United States Patent [19]

Rygg

[11] **4,218,782**

[45] **Aug. 26, 1980**

[54] **HEART VALVE PROSTHESIS AND METHOD FOR THE PRODUCTION THEREOF**

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[73] Assignee: **Biocoating Anpartsselskab**, Copenhagen, Denmark

[21] Appl. No.: **907,580**

[22] Filed: **May 19, 1978**

[30] **Foreign Application Priority Data**

May 25, 1977 [DK] Denmark 2290/77

[51] **Int. Cl.**[2] **A61F 1/22**

[52] **U.S. Cl.** **3/1.5**; 3/1

[58] **Field of Search** 3/1.5, 1.4, 1

[56] **References Cited**

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3,548,418	12/1970	Angell et al.	3/1.5
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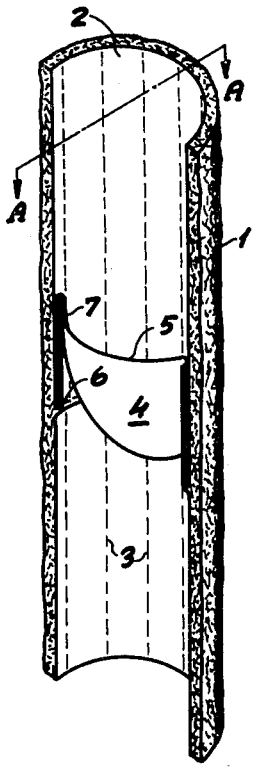
Primary Examiner—Ronald L. Frinks

[57] **ABSTRACT**

A flexible non-stented heart valve prosthesis made from a flat piece of a stabilized biological membrane. The membrane is folded along one or more folding lines and attached to a flat flexible non-biological base material so that one or more leaflets are formed. Preferably the membrane is pericardium and is attached by machine stitching to a woven polymeric base material. Different valve types including ventricular outflow patches and three-leaflet valves such as aortic valves and methods for their production are described.

The aortic valve is preferably made from three separate leaflets provided with narrow base materials serving as attachment margins which are stitched together in a manner to form a three-leaflet valve.

20 Claims, 9 Drawing Figures



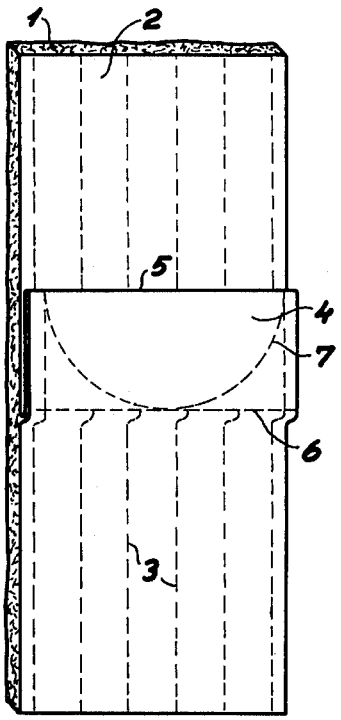


Fig. 1A

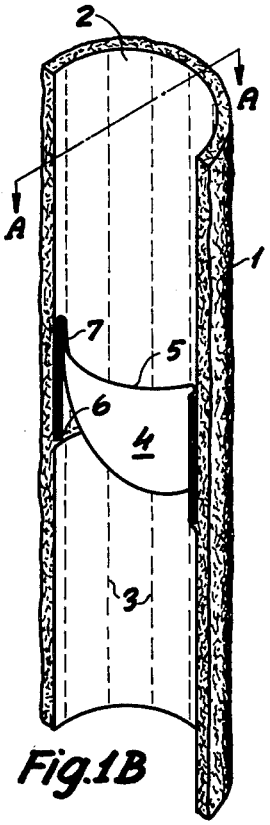


Fig. 1B

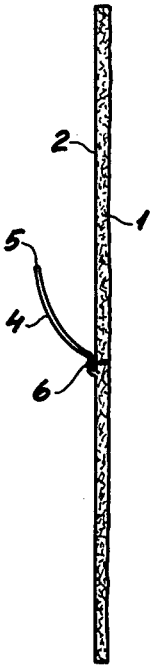


Fig. 1C

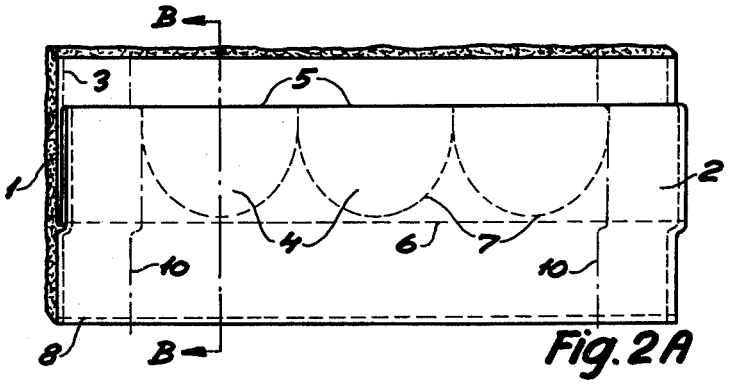


Fig. 2A

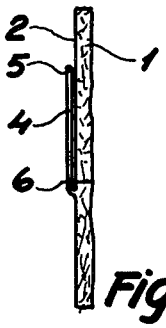


Fig.2B

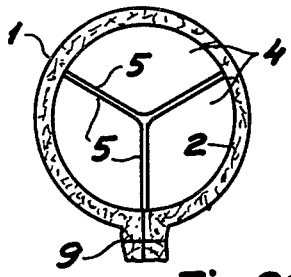


Fig.2C

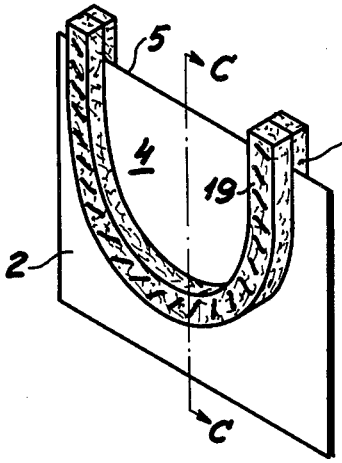


Fig.3A

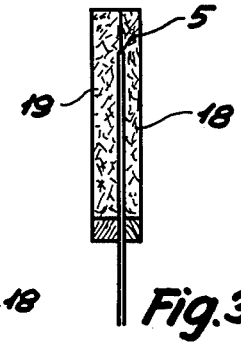


Fig.3B

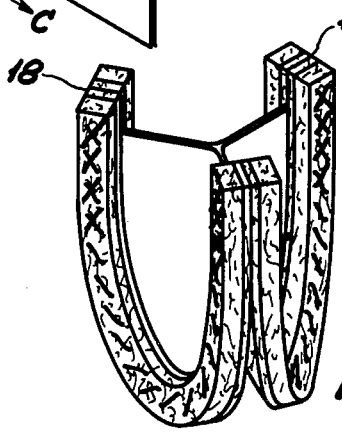


Fig.3C

HEART VALVE PROSTHESIS AND METHOD FOR THE PRODUCTION THEREOF

BACKGROUND OF THE INVENTION

1. Field of the Invention

The present invention relates to a heart valve prosthesis on the basis of a stabilized biological membrane.

2. Description of the Invention

Heart valve prostheses produced from biological membranes have been known for many years. Fascia, pericardium, dura mater, ilium membranes and the like have been used. It has also been proposed to employ cut-out segments of vessels from umbilical cords for coating heart valves, cf. the U.S. Pat. No. 3,988,782.

Both fascia, pericardium and dura mater have been used in the human clinical medicine. A distinction must be made between membranes taken from the patient's own organism, the so-called autologous membranes, and membranes taken from other human beings (homologous membranes), or from animals (heterologous membranes). It has been found that heart valves produced from autologous membranes in contact with circulating blood undergo a specific reaction which is characteristic of a healing process. First, thick deposits of fibrin are formed on the membrane, and then a secondary cellular ingrowth takes place resulting in a thickening and shrinkage simultaneously with some degeneration of the encapsulated tissue. This process is progressive so that heart valves produced from autologous tissue cannot function in the long run.

The reaction of the organism to homologous and heterologous tissue is almost the opposite because the alien tissue has an immunologically different action so that the organism reacts with a kind of rejection reaction, which in this respect may be expedient. There are no fibrin coatings and no secondary cellular reaction apart from the region at the attachment margings. Heart valves produced from homologous or heterologous membranes therefore seem to remain unaffected, but it has been found that also the structure of the alient tissue tends to degenerate and degrade so that gradually the membranes weaken and break. At the same time the membranes tend to yield to pressure strains and expand. Attempts have been made to counteract this disadvantageous change in various manners by stabilizing the membranes with different tanning agents, preferably glutaraldehyde.

The membranes which are used today in the clinics are pericardium and dura mater. Considerable advantages are attached to constructing a heart valve from these membranes instead of utilizing the heretofore most used natural heart valves from animals or dead human beings. The rather difficult and laborious dissection of the heart valve itself is obviated and likewise the shaping and stabilizing of said valve in its naturally dilated state. Further, the valves of the patient as well as of the donor exhibit individual variations, and it is therefore a problem to find suitable sizes. Finally, the problems of suspending or attaching such a prosthesis in a form corresponding to its normal position are obviated. Thus, the use of a biological membrane results in a simplification of the production of the heart valves in several respects and also in a considerably better standardization. It further provides a greater choice of attachment methods, and finally it gives better possibilities of procuring suitable raw materials far more easily.

At present two types of such biological heart valve prostheses are available, one utilizes dissected natural heart valves, preferably from pigs, cf. for example the U.S. Pat. No. 3,548,418, No. 3,570,014, No. 3,755,823 and No. 3,983,581, the other is constructed from biological membranes, preferably porcine pericardium or dura mater. Both types are stabilized by tanning with glutaraldehyde and have the advantages in common that follow from the application of a heterologous material, viz. that they remain thin and movable, and that no deposits are formed on them that may get loose and cause thrombi. Compared with the existing mechanical valve prostheses, cf. for example the U.S. Pat. No. 3,325,827 and No. 3,396,409, they also have the advantages of a better hemodynamic, less hemolysis and no noise problems.

The drawbacks of the heretofore existing biological heart valve prostheses are, however, still that gradually the tissue will deteriorate in some degree in the form of decomposition or degradation of part of the tissue and possibly also wear. There is also a somewhat greater tendency to infection and consequently a greater strain on the material than in the mechanical prostheses. Particularly for the prostheses produced from heterologous biological membranes the weakness in the free margin of the valves is partly a consequence of the production method used up to now.

This type of prostheses are by and large produced by cutting a strip of the biological membrane. This strip is placed around and attached to a stent, which for example may bear a resemblance in appearance to that of the aforementioned U.S. Pat. No. 3,570,014 and which has three apexes between which the strip may be folded towards the centre and thus form a heart valve resembling a natural, three-leaflet valve, such as the aortic valve. The cutting of the strip invariably results in some damage to the margin of the membrane owing to the cutting of its constituents, in particular connective tissue fibrils. The free margin of the heart valve produced therefrom therefore becomes particularly vulnerable, and there is reason to believe that one of the late complications characteristic of this type of prostheses, viz. breaking transversely to the margin, is partly caused by this weakening of the tissue, stemming from the cutting. Furthermore, the suturing to the stent results inevitably in a certain damage of the biological material which is furthermore exposed to an abnormal stress at this suture line caused by the difference in consistency existing between the biological material and the more rigid stent. The stent also in itself exposes the biological material to an abnormal closing stress, giving a tendency to rupture of the free margin.

It is also characteristic of the two most used biological membranes, viz. pericardium and dura mater, that they are covered by a surface cell layer (the mesothelium) only on one side (the inside) and thus only have a microscopic, smooth, even surface on this side, while the other (the outside) is rough and uneven after the removal of fatty tissue and loose connective tissue. Consequently, the thickness and thereby also the strength of these membranes vary considerably.

The drawbacks of the rough side are further that bacteria can stick more easily thereto, and also a degradation or degeneration can take place more easily from this side.

To improve the quality of heart valve prostheses produced from a biological material researches have in recent years been carried out into an improvement of

the preservation of the tissue, which has lead to a method of impregnating and/or coating biological tissue with polymeric materials, cf. the Danish patent application No. 1690/76, corresponding to U.S. application Ser. No. 784,916 filed Apr. 5, 1977 and which is incorporated herein by reference.

These prostheses on the basis of impregnated and/or coated heart valves exhibit considerable advantages compared with mechanical valves as well as valves of the type described above, where for example a porcine valve is attached to a stent, and they do not suffer from the problems which are observed in valves on the basis of biological membranes and which stem from the damaged marginal regions.

However, said Danish application does not obviate the problems relating to the dissection of the heart valve and the placing thereof in its genuine normal position in the patient.

The object of the present invention is to provide a flexible non-stented heart valve prosthesis which has the advantages known from the use of biological membranes without being encumbered with the known drawbacks. This object is achieved by the prosthesis of the invention which is characterized in that a flat piece of a stabilized biological membrane is folded along one or more folding lines and attached to a flat flexible non-biological base material to form one or more leaflets. The biological membrane is stabilized before or after the folding and forming of the leaflets. The most expedient manner of attaching the strip to the base material is by stitching, however, also gluing or a combination of stitching and gluing may be used. Special importance has been attached to the development of a production method which permits machine stitching with the consequent advantages in terms of production. Machine stitching thus makes possible a more accurate, uniform and reproducable stitching, the use of various types of stitches, and also the use of a reinforced suture.

In an embodiment of the prosthesis of the invention the impregnation and/or coating principle described in application No. 1690/76 is utilized because this results in a reinforcement of the membrane. If the biological membrane is of the type which on one side has mesothelial cells it is preferred to impregnate and/or coat from the other side to keep the mesothelial cells intact.

The invention also relates to a method of producing the subject prostheses, and the method of the invention is characterized by folding a flat piece of a biological membrane along one or more folding lines and stitching the strip on a flexible nonbiological base material to form one or more leaflets. Said stitching is preferably effected by machine.

The biological membrane is preferably porcine pericardium because it is easily available and also because it has a thickness suitable for the purpose, but any other thin biological membrane may be used, preferably with one side coated with mesothelial cells.

The base material is preferably a flexible polymeric material, such as a polyester, which is advantageously woven or crocheted so that it is easy to stitch.

In the production the membrane is folded so that the smooth cell clad side faces outwardly. Several advantages are achieved hereby:

1. The produced valve consists of a double layer of membrane.
2. There is a smooth surface layer cell coating on both sides of the valve.
3. The free edge of the heart valve is constituted by an undamaged membrane.
4. As mentioned, a reinforcement of the membrane can be achieved by impregnating and/or coating the rough side with polymeric materials prior to the folding.
5. A further reinforcement can be achieved for example by inserting another suitable material between the two layers prior to the folding, for example polymeric materials, such as polyesters, arranged in parallel.
6. Neither the impregnation and/or coating material nor the reinforcement material is in direct contact with the circulating blood, for which reason it is not specically required that the materials be non-thrombogenic.

In connection with the folding the membrane may be stretched in the direction of the pleat before or during the stabilization and cross-linking known per se of the biological membrane with for example glutaraldehyde. This gives several advantages:

1. A considerable increase in the strength of the membrane is achieved because after the stabilization the orientation of the fibrils resulting from the stretching is maintained.
2. Decreased tendency to subsequent elongation in the stretching direction and thus change of the shape of the valve.
3. Greater uniformity between the biological and non-biological materials of the valve as regards expansion.

Prostheses of the invention are firstly the so-called valved right ventricular outflow patch which is used as a ceiling on a longitudinal incision over the outflow patch from the right ventricle out on the pulmonary artery in case of narrowings at this point, and where the valve prevents the blood from running back to the ventricle.

The invention further comprises prostheses with several, usually three, leaflets to replace the heart valves, such as the aortic valve, the valve of the pulmonary artery and the mitral and tricuspid valves. In the production of the three-leaflet valve prostheses the prosthesis may be given the shape of a tube for example after the folding and forming of the three leaflets, which tube may be circular or have any other desired cross section, such as oval or triangular, the marginal regions being joined, preferably by stitching.

Especially in the production of aortic valve prostheses of the invention it is preferred to form the base material as a narrow tape-shaped attachment margin which is attached, particularly by machine stitching and optionally by gluing in the form of two tapes on either side of a length of a folded biological membrane. When the portion of the membrane is removed that is disposed outside the attachment margin, a tongue-shaped leaflet is obtained. By stitching together three such leaflets in pairs along a section of their attachment margins, a flexible non-stented aortic valve prosthesis with flexible attachment margins is achieved which contrary to the above-mentioned known prostheses where the leaflets are attached to a stent, are not exposed to the above-mentioned abnormal stresses.

BRIEF DESCRIPTION OF THE DRAWINGS

The invention is illustrated in more detail in the drawing in which

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