undue outward force on the tube. The heart valve 22 may be loaded around an inflation balloon, but for the sake of a small profile the balloon is used after expulsion of the valve from the tube at the implantation site.

[0083] With reference again to Fig. 1, the delivery tube 20 is seen in position just prior to complete expulsion and expansion of the prosthetic heart valve 22 from a distal end thereof for implant at the aortic valve AV annulus. The distal end of the delivery tube 20 may optionally be stabilized by a balloon 24 (shown in phantom) inflated against the lumen of the ascending aorta AA, or through other means. The delivery tube 20 is preferably inserted in the vasculature of the patient using a larger diameter introducer 26 through a peripheral vessel such as the femoral artery or femoral vein. Alternatively, the peripheral vessel may be the internal jugular vein, the subclavian artery, the axillary artery, the abdominal aorta, the descending aorta, or any other suitable blood vessel. The introducer 26 may be inserted by surgical cut down or percutaneously using the Seldinger technique.

[0084] The prosthetic heart valve 22 is expelled from the delivery tube 20 by relative movement therebetween - i.e., by pushing the valve from the tube or by retracting the tube from around the valve. The valve 22 desirably self-expands into contact with the surrounding lumen wall, but may also be assisted with an inflation balloon or other such physical expander.

[0085] With reference to Figs. 2A and 2B, the cusps positioners 42 help guide the prosthetic heart valve 22 into position in the aortic valve AV annulus. As mentioned above, the cusp positioners 42 desirably flare outward from the rest of the valve structure and are thus configured to contact the sinuses of the aortic valve AV while the cusps 30 are sized to fit within the annulus. In accordance with one method of implantation, the surgeon or cardiologist expels the heart valve 22 below (i.e., toward the left ventricle) its optimum implant position, and then axially displaces the valve upward into the desired position.

Stated another way, the heart valve 22 is expanded in a location that is inferior to a final implant position such that the cusp positioners 42 contact the surrounding aortic annulus, and the valve is then repositioned by displacing the valve in a superior direction to a final implant position. As the valve 22 ascends, the cusp positioners 42 spring outward into the three valve sinuses and help rotationally orient the valve. That is, the sinuses channel the cusp positioners 42 and correct any rotational misalignment. Finally, the valve 22 is implanted with the cusp positioners 42 in the sinus cavities (preferably below the coronary ostia CO) and the cusps 30 and cusp connectors 40 forming a scalloped yet continuous contact wall against the aortic valve AV annulus or root.

[0086] As mentioned, a physical expander (e.g., balloon) may be used to radially outwardly expand the valve 22 (including the internal support frame 50) beyond its self-expanded diameter so that it is firmly anchored in place. A prosthetic valve possessing hysteresis that is held in a reduced (first or constrained) diameter will exert an outward radial force that is less than the force at which it will resist an inward radial force. Therefore, if deployed in-situ, the device is not expected to exert enough force on the vessel wall to expand to the desired diameter. However, if the expansion is assisted by means of a balloon or other physical expander, the hysteresis of the material will allow it to better maintain its diameter once that diameter is achieved. This is unlike a self-expanding device that relies solely on the outward radial force of the device to achieve its desired diameter. It is also unlike balloon expanded devices that rely on a balloon to plastically deform the device into the desired diameter. Although it is conceivable that a balloon or other physical expander could be used in a self-expanding device made of a material that does not display a hysteresis, the benefits would not be as great.

[0087] It will be appreciated that the invention has been described hereabove with reference to certain examples or preferred embodiments as shown in the drawings. Various additions, deletions, changes and alterations may be made to the above-described embodiments and examples, and it is intended that all such additions, deletions, changes and alterations be included within the scope of the following claims.

WHAT IS CLAIMED IS:

1. A prosthetic heart valve support frame, comprising:

a continuous, undulating valve leaflet frame that mimics the natural fibrous structure of an aortic valve, the leaflet frame having three cusp regions alternating with and intermediate three commissure regions, the three cusp regions being positioned at an inflow end of the support frame and circumferentially about a flow axis defined within the support frame, the three commissure regions being positioned at an outflow end of the support frame and circumferentially about the flow axis; and

three cusp positioners rigidly fixed with respect to the leaflet frame and disposed circumferentially about the flow axis, each cusp positioner being located at the outflow end of the support frame and intermediate two of the commissure regions of the leaflet frame.

2. The heart valve support frame of claim 1, wherein the leaflet frame and the cusp positioners are formed integrally as a single piece.

3. The heart valve support frame of claim 2, wherein the support frame is formed by a process comprising:

providing a two-dimensional blank of the support frame; and

forming the two-dimensional blank into the three-dimensional heart valve support frame.

4. The heart valve support frame of claim 1, wherein the leaflet frame and the cusp positioners are made of Nitinol.

5. The heart valve support frame of claim 1, wherein the Nitinol has a martensitic transition temperature of less than about 5° C and an austenitic transition temperature of more than about 20° C.

6. The heart valve support frame of claim 1, wherein each cusp positioner has a U-shape with an apex of the U-shape pointing toward the outflow end of the support frame and two legs of the U-shape pointing toward the inflow end.

7. The heart valve support frame of claim 6, wherein each of the two legs of each U-shaped cusp positioner is rigidly fixed to the continuous leaflet frame at a location approximately midway between a cusp region and a commissure region thereof.

8. The heart valve support frame of claim 6, further including an anti-migration member rigidly fixed to each cusp positioner and projecting therefrom.

9. The heart valve support frame of claim 8, wherein each anti-migration member comprises an elongated section terminating in an enlarged and rounded head.

10. The heart valve support frame of claim 1, wherein the support frame further includes three cusp connectors rigidly fixed with respect to the leaflet frame and disposed circumferentially about the flow axis, each cusp connector being located at the inflow end of the support frame and intermediate two of the cusp regions of the leaflet frame.

11. The heart valve support frame of claim 10, wherein each cusp connector has a U-shape with an apex of the U-shape pointing toward the inflow end of the support frame and two legs of the U-shape pointing toward the outflow end.

12. The heart valve support frame of claim 10, wherein the leaflet frame, cusp positioners, and cusp connectors are formed integrally as a single piece, and wherein the three cusp positioners and three cusp connectors define a continuous, undulating shape that generally mimics the shape of the leaflet frame but is rotated 60° about the flow axis therefrom.

13. The heart valve support frame of claim 1, wherein the cusp positioners flare outwardly from the rest of the support frame.

14. A collapsible prosthetic heart valve, comprising:

a collapsible leaflet frame having three cusp regions intermediate three commissure regions, the three cusp regions being positioned at an inflow end of the leaflet frame and circumferentially about a flow axis defined within the support frame, the three commissure regions being positioned at an outflow end of the leaflet frame and circumferentially about the flow axis;

three separate, flexible leaflets attached to the leaflet frame, each leaflet having an arcuate cusp edge opposite a free edge and a pair of commissure edges therebetween, the leaflets being attached around the leaflet frame with the cusp edge of each leaflet extending along one of the cusp regions, and a commissure edge of each leaflet meeting a commissure edge of an adjacent leaflet at one of the commissure regions; and

three cusp positioners rigidly fixed with respect to the leaflet frame and disposed circumferentially about the flow axis, each cusp positioner being located at the outflow end of the leaflet frame and intermediate two of the commissure regions of the leaflet frame.

15. The heart valve of claim 14, wherein each cusp positioner has a U-shape with an apex of the U-shape pointing toward the outflow end of the leaflet frame and two legs of the U-shape pointing toward the inflow end.

16. The heart valve of claim 15, wherein each of the two legs of each U-shaped cusp positioner is rigidly fixed to the continuous leaflet frame at a location approximately midway between a cusp region and a commissure region thereof.

17. The heart valve of claim 15, further including an anti-migration member rigidly fixed to each cusp positioner and projecting therefrom.

18. The heart valve of claim 14, wherein the heart valve further includes three cusp connectors rigidly fixed with respect to the leaflet frame and disposed circumferentially about the flow axis, each cusp connector being located at the inflow end of the leaflet frame and intermediate two of the cusp regions of the leaflet frame.

19. The heart valve of claim 18, wherein each cusp connector has a U-shape with an apex of the U-shape pointing toward the inflow end of the leaflet frame and two legs of the U-shape pointing toward the outflow end.

20. The heart valve of claim 19, wherein the leaflet frame, cusp positioners, and cusp connectors are formed integrally as a single piece, and

wherein the three cusp positioners and three cusp connectors define a continuous, undulating shape that generally mimics the shape of the leaflet frame but is rotated 60° about the flow axis therefrom.

21. The heart valve of claim 18, wherein an inflow periphery of the heart valve is defined along the alternating and rigidly fixed cusp regions and cusp connectors.

22. The heart valve of claim 21, wherein the inflow periphery has an external fabric covering, and wherein the heart valve further includes a fabric panel defining an exterior surface of the heart valve between each pair of cusp positioner and cusp connector.

23. The heart valve of claim 14, wherein the leaflet frame has a fabric covering along substantially its entire length, the fabric covering defining a flange, wherein the arcuate cusp edges of the flexible leaflets attach to the fabric covering flange.

24. The heart valve of claim 23, wherein the fabric covering flange projects generally outward from the leaflet frame and the cusp edges of the flexible leaflets extend radially outward past and underneath the leaflet frame and are sewn to the fabric covering flange.

25. The heart valve of claim 14, wherein each flexible leaflet has a pair of tabs extending on either side of its free edge, wherein two tabs of adjacent flexible leaflets meet and pass together to the outside of the adjacent commissure region of the leaflet frame and are attached thereto using sutures through the tabs.

26. A collapsible prosthetic heart valve, comprising:

a continuous, collapsible leaflet frame having three U-shaped cusp regions intermediate three U-shaped commissure regions, the three cusp regions being positioned at an inflow end of the leaflet frame and circumferentially about a flow axis defined within the leaflet frame, the three commissure regions being positioned at an outflow end of the leaflet frame and circumferentially about the flow axis;

a cloth covering extending around the leaflet frame; and

three separate, flexible leaflets attached to the leaflet frame, each leaflet having an arcuate cusp edge opposite a free edge and a pair of commissure edges therebetween, the leaflets being attached around the leaflet frame with the cusp edge of each leaflet extending along one of the cusp regions, and a commissure edge of each leaflet meeting a commissure edge of an adjacent leaflet at one of the commissure regions, the commissure edges of each leaflet further including a tab, wherein the tabs of two adjacent leaflets extend through the U-shape commissure region, diverge on the outside of commissure region, and are attached to the leaflet frame on the outside of the commissure region.

27. The prosthetic heart valve of claim 26, further comprising three cusp positioners rigidly fixed with respect to the leaflet frame and disposed circumferentially about the flow axis, each cusp positioner being located at the outflow end of the support frame and intermediate two of the commissure regions of the leaflet frame, each cusp positioner having a U-shape with an apex of the U-shape pointing toward the outflow end of the leaflet frame and two legs of the U-shape pointing toward the inflow end.

28. The heart valve of claim 26, wherein the heart valve further includes three cusp connectors rigidly fixed with respect to the leaflet frame and

disposed circumferentially about the flow axis, each cusp connector being located at the inflow end of the leaflet frame and intermediate two of the cusp regions of the leaflet frame.

29. The heart valve of claim 28, wherein an inflow periphery of the heart valve is defined along the alternating and rigidly fixed cusp regions and cusp connectors.

30. The heart valve of claim 26, wherein the leaflet frame has a fabric covering along substantially its entire length, the fabric covering defining a flange, wherein the arcuate cusp edges of the flexible leaflets attach to the fabric covering flange.

31. The heart valve of claim 30, wherein the fabric covering flange projects generally outward from the leaflet frame and the cusp edges of the flexible leaflets extend radially outward past and underneath the leaflet frame and are sewn to the fabric covering flange.

32. A method of implanting a prosthetic aortic heart valve, comprising:

providing a collapsible prosthetic heart valve having a collapsible leaflet frame defined by three cusp regions on an inflow end of the valve intermediate three commissure regions on an outflow end of the valve, the valve further including three cusp positioners on the outflow end and intermediate the three commissure regions;

collapsing the prosthetic heart valve within a delivery tube;

advancing the prosthetic heart valve within the delivery tube to an aortic annulus;

expelling the prosthetic heart valve from the delivery tube by relative movement therebetween;

expanding the prosthetic heart valve; and

positioning the prosthetic heart valve such that the cusp positioners contact the two coronary and one non-coronary sinuses of the ascending aorta without blocking the coronary ostia.

33. The method of claim 32, further including:

connecting a holder having flexible members to the commissure regions of the prosthetic heart valve and utilizing the flexible members to perform the step of positioning the prosthetic heart valve.

34. The method of claim 33, further including:

connecting flexible members of the holder to the cusp positioners and utilizing the flexible members to perform the step of positioning the prosthetic heart valve.

35. The method of claim 33, further including utilizing the flexible members to rotate the prosthetic heart valve during the step of positioning.

36. The method of claim 33, further including utilizing the flexible members to re-collapse the prosthetic heart valve after the step of expanding.

37. The method of claim 32, wherein the prosthetic heart valve is expanded in a location that is inferior to a final implant position such that the cusp positioners contact the surrounding aortic annulus, and the step of positioning comprises displacing the valve in a superior direction to a final implant position.

38. The method of claim 37, wherein the cusp positioners are flared outward to define a circle about a flow axis of the valve greater than a circle about the flow axis defined by the three commissure regions, and wherein the step of displacing the valve in a superior direction causes the outwardly flared cusp positioners to be channeled into perspective coronary sinuses.

39. The method of claim 32, wherein the collapsible leaflet frame is formed of a shape memory alloy having an austenitic transition temperature less than body temperature, and wherein the step of collapsing is done with the material of the leaflet frame at a temperature at or below its martensitic transition temperature.

40. The method of claim 39, wherein the step of collapsing is done in conjunction with immersing the prosthetic heart valve in an ice bath to reduce the temperature of the material of leaflet frame to less than or equal to its martensitic transition temperature.

41. The method of claim 32, wherein the collapsible leaflet frame is formed of a shape memory alloy having a memory condition in its expanded state, and wherein the step of expanding the prosthetic heart valve comprises both permitting self-expansion of the valve to an intermediate diameter and then using a physical expander to increase the diameter of the valve to the memory condition of the leaflet frame.

42. A method of implanting a collapsible prosthetic heart valve, comprising:

providing a self-expanding valve comprised of a material displaying hysteresis in the elastic or superelastic region;

permitting the valve to self-expand to a first diameter; and

assisting the valve with a physical expander to further expand to a second diameter.

43. The method of claim 42, wherein the prosthetic heart valve includes a collapsible leaflet frame formed of a shape memory alloy having an austenitic transition temperature less than body temperature, and further including a step of collapsing the valve with the material of the leaflet frame at a temperature at or below its martensitic transition temperature.

44. The method of claim 43, wherein the step of collapsing is done in conjunction with immersing the prosthetic heart valve in an ice bath to reduce the temperature of the material of leaflet frame to less than or equal to its martensitic transition temperature.

45. The method of claim 42, wherein the physical expander is a balloon.

46. The method of claim 42, wherein the prosthetic heart valve has a collapsible leaflet frame defined by three cusp regions on an inflow end of the valve intermediate three commissure regions on an outflow end of the valve, the valve further including three cusp positioners on the outflow end and intermediate the three commissure regions, the method further including:

collapsing the prosthetic heart valve within a delivery tube;

advancing the prosthetic heart valve within the delivery tube to an aortic annulus;

expelling the prosthetic heart valve from the delivery tube by relative movement therebetween;

expanding the prosthetic heart valve by the steps of permitting self-expansion and assisting further expansion; and

positioning the prosthetic heart valve such that the cusp positioners contact the two coronary and one non-coronary sinuses of the ascending aorta without blocking the coronary ostia.

47. The method of claim 46, further including:

connecting a holder having flexible members to the commissure regions of the prosthetic heart valve and utilizing the flexible members to perform the step of positioning the prosthetic heart valve.

48. The method of claim 47, further including:

connecting flexible members of the holder to the cusp positioners and utilizing the flexible members to perform the step of positioning the prosthetic heart valve.

49. The method of claim 47, further including utilizing the flexible members to rotate the prosthetic heart valve during the step of positioning.

50. The method of claim 47, further including utilizing the flexible members to re-collapse the prosthetic heart valve after the step of expanding.

Fig. 1

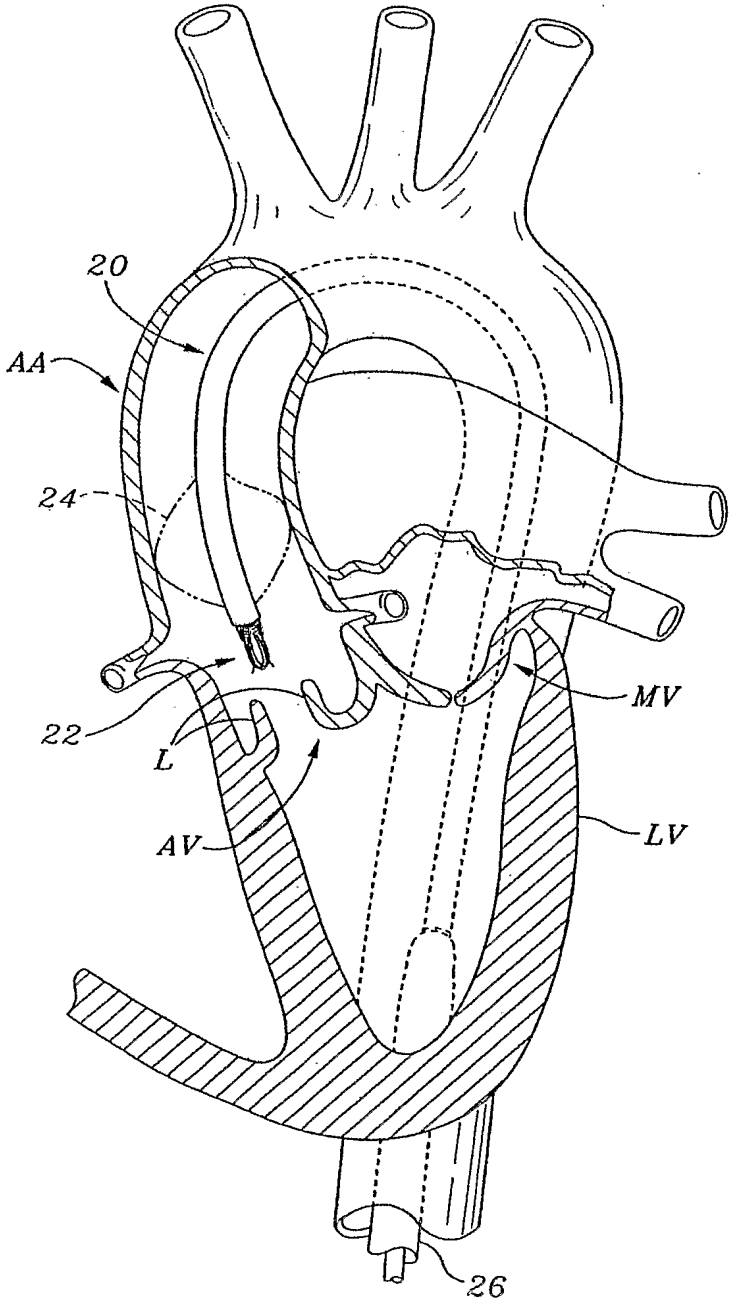


Fig. 2B

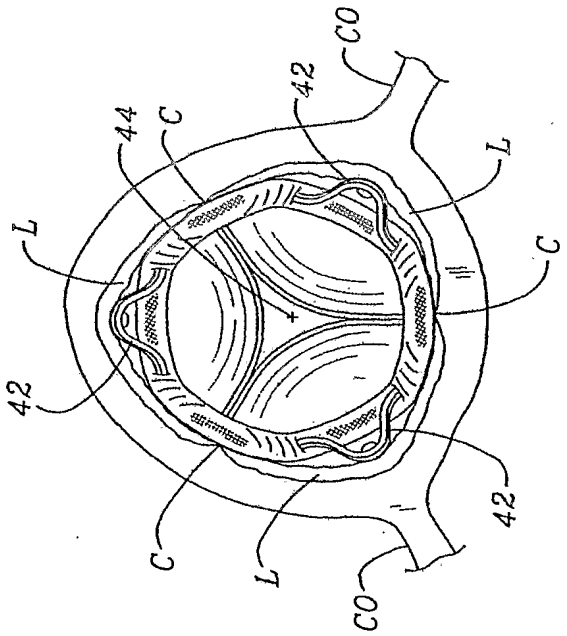


Fig. 2A

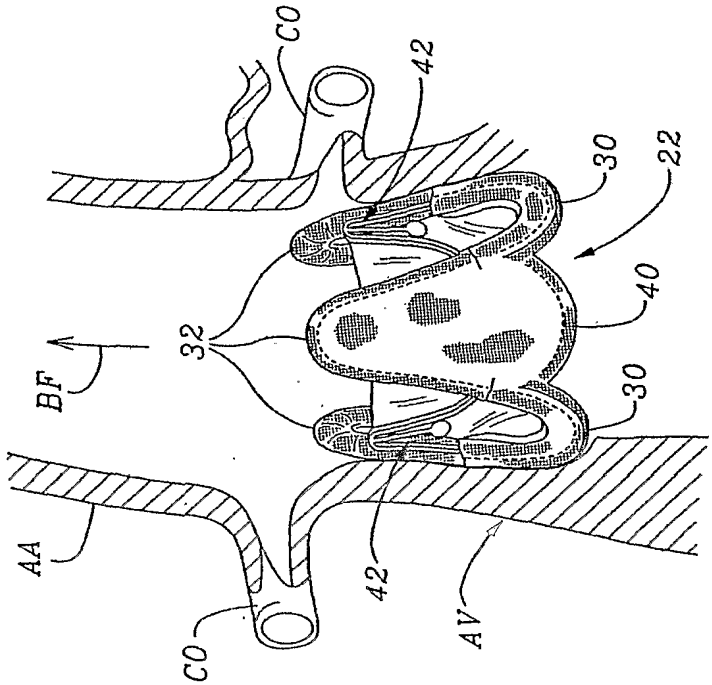


Fig. 3A

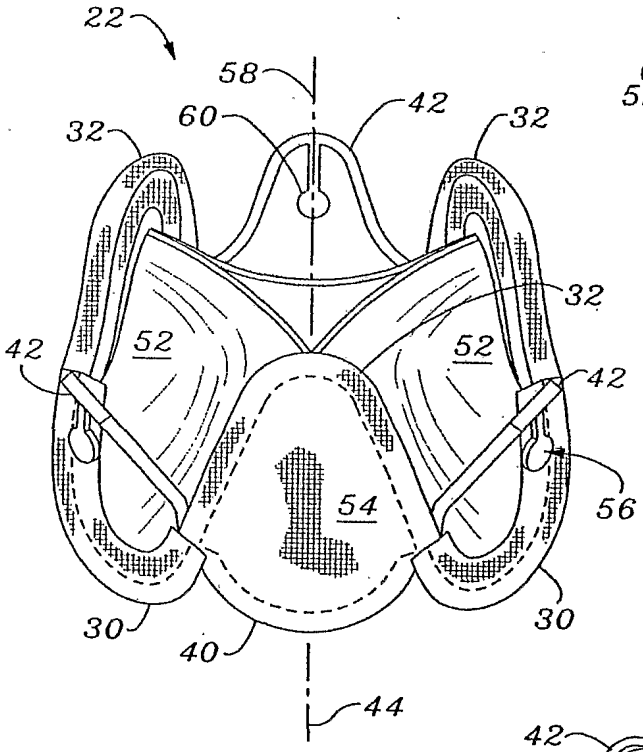


Fig. 3B

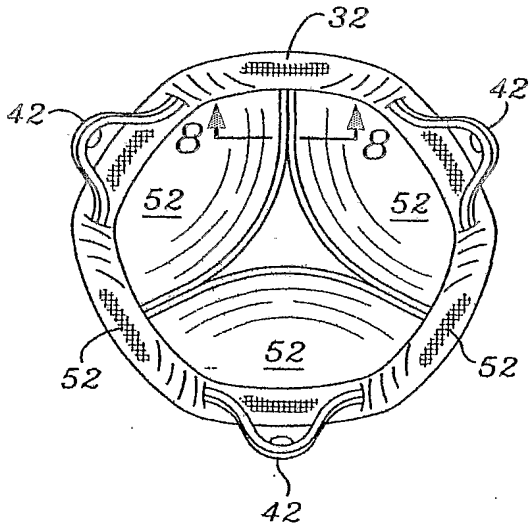


Fig. 3C

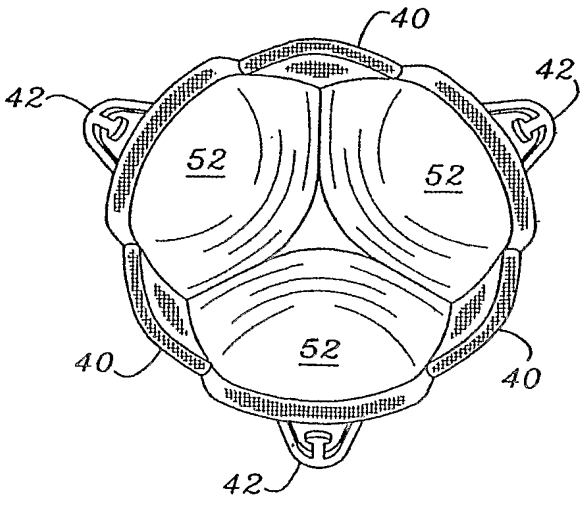


Fig. 4

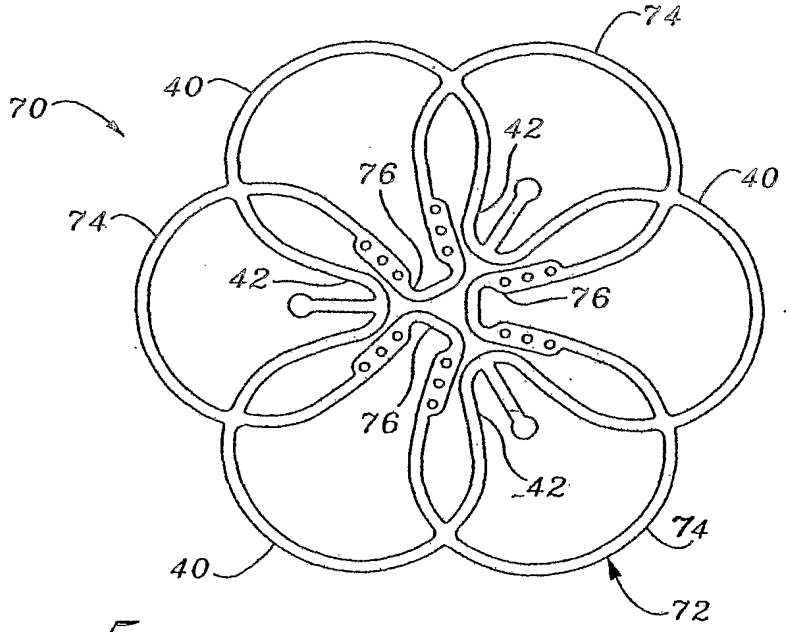
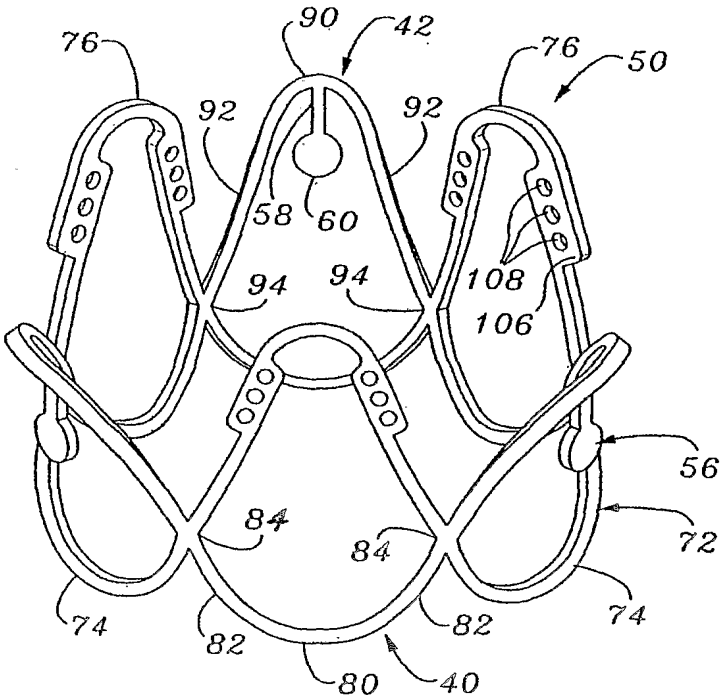


Fig. 5



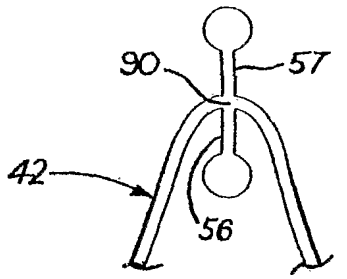


Fig. 5A

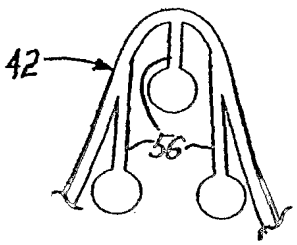


Fig. 5B

Fig. 6A

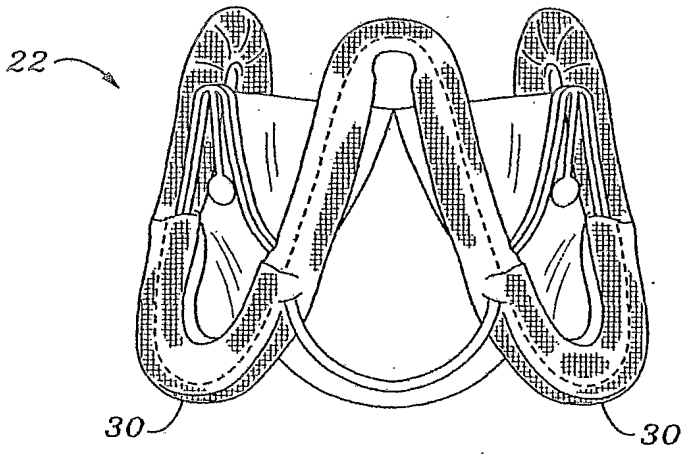


Fig. 6B

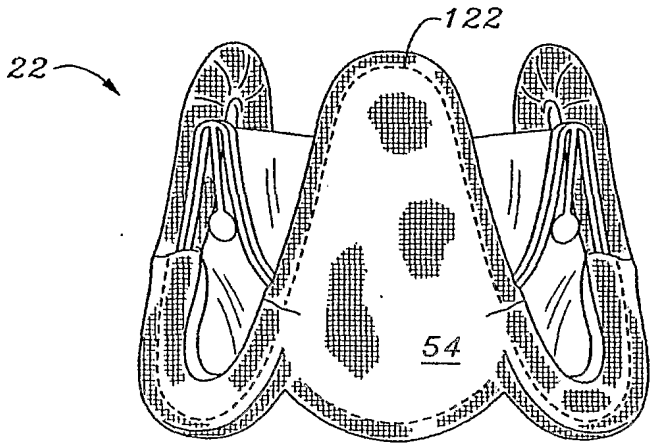


Fig. 7

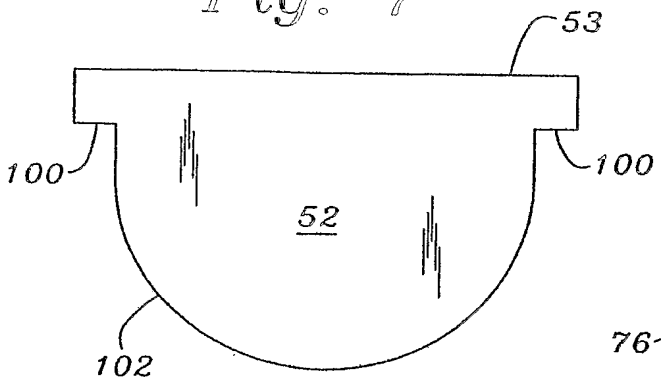
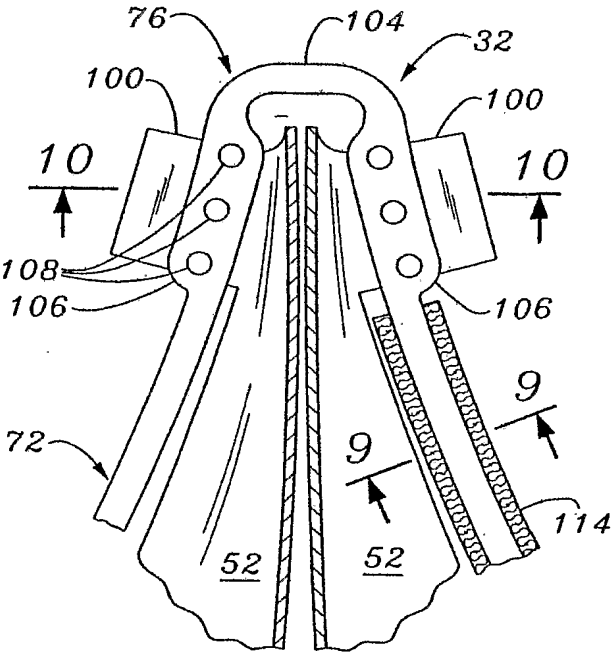


Fig. 8



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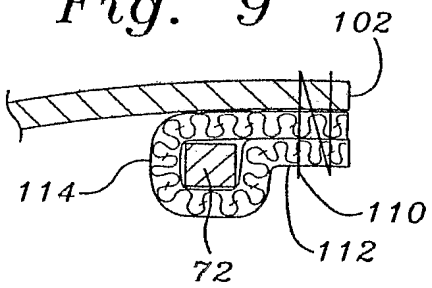


Fig. 10

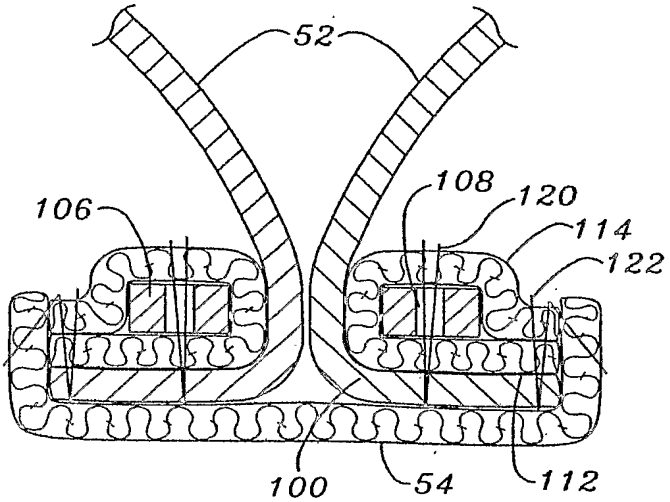


Fig. 11

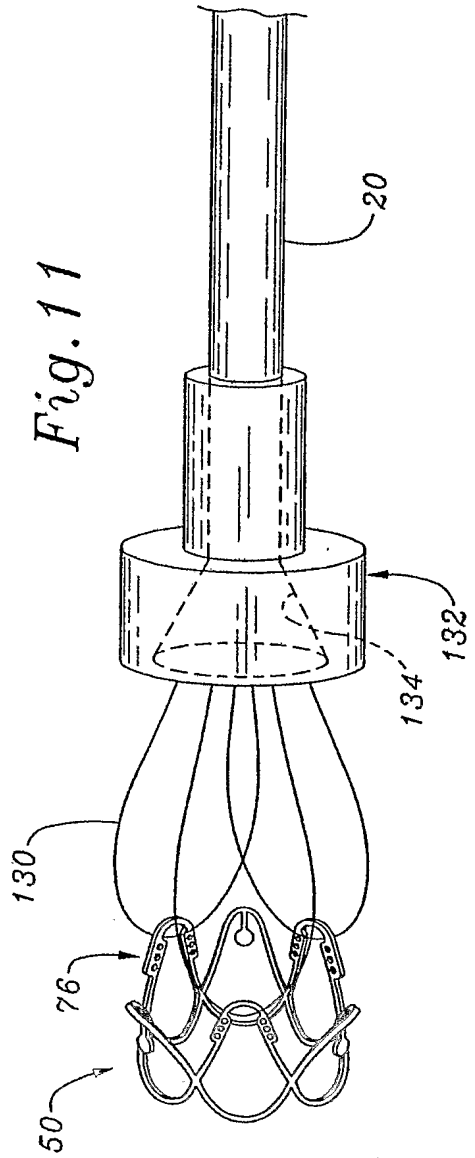
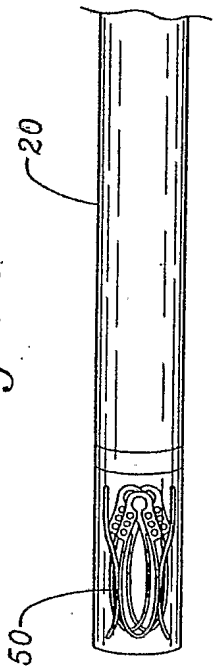


Fig. 12



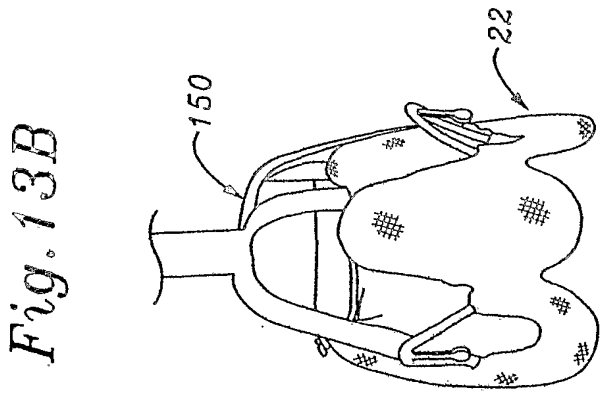


Fig. 13B

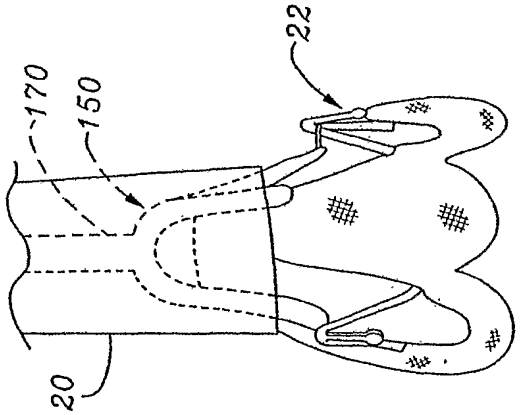


Fig. 14

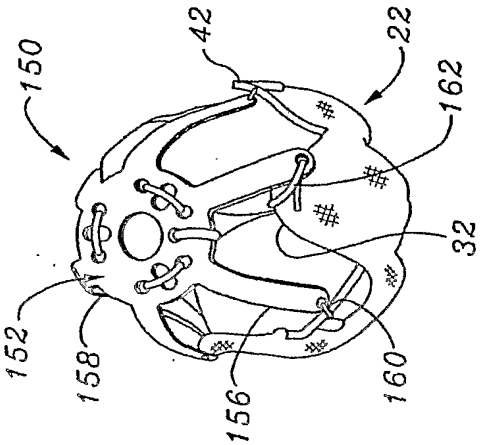


Fig. 13A

Fig. 16

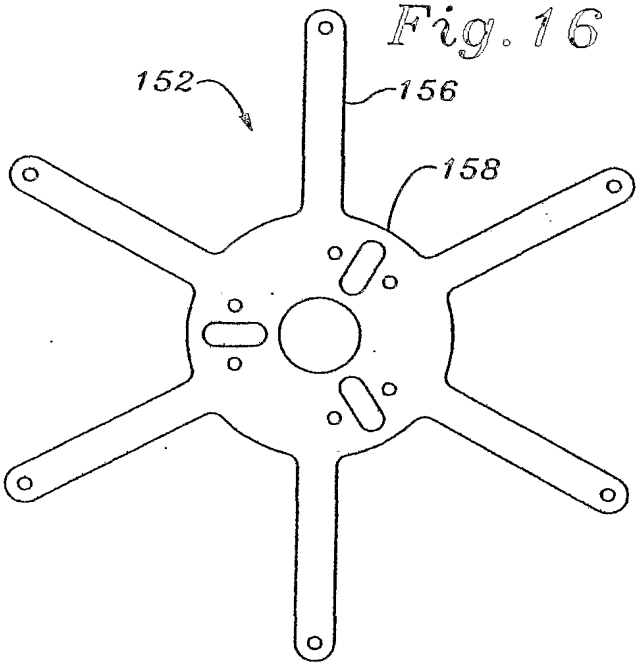


Fig. 17A

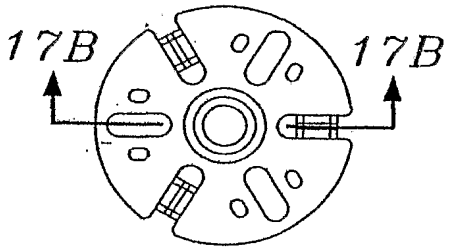


Fig. 17B

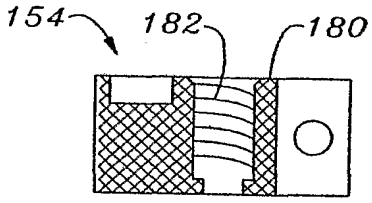
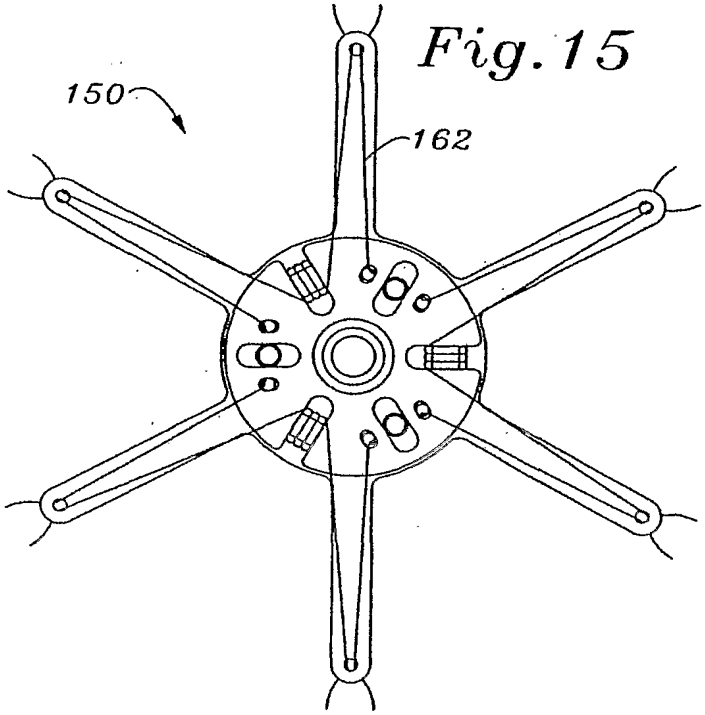


Fig. 15



Electronic Acknowledgement Receipt

EFS ID:	19117331
Application Number:	13675665
International Application Number:	
Confirmation Number:	1995
Title of Invention:	PERCUTANEOUSLY IMPLANTABLE REPLACEMENT HEART VALVE DEVICE AND METHOD OF MAKING SAME
First Named Inventor/Applicant Name:	David Paniagua
Customer Number:	29880
Filer:	Mark Lauren Yaskanin/Carol Donahue
Filer Authorized By:	Mark Lauren Yaskanin
Attorney Docket Number:	109978.10101
Receipt Date:	23-MAY-2014
Filing Date:	13-NOV-2012
Time Stamp:	15:21:58
Application Type:	Utility under 35 USC 111(a)

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Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Information Disclosure Statement (IDS) Form (SB08)	Colibri_10101_Supp_IDS.pdf	555811 4893405e02b32cabcd0822b16649846863dc6c0c	no	7

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2	Foreign Reference	WO-2004-082527.pdf	2197853 f4d0d8ee205f8293529b296c1314228fb54751a7	no	49
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(Not for submission under 37 CFR 1.99)

Application Number	13675665
Filing Date	2012-11-13
First Named Inventor	David PANIAGUA
Art Unit	3738
Examiner Name	Cheryl L. MILLER
Attorney Docket Number	109978.10101

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	2	20030027332		2003-02-06	Lafrance et al.	
	3	20070061008		2007-03-15	Salahieh et al.	
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INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	13675665
	Filing Date	2012-11-13
	First Named Inventor	David PANIAGUA
	Art Unit	3738
	Examiner Name	Cheryl L. MILLER
	Attorney Docket Number	109978.10101

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	1	HILBERT et al., "Biomechanics: Allograft Heart Valves," Cardiac Reconstructions with Allograft Tissues, Springer, New York (2005), pp. 210-212	☐
	2	Office Action issued June 9, 2014, in U.S. Application No. 14/253,650 (109978.10104)	☐
	3	Office Action issued July 8, 2014, in U.S. Application No. 14/253,656 (File: 109978.10113)	☐
	4	Office Action issued August 15, 2014, in U.S. Application No. 14/284,063 (File: 109978.10117)	☐

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	Application Number	13675665
	Filing Date	2012-11-13
	First Named Inventor	David PANIAGUA
	Art Unit	3738
	Examiner Name	Cheryl L. MILLER
	Attorney Docket Number	109978.10101

CERTIFICATION STATEMENT

Please see 37 CFR 1.97 and 1.98 to make the appropriate selection(s):

☐ That each item of information contained in the information disclosure statement was first cited in any communication from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e)(1).

OR

☐ That no item of information contained in the information disclosure statement was cited in a communication from a foreign patent office in a counterpart foreign application, and, to the knowledge of the person signing the certification after making reasonable inquiry, no item of information contained in the information disclosure statement was known to any individual designated in 37 CFR 1.56(c) more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e)(2).

☐ See attached certification statement.

☐ The fee set forth in 37 CFR 1.17 (p) has been submitted herewith.

☒ A certification statement is not submitted herewith.

SIGNATURE

A signature of the applicant or representative is required in accordance with CFR 1.33, 10.18. Please see CFR 1.4(d) for the form of the signature.

Signature	/ Mark L. Yaskanin /	Date (YYYY-MM-DD)	2014-08-29
Name/Print	Mark L. Yaskanin	Registration Number	45246

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 1 hour to complete, including gathering, preparing and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

Privacy Act Statement

The Privacy Act of 1974 (P.L. 93-579) requires that you be given certain information in connection with your submission of the attached form related to a patent application or patent. Accordingly, pursuant to the requirements of the Act, please be advised that: (1) the general authority for the collection of this information is 35 U.S.C. 2(b)(2); (2) furnishing of the information solicited is voluntary; and (3) the principal purpose for which the information is used by the U.S. Patent and Trademark Office is to process and/or examine your submission related to a patent application or patent. If you do not furnish the requested information, the U.S. Patent and Trademark Office may not be able to process and/or examine your submission, which may result in termination of proceedings or abandonment of the application or expiration of the patent.

The information provided by you in this form will be subject to the following routine uses:

1. The information on this form will be treated confidentially to the extent allowed under the Freedom of Information Act (5 U.S.C. 552) and the Privacy Act (5 U.S.C. 552a). Records from this system of records may be disclosed to the Department of Justice to determine whether the Freedom of Information Act requires disclosure of these record s.

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5. A record related to an International Application filed under the Patent Cooperation Treaty in this system of records may be disclosed, as a routine use, to the International Bureau of the World Intellectual Property Organization, pursuant to the Patent Cooperation Treaty.

6. A record in this system of records may be disclosed, as a routine use, to another federal agency for purposes of National Security review (35 U.S.C. 181) and for review pursuant to the Atomic Energy Act (42 U.S.C. 218(c)).

7. A record from this system of records may be disclosed, as a routine use, to the Administrator, General Services, or his/her designee, during an inspection of records conducted by GSA as part of that agency's responsibility to recommend improvements in records management practices and programs, under authority of 44 U.S.C. 2904 and 2906. Such disclosure shall be made in accordance with the GSA regulations governing inspection of records for this purpose, and any other relevant (i.e., GSA or Commerce) directive. Such disclosure shall not be used to make determinations about individuals.

8. A record from this system of records may be disclosed, as a routine use, to the public after either publication of the application pursuant to 35 U.S.C. 122(b) or issuance of a patent pursuant to 35 U.S.C. 151. Further, a record may be disclosed, subject to the limitations of 37 CFR 1.14, as a routine use, to the public if the record was filed in an application which became abandoned or in which the proceedings were terminated and which application is referenced by either a published application, an application open to public inspections or an issued patent.

9. A record from this system of records may be disclosed, as a routine use, to a Federal, State, or local law enforcement agency, if the USPTO becomes aware of a violation or potential violation of law or regulation.

Electronic Acknowledgement Receipt

EFS ID:	20002661
Application Number:	13675665
International Application Number:	
Confirmation Number:	1995
Title of Invention:	PERCUTANEOUSLY IMPLANTABLE REPLACEMENT HEART VALVE DEVICE AND METHOD OF MAKING SAME
First Named Inventor/Applicant Name:	David Paniagua
Customer Number:	29880
Filer:	Mark Lauren Yaskanin/Carol Donahue
Filer Authorized By:	Mark Lauren Yaskanin
Attorney Docket Number:	109978.10101
Receipt Date:	29-AUG-2014
Filing Date:	13-NOV-2012
Time Stamp:	11:15:58
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	no

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Information Disclosure Statement (IDS) Form (SB08)	Colibri_10101_Supp_IDS_2014-08-29.PDF	636455 695c0e0eda75c335307eea3b57112c831ad4dd3f	no	4

Warnings:	
Information:	

2	Non Patent Literature	Hilbert_Biomechanics.PDF	411710 b4851a8736a6654787e31c40da105c179fcf1302	no	4
Warnings:					
Information:					
3	Non Patent Literature	10104_US_14-253650_Office_Action_2014-06-09.PDF	321329 e8440a26ba7de47d56ec1425b05252a020c00f9c	no	8
Warnings:					
Information:					
4	Non Patent Literature	10113_US_14-253656_Office_Action_2014-07-08.PDF	437014 37dc712effb927478d8a4a3f745f32f2fabbfcb2	no	11
Warnings:					
Information:					
5	Non Patent Literature	10117_US_14-284063_Office_Action_2014-08-15.PDF	405746 767cb51c75a56970fcae19c2c2d9362f0c07ac12	no	10
Warnings:					
Information:					
		Total Files Size (in bytes):	2212254		

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New Applications Under 35 U.S.C. 111

If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

National Stage of an International Application under 35 U.S.C. 371

If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office

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PTO/SB/08a (01-10)
Approved for use through 07/31/2012. OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(Not for submission under 37 CFR 1.99)

Application Number	13675665
Filing Date	2012-11-13
First Named Inventor	David PANIAGUA
Art Unit	3738
Examiner Name	Cheryl L. MILLER
Attorney Docket Number	109978.10101

U.S.PATENTS Remove

Examiner Initial*	Cite No	Patent Number	Kind Code[1]	Issue Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
	1	6676698		2004-01-13	McGuckin, Jr.	
	2	6733525		2004-05-11	Yang et al.	

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Examiner Initial*	Cite No	Publication Number	Kind Code[1]	Publication Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
	1					

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Examiner Initial*	Cite No	Foreign Document Number[3]	Country Code[2] i	Kind Code[4]	Publication Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear	T[5]
	1							☐

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NON-PATENT LITERATURE DOCUMENTS Remove

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	13675665
	Filing Date	2012-11-13
	First Named Inventor	David PANIAGUA
	Art Unit	3738
	Examiner Name	Cheryl L. MILLER
	Attorney Docket Number	109978.10101

Examiner Initials*	Cite No	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc), date, pages(s), volume-issue number(s), publisher, city and/or country where published.	T[5]
	1	Office Action issued September 11, 2014, in U.S. Application No. 14/268,190 (File: 109978.10115)	☐
	2	Office Action issued September 3, 2014, in U.S. Application No. 14/284,049 (File: 109978.10116)	☐
	3	Office Action issued September 12, 2014, in U.S. Application No. 14/268,184 (File: 109978.10114)	☐

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Examiner Signature		Date Considered	

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through a citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

[1] See Kind Codes of USPTO Patent Documents at www.USPTO.GOV or MPEP 901.04. [2] Enter office that issued the document, by the two-letter code (WIPO Standard ST.3). [3] For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. [4] Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. [5] Applicant is to place a check mark here if English language translation is attached.

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	13675665
	Filing Date	2012-11-13
	First Named Inventor	David PANIAGUA
	Art Unit	3738
	Examiner Name	Cheryl L. MILLER
	Attorney Docket Number	109978.10101

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☒ A certification statement is not submitted herewith.

SIGNATURE

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Signature	/ Mark L. Yaskanin /	Date (YYYY-MM-DD)	2014-09-17
Name/Print	Mark L. Yaskanin	Registration Number	45246

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Electronic Acknowledgement Receipt

EFS ID:	20168703
Application Number:	13675665
International Application Number:	
Confirmation Number:	1995
Title of Invention:	PERCUTANEOUSLY IMPLANTABLE REPLACEMENT HEART VALVE DEVICE AND METHOD OF MAKING SAME
First Named Inventor/Applicant Name:	David Paniagua
Customer Number:	29880
Filer:	Mark Lauren Yaskanin/Carol Donahue
Filer Authorized By:	Mark Lauren Yaskanin
Attorney Docket Number:	109978.10101
Receipt Date:	17-SEP-2014
Filing Date:	13-NOV-2012
Time Stamp:	17:13:15
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	no

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Information Disclosure Statement (IDS) Form (SB08)	Colibri_10101_Supp_IDS_2014-09-17.PDF	656908 70904b1db64e65b714152b4ef6eb6413e6148a39	no	4

Warnings:	
Information:	

2	Non Patent Literature	10114_US_14-264184_Office_Action_2014-09-12.PDF	459730 b11ce91ce36a866c33d03b2a7d3360d4ff025cfc	no	12
Warnings:					
Information:					
3	Non Patent Literature	10115_US_14-268190_Office_Action_2014-09-11.PDF	789645 6113f5cb5892a4df0d3c7c1a6375cda9a03c1a5d	no	19
Warnings:					
Information:					
4	Non Patent Literature	10116_US_14-284049_Office_Action_2014-09-03.PDF	416178 b343786491136eddbbad5222e392024a2a80ebde	no	11
Warnings:					
Information:					
			Total Files Size (in bytes):	2322461	

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New Applications Under 35 U.S.C. 111

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New International Application Filed with the USPTO as a Receiving Office

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PTO/SB/08a (01-10)
Approved for use through 07/31/2012. OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(Not for submission under 37 CFR 1.99)

Application Number	13675665
Filing Date	2012-11-13
First Named Inventor	David PANIAGUA
Art Unit	3738
Examiner Name	Cheryl L. MILLER
Attorney Docket Number	109978.10101

U.S.PATENTS Remove

Examiner Initial*	Cite No	Patent Number	Kind Code[1]	Issue Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
	1	6530952		2003-03-11	Vesely	

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U.S.PATENT APPLICATION PUBLICATIONS Remove

Examiner Initial*	Cite No	Publication Number	Kind Code[1]	Publication Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
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Examiner Initial*	Cite No	Foreign Document Number[3]	Country Code[2] i	Kind Code[4]	Publication Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear	T[5]
	1							☐

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NON-PATENT LITERATURE DOCUMENTS Remove

Examiner Initials*	Cite No	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc), date, pages(s), volume-issue number(s), publisher, city and/or country where published.	T[5]

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	13675665
	Filing Date	2012-11-13
	First Named Inventor	David PANIAGUA
	Art Unit	3738
	Examiner Name	Cheryl L. MILLER
	Attorney Docket Number	109978.10101

	1	Final Office Action issued September 25, 2014, in U.S. Application No. 14/253,656 (File: 109978.10113)	☐

If you wish to add additional non-patent literature document citation information please click the Add button Add

EXAMINER SIGNATURE

Examiner Signature		Date Considered	

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through a citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

[1] See Kind Codes of USPTO Patent Documents at www.USPTO.GOV or MPEP 901.04. [2] Enter office that issued the document, by the two-letter code (WIPO Standard ST.3). [3] For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. [4] Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. [5] Applicant is to place a check mark here if English language translation is attached.

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
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Signature	/ Mark L. Yaskanin /	Date (YYYY-MM-DD)	2014-09-26
Name/Print	Mark L. Yaskanin	Registration Number	45246

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8. A record from this system of records may be disclosed, as a routine use, to the public after either publication of the application pursuant to 35 U.S.C. 122(b) or issuance of a patent pursuant to 35 U.S.C. 151. Further, a record may be disclosed, subject to the limitations of 37 CFR 1.14, as a routine use, to the public if the record was filed in an application which became abandoned or in which the proceedings were terminated and which application is referenced by either a published application, an application open to public inspections or an issued patent.

9. A record from this system of records may be disclosed, as a routine use, to a Federal, State, or local law enforcement agency, if the USPTO becomes aware of a violation or potential violation of law or regulation.

Electronic Acknowledgement Receipt

EFS ID:	20253380
Application Number:	13675665
International Application Number:	
Confirmation Number:	1995
Title of Invention:	PERCUTANEOUSLY IMPLANTABLE REPLACEMENT HEART VALVE DEVICE AND METHOD OF MAKING SAME
First Named Inventor/Applicant Name:	David Paniagua
Customer Number:	29880
Filer:	Mark Lauren Yaskanin/Carol Donahue
Filer Authorized By:	Mark Lauren Yaskanin
Attorney Docket Number:	109978.10101
Receipt Date:	26-SEP-2014
Filing Date:	13-NOV-2012
Time Stamp:	11:46:59
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	no

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Information Disclosure Statement (IDS) Form (SB08)	Colibri_10101_Supp_IDS_2014-09-26.PDF	655948 454f135446ce10b03d9b616520175a5739c25bfc	no	4

Warnings:	
Information:	

2	Non Patent Literature	10113_US_14-253656_Final_Office_Action_2014-09-25.PDF	538987 cb00303b193a23cd9bb73177ceeba6167d2b91a4	no	14

Warnings:	
Information:	
Total Files Size (in bytes):	1194935

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New Applications Under 35 U.S.C. 111

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National Stage of an International Application under 35 U.S.C. 371

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New International Application Filed with the USPTO as a Receiving Office

If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

PTO/SB/08a (01-10)
Approved for use through 07/31/2012. OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(Not for submission under 37 CFR 1.99)

Application Number	13675665
Filing Date	2012-11-13
First Named Inventor	David PANIAGUA
Art Unit	3738
Examiner Name	Cheryl L. MILLER
Attorney Docket Number	109978.10101

U.S.PATENTS Remove

Examiner Initial*	Cite No	Patent Number	Kind Code[1]	Issue Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
	1	5484444		1996-01-16	Braunschweiler et al.	
	2	5645559		1997-07-08	Hachtman et al.	
	3	5683451		1997-11-04	Lenker et al.	
	4	5876448		1999-03-02	Thompson et al.	
	5	6350278		2002-02-26	Lenker et al.	
	6	6682537		2004-01-27	Ouriel et al.	
	7	6896690		2005-05-24	Lambrecht et al.	
	8	7556646		2009-07-07	Yang et al.	

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INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(Not for submission under 37 CFR 1.99)

Application Number	13675665
Filing Date	2012-11-13
First Named Inventor	David PANIAGUA
Art Unit	3738
Examiner Name	Cheryl L. MILLER
Attorney Docket Number	109978.10101

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Examiner Initial*	Cite No	Publication Number	Kind Code[1]	Publication Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
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Examiner Initial*	Cite No	Foreign Document Number[3]	Country Code[2] i	Kind Code[4]	Publication Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear	T[5]
	1							☐

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NON-PATENT LITERATURE DOCUMENTS Remove

Examiner Initials*	Cite No	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc), date, pages(s), volume-issue number(s), publisher, city and/or country where published.	T[5]
	1	Notice of Allowance issued October 7, 2014, in U.S. Application No. 14/253,656 (File: 109978.10113)	☐

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Examiner Signature		Date Considered	

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through a citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

[1] See Kind Codes of USPTO Patent Documents at www.USPTO.GOV or MPEP 901.04. [2] Enter office that issued the document, by the two-letter code (WIPO Standard ST.3). [3] For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. [4] Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. [5] Applicant is to place a check mark here if English language translation is attached.

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	13675665
	Filing Date	2012-11-13
	First Named Inventor	David PANIAGUA
	Art Unit	3738
	Examiner Name	Cheryl L. MILLER
	Attorney Docket Number	109978.10101

CERTIFICATION STATEMENT

Please see 37 CFR 1.97 and 1.98 to make the appropriate selection(s):

☐ That each item of information contained in the information disclosure statement was first cited in any communication from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e)(1).

OR

☐ That no item of information contained in the information disclosure statement was cited in a communication from a foreign patent office in a counterpart foreign application, and, to the knowledge of the person signing the certification after making reasonable inquiry, no item of information contained in the information disclosure statement was known to any individual designated in 37 CFR 1.56(c) more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e)(2).

☐ See attached certification statement.

☐ The fee set forth in 37 CFR 1.17 (p) has been submitted herewith.

☒ A certification statement is not submitted herewith.

SIGNATURE

A signature of the applicant or representative is required in accordance with CFR 1.33, 10.18. Please see CFR 1.4(d) for the form of the signature.

Signature	/ Mark L. Yaskanin /	Date (YYYY-MM-DD)	2014-10-07
Name/Print	Mark L. Yaskanin	Registration Number	45246

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 1 hour to complete, including gathering, preparing and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

Privacy Act Statement

The Privacy Act of 1974 (P.L. 93-579) requires that you be given certain information in connection with your submission of the attached form related to a patent application or patent. Accordingly, pursuant to the requirements of the Act, please be advised that: (1) the general authority for the collection of this information is 35 U.S.C. 2(b)(2); (2) furnishing of the information solicited is voluntary; and (3) the principal purpose for which the information is used by the U.S. Patent and Trademark Office is to process and/or examine your submission related to a patent application or patent. If you do not furnish the requested information, the U.S. Patent and Trademark Office may not be able to process and/or examine your submission, which may result in termination of proceedings or abandonment of the application or expiration of the patent.

The information provided by you in this form will be subject to the following routine uses:

1. The information on this form will be treated confidentially to the extent allowed under the Freedom of Information Act (5 U.S.C. 552) and the Privacy Act (5 U.S.C. 552a). Records from this system of records may be disclosed to the Department of Justice to determine whether the Freedom of Information Act requires disclosure of these record s.

2. A record from this system of records may be disclosed, as a routine use, in the course of presenting evidence to a court, magistrate, or administrative tribunal, including disclosures to opposing counsel in the course of settlement negotiations.

3. A record in this system of records may be disclosed, as a routine use, to a Member of Congress submitting a request involving an individual, to whom the record pertains, when the individual has requested assistance from the Member with respect to the subject matter of the record.

4. A record in this system of records may be disclosed, as a routine use, to a contractor of the Agency having need for the information in order to perform a contract. Recipients of information shall be required to comply with the requirements of the Privacy Act of 1974, as amended, pursuant to 5 U.S.C. 552a(m).

5. A record related to an International Application filed under the Patent Cooperation Treaty in this system of records may be disclosed, as a routine use, to the International Bureau of the World Intellectual Property Organization, pursuant to the Patent Cooperation Treaty.

6. A record in this system of records may be disclosed, as a routine use, to another federal agency for purposes of National Security review (35 U.S.C. 181) and for review pursuant to the Atomic Energy Act (42 U.S.C. 218(c)).

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Electronic Acknowledgement Receipt

EFS ID:	20354976
Application Number:	13675665
International Application Number:	
Confirmation Number:	1995
Title of Invention:	PERCUTANEOUSLY IMPLANTABLE REPLACEMENT HEART VALVE DEVICE AND METHOD OF MAKING SAME
First Named Inventor/Applicant Name:	David Paniagua
Customer Number:	29880
Filer:	Mark Lauren Yaskanin/Carol Donahue
Filer Authorized By:	Mark Lauren Yaskanin
Attorney Docket Number:	109978.10101
Receipt Date:	07-OCT-2014
Filing Date:	13-NOV-2012
Time Stamp:	18:16:12
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	no

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Non Patent Literature	10113_US_14-253656_Notice_of_Allowance_2014-10-07.PDF	240537 a0f5ed8b9f3c8355dca4c8e4728a4283e7b525c3	no	6

Warnings:	
Information:	

2	Information Disclosure Statement (IDS) Form (SB08)	Colibri_10101_Supp_IDS_2014-10-07.PDF	638497 1ac643590fbccc5cad59236bf1f2ede02c4edfa7	no	4

Warnings:	
Information:	
Total Files Size (in bytes):	879034

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New Applications Under 35 U.S.C. 111

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National Stage of an International Application under 35 U.S.C. 371

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New International Application Filed with the USPTO as a Receiving Office

If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

PTO/SB/08a (01-10)
Approved for use through 07/31/2012. OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(Not for submission under 37 CFR 1.99)

Application Number	13675665
Filing Date	2012-11-13
First Named Inventor	David Paniagua
Art Unit	3738
Examiner Name	Cheryl L. MILLER
Attorney Docket Number	109978.10101

U.S.PATENTS Remove

Examiner Initial*	Cite No	Patent Number	Kind Code[1]	Issue Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
	1					

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U.S.PATENT APPLICATION PUBLICATIONS Remove

Examiner Initial*	Cite No	Publication Number	Kind Code[1]	Publication Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
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Examiner Initial*	Cite No	Foreign Document Number[3]	Country Code[2]	Kind Code[4]	Publication Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear	T[5]
	1							☐

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NON-PATENT LITERATURE DOCUMENTS Remove

Examiner Initials*	Cite No	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc), date, pages(s), volume-issue number(s), publisher, city and/or country where published.	T[5]

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	13675665
	Filing Date	2012-11-13
	First Named Inventor	David Paniagua
	Art Unit	3738
	Examiner Name	Cheryl L. MILLER
	Attorney Docket Number	109978.10101

	1	Final Office Action issued November 7, 2014, in U.S. Application No. 14/253,650 (File: 109978.10104)	☐

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EXAMINER SIGNATURE

Examiner Signature		Date Considered	

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[1] See Kind Codes of USPTO Patent Documents at www.USPTO.GOV or MPEP 901.04. [2] Enter office that issued the document, by the two-letter code (WIPO Standard ST.3). [3] For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. [4] Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. [5] Applicant is to place a check mark here if English language translation is attached.

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	13675665
	Filing Date	2012-11-13
	First Named Inventor	David Paniagua
	Art Unit	3738
	Examiner Name	Cheryl L. MILLER
	Attorney Docket Number	109978.10101

CERTIFICATION STATEMENT

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☐ See attached certification statement.

☐ The fee set forth in 37 CFR 1.17 (p) has been submitted herewith.

☒ A certification statement is not submitted herewith.

SIGNATURE

A signature of the applicant or representative is required in accordance with CFR 1.33, 10.18. Please see CFR 1.4(d) for the form of the signature.

Signature	/ Mark L. Yaskanin /	Date (YYYY-MM-DD)	2014-11-14
Name/Print	Mark L. Yaskanin	Registration Number	45246

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 1 hour to complete, including gathering, preparing and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

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Electronic Acknowledgement Receipt

EFS ID:	20702019
Application Number:	13675665
International Application Number:	
Confirmation Number:	1995
Title of Invention:	PERCUTANEOUSLY IMPLANTABLE REPLACEMENT HEART VALVE DEVICE AND METHOD OF MAKING SAME
First Named Inventor/Applicant Name:	David Paniagua
Customer Number:	29880
Filer:	Mark Lauren Yaskanin/Carol Donahue
Filer Authorized By:	Mark Lauren Yaskanin
Attorney Docket Number:	109978.10101
Receipt Date:	14-NOV-2014
Filing Date:	13-NOV-2012
Time Stamp:	15:11:28
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	no

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Information Disclosure Statement (IDS) Form (SB08)	Colibri_10101_SUPP_IDS.PDF	658994 8b7aed36a6cae4629fe6953afb19a303024cbc4c	no	4

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2	Non Patent Literature	10104_US_14-253650_Final_OA_2014-11-07.PDF	574779 000a68c112ec41bd8dc3f1f478f9cd121ce592d3	no	14

Warnings:

Information:

Total Files Size (in bytes):	1233773

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New Applications Under 35 U.S.C. 111

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PTO/SB/08a (01-10)
Approved for use through 07/31/2012. OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(Not for submission under 37 CFR 1.99)

Application Number	13675665
Filing Date	2012-11-13
First Named Inventor	David Paniagua
Art Unit	3738
Examiner Name	Cheryl L. MILLER
Attorney Docket Number	109978.10101

U.S.PATENTS Remove

Examiner Initial*	Cite No	Patent Number	Kind Code[1]	Issue Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
	1					

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U.S.PATENT APPLICATION PUBLICATIONS Remove

Examiner Initial*	Cite No	Publication Number	Kind Code[1]	Publication Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
	1					

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FOREIGN PATENT DOCUMENTS Remove

Examiner Initial*	Cite No	Foreign Document Number[3]	Country Code[2]	Kind Code[4]	Publication Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear	T[5]
	1							☐

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NON-PATENT LITERATURE DOCUMENTS Remove

Examiner Initials*	Cite No	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc), date, pages(s), volume-issue number(s), publisher, city and/or country where published.	T[5]

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	13675665
	Filing Date	2012-11-13
	First Named Inventor	David Paniagua
	Art Unit	3738
	Examiner Name	Cheryl L. MILLER
	Attorney Docket Number	109978.10101

	1	Cross-reference is made to U.S. Application No. 14/502,453 filed on September 30, 2014, and its associated Preliminary Amendment (109978.10106)	☐

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EXAMINER SIGNATURE

Examiner Signature		Date Considered	

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through a citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

[1] See Kind Codes of USPTO Patent Documents at www.USPTO.GOV or MPEP 901.04. [2] Enter office that issued the document, by the two-letter code (WIPO Standard ST.3). [3] For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. [4] Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. [5] Applicant is to place a check mark here if English language translation is attached.

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	13675665
	Filing Date	2012-11-13
	First Named Inventor	David Paniagua
	Art Unit	3738
	Examiner Name	Cheryl L. MILLER
	Attorney Docket Number	109978.10101

CERTIFICATION STATEMENT

Please see 37 CFR 1.97 and 1.98 to make the appropriate selection(s):

☐ That each item of information contained in the information disclosure statement was first cited in any communication from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e)(1).

OR

☐ That no item of information contained in the information disclosure statement was cited in a communication from a foreign patent office in a counterpart foreign application, and, to the knowledge of the person signing the certification after making reasonable inquiry, no item of information contained in the information disclosure statement was known to any individual designated in 37 CFR 1.56(c) more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e)(2).

☐ See attached certification statement.

☐ The fee set forth in 37 CFR 1.17 (p) has been submitted herewith.

☒ A certification statement is not submitted herewith.

SIGNATURE

A signature of the applicant or representative is required in accordance with CFR 1.33, 10.18. Please see CFR 1.4(d) for the form of the signature.

Signature	/ Mark L. Yaskanin /	Date (YYYY-MM-DD)	2014-11-20
Name/Print	Mark L. Yaskanin	Registration Number	45246

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 1 hour to complete, including gathering, preparing and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

Privacy Act Statement

The Privacy Act of 1974 (P.L. 93-579) requires that you be given certain information in connection with your submission of the attached form related to a patent application or patent. Accordingly, pursuant to the requirements of the Act, please be advised that: (1) the general authority for the collection of this information is 35 U.S.C. 2(b)(2); (2) furnishing of the information solicited is voluntary; and (3) the principal purpose for which the information is used by the U.S. Patent and Trademark Office is to process and/or examine your submission related to a patent application or patent. If you do not furnish the requested information, the U.S. Patent and Trademark Office may not be able to process and/or examine your submission, which may result in termination of proceedings or abandonment of the application or expiration of the patent.

The information provided by you in this form will be subject to the following routine uses:

1. The information on this form will be treated confidentially to the extent allowed under the Freedom of Information Act (5 U.S.C. 552) and the Privacy Act (5 U.S.C. 552a). Records from this system of records may be disclosed to the Department of Justice to determine whether the Freedom of Information Act requires disclosure of these record s.

2. A record from this system of records may be disclosed, as a routine use, in the course of presenting evidence to a court, magistrate, or administrative tribunal, including disclosures to opposing counsel in the course of settlement negotiations.

3. A record in this system of records may be disclosed, as a routine use, to a Member of Congress submitting a request involving an individual, to whom the record pertains, when the individual has requested assistance from the Member with respect to the subject matter of the record.

4. A record in this system of records may be disclosed, as a routine use, to a contractor of the Agency having need for the information in order to perform a contract. Recipients of information shall be required to comply with the requirements of the Privacy Act of 1974, as amended, pursuant to 5 U.S.C. 552a(m).

5. A record related to an International Application filed under the Patent Cooperation Treaty in this system of records may be disclosed, as a routine use, to the International Bureau of the World Intellectual Property Organization, pursuant to the Patent Cooperation Treaty.

6. A record in this system of records may be disclosed, as a routine use, to another federal agency for purposes of National Security review (35 U.S.C. 181) and for review pursuant to the Atomic Energy Act (42 U.S.C. 218(c)).

7. A record from this system of records may be disclosed, as a routine use, to the Administrator, General Services, or his/her designee, during an inspection of records conducted by GSA as part of that agency's responsibility to recommend improvements in records management practices and programs, under authority of 44 U.S.C. 2904 and 2906. Such disclosure shall be made in accordance with the GSA regulations governing inspection of records for this purpose, and any other relevant (i.e., GSA or Commerce) directive. Such disclosure shall not be used to make determinations about individuals.

8. A record from this system of records may be disclosed, as a routine use, to the public after either publication of the application pursuant to 35 U.S.C. 122(b) or issuance of a patent pursuant to 35 U.S.C. 151. Further, a record may be disclosed, subject to the limitations of 37 CFR 1.14, as a routine use, to the public if the record was filed in an application which became abandoned or in which the proceedings were terminated and which application is referenced by either a published application, an application open to public inspections or an issued patent.

9. A record from this system of records may be disclosed, as a routine use, to a Federal, State, or local law enforcement agency, if the USPTO becomes aware of a violation or potential violation of law or regulation.

Electronic Acknowledgement Receipt

EFS ID:	20752745
Application Number:	13675665
International Application Number:	
Confirmation Number:	1995
Title of Invention:	PERCUTANEOUSLY IMPLANTABLE REPLACEMENT HEART VALVE DEVICE AND METHOD OF MAKING SAME
First Named Inventor/Applicant Name:	David Paniagua
Customer Number:	29880
Filer:	Mark Lauren Yaskanin/Carol Donahue
Filer Authorized By:	Mark Lauren Yaskanin
Attorney Docket Number:	109978.10101
Receipt Date:	20-NOV-2014
Filing Date:	13-NOV-2012
Time Stamp:	13:28:33
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	no

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Information Disclosure Statement (IDS) Form (SB08)	Colibri_10101_SUPP_IDS_2014-11-20.PDF	680683 b5069a20d3aa2397a3b21fb103f034bbc5020d59	no	4

Warnings:	
Information:	

A U.S. Patent Number Citation or a U.S. Publication Number Citation is required in the Information Disclosure Statement (IDS) form for autoloading of data into USPTO systems. You may remove the form to add the required data in order to correct the Informational Message if you are citing U.S. References. If you chose not to include U.S. References, the image of the form will be processed and be made available within the Image File Wrapper (IFW) system. However, no data will be extracted from this form. Any additional data such as Foreign Patent Documents or Non Patent Literature will be manually reviewed and keyed into USPTO systems.

2	Non Patent Literature	10106_US_14-502453_Preliminary_Amendment.PDF	138042 d392693ca35db7c7c7b2f546ead31db8e20a94d8	no	10
Warnings:					
Information:					
3	Non Patent Literature	10106_US_14-502453_2nd_Prelim_Amendment_2014-11-19.PDF	119965 2a3ff524e287df719fa75fdd883fb94f44d0285f	no	5
Warnings:					
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		Total Files Size (in bytes):	938690		

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New Applications Under 35 U.S.C. 111

If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

National Stage of an International Application under 35 U.S.C. 371

If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office

If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

PTO/SB/08a (01-10)
Approved for use through 07/31/2012. OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(Not for submission under 37 CFR 1.99)

Application Number	13675665
Filing Date	2012-11-13
First Named Inventor	David Paniagua
Art Unit	3738
Examiner Name	Cheryl L. MILLER
Attorney Docket Number	109978.10101

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Examiner Initial*	Cite No	Patent Number	Kind Code[1]	Issue Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
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Examiner Initial*	Cite No	Publication Number	Kind Code[1]	Publication Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
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Examiner Initial*	Cite No	Foreign Document Number[3]	Country Code[2] i	Kind Code[4]	Publication Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear	T[5]
	1							☐

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NON-PATENT LITERATURE DOCUMENTS Remove

Examiner Initials*	Cite No	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc), date, pages(s), volume-issue number(s), publisher, city and/or country where published.	T[5]

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	13675665
	Filing Date	2012-11-13
	First Named Inventor	David Paniagua
	Art Unit	3738
	Examiner Name	Cheryl L. MILLER
	Attorney Docket Number	109978.10101

	1	Office Action issued December 5, 2014 in U.S. Application No. 14/502,453 (109978.10106)	☐

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EXAMINER SIGNATURE

Examiner Signature		Date Considered	

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through a citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

[1] See Kind Codes of USPTO Patent Documents at www.USPTO.GOV or MPEP 901.04. [2] Enter office that issued the document, by the two-letter code (WIPO Standard ST.3). [3] For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. [4] Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. [5] Applicant is to place a check mark here if English language translation is attached.

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	Application Number	13675665
	Filing Date	2012-11-13
	First Named Inventor	David Paniagua
	Art Unit	3738
	Examiner Name	Cheryl L. MILLER
	Attorney Docket Number	109978.10101

CERTIFICATION STATEMENT

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OR

☐ That no item of information contained in the information disclosure statement was cited in a communication from a foreign patent office in a counterpart foreign application, and, to the knowledge of the person signing the certification after making reasonable inquiry, no item of information contained in the information disclosure statement was known to any individual designated in 37 CFR 1.56(c) more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e)(2).

☐ See attached certification statement.

☐ The fee set forth in 37 CFR 1.17 (p) has been submitted herewith.

☒ A certification statement is not submitted herewith.

SIGNATURE

A signature of the applicant or representative is required in accordance with CFR 1.33, 10.18. Please see CFR 1.4(d) for the form of the signature.

Signature	/ Mark L. Yaskanin /	Date (YYYY-MM-DD)	2015-01-13
Name/Print	Mark L. Yaskanin	Registration Number	45246

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 1 hour to complete, including gathering, preparing and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

Privacy Act Statement

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6. A record in this system of records may be disclosed, as a routine use, to another federal agency for purposes of National Security review (35 U.S.C. 181) and for review pursuant to the Atomic Energy Act (42 U.S.C. 218(c)).

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9. A record from this system of records may be disclosed, as a routine use, to a Federal, State, or local law enforcement agency, if the USPTO becomes aware of a violation or potential violation of law or regulation.

Electronic Acknowledgement Receipt

EFS ID:	21193525
Application Number:	13675665
International Application Number:	
Confirmation Number:	1995
Title of Invention:	PERCUTANEOUSLY IMPLANTABLE REPLACEMENT HEART VALVE DEVICE AND METHOD OF MAKING SAME
First Named Inventor/Applicant Name:	David Paniagua
Customer Number:	29880
Filer:	Mark Lauren Yaskanin/Carol Donahue
Filer Authorized By:	Mark Lauren Yaskanin
Attorney Docket Number:	109978.10101
Receipt Date:	13-JAN-2015
Filing Date:	13-NOV-2012
Time Stamp:	12:46:32
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	no

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Information Disclosure Statement (IDS) Form (SB08)	Colibri_10101_SUPP_IDS_2015-01-13.PDF	719179 ea80c35f84bd650571756df189ca63923f16f3de	no	4

Warnings:	
Information:	

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2	Other Reference-Patent/App/Search documents	10106_Office_Action_2014-12-05.PDF	351762 6e1db64863fa3fa5dd0c8373907e9b3d1a0223cc	no	9

Warnings:

Information:

Total Files Size (in bytes):	1070941

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New Applications Under 35 U.S.C. 111

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National Stage of an International Application under 35 U.S.C. 371

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New International Application Filed with the USPTO as a Receiving Office

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PTO/SB/08a (01-10)
Approved for use through 07/31/2012. OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(Not for submission under 37 CFR 1.99)

Application Number	13675665
Filing Date	2012-11-13
First Named Inventor	David PANIAGUA
Art Unit	3738
Examiner Name	Cheryl L. MILLER
Attorney Docket Number	109978.10101

U.S.PATENTS Remove

Examiner Initial*	Cite No	Patent Number	Kind Code[1]	Issue Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
	1	5554184		1996-09-10	Machiraju	

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U.S.PATENT APPLICATION PUBLICATIONS Remove

Examiner Initial*	Cite No	Publication Number	Kind Code[1]	Publication Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
	1	20020052651		2002-05-02	Myers et al.	
	2	20030209835		2003-11-13	Chun et al.	

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FOREIGN PATENT DOCUMENTS Remove

Examiner Initial*	Cite No	Foreign Document Number[3]	Country Code[2] i	Kind Code[4]	Publication Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear	T[5]
	1	9-501594	JP		1997-02-18		Equivalent to WO/1995/005207	☐
	2	2001-500761	JP		2001-01-23		Equivalent to WO/1998/011935	☐

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	13675665
	Filing Date	2012-11-13
	First Named Inventor	David PANIAGUA
	Art Unit	3738
	Examiner Name	Cheryl L. MILLER
	Attorney Docket Number	109978.10101

	3	2005-103321	JP		2005-04-21		Equivalent to EP0696447	☐
	4	2009/149462	WO		2009-12-10	Edwards Lifesciences Corporation		☐

If you wish to add additional Foreign Patent Document citation information please click the Add button Add

NON-PATENT LITERATURE DOCUMENTS Remove

Examiner Initials*	Cite No	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc), date, pages(s), volume-issue number(s), publisher, city and/or country where published.	T[5]
	1	Declaration Under 37 CFR 1.131 as filed in U.S. Patent Application No. 10/887,688 on December 15, 2008, by co-inventors of that application. (Best available copy)	☐
	2	Final Office Action issued May 8, 2015 in U.S. Application No. 14/502,453 (109978.10106)	☐

If you wish to add additional non-patent literature document citation information please click the Add button Add

EXAMINER SIGNATURE

Examiner Signature		Date Considered	

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[1] See Kind Codes of USPTO Patent Documents at www.USPTO.GOV or MPEP 901.04. [2] Enter office that issued the document, by the two-letter code (WIPO Standard ST.3). [3] For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. [4] Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. [5] Applicant is to place a check mark here if English language translation is attached.

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(Not for submission under 37 CFR 1.99)

Application Number	13675665
Filing Date	2012-11-13
First Named Inventor	David PANIAGUA
Art Unit	3738
Examiner Name	Cheryl L. MILLER
Attorney Docket Number	109978.10101

CERTIFICATION STATEMENT

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☐ See attached certification statement.

☐ The fee set forth in 37 CFR 1.17 (p) has been submitted herewith.

☒ A certification statement is not submitted herewith.

SIGNATURE

A signature of the applicant or representative is required in accordance with CFR 1.33, 10.18. Please see CFR 1.4(d) for the form of the signature.

Signature	/ Mark L. Yaskanin /	Date (YYYY-MM-DD)	2015-06-11
Name/Print	Mark L. Yaskanin	Registration Number	45246

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(54) Title: DUAL VALVE REINFORCED SHEATH AND METHOD

(57) Abstract

A large-diameter expandable sheath for use in introducing a catheter or other medical instrument into a vessel in the body of a patient. The expandable sheath comprises an elongate sheath tube formed of a flexible material which has proximal and distal extremities and a passage extending therethrough of a maximum predetermined diameter. The distal extremity of the elongate sheath tube is folded longitudinally to a smaller folded diameter. The sheath tube may be self-expanding or may be reinforced with a self-expanding wire or expandable stents. A backflow adapter is secured to the proximal extremity of the elongate sheath tube. The backflow adapter has a central opening therein in registration with the passage in the sheath tube. A normally closed primary valve is disposed in the central opening of the backflow adapter and is movable to an open position. A normally open secondary valve, movable to a closed position, may be configured in the backflow adapter proximal the sheath tube and distal the primary valve. The primary and secondary valves when open permit a catheter or other medical instrument to be inserted into the sheath, and when closed form a hemostatic seal about the catheter. A sheath introducer is provided for guiding the distal end of the sheath tube into a vessel and is configured to be positioned within the backflow adapter.

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TITLE

DUAL VALVE REINFORCED SHEATH AND METHOD

This application is a continuation-in-part of application Ser. No. 07/807,089 filed on Dec. 13, 1991, which is hereby incorporated by reference.

BACKGROUND OF THE INVENTION

This invention relates to an expandable sheath and more particularly to a dual valve, reinforced, large-diameter expandable sheath and method of use.

Expandable access catheter assemblies have heretofore been provided to facilitate the placement and removal of diagnostic and therapeutic catheters through the vascular system. Such catheter assemblies included a flexible variable-diameter catheter body, a diameter control stylet and a flexible Y-hub. The flexible Y-hub incorporates an adjustable hemostasis valve and a side port in one branch and a diameter control stylet guide wire in another branch. A flexible variable diameter catheter body is secured to the flexible Y-hub and can be expanded between a collapsed position and an expanded position by the stylet guide wire. Several deficiencies have been found in such a device. For example, the adjustable hemostasis valve is incapable of accepting large catheters. The flexible variable-diameter catheter body is objectionable in that it has a tendency to reduce in diameter and hold onto large-diameter catheters when it is attempted to place the same through the catheter body. In addition, the tip of the stylet guide wire catches a large-diameter catheter which causes elongation of the catheter body and reduction in its diameter to grab and prevent further advancement of the large-diameter catheter. There is therefore a need for a new and improved large-diameter expandable sheath which will overcome these deficiencies.

SUMMARY OF THE INVENTION

The present invention comprises a sheath assembly for use in introducing a catheter or other medical instrument into a corporeal vessel. The sheath assembly includes an elongate

sheath tube formed of a flexible material having proximal and distal extremities and having a passage extending therethrough. The distal extremity of the sheath tube may have a reinforcing means for causing radial expansion of the distal extremity of the sheath tube to an expanded diameter.

The sheath assembly further includes a backflow adapter having a body with a central opening in fluid communication with the sheath tube. The backflow adapter includes a normally closed primary valve and may include a normally open secondary valve. When the primary and secondary valves are open they permit a medical instrument to be inserted into said sheath tube and when closed form a hemostatic seal about the instrument. The sheath assembly may further include a sheath introducer capable of being disposed in the passage of said sheath tube.

The primary valve is disposed proximal the secondary valve. The primary valve has a cylindrical member formed of a flexible material having a proximal end and a distal end configured with a bore therein in fluid communication with the passage of the sheath tube. The primary valve also has a ring gear secured to one end of the cylindrical member, a rack for driving the ring gear to cause relative rotation between the ends of the cylindrical member to cause the cylindrical member to be twisted to close the bore extending through the cylindrical member, and biasing means for urging the rack into a position wherein the cylindrical member is rotated to a closed position.

The secondary valve is secured to the proximal extremity of the sheath tube, and has a cylindrical member formed of a flexible material having a proximal end and a distal end configured with a bore therein in registration with the passage of the sheath tube. The secondary valve includes rotating means for engaging the cylindrical member for causing relative rotation between the ends of the cylindrical member to cause the cylindrical member to be twisted to close the bore extending through the cylindrical member.

In general, it is an object of the present invention to provide an expandable sheath which can be utilized with

large-diameter catheters and method for using the same. Another object of the invention is to provide a sheath of the above character which is folded longitudinally to a small diameter and which can be expanded greatly when a large-diameter catheter is to be passed through it. Another object of the invention is to provide a sheath of the above character which is provided with a backflow adapter which includes a tubular diaphragm that can be moved into an hourglass or iris-like configuration to create a fluid-tight barrier around any tubular device such as a large-diameter catheter passed through the backflow adapter and the tubular diaphragm. Another object of the invention is to provide a sheath of the above character in which a dilator can be utilized for expanding the sheath. Another object of the invention is to provide a sheath of the above character in which the backflow adaptor can be readily controlled.

Other features and advantages of the present invention will become apparent from the following detailed description, taken in conjunction with the accompanying drawings, which illustrate, by way of example, the principles of the invention.

BRIEF DESCRIPTION OF THE DRAWINGS

FIGURE 1 is a side elevational view of a large-diameter expandable sheath assembly incorporating the present invention and in which a sheath introducer is disposed in the sheath tube.

FIG. 2 is an enlarged side elevational view of the sheath introducer shown in the large-diameter expandable sheath assembly of FIG. 1.

FIG. 3 is an enlarged detail view partially in cross-section of the distal extremity of the sheath introducer shown in FIG. 2.

FIG. 4 is a cross-sectional view taken along the line 4-4 of FIG. 1.

FIG. 5 is a partial side elevational view of an alternative embodiment of an expandable sheath tube incorporating the present invention.

FIG. 6 is a cross-sectional view taken along the line 6-6

of FIG. 5.

FIG. 7 is a cross-sectional view similar to FIG. 4 showing the sheath of FIGS. 5 and 6.

FIG. 8 is an enlarged side elevational view partially in cross-section of the proximal extremity of the large expandable sheath of the sheath assembly shown in FIG. 1 and particularly showing the backflow adapter.

FIG. 9 is an end elevational view looking along the line 9-9 of FIG. 8 with certain portions being shown in cross-section and with the valve carried by the backflow adapter being in a normally closed position.

FIG. 10 is a view similar to FIG. 9, but showing the valve in an open position.

FIG. 11 is a side elevational view partially in cross section opposite the side shown in FIG. 8 of the proximal extremity of the expandable sheath.

FIG. 12 is a bottom plan view looking along the line 12-12 of FIG. 11.

FIG. 13 is a top plan view looking along the line 13-13 of FIG. 11.

FIG. 14 is a side elevational view of the valve or diaphragm utilized in the backflow adapter shown in FIGS. 9 and 10.

FIG. 15 is an alternative embodiment of a valve or diaphragm for use in the backflow adapter shown in FIGS. 9 and 10.

FIG. 16 is still another embodiment of a valve or diaphragm for use in the backflow adapter show in FIGS. 9 and 10.

FIG. 17 is a view similar to FIG. 9 but showing an alternative rack and pinion arrangement for the backflow adapter.

FIG. 18 is a cross-sectional view showing another embodiment of a rack for the closing and opening of the valve in the backflow adapter.

FIG. 19 is a cross-sectional view taken along the line 19-19 of FIG. 18.

FIG. 20 is a side elevational view of an alternative embodiment of the sheath assembly incorporating the present

invention and in which a sheath introducer is disposed in the sheath tube.

FIG. 21 is an enlarged elevational view partially in cross-section of the proximal extremity of the sheath assembly shown in FIG. 20 and particularly showing the back-flow adapter.

FIG. 22 is a partial side elevational view of an alternative embodiment of an expandable sheath tube incorporating the present invention.

FIG. 23 is a cross-sectional view taken along the line 23-23 of FIG. 22.

FIG. 24 is an end elevational view looking along the line 24-24 of FIG. 21 with certain portions being shown in cross-section and with the primary valve being in a normally closed position.

FIG. 25 is a side elevational view partly in cross-section of the primary valve shown in FIG. 24 in an open position and held by a keeper.

FIG. 26 is an enlarged detailed view partially in cross-section of an alternate embodiment of the distal extremity of the sheath tube and the sheath introducer, showing the radiopaque marker band on the introducer and a radiopaque marker on the sheath tube.

FIG. 27 is a partial side elevational view in cross-section of an alternate embodiment of an expandable sheath tube incorporating a self-expanding reinforcement means.

FIG. 28 is a partial side elevational view of an alternate embodiment of an expandable sheath tube incorporating a helical coil.

FIG. 29 is a partial side elevational view in cross-section of an alternate embodiment of an expandable sheath tube incorporating a helical coil embedded between an inner sheath tube and an outer sheath tube.

FIG. 30 is a partial side elevational view in cross-section of an alternate embodiment of an expandable sheath tube incorporating stents and a balloon for expanding the stents.

FIG. 31 is a partial side elevational view of an alternate embodiment of an expandable sheath tube incorporating U-shaped

expandable wires.

FIG. 32 is a partial side elevational view of an alternate embodiment of an expandable sheath tube incorporating a wire having a circular distal end.

FIG. 33 is a partial side elevational view of an alternate embodiment of an expandable sheath tube incorporating an expandable wire including two half-circles at the distal end of the sheath tube.

FIG. 34 is a partial side elevational view of an alternate embodiment of an expandable sheath tube incorporating expandable wires forming a "W" pattern at the distal end of the sheath tube.

FIG. 35 is a side elevational view of a sheath assembly inserted into a vessel, wherein an introducer capsule is being removed from the sheath tube.

FIG. 36 is a side elevational view of a sheath assembly inserted in a vessel wherein a removable capsule is being used to withdraw the sheath tube from the vessel.

DESCRIPTION OF THE PREFERRED EMBODIMENTS

In general, the large-diameter expandable sheath is used for introduction of a catheter into the body of a patient. It comprises an elongate sheath tube formed of a flexible material and having proximal and distal extremities and having passage therein of a predetermined maximum diameter. The distal extremity of the elongate sheath tube is folded longitudinally into a smaller diameter. A backflow adapter is secured to the proximal extremity of the elongate sheath tube. The backflow adapter has a central opening therein in registration with the passage in the sheath tube. Valve means is disposed in the central opening in the backflow adapter and is movable between open and closed positions. The valve means when in an open position permits a catheter to be introduced into the sheath and when closed forms a liquid-tight seal about the catheter extending therethrough.

More particularly as shown in FIG. 1 of the drawings, the large-diameter expandable sheath 11 consists of an elongate sheath tube 12 having proximal and distal extremities 13 and 14

and having a flow passage 16 having a maximum diameter extending therethrough. The expandable sheath 11 can have a suitable length as, for example, fifteen to thirty-five centimeters and preferably approximately eighteen centimeters with a maximum outside diameter of one centimeter. The elongate sheath tube is formed of a flexible material having a wall thickness of 0.001 to 0.020 inches (0.0254-0.51 millimeters) and preferably about 0.005 inches (0.127 millimeters) and can be formed of a suitable plastic material such as "TEFLON" (a fluorinated ethylene propylene). An alternate material is "TEFZEL" (ethylene tetrafluoroethylene). The selected material should have physical characteristics which will not be compromised by radiation sterilization.

As shown in FIG. 4, the distal extremity of the sheath tube is pleated or folded longitudinally to provide wraps or folds 17 for a distance of approximately ten centimeters from the distal end to provide a distal extremity of reduced diameter as, for example, a reduction of the outside diameter from 3/8 to 3/16 of an inch (9.52-4.76 millimeters) or approximately one-half the original size. The folding or pleating of the sheath tube 12 in this manner serves two purposes. The first purpose is to reduce the sheath diameter to facilitate introduction of the sheath and to make it less traumatic for the vessel into which it is introduced. The second reason is that with a small-diameter, thin-wall tube, as represented by the elongate sheath tube 12, there is less likelihood of kinking occurring than in a large-diameter, thin-wall tube. The distal extremity of the sheath tube 12, when folded longitudinally in this manner, serves to provide kink resistance in the distal extremity 14 while still being relatively flexible.

If it is desired to further decrease the likelihood of kinking in the large-diameter, thin-wall tube which forms the sheath tube 12, another embodiment of the sheath tube can be provided of the type shown in FIGS. 5, 6 and 7. The sheath tube 18 shown in those figures is provided with a plurality of circumferentially spaced apart flexible elongate elements 19 which are embedded in the wall of the tube 18 and extend

longitudinally along the length thereof as shown in FIG. 5. The proximal extremities are offset or staggered as shown in FIG. 5 with alternate elements 19 being shorter. This offset relationship provides a gradation in stiffness in the proximal extremity of the sheath tube 18. The elongate elements 19 can be in the form of stainless steel wires having a diameter ranging from 0.005 to 0.015 inches (0.127-0.381 millimeters) and preferably a diameter of approximately 0.010 inches (0.254 millimeters). As can be seen from FIG. 6, the sheath tube 18 can bulge outwardly around the elongate elements 19 while being relatively thin between the elongate elements to retain the flexibility of the tube 18. As also can be seen from FIG. 6, the elongate elements 19 are spaced apart in the three groups to facilitate the formation of six folds 20 as shown in FIG. 7. Thus, by way of example, each set of elongate elements can have the elongate elements spaced approximately 35° apart with each set being spaced approximately 85° apart. Spacing of the elongate elements 19 in this manner facilitates the formation of the folds shown in FIG. 7. The elongate elements 19 also provide additional rigidity longitudinally of the tube 18 so as to inhibit accordioning of the tube 18 during removal of the introducer as hereinafter described.

As shown in FIG. 22, sheath tube 12 may be provided with a sheath marker 180 located at the distal end 14 of the sheath tube. The sheath marker is formed of a radiopaque alloy, for example platinum-tungsten or platinum-iridium. The sheath marker is molded inside the distal extremity of the sheath tube to enable the physician to locate the sheath tip during the operative procedure. A laminating patch is created from a tab of sheath material located at the distal tip of the sheath. This tab is folded back over and fused to the sheath tip to laminate the radio opaque marker on the inside tip of the sheath tube. Thus, the marker resides between two laminated layers of the sheath tube. As shown in FIG. 23, the distal end of the sheath tube may be folded into four bifolds 181 to form a square-like configuration, wherein the sheath marker is embedded within one of the sides 182 of the folded square.

A backflow adapter 21 is secured to the proximal extremity

of the elongate sheath tube 12. The backflow adapter 21 consists of a housing or body 22 which is formed of a suitable material, for example, a plastic such as polycarbonate. The housing 22 is provided with a central bore 23 extending therethrough in axial alignment with the passage 16 of the sheath tube 12. A cylindrical sheath tube adapter 26 is disposed in the bore 23 and is provided with an annular recess 27 which receives an inwardly-extending flange 28 provided on the proximal extremity 13 of the sheath tube 12 (see FIG. 8). A tubular insert 29 formed of the same material as the sheath tube 12 but of a greater wall thickness, as for example twice the wall thickness of the sheath tube 12, is secured within an annular recess 30 in the sheath tube adapter 26 by suitable means such as an adhesive. The insert 29 serves as a reinforcement and serves to prevent collapse of the proximal extremities 13 of the sheath tube 12 when the expandable sheath 11 is used. The sheath tube adapter 26 is fixed within a first cylindrical collar 31 seated within the bore 23 and is held in place by solvent bonding the cylindrical collar 31 into the housing or body 22 to prevent longitudinal and/or rotational movement of the first collar 31 relative to the housing or body 22. A second collar 34 is also seated in the bore 23 and is rotatable therein. An annular ring gear 36 having teeth 36 thereon is also rotatably mounted in the bore 23 as hereinafter described.

A cylindrical or tubular valve member or diaphragm 40 is disposed between the first and second collars 31 and 34, and is provided with a bore or flow passage 41 extending therethrough. The valve member 40 is provided with inwardly extending annular lips or flanges 42 and 43 provided on opposite extremities of the same (see FIGS. 8 and 14). The flange 43 is seated in an annular recess 46 in the sheath tube adapter 26 and is retained therein by the first collar 31. The flange 42 is seated in an annular recess 47 provided in a retaining ring 48 and retained therein by the second collar 34. An annular protrusion 49 is formed integral with the retaining ring 48 and engages one side of the toothed ring gear 37 which is secured to the retaining ring 48 by suitable means such as an adhesive. Similarly, the

retaining ring 48 functionally engages the second collar 34 and causes the second collar 34 to rotate therewith.

The diaphragm or valve member 40 can have a suitable size as, for example, a length of 0.3 to 0.45 inches (7.62-11.43 millimeters) and preferably a length of approximately 0.3 inches (7.62 millimeters), and an inside diameter of 0.35 to 0.5 inches (8.89-12.7 millimeters), and preferably an inside diameter of 0.375 inches (9.52 millimeters), with a wall thickness ranging from 0.005 to 0.015 inches (0.127-0.381 millimeters), and preferably a wall thickness of 0.007 inches (0.178 millimeters). The annular lips 42 and 43 can extend inwardly for a distance of 0.032 inches (0.813 millimeters) from the outer wall surface and have a length of approximately 0.050 inches (1.27 millimeters). The diaphragm or valve member 40 can be formed of a suitable material, such as a silicone elastomer, as, for example, Dow "SILASTIC" 97-4720. It can have a Shore A hardness ranging from 20-80 and preferably a Shore hardness of 40A. Alternatively, a low durometer, tear-resistant rubber-like latex material can be utilized.

Other diaphragm or valve members such as shown in FIGS. 15 and 16 can be utilized which have the same physical conformation. In the embodiment shown in FIG. 15, small diener polyester fibers 52 are bonded to the exterior surface of the diaphragm 51 with a silicone adhesive so that the fibers 52 extend circumferentially around the outside surface of the diaphragm 51. Such fibers serve to impede radial and longitudinal distention of the diaphragm or valve member 51. The diaphragm or valve member 56 shown in FIG. 16 is provided with a cylindrical wall 57 which increases in thickness in a direction towards the distal extremity of the diaphragm. This helps the diaphragm to withstand the pressures applied to the diaphragm during use, which may cause the diaphragm to distend and leak.

Means is provided for causing relative rotation between the sheath tube adapter 26 and the retaining ring 48 for opening and closing the bore or flow passage 41 by twisting of the cylindrical valve member or diaphragm 40. This is accomplished by fixing the first collar 31 and the sheath tube

adapter 26 within the housing or body 22 by suitable means such as solvent bonding and causing rotation of the retaining ring 48 by the use of a rack 61. The rack 61 consists of a rod 62 formed of a suitable material such as stainless steel which extends through a hole 63 (see FIG. 11) in the housing or body 22 in a direction which is tangential of the bore 23. The rod 62 is disposed immediately adjacent a flange 64 formed in the body 22 against which the ring gear 36 rotates. The hole 63 opens into the bore 23 so that rack teeth 64 provided on the one side of the rod 62 engage the toothed ring gear 36 whereby upon reciprocatory movement of the rack 61, the ring gear 36 is rotated through an angle ranging from 180° to 360°, and preferably an angle of at least 270°.

An actuator 66 formed of a suitable material such as plastic is mounted on the upper extremity of the rod 62 and is secured thereto by suitable means such as an Allen-head screw 67 set into the rod 62, as shown in FIG. 13. The actuator 66 is generally rectangular in plan and is provided with an upstanding lip 68 so that it conforms to the conformation of the index finger of the hand which is to be utilized for actuating the rack 61. The actuator 66 is provided with a reinforcing rib 69 along one edge of the same. A similar actuator member 71 is provided on the body 22 underlying the actuator 66 and is also provided with a downwardly extending lip 72. The actuator member 71 is secured to the body 22 by suitable means such as an adhesive. The member 71 also has a rectangular configuration in plan and is sized so that it is adapted to be engaged by the thumb of the hand, as shown in FIG. 12. Thus, one hand can be utilized for operating the backflow adapter 21 by the index finger of the hand grasping the actuator 66 and the thumb of the same hand grasping the member 71.

A stabilization and guide rod 76 extends through a tangential bore 77 (see FIG. 11) provided in the body 22 which is spaced apart from the bore 63 and extends in a direction which is parallel thereto. The rod 76 is formed of a material such as stainless steel and is provided with a collar 78 which extends through the reinforcing rib 69 of the actuator 66 and

is secured therein by suitable means such as an Allen-head screw 79.

In an alternative embodiment of the normally closed primary valve if shown in FIGS. 24 and 25, the actuator 66 is turned 90° so that guide or stabilizer rod 76 is positioned on the opposite side of the proximal valve housing 22 to the rack 62. A ring gear 161 is configured into a gear hub 160 which causes rotation of proximal diaphragm retaining ring 158. The distal end of the primary diaphragm 40 is secured to the distal retaining ring 159 which is fixed relative to the proximal valve housing and is positioned proximal a distal retaining hub 162. The primary diaphragm is opened by depressing the actuator which causes the rack to move the ring gear and rotate the gear hub and proximal retaining ring. In addition, a cover 170 is added to the bottom of the body to encase the bottom portions of the rack and stabilizer rod. Also, a "C"-shaped keeper 171 can be used to maintain the actuator in the compressed or open valve position by placing one end over the actuator and the other end over bottom of the cover.

Referring to FIG. 11, means is provided for yieldably returning the rack 61 into a position so that the valve member or diaphragm 40 is in a normally closed position and consists of a coil spring 81 coaxially mounted on the rod 62 and having one end engaging the actuator 66 and having the other end engaging a seat 82 provided in the body 22. Means is provided for preventing the spring 81 from urging the rod 62 out of the bore 63 and consists of a lump 83 of solder or a braising material provided on the rod 62 adjacent the lower extremity of the rack teeth 64. Thus, it can be seen by the hand engaging the backflow adapter 21 using the index finger to engage the actuator 66 and the thumb to engage the actuator member 71, the rack 61 can be reciprocated back and forth to open and close a bore 86 extending through the retaining ring 48 and the sheath tube adapter 26 by forming an hourglass or iris-like closure as shown in FIG. 9 in which the radially extending lines 87 shown represents the folding over of the elastomeric material of the valve member or diaphragm 40. The collar 78 provided on the stabilization rod 76 serves to stop further travel up the rack

when the collar 78 engage a seat 88 provided in the body 22. In this position, the spring 81 is almost completely compressed as shown in FIG. 10. Following the release of the actuator 66, the spring 81 returns the rack 62 to its home position and causes the valve member or diaphragm 40 to be completely closed as shown in FIG. 9.

The ring gear 36 can be formed of a suitable material such as stainless steel and can have any suitable number of teeth. Alternatively, the ring gear can be formed of a suitable plastic such as nylon. The other portions of the backflow adapter 21 as, for example, the body 22, the first collar 31, the second collar 34, the retaining ring 48 can be formed of a suitable plastic such as polycarbonate. The metal parts such as the rod 62, the stabilization rod 76 and the spring 81 can be formed of a suitable material such as stainless steel.

As shown in FIGS. 1 and 8, means is provided for introducing liquid as, for example, a radiopaque liquid, into the bore 86 and consists of a tube 91 formed of a suitable material such as plastic extending through the first collar 31 and through the sheath tube adapter 26 so that it is in communication with the bore 86. Flexible tubing 92 is connected to the tube 91 and has a stopcock 93 of a conventional type mounted thereon which is provided with a Luer-type fitting 94. The stopcock 93 is provided with a knob 96 which can be utilized for moving the stopcock 93 between open and closed positions.

As shown in FIGS. 20-21, an alternate embodiment of the sheath assembly 11 includes a normally open secondary valve assembly 150 located adjacent the primary valve housing 22 of the backflow adapter 21. The secondary valve assembly contains a secondary diagram 151 which operates substantially the same as the primary diaphragm 40 and is actuated by a thumb wheel 152. The secondary diaphragm is made of silicone and is constructed substantially the same as the primary diaphragm. The secondary diaphragm is configured to have a suitable length, diameter and wall thickness to be compatible with the primary diaphragm. Similarly, each of the materials used in the secondary valve assembly for constructing and mounting the secondary diaphragm are substantially the same as the materials

previously described for the backflow adapter assembly.

The primary valve assembly is configured similar to that described above in conjunction with FIGS. 24 and 25. Secondary valve housing 155 is provided with a central bore 165 which is in fluid communication with the central bore 23 of the primary valve housing 22 and the passage 16 of the sheath tube 12. Likewise, secondary diaphragm or valve member 151 is provided with a flow passage extending therethrough. Thus, an instrument such as the sheath introducer 101 may be passed through the primary diaphragm when the secondary diaphragm is closed, thereby preventing blood flow through the proximal end of the large-diameter expandable sheath assembly 11. Also, orifice 163 in the valve housing and orifice 164 in the sheath tube adapter 26 are provided to accept tube 91 connected to the flexible tubing 92 of a introducer sideport assembly (not shown).

As shown in FIG. 21, the secondary valve assembly 150 comprises a secondary valve housing 155 which contains secondary diaphragm 151 and thumb wheel 152. The proximal end of the secondary diaphragm is secured to the thumb wheel by proximal retaining ring 156. The distal end of the secondary diaphragm is fixed relative to the secondary valve housing by distal retaining ring 157. Rotation of the diaphragm is achieved by rotating the thumb wheel so as to cause motion to only the proximal end of the secondary diaphragm. A rotational stop (not shown) is positioned on the thumb wheel to prevent excess rotation of the secondary diaphragm. The rotational stop may be comprised of two 1/32 of an inch (0.79 millimeters) dowel pins located on the thumb wheel and the secondary valve housing which are configured to engage each other to limit the rotation of the thumb wheel. Additionally, a silicone o-ring 153 positioned proximate the thumb wheel in the primary diaphragm distal retaining hub 162 allows rotation of the thumb wheel while preventing fluid from leaking from the backflow adapter housing.

A sheath introducer 101 is provided as a part of the assembly shown in FIG. 1 and as shown in FIG. 2 consists of an elongate tubular member 102 formed in three sections 103, 104

and 106 of different diameters. The elongate tubular member 102 can be formed of a suitable plastic material such as "PEBAX" which is formed of polyether Block Amides which is loaded with approximately 10% barium sulfate to make the same visible under X-rays. Section 103 can have a diameter ranging from 0.15 to 0.3 inches (3.81-7.62 millimeters) and preferably an outside diameter of 3/16 of an inch (4.75 millimeters). The section 104 can have a suitable diameter as, for example, 0.08 to 0.15 inches (2.03-3.81 millimeters) and preferably a diameter of 1/8 of an inch (3.17 millimeters). The section 106 can have a diameter ranging from 0.06 to 0.12 inches (1.52-3.05 millimeters) and preferably a diameter of 0.08 inches (2.03 millimeters). The distal extremities of the sections 103 and 104 are provided with tapers 107 and 108, respectively, so as to provide a tapered transition from one diameter to another. A Luer-type fitting 111 is mounted on the proximal extremity of the tubular section 103. A bore or lumen 112 (see FIG. 4) of a suitable size as, for example, one capable of passing a 0.038 inches (0.97 millimeters) guidewire, is provided in the section 106 as well as in the sections 104 and 103 extending the length of the tubular member 102.

As shown in FIG. 3, a tube 116 is mounted on the distal extremity 106 of the sheath introducer 101 and is formed of a suitable material such as silicone and is retained thereon in a suitable matter by the use of polyethylene shrink tubing 117. A cylindrical enlargement or annular bump 121 is provided on the tubular section 106 adjacent the distal extremity of the shrink tubing 117 and serves to prevent the sleeve 116 and the shrink tubing 117 from accidentally slipping off of the distal extremity of the tubular section 106.

When the sheath introducer 101 is disposed in the expandable sheath 11, as shown in FIG. 1, the proximal extremity of the silicone sleeve 116 is disposed over the distal extremity of the sheath tube 12 and serves to prevent the sharp edges of the folded sheath tube 12 from causing trauma to the interior wall of a vessel when it is introduced into the vessel when the sheath is introduced as hereinafter described. A vent hole 123 is provided in the sheath

introducer 101 which is in communication with the passage 112 proximal of the silicone sleeve 116, as shown in FIG. 3. The vent hole 123 can be utilized for flushing the elongate sheath tube 12 through the side port fitting 94 prior to use of the expandable sheath in a surgical procedure.

As shown in FIG. 26, a radiopaque marker band 185 may be positioned proximal to distal end of the sheath introducer 101. The marker band is made of a radiopaque alloy, platinum-tungsten or platinum-iridium. The marker band is positioned just proximal the retaining bump 121 over the elongate tubular member 102 and within silicone sleeve 116 and polyethylene shrink tubing 117. The platinum alloy band is held in place by both the silicone sleeve and the polyethylene shrink tubing. As appropriate, the marker band may be positioned elsewhere along the length of the sheath introducer, such as within the most distal tubular section 106.

Operation and use of the expandable sheath 11 in conjunction with the sheath introducer 101 may now be briefly described as follows. Let it be assumed that the patient has been prepared in a conventional manner and that it is desired to enter a peripheral vessel such as an artery or a vein of the patient. The desired vessel is exposed and a longitudinal or transverse incision made into that vessel. A guidewire of a suitable size is then selected as, for example, a guidewire having a diameter of 0.038 inches (0.97 millimeters). The guidewire (not shown) is introduced into the vessel and then the expandable sheath assembly 11 shown in FIG. 1 is placed over the guidewire by placing the proximal extremity of the guidewire into the lumen 112 provided in the elongate tubular member 102 and advanced through the Luer fitting 111. The rounded tip and the small diameter of the section 106 of the tubular member 102 facilitate advancement of the sheath introducer 101 into the vessel without traumatizing the vessel. The small-diameter tip section 106 is followed by the elongate sheath tube 12 which has been collapsed as hereinbefore described about the tubular section 106 until the sheath tube 12 has been introduced to the proper depth in the vessel. As soon as the sheath tube 12 has been positioned in the vessel,

the sheath introducer 101 is advanced relative to the elongate sheath tube 12 by using one hand to hold the backflow adapter 21 which is connected to the sheath tube 12 and the other hand to push the sheath introducer 101 so that the proximal extremity of the silicone sleeve 116 moves off of the distal extremity of the sheath tube 12 to expose the same.

As soon as this has been accomplished, the sheath introducer 101 is pushed forward so that section 103 enters the collapsed section of the sheath tube 12 to commence opening of the same. The sheath introducer 101 is then removed through the backflow adapter 21. The sheath introducer can be removed by grasping the backflow adapter 21 by the fingers of the hand as hereinafter described to at least partially open the same to permit removal of the sheath introducer and dilator 101 while minimizing the flow of blood from the sheath tube 12. The backflow adapter can then be released. The sheath 11 and its backflow adapter is now in its normally closed state to provide a hemostatic seal closing the flow passage 86.

The physician conducting the procedure then selects the desired catheter or other device which is desired to be introduced through the expandable sheath 11. Such a device should have a diameter of 8.5 millimeters or less or which is at least slightly less than the diameter of the bore 86. The physician grasps the actuator members 66 and 71 and presses the same to operate the rack 61 to open the diaphragm or valve member 40 permitting the physician to insert the device as, for example, the catheter through the expandable sheath 11. As soon as the catheter has been advanced as far as desired, the physician releases the pressure on the actuator members 66 and 71 permitting the diaphragm 40 to close around the device as, for example, the catheter inserted through to form a hemostatic seal about the catheter. If it is desired to reposition the catheter, it is merely necessary to push or pull the catheter and it will slide freely through the diaphragm. When it is desired to remove the catheter, the catheter need only be pulled out of the sheath 101 and the diaphragm will seal closed forming a hemostatic seal.

A silicone coating may be applied to the pleated sheath

tube 12. Coating may be applied to the inner and outer surfaces prior to attachment to the backflow adapter 21. The silicone coating on the inside diameter of the sheath tube reduces the amount of force required to advance catheters and the like through the sheath tube. Additionally, the silicone coating on the outside of the sheath tube may reduce the amount of force required to advance the expandable sheath 11 into a vessel. A suitable silicone coating material is "HYDRO-SIL-D 1.0" available from TUA systems of Sarasota, Florida. Additionally, a silicone lubricant may be applied to the ring gear 36 on the primary valve assembly and the adjacent to bearing surfaces.

The method for introducing a medical instrument into the body of a patient using the dual valve expandable sheath assembly 11 shown in FIGS. 21-26 involves opening the valves to minimize blood flow through the sheath assembly 11. First, the sheath introducer 101 is placed within the sheath assembly such that the distal end 14 of the sheath tube 12 resides in the introducer sleeve 116, as shown in FIG. 26. This step may be performed as part of the manufacturing process. After the patient is prepared for the procedure, the sheath tube and the sheath introducer are intraluminally inserted into the patient, usually through a cutdown in a vessel such as a femoral artery. The distal end 106 of the sheath introducer is then inserted into the vessel until the distal end of the sheath tube is within the vessel. The sheath introducer is then advanced into the vessel relative to the sheath tube, allowing the distal end of the sheath tube to expand. In addition, the sheath introducer may be further advanced into the sheath assembly to dilate the distal end of the sheath tube.

Next, the sheath introducer 101 is removed from the sheath assembly 11. As the distal end 106 of the sheath introducer is removed from the sheath tube 12, the secondary valve 151 is closed to form a substantially fluid tight seal between the passage 16 in the sheath tube and the secondary valve assembly 150. After the secondary diaphragm 151 is closed, the primary diaphragm 40 may be opened to fully remove the sheath introducer. Then the distal end of a catheter or other medical

instrument may be inserted through the primary valve. The primary diaphragm is then closed to form a substantially fluid tight seal around the medical instrument. Next, the secondary diaphragm is opened to allow the distal end of the medical instrument to be inserted through the secondary valve assembly, through the passage in the sheath tube and into the vessel of the patient. After the procedure has been completed, the medical instrument and the sheath assembly can be removed from the vessel and the incision which has been made in the vessel for permitting passage of the sheath assembly can be sutured.

It can be seen from the foregoing that there has been provided an expandable sheath 11 which can be made in various sizes to accommodate large-diameter devices while still providing the desired hemostatic seal. The expandable sheath can be readily inserted and removed. The sheath introducer 101 facilitates this introduction. It is provided with a distal extremity 106 which is small in diameter to permit the sheath tube 12 to be wrapped about the same as hereinbefore described. The sheath introducer 101 is provided with sections 103 and 104 of larger diameters to provide additional rigidity to the sheath introducer 101 to facilitate pushing of the sheath introducer when introducing the expandable sheath 11 into the vessel of the patient.

An alternative mechanism for actuating the diaphragm 40 is shown in FIG. 17 and consists of a pinion 131 which engages the ring gear 36 and is disposed in a cylindrical recess 132 provided in the body 22. The pinion 131 is mounted on a shaft 133. Another gear 134 is mounted on the shaft 133 and has a smaller diameter than the diameter of the pinion 131 and engages the rack teeth 64 provided on the rod 62. By providing such a gear arrangement, it can be seen that it is possible to provide a shorter rack to achieve the same degree of ring gear rotation for opening and closing of the diaphragm 40.

As can be seen in FIGS. 18 and 19, there is shown another embodiment of a mechanism for actuating the diaphragm 40. As shown therein it consists of a flexible rack 141 that is comprised of a flexible member 142 which is provided with rack teeth 143 on one side of the same which are adaptable to engage

the ring gear 36. The member 142 extends through a semi-circular slot 144 provided in the body so that it extends through the body and around the ring gear 36. An actuator 146 is provided formed integral with the rack 141 for operating the rack 141 with the fingers of the hand. In this construction the rack is substantially contained within the body 22.

As shown in FIGS. 27-36, the expandable sheath 11 may include a reinforced sheath tube 200. The reinforced sheath tube is similar to the elongate sheath tube 12 and similarly has proximal and distal extremities 201 and 202. A flow passage 203 is provided having a maximum diameter extending therethrough. One suitable material for the reinforced sheath is in an expanded PTFE (polytetrafluoroethylene). Such materials may be obtained from Impra of Temp, Arizona and W. L. Gore of Flagstaff, Arizona. An example of a suitable size for a sheath tube for use with large catheter systems would include an outer diameter of approximately 0.345 inches (8.76 millimeters) with a wall thickness of 0.005 inches (0.127 millimeters) and having a length of about twenty centimeters.

The reinforced sheath tube 200 could be supported by stents, coiled wire, coiled plastic or similar means. As shown in FIG. 27, a series of self-expanding supports 210 may be placed within the sheath tube for radial expansion. Similarly, as shown in FIG. 28, a coil 211 may be attached to the outside of the sheath tube to allow for self-expansion. Alternatively, the coil support may be embedded within an inner sheath tube 212 and outer sheath tube 213, as shown in FIG. 29. The coil or expansion system may be made of a 0.012 inches (0.3 millimeters) nitinol or similar alloy wire. As shown in FIG. 30, the reinforced sheath may include balloon expandable stents 214 which may be expanded by a balloon 215 and catheter 216 or similar means.

Alternatively, the sheath tube 200 may be made of a dacron graft 217 supported by longitudinally positioned nitinol wires 218 as shown in FIGS. 31-34. As shown in FIG. 31, the reinforcement wires may be run as tightly parallel U-shaped expansion means. Likewise, a single wire forming a circle at the distal end 202 of the sheath tube may be used. Similarly,

two wires forming half-circles at the distal end may be used to reinforce and expand the sheath as shown in FIG. 33. Alternatively, the wires may form a "W" shape at the distal end of the sheath tube to provide radial expansion, as shown in FIG. 34.

As shown in FIG. 35, the large-diameter expandable sheath assembly 11 includes an introducer capsule 220. The reinforced sheath tube 200 is packed into the introducer capsule for deployment. The introducer capsule has a significantly less inner diameter than the outer diameter of the expanded sheath tube. The introducer capsule is configured such that it will peel away from the proximal end 201 of the reinforced sheath tube as the introducer capsule is withdrawn from the distal end 202 of the sheath tube. As the sheath introducer capsule is withdrawn, the reinforced sheath tube expands radially within the vessel.

As shown in FIG. 36, a removal capsule 225 may be fitted around the proximal 201 end of the reinforced sheath tube 200 to collapse the expanded sheath tube after the sheath tube has been deployed in a vessel. The removal capsule is configured with a lengthwise slit so it may be fitted over the proximal end of the secondary valve without having to fit over the backflow adapter 21. The removal capsule outer diameter is less than the outer diameter of the expanded sheath tube so as to radial collapse the sheath tube to a smaller diameter state. Once the reinforced sheath tube is collapsed, the removal capsule and sheath tube are then removed from the vessel. This retrieval reduces potential vessel trauma from removing a large diameter sheath.

While several particular forms of the invention have been illustrated and described, it will be apparent that various modifications can be made without departing from the spirit and scope of the invention. For example, references to materials of construction and specific dimensions are also not intended to be limiting in any manner and other materials and dimensions could be substituted and remain within the spirit and scope of the invention. Accordingly, it is not intended that the invention be limited, except as by the appended claims.

CLAIMS

What is claimed is:

1. A sheath assembly comprising:

an elongate sheath tube formed of a flexible material having proximal and distal extremities and having a passage extending therethrough;

a first valve secured to the proximal extremity of said sheath tube and movable between open and closed positions, said first valve having a central opening therein in registration with the passage in said sheath tube; and

a second valve disposed proximal said first valve and movable between open and closed positions, said second valve having a central opening therein in registration with the central opening in said first valve and with the passage in said sheath tube,

wherein said first valve and said second valve when open permit a medical instrument to be inserted into said sheath tube and when closed form a hemostatic seal about the instrument.

2. The sheath assembly of claim 1, wherein said first valve comprises:

a first cylindrical member formed of a flexible material having a proximal end and a distal end configured with a bore therein in registration with the passage of said sheath tube; and

first rotating means for engaging the cylindrical member for causing relative rotation between the ends of the cylindrical member to cause the cylindrical member to be twisted to close the bore extending through the cylindrical member.

3. The sheath assembly of claim 2, wherein said second valve comprises:

a second cylindrical member formed of a flexible material having a proximal end and a distal end configured with a bore therein in registration with the bore of said first cylindrical member; and

second rotating means for engaging the second cylindrical member for causing relative rotation between the ends of the second cylindrical member to cause the second cylindrical member to be twisted to close the bore extending through the second cylindrical member.

4. The sheath assembly of claim 3, wherein the second rotating means of said second valve includes a ring gear secured to one end of the second cylindrical member, and a rack for driving the ring gear to cause rotation of the second cylindrical member.

5. The sheath assembly of claim 4, wherein the second rotating means of said second valve further comprises biasing means for urging the rack into a position wherein the second cylindrical member is rotated to a normally closed position.

6. The sheath assembly of claim 5, wherein the second rotating means of said second valve further comprises an actuator carried by the rack and configured to be engaged by the fingers of a human hand for moving the rack against the force of the biasing means to move the second valve to an open position.

7. The sheath assembly of claim 6, wherein the second rotating means of said second valve further comprises a stabilizer rod slidably mounted parallel to the rack and secured to the actuator.

8. The sheath assembly of claim 1, wherein said sheath tube includes reinforcing means for causing radial expansion of said sheath tube.

9. The sheath assembly of claim 8, wherein said reinforcing means includes a self-expanding wire.

10. The sheath assembly of claim 1, wherein the distal extremity of said sheath tube is provided with a radiopaque

marker.

11. The sheath assembly of claim 1, wherein said sheath tube is provided with a lubricating coating.

12. The sheath assembly of claim 2, wherein the first rotating means of said first valve is provided with a lubricating coating.

13. The sheath assembly of claim 3, wherein the second rotating means of said second valve is provided with a lubricating coating.

14. The sheath assembly of claim 1, wherein the distal extremity of said sheath tube is folded longitudinally to a smaller folded diameter.

15. The sheath assembly of claim 14, further comprising a sheath introducer capable of being disposed in the passage of said sheath tube, said sheath introducer having a distal extremity extending beyond the proximal extremity of said sheath tube and dilation means positioned at the distal extremity of the sheath introducer for unfolding the sheath tube.

16. The sheath assembly of claim 15, wherein the distal extremity of said sheath introducer is provided with a radiopaque marker.

17. A sheath assembly for use in introducing a catheter into a corporeal vessel, the sheath assembly comprising:

an elongate sheath tube formed of a flexible material having proximal and distal extremities and having a passage extending therethrough, the distal extremity of said sheath tube having a reinforcing means for causing radial expansion of the distal extremity of said sheath tube to an expanded diameter;

a first valve secured to the proximal extremity of said

sheath tube, said first valve having a first cylindrical member formed of a flexible material having a proximal end and a distal end configured with a bore therein in registration with the passage of said sheath tube, and having first rotating means for engaging the cylindrical member for causing relative rotation between the ends of the cylindrical member to cause the cylindrical member to be twisted to close the bore extending through the cylindrical member; and

a second valve disposed proximal said first valve, said second valve having a second cylindrical member formed of a flexible material having a proximal end and a distal end configured with a bore therein in registration with the bore of said first cylindrical member, a ring gear secured to one end of the second cylindrical member, a rack for driving the ring gear to cause relative rotation between the ends of the second cylindrical member to cause the second cylindrical member to be twisted to close the bore extending through the second cylindrical member, and biasing means for urging the rack into a position wherein the second cylindrical member is rotated to a closed position.

18. The sheath assembly of claim 17, wherein said reinforcing means includes a self-expanding wire.

19. The sheath assembly of claim 18, wherein the self-expanding wire of said reinforcing means is configured to transverse the length of said sheath tube and to form a sinusoidal shape along the perimeter of the distal extremity of said sheath tube.

20. The sheath assembly of claim 17, further comprising a sheath introducer disposed around said sheath tube, said sheath introducer having a distal extremity which has a diameter less than the expanded diameter of said sheath tube.

21. The sheath assembly of claim 18, wherein the distal extremity of said sheath tube is provided with a radiopaque marker, and the distal extremity of said sheath introducer is

provided with a radiopaque marker.

22. A backflow adapter having a body with a central opening in fluid communication with a sheath tube, the backflow adapter comprising:

a first diaphragm disposed in the central opening of said backflow adapter, said first diaphragm having a first end and a second end and being movable between open and closed positions;

first retaining means for engaging said first diaphragm for causing relative rotation between the ends of said first diaphragm;

a second diaphragm disposed in the central opening of said backflow adapter and adjacent the second end of said first diaphragm, said second diaphragm having a first end and a second end and being movable between open and closed positions; and

second retaining means for engaging said second diaphragm for causing relative rotation between the ends of said second diaphragm.

23. The backflow adapter of claim 22, wherein said second retaining means includes a gear secured to the second diaphragm and a rack for driving the gear to cause rotation of the second diaphragm.

24. The sheath assembly of claim 23, wherein the second retaining means further comprises biasing means for urging the rack into a position wherein the second diaphragm is rotated to a closed position.

25. The sheath assembly of claim 24, wherein the second retaining means further comprises an actuator carried by the rack for moving the rack against the force of the biasing means to move the second diaphragm to an open position.

26. The sheath assembly of claim 25, wherein the second retaining means further comprises a stabilizer rod slidably

mounted parallel to the rack and secured to the actuator.

27. The backflow adapter of claim 22, further comprising a sheath tube adapter secured to the body of said backflow adaptor and secured to a sheath tube so as to prevent rotation of said sheath tube adapter when either said first diaphragm or said second diaphragm are rotated within the body of said backflow adapter.

28. An expandable sheath for use in introducing a medical instrument into a body, the sheath comprising:

an elongate sheath tube having proximal and distal ends having an annular passage therethrough, said elongate sheath tube having a wall of substantially uniform thickness and being formed of a flexible material; and

reinforcing means for causing radial expansion of said sheath tube.

29. The expandable sheath of claim 28, wherein said reinforcing means includes a self-expanding wire.

30. The expandable sheath of claim 29, wherein the self-expanding wire of said reinforcing means is sinusoidal in configuration.

31. The expandable sheath of claim 29, wherein the self-expanding wire of said reinforcing means is helical in configuration.

32. The expandable sheath of claim 29, wherein the self-expanding wire of said reinforcing means is configured to transverse the length of said sheath tube and to encircle the perimeter of the distal end of said sheath tube.

33. The expandable sheath of claim 29, wherein the self-expanding wire of said reinforcing means is configured to transverse the length of said sheath tube and to form a sinusoidal shape along the perimeter of the distal end of said

sheath tube.

34. A method for introducing a medical instrument into the body of a patient, the steps of the method comprising:

providing an expandable sheath assembly including an elongate sheath tube with proximal and distal extremities and having a passage extending therethrough, means for radially expanding the distal extremity of the sheath tube, a normally open first valve positioned proximate the proximal extremity of the sheath tube, a normally closed second valve positioned proximal the first valve, and a sheath introducer slidably mounted on at least the distal extremity of the sheath tube;

introducing the sheath tube and the sheath introducer into the body of a patient;

removing the sheath introducer from the distal extremity of the sheath tube;

expanding the distal extremity of the sheath tube;

closing the first valve to form a substantially fluid tight seal between the passage in the sheath tube and the second valve;

opening the second valve;

inserting the distal end of the medical instrument through the second valve;

closing the second valve to form a substantially fluid tight seal around the medical instrument;

opening the first valve; and

guiding the distal end of the medical instrument through the first valve, through the passage in the sheath tube and into the body of the patient.

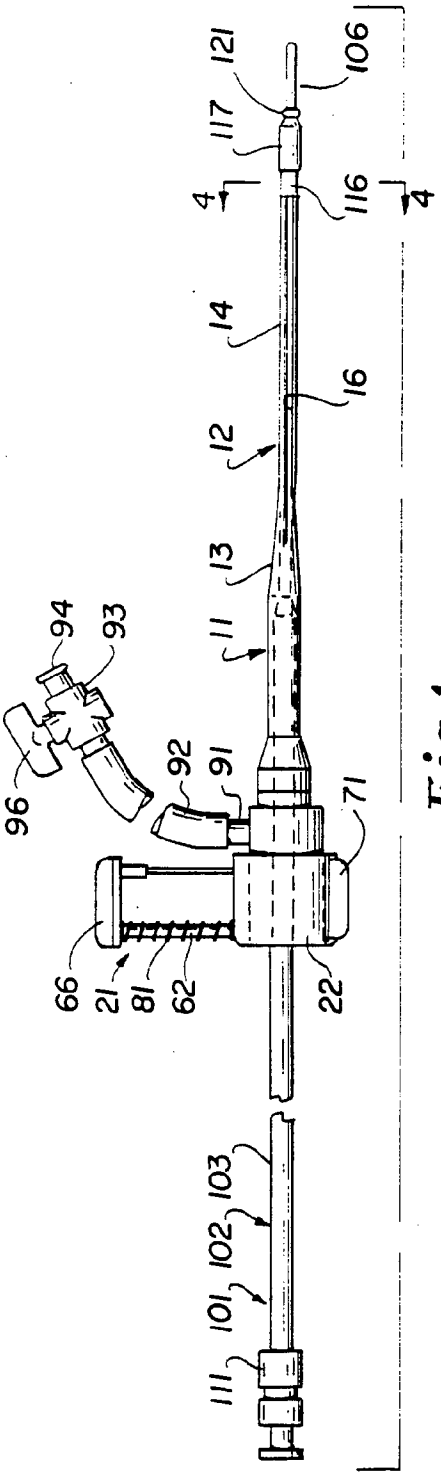


Fig.1

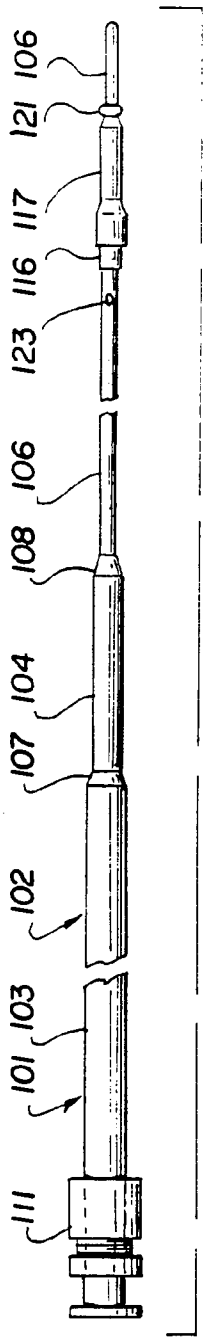


Fig.2

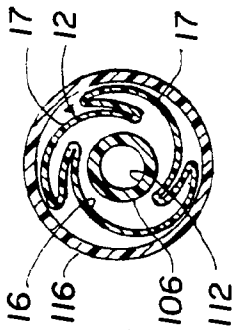


Fig.4

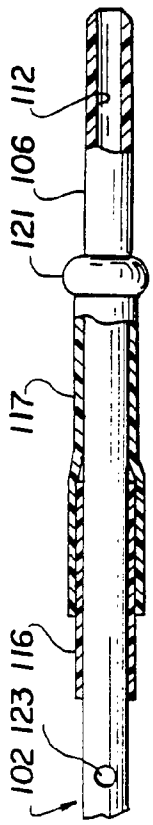


Fig.3

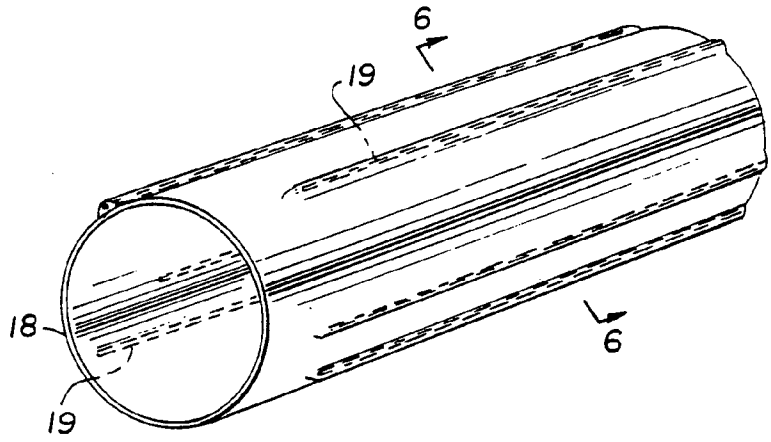


Fig.5

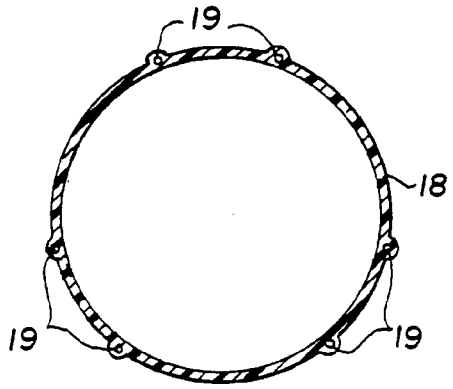


Fig.6

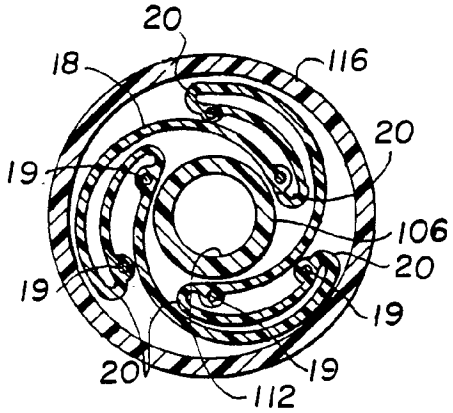


Fig.7

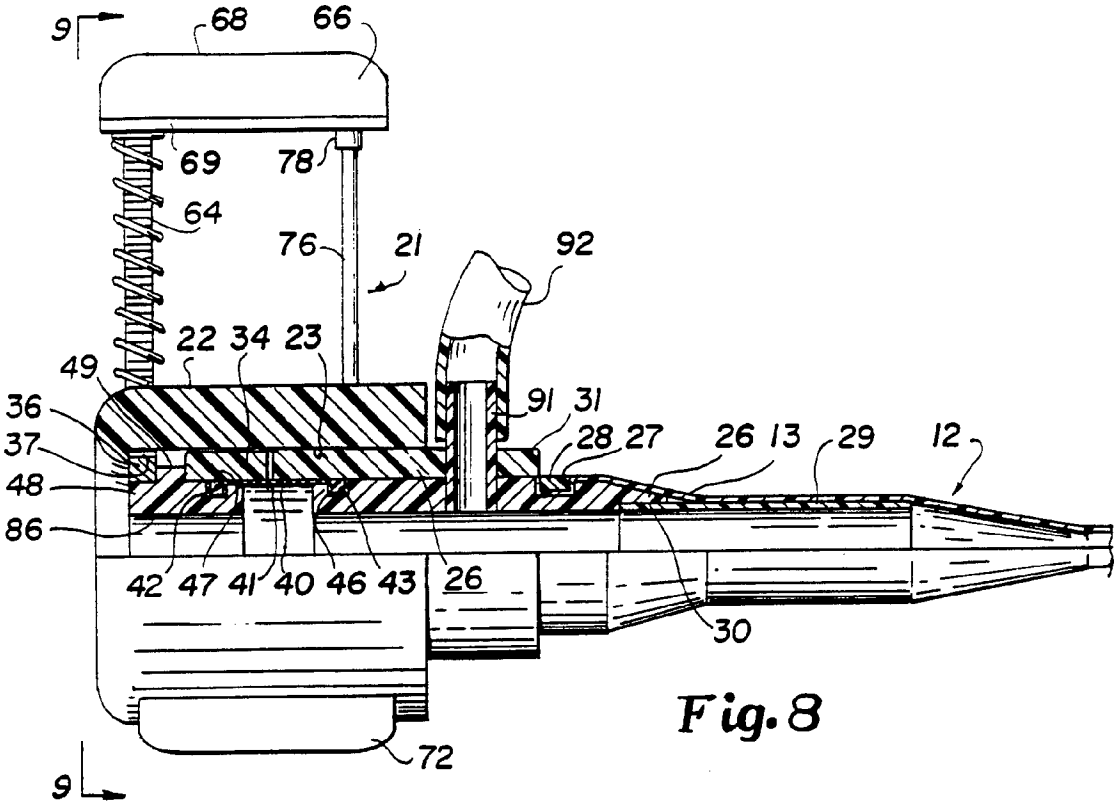


Fig. 8

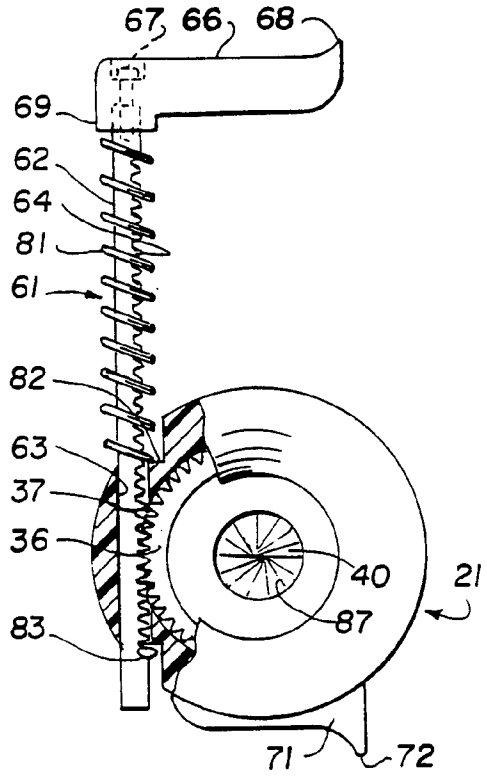


Fig. 9

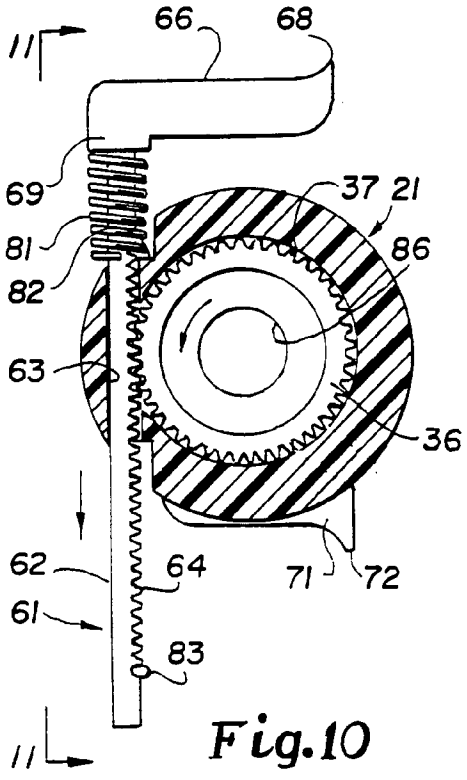


Fig. 10

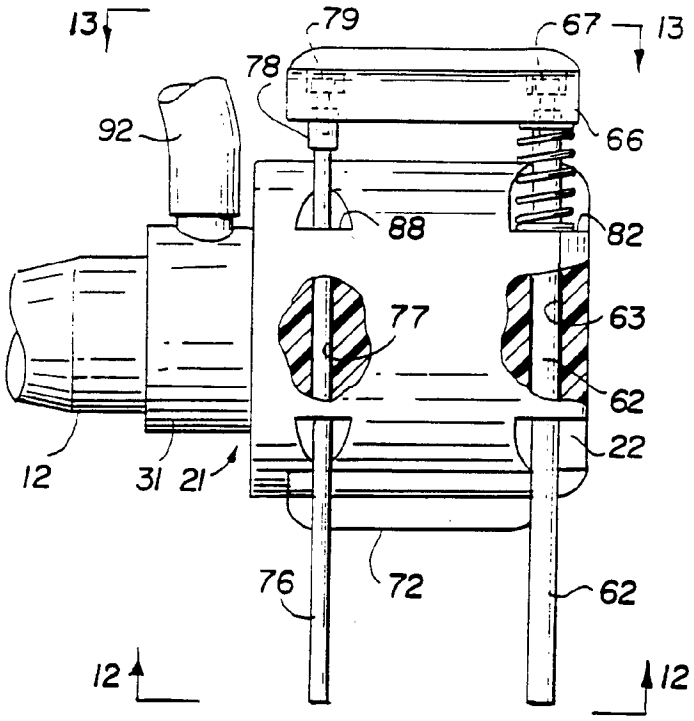


Fig.11

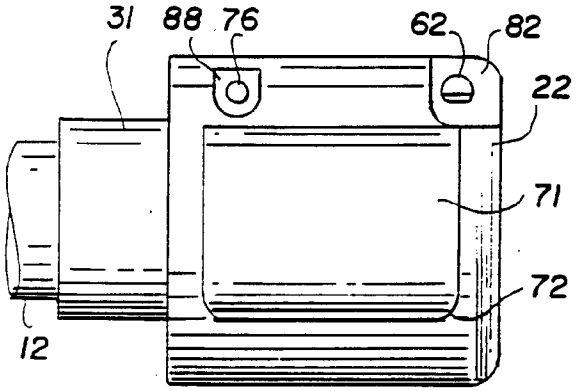


Fig.12

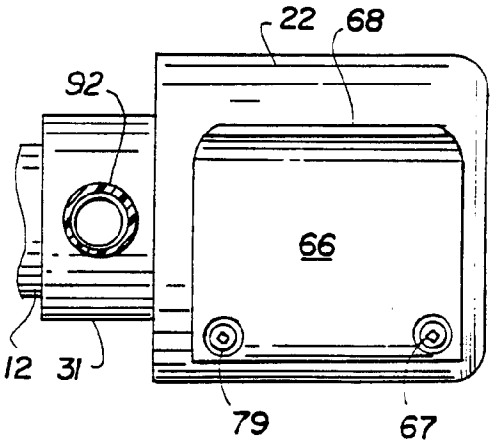


Fig.13

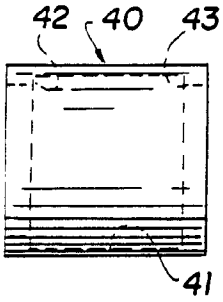


Fig.14

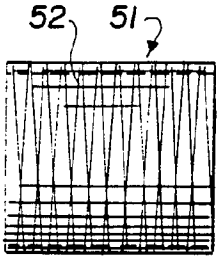


Fig.15

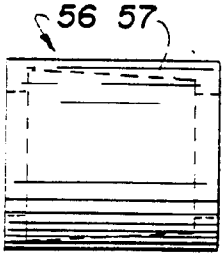


Fig.16

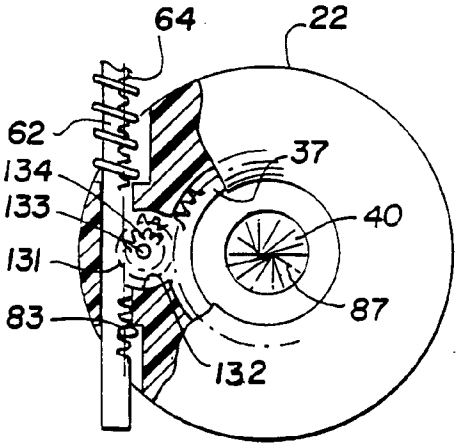


Fig.17

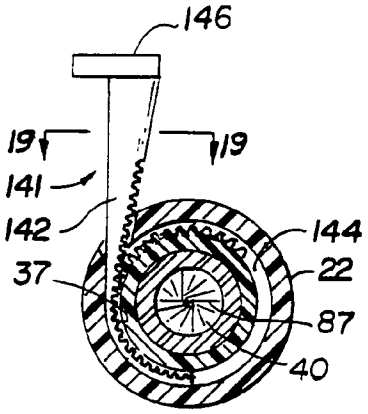


Fig.18

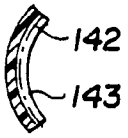
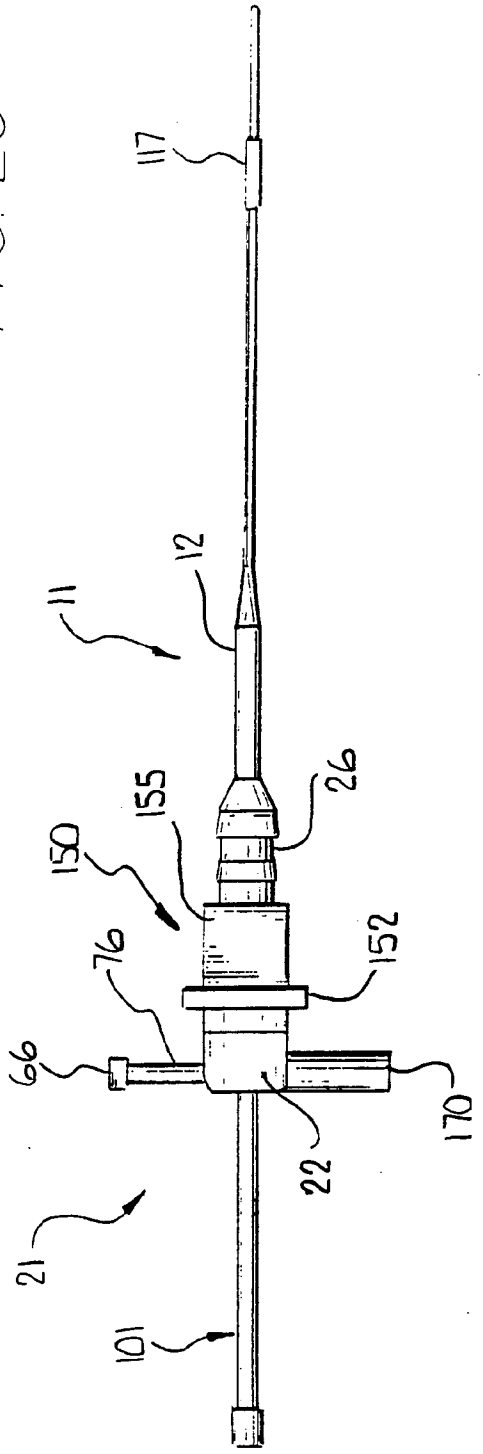


Fig.19

FIG. 20



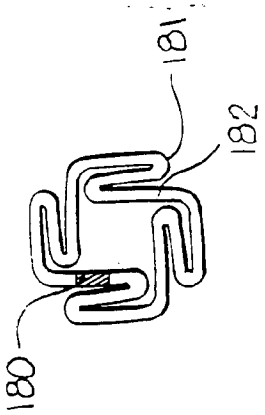


FIG. 23

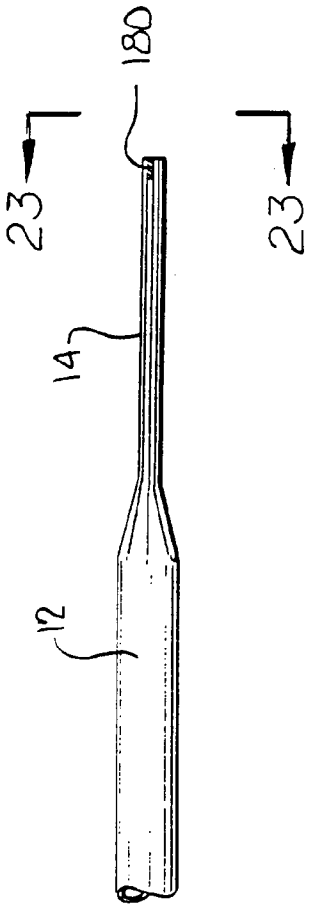


FIG. 22

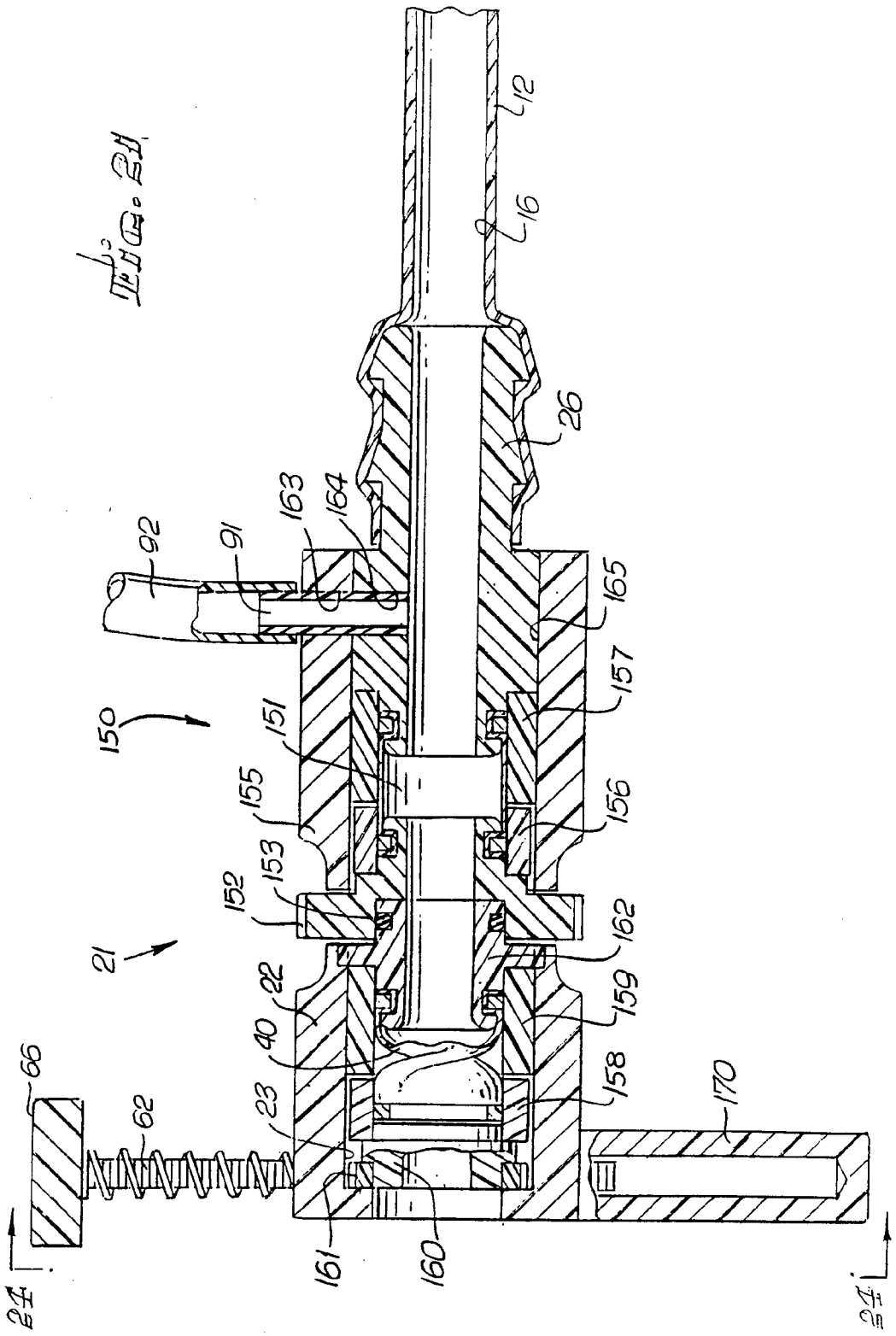


FIG. 2H
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FIG.24

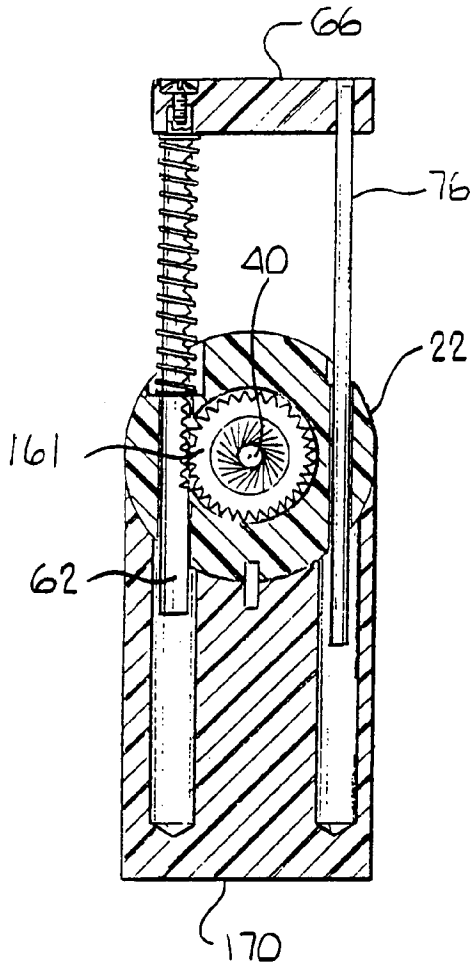
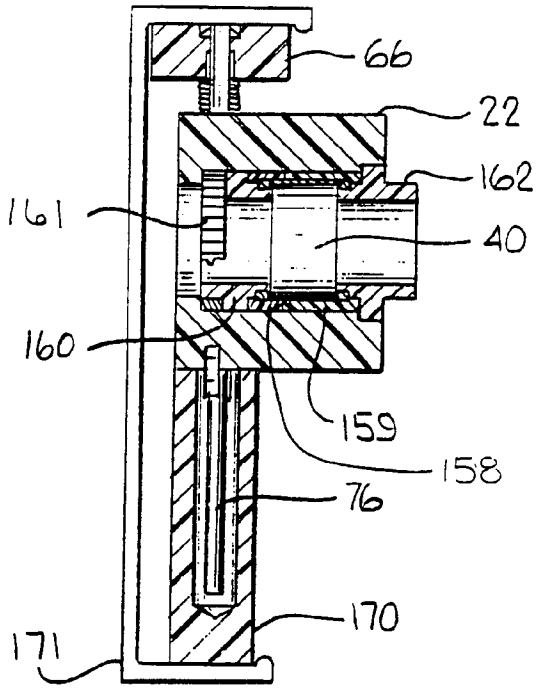


FIG. 25



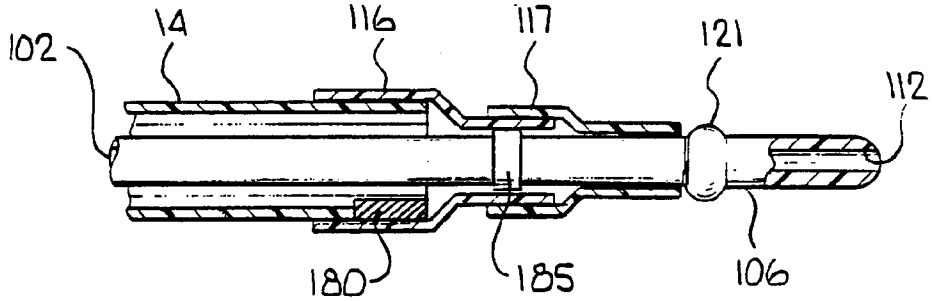


FIG. 26

FIG. 27

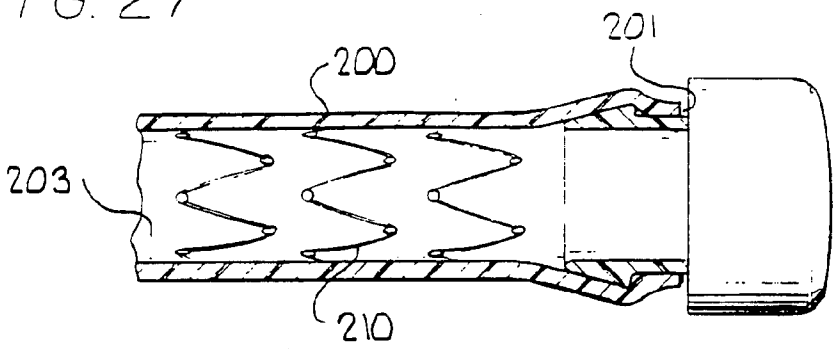


FIG. 28

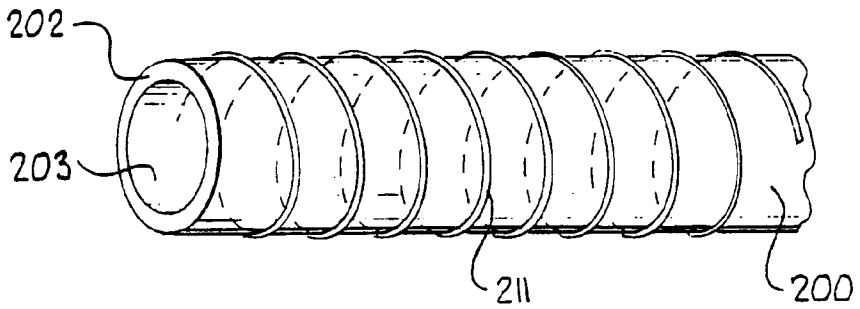


FIG. 29

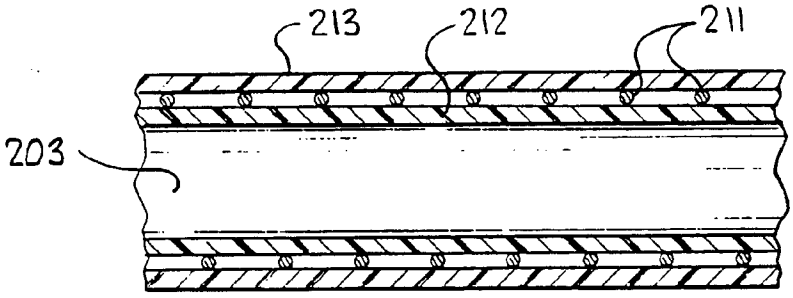


FIG. 30

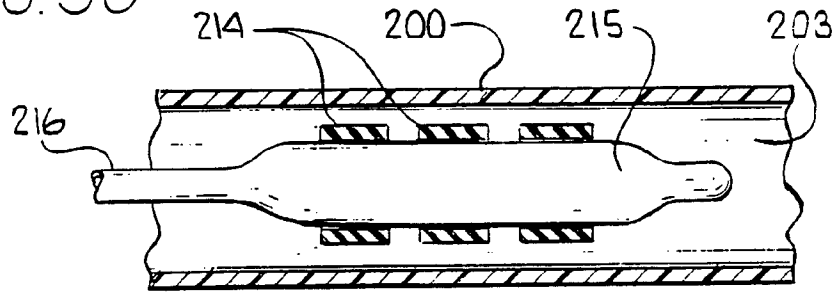


FIG. 31

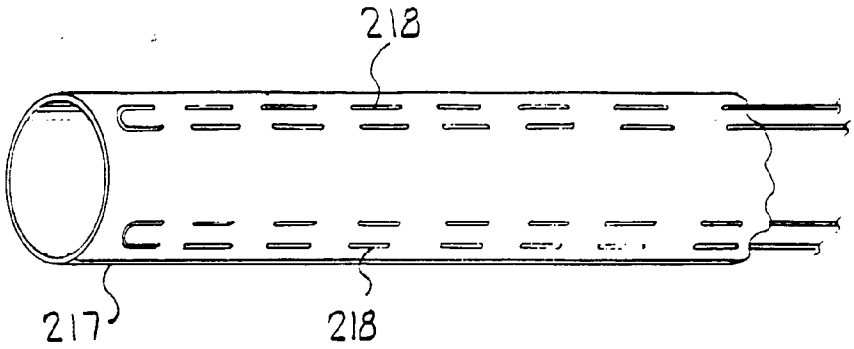


FIG. 32

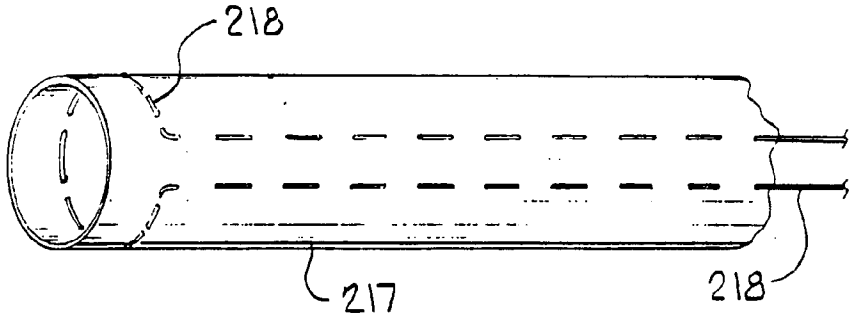


FIG. 33

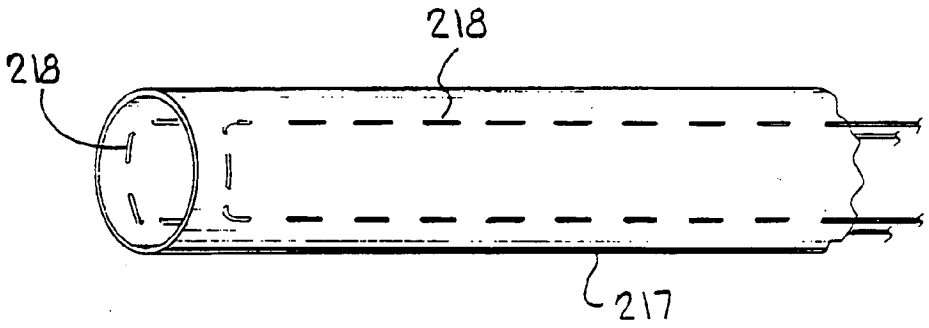
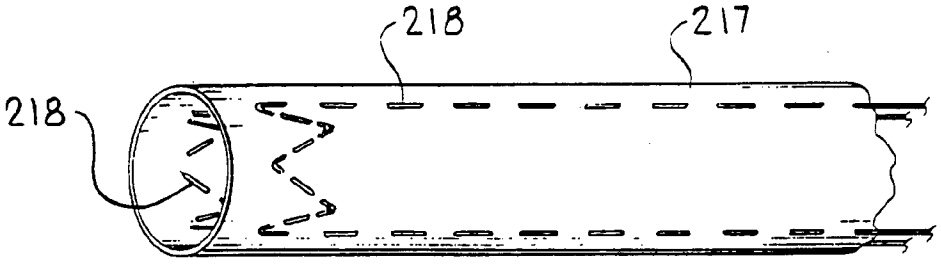


FIG. 34



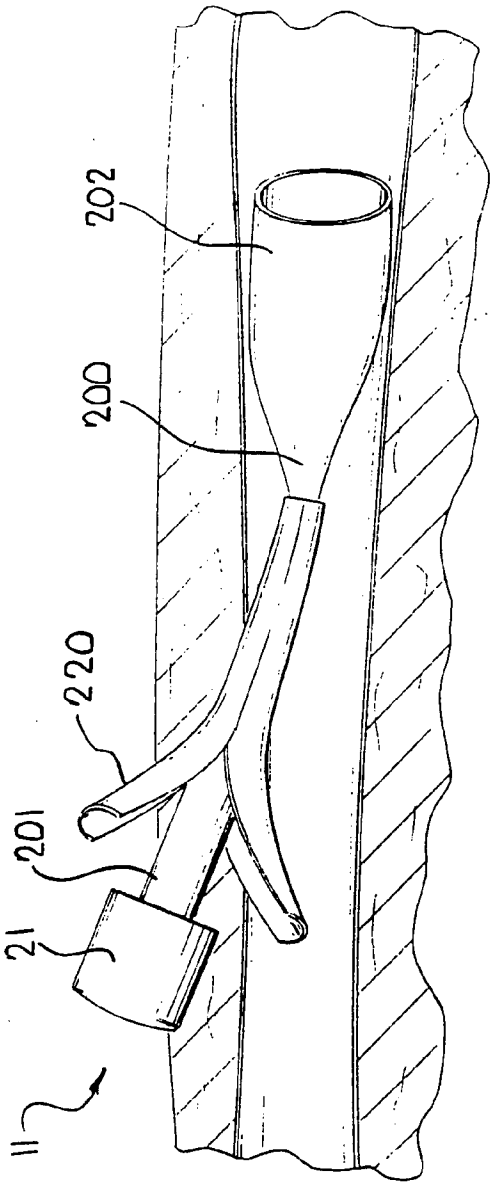


FIG. 35

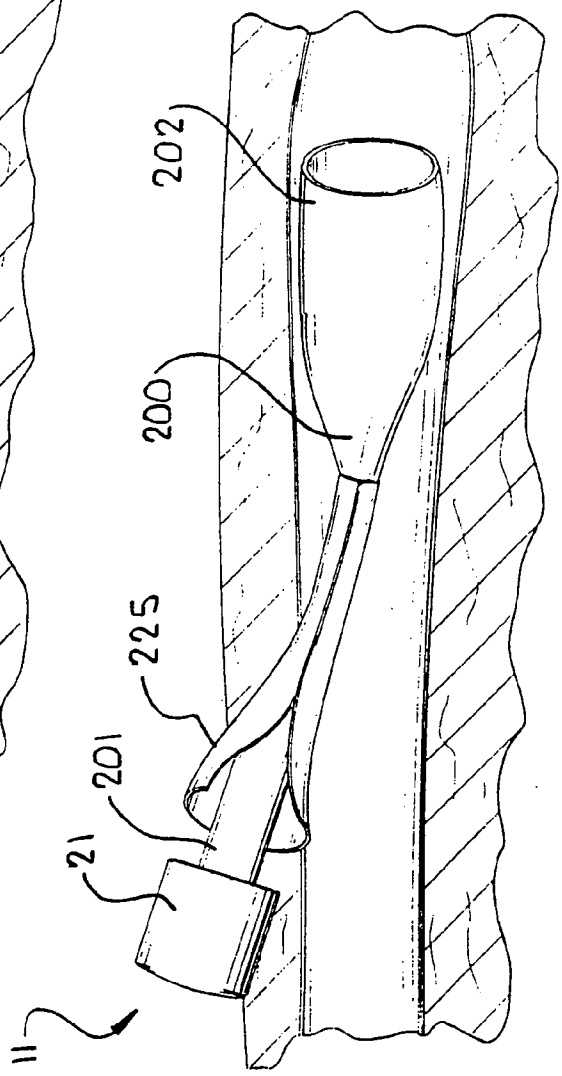


FIG. 36

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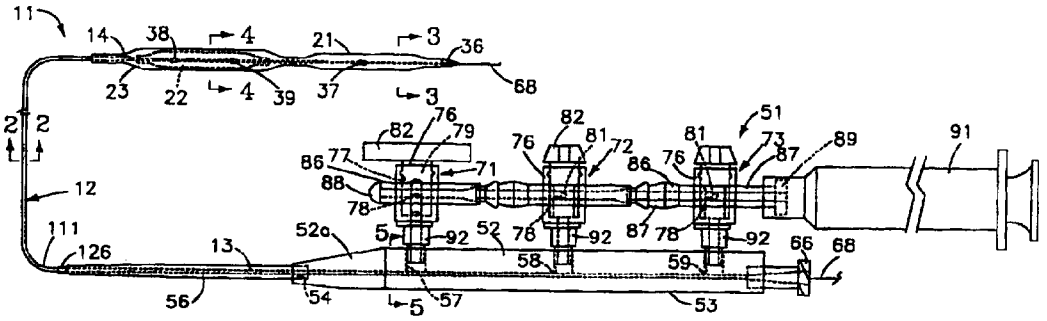

(57) Abstract

This invention is a multiple balloon catheter (11) for use in a vessel of a patient, and for use with an inflation/deflation device. A flexible elongate tubular member (12) with proximal and distal extremities (13, 14) has a distal balloon (21) mounted on the distal extremity (14) of the flexible elongate tubular member (12). Coaxial inner and outer balloons (22, 23) are mounted on the distal extremity (14) of the flexible elongate member (12) proximal of the distal balloon (21). The flexible elongate tubular member (12) has the balloon inflation lumens (17, 18, 19) therein in communication with the interiors of the distal balloon (21) and the inner and outer coaxial balloons (22, 23). A manifold is secured to the proximal extremity of the flexible elongate tubular member (12) in communication with the inflation lumens (17, 18, 19), and is adjusted to be coupled to the inflation/deflation device. Valves are carried by the inflation/deflation manifold for inflating the distal balloon in the inner and outer coaxial balloons (22, 23) one at a time, or in unison without removal of the inflation/deflation device from the manifold.

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MULTIPLE BALLOON STENT DELIVERY CATHETER AND METHOD

This invention relates to a multiple balloon stent delivery catheter and method for deploying the same in vessels of humans.

Heretofore stents have been delivered into vessels in the human body as for example arterial vessels in the heart. In delivering a stent to a lesion in such an arterial vessel, it has been the practice to first cross the lesion with a guide wire followed by a dilatation balloon catheter after which the dilatation balloon is inflated to dilate the lesion. The balloon is then deflated and the balloon catheter removed along with the guide wire. Thereafter, another guide wire is advanced through the stenosis. A stent delivery catheter is then advanced over this guide wire until the stent is disposed within the stenosis. Thereafter, the balloon of the stent delivery catheter is inflated to expand the stent into engagement with the stenosis after which the balloon is deflated and the balloon stent delivery catheter is withdrawn. Often a high pressure balloon is then advanced into the stent and inflated to more snugly secure the stent against the arterial wall. Thereafter, the high pressure balloon is deflated and the high pressure balloon catheter and

the guide wire are removed from the vessel. It has been found that such a procedure is time consuming and in addition requires the use of many different devices which require many insertions into the patient and removals of such devices from the patient. There is therefore need for a new and improved medical device for delivering stents and a method which overcomes these difficulties.

In general, it is an object of the present invention to provide a multiple balloon stent delivery catheter and method which makes it possible to deliver a stent to a desired location with a minimum number of devices inserted into and removed from the patient.

Another object of the invention is to provide a multiple balloon stent delivery catheter which can perform multiple functions.

Another object of the invention is to provide a multiple balloon stent delivery catheter in which a manifold is provided making it possible to inflate the multiple balloons one at a time or in unison without removing the catheter from the patient.

Another object of the invention is to provide a multiple balloon stent delivery catheter of the above character which makes it possible to attain different diameters for dilations of stenoses.

Another object of the invention is to provide a multiple balloon stent delivery catheter in which multiple diameter sized balloons are provided on a single catheter eliminating the need for catheter exchanges.

Another object of the invention is to provide a multiple balloon stent delivery catheter having tapered balloons.

Another object of the invention is to provide a multiple balloon stent delivery catheter of the above character in which various balloon profiles can be provided.

Additional objects and features of the invention will appear from the following description in which the preferred embodiments are set forth in detail in conjunction with the accompanying drawings.

FIGURE 1 is a side-elevational view of a multiple balloon catheter and a manifold for use with the same.

FIGURE 2 is an enlarged cross-sectional view taken along the line 2-2 of Figure 1.

FIGURE 3 is an enlarged cross-sectional view taken along the line 3-3 of Figure 1.

FIGURE 4 is an enlarged cross-sectional view taken along the line 4-4 of Figure 1.

FIGURE 5 is an enlarged cross-sectional view taken along the line 5-5 of Figure 1.

FIGURE 6 is an enlarged partial view in section of the coaxial balloons shown in Figure 1.

FIGURE 7 is a side-elevational view of a multiple balloon stent delivery catheter and manifold for use with the same.

FIGURE 8 is an enlarged cross-sectional view taken along the line 7-7 of Figure 7.

FIGURE 9 is a cross sectional view similar to that shown in Figure 7 but showing the outer balloon inflated to place the stent.

FIGURES 10, 11, 12, and 13 are side-elevational views of additional embodiments of multiple balloon catheters incorporating the present invention.

In general, the multiple balloon catheter is for use in the vessel of a patient with an inflation/deflation device. It is comprised of a flexible elongate tubular member having proximal and distal extremities. A distal balloon is mounted on the distal extremity of the flexible elongate tubular member. Coaxial inner and outer balloons are mounted on the distal extremity of the flexible elongate member proximal of the distal balloon. The flexible elongate tubular member has balloon inflation lumens therein in communication with the interiors of the distal balloon and the inner and outer coaxial balloons. An inflation manifold is secured to the proximal extremity of the flexible elongate tubular member and is in communication with the inflation lumens and is adapted to be connected to the inflation/deflation device. Valve means is carried by the inflation/deflation manifold for inflating the distal balloon in the inner and outer coaxial balloons one at a time or in unison without removal of the inflation/deflation device.

More in particular as shown in Figures 1 through 5 of the drawings, the multiple balloon catheter 11 consists of a flexible elongate tubular member 12 having proximal and distal extremities 13 and 14 serving as a shaft for the multiple balloon catheter 11. The

flexible elongate tubular member 12 is formed of a suitable lubricous plastic such as Nylon or a copolymer of Nylon such as Pebax or other high lubricous materials such as polyethylene. Nylon 11 has been found to be a particularly suitable material. Other Nylons such as Nylon 12 or Nylon 66 can be utilized. The diameter of the shaft can be of a suitable size such as 3-French corresponding to 0.039" of the outside diameter. The shaft 12 has a suitable length ranging from 130 to 175 centimeters and typically approximately 150 centimeters when used for angioplasty. The flexible elongate tubular member or shaft 12 is typically an extrusion and is provided with a plurality of extruded lumens therein. Thus, as shown in Figure 2 the shaft 12 is provided with a guide wire lumen 16 which is sized to receive a conventional guide wire 68, as for example one having a diameter of .014", and thus is provided with a diameter of 0.017". The shaft is also provided with three balloon inflation lumens, 17, 18 and 19 in which lumen 17 and 18 are generally crescent- shaped and lumen 19 is generally circular in cross section. A plurality of inflatable balloons is provided on the distal extremity 14 of the flexible elongate tubular member 12. Thus, as shown in Figure 1, there is provided a distal balloon 21, an inner balloon 22 which is proximal of the distal balloon 21, and an outer balloon 23 which is coaxial with the inner balloon 22. The balloons 21, 22 and 23 are formed of a non-compliant or low-compliant high pressure material which is capable of withstanding pressures in the range of 18 to 20 atmospheres. Such high strength balloon materials typically incorporate materials such as Nylon 12 or Nylon 11. The distal balloon 21 can have a diameter ranging from 1.5 to 3 millimeters and typically approximately 2 millimeters. The inner balloon 22 can have a diameter ranging from 2.0 to 4.0 millimeters and typically 2.5 or 3

millimeters, whereas the outer balloon 23 can have a diameter ranging from 2.5 to 5 millimeters and typically 3 millimeters to 3.5 millimeters. The balloons can have a wall thickness ranging from 0.0005" to 0.0015" and preferably a thickness of approximately 0.00075". The balloons 21, 22 and 23 can have a suitable working length, as for example the distal balloon 21 can have a working length of 20 millimeters, the inner balloon 22 a working length of 20 millimeters and the outer balloon 23 a working length of 22 millimeters. It should be appreciated that the balloons, if desired, can have increased or decreased lengths as desired. The balloons 21, 22 and 23 are bonded in appropriate locations on the distal extremity 14 of the flexible elongate tubular member 12 in a suitable conventional manner as for example by the use of an adhesive, heat bonding or solvent bonding to form fluid tight seals so that the balloons can be inflated. Thus as shown in Figures 3 and 4, an adhesive 26 has been provided for securing the extremities of the balloons 21, 22 and 23 to the distal extremity 14 of the flexible elongate member 12. Thus, as shown in partial view in Figure 6, an adhesive 26 is utilized for making these bonds. The flexible elongate extremity 14 is also provided with holes of ports establishing communication with the balloon inflation lumens and the interior of the associated balloons. Thus there is provided an opening or port 31 establishing communication between the interior of the distal balloon 21 and lumen 19. Similarly, there is provided an opening or port 32 establishing communication between the lumen 17 and the interior of the inner balloon 22. A port 33 establishes communication between the lumen 18 and the interior of the outer balloon 23. A soft atraumatic tip 36 is provided on the distal extremity 14 and is secured thereto by suitable means such as adhesive (not shown).

The tip can be formed of a soft plastic material as for example Pebax.

Radiopaque markers are provided on the distal extremity 14 of the flexible elongate tubular member 12 to aid in locating the positions of the balloons 21, 22 and 23 during use and consist of a radiopaque marker 37 mounted on the flexible elongate tubular member 12 equidistant between the ends of the distal balloon 21. A pair of markers 38 and 39 is also provided on the distal extremity of the flexible elongate tubular member 12 proximal of the marker 37 and spaced apart near the opposite ends of the inner balloon 22. The radiopaque markers can be formed of a suitable radiopaque material such as gold or platinum. By placing two radiopaque markers in the inner balloon 22 and a single radiopaque marker on the distal balloon 21, it is easy to differentiate the distal balloon 21 from the proximal coaxial balloons 22 and 23.

A manifold assembly 51 is secured to the proximal extremity 13 of the flexible elongate tubular member 12 which can be utilized for inflating and deflating the balloons individually without having to disconnect and reconnect an inflation/deflation device 91. The manifold assembly 51 consists of an elongate cylindrical body 52 formed of a suitable material such as polycarbonate plastic which is provided with a flat 53 so that the manifold assembly 51 will remain in an upright position when resting on a flat surface. The body 52 is provided with a tapered or cone-shaped distal extremity 52a which has a bore 54 therein which has the proximal extremity 13 of the flexible elongate tubular member 12 sealed therein and bonded therein by suitable means such as an adhesive (not shown). A strain relief sleeve 56 is provided on the proximal extremity 13. The manifold body 52 is provided with

spaced-apart balloon inflation chambers, namely a distal balloon chamber 57, an inner balloon chamber 58 and an outer balloon chamber 59. The inner balloon chamber 58 is disposed proximally of the distal balloon chamber 57 and the outer balloon chamber 59 is disposed proximally of the inner balloon chamber 58. The body 52 is provided with a plurality of longitudinally extending bores. Thus, as shown in Figure 5, there is provided a guide wire bore 61 in alignment with the guide wire lumen 16 in the flexible elongate tubular member 12. Similarly, there are provided balloon inflation bores 62, 63 and 64 in communication with balloon inflation lumens 17, 18 and 19 respectively. The chambers 57, 58 and 59 are in communication, respectively, with the bores 64, 63 and 62.

A Luer fitting 66 is mounted on the body 52 and is in communication with the guide wire bore 61 to provide a guide wire port which, as shown, has a guide wire 68 disposed therein. The guide wire 68 is of a conventional type such as an 0.014" diameter guide wire. A Tuohy-Borst adapter (not shown) typically is carried by the Luer fitting 66 to prevent blood from seeping around the guide wire while the catheter 11 is in use.

The manifold assembly 51 includes means for supplying an inflation fluid to the chambers 57, 58 and 59 and consists of valve assemblies 71, 72 and 73 connected, respectively, to the chambers 57, 58 and 59. Each of the valve assemblies 71, 72 and 73 consist of a cylindrical valve body 76 having a bore 77 therein and another bore 78 extending transversely therethrough. A stem 79 is rotatably mounted in the bore 77 and has a bore 81 extending transversely therethrough and adapted to be moved into and out of registration with the bore 78 in the valve body 76. A handle 82 is

provided on the stem 79. Each valve body 76 is connected to adjacent valve body 76. Thus as shown each valve body 76 is provided with a male fitting 86 and a female fitting 87 in communication with the transverse bore 78 in the valve body 76. As shown in Figure 1, the male fitting 86 on one valve body 76 mates with the female fitting 87 of the adjacent valve body 76 so that a fluid communication channel is established between the valve assemblies 71, 72 and 73. The most distal male fitting 86 is truncated and is plugged with a plug 88. A Luer fitting 89 is provided on the most proximal female fitting 87 and has mounted thereon a conventional ENDOFLATER™ or syringe 91. Each valve assembly 71, 72 and 73 also includes a coupling 92 which couples the bore 77 into the respective chambers 57, 58 and 59.

With such a manifold assembly, balloons 21, 22 and 23 can be inflated and deflated individually or can be inflated simultaneously as desired merely by operation of the valve assemblies 71, 72 and 73 in an appropriate manner as hereinafter described. Thus, for example, if it is desired to inflate only the distal balloon 21, all of the valve assemblies 71, 72 and 73 are turned to the closed position. The valve assembly 71 is then rotated by 90° to turn it to an open position as shown in Figure 1, after which an inflation/deflation device 91 is operated to introduce an inflation fluid chamber 57 and then into the bore 64 and into the lumen 19 for inflating the distal balloon 21. The balloon 21 can also then be deflated. If that is not desired, the valve assembly 71 can be turned another 90° to close it to prevent deflation of the balloon 21 or, alternatively, to deflate the balloon 21 and hold it uninflated, after which the catheter 11 can be moved as hereinafter described and the next balloon, as for example inner balloon 22 can be inflated by rotating

the valve 72 to the open position. Thereafter in a similar manner, the outer balloon 73 can be inflated.

Also incorporating the present invention is a multiple balloon stent delivery catheter 101 which is shown in Figure 7. This multiple balloon stent delivery catheter 101 is very similar to the multiple balloon catheter 11 hereinbefore described. It consists of a flexible elongate tubular member 12 having proximal and distal extremities 13 and 14 with a distal balloon 21 and inner and outer balloons 22 and 23. A balloon expandable stent 102 is frictionally mounted on the coaxial inner and outer balloons 22 and 23. As shown in Figure 8, the balloons 22 and 23 are not inflated and the balloon expandable stent 102 is frictionally secured to the outer balloon 23 sufficiently tightly so that a force in excess of approximately one-half pound is required to remove the stent 102 from the outer balloon 23. Such a frictional force is desirable in order to prevent inadvertent displacement of the stent 102 from the outer balloon 23 during deployment. The balloon stent 102 can be of any conventional type and can be formed of a suitable material such as stainless steel or a nickel titanium alloy. A stent of desired length can be provided. Also if desired, stents can be provided in tandem on the outer balloon 23.

As shown, the stent 102 is positioned relative to the radiopaque markers 38 and 39 so that the positioning of the stent can be precisely ascertained during deployment as hereinafter described.

Means is provided for covering the stent 102 until it has been deployed and consists of a sheath 106 and can be formed of a very thin molded plastic having a lubricous outer surface such as one made of Teflon. The sheath 106 can have a single wall thickness ranging

from 0.001" to 0.005" and preferably a wall thickness of approximately 0.0015". The sheath 106 should have a wall thickness which will resist elongation while being withdrawn as hereinafter described. The sheath 106 has a distal extremity 107 which extends slightly beyond the distal extremity of the balloon expandable stent 102, as for example a distance of approximately 1 millimeter. The sheath 106 then extends proximally over the flexible elongate tubular member shaft 12 to the proximal extremity 13 thereof. The proximal extremity 108 of the sheath 106 is secured to a cylindrical fitting 111 forming a part of a hemostasis valve assembly 112. The hemostasis valve assembly 112 includes an internally threaded cap 116 which is threadedly mounted on the cylindrical fitting 111 and engages an O-ring 117 to form a liquid-tight seal between the fitting 111 and the proximal extremity 13 of the flexible elongate member 12. A Luer-type fitting 121 in the form of a side arm is secured to the fitting 111 and provides a port 122 for introducing a flushing saline liquid which can pass into the annular space 123 between the exterior of the flexible elongate tubular member or shaft 12 over the outer balloon 23 within the sheath 106 and exiting out the distal extremity 107 of the sheath 106 to be utilized for a purpose hereinafter described.

A marker 126 visible to the human eye formed of a suitable material such as a paint or a colored tape is provided on the proximal extremity 13 of the flexible elongate tubular member 12 proximal of the hemostasis valve assembly 112. The spacing between the proximal extremity of the hemostasis valve assembly 112 and the marker 126 should be a distance at least equal to or slightly greater than the length of the stent 102 so that when the threaded cap 116 is loosened, the fitting 111 can be retracted to pull with it the sheath 106.

When the threaded cap 106 is adjacent to or overlies the marker 126, the sheath 106 will have cleared the stent 102 to permit placement of the stent 102 as hereinafter described.

A manifold assembly 51 is provided which is substantially identical to the manifold assembly 51 hereinbefore described.

Operation and use of the multiple balloon catheter 11 may now be briefly described as follows. Let it be assumed that it is desired to perform a balloon angioplasty procedure to enlarge an opening in a stenosis in an arterial vessel of the heart of a human patient. The femoral artery of the patient is accessed in a conventional manner by advancing the guide wire 68 until it extends through the stenosis. Thereafter, the multiple balloon catheter 11 is inserted into the femoral artery utilizing the guide wire 68 as a guide to advance the distal extremity 14 of the flexible elongate tubular member 12 so that the distal balloon 21 is disposed within the stenosis. As soon as this has been accomplished by observation of the marker 37 under fluoroscopy, the distal balloon 21 can be inflated by rotating the valve 71 to an open position and then introducing a suitable inflation medium such as a contrast medium to inflate the balloon to its maximum diameter and to cause a flow passage of increased size to be created in the stenosis. After this has been accomplished, the distal balloon 21 is deflated by removing the inflation medium using the inflation/deflation device or syringe 91. After this larger opening has been formed in the stenosis by the distal balloon 21, the distal extremity 14 of the flexible elongate tubular member 12 is then further advanced into the stenosis until the coaxial inner and outer balloons 22 and 23 are positioned within the

stenosis. This again can be visualized by observing the positioning of the markers 38 and 39 under fluoroscopy. The valve assembly 71 is then turned to a closed position and the valve assembly 72 is turned to an open position and an inflation medium is introduced into the inner balloon 22 which moves the outer uninflated balloon 23 into engagement with the stenosis to cause a larger size opening to be formed in the stenosis. If a still larger size opening is desired in the stenosis, the valve 73 can be turned to an open position and the outer balloon 23 can be inflated with a contrast medium or other suitable fluid. After a suitable dilation of the stenosis has occurred, the outer and inner balloons 23 and 22 can be deflated by withdrawing the inflation medium. The multiple balloon catheter 11 and the guide wire 68 can be removed from the femoral artery and the femoral artery closed surgically in a conventional manner. From the foregoing, it can be seen that all three of the balloons 21, 22 and 23 can be inflated individually or, alternatively, can be inflated in unison if desired without removal of the inflation/deflation device 91. This is made possible by use of the manifold assembly 51.

Operation and use of the multiple balloon stent delivery catheter 101 may now be briefly described as follows. Assuming that the multiple balloon stent delivery catheter 101 has been assembled as shown in Figure 7 with the stent 102 in place and with the sheath 106 overlying the same, let it be assumed that it is desired to treat a stenosis occurring in an arterial vessel of the heart of the human patient. This vessel typically is accessed through the femoral artery of the patient. A guide wire 68 is introduced into the femoral artery in a conventional manner and is advanced until its distal extremity has passed through

the stenosis. Thereafter, the multiple balloon stent delivery catheter 101 is advanced over the guide wire 68 until the small distal balloon 21 has been advanced into registration with the stenosis by observation of the marker 37. As soon as this has been accomplished, the valve 71 is opened and an inflation medium is introduced through the manifold 51 with the valves 72 and 73 in closed positions to inflate the distal balloon 21 to increase the size of the flow passage through the stenosis. After this has been accomplished, the distal balloon 21 is deflated. The distal extremity 14 of the multiple balloon stent delivery catheter 101 is advanced until the coaxial inner and outer balloons 22 and 23 are disposed within the stenosis by observation of the spaced apart markers 38 and 39. When this has occurred, the stent 102 is also positioned within the stenosis as well as the distal extremity 107 of the sheath 106.

After these desired procedures have been accomplished, the position of the stent 102 is again verified. If it is desired to change the position of the stent 102, the distal extremity 14 of the multiple balloon stent delivery catheter 101 can be changed after which the distal balloon 21 can be again inflated in the vessel to serve as an anchor for the distal extremity 14 of the flexible elongate tubular member 12. Thereafter, the sheath 106 can be removed from over the stent 102 by retracting proximally the hemostatic valve assembly 112 after loosening the threaded cap 116 and pulling it proximally until the cap 116 is in registration with the marker 126 to assure that the sheath has cleared the stent 102.

As soon as this has been accomplished, the inner balloon 22 can be inflated by opening the valve assembly 72 and leaving the valve assembly 73 closed

and supplying an inflation medium to the inner balloon 22 to expand the stent 102 radially and outwardly to increase the size of the opening or flow passage through the stenosis. If it is desired to further increase the size of the opening in the stenosis, the outer balloon 23 can then be inflated by opening of the valve 73 and supplying additional inflation medium to the manifold assembly 51 to inflate the outer balloon 23 and to carry with it and expand the stent 102 to further increase the size of the opening through the stenosis. As soon as it has been established that the stent 102 has been fully expanded to the desired diameter and embedded in the vessel wall, the balloons 21, 22 and 23 can be deflated by withdrawing inflation medium from the same. The entire multiple balloon stent delivery catheter 101 along with the guide wire 68 can then be removed from the femoral artery and the femoral artery closed surgically in a conventional manner.

It should be appreciated that in connection with the multiple balloon catheter 11 and the multiple balloon stent delivery catheter 101, that the distal balloon 21 can have any appropriate size. For example, it can be a small size balloon as hereinbefore described or, if desired, it can be a larger size balloon substantially the same size as the outer balloon 23.

It also should be appreciated that in place of one distal balloon 21, a plurality of distal balloons can be provided which are disposed in tandem, as for example as shown in Figure 11 in which another distal balloon 21a proximal of the other distal balloon 21 has been provided in the multiple balloon catheter 136. An additional marker 37a has been provided in the balloon 21a.

Another multiple balloon catheter 141 incorporating the present invention is shown in Figure 12 in which a stepped outer coaxial balloon 23a is provided having a distal extremity of lesser diameter than the proximal extremity of the balloon 23a. The proximal and distal portions of the balloon 23a can be of various lengths as desired.

In connection with the foregoing embodiments it also should be appreciated that the balloons provided on the multiple balloon catheters 11 and 101 can have various configurations. Thus, for example, as shown in Figure 13, the outer balloon 23b can be in the form of a tapered balloon having a taper which gradually decreases in a distal direction.

The balloon catheters 11 and 101 are high pressure substantially non-distensible balloons which can be distended at highly controlled and predictable rates. The balloons can be of various sizes ranging from 1 to 8 millimeters in diameter and 10 to 40 millimeters in length. The balloons can have various profiles, as for example straight, tapered, center or ends bulging portions. The catheters can be formed for over-the-wire use or can be provided with a fixed guide wire. The distal balloon can be utilized for maintaining an anatomical position for the catheter while other functions are being performed with the catheter, as for example deployment of a stent as hereinbefore described.

Various methods can be performed utilizing the multiple balloon catheter hereinbefore described. First it should be appreciated that the multiple balloon catheter can be utilized for delivering a stent without having a sheath covering the stent when that is desired as for example for purposes of economy. The method of

the present invention can be utilized with a multiple balloon stent delivery catheter which has an outer coaxial balloon which is a stepped balloon having proximal and distal portions with the distal portion having a diameter less than the diameter of the proximal portion. The stent can be mounted on the distal portion of smaller diameter. When this is the case, the sheath can be withdrawn to uncover the stent while still covering the proximal portion of the outer coaxial balloon. Thereafter, the outer coaxial balloon can be inflated to cause expansion of the uncovered distal portion to cause deployment of the stent. Alternatively, the stent can be mounted on the proximal portion of larger diameter and covered by the sheath. The distal portion of smaller diameter can then be advanced into the stenosis and can be utilized for predilating the stenosis. The outer coaxial balloon can then be delated and the catheter advanced so that the proximal portion of larger diameter with the stent thereon can be moved into the stenosis through the larger flow passage formed in inflation of the distal portion. Thereafter, the sheath can be withdrawn and the proximal portion of the distal balloon can be inflated to deploy the stent. The method can be utilized in a similar manner with the tapered outer coaxial balloon with the stent being carried by the tapered outer balloon and being advanced into the stenosis. The sheath can be withdrawn to uncover the stent after which the balloon can be inflated to deploy the stent.

Although the stent delivery catheter of the present invention has been described for delivering a single stent at a time, it should be appreciated that a plurality of shorter segmented stents all mounted on a balloon and, if necessary, on a longer balloon and then

deployed as hereinbefore described to treat longer lesions or a plurality of lesions in a vessel.

Although the present multiple balloon catheter has been described principally as a stent delivery catheter, it should be appreciated that it also can be utilized for dilating one or more stenoses in a vessel. This can be readily accomplished by deploying the catheter into the vessel as hereinbefore described and then advancing the distal balloon into a stenosis and dilating that stenosis to increase the size of the flow passage therethrough. The distal balloon can be then deflated and the catheter advanced to advance the coaxial outer and inner balloons into registration with the stenosis after which at least one of the inner and outer balloons can be inflated to increase the size of the flow passage in the stenosis. Alternatively, the inner coaxial balloon can be inflated followed by inflation of the outer coaxial balloon when a larger size flow passage is desired through the stenosis. It should be appreciated that if there are additional stenoses in the same vessel, the multiple balloons can be further advanced into the vessel to perform the same dilating procedure with additional stenoses in the vessel.

Although the catheters 11 and 101 have been described principally in connection with angioplasty procedures involving stenoses in vessels of the heart, it should be appreciated that the teaching herein is equally applicable to procedures in carotid arteries and other vessels in the human body.

CLAIMS:

1. A multiple balloon catheter for use in a vessel of a patient and for use with an inflation/deflation device comprising a flexible elongate tubular member having proximal and distal extremities, a distal balloon mounted on the distal extremity of the flexible elongate tubular member, coaxial inner and outer balloons mounted on the distal extremity of the flexible elongate member proximal of the distal balloon, said flexible elongate tubular member having balloon inflation lumens therein in communication with the interiors of the distal balloon and the inner and outer coaxial balloons and a manifold secured to the proximal extremity of the flexible elongate tubular member in communication with the inflation lumens and adjusted to be coupled to the inflation/deflation device and valve means carried by the inflation/deflation manifold for inflating the distal balloon in the inner and outer coaxial balloons one at a time or in unison without removal of the inflation/deflation device from the manifold

2. A catheter as in Claim 1 further comprising an expandable stent carried by the outer balloon, a protective sheath overlying the stent extending from the stent to the proximal extremity of the flexible elongate tubular member and means secured to the sheath for removing the sheath proximally to clear the stent.

3. A catheter as in Claim 2 wherein said means for removing the stent includes means for introducing a fluid into the annular space between the sheath and the flexible elongate tubular member.

4. A catheter as in Claim 2 wherein said means for removing the sheath includes a hemostasis valve assembly, said hemostasis valve assembly including a port for introducing a fluid into the annular space between the sheath and the flexible elongate tubular member.

5. A catheter as in Claim 1 wherein said inflation manifold further comprises ganged valve assemblies movable between open and closed positions.

6. A catheter as in Claim 4 further comprising a marker carried by the proximal extremity of the flexible elongate tubular member and spaced a predetermined distance from the hemostasis valve assembly when the sheath overlies the stent to provide a gauge visible to the human eye to designate the distance the hemostasis valve assembly must be retracted to uncover the stent.

7. A catheter as in Claim 1 wherein said outer balloon has a tapered configuration.

8. A catheter as in Claim 1 wherein said outer balloon has a stepped configuration.

9. A catheter as in Claim 1 further including an additional distal balloon proximal of the distal balloon and distal of the coaxial inner and outer balloons.

10. A catheter as in Claim 1 further comprising a stent carried by the coaxial inner and outer balloons.

11. A multiple balloon stent delivery catheter comprising a flexible elongate tubular member having

proximal and distal extremities, a distal balloon mounted on the distal extremity of the flexible elongate tubular member, coaxial inner and outer balloons mounted on the distal extremity of the flexible elongate member proximal of the distal balloon, the flexible elongate tubular member being formed with balloon inflation lumens in communication with the interiors of the distal balloon and the inner and outer balloons, a stent carried by the outer balloon, a sheath overlying the stent and extending proximally of the stent to the proximal extremity of the flexible elongate tubular member and an attachment secured to the proximal extremity of the sheath for facilitating withdrawing the sheath to uncover the stent.

12. A catheter as in Claim 11 further comprising a first radiopaque marker carried by the distal extremity of the flexible elongate member and being disposed substantially equidistant from the ends of the distal balloon, second and third radiopaque markers carried by the distal extremity of the flexible elongate tubular member spaced apart within the confines of the inner balloon whereby the position of the inner balloon can be distinguished from that of the position of the distal balloon.

13. A catheter as in Claim 11 further comprising a marker visible to the human eye carried by the proximal extremity of the flexible elongate tubular member and providing a visual indication of the distance the sheath must be retracted in order to uncover the stent.

14. A method for deploying a stent into a vessel having a blood flow lumen therein and having stenosis in the vessel at least partially occluding blood flow

in the vessel by the use of a multiple balloon stent delivery catheter having a distal extremity and a proximal extremity with a distal balloon mounted on the distal extremity and coaxial inner and outer balloons mounted on the distal extremity proximal of the distal extremity a stent carried by the outer balloon comprising advancing the distal extremity of the catheter until the distal balloon is advanced into the stenosis, inflating the distal balloon to increase the size of the flow passage in the stenosis, deflating the distal balloon, advancing the distal extremity of the catheter until the stent is disposed in the stenosis, inflating the distal balloon in the vessel to anchor the distal extremity of the catheter in the vessel, inflating at least one of the inner and outer coaxial balloons to expand the stent to embed the stent in the wall of the vessel, deflating the distal balloon and at least one of the inner and outer coaxial balloons and removing the catheter from the vessel.

15. A method as in Claim 14 by the use of a sheath covering the stent and extending to the proximal extremity of the flexible elongate tubular member and including the step of withdrawing the sheath to uncover the stent prior to inflating at least one of the inner and outer coaxial balloons.

16. A method as in Claim 15 further comprising the step of inflating the outer balloon after the inner balloon has been inflated to further expand the stent to further embed the stent in the vessel and thereafter deflating the outer balloon and the inner balloon and the distal balloon and removing the catheter from the vessel.

17. A method as in Claim 14 further comprising the steps of prior to inflation of the inner balloon or the outer balloon of utilizing the annular space between the sheath and the flexible elongate tubular member for flushing the stent.

18. A method as in Claim 14 for use with a guide wire and further comprising advancing the guide wire through the stenosis and thereafter advancing the catheter over the guide wire into the stenosis.

19. A method as in claim 14 wherein the multiple balloon stent delivery catheter has an outer coaxial balloon which is a stepped balloon having proximal and distal portions with the distal portion having a diameter less than the diameter of the proximal portion and further comprising the step of mounting the stent on the distal portion of smaller diameter and only withdrawing the sheath to uncover the stent while still covering the proximal portion of the outer coaxial balloon and thereafter inflating the outer coaxial balloon to inflate the uncovered distal portion.

20. A method as in Claim 14 wherein the multiple balloon stent delivery catheter has an outer coaxial balloon which is a stepped balloon having proximal and distal portions with the distal portion having a diameter less than the diameter of the proximal portion and further comprising the step of mounting the stent on the proximal portion of the larger diameter of the stepped balloon and further comprising the step of predilating the stenosis with the distal portion of the stepped balloon while the stent is covered by the sheath, thereafter deflating the stepped balloon, advancing the catheter so that the stent is disposed in the stenosis, retracting the sheath to expose the stent and inflating the outer coaxial stepped balloon to deploy the stent.

21. A method as in Claim 14 wherein the multiple balloon stent delivery catheter has an outer coaxial balloon which is tapered and having proximal and distal portions with the distal portion having a smaller diameter than the diameter of the proximal portion, and further comprising the step of mounting the stent on the tapered balloon.

22. A method as in Claim 14 wherein the stent is a plurality of stents carried by the outer balloon and further comprising the step of placing the plurality of stents on the outer balloon at the same time.

23. A method for performing angioplasty in a vessel having a blood flow lumen therein and having at least one stenosis in the vessel at least partially occluding blood flow in the vessel by the use of a multiple balloon delivery catheter having a distal extremity and a proximal extremity with a distal balloon mounted on the distal extremity and coaxial inner and outer balloons mounted on the distal extremity proximal of the distal balloon comprising advancing the distal extremity of the catheter until the distal balloon is advanced into the stenosis, inflating the distal balloon to increase the size of the flow passage in the stenosis, deflating the distal balloon, advancing the distal extremity of the catheter until the inner and outer coaxial balloon are disposed in the stenosis, inflating at least one of the inner and outer coaxial balloons to further increase the size of the flow passage in the stenosis, deflating the distal balloon and the at least one of the inner and outer coaxial balloons and removing the catheter from the vessel.

24. A method as in Claim 23 further including the step of first inflating the inner coaxial balloon and thereafter inflating the outer balloon to further increase the size of the flow passage through the stenosis.

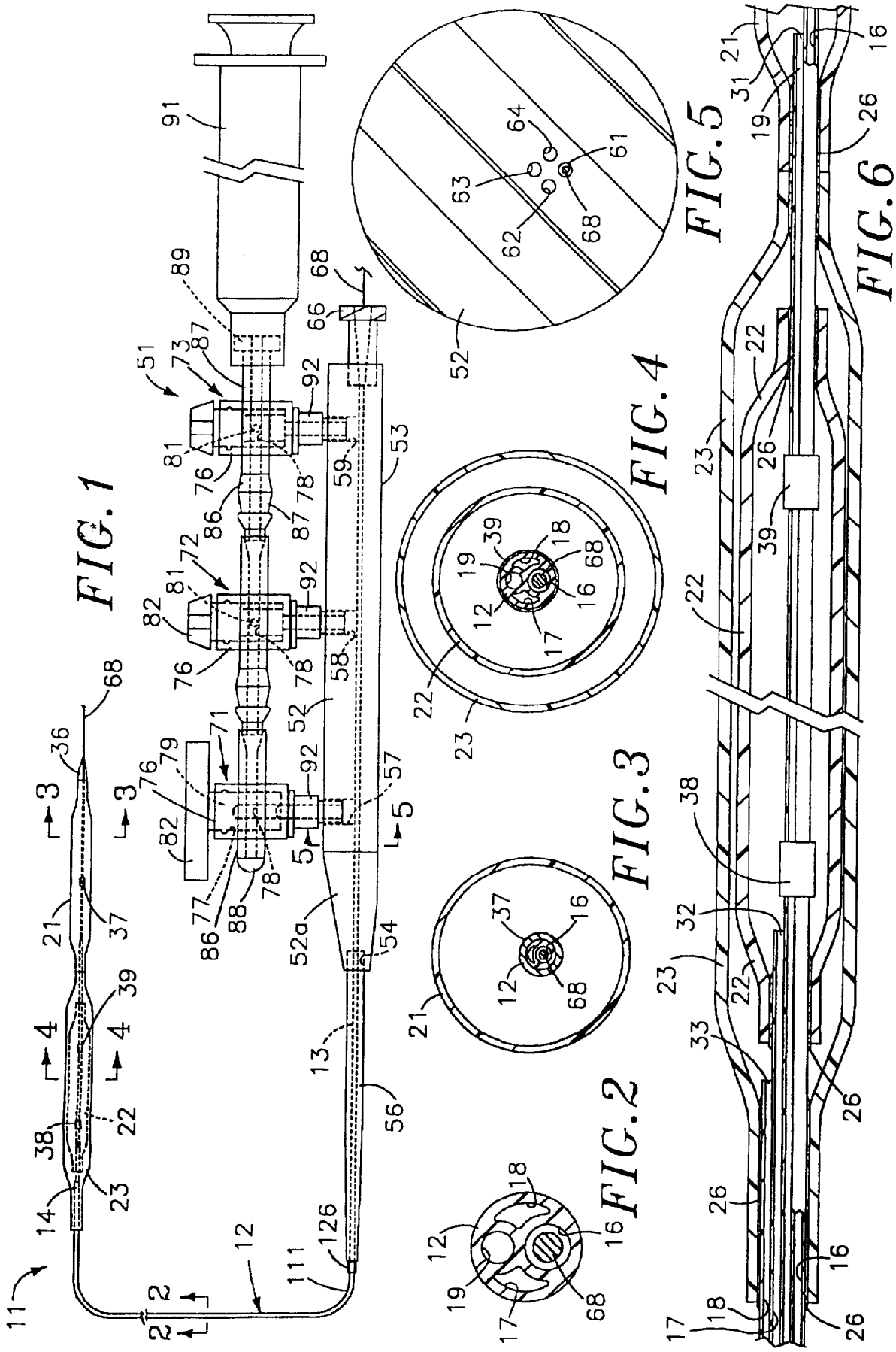

FIG. 1

FIG. 2

FIG. 3

FIG. 4

FIG. 5

FIG. 6

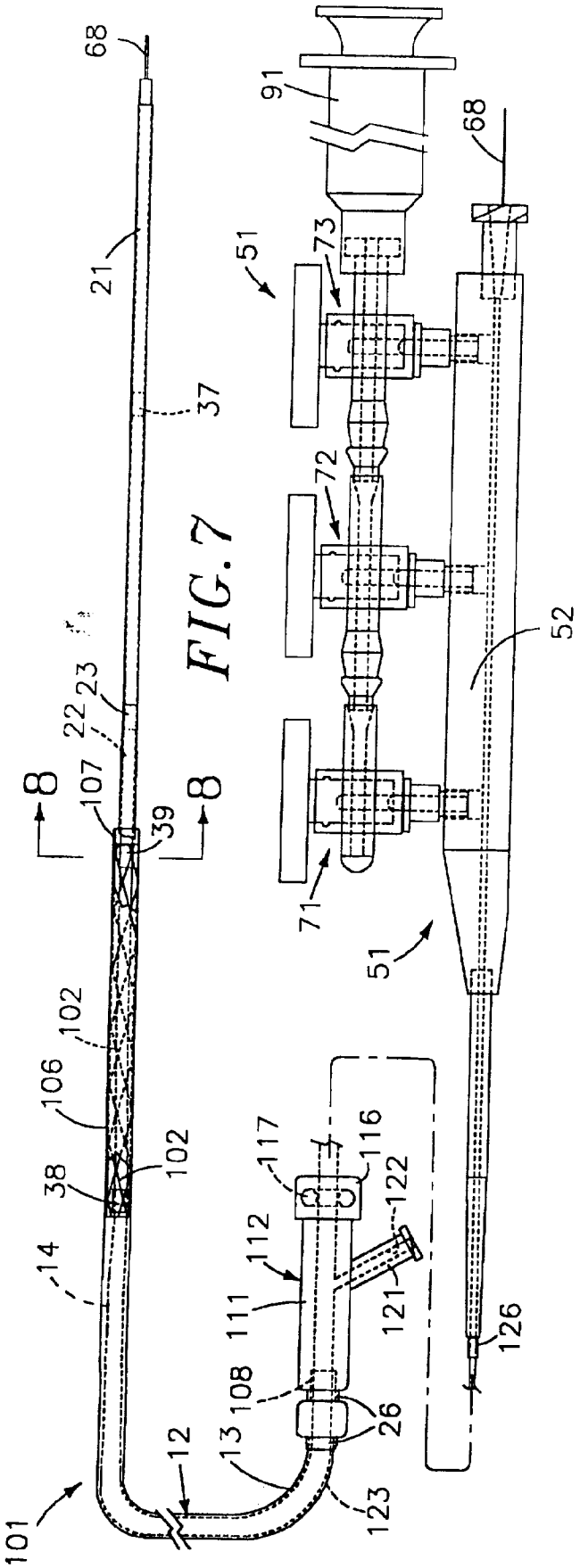

FIG. 7

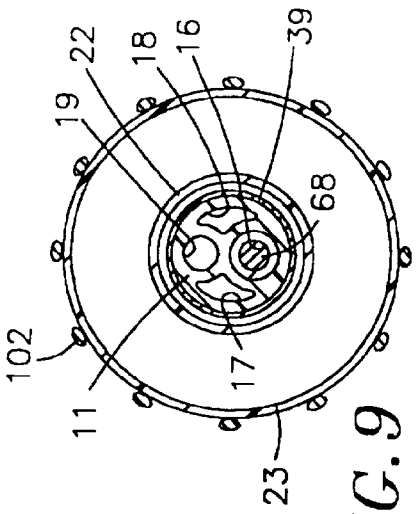

FIG. 9

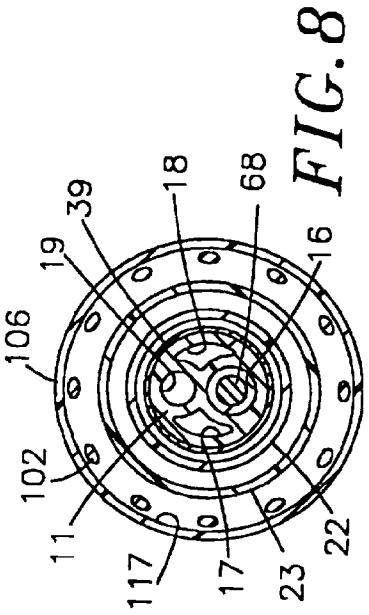

FIG. 8

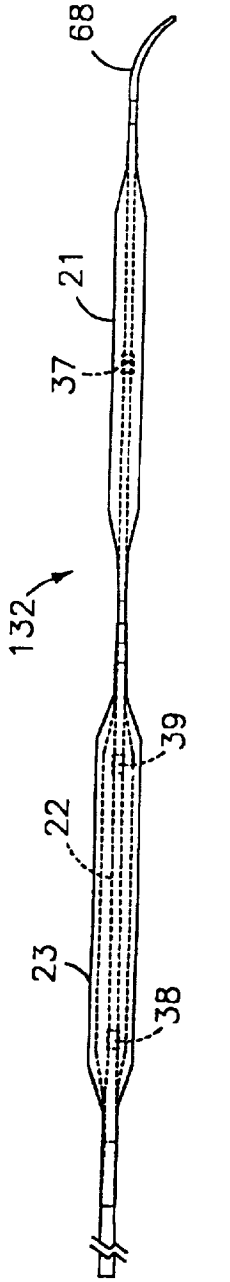

FIG. 10

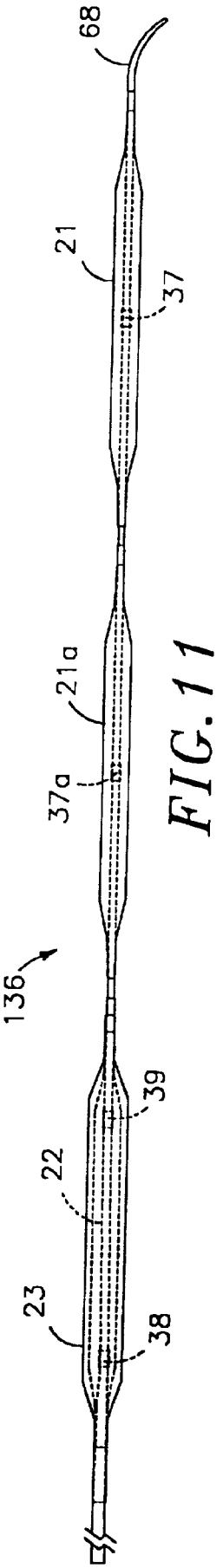

FIG. 11

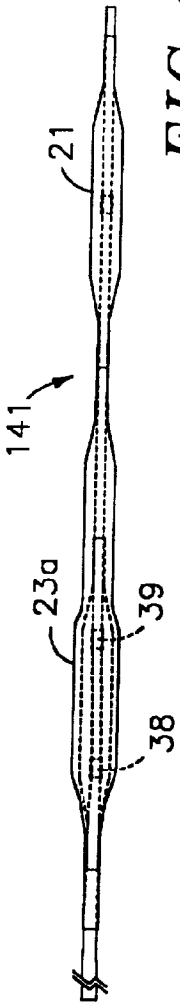

FIG. 12

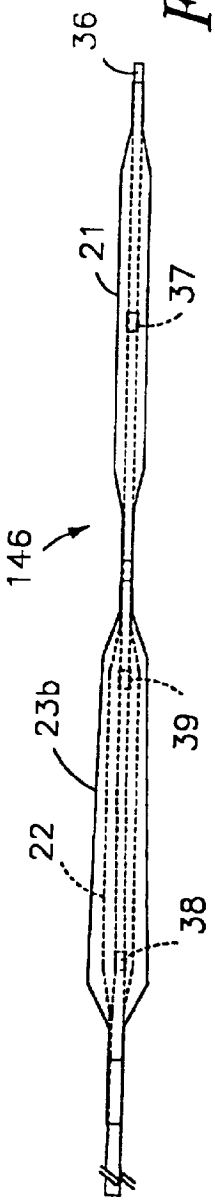

FIG. 13

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US97/16326

A. CLASSIFICATION OF SUBJECT MATTER

IPC(6) :A61M 29/00
US CL :606/194, 198

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 606/194, 198

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

NONE

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

NONE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 5,456,694 A (MARIN et al) 10 October 1995, entire document.	1-24
A, P	US 5,632,760 A (SHEIBAN et al) 27 May 1997, entire document.	1-24

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

*	Special categories of cited documents:	"T"	later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"A"	document defining the general state of the art which is not considered to be of particular relevance	"X"	document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"E"	earlier document published on or after the international filing date	"Y"	document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"L"	document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"&"	document member of the same patent family
"O"	document referring to an oral disclosure, use, exhibition or other means		
"P"	document published prior to the international filing date but later than the priority date claimed		

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Name and mailing address of the ISA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703) 305-3230	Authorized officer KEVIN TRUONG Telephone No. (703) 308-3767

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(54) **Apparatus for deployment release of intraluminal prostheses**

Vorrichtung zum Positionieren einer intraluminalen Prothese

Dispositif pour la mise an place d'une prothèse intraluminale

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(60) Divisional application: **99113203.6 / 0 948 946**
99113204.4 / 0 943 302

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US-A- 5 078 720

EP 0 696 447 B1

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Description

BACKGROUND OF THE INVENTION

1. Field of the Invention

[0001] The present invention relates generally to a delivery catheter for the endoluminal placement of resilient tubular prostheses, such as grafts, stents, stent-grafts, and other structures. More particularly, the present invention relates to a delivery catheter for the initial placing and optional repositioning of such intraluminal tubular protheses in body lumens, including blood vessels, for the treatment of abdominal and other aneurysms.

[0002] Vascular aneurysms are the result of abnormal dilation of a blood vessel, usually resulting from disease and/or genetic predisposition which can weaken the arterial wall and allow it to expand. While aneurysms can occur in any blood vessel, most occur in the aorta and peripheral arteries, with the majority of aortic aneurysms occurring in the abdominal aorta, usually beginning below the renal arteries and often extending distally into one or both of the iliac arteries.

[0003] Aortic aneurysms are most commonly treated in open surgical procedures where the diseased vessel segment is bypassed and repaired with an artificial vascular graft. While considered to be an effective surgical technique, particularly considering the alternative of a usually fatal ruptured abdominal aortic aneurysm, conventional vascular graft surgery suffers from a number of disadvantages. The surgical procedure is complex and requires experienced surgeons and well equipped surgical facilities. Even with the best surgeons and equipment, however, patients being treated frequently are elderly and weakened from cardiovascular and other diseases, reducing the number of eligible patients. Even for eligible patients prior to rupture, conventional aneurysm repair has a relatively high mortality rate, usually from 3% to 10%. Morbidity related to the conventional surgery includes myocardial infarction, renal failure, impotence, paralysis, and other conditions. Additionally, even with successful surgery, recovery takes several weeks, and often requires a lengthy hospital stay.

[0004] In order to overcome some or all of these drawbacks, endovascular graft placement for the treatment of aneurysms has been proposed. Although very promising, many of the proposed methods and apparatus suffer from other problems. In particular, delivery and placement of the endovascular graft within the vasculature can be problematic. Proper positioning and sizing of the endovascular graft is critical to the successful treatment of an aneurysm. With many endovascular graft structures and their associated delivery catheters, it is difficult or impossible to retract a partially released graft structure. Thus, improper initial placement of a vascular graft can sometimes require open surgical procedures for correction. Additionally, proper sizing of the graft can require maintenance of a large inventory of graft delivery catheters, where each catheter carries a graft having a different length and/or expansible diameter.

[0005] Furthermore, grafts are often resilient, biased to expand and anchor the graft within the body lumen. These resiliently expanding grafts are tightly compressed within the catheter and impose significant forces against the surrounding catheter bodies, often leading to excess friction between the graft and the catheter wall. These forces complicate the loading of the graft into the catheter, as well as the accurate release of grafts and stents in body lumens. Moreover, the catheters must maneuver the graft within the vascular system. Thus, the catheters are required to have flexible, elongate bodies which are particularly susceptible to the expanding graft, often resulting in invagination of the graft in the soft material of the catheter wall.

[0006] For these reasons, it would be desirable to provide an improved apparatus for endovascular placement of intraluminal protheses, including grafts, stents, and stent-grafts, for treating aneurysms and other conditions.

[0007] It would be particularly desirable to provide delivery catheters for the placement of endoluminal tubular prostheses which would facilitate the controlled release of resilient tubular prostheses. It would be particularly desirable to provide delivery catheters for the placement of endoluminal and other tubular prostheses which permit the repositioning and/or retrieval of partially released prostheses. It would be further desirable if such delivery catheters were able to contain the protheses firmly within the catheter until the final release of the prostheses into the blood vessel. It would also be particularly desirable to provide delivery catheters which reduce the frictional forces created by the resilient expansion against the catheter during loading and release of the prostheses.

2. Description of the Background Art

[0008] Vascular grafts and devices for their endoluminal placement are described in U.S. Patent Nos. 5,282,824; 5,242,399; 5,219,355; 5,211,658; 5,201,757; 5,192,297; 5,190,058; 5,158,548; 5,147,370; 5,104,399; 5,092,877; 5,078,726; 5,019,085; 4,990,151; 4,950,227; 4,913,141; 4,886,062; 4,820,298; 4,787,899; 4,617,932; 4,562,596; 4,577,631; and 4,140,126; and European Patent Publications 539,237; 533,511; 518,839; 518,704; 508 473; 505,686; 466 518; and 461 791. Catheters for placing vascular stents are described in U.S. Patent Nos. 5,192,297; 5,092,877; 5,089,005; 5,037,427; 4,969,890; and 4,886,062. Catheters carding a graft structure in a tube or capsule are described in U.S. Patent Nos. 5,275,622; 5,104,399; and 4,787,899; and EP466518. EP-A-364 420 describes a delivery catheter according to the preamble of inde-

pendent claim 1.

SUMMARY OF THE INVENTION

[0009] The present invention provides a delivery catheter as defined in independent claim 1. Prefered embodiments are further specified in the dependent claims.

BRIEF DESCRIPTION OF THE DRAWINGS

[0010]

Fig. 1 is a side view of a vascular graft which is exemplary of the type of radially compressible tubular prosthesis which may be placed using the delivery catheter of the present invention.

Figs. 2-18; Figs 19A-D; Figs 24A-C illustrate the use of a delivery catheter in placement of a radially compressible tubular prosthesis in a body lumen.

Figs. 20A and 20B;

Figs. 21A and 21B;

Figs. 22A and 22B; and

Figs. 23A and 23B illustrate embodiments of the retaining structure of the delivery catheter according to the invention.

Fig. 25 is a perspective view of another embodiment of a delivery catheter of the present invention, with a portion of the distal end broken away to disclose a prosthesis therein.

Figs. 26A and 26B illustrate the loading of a graft into the delivery catheter of Fig. 25.

Figs. 27A-27C illustrate the use of the delivery catheter of Fig. 25 in placement of a radially compressible tubular prosthesis in a body lumen.

Fig. 28 illustrates a preferred method of use of the delivery catheter of Fig. 25, in which tapered nosecone is withdrawn independently of the runners.

Fig. 29A is an exploded cross-sectional view of the delivery catheter of Fig. 25.

Fig. 29B is a cross-section of an alternative shaft structure and cover having increased flexibility.

Fig. 30 illustrates a housing at the proximal end of the delivery catheter of Fig. 25 which provides a mechanical advantage for withdrawing the cover.

Fig. 31 illustrates a delivery catheter cover having a rounded, atraumatic distal end with a split tip.

Fig. 32 illustrates a delivery catheter cover having runners imbedded within the distal end.

Figs. 33A and 33B are alternative cross-sectional views of a delivery catheter cover.

Fig. 34 illustrates a brace which restrains the prosthesis at a target location during deployment.

DESCRIPTION OF THE PREFERRED EMBODIMENT

[0011] The present invention provides a delivery catheter as defined in claim 1 for the endoluminal placement of intraluminal tubular prostheses, particularly grafts, stents, and stent-grafts. The tubular prostheses will be radially compressible, and the apparatus of the present invention will maintain the prostheses under compression in a narrow-diameter configuration while they are being introduced to the body lumen, typically during surgical cutdown or percutaneous introduction procedures. Placement of the tubular prosthesis is effected by releasing the prosthesis at a target location in the lumen. Thus, it is necessary that the prosthesis be sufficiently resilient and conformable to expand against the interior wall of the body lumen. It will be appreciated, however, that the prosthesis may be formed at least partly from malleable components which permit it to be subsequently further expanded, typically by inflation of a balloon within the lumen of the prosthesis.

[0012] The present invention will find greatest use in the percutaneous placement of endovascular prostheses for the treatment of diseases of the vasculature, particularly aneurysms, stenoses, and the like. Suitable prosthesis structures which may be deployed by the delivery catheter of the present invention are described in copending application Serial No. 08/255,681. One exemplary graft structure 10 is illustrated in Fig. 1. Prosthesis 10 comprises a perforate tubular frame 12 which includes a plurality of independent (non-connected) band members 14 separated from each other by small gaps 16. The tubular frame 12 is covered by an inner liner 18 and an outer liner 20, where the inner and outer liners together encase or sandwich the otherwise free-floating band members 14 therebetween. In order to secure the band members 14 in place, and secure the liners to the perforate tubular frame 12, the inner and outer liners are joined together along circumferential lines 22, preferably aligned with the gaps 16 between adjacent band members 14. The liners may be joined together by stitching, heat welding, ultrasonic welding, or the like. In the exemplary embodiment, the liners 18 and 20 are formed from polymeric sheet material and are joined together by ultrasonic welding. The band members 14 at each end of the graft 10 will have to be further secured to the liners 18 and 20. For example, they could be stitched, welded, or otherwise joined to the liners to hold them in place. The graft 10 will typically have a length in the range from about 50 mm to 500 mm, preferably from 80 mm to 200 mm, with a relaxed diameter in the range from about 4 mm to 45 mm, preferably being in the range from 5 mm to 25 mm. Such graft structures will be particularly suitable for treating vascular aneurysms.

[0013] In connection with the present invention, it has been discovered that the placement of resilient tubular prostheses imposes serious demands on delivery and imaging systems, as well as on the attending medical personnel. Prostheses are highly compressed within delivery catheters to allow maneuvering within the vascular system. The compressive forces have been found to lead to excessive friction during deployment from the delivery catheters of the prior art. Additionally, visuali-

zation of compressed prostheses within the catheter is problematic, particularly when a branched prosthesis must be placed in a branching body lumen in a specific orientation.

[0014] The delivery catheters facilitate deployment of resilient prostheses by reducing friction at the prosthesis/catheter interface, avoiding any increase in the stiffness of the delivery system where it is not needed. It has been discovered that compressed prostheses are largely rigid, which reduces any penalty in flexibility imposed by including hard, friction-reducing runners around the prosthesis.

[0015] Referring now to Fig. 2, a delivery catheter 30 comprises a sheath 32 and a shaft or inner catheter body 34. The sheath 32 has a central lumen 36 extending from a distal end 38 to a proximal handle 40. The shaft 34 is slidably received within the central lumen 36 and has a distal end 42 and a proximal handle 44. The delivery catheter 30 receives a radially compressible tubular prosthesis P within the annular space between the outer surface of the shaft 34 and the inner surface of the lumen through sheath 32. For convenience, the prosthesis is illustrated as a radially compressed helical coil which expands by unwinding and axial shortening. The delivery catheters, however, can be used with virtually any radially compressible prosthesis, as described above.

[0016] The delivery catheter of Fig. 2 relies on maintaining the radial compression of prosthesis P by direct pressure from the sheath 32. As will be discussed in detail below in connection with Figs. 19-24, prosthesis compression may also be provided by a retaining structure which comprises a cover, spaced-apart anchors, or other equivalent structure which maintains the radial compression regardless of the position of the sheath. Using such embodiments, the prosthesis may be uncovered and located prior to release and radial expansion.

[0017] In the embodiment of Fig. 2, the prosthesis P is anchored by a plurality of penetrating stay members 50 which are circumferentially spaced-apart over the exterior of the shaft 34. The stays 50 will be spaced proximally from the distal end 42 of the shaft 34 by a distance which corresponds generally to that of the tubular prosthesis P which is to be maintained on the delivery catheter 30. The penetrating stays 50 will extend radially outward by a distance sufficient to engage the interior surface of the lumen 36 of the sheath 32. In that way, the penetrating stays 50 will be able to anchor the proximal end of the tubular prothesis P when it is held within the catheter. In particular, the prosthesis P will remain anchored as the sheath 32 is drawn proximally over the shaft 34, as illustrated in Figs. 3-5.

[0018] When initially placed in a body lumen L, the sheath 32 covers substantially the entire length of the prosthesis P with the penetrating stays 50 engaging the proximal portion of the prosthesis P, as illustrated in Fig. 3. The sheath 32 may then be retracted proximally, partially releasing the prosthesis P, as illustrated in Fig. 4. The proximal portion of the prosthesis P, however, remains anchored by the penetrating stays 50 so long as the sheath 32 remains positioned over the stays. Once the sheath 32 is withdrawn to the proximal side of the stays 50, as illustrated in Fig. 5, the prosthesis P will be fully released. Prior to such full release, however, the prosthesis P may be recaptured by advancing the sheath 32 in the distal direction relative to the shaft 32.

[0019] Referring now to Fig. 6, the catheter 30 may optionally be provided with a journal sleeve 60 near its proximal end. The journal sleeve 60 is preferably mechanically coupled to the shaft 34 by pins 62 which extend through slots 64 in the sheath 32. The journal sleeve 60 can be anchored within an introducer sleeve or other access device (not illustrated) which is used to provide percutaneous access to the body lumen being treated. After initial positioning of the catheter 30 so that the prosthesis P is located at the target location within the lumen, it is desirable to firmly anchor the catheter 30 within the introducer sheath. Journal sleeve 60 permits anchoring of the shaft 34 (which carries the prosthesis P) while allowing the sheath 34 to remain freely translatable relative to both the journal sleeve 60 and the catheter shaft 34.

[0020] The dimensions and materials of construction of the catheter 30 may vary widely, depending on the intended usage. For vascular applications, the catheter 30 will typically have a length in the range from about 50 cm to 250 cm, preferably from 100 cm to 200 cm, and a diameter in the length from about 3 mm to 8 mm, preferably from 4 mm to 6 mm. These dimensions generally refer to the exterior dimensions of the sheath 32. It will be appreciated that the catheter shaft 34 will have a smaller diameter, typically in the range from 1 mm to 5 mm, preferably from about 1.5 mm to 3 mm, allowing a sufficient annular space therebetween to receive the prosthesis P. The catheter shaft will also have a length which is greater than that of the sheath, usually by a distance sufficient to accommodate the length of the prosthesis which is being delivered, typically from 5 cm to 25 cm, preferably from 7.5 cm to 15 cm. The catheters will generally be constructed of natural or synthetic polymers, such as silicone rubber, natural rubber, polyvinylchloride, polyurethanes, polyesters, polyethylenes, polytetrafluoro-ethylenes (PTFE), and the like. Optionally, the catheter sheath and shaft may be formed as composites having a reinforcement layer incorporated within a polymeric body in order to enhance strength, flexibility, and toughness. Suitable reinforcement layers include wire mesh layers, braided layers, and the like. The tubular members of the present invention may be formed by extrusion, with the tubular diameter modified by heat expansion and/or shrinkage using conventional techniques. Particular techniques for forming vascular and other catheters suitable for use in the present invention are well described in the patent and medical literature.

[0021] Referring now to Figs. 7 and 8, a catheter 70

having a sheath 72 with a deployable flared end will be described. Catheter 70 comprises the sheath 72, a shaft 74, and a prosthesis-containment sheath 76. A prosthesis P is contained between the sheath 72 and the shaft 74, generally as described above in connection with delivery catheter 30. The sheath 72, however, differs from that of sheath 32 in that sheath 72 has an outwardly flared distal end 78, as best seen in Fig. 8. The distal end 78 is a resilient structure, typically formed from the material of the sheath 72 itself and optionally having a plurality of elastic reinforcement elements imbedded therein to maintain the desired flared configuration, and may be radially collapsed by the containment sleeve 76, as illustrated in Fig. 7. The flared distal end of the sheath 72 is advantageous since it facilitates the release and recapture of the prosthesis P.

[0022] The flared distal end 78 of catheter 70 will usually have a fully expanded diameter d at the distal tip 79 in the range from 10 mm to 30 mm, preferably from 15 mm to 25 mm. The distal tip of diameter d will usually be greater than the diameter of the proximal portions of the sheath 72 by a factor from 2 to 8, preferably being from 2.5 to 5. The flare will extend over an axial length ℓ in the range from 3 mm to 30 mm, preferably from 5 mm to 20 mm. These flare dimensions will generally be applicable to all embodiments of the present invention where the prosthesis-containment sheath has a flared distal end.

[0023] Referring now to Figs. 9 and 10, a catheter 80 having an alternate mechanism for deploying a flared distal tip on a prosthesis-containing sheath structure 82 will be described. Catheter 80 comprises the sheath 82 having an annular lumen 84 extending from its proximal end 86 to its distal end 88. The annular lumen 84 is connected to an inflation port 90 on a proximal housing 92. A shaft 94 extends through the central lumen of the sheath 82 and carries a prosthesis P near it distal end.

[0024] The distal end of the sheath 82 is formed so that, upon inflation with a non-compressible fluid medium, typically saline or other biocompatible liquid, it assumes the outwardly flared configuration shown in Fig. 10. The structure is sufficiently elastic, however, so that removal of the inflation medium will permit the sheath 82 to resume its non-flared configuration, as illustrated in Fig. 9. Flaring of the distal end of sheath 82 facilitates both release and recapture of the prosthesis P, as with the embodiment of Figs. 7 and 8.

[0025] Conveniently, distal end 88 of sheath structure 82 comprises an outer layer 91 secured to an inner layer 92 at their respective distal ends. Both layers 91 and 92 will be composed of a flexible, non-distendable material, such as polyethylene terephthalate (PET), or other reinforced material, such as an elastomeric or non-elastomeric material reinforced with a non-distendable mesh. The outer layer will be shorter than the inner layer so that when the annular lumen 84 is inflated, the distal end will flare as shown in Fig. 10.

[0026] Alternative mechanisms for providing a deployable flare at the distal end of a prosthesis-containment sheath are illustrated in Figs. 11 and 12. The sheath 100 in Fig. 11 has a distal end 102 including a plurality of axially aligned, circumferentially spaced-apart heat memory alloy members 104. The heat memory alloys are selected to have a temperature transition where they assume a straight, non-flared configuration at low temperatures, as illustrated in full line in Fig. 11. At body temperature, however, the members 104 assume an outwardly flared configuration, as illustrated in broken line. Suitable alloy materials include nickel-titanium alloys which may be heat treated to provide the proper shapes and transition temperature.

[0027] Sheath 110 illustrated in Fig. 12 has a resilient, flared structure formed at its distal end 112. The flared distal end 112 is contained in an end cap 114 which may be distally advanced (as illustrated in broken line) by shaft 116 to release the flared end structure, as shown in broken line.

[0028] An alternative structure for facilitating the release and recapture of a prosthesis from a delivery catheter is illustrated in Figs. 13-15. A catheter 118 is provided with a sheath 120, shaft 122, and penetrating stays 124, generally as described above in connection with Figs. 2-5.

[0029] The catheter 118 further includes an eversible membrane 126 which is attached at a first end 128 to the shaft 122, and at a second end 130 to the inner surface of the lumen of sheath 120. The membrane 126 will be formed from a flexible, preferably lubricous and non-compliant material, such as PET, nylon, polytetrafluoroethylene (PTFE), any of which may be wire- or braid-reinforced, or the like. The prosthesis P will remain anchored on the shaft 122 by penetrating stays 124 as the sheath 120 is partially withdrawn (Fig. 14). The membrane 126 folds back over itself (everts) as the sheath 120 is retracted so that there are always two layers of the membrane between the distal end of the sheath and the prosthesis P. The double-layer structure of the membrane provides a high degree of lubricity during the release and optional recapture of the prosthesis P. Complete release of the prosthesis P is illustrated in Fig. 15.

[0030] Referring now to Fig. 16, an alternative prosthesis anchoring mechanism for a delivery catheter 150 is illustrated. The delivery catheter 150 includes a shaft 152 having a pair of axially spaced-apart stays 154 and 156. A pull wire 158 extends through a lumen 160 of shaft 152 and through protrusions on each of the stays 154 and 156. A guide wire GW is received through the shaft 152 in order to permit vascular introduction by conventional techniques. The radially compressible prosthesis P (such as graft 10) is placed over the distal end of the shaft extension 162, generally being aligned between the stays 154 and 156. The pull wire 158 is then advanced through the stays 154 and 156 so that it passes through each end of the prosthesis P to maintain the prosthesis P in place until the pull wire is withdrawn. While the pull wire 158 remains in place, a prosthesis-

containment sheath 164 may be axially advanced over the graft to radially compress the graft into its desired low profile diameter. The sheath 164 includes a flared (i.e., outwardly tapered) distal end 166 to facilitate advancing the sheath over the prosthesis P, in particular so that the prosthesis P may be recaptured when it is partially deployed. The outward flare may be permanently fixed in the body of the sheath, but will preferably be selectively deployable between the flared and non-flared configuration, using any of the mechanisms described above.

[0031] Referring now to Fig. 17 and 18, a prosthesis cartridge 200 comprises a sheath extension 202 having a distal end 204 and a proximal end 206. A prosthesis P is contained within the sheath extension 202 and is mounted over a shaft extension 208. Typically, the prosthesis P will be anchored on the shaft extension 208 using penetrating stays (not shown) as described in connection with previous embodiments. The prosthesis cartridge 200 is releasably connectable to a delivery catheter 221 including a sheath 220 (or other elongate member) and shaft 222. The proximal end of the cartridge sheath 202 is configured to couple to the distal end of the catheter sheath 220. Similarly, the proximal end of the shaft extension 208 is configured to selectively couple to the distal end of the shaft 222. In this way, a user can select the diameter, length, and other characteristics of the prosthesis P which are desired to be employed in a procedure. The prosthesis, which is part of cartridge 200 (and preferably packaged in a separate, sterile pouch or other container) may then be attached to the distal end of the delivery catheter (which is separately packaged in a sterile pouch or other container) having the necessary sheath and shaft connections. The catheter sheath 220 could alternatively comprise other, non-tubular structures (elongate members). It is necessary only that the elongate member be able to connect to the sheath extension 202 to be proximally retracted over the prothesis P (and optionally distally advanced) to effect release and recapture of the prosthesis as described above.

[0032] Referring now to Figs. 19A-19D, yet another embodiment of a delivery catheter 250 will be described. Delivery catheter 250 includes flexible shaft 252 having a central lumen for receiving a guide wire GW. A sheath 254 is slidably mounted over the shaft 252, generally as described for previous embodiments. The catheter 250 differs from previous embodiments, however, in the nature of the retaining structure which is used for holding prosthesis P in place on the flexible shaft 252. The retaining structure comprises a distal anchor 256, which is conveniently in the form of a cap or other receptacle which can receive a distal end of the prosthesis therein. A proximal anchor 258 is mounted at the distal end of a sliding tube 260. As shown in Fig. 19A, when the catheter 250 is introduced to blood vessel BV the prosthesis P will be maintained in its collapsed configuration by the anchors 256 and 258, and sheath 254 will cover the prosthesis and anchor structures.

[0033] After introduction, as illustrated in Fig. 19B, the sheath 254 may be withdrawn proximally to expose the prosthesis P. The prosthesis P, however, remains radially compressed by the anchors 256 and 258, even after the sheath 254 has been fully withdrawn, as illustrated in Fig. 19C. The prosthesis P may be fully released by moving the anchors 256 and 218 axially apart in order to free the compressed ends of the prosthesis, as illustrated in Fig. 19D. Prior to release, however, the exposed prostheses can be carefully positioned without interference from the sheath 254. It is a particular advantage that such partial release is achieved while still being able to readily recapture the prosthesis by readvancing the sheath 254.

[0034] Referring now to Figs. 20A and 20B, an embodiment of a delivery catheter constructed in accordance with the principles of the present invention is illustrated. The retaining structure 280 will fully cover and compress the prostheses P, and will usually be maintained within an outer sheath (not shown) equivalent to the delivery catheter sheaths illustrated previously. The retaining structure 280 will maintain radial compression of the prosthesis P within the sheath, regardless of whether the sheath covers the prosthesis. Thus, the sheath of the associated delivery catheter may be proximally retracted prior to release of the prostheses P.

[0035] The retaining structure 280 comprises a helically wound ribbon, which may optionally be formed as a helically scored or perforated cylinder. The retaining structure 280 is mounted on flexible shaft 284, typically with a distal portion of the helical ribbon attached directly or indirectly to the shaft. A pull cord 286 is attached to a proximal end of the helical ribbon, and the ribbon may be withdrawn from over the prostheses P by pulling proximally on the pull cord, as illustrated in Fig. 20b.

[0036] Yet another embodiment of the retaining structure is illustrated in Figs. 21A and 21B. Retaining structure 300 comprises a cylinder 302 having a helical wire 304 disposed over its surface. The wire 304, when pulled from the cylinder 302, separates adjacent sections of the cylinder so that they break apart, as illustrated in Fig. 21B. Thus, by attaching a first pull cord 306 to a proximal end of the wire 304, the wire can be withdrawn by pulling proximally. The resulting ribbon-like section of the cylinder may then be withdrawn by pulling on a second pull cord 308, also as shown in Fig. 21B. The prostheses P is thus released from the catheter.

[0037] Yet another embodiment of a retaining structure is illustrated in Figs. 22A and 22B structure 320 is a cylinder 322 having a single axial break line 324 formed along one side thereof. It will be appreciated that more than one axial break line may be provided. Only one is illustrated, however, for convenience. A slide structure 326 secured to the cylinder 322 at a distal end of the break line 324. A pull cord 328 is attached to the slide structure 326. Optionally, multiple pull cords could be used. The slide structure 326 may be drawn proxi-

mally in order to open the breakline 324 in the manner of a zipper, as illustrated in Fig. 22B. In this way, the prostheses P can be released.

[0038] Yet another embodiment of the retaining structure 340 is illustrated in Figs. 23A and 23B. The retaining structure 340 comprises a plurality of individual resilient axial members 342 which are captured at their distal ends and an anchor 344. The axial elements 342 are permanently mounted in a ring structure 346 at the distal end of catheter body 348. The anchor 344 is secured at the distal end of a flexible shaft 350. The axial elements 342 are spring-loaded so that when the anchor 344 is moved distally by advancing the shaft 350, as illustrated in Fig. 23b, the individual elements will spring radially apart at the distal end. In this way, prosthesis P can be released from the retaining structure 340.

[0039] Referring now to Figs. 24A-24C, another embodiment of a retaining structure not falling under the scope of the claims will be described. The retaining structure 360 is a thin-walled tube 362 which is weakened along a circumferential (or helical) line 364, typically in the form of a score, perforation, or the like. Flexible shaft 366 secured to a distal end cap 368. By axially advancing the shaft 366, the end cap 368 and the attached portion of cylinder 362 between the score line 364 and the end cap will be pulled away from the remainder of the cylinder 362. In this way, the prostheses P can be released. The prostheses is first partially released, as shown in Fig. 24B. After the cylinder segments are fully spaced-apart, the prostheses is fully released, as shown in Fig. 24C.

[0040] Referring now to Fig. 25, a delivery catheter 430 constructed in accordance with the principles of the present invention comprises a tubular cover 432 and a shaft or inner catheter body 434. Cover 432 has a central lumen 36 extending from a proximal end 438 to a distal end 440. Shaft 434 is slidably received within central lumen 436 and extends proximally of the proximal end of cover 432.

[0041] A plurality of runners 442 extend distally from the distal end of shaft 434. Runners 442 line a portion of the inner surface of lumen 436, and slide within the lumen with the shaft. Shaft 434 also has a lumen, in which a core shaft 444 is slidably disposed. Core shaft 444 has a guidewire lumen 446. Guidewire lumen 446 optionally receives an intravascular ultrasound (IVUS) imaging transducer to provide imaging prior to, during, and after deployment of the prosthesis. Nosecone 448 is fixed to the distal end of core shaft 444, and can therefore move independently of runners 442.

[0042] Graft 10 is radially compressed and restrained within the plurality of runners 442. In turn, cover 432 prevents runners 442 from expanding outward. Runners 442 are formed from a hard material, and distribute the expansion load of prosthesis 10 over the inner surface of central lumen 436. Advantageously, the prosthesis does not invaginate in the lumen surface, and is thus able to slide relative to the cover in response to a moderate distal force. In the embodiment of Fig. 25, the deploying force is applied proximally against a slider 450 attached to distal end 438 of cover 430, while holding a lure fitting 452 at the distal end of shaft 434. An additional lure adaptor 454 at the distal end of core shaft 444 allows the core shaft to be releasably secured to the shaft 434.

[0043] Referring now to Figs. 26A and 26B, loading of graft 10 into the distal end 440 of cover 432 is facilitated by use of runners 442. As seen in Fig. 26A, extending shaft 434 distally allows runners 442 to flex outward. Graft 10 may be inserted between the outward flexed runners and compressed by withdrawing runners 442 and shaft 434 into the distal end 440 of cover 432. Nosecone 448 and core shaft 444 are shown attached to shaft 434 during loading. Alternatively, nosecone 448 may be attached to core shaft 444 after the loading of prosthesis 10. Prosthesis 10 is preferably formed of a heat memory alloy such as Nitinol™. To maintain graft 10 in a compressed state, the loading process may be done in a cold environment, such as that provided by a cold spray, liquid nitrogen, freon, an air vortex, or the like.

[0044] Referring now to Figs. 27A through 28, placement of graft 10 within a body lumen 460 begins by positioning catheter 430 at a target location. As illustrated in Fig. 27B, graft 10 is allowed to expand by retracting cover 432, proximally relative to shaft 434 and core shaft 444. As cover 432 is retracted, runners 442 maintain their axial position, sliding over the inner surface of cover 432. Once the graft 10 has fully expanded within body lumen 60, it is axially anchored by expansion against the lumen wall between the runners. Runners 442 may then be retracted proximally with shaft 434 and nosecone 448. The hard surface of runner 442 allows shaft 434 to be retracted smoothly, with little possibility of dragging graft 10 from the target position. The graft cover may also help to reduce friction during deployment. The possibility of dragging the prosthesis is further reduced by retracting nosecone 448 having a tapered proximal end 464 independently from shaft 434, as illustrated in Fig. 28. Finally, it will be recognized that the runners may also be used to help recapture a partially-deployed prosthesis.

[0045] Referring now to Fig. 29A, the elements of the present graft delivery catheter will be described. Cover 432 must be strong enough to withstand the expansion force of graft 10 but must also be flexible to allow intravascular atraumatic maneuvering. Cover 432 is optionally formed of a high strength thermoplastic elastomer such as Hytrel™. Alternatively, cover 432 may be formed of a braided reinforced polymer tubing or a linear reinforced tubing, preferably having fibers of a polyamide such as Kevlar™, Spectra™, or the like, embedded to improve tensile strength without reducing flexibility. Preferably, the cover includes a radiopaque contrast medium, e.g., a B_4SO_4 compound, to allow imaging of the placement of catheter 30 within a body lumen using

fluoroscopy. Shaft 434 is preferably formed from PEEK, nylon, or the like, to provide column strength. Runners 442 are formed from a high strength biocompatible alloy such as Nitinol™, stainless steel, or a stainless steel alloy. Runners 442 are bonded to shaft 434, preferably being laminated between inner and outer layers of nylon, a thermoplastic elastomer such as Pebax™, or the like. Core shaft 444 is also preferably formed of PEEK. Nosecone 448 may be formed of stainless steel and bonded to the distal end of core shaft 444, or may alternatively be molded of a radiopaque plastic comprising Pebax™, nylon, Hytrel™, or the like. In any case, nosecone 448 preferably includes a radiopaque element, thereby giving an indication of the location of the distal end of graft 10 during fluoroscopically guided prostheses placement. In certain embodiments, core shaft 444 further supports marker ring 466, comprising platinum, barium, or the like, to provide a sharp radiographic contrast. Optionally, distal force imparting structure 467 is bonded to the core shaft to slide the compressed prosthesis distally over the runners.

[0046] Referring now to Fig. 29B, a helical shaft 435 provides high column strength with flexibility. Helical shaft 435 is formed from a tightly wound, high strength metal, preferably comprising stainless steel. Helical shaft 435 is easily welded to runners 442, where similar metals are used for both. Alternatively, runners 442 are laminated to helical shaft 435 with inner and/or outer layers of nylon, Pebax™, or the like. A composite cover 433 comprising polymer reinforced tubing having braided or linear Kevlar™, Spectra™, or the like, further enhances flexibility of the delivery catheter of the present invention.

[0047] The delivery catheters of the present invention significantly reduce the force required to deploy a prosthesis within a body lumen. Nonetheless, the force required to withdraw cover 432 remains substantial. For this reason, the present invention further provides a housing 470 to be attached to the distal end of shaft 434, as illustrated in Fig. 30. Rotation of handle 472 moves follower 474 along a linear screw. Slider 450 at the proximal end of cover 432 is driven axially by the movement of the follower. Cover 432 is withdrawn during deployment of the prosthesis by articulating handle 472 so as to drive slider 450 toward lure fitting 452 at the proximal end of shaft 434. The force required to withdraw the cover is typically on the order of 1 to 10 lbs., requiring only a modest mechanical advantage. However, a mechanical advantage ratio in the range from 5 to 50, as measured from the linear travel at the outside edge of handle 472 to the linear motion of follower 474, provides a highly controlled deployment. Clearly, a wide variety of mechanical linkages are available to provide such a mechanical advantage. It is particularly advantageous to provide a mechanism which allows manipulation with a single hand, as this leaves the alternate hand free to manipulate the cover relative to an introducer sheath. It will be noted that housing 470 allows independent manipulation of core shaft 444 using second lure fitting 454, as described above regarding Fig. 28.

[0048] Referring now to Fig. 31, an alternative cover 480 provides an atraumatic distal end 482 with a reduced nosecone diameter, or, alternatively, no nosecone at the distal end of core shaft 444. Atraumatic cover 480 includes a series of splits 484 to allow the distal tip of atraumatic cover 480 to open during deployment of prosthesis 10.

[0049] Referring now to Fig. 32, a further alternative cover 490, having runners 492 embedded within the central lumen, will also reduce the friction between the prosthesis and the cover during prosthesis placement. Furthermore, such a structure eliminates any danger of injury to the walls of a body lumen during placement by a distal movement of the exposed runners. Moreover, similar safety advantages could be obtained using the delivery catheter of Fig. 25 by retaining runners 442 within cover 432 during deployment of prosthesis 10. An alternative structure must be provided to apply a distal force against the prosthesis, such as distal force imparting structure 467 shown in Fig. 29A.

[0050] Referring now to Figs. 33A and 33B, alternative cross sections 494 and 496 for a delivery catheter tubular cover or shaft will provide additional column strength without a corresponding increase in stiffness. Slots 495 are also suitable for receiving the runners, thus forming the runner/shaft laminated bond. Indents 497 may receive the free distal portion of the runners to prevent rotation of the prosthesis relative to the cover during manipulation of the shaft. Alternatively, a smooth cover lumen facilitates such rotation by allowing the runners to slidingly rotate against the cover lumen surface.

[0051] Referring now to Fig. 34, a brace 590 optionally restrains the prosthesis at the target location while withdrawing cover 432. Brace 590 attaches to introducer sheath 580 with a locking collar 592. Bar 594 extends proximally from locking collar 592, and is slidably received by tabs 596 protruding from housing 470. Once the prosthesis is positioned at the target location, a set screw 598 is tightened to fix the distance between the proximal end of delivery catheter 430 and the introduction sheath 580. Rotating handle 472 thus withdraws cover 430 proximally through introduction sheath 580 without distally advancing shaft 434. This minimizes the danger of advancing the exposed runners into the lumen wall during deployment, and thus allows deployment by a single surgeon. The compressive load on bar 594 is reduced by friction reducer tube 570.

[0052] A wide variety of compression bearing structures could be used in place of bar 590. A telescoping tube with single or multiple overlapping sections having set screws would eliminate the protruding proximal end of the rod. Such a telescoping tube may optionally surround catheter 430 between the introducer sheath and housing. Alternatively, a flexible tube having good column stiffness disposed over the delivery catheter also prevents axial movement of the prosthesis, and avoids

the long, rigid, and potentially cumbersome bar structure. Such a flexible tube preferably comprises a tightly wound coil analogous to flexible shaft 435 shown in Fig. 29B. Although a fixed length tube may be used, telescoping flexible overlapped tubes, usually having a locking device such as set screws, compressive clamps, or the like, are preferred.

[0053] The brace of the present invention may advantageously be used with alternative proximal housings having a wide variety of mechanisms for translating the cover relative to the shaft, including electric motors, foot operated linkages, and the like.

[0054] Although the foregoing invention has been described in some detail by way of illustration and example, for purposes of clarity and understanding, certain changes and modifications will be obvious to those of skill in the art. For example, the present cover and/or runners may be attached to the elongate shaft as a cartridge, preferably preloaded with a prosthesis. Thus, the scope of the present invention is limited only by the appended claims.

Claims

1. A delivery catheter for positioning radially compressible prostheses (P), comprising an elongate flexible shaft (350, 444) having a proximal end and a distal end, a retaining structure (280, 300, 320, 340) near the distal end of the shaft (350, 444) which releasably holds the axial position of the prosthesis (P) on the shaft (350, 444), and a sheath (254, 434) slidably received over the shaft (350, 444) to cover the prosthesis (P) while the prosthesis (P) is held on the shaft (350, 444) by the retaining structure (280, 300, 320, 340) which comprises means (282, 302, 322, 342, 442) for circumferentially supporting the prosthesis (P) within the sheath (254, 434), **characterized** in that the retaining structure (280, 300, 320, 340) is adapted to extend from a proximal end of the prosthesis (P) to the distal end of the prosthesis (P) so that said means (282, 302, 322, 342, 442) for circumferentially supporting the prosthesis (P) supports the prosthesis (P) over its full length.

2. The catheter of claim 1, characterized in that the supporting means comprises a plurality of axial elements (342, 442) attached to the shaft (350).

3. The catheter of claim 2, characterized in that the elements (342, 442) are flexible radially outwardly to release the prosthesis (P).

4. The catheter of claim 3, characterized in that the elements (442) are runners having proximal ends being affixed together.

5. The catheter of claim 4, characterized in that the proximal ends of the runners (442) are affixed to the sheath (434).

6. The catheter of claim 5, characterized in that the supporting means comprises a cover (432) releasably disposed over the elements (442).

7. The catheter of claim 1, characterized in that the supporting means comprises a cover (282, 302, 322) releasably disposed over the prosthesis (P).

8. The catheter of anyone of the claims 1 to 7, characterized in that the retaining structure (280, 300, 320, 340) extends between the prothesis (P) and the surrounding sheath (254, 434).

9. The catheter of anyone of the claims 1 to 8, characterized in that the sheath (254, 434) comprises a flexible polymer material and the retaining structure (280, 300, 320, 340) a material which is harder than that of the sheath (254, 434).

10. The catheter of anyone of the claims 1 to 9, characterized in that a deployable outwardly flarable distal end and means for reconfiguring the distal end of the sheath (254, 434) between a non-flared and a flared configuration are provided.

11. The catheter of anyone of the claims 1 to 10, characterized in that a shaft extension (208) coupling at the distal end of the shaft (222) and a sheath extension (202) coupling at the distal end of the sheath (220) are provided, the prosthesis (P) being radially compressed over the shaft extension (208) and within the sheath extension (202).

Patentansprüche

1. Einführkatheter zum Positionieren radial komprimierbarer Prothesen (P), mit einem langen, flexiblen Schaft (350, 444), der ein proximales Ende und ein distales Ende besitzt, einer Haltestruktur (280, 300, 320, 340) in der Nähe des distalen Endes des Schafts (350, 444), die die axiale Position der Prothese (P) am Schaft (350, 444) lösbar hält, und einer Hülse (254, 434), die über dem Schaft (350, 444) gleitend aufgenommen ist, um die Prothese (P) zu bedecken, während die Prothese (P) auf dem Schaft (350, 444) durch die Haltestruktur (280, 300, 320, 340) gehalten wird, die eine Einrichtung (282, 302, 322, 342, 442) umfaßt, um die Prothese (P) in der Hülse (254, 434) in Umfangsrichtugn zu unterstützen, **dadurch gekennzeichnet**, daß die Haltestruktur (280, 300, 320, 340) so beschaffen ist, daß sie sich von einem proximalen Ende der Prothese (P) zum distalen Ende der Prothese (P) erstreckt,

so daß die Einrichtung (282, 302, 322, 342, 442) zum Stützen der Prothese (P) in Umfangsrichtung die Prothese (P) auf ihrer gesamten Länge stützt.

2. Katheter nach Anspruch 1, dadurch gekennzeichnet, daß die Stützeinrichtung mehrere axiale Elemente (342, 442) umfaßt, die am Schaft (350) befestigt sind.

3. Katheter nach Anspruch 2, dadurch gekennzeichnet, daß die Elemente (342, 442) radial auswärts flexibel sind, um die Prothese (P) freizugeben.

4. Katheter nach Anspruch 3, dadurch gekennzeichnet, daß die Elemente (442) Kufen sind, deren proximale Enden aneinander befestigt sind.

5. Katheter nach Anspruch 4, dadurch gekennzeichnet, daß die proximalen Enden der Kufen (442) an der Hülse (434) befestigt sind.

6. Katheter nach Anspruch 5, dadurch gekennzeichnet, daß die Stützeinrichtung eine Abdeckung (432) aufweist, die über den Elementen (442) lösbar angeordnet ist.

7. Katheter nach Anspruch 1, dadurch gekennzeichnet, daß die Stützeinrichtung eine Abdeckung (282, 302, 322) umfaßt, die über der Prothese (P) lösbar angeordnet ist.

8. Katheter nach einem der Ansprüche 1 bis 7, dadurch gekennzeichnet, daß sich die Haltestruktur (280, 300, 320, 340) zwischen der Prothese (P) und der umgebenden Hülse (254, 434) erstreckt.

9. Katheter nach einem der Ansprüche 1 bis 8, dadurch gekennzeichnet, daß die Hülse (254, 434) ein flexibles Polymermaterial umfaßt und die Haltestruktur (280, 300, 320, 340) ein Material, das härter als dasjenige der Hülse (254, 434) ist, umfaßt.

10. Katheter nach einem der Ansprüche 1 bis 9, dadurch gekennzeichnet, daß ein nach außen entfaltbares, bauschbares distales Ende und eine Einrichtung zum Umkonfigurieren des distalen Endes der Hülse (254, 434) zwischen einer nicht gebauschten und einer gebauschten Konfiguration vorgesehen sind.

11. Katheter nach einem der Ansprüche 1 bis 10, dadurch gekennzeichnet, daß eine Schaftverlängerung (208), die mit dem distalen Ende des Schafts (222) gekoppelt ist, und eine Hülsenverlängerung (202), die mit dem distalen Ende der Hülse (220) gekoppelt ist, vorgesehen sind, wobei die Prothese (P) über der Schaftverlängerung (208) und in der Hülsenverlängerung (202) radial komprimiert ist.

Revendications

1. Cathéter d'introduction destiné à positionner radialement des prothèses pouvant être compressées (P), comprenant une tige flexible allongée (350, 444) présentant une extrémité proximale et une extrémité distale, une structure de retenue (280, 300, 320, 340) à proximité de l'extrémité distale de la tige (350, 444) qui maintient de manière amovible la position axiale de la prothèse (P) sur la tige (350, 444), et une gaine (254, 434) reçue de manière à pouvoir coulisser sur la tige (350, 444) afin de recouvrir la prothèse (P) lorsque la prothèse (P) est maintenue sur la tige (350, 444) par la structure de retenue (280, 300, 320, 340) qui comprend des moyens (282, 302, 322, 342, 442) destinés à supporter circonférentiellement la prothèse (P) à l'intérieur de la gaine (254, 434), caractérisé en ce que la structure de retenue (280, 300 320, 340) est conçue de manière à s'étendre depuis une extrémité proximale de la prothèse (P) vers l'extrémité distale de la prothèse (P) de telle sorte que lesdits moyens (282, 302, 322, 342, 442) destinés à supporter circonférentiellement la prothèse (P) supportent la prothèse (P) sur la totalité de sa longueur.

2. Cathéter selon la revendication 1, caractérisé en ce que les moyens support comprennent une pluralité d'éléments axiaux (342, 442) fixés sur la tige (350).

3. Cathéter selon la revendication 2, caractérisé en ce que les éléments (342, 442) sont flexibles radialement vers l'extérieur afin de relâcher la prothèse (P).

4. 'Cathéter selon la revendication 3, caractérisé en ce que les éléments (442) sont des broches dont les extrémités proximales sont fixées ensemble.

5. Cathéter selon la revendication 4, caractérisé en ce que les extrémités proximales des broches (442) sont fixées sur la gaine (434).

6. Cathéter selon la revendication 5, caractérisé en ce que les moyens support comprennent un couvercle (432) disposé de manière amovible au-dessus des éléments (442).

7. Cathéter selon la revendication 1, caractérisé en ce que les moyens support comprennent un couvercle (282, 302, 322) disposé de manière amovible au-dessus de la prothèse (P).

8. Cathéter selon l'une quelconque des revendications 1 à 7, caractérisé en ce que la structure de retenue (280, 300, 320, 340) s'étend entre la prothèse (P) et la gaine enveloppe (254, 434).

9. Cathéter selon l'une quelconque des revendications 1 à 8, caractérisé en ce que la gaine (254, 434) est constituée en un matériau polymère souple et la structure de retenue (280, 300, 320, 340) en un matériau qui est plus dur que celui de la gaine (254, 434).

10. Cathéter selon l'une quelconque des revendications 1 à 9, caractérisé en ce qu'une extrémité distale déployable pouvant s'évaser vers l'extérieur et des moyens destinés à modifier la configuration de l'extrémité distale de la gaine (254, 434), entre une configuration non évasée et évasée, sont prévus.

11. Cathéter selon l'une quelconque des revendications 1 à 10, caractérisé en ce qu'une extension de tige (208) pouvant être couplée à l'extrémité distale de la tige (222) et une extension de gaine (202) pouvant être couplée à l'extrémité distale de la gaine (220) sont prévues, la prothèse (P) étant comprimée radialement au-dessus de l'extension de tige (208) et à l'intérieur de l'extension de gaine (202).

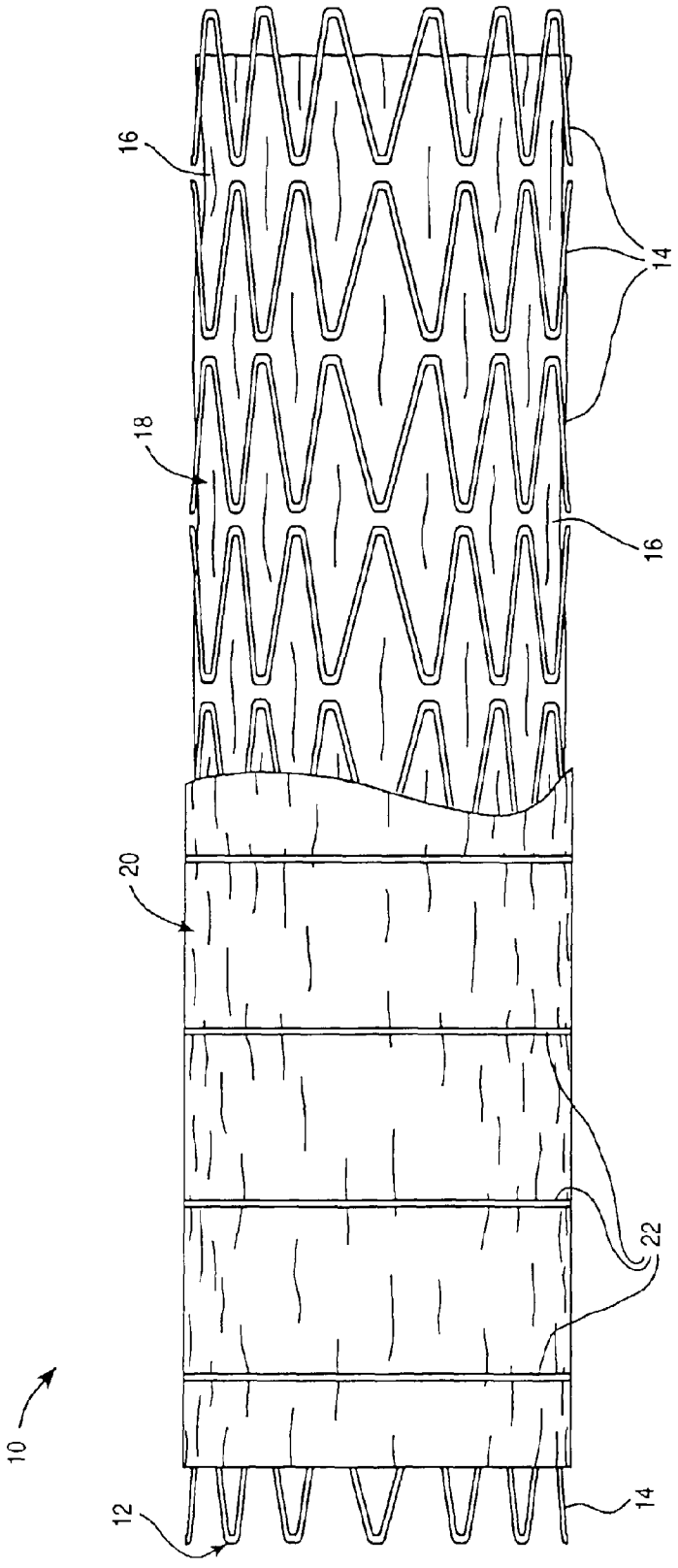

FIG. 1

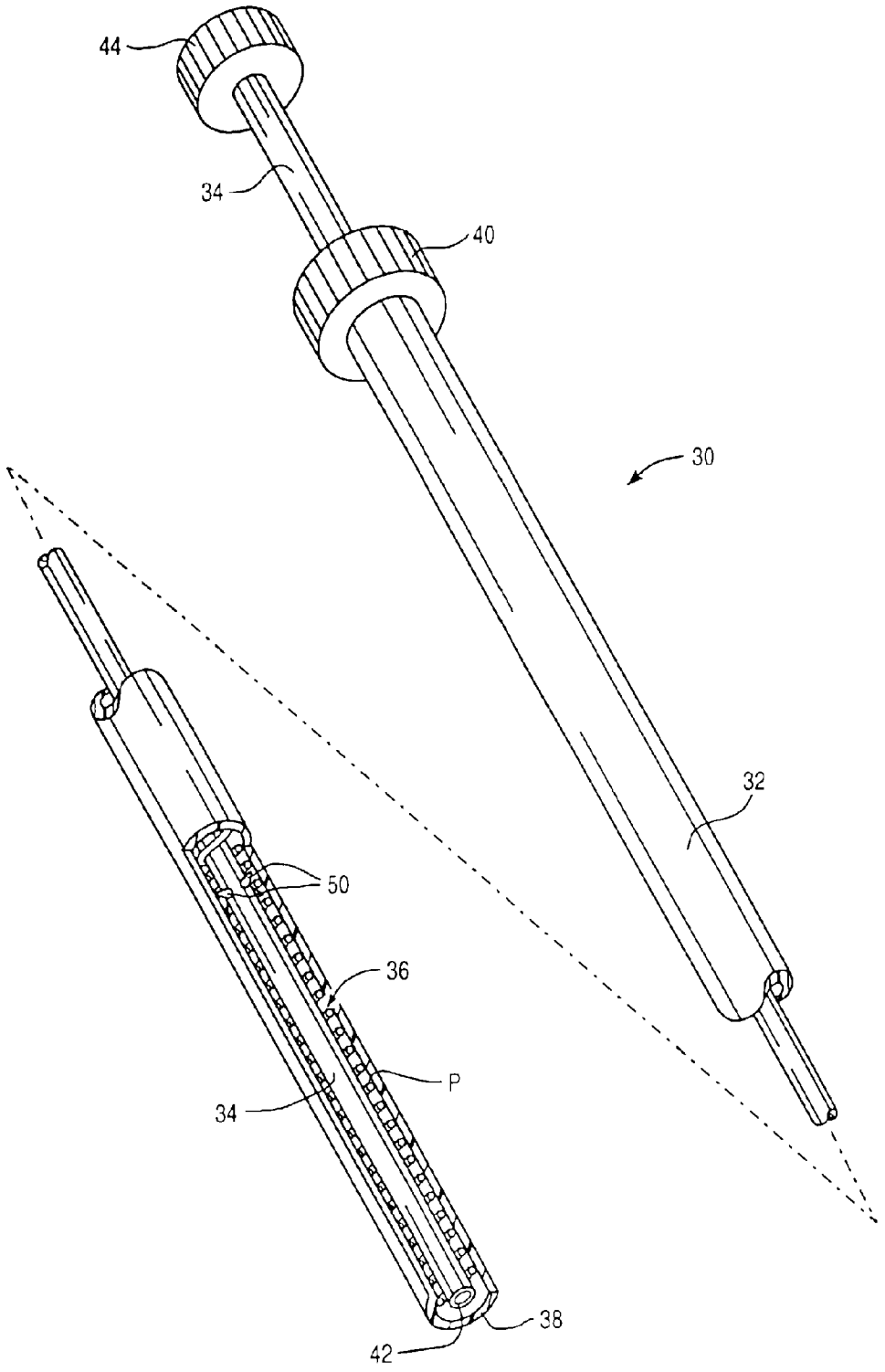

FIG. 2

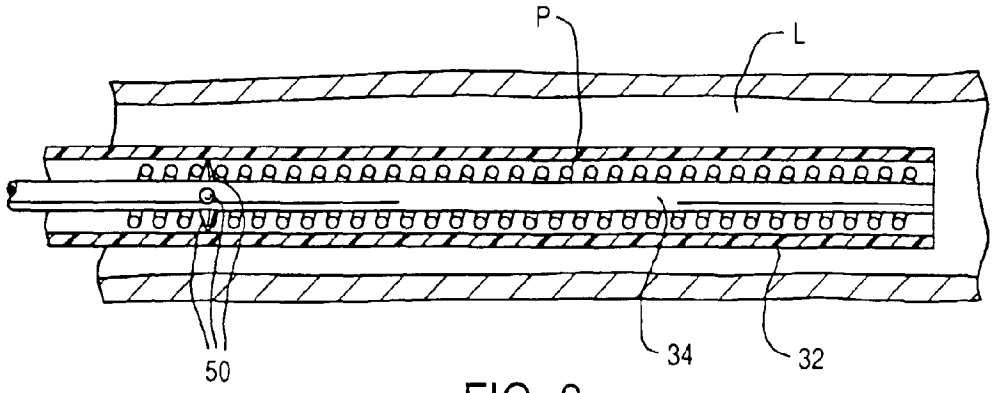

FIG. 3

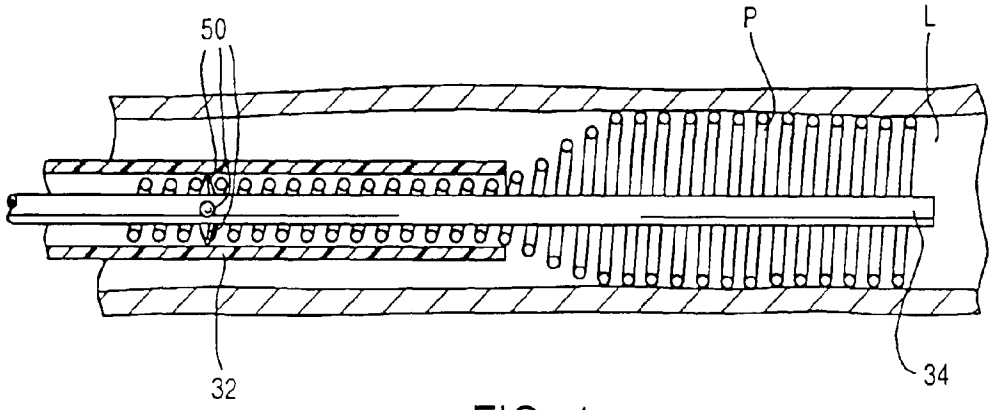

FIG. 4

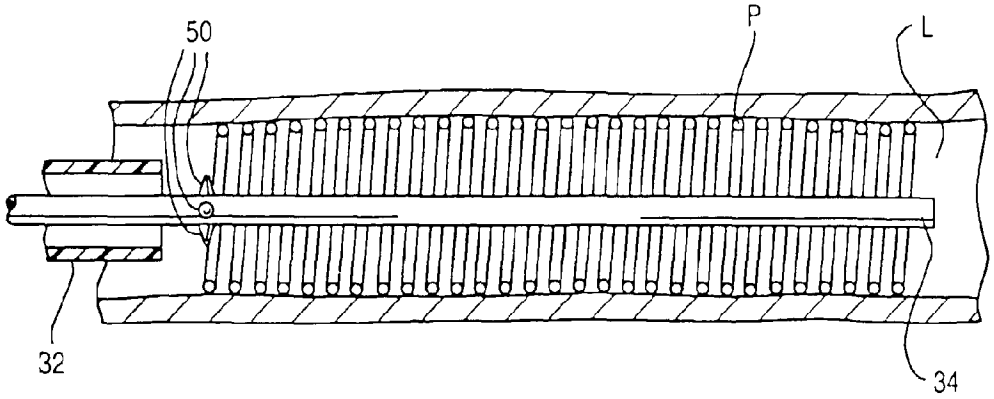

FIG. 5

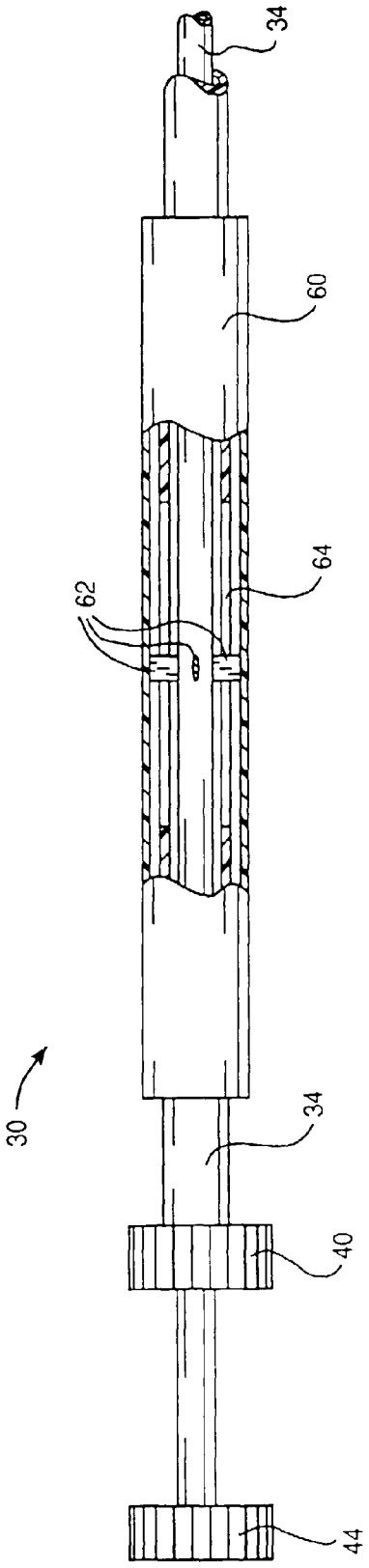

FIG. 6

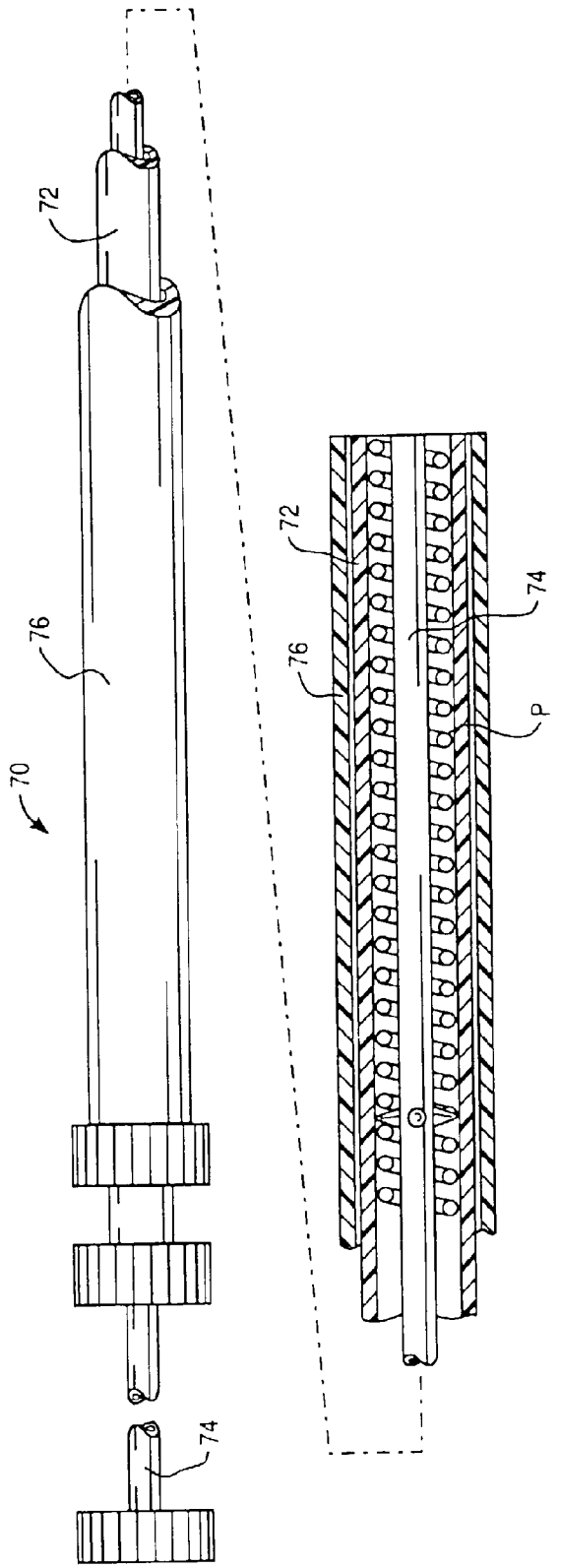

FIG. 7

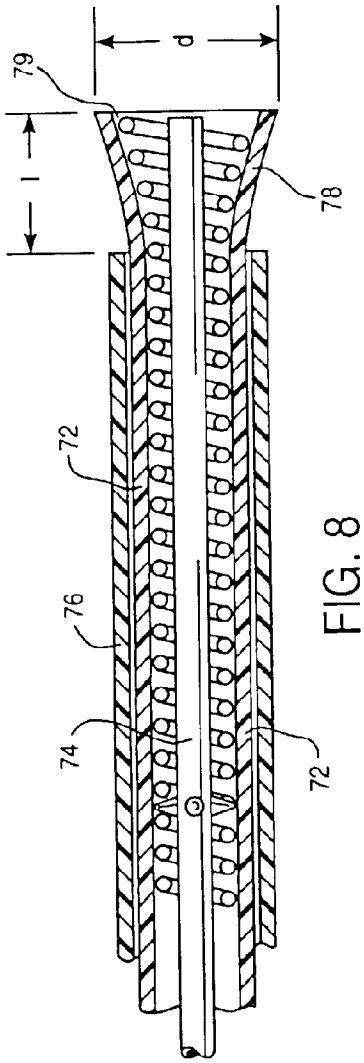

FIG. 8

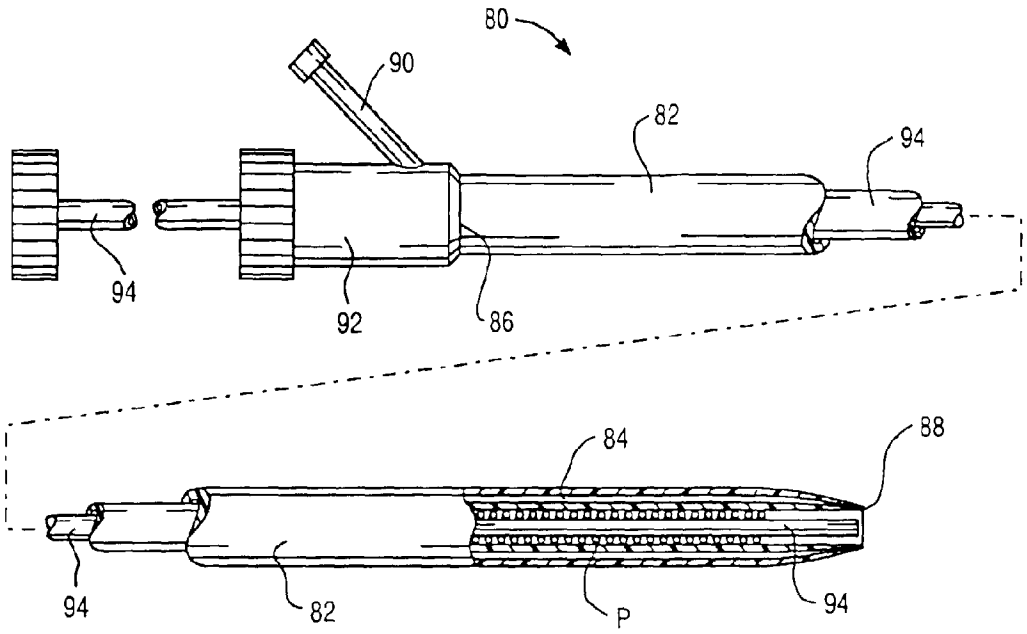

FIG. 9

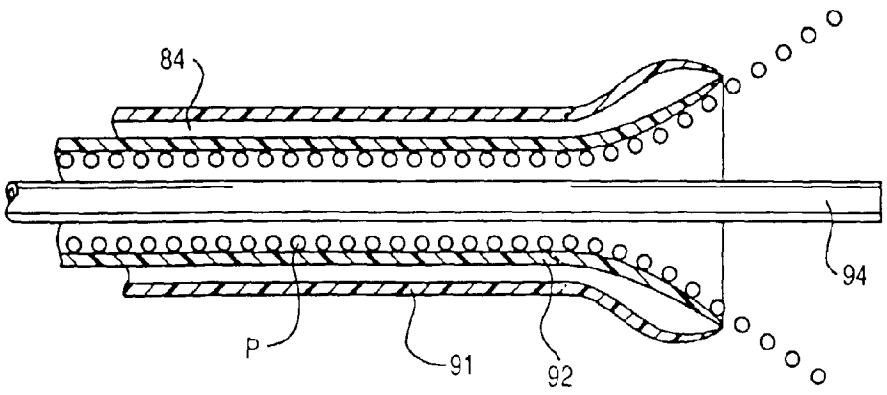

FIG. 10

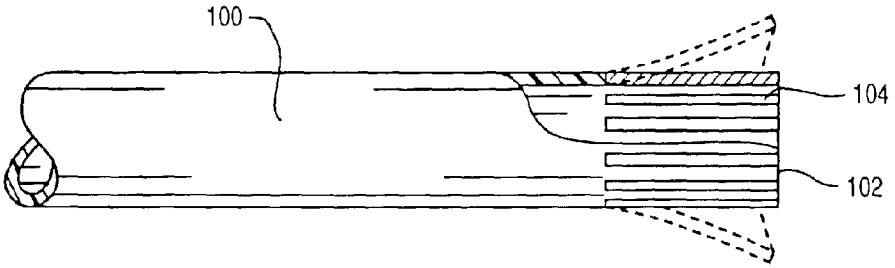

FIG. 11

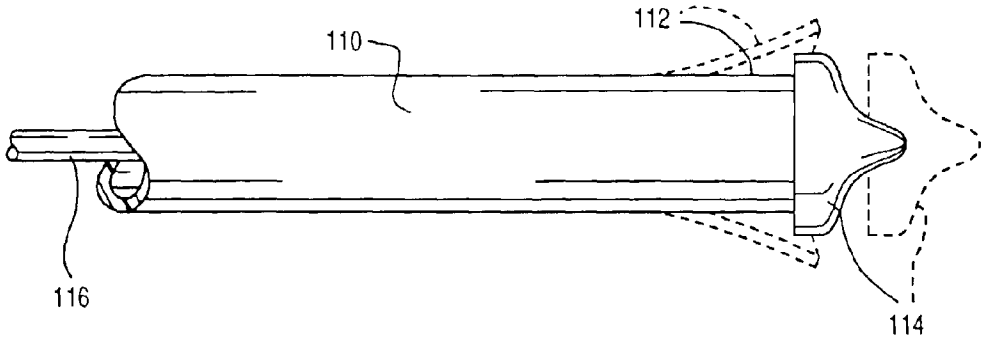

FIG. 12

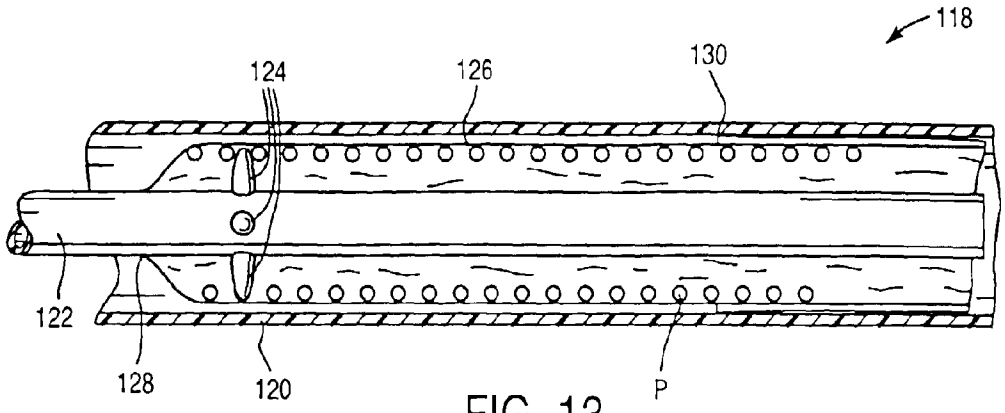

FIG. 13

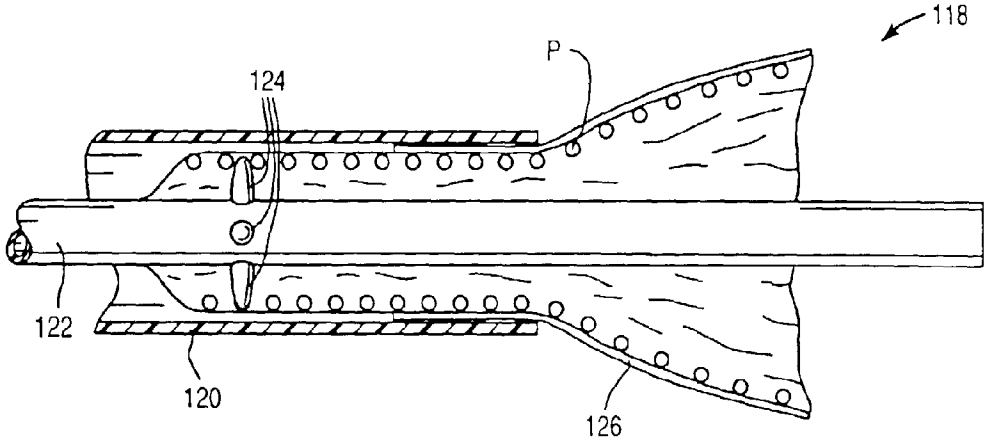

FIG. 14

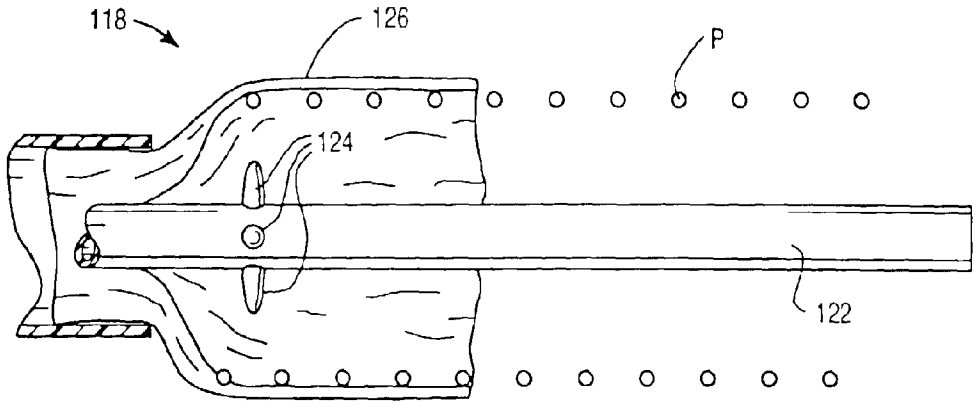

FIG. 15

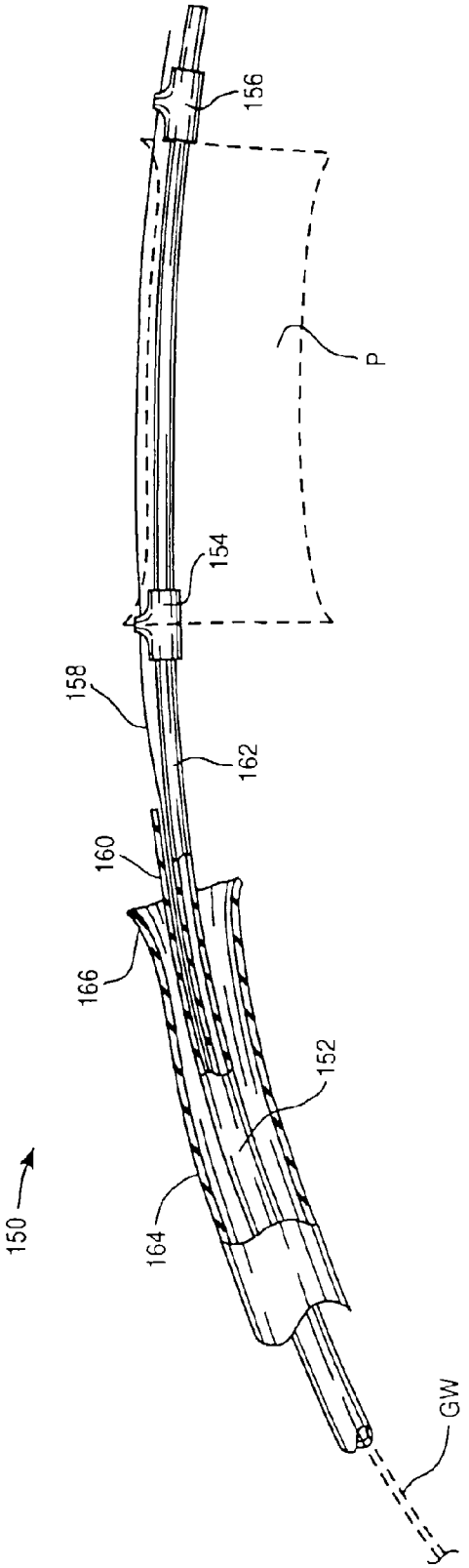

FIG. 16

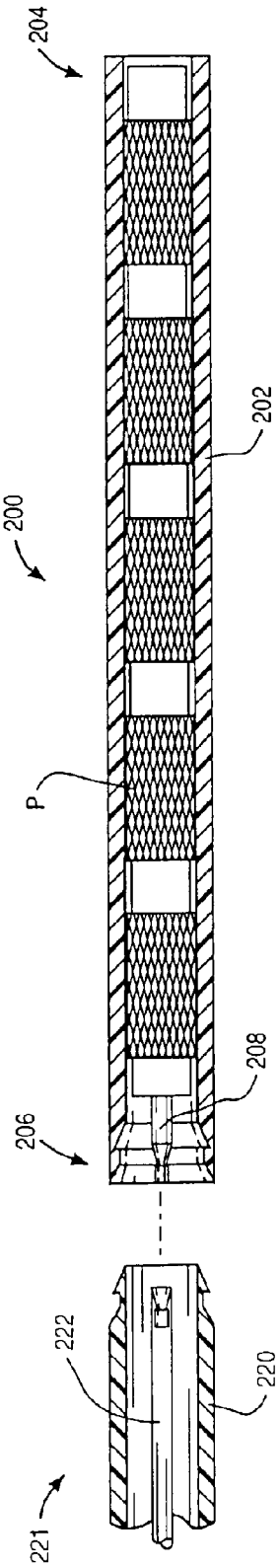

FIG. 17

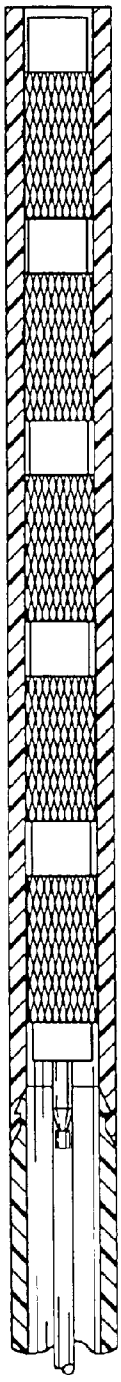

FIG. 18

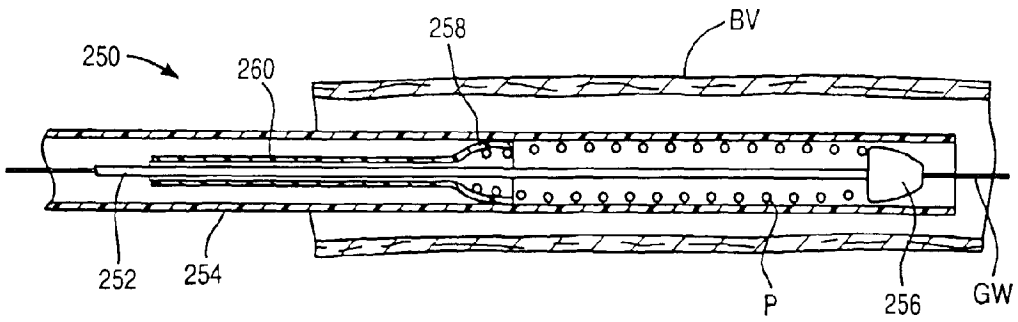

FIG. 19A

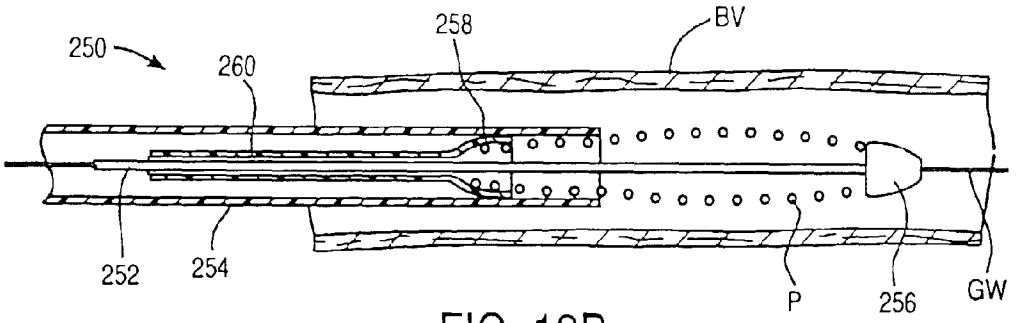

FIG. 19B

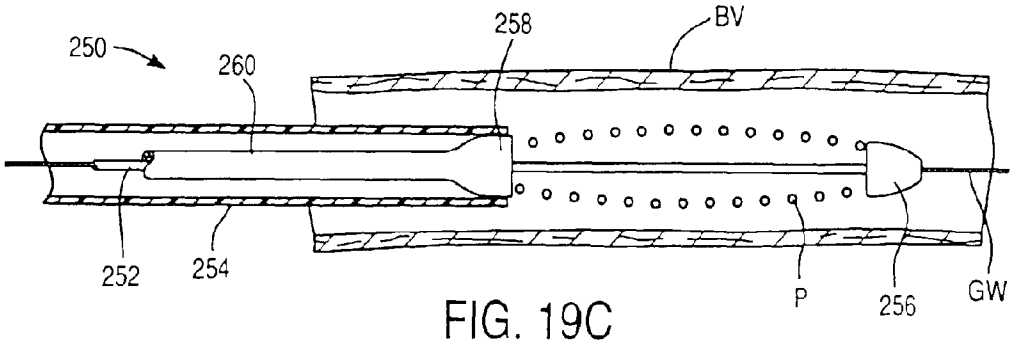

FIG. 19C

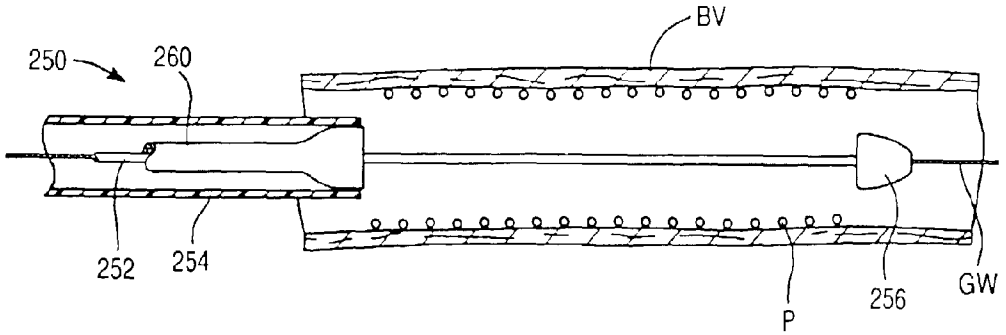

FIG. 19D

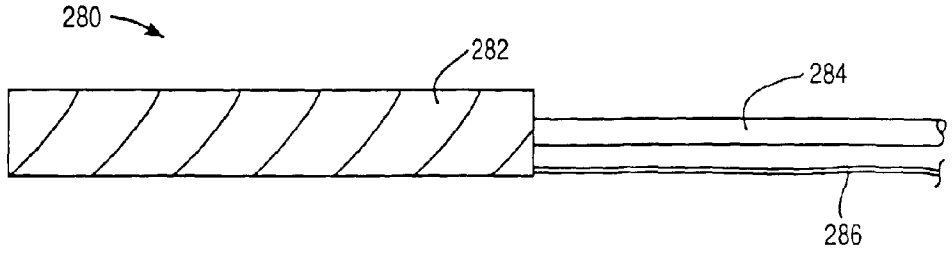

FIG. 20A

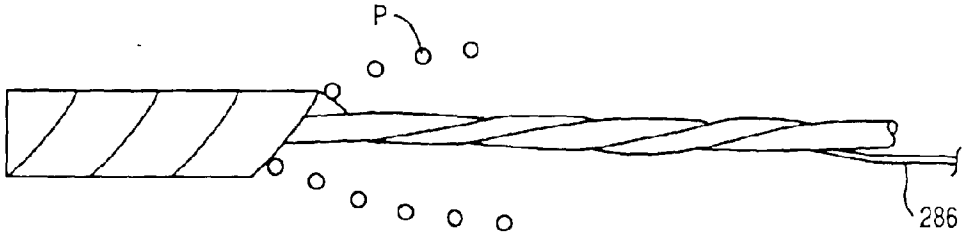

FIG. 20B

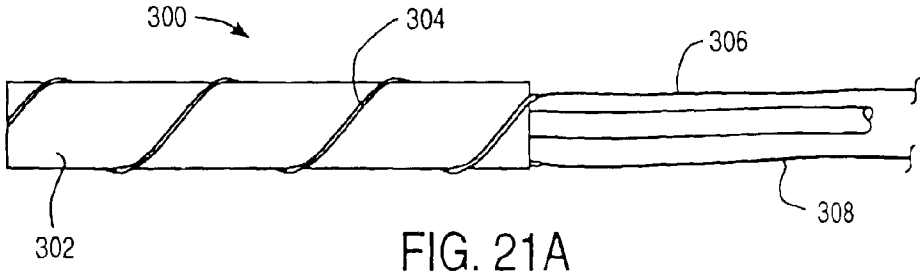

FIG. 21A

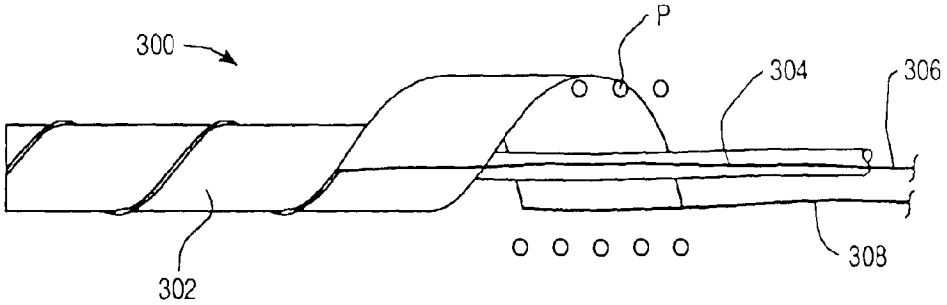

FIG. 21B

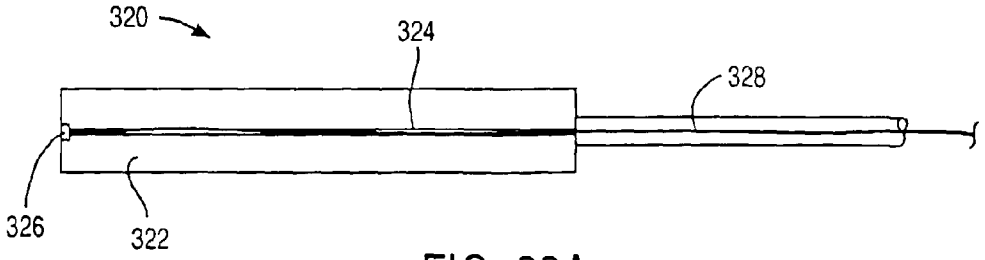

FIG. 22A

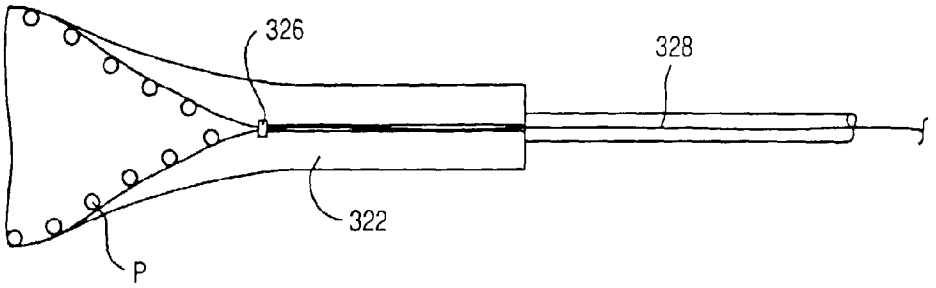

FIG. 22B

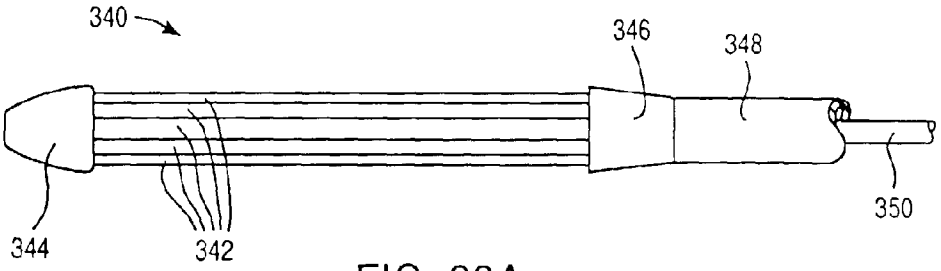

FIG. 23A

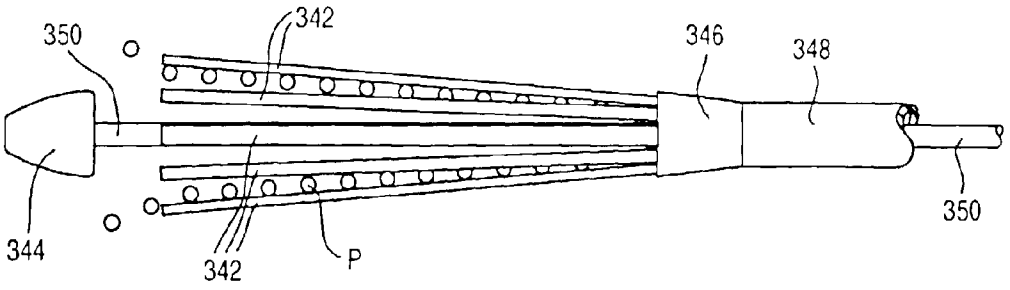

FIG. 23B

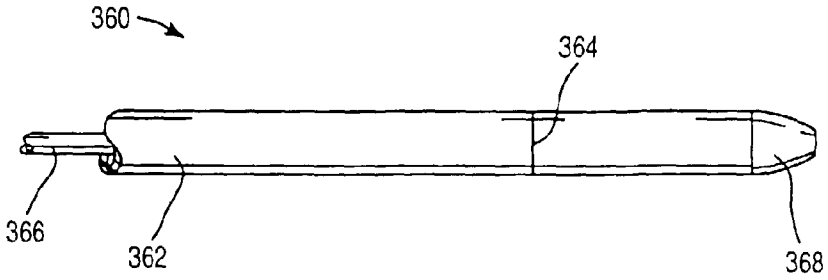

FIG. 24A

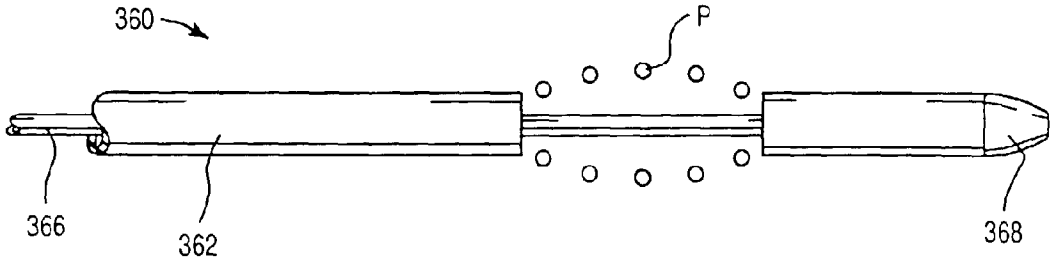

FIG. 24B

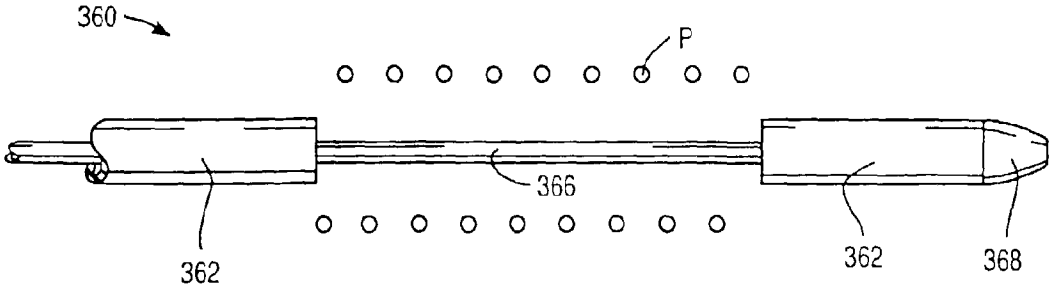

FIG. 24C

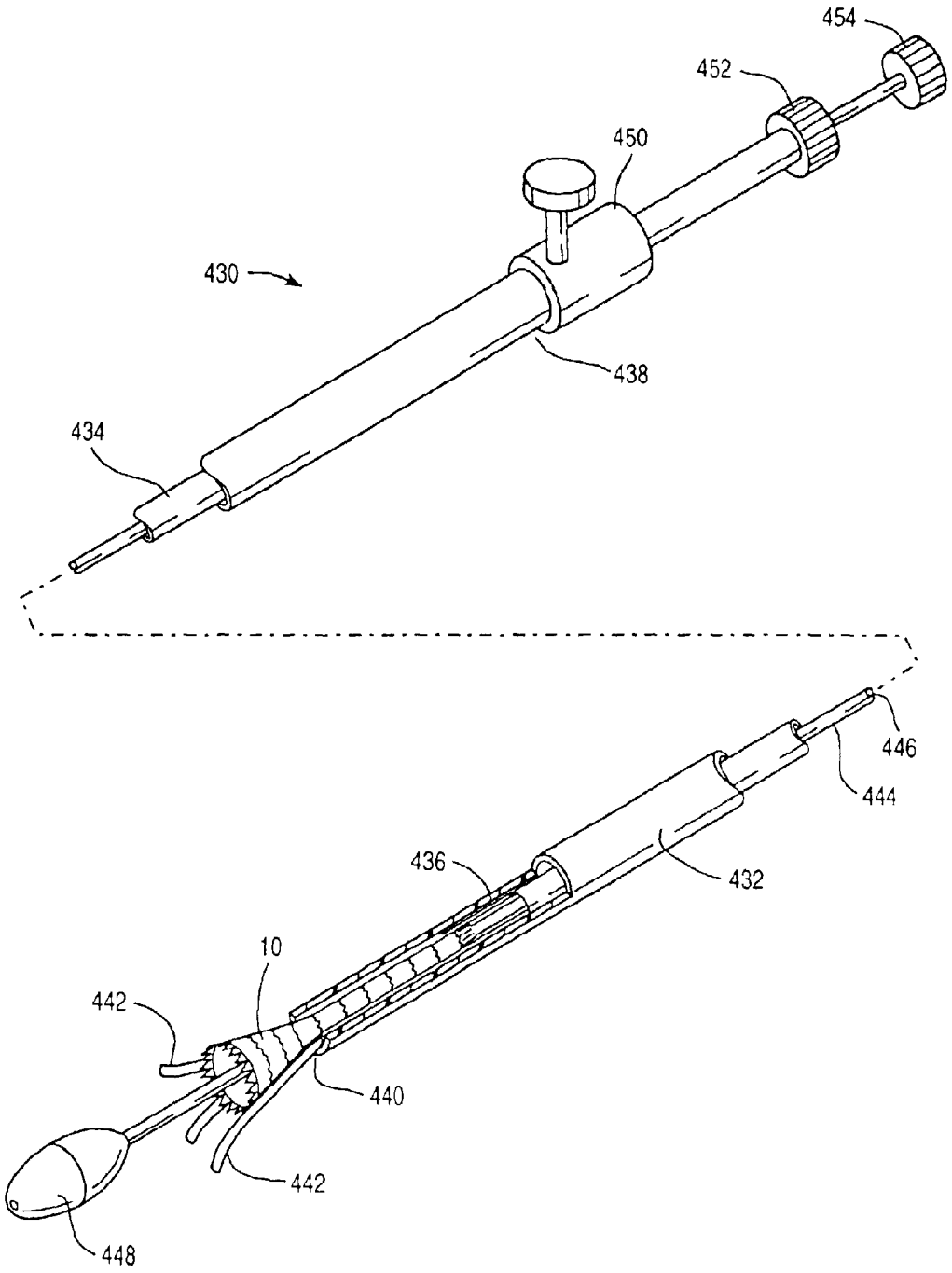

FIG. 25

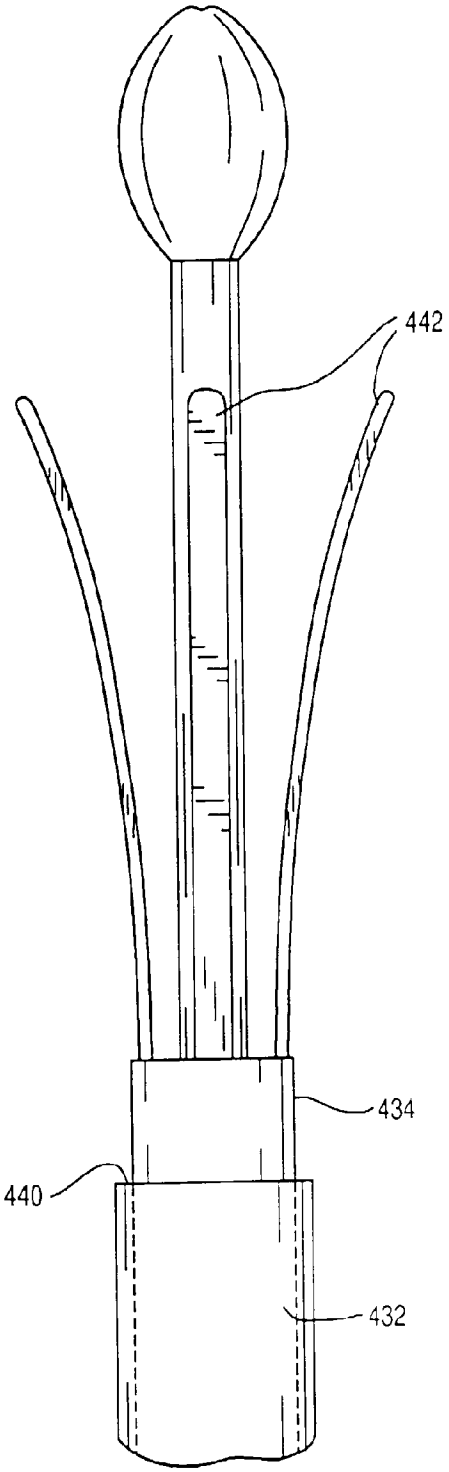

FIG. 26A

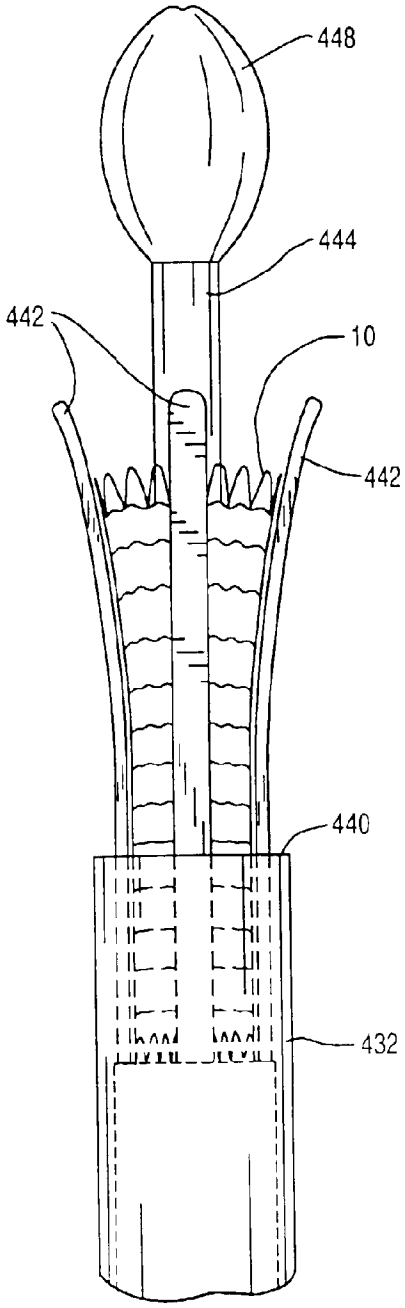

FIG. 26B

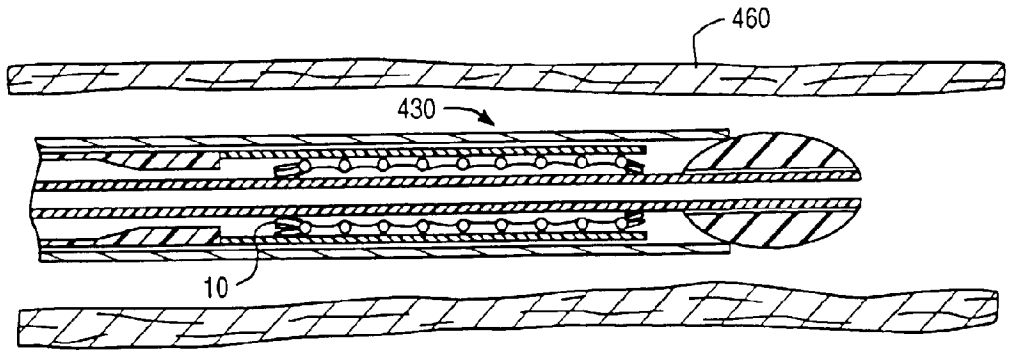

FIG. 27A

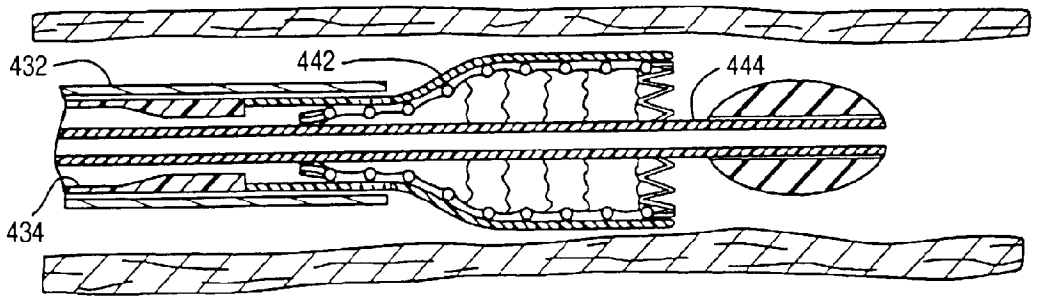

FIG. 27B

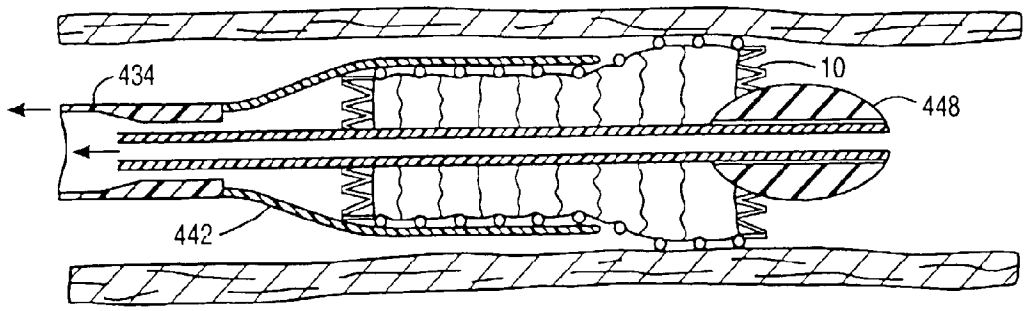

FIG. 27C

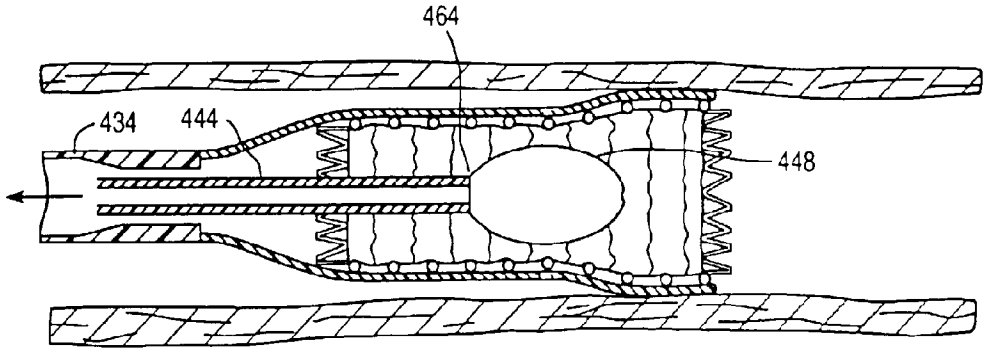

FIG. 28

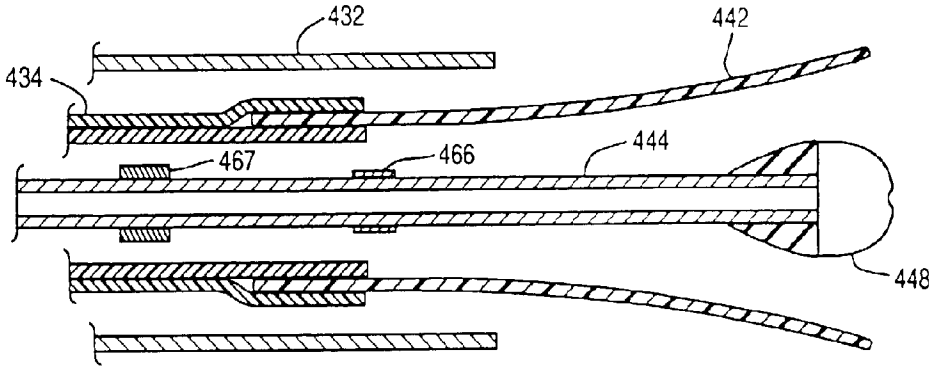

FIG. 29A

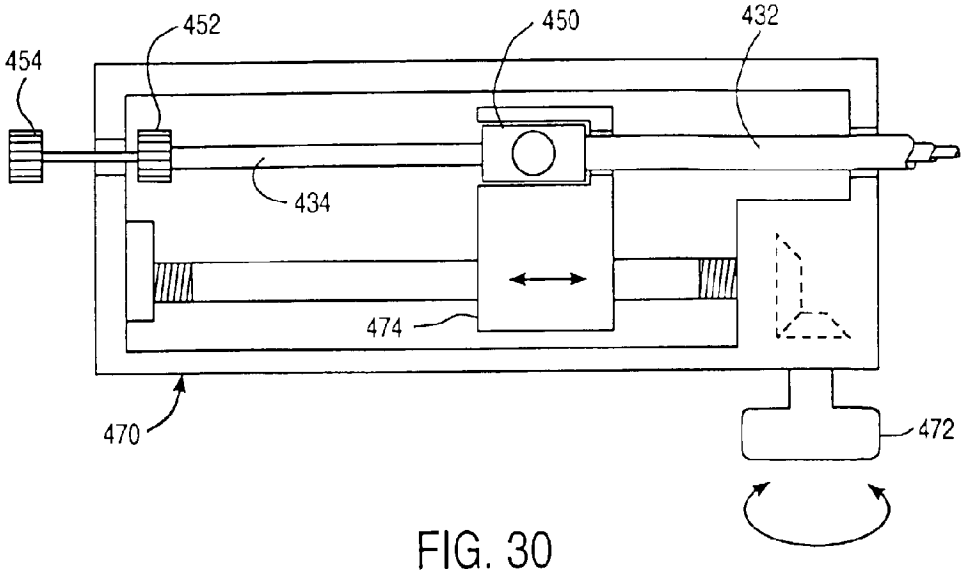

FIG. 30

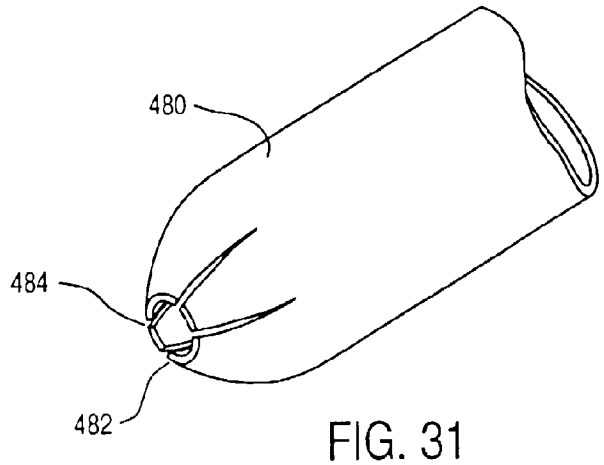

FIG. 31

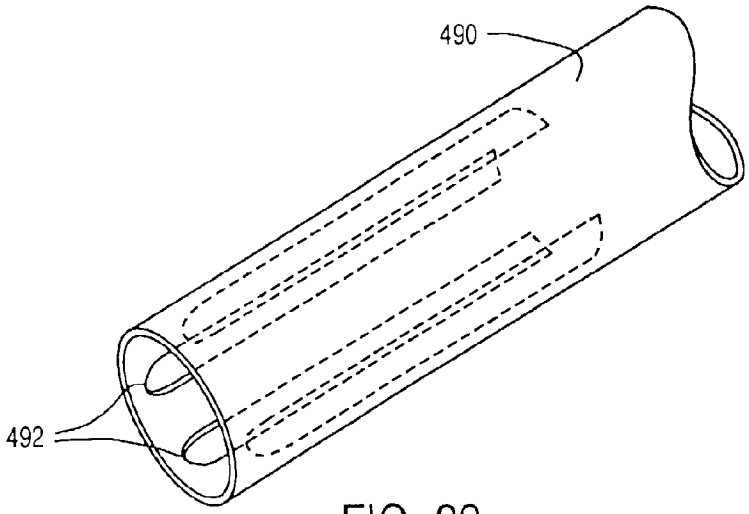

FIG. 32

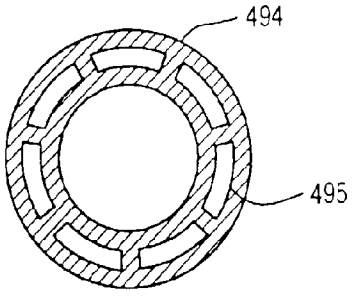

FIG. 33A

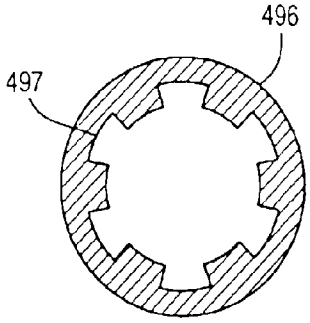

FIG. 33B

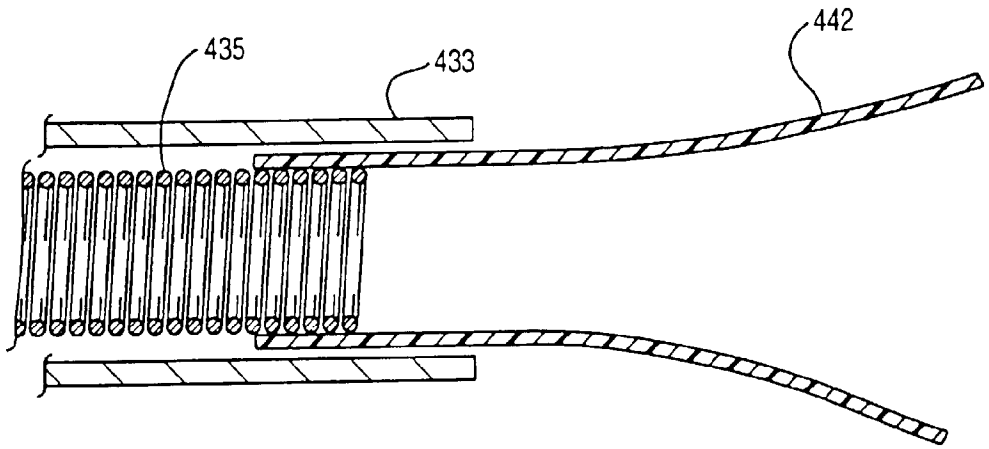

FIG. 29B

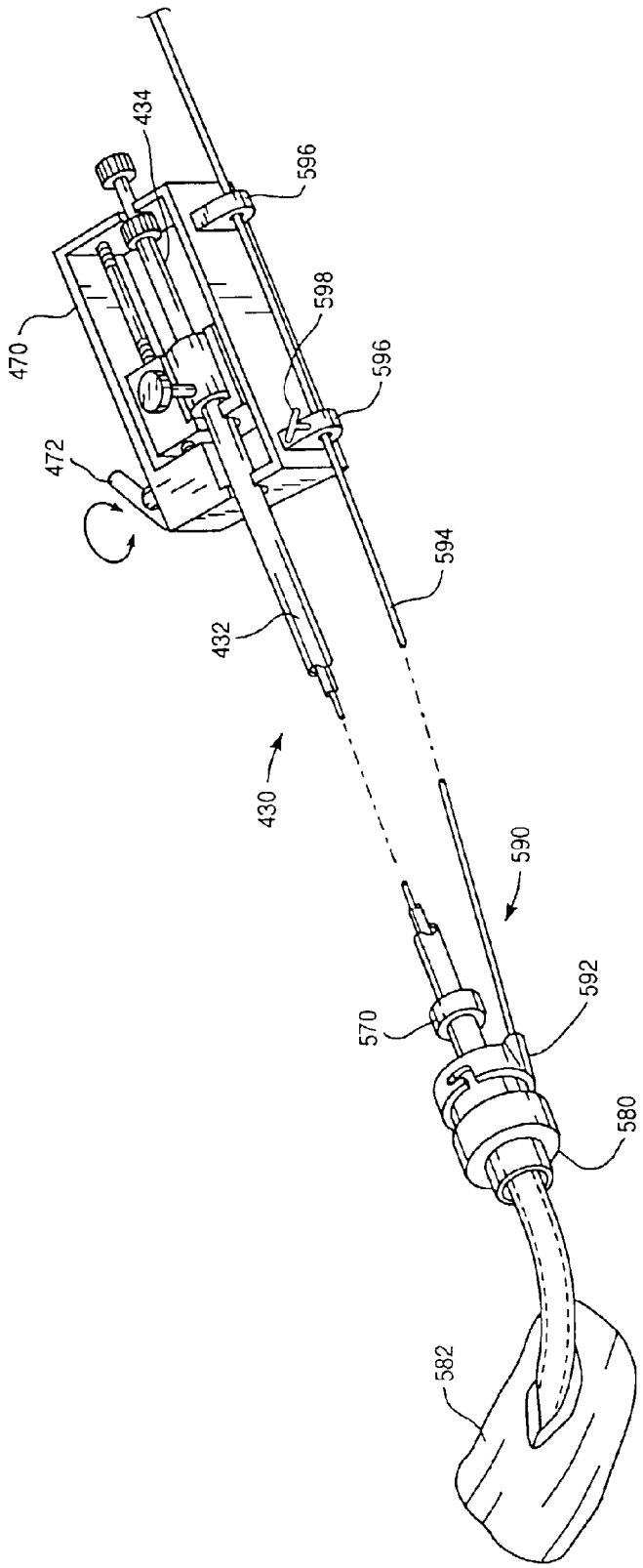

FIG. 34

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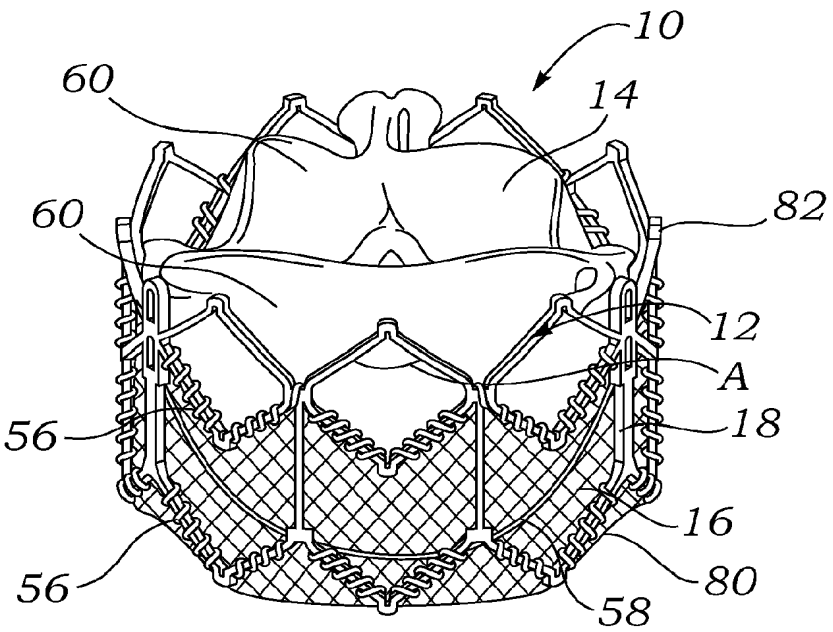
[Continued on next page]

(54) Title: LOW PROFILE TRANSCATHETER HEART VALVE

Fig. 1



(57) Abstract: An implantable prosthetic valve, according to one embodiment, comprises a frame, a leaflet structure, and a skirt member. The frame can have a plurality of axial struts interconnected by a plurality of circumferential struts. The leaflet structure comprises a plurality of leaflets (e.g., three leaflets arrange to form a tricuspid valve). The leaflet structure has a scalloped lower edge portion secured to the frame. The skirt member can be disposed between the leaflet structure and the frame.

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LOW PROFILE TRANSCATHETER HEART VALVE

FIELD

[001] The present disclosure relates to implantable devices and, more particularly, to valve prosthetics for implantation into body ducts, such as native heart valve annuluses.

DESCRIPTION OF THE RELATED ART

[002] The human heart can suffer from various valvular diseases. These valvular diseases can result in significant malfunctioning of the heart and ultimately require replacement of the native valve with an artificial valve. There are a number of known artificial valves and a number of known methods of implanting these artificial valves in humans.

[003] Various surgical techniques may be used to repair a diseased or damaged valve. In a valve replacement operation, the damaged leaflets are excised and the annulus sculpted to receive a replacement valve. Due to aortic stenosis and other heart valve diseases, thousands of patients undergo surgery each year wherein the defective native heart valve is replaced by a prosthetic valve, either bioprosthetic or mechanical. Another less drastic method for treating defective valves is through repair or reconstruction, which is typically used on minimally calcified valves. The problem with surgical therapy is the significant insult it imposes on these chronically ill patients with high morbidity and mortality rates associated with surgical repair.

[004] When the valve is replaced, surgical implantation of the prosthetic valve typically requires an open-chest surgery during which the heart is stopped and patient placed on cardiopulmonary bypass (a so-called "heart-lung machine"). In one common surgical procedure, the diseased native valve leaflets are excised and a prosthetic valve is sutured to the surrounding tissue at the valve annulus. Because of the trauma associated with the procedure and the attendant duration of extracorporeal blood circulation, some patients do not

survive the surgical procedure or die shortly thereafter. It is well known that the risk to the patient increases with the amount of time required on extracorporeal circulation. Due to these risks, a substantial number of patients with defective valves are deemed inoperable because their condition is too frail to withstand the procedure. By some estimates, more than 50% of the subjects suffering from aortic stenosis who are older than 80 years cannot be operated on for aortic valve replacement.

[005] Because of the drawbacks associated with conventional open-heart surgery, percutaneous and minimally-invasive surgical approaches are garnering intense attention. In one technique, a prosthetic valve is configured to be implanted in a much less invasive procedure by way of catheterization. For instance, U.S. Patent Nos. 5,411,522 and 6,730,118, which are incorporated herein by reference, describe collapsible transcatheter heart valves that can be percutaneously introduced in a compressed state on a catheter and expanded in the desired position by balloon inflation or by utilization of a self-expanding frame or stent.

[006] An important design parameter of a transcatheter heart valve is the diameter of the folded or crimped profile. The diameter of the crimped profile is important because it directly influences the physician's ability to advance the valve through the femoral artery or vein. More particularly, a smaller profile allows for treatment of a wider population of patients, with enhanced safety.

SUMMARY

[007] The present disclosure is directed toward new and non-obvious methods and apparatuses relating to prosthetic valves, such as heart valves.

[008] In one representative embodiment, an implantable prosthetic valve comprises a radially collapsible and expandable frame, or stent, and a leaflet structure comprising a plurality of leaflets. The leaflet structure has a scalloped lower edge portion that is positioned inside of and secured to the frame. The valve can further include an annular skirt member, which can be disposed

between the frame and the leaflet structure such that the scalloped lower edge portion can be attached to an inner surface of the skirt member. Each leaflet can have an upper edge, a curved lower edge and two side flaps extending between respective ends of the upper edge and the lower edge, wherein each side flap is secured to an adjacent side flap of another leaflet to form commissures of the leaflet structure. Each commissure can be attached to one of the commissure attachment posts, and a reinforcing bar can be positioned against each side flap for reinforcing the attachments between the commissures and the commissure attachment posts.

[009] The frame can comprise a plurality of angularly spaced, axial struts that are interconnected by a plurality of rows of circumferential struts. Each row of circumferential struts desirably includes struts arranged in a zig-zag or saw-tooth pattern extending around the circumference of the frame.

[010] In certain embodiments, at least one row, and preferably all rows, of circumferential struts include pairs of circumferential struts extending between two axial struts. Each strut of the pair has one end connected to a respective axial strut and another end interconnected to an adjacent end of the other strut of the same pair by a crown portion such that a gap exists between the adjacent ends of the struts. The angle between the struts of each pair desirably is between about 90 and 110 degrees, with about 100 degrees being a specific example. The frame desirably is made of a nickel-cobalt based alloy, such as a nickel cobalt chromium molybdenum alloy (e.g., MP35N™).

[011] In another representative embodiment, an implantable prosthetic valve comprises a radially collapsible and expandable annular frame and a leaflet structure supported by the frame. The frame can comprise a plurality of interconnected struts defining a plurality of open cells in the frame. The valve further includes an annular cover member disposed on and covering the cells of at least a portion of the frame. The cover member desirably comprises an elastomer, such as silicon, that can expand and stretch when the valve is expanded from a crimped state to an expanded state.

[012] The cover member may be a thin sleeve of silicon that surrounds at least a portion of the frame. Alternatively, the cover member may be formed by dipping at least a portion of the frame in silicon or another suitable elastomer in liquefied form.

[013] In another representative embodiment, a method is disclosed for crimping an implantable prosthetic valve having a frame and leaflets supported by the frame. The method comprises placing the valve in the crimping aperture of a crimping device such that a compressible material is disposed between the crimping jaws of the crimping device and the frame of the valve. Pressure is applied against the compressible material and the valve with the crimping jaws to radially crimp the valve to a smaller profile and compress the compressible material against the valve such that the compressible material extends into open cells of the frame and pushes the leaflets away from the inside of the frame.

[014] The foregoing and other features and advantages of the invention will become more apparent from the following detailed description, which proceeds with reference to the accompanying figures.

BRIEF DESCRIPTION OF THE DRAWINGS

[015] FIG. 1 is a perspective view of a representative embodiment of a prosthetic heart valve.

[016] FIG. 2 is another perspective view of the prosthetic valve of FIG. 1.

[017] FIG. 3 is another perspective view of the prosthetic valve of FIG. 1.

[018] FIG. 4 is an enlarged view of a section of the valve shown in FIG. 3.

[019] FIG. 5 is a bottom perspective view of the prosthetic valve of FIG. 1 showing the inside of the valve.

[020] FIG. 6 is a top plan view of the prosthetic valve of FIG. 1.

[021] FIG. 6A is an enlarged partial top view of the valve of FIG. 1 illustrating the positioning of the reinforcing bars with respect to the commissure attachment posts of the frame.

[022] FIG. 7 is a perspective view of the frame of the prosthetic valve of FIG. 1.

[023] FIG. 8 is a perspective view of an alternative embodiment of a frame that can be used in the prosthetic valve of FIG. 1.

[024] FIG. 9 is a flattened view of 120-degree segment of the frame shown in FIG. 7.

[025] FIG. 10 is a flattened view of 120-degree segment of the frame shown in FIG. 8.

[026] FIG. 11 is a front view of a reinforcing bar that can be used to reinforce the connection of the valve leaflets to a frame in a prosthetic valve such as shown in FIG. 1.

[027] FIG. 12 is a perspective view of the reinforcing bar of FIG. 11 and a PET sleeve that can be used to cover the bar.

[028] FIG. 13 is a flattened view of a leaflet of the valve shown in FIG. 1.

[029] FIG. 14 is a flattened view of the opposite side of the leaflet showing a reinforcing strip secured adjacent the bottom edge of the leaflet.

[030] FIG. 15 is a top plan view of the leaflet structure of the valve of FIG. 1 prior to attachment to the frame.

[031] FIG. 16 is a flattened view of the skirt used in the valve shown in FIG. 1.

[032] FIG. 18 is a bottom perspective view of the leaflet structure connected to the skirt so as to form a leaflet assembly.

[033] FIG. 19 is a side view of a balloon catheter and a prosthetic valve crimped onto the balloon of the balloon catheter.

[034] FIG. 20 is a front view of a crimping device showing a prosthetic valve positioned in the crimping aperture of the crimping device with a protective sleeve disposed between the valve and the crimping jaws.

[035] FIG. 21 is a front view of the crimping device shown after the crimping jaws are forced inwardly to compress the valve and the protective sleeve.

[036] FIG. 22 is a side view of the valve and protective sleeve after removal from the crimping device.

[037] FIG. 23 is a side view of a prosthetic valve that has been crimped onto a balloon of a balloon catheter without a protective sleeve.

[038] FIG. 24 is a side view of a prosthetic valve that has been crimped onto a balloon of a balloon catheter using a protective sleeve in the manner shown in FIGS. 20-21.

[039] FIG. 25 is a side view of a frame for a prosthetic valve having a silicon skirt, or sleeve, disposed on the outside of the frame.

[040] FIG. 26 is a side view of a frame for a prosthetic valve having a silicon encapsulating layer covering the inside and outside of the frame.

[041] FIG. 27 is a perspective view of a prosthetic valve comprising a frame having a silicon encapsulating layer.

[042] FIG. 28 is a perspective view of the valve of FIG. 27 after it has been crimped to a smaller diameter.

[043] FIG. 29 is a side view of the valve of FIG. 27 after it has been expanded by a balloon catheter.

[044] FIGS. 30A-30C are graphs illustrating the results of respective uniaxial tests performed on respective silicon test strips.

[045] FIGS. 31A-31F are graphs illustrating the results of respective uniaxial tests performed on respective silicon test strips having deliberately introduced tears.

DETAILED DESCRIPTION

[046] FIGS. 1 and 2 illustrate an implantable prosthetic valve 10, according to one embodiment. Valve 10 in the illustrated embodiment generally comprises a frame, or stent, 12, a leaflet structure 14 supported by the frame, and a skirt 16

secured to the outer surface of the leaflet structure. Valve 10 typically is implanted in the annulus of the native aortic valve but also can be adapted to be implanted in other native valves of the heart or in various other ducts or orifices of the body. Valve 10 has a "lower" end 80 and an "upper" end 82. In the context of the present application, the terms "lower" and "upper" are used interchangeably with the terms "inflow" and "outflow", respectively. Thus, for example, the lower end 80 of the valve is its inflow end and the upper end 82 of the valve is its outflow end.

[047] Valve 10 and frame 12 are configured to be radially collapsible to a collapsed or crimped state for introduction into the body on a delivery catheter and radially expandable to an expanded state for implanting the valve at a desired location in the body (e.g., the native aortic valve). Frame 12 can be made of a plastically-expandable material that permits crimping of the valve to a smaller profile for delivery and expansion of the valve using an expansion device such as the balloon of a balloon catheter. Exemplary plastically-expandable materials that can be used to form the frame are described below. Alternatively, valve 10 can be a so-called self-expanding valve wherein the frame is made of a self-expanding material such as Nitinol. A self-expanding valve can be crimped to a smaller profile and held in the crimped state with a restraining device such as a sheath covering the valve. When the valve is positioned at or near the target site, the restraining device is removed to allow the valve to self-expand to its expanded, functional size.

[048] Referring also to FIG. 7 (which shows the frame alone for purposes of illustration), frame 12 is an annular, stent-like structure having a plurality of angularly spaced, vertically extending, commissure attachment posts, or struts, 18. Posts 18 can be interconnected via a lower row 36a of circumferentially extending struts 20 and first and second rows upper rows 36b, 36c, respectively, of circumferentially extending struts 22 and 24, respectively. The struts in each row desirably are arranged in a zig-zag or generally saw-tooth like pattern extending in the direction of the circumference of the frame as shown. Adjacent struts in the same row can be interconnected to one another as shown in FIGS. 1

and 5 to form an angle A, which desirably is between about 90 and 110 degrees, with about 100 degrees being a specific example. The selection of angle A between approximately 90 and 110 degrees optimizes the radial strength of frame 12 when expanded yet still permits the frame 12 to be evenly crimped and then expanded in the manner described below.

[049] In the illustrated embodiment, pairs of adjacent circumferential struts in the same row are connected to each other by a respective, generally U-shaped crown structure, or crown portion, 26. Crown structures 26 each include a horizontal portion extending between and connecting the adjacent ends of the struts such that a gap 28 is defined between the adjacent ends and the crown structure connects the adjacent ends at a location offset from the strut's natural point of intersection. Crown structures 26 significantly reduce residual strains on the frame 12 at the location of struts 20, 22, 24 during crimping and expanding of the frame 20 in the manner described below. Each pair of struts 22 connected at a common crown structure 26 forms a cell with an adjacent pair of struts 24 in the row above. Each cell can be connected to an adjacent cell at a node 32. Each node 32 can be interconnected with the lower row of struts by a respective vertical (axial) strut 30 that is connected to and extends between a respective node 32 and a location on the lower row of struts 20 where two struts are connected at their ends opposite crown structures 26.

[050] In certain embodiments, lower struts 20 have a greater thickness or diameter than upper struts 22, 24. In one implementation, for example, lower struts 20 have a thickness T (FIG. 9) of about 0.42 mm and upper struts 22, 24 have a thickness T of about 0.38 mm. Because there is only one row of lower struts 20 and two rows of upper struts 22, 24 in the illustrated configuration, enlargement of lower struts 20 with respect to upper struts 22, 24 enhances the radial strength of the frame at the lower area of the frame and allows for more uniform expansion of the frame.

[051] FIG. 9 shows a flattened view of a 120-degree segment of frame 12 shown in FIG. 7, the segment comprising a portion of the frame extending

between two posts 18. As shown, the frame segment has three columns 34 and three rows 36a, 36b, 36c of struts per segment. Each column 34 is defined by the adjoining pairs of struts 20, 22, 24 extending between two axially extending struts 18, 30. Frame 12 desirably is comprised of three 120-degree segments, with each segment being bounded by two posts 18. Accordingly, frame 12 in the illustrated embodiment includes 9 total columns per frame.

[052] The number of columns and rows desirably is minimized to reduce the overall crimp profile of the valve, as further discussed below. The arrangement of FIGS. 7 and 9 typically is used for valves that are less than about 29 mm in diameter, and are most suitable for valves that are about 20-26 mm in diameter. In working examples of valves comprising frame 12, a 20-mm valve can be crimped to a diameter of about 17 Fr, a 23-mm valve can be crimped to a diameter of about 18 Fr and a 26-mm valve can be crimped to a diameter of about 19 Fr. For valves that are about 29 mm and larger in diameter, it may be desirable to add another row and column of struts.

[053] For example, FIGS. 8 and 10 show an alternative frame 40 that is similar to frame 12 except that frame 40 has four rows of struts (a lowermost, first row 52a of struts 42, a second row 52b of struts 44, a third row 52c of struts 46, and an uppermost row 52d of struts 48) instead of three rows of struts, as well as four columns 50 of struts for each 120-degree frame segment instead of three columns of struts. FIG. 10 shows a flattened view of a 120-degree segment of frame 40 shown in FIG. 8. Frame 40 in the illustrated embodiment includes three such 120-degree segments, providing 12 total columns 50 of struts for the frame.

[054] Struts 46 of the third row desirably are facing in the opposite direction of the struts 48 of the fourth row (i.e., the apexes or crown portions are facing in the opposite direction), to help avoid buckling of the vertical posts of the frame during crimping and expansion of the valve. Struts 44 of the second row can be arranged so as to be facing in the same direction as the struts 42 of the first row as shown (i.e., the apexes or crown portions are facing in the same direction).

Alternatively, struts 44 of the second row can be facing in the opposing direction from struts 42 of the first row so as to form square cells, like the cells formed by the struts 46, 48 of the third and fourth rows, respectively. Frame 40 can also include axially extending struts 54 connected to and extending between the ends of each strut 42, 44, 46, 48 aligned in a column 50 that are not connected to a post 18. As noted above, frame 40 is most suitable for valves 29 mm and larger in diameter (when expanded to its functional size). In a working example of a valve incorporating frame 40, a 29-mm valve can be crimped to a diameter of about 21 Fr.

[055] Suitable plastically-expandable materials that can be used to form the frame include, without limitation, stainless steel, a nickel based alloy (e.g., a nickel-cobalt-chromium alloy), polymers, or combinations thereof. In particular embodiments, frame 20 is made of a nickel-cobalt-chromium-molybdenum alloy, such as MP35N™ (tradename of SPS Technologies), which is equivalent to UNS R30035 (covered by ASTM F562-02). MP35N™/UNS R30035 comprises 35% nickel, 35% cobalt, 20% chromium, and 10% molybdenum, by weight. It has been found that the use of MP35N to form frame 20 provides superior structural results over stainless steel. In particular, when MP35N is used as the frame material, less material is needed to achieve the same or better performance in radial and crush force resistance, fatigue resistances, and corrosion resistance. Moreover, since less material is required, the crimped profile of the frame can be reduced, thereby providing a lower profile valve assembly for percutaneous delivery to the treatment location in the body.

[056] Referring again to FIG. 1, skirt 16 can be formed, for example, of polyethylene terephthalate (PET) ribbon. The thickness of the skirt can vary, but is desirably less than 6 mil, and desirably less than 4 mil, and even more desirably about 2 mil. Skirt 16 can be secured to the inside of frame 12 via Lenzing sutures 56, as shown in FIG. 1. Leaflet structure 14 can be attached to the skirt via a thin PET reinforcing strip 68 (or sleeve), discussed below, which enables a secure suturing and protects the pericardial tissue of the leaflet structure from tears. Leaflet structure 14 can be sandwiched between skirt 16

and the thin PET strip 68 as shown. Suture 58, which secures the PET strip and the leaflet structure 14 to skirt 16 can be any suitable suture, such as an Ethibond suture. Suture 58 desirably tracks the curvature of the bottom edge of leaflet structure 14, as described in more detail below. Leaflet structure 14 can be formed of bovine pericardial tissue, biocompatible synthetic materials, or various other suitable natural or synthetic materials as known in the art and described in U.S. Patent No. 6,730,118, which is incorporated by reference herein.

[057] Leaflet structure 14 can comprise three leaflets 60, which can be arranged to collapse in a tricuspid arrangement, as best shown in FIGS. 2 and 6. The lower edge of leaflet structure 14 desirably has an undulating, curved scalloped shape (suture line 58 shown in FIG. 1 tracks the scalloped shape of the leaflet structure). By forming the leaflets with this scalloped geometry, stresses on the leaflets are reduced, which in turn improves durability of the valve. Moreover, by virtue of the scalloped shape, folds and ripples at the belly of each leaflet (the central region of each leaflet), which can cause early calcification in those areas, can be eliminated or at least minimized. The scalloped geometry also reduces the amount of tissue material used to form leaflet structure, thereby allowing a smaller, more even crimped profile at the inflow end of the valve.

[058] Leaflets 60 can be secured to one another at their adjacent sides to form commissures 84 of the leaflet structure (the edges where the leaflets come together). Leaflet structure 14 can be secured to frame 12 using suitable techniques and mechanisms. For example, as best shown in FIG. 6, commissures 84 of the leaflet structure desirably are aligned with the support posts 18 and secured thereto using sutures. The point of attachment of the leaflets to the posts 18 can be reinforced with bars 62 (FIG. 11), which desirably are made of a relatively rigid material (compared to the leaflets), such as stainless steel.

[059] FIG. 13 shows a single leaflet 60, which has a curved lower edge 64 and two flaps 66 extending between the upper edge and curved lower edge of the leaflet. The curved lower edge 64 forms a single scallop. When secured to two other leaflets to form leaflet structure 14, the curved lower edges of the leaflets collectively form the scalloped shaped lower edge portion of the leaflet structure (as best shown in FIG. 18). As further shown in FIG. 13, two reinforcing bars 62 can be secured to the leaflet adjacent to flaps 66 (e.g., using sutures). The flaps can then be folded over bars 62 and secured in the folded position using sutures. If desired, as shown in FIG. 12, each bar 62 can be placed in a protective sleeve 68 (e.g., a PET sleeve) before being secured to a leaflet.

[060] As shown in FIG. 14, the lower curved edge 64 of the leaflet can be reinforced for later securement to the skirt 16, such as by securing a reinforcing strip 68 along the curved lower edge between flaps 66 on the side of the leaflet opposite bars 62. Three such leaflets 60 can be prepared in the same manner and then connected to each other at their flaps 66 in a tricuspid arrangement to form leaflet structure 14, as shown in FIG. 15. The reinforcing strips 68 on the leaflets collectively define a ribbon or sleeve that extends along the lower edge portion of the inside surface of the leaflet structure.

[061] As noted above, leaflet structure 14 can be secured to frame 12 with skirt 16. Skirt 16 desirably comprises a tough, tear resistant material such as PET, although various other synthetic or natural materials can be used. Skirt 16 can be much thinner than traditional skirts. In one embodiment, for example, skirt 16 is a PET skirt having a thickness of about 0.07 mm at its edges and about 0.06 mm at its center. The thinner skirt can provide for better crimping performances while still providing good perivalvular sealing.

[062] FIG. 16 shows a flattened view of the skirt before the opposite ends are secured to each other to form the annular shape shown in FIG. 17. As shown, the upper edge of skirt 16 desirably has an undulated shape that generally follows the shape of the second row of struts 22 of the frame. In this manner,

the upper edge of skirt 16 can be tightly secured to struts 22 with sutures 56 (as best shown in FIG. 1). Skirt 16 can also be formed with slits 70 to facilitate attachment of the skirt to the frame. Slits 70 are aligned with crown structures 26 of struts 22 when the skirt is secured to the frame. Slits 70 are dimensioned so as to allow an upper edge portion of skirt to be partially wrapped around struts 22 and reduce stresses in the skirt during the attachment procedure. For example, in the illustrated embodiment, skirt 16 is placed on the inside of frame 12 and an upper edge portion of the skirt is wrapped around the upper surfaces of struts 22 and secured in place with sutures 56. Wrapping the upper edge portion of the skirt around struts 22 in this manner provides for a stronger and more durable attachment of the skirt to the frame. Although not shown, the lower edge of the skirt can be shaped to conform generally to the contour of the lowermost row of struts 22 to improve the flow of blood past the inflow end of the valve.

[063] As further shown in FIG. 17, various suture lines can be added to the skirt to facilitate attachment of the skirt to the leaflet structure and to the frame. For example, a scalloped shaped suture line 72 can be used as a guide to suture the lower edge of the leaflet structure at the proper location against the inner surface of the skirt using suture 59 (as best shown in FIG. 5). Another scalloped shaped suture line 74 (FIG. 17) can be use as a guide to suture the leaflet structure to the skirt using sutures 58 (FIG. 1). Reinforcing strips 68 secured to the lower edge of the leaflets reinforces the leaflets along suture line 58 and protects against tearing of the leaflets. FIG. 18 shows a leaflet assembly comprised of skirt 16 and leaflet structure 14 secured to the skirt. The leaflet assembly can then be secured to frame 12 in the manner described below. In alternative embodiments, the skirt, without the leaflet structure, can be connected to the frame first, and then the leaflet structure can be connected to the skirt.

[064] FIG. 6 shows a top view of the valve assembly attached to frame 12. Leaflets 60 are shown in a generally closed position. As shown, the commissures of the leaflets are aligned with posts 18 of the frame. The leaflets

can be secured to the frame using sutures extending through flaps 66 of the leaflets, openings 76 in bars 62, and openings 78 in posts 18, effectively securing flaps 66 to posts 18. As noted above, bars 62 reinforce the flaps at the area of connection with posts and protect against tearing of the leaflets.

[065] As shown in FIG. 6A, bars 62 desirably are aligned perpendicular and as straight as possible with respect to posts 18 of the frame, such that bars 62 and post 18 at each commissure form a "T" shape. The width of bars 62 and the attachment of the commissures via the bars provides a clearance between the deflectable portions of the leaflets 60 (the portions not secured by sutures to the frame) and the frame, while the edge radius (thickness) of bars 62 serves as a flex hinge for the leaflets 60 during valve opening and closing, thereby increasing the space between the leaflets and the frame. By increasing the space between the moving portions of the leaflets and frame and by having the leaflets flex against an edge radius of bars 62, contact between the moving portions of the leaflets (especially the outflow edges of the leaflets) and the frame can be avoided during working cycles, which in turn improves the durability of the valve assembly. This configuration also enhances perfusion through the coronary sinuses.

[066] FIG. 19 depicts a side view of a valve 10 crimped on a balloon delivery catheter 100. The valve is crimped onto balloon 110 of balloon catheter 100. It is desirable to protect leaflet structure 14 of the valve from damage during crimping to ensure durability of the leaflet structure and at the same time, it is desirable to reduce as much as possible the crimped profile size of the valve. During the crimping procedure the tissue of the leaflet structure (e.g., bovine pericardial tissue or other suitable tissue) is pressed against against the inner surface of the metal frame and portions of the tissue can protrude into the open cells of the frame between the struts and can be pinched due to the scissor-like motion of the struts of the frame. If the valve is severely crimped to achieve a small crimping size, this scissor-like motion can result in cuts and rupture of the tissue leaflets.

[067] Skirt 16, described above, can protect against damage to the leaflet structure during crimping to a certain degree. However, the skirt's main purpose is structural and it does not in certain embodiments cover the entire frame. Therefore, in such embodiments, the skirt may not fully protect the leaflet structure during crimping and as such, the frame can still cause damage to the leaflet structure.

[068] FIGS. 20 and 21 show an embodiment of a crimping apparatus for atraumatic crimping of a valve onto a balloon in a manner that further protects against damage to the leaflets. The crimping apparatus (also referred to as a crimper), indicated generally at 200, has an aperture 202 sized to receive a valve in an expanded state. FIG. 20 shows aperture 202 in a fully open or dilated state with a valve 10 positioned inside aperture 202. Crimping apparatus 200 has a plurality of crimper jaws 206 (12 in the illustrated embodiment) which are configured to move radially inwardly to radially compress (crimp) the valve to a smaller profile around the balloon of a balloon catheter.

[069] A deformable material is positioned between the outside of the frame and the crimping jaws 206. In the illustrated embodiment, the deformable material comprises a protective sleeve, or covering, 204 that is placed around the valve so that it covers the outer surface of the frame of the valve and prevents the hard surface of the crimping jaws from directly contacting the frame of the valve. The sleeve 204 desirably is sized to fully cover the outer surface of the frame. Sleeve 204 desirably is made of a soft, flexible and compressible material. The sleeve can be formed from generally available materials, including, but not limited to, natural or synthetic sponge (e.g., polyurethane sponge), a foamed material made of a suitable polymer such as polyurethane or polyethylene, or any of various suitable elastomeric materials, such as polyurethane, silicon, polyolefins or a variety of hydrogels, to name a few.

[070] The sleeve is desirably stored in a wet environment (e.g., immersed in saline) prior to use. After placing sleeve 204 around the valve, the valve and

the sleeve are placed into crimping apparatus 200 as shown in FIG. 20. Balloon 110 of a balloon catheter can then be positioned within the leaflets 60 of the valve (FIG. 21). FIG. 21 shows crimper jaws 206 surrounding sleeve 204, which in turn surrounds frame 12 and leaflet structure 14 of valve 10. Balloon 110 typically is placed at the center of the valve so that the valve can be evenly expanded during implantation of the valve within the body.

[071] As seen in FIG. 21, during crimping, the sponge-like material of protective sleeve 204 protrudes into the open cells of frame 12 and occupies this space, thereby preventing leaflet structure 14 from entering this space and being pinched or otherwise damaged. After crimping is completed, the valve with the protective sleeve is removed from the crimping apparatus. Sleeve 204 can then be gently peeled away from the frame. Because the protective sleeve presses the leaflet structure inwardly and away from the frame during crimping, the valve can be crimped to a small profile without damaging the leaflet structure.

[072] FIGS. 23 and 24 illustrate an advantage that can be gained by using protective sleeve 204. FIG. 23 shows a prosthetic valve that was crimped without using the protective sleeve. Dotted line 300 identifies an area of the valve where leaflet structure 302 has been pressed between struts of a frame 304, which can damage the leaflet structure as discussed above.

[073] In contrast, FIG. 24 shows a prosthetic valve that was crimped using protective sleeve 204. In this example, leaflet structure 302 was pressed inwardly and away from the inside of frame 304 and, therefore, the leaflet structure was not pinched or squeezed between the struts of the frame.

[074] Accordingly, since the leaflet structure is pushed away from the frame when the protective sleeve is used, the leaflet structure is less likely to be pinched or cut during the crimping process. Also, when using a protective sleeve, a very ordered structure of balloon-leaflets-frame (from inward to outward) can be achieved. When no such protective sleeve is utilized, some portion of the balloon, leaflets, and frame are much more likely to overlap after

the crimping procedure and the resulting structure is less predictable and uniform.

[075] In addition to the foam or sponge-type protective sleeve described above, other types of sleeves or protective layers of deformable material can be used to protect the leaflets against damage during crimping of a valve. In one implementation, for example, a layer (e.g., rectangular slices) of deformable material (e.g., sponge, rubber, silicon, polyurethane, etc.) can be disposed on each crimping jaw 206 so as to form a sleeve around the valve upon crimping. Alternatively, deformable packets filled with a flowable, deformable material, such as a gel or gas, can be disposed on each crimping jaw for contacting the valve upon crimping. In addition, the deformable material (e.g., sleeve 204) can be covered with a thin PET cloth, among many other fabric materials or other suitable materials, to prevent particles of the deformable materials from migrating to the valve during crimping.

[076] The skirt of a prosthetic valve serves several functions. In particular embodiments, for example, the skirt functions to seal and prevent (or decrease) perivalvular leakage, to anchor the leaflet structure to the frame, and to protect the leaflets against damage caused by contact with the frame during crimping and during working cycles of the valve. The skirt used with the prosthetic valve discussed above has been described as being a fabric, such as a PET cloth. PET or other fabrics are substantially non-elastic (i.e., substantially non-stretchable and non-compressible). As such, the skirt in certain implementations limits the smallest achievable crimping diameter of the valve and can wrinkle after expansion from the crimped diameter.

[077] In alternative embodiments, such as discussed below, a prosthetic valve can be provided with a skirt that is made of a stretchable and/or compressible material, such as silicon. Due to the compressibility of such a skirt, the valve can be crimped to a relatively smaller diameter as compared to a valve having a non-compressible skirt. Furthermore, such a skirt can recover its original,

smooth surfaces with little or no wrinkling after expansion from the crimped state.

[078] FIG. 25 shows an embodiment of a frame 12 that has an elastic "over-tube" skirt or sleeve 340 that extends completely around and covers at least a portion of the outside of the frame. In particular embodiments, skirt 340 is made of silicon, which can undergo large deformations while maintaining its elasticity. Such a silicon skirt can be a thin sleeve that covers a portion of frame 12 from the outside. In the illustrated embodiment, the height of the skirt is less than the overall height of frame 12, however, the skirt can vary in height and need not be the height shown in FIG. 25. For example, the height of the skirt can be the same as or greater than that of the frame so as to completely cover the outside of the frame. In an alternative embodiment, the skirt 340 can be mounted to the inside of the frame using, for example, sutures or an adhesive. When mounted inside of the frame, the skirt can protect the leaflets from abrasion against the inside of the frame. Other materials that can be used to form the skirt or sleeve include, but are not limited to, PTFE, ePTFE, polyurethane, polyolefins, hydrogels, biological materials (e.g., pericardium or biological polymers such as collagen, gelatin, or hyaluronic acid derivatives) or combinations thereof.

[079] In another embodiment, the entire frame or a portion thereof can be dipped in liquefied material (e.g., liquid silicon or any of the materials described above for forming the sleeve 340 that can be liquefied for dip coating the frame) in order to encapsulate the entire frame (or at least that portion that is dipped) in silicon. FIG. 26 is a side view of a frame 12 that has been dipped in silicon to form a continuous cylindrical silicon covering 342 encapsulating the struts of the frame and filling the spaces between the struts. FIG. 26 shows the covering 342 before it is trimmed to remove excess material extending beyond the ends of the frame. Although less desirable, the frame can be dipped such that the silicon encapsulates the struts of the frame but does not fill the open spaces between the struts of the frame.

[080] FIG. 27 shows an embodiment of a prosthetic valve 400 comprising a frame 402 and a leaflet structure 404 mounted to the inside of the frame (e.g., using sutures as shown). Frame 402 has a skirt in the form of silicon covering 406 that is formed, for example, by dipping the frame into liquid silicon. FIG. 27 shows valve 400 in its expanded state. In FIG. 28, valve 400 has been crimped to a smaller profile. During crimping, coating 406, which extends across and fills the open cells between the struts of the frame, is effective to push leaflet structure 404 inward and away from the frame, thereby protecting the leaflet structure from pinching or tearing. FIG. 29 shows valve 400 after being expanded by a balloon of a balloon catheter.

[081] In order to test the durability and stretch resistance of the silicon used, several uniaxial tests were conducted. In particular, silicon strips of about 5x50 mm (with a thickness of about 0.85 mm) were tested in a uniaxial tester. FIGS. 30A-30C show graphs of the results of the uniaxial testing of silicon strips. In addition, tears were deliberately introduced into silicon strips at a middle of the strips and at the edge of the strips while the strips were stretched on a uniaxial tester. The tears were introduced by making holes in the silicon strips with a needle. FIGS. 31A-31F show graphs of the results of the uniaxial testing of silicon strips with deliberately introduced tears.

[082] It was found that ultimate tensile stretch for a thin layer of silicon was over 500% and that samples that had tears that were deliberately introduced continued to show notable strength. Accordingly, the elasticity of silicon permits silicon dipped frames to be crimped to very low profiles and expanded back out to larger profiles without significant damage to the silicon layer. In addition, the silicon material can increase friction between the frame and the native annulus where the prosthetic valve is implanted, resulting in better anchoring and preventing/reducing perivalvular leaks.

[083] A silicon skirt can be mounted on a frame by various means, including by using a mandrel. Also, it may be desirable to use a silicon skirt in combination with a cloth or fabric skirt. For example, it may be desirable to

place a silicon skirt on the outside of a cloth or fabric skirt that is surrounding at least a portion of a frame.

[084] Alternatively or additionally, a silicon skirt could also be placed on the inside of the frame and attached to the frame so that it offers the leaflets improved protecting during working cycles. Alternatively, instead of silicon, the skirt can be made of an auxetic and/or swelling material, such as synthetic or natural hydrogels. An auxetic material is one that expands laterally while stretched longitudinally, which means that this material has a negative Poisson ration. If the frame is covered with an auxetic material it can expand radially while being stretched circumferentially when the valve is expanded from its crimped state. Such expansion can improve the fit of the valve at the native valve annulus, thereby preventing or reducing perivalvular leakage.

[085] In view of the many possible embodiments to which the principles of the disclosed invention may be applied, it should be recognized that the illustrated embodiments are only preferred examples of the invention and should not be taken as limiting the scope of the invention. Rather, the scope of the invention is defined by the following claims. We therefore claim as our invention all that comes within the scope and spirit of these claims.

We claim:

1. An implantable prosthetic valve comprising:

a radially collapsible and expandable annular frame, the frame having a plurality of angularly spaced commissure attachment posts;

an annular skirt member positioned inside of and secured to the frame; and

a leaflet structure comprising a plurality of leaflets, the leaflet structure having a scalloped lower edge portion secured to an inner surface of the skirt member, each leaflet having an upper edge, a curved lower edge and two side flaps extending between respective ends of the upper edge and the lower edge, wherein each side flap is secured to an adjacent side flap of another leaflet to form commissures of the leaflet structure, each commissure being attached to one of the commissure attachment posts; and

a reinforcing bar positioned against each side flap for reinforcing the attachments between the commissures and the commissure attachment posts.

2. The prosthetic valve of claim 1, wherein the commissures are attached to the commissure attachment posts with sutures extending through the side flaps, the reinforcing bars and the commissure attachment posts.

3. The prosthetic valve of claim 1, further comprising an elastomeric sleeve disposed on the outside of the frame.

4. The prosthetic valve of claim 1, further comprising an annular elastomeric layer encapsulating at least a portion of the frame.

5. The valve of claim 1, wherein the frame comprises a plurality of axial struts and a plurality of rows of circumferential struts extending between and interconnecting the axial struts.

6. The valve of claim 5, wherein at least one row of circumferential struts includes pairs of circumferential struts extending between two axial struts, the struts of each pair having adjacent ends interconnected by a generally U-shaped crown portion defining a gap between the adjacent ends.

7. The valve of claim 6, wherein an angle between each pair of struts is between about 90 and 110 degrees.

8. The valve of claim 1, wherein the frame comprises a nickel cobalt chromium alloy.

9. The valve of claim 4, wherein the nickel cobalt chromium alloy comprises MP35N.

10. The valve of claim 1, wherein the leaflets are connected to each other at adjacent sides to form commissures of the leaflet structure, each leaflet having a curved lower edge portion comprising a scallop extending between two commissures, the curved lower edge portions of the leaflets collectively defining the scalloped lower edge portion of the leaflet structure.

11. The valve of claim 10, further comprising an annular skirt secured to the inside of the frame.

12. The valve of claim 11, wherein the lower edge portion of the leaflet structure is secured to the inside of the skirt and the commissures are secured to respective axial struts of the frame.

13. The valve of claim 12, further comprising a reinforcing strip, separate from the skirt, that is secured to an inner surface of the lower edge portion of the leaflet structure.

14. The valve of claim 5, wherein the rows of circumferential struts includes at least a first row of circumferential struts adjacent the inflow end of the valve and a second row of circumferential struts adjacent the outflow end of the valve, wherein the struts of the first row are thicker than the struts of the second row.

15. An implantable prosthetic valve comprising:

a radially collapsible and expandable annular frame, the frame comprising a plurality of interconnected struts defining a plurality of open cells in the frame;

a leaflet structure supported by the frame and comprising a plurality of leaflets; and

an annular cover member disposed on and covering the cells of at least a portion of the frame, the cover member being made of silicon.

16. The valve of claim 15, wherein the cover member comprises a sleeve.

17. The valve of claim 15, wherein the sleeve is disposed on the outside of the frame.

18. The valve of claim 15, wherein the cover member is an encapsulating layer encapsulating said at least a portion of the frame and filling the cells of said at least a portion of the frame.

19. The valve of claim 15, wherein the leaflets are connected to each other at adjacent sides to form commissures of the leaflet structure, each leaflet having a curved lower edge portion comprising a scallop extending between two commissures, the curved lower edge portions of the leaflets collectively defining a scalloped lower edge portion of the leaflet structure that is positioned inside and secured to the frame.

Fig. 1

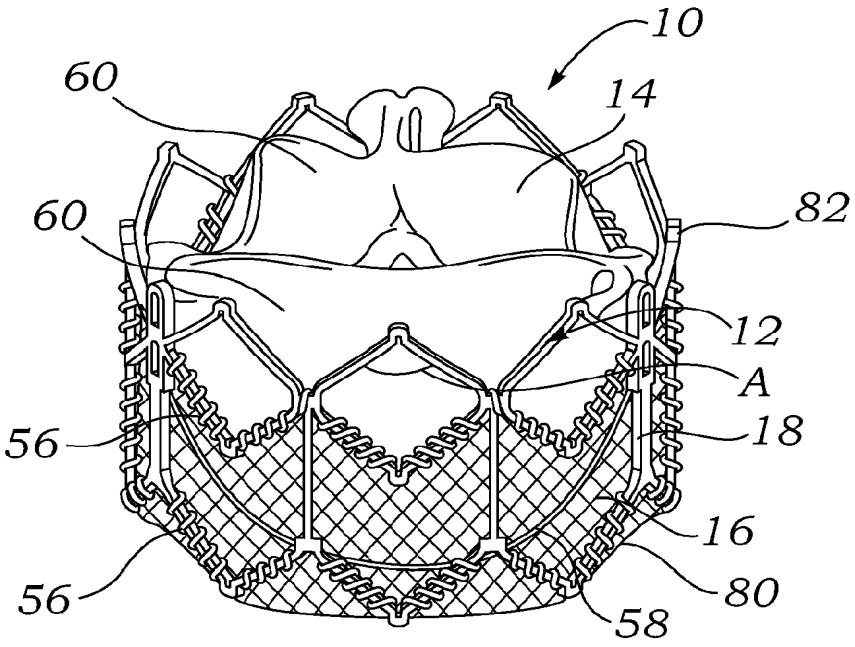


Fig. 2

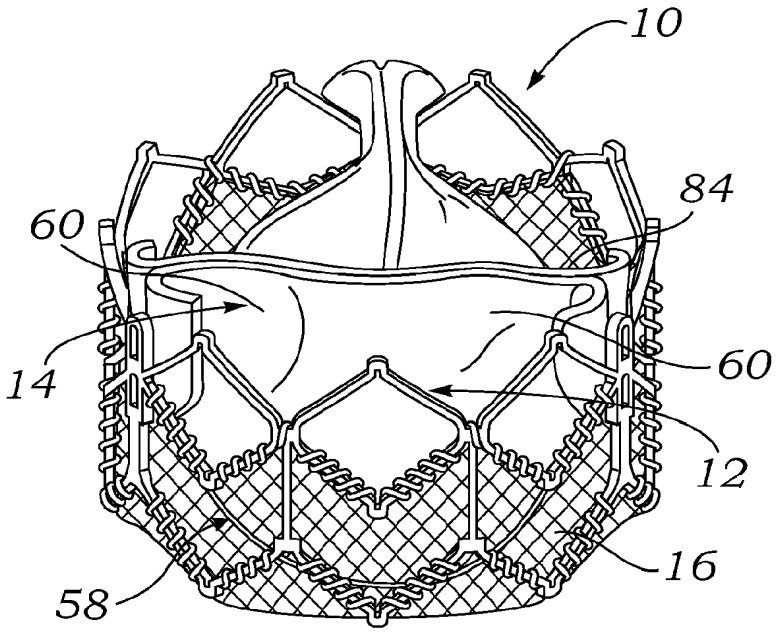


Fig. 3

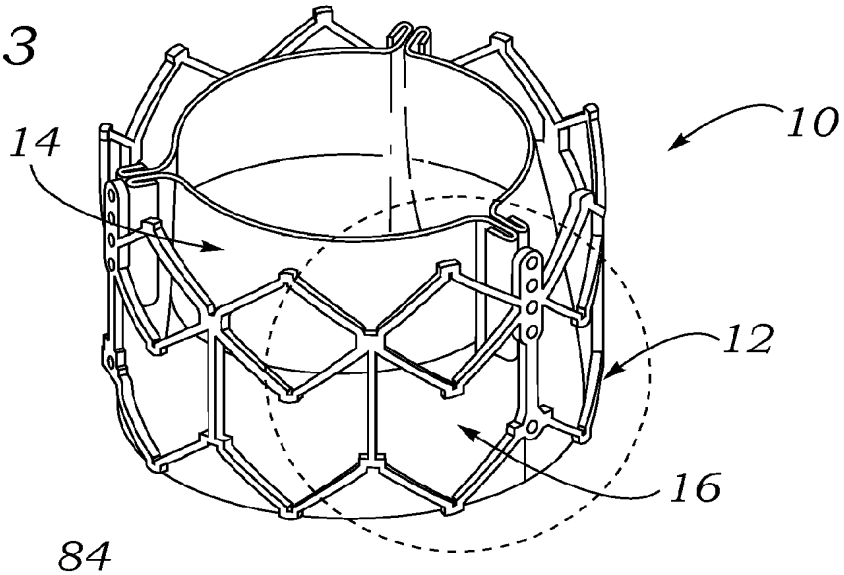


Fig. 4

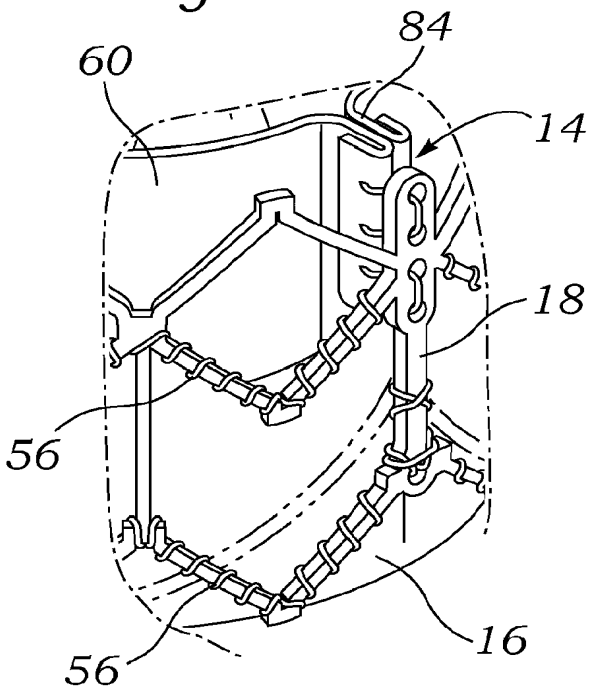
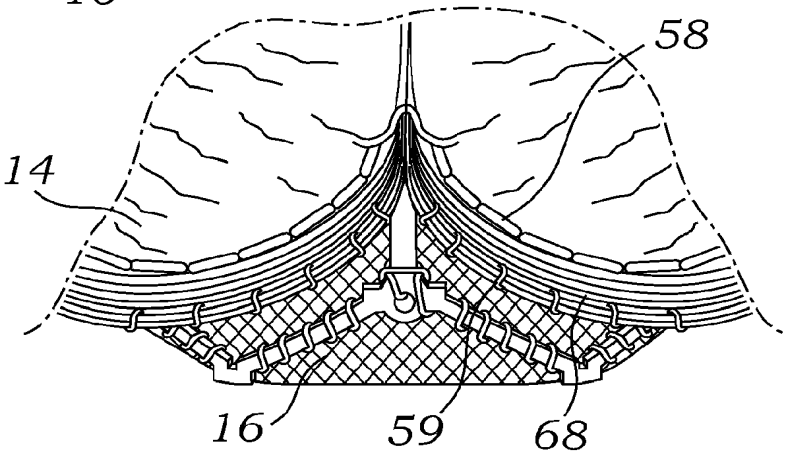


Fig. 5



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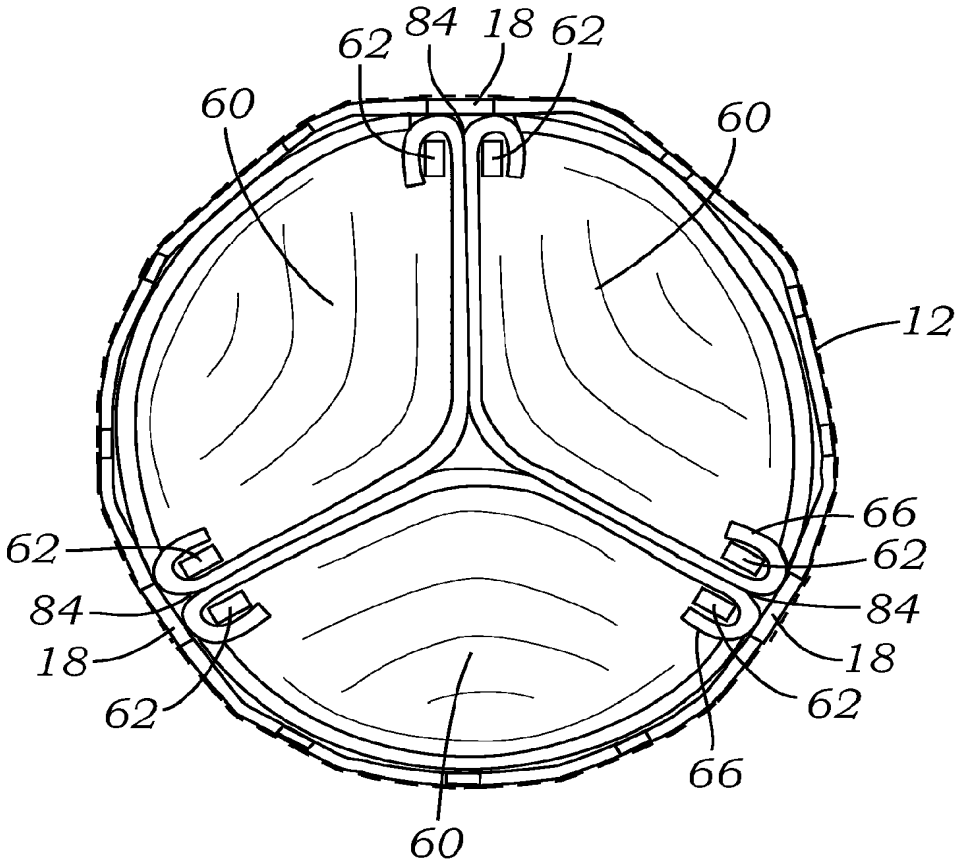

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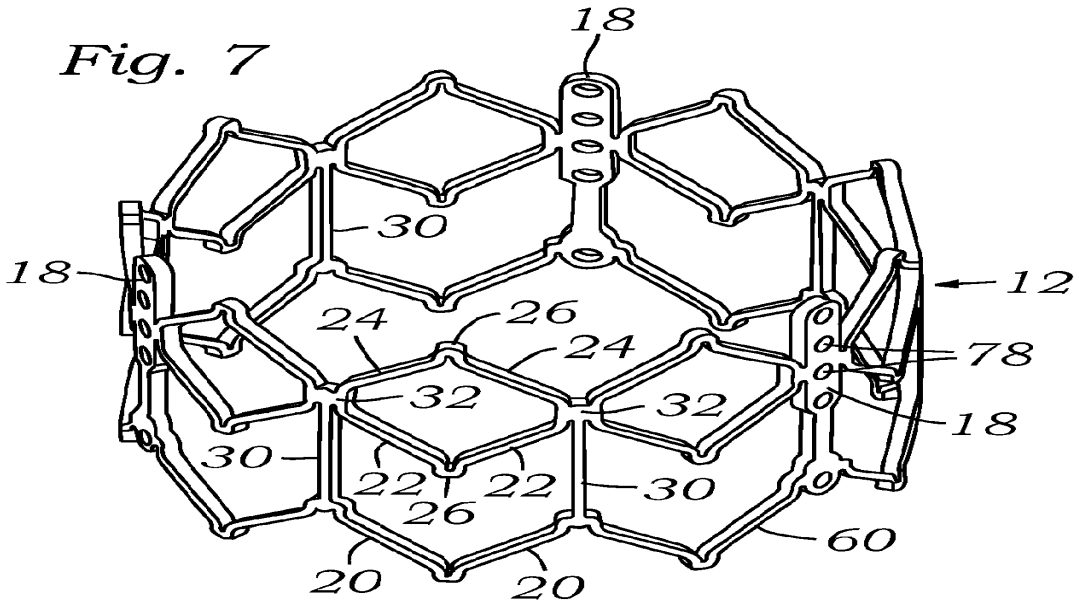

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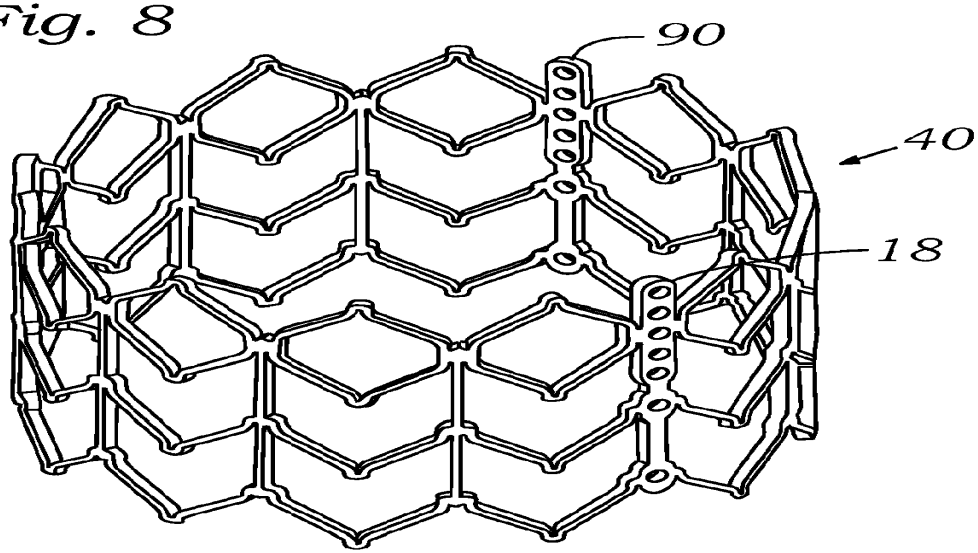

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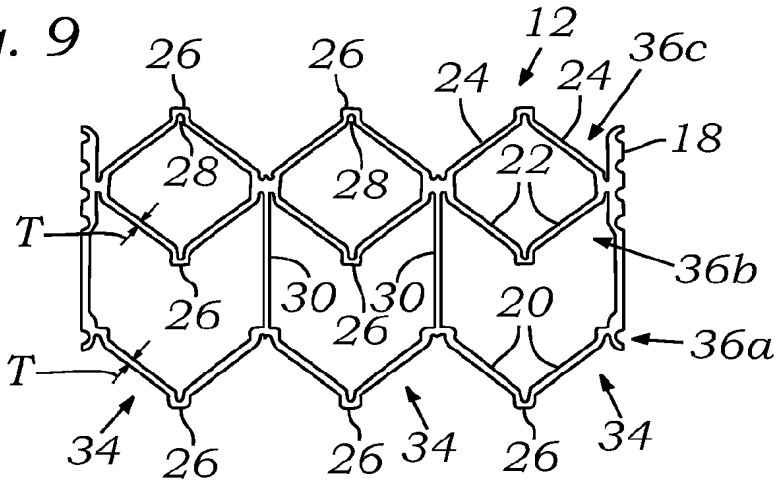

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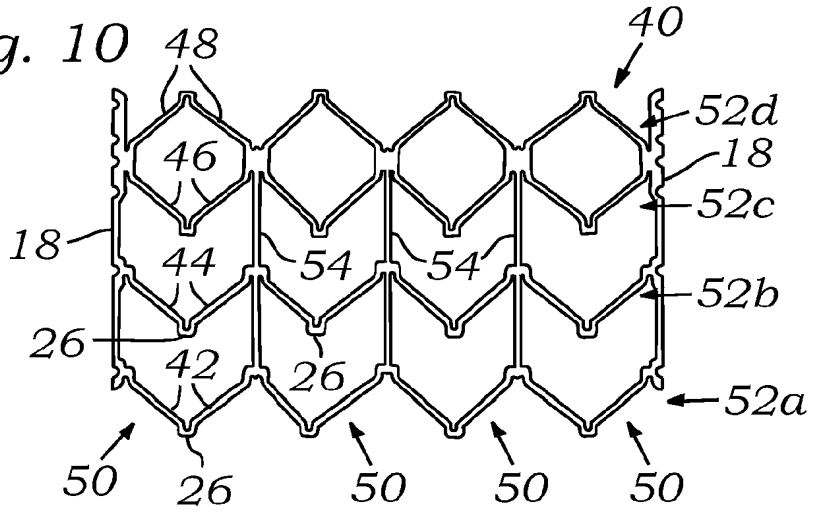

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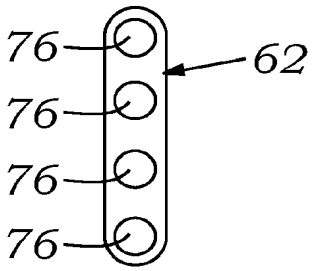

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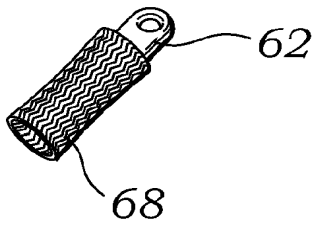

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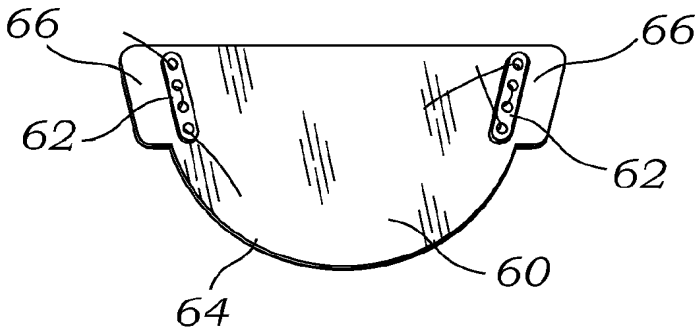

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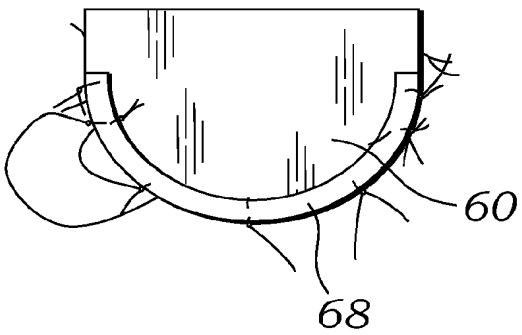


Fig. 15

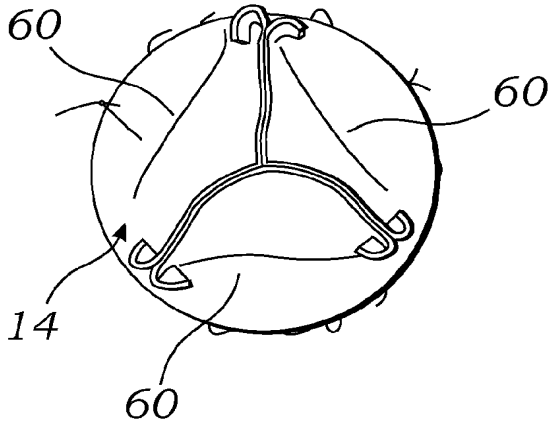
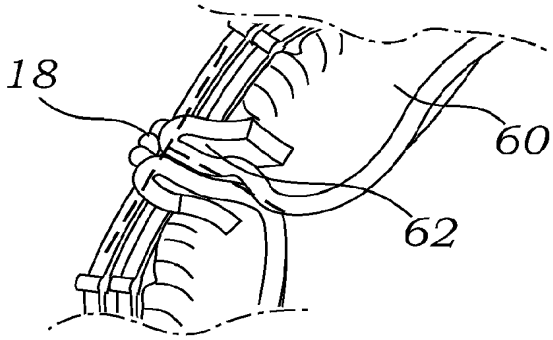


Fig. 6A



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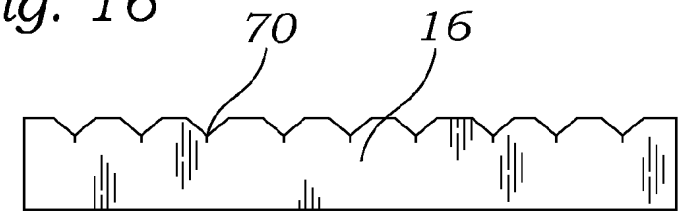

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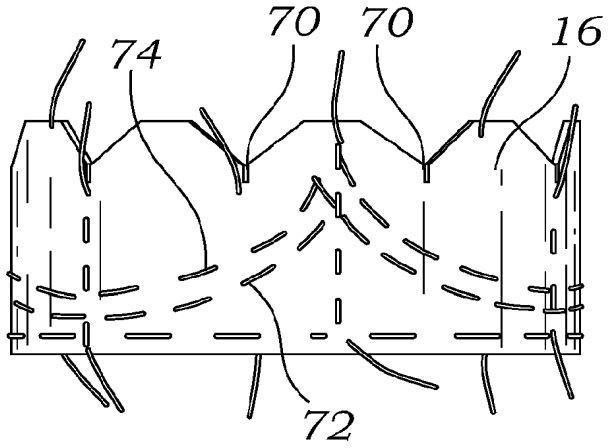

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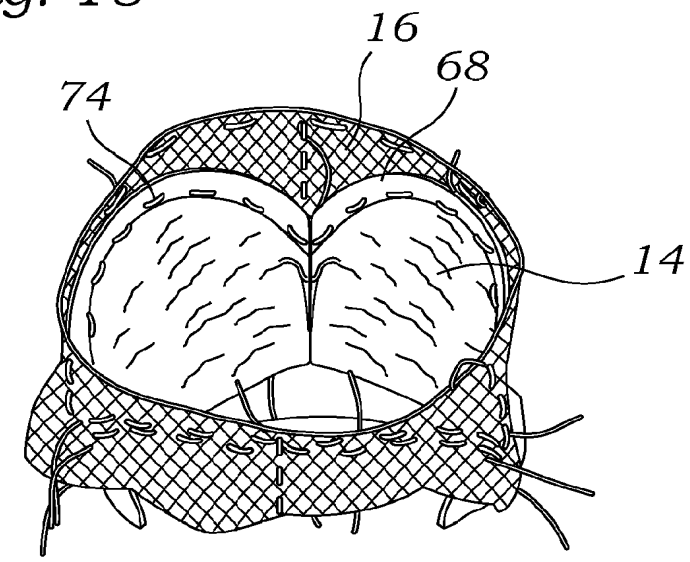

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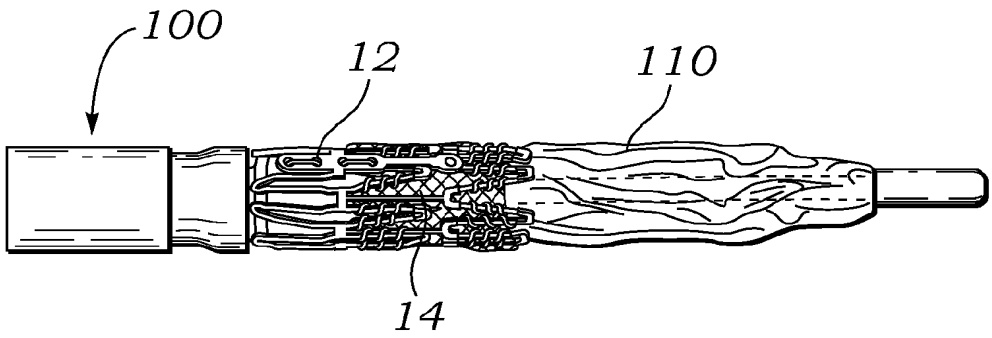

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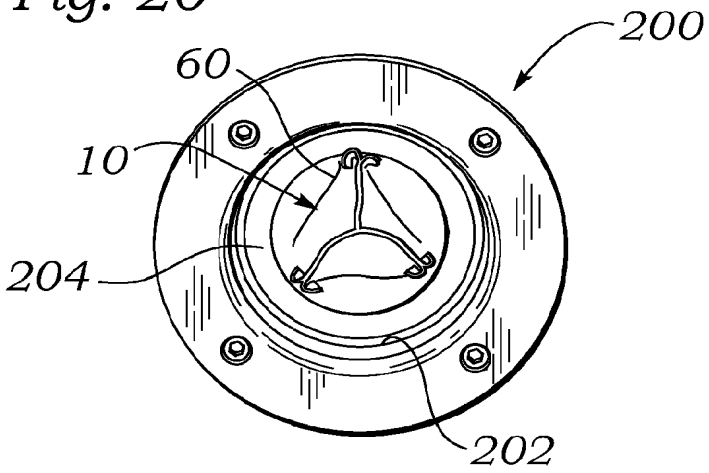

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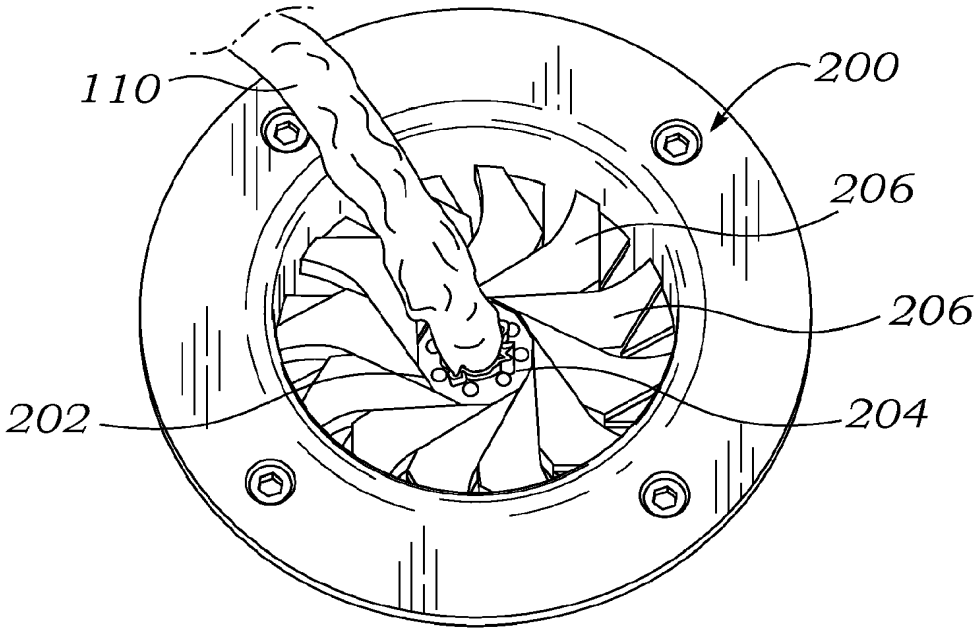

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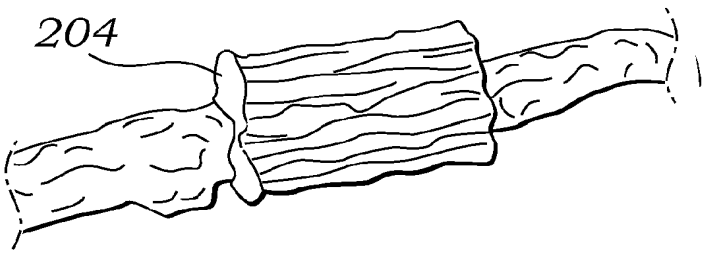
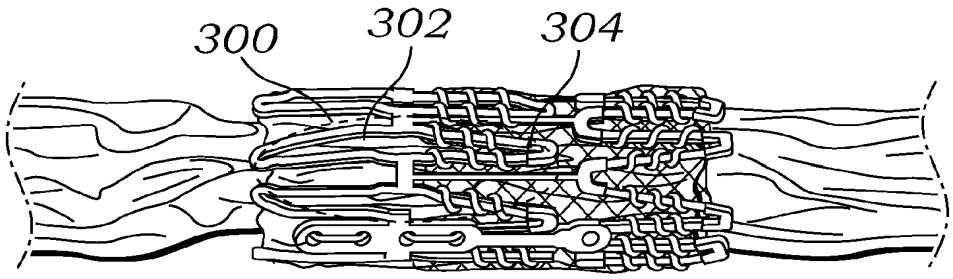


Fig. 23



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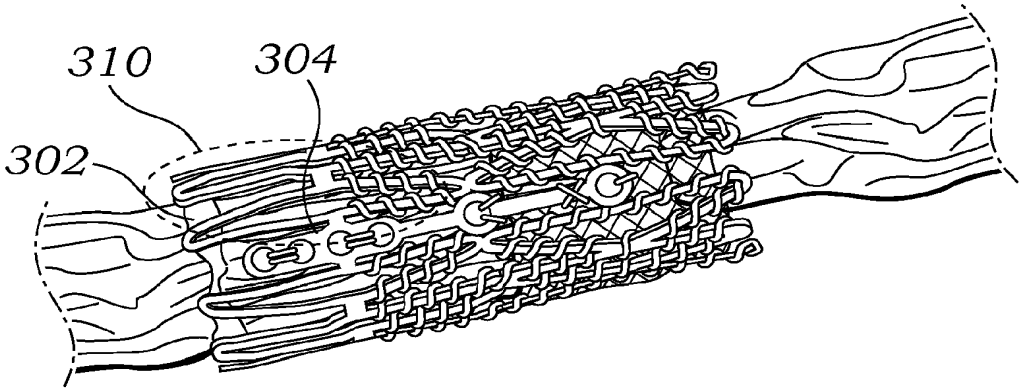

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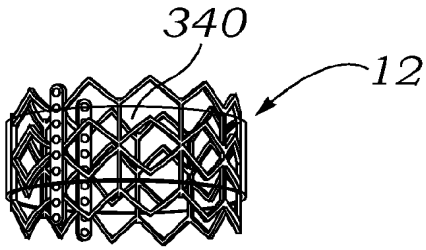

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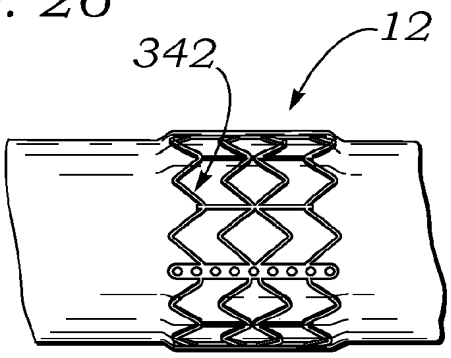

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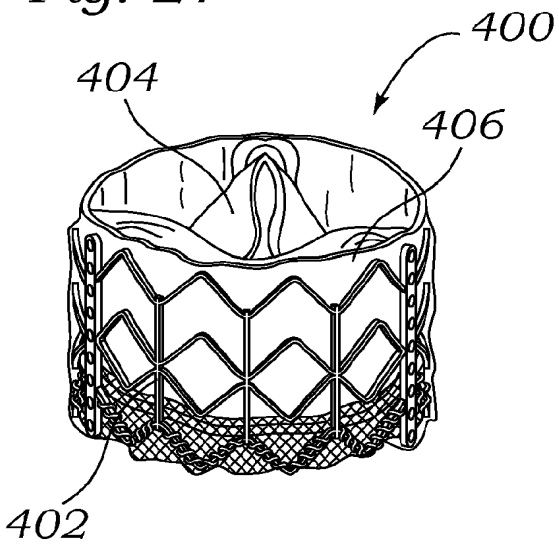

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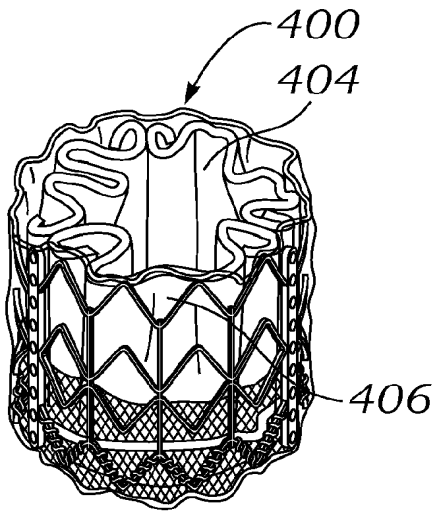

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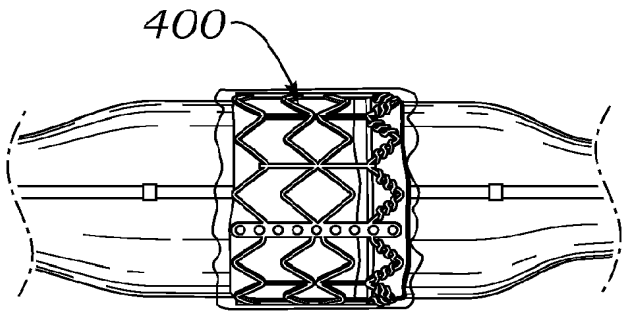


Fig. 30A

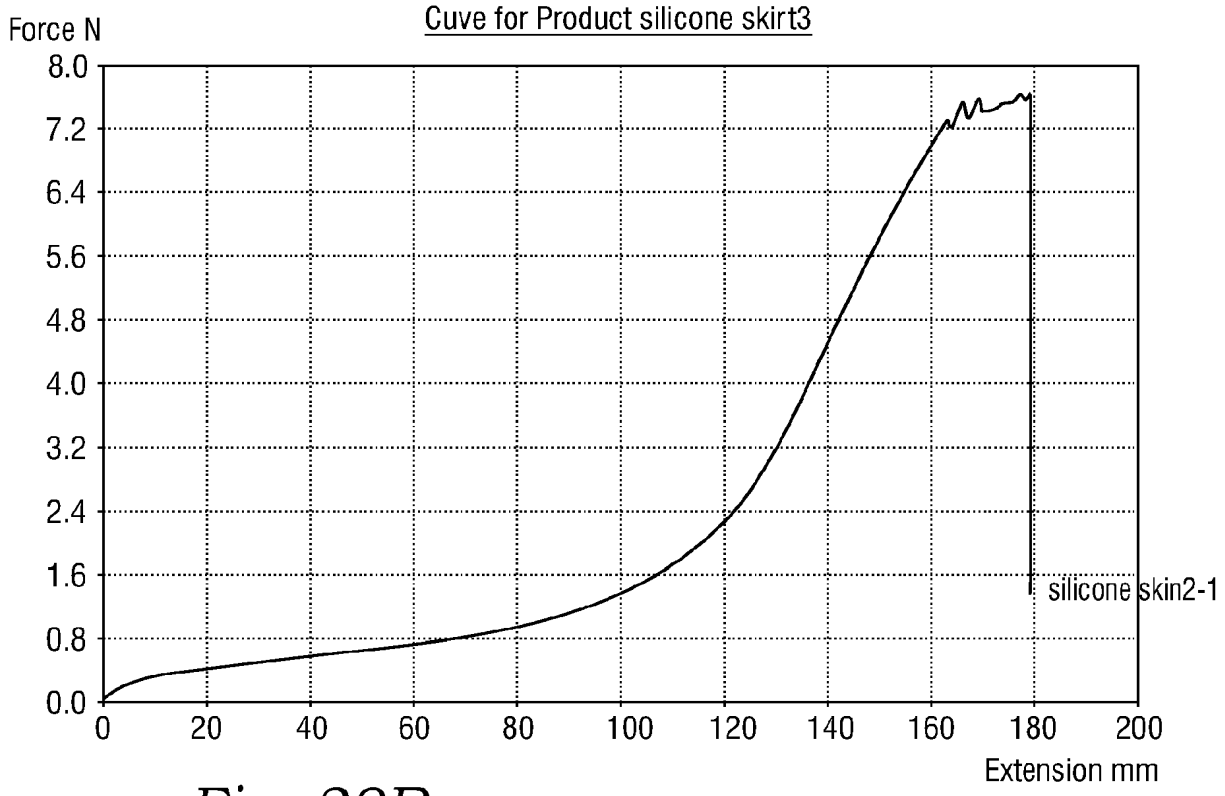


Fig. 30B

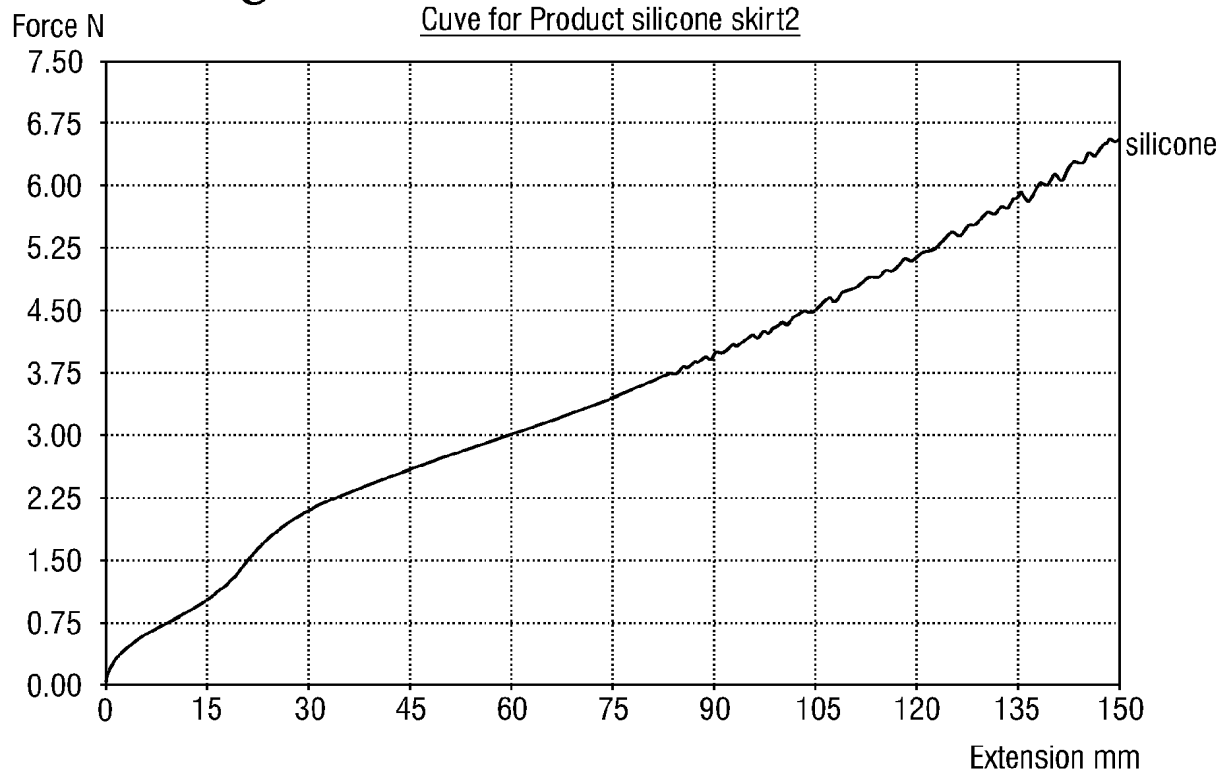


Fig. 30C

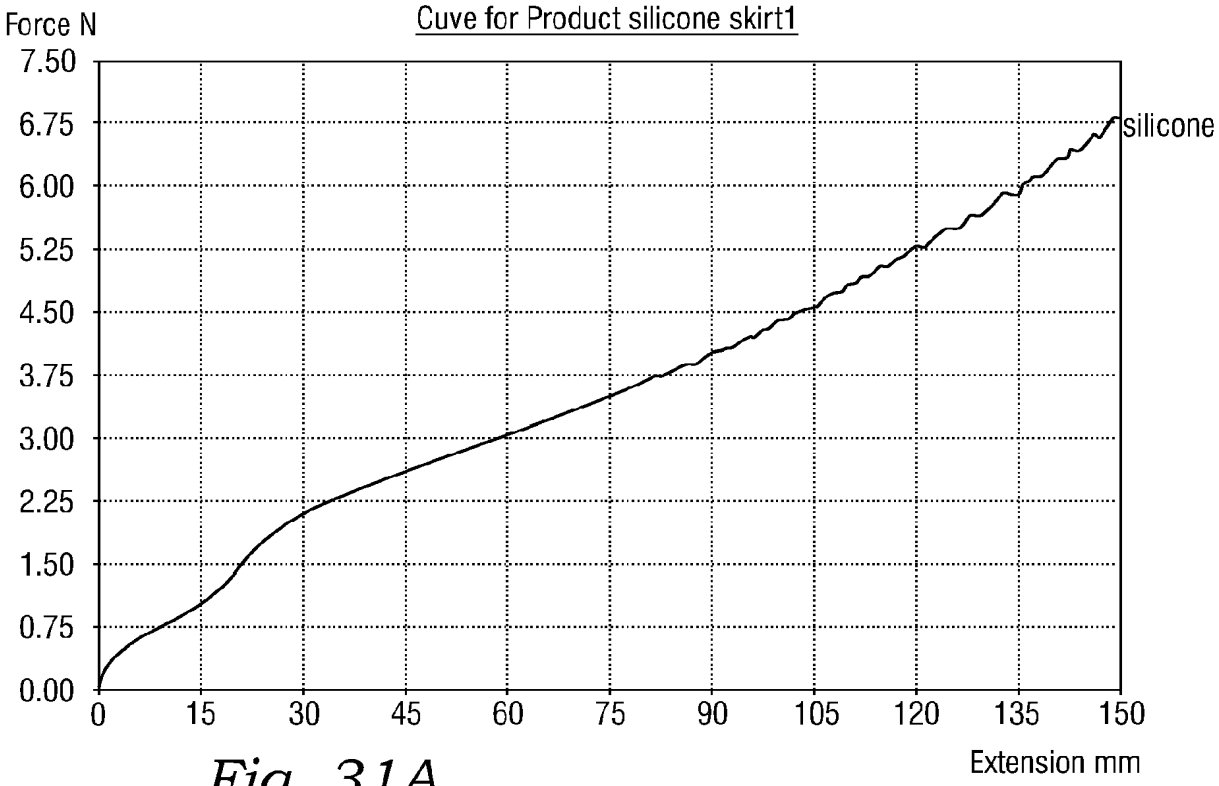


Fig. 31A

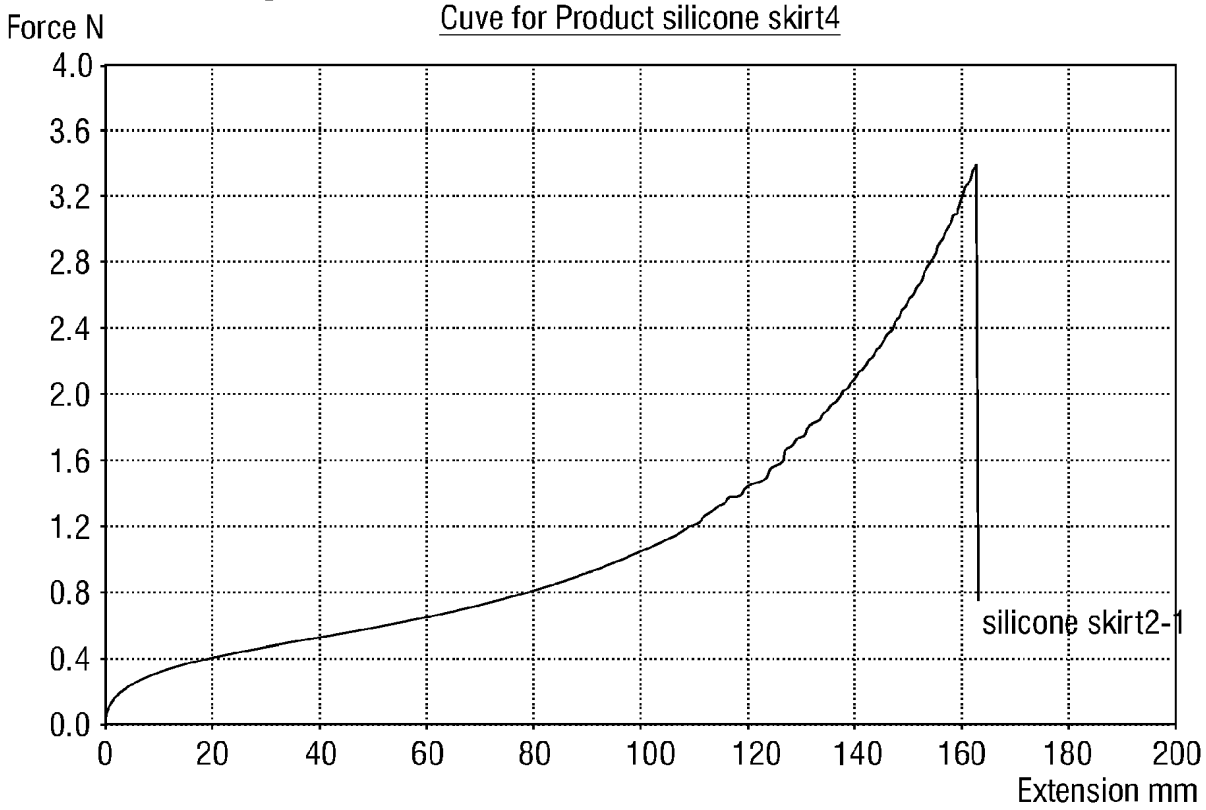


Fig. 31B

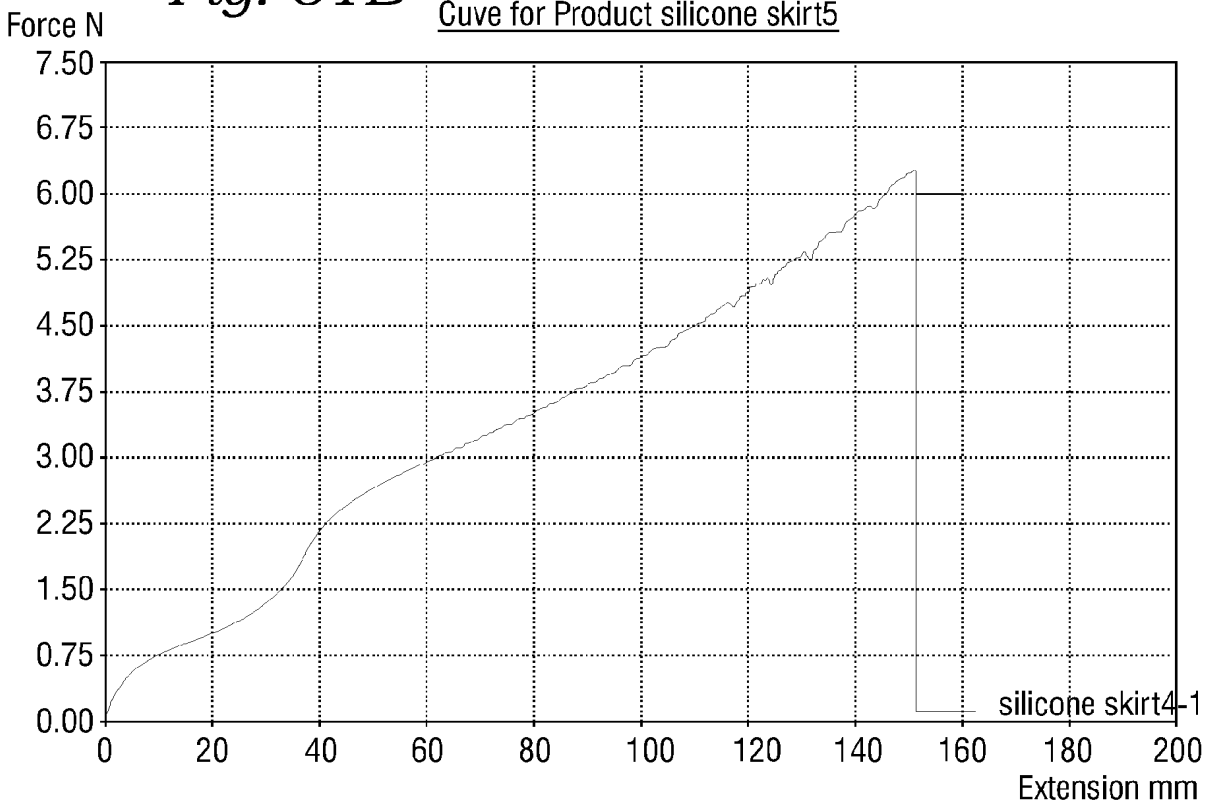


Fig. 31C

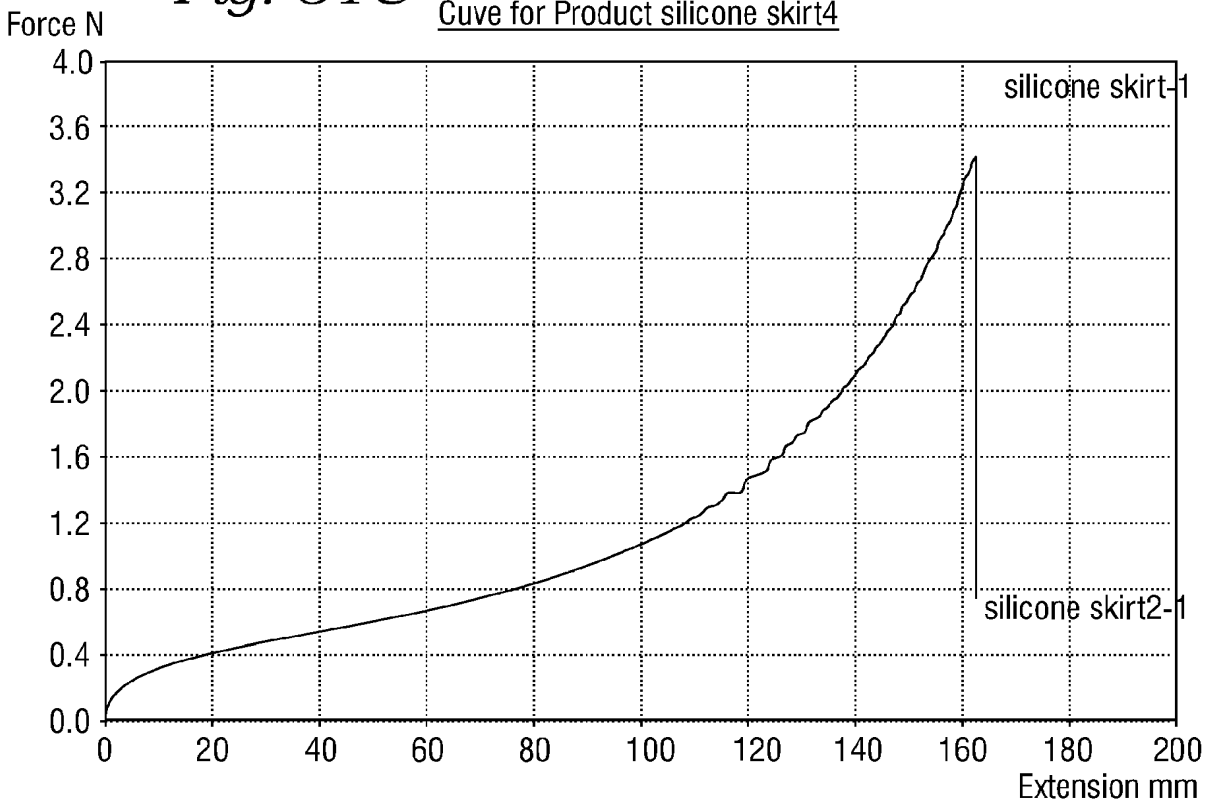


Fig. 31D

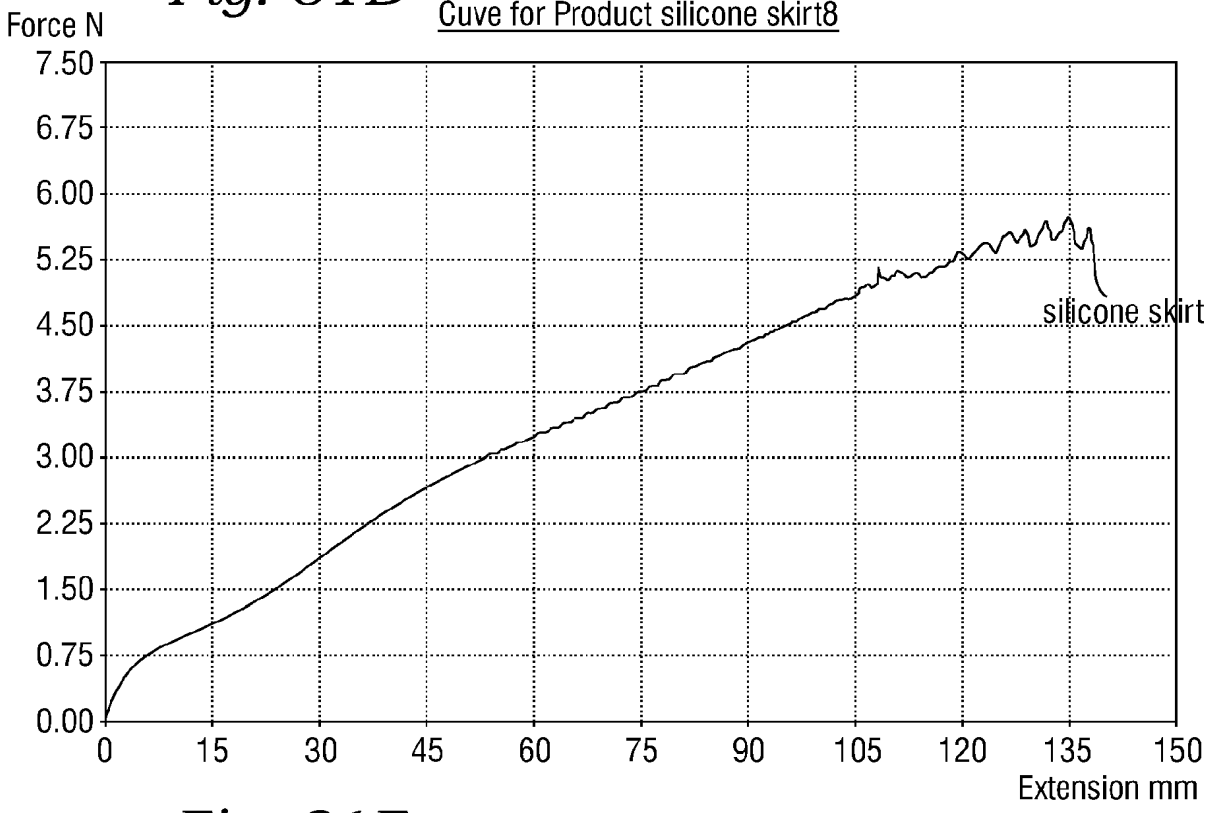


Fig. 31E

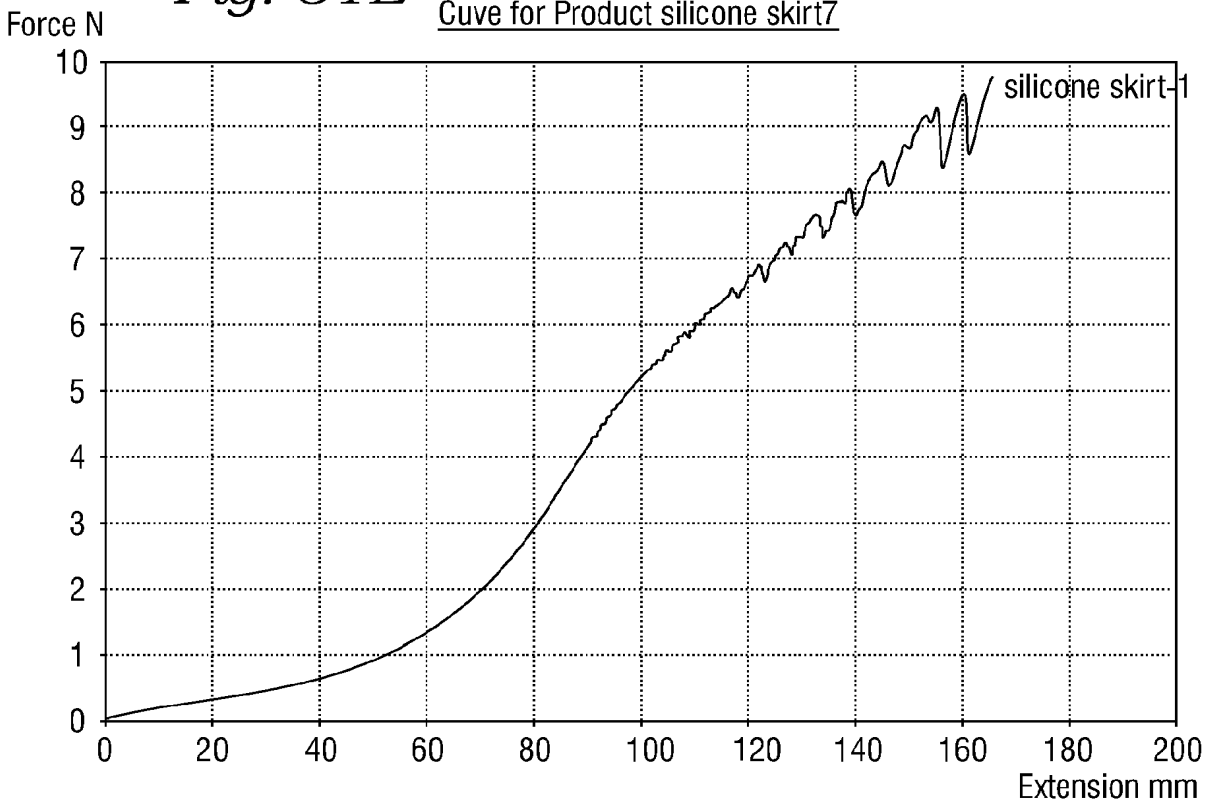
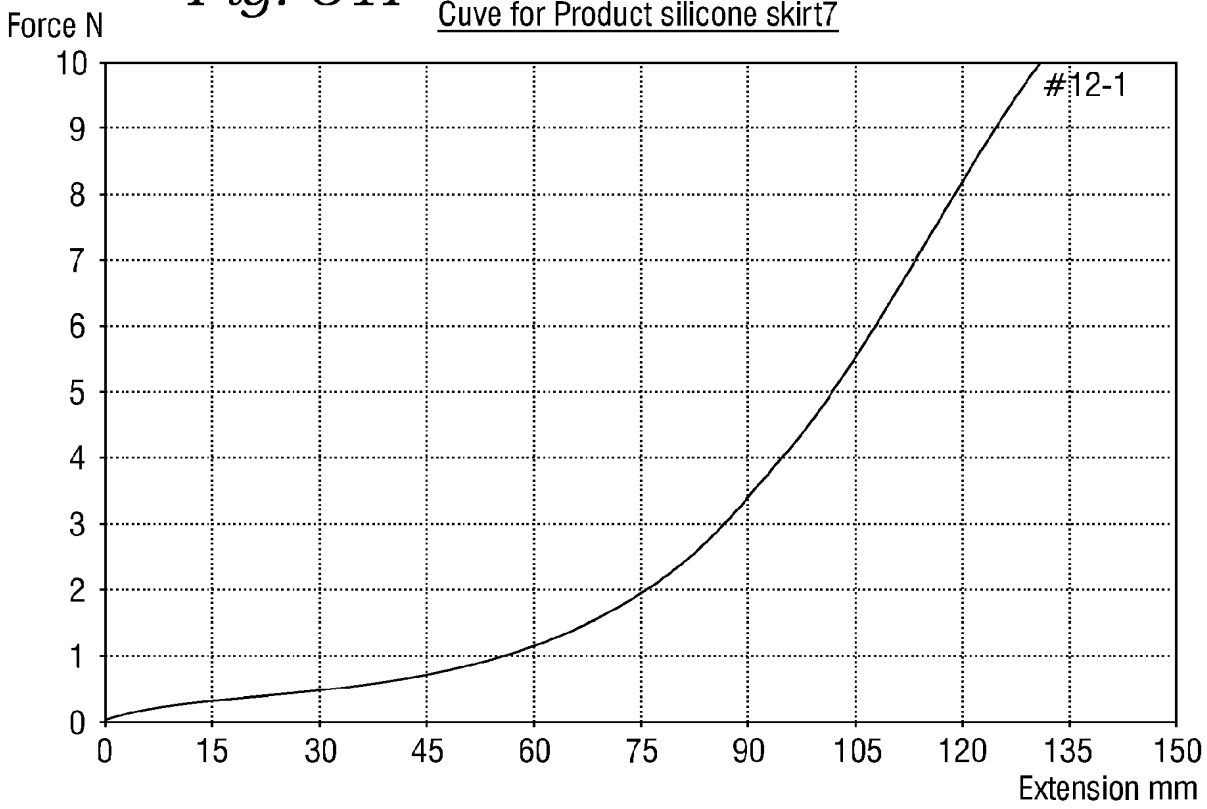


Fig. 31F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Electronic Acknowledgement Receipt

EFS ID:	22601705
Application Number:	13675665
International Application Number:	
Confirmation Number:	1995
Title of Invention:	PERCUTANEOUSLY IMPLANTABLE REPLACEMENT HEART VALVE DEVICE AND METHOD OF MAKING SAME
First Named Inventor/Applicant Name:	David Paniagua
Customer Number:	29880
Filer:	Mark Lauren Yaskanin/Carol Donahue
Filer Authorized By:	Mark Lauren Yaskanin
Attorney Docket Number:	109978.10101
Receipt Date:	11-JUN-2015
Filing Date:	13-NOV-2012
Time Stamp:	13:27:51
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	no

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Information Disclosure Statement (IDS) Form (SB08)	Colibri_10101_Supp_IDS_2015-06-11.PDF	630914 cb7e1b14285a606c19e0412f70eb4b4518ef661e	no	4

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2	Foreign Reference	WO-1995-005207.PDF	1830719 8d8439b132e183e99b8eda6fd6531f7684b0a3a4	no	41
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New International Application Filed with the USPTO as a Receiving Office

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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
13/675,665	11/13/2012	David Paniagua	109978.10101	1995

29880 7590 07/06/2015

FOX ROTHSCHILD LLP
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EXAMINER
MILLER, CHERYL L

ART UNIT	PAPER NUMBER
3738	

NOTIFICATION DATE	DELIVERY MODE
07/06/2015	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

ipdocket@foxrothschild.com

Office Action Summary	Application No. 13/675,665	Applicant(s) PANIAGUA ET AL.	
	Examiner CHERYL MILLER	Art Unit 3738	AIA (First Inventor to File) Status No

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTHS FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *7/11/2013*.

☐ A declaration(s)/affidavit(s) under **37 CFR 1.130(b)** was/were filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on _____; the restriction requirement and election have been incorporated into this action.

4)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims*

5)☒ Claim(s) *1-10,27-29 and 33* is/are pending in the application.

5a) Of the above claim(s) _____ is/are withdrawn from consideration.

6)☐ Claim(s) _____ is/are allowed.

7)☒ Claim(s) *1-10,27-29 and 33* is/are rejected.

8)☐ Claim(s) _____ is/are objected to.

9)☐ Claim(s) _____ are subject to restriction and/or election requirement.

* If any claims have been determined allowable, you may be eligible to benefit from the **Patent Prosecution Highway** program at a participating intellectual property office for the corresponding application. For more information, please see http://www.uspto.gov/patents/init_events/pph/index.jsp or send an inquiry to PPHfeedback@uspto.gov.

Application Papers

10)☐ The specification is objected to by the Examiner.

11)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

Certified copies:

a)☐ All b)☐ Some** c)☐ None of the:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

** See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)

2) ☒ Information Disclosure Statement(s) (PTO/SB/08a and/or PTO/SB/08b) Paper No(s)/Mail Date _____.

3) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .

4) ☐ Other: _____.

DETAILED ACTION

Notice of Pre-AIA or AIA Status

The present application is being examined under the pre-AIA first to invent provisions.

Claim Rejections - 35 USC § 112

The following is a quotation of 35 U.S.C. 112(b):
(b) CONCLUSION.—The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the inventor or a joint inventor regards as the invention.

The following is a quotation of 35 U.S.C. 112 (pre-AIA), second paragraph:
The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-10, 27-29, and 33 are rejected under 35 U.S.C. 112(b) or 35 U.S.C. 112 (pre-AIA), second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which the inventor or a joint inventor, or for pre-AIA the applicant regards as the invention.

Claim 1 recites the limitations "the inner cavity" and “said artificial valve’s outer surface” in lines 3 and 4 respectively. There is insufficient antecedent basis for these limitations in the claim. Claims 2-10 depend upon claim 1 and inherit all issues with the claim.

Also in claim 1, line 3 recites “and disposed within the inner cavity of said stent member affixed at one or more points". It is unclear 1) what exactly is disposed in the inner cavity, and 2) what is affixed. The clause seems to be a plurality of fragments that does not appear to be grammatically clear. The claim lacks a colon after the preamble and seems to missing dividing commas or semicolons within the claim.

Claim 1 lines 5-7 recites, “cusps or leaflets formed by folding of a sheet of said biocompatible tissue material without affixing of separate cusps or leaflets or cutting slits into

said material to form said cusps or leaflets." This is unclear as to 1) what the separate cusps are not affixed to, 2) “or leaflets" in an incomplete fragment, 3) if cutting slits is intended to be an option or if it is supposed to mean without cutting slits, 4) is "to form said cusps or leaflets” different/in addition to “cusps or leaflets formed by” or intended to refer to the same forming process.

Claim 6 recites the limitation "the patient" in line 3. There is insufficient antecedent basis for this limitation in the claim.

Claim 7 is indefinite as the biocompatible tissue material is required to be synthetic. Tissue and synthetic appear to be alternatives to one another and thus in direct conflict with one another. Claim 8 depends upon claim 7 and inherits all issues associated with the claim.

Claim 8 appears to be a Markush style claim, however is missing an “and” following “metal alloy”.

Claim 27 recites the limitations "the inner cavity", “said artificial valve’s outer surface”, “said sheet”, and “said cusps” in lines 3, 4, 7, and 7 respectively. There is insufficient antecedent basis for these limitations in the claim. Claims 28-29 depend upon claim 27 and inherit all issues with the claim.

Also in claim 27, line 3 recites “and disposed within the inner cavity of said stent member affixed at one or more points". It is unclear 1) what exactly is disposed in the inner cavity, and 2) what is affixed. The clause seems to be a plurality of fragments that does not appear to be grammatically clear. The claim lacks a colon after the preamble and seems to missing dividing commas or semicolons within the claim.

Claim 27 lines 5-7 recites, “a leaflet or cusp portion formed by folding of a first sheet portion of said biocompatible tissue material without affixing of separate cusps or leaflets or cutting slits into said sheet to form said cusps or leaflets." This is unclear as to 1) what the separate cusps are not affixed to, 2) “or leaflets" in an incomplete fragment, 3) if cutting slits is intended to be an option or if it is supposed to mean without cutting slits, 4) is "to form said cusps or leaflets” different than “a leaflet or cusp portion formed by” or intended to refer to the same forming process (one is singular and other is plural, and the separate cusps or leaflets of line 6 are not affixed thus not present to form by cutting slits).

Claim 29 recites the limitation "the form" in line 1. There is insufficient antecedent basis for this limitation in the claim. Applicant may consider changing "suturing is in the form of double continuous sutures” to recite --suturing comprises double continuous sutures--.

Claim 33 recites the limitations "the inner cavity", “said artificial valve’s outer surface”, “said sheet”, and “said cusps” in lines 3, 4, 7, and 7 respectively. There is insufficient antecedent basis for these limitations in the claim.

Also in claim 33, line 3 recites “and disposed within the inner cavity of said stent member affixed at one or more points". It is unclear 1) what exactly is disposed in the inner cavity, and 2) what is affixed. The clause seems to be a plurality of fragments that does not appear to be grammatically clear. The claim lacks a colon after the preamble and seems to missing dividing commas or semicolons within the claim.

Claim 33 lines 5-7 recites, “a leaflet or cusp portion formed by folding of a first sheet portion of said biocompatible tissue material without affixing of separate cusps or leaflets or cutting slits into said sheet to form said cusps or leaflets." This is unclear as to 1) what the

separate cusps are not affixed to, 2) “or leaflets" in an incomplete fragment, 3) if cutting slits is intended to be an option or if it is supposed to mean without cutting slits, 4) is "to form said cusps or leaflets” different than “a leaflet or cusp portion formed by” or intended to refer to the same forming process.

Here is an example of a modified claim 1 that would seemingly clear up any 112 2nd indefiniteness (emphasis added):

> A percutaneously implantable replacement heart valve device comprising**:**
>
> an expandable stent member **having an inner cavity;** and
>
> a flexible, compressible artificial valve **having leaflets**;
>
> the artificial valve disposed within the inner cavity of the stent member, **and an outer surface** of the artificial valve being affixed **to** said stent member at one or more points,
>
> said leaflets formed by folding a sheet of biocompatible tissue material without affixing separate leaflets **together and without** cutting slits into said material.

Product-by-Process

It is noted that claims 1, 27, and 33 each contain a product by process limitation wherein the leaflets or cusps (or leaflet/cusp portion) is *formed by* folding a sheet portion without affixing separate cusps or cutting slits to form cusps/leaflets. Because these are product claims, patentable weight has been given to the end product structure, and not the method of manufacture/forming. See MPEP 2113.

"[E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." *In re Thorpe*, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985) (citations omitted).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of pre-AIA 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-2, 7-8, 10, 27-28, and 33 are rejected under pre-AIA 35 U.S.C. 102e as being anticipated by Cribier (US 6,908,481 B2). Referring to claims 1, 33, Cribier discloses a percutaneously implantable replacement heart valve device (13; fig.4, 6b for example; col.1, lines 15-19) comprising an expandable stent (10; expands from compressed state in fig.4a to expanded state in fig.4b; col.10, lines 49-51) and a flexible, compressible artificial valve (14 or 14+19) made of biocompatible tissue material (col.10, lines 52-58) and disposed within the inner cavity of the stent (see fig.4, 6b, 6d) affixed at one or more points on the valves outer surface to the stent (at point 18, see fig.6b; col.11, lines 34-36), the valve (14 or 14+19) having cusps or leaflets (cusp/leaflet portion, 16) formed by folding a sheet of the material (synthetic or

pericardium, col.14 line 61-col.15 line 9; folds/pleats made so material will collapse along these folds/pleats, col.15, lines 36-52; col.5, lines 7-11) without affixing separate cusps or leaflets.

Referring to claims 2, 7-8, and 10, Cribier discloses the stent member (10) to be made of stainless steel (col.5, lines 55-57), the valve (14) comprising a biological material (pericardium) or a synthetic material such as PTFE (Teflon, col.5, lines 20-27), the stent (10) is balloon catheter expandable (col.9, lines 11-13; fig.12-13).

Referring to claims 27-28, Cribier further discloses the leaflet or cusp (16) formed by folding a first sheet portion (folds/pleats in 14; col.15, lines 36-53; col.4, lines 51-52; col.5, lines 7-11), and an outer tubular cuff (19) formed by folding a second sheet portion (see fig.6d for example; fold at bottom of stent), the first (14) and second (19) sheet portions affixed together (see fig.6d; col.13, lines 57-65), such as by continuous suturing (sewing, col.13, lines 57-65, continuous suture, col.13, lines 33-35).

Claims 1 and 9 are rejected under pre-AIA 35 U.S.C. 102e as being anticipated by Spenser et al. (US 6,893,460 B2). Spenser discloses a percutaneously implantable replacement heart valve device (fig.23e) comprising an expandable stent (380; col.16, lines 11-20) and a flexible, compressible artificial valve (370/371; fig.23b) made of biocompatible tissue material (may be pericardium patch, col.15, lines 51-54) and disposed within the inner cavity of the stent (fig.23e) affixed at one or more points on the valves outer surface to the stent (fig.23e, suture lines), the valve (370/371) having cusps or leaflets (378) formed by folding a sheet of the material (fold 370/371 from a sheet into a tube, and fold at suture lines 373; col.15, lines 44-46,

57-61) without affixing separate cusps or leaflets (see figs.23a-23e). Spenser discloses the stent (380) to be self-expandable (shape memory, col.8, lines 24-34).

Claim Rejections - 35 USC § 103

The following is a quotation of pre-AIA 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 3-5 are rejected under pre-AIA 35 U.S.C. 103(a) as being unpatentable over Cribier (US 6,908,481 B2) in view of Dewanjee (US 4,553,974). Cribier discloses the tissue material to be pericardium for example, and is silent to the specific source of pericardium, however discloses such materials are common in cardiac surgery (col.5, lines 20-30; col.15, lines 6-9). Dewanjee teaches in the same field of tissues useful as prostheses such as heart valve leaflets (col.1, lines 8-11; col.3, lines 50-55), specific sources of pericardium to include calf pericardium (juvenile) and porcine pericardium (col.3, lines 50-55; col.10, lines 53-58). It would have been obvious to one having ordinary skill in the art at the time the invention was made to combine Cribier's implant having pericardium tissue generically, with Dewanjee's teaching of known specific types of pericardium (bovine calf and porcine) for valve leaflet applications, as such is shown to be an obvious known material in the art.

Claim 6 is rejected under pre-AIA 35 U.S.C. 103(a) as being unpatentable over Cribier (US 6,908,481 B2) in view of Cox (US 2002/0032482 A1). Cribier discloses the tissue material to be pericardium for example, and is silent to the specific source of pericardium, however

discloses such materials are common in cardiac surgery (col.5, lines 20-30; col.15, lines 6-9). Cox teaches in the same field of tissues useful as prostheses such as heart valve leaflets that may or may not be stented (P0105, P0115, P0116), specific materials being autologous flat sheet pericardium as a known type of pericardium for valve leaflet use as it provides more biocompatibility than foreign tissues sources (P0072, P0122, P0125). It would have been obvious to one having ordinary skill in the art at the time the invention was made to combine Cribier's implant having pericardium tissue generically, with Cox's teaching of specifically autologous pericardium as a known pericardium for valve leaflet applications, as such is shown to be an obvious known material in the art that provides increased biocompatibility.

Claim 29 is rejected under pre-AIA 35 U.S.C. 103(a) as being unpatentable over Cribier (US 6,908,481 B2) in view of Deac (US 5,344,442). Cribier discloses the replacement heart valve substantially as claimed (see above), comprising two sheet portions sutured together by continuous suture lines (sewing, col.13, lines 57-65, continuous suture, col.13, lines 33-35), however is silent to mention if they are single or double. Deac teaches in the same field of heart valve prostheses, use of double continuous sutures to affix two tissue sheets together (col.5, lines 36-60; col.6, lines 45-55) as a known suturing technique for sewing tissue membrane material. It would have been obvious to one having ordinary skill in the art at the time the invention was made to combine Deac's taught double continuous suturing technique with Cribier's implant having membranes sutured, so as to use Deac's specific suturing as such is taught to be known mode for suturing tissue in the field of heart valve prostheses.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Cheryl Miller whose telephone number is 571-272-4755. The examiner can normally be reached on M- F (8am-5:30pm).

If attempts to reach the examiner by telephone are unsuccessful, please contact the examiner's supervisor, Thomas Sweet at 571-272-4761. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/C. M./
Examiner, Art Unit 3738
/THOMAS J SWEET/
Supervisory Patent Examiner, Art Unit 3738

Notice of References Cited	Application/Control No. 13/675,665	Applicant(s)/Patent Under Reexamination PANIAGUA ET AL.	
	Examiner CHERYL MILLER	Art Unit 3738	Page 1 of 1

U.S. PATENT DOCUMENTS

*		Document Number Country Code-Number-Kind Code	Date MM-YYYY	Name	Classification
*	A	US-6,908,481 B2	06-2005	Cribier, Alain	623/2.11
*	B	US-6,893,460 B2	05-2005	Spenser et al.	623/2.14
*	C	US-2002/0032482 A1	03-2002	Cox, James L.	623/2.16
*	D	US-4,553,974	11-1985	Dewanjee, Mrinal K.	8/94.11
*	E	US-5,344,442	09-1994	Deac, Radu	623/2.12
	F	US-			
	G	US-			
	H	US-			
	I	US-			
	J	US-			
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	L	US-			
	M	US-			

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*		Include as applicable: Author, Title Date, Publisher, Edition or Volume, Pertinent Pages)
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*A copy of this reference is not being furnished with this Office action. (See MPEP § 707.05(a).)
Dates in MM-YYYY format are publication dates. Classifications may be US or foreign.

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(Not for submission under 37 CFR 1.99)

Application Number	13675665
Filing Date	2012-11-13
First Named Inventor	David Paniagua
Art Unit	3738
Examiner Name	Cheryl L. MILLER
Attorney Docket Number	109978.10101

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Examiner Initial*	Cite No	Patent Number	Kind Code[1]	Issue Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
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Examiner Initials*	Cite No	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc), date, pages(s), volume-issue number(s), publisher, city and/or country where published.	T[5]

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /CM/

Receipt date: 11/20/2014	Application Number	13675665 13675665 - GAU: 3738
INFORMATION DISCLOSURE STATEMENT BY APPLICANT (**Not for submission under 37 CFR 1.99)**	Filing Date	2012-11-13
	First Named Inventor	David Paniagua
	Art Unit	3738
	Examiner Name	Cheryl L. MILLER
	Attorney Docket Number	109978.10101

	1	Cross-reference is made to U.S. Application No. 14/502,453 filed on September 30, 2014, and its associated Preliminary Amendment (109978.10106)	☐

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EXAMINER SIGNATURE

Examiner Signature	/Cheryl Miller/	Date Considered	06/27/2015

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through a citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

[1] See Kind Codes of USPTO Patent Documents at www.USPTO.GOV or MPEP 901.04. [2] Enter office that issued the document, by the two-letter code (WIPO Standard ST.3). [3] For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. [4] Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. [5] Applicant is to place a check mark here if English language translation is attached.

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /CM/

Receipt date: 11/20/2014	Application Number	13675665	13675665 - GAU: 3738
INFORMATION DISCLOSURE STATEMENT BY APPLICANT (**Not for submission under 37 CFR 1.99)**	Filing Date	2012-11-13	
	First Named Inventor	David Paniagua	
	Art Unit	3738	
	Examiner Name	Cheryl L. MILLER	
	Attorney Docket Number	109978.10101	

CERTIFICATION STATEMENT

Please see 37 CFR 1.97 and 1.98 to make the appropriate selection(s):

☐ That each item of information contained in the information disclosure statement was first cited in any communication from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e)(1).

OR

☐ That no item of information contained in the information disclosure statement was cited in a communication from a foreign patent office in a counterpart foreign application, and, to the knowledge of the person signing the certification after making reasonable inquiry, no item of information contained in the information disclosure statement was known to any individual designated in 37 CFR 1.56(c) more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e)(2).

☐ See attached certification statement.

☐ The fee set forth in 37 CFR 1.17 (p) has been submitted herewith.

☒ A certification statement is not submitted herewith.

SIGNATURE

A signature of the applicant or representative is required in accordance with CFR 1.33, 10.18. Please see CFR 1.4(d) for the form of the signature.

Signature	/ Mark L. Yaskanin /	Date (YYYY-MM-DD)	2014-11-20
Name/Print	Mark L. Yaskanin	Registration Number	45246

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 1 hour to complete, including gathering, preparing and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

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Privacy Act Statement

The Privacy Act of 1974 (P.L. 93-579) requires that you be given certain information in connection with your submission of the attached form related to a patent application or patent. Accordingly, pursuant to the requirements of the Act, please be advised that: (1) the general authority for the collection of this information is 35 U.S.C. 2(b)(2); (2) furnishing of the information solicited is voluntary; and (3) the principal purpose for which the information is used by the U.S. Patent and Trademark Office is to process and/or examine your submission related to a patent application or patent. If you do not furnish the requested information, the U.S. Patent and Trademark Office may not be able to process and/or examine your submission, which may result in termination of proceedings or abandonment of the application or expiration of the patent.

The information provided by you in this form will be subject to the following routine uses:

1. The information on this form will be treated confidentially to the extent allowed under the Freedom of Information Act (5 U.S.C. 552) and the Privacy Act (5 U.S.C. 552a). Records from this system of records may be disclosed to the Department of Justice to determine whether the Freedom of Information Act requires disclosure of these record s.

2. A record from this system of records may be disclosed, as a routine use, in the course of presenting evidence to a court, magistrate, or administrative tribunal, including disclosures to opposing counsel in the course of settlement negotiations.

3. A record in this system of records may be disclosed, as a routine use, to a Member of Congress submitting a request involving an individual, to whom the record pertains, when the individual has requested assistance from the Member with respect to the subject matter of the record.

4. A record in this system of records may be disclosed, as a routine use, to a contractor of the Agency having need for the information in order to perform a contract. Recipients of information shall be required to comply with the requirements of the Privacy Act of 1974, as amended, pursuant to 5 U.S.C. 552a(m).

5. A record related to an International Application filed under the Patent Cooperation Treaty in this system of records may be disclosed, as a routine use, to the International Bureau of the World Intellectual Property Organization, pursuant to the Patent Cooperation Treaty.

6. A record in this system of records may be disclosed, as a routine use, to another federal agency for purposes of National Security review (35 U.S.C. 181) and for review pursuant to the Atomic Energy Act (42 U.S.C. 218(c)).

7. A record from this system of records may be disclosed, as a routine use, to the Administrator, General Services, or his/her designee, during an inspection of records conducted by GSA as part of that agency's responsibility to recommend improvements in records management practices and programs, under authority of 44 U.S.C. 2904 and 2906. Such disclosure shall be made in accordance with the GSA regulations governing inspection of records for this purpose, and any other relevant (i.e., GSA or Commerce) directive. Such disclosure shall not be used to make determinations about individuals.

8. A record from this system of records may be disclosed, as a routine use, to the public after either publication of the application pursuant to 35 U.S.C. 122(b) or issuance of a patent pursuant to 35 U.S.C. 151. Further, a record may be disclosed, subject to the limitations of 37 CFR 1.14, as a routine use, to the public if the record was filed in an application which became abandoned or in which the proceedings were terminated and which application is referenced by either a published application, an application open to public inspections or an issued patent.

9. A record from this system of records may be disclosed, as a routine use, to a Federal, State, or local law enforcement agency, if the USPTO becomes aware of a violation or potential violation of law or regulation.

/Cheryl Miller/ 06/27/2015

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INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(Not for submission under 37 CFR 1.99)

Application Number	13675665
Filing Date	2012-11-13
First Named Inventor	David PANIAGUA
Art Unit	3738
Examiner Name	Cheryl L. MILLER
Attorney Docket Number	109978.10101

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	1	20020032481		2002-03-14	Gabbay	
	2	20030027332		2003-02-06	Lafrance et al.	
	3	20070061008		2007-03-15	Salahieh et al.	
	4	20100043197		2010-02-25	Abbate et al.	

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Receipt date: 08/29/2014	Application Number	13675665	13675665 - GAU: 3738
INFORMATION DISCLOSURE STATEMENT BY APPLICANT (**Not for submission under 37 CFR 1.99)**	Filing Date	2012-11-13	
	First Named Inventor	David PANIAGUA	
	Art Unit	3738	
	Examiner Name	Cheryl L. MILLER	
	Attorney Docket Number	109978.10101	

	1							☐

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Examiner Initials*	Cite No	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc), date, pages(s), volume-issue number(s), publisher, city and/or country where published.	T[5]
	1	HILBERT et al., "Biomechanics: Allograft Heart Valves," Cardiac Reconstructions with Allograft Tissues, Springer, New York (2005), pp. 210-212	☐
	2	Office Action issued June 9, 2014, in U.S. Application No. 14/253,650 (109978.10104)	☐
	3	Office Action issued July 8, 2014, in U.S. Application No. 14/253,656 (File: 109978.10113)	☐
	4	Office Action issued August 15, 2014, in U.S. Application No. 14/284,063 (File: 109978.10117)	☐

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Examiner Signature	/Cheryl Miller/	Date Considered	06/27/2015

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Receipt date: 08/29/2014	Application Number	13675665	13675665 - GAU: 3738
INFORMATION DISCLOSURE STATEMENT BY APPLICANT (**Not for submission under 37 CFR 1.99)**	Filing Date	2012-11-13	
	First Named Inventor	David PANIAGUA	
	Art Unit	3738	
	Examiner Name	Cheryl L. MILLER	
	Attorney Docket Number	109978.10101	

CERTIFICATION STATEMENT

Please see 37 CFR 1.97 and 1.98 to make the appropriate selection(s):

☐ That each item of information contained in the information disclosure statement was first cited in any communication from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e)(1).

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☐ That no item of information contained in the information disclosure statement was cited in a communication from a foreign patent office in a counterpart foreign application, and, to the knowledge of the person signing the certification after making reasonable inquiry, no item of information contained in the information disclosure statement was known to any individual designated in 37 CFR 1.56(c) more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e)(2).

☐ See attached certification statement.

☐ The fee set forth in 37 CFR 1.17 (p) has been submitted herewith.

☒ A certification statement is not submitted herewith.

SIGNATURE

A signature of the applicant or representative is required in accordance with CFR 1.33, 10.18. Please see CFR 1.4(d) for the form of the signature.

Signature	/ Mark L. Yaskanin /	Date (YYYY-MM-DD)	2014-08-29
Name/Print	Mark L. Yaskanin	Registration Number	45246

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 1 hour to complete, including gathering, preparing and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

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6. A record in this system of records may be disclosed, as a routine use, to another federal agency for purposes of National Security review (35 U.S.C. 181) and for review pursuant to the Atomic Energy Act (42 U.S.C. 218(c)).

7. A record from this system of records may be disclosed, as a routine use, to the Administrator, General Services, or his/her designee, during an inspection of records conducted by GSA as part of that agency's responsibility to recommend improvements in records management practices and programs, under authority of 44 U.S.C. 2904 and 2906. Such disclosure shall be made in accordance with the GSA regulations governing inspection of records for this purpose, and any other relevant (i.e., GSA or Commerce) directive. Such disclosure shall not be used to make determinations about individuals.

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INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(Not for submission under 37 CFR 1.99)

Application Number	13675665
Filing Date	2012-11-13
First Named Inventor	David PANIAGUA
Art Unit	3738
Examiner Name	Cheryl L. MILLER
Attorney Docket Number	109978.10101

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Examiner Initial*	Cite No	Patent Number	Kind Code[1]	Issue Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
	1	6676698		2004-01-13	McGuckin, Jr.	
	2	6733525		2004-05-11	Yang et al.	

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Receipt date: 09/17/2014	Application Number	13675665	13675665 - GAU: 3738
INFORMATION DISCLOSURE STATEMENT BY APPLICANT (**Not for submission under 37 CFR 1.99)**	Filing Date	2012-11-13	
	First Named Inventor	David PANIAGUA	
	Art Unit	3738	
	Examiner Name	Cheryl L. MILLER	
	Attorney Docket Number	109978.10101	

Examiner Initials*	Cite No	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc), date, pages(s), volume-issue number(s), publisher, city and/or country where published.	T[5]
	1	Office Action issued September 11, 2014, in U.S. Application No. 14/268,190 (File: 109978.10115)	☐
	2	Office Action issued September 3, 2014, in U.S. Application No. 14/284,049 (File: 109978.10116)	☐
	3	Office Action issued September 12, 2014, in U.S. Application No. 14/268,184 (File: 109978.10114)	☐

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Examiner Signature	/Cheryl Miller/	Date Considered	06/27/2015

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Name/Print	Mark L. Yaskanin	Registration Number	45246

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/Cheryl Miller/ 06/27/2015

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INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(Not for submission under 37 CFR 1.99)

Application Number	13675665
Filing Date	2012-11-13
First Named Inventor	David PANIAGUA
Art Unit	3738
Examiner Name	not assigned
Attorney Docket Number	109978.10101

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Examiner Initial*	Cite No	Patent Number	Kind Code[1]	Issue Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
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Examiner Initial*	Cite No	Publication Number	Kind Code[1]	Publication Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
	1	20020095994		2002-07-25	Vesely et al.	
	2	20020123789		2002-09-05	Francis et al.	
	3	20020128708		2002-09-21	Northrup et al.	
	4	20030078659		2003-04-24	Yang	
	5	20030102000		2003-06-05	Stevens et al.	

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Receipt date: 09/23/2013	Application Number	13675665	13675665 - GAU: 3738
INFORMATION DISCLOSURE STATEMENT BY APPLICANT (**Not for submission under 37 CFR 1.99)**	Filing Date	2012-11-13	
	First Named Inventor	David PANIAGUA	
	Art Unit	3738	
	Examiner Name	not assigned	
	Attorney Docket Number	109978.10101	

	6	20030130727		2003-07-10	Drasler et al.	
	7	20030130729		2003-07-10	Paniagua et al.	
	8	20030130731		2003-07-10	Vidlund et al.	
	9	20030153974		2003-08-14	Spenser et al.	
	10	20030187362		2003-10-02	Murphy et al.	
	11	20030195620		2003-10-16	Huynh et al.	
	12	20030204023		2003-10-30	Koob et al.	
	13	20030212460		2003-11-13	Darois et al.	
	14	20030212462		2003-11-13	Gryska et al.	
	15	20030217415		2003-11-27	Crouch et al.	
	16	20040024452		2004-02-05	Kruse et al.	

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	Art Unit	3738	
	Examiner Name	not assigned	
	Attorney Docket Number	109978.10101	

	17	20040055608		2004-03-25	Stevens et al.	
	18	20040059418		2004-03-25	McKay et al.	
	19	20040098092		2004-05-20	Butaric et al.	
	20	20040193261		2004-09-30	Berreklouw	
	21	20040243153		2004-12-02	Liddicoat et al.	
	22	20040243229		2004-12-02	Vidlund et al.	
	23	20050004668		2005-01-06	Aklog et al.	
	24	20050027369		2005-02-03	Eldridge et al.	
	25	20050043819		2005-02-24	Schmidt et al.	
	26	20050096673		2005-05-05	Stack et al.	
	27	20050113910		2005-05-26	Paniagua et al.	

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	Art Unit	3738	
	Examiner Name	not assigned	
	Attorney Docket Number	109978.10101	

	28	20050137681		2005-06-23	Shoemaker et al.	
	29	20050137682		2005-06-23	Justino	
	30	20050142163		2005-06-30	Hunter et al.	
	31	20050147562		2005-07-07	Hunter et al.	
	32	20050147599		2005-07-07	Hunter et al.	
	33	20050147643		2005-07-07	Hunter et al.	
	34	20050148512		2005-07-07	Hunter et al.	
	35	20050158274		2005-07-21	Hunter et al.	
	36	20050159811		2005-07-21	Lane	
	37	20050169958		2005-08-04	Hunter et al.	
	38	20050169959		2005-08-04	Hunter et al.	

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	39	20050175657		2005-08-11	Hunter et al.	
	40	20050187618		2005-08-25	Gabbay	
	41	20050191248		2005-09-01	Hunter et al.	
	42	20050228494		2005-10-13	Marquez	
	43	20050246035		2005-11-03	Wolfinbarger, Jr. et al.	
	44	20050247320		2005-11-10	Stack et al.	
	45	20050267529		2005-12-01	Crockett et al.	
	46	20060004439		2006-01-05	Spenser et al.	
	47	20060004443		2006-01-05	Liddicoat et al.	
	48	20060020336		2006-01-26	Liddicoat	
	49	20060025800		2006-02-02	Suresh	

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	Art Unit	3738	
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	50	20060041306		2006-02-23	Vidlund et al.	
	51	20060074486		2006-04-06	Liddicoat et al.	
	52	20060089708		2006-04-27	Osse et al.	
	53	20060111733		2006-05-25	Shriver	
	54	20060129225		2006-06-15	Kopia et al.	
	55	20060134079		2006-06-22	Sih et al.	
	56	20060140916		2006-06-29	Siani-Rose et al.	
	57	20060173475		2006-08-03	Lafontaine et al.	
	58	20060178740		2006-08-10	Stacchino et al.	
	59	20060190074		2006-08-24	Hill et al.	
	60	20060193885		2006-08-31	Neethling et al.	

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	61	20060195010		2006-08-31	Arnal et al.	
	62	20060195183		2006-08-31	Navia et al.	
	63	20060206203		2006-09-14	Yang et al.	
	64	20060229701		2006-10-12	Gurm et al.	
	65	20060240063		2006-10-26	Hunter et al.	
	66	20060240064		2006-10-26	Hunter et al.	
	67	20060259134		2006-11-16	Schwammenthal et al.	
	68	20060259135		2006-11-16	Navia et al.	
	69	20060259137		2006-11-16	Artof et al.	
	70	20060265056		2006-11-23	Nguyen et al.	
	71	20060287571		2006-12-21	Gozzi et al.	

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	72	20060292125		2006-12-28	Kellar et al.	
	73	20070010857		2007-01-11	Sugimoto et al.	
	74	20070043431		2007-02-22	Melsheimer	
	75	20070050014		2007-03-01	Johnson	
	76	20070050022		2007-03-01	Vidlund et al.	
	77	20070056346		2007-03-15	Spenser et al.	
	78	20070060932		2007-03-15	Stack et al.	
	79	20070100426		2007-05-03	Rudakov et al.	
	80	20070128174		2007-06-07	Kleinsek et al.	
	81	20070173861		2007-07-26	Strommer et al.	
	82	20070213813		2007-09-13	Von Segessler et al.	

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A signature of the applicant or representative is required in accordance with CFR 1.33, 10.18. Please see CFR 1.4(d) for the form of the signature.

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Name/Print	Mark L. Yaskanin	Registration Number	45246

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	31	4291420		1981-09-29	Reul	
	32	4340977		1982-07-27	Brownlee et al.	
	33	4350492		1982-09-21	Wright et al.	
	34	4364127		1982-12-21	Pierce et al.	
	35	4388735		1983-06-21	Ionescu et al.	
	36	4423525		1984-01-03	Vallana et al.	
	37	4441216		1984-04-10	Ionescu et al.	
	38	4456589		1984-06-26	Holman et al.	
	39	4473423		1984-09-25	Kolff	
	40	4477930		1984-10-23	Totten et al.	
	41	4490859		1985-01-01	Black et al.	

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	42	4517687		1985-05-21	Liebig et al.	
	43	4545082		1985-10-08	Hood	
	44	4597762		1986-07-01	Walter et al.	
	45	4600533		1986-07-15	Chu	
	46	4631052		1986-12-23	Kensey	
	47	4666442		1987-05-19	Arru et al.	
	48	4728328		1998-03-01	Hughes et al.	
	49	4759758		1988-07-26	Gabbay	
	50	4759759		1988-07-26	Walker et al.	
	51	4798611		1989-01-17	Freeman, Jr.	
	52	4801299		1989-01-31	Brendel et al.	

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	53	4870966		1989-10-03	Dellon et al.	
	54	4883458		1989-11-28	Shiber	
	55	4892539		1990-01-09	Koch	
	56	4966604		1990-10-30	Reiss	
	57	4976733		1990-12-11	Giradot	
	58	4979939		1990-12-25	Shiber	
	59	5006104		1991-04-09	Smith et al.	
	60	5007896		1991-04-16	Shiber	
	61	5011488		1991-04-30	Ginsburg	
	62	5026366		1991-06-25	Leckrone	
	63	5032128		1991-07-16	Alonso	

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	64	5047041		1991-09-10	Samuels	
	65	5047050		1991-09-10	Arpesani	
	66	5061277		1991-10-29	Carpentier et al.	
	67	5080660		1992-01-14	Buelna	
	68	5052771		1991-10-01	Williams et al.	
	69	5139515		1992-08-18	Robicsek	
	70	5163955		1992-11-17	Love et al.	
	71	5171273		1992-12-15	Silver et al.	
	72	5226889		1993-07-13	Sheiban	
	73	5261878		1993-11-16	Galindo	
	74	5282847		1994-02-01	Trescony et al.	

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	75	5326370		1994-07-05	Love et al.	
	76	5326371		1994-07-05	Love et al.	
	77	5332402		1994-07-26	Teitelbaum	
	78	5336616		1994-08-09	Livesey et al.	
	79	5360443		1994-11-01	Barone et al.	
	80	5374539		1994-12-20	Nimni et al.	
	81	5376110		1994-12-27	Tu et al.	
	82	5383927		1995-01-24	De Goiceochea et al.	
	83	5411552		1995-05-02	Anderson et al.	
	84	5413601		1995-05-09	Keshelava	
	85	5449384		1995-09-12	Johnson	

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	86	5476506		1995-12-19	Lunn	
	87	5480424		1996-01-02	Cox	
	88	5489297		1996-02-06	Duran	
	89	5500015		1996-03-19	Deac	
	90	5509930		1996-04-23	Love	
	91	5522879		1995-06-04	Scopelianos	
	92	5522881		1996-06-04	Lentz	
	93	5545215		1996-08-13	Duran	
	94	5549664		1996-08-27	Hirata et al.	
	95	5549666		1996-08-27	Hata et al.	
	96	5571170		1996-11-05	Palmaz et al.	

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	97	5571173		1996-11-05	Parodi	
	98	5571174		1996-11-05	Love et al.	
	99	5578071		1996-11-26	Parodi	
	100	5578072		1996-11-26	Barone et al.	
	101	5582168		1996-12-10	Samuels et al.	
	102	5591229		1997-01-07	Parodi	
	103	5634928		1997-06-03	Fischell et al.	
	104	5653749		1997-08-05	Love et al.	
	105	5713953		1998-02-03	Vallana et al.	
	106	5728152		1998-03-17	Mirsch, II et al.	
	107	5733299		1998-03-21	Sheiban et al.	

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	108	5741333		1998-04-21	Frid	
	109	5746775		1998-05-05	Levy et al.	
	110	5769780		1998-06-23	Hata et al.	
	111	5782914		1998-07-21	Schankerel	
	112	5787887		1998-08-04	Klingenbeck-Regn	
	113	5840081		1998-11-24	Anderson et al.	
	114	5855601		1999-01-05	Bessler et al.	
	115	5861028		1999-01-19	Angell	
	116	5862806		1999-01-26	Cheung	
	117	5895420		1999-04-20	Mirsch, II et al.	
	118	5931969		1999-08-03	Carpentier et al.	

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	119	5957949		1999-09-28	Leonhardt et al.	
	120	5961539		1999-10-05	Northup et al.	
	121	5961549		1999-10-05	Nguyen et al.	
	122	5972030		1999-10-26	Garrison et al.	
	123	5976179		1999-11-02	Inoue	
	124	6004328		1999-12-21	Solar	
	125	6004330		1999-12-21	Middleman et al.	
	126	6010531		2000-01-04	Donlon et al.	
	127	6029671		2000-02-29	Stevens et al.	
	128	6045576		2000-04-04	Starr et al.	
	129	6053938		2000-04-25	Goldmann et al.	

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	130	6091984		2000-07-18	Perelman et al.	
	131	6102944		2000-08-15	Huynh et al.	
	132	6117169		2000-09-12	Moe	
	133	6125852		2000-10-03	Stevens et al.	
	134	6126686		2000-10-03	Badylak et al.	
	135	6129756		2000-10-10	Kugler	
	136	6162245		2000-12-19	Jayaraman	
	137	6168614		2001-01-02	Andersen et al.	
	138	6168619		2001-01-02	Dinh et al.	
	139	6171335		2001-01-09	Wheatley et al.	
	140	6174327		2001-01-16	Mertens et al.	

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	141	6186999		2001-02-13	Chen	
	142	6197143		2001-03-06	Bodnar	
	143	6214055		2001-04-10	Simionescu et al.	
	144	6221091		2001-04-24	Khosravi	
	145	6231602		2001-05-15	Carpentier et al.	
	146	6254629		2001-07-03	Inoue	
	147	6254630		2001-07-03	Inoue	
	148	6254636		2001-07-03	Peredo	
	149	6264691		2001-07-24	Gabbay	
	150	6269819		2001-08-07	Oz et al.	
	151	6270526		2001-08-07	Cox	

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	152	6277397		2001-08-21	Shimizu	
	153	6277555		2001-08-21	Duran et al.	
	154	6287335		2001-09-11	Drasler et al.	
	155	6293970		2001-09-25	Wolfinbarger, Jr. et al.	
	156	6312462		2001-11-06	McDermott et al.	
	157	6312474		2001-11-06	Francis et al.	
	158	6334873		2002-01-01	Lane et al.	
	159	6342069		2002-01-29	Deac et al.	
	160	6350282		2002-02-26	Eberhardt	
	161	6352554		2002-03-05	De Paulis	
	162	6352708		2002-03-05	Duran et al.	

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	163	6358275		2002-03-19	McIlroy et al.	
	164	6358284		2002-03-19	Fearnot et al.	
	165	6371980		2002-04-16	Rudakov et al.	
	166	6376244		2002-04-23	Atala et al.	
	167	6378221		2002-04-30	Ekholm, Jr. et al.	
	168	6383171		2002-05-07	Gifford et al.	
	169	6391333		2002-05-21	Li et al.	
	170	6409755		2002-06-25	Vrba	
	171	6418339		2002-07-09	Essenpreis et al.	
	172	6425916		2002-07-30	Garrison et al.	
	173	6432712		2002-08-13	Wolfinbarger, Jr. et al.	

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	174	6440167		2002-08-27	Shimizu	
	175	6458153		2002-10-01	Bailey et al.	
	176	6461382		2002-10-08	Cao	
	177	6468313		2002-10-22	Claeson et al.	
	178	6471723		2002-10-29	Ashworth et al.	
	179	6482227		2002-11-19	Solovay	
	180	6482228		2002-11-19	Norred	
	181	6482240		2002-11-19	Echmayer et al.	
	182	6491719		2002-12-10	Fogarty et al.	
	183	6494909		2002-12-17	Greenhalgh	
	184	6503272		2003-01-07	Duerig et al.	

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	185	6534004		2003-03-18	Chen et al.	
	186	6558418		2003-05-06	Carpentier et al.	
	187	6569200		2003-05-27	Wolfinbarger Jr. et al.	
	188	6565960		2003-05-20	Koob et al.	
	189	6582458		2003-06-24	White et al.	
	190	6582462		2003-06-24	Andersen et al.	
	191	6582464		2003-06-24	Gabbay	
	192	6599524		2003-07-29	Li et al.	
	193	6624890		2003-09-23	Backman et al.	
	194	6626938		2003-09-30	Butaric et al.	
	195	6652577		2003-11-25	Gianotti	

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	196	6652578		2003-11-25	Bailey et al.	
	197	6553681		2003-04-29	Ekholm, Jr. et al.	
	198	6610088		2003-08-26	Gabbay	
	199	6666886		2003-12-23	Tranquillo et al.	
	200	6682559		2004-01-27	Myers et al.	
	201	6685739		2004-02-03	Dimatteo et al.	
	202	6696074		2004-02-24	Dia et al.	
	203	6719788		2004-04-13	Cox	
	204	6719789		2004-04-13	Cox	
	205	6702826		2004-03-09	Liddicoat et al.	
	206	6736823		2004-05-18	Darios et al.	

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	207	6764510		2004-07-20	Vidlund et al.	
	208	6773456		2004-08-10	Gordon et al.	
	209	6773457		2004-08-10	Ivancev	
	210	6790229		2004-09-14	Berreklouw	
	211	6792979		2004-09-21	Konya et al.	
	212	6802319		2004-10-12	Stevens et al.	
	213	6802806		2004-10-12	McCarthy et al.	
	214	6821530		2004-11-23	Koob et al.	
	215	6893460		2005-05-17	Spenser et al.	
	216	6908481		2005-06-21	Cribier	
	217	6913608		2005-07-02	Liddicoat et al.	

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	218	6916338		2005-07-12	Speziali	
	219	6942694		2005-09-13	Liddicoat et al.	
	220	6951571		2005-10-04	Srivastava	
	221	6961123		2005-11-01	Wang et al.	
	222	6977231		2005-12-20	Matsuda	
	223	6986735		2006-01-17	Abraham et al.	
	224	7004925		2006-02-28	Navia et al.	
	225	7008763		2006-03-07	Cheung	
	226	7011688		2006-03-14	Gryska et al.	
	227	7018404		2006-03-28	Holmberg et al.	
	228	7022348		2006-04-04	Ketharananthan	

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	229	7025780		2006-04-11	Gabbay	
	230	7037333		2006-05-02	Myers et al.	
	231	7039446		2006-05-02	Ruchti et al.	
	232	7041132		2006-05-09	Quijano et al.	
	233	7053051		2006-05-30	Hendriks et al.	
	234	7060092		2006-06-13	Kuribayashi et al.	
	235	7070616		2006-07-04	Majercak et al.	
	236	7077862		2006-07-18	Vidlund et al.	
	237	7084082		2006-08-01	Shimizu	
	238	7138226		2006-11-21	Vincek et al.	
	239	7153324		2006-12-26	Case et al.	

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	240	7160322		2007-01-09	Gabbay	
	241	7164145		2007-01-16	Shakespeare	
	242	7166570		2007-01-23	Hunter et al.	
	243	7189259		2007-03-13	Simionescu et al.	
	244	7213601		2007-05-08	Stevens et al.	
	245	7214242		2007-05-08	Abraham et al.	
	246	7232461		2007-06-19	Ramer	
	247	7261732		2007-08-28	Justino	
	248	7289211		2007-10-30	Walsh, Jr. et al.	
	249	7309461		2007-12-18	Kujawski et al.	
	250	7311730		2007-12-25	Gabbay	

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	251	7318998		2008-01-15	Goldstein et al.	
	252	7331993		2008-02-19	White	
	253	7329279		2008-02-12	Haug et al.	
	254	7354702		2008-04-08	Dai et al.	
	255	7381218		2008-06-03	Schreck	
	256	7381219		2008-06-03	Salahieh et al.	
	257	7399315		2008-07-15	Iobbi	
	258	7427291		2008-09-23	Liddicoat e al.	
	259	7431725		2008-10-07	Stack et al.	
	260	7468073		2008-12-23	Johnson et al.	
	261	7473237		2009-01-06	Navia et al.	

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	262	7481838		2009-01-27	Carpentier et al.	
	263	7503929		2009-03-17	Johnson et al.	
	264	7510571		2009-03-31	Spiridigliozzi et al.	
	265	7510575		2009-03-31	Spenser et al.	
	266	7524330		2009-04-28	Berreklouw	
	267	7566343		2009-07-28	Jenson et al.	
	268	7585321		2009-09-08	Cribier	
	269	7604661		2009-10-20	Pavcnik et al.	
	270	7618446		2009-11-17	Andersen et al.	
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INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(Not for submission under 37 CFR 1.99)

Application Number	13675665
Filing Date	2012-11-13
First Named Inventor	David PANIAGUA
Art Unit	3738
Examiner Name	Cheryl L. MILLER
Attorney Docket Number	109978.10101

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Examiner Initial*	Cite No	Patent Number	Kind Code[1]	Issue Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
	1	6530952		2003-03-11	Vesely	

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Receipt date: 09/26/2014	Application Number	13675665	13675665 - GAU: 3738
INFORMATION DISCLOSURE STATEMENT BY APPLICANT (**Not for submission under 37 CFR 1.99)**	Filing Date	2012-11-13	
	First Named Inventor	David PANIAGUA	
	Art Unit	3738	
	Examiner Name	Cheryl L. MILLER	
	Attorney Docket Number	109978.10101	

	1	Final Office Action issued September 25, 2014, in U.S. Application No. 14/253,656 (File: 109978.10113)	☐

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Examiner Signature	/Cheryl Miller/	Date Considered	06/27/2015

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Signature	/ Mark L. Yaskanin /	Date (YYYY-MM-DD)	2014-09-26
Name/Print	Mark L. Yaskanin	Registration Number	45246

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/Cheryl Miller/ 06/27/2015

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	1	5484444		1996-01-16	Braunschweiler et al.	
	2	5645559		1997-07-08	Hachtman et al.	
	3	5683451		1997-11-04	Lenker et al.	
	4	5876448		1999-03-02	Thompson et al.	
	5	6350278		2002-02-26	Lenker et al.	
	6	6682537		2004-01-27	Ouriel et al.	
	7	6896690		2005-05-24	Lambrecht et al.	
	8	7556646		2009-07-07	Yang et al.	

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	1	Notice of Allowance issued October 7, 2014, in U.S. Application No. 14/253,656 (File: 109978.10113)	☐

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Signature	/ Mark L. Yaskanin /	Date (YYYY-MM-DD)	2014-10-07
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	1	Final Office Action issued November 7, 2014, in U.S. Application No. 14/253,650 (File: 109978.10104)	☐

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	2	4657133		1987-04-14	Komatsu et al.	
	3	4743231		1988-05-10	Kay et al.	
	4	6124523		2000-09-26	Banas et al.	
	5	6245102		2001-06-12	Jayaraman	
	6	6540782		2003-04-01	Snyders	
	7	6821297		2004-11-23	Snyders	
	8	6830584		2004-12-14	Seguin	

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Receipt date: 05/23/2014	Application Number	13675665	13675665 - GAU: 3738
INFORMATION DISCLOSURE STATEMENT BY APPLICANT (**Not for submission under 37 CFR 1.99)**	Filing Date	2012-11-13	
	First Named Inventor	David PANIAGUA	
	Art Unit	3738	
	Examiner Name	Cheryl L. Miller	
	Attorney Docket Number	109978.10101	

	9	7018406		2006-03-28	Seguin et al.	
	10	8512401		2013-08-20	Murray et al.	
	11	8512403		2013-08-20	Navia et al.	

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U.S.PATENT APPLICATION PUBLICATIONS Remove

Examiner Initial*	Cite No	Publication Number	Kind Code[1]	Publication Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
	1	20020151970		2002-10-17	Garrison et al.	
	2	20030149477		2003-08-07	Gabbay	
	3	20040039442		2004-02-26	St. Goar	
	4	20040158321		2004-08-12	Reuter et al.	
	5	20040230285		2004-11-18	Gifford, III et al.	
	6	20050241981		2005-11-03	Gupta et al.	

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	First Named Inventor	David PANIAGUA	
	Art Unit	3738	
	Examiner Name	Cheryl L. Miller	
	Attorney Docket Number	109978.10101	

	7	20070104395		2007-05-10	Kinigakis et al.	
	8	20070203575		2007-08-30	Forster et al.	
	9	20070276461		2007-11-29	Andreas et al.	
	10	20090005857		2009-01-01	Ischinger	
	11	20090054969		2009-02-26	Salahieh	
	12	20100241069		2010-09-23	Hatten	
	13	20110240511		2011-10-06	Bolton et al.	
	14	20130304201		2013-11-14	Navia et al.	
	15	20140039613		2014-02-06	Navia et al.	

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Examiner Initial*	Cite No	Foreign Document Number[3]	Country Code[2] i	Kind Code[4]	Publication Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear	T[5]

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Receipt date: 05/23/2014	Application Number	13675665	13675665 - GAU: 3738
INFORMATION DISCLOSURE STATEMENT BY APPLICANT	Filing Date	2012-11-13	
(Not for submission under 37 CFR 1.99)	First Named Inventor	David PANIAGUA	
	Art Unit	3738	
	Examiner Name	Cheryl L. Miller	
	Attorney Docket Number	109978.10101	

	1	2004/082527	WO		2004-09-30	Edwards Lifesciences Corp.		☐

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NON-PATENT LITERATURE DOCUMENTS Remove

Examiner Initials*	Cite No	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc), date, pages(s), volume-issue number(s), publisher, city and/or country where published.	T[5]
	1	MENDELSON, Karen et al., "Heart Valve Tissue Engineering: Concepts, Approaches, Progress, and Challenges" Ann Biomed Eng, 2006 Dec; 34(12); pp. 1799-1819; published online 2006 October 12 doi:10.1007/s/10439-006-9163-z	☐
	2	SCHMIDT, Dorthe et al., "Tissue engineering of heart valves using decellularized xenogeneic of polymeric starter matrices" Philos Trans R Soc Lond B Bio Sci., Aug 29, 2007, 362(1484); 1505-1512; published online June 22, 2007, doi: 10.1098/rstb.2007.2131	☐
	3	WERNER, S. et al., "Testing the Hydrodynamic properties of heart valve prostheses with a new test apparatus", Biomed Tech (Berl) 1994 Sep; 30(9); pp. 204-210 (Abstract only)	☐
	4	Office Action issued in U.S. Application No. 14/136,516, dated March 10, 2014 (109978.10102)	☐
	5	Notice of Allowance issued in U.S. Application No. 14/136,516, dated March 31, 2014 (109978.10102)	☐
	6	Cross-reference is made to U.S. Application No. 14/253,650 filed on April 15, 2014, and its associated Preliminary Amendment (109978.10104)	☐
	7	Cross-reference is made to U.S. Application No. 14/253,656 filed on April 15, 2014, and its associated Preliminary Amendment (109978.10113)	☐
	8	Cross-reference is made to U.S. Application No. 14/268,184 filed on May 2, 2014, and its associated Preliminary Amendment (109978.10114)	☐

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Receipt date: 05/23/2014	Application Number	13675665	13675665 - GAU: 3738
INFORMATION DISCLOSURE STATEMENT BY APPLICANT (**Not for submission under 37 CFR 1.99)**	Filing Date	2012-11-13	
	First Named Inventor	David PANIAGUA	
	Art Unit	3738	
	Examiner Name	Cheryl L. Miller	
	Attorney Docket Number	109978.10101	

	9	Cross-reference is made to U.S. Application No. 14/268,190 filed on May 2, 2014, and its associated Preliminary Amendment (109978.10115)	☐
	10	Cross-reference is made to U.S. Application No. 14/284,049 filed on May 21, 2014, and its associated Preliminary Amendment (109978.10116)	☐
	11	Cross-reference is made to U.S. Application No. 14/284,063 filed on May 21, 2014, and its associated Preliminary Amendment (109978.10117)	☐

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EXAMINER SIGNATURE

Examiner Signature	/Cheryl Miller/	Date Considered	06/27/2015

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through a citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

[1] See Kind Codes of USPTO Patent Documents at www.USPTO.GOV or MPEP 901.04. [2] Enter office that issued the document, by the two-letter code (WIPO Standard ST.3). [3] For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. [4] Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. [5] Applicant is to place a check mark here if English language translation is attached.

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Receipt date: 05/23/2014	Application Number	13675665	13675665 - GAU: 3738
INFORMATION DISCLOSURE STATEMENT BY APPLICANT (**Not for submission under 37 CFR 1.99)**	Filing Date	2012-11-13	
	First Named Inventor	David PANIAGUA	
	Art Unit	3738	
	Examiner Name	Cheryl L. Miller	
	Attorney Docket Number	109978.10101	

CERTIFICATION STATEMENT

Please see 37 CFR 1.97 and 1.98 to make the appropriate selection(s):

☐ That each item of information contained in the information disclosure statement was first cited in any communication from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e)(1).

OR

☐ That no item of information contained in the information disclosure statement was cited in a communication from a foreign patent office in a counterpart foreign application, and, to the knowledge of the person signing the certification after making reasonable inquiry, no item of information contained in the information disclosure statement was known to any individual designated in 37 CFR 1.56(c) more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e)(2).

☐ See attached certification statement.

☐ The fee set forth in 37 CFR 1.17 (p) has been submitted herewith.

☒ A certification statement is not submitted herewith.

SIGNATURE

A signature of the applicant or representative is required in accordance with CFR 1.33, 10.18. Please see CFR 1.4(d) for the form of the signature.

Signature	/ Mark L. Yaskanin /	Date (YYYY-MM-DD)	2014-05-23
Name/Print	Mark L. Yaskanin	Registration Number	45246

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 1 hour to complete, including gathering, preparing and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

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The information provided by you in this form will be subject to the following routine uses:

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2. A record from this system of records may be disclosed, as a routine use, in the course of presenting evidence to a court, magistrate, or administrative tribunal, including disclosures to opposing counsel in the course of settlement negotiations.

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5. A record related to an International Application filed under the Patent Cooperation Treaty in this system of records may be disclosed, as a routine use, to the International Bureau of the World Intellectual Property Organization, pursuant to the Patent Cooperation Treaty.

6. A record in this system of records may be disclosed, as a routine use, to another federal agency for purposes of National Security review (35 U.S.C. 181) and for review pursuant to the Atomic Energy Act (42 U.S.C. 218(c)).

7. A record from this system of records may be disclosed, as a routine use, to the Administrator, General Services, or his/her designee, during an inspection of records conducted by GSA as part of that agency's responsibility to recommend improvements in records management practices and programs, under authority of 44 U.S.C. 2904 and 2906. Such disclosure shall be made in accordance with the GSA regulations governing inspection of records for this purpose, and any other relevant (i.e., GSA or Commerce) directive. Such disclosure shall not be used to make determinations about individuals.

8. A record from this system of records may be disclosed, as a routine use, to the public after either publication of the application pursuant to 35 U.S.C. 122(b) or issuance of a patent pursuant to 35 U.S.C. 151. Further, a record may be disclosed, subject to the limitations of 37 CFR 1.14, as a routine use, to the public if the record was filed in an application which became abandoned or in which the proceedings were terminated and which application is referenced by either a published application, an application open to public inspections or an issued patent.

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/Cheryl Miller/ 06/27/2015

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INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(Not for submission under 37 CFR 1.99)

Application Number	13675665
Filing Date	2012-11-13
First Named Inventor	David Paniagua
Art Unit	3738
Examiner Name	Cheryl L. MILLER
Attorney Docket Number	109978.10101

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Examiner Initial*	Cite No	Patent Number	Kind Code[1]	Issue Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
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Examiner Initial*	Cite No	Foreign Document Number[3]	Country Code[2] i	Kind Code[4]	Publication Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear	T[5]
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Examiner Initials*	Cite No	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc), date, pages(s), volume-issue number(s), publisher, city and/or country where published.	T[5]

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Receipt date: 01/13/2015	Application Number	13675665 13675665 - GAU: 3738
INFORMATION DISCLOSURE STATEMENT BY APPLICANT (**Not for submission under 37 CFR 1.99)**	Filing Date	2012-11-13
	First Named Inventor	David Paniagua
	Art Unit	3738
	Examiner Name	Cheryl L. MILLER
	Attorney Docket Number	109978.10101

	1	Office Action issued December 5, 2014 in U.S. Application No. 14/502,453 (109978.10106)	☐

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Examiner Signature	/Cheryl Miller/	Date Considered	06/27/2015

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INFORMATION DISCLOSURE STATEMENT BY APPLICANT (**Not for submission under 37 CFR 1.99)**	Filing Date	2012-11-13	
	First Named Inventor	David Paniagua	
	Art Unit	3738	
	Examiner Name	Cheryl L. MILLER	
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Signature	/ Mark L. Yaskanin /	Date (YYYY-MM-DD)	2015-01-13
Name/Print	Mark L. Yaskanin	Registration Number	45246

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/Cheryl Miller/ 06/27/2015

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /CM/

Search Notes	Application/Control No.	Applicant(s)/Patent Under Reexamination
	13675665	PANIAGUA ET AL.
	Examiner	Art Unit
	CHERYL MILLER	3738

CPC- SEARCHED		
Symbol	Date	Examiner

CPC COMBINATION SETS - SEARCHED		
Symbol	Date	Examiner

US CLASSIFICATION SEARCHED			
Class	Subclass	Date	Examiner

SEARCH NOTES		
Search Notes	Date	Examiner
East text search, review parent application files	6/27/2015	cm

INTERFERENCE SEARCH			
US Class/ CPC Symbol	US Subclass / CPC Group	Date	Examiner

/C.M./ Examiner.Art Unit 3738	

EAST Search History

EAST Search History (Prior Art)

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
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L11	162	9 and (resilient or "self-expandable" or "self-expanding" or "self-expands") and (sheet or patch)	US-PGPUB; USPAT; USOCR	OR	ON	2015/06/27 22:50
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L13	126	623/2.$2.ccls. and ((autologous or autograft) with pericardi$2)	US-PGPUB; USPAT; USOCR	OR	ON	2015/06/27 23:07
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		"3574865" | "3626518" | "3911502" | "4580568" | "4648383").PN.	PGPUB; USPAT; USOCR			11:43
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S9	2	("4038703" | "4106129").PN.	US-PGPUB; USPAT; USOCR	OR	OFF	2014/06/02 11:45
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S14	2098	623/1.24.ccls. or 623/1.26.ccls. or 623/2.12.ccls. or 623/2.13.ccls. or 623/2.14.ccls. or 623/2.15.ccls. or 623/2.16.ccls. or 623/2.17.ccls. or 623/2.18.ccls. or 623/2.19.ccls. or 623/900.ccls.	US-PGPUB; USPAT; USOCR	OR	ON	2014/11/02 16:25
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S24	279	S23 and (valve with pericardi$3)	US-PGPUB; USPAT; USOCR	OR	ON	2014/11/02 20:44
S25	199	S23 and (leaflets with pericardi$3)	US-PGPUB; USPAT; USOCR	OR	ON	2014/11/02 20:44
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S41	5	"10/037,266"	USPAT; USOCR	OR	ON	2015/06/26 23:32
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INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(Not for submission under 37 CFR 1.99)

Application Number	13675665
Filing Date	2012-11-13
First Named Inventor	David PANIAGUA
Art Unit	3738
Examiner Name	Cheryl L. MILLER
Attorney Docket Number	109978.10101

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Examiner Initial*	Cite No	Patent Number	Kind Code[1]	Issue Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
	1	5554184		1996-09-10	Machiraju	

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	1	20020052651		2002-05-02	Myers et al.	
	2	20030209835		2003-11-13	Chun et al.	

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	1	9-501594	JP		1997-02-18		Equivalent to WO/1995/005207	☐
	2	2001-500761	JP		2001-01-23		Equivalent to WO/1998/011935	☐

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Receipt date: 06/11/2015	Application Number	13675665	13675665 - GAU: 3738
INFORMATION DISCLOSURE STATEMENT BY APPLICANT	Filing Date	2012-11-13	
(Not for submission under 37 CFR 1.99)	First Named Inventor	David PANIAGUA	
	Art Unit	3738	
	Examiner Name	Cheryl L. MILLER	
	Attorney Docket Number	109978.10101	

	3	2005-103321	JP		2005-04-21		Equivalent to EP0696447	☐
	4	2009/149462	WO		2009-12-10	Edwards Lifesciences Corporation		☐

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Examiner Initials*	Cite No	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc), date, pages(s), volume-issue number(s), publisher, city and/or country where published.	T[5]
	1	Declaration Under 37 CFR 1.131 as filed in U.S. Patent Application No. 10/887,688 on December 15, 2008, by co-inventors of that application. (Best available copy)	☐
	2	Final Office Action issued May 8, 2015 in U.S. Application No. 14/502,453 (109978.10106)	☐

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EXAMINER SIGNATURE

Examiner Signature	/Cheryl Miller/	Date Considered	06/27/2015

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through a citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

[1] See Kind Codes of USPTO Patent Documents at www.USPTO.GOV or MPEP 901.04. [2] Enter office that issued the document, by the two-letter code (WIPO Standard ST.3). [3] For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. [4] Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. [5] Applicant is to place a check mark here if English language translation is attached.

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Receipt date: 06/11/2015	Application Number	13675665	13675665 - GAU: 3738
INFORMATION DISCLOSURE STATEMENT BY APPLICANT (**Not for submission under 37 CFR 1.99)**	Filing Date	2012-11-13	
	First Named Inventor	David PANIAGUA	
	Art Unit	3738	
	Examiner Name	Cheryl L. MILLER	
	Attorney Docket Number	109978.10101	

CERTIFICATION STATEMENT

Please see 37 CFR 1.97 and 1.98 to make the appropriate selection(s):

☐ That each item of information contained in the information disclosure statement was first cited in any communication from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e)(1).

OR

☐ That no item of information contained in the information disclosure statement was cited in a communication from a foreign patent office in a counterpart foreign application, and, to the knowledge of the person signing the certification after making reasonable inquiry, no item of information contained in the information disclosure statement was known to any individual designated in 37 CFR 1.56(c) more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e)(2).

☐ See attached certification statement.

☐ The fee set forth in 37 CFR 1.17 (p) has been submitted herewith.

☒ A certification statement is not submitted herewith.

SIGNATURE

A signature of the applicant or representative is required in accordance with CFR 1.33, 10.18. Please see CFR 1.4(d) for the form of the signature.

Signature	/ Mark L. Yaskanin /	Date (YYYY-MM-DD)	2015-06-11
Name/Print	Mark L. Yaskanin	Registration Number	45246

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 1 hour to complete, including gathering, preparing and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

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4. A record in this system of records may be disclosed, as a routine use, to a contractor of the Agency having need for the information in order to perform a contract. Recipients of information shall be required to comply with the requirements of the Privacy Act of 1974, as amended, pursuant to 5 U.S.C. 552a(m).

5. A record related to an International Application filed under the Patent Cooperation Treaty in this system of records may be disclosed, as a routine use, to the International Bureau of the World Intellectual Property Organization, pursuant to the Patent Cooperation Treaty.

6. A record in this system of records may be disclosed, as a routine use, to another federal agency for purposes of National Security review (35 U.S.C. 181) and for review pursuant to the Atomic Energy Act (42 U.S.C. 218(c)).

7. A record from this system of records may be disclosed, as a routine use, to the Administrator, General Services, or his/her designee, during an inspection of records conducted by GSA as part of that agency's responsibility to recommend improvements in records management practices and programs, under authority of 44 U.S.C. 2904 and 2906. Such disclosure shall be made in accordance with the GSA regulations governing inspection of records for this purpose, and any other relevant (i.e., GSA or Commerce) directive. Such disclosure shall not be used to make determinations about individuals.

8. A record from this system of records may be disclosed, as a routine use, to the public after either publication of the application pursuant to 35 U.S.C. 122(b) or issuance of a patent pursuant to 35 U.S.C. 151. Further, a record may be disclosed, subject to the limitations of 37 CFR 1.14, as a routine use, to the public if the record was filed in an application which became abandoned or in which the proceedings were terminated and which application is referenced by either a published application, an application open to public inspections or an issued patent.

9. A record from this system of records may be disclosed, as a routine use, to a Federal, State, or local law enforcement agency, if the USPTO becomes aware of a violation or potential violation of law or regulation.

/Cheryl Miller/ 06/27/2015

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /CM/

PTO/SB/08a (03-15)
Approved for use through 07/31/2016. OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(Not for submission under 37 CFR 1.99)

Application Number	13675665
Filing Date	2012-11-13
First Named Inventor	David Paniagua
Art Unit	3738
Examiner Name	Cheryl L. Miller
Attorney Docket Number	109978.10101

U.S.PATENTS Remove

Examiner Initial*	Cite No	Patent Number	Kind Code[1]	Issue Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
	1	4275469		1981-06-30	Gabbay	
	2	5558875		1996-09-24	Wang	
	3	7214344		2007-01-14	Carpentier et al.	

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Examiner Initial*	Cite No	Publication Number	Kind Code[1]	Publication Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
	1	20020119437		2002-08-29	Grooms et al.	
	2	20020146393		2002-10-10	Bell et al.	
	3	20030118560		2003-06-25	Kelly et al.	

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	13675665
	Filing Date	2012-11-13
	First Named Inventor	David Paniagua
	Art Unit	3738
	Examiner Name	Cheryl L. Miller
	Attorney Docket Number	109978.10101

	4	20060212111		2006-09-21	Case et al.		

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Examiner Initial*	Cite No	Foreign Document Number[3]	Country Code[2] ¡	Kind Code[4]	Publication Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear	T[5]
	1							☐

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Examiner Initials*	Cite No	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc), date, pages(s), volume-issue number(s), publisher, city and/or country where published.	T[5]
	1	Office Action issued July 6, 2015, in U.S. Application No. 13/367,252 (109978.10111)	☐
	2	Notice of Allowance issued August 14, 2015, in U.S. Application No. 13/367,252 (109978.10111)	☐

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EXAMINER SIGNATURE

Examiner Signature		Date Considered	

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through a citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

[1] See Kind Codes of USPTO Patent Documents at www.USPTO.GOV or MPEP 901.04. [2] Enter office that issued the document, by the two-letter code (WIPO Standard ST.3). [3] For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. [4] Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. [5] Applicant is to place a check mark here if English language translation is attached.

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	13675665
	Filing Date	2012-11-13
	First Named Inventor	David Paniagua
	Art Unit	3738
	Examiner Name	Cheryl L. Miller
	Attorney Docket Number	109978.10101

CERTIFICATION STATEMENT

Please see 37 CFR 1.97 and 1.98 to make the appropriate selection(s):

☐ That each item of information contained in the information disclosure statement was first cited in any communication from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e)(1).

OR

☒ That no item of information contained in the information disclosure statement was cited in a communication from a foreign patent office in a counterpart foreign application, and, to the knowledge of the person signing the certification after making reasonable inquiry, no item of information contained in the information disclosure statement was known to any individual designated in 37 CFR 1.56(c) more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e)(2).

☐ See attached certification statement.

☐ The fee set forth in 37 CFR 1.17 (p) has been submitted herewith.

☐ A certification statement is not submitted herewith.

SIGNATURE

A signature of the applicant or representative is required in accordance with CFR 1.33, 10.18. Please see CFR 1.4(d) for the form of the signature.

Signature	/ Mark L. Yaskanin /	Date (YYYY-MM-DD)	2015-09-10
Name/Print	Mark L. Yaskanin	Registration Number	45246

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 1 hour to complete, including gathering, preparing and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

Privacy Act Statement

The Privacy Act of 1974 (P.L. 93-579) requires that you be given certain information in connection with your submission of the attached form related to a patent application or patent. Accordingly, pursuant to the requirements of the Act, please be advised that: (1) the general authority for the collection of this information is 35 U.S.C. 2(b)(2); (2) furnishing of the information solicited is voluntary; and (3) the principal purpose for which the information is used by the U.S. Patent and Trademark Office is to process and/or examine your submission related to a patent application or patent. If you do not furnish the requested information, the U.S. Patent and Trademark Office may not be able to process and/or examine your submission, which may result in termination of proceedings or abandonment of the application or expiration of the patent.

The information provided by you in this form will be subject to the following routine uses:

1. The information on this form will be treated confidentially to the extent allowed under the Freedom of Information Act (5 U.S.C. 552) and the Privacy Act (5 U.S.C. 552a). Records from this system of records may be disclosed to the Department of Justice to determine whether the Freedom of Information Act requires disclosure of these record s.

2. A record from this system of records may be disclosed, as a routine use, in the course of presenting evidence to a court, magistrate, or administrative tribunal, including disclosures to opposing counsel in the course of settlement negotiations.

3. A record in this system of records may be disclosed, as a routine use, to a Member of Congress submitting a request involving an individual, to whom the record pertains, when the individual has requested assistance from the Member with respect to the subject matter of the record.

4. A record in this system of records may be disclosed, as a routine use, to a contractor of the Agency having need for the information in order to perform a contract. Recipients of information shall be required to comply with the requirements of the Privacy Act of 1974, as amended, pursuant to 5 U.S.C. 552a(m).

5. A record related to an International Application filed under the Patent Cooperation Treaty in this system of records may be disclosed, as a routine use, to the International Bureau of the World Intellectual Property Organization, pursuant to the Patent Cooperation Treaty.

6. A record in this system of records may be disclosed, as a routine use, to another federal agency for purposes of National Security review (35 U.S.C. 181) and for review pursuant to the Atomic Energy Act (42 U.S.C. 218(c)).

7. A record from this system of records may be disclosed, as a routine use, to the Administrator, General Services, or his/her designee, during an inspection of records conducted by GSA as part of that agency's responsibility to recommend improvements in records management practices and programs, under authority of 44 U.S.C. 2904 and 2906. Such disclosure shall be made in accordance with the GSA regulations governing inspection of records for this purpose, and any other relevant (i.e., GSA or Commerce) directive. Such disclosure shall not be used to make determinations about individuals.

8. A record from this system of records may be disclosed, as a routine use, to the public after either publication of the application pursuant to 35 U.S.C. 122(b) or issuance of a patent pursuant to 35 U.S.C. 151. Further, a record may be disclosed, subject to the limitations of 37 CFR 1.14, as a routine use, to the public if the record was filed in an application which became abandoned or in which the proceedings were terminated and which application is referenced by either a published application, an application open to public inspections or an issued patent.

9. A record from this system of records may be disclosed, as a routine use, to a Federal, State, or local law enforcement agency, if the USPTO becomes aware of a violation or potential violation of law or regulation.

Electronic Acknowledgement Receipt

EFS ID:	23450275
Application Number:	13675665
International Application Number:	
Confirmation Number:	1995
Title of Invention:	PERCUTANEOUSLY IMPLANTABLE REPLACEMENT HEART VALVE DEVICE AND METHOD OF MAKING SAME
First Named Inventor/Applicant Name:	David Paniagua
Customer Number:	29880
Filer:	Mark Lauren Yaskanin/Carol Donahue
Filer Authorized By:	Mark Lauren Yaskanin
Attorney Docket Number:	109978.10101
Receipt Date:	10-SEP-2015
Filing Date:	13-NOV-2012
Time Stamp:	11:18:32
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	no

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Information Disclosure Statement (IDS) Form (SB08)	Colibri_10101_SUPP_IDS.PDF	1124144 d60be5aa63c4f633f3f49a02fde586cdff8990b9	no	4
Warnings:					
Information:					

2	Non Patent Literature	10111_US_13-367252_Office_Action_2015-07-06.PDF	383589 2c373b764fa1342e0bf2e006e4d71b8c29fd8c51	no	10
Warnings:					
Information:					
3	Non Patent Literature	10111_US_13-367252_Notice-of_Allowance_2015-08-14.PDF	309772 77609b22cc76e8db995167747e488a38c13926a2	no	6
Warnings:					
Information:					
		Total Files Size (in bytes):	1817505		

This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

New Applications Under 35 U.S.C. 111
If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

National Stage of an International Application under 35 U.S.C. 371
If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office
If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In Re the Application of:	)	Group Art Unit: 3738
	)	
David Panigua et al.	)	Confirmation No. 1995
	)	
Application No.: 13/675,665	)	Examiner: Cheryl L. Miller
	)	
Filed: November 13, 2012	)	AMENDMENT AND RESPONSE
	)	
Atty. File No.: 109978.10101	)	**Filed Electronically**
	)	
Entitled: PERCUTANEOUSLY IMPLANTABLE REPLACEMENT HEART VALVE DEVICE AND METHOD OF MAKING SAME	)	

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313

Dear Madam:

In response to the July 6, 2015 Office Action (the "Office Action"), please amend the above-identified application as follows:

Amendments to the Claims begin on page 2 of this paper.

Remarks/Arguments begin on page 4 of this paper.

Applicants concurrently submit a three-month request for extension of time with the requisite small entity fee. Please credit any over payment or debit any under payment to Deposit Account No. 50-1943.

AMENDMENTS TO THE CLAIMS

The listing of claims will replace all prior versions and listings of claims in the application:

Listing of Claims:

1. **(Currently Amended)** A percutaneously implantable replacement heart valve device for implantation in a patient, comprising:

an expandable stent member having an inner channel, the expandable stent member collapsible and configured for percutaneous delivery; and

a valve means ~~a flexible, compressible artificial valve~~ made of biocompatible tissue material and attached to the expandable stent member, the valve means including an outer cuff layer and two to four individual leaflets, wherein each of the two to four individual leaflets is rectangular in shape in side elevation view, wherein a crease is located between the two to four individual leaflets and the outer cuff layer at a base of the two to four individual leaflets, and wherein after implantation in the patient, the valve means resides as a single element entirely within the inner channel of the expandable stent member, wherein only the two to four individual leaflets reside radially inward from the outer cuff layer, and wherein the valve means is formed without ~~and disposed within the inner cavity of said stent member affixed at one or more points on said artificial valve's outer surface to said stent member, said artificial valve having cusps or leaflets formed by folding of a sheet of said biocompatible tissue material without affixing of separate cusps or leaflets or~~ cutting slits into said biocompatible tissue material to form said ~~cusps or~~ leaflets.

2. **(Original)** The percutaneously implantable replacement heart valve device of claim 1, wherein said expandable stent member is made of a metal or alloy of metals selected from the group consisting of nickel-titanium alloy, titanium and stainless steel.

3. **(Canceled)**

4. **(Currently Amended)** The percutaneously implantable replacement heart valve device of claim 1, wherein said biocompatible tissue material of said ~~artificial~~ valve means comprises porcine pericardium tissue.

5. **(Canceled)**

6. **(Currently Amended)** The percutaneously implantable replacement heart valve device of claim 1, wherein said biocompatible tissue material of said ~~artificial~~ valve means comprises autologous tissue obtained from the patient into whom said replacement heart valve device will be implanted.

7.-8. **(Canceled)**

9. **(Currently Amended)** The percutaneously implantable heart valve device of claim 1, wherein said expandable stent member is self-expanding when implanted.

10. **(Currently Amended)** The percutaneously implantable heart valve device of claim 1, wherein said expandable stent member is balloon catheter expandable when implanted.

11.-33. **(Cancelled)**

REMARKS/ARGUMENTS

The present Amendment and Response comprises Applicant's reply to the Examiner's July 6, 2015 Office Action. Claims 3, 5, 7-8 and 11-33 are cancelled. Claims 1, 4, 6, 9 and 10 are amended. No new claims have been added. Accordingly, Claims 1, 2, 4, 6, 9 and 10 are now pending in view of the above amendments.

Applicants believe that no new matter has been added with regard to the claim amendments provided herein. Applicants do not donate or disclaim any claims or subject matter with the claim amendments made herein, and the Applicants expressly reserve the right to prosecute the original claims, prior version of claims or any unclaimed subject matter in one or more future filed continuing applications. Applicants do not acquiesce to any of the rejections set forth in the Office Action.

Reconsideration of the application is respectfully requested in view of the above amendments to the claims and the following remarks. Please note that the following remarks are not intended to be an exhaustive enumeration of the distinctions between any cited reference and the claimed invention. Rather, the distinctions identified and discussed below are presented solely by way of example to illustrate some of the differences between the claimed invention and the cited references. In addition, the Applicants request that the Examiner carefully review any references discussed below to ensure that Applicants' understanding and discussion of the references, if any, is consistent with the Examiner's understanding. Also, Applicants' arguments related to each cited reference are not an admission that the cited references are, in fact, prior art.

I. Rejections Under 35 U.S.C. § 112, Second Paragraph

The Examiner rejected Claims 1-10, 27-29 and 33 under 35 U.S.C. § 112, Second Paragraph for indefiniteness on the grounds that they do not distinctly claim the subject matter of the invention. In response, Claim 1 has been amended to delete the wording "the inner cavity of said stent member affixed at one or more points on said artificial valve's outer surface." In addition, the Applicants have amended "said artificial valve having cusps or leaflets formed by folding of a sheet of said biocompatible tissue material without affixing of separate cusps or leaflets or cutting slits into said material to form said cusps or leaflets" to read "wherein the valve means is formed without cutting slits into said biocompatible tissue material to form said leaflets." Applicants believe that the changes to Claim 1 address the 35 U.S.C. § 112, Second Paragraph, rejections and request the Examiner to withdraw the indefinite rejections of Claim 1.

With regard to Claim 6, "a patient" is now recited in the preamble of Claim 1, and therefore, there is now antecedent basis for "the patient" in Claim 6. Accordingly, the Examiner is requested to withdraw the 35 U.S.C. § 112, Second Paragraph, rejection of Claim 6.

Claims 7, 8, 27 and 33 are cancelled. Therefore the 35 U.S.C. § 112, Second Paragraph, rejections of these claims are now moot.

Based on the amendments the claims, the Examiner is requested to withdraw the 35 U.S.C. § 112, Second Paragraph, rejections of the pending claims.

II. Prior Art Rejections

A. Rejections Under 35 U.S.C. § 102(e)

The Examiner rejected Claims 1-2, 7-8, 10, 27-28 and 33 under pre-AIA 35 U.S.C. § 102(e) as being anticipated by United States Patent No. 6,908,481 to Cribier ("Cribier").

Because the Examiner has asserted Cribier under 35 U.S.C. § 102(e), Applicants do not admit that Cribier is in fact prior art to the claimed invention but reserve the right to swear behind Cribier if necessary to remove it as a reference. In the Office Action, the Examiner asserted that the present invention is unpatentable over Cribier.

It is well recognized that claims are anticipated if, and only if, each and every element, as set forth in the claim is found in a single prior art reference. Vertegaal Bros. v. Union Oil Co. of Calif., 814 F.2d 628, 631 (Fed. Cir. 1987). Furthermore, "[t]he identical invention must be shown in as a complete detail as is contained in the . . . claim." Richardson v. Suzuki Motor Co., 868 F.2d 1226, 1236 (Fed. Cir. 1989). See MPEP § 2131. To constitute anticipation, all material elements of the claim must be found in one prior art source. In re Marshall, 198 U.S.P.Q. 344 (C.C.P.A. 1978). Additionally, the elements of the reference must be arranged as required by the claim. In re Bond, 15 U.S.P.Q. 2d 1566 (Fed. Cir. 1999). Applicant respectfully submits that the cited reference does not teach all the materials elements and do not arrange the elements as required by the rejected claim, as amended.

Independent Claim 1 has been amended to read as follows:

> 1. A percutaneously implantable replacement heart valve device for implantation in a patient, comprising:
>
> an expandable stent member having an inner channel, the expandable stent member collapsible and configured for percutaneous delivery; and
>
> a valve means made of biocompatible tissue material and attached to the expandable stent member, the valve means including an outer cuff layer and two to four individual leaflets, wherein each of the two to four individual leaflets is rectangular in shape in side elevation view, wherein a crease is located between the two to four individual leaflets and the outer cuff layer at a base of the two to four individual leaflets, and wherein after implantation in the patient, the valve means resides as a single element entirely within the inner channel of the expandable stent member, wherein only the two to four individual leaflets reside radially inward from the

outer cuff layer, and wherein the valve means is formed without cutting slits into said biocompatible tissue material to form said leaflets.

Applicants believe that support for all amendments to the claims in this reply reside within U.S. Pat. App. No. 10/037,266 filed on January 4, 2002, including at least Figures 1-3B, as well as the associated portions of the specification. Applicants further note to the Examiner's attention that Claim 1, as amended, includes some limitations recited in Claim 1 of Applicants' granted U.S. Pat. No. 8,790,398.

In view of the amendments made to Claim 1, at the least, Cribier fails to disclose the limitations that the valve means resides as a single element entirely within the inner channel of the expandable stent member, as well as having two to four individual leaflets that are rectangular in shape in side elevation view. Other limitations may also distinguishable. Figs. 11a-11e of Cribier are provided below (it is noted that Cribier includes other figures):

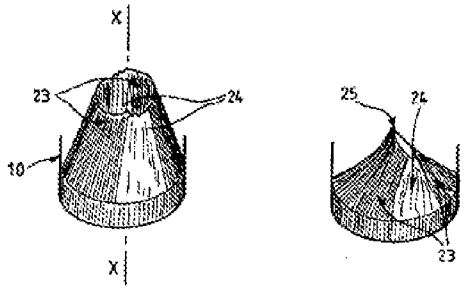


FIG_11a

FIG_11b

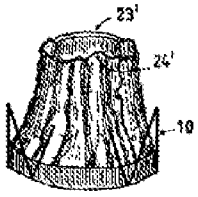


FIG_11c

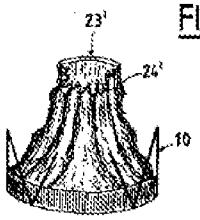


FIG_11d

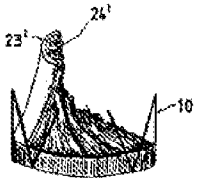
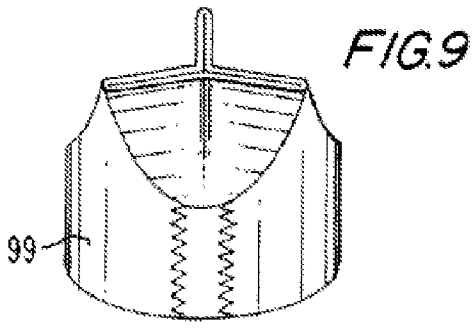


FIG_11e

The valve means of Cribier appears to extend beyond the frame 10 and does not include two to four individual leaflets that are rectangular in shape in side elevation view. Based on the foregoing, the Examiner is requested to withdraw the pre-AIA 35 U.S.C. § 102(e) rejection of amended Claim 1 based on Cribier.

The Examiner rejected Claims 1 and 9 under pre-AIA 35 U.S.C. § 102(e) as being anticipated by United States Patent No. 6,893,460 to Spenser ("Spenser"). Because the Examiner has asserted Spenser under 35 U.S.C. § 102(e), Applicants do not admit that Spenser is in fact prior art to the claimed invention, but reserve the right to swear behind Spenser if necessary to remove it as a reference. In the Office Action, the Examiner asserted that the present invention is unpatentable over Spenser.

At the least, Spenser fails to disclose the limitations that the two to four individual leaflets that are rectangular in shape in side elevation view (other limitations may also distinguishable). More particularly, the valve means of Spenser appears to include arcuate-shaped leaflet portions, such as those shown in Fig. 9 below (it is noted that Spenser includes other figures):



Based on the foregoing, the Examiner is requested to withdraw the pre-AIA 35 U.S.C. § 102(e) rejection of amended Claim 1 based on Spenser.

B. Rejection Under 35 U.S.C. § 103(a)

The Examiner rejected Claims 3-5 under pre-AIA 35 U.S.C. § 103(a) as being unpatentable over Cribier in view of U.S. Patent No. 4,553,974 to Dewanjee ("Dewanjee"); Claim 6 is rejected under pre-AIA 35 U.S.C. § 103(a) as being unpatentable over Cribier in view of U.S. Patent Application Publication No. 2002/0032482 to Cox ("Cox"); and Claim 29 is rejected under pre-AIA 35 U.S.C. § 103(a) as being unpatentable over Cribier in view of U.S. Patent No. 5,344,442 to Deac ("Deac").

If an independent claim is nonobvious under 35 U.S.C. §103, then any claim depending therefrom is nonobvious. In re Fine, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988). See MPEP §2143.03. Based on the cited references, Claim 1 appears to be nonobvious under 35 U.S.C. §103. Accordingly, the Examiner is requested to withdraw the 35 U.S.C. §103 rejections of previously rejected, but still pending Claims 3, 5 and 6 that depend from Claim 1.

CONCLUSION

In view of the foregoing, Applicants believe the claims as amended are in allowable form. In the event that the Examiner finds a remaining impediment to a prompt allowance of this application that may be clarified through a telephone interview, or which may be overcome by an Examiner's Amendment, the Examiner is requested to contact the undersigned attorney.

Respectfully submitted,

FOX ROTHSCHILD LLP

/ Mark L. Yaskanin /

Mark L. Yaskanin
Registration No. 45,246
Customer No. 29880
Phone: (303) 446.3852
Facsimile: (303) 292.1300

Dated: January 6, 2016

Electronic Patent Application Fee Transmittal

Application Number:	13675665
Filing Date:	13-Nov-2012
Title of Invention:	PERCUTANEOUSLY IMPLANTABLE REPLACEMENT HEART VALVE DEVICE AND METHOD OF MAKING SAME
First Named Inventor/Applicant Name:	David Paniagua
Filer:	Mark Lauren Yaskanin/Carol Donahue
Attorney Docket Number:	109978.10101

Filed as Small Entity

Filing Fees for Utility under 35 USC 111(a)

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Basic Filing:				
Pages:				
Claims:				
Miscellaneous-Filing:				
Petition:				
Patent-Appeals-and-Interference:				
Post-Allowance-and-Post-Issuance:				
Extension-of-Time:				

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Extension - 3 months with $0 paid	2253	1	700	700
Miscellaneous:				
Submission- Information Disclosure Stmt	2806	1	90	90
		Total in USD ($)		**790**

Electronic Acknowledgement Receipt

EFS ID:	24547159
Application Number:	13675665
International Application Number:	
Confirmation Number:	1995
Title of Invention:	PERCUTANEOUSLY IMPLANTABLE REPLACEMENT HEART VALVE DEVICE AND METHOD OF MAKING SAME
First Named Inventor/Applicant Name:	David Paniagua
Customer Number:	29880
Filer:	Mark Lauren Yaskanin/Carol Donahue
Filer Authorized By:	Mark Lauren Yaskanin
Attorney Docket Number:	109978.10101
Receipt Date:	06-JAN-2016
Filing Date:	13-NOV-2012
Time Stamp:	18:01:03
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	yes
Payment Type	Credit Card
Payment was successfully received in RAM	$790
RAM confirmation Number	5050
Deposit Account	501943
Authorized User	YASKANIN, MARK L.

The Director of the USPTO is hereby authorized to charge indicated fees and credit any overpayment as follows:

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Charge any Additional Fees required under 37 CFR 1.17 (Patent application and reexamination processing fees)

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Charge any Additional Fees required under 37 CFR 1.20 (Post Issuance fees)

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File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Extension of Time	Colibri_10101_Extension-Request.PDF	156706 92b6ba9641fd624d902e6a7f0f30f5890bffdb2c	no	2
Warnings:					
Information:					
2	Information Disclosure Statement (IDS) Form (SB08)	Colibri_10101_SUPP_IDS.PDF	1070992 14dece3c9799b87bcf317062fc4b5b4fd142ebd8	no	4
Warnings:					
Information:					
3	Foreign Reference	WO-2010-141847.PDF	1544183 f87e43199ce67e82339efeb48d086d50ce429253	no	30
Warnings:					
Information:					
4	Non Patent Literature	NPL_Sacks_Orthotropic-Mechanical-Properties.PDF	1342139 5a8c5d283cc2913d281d59c05ef0008ce8858944	no	11
Warnings:					
Information:					
5	Non Patent Literature	10110_US_12-229192_Notice-of-Allowance_2011-09-22.PDF	196253 d25ac9ebd4c20c489d8480f1c7c1ec0dfc99fb32	no	4
Warnings:					
Information:					
6		10101_OA_Response_2016-01-06.PDF	202590 218ef324ebef7ba69be23945e3efbdff17ea8843	yes	10

Multipart Description/PDF files in .zip description

Document Description	Start	End
Amendment/Req. Reconsideration-After Non-Final Reject	1	1
Claims	2	3
Applicant Arguments/Remarks Made in an Amendment	4	10

Warnings:					
Information:					
7	Fee Worksheet (SB06)	fee-info.pdf	32961 19427d8cd97aa626ac4f4629f703eb850535d723	no	2
Warnings:					
Information:					
		Total Files Size (in bytes):	4545824		

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If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

National Stage of an International Application under 35 U.S.C. 371

If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office

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PTO/AIA/22 (03-13)
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U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

PETITION FOR EXTENSION OF TIME UNDER 37 CFR 1.136(a)

Docket Number (Optional): 109978.10101

Application Number: 13/675,665

Filed: 2012-11-13

For: Percutaneously Implantable Replacement Heart Valve Device and Method of Making Same

Art Unit: 3738

Examiner: Cheryl L. Miller

This is a request under the provisions of 37 CFR 1.136(a) to extend the period for filing a reply in the above-identified application.

The requested extension and fee are as follows (check time period desired and enter the appropriate fee below):

	Fee	Small Entity Fee	Micro Entity Fee	
☐ One month (37 CFR 1.17(a)(1))	$200	$100	$50	$
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☐ Four months (37 CFR 1.17(a)(4))	$2,200	$1,100	$550	$
☐ Five months (37 CFR 1.17(a)(5))	$3,000	$1,500	$750	$

☑ Applicant asserts small entity status. See 37 CFR 1.27.

☐ Applicant certifies micro entity status. See 37 CFR 1.29.
Form PTO/SB/15A or B or equivalent must either be enclosed or have been submitted previously.

☐ A check in the amount of the fee is enclosed.

☐ Payment by credit card. Form PTO-2038 is attached.

☐ The Director has already been authorized to charge fees in this application to a Deposit Account.

☑ The Director is hereby authorized to charge any fees which may be required, or credit any overpayment, to Deposit Account Number 50-1943.

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I am the

☐ applicant.

☑ attorney or agent of record. Registration number 45246.

☐ attorney or agent acting under 37 CFR 1.34. Registration number _____.

/ Mark L. Yaskanin / — Signature

2016-01-06 — Date

Mark L. Yaskanin — Typed or printed name

303-446-3852 — Telephone Number

NOTE: This form must be signed in accordance with 37 CFR 1.33. See 37 CFR 1.4 for signature requirements and certifications. Submit multiple forms if more than one signature is required, see below*.

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5. A record related to an International Application filed under the Patent Cooperation Treaty in this system of records may be disclosed, as a routine use, to the International Bureau of the World Intellectual Property Organization, pursuant to the Patent Cooperation Treaty.
6. A record in this system of records may be disclosed, as a routine use, to another federal agency for purposes of National Security review (35 U.S.C. 181) and for review pursuant to the Atomic Energy Act (42 U.S.C. 218(c)).
7. A record from this system of records may be disclosed, as a routine use, to the Administrator, General Services, or his/her designee, during an inspection of records conducted by GSA as part of that agency's responsibility to recommend improvements in records management practices and programs, under authority of 44 U.S.C. 2904 and 2906. Such disclosure shall be made in accordance with the GSA regulations governing inspection of records for this purpose, and any other relevant (*i.e.*, GSA or Commerce) directive. Such disclosure shall not be used to make determinations about individuals.
8. A record from this system of records may be disclosed, as a routine use, to the public after either publication of the application pursuant to 35 U.S.C. 122(b) or issuance of a patent pursuant to 35 U.S.C. 151. Further, a record may be disclosed, subject to the limitations of 37 CFR 1.14, as a routine use, to the public if the record was filed in an application which became abandoned or in which the proceedings were terminated and which application is referenced by either a published application, an application open to public inspection or an issued patent.
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INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(Not for submission under 37 CFR 1.99)

Application Number	13675665
Filing Date	2012-11-13
First Named Inventor	David Paniagua
Art Unit	3738
Examiner Name	Cheryl L. Miller
Attorney Docket Number	109978.10101

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	1	20080131522		2008-06-05	Liu et al.	

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	1	2010/141847	WO		2010-12-09	ATS Medical, Inc.		

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INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	13675665
	Filing Date	2012-11-13
	First Named Inventor	David Paniagua
	Art Unit	3738
	Examiner Name	Cheryl L. Miller
	Attorney Docket Number	109978.10101

	1	SACKS, Michael S. et al., "Orthotropic Mechanical Properties of Chemically Treated Bovine Pericardium" Annals of Biomedical Engineering, 1998, vol. 26, pp. 892-902 (10254 OA, 12/03/15)
	2	Notice of Allowance issued September 22, 2011, in U.S. Application No. 12/228,192 (109978.10110)

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Examiner Signature		Date Considered	

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INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	13675665
	Filing Date	2012-11-13
	First Named Inventor	David Paniagua
	Art Unit	3738
	Examiner Name	Cheryl L. Miller
	Attorney Docket Number	109978.10101

CERTIFICATION STATEMENT

Please see 37 CFR 1.97 and 1.98 to make the appropriate selection(s):

That each item of information contained in the information disclosure statement was first cited in any communication from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e)(1).

OR

☐ That no item of information contained in the information disclosure statement was cited in a communication from a foreign patent office in a counterpart foreign application, and, to the knowledge of the person signing the certification after making reasonable inquiry, no item of information contained in the information disclosure statement was known to any individual designated in 37 CFR 1.56(c) more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e)(2).

See attached certification statement.

☒ The fee set forth in 37 CFR 1.17 (p) has been submitted herewith.

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SIGNATURE

A signature of the applicant or representative is required in accordance with CFR 1.33, 10.18. Please see CFR 1.4(d) for the form of the signature.

Signature	/ Mark L. Yaskanin /	Date (YYYY-MM-DD)	2016-01-06
Name/Print	Mark L. Yaskanin	Registration Number	45246

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7. A record from this system of records may be disclosed, as a routine use, to the Administrator, General Services, or his/her designee, during an inspection of records conducted by GSA as part of that agency's responsibility to recommend improvements in records management practices and programs, under authority of 44 U.S.C. 2904 and 2906. Such disclosure shall be made in accordance with the GSA regulations governing inspection of records for this purpose, and any other relevant (i.e., GSA or Commerce) directive. Such disclosure shall not be used to make determinations about individuals.

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(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

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(25) Filing Language: English

(26) Publication Language: English

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61/184,519 5 June 2009 (05.06.2009) US

(71) Applicant *(for all designated States except US)*: **ATS MEDICAL, INC.** [US/US]; 3905 Annapolis Lane, Suite 105, Plymouth, Minnesota 55447 (US).

(72) Inventors; and
(75) Inventors/Applicants *(for US only)*: **MALEWICZ, Andrzej M.** [PL/US]; 4139 Garfield Avenue South, Minneapolis, Minnesota 55409 (US). **WESTON, Matthew W.** [US/US]; 828 Aspen Circle, Little Canada, Minnesota 55109 (US).

(74) Agent: **WRIGLEY, Barbara A.**; OPPENHEIMER WOLFF & DONNELLY LLP, Plaza VII, Suite 3300, 45 South Seventh Street, Minneapolis, MN 55402-1609 (US).

(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PE, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

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Declarations under Rule 4.17:

— *as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii))*

— *as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii))*

— *of inventorship (Rule 4.17(iv))*

[Continued on next page]

(54) **Title**: FLEXIBLE COMMISSURE STRUCTURE FOR ATTACHING VALVE BIOPROSTHESIS

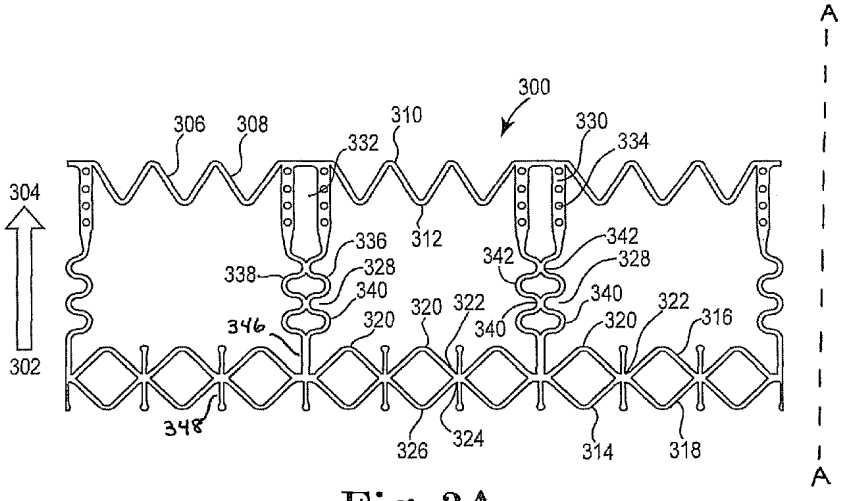

Fig. 3A

(57) **Abstract**: A cylindrical anchoring structure for supporting a tissue heart valve is disclosed. The cylindrical anchoring structure defines a central longitudinal axis and includes an inflow ring having at least one sinusoidal-shaped wire with a plurality of peaks and troughs and an outflow ring having at least one sinusoidal-shaped wire with a plurality of peaks and troughs. A flexible commissure post having a longitudinal axis connects the inflow ring and the outflow ring. The flexible commissure post has a bending flexibility along a plane defined by a surface containing all straight lines connecting any point on the central longitudinal axis of the cylindrical anchoring structure and any point on the longitudinal axis of the flexible commissure post.

WO 2010/141847 A1

Published:

— *with international search report (Art. 21(3))*

FLEXIBLE COMMISSURE STRUCTURE FOR ATTACHING VALVE BIOPROSTHESIS

BACKGROUND OF THE INVENTION

Field of the Invention.

[0001] The present invention relates to bioprosthetic heart valve replacement systems. More particularly, the present invention relates to a bioprosthetic heart valve supported by a tubular, expandable anchoring structure having commissure posts of improved bending flexibility.

Description of the Related Art.

[0002] Prosthetic heart valves may be used to replace diseased natural heart valves in human patients. Minimally invasive bioprosthetic heart valves typically include a proximal end or inflow ring and a distal end or outflow ring. At least two, but typically three, support structures extend from and connect the inflow ring to the outflow ring. These support structures are commonly referred to as commissure posts. In conventional devices these posts are rigid to provide support to the heart valve, but are also somewhat longitudinally flexible to allow them to be manipulated during implantation. The commissure posts define the juncture between adjacent tissue or synthetic leaflets otherwise secured thereto.

[0003] The body of the heart valve typically includes a plurality of multiple leaflets of valve tissue joined by seams with each seam formed by the junction of two leaflets. The inlet comprises an inflow annulus, preferably with either a scalloped or straight edge. The inflow ring may further optionally include a reinforcement structure, such as fabric, that can be stitched to it. Both the inflow and outflow rings are typically formed with an undulating or sinusoidal configuration, which are connected by the rigid commissure posts. The anchoring structure for a minimally invasive heart valve is typically made from a wire frame of metal that exhibits a high modulus of elasticity and that is biocompatible, such as Nitinol, as such materials exhibiting superior radial compressibility allow the

anchoring structure to self-expand upon the release of the radially compressive forces. Optional, integrally formed commissural tabs attach the tissue segments to the commissural posts of the stent. Alternatively, the tissue heart valve may simply be attached to the commissural posts along the seam line or at a portion of the outflow end. During delivery and deployment, the stented heart valve resides in a radially-compressed or folded configuration in a delivery tool or catheter.

[0004] One problem associated with the delivery and deployment of a conventional stented bioprosthetic heart valves with rigid commissural posts is that binding, overlapping or interference can occur between adjacent heart valve segments. For example, the stented heart valve is typically placed in a delivery mechanism. As the delivery mechanism is threaded through the vasculature it bends as it follows the artery. In addition, upon deployment the delivery system containing the stented heart valve may curve slightly. In both of these cases, the inside radius of the bend causes wire segments of the anchoring structure to move toward each other causing overlapping. Moreover, on the outside radius of the bend, the wire segments may move away from each other, leaving large gaps that prevent the inflow ring from effectively seating the valve in the annulus. This can lead to improper annulus support, trauma, flow disturbance, kinking, paravalvular leakage, and interference with coronary ostia.

[0005] Still a further problem associated with minimally invasive bioprosthetic heart valves is the failure of the commissure posts to accommodate a curved aortic profile. This in turn leads to leaking, improper support of the annulus and potential trauma to the aortic wall.

[0006] Yet another problem is that the rigid commissure posts in conventional designs fail to allow the inflow and outflow rings to fully radially expand leading to leaking and improper seating of the valve in the annulus.

[0007] The present invention is directed to solving, or at least reducing, some or all of the aforementioned problems.

SUMMARY OF THE INVENTION

[0008] The present invention advantageously provides a stented heart valve that includes a commissure structure which has a bending flexibility that is greater than those of conventional structures and avoids the problems associated with conventional stented bioprosthetic valves and also exhibits improved overall flexibility.

[0009] An exemplary embodiment of the invention provides a stented bioprosthetic heart valve that includes a plurality of commissural posts formed from a single wire having a sinusoidal wave pattern cut along a longitudinal axis thereof.

[0010] Another exemplary embodiment of the invention provides a minimally invasive bioprosthetic heart valve that includes a plurality of commissural posts formed from multiple wires each having a sinusoidal wave pattern cut along a longitudinal axis thereof.

[0011] Yet another exemplary embodiment of the invention provides a stented bioprosthetic heart valve that includes commissural posts formed by a single or double wire each including a generally sinusoidal wave pattern cut along a longitudinal length thereof wherein the bending flexibility of the commissure post increases as the frequency of the generally sinusoidal wave increases.

[0012] In yet another exemplary embodiment of the invention, a stented bioprosthetic heart valve includes commissural posts formed by a single or double wire each including a generally sinusoidal wave pattern cut along a longitudinal length thereof wherein the bending flexibility of the commissure post increases as the amplitude or wave height of the generally sinusoidal waves increases.

[0013] In yet another exemplary embodiment of the invention, a stented bioprosthetic heart valve includes commissural posts formed by a single or double wire each including a generally sinusoidal wave pattern cut along a longitudinal

length thereof wherein the bending flexibility of the commissure post increases as the frequency and amplitude of the generally sinusoidal waves increases.

[0014] In yet another exemplary embodiment of the invention, a stented bioprosthetic heart valve includes commissural posts formed by a single or double wire each including a generally sinusoidal wave pattern cut along a longitudinal length thereof wherein the bending flexibility of the commissure post increases as the wavelength, or peak to peak distance, decreases.

[0015] In yet another exemplary embodiment of the invention, the flexible commissure posts have a bending flexibility along a plane defined by a surface containing all straight lines connecting any point on the central longitudinal axis of the cylindrical anchoring structure and any point on the longitudinal axis of the flexible commisure posts.

[0016] In yet another exemplary embodiment of the invention, a stented bioprosthetic heart valve includes commissural posts that are especially designed for replacement of aortic and pulmonary valves.

[0017] In another exemplary embodiment of the invention a valve assembly is provided, comprising a valve and anchoring structure with flexible commissure posts, in which the valve comprises a body having a proximal end and a distal end, an inlet at the proximal end, and an outlet at the distal end. The inlet comprises an inflow annulus, preferably with either a scalloped or straight edge. The outlet comprises a plurality of tabs that are supported by the commissural posts anchoring structure at the outlet end. In exemplary embodiments of the invention, the plurality of tabs is spaced evenly around the circumference of the valve.

[0018] It should be noted that for the purposes of this invention, the phrase "generally sinusoidal" is intended to include waves characterized by sine and cosine functions as well as waves which are not rigorously characterized by those functions, but nevertheless resemble such waves. In a more general way, such waves include those which are characterized as having one or more peaks and

troughs. As an example, a wave whose peaks and troughs are U-shaped or bulbous is intended to be included. Also intended to be included, without limiting the definition, are waves which are more triangular in shape such as a saw-tooth wave or waves whose peaks and troughs are rectangular.

[0019] The flexible commissure post in accordance with the invention ensures complete or full radial expansion and deployment of the inflow and outflow rings thus providing for precise placement of the heart valve and a more open path for blood flow.

BRIEF DESCRIPTION OF THE DRAWINGS

[0020] FIG. 1 shows an exemplary valve during normal operation. FIG. 1A shows the valve in the open position during peak flow. FIG. 1B shows the valve in closed position to prevent backflow of the fluid across the valve.

[0021] FIG. 2 is an exemplary bioprosthetic tissue valve for use with the present invention.

[0022] FIG. 3A depicts an exemplary embodiment of a tubular anchoring device including flexible commissure posts in accordance with one aspect of the present invention cut along line A-A and laid flat.

[0023] FIG. 3B depicts a variation of the tubular anchoring device with flexible commissure posts illustrated in FIG. 3A.

[0024] FIG. 4A depicts a further embodiment of one aspect of a tubular anchoring device with flexible commissure posts in accordance with the present invention cut along line B-B and laid flat.

[0025] FIG. 4B depicts a variation of the tubular anchoring device with flexible commissure posts illustrated in FIG. 4A.

[0026] FIG. 5A depicts an exemplary embodiment of the bioprosthetic heart valve of FIG. 2 supported by the tubular anchoring structure with flexible commisure posts of the present invention.

[0027] FIG. 5B is a top view of the cylindrical anchoring structure showing the longitudinal axis L' through the center of the cylindrical anchoring structure.

[0028] FIG. 6 depicts the exemplary bioprosthetic heart valve supported by the tubular anchoring structure with flexible commisure posts of the present invention positioned within an aorta.

DETAILED DESCRIPTION OF THE INVENTION

[0029] While this invention may be embodied in many different forms, there are described in detail herein various embodiments of the invention. This description is an exemplification of the principles of the invention and is not intended to limit the invention to the particular embodiments illustrated.

[0030] When referring to the terms "peak" and "trough" as they relate to the commissure posts these terms are defined with respect to the left and right sides of the figures, respectively. As seen in the figures, each of the commissure posts has a paddle end and a proximal/straight end. With regard to the commissure posts, peaks are the first and subsequent sinusoidal wave commencing at the inflow end and are concave relative to the right side of the respective figure and convex relative to the left side of the respective figure. Troughs as they pertain to the commissure post, on the other hand, are convex relative to the right side of the figure and concave relative to the left side of the figure. As may be appreciated by those of ordinary skill in the art, the commissure post may have a sinusoidal wave formed from one wire, as depicted in FIGS. 4A and 4B or may have sinusoidal waves formed from multiple wires, as depicted in FIGS. 3A and 3B.

[0031] In addition given constant wave amplitude, as the frequency of the sinusoidal waves increases, the bending flexibility of the commissure posts increases. Further, given constant wave frequency, as the amplitude of the waves increases the bending flexibility of the commissure posts increases. Moreover, increasing wave amplitude and wave frequency result in an increase in commissure post bending flexibility. In addition, as the peak to peak distance,

or wavelength, between each wave decreases, the bending flexibility of the commissure post increases.

[0032] As seen in the figures, the tubular or generally cylindrical anchoring structure includes an inflow end with an inflow ring and an outflow end with an outflow ring. With respect to the inflow and outflow rings peaks are concave relative to the proximal end of the anchoring structure and convex relative to the distal end of the anchoring structure. Troughs, on the other hand, are convex relative to the proximal end of the anchoring structure and concave relative to the distal end of the anchoring structure.

[0033] In addition, by "flexible" commissure posts and enhanced or greater "flexibility" we mean the bending capacity or bending flexibility of the commissure posts of the stented heart valve in or along a plane defined by the surface containing all the straight lines that connect any point on the longitudinal axis running through the center of the cylindrical anchoring structure (as seen in FIG. 5B) and any point on the longitudinal axis of the commissure post (as seen in FIG. 5A). The bending flexibility of the commissure posts in accordance with the invention is 10% or more than conventional rigid posts, which tend to flex only along the longitudinal axis of the post.

[0034] Turning now to the figures, the invention relates to valve replacement systems including a tubular anchoring structure that has flexible commissure posts. As illustrated in FIG. 1, a valve (1) comprises a distal or outflow end (2), leaflets (3) and a proximal or inflow end (4). A typical valve functions similar to a collapsible tube in that it opens widely during systole or in response to muscular contraction, to enable unobstructed forward flow across the valvular orifice (FIG. 1A). In contrast, at the end of systole or contraction, as illustrated in FIG. 1B, as forward flow decelerates, the walls of the tube are forced centrally between the sites of attachment to the vessel wall and the valve closes completely.

[0035] One embodiment of a bioprosthetic valve 5 for use with the system of the present invention is illustrated in FIG. 2 and is comprised of a body having a

proximal end or inflow portion 6 and a distal end or outflow portion 7. The body is comprised of multiple leaflets of valve tissue joined by seams 8, wherein each seam is formed by a junction of two leaflets. An optional commissural tab region 9, which may be integrally formed from adjacent leaflets, extends from each seam at the distal end of the valve body. The proximal end 6 has a peripheral edge that can be scalloped or straight. The proximal end or inflow 6 of the valve can further comprise an optional reinforcement structure 10 that can be stitched to it. In preferred embodiments of the invention, the inflow edge of the valve is scalloped. The novel design for a bioprosthetic heart valve system supported by a tubular, expandable anchoring structure having commissure posts of improved bending flexibility is not limited, however, to the specific valve illustrated in FIG. 2.

[0036] Turning now to FIG. 3A one exemplary embodiment of a tubular, expandable anchoring structure 300 including commissure posts of improved bending flexibility is shown. Blood inflow is depicted at 302 and outflow is depicted at 304. The anchoring structure is generally cylindrical in shape but for purposes of illustration is depicted as being cut along line A-A and laid flat. The anchoring structure 300 includes an outflow ring 306 having a single sinusoidal-shaped wire 308 including peaks 310 and troughs 312. Anchoring structure 300 also includes inflow ring 314 having two sinusoidal-shaped wires designated as distal inflow wire ring 316 and proximal inflow wire ring 318. Distal inflow wire ring 316 includes peaks 320 and troughs 322. Proximal inflow wire ring 318 includes peaks 324 and troughs 326. As can be seen from FIG. 3A the troughs 322 of distal inflow wire ring 316 are joined to the peaks 324 of proximal inflow wire ring 318. Those of ordinary skill in the art will appreciate that although two inflow wires forming inflow ring 314 are depicted, a single wire, triple wires or any other configuration may also be used. At the outflow end, flexible commissure posts 328 include paddle portion 330 that couples the commissure posts 328 to the outflow ring 306. Paddle portion 330 with axial slot 332 extends along the longitudinal axis of commissure post 330. Suturing holes 334 are positioned on the outer periphery of paddle 330 and are used to suture a bioprosthetic heart valve, such as shown in FIG. 2, to the anchoring structure 300.

Commissure post 328 includes first and second commissure post wires 336, 338 each with peaks 340 and troughs 342 that converge to a single wire 346 at the inflow end that couples the flexible commisure posts to the inflow ring 314. As can be seen from FIG. 3A the first commissure post wire 336 is joined at trough 342 to a peak 340 of the second commissure wire 338. The number of commissure posts 328 in this embodiment can range from two to four, depending on the number of leaflets present in the valve sinus. Thus, in one embodiment the anchoring structure comprises three support posts for a three-leaflet valve with a sinus that features three natural commissural posts. The commissure posts 328 of the anchoring structure 300 are configured to coincide with the natural commissural points of the sinus. The inflow ring 314 optionally includes finger-like elements 348 positioned between distal and proximal inflow wires and extend in an axial direction therefrom. Finger-like elements 348 are designed to lend additional support to fabric that may cover inflow rim 314 to anchor the fabric and permit tissue ingrowth. In addition, although only two waves are shown those of ordinary skill in the art will appreciate that the number of waves may be varied to achieve the desired bending flexibility.

[0037] FIG. 3B depicts a variation of the tubular, expandable anchoring structure 300 including commissure posts of improved bending flexibility of FIG. 3A. In FIG. 3B paddle portion 330 has been eliminated and a single wire 346' extends from the commissure post which couples the commissure post directly to the outflow ring. Single wire 346' may contain suturing holes to attach the tissue heart valve to the commisure posts. The anchoring structure 300 includes an outflow ring 306 having a single sinusoidal-shaped wire 308 including peaks 310 and troughs 312. Anchoring structure 300 also includes inflow ring 314 having two sinusoidal-shaped wires designated as distal inflow wire ring 316 and proximal inflow wire ring 318. Distal inflow wire ring 316 includes peaks 320 and troughs 322. Proximal inflow wire ring 318 includes peaks 324 and troughs 326. As can be seen from FIG. 3B the troughs 322 of distal inflow wire ring 316 are joined to the peaks 324 of proximal inflow wire ring 318. Those of ordinary skill in the art will appreciate that although two inflow wires forming inflow ring 314 are depicted, a single wire, triple wires or any other configuration may also be

used. Commissure post 328 includes first and second commissure post wires 336, 338 each with peaks 340 and troughs 342. As can be seen from FIG. 3B the first commissure post wire 336 is joined at trough 342 to a peak 340 of the second commissure wire 338. The number of commissure posts 328 in this embodiment can range from two to four, depending on the number of leaflets present in the valve sinus. Thus, in one embodiment the anchoring structure comprises three support posts for a three-leaflet valve with a sinus that features three natural commissural posts. The commissure posts 328 of the anchoring structure 300 are configured to coincide with the natural commissural points of the sinus. In addition, while multiple waves are depicted the actual number of waves may vary depending on the desired bending flexibility.

[0038] Turning now to FIG. 4A another exemplary embodiment of a tubular, expandable anchoring structure 400 including commissure posts of improved bending flexibility is shown. Blood inflow is depicted at 402 and outflow is depicted at 404. The anchoring structure 400 includes an outflow ring 406 having a single sinusoidal-shaped wire 408 including peaks 410 and troughs 412. Anchoring structure 400 also includes inflow ring 414 having first and second sinusoidal-shaped wires designated as distal inflow wire ring 416 and proximal inflow wire ring 418. Distal inflow wire ring 416 includes peaks 420 and troughs 422. Proximal inflow wire ring 418 includes peaks 424 and troughs 426. As can be seen from FIG. 4A the troughs 422 of distal inflow wire ring 416 are joined to the peaks 424 of proximal inflow wire ring 418. One of ordinary skill in the art will appreciate that although two inflow wires forming inflow ring 414 are depicted, a single wire, triple wires or any other configuration may also be used. Flexible commissure posts 428 include paddle portion 430 with axial slot 432 at the outflow end and extending along the longitudinal axis of commissure post 430. Suturing holes 434 are positioned on the outer periphery of paddle 430 and are used to suture a bioprosthetic heart valve, such as shown in FIG. 2, to the anchoring structure 400. Commissure post 428 includes a single sinusoidal wave like wire 436 with peaks 440 and troughs 442 which couples to the inflow ring 414 by single wire 446. The number of commissure posts 428 in this embodiment

can range from two to four, depending on the number of leaflets present in the valve sinus. Thus, in one embodiment the anchoring structure comprises three support posts for a three-leaflet valve with a sinus that features three natural commissural posts. The commissure posts 428 of the anchoring structure 400 are configured to coincide with the natural commissural posts of the sinus. In addition, although only two waves are shown those of ordinary skill in the art will appreciate that the number of waves may be varied to achieve the desired bending flexibility.

[0039] FIG. 4B depicts a variation of the tubular, expandable anchoring structure 400 including commissure posts of improved bending flexibility of FIG. 4A. In FIG. 4B paddle portion 430 has been eliminated and a single wire 446' extends from the commissure post which couples the commissure post directly to the outflow ring. Single wire 346' may contain suturing holes to attach the tissue heart valve to the commisure posts. The anchoring structure 400 includes an outflow ring 406 having a single sinusoidal-shaped wire 408 including peaks 410 and troughs 412. Anchoring structure 400 also includes inflow ring 414 having two sinusoidal-shaped wires designated as distal inflow wire ring 416 and proximal inflow wire ring 418. Distal inflow wire ring 416 includes peaks 420 and troughs 422. Proximal inflow wire ring 418 includes peaks 424 and troughs 426. As can be seen from FIG. 4B the troughs 422 of distal inflow wire ring 416 are joined to the peaks 424 of proximal inflow wire ring 418. Those of ordinary skill in the art will appreciate that although two inflow wires forming inflow ring 414 are depicted, a single wire, triple wires or any other configuration may also be used. Commissure post 428 includes a single commissure post wire 436 each with peaks 440 and troughs 442. The number of commissure posts 428 in this embodiment can range from two to four, depending on the number of leaflets present in the valve sinus. Thus, in one embodiment the anchoring structure comprises three support posts for a three-leaflet valve with a sinus that features three natural commissural posts. The commissure posts 428 of the anchoring structure 400 are configured to coincide with the natural commissural points of the

sinus. In addition, while multiple waves are depicted the actual number of waves may vary depending on the desired bending flexibility.

[0040] FIG. 5 shows an exemplary bioprosthetic valve system including the exemplary anchoring structure with flexible commissure posts depicted in FIGS. 4A. Those of ordinary skill in the art will appreciate that the anchoring structure of FIG. 3A, 3B or 4B may also be used.

[0041] The anchoring structure 500 is adapted to support a valve such as that illustrated in FIG. 2. As seen in FIG. 5A, the anchoring structure 500 has a generally tubular or cylindrical configuration within which a bioprosthetic heart valve 5 is secured. The valve 5 is secured at its proximal (inflow) annulus by attachment to the inflow ring 514 of the anchoring structure 500 and at its distal end via the optional commissural tabs 9 that are threaded through the axially extending slots 532 of the paddle portion 530. Paddle portion 530 couples the flexible commissure posts 528 to the outflow ring 506 of the anchoring structure 500, whereas the proximal end of the commissure posts 528 are coupled to the inflow ring 514 of the anchoring structure 500 by single wire connector 546.

[0042] In FIG. 5A the outflow ring 506 of the anchoring structure 500 is depicted as comprising a single sinusoidal-shaped wire that extends between commisure posts 528 generally at or above the axially extending slots 532 that reside therein. The single wire of the outflow ring 506 is configured in an undulating or sinusoidal pattern forming peaks 510 and troughs 512. Anchoring structure 500 also includes inflow ring 514 having first and second sinusoidal-shaped wires designated as distal inflow wire ring 516 and proximal inflow wire ring 518. Distal inflow wire ring 516 includes peaks 520 and troughs 522. Proximal inflow wire ring 518 includes peaks 524 and troughs 526. As can be seen from FIG. 5A the troughs 522 of distal inflow wire ring 516 are joined to the peaks 524 of proximal inflow wire ring 518. This arrangement allows the distal inflow wire ring and proximal inflow wire ring to move together when the valve is in its radially compressed state prior to delivery thus preventing possible damage to the bioprosthetic heart valve.

[0043] Flexible commissure posts 528 include paddle portion 530 with axial slot 532 extending along the longitudinal axis (L) of commissure post 528. Suturing holes 534 are positioned on the outer periphery of paddle 530 and are used to suture a bioprosthetic heart valve, such as shown in FIG. 2, to the anchoring structure 500. Paddle portion 530 of commissure post 528 connects commissure post 528 to the single wire of inflow ring 506 at trough 512. The single wire connector 546 couples commissure post 528 to the inflow ring 514. Single wire connector 546 is designed to stabilize the anchoring structure and to prevent distortion of the valve during compression and expansion. The single wire connector 546 extends longitudinally in the axial direction of the cylindrical anchoring structure 500. Those of ordinary skill in the art will appreciate that both the inflow ring 514 and outflow ring 506 can be comprised of any number of wires without deviating from the spirit of the present invention.

[0044] Both the inflow 514 and outflow 506 rings of the anchoring structure 500 are formed with an sinusoidal wave configuration, although the inflow ring 514 may have a longer wavelength (circumferential dimension from peak to peak) and a lesser wave height (axial dimension from peak to peak) than the outflow ring 506. The wavelengths and wave heights of the inflow 514 and outflow 506 rings are selected to ensure uniform compression and expansion of the anchoring structure without distortion. The wavelength of the inflow rim 514 is further selected to support the geometry of the scalloped inflow annulus of a preferred valve of the present invention. Notably, as shown in FIG. 5, the sinusoidal wave pattern that forms the distal and proximal wires 516, 518 of inflow ring 514 is configured such that the single wire connector 546 is connected to the point at which peaks 524 and troughs 522 meet. Similarly, the undulating or sinusoidal wave pattern that forms the outflow ring 506 of the anchoring structure 500 is configured such that the paddle portion 530 of the commissure posts 528 is connected to the trough 512 of the single wire outflow ring 506. Locating the paddle portion of the commissure post 528 at the troughs 512 of the outflow ring 506 will prevent the longitudinal extension of outflow ring in the direction of the valve secured within the lumen of the anchoring structure upon compression of

the valve assembly, thereby eliminating any contact between valve and anchoring structure. Thus, compression of the valve and anchoring structure 500 does not lead to distortion of or injury to the tissue valve.

[0045] FIG. 5 further shows that the commissure posts 528 include sinusoidal-shaped waves cut thereinto. An important function of the commissure posts 528 is the stabilization of the valve in general, and in particular the prevention of any longitudinal extension at points of valve attachment to preclude valve stretching or distortion upon compression of the device. Another important function of the sinusoidal-shaped commissure posts is to provide for axial and bending decoupling of the inflow and outflow rings to ensure complete circumferential expansion and deployment of the inflow and outflow rings during placement thus providing a more open path for blood flow to the coronary ostia and through the coronary artery. As will be appreciated by those of skill in the art, the wavelengths, frequency and amplitude of the waves of the commissure posts in accordance with the present invention are selected to ensure uniform compression and expansion of the anchoring structure without distortion upon deployment and to ensure that the inflow ring expands to its full circumferential profile to allow for proper seating within the annulus.

[0046] The number of support posts 528 in this preferred embodiment can range from two to four, depending on the number of commissural posts present in the valve sinus. Thus, in a preferred embodiment, the anchoring structure comprises three support posts for a three-leaflet valve with a sinus that features three natural commissural posts. The support posts 528 of the anchoring structure 500 are configured to coincide with the natural commissural posts of the sinus.

[0047] As can be seen from FIG. 5, inflow ring 514 may be covered with a cloth or fabric material 550. The fabric 550 may comprise any suitable material including, but not limited to, woven polyester, polyester velour, polyethylene terepthalate, polytetrafluoroethylene (PTFE), or other biocompatible material. Fabric 550 permits for tissue ingrowth over time to firmly position the minimally invasive bioprosthetic valve system in the annulus.

[0048] FIG. 5B depicts the longitudinal axis (L') running through the center of the cylindrical anchoring structure, which in turn defines the plane of commissural post bending flexibility as hereinbefore noted.

[0049] FIG. 6 shows a bioprosthetic valve system including the exemplary anchoring structure with flexible commissure posts of FIG. 4A fully seated within an aorta after deployment. Those of ordinary skill in the art will appreciate that the anchoring structure of FIG. 3A, 3B or 4B and variations thereof may also be used. In the exemplary embodiment discussed above, a crimping tool may be used to crimp the exemplary heart valve supported by the anchoring structure with flexible commissure posts. The crimped valve is loaded into a delivery device, known to those of ordinary skill in the art, which is then used to deliver the crimped stented heart valve to an aortic annulus. The crimped stented heart valve may be delivered surgically or transapically. In surgical placement, the patient may be put on bypass and the aorta at least partially transected. The surgeon then positions the delivery device within the aortic annulus 630, radially compressing the native leaflets 632 as the crimped heart valve expands, such that the exposed inflow end 602 is substantially aligned with the inflow annulus of the native valve. As will be appreciated by those of ordinary skill in the art, warm bodily fluids may cause the exposed portion of the stented heart valve 600, i.e. the inflow end 602, to start to expand to the "remembered" shape as further illustrated in FIG. 6. Alternatively or in addition, the surgeon may apply a warm solution to the implantation site to promote re-expansion of the stented heart valve 600, such as a warm saline solution.

[0050] As the stented heart valve 600 starts to expand the delivery device 630 may be retracted to expose an additional length of the inflow end 602 of the stented heart valve 600 until the stented heart valve 600 completely expands in the aortic annulus 630 where it friction fits and seals into place. The bending flexibility of the commissure posts ensures that binding, overlapping and/or interference between adjacent segments of the anchoring structure with heart valve is minimized and/or eliminated. In addition, the enhanced bending flexibility of the commissure posts ensures that the heart valve is properly seated in the aortic annulus.

[0051] Although the present invention has been described with reference to preferred embodiments, workers skilled in the art will recognize that changes may be made in form and detail without departing from the spirit and scope of the invention.

CLAIMS

We claim:

1. A structure for supporting a bioprosthetic heart valve comprising:
a cylindrical anchoring structure defining a central longitudinal axis, the cylindrical anchoring structure comprising:
an inflow ring including at least one sinusoidal-shaped wire having a plurality of peaks and troughs;
an outflow ring including at least one sinusoidal-shaped wire having a plurality of peaks and troughs; and
at least one flexible commissure post having a longitudinal axis, the flexible commissure post connecting the inflow ring and the outflow ring,
wherein the flexible commissure post has a bending flexibility along a plane defined by a surface containing all straight lines connecting any point on the central longitudinal axis of the cylindrical anchoring structure and any point on the longitudinal axis of the flexible commisure post.

2. The anchoring structure of claim 1 wherein the at least one flexible commissure post includes a paddle portion operably connected to the outflow ring, the paddle portion including an axial slot extending along the longitudinal axis thereof.

3. The anchoring structure of claims 1 or 2 wherein the at least one flexible commissure post includes a single wire having at least one peak and one trough.

4. The anchoring structure of claim 3 wherein the single wire has a plurality of peaks and troughs forming a plurality of generally sinusoidal waves.

5. The anchoring structure of claim 4 wherein the frequency of the sinusoidal waves varies along the longitudinal axis of the flexible commissure post.

6. The anchoring structure of claim 4 wherein the wavelength of the sinusoidal waves varies along the longitudinal axis of the flexible commissure post.

7. The anchoring structure of claim 4 wherein the wavelength of the sinusoidal waves is substantially constant along the longitudinal axis of the flexible commissure post.

8. The anchoring structure of claim 4 wherein the bending flexibility of the flexible commissure post increases as the frequency of the sinusoidal waves increases.

9. The anchoring structure of claim 4 wherein the bending flexibility of the flexible commissure post increases as the wave height of the sinusoidal waves increases.

10. The anchoring structure of claim 4 wherein the bending flexibility of the flexible commissure post increases as the peak-to-peak distance between adjacent waves decreases.

11. The anchoring structure of claim 3 wherein the inflow ring includes a first sinusoidal-shaped wire and a second sinusoidal-shaped wire, the first and second sinusoidal-shape wires each having a plurality of peaks and troughs.

12. The anchoring structure of claim 11 wherein the peaks of the first sinusoidal-shaped wire are joined to the troughs of the second sinusoidal-shaped wire.

13. The anchoring structure of claim 12 wherein the at least one flexible commissure post includes a vertical connection member, the vertical connection member joined to the inflow ring at the intersection between one of the peaks of the first sinusoidal-shaped wire and one of the troughs of the second sinusoidal-shaped wire.

14. The anchoring structure of claims 1 or 2 wherein the at least one flexible commissure post includes first and second wires, each of the wires including at least one peak and one trough.

15. The anchoring structure of claim 14 wherein the at least one peak of the first wire abuts the at least one trough of the second wire.

16. The anchoring structure of claim 15 wherein the first and second wires each include a plurality of peaks and troughs forming a plurality of generally sinusoidal waves.

17. The anchoring structure of claim 16 wherein the bending flexibility of the flexible commissure post increases as the frequency of the sinusoidal waves of the first and second wires increases.

18. The anchoring structure of claim 16 wherein the bending flexibility of the flexible commissure post increases as the wave height of the sinusoidal waves of the first and second wires increases.

19. The anchoring structure of claim 16 wherein the bending flexibility of the flexible commissure post increases as the peak-to-peak distance between adjacent waves of the first and second wires decreases.

20. The anchoring structure of claims 1 or 2 wherein the bending flexibility of the commissure post is greater than 10% of a rigid or semi-rigid commissure post.

21. The anchoring structure of claim 2 wherein the paddle portion of the at least one flexible commissure post is connected to one of the troughs of the outflow ring.

22. The anchoring structure of claim 2 wherein the paddle portion of the at least one flexible commissure post is connected to one of the peaks of the outflow ring.

23. The anchoring structure of claim 2 further comprising a bioprosthetic heart valve disposed within the cylindrical anchoring structure, the bioprosthetic heart valve including a plurality of leaflets defining a valve body having an inflow end and an outflow end.

24. The anchoring structure of claim 23 wherein adjacent leaflets are joined together by a seam at the junction of the leaflets, and wherein a commissural tab extends from each of the seams near the outflow end of the valve body.

25. The anchoring structure of claim 24 wherein the cylindrical anchoring structure includes a plurality of flexible commissure posts, and wherein the bioprosthetic heart valve is secured to the cylindrical anchoring structure by threading the commissural tabs through the axial slots in the paddle portions of the flexible commissure posts.

26. The anchoring structure of claim 25 wherein the commissural tabs are formed integral with the leaflets.

27. The anchoring structure of claim 25 further comprising at least one suture hole formed in each of the paddle portions for suturing the commissural tabs to the paddle portions.

28. The anchoring structure of claim 25 further comprising a biocompatible cloth covering positioned around at least a portion of the inflow ring.

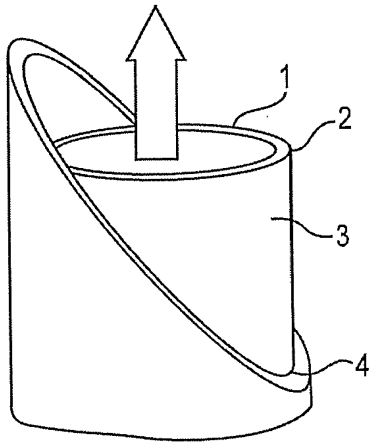

Fig. 1A

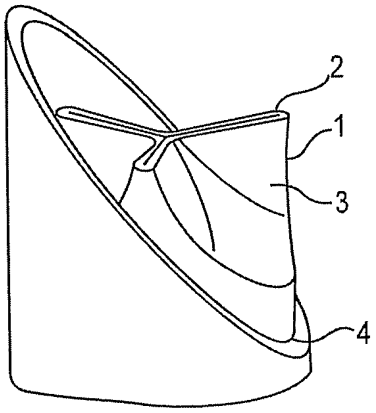

Fig. 1B

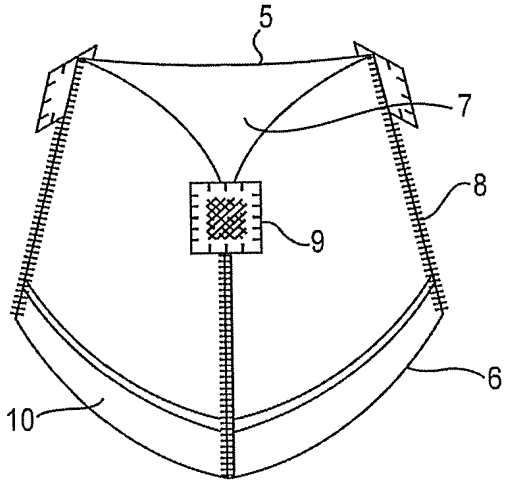

Fig. 2

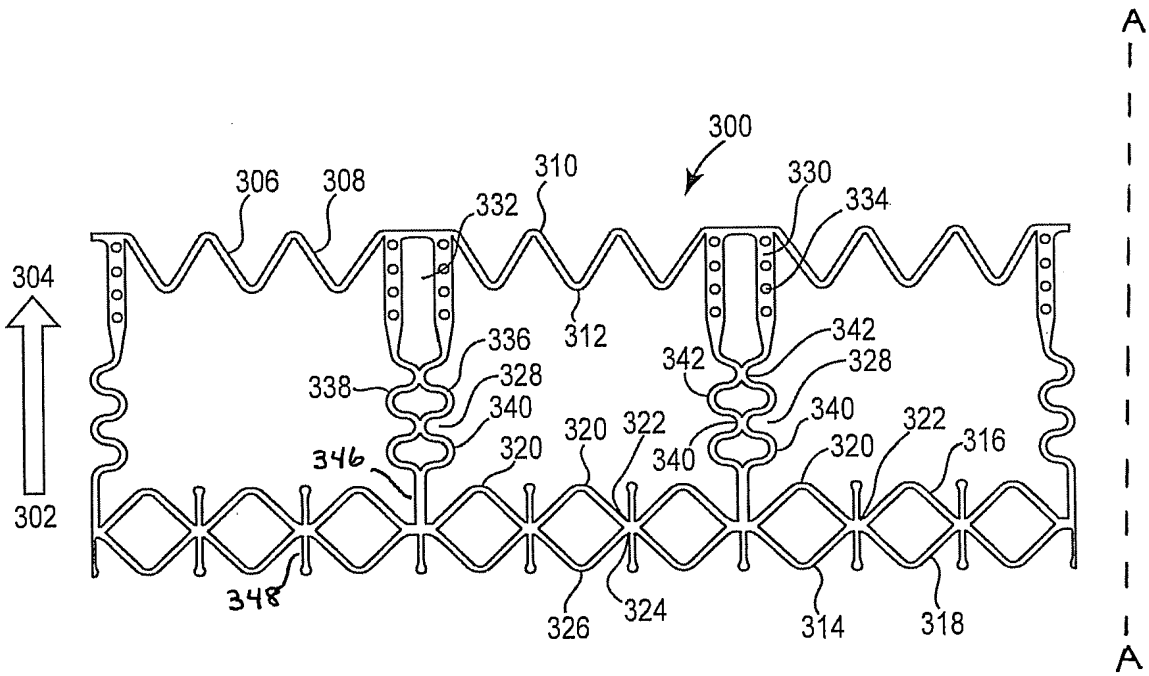
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Fig. 3A

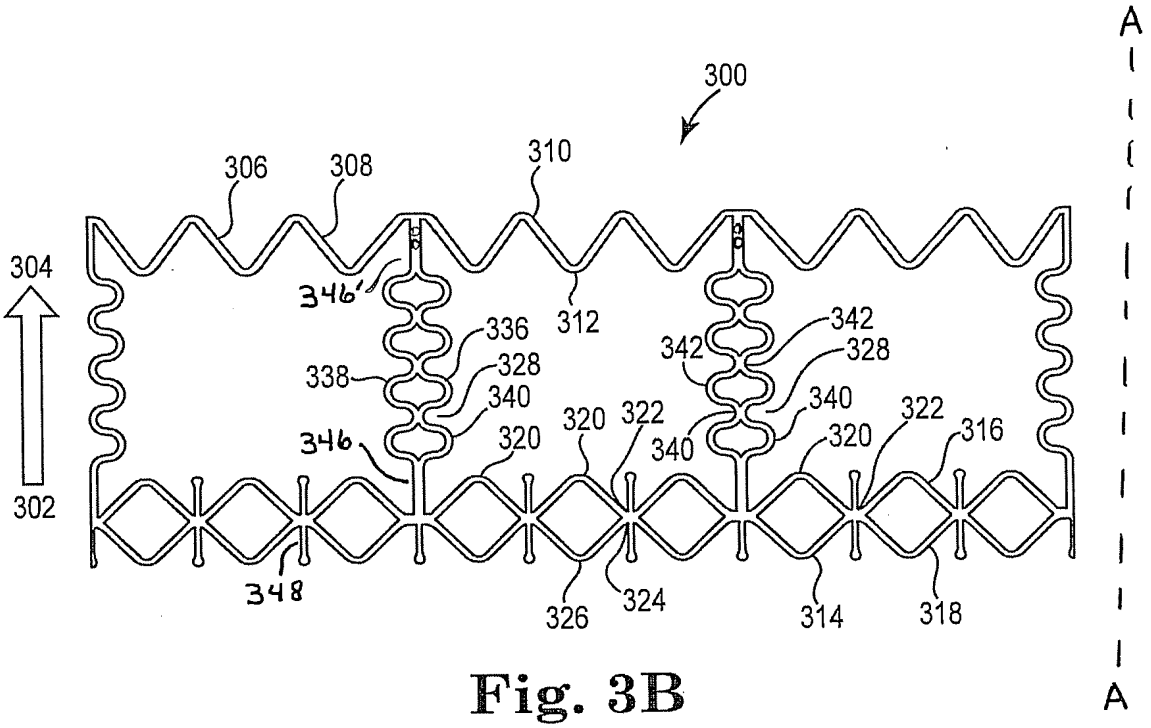
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Fig. 3B

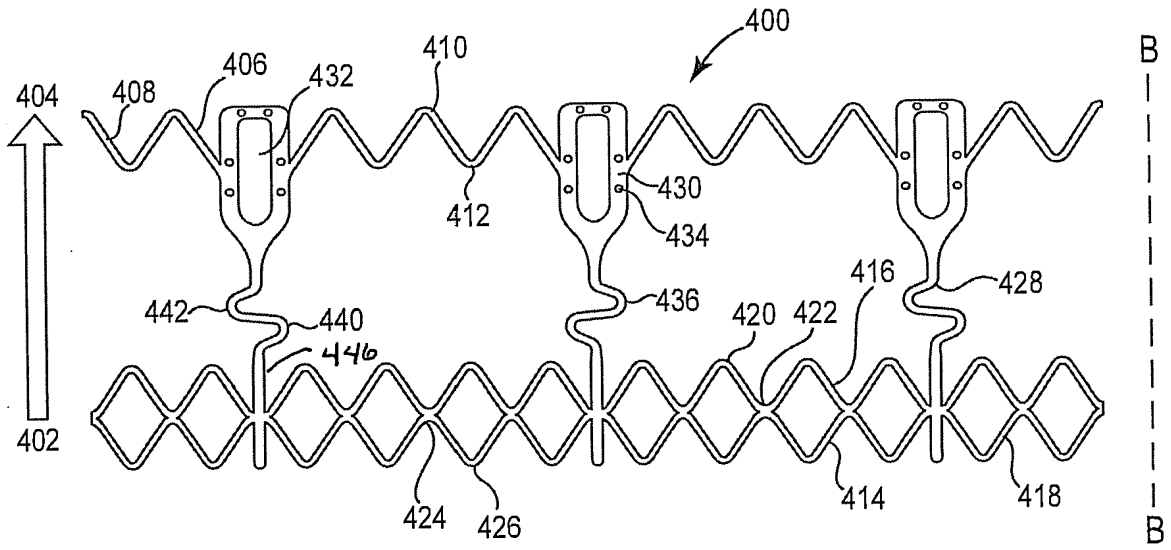
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Fig. 4A

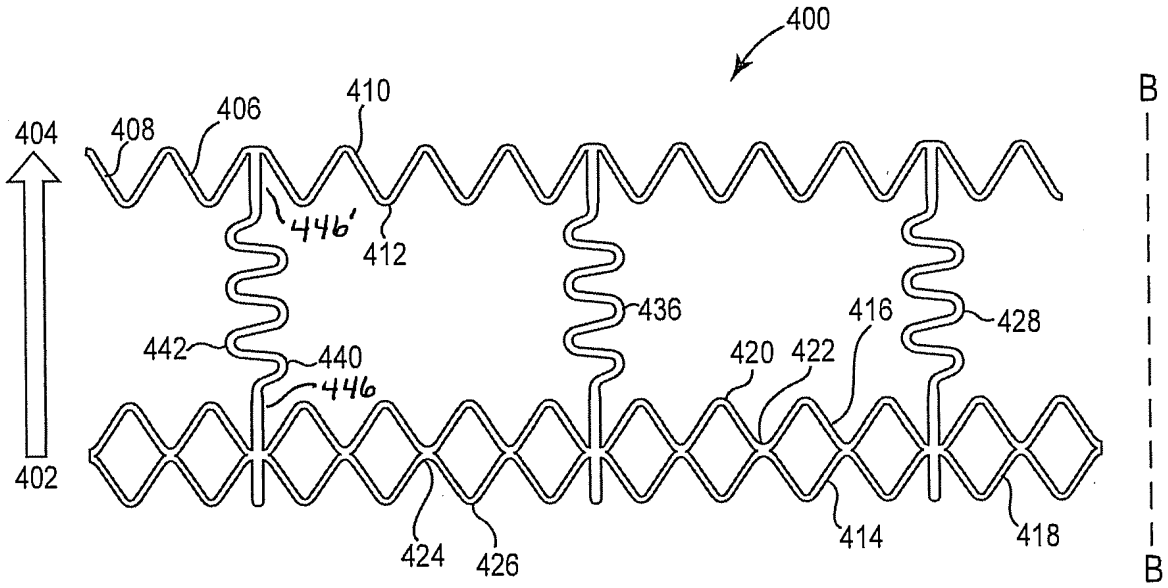
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Fig. 4B

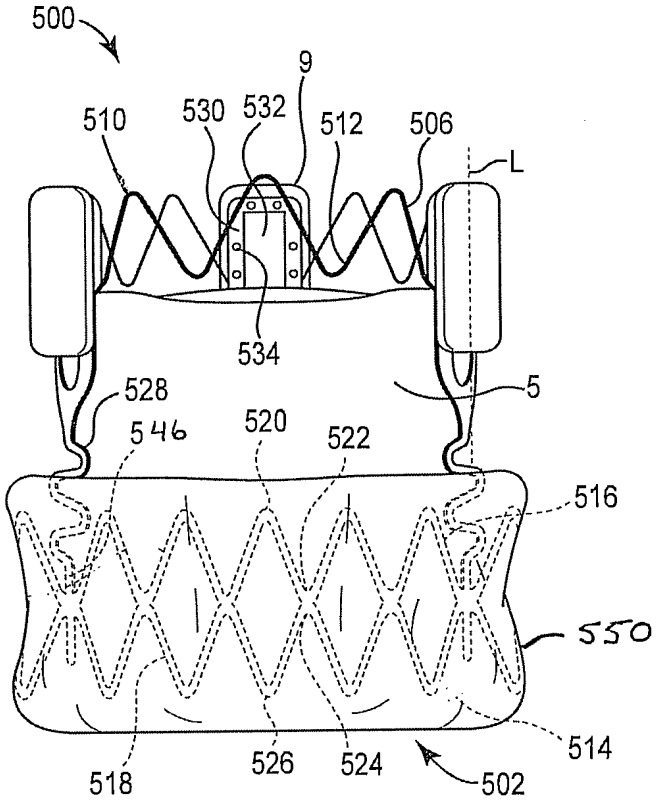
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Fig. 5A

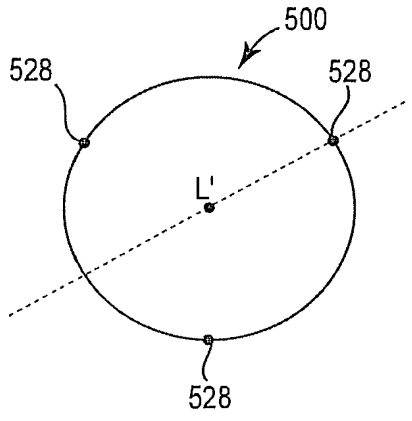
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Fig. 5B

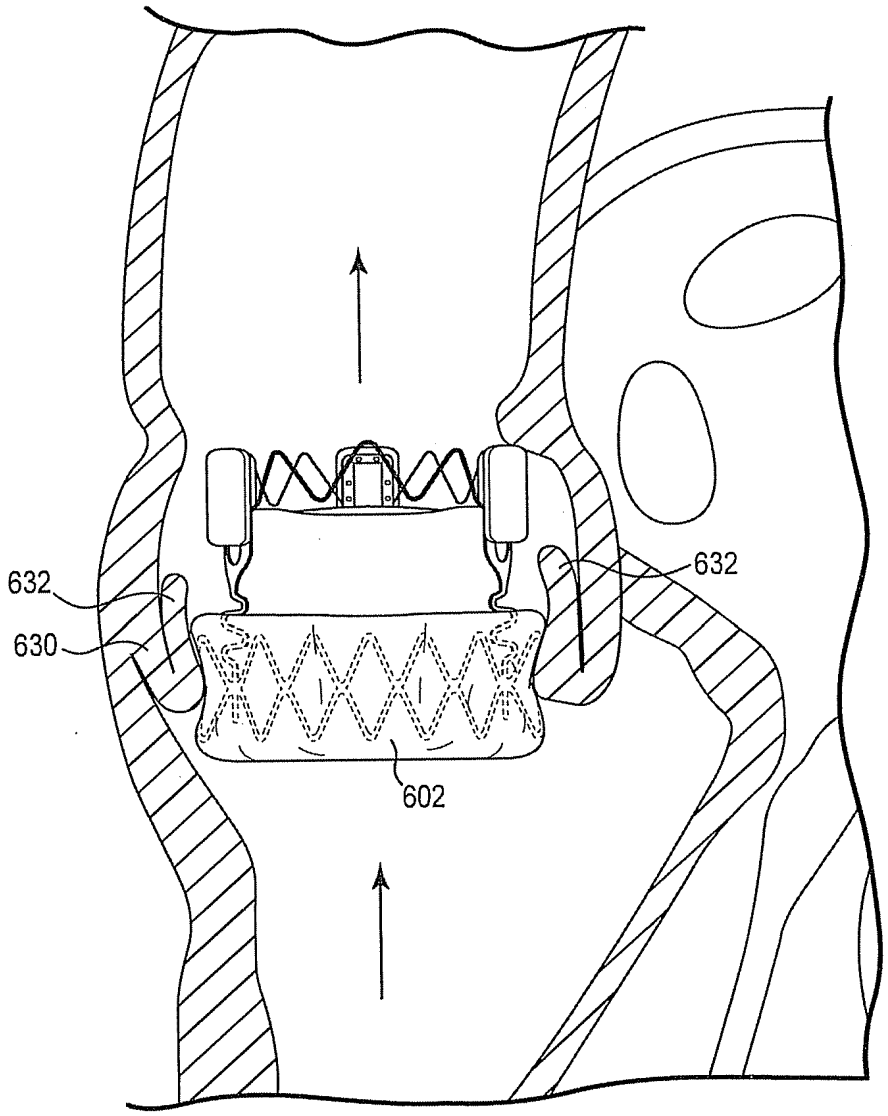

Fig. 6

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2010/037445

A. CLASSIFICATION OF SUBJECT MATTER
IPC(8) - A61F 2/24 (2010.01)
USPC - 623/2.38
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC(8) - A61F 2/24 (2010.01)
USPC - 623/2.11, 2.18, 2.38; 600/587

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
PatBase

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X -- Y	WO 2009/045338 A1 (BRAIDO) 09 April 2009 (09.04.2009) entire document	1, 3-12, 14-20 ---------- 2, 13, 21-28
Y	US 2005/0075584 A1 (CALI) 07 April 2005 (07.04.2005) entire document	2, 13, 21-28
A	US 2006/0178740 A1 (STACCHINO et al) 10 August 2006 (10.08.2006) entire document	1-28

☐ Further documents are listed in the continuation of Box C. ☐

* Special categories of cited documents:
"A" document defining the general state of the art which is not considered to be of particular relevance
"E" earlier application or patent but published on or after the international filing date
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
"O" document referring to an oral disclosure, use, exhibition or other means
"P" document published prior to the international filing date but later than the priority date claimed
"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
29 July 2010	10 AUG 2010
Name and mailing address of the ISA/US Mail Stop PCT, Attn: ISA/US, Commissioner for Patents P.O. Box 1450, Alexandria, Virginia 22313-1450 Facsimile No. 571-273-3201	Authorized officer: Blaine R. Copenheaver PCT Helpdesk: 571-272-4300 PCT OSP: 571-272-7774

Form PCT/ISA/210 (second sheet) (July 2009)

PTO/SB/06 (09-11)
Approved for use through 1/31/2014. OMB 0651-0032
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

PATENT APPLICATION FEE DETERMINATION RECORD Substitute for Form PTO-875	Application or Docket Number 13/675,665	Filing Date 11/13/2012	☐ To be Mailed

ENTITY: ☐ LARGE ☒ SMALL ☐ MICRO

APPLICATION AS FILED – PART I

	(Column 1)	(Column 2)		
FOR	NUMBER FILED	NUMBER EXTRA	RATE ($)	FEE ($)
☒ BASIC FEE (37 CFR 1.16(a), (b), or (c))	N/A	N/A	N/A	**195**
☐ SEARCH FEE (37 CFR 1.16(k), (i), or (m))	N/A	N/A	N/A	
☐ EXAMINATION FEE (37 CFR 1.16(o), (p), or (q))	N/A	N/A	N/A	
TOTAL CLAIMS (37 CFR 1.16(i))	minus 20 =	*	X $ =	
INDEPENDENT CLAIMS (37 CFR 1.16(h))	minus 3 =	*	X $ =	
☐ APPLICATION SIZE FEE (37 CFR 1.16(s))	If the specification and drawings exceed 100 sheets of paper, the application size fee due is $310 ($155 for small entity) for each additional 50 sheets or fraction thereof. See 35 U.S.C. 41(a)(1)(G) and 37 CFR 1.16(s).			
☐ MULTIPLE DEPENDENT CLAIM PRESENT (37 CFR 1.16(j))				
* If the difference in column 1 is less than zero, enter "0" in column 2.			TOTAL	**195**

APPLICATION AS AMENDED – PART II

		(Column 1)		(Column 2)	(Column 3)		
AMENDMENT	**01/06/2016**	CLAIMS REMAINING AFTER AMENDMENT		HIGHEST NUMBER PREVIOUSLY PAID FOR	PRESENT EXTRA	RATE ($)	ADDITIONAL FEE ($)
	Total (37 CFR 1.16(i))	* 6	Minus	** 20	= 0	X $40 =	0
	Independent (37 CFR 1.16(h))	* 1	Minus	***3	= 0	X $210 =	0
	☐ Application Size Fee (37 CFR 1.16(s))						
	☐ FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))						
						TOTAL ADD'L FEE	**0**

		(Column 1)		(Column 2)	(Column 3)		
AMENDMENT		CLAIMS REMAINING AFTER AMENDMENT		HIGHEST NUMBER PREVIOUSLY PAID FOR	PRESENT EXTRA	RATE ($)	ADDITIONAL FEE ($)
	Total (37 CFR 1.16(i))	*	Minus	**	=	X $ =	
	Independent (37 CFR 1.16(h))	*	Minus	***	=	X $ =	
	☐ Application Size Fee (37 CFR 1.16(s))						
	☐ FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))						
						TOTAL ADD'L FEE	

* If the entry in column 1 is less than the entry in column 2, write "0" in column 3.
** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 20, enter "20".
*** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 3, enter "3".
The "Highest Number Previously Paid For" (Total or Independent) is the highest number found in the appropriate box in column 1.

LIE
/GLORIA J. TRAMMELL/

UNITED STATES PATENT AND TRADEMARK OFFICE

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United States Patent and Trademark Office
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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
13/675,665	11/13/2012	David Paniagua	109978.10101	1995

29880 7590 04/22/2016

FOX ROTHSCHILD LLP
PRINCETON PIKE CORPORATE CENTER
997 LENOX DRIVE
BLDG. #3
LAWRENCEVILLE, NJ 08648

EXAMINER
MILLER, CHERYL L

ART UNIT	PAPER NUMBER
3738	

NOTIFICATION DATE	DELIVERY MODE
04/22/2016	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

ipdocket@foxrothschild.com

Office Action Summary	Application No. 13/675,665	Applicant(s) PANIAGUA ET AL.	
	Examiner CHERYL MILLER	Art Unit 3738	AIA (First Inventor to File) Status No

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTHS FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *1/6/2016*.

☐ A declaration(s)/affidavit(s) under **37 CFR 1.130(b)** was/were filed on _____.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on _____; the restriction requirement and election have been incorporated into this action.

4)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims*

5)☒ Claim(s) *1,2,4,6,9 and 10* is/are pending in the application.

5a) Of the above claim(s) _____ is/are withdrawn from consideration.

6)☐ Claim(s) _____ is/are allowed.

7)☒ Claim(s) *1,2,4,6, 9 and 10* is/are rejected.

8)☐ Claim(s) _____ is/are objected to.

9)☐ Claim(s) _____ are subject to restriction and/or election requirement.

* If any claims have been determined allowable, you may be eligible to benefit from the **Patent Prosecution Highway** program at a participating intellectual property office for the corresponding application. For more information, please see http://www.uspto.gov/patents/init_events/pph/index.jsp or send an inquiry to PPHfeedback@uspto.gov.

Application Papers

10)☐ The specification is objected to by the Examiner.

11)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

Certified copies:

a)☐ All b)☐ Some** c)☐ None of the:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

** See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)

2) ☒ Information Disclosure Statement(s) (PTO/SB/08a and/or PTO/SB/08b) Paper No(s)/Mail Date _____.

3) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .

4) ☐ Other: _____.

DETAILED ACTION

Notice of Pre-AIA or AIA Status

The present application is being examined under the pre-AIA first to invent provisions.

Response to Arguments

Applicant's arguments with respect to claims 1-2, 4, 6, and 9-10 have been considered but are moot because the amendment has necessitated new grounds for rejection (see below).

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory double patenting rejection is appropriate where the claims at issue are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); In re Vogel, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the reference application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope

of a joint research agreement. See MPEP § 717.02 for applications subject to examination under the first inventor to file provisions of the AIA as explained in MPEP § 2159. See MPEP §§ 706.02(l)(1) - 706.02(l)(3) for applications not subject to examination under the first inventor to file provisions of the AIA. A terminal disclaimer must be signed in compliance with 37 CFR 1.321(b).

The USPTO Internet website contains terminal disclaimer forms which may be used. Please visit www.uspto.gov/forms/. The filing date of the application in which the form is filed determines what form (e.g., PTO/SB/25, PTO/SB/26, PTO/AIA/25, or PTO/AIA/26) should be used. A web-based eTerminal Disclaimer may be filled out completely online using web-screens. An eTerminal Disclaimer that meets all requirements is auto-processed and approved immediately upon submission. For more information about eTerminal Disclaimers, refer to http://www.uspto.gov/patents/process/file/efs/guidance/eTD-info-I.jsp.

Claims 1-2 and 4 are rejected on the ground of nonstatutory double patenting as being unpatentable over claims 1-17 of U.S. Patent No. 8,308,797 B2. Although the claims at issue are not identical, they are not patentably distinct from each other because the application claims are merely broader than the patent claims.

Claim 1 is rejected on the ground of nonstatutory double patenting as being unpatentable over claim 4 of U.S. Patent No. 8,790,398 B2. Although the claims at issue are not identical, they are not patentably distinct from each other because the application claim is merely broader than the patent claim.

Claim Rejections - 35 USC § 112

The following is a quotation of 35 U.S.C. 112(b):
(b) CONCLUSION.—The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the inventor or a joint inventor regards as the invention.

The following is a quotation of 35 U.S.C. 112 (pre-AIA), second paragraph:
The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-2, 4, 6, and 9-10 are rejected under 35 U.S.C. 112(b) or 35 U.S.C. 112 (pre-AIA), second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which the inventor or a joint inventor, or for pre-AIA the applicant regards as the invention.

Claim 1, lines 8-9 recites "wherein a crease is located between the two to four individual leaflets and the outer cuff layer at a base of the two to four individual leaflets". This statement is somewhat unclear since the crease is claimed to be located in two different locations (*between* the leaflets and the cuff; and also *at* the base of the leaflets-thus on the leaflets). It is unclear how the crease could possibly be located *at* the base (thus part of the leaflets), while also being located *between* the leaflets and cuff. These two locations are contradictory. It seems applicant may have intended to describe the crease between bases of the leaflets and the outer cuff layer. Applicant may consider either removing the language "at a base of the two to four individual leaflets" from the claim; or alternately, changing "between the two to four individual leaflets" to recite --between bases of the two to four individual leaflets--. Claims 2, 4, 6, and 9-10 depend upon claim 1 and inherit all issues associated with the claim.

Conclusion

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Wittens (US 2011/0004295 A1) discloses a tube shaped valve with stent; Schreck

(US 2002/0198594 A1) discloses stent with attached tube valve; Jayaraman (US 5,855,597) discloses a stent with attached patches as valve leaflets; and Gabbay (US 4,491,986) discloses a stent with tube valve. Also worth noting, Garrison et al. (US 2002/0151970 A1, previously cited in IDS) stent valve of figures 32-38 is similar however seems to lack a crease between leaflets and cuff and Cox (US 2002/0032482 A1, previously cited) discloses a similar valve with optional stent (P0115-P0116), however lacking details of the stent structure and whether it is expandable and configured for percutaneous delivery and the valve further appears to lack a defined crease.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Cheryl Miller whose telephone number is 571-272-4755. The examiner can normally be reached on M- F (8am-5:30pm).

If attempts to reach the examiner by telephone are unsuccessful, please contact the examiner's supervisor, Thomas Sweet at 571-272-4761. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/C. M./
Examiner, Art Unit 3738
/THOMAS J SWEET/
Supervisory Patent Examiner, Art Unit 3738

Notice of References Cited	Application/Control No. 13/675,665	Applicant(s)/Patent Under Reexamination PANIAGUA ET AL.	
	Examiner CHERYL MILLER	Art Unit 3738	Page 1 of 1

U.S. PATENT DOCUMENTS

*		Document Number Country Code-Number-Kind Code	Date MM-YYYY	Name	CPC Classification	US Classification
*	A	US-8,308,797 B2	11-2012	Paniagua; David	A61F2/2412	623/2.14
*	B	US-8,790,398 B2	07-2014	Paniagua; David	A61F2/2412	623/1.24
*	C	US-2011/0004295 A1	01-2011	Wittens; Cornelis Hendrikus Anna	A61F2/2418	623/1.24
*	D	US-2002/0198594 A1	12-2002	Schreck, Stefan	A61F2/2418	623/2.11
*	E	US-5,855,597 A	01-1999	Jayaraman; Swaminathan	A61F2/2412	623/1.16
*	F	US-4,491,986 A	01-1985	Gabbay; Shlomo	A61F2/2418	623/2.18
	G	US-				
	H	US-				
	I	US-				
	J	US-				
	K	US-				
	L	US-				
	M	US-				

FOREIGN PATENT DOCUMENTS

*		Document Number Country Code-Number-Kind Code	Date MM-YYYY	Country	Name	CPC Classification
	N					
	O					
	P					
	Q					
	R					
	S					
	T					

NON-PATENT DOCUMENTS

*		Include as applicable: Author, Title Date, Publisher, Edition or Volume, Pertinent Pages)
	U	
	V	
	W	
	X	

*A copy of this reference is not being furnished with this Office action. (See MPEP § 707.05(a).)
Dates in MM-YYYY format are publication dates. Classifications may be US or foreign.

EAST Search History

EAST Search History (Prior Art)

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
S1	1973	623/1.24.ccls. or 623/1.26.ccls. or 623/2.12.ccls. or 623/2.13.ccls. or 623/2.14.ccls. or 623/2.15.ccls. or 623/2.16.ccls. or 623/2.17.ccls. or 623/2.18.ccls. or 623/2.19.ccls. or 623/900.ccls.	US-PGPUB; USPAT; USOCR	OR	ON	2014/06/02 11:02
S2	410	S1 and @rlad<"20020104"	US-PGPUB; USPAT; USOCR	OR	ON	2014/06/02 11:02
S3	430	S1 and @ad<"20020104"	US-PGPUB; USPAT; USOCR	OR	ON	2014/06/02 11:03
S4	674	S2 S3	US-PGPUB; USPAT; USOCR	OR	ON	2014/06/02 11:03
S5	8	"09/973,609"	US-PGPUB; USPAT; USOCR	OR	ON	2014/06/02 11:17
S6	275	("3130419" | "3143742" | "3571815" | "3574865" | "3626518" | "3911502" | "4580568" | "4648383").PN. OR ("5397351").URPN.	US-PGPUB; USPAT; USOCR	OR	OFF	2014/06/02 11:42
S7	11	("3130419" | "3143742" | "3571815" | "3574865" | "3626518" | "3911502" | "4580568" | "4648383").PN.	US-PGPUB; USPAT; USOCR	OR	OFF	2014/06/02 11:43
S8	9	("3626518" | "3691567" | "3868956" | "3911502" | "4030142" | "4503569" | "4759758" | "4994077").PN.	US-PGPUB; USPAT; USOCR	OR	OFF	2014/06/02 11:43
S9	2	("4038703" | "4106129").PN.	US-PGPUB; USPAT; USOCR	OR	OFF	2014/06/02 11:45
S10	0	"a61f2002.""3601".cpc.	US-PGPUB; USPAT; USOCR	OR	ON	2014/06/03 14:01
S11	0	a61f2002/3601.cpc.	US-PGPUB; USPAT; USOCR	OR	ON	2014/06/03 14:01
S12	4	"4759758".pn. or "5935163".pn. or "5861028".pn. or "5855602".pn.	US-PGPUB; USPAT;	OR	ON	2014/11/02 15:29

			USOCR			
S13	4	S12 and pericardium	US-PGPUB; USPAT; USOCR	OR	ON	2014/11/02 15:29
S14	2098	623/1.24.ccls. or 623/1.26.ccls. or 623/2.12.ccls. or 623/2.13.ccls. or 623/2.14.ccls. or 623/2.15.ccls. or 623/2.16.ccls. or 623/2.17.ccls. or 623/2.18.ccls. or 623/2.19.ccls. or 623/900.ccls.	US-PGPUB; USPAT; USOCR	OR	ON	2014/11/02 16:25
S15	416	S14 and @rlad<"20020104"	US-PGPUB; USPAT; USOCR	OR	ON	2014/11/02 16:25
S16	430	S14 and @ad<"20020104"	US-PGPUB; USPAT; USOCR	OR	ON	2014/11/02 16:25
S17	680	S15 S16	US-PGPUB; USPAT; USOCR	OR	ON	2014/11/02 16:25
S18	199	S17 and (leaflets with pericardi$3)	US-PGPUB; USPAT; USOCR	OR	ON	2014/11/02 16:26
S19	1	"6579307".pn.	US-PGPUB; USPAT; USOCR	OR	ON	2014/11/02 16:34
S20	2098	623/1.24.ccls. or 623/1.26.ccls. or 623/2.12.ccls. or 623/2.13.ccls. or 623/2.14.ccls. or 623/2.15.ccls. or 623/2.16.ccls. or 623/2.17.ccls. or 623/2.18.ccls. or 623/2.19.ccls. or 623/900.ccls.	US-PGPUB; USPAT; USOCR	OR	ON	2014/11/02 20:44
S21	416	S20 and @rlad<"20020104"	US-PGPUB; USPAT; USOCR	OR	ON	2014/11/02 20:44
S22	430	S20 and @ad<"20020104"	US-PGPUB; USPAT; USOCR	OR	ON	2014/11/02 20:44
S23	680	S21 S22	US-PGPUB; USPAT; USOCR	OR	ON	2014/11/02 20:44
S24	279	S23 and (valve with pericardi$3)	US-PGPUB; USPAT; USOCR	OR	ON	2014/11/02 20:44
S25	199	S23 and (leaflets with pericardi$3)	US-PGPUB; USPAT; USOCR	OR	ON	2014/11/02 20:44
S26	85	S24 not S25	US-PGPUB;	OR	ON	2014/11/02 20:44

			USPAT; USOCR			
S27	364	S23 and (pericardi$3)	US-PGPUB; USPAT; USOCR	OR	ON	2014/11/02 20:59
S28	85	S27 not S24	US-PGPUB; USPAT; USOCR	OR	ON	2014/11/02 21:00
S29	80	S28 not S25	US-PGPUB; USPAT; USOCR	OR	ON	2014/11/02 21:00
S30	1	"6676698".pn.	US-PGPUB; USPAT; USOCR	OR	ON	2014/11/02 21:32
S31	1	"6652578".pn.	US-PGPUB; USPAT; USOCR	OR	ON	2014/11/03 10:38
S32	1	"7556646".pn.	US-PGPUB; USPAT; USOCR	OR	ON	2014/11/03 13:32
S33	1	"6733525".pn.	US-PGPUB; USPAT; USOCR	OR	ON	2014/11/03 14:12
S34	1	bessler.in. and 623/2.$2.ccls.	US-PGPUB; USPAT; USOCR	OR	ON	2015/06/26 13:59
S35	2	"6197143".pn. or "20030060875".pn.	US-PGPUB; USPAT; USOCR	OR	ON	2015/06/26 15:53
S36	2	"20020052651".pn. or "5554184".pn.	US-PGPUB; USPAT; USOCR	OR	ON	2015/06/26 15:55
S37	1	"20030209835".pn.	US-PGPUB; USPAT; USOCR	OR	ON	2015/06/26 15:57
S38	19	"10/037,266"	US-PGPUB; USPAT; USOCR	OR	ON	2015/06/26 21:10
S39	2	"20100268332".pn. or "20100217371".pn.	US-PGPUB; USPAT; USOCR	OR	ON	2015/06/26 21:30
S40	1	"8308797".pn.	US-PGPUB; USPAT; USOCR	OR	ON	2015/06/26 23:11

S41	5	"10/037,266"	USPAT; USOCR	OR	ON	2015/06/26 23:32
S42	43	bessler.in. and valve	US-PGPUB; USPAT; USOCR	OR	ON	2015/06/27 14:05
S43	1	bessler.in. and 623/2.$2.ccls.	US-PGPUB; USPAT; USOCR	OR	ON	2015/06/27 14:06
S44	38	myers.in. and 623/2.$2.ccls.	US-PGPUB; USPAT; USOCR	OR	ON	2015/06/27 14:07
S45	30	cox.in. and 623/2.$2.ccls. and tube	US-PGPUB; USPAT; USOCR	OR	ON	2015/06/27 14:09
S46	2	"4470157".pn. or "5163955".pn.	US-PGPUB; USPAT; USOCR	OR	ON	2015/06/27 14:14
S47	1	"5411552".pn.	US-PGPUB; USPAT; USOCR	OR	ON	2015/06/27 14:32
S48	1	"6908481".pn.	US-PGPUB; USPAT; USOCR	OR	ON	2015/06/27 15:34
S49	139	("20010010017" | "20010023372" | "20010049558" | "20020005073" | "20020028243" | "20020029783" | "20020037940" | "20020042621" | "20020091441" | "20020095167" | "3014024" | "3029819" | "3105492" | "3320972" | "3409914" | "3548417" | "3562820" | "3588920" | "3671979" | "3709175" | "3878565" | "3945052" | "3966401" | "3983581" | "3986828" | "4035849" | "4055861" | "4056854" | "4060081" | "4082507" | "4084268" | "4106129" | "4164045" | "4172295" | "4218782" | "4222126" | "4233493" | "4265694" | "4291420" | "4340977" | "4350492" | "4364127" | "4388735" | "4423525" | "4441216" | "4456589" | "4473423" | "4477930" | "4490859" | "4517687" | "4545082" | "4597762" | "4600533" | "4631052" | "4666442" | "4728328" | "4759758" | "4759759" | "4798611" | "4801299" | "4870966" | "4883458" | "4892539" | "4966604" | "4976733" | "4979939" | "5006104" | "5007896" | "5011488" | "5026366" | "5032128" | "5047041" | "5047050" | "5052771" | "5061277" | "5080660" | "5139515" | "5163955" | "5171273" | "5226889" | "5261878" | "5282847" | "5326370" | "5326371" | "5332402" | "5336616" | "5360443" | "5374539" |	US-PGPUB; USPAT; USOCR	OR	ON	2015/06/27 19:46

		"5376110" | "5383927" | "5411552" | "5413601" | "5449384" | "5476506" | "5480424" | "5489297" | "5500015" | "5509930" | "5522879" | "5522881" | "5545215" | "5549664" | "5549666" | "5571170" | "5571173" | "5571174" | "5578071" | "5578072" | "5582168" | "5591229" | "5634928" | "5653749" | "5713953" | "5728152" | "5733299" | "5741333" | "5746775" | "5769780" | "5782914" | "5787887" | "5840081" | "5855601" | "5861028" | "5862806" | "5895420" | "5931969" | "5957949" | "5961539" | "5961549" | "5972030" | "5976179").PN.				
S50	169	("6004328" | "6004330" | "6010531" | "6029671" | "6045576" | "6053938" | "6091984" | "6102944" | "6117169" | "6125852" | "6126686" | "6129756" | "6162245" | "6168614" | "6168619" | "6171335" | "6174327" | "6186999" | "6197143" | "6214055" | "6221091" | "6231602" | "6254629" | "6254630" | "6254636" | "6264691" | "6269819" | "6270526" | "6277397" | "6277555" | "6287335" | "6293970" | "6312462" | "6312474" | "6334873" | "6342069" | "6350282" | "6352554" | "6352708" | "6358275" | "6358284" | "6371980" | "6376244" | "6378221" | "6383171" | "6391333" | "6409755" | "6418339" | "6425916" | "6432712" | "6440167" | "6458153" | "6461382" | "6468313" | "6471723" | "6482227" | "6482228" | "6482240" | "6491719" | "6494909" | "6503272" | "6534004" | "6553681" | "6558418" | "6565960" | "6569200" | "6582458" | "6582462" | "6582464" | "6599524" | "6610088" | "6624890" | "6626938" | "6652577" | "6652578" | "6666886" | "6682559" | "6685739" | "6696074" | "6702826" | "6719788" | "6719789" | "6736823" | "6764510" | "6773456" | "6773457" | "6790229" | "6792979" | "6802319" | "6802806" | "6821530" | "6893460" | "6908481" | "6913608" | "6916338" | "6942694" | "6951571" | "6961123" | "6977231" | "6986735" | "7004925" | "7008763" | "7011688" | "7018404" | "7022348" | "7025780" | "7037333" | "7039446" | "7041132" | "7053051" | "7060092" | "7070616" | "7077862" | "7084082" | "7138226" | "7153324" | "7160322" | "7164145" | "7166570" | "7189259" | "7213601" | "7214242" | "7232461" | "7261732" | "7289211" | "7309461" | "7311730" | "7318998" | "7329279" | "7331993" | "7354702" | "7381218" | "7381219" | "7399315" | "7427291" | "7431725" | "7468073" | "7473237" | "7481838" | "7503929" | "7510571" | "7510575" | "7524330" | "7566343" | "7585321" | "7604661" | "7618446" |	US-PGPUB; USPAT; USOCR	OR	ON	2015/06/27 19:47

		"7622276" | "7628805" | "7648676" | "7670368" | "7708775" | "7758632" | "7780722" | "7789909" | "7846203" | "7846204" | "7871431" | "7892281" | "7914576" | "7967833" | "7981151" | "8002825" | "8007992" | "8057540" | "8080054" | "8105375" | "RE40404" | "RE42395").PN.				
S51	148	("20020095994" | "20020123789" | "20020128708" | "20030078659" | "20030102000" | "20030130727" | "20030130729" | "20030130731" | "20030153974" | "20030187362" | "20030195620" | "20030204023" | "20030212460" | "20030212462" | "20030217415" | "20040024452" | "20040055608" | "20040059418" | "20040098092" | "20040193261" | "20040243153" | "20040243229" | "20050004668" | "20050027369" | "20050043819" | "20050096673" | "20050113910" | "20050137681" | "20050137682" | "20050142163" | "20050147562" | "20050147599" | "20050147643" | "20050148512" | "20050158274" | "20050159811" | "20050169958" | "20050169959" | "20050175657" | "20050187618" | "20050191248" | "20050228494" | "20050246035" | "20050247320" | "20050267529" | "20060004439" | "20060004443" | "20060020336" | "20060025800" | "20060041306" | "20060074486" | "20060089708" | "20060111733" | "20060129225" | "20060134079" | "20060140916" | "20060173475" | "20060178740" | "20060190074" | "20060193885" | "20060195010" | "20060195183" | "20060206203" | "20060229701" | "20060240063" | "20060240064" | "20060259134" | "20060259135" | "20060259137" | "20060265056" | "20060287571" | "20060292125" | "20070010857" | "20070043431" | "20070050014" | "20070050022" | "20070056346" | "20070060932" | "20070100426" | "20070128174" | "20070173861" | "20070213813" | "20070250154" | "20070263226" | "20070276432" | "20080004686" | "20080009667" | "20080009940" | "20080029105" | "20080039871" | "20080039926" | "20080058798" | "20080082113" | "20080102439" | "20080133004" | "20080147182" | "20080154356" | "20080177381" | "20080183280" | "20080183283" | "20080190989" | "20080195200" | "20080199843" | "20080200977" | "20090030511" | "20090043383" | "20090062907" | "20090112309" | "20090132032" | "20090157175" | "20090164005" | "20090187241"	US-PGPUB; USPAT; USOCR	OR	ON	2015/06/27 19:48

		"20090248149" | "20090254175" | "20090281609" | "20100030259" | "20100036479" | "20100036484" | "20100048987" | "20100049312" | "20100131054" | "20100161036" | "20100185277" | "20100217382" | "20100234878" | "20100249918" | "20100256749" | "20100256751" | "20100312333" | "20110004299" | "20110015728" | "20110040375" | "20110087322" | "20110137409" | "20110146361" | "20110153009" | "20110166636" | "20110178597" | "20110218619" | "20110224607" | "20110300625" | "20110301700" | "20120078343" | "20120078356" | "20120095551" | "20120158128" | "20120185038" | "20120310041").PN.				
S52	26	("20020151970" | "20030149477" | "20040039442" | "20040158321" | "20040230285" | "20050241981" | "20070104395" | "20070203575" | "20070276461" | "20090005857" | "20090054969" | "20100241069" | "20110240511" | "20130304201" | "20140039613" | "4011947" | "4657133" | "4743231" | "6124523" | "6245102" | "6540782" | "6821297" | "6830584" | "7018406" | "8512401" | "8512403").PN.	US-PGPUB; USPAT; USOCR	OR	ON	2015/06/27 19:48
S53	4	("20020032481" | "20030027332" | "20070061008" | "20100043197").PN.	US-PGPUB; USPAT; USOCR	OR	ON	2015/06/27 19:49
S54	2	("6676698" | "6733525").PN.	US-PGPUB; USPAT; USOCR	OR	ON	2015/06/27 19:49
S55	1	("6530952").PN.	US-PGPUB; USPAT; USOCR	OR	ON	2015/06/27 19:49
S56	8	("5484444" | "5645559" | "5683451" | "5876448" | "6350278" | "6682537" | "6896690" | "7556646").PN.	US-PGPUB; USPAT; USOCR	OR	ON	2015/06/27 19:49
S57	3	("20020052651" | "20030209835" | "5554184").PN.	US-PGPUB; USPAT; USOCR	OR	ON	2015/06/27 19:50
S58	500	S49 or S50 or S51 or S52 or S53 or S54 or S55 or S56 or S57	US-PGPUB; USPAT; USOCR	OR	ON	2015/06/27 19:51
S59	222	S58 and @rlad<"20040710"	US-PGPUB; USPAT; USOCR	OR	ON	2015/06/27 19:51
S60	321	S58 and @ad<"20040710"	US-PGPUB; USPAT; USOCR	OR	ON	2015/06/27 19:51

S61	389	S59 S60	US-PGPUB; USPAT; USOCR	OR	ON	2015/06/27 19:51
S62	1	"4056854".pn.	US-PGPUB; USPAT; USOCR	OR	ON	2015/06/27 20:01
S63	381	623/2.1$1.ccls. and (sheet with (tissue or pericardi$2))	US-PGPUB; USPAT; USOCR	OR	ON	2015/06/27 22:28
S64	92	S63 and @rlad<"20020104"	US-PGPUB; USPAT; USOCR	OR	ON	2015/06/27 22:30
S65	46	S63 and @ad<"20020104"	US-PGPUB; USPAT; USOCR	OR	ON	2015/06/27 22:30
S66	117	S64 S65	US-PGPUB; USPAT; USOCR	OR	ON	2015/06/27 22:30
S67	1762	623/2.$2.ccls. and pericardi$2 and (stent or frame)	US-PGPUB; USPAT; USOCR	OR	ON	2015/06/27 22:46
S68	1011	623/2.$2.ccls. and ((calf or juvenile or porcine or animal or mammal) with pericardi$2) and (stent or frame)	US-PGPUB; USPAT; USOCR	OR	ON	2015/06/27 22:47
S69	317	S68 and @rlad<"20040710"	US-PGPUB; USPAT; USOCR	OR	ON	2015/06/27 22:48
S70	263	S68 and @ad<"20040710"	US-PGPUB; USPAT; USOCR	OR	ON	2015/06/27 22:48
S71	458	S69 S70	US-PGPUB; USPAT; USOCR	OR	ON	2015/06/27 22:48
S72	240	S71 and (resilient or "self-expandable" or "self-expanding" or "self-expands")	US-PGPUB; USPAT; USOCR	OR	ON	2015/06/27 22:49
S73	162	S71 and (resilient or "self-expandable" or "self-expanding" or "self-expands") and (sheet or patch)	US-PGPUB; USPAT; USOCR	OR	ON	2015/06/27 22:50
S74	97	623/2.$2.ccls. and (autologous with pericardi$2)	US-PGPUB; USPAT; USOCR	OR	ON	2015/06/27 23:07
S75	126	623/2.$2.ccls. and ((autologous or autograft) with pericardi$2)	US-PGPUB; USPAT;	OR	ON	2015/06/27 23:07

			USOCR			
S76	37	S75 and @rlad<"20020104"	US-PGPUB; USPAT; USOCR	OR	ON	2015/06/27 23:07
S77	39	S75 and @ad<"20020104"	US-PGPUB; USPAT; USOCR	OR	ON	2015/06/27 23:08
S78	57	S76 S77	US-PGPUB; USPAT; USOCR	OR	ON	2015/06/27 23:08
S79	129	("3989701" | "4261342" | "4790844" | "4960424").PN. OR ("5344442").URPN.	US-PGPUB; USPAT; USOCR	OR	OFF	2015/06/27 23:18
S80	1	"6908481".pn.	US-PGPUB; USPAT; USOCR	OR	OFF	2015/06/28 00:06
S81	1	"20020032482".pn.	US-PGPUB; USPAT; USOCR	OR	OFF	2015/06/28 00:12
S82	1	"6893460".pn.	US-PGPUB; USPAT; USOCR	OR	OFF	2015/06/28 00:23
S83	21	623/2.$2.ccls. and (double with continuous with sutur$4)	US-PGPUB; USPAT; USOCR	OR	OFF	2015/06/28 00:52
S84	3728	a61f2/2412.cpc. or a61f2/2415.cpc. or a61f2/2418.cpc.	US-PGPUB; USPAT; USOCR	OR	ON	2016/04/11 14:52
S85	625	S84 and @rlad<"20020104"	US-PGPUB; USPAT; USOCR	OR	ON	2016/04/11 14:53
S86	454	S84 and @ad<"20020104"	US-PGPUB; USPAT; USOCR	OR	ON	2016/04/11 14:53
S87	891	S85 S86	US-PGPUB; USPAT; USOCR	OR	ON	2016/04/11 14:53
S88	52	(US-20100114299-$ or US-20060167543-$ or US-20060142848-$ or US-20050065594-$ or US-20040193253-$ or US-20030040792-$ or US-20020151970-$ or US-20110137409-$ or US-20030078652-$ or US-20020052651-$ or US-20020032482-$ or US-20020198594-$ or US-20030023303-$ or US-20040186565-$ or US-20050075725-$ or US-20060004442-$ or US-20090118826-$).did. or (US-7947072-$ or US-6733525-$ or US-6730121-$ or US-	US-PGPUB; USPAT	OR	OFF	2016/04/12 13:07

		6425916-$ or US-6299637-$ or US-6027525-$ or US-5957949-$ or US-5855601-$ or US-5607465-$ or US-5449384-$ or US-5163953-$ or US-4601718-$ or US-4759758-$ or US-7547322-$ or US-5895420-$ or US-5713953-$ or US-5509930-$ or US-5489297-$ or US-4340977-$ or US-5358518-$ or US-4343048-$ or US-4491986-$ or US-8308797-$ or US-8790398-$ or US-4470157-$ or US-4056854-$).did. or (US-4297749-$ or US-5545215-$ or US-6553681-$ or US-6682559-$ or US-6736846-$ or US-8613763-$ or US-5344442-$ or US-6358277-$ or US-4790844-$).did.				
S89	52	(US-20100114299-$ or US-20060167543-$ or US-20060142848-$ or US-20050065594-$ or US-20040193253-$ or US-20030040792-$ or US-20020151970-$ or US-20110137409-$ or US-20030078652-$ or US-20020052651-$ or US-20020032482-$ or US-20020198594-$ or US-20030023303-$ or US-20040186565-$ or US-20050075725-$ or US-20060004442-$ or US-20090118826-$).did. or (US-7947072-$ or US-6733525-$ or US-6730121-$ or US-6425916-$ or US-6299637-$ or US-6027525-$ or US-5957949-$ or US-5855601-$ or US-5607465-$ or US-5449384-$ or US-5163953-$ or US-4601718-$ or US-4759758-$ or US-7547322-$ or US-5895420-$ or US-5713953-$ or US-5509930-$ or US-5489297-$ or US-4340977-$ or US-5358518-$ or US-4343048-$ or US-4491986-$ or US-8308797-$ or US-8790398-$ or US-4470157-$ or US-4056854-$).did. or (US-4297749-$ or US-5545215-$ or US-6553681-$ or US-6682559-$ or US-6736846-$ or US-8613763-$ or US-5344442-$ or US-6358277-$ or US-4790844-$).did.	US-PGPUB; USPAT; USOCR	OR	ON	2016/04/12 13:07
S90	29	paniagua.in. and valve	US-PGPUB; USPAT; USOCR	OR	ON	2016/04/12 15:39
S91	9	paniagua.in. and valve	USPAT; USOCR	OR	ON	2016/04/12 15:39
S92	3733	a61f2/2412.cpc. or a61f2/2415.cpc. or a61f2/2418.cpc.	US-PGPUB; USPAT; USOCR	OR	ON	2016/04/12 16:00
S93	625	S92 and @rlad<"20020104"	US-PGPUB; USPAT; USOCR	OR	ON	2016/04/12 16:00
S94	454	S92 and @ad<"20020104"	US-PGPUB; USPAT; USOCR	OR	ON	2016/04/12 16:00
S95	891	S93 S94	US-PGPUB; USPAT; USOCR	OR	ON	2016/04/12 16:00
S96	299	S95 and pericardi$3	USPAT; USOCR	OR	ON	2016/04/12 16:00
S97	498	S95 and pericardi$3	US-	OR	ON	2016/04/12

			PGPUB; USPAT; USOCR			16:00
S98	344	S95 and pericardi$3 and (expand$4 or collaps$4)	US-PGPUB; USPAT; USOCR	OR	ON	2016/04/12 16:01
S99	286	S95 and pericardi$3 and (expand$4 or collaps$4) and (cuff or crease or fold$4 or invert$3 or evert$3)	US-PGPUB; USPAT; USOCR	OR	ON	2016/04/12 16:02
S100	425	S95 and (pericardi$3 or tube) and (expand$4 or collaps$4) and (cuff or crease or fold$4 or invert$3 or evert$3)	US-PGPUB; USPAT; USOCR	OR	ON	2016/04/12 16:02
S101	57	(US-20100114299-$ or US-20060167543-$ or US-20060142848-$ or US-20050065594-$ or US-20040193253-$ or US-20030040792-$ or US-20020151970-$ or US-20110137409-$ or US-20030078652-$ or US-20020052651-$ or US-20020032482-$ or US-20020198594-$ or US-20030023303-$ or US-20040186565-$ or US-20050075725-$ or US-20060004442-$ or US-20090118826-$).did. or (US-7947072-$ or US-6733525-$ or US-6730121-$ or US-6425916-$ or US-6299637-$ or US-6027525-$ or US-5957949-$ or US-5855601-$ or US-5607465-$ or US-5449384-$ or US-5163953-$ or US-4601718-$ or US-4759758-$ or US-7547322-$ or US-5895420-$ or US-5713953-$ or US-5509930-$ or US-5489297-$ or US-4340977-$ or US-5358518-$ or US-4343048-$ or US-4491986-$ or US-8308797-$ or US-8790398-$ or US-4470157-$ or US-4056854-$).did. or (US-4297749-$ or US-5545215-$ or US-6553681-$ or US-6682559-$ or US-6736846-$ or US-8613763-$ or US-5344442-$ or US-6358277-$ or US-4790844-$ or US-8109995-$ or US-8361144-$ or US-8900294-$ or US-9125739-$ or US-9186248-$).did.	US-PGPUB; USPAT	OR	OFF	2016/04/12 16:03
S102	400	S100 not S101	US-PGPUB; USPAT; USOCR	OR	ON	2016/04/12 16:03
S103	1	"6579307".pn.	US-PGPUB; USPAT; USOCR	OR	ON	2016/04/12 16:19
S104	8	("20080131522").PN. or ("20020119437" | "20020146393" | "20030118560" | "20060212111" | "4275469" | "5558875" | "7214344").PN.	US-PGPUB; USPAT; USOCR	OR	ON	2016/04/12 16:36
S105	1	"20020032482".pn.	US-PGPUB; USPAT; USOCR	OR	ON	2016/04/15 15:35
S106	1	"8308797".pn.	US-PGPUB; USPAT; USOCR	OR	ON	2016/04/15 19:36

S107	23	"10/037,266"	US-PGPUB; USPAT; USOCR	OR	ON	2016/04/15 19:39
S108	4	"10/037,266" and crease	US-PGPUB; USPAT; USOCR	OR	ON	2016/04/15 19:44

4/ 16/ 2016 7:11:02 PM
C:\ Users\ cmiller2\ Documents\ EAST\ Workspaces\ 13675665.wsp

Doc code: IDS
Doc description: Information Disclosure Statement (IDS) Filed

PTO/SB/08a (03-15)
Approved for use through 07/31/2016. OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(Not for submission under 37 CFR 1.99)

Application Number	13675665
Filing Date	2012-11-13
First Named Inventor	David Paniagua
Art Unit	3738
Examiner Name	Cheryl L. Miller
Attorney Docket Number	109978.10101

U.S.PATENTS Remove

Examiner Initial*	Cite No	Patent Number	Kind Code[1]	Issue Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
	1					

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U.S.PATENT APPLICATION PUBLICATIONS Remove

Examiner Initial*	Cite No	Publication Number	Kind Code[1]	Publication Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
	1	20080131522		2008-06-05	Liu et al.	

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FOREIGN PATENT DOCUMENTS Remove

Examiner Initial*	Cite No	Foreign Document Number[3]	Country Code[2] i	Kind Code[4]	Publication Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear	T[5]
	1	2010/141847	WO		2010-12-09	ATS Medical, Inc.		

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NON-PATENT LITERATURE DOCUMENTS Remove

Examiner Initials*	Cite No	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc), date, pages(s), volume-issue number(s), publisher, city and/or country where published.	T[5]

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /CM/

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Application Number	13675665
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First Named Inventor	David Paniagua
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Attorney Docket Number	109978.10101

	1	SACKS, Michael S. et al., "Orthotropic Mechanical Properties of Chemically Treated Bovine Pericardium" Annals of Biomedical Engineering, 1998, vol. 26, pp. 892-902 (10254 OA, 12/03/15)
	2	Notice of Allowance issued September 22, 2011, in U.S. Application No. 12/228,192 (109978.10110)

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EXAMINER SIGNATURE

Examiner Signature	/Cheryl Miller/	Date Considered	04/16/2016

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[1] See Kind Codes of USPTO Patent Documents at www.USPTO.GOV or MPEP 901.04. [2] Enter office that issued the document, by the two-letter code (WIPO Standard ST.3). [3] For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. [4] Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. [5] Applicant is to place a check mark here if English language translation is attached.

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /CM/

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Attorney Docket Number	109978.10101

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Examiner Initial*	Cite No	Patent Number	Kind Code[1]	Issue Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
	1	4275469		1981-06-30	Gabbay	
	2	5558875		1996-09-24	Wang	
	3	7214344		2007-01-14	Carpentier et al.	

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Examiner Initial*	Cite No	Publication Number	Kind Code[1]	Publication Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
	1	20020119437		2002-08-29	Grooms et al.	
	2	20020146393		2002-10-10	Bell et al.	
	3	20030118560		2003-06-25	Kelly et al.	

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Examiner Name	Cheryl L. Miller
Attorney Docket Number	109978.10101

	4	20060212111		2006-09-21	Case et al.	

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Examiner Initials*	Cite No	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc), date, pages(s), volume-issue number(s), publisher, city and/or country where published.	T[5]
	1	Office Action issued July 6, 2015, in U.S. Application No. 13/367,252 (109978.10111)	☐
	2	Notice of Allowance issued August 14, 2015, in U.S. Application No. 13/367,252 (109978.10111)	☐

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Examiner Signature	/Cheryl Miller/	Date Considered	04/16/2016

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ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /CM/

Search Notes	Application/Control No.	Applicant(s)/Patent Under Reexamination
	13675665	PANIAGUA ET AL.
	Examiner	Art Unit
	CHERYL MILLER	3738

CPC- SEARCHED		
Symbol	Date	Examiner
A61f2/2418, 2412, 2415	4/12/2016	cm

CPC COMBINATION SETS - SEARCHED		
Symbol	Date	Examiner

US CLASSIFICATION SEARCHED			
Class	Subclass	Date	Examiner

SEARCH NOTES		
Search Notes	Date	Examiner
East text search, review parent application files	6/27/2015	cm
Inventor name search	4/12/2016	cm

INTERFERENCE SEARCH			
US Class/ CPC Symbol	US Subclass / CPC Group	Date	Examiner

/C.M./ Examiner.Art Unit 3738	

PTO/SB/08a (03-15)
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First Named Inventor	David PANIAGUA
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Examiner Name	Cheryl L. MILLER
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Examiner Initial*	Cite No	Patent Number	Kind Code[1]	Issue Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
	1	5080670		1992-01-14	Imamura	

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Examiner Initial*	Cite No	Publication Number	Kind Code[1]	Publication Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
	1	20030138945		2003-07-24	McAllister	
	2	20060155366		2006-07-13	LaDuca et al.	
	3	20060229716		2006-10-12	Mitrev	
	4	20090054976		2009-02-26	Tuval et al.	

If you wish to add additional U.S. Published Application citation information please click the Add button. Add

FOREIGN PATENT DOCUMENTS Remove

Examiner Initial*	Cite No	Foreign Document Number[3]	Country Code[2] i	Kind Code[4]	Publication Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear	T[5]

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	13675665
	Filing Date	2012-11-13
	First Named Inventor	David PANIAGUA
	Art Unit	3738
	Examiner Name	Cheryl L. MILLER
	Attorney Docket Number	109978.10101

	1						

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Examiner Initials*	Cite No	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc), date, pages(s), volume-issue number(s), publisher, city and/or country where published.	T[5]
	1	Office Action issued April 8, 2016 in U.S. Application No. 14/502,453 (File: 109978.10106)	

If you wish to add additional non-patent literature document citation information please click the Add button Add

EXAMINER SIGNATURE

Examiner Signature		Date Considered	

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through a citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

[1] See Kind Codes of USPTO Patent Documents at www.USPTO.GOV or MPEP 901.04. [2] Enter office that issued the document, by the two-letter code (WIPO Standard ST.3). [3] For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. [4] Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. [5] Applicant is to place a check mark here if English language translation is attached.

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(Not for submission under 37 CFR 1.99)

Application Number	13675665
Filing Date	2012-11-13
First Named Inventor	David PANIAGUA
Art Unit	3738
Examiner Name	Cheryl L. MILLER
Attorney Docket Number	109978.10101

CERTIFICATION STATEMENT

Please see 37 CFR 1.97 and 1.98 to make the appropriate selection(s):

That each item of information contained in the information disclosure statement was first cited in any communication from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e)(1).

OR

☐ That no item of information contained in the information disclosure statement was cited in a communication from a foreign patent office in a counterpart foreign application, and, to the knowledge of the person signing the certification after making reasonable inquiry, no item of information contained in the information disclosure statement was known to any individual designated in 37 CFR 1.56(c) more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e)(2).

See attached certification statement.

The fee set forth in 37 CFR 1.17 (p) has been submitted herewith.

☒ A certification statement is not submitted herewith.

SIGNATURE

A signature of the applicant or representative is required in accordance with CFR 1.33, 10.18. Please see CFR 1.4(d) for the form of the signature.

Signature	/Gunjan Agarwal/	Date (YYYY-MM-DD)	2016-07-19
Name/Print	Gunjan Agarwal	Registration Number	69661

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 1 hour to complete, including gathering, preparing and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

Privacy Act Statement

The Privacy Act of 1974 (P.L. 93-579) requires that you be given certain information in connection with your submission of the attached form related to a patent application or patent. Accordingly, pursuant to the requirements of the Act, please be advised that: (1) the general authority for the collection of this information is 35 U.S.C. 2(b)(2); (2) furnishing of the information solicited is voluntary; and (3) the principal purpose for which the information is used by the U.S. Patent and Trademark Office is to process and/or examine your submission related to a patent application or patent. If you do not furnish the requested information, the U.S. Patent and Trademark Office may not be able to process and/or examine your submission, which may result in termination of proceedings or abandonment of the application or expiration of the patent.

The information provided by you in this form will be subject to the following routine uses:

1. The information on this form will be treated confidentially to the extent allowed under the Freedom of Information Act (5 U.S.C. 552) and the Privacy Act (5 U.S.C. 552a). Records from this system of records may be disclosed to the Department of Justice to determine whether the Freedom of Information Act requires disclosure of these record s.

2. A record from this system of records may be disclosed, as a routine use, in the course of presenting evidence to a court, magistrate, or administrative tribunal, including disclosures to opposing counsel in the course of settlement negotiations.

3. A record in this system of records may be disclosed, as a routine use, to a Member of Congress submitting a request involving an individual, to whom the record pertains, when the individual has requested assistance from the Member with respect to the subject matter of the record.

4. A record in this system of records may be disclosed, as a routine use, to a contractor of the Agency having need for the information in order to perform a contract. Recipients of information shall be required to comply with the requirements of the Privacy Act of 1974, as amended, pursuant to 5 U.S.C. 552a(m).

5. A record related to an International Application filed under the Patent Cooperation Treaty in this system of records may be disclosed, as a routine use, to the International Bureau of the World Intellectual Property Organization, pursuant to the Patent Cooperation Treaty.

6. A record in this system of records may be disclosed, as a routine use, to another federal agency for purposes of National Security review (35 U.S.C. 181) and for review pursuant to the Atomic Energy Act (42 U.S.C. 218(c)).

7. A record from this system of records may be disclosed, as a routine use, to the Administrator, General Services, or his/her designee, during an inspection of records conducted by GSA as part of that agency's responsibility to recommend improvements in records management practices and programs, under authority of 44 U.S.C. 2904 and 2906. Such disclosure shall be made in accordance with the GSA regulations governing inspection of records for this purpose, and any other relevant (i.e., GSA or Commerce) directive. Such disclosure shall not be used to make determinations about individuals.

8. A record from this system of records may be disclosed, as a routine use, to the public after either publication of the application pursuant to 35 U.S.C. 122(b) or issuance of a patent pursuant to 35 U.S.C. 151. Further, a record may be disclosed, subject to the limitations of 37 CFR 1.14, as a routine use, to the public if the record was filed in an application which became abandoned or in which the proceedings were terminated and which application is referenced by either a published application, an application open to public inspections or an issued patent.

9. A record from this system of records may be disclosed, as a routine use, to a Federal, State, or local law enforcement agency, if the USPTO becomes aware of a violation or potential violation of law or regulation.

Electronic Patent Application Fee Transmittal

Application Number:	13675665
Filing Date:	13-Nov-2012
Title of Invention:	PERCUTANEOUSLY IMPLANTABLE REPLACEMENT HEART VALVE DEVICE AND METHOD OF MAKING SAME
First Named Inventor/Applicant Name:	David Paniagua
Filer:	Gunjan Agarwal/Carol Donahue
Attorney Docket Number:	109978.10101

Filed as Small Entity

Filing Fees for Utility under 35 USC 111(a)

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Basic Filing:				
Pages:				
Claims:				
Miscellaneous-Filing:				
Petition:				
Patent-Appeals-and-Interference:				
Post-Allowance-and-Post-Issuance:				
Extension-of-Time:				

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Miscellaneous:				
Request for Continued Examination	2801	1	600	600
		Total in USD ($)		**600**

Electronic Acknowledgement Receipt

EFS ID:	26389875
Application Number:	13675665
International Application Number:	
Confirmation Number:	1995
Title of Invention:	PERCUTANEOUSLY IMPLANTABLE REPLACEMENT HEART VALVE DEVICE AND METHOD OF MAKING SAME
First Named Inventor/Applicant Name:	David Paniagua
Customer Number:	29880
Filer:	Gunjan Agarwal/Carol Donahue
Filer Authorized By:	Gunjan Agarwal
Attorney Docket Number:	109978.10101
Receipt Date:	19-JUL-2016
Filing Date:	13-NOV-2012
Time Stamp:	14:34:16
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	yes
Payment Type	CARD
Payment was successfully received in RAM	$600
RAM confirmation Number	072016INTEFSW14345700
Deposit Account	5690
Authorized User	Carol Donahue

The Director of the USPTO is hereby authorized to charge indicated fees and credit any overpayment as follows:

37 CFR 1.16 (National application filing, search, and examination fees)

37 CFR 1.17 (Patent application and reexamination processing fees)

37 CFR 1.19 (Document supply fees)

37 CFR 1.20 (Post Issuance fees)

37 CFR 1.21 (Miscellaneous fees and charges)

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Request for Continued Examination (RCE)	10101_RCE.PDF	1379945 748d060eae0a6baf846064308d033030ef3546c0	no	3
Warnings:					
Information:					
2		10101_OAResponse.pdf	21592 c659dcab93616d94b4c403ca0202b9eaf2f35b70	yes	6
	Multipart Description/PDF files in .zip description				
	Document Description		**Start**	**End**	
	Response After Final Action		1	1	
	Claims		2	3	
	Applicant Arguments/Remarks Made in an Amendment		4	6	
Warnings:					
Information:					
3	Transmittal Letter	10101_IDS_Transmittal.pdf	26921 c52f5607a3e19bc2cfb2e16b756af259aca9204a	no	5
Warnings:					
Information:					
4	Information Disclosure Statement (IDS) Form (SB08)	10101_Supp_IDS.PDF	1085941 36b2b67242c4a1ad21a1af5a654f484de2f17d72	no	4
Warnings:					
Information:					
5	Non Patent Literature	10106_US_14-502453_Office_Action_2016-04-08.PDF	222548 9c49a591349215df65d5063a0f430331049af1f9	no	6

Warnings:					
Information:					
6	Fee Worksheet (SB06)	fee-info.pdf	30982 27afb385cf87328d18b0a8e755ec946649c2f420	no	2
Warnings:					
Information:					
			Total Files Size (in bytes):	2767929	

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New Applications Under 35 U.S.C. 111

If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

National Stage of an International Application under 35 U.S.C. 371

If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office

If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

PTO/SB/30EFS (07-14)
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U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

REQUEST FOR CONTINUED EXAMINATION(RCE)TRANSMITTAL
(Submitted Only via EFS-Web)

Application Number	13675665	Filing Date	2012-11-13	Docket Number (if applicable)	109978.10101	Art Unit	3738
First Named Inventor	David Paniagua			Examiner Name	Cheryl L. Miller		

This is a Request for Continued Examination (RCE) under 37 CFR 1.114 of the above-identified application.
Request for Continued Examination (RCE) practice under 37 CFR 1.114 does not apply to any utility or plant application filed prior to June 8, 1995, to any international application that does not comply with the requirements of 35 U.S.C. 371, or to any design application. The Instruction Sheet for this form is located at WWW.USPTO.GOV.

SUBMISSION REQUIRED UNDER 37 CFR 1.114

Note: If the RCE is proper, any previously filed unentered amendments and amendments enclosed with the RCE will be entered in the order in which they were filed unless applicant instructs otherwise. If applicant does not wish to have any previously filed unentered amendment(s) entered, applicant must request non-entry of such amendment(s).

☐ Previously submitted. If a final Office action is outstanding, any amendments filed after the final Office action may be considered as a submission even if this box is not checked.

- ☐ Consider the arguments in the Appeal Brief or Reply Brief previously filed on _____
- ☐ Other _____

☒ Enclosed

- ☒ Amendment/Reply
- ☒ Information Disclosure Statement (IDS)
- ☐ Affidavit(s)/ Declaration(s)
- ☐ Other _____

MISCELLANEOUS

☐ Suspension of action on the above-identified application is requested under 37 CFR 1.103(c) for a period of months _____ (Period of suspension shall not exceed 3 months; Fee under 37 CFR 1.17(i) required)

☐ Other _____

FEES

The RCE fee under 37 CFR 1.17(e) is required by 37 CFR 1.114 when the RCE is filed.

☒ The Director is hereby authorized to charge any underpayment of fees, or credit any overpayments, to Deposit Account No 501943

SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT REQUIRED

☒ Patent Practitioner Signature

Applicant Signature

PTO/SB/30EFS (07-14)
Approved for use through 07/31/2016. OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

Signature of Registered U.S. Patent Practitioner			
Signature	/Gunjan Agarwal/	Date (YYYY-MM-DD)	2016-07-19
Name	Gunjan Agarwal	Registration Number	69661

This collection of information is required by 37 CFR 1.114. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.11 and 1.14. This collection is estimated to take 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450.

If you need assistance in completing the form, call 1-800-PTO-9199 and select option 2.

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The Privacy Act of 1974 (P.L. 93-579) requires that you be given certain information in connection with your submission of the attached form related to a patent application or patent. Accordingly, pursuant to the requirements of the Act, please be advised that: (1) the general authority for the collection of this information is 35 U.S.C. 2(b)(2); (2) furnishing of the information solicited is voluntary; and (3) the principal purpose for which the information is used by the U.S. Patent and Trademark Office is to process and/or examine your submission related to a patent application or patent. If you do not furnish the requested information, the U.S. Patent and Trademark Office may not be able to process and/or examine your submission, which may result in termination of proceedings or abandonment of the application or expiration of the patent.

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5. A record related to an International Application filed under the Patent Cooperation Treaty in this system of records may be disclosed, as a routine use, to the International Bureau of the World Intellectual Property Organization, pursuant to the Patent Cooperation Treaty.

6. A record in this system of records may be disclosed, as a routine use, to another federal agency for purposes of National Security review (35 U.S.C. 181) and for review pursuant to the Atomic Energy Act (42 U.S.C. 218(c)).

7. A record from this system of records may be disclosed, as a routine use, to the Administrator, General Services, or his/her designee, during an inspection of records conducted by GSA as part of that agency's responsibility to recommend improvements in records management practices and programs, under authority of 44 U.S.C. 2904 and 2906. Such disclosure shall be made in accordance with the GSA regulations governing inspection of records for this purpose, and any other relevant (i.e., GSA or Commerce) directive. Such disclosure shall not be used to make determinations about individuals.

8. A record from this system of records may be disclosed, as a routine use, to the public after either publication of the application pursuant to 35 U.S.C. 122(b) or issuance of a patent pursuant to 35 U.S.C. 151. Further, a record may be disclosed, subject to the limitations of 37 CFR 1.14, as a routine use, to the public if the record was filed in an application which became abandoned or in which the proceedings were terminated and which application is referenced by either a published application, an application open to public inspections or an issued patent.

9. A record from this system of records may be disclosed, as a routine use, to a Federal, State, or local law enforcement agency, if the USPTO becomes aware of a violation or potential violation of law or regulation.

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:	:	
	:	
David Paniagua et al.	:	Confirmation No.: 1995
	:	
Application No.: 13/675,665	:	Group Art Unit: 3738
	:	
Filed: November 13, 2012	:	Examiner: Cheryl L. Miller

Title: PERCUTANEOUSLY IMPLANTABLE REPLACEMENT HEART VALVE DEVICE AND METHOD OF MAKING SAME

AMENDMENT AND RESPONSE TO OFFICE ACTION, REQUEST FOR CONTINUED EXAMINATION AND REQUEST FOR EXAMINER INTERVIEW

This Amendment And Response To Final Office Action, Request for Continued Examination And Request For Examiner Interview is in reply to the Final Office Action issued on April 22, 2016 in the application captioned above. The following remarks are respectfully submitted.

AMENDMENTS TO THE CLAIMS

The following listing of claims replaces all prior versions, and listings, of the claims in the application.

1. (Currently Amended) A percutaneously implantable replacement heart valve device for implantation in a patient, comprising:

an expandable stent member having an inner channel, the expandable stent member collapsible and configured for percutaneous delivery; and

a valve means made of biocompatible tissue material and attached to the expandable stent member, the valve means including an outer cuff layer and two to four individual leaflets, wherein each of the two to four individual leaflets is rectangular in shape in side elevation view, wherein a crease is located between a base of the two to four individual leaflets and the outer cuff layer ~~at a base of the two to four individual leaflets~~, and wherein after implantation in the patient, the valve means resides as a single element entirely within the inner channel of the expandable stent member, wherein only the two to four individual leaflets reside radially inward from the outer cuff layer, and wherein the valve means is formed without cutting slits into said biocompatible tissue material to form said leaflets.

2. (Original) The percutaneously implantable replacement heart valve device of claim 1, wherein said expandable stent member is made of a metal or alloy of metals selected from the group consisting of nickel-titanium alloy, titanium and stainless steel.

3. (Canceled)

4. (Previously Presented) The percutaneously implantable replacement heart valve device of claim 1, wherein said biocompatible tissue material of said valve means comprises porcine pericardium tissue.

5. (Canceled)

6. (Previously Presented) The percutaneously implantable replacement heart valve device of claim 1, wherein said biocompatible tissue material of said valve means comprises autologous tissue obtained from the patient into whom said replacement heart valve device will be implanted.

7.-8. (Canceled)

9. (Previously Presented) The percutaneously implantable heart valve device of claim 1, wherein said expandable stent member is self-expanding when implanted.

10. (Previously Presented) The percutaneously implantable heart valve device of claim 1, wherein said expandable stent member is balloon catheter expandable when implanted.

11.-33. (Cancelled)

REMARKS

In the Office Action, the Office rejected claims 1, 2, 4, 6, 9 and 10. More specifically:

- The Office rejected claims 1-2 and 4 under nonstatutory double patenting as being unpatentable over claims 1-17 of U.S. Patent No. 8,308,797;
- The Office rejected claim 1 under nonstatutory double patenting as being unpatentable over claim 4 of U.S. Patent No. 8,790,398; and
- The Office rejected claims 1-2, 4, 6 and 9-10 under 35 U.S.C. §112 pre-AIA, second paragraph, as failing to point out and distinctly claim the subject matter regarded as the invention.

Claim 1 has been amended. Support for these amendments can be found in at least paragraphs [0046] and FIGS. 3A and 3B of the published application. Upon entry of these amendments and remarks, claims 1, 2, 4, 6, 9 and 10 will remain pending. For the reasons set forth below, Applicant asks the Office to withdraw the rejections associated with the claims.

Rejections Under Double Patenting

The Office rejected claims 1-2 and 4 under nonstatutory double patenting as being unpatentable over claims 1-17 of U.S. Patent No. 8,308,797; and claim 1 under nonstatutory double patenting as being unpatentable over claim 4 of U.S. Patent No. 8,790,398.

Applicant does not necessarily agree with the Office's assertions, and hereby respectfully reserves the right to refute and contest any and all contentions made by the Office in issuing these rejections. Nevertheless, Applicant notes that there has not yet been any indication of allowable subject matter in the present application, and accordingly applicants respectfully request that the Office hold these rejections in abeyance until allowable subject matter is

indicated. At that time applicants will consider the possibility of filing, solely in order to advance prosecution, one or more Terminal Disclaimers under 37 CFR 1.321(c).

Rejections Under 35 U.S.C. §112 pre-AIA, second paragraph

On page 4 of the Office Action, the Office rejected claims 1, 2, 4, 6, 9 and 10 under 35 U.S.C. §112 pre-AIA, second paragraph, as being indefinite for failing to particularly point out and distinctly claims the subject matter of the invention. Specifically, the Office asserted that it is unclear how the crease could be located at the base of the leaflets while also being located between the leaflets and the cuff.

Without conceding the merits of the rejection, and solely to advance prosecution, Applicant has amended claim 1 to recite "wherein a crease is located between a base of the two to four individual leaflets and the outer cuff layer."

Accordingly, Applicant respectfully requests that the Office withdraw the §112, second paragraph, rejections associated with claims 1-2, 4, 6 and 9-10.

CONCLUSION AND REQUEST FOR INTERVIEW

For the reasons discussed above, Applicant respectfully asks the Examiner to reconsider and withdraw all outstanding rejections.

If the next Office Action will not result in allowance of the claims, Applicant requests an interview to discuss any remaining issues. Applicant invites the Examiner to contact the undersigned attorney to schedule a convenient time.

The Commissioner is hereby authorized to charge any additional fees which may be required for this Amendment, or credit any overpayment, to Deposit Account No. 50-1943.

Respectfully submitted,

FOX ROTHSCHILD LLP

/Gunjan Agarwal/
Gunjan Agarwal
Registration No. 69,661

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Telephone: 412-391-2414
Facsimile: 609-896-1469
Date: July 19 2016

Docket No.: 109978.10101
(PATENT)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of:
David Paniagua et al.

Application No.: 13/675,665 Confirmation No.: 1995

Filed: November 13, 2012 Art Unit: 3738

For: Percutaneously Implantable Replacement Heart Valve Device and Method of Making Same Examiner: C. L. Miller

INFORMATION DISCLOSURE STATEMENT (IDS)

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

This Information Disclosure Statement is submitted in accordance with 37 C.F.R. 1.97, 1.98, and it is requested that the information set forth in this statement and in the listed documents be considered during the pendency of the above-identified application, and any other application relying on the filing date of the above-identified application or cross-referencing it as a related application.

1. This IDS should be considered, in accordance with 37 C.F.R. 1.97, as it is filed: (Check one of the boxes A-D)

- [ ] A. within three months of the filing date of the above-identified national application or within three months of the entry into the national stage of the above identified national application
- [x] B. before the mailing date of a first office action on the merits, or a first office action after filing a request for continued examination.
- [ ] C. after (A) and (B) above, but before final rejection or allowance, and Applicants have made the necessary statement in box "i" below or paid the necessary fee in box "ii" below.

(check one of the boxes "i" and "ii" below:)

☐ i. Counsel states that, upon information and belief, each item of information listed herein was (check one of boxes (a) or (b))

☐ (a) first cited in any communication from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of this IDS; or

☐ (b) not cited in a communication from a foreign patent office in a counterpart foreign application and, to the knowledge of undersigned after making reasonable inquiry, was not known to any individual designated in 1.56(c) more than three months prior to the filing of this IDS.

☐ ii. Payment in the amount of the fee set forth in 1. 17(p), presently believed to be $180, is enclosed.

☐ D. after (A), (B) and (C) above, but before payment of the issue fee: Applicant petitions under 37 C.F.R. 1.97(d) for the consideration of this IDS. Under 37 CFR 1.17(p) payment in the amount of $180.00 is enclosed. Counsel certifies that, upon information and belief, each item of information listed herein was

(check one of the boxes "a" and "b" below:)

☐ (a) first cited in any communication from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of this IDS; or

☐ (b) was not cited in a communication from a foreign patent office in a counterpart foreign application and, to the knowledge of undersigned after making reasonable inquiry, was not known to any individual designated in 1.56(c) more than three months prior to the filing of this IDS.

2. In accordance with 37 C.F.R. 1.98, this IDS includes a list (e.g., form PTO/SB/08) of all patents, publications, or other information submitted for consideration by the office, either incorporated into this IDS or as an attachment hereto. A copy of each document listed is attached, except as explained below.

(check boxes A, B and/or C and fill in blanks, if appropriate.)

[x] A. Pursuant to the Notice issued by the United States Patent and Trademark Office dated August 5, 2003 waiving the requirements of 37 C.F.R. § 1.98(a)(2)(ii), a copy/copies of the U.S. Patent(s) and/or U.S. Patent Application Publication(s) on PTO/SB/08 is/are not being submitted.

[ ] B. Document(s) _____is (are) deemed substantially cumulative to document(s) _____ , and, in accordance with 1.98(c), only a copy of each of the latter documents is enclosed.

[ ] C. Certain documents were previously cited by or submitted to the Office in the following prior applications, which are relied upon under 35 U.S.C. 120:

<<INSERT SERIAL NO. & FILING DATE>>

Applicant identifies these documents by attaching hereto copies of the forms PTO-892, PTO-1449 and/or PTO/SB/08 from the files of the prior application(s) or a fresh PTO/SB/08 listing these documents, and request that they be considered and made of record in accordance with 1.98(d). Per 37 CFR 1.98(d), copies of these documents need not be filed in this application.

[ ] 3. Cite Nos. _____ are not in the English language. In accordance with 1.98(c), Applicant states:

[ ] An English translation of each document (or of the pertinent portions thereof), or a copy of each corresponding English-language patent or application , or English-language abstract (or claim) is enclosed.

[ ] The requirement for a concise explanation of the relevance of any foreign language document is satisfied by the attached search report; citation of the documents cited in the search report shall not be construed as an admission that they are or are considered to be, material to patentability of the subject matter claimed herein (See MPEP §609).

[ ] A concise explanation of the relevance of document(s) _____ is set forth as follows: [Insert concise explanation of relevance]

[ ] A concise explanation of the relevance of document(s) _____ can be found on page(s) _____ of the specification.

[ ] A concise explanation of document(s) _____ can be found on the attached sheet.

☐ 4. No explanation of relevance is necessary for documents in the English language (see reply to Comments 67 in the preamble to the final rules; 1135 OG 13 at 20).

☐ 5. Other information being provided for the examiner's consideration follows:

6. Related Patents and Patent Applications. The Examiner is hereby advised of the existence of the patents, patent applications, and/or other proceedings before the Patent Office listed below which: (1) share at least some common disclosure with the instant application, (2) serve as the basis of priority for the instant application, and/or (3) otherwise may relate to the instant application or one or more of the other matters listed below. For completeness, the instant application is also included in the list.

It is respectfully requested that the Examiner review each matter listed below and its associated prosecution history (e.g., Office Actions, Responses to Office Actions, Interview Summaries, Notice of Allowances, and so forth) as part of evaluating the instant application. The prosecution history for each matter listed below should be readily available to the Examiner through the Patent Office's internal systems. Since these materials are already easily accessible to the Examiner, a hard copy has not been provided. However, at the Examiner's request, Applicant will provide a hard copy of any matter listed below including its prosecution history (or one or more individual documents from the prosecution history). Applicant believes that this is an efficient and effective way to allow the Examiner to consider the applicability of the matters listed below to the instant application.

The attached form PTO/SB/08b includes a reference to the information listed below concerning related patents and patent applications. Applicant requests that the Examiner initial the attached PTO/SB/08b form next to this reference to indicate that the Examiner has considered this information as part of evaluating the instant application. By initialing the form in this manner, the Examiner expressly acknowledges that he/she has considered each matter listed below, as well as all of the documents included in its prosecution history, as part of examining the instant application.

Application Serial No.	**Filing Date**	**Title of Invention**

7. In accordance with 37 C.F.R. 1.97(g) and (h), the filing of this IDS should not be construed as a representation that a search has been made or that information cited is, or is considered to be, material to patentability as defined in §1.56 (b), or that any cited document listed or attached is (or constitutes) prior art. Unless other-wise indicated, the date of publication indicated

for an item is taken from the face of the item and Applicant reserves the right to prove that the date of publication is in fact different.

Early and favorable consideration is earnestly solicited.

The Director is hereby authorized to charge any deficiency in the fees filed, asserted to be filed or which should have been filed herewith (or with any paper hereafter filed in this application by this firm) to our Deposit Account No. 50-1943, under Order No. 109978.10101.

Applicant believes no fee is due with this response. However, if a fee is due, please charge our Deposit Account No. 50-1943, under Order No. 109978.10101 from which the undersigned is authorized to draw.

Dated: July 19, 2016

Respectfully submitted,

By/Gunjan Agarwal/
Gunjan Agarwal
Registration No.: 69,661
FOX ROTHSCHILD LLP
997 Lenox Drive, Building 3
Lawrenceville, New Jersey 08648-2311
(412) 391-2414
(609) 896-1469 (Fax)
Attorneys/Agents For Applicant

PTO/SB/06 (09-11)
Approved for use through 1/31/2014. OMB 0651-0032
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

PATENT APPLICATION FEE DETERMINATION RECORD Substitute for Form PTO-875	Application or Docket Number 13/675,665	Filing Date 11/13/2012	☐ To be Mailed

ENTITY: ☐ LARGE ☒ SMALL ☐ MICRO

APPLICATION AS FILED – PART I

FOR	(Column 1) NUMBER FILED	(Column 2) NUMBER EXTRA	RATE ($)	FEE ($)
☐ BASIC FEE (37 CFR 1.16(a), (b), or (c))	N/A	N/A	N/A	
☐ SEARCH FEE (37 CFR 1.16(k), (i), or (m))	N/A	N/A	N/A	
☐ EXAMINATION FEE (37 CFR 1.16(o), (p), or (q))	N/A	N/A	N/A	
TOTAL CLAIMS (37 CFR 1.16(i))	minus 20 =	*	X $ =	
INDEPENDENT CLAIMS (37 CFR 1.16(h))	minus 3 =	*	X $ =	
☐ APPLICATION SIZE FEE (37 CFR 1.16(s))	If the specification and drawings exceed 100 sheets of paper, the application size fee due is $310 ($155 for small entity) for each additional 50 sheets or fraction thereof. See 35 U.S.C. 41(a)(1)(G) and 37 CFR 1.16(s).			
☐ MULTIPLE DEPENDENT CLAIM PRESENT (37 CFR 1.16(j))				
* If the difference in column 1 is less than zero, enter "0" in column 2.			TOTAL	

APPLICATION AS AMENDED – PART II

AMENDMENT **07/19/2016**

	(Column 1) CLAIMS REMAINING AFTER AMENDMENT		(Column 2) HIGHEST NUMBER PREVIOUSLY PAID FOR	(Column 3) PRESENT EXTRA	RATE ($)	ADDITIONAL FEE ($)
Total (37 CFR 1.16(i))	* 6	Minus	** 20	= 0	X $40 =	0
Independent (37 CFR 1.16(h))	* 1	Minus	***3	= 0	X $210 =	0
☐ Application Size Fee (37 CFR 1.16(s))						
☐ FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))						
					TOTAL ADD'L FEE	0

AMENDMENT

	(Column 1) CLAIMS REMAINING AFTER AMENDMENT		(Column 2) HIGHEST NUMBER PREVIOUSLY PAID FOR	(Column 3) PRESENT EXTRA	RATE ($)	ADDITIONAL FEE ($)
Total (37 CFR 1.16(i))	*	Minus	**	=	X $ =	
Independent (37 CFR 1.16(h))	*	Minus	***	=	X $ =	
☐ Application Size Fee (37 CFR 1.16(s))						
☐ FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))						
					TOTAL ADD'L FEE	

* If the entry in column 1 is less than the entry in column 2, write "0" in column 3.
** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 20, enter "20".
*** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 3, enter "3".
The "Highest Number Previously Paid For" (Total or Independent) is the highest number found in the appropriate box in column 1.

LIE
/STELLA LITTLE/

Electronic Acknowledgement Receipt

EFS ID:	26389875
Application Number:	13675665
International Application Number:	
Confirmation Number:	1995
Title of Invention:	PERCUTANEOUSLY IMPLANTABLE REPLACEMENT HEART VALVE DEVICE AND METHOD OF MAKING SAME
First Named Inventor/Applicant Name:	David Paniagua
Customer Number:	29880
Filer:	Gunjan Agarwal/Carol Donahue
Filer Authorized By:	Gunjan Agarwal
Attorney Docket Number:	109978.10101
Receipt Date:	19-JUL-2016
Filing Date:	13-NOV-2012
Time Stamp:	14:34:16
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	yes
Payment Type	CARD
Payment was successfully received in RAM	$600
RAM confirmation Number	072016INTEFSW14345700
Deposit Account	501943
Authorized User	Carol Donahue

The Director of the USPTO is hereby authorized to charge indicated fees and credit any overpayment as follows:

37 CFR 1.16 (National application filing, search, and examination fees)

37 CFR 1.17 (Patent application and reexamination processing fees)

37 CFR 1.19 (Document supply fees)

37 CFR 1.20 (Post Issuance fees)

37 CFR 1.21 (Miscellaneous fees and charges)

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Request for Continued Examination (RCE)	10101_RCE.PDF	1379945 748d060eae0a6baf846064308d033030ef3546c0	no	3
Warnings:					
Information:					
2		10101_OAResponse.pdf	21592 c659dcab93616d94b4c403ca0202b9eaf2f35b70	yes	6

Multipart Description/PDF files in .zip description

Document Description	Start	End
Response After Final Action	1	1
Claims	2	3
Applicant Arguments/Remarks Made in an Amendment	4	6

Warnings:					
Information:					
3	Transmittal Letter	10101_IDS_Transmittal.pdf	26921 c52f5607a3e19bc2cfb2e16b756af259aca9204a	no	5
Warnings:					
Information:					
4	Information Disclosure Statement (IDS) Form (SB08)	10101_Supp_IDS.PDF	1085941 36b2b67242c4a1ad21a1af5a654f484de2f17d72	no	4
Warnings:					
Information:					
5	Non Patent Literature	10106_US_14-502453_Office_Action_2016-04-08.PDF	222548 9c49a591349215df65d5063a0f430331049af1f9	no	6

Warnings:					
Information:					
6	Fee Worksheet (SB06)	fee-info.pdf	30982 27afb385cf87328d18b0a8e755ec946649c2f420	no	2
Warnings:					
Information:					
			Total Files Size (in bytes):	2767929	

This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

New Applications Under 35 U.S.C. 111

If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

National Stage of an International Application under 35 U.S.C. 371

If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office

If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
13/675,665	11/13/2012	David Paniagua	109978.10101	1995

29880 7590 07/29/2016

FOX ROTHSCHILD LLP
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BLDG. #3
LAWRENCEVILLE, NJ 08648

EXAMINER
MILLER, CHERYL L

ART UNIT	PAPER NUMBER
3738	

NOTIFICATION DATE	DELIVERY MODE
07/29/2016	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

ipdocket@foxrothschild.com

Office Action Summary	Application No. 13/675,665	Applicant(s) PANIAGUA ET AL.	
	Examiner CHERYL MILLER	Art Unit 3738	AIA (First Inventor to File) Status No

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTHS FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *7/19/2016*.

☐ A declaration(s)/affidavit(s) under **37 CFR 1.130(b)** was/were filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on _____; the restriction requirement and election have been incorporated into this action.

4)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims*

5)☒ Claim(s) *1,2,4,6,9 and 10* is/are pending in the application.

5a) Of the above claim(s) _____ is/are withdrawn from consideration.

6)☐ Claim(s) _____ is/are allowed.

7)☒ Claim(s) *1,2 and 4* is/are rejected.

8)☒ Claim(s) *6,9 and 10* is/are objected to.

9)☐ Claim(s) _____ are subject to restriction and/or election requirement.

* If any claims have been determined allowable, you may be eligible to benefit from the **Patent Prosecution Highway** program at a participating intellectual property office for the corresponding application. For more information, please see http://www.uspto.gov/patents/init_events/pph/index.jsp or send an inquiry to PPHfeedback@uspto.gov.

Application Papers

10)☐ The specification is objected to by the Examiner.

11)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

Certified copies:

a)☐ All b)☐ Some** c)☐ None of the:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

** See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)

2) ☒ Information Disclosure Statement(s) (PTO/SB/08a and/or PTO/SB/08b) Paper No(s)/Mail Date _____.

3) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .

4) ☐ Other: _____.

DETAILED ACTION

Notice of Pre-AIA or AIA Status

The present application is being examined under the pre-AIA first to invent provisions.

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on July 19, 2016 has been entered.

Response to Arguments

Applicant's amendment filed July 19, 2016 has overcome the previous 112 2nd rejections.

The previous double patenting rejections have been maintained herein, because a terminal disclaimer was not filed with applicant's response.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory double patenting rejection is appropriate where the claims at issue are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d

1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); In re Vogel, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the reference application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement. See MPEP § 717.02 for applications subject to examination under the first inventor to file provisions of the AIA as explained in MPEP § 2159. See MPEP §§ 706.02(l)(1) - 706.02(l)(3) for applications not subject to examination under the first inventor to file provisions of the AIA. A terminal disclaimer must be signed in compliance with 37 CFR 1.321(b).

The USPTO Internet website contains terminal disclaimer forms which may be used. Please visit www.uspto.gov/forms/. The filing date of the application in which the form is filed determines what form (e.g., PTO/SB/25, PTO/SB/26, PTO/AIA/25, or PTO/AIA/26) should be used. A web-based eTerminal Disclaimer may be filled out completely online using web-screens. An eTerminal Disclaimer that meets all requirements is auto-processed and approved immediately upon submission. For more information about eTerminal Disclaimers, refer to http://www.uspto.gov/patents/process/file/efs/guidance/eTD-info-I.jsp.

Claims 1-2 and 4 are rejected on the ground of nonstatutory double patenting as being unpatentable over claims 1-17 of U.S. Patent No. 8,308,797 B2, cited previously. Although the claims at issue are not identical, they are not patentably distinct from each other because the application claims are merely broader than the patent claims.

Claim 1 is rejected on the ground of nonstatutory double patenting as being unpatentable over claim 4 of U.S. Patent No. 8,790,398 B2, cited previously. Although the claims at issue are not identical, they are not patentably distinct from each other because the application claim is merely broader than the patent claim.

Allowable Subject Matter

Claims 6, 9, and 10 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Conclusion

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Dzemeshkevich et al. (US 4,692,164) discloses a two layer tissue valve with resilient frame; Schwartz et al. (US 2002/0099439 A1) discloses a frame with a plurality of cusps therein (fig.25-27); Obermiller et al. (US 2004/0049262 A1) discloses a stent with valve pockets; and McGuckin et al. (US 2002/0055772 A1) discloses a stent with valve therein (fig.42-44).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Cheryl Miller whose telephone number is 571-272-4755. The examiner can normally be reached on M- F (8am-5:30pm).

If attempts to reach the examiner by telephone are unsuccessful, please contact the examiner's supervisor, Thomas Sweet at 571-272-4761. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/C. M./
Examiner, Art Unit 3738
/THOMAS J SWEET/

Supervisory Patent Examiner, Art Unit 3738

Notice of References Cited	Application/Control No. 13/675,665	Applicant(s)/Patent Under Reexamination PANIAGUA ET AL.	
	Examiner CHERYL MILLER	Art Unit 3738	Page 1 of 1

U.S. PATENT DOCUMENTS

*		Document Number Country Code-Number-Kind Code	Date MM-YYYY	Name	CPC Classification	US Classification
*	A	US-4,692,164 A	09-1987	Dzemeshkevich; Sergei L.	A61F2/2412	623/2.14
*	B	US-2002/0099439 A1	07-2002	Schwartz, Robert S.	A61F2/2412	623/1.24
*	C	US-2004/0049262 A1	03-2004	Obermiller, Joseph F.	A61F2/2418	623/1.15
*	D	US-2002/0055772 A1	05-2002	McGuckin, James F. JR.	A61B17/12036	623/1.24
	E	US-				
	F	US-				
	G	US-				
	H	US-				
	I	US-				
	J	US-				
	K	US-				
	L	US-				
	M	US-				

FOREIGN PATENT DOCUMENTS

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	N					
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NON-PATENT DOCUMENTS

*		Include as applicable: Author, Title Date, Publisher, Edition or Volume, Pertinent Pages)
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*A copy of this reference is not being furnished with this Office action. (See MPEP § 707.05(a).)
Dates in MM-YYYY format are publication dates. Classifications may be US or foreign.

Doc code: IDS
Doc description: Information Disclosure Statement (IDS) Filed

PTO/SB/08a (03-15)
Approved for use through 07/31/2016. OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(Not for submission under 37 CFR 1.99)

Application Number	13675665
Filing Date	2012-11-13
First Named Inventor	David PANIAGUA
Art Unit	3738
Examiner Name	Cheryl L. MILLER
Attorney Docket Number	109978.10101

U.S.PATENTS Remove

Examiner Initial*	Cite No	Patent Number	Kind Code[1]	Issue Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
	1	5080670		1992-01-14	Imamura	

If you wish to add additional U.S. Patent citation information please click the Add button. Add

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Examiner Initial*	Cite No	Publication Number	Kind Code[1]	Publication Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
	1	20030138945		2003-07-24	McAllister	
	2	20060155366		2006-07-13	LaDuca et al.	
	3	20060229716		2006-10-12	Mitrev	
	4	20090054976		2009-02-26	Tuval et al.	

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Examiner Initial*	Cite No	Foreign Document Number[3]	Country Code[2] i	Kind Code[4]	Publication Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear	T[5]

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /C.L.M/

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(Not for submission under 37 CFR 1.99)

Application Number	13675665
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First Named Inventor	David PANIAGUA
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Examiner Name	Cheryl L. MILLER
Attorney Docket Number	109978.10101

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Examiner Initials*	Cite No	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc), date, pages(s), volume-issue number(s), publisher, city and/or country where published.	T[5]
	1	Office Action issued April 8, 2016 in U.S. Application No. 14/502,453 (File: 109978.10106)	

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EXAMINER SIGNATURE

Examiner Signature	/CHERYL L MILLER/	Date Considered	07/23/2016

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through a citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

[1] See Kind Codes of USPTO Patent Documents at www.USPTO.GOV or MPEP 901.04. [2] Enter office that issued the document, by the two-letter code (WIPO Standard ST.3). [3] For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. [4] Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. [5] Applicant is to place a check mark here if English language translation is attached.

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /C.L.M/

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(Not for submission under 37 CFR 1.99)

Application Number	13675665
Filing Date	2012-11-13
First Named Inventor	David PANIAGUA
Art Unit	3738
Examiner Name	Cheryl L. MILLER
Attorney Docket Number	109978.10101

CERTIFICATION STATEMENT

Please see 37 CFR 1.97 and 1.98 to make the appropriate selection(s):

That each item of information contained in the information disclosure statement was first cited in any communication from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e)(1).

OR

☐ That no item of information contained in the information disclosure statement was cited in a communication from a foreign patent office in a counterpart foreign application, and, to the knowledge of the person signing the certification after making reasonable inquiry, no item of information contained in the information disclosure statement was known to any individual designated in 37 CFR 1.56(c) more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e)(2).

See attached certification statement.

The fee set forth in 37 CFR 1.17 (p) has been submitted herewith.

☒ A certification statement is not submitted herewith.

SIGNATURE

A signature of the applicant or representative is required in accordance with CFR 1.33, 10.18. Please see CFR 1.4(d) for the form of the signature.

Signature	/Gunjan Agarwal/	Date (YYYY-MM-DD)	2016-07-19
Name/Print	Gunjan Agarwal	Registration Number	69661

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 1 hour to complete, including gathering, preparing and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

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The Privacy Act of 1974 (P.L. 93-579) requires that you be given certain information in connection with your submission of the attached form related to a patent application or patent. Accordingly, pursuant to the requirements of the Act, please be advised that: (1) the general authority for the collection of this information is 35 U.S.C. 2(b)(2); (2) furnishing of the information solicited is voluntary; and (3) the principal purpose for which the information is used by the U.S. Patent and Trademark Office is to process and/or examine your submission related to a patent application or patent. If you do not furnish the requested information, the U.S. Patent and Trademark Office may not be able to process and/or examine your submission, which may result in termination of proceedings or abandonment of the application or expiration of the patent.

The information provided by you in this form will be subject to the following routine uses:

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2. A record from this system of records may be disclosed, as a routine use, in the course of presenting evidence to a court, magistrate, or administrative tribunal, including disclosures to opposing counsel in the course of settlement negotiations.

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5. A record related to an International Application filed under the Patent Cooperation Treaty in this system of records may be disclosed, as a routine use, to the International Bureau of the World Intellectual Property Organization, pursuant to the Patent Cooperation Treaty.

6. A record in this system of records may be disclosed, as a routine use, to another federal agency for purposes of National Security review (35 U.S.C. 181) and for review pursuant to the Atomic Energy Act (42 U.S.C. 218(c)).

7. A record from this system of records may be disclosed, as a routine use, to the Administrator, General Services, or his/her designee, during an inspection of records conducted by GSA as part of that agency's responsibility to recommend improvements in records management practices and programs, under authority of 44 U.S.C. 2904 and 2906. Such disclosure shall be made in accordance with the GSA regulations governing inspection of records for this purpose, and any other relevant (i.e., GSA or Commerce) directive. Such disclosure shall not be used to make determinations about individuals.

8. A record from this system of records may be disclosed, as a routine use, to the public after either publication of the application pursuant to 35 U.S.C. 122(b) or issuance of a patent pursuant to 35 U.S.C. 151. Further, a record may be disclosed, subject to the limitations of 37 CFR 1.14, as a routine use, to the public if the record was filed in an application which became abandoned or in which the proceedings were terminated and which application is referenced by either a published application, an application open to public inspections or an issued patent.

9. A record from this system of records may be disclosed, as a routine use, to a Federal, State, or local law enforcement agency, if the USPTO becomes aware of a violation or potential violation of law or regulation.

/CHERYL L MILLER/ 07/23/2016

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /C.L.M/

Search Notes	Application/Control No.	Applicant(s)/Patent Under Reexamination
	13675665	PANIAGUA ET AL.
	Examiner	Art Unit
	CHERYL MILLER	3738

CPC- SEARCHED		
Symbol	Date	Examiner
A61f2/2418, 2412, 2415	4/12/2016	cm
update	7/22/2016	cm

CPC COMBINATION SETS - SEARCHED		
Symbol	Date	Examiner

US CLASSIFICATION SEARCHED			
Class	Subclass	Date	Examiner

SEARCH NOTES		
Search Notes	Date	Examiner
East text search, review parent application files	6/27/2015	cm
Inventor name search	4/12/2016	cm

INTERFERENCE SEARCH			
US Class/ CPC Symbol	US Subclass / CPC Group	Date	Examiner

/C.M./ Examiner.Art Unit 3738	

EAST Search History

EAST Search History (Prior Art)

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			USOCR			
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S67	1762	623/2.$2.ccls. and pericardi$2 and (stent or frame)	US-PGPUB; USPAT; USOCR	OR	ON	2015/06/27 22:46
S68	1011	623/2.$2.ccls. and ((calf or juvenile or porcine or animal or mammal) with pericardi$2) and (stent or frame)	US-PGPUB; USPAT; USOCR	OR	ON	2015/06/27 22:47

S69	317	S68 and @rlad<"20040710"	US-PGPUB; USPAT; USOCR	OR	ON	2015/06/27 22:48
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S71	458	S69 S70	US-PGPUB; USPAT; USOCR	OR	ON	2015/06/27 22:48
S72	240	S71 and (resilient or "self-expandable" or "self-expanding" or "self-expands")	US-PGPUB; USPAT; USOCR	OR	ON	2015/06/27 22:49
S73	162	S71 and (resilient or "self-expandable" or "self-expanding" or "self-expands") and (sheet or patch)	US-PGPUB; USPAT; USOCR	OR	ON	2015/06/27 22:50
S74	97	623/2.$2.ccls. and (autologous with pericardi$2)	US-PGPUB; USPAT; USOCR	OR	ON	2015/06/27 23:07
S75	126	623/2.$2.ccls. and ((autologous or autograft) with pericardi$2)	US-PGPUB; USPAT; USOCR	OR	ON	2015/06/27 23:07
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S82	1	"6893460".pn.	US-PGPUB; USPAT; USOCR	OR	OFF	2015/06/28 00:23
S83	21	623/2.$2.ccls. and (double with continuous with sutur$4)	US-PGPUB; USPAT;	OR	OFF	2015/06/28 00:52

			USOCR			
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S85	625	S84 and @rlad<"20020104"	US-PGPUB; USPAT; USOCR	OR	ON	2016/04/11 14:53
S86	454	S84 and @ad<"20020104"	US-PGPUB; USPAT; USOCR	OR	ON	2016/04/11 14:53
S87	891	S85 S86	US-PGPUB; USPAT; USOCR	OR	ON	2016/04/11 14:53
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		$ or US-6358277-$ or US-4790844-$).did.				
S90	29	paniagua.in. and valve	US-PGPUB; USPAT; USOCR	OR	ON	2016/04/12 15:39
S91	9	paniagua.in. and valve	USPAT; USOCR	OR	ON	2016/04/12 15:39
S92	3733	a61f2/2412.cpc. or a61f2/2415.cpc. or a61f2/2418.cpc.	US-PGPUB; USPAT; USOCR	OR	ON	2016/04/12 16:00
S93	625	S92 and @rlad<"20020104"	US-PGPUB; USPAT; USOCR	OR	ON	2016/04/12 16:00
S94	454	S92 and @ad<"20020104"	US-PGPUB; USPAT; USOCR	OR	ON	2016/04/12 16:00
S95	891	S93 S94	US-PGPUB; USPAT; USOCR	OR	ON	2016/04/12 16:00
S96	299	S95 and pericardi$3	USPAT; USOCR	OR	ON	2016/04/12 16:00
S97	498	S95 and pericardi$3	US-PGPUB; USPAT; USOCR	OR	ON	2016/04/12 16:00
S98	344	S95 and pericardi$3 and (expand$4 or collaps$4)	US-PGPUB; USPAT; USOCR	OR	ON	2016/04/12 16:01
S99	286	S95 and pericardi$3 and (expand$4 or collaps$4) and (cuff or crease or fold$4 or invert$3 or evert$3)	US-PGPUB; USPAT; USOCR	OR	ON	2016/04/12 16:02
S100	425	S95 and (pericardi$3 or tube) and (expand$4 or collaps$4) and (cuff or crease or fold$4 or invert$3 or evert$3)	US-PGPUB; USPAT; USOCR	OR	ON	2016/04/12 16:02
S101	57	(US-20100114299-$ or US-20060167543-$ or US-20060142848-$ or US-20050065594-$ or US-20040193253-$ or US-20030040792-$ or US-20020151970-$ or US-20110137409-$ or US-20030078652-$ or US-20020052651-$ or US-20020032482-$ or US-20020198594-$ or US-20030023303-$ or US-20040186565-$ or US-20050075725-$ or US-20060004442-$ or US-20090118826-$).did. or (US-7947072-$ or US-6733525-$ or US-6730121-$ or US-6425916-$ or US-6299637-$ or US-6027525-$ or US-5957949-$ or US-5855601-$ or US-5607465-$ or US-5449384-$ or US-5163953-$ or US-4601718-$ or US-4759758-$ or US-7547322-$ or US-5895420-$ or US-5713953-$ or US-5509930-$ or US-5489297-$ or US-4340977-$ or US-5358518-$ or US-4343048-$ or US-4491986-$ or US-8308797-$ or US-8790398-$ or US-4470157-$ or US-4056854-	US-PGPUB; USPAT	OR	OFF	2016/04/12 16:03

		$).did. or (US-4297749-$ or US-5545215-$ or US-6553681-$ or US-6682559-$ or US-6736846-$ or US-8613763-$ or US-5344442-$ or US-6358277-$ or US-4790844-$ or US-8109995-$ or US-8361144-$ or US-8900294-$ or US-9125739-$ or US-9186248-$).did.				
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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:	:	
	:	
David Paniagua et al.	:	Confirmation No.: 1995
	:	
Application No.: 13/675,665	:	Group Art Unit: 3738
	:	
Filed: November 13, 2012	:	Examiner: Cheryl L. Miller

Title: PERCUTANEOUSLY IMPLANTABLE REPLACEMENT HEART VALVE DEVICE AND METHOD OF MAKING SAME

AMENDMENT AND RESPONSE TO OFFICE ACTION AND REQUEST FOR EXAMINER INTERVIEW

This Amendment And Response To Office Action And Request For Examiner Interview is in reply to the Office Action issued on July 29, 2016 in the application captioned above. The following remarks are respectfully submitted.

AMENDMENTS TO THE CLAIMS

The following listing of claims replaces all prior versions, and listings, of the claims in the application.

1. (Previously Presented) A percutaneously implantable replacement heart valve device for implantation in a patient, comprising:

an expandable stent member having an inner channel, the expandable stent member collapsible and configured for percutaneous delivery; and

a valve means made of biocompatible tissue material and attached to the expandable stent member, the valve means including an outer cuff layer and two to four individual leaflets, wherein each of the two to four individual leaflets is rectangular in shape in side elevation view, wherein a crease is located between a base of the two to four individual leaflets and the outer cuff layer, and wherein after implantation in the patient, the valve means resides as a single element entirely within the inner channel of the expandable stent member, wherein only the two to four individual leaflets reside radially inward from the outer cuff layer, and wherein the valve means is formed without cutting slits into said biocompatible tissue material to form said leaflets.

2. (Original) The percutaneously implantable replacement heart valve device of claim 1, wherein said expandable stent member is made of a metal or alloy of metals selected from the group consisting of nickel-titanium alloy, titanium and stainless steel.

3. (Canceled)

4. (Previously Presented) The percutaneously implantable replacement heart valve device of claim 1, wherein said biocompatible tissue material of said valve means comprises porcine pericardium tissue.

5. (Canceled)

6. (Previously Presented) The percutaneously implantable replacement heart valve device of claim 1, wherein said biocompatible tissue material of said valve means comprises autologous tissue obtained from the patient into whom said replacement heart valve device will be implanted.

7.-8. (Canceled)

9. (Previously Presented) The percutaneously implantable heart valve device of claim 1, wherein said expandable stent member is self-expanding when implanted.

10. (Previously Presented) The percutaneously implantable heart valve device of claim 1, wherein said expandable stent member is balloon catheter expandable when implanted.

11.-33. (Cancelled)

REMARKS

In the Office Action, the Office rejected claims 1, 2, and 4 and objected to claims 6, 9 and 10. More specifically:

- The Office rejected claims 1, 2 and 4 under nonstatutory double patenting as being unpatentable over claims 1-17 of U.S. Patent No. 8,308,797;
- The Office rejected claim 1 under nonstatutory double patenting as being unpatentable over claim 4 of U.S. Patent No. 8,790,398; and
- The Office objected claims 6, 9 and 10 as being dependent upon a rejected based claim, but would be allowable if rewritten in independent form including all of the limitations of the baes claim and any intervening claims.

No claims have been amended. For the reasons set forth below, Applicant asks the Office to withdraw the rejections associated with the claims.

Rejections Under Double Patenting

The Office rejected claims 1-2 and 4 under nonstatutory double patenting as being unpatentable over claims 1-17 of U.S. Patent No. 8,308,797; and claim 1 under nonstatutory double patenting as being unpatentable over claim 4 of U.S. Patent No. 8,790,398.

While Applicant does not necessarily agree with the Office's assertions, in order to progress this application to allowance, Applicant submits the requested Terminal Disclaimers Accordingly, Applicant respectfully requests that the Office withdraw the double patenting rejections associated with claims 1, 2 and 4.

Objections to Claims 6, 9 and 10

Applicant asserts that with the submission of the Terminal Disclaimers for claims 1, 2 and 4, claims 6, 9 and 10 are no longer dependent upon rejected claims.

Accordingly, Applicant respectfully requests that the Office withdraw the objections associated with claims 6, 9 and 10.

CONCLUSION AND REQUEST FOR INTERVIEW

For the reasons discussed above, Applicant respectfully asks the Examiner to reconsider and withdraw all outstanding rejections.

If the next Office Action will not result in allowance of the claims, Applicant requests an interview to discuss any remaining issues. Applicant invites the Examiner to contact the undersigned attorney to schedule a convenient time.

The Commissioner is hereby authorized to charge any additional fees which may be required for this Amendment, or credit any overpayment, to Deposit Account No. 50-1943.

Respectfully submitted,

FOX ROTHSCHILD LLP

/Gunjan Agarwal/
Gunjan Agarwal
Registration No. 69,661

Fox Rothschild LLP
Princeton Pike Corporate Center
997 Lenox Drive, Building 3
Lawrenceville, NJ 08648-2311
Telephone: 412-391-2414
Facsimile: 609-896-1469
Date: October 26, 2016

PTO/AIA/26 (04-14)
Approved for use through 07/31/2016. OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

TERMINAL DISCLAIMER TO OBVIATE A DOUBLE PATENTING REJECTION OVER A "PRIOR" PATENT

Docket Number (Optional)
109978.10101

In re Application of: David Panigua

Application No.: 13/675,665

Filed: 2012-11-13

For: PERCUTANEOUSLY IMPLANTABLE REPLACEMENT HEART VALVE DEVICE AND METHOD OF MAKING SAME

The applicant, COLIBRI HEART VALVE LLC, owner of 100 percent interest in the instant application hereby disclaims, except as provided below, the terminal part of the statutory term of any patent granted on the instant application which would extend beyond the expiration date of the full statutory term of **prior patent** No. 8790398 as the term of said **prior patent** is presently shortened by any terminal disclaimer. The applicant hereby agrees that any patent so granted on the instant application shall be enforceable only for and during such period that it and the **prior patent** are commonly owned. This agreement runs with any patent granted on the instant application and is binding upon the grantee, its successors or assigns.

In making the above disclaimer, the applicant does not disclaim the terminal part of the term of any patent granted on the instant application that would extend to the expiration date of the full statutory term of the **prior patent**, "as the term of said **prior patent** is presently shortened by any terminal disclaimer," in the event that said **prior patent** later:

expires for failure to pay a maintenance fee;
is held unenforceable;
is found invalid by a court of competent jurisdiction;
is statutorily disclaimed in whole or terminally disclaimed under 37 CFR 1.321;
has all claims canceled by a reexamination certificate;
is reissued; or
is in any manner terminated prior to the expiration of its full statutory term as presently shortened by any terminal disclaimer.

Check either box 1 or 2 below, if appropriate.

1. ☐ The undersigned is the applicant. If the applicant is an assignee, the undersigned is authorized to act on behalf of the assignee.

I hereby acknowledge that any willful false statements made are punishable under 18 U.S.C. 1001 by fine or imprisonment of not more than five (5) years, or both.

2. ☑ The undersigned is an attorney or agent of record. Reg. No. 69661

/Gunjan Agarwal/ — Signature
10/26/2016 — Date

Gunjan Agarwal — Typed or printed name

Patent Attorney of Record — Title
412-391-2414 — Telephone Number

☑ Terminal disclaimer fee under 37 CFR 1.20(d) included.

WARNING: Information on this form may become public. Credit card information should not be included on this form. Provide credit card information and authorization on PTO-2038.

Privacy Act Statement

The **Privacy Act of 1974 (P.L. 93-579)** requires that you be given certain information in connection with your submission of the attached form related to a patent application or patent. Accordingly, pursuant to the requirements of the Act, please be advised that: (1) the general authority for the collection of this information is 35 U.S.C. 2(b)(2); (2) furnishing of the information solicited is voluntary; and (3) the principal purpose for which the information is used by the U.S. Patent and Trademark Office is to process and/or examine your submission related to a patent application or patent. If you do not furnish the requested information, the U.S. Patent and Trademark Office may not be able to process and/or examine your submission, which may result in termination of proceedings or abandonment of the application or expiration of the patent.

The information provided by you in this form will be subject to the following routine uses:

1. The information on this form will be treated confidentially to the extent allowed under the Freedom of Information Act (5 U.S.C. 552) and the Privacy Act (5 U.S.C 552a). Records from this system of records may be disclosed to the Department of Justice to determine whether disclosure of these records is required by the Freedom of Information Act.
2. A record from this system of records may be disclosed, as a routine use, in the course of presenting evidence to a court, magistrate, or administrative tribunal, including disclosures to opposing counsel in the course of settlement negotiations.
3. A record in this system of records may be disclosed, as a routine use, to a Member of Congress submitting a request involving an individual, to whom the record pertains, when the individual has requested assistance from the Member with respect to the subject matter of the record.
4. A record in this system of records may be disclosed, as a routine use, to a contractor of the Agency having need for the information in order to perform a contract. Recipients of information shall be required to comply with the requirements of the Privacy Act of 1974, as amended, pursuant to 5 U.S.C. 552a(m).
5. A record related to an International Application filed under the Patent Cooperation Treaty in this system of records may be disclosed, as a routine use, to the International Bureau of the World Intellectual Property Organization, pursuant to the Patent Cooperation Treaty.
6. A record in this system of records may be disclosed, as a routine use, to another federal agency for purposes of National Security review (35 U.S.C. 181) and for review pursuant to the Atomic Energy Act (42 U.S.C. 218(c)).
7. A record from this system of records may be disclosed, as a routine use, to the Administrator, General Services, or his/her designee, during an inspection of records conducted by GSA as part of that agency's responsibility to recommend improvements in records management practices and programs, under authority of 44 U.S.C. 2904 and 2906. Such disclosure shall be made in accordance with the GSA regulations governing inspection of records for this purpose, and any other relevant (*i.e.*, GSA or Commerce) directive. Such disclosure shall not be used to make determinations about individuals.
8. A record from this system of records may be disclosed, as a routine use, to the public after either publication of the application pursuant to 35 U.S.C. 122(b) or issuance of a patent pursuant to 35 U.S.C. 151. Further, a record may be disclosed, subject to the limitations of 37 CFR 1.14, as a routine use, to the public if the record was filed in an application which became abandoned or in which the proceedings were terminated and which application is referenced by either a published application, an application open to public inspection or an issued patent.
9. A record from this system of records may be disclosed, as a routine use, to a Federal, State, or local law enforcement agency, if the USPTO becomes aware of a violation or potential violation of law or regulation.

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U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

TERMINAL DISCLAIMER TO OBVIATE A DOUBLE PATENTING REJECTION OVER A "PRIOR" PATENT	Docket Number (Optional) 109978.10101

In re Application of: David Panigua

Application No.: 13/675,665

Filed: 2012-11-13

For: PERCUTANEOUSLY IMPLANTABLE REPLACEMENT HEART VALVE DEVICE AND METHOD OF MAKING SAME

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is held unenforceable;
is found invalid by a court of competent jurisdiction;
is statutorily disclaimed in whole or terminally disclaimed under 37 CFR 1.321;
has all claims canceled by a reexamination certificate;
is reissued; or
is in any manner terminated prior to the expiration of its full statutory term as presently shortened by any terminal disclaimer.

Check either box 1 or 2 below, if appropriate.

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I hereby acknowledge that any willful false statements made are punishable under 18 U.S.C. 1001 by fine or imprisonment of not more than five (5) years, or both.

2. ☑ The undersigned is an attorney or agent of record. Reg. No. 69661

/Gunjan Agarwal/ — Signature
10/26/2016 — Date

Gunjan Agarwal — Typed or printed name

Patent Attorney of Record — Title
412-391-2414 — Telephone Number

☑ Terminal disclaimer fee under 37 CFR 1.20(d) included.

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7. A record from this system of records may be disclosed, as a routine use, to the Administrator, General Services, or his/her designee, during an inspection of records conducted by GSA as part of that agency's responsibility to recommend improvements in records management practices and programs, under authority of 44 U.S.C. 2904 and 2906. Such disclosure shall be made in accordance with the GSA regulations governing inspection of records for this purpose, and any other relevant (*i.e.*, GSA or Commerce) directive. Such disclosure shall not be used to make determinations about individuals.
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9. A record from this system of records may be disclosed, as a routine use, to a Federal, State, or local law enforcement agency, if the USPTO becomes aware of a violation or potential violation of law or regulation.

Electronic Patent Application Fee Transmittal

Application Number:	13675665
Filing Date:	13-Nov-2012
Title of Invention:	PERCUTANEOUSLY IMPLANTABLE REPLACEMENT HEART VALVE DEVICE AND METHOD OF MAKING SAME
First Named Inventor/Applicant Name:	David Paniagua
Filer:	Gunjan Agarwal/Carol Donahue
Attorney Docket Number:	109978.10101

Filed as Small Entity

Filing Fees for Utility under 35 USC 111(a)

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Basic Filing:				
Pages:				
Claims:				
Miscellaneous-Filing:				
Petition:				
Patent-Appeals-and-Interference:				
Post-Allowance-and-Post-Issuance:				
Extension-of-Time:				

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Miscellaneous:				
STATUTORY OR TERMINAL DISCLAIMER	2814	2	160	320
		Total in USD ($)		**320**

Electronic Acknowledgement Receipt

EFS ID:	27331858
Application Number:	13675665
International Application Number:	
Confirmation Number:	1995
Title of Invention:	PERCUTANEOUSLY IMPLANTABLE REPLACEMENT HEART VALVE DEVICE AND METHOD OF MAKING SAME
First Named Inventor/Applicant Name:	David Paniagua
Customer Number:	29880
Filer:	Gunjan Agarwal/Carol Donahue
Filer Authorized By:	Gunjan Agarwal
Attorney Docket Number:	109978.10101
Receipt Date:	26-OCT-2016
Filing Date:	13-NOV-2012
Time Stamp:	16:46:50
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	yes
Payment Type	CARD
Payment was successfully received in RAM	$320
RAM confirmation Number	102716INTEFSW16472700
Deposit Account	501943
Authorized User	Carol Donahue

The Director of the USPTO is hereby authorized to charge indicated fees and credit any overpayment as follows:

37 CFR 1.16 (National application filing, search, and examination fees)

37 CFR 1.17 (Patent application and reexamination processing fees)

37 CFR 1.19 (Document supply fees)

37 CFR 1.20 (Post Issuance fees)

37 CFR 1.21 (Miscellaneous fees and charges)

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1		10101_Response.pdf	34663 47f912c6c4c2294bfe1c7285d021dedb020e0ffa	yes	6
	Multipart Description/PDF files in .zip description				
	Document Description		**Start**	**End**	
	Amendment/Req. Reconsideration-After Non-Final Reject		1	1	
	Claims		2	3	
	Applicant Arguments/Remarks Made in an Amendment		4	6	
Warnings:					
Information:					
2	Terminal Disclaimer Filed	10101_Terminal_Disclaimer_Pat_8790398.PDF	167727 845383ec99dcc0c84789dd1bf940a0d2242fe454	no	2
Warnings:					
Information:					
3	Terminal Disclaimer Filed	10101_Terminal_Disclaimer_Pat_8308797.PDF	167594 643b02bd65295e4e40cc3ae5ca8f76fecfb64a45	no	2
Warnings:					
Information:					
4	Fee Worksheet (SB06)	fee-info.pdf	30765 4e5e15e2dff2cfb94ff645cd610b5adea82788fd	no	2
Warnings:					
Information:					
		Total Files Size (in bytes):	400749		

This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

New Applications Under 35 U.S.C. 111

If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

National Stage of an International Application under 35 U.S.C. 371

If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office

If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

Application Number	Application/Control No.	Applicant(s)/Patent under Reexamination	
	13/675,665	PANIAGUA ET AL.	

Document Code - DISQ	Internal Document – DO NOT MAIL

TERMINAL DISCLAIMER	☒ APPROVED	☐ DISAPPROVED
Date Filed : 26 October, 2016	This patent is subject to a Terminal Disclaimer	

Approved/Disapproved by:

/CRYSTAL QUEEN/

Technology Center: PLRC

Telephone: _____

2 TD'S APPROVED.

U.S. Patent and Trademark Office

PTO/SB/06 (09-11)
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PATENT APPLICATION FEE DETERMINATION RECORD Substitute for Form PTO-875	Application or Docket Number 13/675,665	Filing Date 11/13/2012	☐ To be Mailed

ENTITY: ☐ LARGE ☒ SMALL ☐ MICRO

APPLICATION AS FILED – PART I

FOR	(Column 1) NUMBER FILED	(Column 2) NUMBER EXTRA	RATE ($)	FEE ($)
☐ BASIC FEE (37 CFR 1.16(a), (b), or (c))	N/A	N/A	N/A	
☐ SEARCH FEE (37 CFR 1.16(k), (i), or (m))	N/A	N/A	N/A	
☐ EXAMINATION FEE (37 CFR 1.16(o), (p), or (q))	N/A	N/A	N/A	
TOTAL CLAIMS (37 CFR 1.16(i))	minus 20 =	*	X $ =	
INDEPENDENT CLAIMS (37 CFR 1.16(h))	minus 3 =	*	X $ =	
☐ APPLICATION SIZE FEE (37 CFR 1.16(s))	If the specification and drawings exceed 100 sheets of paper, the application size fee due is $310 ($155 for small entity) for each additional 50 sheets or fraction thereof. See 35 U.S.C. 41(a)(1)(G) and 37 CFR 1.16(s).			
☐ MULTIPLE DEPENDENT CLAIM PRESENT (37 CFR 1.16(j))				
* If the difference in column 1 is less than zero, enter "0" in column 2.			TOTAL	

APPLICATION AS AMENDED – PART II

AMENDMENT	10/26/2016	(Column 1) CLAIMS REMAINING AFTER AMENDMENT		(Column 2) HIGHEST NUMBER PREVIOUSLY PAID FOR	(Column 3) PRESENT EXTRA	RATE ($)	ADDITIONAL FEE ($)
	Total (37 CFR 1.16(i))	* 6	Minus	** 20	= 0	X $40 =	0
	Independent (37 CFR 1.16(h))	* 1	Minus	***3	= 0	X $210 =	0
	☐ Application Size Fee (37 CFR 1.16(s))						
	☐ FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))						
						TOTAL ADD'L FEE	0

AMENDMENT		(Column 1) CLAIMS REMAINING AFTER AMENDMENT		(Column 2) HIGHEST NUMBER PREVIOUSLY PAID FOR	(Column 3) PRESENT EXTRA	RATE ($)	ADDITIONAL FEE ($)
	Total (37 CFR 1.16(i))	*	Minus	**	=	X $ =	
	Independent (37 CFR 1.16(h))	*	Minus	***	=	X $ =	
	☐ Application Size Fee (37 CFR 1.16(s))						
	☐ FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))						
						TOTAL ADD'L FEE	

* If the entry in column 1 is less than the entry in column 2, write "0" in column 3.
** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 20, enter "20".
*** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 3, enter "3".
The "Highest Number Previously Paid For" (Total or Independent) is the highest number found in the appropriate box in column 1.

LIE
/DORIAN EVANS/

PTO/SB/08a (03-15)
Approved for use through 07/31/2016. OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(Not for submission under 37 CFR 1.99)

Application Number	13675665
Filing Date	2012-11-13
First Named Inventor	David PANIAGUA
Art Unit	3738
Examiner Name	Cheryl L. MILLER
Attorney Docket Number	109978.10101

U.S.PATENTS Remove

Examiner Initial*	Cite No	Patent Number	Kind Code[1]	Issue Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
	1	6166184		2000-12-26	Hendriks et al.	
	2	7632309		2009-12-15	Brendzel et al.	

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U.S.PATENT APPLICATION PUBLICATIONS Remove

Examiner Initial*	Cite No	Publication Number	Kind Code[1]	Publication Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
	1	20010007956		2001-07-12	Letac et al.	

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FOREIGN PATENT DOCUMENTS Remove

Examiner Initial*	Cite No	Foreign Document Number[3]	Country Code[2] i	Kind Code[4]	Publication Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear	T[5]
	1							

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NON-PATENT LITERATURE DOCUMENTS Remove

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

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Application Number	13675665
Filing Date	2012-11-13
First Named Inventor	David PANIAGUA
Art Unit	3738
Examiner Name	Cheryl L. MILLER
Attorney Docket Number	109978.10101

Examiner Initials*	Cite No	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc), date, pages(s), volume-issue number(s), publisher, city and/or country where published.	T[5]
	1	Notice of Allowance issued September 19, 2016 in U.S. Application No. 14/502,453 (File: 109978.10106)	
	2	Office Action issued October 7, 2016, in U.S. Application No. 14/829,349 (File: 109978.10120)	

If you wish to add additional non-patent literature document citation information please click the Add button Add

EXAMINER SIGNATURE

Examiner Signature		Date Considered	

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through a citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

[1] See Kind Codes of USPTO Patent Documents at www.USPTO.GOV or MPEP 901.04. [2] Enter office that issued the document, by the two-letter code (WIPO Standard ST.3). [3] For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. [4] Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. [5] Applicant is to place a check mark here if English language translation is attached.

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(Not for submission under 37 CFR 1.99)

Application Number	13675665
Filing Date	2012-11-13
First Named Inventor	David PANIAGUA
Art Unit	3738
Examiner Name	Cheryl L. MILLER
Attorney Docket Number	109978.10101

CERTIFICATION STATEMENT

Please see 37 CFR 1.97 and 1.98 to make the appropriate selection(s):

That each item of information contained in the information disclosure statement was first cited in any communication from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e)(1).

OR

☐ That no item of information contained in the information disclosure statement was cited in a communication from a foreign patent office in a counterpart foreign application, and, to the knowledge of the person signing the certification after making reasonable inquiry, no item of information contained in the information disclosure statement was known to any individual designated in 37 CFR 1.56(c) more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e)(2).

See attached certification statement.

☒ The fee set forth in 37 CFR 1.17 (p) has been submitted herewith.

☒ A certification statement is not submitted herewith.

SIGNATURE

A signature of the applicant or representative is required in accordance with CFR 1.33, 10.18. Please see CFR 1.4(d) for the form of the signature.

Signature	/Gunjan Agarwal/	Date (YYYY-MM-DD)	2016-11-15
Name/Print	Gunjan Agarwal	Registration Number	69661

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 1 hour to complete, including gathering, preparing and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

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1. The information on this form will be treated confidentially to the extent allowed under the Freedom of Information Act (5 U.S.C. 552) and the Privacy Act (5 U.S.C. 552a). Records from this system of records may be disclosed to the Department of Justice to determine whether the Freedom of Information Act requires disclosure of these record s.

2. A record from this system of records may be disclosed, as a routine use, in the course of presenting evidence to a court, magistrate, or administrative tribunal, including disclosures to opposing counsel in the course of settlement negotiations.

3. A record in this system of records may be disclosed, as a routine use, to a Member of Congress submitting a request involving an individual, to whom the record pertains, when the individual has requested assistance from the Member with respect to the subject matter of the record.

4. A record in this system of records may be disclosed, as a routine use, to a contractor of the Agency having need for the information in order to perform a contract. Recipients of information shall be required to comply with the requirements of the Privacy Act of 1974, as amended, pursuant to 5 U.S.C. 552a(m).

5. A record related to an International Application filed under the Patent Cooperation Treaty in this system of records may be disclosed, as a routine use, to the International Bureau of the World Intellectual Property Organization, pursuant to the Patent Cooperation Treaty.

6. A record in this system of records may be disclosed, as a routine use, to another federal agency for purposes of National Security review (35 U.S.C. 181) and for review pursuant to the Atomic Energy Act (42 U.S.C. 218(c)).

7. A record from this system of records may be disclosed, as a routine use, to the Administrator, General Services, or his/her designee, during an inspection of records conducted by GSA as part of that agency's responsibility to recommend improvements in records management practices and programs, under authority of 44 U.S.C. 2904 and 2906. Such disclosure shall be made in accordance with the GSA regulations governing inspection of records for this purpose, and any other relevant (i.e., GSA or Commerce) directive. Such disclosure shall not be used to make determinations about individuals.

8. A record from this system of records may be disclosed, as a routine use, to the public after either publication of the application pursuant to 35 U.S.C. 122(b) or issuance of a patent pursuant to 35 U.S.C. 151. Further, a record may be disclosed, subject to the limitations of 37 CFR 1.14, as a routine use, to the public if the record was filed in an application which became abandoned or in which the proceedings were terminated and which application is referenced by either a published application, an application open to public inspections or an issued patent.

9. A record from this system of records may be disclosed, as a routine use, to a Federal, State, or local law enforcement agency, if the USPTO becomes aware of a violation or potential violation of law or regulation.

Electronic Patent Application Fee Transmittal

Application Number:	13675665
Filing Date:	13-Nov-2012
Title of Invention:	PERCUTANEOUSLY IMPLANTABLE REPLACEMENT HEART VALVE DEVICE AND METHOD OF MAKING SAME
First Named Inventor/Applicant Name:	David Paniagua
Filer:	Gunjan Agarwal/Carol Donahue
Attorney Docket Number:	109978.10101

Filed as Small Entity

Filing Fees for Utility under 35 USC 111(a)

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Basic Filing:				
Pages:				
Claims:				
Miscellaneous-Filing:				
Petition:				
Patent-Appeals-and-Interference:				
Post-Allowance-and-Post-Issuance:				
Extension-of-Time:				

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Miscellaneous:				
SUBMISSION- INFORMATION DISCLOSURE STMT	2806	1	90	90
		Total in USD ($)		**90**

Electronic Acknowledgement Receipt

EFS ID:	27519553
Application Number:	13675665
International Application Number:	
Confirmation Number:	1995
Title of Invention:	PERCUTANEOUSLY IMPLANTABLE REPLACEMENT HEART VALVE DEVICE AND METHOD OF MAKING SAME
First Named Inventor/Applicant Name:	David Paniagua
Customer Number:	29880
Filer:	Gunjan Agarwal/Carol Donahue
Filer Authorized By:	Gunjan Agarwal
Attorney Docket Number:	109978.10101
Receipt Date:	15-NOV-2016
Filing Date:	13-NOV-2012
Time Stamp:	16:28:51
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	yes
Payment Type	CARD
Payment was successfully received in RAM	$90
RAM confirmation Number	111616INTEFSW16301500
Deposit Account	501943
Authorized User	Carol Donahue

The Director of the USPTO is hereby authorized to charge indicated fees and credit any overpayment as follows:

37 CFR 1.16 (National application filing, search, and examination fees)

37 CFR 1.17 (Patent application and reexamination processing fees)

37 CFR 1.19 (Document supply fees)

37 CFR 1.20 (Post Issuance fees)

37 CFR 1.21 (Miscellaneous fees and charges)

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Transmittal Letter	10101_IDS_Transmittal.pdf	40640 2736a559b3191af3f8a5f3733af8cfa778d088e3	no	5
Warnings:					
Information:					
2	Information Disclosure Statement (IDS) Form (SB08)	10101_IDS.pdf	1081320 9399b636d24c280924d540b1c4bb8dfccff332db	no	4
Warnings:					
Information:					
3	Non Patent Literature	10106_US_14-502453_Notice-of-Allowance_2016-09-19.pdf	658913 42bbcd18b5f0341a2b4d66b27d98a66db3c0e927	no	8
Warnings:					
Information:					
4	Non Patent Literature	10120_US_14-829349_Office-Action_2016-10-07.pdf	563355 f728706ed8b23bfdf3cce0d1b88df2cdd7409038	no	9
Warnings:					
Information:					
5	Fee Worksheet (SB06)	fee-info.pdf	30754 27eb4ba695bf808429ac81601ae6512d29b69a2d	no	2
Warnings:					
Information:					
		Total Files Size (in bytes):	2374982		

This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

New Applications Under 35 U.S.C. 111

If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

National Stage of an International Application under 35 U.S.C. 371

If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office

If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

Docket No.: 109978.10101
(PATENT)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of:
David Paniagua et al.

Application No.: 13/675,665 Confirmation No.: 1995

Filed: November 13, 2012 Art Unit: 3738

For: Percutaneously Implantable Replacement Heart Valve Device and Method of Making Same Examiner: C. L. Miller

INFORMATION DISCLOSURE STATEMENT (IDS)

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

This Information Disclosure Statement is submitted in accordance with 37 C.F.R. 1.97, 1.98, and it is requested that the information set forth in this statement and in the listed documents be considered during the pendency of the above-identified application, and any other application relying on the filing date of the above-identified application or cross-referencing it as a related application.

1. This IDS should be considered, in accordance with 37 C.F.R. 1.97, as it is filed: (Check one of the boxes A-D)

- [ ] A. within three months of the filing date of the above-identified national application or within three months of the entry into the national stage of the above identified national application
- [ ] B. before the mailing date of a first office action on the merits, or a first office action after filing a request for continued examination.
- [X] C. after (A) and (B) above, but before final rejection or allowance, and Applicants have made the necessary statement in box "i" below or paid the necessary fee in box "ii" below.

(check one of the boxes "i" and "ii" below:)

☐ i. Counsel states that, upon information and belief, each item of information listed herein was (check one of boxes (a) or (b))

☐ (a) first cited in any communication from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of this IDS; or

☐ (b) not cited in a communication from a foreign patent office in a counterpart foreign application and, to the knowledge of undersigned after making reasonable inquiry, was not known to any individual designated in 1.56(c) more than three months prior to the filing of this IDS.

☒ ii. Payment in the amount of the fee set forth in 1. 17(p), presently believed to be $180, is enclosed.

☐ D. after (A), (B) and (C) above, but before payment of the issue fee: Applicant petitions under 37 C.F.R. 1.97(d) for the consideration of this IDS. Under 37 CFR 1.17(p) payment in the amount of $180.00 is enclosed. Counsel certifies that, upon information and belief, each item of information listed herein was

(check one of the boxes "a" and "b" below:)

☐ (a) first cited in any communication from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of this IDS; or

☐ (b) was not cited in a communication from a foreign patent office in a counterpart foreign application and, to the knowledge of undersigned after making reasonable inquiry, was not known to any individual designated in 1.56(c) more than three months prior to the filing of this IDS.

2. In accordance with 37 C.F.R. 1.98, this IDS includes a list (e.g., form PTO/SB/08) of all patents, publications, or other information submitted for consideration by the office, either incorporated into this IDS or as an attachment hereto. A copy of each document listed is attached, except as explained below.

(check boxes A, B and/or C and fill in blanks, if appropriate.)

[x] A. Pursuant to the Notice issued by the United States Patent and Trademark Office dated August 5, 2003 waiving the requirements of 37 C.F.R. § 1.98(a)(2)(ii), a copy/copies of the U.S. Patent(s) and/or U.S. Patent Application Publication(s) on PTO/SB/08 is/are not being submitted.

[ ] B. Document(s) _____is (are) deemed substantially cumulative to document(s) _____ , and, in accordance with 1.98(c), only a copy of each of the latter documents is enclosed.

[ ] C. Certain documents were previously cited by or submitted to the Office in the following prior applications, which are relied upon under 35 U.S.C. 120:

<<INSERT SERIAL NO. & FILING DATE>>

Applicant identifies these documents by attaching hereto copies of the forms PTO-892, PTO-1449 and/or PTO/SB/08 from the files of the prior application(s) or a fresh PTO/SB/08 listing these documents, and request that they be considered and made of record in accordance with 1.98(d). Per 37 CFR 1.98(d), copies of these documents need not be filed in this application.

[ ] 3. Cite Nos. _____ are not in the English language. In accordance with 1.98(c), Applicant states:

[ ] An English translation of each document (or of the pertinent portions thereof), or a copy of each corresponding English-language patent or application , or English-language abstract (or claim) is enclosed.

[ ] The requirement for a concise explanation of the relevance of any foreign language document is satisfied by the attached search report; citation of the documents cited in the search report shall not be construed as an admission that they are or are considered to be, material to patentability of the subject matter claimed herein (See MPEP §609).

[ ] A concise explanation of the relevance of document(s) _____ is set forth as follows: [Insert concise explanation of relevance]

[ ] A concise explanation of the relevance of document(s) _____ can be found on page(s) _____ of the specification.

[ ] A concise explanation of document(s) _____ can be found on the attached sheet.

☐ 4. No explanation of relevance is necessary for documents in the English language (see reply to Comments 67 in the preamble to the final rules; 1135 OG 13 at 20).

☐ 5. Other information being provided for the examiner's consideration follows:

6. Related Patents and Patent Applications. The Examiner is hereby advised of the existence of the patents, patent applications, and/or other proceedings before the Patent Office listed below which: (1) share at least some common disclosure with the instant application, (2) serve as the basis of priority for the instant application, and/or (3) otherwise may relate to the instant application or one or more of the other matters listed below. For completeness, the instant application is also included in the list.

It is respectfully requested that the Examiner review each matter listed below and its associated prosecution history (e.g., Office Actions, Responses to Office Actions, Interview Summaries, Notice of Allowances, and so forth) as part of evaluating the instant application. The prosecution history for each matter listed below should be readily available to the Examiner through the Patent Office's internal systems. Since these materials are already easily accessible to the Examiner, a hard copy has not been provided. However, at the Examiner's request, Applicant will provide a hard copy of any matter listed below including its prosecution history (or one or more individual documents from the prosecution history). Applicant believes that this is an efficient and effective way to allow the Examiner to consider the applicability of the matters listed below to the instant application.

The attached form PTO/SB/08b includes a reference to the information listed below concerning related patents and patent applications. Applicant requests that the Examiner initial the attached PTO/SB/08b form next to this reference to indicate that the Examiner has considered this information as part of evaluating the instant application. By initialing the form in this manner, the Examiner expressly acknowledges that he/she has considered each matter listed below, as well as all of the documents included in its prosecution history, as part of examining the instant application.

Application Serial No.	**Filing Date**	**Title of Invention**

7. In accordance with 37 C.F.R. 1.97(g) and (h), the filing of this IDS should not be construed as a representation that a search has been made or that information cited is, or is considered to be, material to patentability as defined in §1.56 (b), or that any cited document listed or attached is (or constitutes) prior art. Unless other-wise indicated, the date of publication indicated

for an item is taken from the face of the item and Applicant reserves the right to prove that the date of publication is in fact different.

Early and favorable consideration is earnestly solicited.

Please charge our Credit Card in the amount of $90.00 covering the fee set forth in 37 C.F.R. § 1.17(p). The Director is hereby authorized to charge any deficiency in the fees filed, asserted to be filed or which should have been filed herewith (or with any paper hereafter filed in this application by this firm) to our Deposit Account No. 50-1943, under Order No. 109978.10101.

Dated: November 15, 2016

Respectfully submitted,

By/Gunjan Agarwal/
Gunjan Agarwal
Registration No.: 69,661
FOX ROTHSCHILD LLP
997 Lenox Drive, Building 3
Lawrenceville, New Jersey 08648-2311
(412) 391-2414
(609) 896-1469 (Fax)
Attorneys/Agents For Applicant

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

NOTICE OF ALLOWANCE AND FEE(S) DUE

29880 7590 11/18/2016

FOX ROTHSCHILD LLP
PRINCETON PIKE CORPORATE CENTER
997 LENOX DRIVE
BLDG. #3
LAWRENCEVILLE, NJ 08648

EXAMINER
MILLER, CHERYL L

ART UNIT	PAPER NUMBER
3738	

DATE MAILED: 11/18/2016

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
13/675,665	11/13/2012	David Paniagua	109978.10101	1995

TITLE OF INVENTION: PERCUTANEOUSLY IMPLANTABLE REPLACEMENT HEART VALVE DEVICE AND METHOD OF MAKING SAME

APPLN. TYPE	ENTITY STATUS	ISSUE FEE DUE	PUBLICATION FEE DUE	PREV. PAID ISSUE FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	SMALL	$480	$0	$0	$480	02/21/2017

THE APPLICATION IDENTIFIED ABOVE HAS BEEN EXAMINED AND IS ALLOWED FOR ISSUANCE AS A PATENT. PROSECUTION ON THE MERITS IS CLOSED. THIS NOTICE OF ALLOWANCE IS NOT A GRANT OF PATENT RIGHTS. THIS APPLICATION IS SUBJECT TO WITHDRAWAL FROM ISSUE AT THE INITIATIVE OF THE OFFICE OR UPON PETITION BY THE APPLICANT. SEE 37 CFR 1.313 AND MPEP 1308.

THE ISSUE FEE AND PUBLICATION FEE (IF REQUIRED) MUST BE PAID WITHIN THREE MONTHS FROM THE MAILING DATE OF THIS NOTICE OR THIS APPLICATION SHALL BE REGARDED AS ABANDONED. THIS STATUTORY PERIOD CANNOT BE EXTENDED. SEE 35 U.S.C. 151. THE ISSUE FEE DUE INDICATED ABOVE DOES NOT REFLECT A CREDIT FOR ANY PREVIOUSLY PAID ISSUE FEE IN THIS APPLICATION. IF AN ISSUE FEE HAS PREVIOUSLY BEEN PAID IN THIS APPLICATION (AS SHOWN ABOVE), THE RETURN OF PART B OF THIS FORM WILL BE CONSIDERED A REQUEST TO REAPPLY THE PREVIOUSLY PAID ISSUE FEE TOWARD THE ISSUE FEE NOW DUE.

HOW TO REPLY TO THIS NOTICE:

I. Review the ENTITY STATUS shown above. If the ENTITY STATUS is shown as SMALL or MICRO, verify whether entitlement to that entity status still applies.

If the ENTITY STATUS is the same as shown above, pay the TOTAL FEE(S) DUE shown above.

If the ENTITY STATUS is changed from that shown above, on PART B - FEE(S) TRANSMITTAL, complete section number 5 titled "Change in Entity Status (from status indicated above)".

For purposes of this notice, small entity fees are 1/2 the amount of undiscounted fees, and micro entity fees are 1/2 the amount of small entity fees.

II. PART B - FEE(S) TRANSMITTAL, or its equivalent, must be completed and returned to the United States Patent and Trademark Office (USPTO) with your ISSUE FEE and PUBLICATION FEE (if required). If you are charging the fee(s) to your deposit account, section "4b" of Part B - Fee(s) Transmittal should be completed and an extra copy of the form should be submitted. If an equivalent of Part B is filed, a request to reapply a previously paid issue fee must be clearly made, and delays in processing may occur due to the difficulty in recognizing the paper as an equivalent of Part B.

III. All communications regarding this application must give the application number. Please direct all communications prior to issuance to Mail Stop ISSUE FEE unless advised to the contrary.

IMPORTANT REMINDER: Utility patents issuing on applications filed on or after Dec. 12, 1980 may require payment of maintenance fees. It is patentee's responsibility to ensure timely payment of maintenance fees when due.

PART B - FEE(S) TRANSMITTAL

Complete and send this form, together with applicable fee(s), to: Mail **Mail Stop ISSUE FEE**
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450
or Fax (571)-273-2885

INSTRUCTIONS: This form should be used for transmitting the ISSUE FEE and PUBLICATION FEE (if required). Blocks 1 through 5 should be completed where appropriate. All further correspondence including the Patent, advance orders and notification of maintenance fees will be mailed to the current correspondence address as indicated unless corrected below or directed otherwise in Block 1, by (a) specifying a new correspondence address; and/or (b) indicating a separate "FEE ADDRESS" for maintenance fee notifications.

CURRENT CORRESPONDENCE ADDRESS (Note: Use Block 1 for any change of address)

29880 7590 11/18/2016
FOX ROTHSCHILD LLP
PRINCETON PIKE CORPORATE CENTER
997 LENOX DRIVE
BLDG. #3
LAWRENCEVILLE, NJ 08648

Note: A certificate of mailing can only be used for domestic mailings of the Fee(s) Transmittal. This certificate cannot be used for any other accompanying papers. Each additional paper, such as an assignment or formal drawing, must have its own certificate of mailing or transmission.

Certificate of Mailing or Transmission
I hereby certify that this Fee(s) Transmittal is being deposited with the United States Postal Service with sufficient postage for first class mail in an envelope addressed to the Mail Stop ISSUE FEE address above, or being facsimile transmitted to the USPTO (571) 273-2885, on the date indicated below.

(Depositor's name)
(Signature)
(Date)

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
13/675,665	11/13/2012	David Paniagua	109978.10101	1995

TITLE OF INVENTION: PERCUTANEOUSLY IMPLANTABLE REPLACEMENT HEART VALVE DEVICE AND METHOD OF MAKING SAME

APPLN. TYPE	ENTITY STATUS	ISSUE FEE DUE	PUBLICATION FEE DUE	PREV. PAID ISSUE FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	SMALL	$480	$0	$0	$480	02/21/2017

EXAMINER	ART UNIT	CLASS-SUBCLASS
MILLER, CHERYL L	3738	623-001200

1. Change of correspondence address or indication of "Fee Address" (37 CFR 1.363).
- ❑ Change of correspondence address (or Change of Correspondence Address form PTO/SB/122) attached.
- ❑ "Fee Address" indication (or "Fee Address" Indication form PTO/SB/47; Rev 03-02 or more recent) attached. **Use of a Customer Number is required.**

2. For printing on the patent front page, list
(1) The names of up to 3 registered patent attorneys or agents OR, alternatively,
(2) The name of a single firm (having as a member a registered attorney or agent) and the names of up to 2 registered patent attorneys or agents. If no name is listed, no name will be printed.
1 _____
2 _____
3 _____

3. ASSIGNEE NAME AND RESIDENCE DATA TO BE PRINTED ON THE PATENT (print or type)

PLEASE NOTE: Unless an assignee is identified below, no assignee data will appear on the patent. If an assignee is identified below, the document has been filed for recordation as set forth in 37 CFR 3.11. Completion of this form is NOT a substitute for filing an assignment.

(A) NAME OF ASSIGNEE (B) RESIDENCE: (CITY and STATE OR COUNTRY)

Please check the appropriate assignee category or categories (will not be printed on the patent) : ❑ Individual ❑ Corporation or other private group entity ❑ Government

4a. The following fee(s) are submitted:
- ❑ Issue Fee
- ❑ Publication Fee (No small entity discount permitted)
- ❑ Advance Order - # of Copies _____

4b. Payment of Fee(s): **(Please first reapply any previously paid issue fee shown above)**
- ❑ A check is enclosed.
- ❑ Payment by credit card. Form PTO-2038 is attached.
- ❑ The director is hereby authorized to charge the required fee(s), any deficiency, or credits any overpayment, to Deposit Account Number _____ (enclose an extra copy of this form).

5. **Change in Entity Status** (from status indicated above)
- ❑ Applicant certifying micro entity status. See 37 CFR 1.29 — NOTE: Absent a valid certification of Micro Entity Status (see forms PTO/SB/15A and 15B), issue fee payment in the micro entity amount will not be accepted at the risk of application abandonment.
- ❑ Applicant asserting small entity status. See 37 CFR 1.27 — NOTE: If the application was previously under micro entity status, checking this box will be taken to be a notification of loss of entitlement to micro entity status.
- ❑ Applicant changing to regular undiscounted fee status. — NOTE: Checking this box will be taken to be a notification of loss of entitlement to small or micro entity status, as applicable.

NOTE: This form must be signed in accordance with 37 CFR 1.31 and 1.33. See 37 CFR 1.4 for signature requirements and certifications.

Authorized Signature _____ Date _____

Typed or printed name _____ Registration No. _____

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
13/675,665	11/13/2012	David Paniagua	109978.10101	1995

29880 7590 11/18/2016

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BLDG. #3
LAWRENCEVILLE, NJ 08648

EXAMINER	
MILLER, CHERYL L	

ART UNIT	PAPER NUMBER
3738	

DATE MAILED: 11/18/2016

Determination of Patent Term Adjustment under 35 U.S.C. 154 (b)
(Applications filed on or after May 29, 2000)

The Office has discontinued providing a Patent Term Adjustment (PTA) calculation with the Notice of Allowance.

Section 1(h)(2) of the AIA Technical Corrections Act amended 35 U.S.C. 154(b)(3)(B)(i) to eliminate the requirement that the Office provide a patent term adjustment determination with the notice of allowance. See Revisions to Patent Term Adjustment, 78 Fed. Reg. 19416, 19417 (Apr. 1, 2013). Therefore, the Office is no longer providing an initial patent term adjustment determination with the notice of allowance. The Office will continue to provide a patent term adjustment determination with the Issue Notification Letter that is mailed to applicant approximately three weeks prior to the issue date of the patent, and will include the patent term adjustment on the patent. Any request for reconsideration of the patent term adjustment determination (or reinstatement of patent term adjustment) should follow the process outlined in 37 CFR 1.705.

Any questions regarding the Patent Term Extension or Adjustment determination should be directed to the Office of Patent Legal Administration at (571)-272-7702. Questions relating to issue and publication fee payments should be directed to the Customer Service Center of the Office of Patent Publication at 1-(888)-786-0101 or (571)-272-4200.

OMB Clearance and PRA Burden Statement for PTOL-85 Part B

The Paperwork Reduction Act (PRA) of 1995 requires Federal agencies to obtain Office of Management and Budget approval before requesting most types of information from the public. When OMB approves an agency request to collect information from the public, OMB (i) provides a valid OMB Control Number and expiration date for the agency to display on the instrument that will be used to collect the information and (ii) requires the agency to inform the public about the OMB Control Number's legal significance in accordance with 5 CFR 1320.5(b).

The information collected by PTOL-85 Part B is required by 37 CFR 1.311. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, Virginia 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450. Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

Privacy Act Statement

The Privacy Act of 1974 (P.L. 93-579) requires that you be given certain information in connection with your submission of the attached form related to a patent application or patent. Accordingly, pursuant to the requirements of the Act, please be advised that: (1) the general authority for the collection of this information is 35 U.S.C. 2(b)(2); (2) furnishing of the information solicited is voluntary; and (3) the principal purpose for which the information is used by the U.S. Patent and Trademark Office is to process and/or examine your submission related to a patent application or patent. If you do not furnish the requested information, the U.S. Patent and Trademark Office may not be able to process and/or examine your submission, which may result in termination of proceedings or abandonment of the application or expiration of the patent.

The information provided by you in this form will be subject to the following routine uses:

1. The information on this form will be treated confidentially to the extent allowed under the Freedom of Information Act (5 U.S.C. 552) and the Privacy Act (5 U.S.C 552a). Records from this system of records may be disclosed to the Department of Justice to determine whether disclosure of these records is required by the Freedom of Information Act.
2. A record from this system of records may be disclosed, as a routine use, in the course of presenting evidence to a court, magistrate, or administrative tribunal, including disclosures to opposing counsel in the course of settlement negotiations.
3. A record in this system of records may be disclosed, as a routine use, to a Member of Congress submitting a request involving an individual, to whom the record pertains, when the individual has requested assistance from the Member with respect to the subject matter of the record.
4. A record in this system of records may be disclosed, as a routine use, to a contractor of the Agency having need for the information in order to perform a contract. Recipients of information shall be required to comply with the requirements of the Privacy Act of 1974, as amended, pursuant to 5 U.S.C. 552a(m).
5. A record related to an International Application filed under the Patent Cooperation Treaty in this system of records may be disclosed, as a routine use, to the International Bureau of the World Intellectual Property Organization, pursuant to the Patent Cooperation Treaty.
6. A record in this system of records may be disclosed, as a routine use, to another federal agency for purposes of National Security review (35 U.S.C. 181) and for review pursuant to the Atomic Energy Act (42 U.S.C. 218(c)).
7. A record from this system of records may be disclosed, as a routine use, to the Administrator, General Services, or his/her designee, during an inspection of records conducted by GSA as part of that agency's responsibility to recommend improvements in records management practices and programs, under authority of 44 U.S.C. 2904 and 2906. Such disclosure shall be made in accordance with the GSA regulations governing inspection of records for this purpose, and any other relevant (i.e., GSA or Commerce) directive. Such disclosure shall not be used to make determinations about individuals.
8. A record from this system of records may be disclosed, as a routine use, to the public after either publication of the application pursuant to 35 U.S.C. 122(b) or issuance of a patent pursuant to 35 U.S.C. 151. Further, a record may be disclosed, subject to the limitations of 37 CFR 1.14, as a routine use, to the public if the record was filed in an application which became abandoned or in which the proceedings were terminated and which application is referenced by either a published application, an application open to public inspection or an issued patent.
9. A record from this system of records may be disclosed, as a routine use, to a Federal, State, or local law enforcement agency, if the USPTO becomes aware of a violation or potential violation of law or regulation.

Notice of Allowability	Application No. 13/675,665	Applicant(s) PANIAGUA ET AL.	
	Examiner CHERYL MILLER	Art Unit 3738	AIA (First Inventor to File) Status No

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to *the response with terminal disclaimers filed 10/26/2016*.
   ☐ A declaration(s)/affidavit(s) under **37 CFR 1.130(b)** was/were filed on_____.
2. ☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on _____; the restriction requirement and election have been incorporated into this action.
3. ☒ The allowed claim(s) is/are *1,2,4,6,9 and 10*. As a result of the allowed claim(s), you may be eligible to benefit from the **Patent Prosecution Highway** program at a participating intellectual property office for the corresponding application. For more information, please see http://www.uspto.gov/patents/init_events/pph/index.jsp or send an inquiry to PPHfeedback@uspto.gov.
4. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

   Certified copies:

   a) ☐ All b) ☐ Some *c) ☐ None of the:
   1. ☐ Certified copies of the priority documents have been received.
   2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
   3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

   * Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.
THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

5. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
   ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.

   Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).
6. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

1. ☐ Notice of References Cited (PTO-892)
2. ☐ Information Disclosure Statements (PTO/SB/08), Paper No./Mail Date _____
3. ☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material
4. ☐ Interview Summary (PTO-413), Paper No./Mail Date _____ .
5. ☐ Examiner's Amendment/Comment
6. ☐ Examiner's Statement of Reasons for Allowance
7. ☐ Other _____.

/C. M./ Examiner, Art Unit 3738	/THOMAS J SWEET/ Supervisory Patent Examiner, Art Unit 3738

EAST Search History

EAST Search History (Prior Art)

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	4024	a61f2/2412.cpc. or a61f2/2418.cpc. or a61f2/2475.cpc.	US-PGPUB; USPAT; USOCR	OR	ON	2016/11/03 16:16
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L3	415	L1 and @ad<"20020104"	US-PGPUB; USPAT; USOCR	OR	ON	2016/11/03 16:16
L4	850	2 3	US-PGPUB; USPAT; USOCR	OR	ON	2016/11/03 16:16
L5	4	L4 and @pd>"20160701"	US-PGPUB; USPAT; USOCR	OR	ON	2016/11/03 16:17
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S17	680	S15 S16	US-PGPUB; USPAT; USOCR	OR	ON	2014/11/02 16:25
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S44	38	myers.in. and 623/2.$2.ccls.	US-PGPUB; USPAT; USOCR	OR	ON	2015/06/27 14:07
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S65	46	S63 and @ad<"20020104"	US-PGPUB; USPAT; USOCR	OR	ON	2015/06/27 22:30
S66	117	S64 S65	US-PGPUB; USPAT; USOCR	OR	ON	2015/06/27 22:30
S67	1762	623/2.$2.ccls. and pericardi$2 and (stent or frame)	US-PGPUB; USPAT; USOCR	OR	ON	2015/06/27 22:46
S68	1011	623/2.$2.ccls. and ((calf or juvenile or porcine or animal or mammal) with pericardi$2) and (stent or frame)	US-PGPUB; USPAT; USOCR	OR	ON	2015/06/27 22:47
S69	317	S68 and @rlad<"20040710"	US-PGPUB; USPAT; USOCR	OR	ON	2015/06/27 22:48
S70	263	S68 and @ad<"20040710"	US-PGPUB; USPAT;	OR	ON	2015/06/27 22:48

			USOCR			
S71	458	S69 S70	US-PGPUB; USPAT; USOCR	OR	ON	2015/06/27 22:48
S72	240	S71 and (resilient or "self-expandable" or "self-expanding" or "self-expands")	US-PGPUB; USPAT; USOCR	OR	ON	2015/06/27 22:49
S73	162	S71 and (resilient or "self-expandable" or "self-expanding" or "self-expands") and (sheet or patch)	US-PGPUB; USPAT; USOCR	OR	ON	2015/06/27 22:50
S74	97	623/2.$2.ccls. and (autologous with pericardi$2)	US-PGPUB; USPAT; USOCR	OR	ON	2015/06/27 23:07
S75	126	623/2.$2.ccls. and ((autologous or autograft) with pericardi$2)	US-PGPUB; USPAT; USOCR	OR	ON	2015/06/27 23:07
S76	37	S75 and @rlad<"20020104"	US-PGPUB; USPAT; USOCR	OR	ON	2015/06/27 23:07
S77	39	S75 and @ad<"20020104"	US-PGPUB; USPAT; USOCR	OR	ON	2015/06/27 23:08
S78	57	S76 S77	US-PGPUB; USPAT; USOCR	OR	ON	2015/06/27 23:08
S79	129	("3989701" | "4261342" | "4790844" | "4960424").PN. OR ("5344442").URPN.	US-PGPUB; USPAT; USOCR	OR	OFF	2015/06/27 23:18
S80	1	"6908481".pn.	US-PGPUB; USPAT; USOCR	OR	OFF	2015/06/28 00:06
S81	1	"20020032482".pn.	US-PGPUB; USPAT; USOCR	OR	OFF	2015/06/28 00:12
S82	1	"6893460".pn.	US-PGPUB; USPAT; USOCR	OR	OFF	2015/06/28 00:23
S83	21	623/2.$2.ccls. and (double with continuous with sutur$4)	US-PGPUB; USPAT; USOCR	OR	OFF	2015/06/28 00:52
S84	3728	a61f2/2412.cpc. or a61f2/2415.cpc. or a61f2/2418.cpc.	US-PGPUB; USPAT; USOCR	OR	ON	2016/04/11 14:52
S85	625	S84 and @rlad<"20020104"	US-	OR	ON	2016/04/11

			PGPUB; USPAT; USOCR			14:53
S86	454	S84 and @ad<"20020104"	US-PGPUB; USPAT; USOCR	OR	ON	2016/04/11 14:53
S87	891	S85 S86	US-PGPUB; USPAT; USOCR	OR	ON	2016/04/11 14:53
S88	52	(US-20100114299-$ or US-20060167543-$ or US-20060142848-$ or US-20050065594-$ or US-20040193253-$ or US-20030040792-$ or US-20020151970-$ or US-20110137409-$ or US-20030078652-$ or US-20020052651-$ or US-20020032482-$ or US-20020198594-$ or US-20030023303-$ or US-20040186565-$ or US-20050075725-$ or US-20060004442-$ or US-20090118826-$).did. or (US-7947072-$ or US-6733525-$ or US-6730121-$ or US-6425916-$ or US-6299637-$ or US-6027525-$ or US-5957949-$ or US-5855601-$ or US-5607465-$ or US-5449384-$ or US-5163953-$ or US-4601718-$ or US-4759758-$ or US-7547322-$ or US-5895420-$ or US-5713953-$ or US-5509930-$ or US-5489297-$ or US-4340977-$ or US-5358518-$ or US-4343048-$ or US-4491986-$ or US-8308797-$ or US-8790398-$ or US-4470157-$ or US-4056854-$).did. or (US-4297749-$ or US-5545215-$ or US-6553681-$ or US-6682559-$ or US-6736846-$ or US-8613763-$ or US-5344442-$ or US-6358277-$ or US-4790844-$).did.	US-PGPUB; USPAT	OR	OFF	2016/04/12 13:07
S89	52	(US-20100114299-$ or US-20060167543-$ or US-20060142848-$ or US-20050065594-$ or US-20040193253-$ or US-20030040792-$ or US-20020151970-$ or US-20110137409-$ or US-20030078652-$ or US-20020052651-$ or US-20020032482-$ or US-20020198594-$ or US-20030023303-$ or US-20040186565-$ or US-20050075725-$ or US-20060004442-$ or US-20090118826-$).did. or (US-7947072-$ or US-6733525-$ or US-6730121-$ or US-6425916-$ or US-6299637-$ or US-6027525-$ or US-5957949-$ or US-5855601-$ or US-5607465-$ or US-5449384-$ or US-5163953-$ or US-4601718-$ or US-4759758-$ or US-7547322-$ or US-5895420-$ or US-5713953-$ or US-5509930-$ or US-5489297-$ or US-4340977-$ or US-5358518-$ or US-4343048-$ or US-4491986-$ or US-8308797-$ or US-8790398-$ or US-4470157-$ or US-4056854-$).did. or (US-4297749-$ or US-5545215-$ or US-6553681-$ or US-6682559-$ or US-6736846-$ or US-8613763-$ or US-5344442-$ or US-6358277-$ or US-4790844-$).did.	US-PGPUB; USPAT; USOCR	OR	ON	2016/04/12 13:07
S90	29	paniagua.in. and valve	US-PGPUB; USPAT; USOCR	OR	ON	2016/04/12 15:39
S91	9	paniagua.in. and valve	USPAT;	OR	ON	2016/04/12

			USOCR			15:39
S92	3733	a61f2/2412.cpc. or a61f2/2415.cpc. or a61f2/2418.cpc.	US-PGPUB; USPAT; USOCR	OR	ON	2016/04/12 16:00
S93	625	S92 and @rlad<"20020104"	US-PGPUB; USPAT; USOCR	OR	ON	2016/04/12 16:00
S94	454	S92 and @ad<"20020104"	US-PGPUB; USPAT; USOCR	OR	ON	2016/04/12 16:00
S95	891	S93 S94	US-PGPUB; USPAT; USOCR	OR	ON	2016/04/12 16:00
S96	299	S95 and pericardi$3	USPAT; USOCR	OR	ON	2016/04/12 16:00
S97	498	S95 and pericardi$3	US-PGPUB; USPAT; USOCR	OR	ON	2016/04/12 16:00
S98	344	S95 and pericardi$3 and (expand$4 or collaps$4)	US-PGPUB; USPAT; USOCR	OR	ON	2016/04/12 16:01
S99	286	S95 and pericardi$3 and (expand$4 or collaps$4) and (cuff or crease or fold$4 or invert$3 or evert$3)	US-PGPUB; USPAT; USOCR	OR	ON	2016/04/12 16:02
S100	425	S95 and (pericardi$3 or tube) and (expand$4 or collaps$4) and (cuff or crease or fold$4 or invert$3 or evert$3)	US-PGPUB; USPAT; USOCR	OR	ON	2016/04/12 16:02
S101	57	(US-20100114299-$ or US-20060167543-$ or US-20060142848-$ or US-20050065594-$ or US-20040193253-$ or US-20030040792-$ or US-20020151970-$ or US-20110137409-$ or US-20030078652-$ or US-20020052651-$ or US-20020032482-$ or US-20020198594-$ or US-20030023303-$ or US-20040186565-$ or US-20050075725-$ or US-20060004442-$ or US-20090118826-$).did. or (US-7947072-$ or US-6733525-$ or US-6730121-$ or US-6425916-$ or US-6299637-$ or US-6027525-$ or US-5957949-$ or US-5855601-$ or US-5607465-$ or US-5449384-$ or US-5163953-$ or US-4601718-$ or US-4759758-$ or US-7547322-$ or US-5895420-$ or US-5713953-$ or US-5509930-$ or US-5489297-$ or US-4340977-$ or US-5358518-$ or US-4343048-$ or US-4491986-$ or US-8308797-$ or US-8790398-$ or US-4470157-$ or US-4056854-$).did. or (US-4297749-$ or US-5545215-$ or US-6553681-$ or US-6682559-$ or US-6736846-$ or US-8613763-$ or US-5344442-$ or US-6358277-$ or US-4790844-$ or US-8109995-$ or US-8361144-$ or US-8900294-$ or US-9125739-$ or US-9186248-$).did.	US-PGPUB; USPAT	OR	OFF	2016/04/12 16:03

S102	400	S100 not S101	US-PGPUB; USPAT; USOCR	OR	ON	2016/04/12 16:03
S103	1	"6579307".pn.	US-PGPUB; USPAT; USOCR	OR	ON	2016/04/12 16:19
S104	8	("20080131522").PN. or ("20020119437" | "20020146393" | "20030118560" | "20060212111" | "4275469" | "5558875" | "7214344").PN.	US-PGPUB; USPAT; USOCR	OR	ON	2016/04/12 16:36
S105	1	"20020032482".pn.	US-PGPUB; USPAT; USOCR	OR	ON	2016/04/15 15:35
S106	1	"8308797".pn.	US-PGPUB; USPAT; USOCR	OR	ON	2016/04/15 19:36
S107	23	"10/037,266"	US-PGPUB; USPAT; USOCR	OR	ON	2016/04/15 19:39
S108	4	"10/037,266" and crease	US-PGPUB; USPAT; USOCR	OR	ON	2016/04/15 19:44
S109	5	"5080670".pn. or "20030138945".pn. or "20060155366".pn. or "20060229716".pn. or "20090054976".pn.	US-PGPUB; USPAT; USOCR	OR	ON	2016/07/21 17:28
S110	1	"4692164".pn.	US-PGPUB; USPAT; USOCR	OR	ON	2016/07/23 00:12
S111	3897	a61f2/2412.cpc. or a61f2/2415.cpc. or a61f2/2418.cpc.	US-PGPUB; USPAT; USOCR	OR	ON	2016/07/23 00:15
S112	628	S111 and @rlad<"20020104"	US-PGPUB; USPAT; USOCR	OR	ON	2016/07/23 00:15
S113	454	S111 and @ad<"20020104"	US-PGPUB; USPAT; USOCR	OR	ON	2016/07/23 00:15
S114	894	S112 S113	US-PGPUB; USPAT; USOCR	OR	ON	2016/07/23 00:15
S115	894	S114	US-PGPUB; USPAT; USOCR	OR	ON	2016/07/23 00:15
S116	2	S115 and @pd>"20160401"	US-PGPUB; USPAT;	OR	ON	2016/07/23 00:15

			USOCR				

11/3/2016 4:46:08 PM
C:\Users\cmiller2\Documents\EAST\Workspaces\13675665.wsp

Search Notes	Application/Control No.	Applicant(s)/Patent Under Reexamination
	13675665	PANIAGUA ET AL.
	Examiner	Art Unit
	CHERYL MILLER	3738

CPC- SEARCHED		
Symbol	Date	Examiner
A61f2/2418, 2412, 2415	4/12/2016	cm
update	7/22/2016	cm
A61f2/2412, 2418, 2475	11/3/2016	cm

CPC COMBINATION SETS - SEARCHED		
Symbol	Date	Examiner

US CLASSIFICATION SEARCHED			
Class	Subclass	Date	Examiner

SEARCH NOTES		
Search Notes	Date	Examiner
East text search, review parent application files	6/27/2015	cm
Inventor name search	4/12/2016	cm

INTERFERENCE SEARCH			
US Class/ CPC Symbol	US Subclass / CPC Group	Date	Examiner
Claim text search		11/3/2016	cm

/C.M./ Examiner.Art Unit 3738	

Issue Classification	Application/Control No.	Applicant(s)/Patent Under Reexamination
	13675665	PANIAGUA ET AL.
	Examiner	**Art Unit**
	CHERYL MILLER	3738

CPC							
Symbol						**Type**	**Version**
A61F		2	/	2412		F	2013-01-01
A61F		2002	/	9534		A	2013-01-01
A61F		2	/	2439		A	2013-01-01
Y10T		29	/	49412		A	2015-01-15
A61F		2230	/	0078		A	2013-01-01
A61F		2210	/	0076		A	2013-01-01
A61F		2240	/	001		A	2013-01-01
A61L		27	/	3604		A	2013-01-01
A61L		27	/	3683		A	2013-01-01
A61L		27	/	3691		A	2013-01-01
A61L		27	/	3687		A	2013-01-01
Y10S		623	/	918		A	2013-01-01
A61F		2220	/	0025		A	2013-01-01
A61F		2230	/	001		A	2013-01-01
A61F		2230	/	0013		A	2013-01-01
A61F		2230	/	0095		A	2013-01-01
A61F		2230	/	0067		A	2013-01-01
A61F		2310	/	00371		A	2013-01-01
A61F		2	/	2415		I	2013-01-01
A61F		2	/	2418		I	2013-01-01
A61F		2	/	2436		I	2013-01-01
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A61F		2	/	2475		I	2013-01-01
A61F		2250	/	0039		A	2013-01-01
A61B		8	/	12		I	2013-01-01
A61F		2	/	2433		I	2013-01-01
A61F		2	/	2427		I	2013-01-01
A61F		2220	/	0008		A	2013-01-01
A61F		2220	/	0016		A	2013-01-01
A61F		2220	/	0075		A	2013-01-01

/C.M./ Examiner.Art Unit 3738	11/03/2016	**Total Claims Allowed:**	
(Assistant Examiner)	(Date)	6	
/THOMAS J SWEET/ Supervisory Patent Examiner.Art Unit 3738	11/14/2016	O.G. Print Claim(s)	O.G. Print Figure
(Primary Examiner)	(Date)	1	5

Issue Classification	Application/Control No.	Applicant(s)/Patent Under Reexamination
	13675665	PANIAGUA ET AL.
	Examiner	**Art Unit**
	CHERYL MILLER	3738

A61F		2210	/	0014	A	2013-01-01

CPC Combination Sets					
Symbol				**Type**	**Set**	**Ranking**	**Version**
			/				
			/				

/C.M./ Examiner.Art Unit 3738	11/03/2016	**Total Claims Allowed:**	
(Assistant Examiner)	(Date)	6	
/THOMAS J SWEET/ Supervisory Patent Examiner.Art Unit 3738	11/14/2016	O.G. Print Claim(s)	O.G. Print Figure
(Primary Examiner)	(Date)	1	5

Issue Classification	Application/Control No.	Applicant(s)/Patent Under Reexamination
	13675665	PANIAGUA ET AL.
	Examiner	**Art Unit**
	CHERYL MILLER	3738

US ORIGINAL CLASSIFICATION		INTERNATIONAL CLASSIFICATION										
CLASS	SUBCLASS	CLAIMED					NON-CLAIMED					
		A	6	1	F	2 / 24 (2006.01.01)						
CROSS REFERENCE(S)												
CLASS	SUBCLASS (ONE SUBCLASS PER BLOCK)											

/C.M./ Examiner.Art Unit 3738	11/03/2016	**Total Claims Allowed:**	
(Assistant Examiner)	(Date)	6	
/THOMAS J SWEET/ Supervisory Patent Examiner.Art Unit 3738	11/14/2016	O.G. Print Claim(s)	O.G. Print Figure
(Primary Examiner)	(Date)	1	5

Issue Classification	Application/Control No.	Applicant(s)/Patent Under Reexamination
	13675665	PANIAGUA ET AL.
	Examiner	**Art Unit**
	CHERYL MILLER	3738

☐ Claims renumbered in the same order as presented by applicant ☐ CPA ☒ T.D. ☐ R.1.47

Final	Original	Final	Original	Final	Original	Final	Original	Final	Original	Final	Original	Final	Original	Final	Original
1	1		17		33										
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	3		19												
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	11		27												
	12		28												
	13		29												
	14		30												
	15		31												
	16		32												

/C.M./ Examiner.Art Unit 3738	11/03/2016	**Total Claims Allowed:**	
(Assistant Examiner)	(Date)	6	
/THOMAS J SWEET/ Supervisory Patent Examiner.Art Unit 3738	11/14/2016	O.G. Print Claim(s)	O.G. Print Figure
(Primary Examiner)	(Date)	1	5

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BIB DATA SHEET

CONFIRMATION NO. 1995

SERIAL NUMBER	FILING or 371(c) DATE RULE	CLASS	GROUP ART UNIT	ATTORNEY DOCKET NO.
13/675,665	11/13/2012	623	3738	109978.10101

APPLICANTS

COLIBRI HEART VALVE LLC, Broomfield, CO;

INVENTORS

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R. David Fish, Houston, TX;
Eduardo Induni, Alajuela, COSTA RICA;
Carlos Meija, Houston, TX;
Fransisco Lopez-Jimenez, Rochester, MN;

**** CONTINUING DATA ************************

This application is a CON of 10/887,688 07/10/2004 PAT 8308797 *
which is a CIP of 10/037,266 01/04/2002 ABN
(*)Data provided by applicant is not consistent with PTO records.

**** FOREIGN APPLICATIONS ************************

**** IF REQUIRED, FOREIGN FILING LICENSE GRANTED **** ** SMALL ENTITY **
12/05/2012

Foreign Priority claimed ☐ Yes ☑ No 35 USC 119(a-d) conditions met ☐ Yes ☑ No Verified and Acknowledged /CHERYL L MILLER/ Examiner's Signature	☐ Met after Allowance Initials	STATE OR COUNTRY	SHEETS DRAWINGS	TOTAL CLAIMS	INDEPENDENT CLAIMS
		TX	12	~~14~~ 6	~~3~~ 1

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PRINCETON PIKE CORPORATE CENTER
997 LENOX DRIVE
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LAWRENCEVILLE, NJ 08648
UNITED STATES

TITLE

PERCUTANEOUSLY IMPLANTABLE REPLACEMENT HEART VALVE DEVICE AND METHOD OF MAKING SAME

FILING FEE RECEIVED		
800	FEES: Authority has been given in Paper No._____ to charge/credit DEPOSIT ACCOUNT No._____ for following:	☐ All Fees ☐ 1.16 Fees (Filing) ☐ 1.17 Fees (Processing Ext. of time) ☐ 1.18 Fees (Issue) ☐ Other _____ ☐ Credit

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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
13/675,665	11/13/2012	David Paniagua	109978.10101	1995

29880 7590 12/07/2016

FOX ROTHSCHILD LLP
PRINCETON PIKE CORPORATE CENTER
997 LENOX DRIVE
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LAWRENCEVILLE, NJ 08648

EXAMINER	
MILLER, CHERYL L	

ART UNIT	PAPER NUMBER
3738	

NOTIFICATION DATE	DELIVERY MODE
12/07/2016	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

ipdocket@foxrothschild.com

Corrected Notice of Allowability	Application No. 13/675,665	Applicant(s) PANIAGUA ET AL.	
	Examiner CHERYL MILLER	Art Unit 3738	AIA (First Inventor to File) Status No

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to *the IDS filed 11/15/2016*.
   ☐ A declaration(s)/affidavit(s) under **37 CFR 1.130(b)** was/were filed on_____.
2. ☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on _____; the restriction requirement and election have been incorporated into this action.
3. ☒ The allowed claim(s) is/are *1,2,4,6,9 and 10*. As a result of the allowed claim(s), you may be eligible to benefit from the **Patent Prosecution Highway** program at a participating intellectual property office for the corresponding application. For more information, please see http://www.uspto.gov/patents/init_events/pph/index.jsp or send an inquiry to PPHfeedback@uspto.gov.
4. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

   Certified copies:

   a) ☐ All b) ☐ Some *c) ☐ None of the:
   1. ☐ Certified copies of the priority documents have been received.
   2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
   3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

   * Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.
THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

5. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
   ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.

   Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).
6. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

1. ☐ Notice of References Cited (PTO-892)
2. ☒ Information Disclosure Statements (PTO/SB/08), Paper No./Mail Date _____
3. ☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material
4. ☐ Interview Summary (PTO-413), Paper No./Mail Date _____ .
5. ☐ Examiner's Amendment/Comment
6. ☐ Examiner's Statement of Reasons for Allowance
7. ☐ Other _____.

/CHRISTIAN SEVILLA/ Primary Examiner, Art Unit 3775	/C. M./ Examiner, Art Unit 3738

PTO/SB/08a (03-15)
Approved for use through 07/31/2016. OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(Not for submission under 37 CFR 1.99)

Application Number	13675665
Filing Date	2012-11-13
First Named Inventor	David PANIAGUA
Art Unit	3738
Examiner Name	Cheryl L. MILLER
Attorney Docket Number	109978.10101

U.S.PATENTS Remove

Examiner Initial*	Cite No	Patent Number	Kind Code[1]	Issue Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
	1	6166184		2000-12-26	Hendriks et al.	
	2	7632309		2009-12-15	Brendzel et al.	

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	1	20010007956		2001-07-12	Letac et al.	

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Examiner Initial*	Cite No	Foreign Document Number[3]	Country Code[2] i	Kind Code[4]	Publication Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear	T[5]
	1							

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/CHERYL L MILLER/ 12/01/2016

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /C.L.M/

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(Not for submission under 37 CFR 1.99)

Application Number	13675665
Filing Date	2012-11-13
First Named Inventor	David PANIAGUA
Art Unit	3738
Examiner Name	Cheryl L. MILLER
Attorney Docket Number	109978.10101

Examiner Initials*	Cite No	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc), date, pages(s), volume-issue number(s), publisher, city and/or country where published.	T[5]
	1	Notice of Allowance issued September 19, 2016 in U.S. Application No. 14/502,453 (File: 109978.10106)	
	2	Office Action issued October 7, 2016, in U.S. Application No. 14/829,349 (File: 109978.10120)	

If you wish to add additional non-patent literature document citation information please click the Add button Add

EXAMINER SIGNATURE

Examiner Signature	/CHERYL L MILLER/	Date Considered	12/01/2016

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through a citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

[1] See Kind Codes of USPTO Patent Documents at www.USPTO.GOV or MPEP 901.04. [2] Enter office that issued the document, by the two-letter code (WIPO Standard ST.3). [3] For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. [4] Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. [5] Applicant is to place a check mark here if English language translation is attached.

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /C.L.M/

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Art Unit	3738
Examiner Name	Cheryl L. MILLER
Attorney Docket Number	109978.10101

CERTIFICATION STATEMENT

Please see 37 CFR 1.97 and 1.98 to make the appropriate selection(s):

That each item of information contained in the information disclosure statement was first cited in any communication from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e)(1).

OR

☐ That no item of information contained in the information disclosure statement was cited in a communication from a foreign patent office in a counterpart foreign application, and, to the knowledge of the person signing the certification after making reasonable inquiry, no item of information contained in the information disclosure statement was known to any individual designated in 37 CFR 1.56(c) more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e)(2).

See attached certification statement.

☒ The fee set forth in 37 CFR 1.17 (p) has been submitted herewith.

☒ A certification statement is not submitted herewith.

SIGNATURE

A signature of the applicant or representative is required in accordance with CFR 1.33, 10.18. Please see CFR 1.4(d) for the form of the signature.

Signature	/Gunjan Agarwal/	Date (YYYY-MM-DD)	2016-11-15
Name/Print	Gunjan Agarwal	Registration Number	69661

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 1 hour to complete, including gathering, preparing and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

/CHERYL L MILLER/ 12/01/2016

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Privacy Act Statement

The Privacy Act of 1974 (P.L. 93-579) requires that you be given certain information in connection with your submission of the attached form related to a patent application or patent. Accordingly, pursuant to the requirements of the Act, please be advised that: (1) the general authority for the collection of this information is 35 U.S.C. 2(b)(2); (2) furnishing of the information solicited is voluntary; and (3) the principal purpose for which the information is used by the U.S. Patent and Trademark Office is to process and/or examine your submission related to a patent application or patent. If you do not furnish the requested information, the U.S. Patent and Trademark Office may not be able to process and/or examine your submission, which may result in termination of proceedings or abandonment of the application or expiration of the patent.

The information provided by you in this form will be subject to the following routine uses:

1. The information on this form will be treated confidentially to the extent allowed under the Freedom of Information Act (5 U.S.C. 552) and the Privacy Act (5 U.S.C. 552a). Records from this system of records may be disclosed to the Department of Justice to determine whether the Freedom of Information Act requires disclosure of these record s.

2. A record from this system of records may be disclosed, as a routine use, in the course of presenting evidence to a court, magistrate, or administrative tribunal, including disclosures to opposing counsel in the course of settlement negotiations.

3. A record in this system of records may be disclosed, as a routine use, to a Member of Congress submitting a request involving an individual, to whom the record pertains, when the individual has requested assistance from the Member with respect to the subject matter of the record.

4. A record in this system of records may be disclosed, as a routine use, to a contractor of the Agency having need for the information in order to perform a contract. Recipients of information shall be required to comply with the requirements of the Privacy Act of 1974, as amended, pursuant to 5 U.S.C. 552a(m).

5. A record related to an International Application filed under the Patent Cooperation Treaty in this system of records may be disclosed, as a routine use, to the International Bureau of the World Intellectual Property Organization, pursuant to the Patent Cooperation Treaty.

6. A record in this system of records may be disclosed, as a routine use, to another federal agency for purposes of National Security review (35 U.S.C. 181) and for review pursuant to the Atomic Energy Act (42 U.S.C. 218(c)).

7. A record from this system of records may be disclosed, as a routine use, to the Administrator, General Services, or his/her designee, during an inspection of records conducted by GSA as part of that agency's responsibility to recommend improvements in records management practices and programs, under authority of 44 U.S.C. 2904 and 2906. Such disclosure shall be made in accordance with the GSA regulations governing inspection of records for this purpose, and any other relevant (i.e., GSA or Commerce) directive. Such disclosure shall not be used to make determinations about individuals.

8. A record from this system of records may be disclosed, as a routine use, to the public after either publication of the application pursuant to 35 U.S.C. 122(b) or issuance of a patent pursuant to 35 U.S.C. 151. Further, a record may be disclosed, subject to the limitations of 37 CFR 1.14, as a routine use, to the public if the record was filed in an application which became abandoned or in which the proceedings were terminated and which application is referenced by either a published application, an application open to public inspections or an issued patent.

9. A record from this system of records may be disclosed, as a routine use, to a Federal, State, or local law enforcement agency, if the USPTO becomes aware of a violation or potential violation of law or regulation.

12/01/2016

/CHERYL L MILLER/

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PART B - FEE(S) TRANSMITTAL

Complete and send this form, together with applicable fee(s), to: Mail **Mail Stop ISSUE FEE**
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450
or Fax (571)-273-2885

INSTRUCTIONS: This form should be used for transmitting the ISSUE FEE and PUBLICATION FEE (if required). Blocks 1 through 5 should be completed where appropriate. All further correspondence including the Patent, advance orders and notification of maintenance fees will be mailed to the current correspondence address as indicated unless corrected below or directed otherwise in Block 1, by (a) specifying a new correspondence address; and/or (b) indicating a separate "FEE ADDRESS" for maintenance fee notifications.

CURRENT CORRESPONDENCE ADDRESS (Note: Use Block 1 for any change of address)

29880 7590 11/18/2016
FOX ROTHSCHILD LLP
PRINCETON PIKE CORPORATE CENTER
997 LENOX DRIVE
BLDG. #3
LAWRENCEVILLE, NJ 08648

Note: A certificate of mailing can only be used for domestic mailings of the Fee(s) Transmittal. This certificate cannot be used for any other accompanying papers. Each additional paper, such as an assignment or formal drawing, must have its own certificate of mailing or transmission.

Certificate of Mailing or Transmission
I hereby certify that this Fee(s) Transmittal is being deposited with the United States Postal Service with sufficient postage for first class mail in an envelope addressed to the Mail Stop ISSUE FEE address above, or being facsimile transmitted to the USPTO (571) 273-2885, on the date indicated below.

(Depositor's name)
(Signature)
(Date)

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
13/675,665	11/13/2012	David Paniagua	109978.10101	1995

TITLE OF INVENTION: PERCUTANEOUSLY IMPLANTABLE REPLACEMENT HEART VALVE DEVICE AND METHOD OF MAKING SAME

APPLN. TYPE	ENTITY STATUS	ISSUE FEE DUE	PUBLICATION FEE DUE	PREV. PAID ISSUE FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	SMALL	$480	$0	$0	$480	02/21/2017

EXAMINER	ART UNIT	CLASS-SUBCLASS
MILLER, CHERYL L	3738	623-001200

1. Change of correspondence address or indication of "Fee Address" (37 CFR 1.363).
- ☐ Change of correspondence address (or Change of Correspondence Address form PTO/SB/122) attached.
- ☐ "Fee Address" indication (or "Fee Address" Indication form PTO/SB/47; Rev 03-02 or more recent) attached. **Use of a Customer Number is required.**

2. For printing on the patent front page, list
(1) The names of up to 3 registered patent attorneys or agents OR, alternatively,
(2) The name of a single firm (having as a member a registered attorney or agent) and the names of up to 2 registered patent attorneys or agents. If no name is listed, no name will be printed.

1 FOX ROTHSCHILD LLP
2
3

3. ASSIGNEE NAME AND RESIDENCE DATA TO BE PRINTED ON THE PATENT (print or type)

PLEASE NOTE: Unless an assignee is identified below, no assignee data will appear on the patent. If an assignee is identified below, the document has been filed for recordation as set forth in 37 CFR 3.11. Completion of this form is NOT a substitute for filing an assignment.

(A) NAME OF ASSIGNEE: COLIBRI HEART VALVE LLC

(B) RESIDENCE: (CITY and STATE OR COUNTRY): Broomfield, Colorado

Please check the appropriate assignee category or categories (will not be printed on the patent) : ☐ Individual ☒ Corporation or other private group entity ☐ Government

4a. The following fee(s) are submitted:
- ☒ Issue Fee
- ☐ Publication Fee (No small entity discount permitted)
- ☐ Advance Order - # of Copies _____

4b. Payment of Fee(s): **(Please first reapply any previously paid issue fee shown above)**
- ☐ A check is enclosed.
- ☐ Payment by credit card. Form PTO-2038 is attached.
- ☒ The director is hereby authorized to charge the required fee(s), any deficiency, or credits any overpayment, to Deposit Account Number 50-1943 (enclose an extra copy of this form).

5. **Change in Entity Status** (from status indicated above)
- ☐ Applicant certifying micro entity status. See 37 CFR 1.29 — NOTE: Absent a valid certification of Micro Entity Status (see forms PTO/SB/15A and 15B), issue fee payment in the micro entity amount will not be accepted at the risk of application abandonment.
- ☐ Applicant asserting small entity status. See 37 CFR 1.27 — NOTE: If the application was previously under micro entity status, checking this box will be taken to be a notification of loss of entitlement to micro entity status.
- ☐ Applicant changing to regular undiscounted fee status. — NOTE: Checking this box will be taken to be a notification of loss of entitlement to small or micro entity status, as applicable.

NOTE: This form must be signed in accordance with 37 CFR 1.31 and 1.33. See 37 CFR 1.4 for signature requirements and certifications.

Authorized Signature /Gunjan Agarwal/ Date 16 February 2017

Typed or printed name Gunjan Agarwal Registration No. 69661

Electronic Patent Application Fee Transmittal

Application Number:	13675665
Filing Date:	13-Nov-2012
Title of Invention:	PERCUTANEOUSLY IMPLANTABLE REPLACEMENT HEART VALVE DEVICE AND METHOD OF MAKING SAME
First Named Inventor/Applicant Name:	David Paniagua
Filer:	Gunjan Agarwal/Carol Donahue
Attorney Docket Number:	109978.10101

Filed as Small Entity

Filing Fees for Utility under 35 USC 111(a)

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Basic Filing:				
Pages:				
Claims:				
Miscellaneous-Filing:				
Petition:				
Patent-Appeals-and-Interference:				
Post-Allowance-and-Post-Issuance:				
UTILITY APPL ISSUE FEE	2501	1	480	480

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Extension-of-Time:				
Miscellaneous:				
			Total in USD ($)	**480**

Electronic Acknowledgement Receipt

EFS ID:	28377435
Application Number:	13675665
International Application Number:	
Confirmation Number:	1995
Title of Invention:	PERCUTANEOUSLY IMPLANTABLE REPLACEMENT HEART VALVE DEVICE AND METHOD OF MAKING SAME
First Named Inventor/Applicant Name:	David Paniagua
Customer Number:	29880
Filer:	Gunjan Agarwal/Carol Donahue
Filer Authorized By:	Gunjan Agarwal
Attorney Docket Number:	109978.10101
Receipt Date:	16-FEB-2017
Filing Date:	13-NOV-2012
Time Stamp:	13:54:35
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	yes
Payment Type	CARD
Payment was successfully received in RAM	$480
RAM confirmation Number	021717INTEFSW13554800
Deposit Account	501943
Authorized User	Carol Donahue

The Director of the USPTO is hereby authorized to charge indicated fees and credit any overpayment as follows:

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37 CFR 1.17 (Patent application and reexamination processing fees)

37 CFR 1.19 (Document supply fees)

37 CFR 1.20 (Post Issuance fees)

37 CFR 1.21 (Miscellaneous fees and charges)

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Issue Fee Payment (PTO-85B)	10101_Issue_Fee_Transmittal.pdf	138336 73a0c0ee45e9ec8332746da02d90ef944f49ab84	no	1
Warnings:					
Information:					
2	Fee Worksheet (SB06)	fee-info.pdf	30898 5ce97089049aca59379346e87fc461af955e32dc	no	2
Warnings:					
Information:					
		Total Files Size (in bytes):	169234		

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New Applications Under 35 U.S.C. 111

If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

National Stage of an International Application under 35 U.S.C. 371

If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office

If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

Doc code: IDS
Doc description: Information Disclosure Statement (IDS) Filed

PTO/SB/08a (03-15)
Approved for use through 07/31/2016. OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(Not for submission under 37 CFR 1.99)

Application Number	13675665
Filing Date	2012-11-13
First Named Inventor	David Paniagua
Art Unit	3738
Examiner Name	Cheryl L. Miller
Attorney Docket Number	109978.10101

U.S.PATENTS Remove

Examiner Initial*	Cite No	Patent Number	Kind Code[1]	Issue Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
	1	4275469		1981-06-30	Gabbay	
	2	5558875		1996-09-24	Wang	
	3	7214344		05/2007 ~~2007-01-14~~	Carpentier et al.	

Change(s) applied to document. /N.W.S./ 12/14/2016

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U.S.PATENT APPLICATION PUBLICATIONS Remove

Examiner Initial*	Cite No	Publication Number	Kind Code[1]	Publication Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
	1	20020119437		2002-08-29	Grooms et al.	
	2	20020146393		2002-10-10	Bell et al.	
	3	20030118560		2003-06-25	Kelly et al.	

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /CM/

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Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	ISSUE DATE	PATENT NO.	ATTORNEY DOCKET NO.	CONFIRMATION NO.
13/675,665	04/04/2017	9610158	109978.10101	1995

29880 7590 03/15/2017

FOX ROTHSCHILD LLP
PRINCETON PIKE CORPORATE CENTER
997 LENOX DRIVE
BLDG. #3
LAWRENCEVILLE, NJ 08648

ISSUE NOTIFICATION

The projected patent number and issue date are specified above.

Determination of Patent Term Adjustment under 35 U.S.C. 154 (b)
(application filed on or after May 29, 2000)

The Patent Term Adjustment is 630 day(s). Any patent to issue from the above-identified application will include an indication of the adjustment on the front page.

If a Continued Prosecution Application (CPA) was filed in the above-identified application, the filing date that determines Patent Term Adjustment is the filing date of the most recent CPA.

Applicant will be able to obtain more detailed information by accessing the Patent Application Information Retrieval (PAIR) WEB site (http://pair.uspto.gov).

Any questions regarding the Patent Term Extension or Adjustment determination should be directed to the Office of Patent Legal Administration at (571)-272-7702. Questions relating to issue and publication fee payments should be directed to the Application Assistance Unit (AAU) of the Office of Data Management (ODM) at (571)-272-4200.

APPLICANT(s) (Please see PAIR WEB site http://pair.uspto.gov for additional applicants):

COLIBRI HEART VALVE LLC, Broomfield, CO;
David Paniagua, Houston, TX;
R. David Fish, Houston, TX;
Eduardo Induni, Alajuela, COSTA RICA;
Carlos Meija, Houston, TX;
Fransisco Lopez-Jimenez, Rochester, MN;