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INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 6 : A61L 27/00, C12M 3/04 — A1

(11) International Publication Number: **WO 95/01810**

(43) International Publication Date: 19 January 1995 (19.01.95)

(21) International Application Number: PCT/GB94/01455

(22) International Filing Date: 5 July 1994 (05.07.94)

(30) Priority Data:

9314057.2	7 July 1993 (07.07.93)	GB
9314471.5	7 July 1993 (07.07.93)	GB
9314056.4	7 July 1993 (07.07.93)	GB
9314580.3	14 July 1993 (14.07.93)	GB
9320352.9	2 October 1993 (02.10.93)	GB
9320368.5	2 October 1993 (02.10.93)	GB

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(81) Designated States: AT, AU, BB, BG, BR, BY, CA, CH, CZ, DE, DK, ES, FI, GB, HU, JP, KP, KR, KZ, LK, LU, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SK, UA, US, VN, European patent (AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG).

Published
With international search report.

(54) Title: IMPLANTABLE PROSTHESIS, KIT AND DEVICE FOR MANUFACTURING THE SAME

(57) Abstract

An implantable prosthesis comprises a biocompatible, synthetic, substantially bioresorbable matrix material seeded with fibroblasts.

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IMPLANTABLE PROSTHESES, KIT AND DEVICE FOR MANUFACTURING THE SAME

The present invention relates to methods suitable for replacing or repairing broken or damaged connective tissue such as ligaments or tendons and to prostheses for use in such methods. Also disclosed is a device for use in forming such prostheses, as well as kits from which the prostheses can be formed.

It is known from United States Patent No. US5078744 to repair damaged ligaments such as the anterior cruciate ligament (ACL) by replacing part of the damaged ligament by a prosthetic ligament comprising purified connective animal tendon or ligament tissue fibres which are cross-linked and formed into groups of aligned fibres.

The most common method of repair or reconstruction of the ACL is to implant a prosthetic graft comprising autogenous tissues. Thus it is common surgical practice to harvest autogenous tissue eg. patellar tendon from the host and to form a prosthesis for implantation.

A number of synthetic non-bioresorbable materials have been used in the manufacture of prosthetic ligaments, the materials being chosen for their affinity for supporting or encouraging the ingrowth of fibroblasts, after implantation of the prosthesis.

According to the present invention there is provided an implantable prosthesis which, in a form prior to implantation in a host, comprises a biocompatible, synthetic, substantially bioresorbable matrix material seeded with fibroblasts.

By "synthetic", is merely meant a material which is not used naturally by the mammalian body in connective tissue repair or which is not a chemically modified form of such a material. Thus this term excludes collagen and artificially cross-linked collagen matrixes (although, if desired, collagen can be used in addition to the synthetic material).

The term "fibroblast" includes cells which are sometimes referred to as fibroblast, fibrocyte, tenocyte or synovioctye cells. This term also covers precursor cells to any of these cells.

By "substantially bioresorbable matrix material" is meant a three dimensional structure for supporting fibroblasts (which may be in the form of a scaffold, mesh or solid structure, for example) and which, in the implanted prosthesis, degrades substantially over time in a mammalian body, due to the chemical/biological action of body components (as opposed to simply breaking due to physical strain on to the prosthesis). Desirably after the prosthesis has been implanted in an adult human for five years (more preferably after only one year's implantation) the bioresorbable material will have degraded to such an extent so that it makes no substantial contribution to the structural integrity of the prosthesis.

Preferably the matrix may additionally comprise one or more of the following molecules: proteoglycans, glycosaminoglycans, fibronectin or its active binding domain, or one or more growth factors e.g. bone morphogenetic protein (BMP) fibroblast growth factor, angiogensis factor or other stimulatory factors.

In a further embodiment of the invention, the prosthesis or part thereof (e.g. area(s) of the prosthesis which will come into contact with bone after implantation), may be impregnated with osteoinductive or osteoconductive agents, to enable more easy infiltration by bone cells. Examples of suitable osteoinductive materials susceptible to infiltration include hydroxyapatite, freeze-dried or demineralised bone, growth factors (e.g. bone morphogenetic protein) etc. Impregnation may suitably be just before implantation of the prosthesis. Aptly such materials are incorporated into ends of the prosthesis.

In a further embodiment of the present invention, there is provided a method of repairing or replacing damaged connective tissue in a human or non-human animal comprising the steps of: incubating a biocompatible, synthetic, substantially bioresorbable

matrix material in the presence of a suitable culture medium and of fibroblasts under suitable conditions for fibroblast seeding on or in the matrix and thereafter implanting the seeded matrix into a host.

Examples of suitable substantially bioresorbable synthetic polymers include polylactide (PLA), polyglycolide (PGA), polydioxanone, poly caprolactone (PCL), polyhydroxybutyrate (ICI BIOPOL™), polyhydroxybutyrate-co-hydroxyvalerate (ICI BIOPOL™), polyanhydrides, polyorthoesters, polyorthocarbonates, polyaminocarbonates, polytrimethylene carbonate and co-polymers incorporating monomers from which the aforesaid polymers can be formed.

When the prosthesis according to the present invention comprises a copolymer, the copolymer may incorporate hydroxyvalerate and hydroxybutyrate monomers. In such copolymers the amount of hydroxyvalerate present may be from 1 to 47% mol. Other particularly suitable copolymers are PLA/PGA and PLA/PCL copolymers.

Composites of a plurality the above substantially bioresorbable materials may also be suitable as or as part of the matrix material.

The matrix be fabricated of two or more distinct materials (e.g. distinct fibre types) with different degradation rates, providing a two or more phase loss of mechanical properties with time. Also, the different fibre types may possess different mechanical properties. For example, highly extendable fibres may be combined with less extendable fibres. The matrix may be designed to elongate to a specified extent before the less extendable fibres prevent further extension. This design may be advantageous in exposing the cells to limited and controlled strain while protecting against damage to the forming tissue. For example, polycaprolactone fibres have a lower Young's modulus than polylactide fibres.

Furthermore, one polymer may be coated with another polymer. This is advantageous where the material of choice on the

basis of mechanical properties is not necessarily the material of choice for cell culture (unless it is modified). Here a more biocompatible polymer may be used to coat a less biocompatible base material. For example, polylactide provides a better substrate for fibroblast proliferation than polycaprolactone. Polycaprolactone fibres could be coated with polylactide to improve compatibility with fibroblasts.

As indicated above, copolymeric materials may be used. This can be advantageous where the copolymers possess degradation rates intermediate between the rates of the homopolymers of which they are composed. Therefore, the degradation rate may be controlled by controlling the composition of the copolymer. Also, production of copolymer fibres by fibre spinning or extrusion may yield fibres with mechanical properties superior to those of homopolymers. Polylactide-Polyglycolide copolymers are good examples of both of these points.

Suitable fibroblasts for use in seeding the matrix may be autogenic fibroblasts, allogenic fibroblasts or xenogenic fibroblasts. Preferably, the fibroblasts are autogenic. The fibroblasts may originate from for example the dermis, tendons or ligaments. The fibroblasts for use in seeding the matrix may comprise a mixture of one or more of the above types of fibroblasts. Where the fibroblasts are autogenic, it is preferable to isolate them from the dermis, as this avoids the need for extensive invasive surgery.

The fibroblasts may be obtained according to any suitable method. A preferred method is by carrying out a skin biopsy.

The matrix material may be seeded with fibroblasts by placing the matrix in a culture vessel containing an appropriate culture medium (e.g. DMEM), in the presence of fibroblasts and incubating under cell culture conditions. The fibroblasts may be suspended in the culture medium and the resultant suspension added to the culture vessel either before or after addition of the matrix. The

number of fibroblasts/ml of medium may be varied according to the degree of seeding it is desired to establish.

The prosthesis of the present invention may be used to either partially or totally replace a damaged ligament, tendon, cornea, dermis, dura (or other body part comprising connective tissue). Where the damage is substantial, the damaged ligament or tendon may be totally surgically replaced by the prosthesis. Where the damage is less substantial the matrix may be designed so as to be joined (e.g. by suturing) to the existing damaged ligament or tendon.

The matrix may be designed according to any one of a number of possibilities. Aptly the matrix is a fibrous structure. It may have loops or other structures at each end for aiding fixation to bone (using for example either the "two tunnel" or the "over-the-top" technique). It may be formed by any appropriate technique - e.g. braiding, knitting, weaving, crocheting etc. The matrix is desirably in elongate form and is preferably flexible.

The device may closely mimic the natural structure and fixation of the ligament or tendon. For example, for ACL reconstruction, the device could be composed of a hierarchy of fibres bundled together in fasicular units, passing directly from the femur to the tibia or taking a spiral path around the axis of the device. Fixation may be to the natural fixation areas of the ligament or tendon. Any appropriate fixation means may be used (e.g. screws, nails, staples or sutines). The fixation means may itself be bioresorbable, for example it may be formed of polyhydroxybutyrate.

The present invention further provides a kit for forming the prosthesis of the present invention comprising a synthetic biocompatible matrix material and a source of fibroblasts.

On incubation under suitable conditions, the fibroblasts will grow on and/or in the matrix, thus producing a matrix seeded with fibroblasts.

The kit may additionally comprise a suitable medium for the proliferation of fibroblasts.

Ideally the kit is presented in a sterile package. Alternatively the parts of the kit may be sterilised just before use. Prior to implantation, the components of the kit can be incubated together under appropriate culture conditions as above described to allow the fibroblasts to seed the prosthesis.

The fibroblasts may be in any suitable form ready for use. Thus aptly the fibroblasts may be cryopreserved.

The matrix, or components/precursors thereof, may be provided in lyophilised form.

In a preferred embodiment, the present invention comprises, an implantable prosthesis which in a form prior to implantation comprises a biocompatible synthetic substantially bioresorbable matrix material having a polymeric gel in intimate contact therewith, the gel having fibroblasts dispersed therein. This is advantageous in that the gel can support the cells in a true three-dimensional arrangement rather than merely supporting a monolayer on the surface of a material. The environment closely mimics the natural physiological environment of the cells. Also, incorporation of cells in a gel can provide for even cell distribution, preventing cells from pooling which might otherwise occur due to gravitational influence.

The present invention provides a method of repairing or replacing connective tissue in a human or other animal, comprising the steps of: incubating a biocompatible matrix material in the presence of a gel-forming composition and of fibroblasts under suitable conditions to form a prosthesis comprising a matrix contacting a polymeric gel, the gel having fibroblasts dispersed therein, and thereafter implanting the prosthesis into a host.

Suitable gel forming compositions include collagen gel forming compositions and fibrin gel forming compositions.

Fibroblasts in a collagen gel are capable of utilising the collagen and reorganising it. Under an appropriate mechanical stimulus they are capable of reorganising the fibrils into non-randomly orientated, organised structures resembling the natural ultrastructure of ligament and tendons. A mechanical stimulus may be the prevention of gel contraction which would otherwise occur over time by fixing the gel at two points. The matrix may be designed to achieve this. Alternatively, the gel on or in the matrix may be exposed to applied strain using a mechanised straining device to stimulate fibroblast alignment.

The method may comprise an additional step of incubating a gel-contacting matrix under suitable conditions for fibroblast proliferation in the gel and thereafter implanting the matrix into a host.

In the preferred embodiment of the present invention, the matrix is seeded by means of incubating the matrix in the presence of a suitable culture medium, a gel-forming composition and the fibroblasts to be seeded. An appropriate agent for causing gelation of the gel forming composition may also be used, if necessary.

Seeding the matrix in the presence of a gel-forming composition, fibroblasts (and a gelling agent, if required) results in a gel-coated or filled matrix, the gel having fibroblasts dispersed therein. The gel can be formed by the interaction of the gelling agent and the gel-forming composition. A preferred gel is a collagen gel. A Type I, II or III collagen solution may be prepared using an appropriate source of collagen. Thus for example a Type I collagen solution may be prepared from dermis (Type I collagen forms up to 70% of extracellular protein found in skin) as above described. Alternatively a Type I collagen solution may be prepared tendons, e.g. rat or bovine tendons, which comprise almost exclusively Type 1 collagen. The collagen may be extracted according to any of the standard methods known by those skilled in the art.

There are a number of suitable ways of incorporating the gel in or on the matrix. For example, the matrix may be suspended in such a manner that the gel-forming solution (optionally comprising fibroblasts) completely surrounds the matrix. A mould which surrounds the matrix may be used. Centrifugation or suction may alternatively be used to direct gel towards the matrix.

A kit for use in forming the prosthesis of the preferred embodiment can comprise a biocompatible matrix, a gel-forming composition and a source of fibroblasts.

Alternatively the kit may comprise a biocompatible matrix having a coating comprising a polymeric gel and/or having a polymeric gel incorporated therein and a source of fibroblasts. On incubation under suitable conditions the fibroblasts can invade the gel, thus producing a matrix bearing a gel having fibroblasts therein.

The prosthesis of the present invention offers an advantage over previously known prostheses which were designed to enhance ingrowth of fibroblasts after implantation and act as a scaffold through which fibroblasts can grow and form a new ligament, since it comprises fibroblasts prior to implantation. Thus the damaged tissue may be replaced by a prosthesis comprising viable fibroblasts which may be replicating. The fibroblasts may already substantially be aligned on implantation or at least oriented in a non-random manner. This process is speedier than previously known methods which rely on infiltration of prostheses by fibroblasts after implantation. It will be clear that the prosthesis may be implanted after an initial predetermined incubation period timed to result in seeding of the prosthesis with fibroblasts. Alternatively the prosthesis may be incubated for a longer incubation period than the initial incubation period so that the fibroblasts will be replicating and will have already started to secrete collagen fibrils when the prosthesis is implanted.

The prosthesis and method of the present invention offers other advantages over the common surgical practice or harvesting

host patellar tendon in that it avoids the need for carrying out an extensive surgical operation to harvest the tendon. A simple skin biopsy (a standard procedure which does not result in substantial scarring) can be used to obtain fibroblasts which can then be proliferated in culture. In addition, the prosthesis can be designed to optimise fibroblast orientation. The cumulative effect of these advantages can result in a reduction in the length of a hospital stay.

In one preferred embodiment of the present invention, where a collagen gel contacts the matrix, the prosthesis of the present invention provides a source of collagen which can be used by the fibroblasts. The collagen in the gel is preferably in a non-cross-linked form.

In another preferred embodiment of the present invention a fibrin gel is used.

According to a further aspect of the present invention there is provided a device for culturing cells for use in forming a prosthesis according to the present invention, comprising a chamber for maintaining fibroblasts in a viable condition, the chamber being provided with means for releasably securing the matrix material and means adapted for applying strain to the matrix material along a single axis only. Such a device can be included in a kit as aforesaid.

If several straining means are present, the device of the present invention can apply strain to a plurality of samples at any one time. Thus the device may have one or more chambers adapted to retain a culture medium and may be provided with means for releasably securing a plurality of matrix materials. This may be done simultaneously. Each of several chambers may be provided with means for releasably securing a plurality of matrix materials. Alternatively each chamber may be provided with means for releasably securing a single matrix material.

A chamber may be permanently fixed within the device. Alternatively the chamber may be releasably fixed so that it may be

removed from the device as desired, e.g. the chamber(s) may be removed to facilitate the securing and release of the matrix material.

A chamber may be made from any material which may be sterilised by suitable methods of sterilisation, e.g. gamma irradiation, steam sterilisation or ethylene oxide (ETO) sterilisation.

A chamber may have any desirable shape and size. Suitably the chamber may be cylindrical, cuboid or spherical. The dimensions of the chamber should be such that they enable the matrix material to be secured and to be subsequently extended on the application of strain. The device of the present invention can be adapted to apply a strain which causes e.g. up to 100% extension of the matrix material (relative to the material in unextended form). Generally speaking however, an extension of up to 10%, or of up to 5% may be sufficient.

Thus the dimensions of the chamber can be such that they enable the matrix material to be extended to the desired level.

The dimensions of a chamber are desirably such that the chamber has a capacity of up to $75cm^3$, e.g. up to $50cm^3$. The chamber may be made from any suitable material, e.g. stainless steel or Perspex™ material. Preferably the material is autoclavable to facilitate sterilisation.

Preferably the chamber is provided with a transparent or translucent window to enable the matrix material to be viewed during the time of culture. Examples of suitable materials include glass and polymethylmethacrylate (PERSPEX).

The chamber may comprise a closure, which may be removably or hingedly mounted to allow access to the inside of the chamber. Thus for example the chamber may comprise a glass cylinder wherein at least one of the ends is removable. Aptly the chamber may be collapsible or telescopic.

The chamber is desirably thermostatically controlled and may be heated via a water jacket or other heating means. It may be provided with various sensors e.g. sensors of the CO_2 content within a head space of the chamber. A CO_2 source may also be provided.

The matrix material may be releasably secured by securing means within the chamber.

The means for applying strain may compare two elements which are movable within the chamber so that the spacing between the elements can be varied. Alternatively one element may be movable but the other may be fixed.

The securing means may be any suitable means for releasably securing the matrix sample. The design of the securing means depends upon the design of the ends of the matrix material. Thus for example where the matrix material comprises looped ends the securing means may comprise a pair of clips or hooks. Suitably the securing means may comprise for example a chuck or a lathe or jaws which may screw together or be held by springs. Aptly the securing means may be in the form of a slot or other opening such that the ends of the matrix material are designed to fit thereon. Thus for example the ends of the matrix material may be embedded in a resin which may be retained in a slot. The opposite arrangement can be used in which the opening is in the matrix material and the securing means fit therein. A yet further way of releasably securing the matrix material is to provide a spool, which may be generally cylindrical, about which matrix material can be wrapped and held in position by friction. The spool may be held in place by a gripping device. Two such spools may be provided - one for each of two gripping devices.

The matrix material to which strain is to be applied by the device of the present invention may comprise any suitable material for supporting viable cells. Cells may be present in or along the entire length of the matrix material. Alternatively part of the matrix

material, e.g. the ends thereof, may have no cells. The cells may be applied to the matrix material either before or after the matrix material has been secured under extension. It is preferable however to apply the cells to the material before securing the material under extension in the chamber.

The matrix material may be designed in the form of a prosthetic ligament or tendon. Where for example the matrix material is in the form of a prosthetic ligament, the ligament when unstrained is preferably in the range of from 1 to 30cm long. The matrix material should be chosen so that it is suitable for withstanding the magnitudes of strain which it will be subjected to on implantation, e.g. in the knee.

The means for applying strain may act by pulling both ends or one end of the matrix material, resulting in an extension of the matrix material. This may be done by various means, e.g. mechanical, electrochemical, electrical, piezoelectric, pneumatic, hydraulic or other means. The matrix material may be releasably attached to a stationary element at one end of the chamber and the opposing end of the matrix material may be attached to a tension applying member (for example a winding device). Suitably strain may be applied to the matrix material by means of a diaphragm, one side of the diaphragm lying within the chamber and the opposing side lying outside the chamber. A pivotally mounted lever may be used to apply strain.

The present invention also provides a method of culturing cells under strain which method comprises the steps of releasably securing a matrix material having viable cells in intimate contact therewith in a chamber, the chamber comprising an adequate amount of culture medium to cover the matrix and cells, and applying strain to the matrix material along a single axis.

Materials suitable for use in a matrix of the present invention can be assessed as exemplified below:-

Assessment of Materials

In order to make an initial assessment of suitable materials for supporting fibroblast growth, various materials were obtained (which are not to be construed as limiting), as indicated in Table 1 below, and moulded into films for 5min at 2.5 Tons at the following temperatures: Polylactide 170°C; polyglycolide, 245°C; polyhydroxybutyrate, 185°C; and polycaprolactone, 65°C.

Table 1

Material	Supplier	Fig.
Polylactide	Medisorb, Cincinnati, Ohio, USA	1a
Polyglycolide	Medisorb, Cincinnati, Ohio, USA	1b
Polyhydroxybutyrate	Goodfellows, Cambridge, UK	1c
Polycaprolactone	Birmingham Polymers Inc. Alabama, USA	1d

Fibroblasts were seeded onto the surfaces of these materials at a density of 1×10^4 cells/cm^2 of material and incubated for 3 days under culture conditions.

After the incubation period, photomicrographs were taken of the cell-seeded samples. These are shown in Figs. 1a to 1d for the samples indicated in Table 1 above (photocopies of all of the photographs provided for this application are provided immediately after the relevant photographs).

Fibroblasts can be seen to be well adhered to the surfaces of all of the materials and to exhibit the morphology typical of healthy cultural fibroblasts.

One sample of fibroblasts was grown on polylactide as described above apart from the fact that a longer (16 day) culture period was used.

After this period the cells were stained with a viable stain (calcein AM (2μM)) and visualised by fluorescence microscopy using a fluorescein filter. A confluent monolayer of viable cells was observed, showing that polylactide is capable of supporting viable fibroblasts for extended periods of culture.

Figure 2 is a graph showing the relative rate of proliferation of fibroblasts on four examples of bioresorbable synthetic materials: polylactide (PLA); polyglycolide (PGA) polyhydroxybutyrate (PHB) and polycaprolactone (PCL) (all as described above) in comparison with a tissue culture treated polystyrene (TCP) control (since TCP is known to support good fibroblast growth).

Figures 2a) to e) show each of these materials on a single graph (for each of reference). Cells were seeded at 1 $x10^4$ cells.cm^{-2} in triplicate and the rate of proliferation determined by measuring the uptake of tritiated thymidine into cellular DNA at timepoints up to 7 days after incubation using standard cell culture techniques. The medium was changed at 2, 4 and 6 days. The points represent the mean of three determinations and the error bars represent the range. All polymers supported fibroblast proliferation.

Figure 3 is a photomicrograph of fibroblasts embedded within a three dimensional collagen gel after 15 days of culture. The cell-seeded gel was prepared as described in example 2 (which will be described later) apart from the fact that it was not used to contact a matrix. The gel provides a three-dimensional structure in which the cells are embedded and can form interactions with collagen molecules via membrane integrin receptors. The cells are randomly arranged, exhibit long processes and are capable of reorganising collagen fibrils within the gel.

Figure 4 is a photomicrograph of fibroblasts embedded within a three dimensional collagen gel as described for Fig. 3 above, apart from the fact that the gel has now been constrained from contracting in one direction by two stainless steel pegs glued to a culture dish with a tissue culture compatible adhesive. The cells are arranged in a highly orientated fashion, their long axes being parallel to the axis between the contraining pegs. The collagen fibrils align along the same axis. This effect is due to the pegs preventing the gel contracting, as would otherwise occur in the presence of fibroblasts in culture.

The following examples, which are not to be construed as limiting, illustrate how various cell-seeded matrixes can be produced.

Example 1 : Preparation of a fibroblast seeded polylactide matrix prosthesis

a) Preparation of Cells

A biopsy is washed three times in phosphate buffered saline (PBS), and rinsed in 70% alcohol. The rinsed biopsy is then dipped into Dulbecco's Modified Essential Medium (DMEM) and incubated at 37°C for 24 hours. After incubation, the biopsy is cut into small pieces under PBS. The cut pieces are transferred to a 50mm petri dish, containing about 5ml of collagenase solution to allow digestion. The epidermal sheets are removed from the collagenase solution. The resultant solution is centrifuged. The fibroblast cell pellet is resuspended in DMEM and thereafter seeded in a 35mm petri dish using DMEM. The cells may be confluent in from 2-4 days. Thereafter the cells may be cultured to provide an appropriate quantity of fibroblasts for seeding the matrix.

A suitable medium for culturing the isolated fibroblasts may comprise DMEM which may be supplemented with the following: glutamine, foetal calf serum, non essential amino acids and antibiotics. In addition the medium may have a buffering agent such as bicarbonate.

b) Preparation of matrix material

A polylactide matrix material suitable for use in a prosthesis for replacing a ligament can be prepared by obtaining polylactide fibres and then braiding them to form a braid of appropriate dimensions to replace the ligament.

Polylactide fibres can be obtained by extrusion, fibre spinning, melt-spinning, drawing, heat annealing etc.

Braiding of the fibres can be done by standard braiding techniques, the length and thickness of the braid, number of fibres present and diameter of fibres present being selected to form a braid with appropriate properties.

The ends of the device are constructed in a suitable way to aid fixation of the device by a screw or other fixation means. This is done by forming eyelets at the ends.

c) Seeding of matrix material with cells

The braided device is incubated in a medium containing 10% v/v serum for 24 hours and is then seeded with cells by pipetting a cell suspension over the surface of the matrix material until the latter is completely covered with cell suspension. (Alternatively the matrix may be incubated together with the cell suspension for a period of about six hours under conditions of agitation, e.g. on a bottle roller. Other alternatives are to seed the device by sucking cell suspension through it under vacuum (if it is porous) or by centrifuging cell suspension through the device).

d) Straining of the cell-seeded matrix

The cell seeded device is gripped at both ends in a straining apparatus which causes the device to be strained along a single longitudinal axis. This is done for sufficient time so as to cause the fibroblasts substantially to align along the general direction of the longitudinal axis, as can be assessed by microscopic analysis of the cells. The apparatus comprises a culture chamber so that straining can occur over several hours or even several days and yet the cells can remain viable. Typically the device is strained at 37°C.

During straining a culture medium is used to culture the cells under suitable conditions. This includes serum, ascorbate or stable analogues thereof, together with growth factors.

The ascorbate stimulates the fibroblasts to synthesise collagen; the serum contains factors promoting cell proliferation and cell adherence and the growth factors can stimulate cell proliferation, development and migration.

e) Implantation of the cell-seeded matrix

Once the cell-seeded device has been strained for a sufficient period to obtain a desired degree of alignment of fibroblasts, it is removed from the cell-straining device and implanted into a patient by any desired technique.

Minimal invasive surgery is preferred. For a prosthetic anterior cruciate ligament implantation be done utilising the "two-tunnel" or the "over the top" techniques. Fixation can be achieved by using screws (or other fixation elements) placed through the eyelets of the matrix. The screws are suitably formed of a biodegradable material, such as polyhydroxybutyrate.

Example 2 : Preparation of a fibroblast seeded polylactide matrix prosthesis comprising a collagen gel in which the fibroblasts are incorporated

This can be done in an analogous manner to the method described in Example 1, except for the inclusion of an alternative procedure whereby fibroblasts are incorporated in a collagen gel which is used to seed the polylactide matrix. This extra procedure is described below:-

a) Preparation of collagen

It is desired to form the collagen in a form which is acid soluble and which is not cross-linked. This can be done as follows:-

Type I collagen is prepared from tendon but could be from other tissue e.g. skin. The tissue is minced finely, disinfected in 70% (v/v) ethanol for at least 30 mins, dispersed in acetic acid (1% v/v) and incubated with agitation at 4°C. The supernatant is removed and neutralised by addition of an appropriate volume of 1.0M sodium hydroxide. The precipitated type I collagen is pelleted by centrifugation at 8,000 x g and the pellet resuspended in an appropriate volume of acetic acid (1% v/v). The collagen concentration of this solution is determined by any appropriate method (e.g. a total protein assay - the BCA assay) and the concentration of the collagen solution adjusted appropriately (e.g. $3mg.ml^{-1}$ can be used).

If the product is a kit, sterile collagen solution may be lyophilised and stored under vacuum or an inert gas (e.g. argon) to prevent cross-linking. A diluent (acetic acid) could also be provided. Alternatively, it could be provided as a solution and stored at 4°C to -20°C.

b) Seeding of matrix material with cells

Three components are typically used to seed the matrix:- cells suspended in an appropriate medium, collagen solution and a gelling agent - (e.g. 1M sodium hydroxide). The final collagen concentration may be approximately $1mg.ml^{-1}$ and the seeding density approx. $3x10^4$ cells per ml of gel (or volume within the matrix). The three components are maintained at 0°C to 4°C, mixed and added to the matrix. Once the matrix is fully impregnated, it is incubated at 37°C and gelling is initiated.

The impregnation of the matrix may be achieved by any suitable method. The matrix may be merely immersed in the solution within a mould. Alternatively the solution may be sucked into the scaffold by use of a vaccum or forced in by centrifugation (for example within a mould centrifuged at 500rpm for 5min at 0-4°C).

The rate of setting of the gel may be varied by varying the temperature.

Example 3 : Preparation of a fibroblast seeded polylactide matrix prosthesis comprising a fibrin gel in which the fibroblasts are incorporated

This can be done by an analogous method to that described in Example 2, except that a fibrin gel rather than a collagen gel is used.

Again, three components are used: cell suspension, fibrinogen solution and thrombin solution containing calcium chloride (mM). The final cell concentration may be $3x10^4$ cells per ml, the fibrinogen concentration may be 3mg/ml, the thrombin activity 2.5 Units/ml and the calcium chloride concentration 5mM. The reagents are mixed and then incubated with the matrix. Once impregnated with the solution, the matrix is incubated at 37°C to allow rapid gelling. Impregnation of the matrix may be conducted by any of the techniques described above.

The rate of gelling may be varied by varying the thrombin activity and/or the temperature.

The cell straining device referred to previously will now be described by way of example only with reference to Figs. 5 a), b), c), d), and e) which show various components which can be put together to form the device.

The device comprises a Perspex™ container 10 (shown in cut-away section) and lid 20 (see Figs. 5a) and 5e)). Container 10 can be used to contain an extensible material seeded with fibroblasts under cell culture conditions. For ease of reference thermostats, sensors, inlets for topping up culture media and other components which would be well known to those skilled in the art are not shown.

The device further comprises first and second grips 30 and 40, each of which has two parallel arms 45 bearing pegs 50 (see Figs. 5c) and e)).

One of the grips (grip 40) is provided with a support 60 which can be moved towards or away from the other grip 30 along a single longitudinal axis by a motor (not shown). The other grip 30 is fixedly mounted to an end wall 35 of the device.

The grips 30 and 40 function to receive and hold spools 70 and 80 (see Figs. 5c) and 5e)). This is achieved by pegs 50 fitting into grooves 90, thereby attaching the spools 70 and 80 to grips 30 and 40 in a manner which prevents rotation of the spools 70 and 80 relative to the grips 30 and 40 respectively.

Spools 70 and 80 function to hold an extensible material seeded with fibroblasts, indicated by cell seeded polylactide braid prosthesis 100.

This is achieved by threading opposite ends of the prosthesis 100 through apertures 110 and 120 and then rotating the spools 70 and 80 several times about axes A and B respectively so that the prosthesis 100 is secured to the spools 70 and 80 by friction (see Fig. 5b).

The spools 70 and 80 can then be slotted onto grips 30 and 40 as aforesaid (see Fig. 5c) and the prosthesis 100 can be extended by causing support 60 to retract within the container so that grips 30 and 40 become increasingly spaced. Once a desired degree of extension has been achieved support 60 can be held in position by a releasable locking device (not shown) and the extended prosthesis 100 can be incubated under culture conditions for as long as desired.

In order that the prosthesis 100 can be easily seen a window 130 is provided formed of a transparent on translucent material. This can be used for microscopic analysis of fibroblasts growing on the prosthesis 100 in order to determine when the prosthesis 100 is ready for implantation.

A grooved transparent or translucent block 140 is also provided for positioning at the bottom of container 10 (see Fig. 5d). The block is sized so that groove 150 can accommodate sufficient culture medium to cover the prosthesis 100 when positioned on spools 70 and 80 with the spools 70 and 80 being held by grips 30 and 40. This enables economical amounts of culture medium to be used.

The materials used to form the components of the straining device are autoclavable and sterilisable with alcohol. Typically the device is operated at a temperature of 37°C and with an atmosphere of 5% CO_2.

CLAIMS

1. An implantable prosthesis which in a form prior to implantation comprises a biocompatible, synthetic, substantially bioresorbable matrix material seeded with fibroblasts.

2. A prosthesis according to claim 1 wherein the bioresorbable matrix material comprises a polylactide, a polyglycolide, a polydioxanone, a poly caprolactone, a polyhydroxybutyrate, a polyhydroxybutyrate-co-hydroxyvalerate, a polyanhydride, a polyorthoester, a polyorthocarbonate, a polyaminocarbonate, a polytrimethylene carbonate or a co-polymer which incorporates monomers from which the abovementioned polymers are formed.

3. A prosthesis according to claim 1 or claim 2, further comprising a non-bioresorbable matrix material.

4. A prosthesis according to claim 3 wherein the non-bioresorbable matrix material is a polyester, a polyethylene, a polypropylene, PTFE, carbon fibre, or a composite of two or more of the aforesaid materials.

5. A prosthesis according to any preceding claims wherein the matrix further comprise one or more of the following:- proteoglycans, glycosaminoglylycans, fibronectin or its active binding domain, growth factors, osteoinductive or osteoconductive materials.

6. A prosthesis according to any preceding claim wherein the prosthesis comprises a gel in intimate contact with the bioresorbable matrix material, the gel having fibroblasts dispersed therein.

7. A prosthesis according to claim 6, wherein the gel is a collagen or fibrin gel.

8. A prosthesis according to claim 7 wherein the gel is in the form of a coating and/or a filling.

9. A prosthesis according to any of claims 6 to 8, wherein the bioresorbable matrix material is polyhydroxybutyrate or a copolymer incorporating a plurality of hydroxybutyrate monomers.

10. A prosthesis according to any preceding claim wherein the matrix is flexible.

11. A prosthesis according to any preceding claim which is in the form of a fibrous member.

12. A prosthesis according to any preceding claim which is in the form of a woven, knitted, crocheted or braided member.

13. A prosthesis according to any preceding claim comprising a plurality of bioresorbable matrix materials having different rates of bioresorbtion.

14. A prosthesis according to any preceding claim, wherein the fibroblasts are non-randomly oriented.

15. A prosthesis according to claim 14 wherein the fibroblasts are substantially aligned.

16. A kit for producing a prosthesis according to claim 1 comprising a fibroblast cell source or a device adapted for extracting fibroblasts from a mammalian body and a bioresorbable matrix material.

17. A kit for producing a prosthesis according to claim 6 comprising a fibroblast cell source or a device adapted for extracting fibroblasts from a mammalian body, a bioresorbable matrix material and a polymeric gel or a composition for forming the polymeric gel.

18. A device for use in manufacturing a prosthesis according to claim 14 or claim 15, wherein the device comprises a chamber for maintaining fibroblasts in a viable condition, the chamber being

provided with means for releasably securing the matrix material and means adapted for applying strain to the matrix material along a single axis only.

19. A method of repairing or replacing damaged connective tissue in a human or animal, comprising incubating a biocompatible synthetic substantially bioresorbable matrix material in the presence of a suitable culture medium and of fibroblasts under suitable conditions for fibroblast seeding on or in the matrix and thereafter implanting the matrix seeded with fibroblasts into a host.

20. A method according to claim 19 further comprising the step of applying strain to the matrix material when seeded with fibroblasts so as to cause non-random orientation of the fibroblasts.

21. A method according to claim 19 wherein the non-random orientation is a substantial alignment of fibroblasts.

22. A method according to claim 20 or claim 21 wherein the fibroblasts are incorporated in a gel.

23. A method according to claim 22 wherein the gel is a collagen gel or a fibrin gel.

Fig 1a

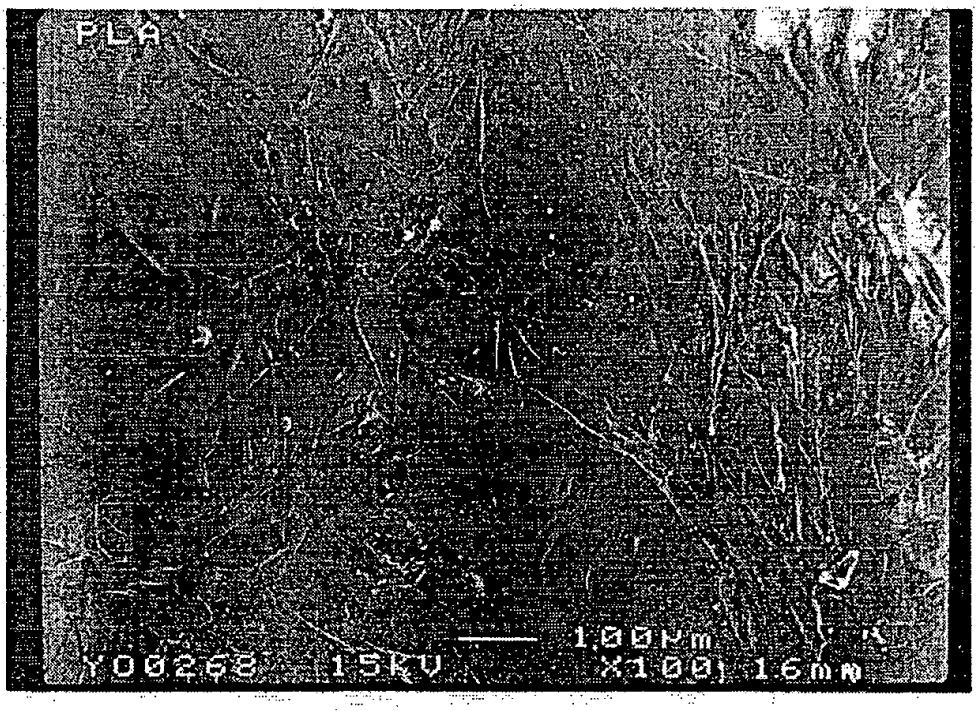


Fig 1b

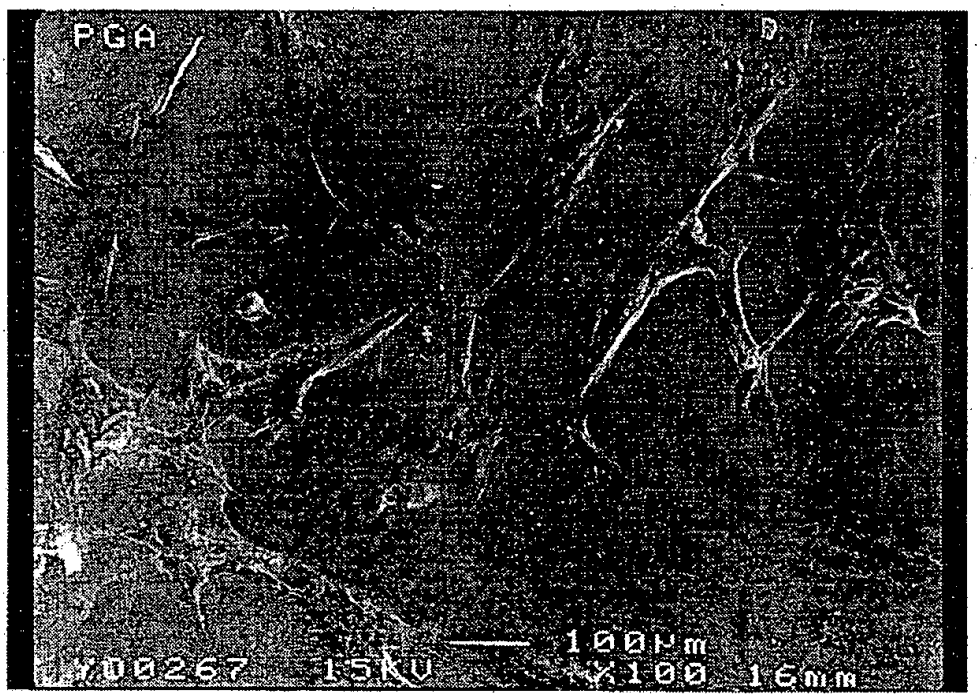


Fig 1c

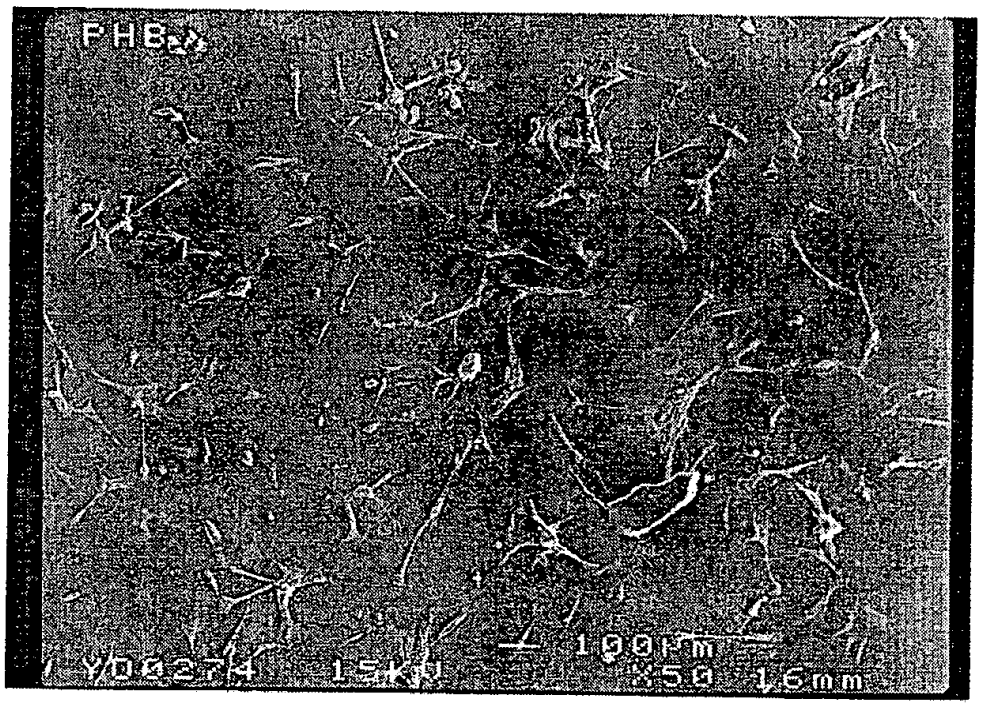


Fig 1d

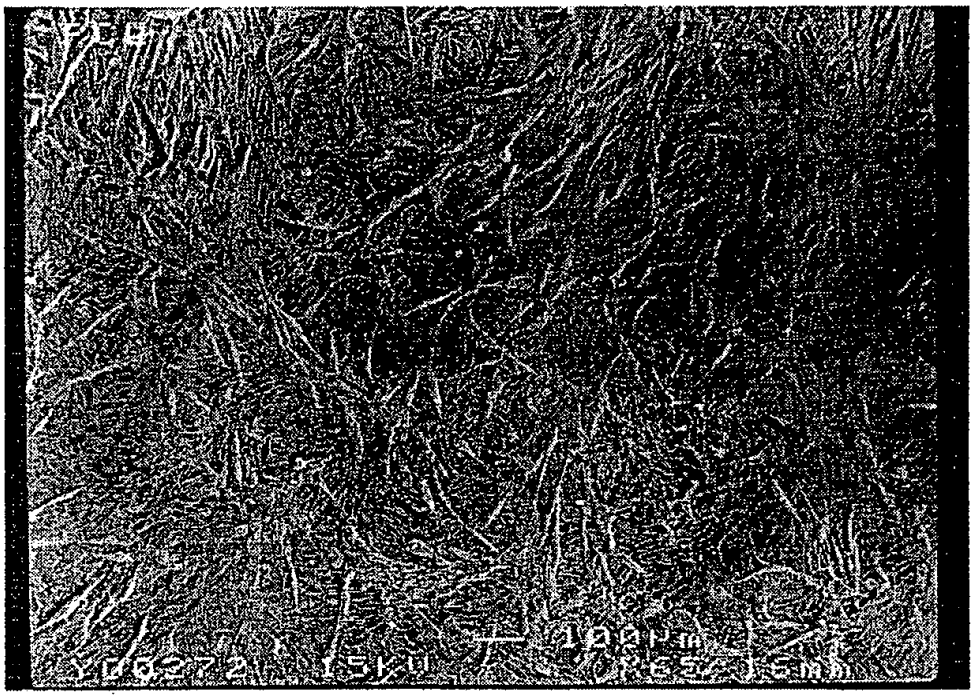


Fig 2a

Cell Proliferation on Tissue Culture Plastic

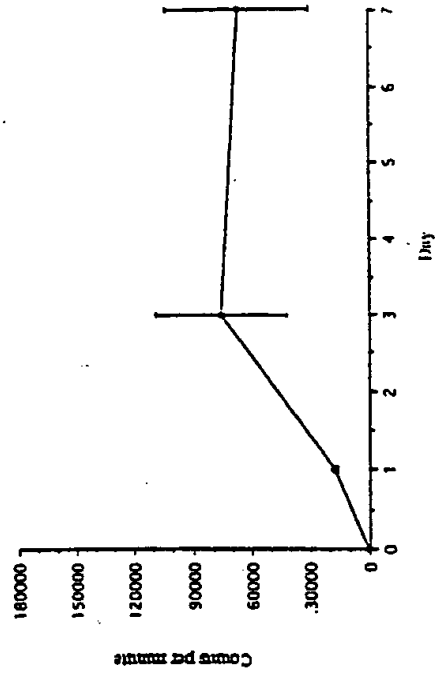


Fig 2c

Cell Proliferation on PHB

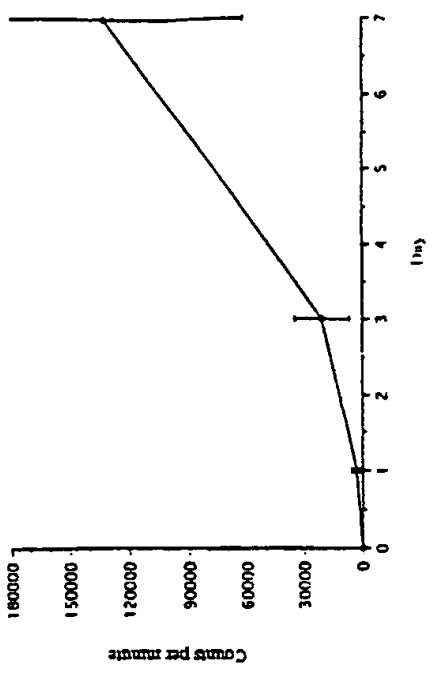


Fig 2

Cell Proliferation on a Range of Polymers

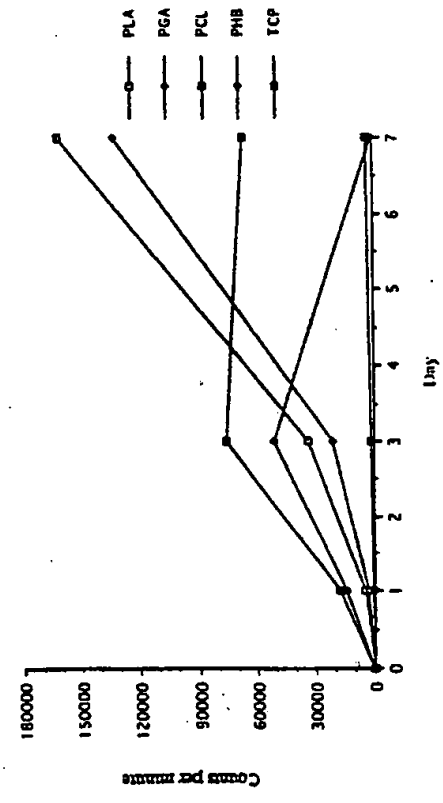
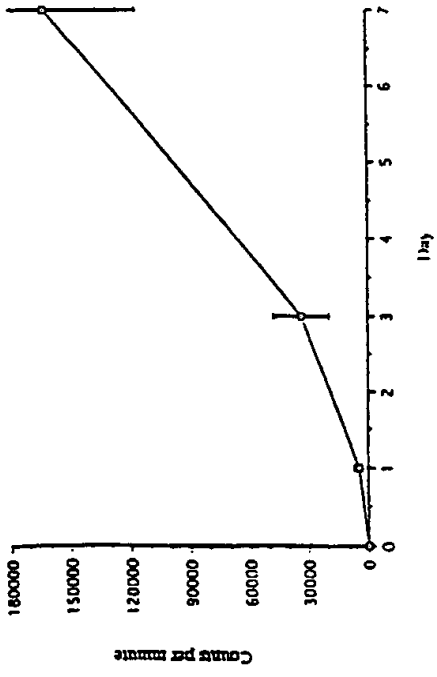


Fig 2b

Cell Proliferation on PLA



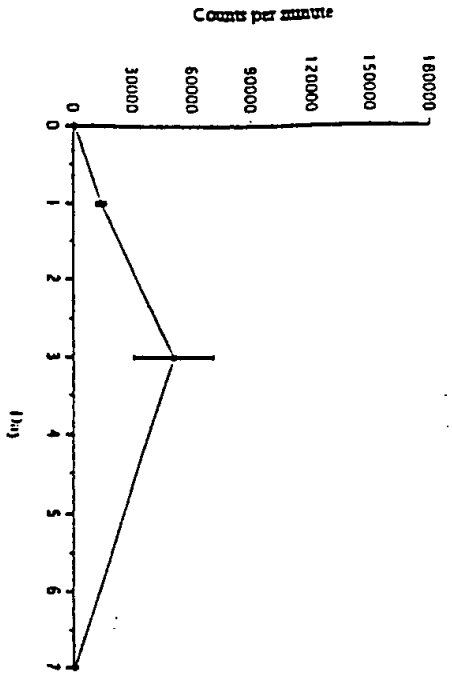


Fig 2d.

Cell Proliferation on FGA

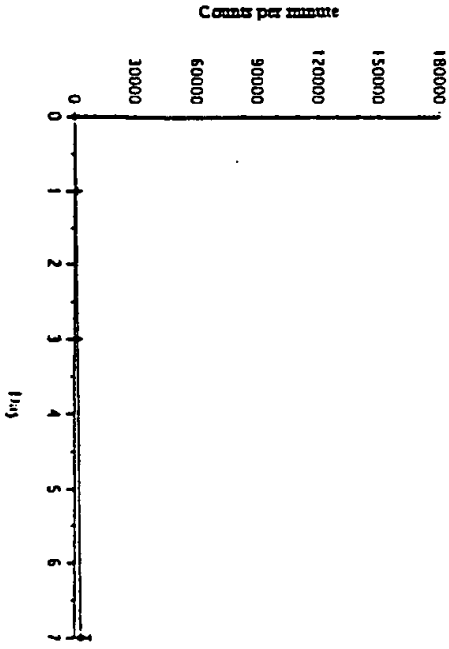


Fig 2e

Cell Proliferation on FCL

Fig 3

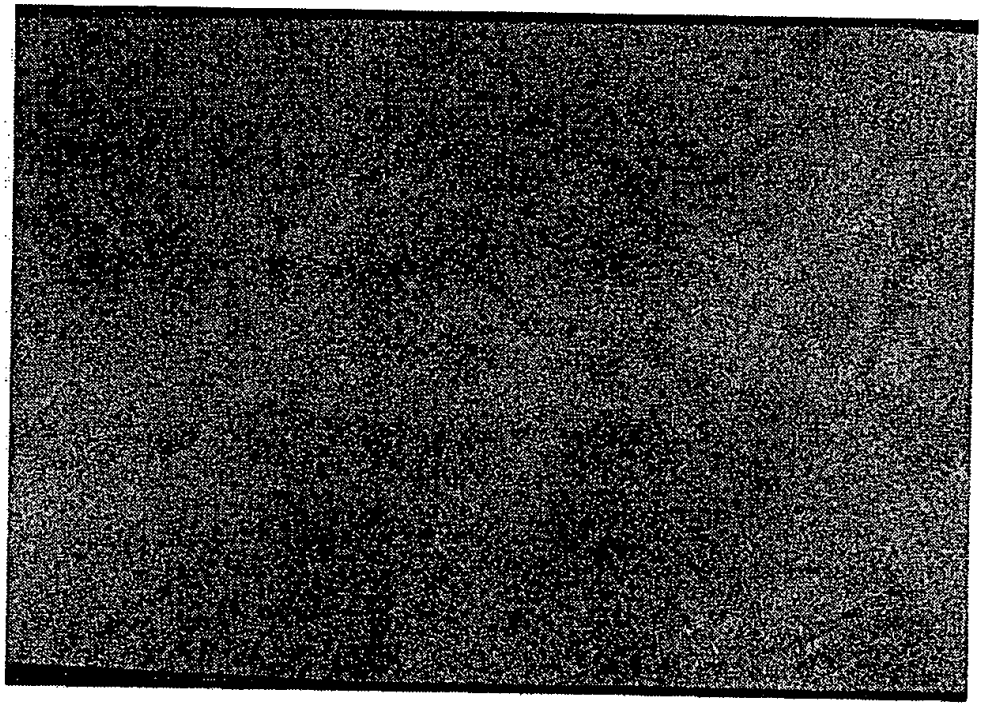


Fig 4

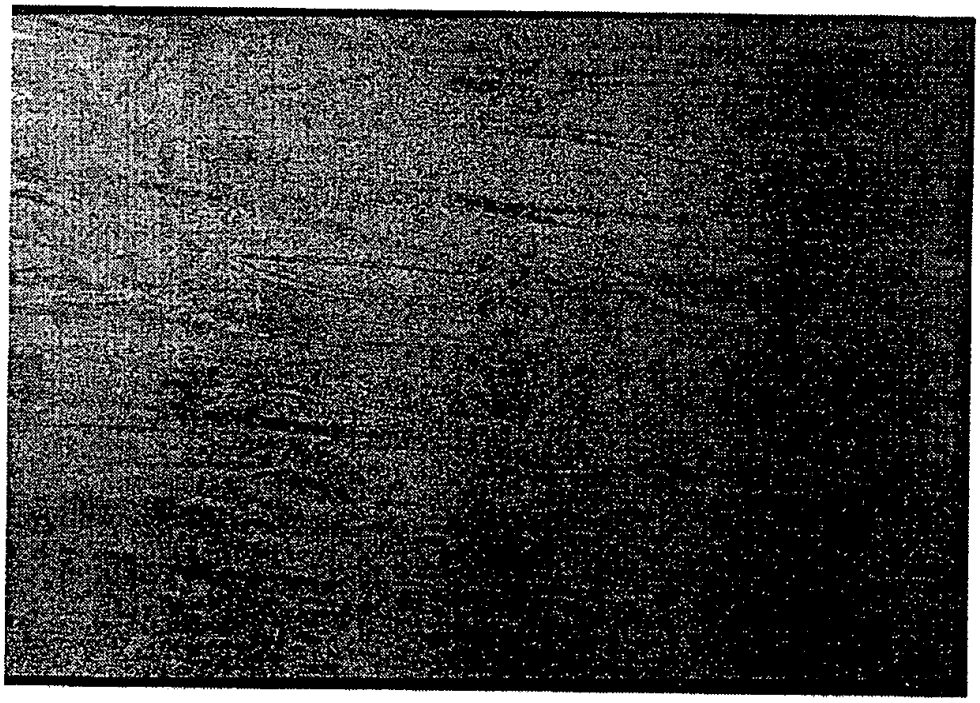
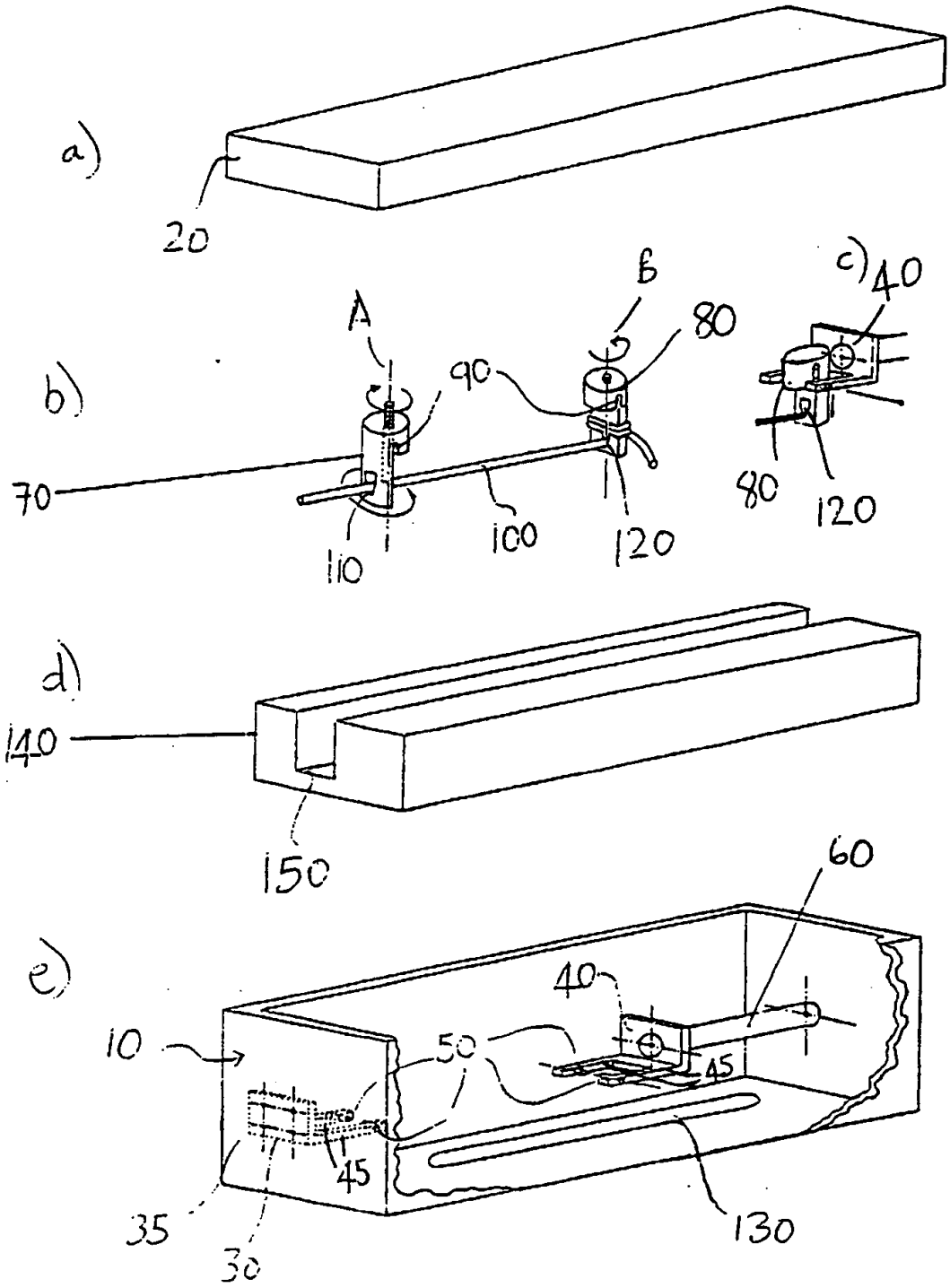


Fig 5


a)
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INTERNATIONAL SEARCH REPORT

International application No.
PCT/GB 94/01455

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 A61L27/00 C12M3/04

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 6 A61L C12M

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)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO,A,90 12603 (VACANTI, JOSEPH, P. ET AL.) 1 November 1990 see page 6, line 9 - line 28 see page 8, line 13 - line 33 see page 11, line 23 - line 35 ---	1-15
X	WO,A,88 03785 (VACANTI JOSEPH, P. ET AL.) 2 June 1988 see page 22, line 14 - line 28; claims ---	1-3
X	WO,A,85 04185 (CAPLAN, ARNOLD, I.) 26 September 1985 see claims ---	1
Y	WO,A,92 15259 (COLORADO STATE UNIVERSITY RESEARCH FOUNDATION.) 17 September 1992 see claims --- -/--	1-23

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

[X] Patent family members are listed in annex.

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Date of the actual completion of the international search	Date of mailing of the international search report
12 October 1994	28. 10. 94
Name and mailing address of the ISA European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+ 31-70) 340-2040, Tx. 31 651 epo nl, Fax (+ 31-70) 340-3016	Authorized officer ESPINOSA, M

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	WO,A,93 07913 (CHILDREN'S MEDICAL CENTER CORPORATION.) 29 April 1993 see claims	1-23
P,Y	WO,A,93 19701 (BAXTER INTERNATIONAL INC.) 14 October 1993 see examples 1-3	1-23
A	WO,A,93 08850 (MASSACHUSETTS INSTITUTE OF TECHNOLOGY) 13 May 1993 see page 8, line 3 - line 26; claims	1

2

Form PCT/ISA/210 (continuation of second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

International application No.
PCT/GB94/01455

Box I Observations where certain claims were found unsearchable (Continuation of item 1 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.: 19-23
because they relate to subject matter not required to be searched by this Authority, namely:
Remark: Although claims 19-23 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

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 II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

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

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

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

3. [ ] As only some of the required additional search fees were timely paid by the applicant, this international search report covers 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.

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

Form PCT/ISA/210 (continuation of first sheet (1)) (July 1992)

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No.
PCT/GB 94/01455

Patent document cited in search report	Publication date	Patent family member(s)		Publication date
WO-A-9012603	01-11-90	US-A-	5041138	20-08-91
		AU-B-	635025	11-03-93
		AU-A-	5556890	16-11-90
		CA-A-	2051663	18-10-90
		EP-A-	0469070	05-02-92
		JP-B-	6006155	26-01-94
		JP-T-	4505717	08-10-92
WO-A-8803785	02-06-88	EP-A-	0299010	18-01-89
		JP-T-	1501362	18-05-89
		US-A-	5041138	20-08-91
WO-A-8504185	26-09-85	US-A-	4609551	02-09-86
		AU-A-	4153985	11-10-85
		EP-A-	0175762	02-04-86
WO-A-9215259	17-09-92	US-A-	5192312	09-03-93
		AU-A-	1577792	06-10-92
		CA-A-	2105478	06-09-92
		EP-A-	0574527	22-12-93
WO-A-9307913	29-04-93	AU-A-	2900792	21-05-93
WO-A-9319701	14-10-93	NONE		
WO-A-9308850	13-05-93	CA-A-	2121040	13-05-93
		EP-A-	0610423	17-08-94

Form PCT/ISA/210 (patent family annex) (July 1992)

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INTERNATIONAL APPLICATION PUBLISHED UNDER

(51) International Patent Classification 6 :
A61B 17/70

A1

(11) In

WO 9608205A1

(43) International Publication Date: 21 March 1996 (21.03.96)

(21) International Application Number: PCT/US95/11281

(22) International Filing Date: 8 September 1995 (08.09.95)

(30) Priority Data:
08/306,879 15 September 1994 (15.09.94) US

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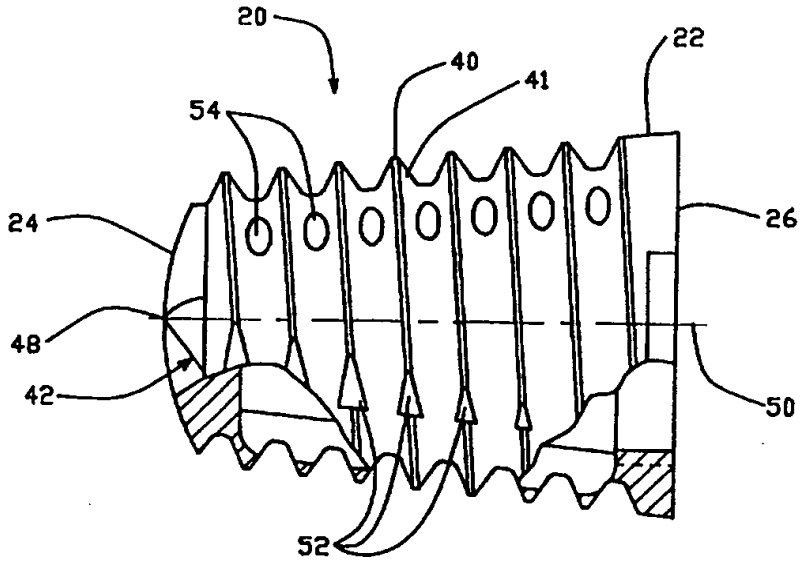
(74) Agent: MEYER, Sheldon, R.; Fliesler, Dubb, Meyer and Lovejoy, Suite 400, Four Embarcadero Center, San Francisco, CA 94111-4156 (US).

(81) Designated States: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TT, UA, UG, UZ, VN, European patent (AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG), ARIPO patent (KE, MW, SD, SZ, UG).

Published
With international search report.

(54) Title: CONICALLY-SHAPED ANTERIOR FUSION CAGE AND METHOD OF IMPLANTATION



(57) Abstract

A fusion cage (20) for anterior vertebral body fusion is conically shaped and includes a rounded distal end (24). A thread (40) is formed as part of the external conical surface of the fusion cage (20). The thread (40) defines one or more flutes (52) which enhance the ability of the fusion cage (20) to be self-tapping. Apertures (54, 206, 322) are defined through the fusion cage in order to provide for contact between the engaged vertebral bone structures and bone growth inducing substances packed within the fusion cage. The fusion cage (20) is introduced through an anterior procedure and maintains or increases the lordosis between adjacent vertebral bone structures.

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CONICALLY-SHAPED ANTERIOR FUSION CAGE AND METHOD OF IMPLANTATION

BACKGROUND

Field of the Invention

The present invention is directed to devices and methods for facilitating the fusing of bone structures and more particularly the fusing together of adjacent vertebral bodies or bone structures.

Background of the Invention

Technical literature and patent documents disclose a number of devices and methods for fusing bones together. One such device which has proven to be successful is disclosed in U.S. Patent 4,961,740, entitled "V-THREAD FUSION CAGE AND METHOD OF FUSING A BONE JOINT," which patent has been assigned the present assignee and which patent is incorporated herein by reference. The referenced patent discloses a fusion cage which is preferably cylindrical and has a thread formed as part of the external cylindrical surface. The fusion cage defines an internal cavity and apertures through the wall of the cage which communicate the external cylindrical surface with the internal cavity. The apertures are formed in the valleys of the thread. Normally two such cages are used to stabilized and fuse together adjacent vertebral bodies or bone structures.

In practice, using a posterior approach, a patient's vertebral bone structures are exposed and degenerate disk material located between the vertebral bone structures is removed. A threaded tap is used to tap a complementary thread in the upper and lower vertebral bone structures preparatory to the insertion of the above fusion cage. Once such tapping has been accomplished, using an introduction tool, the fusion cage is screwed into the space between the adjacent vertebral bone structures. The thread bites into the bone of the upper and lower vertebral bone structures, stabilizing the bone structures, and preventing the fusion cage from working out of this position due to patient movement. Generally two

such fusion cages are applied using this technique. Once the two implants have been positioned, then bone growth inducing substances, such as bone chips, are packed into the internal cavity of the fusion cages. These bone growth inducing substances come into immediate contact with the bone from the vertebral bone structures which project into the internal cavity through the apertures. Such projection of bone is due to the fact that the apertures are formed in the valleys of the external thread of the fusion cage. Such immediate bone to bone contact between the vertebral bone structures and the bone pack within the fusion cages results in more rapid propagation of bone cells between the adjacent vertebral bone structures and thus a more rapid fusion of the adjacent vertebral bone structures.

Summary of the Invention

The present invention is directed to a fusion cage which has been designed to be implanted using an anterior approach to the vertebral bone structures.

In a first embodiment of the present invention, the fusion cage includes a conically-shaped cage body having a proximal end and a distal end, said distal end having a diameter which is smaller than the diameter of the proximal end. The distal end further is rounded with for example a bull nose in order to facilitate the insertion of the cage body relative to one or more bone structures. The conically-shaped cage body is particularly advantageous for use with an anterior approach to vertebral bone structure fusion. This is due to the fact that the normal lordosis of the vertebral bone structures defines a wedged-shape space for a vertebral disk between, for example, lumbar vertebrae. Accordingly, the conically-shaped body cage can be sized and selected in order to maintain or enlarge upon the normal lordosis.

In a second embodiment of the present invention, a fusion cage includes a conically-shaped cage body having a proximal end and a distal end with the distal end having a diameter which is smaller than the

diameter of the proximal end. The conically-shaped cage body has a conically-shaped outer surface and at least one flute formed in the conically-shaped outer surface. The flute acts as a relief much as the flute placed on self-tapping screws in order to facilitate the insertion of the fusion cage using a twisting motion between two vertebral bone structures.

In a third embodiment of the invention, a fusion cage includes a conically-shaped cage body having a proximal end and a distal end, the distal end having a diameter which is smaller than the diameter of the proximal end. The conically-shaped cage body has a conically-shaped outer surface and a thread formed as part of the conically-shaped outer surface. The thread allows the cage body to be inserted using an anterior approach. Due to the fact that the cage body is conically-shaped, the requirement for pretapping the vertebral bone structures to receive the fusion cage is eliminated with the fusion cage being self-tapping. Also the cage gradually spreads apart the vertebral bone structures as the cage is inserted in order to regain or enlarge the natural lordosis of the adjacent vertebral bone structures. As with other embodiments of the present invention, flutes can be provided through the thread in order to allow for enhanced thread tapping by the cage and for a smoother insertion of the fusion cage between the vertebral bone structures. Preferably two or three flutes would be formed spaced about the fusion cage in order that one flute would be engaging with or adjacent to an upper vertebral bone structures with another flute being engaging with or adjacent to a lower vertebral bone structure. Such a relationship maintains alignment of the fusion cage and prevent wandering as the fusion cage is introduced between the two vertebral bone structures. Without two or more flutes, wandering might occur due to the fact that the thread is only substantially engaged with the vertebral bone structures and not with the disk material between the vertebral bone structures, which disk material does not provide support to the thread.

In a further aspect of the invention, any of the above embodiments can be provided with a plurality of apertures through the fusion cage and an internal cavity with the apertures communicating between the internal cavity and the external surface of the fusion cage. Bone growth inducing substances, such as bone chips, can be packed into the internal cavity either before the fusion cage is inserted or after the fusion cage has reached a final insertion position. The bone chips come in contact with the vertebral bone structures through the apertures in order to facilitate fusion between the adjacent vertebral bone structures.

In another aspect of the invention which can be included in any of the above embodiments, the cage body can have a round or bull nose distal end with one or more flutes formed in the round or bull nose distal end in order to enhance the self-tapping nature of the fusion cage.

In yet another aspect of the invention, introduction tools allow the fusion cage to be accurately positioned between the vertebral bone structures.

The method of the present invention affords access to adjacent vertebral bone structures using an anterior approach and procedure. Such anterior approach and procedure can be preferably performed laparoscopically using an introduction set including a cannula. A laparoscopic procedure is minimally invasive as the abdomen muscle tissue can be spread using a set of cannula of increasing size and a small opening thereby developed through which a fusion cage can be inserted. Such a procedure is less traumatic to the tissue than an alternate anterior approach and procedure, also known as an anterior lumbar interbody fusion, where an incision, perhaps up to five inches long is made, through the abdomen muscle tissue. It is to be understood however that either anterior approach and procedure can be used with the fusion cage and fall within the scope of the invention.

After such access, using preferably a laparoscopic technique, degenerate disk material can be removed and, using a cannula and insertion tool, an appropriately shaped fusion cage can be screwed into

place between the vertebral bone structures in order to stabilize the vertebral bone structures and allow for fusion. Either preparatory to insertion of the fusion cage or after it has been inserted, bone chips or other bone growth inducing substances can be inserted into the fusion cage to promote bone to bone contact and subsequent fusion.

It is to be understood that although the above-embodiments have been described with respect to the fusion of adjacent vertebral bodies or bone structures, that the present invention can be used to fuse together a variety of bone structures, in addition to being fused to one bone structure and used as, for example, a base for an implant.

Other objects and advantages of the invention can be obtained through a review of the specification and the figures.

Brief Description of the Figure

Figure 1 is a partially sectional side view of an embodiment of the fusion cage of the invention.

Figure 2 depicts a left end (distal end) view of the fusion cage of Figure 1.

Figure 3 depicts a right end (proximal end) view of the fusion cage of Figure 1.

Figure 4 depicts a view through line 4-4 of the fusion cage of Figure 1.

Figure 5 depicts the fusion cage of Figure 1 in conjunction with an introduction tool.

Figure 6 depicts an alternative embodiment of the introduction tool.

Figures 7, 8, and 9 depict the progressive stages in the method of inserting the fusion cage between adjacent vertebral bone structures.

Figure 10 depicts a side view of an alternative embodiment of the fusion cage of the invention.

Figure 11 depicts the left end (distal end) view of the fusion cage of Figure 10.

Figure 12 depicts the right end (proximal end) view of the fusion cage of Figure 10.

Figure 13 depicts a side view of yet another embodiment of the fusion cage of the present invention.

Figure 14 depicts a left distal end (distal end) view of the fusion cage of the invention of Figure 13.

Figure 15 depicts a right end (proximal end) view of the fusion cage of the invention of Figure 13.

Figure 16 depicts a sectional view taken through line 16-16 of Figure 13.

Detailed Description of the Preferred Embodiment

With respect to the figures in a particular Figure 1, a side view of the preferred embodiment of the fusion cage 20 is depicted. Fusion cage 20 includes a fusion cage body 22 which in this preferred embodiment is provided in the shape of a cone. Fusion cage 20 includes a distal end 24 and a proximal end 26. The distal end 24 in a preferred embodiment is rounded or bull nosed in order to facilitate the insertion of the fusion cage 20 relative to one or more bone structures. The proximal end 26 includes an opening 28 which communicates with an internal cavity 30 defined by the fusion cage 20. The opening 28 in a preferred embodiment is threaded so that it can receive an end cap or plug 32 (Figure 5). End cap 32 is used to close off the proximal end 26 and retain bone growth inducing substances packed therein as described herein-below. As can be seen in Figure 5, end cap 32 includes a threaded bore 34 which is designed to receive an insertion tool. The threaded bore 34 has an initial unthreaded, hex-shaped section 35 which can be used with a socket wrench to tightly position end cap 32 in opening 28. The proximal end 26 further define first and second peripheral indentations 36, 38. These peripheral indentations 36, 38 receive tangs from an insertion tool as described hereinbelow for facilitating the insertion of the fusion cage 20.

A thread 40 is defined as part of the outer cylindrical surface 41 of the body 22. It is to be understood that the thread can be replaced with a plurality of discrete threads or a plurality of projections, ridges, protrusions, barbs, or spurs and be within the spirit and scope of the invention.

The rounded distal end 24, and at least some of the turns of thread 40 defined flutes or relief grooves 42, 44, and 46. (Figures 1, 2.) In a preferred embodiment, flutes 42, 44, and 46 meet at a central point 48 of the distal end 24 on the longitudal axis 50 of the fusion cage 20. In other embodiments the flutes can be smaller and not extend all the way to the central point 48 on the longitude axis 50. Still in other embodiments, the flutes can be eliminated from the distal end 24 and such embodiments are still within the spirit and scope of the invention.

The flutes extend from the distal end 24 toward the proximal end 26 as shown in Figure 1 with respect to flute 42. These flutes are defined by the sections 52 which are removed from the thread. In a preferred embodiment, the flutes become narrower as they approach the proximal end 26 due to the fact that thread relief for purposes of self-tapping becomes less important as the cage reaches a final resting position. As shown in other embodiments, the flutes can be deeper and extend from the distal end completely to the proximal end. Still further in other embodiments the flutes can be confined to the first several turns of the thread adjacent to the distal end and/or to just the distal end.

As can be seen in Figures 1, 4, a plurality of apertures 54 are provided through wall 56 of the fusion cage 20. In a preferred embodiment, these apertures 54 are formed by broaching grooves 58 in the internal surface 60 of the interna. cavity 30. The effect of such roaching is to remove material from the valleys between the turns of the thread 40, thus defining the aperture 54. The advantages of such an arrangement are taught by the above-referenced U.S. Patent No. 4,961,740, which patent is incorporated herein by reference and allows for immediate bone to bone contact between the vertebral bodies or bone

structures and the bone packed within the internal cavity 30 of the fusion cage 20.

The apertures 54 in a preferred embodiment increase in size from smaller apertures closer to the distal end 24 to a larger aperture closer to the proximal end 26. This increase in size allows for more bone to bone contact. Alternatively in the embodiment as shown in Figure 1, all the apertures are of the same size.

As can be seen in Figure 4, the apertures are clustered about a transverse axis 51, both at the upper and lower end of the axis. This is so that in position, the apertures come into contact with the upper and lower vertebral bone structures (Figure 9) to encourage bone growth through the fusion cage from the vertebral bone structures. The lateral section of the fusion cage found along the other transverse axis 53 do not have apertures in order to prevent growth of disk material which might interfere with the bone fusing process.

A preferred embodiment of the conically-shaped fusion cage 20 includes a fusion cage which is 23 millimeters in length having a distal end 24 with a diameter of 14 millimeters and a proximal end 26 with a diameter of 18 millimeters. The cage body is a right circular cone. The thread has a pitch of 30° and there are ten turns per inch with a thread depth of .053 inches. Further the cage is made of a titanium material. Preferably this and the other disclosed fusion cages disclosed are machined. However, the processes such as molding can be used to accomplished formation of the fusion cages.

The cage is inserted between vertebral bodies using an insertion tool 62 (Figure 5). Insertion tool 62 includes an inner handle 64 and an outer handle 66. The outer handle includes a bore 68 for receiving the inner handle 64. Handles 64, 66 include knobs 70, 72 respectively. The distal end of inner handle 64 defines a threaded shaft 74, having a reverse thread to facilitate easy removal, and the distal end of handle 66 define a cylindrical disk 76 which has first and second tangs 78, 80, projecting from the peripheral edge of the cylindrical disk 76. These tangs 78, 80

are designed to mate with the peripheral indentation 36, 38 of the fusion cage 20. For purposes of inserting the fusion cage between the vertebral bodies, the end cap 32 is inserted into the fusion cage 20 as shown in Figure 5. Then the threaded shaft 74 of the inner handle is introduced into the threaded bore 34 of the end cap 32. After this is accomplished, the outer handle 66 is slid over the inner handle 64 and the tangs 78, 80 are positioned into engagement with the indentations 36, 38. In this arrangement, the fusion cage 20 can be anteriorly inserted into the space between the vertebral body structure using the insertion tool 62.

An alternative embodiment of the insertion tool is shown in Figure 6. In this figure, insertion tool 82 includes a handle 84 with a knob 86. At the end of the insertion tool 82 distal from the knob 86 is a cylindrical disk 88 which has first and second tangs 90, 92, which have the same function as the above tangs 78, 80. Extending from the center of the cylindrical disk 88 along the centerline of the insertion tool 82 is a shaft 94 which has a ball detent 96. For use with insertion tool 82, the threaded bore 34 of the end cap 32 would be replaced with a bore having a lip which could engage with the ball detent 96 of the insertion tool 82.

The method for inserting the fusion cage 20 of Figure 1 using an anterior approach and procedure to the vertebral bodies is as follows. It is to be understood that although the focus of this discussion is on a laparoscopic procedure, that the anterior approach and procedure can also include a more invasive procedure where a long incision is made in the abdomen wall.

With an anterior approach, using an introduction set such as described by way of example only, in U.S. Patent 4,863,430, entitled "INTRODUCTION SET WITH FLEXIBLE TROCAR WITH CURVED CANNULA," which is incorporated by reference, but however with larger diameter instruments, an amount of disk material is removed between the two vertebral bodies or bone structures which are to be fused together. This procedure is accomplished through a cannula position adjacent to the vertebral bone structures. With the same or a larger diameter cannula, the

fusion cage 20 can be introduced adjacent to the vertebral bone structures. In a first procedure, the fusion cage is packed with bone growth substances and the end cap 32 is affixed to the fusion cage 20. Insertion tool 62 is then secured to the fusion cage 20 and the fusion cage is guided through the cannula to a location adjacent to the upper and lower vertebral body such as presented schematically in Figures 7, 8, 9, by upper body 98 and lower body 100. In the initial position as shown in Figure 7, the fusion cage 20 is adjacent to the anterior sections 102, 104 of the vertebral bodies 98, 100. As the introduction tool is turned, the thread 40 of the fusion cage 20 bites into the vertebral bodies 98, 100. Further turning of the introduction tool causes the fusion cage to move through the position shown in Figure 8 to the final resting position shown in Figure 9, where the distal end 24 is moved adjacent to the posterior sections 106, 108 of the vertebral bone structures 98, 100. As this occurs, the fusion cage 20 increases the lordosis or spacing between the vertebral bodies, basically distracting the vertebral bodies and causing the vertebral bodies to pivot about the posterior sections 106, 108, with such posterior sections acting like a hinge. It is noted that most of the distraction occurs adjacent to the anterior sections, but that distractions also occur at the posterior sections where the hinged effect is exhibited. Preferably, the lordosis is increased over the normal lordosis in order to stabilize the vertebral bone structures prior to fusion occurring. Stabilization occurs due to the fact that increased lordosis places additional stress on the anterior longitudinal ligaments which are part of the anatomy holding the vertebral bodies in place.

Once the fusion cage 20 is appropriately positioned, the handle 64 of the insertion tool 62 is unscrewed from the cap 32 and the insertion tool 62 is pulled away from the fusion cage.

An alternative embodiment of a fusion cage 200 is shown in Figures 10, 11, and 12. Fusion cage 200 includes a distal end 202 and an a proximal end 204. Fusion cage 200 includes an internal cavity 206. End caps not shown can be used to close the ports 208, 210 of distal and

proximal ends 202, 204. A plurality of threads 212 is defined on the external conical surface 214 of the fusion cage 200. Defined by the thread 212 are first and second flutes 216, 218, which in this embodiment extend from the distal end 202 to the proximal end 204. These flutes provide thread relief allowing the fusion cage 200 to be self-tapping.

The fusion cage 200 includes a plurality of elongated apertures 220 which are formed through the side walls of a fusion cage 200. The elongated apertures 202 are formed in such a way that the internal conical surface 214 is spaced away from the internal surface 224 of the internal cavity 206 by the thickness of the sidewall 222.

A further embodiment of the invention is shown in Figures 13, 14, 15 and 16. In Figure 16 the fusion cage 300 has distal and proximal ends 302 and 304 respectively. The fusion cage 300 defines an internal cavity 306, and ports 308 and 310 defined through the distal and proximal ends 302 and 304 respectfully. A thread 312 is defined as part of the external conical surface 314 of the fusion cage 200. First, second and third flutes 316, 318, and 320, are defined in the thread 312 from the distal end 302 to the proximal end 304. These flutes give the fusion cage 300 an enhanced self-tapping advantage. These flutes are equally spaced about the fusion cage 300 in a manner similar to the flutes of the fusion cage embodiment 20 in Figure 1.

A plurality of aperture 322 is provided through the external conical surface 314 of the fusion cage 300 and through the side wall 324 opening into the internal cavity 306. Accordingly, at the location of the aperture 322 the external surface 314 is held away from the internal surface 326 by the thickness of the side wall 324.

Industrial Applicability

The present invention affords the advantages of a fusion cage which can be introduced through an anterior approach in order to maintain or increase lordosis between adjacent vertebral bodies. The fusion cage has the advantage of being conically-shaped and self-tapping through the

use of external flutes. The flutes additionally assist in keeping the fusion cage aligned and centered as the cage is being inserted between the vertebral bone structures.

Other advantages, aspects, and objects of the invention can be obtained through a review of the claims and the appended figures.

It is to be understood that additional embodiments of the invention can be constructed and fall within the spirit and scope of the claims.

We claim:

1. A fusion cage for promoting fusion with one or more bone structures comprising:

a conically-shaped cage body having a proximal end and a distal end, said distal end having a diameter which is smaller than a diameter of said proximal end; and

said distal end being rounded in order to facilitate insertion relative to one or more bone structures.

2. The fusion cage of claim 1 including:

said conically-shaped cage body having a conically-shaped outer surface and at least one flute formed in the conically-shaped outer surface.

3. The fusion cage of claim 2 including:

said conically-shaped cage body wherein said flute extends from the distal end toward the proximal end.

4. The fusion cage of claim 2 including:

at least three flutes formed in the conically-shaped outer surface.

5. The fusion cage of claim 4 including:

said three flutes are equally spaced about said distal end.

6. The fusion cage of claim 2 including:

said flute being additionally formed in the rounded distal end.

7. The fusion cage of claim 4 including:

said three flutes being additionally formed in the rounded distal end.

8. The fusion cage of claim 1 including:

said conically-shaped cage body having a conically-shaped outer surface and a thread formed into said conically-shaped outer surface.

9. The fusion cage of claim 8 including:

at least one flute formed in the thread.

10. The fusion cage of claim 8 including:

said conically-shaped cage body having a conically-shaped outer surface and an internal cavity; and

a plurality of apertures formed through the conically-shaped body which communicate said conically-shaped outer surface with said internal cavity.

11. The fusion cage of claim 1 including:

said conically-shaped cage body is a right circular cone.

12. A fusion cage for promoting fusion with between two spaced apart vertebral bone structures which have posterior sections and anterior sections and with a posterior interspace defined between the posterior sections and an anterior interspace defined between the anterior sections, said fusion cage comprising:

a conically-shaped cage body having a proximal end and a distal end, said distal end having a diameter which is smaller than a diameter of said proximal end, with said distal end positionable in the posterior interspace between the posterior sections of the vertebral bone structures and with said proximal end positionable in the anterior interspace between the anterior sections of said vertebral bone structures in order to maintain the height of the anterior interspace larger than the height of the posterior interspace; and

said conically-shaped cage body having a conically-shaped outer surface and a thread formed into said conically-shaped outer surface in

order to engage the vertebral bone structures as the cage body is inserted from the anterior interspace toward the posterior interspace.

13. The fusion cage of claim 12 including:

said distal end being rounded in order to facilitate insertion of the fusion cage between the vertebral bone structures, from the anterior interspace toward the posterior interspace.

14. The fusion cage of claim 12 including:

at least one flute formed in the thread.

15. The fusion cage of claim 14 including:

said flute extends from the distal end toward the proximal end.

16. The fusion cage of claim 12 including:

at least three flutes formed in the thread.

17. The fusion cage of claim 16 including:

said three flutes are equally spaced about said distal end.

18. The fusion cage of clam 13 including:

at least one flute being formed in the rounded distal end.

19. The fusion cage of claim 18 including:

three flutes being formed in the rounded distal end.

20. The fusion cage of claim 12 including:

said conically-shaped cage body having an internal cavity; and

a plurality of apertures formed through the conically-shaped body which communicate said conically-shaped outer surface with said internal cavity.

21. The fusion cage of claim 12 including:

said conically-shaped cage body is a right circular cone.

22. A fusion cage for promoting fusion with one or more bone structures comprising:

a conically-shaped cage body having a proximal end and a distal end, said distal end having a diameter which is smaller than a diameter of said proximal end; and

said conically-shaped cage body having a conically-shaped outer surface and at least one flute formed in the conically-shaped outer surface.

23. The fusion cage of claim 22 including:

said distal end being rounded in order to facilitate insertion relative to one or more bone structures.

24. The fusion cage of claim 22 including:

said conically-shaped cage body wherein said flute extends from the distal end toward the proximal end.

25. The fusion cage of claim 22 including:

at least three flutes formed in the conically-shaped outer surface.

26. The fusion cage of claim 22 including:

three flutes equally spaced about said distal end.

27. The fusion cage of clam 23 including:

a flute formed in the rounded distal end.

28. The fusion cage of claim 25 including:

said distal end being rounded in order to facilitate insertion relative to the one or more bone structures;

and

said three flutes being additionally formed in the rounded distal end.

29. The fusion cage of claim 22 including:

a thread formed into said conically-shaped outer surface.

30. The fusion cage of claim 29 including:

said at least one flute formed in the thread.

31. The fusion cage of claim 22 including:

said conically-shaped cage body an internal cavity; and

a plurality of apertures formed through the conically-shaped body which communicate said conically-shaped outer surface with said internal cavity.

32. An anterior fusion cage for promoting fusion between vertebral bone structures comprising:

a conically-shaped cage body having a proximal end and a distal end, said distal end having a diameter which is smaller than a diameter of said proximal end, said distal end for initial insertion between vertebral bone structures from an anterior approach;

said conically-shaped cage body having a conically-shaped outer surface and a thread with a plurality of turns formed into said conically-shaped outer surface, and a flute formed in at least one said turns;

said conically-shaped cage body having an interior cavity; and

a plurality of apertures formed through the conically-shaped body which communicate said conically-shaped outer surface with said internal cavity.

33. The fusion cage of claim 32 including:

said distal end being rounded in order to facilitate insertion between the vertebral bone structures from an anterior location towards a posterior location.

34. The fusion cage of claim 32 including:

said conically-shaped cage body wherein said flute extends from the distal end toward the proximal end.

35. The fusion cage of claim 32 including:

at least three flutes formed in at least one of the turns.

36. The fusion cage of claim 32 including:

three flutes equally spaced about said distal end.

37. The fusion cage of clam 33 including:

said flute being additionally formed in the rounded distal end.

38. The fusion cage of claim 33 including:

three flutes are formed in the rounded distal end.

39. A fusion cage for promoting fusion with one or more bone structures comprising:

a conically-shaped cage body having a proximal end and a distal end, said distal end having a diameter which is smaller than a diameter of said proximal end; and

said conically-shaped cage body having a conically-shaped outer surface and a thread formed into said conically-shaped outer surface.

40. The fusion cage of claim 39 including:

said distal end being rounded in order to facilitate insertion relative to one or more bone structures.

41. The fusion cage of claim 39 including:

at least one flute formed in the thread.

42. The fusion cage of claim 41 including:

said flute extends from the distal end toward the proximal end.

43. The fusion cage of claim 39 including:
at least three flutes formed in the thread.

44. The fusion cage of claim 43 including:
said three flutes are equally spaced about said distal end.

45. The fusion cage of clam 40 including:
at least one flute being formed in the rounded distal end.

46. The fusion cage of claim 40 including:
three flutes being formed in the rounded distal end.

47. A fusion cage for promoting fusion with one or more bone structures comprising:
a cage body having a proximal end and a distal end; and
said cage body having an outer surface and at least one flute formed in the outer surface in order to facilitate the insertion of the fusion cage in the one or more bone structures.

48. The fusion cage of claim 47 including:
said distal end being rounded in order to facilitate insertion relative to one or more bone structures.

49. The fusion cage of claim 47 including:
said flute extends from the distal end toward the proximal end.

50. The fusion cage of claim 47 including:
at least three flutes formed in the outer surface.

51. The fusion cage of claim 50 including:

three flutes are equally spaced about said distal end.

52. The fusion cage of clam 48 including:

said flute being additionally formed in the rounded distal end.

53. The fusion cage of claim 47 including:

said cage body having a thread formed into said outer surface.

54. The fusion cage of claim 53 including:

said flute formed in the thread.

55. The fusion cage of claim 1 in combination with an insertion tool, said fusion cage and said insertion tool including:

said proximal end having a opening which communicates with an internal cavity;

an end cap which can fit into said opening in order to close off said internal cavity;

said proximal end including at least one insertion tool receiving indentation;

said end cap including an insertion tool receiving threaded bore; and

said insertion tool having a tang for being received in said indentation and a threaded shaft for being received in said threaded bore. said insertion tool for being engaged with said fusion cage for inserting said fusion cage relative to the one or more bone structures.

56. The fusion cage of claim 10 including:

said apertures are elongated in order to increase the amount of communication between the internal cavity and the one or more bone structures.

57. A method for fusing together two spaced apart vertebral bone structures which have posterior sections and anterior sections and

with a posterior interspace defined between the posterior sections and an anterior interspace defined between the anterior sections, with the height of the anterior interspace being about the same as or larger than the height of the posterior interspace, the method comprising the steps of:

accessing the vertebral bone structures from the anterior sections;

selecting a fusion cage with a conically-shaped cage body having a proximal end and a distal end, said distal end having a diameter which is smaller than a diameter of said proximal end, with said distal end positionable in the posterior interspace between the posterior sections of the vertebral bone structures and with said proximal end positionable in the anterior interspace between the anterior sections of said vertebral bone structures in order to maintain the height of the anterior interspace relative to the height of the posterior interspace, and said conically-shaped cage body having a conically-shaped outer surface and a thread formed into said conically-shaped outer surface;

position the fusion cage body adjacent to the anterior sections of the vertebral bone structures;

causing said fusion cage to be inserted between the vertebral bone structures by moving the fusion cage from (1) a position with the distal end adjacent to the anterior section of the vertebral bone structures to (2) a position with the distal end adjacent to the posterior sections and the proximal end adjacent to the anterior sections of said vertebral body structures.

58. The method of claim 57 including:

said causing step includes turning the fusion cage so that the thread formed as part of the outer surfaces and engage the vertebral bone structures in order to hold the fusion cage in place and stabilize the vertebral bone structures.

59. The method of claim 57 including:

said causing step includes turning the fusion cage so that the thread self-taps a complementary thread in the vertebral bone structures.

60. A method of achieving a desired lordosis of the spinal column of a patient including the steps of:

accessing the vertebral bone structures from the anterior;

positioning a conically-shaped fusion cage adjacent to anterior sections of the vertebral bone structures using an anterior procedure;

urging the conically-shaped fusion cage into the disk space between adjacent vertebral bone structures in a direction from the anterior to the posterior of the vertebral bone structures in order to restore a desired lordosis.

61. The method of claim 60 including the step of:

preparatory to the positioning step, the step selecting a conically shaped fusion cage of an appropriate size in order to achieve the desired lordosis.

62. The method of claim 60 including the step of:

preparatory to the positioning step, the step of selecting a conically-shaped fusion cage of an appropriate size in order to stretch the anterior longitudinal ligaments in order to stabilize the vertebral bone structures about the fusion cage.

63. The fusion cage of claim 10 including:

said apertures increase in size from the distal end toward the proximal end.

64. A fusion cage (1) for promoting fusion between two spaced apart vertebral bone structures which have posterior sections and anterior sections with a posterior interspace defined between the posterior sections and an anterior interspace defined between the anterior positions, and (2)

for achieving a desired lordosis as the fusion cage is implanted by urging the fusion cage from the anterior sections toward the posterior sections using an anterior approach, the fusion cage comprising:

a conically-shaped cage body having a proximal end and a distal end, said distal end having a diameter which is smaller than a diameter of said proximal end, with said distal end positionable in the posterior interspace between the posterior sections of the vertebral bone structures and with said proximal end positionable in the anterior interspace between the anterior sections of said vertebral bone structures as the conically-shaped cage body is urged using an anterior approach from an initial position where the distal end is positioned adjacent to the anterior sections to a final position where the proximal end is positioned in the anterior interspace and the distal end is positioned in the posterior innerspace.

65. The fusion cage of claim 64 including:

said conically-shaped cage body having a conically-shaped outer surface and a thread formed into said conically-shaped outer space in order to engage the vertebral bone structures as the cage body is inserted from the anterior interspace toward the posterior interspace.

66. The fusion cage of claim 65 including:

said distal end of said cage body is rounded in order to facilitate insertion between the vertebral body structures.

67. The method of claim 57 including:

using a laparoscopic procedure to access the vertebral bone structures and to insert the fusion cage.

68. The method of claim 57 including:

said causing step distracting the anterior sections more than the posterior sections, and for causing the vertebral bone structures to pivot about the posterior sections.

69. The method of claim 60 including:

using a laparoscopic procedure to access the vertebral bone structures and to insert the fusion cage.

70. The method of claim 60 including:

said urging step for distracting the anterior sections more than the posterior sections of the vertebral bone structures, and for causing the vertebral bone structures to pivot about the posterior sections.

71. A fusion cage for promoting fusion with one or more bone structures comprising:

a cage body having a proximal end and a distal end, said distal end having a diameter which is smaller than a diameter of said proximal end; and

said distal end being rounded in order to facilitate insertion relative to one or more bone structures.

72. The fusion cage of claim 71 including:

said cage body having an outer surface and at least one flute formed in the outer surface.

73. The fusion cage of claim 72 including:

said cage body wherein said flute extends from the distal end toward the proximal end.

74. The fusion cage of claim 72 including:

at least three flutes formed in the outer surface.

75. The fusion cage of claim 71 including:

at least one flute formed in the rounded distal end.

76. The fusion cage of claim 71 including:

three flutes formed in the rounded distal end.

77. The fusion cage of claim 71 including:

said cage body having an outer surface and a thread formed into said outer surface.

78. The fusion cage of claim 77 including:

at least one flute formed in the thread.

79. A fusion cage for promoting fusion with between two spaced apart vertebral bone structures which have posterior sections and anterior sections and with a posterior interspace defined between the posterior sections and an anterior interspace defined between the anterior sections, said fusion cage comprising:

a cage body having a proximal end and a distal end, said distal end having a diameter which is smaller than a diameter of said proximal end, with said distal end positionable in the posterior interspace between the posterior sections of the vertebral bone structures and with said proximal end positionable in the anterior interspace between the anterior sections of said vertebral bone structures in order to maintain the height of the anterior interspace larger than the height of the posterior interspace; and

said cage body having an outer surface and a thread formed into said outer surface in order to engage the vertebral bone structures as the cage body is inserted from the anterior interspace toward the posterior interspace.

80. The fusion cage of claim 79 including:

said distal end being rounded in order to facilitate insertion of the fusion cage between the vertebral bone structures, from the anterior interspace toward the posterior interspace.

81. A fusion cage for promoting fusion with one or more bone structures comprising:

a cage body having a proximal end and a distal end, said distal end having a diameter which is smaller than a diameter of said proximal end; and

said cage body having an outer surface and at least one flute formed in the outer surface.

82. The fusion cage of claim 81 including:

said distal end being rounded in order to facilitate insertion relative to one or more bone structures.

83. A fusion cage for promoting fusion between vertebral bone structures comprising:

a cage body having a proximal end and a distal end, said distal end having a diameter which is smaller than a diameter of said proximal end, said distal end for initial insertion between vertebral bone structures from an anterior approach;

said cage body having an outer surface and a thread with a plurality of turns formed into said outer surface,;

said cage body having an interior cavity; and

a plurality of apertures formed through the body which communicate said outer surface with said internal cavity.

84. The fusion cage of claim 83 wherein:

a flute is formed in at least one of said turns.

85. A fusion cage for promoting fusion with one or more bone structures comprising:

a cage body having a proximal end and a distal end, said distal end having a diameter which is smaller than a diameter of said proximal end; and

said cage body having an outer surface and a thread formed into said outer surface.

86. The fusion cage of claim 85 including:

said cage body being conically-shaped.

87. A fusion cage for promoting fusion with one or more bone structures comprising:

a cage body having a proximal end and a distal end; and

said cage body having at least one flute formed in the distal end in order to facilitate the insertion of the fusion cage in the one or more bone structures.

88. The fusion cage of claim 87 including:

said distal end being rounded in order to facilitate insertion relative to one or more bone structures.

89. The fusion cage of claim 87 including:

said flute extends from the distal end toward the proximal end.

90. A method for fusing together two spaced apart vertebral bone structures which have posterior sections and anterior sections and with a posterior interspace defined between the posterior sections and an anterior interspace defined between the anterior sections, with the height of the anterior interspace being about the same as or larger than the height of the posterior interspace, the method comprising the steps of:

accessing the vertebral bone structures from the anterior sections;

selecting a fusion cage with a cage body having a proximal end and a distal end, said distal end having a diameter which is smaller than a diameter of said proximal end, with said distal end positionable in the posterior interspace between the posterior sections of the vertebral bone structures and with said proximal end positionable in the anterior

interspace between the anterior sections of said vertebral bone structures in order to maintain the height of the anterior interspace relative to the height of the posterior interspace, and said conically-shaped cage body having an outer surface and a thread formed into said outer surface;

position the fusion cage body adjacent to the anterior sections of the vertebral bone structures;

causing said fusion cage to be inserted between the vertebral bone structures by moving the fusion cage from (1) a position with the distal end adjacent to the anterior section of the vertebral bone structures to (2) a position with the distal end adjacent to the posterior sections and the proximal end adjacent to the anterior sections of said vertebral body structures.

91. A fusion cage (1) for promoting fusion between two spaced apart vertebral bone structures which have posterior sections and anterior sections with a posterior interspace defined between the posterior sections and an anterior interspace defined between the anterior positions, and (2) for achieving a desired lordosis as the fusion cage is implanted by urging the fusion cage from the anterior sections toward the posterior sections using an anterior approach, the fusion cage comprising:

a conically-shaped cage body having a proximal end and a distal end, said distal end having a diameter which is smaller than a diameter of said proximal end, with said distal end positionable in the posterior interspace between the posterior sections of the vertebral bone structures and with said proximal end positionable in the anterior interspace between the anterior sections of said vertebral bone structures as the conically-shaped cage body is urged using an anterior approach from an initial position where the distal end is positioned adjacent to the anterior sections to a final position where the proximal end is positioned in the anterior interspace and the distal end is positioned in the posterior innerspace.

92. The fusion cage of claim 91 including:

said conically-shaped cage body having a conically-shaped outer surface and a thread formed into said conically-shaped outer space in order to engage the vertebral bone structures as the cage body is inserted from the anterior interspace toward the posterior interspace.

93. The fusion cage of claim 91 including:

said posterior end of said cage body is rounded in order to facilitate insertion between the vertebral body structures.

94. The method of claim 90 including:

using a laparoscopic procedure to access the vertebral bone structures and to insert the fusion cage.

95. The method of claim 90 including:

said causing step distracting the anterior sections more than the posterior sections, and for causing the vertebral bone structures to pivot about the posterior sections.

96. The method of claim 90 including:

using a laparoscopic procedure to access the vertebral bone structures and to insert the fusion cage.

97. The method of claim 90 including:

said causing step for distracting the anterior sections more than the posterior sections of the vertebral bone structures, and for causing the vertebral bone structures to pivot about the posterior sections.

98. A fusion cage for promoting fusion with between two spaced apart vertebral bone structures which have posterior sections and anterior sections and with a posterior interspace defined between the posterior sections and an anterior interspace defined between the anterior sections, said fusion cage comprising:

a cage body having a proximal end and a distal end, said distal end having a diameter which is smaller than a diameter of said proximal end, with said distal end positionable in the posterior interspace between the posterior sections of the vertebral bone structures and with said proximal end positionable in the anterior interspace between the anterior sections of said vertebral bone structures in order to maintain the height of the anterior interspace larger than the height of the posterior interspace.

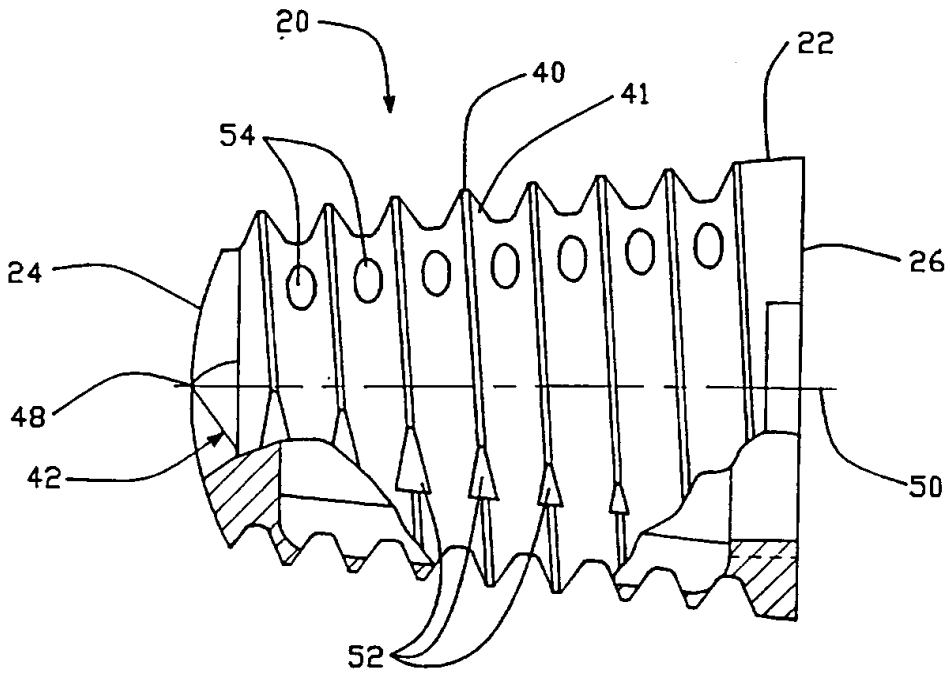

FIG.—1

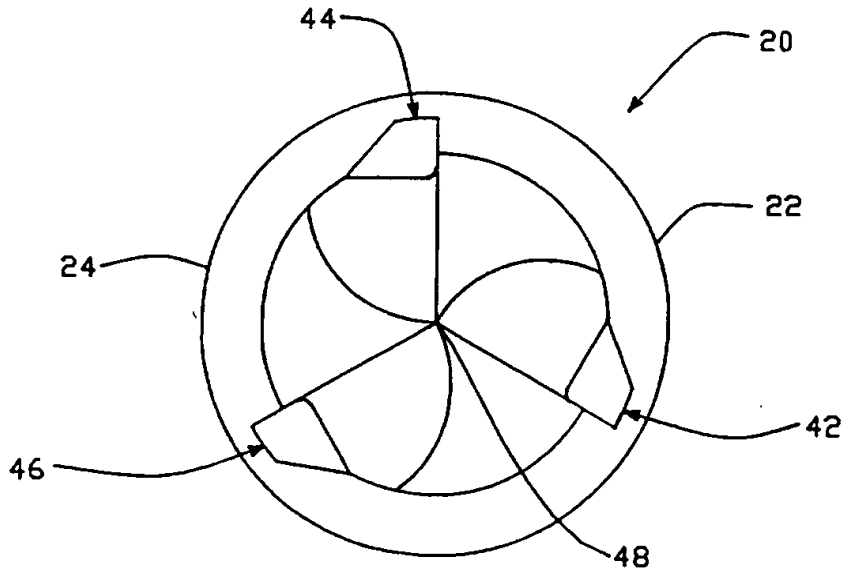

FIG.—2

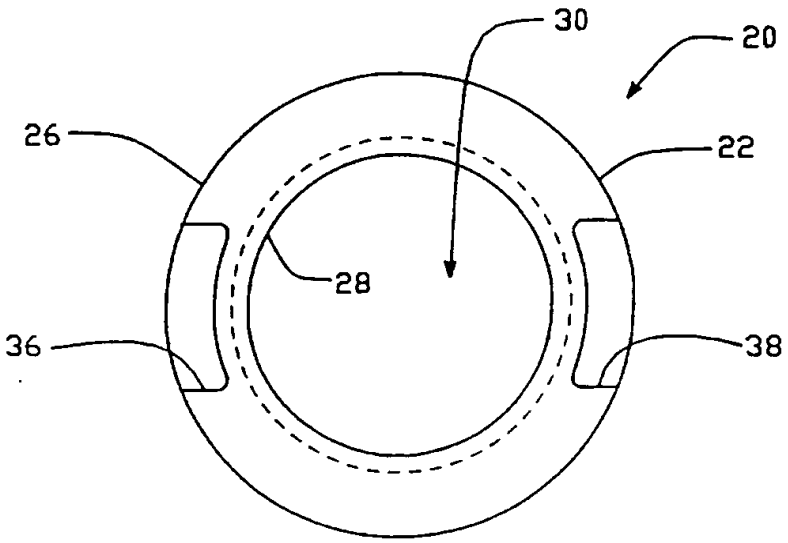

FIG.—3

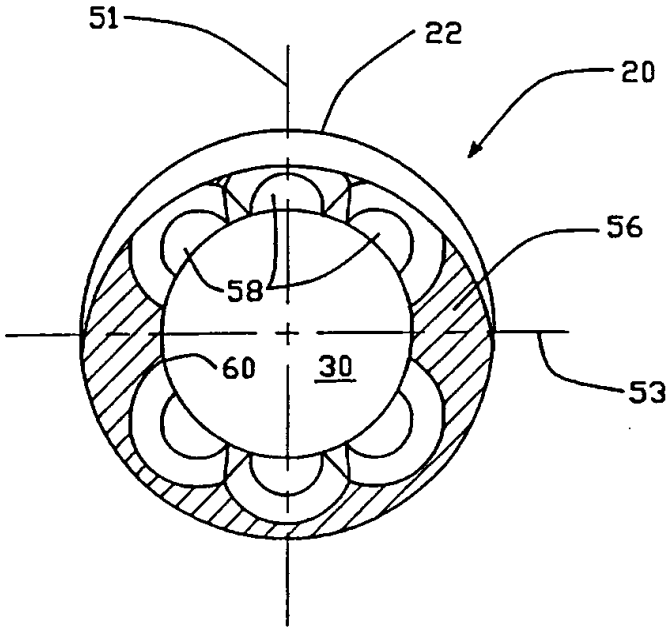

FIG.—4

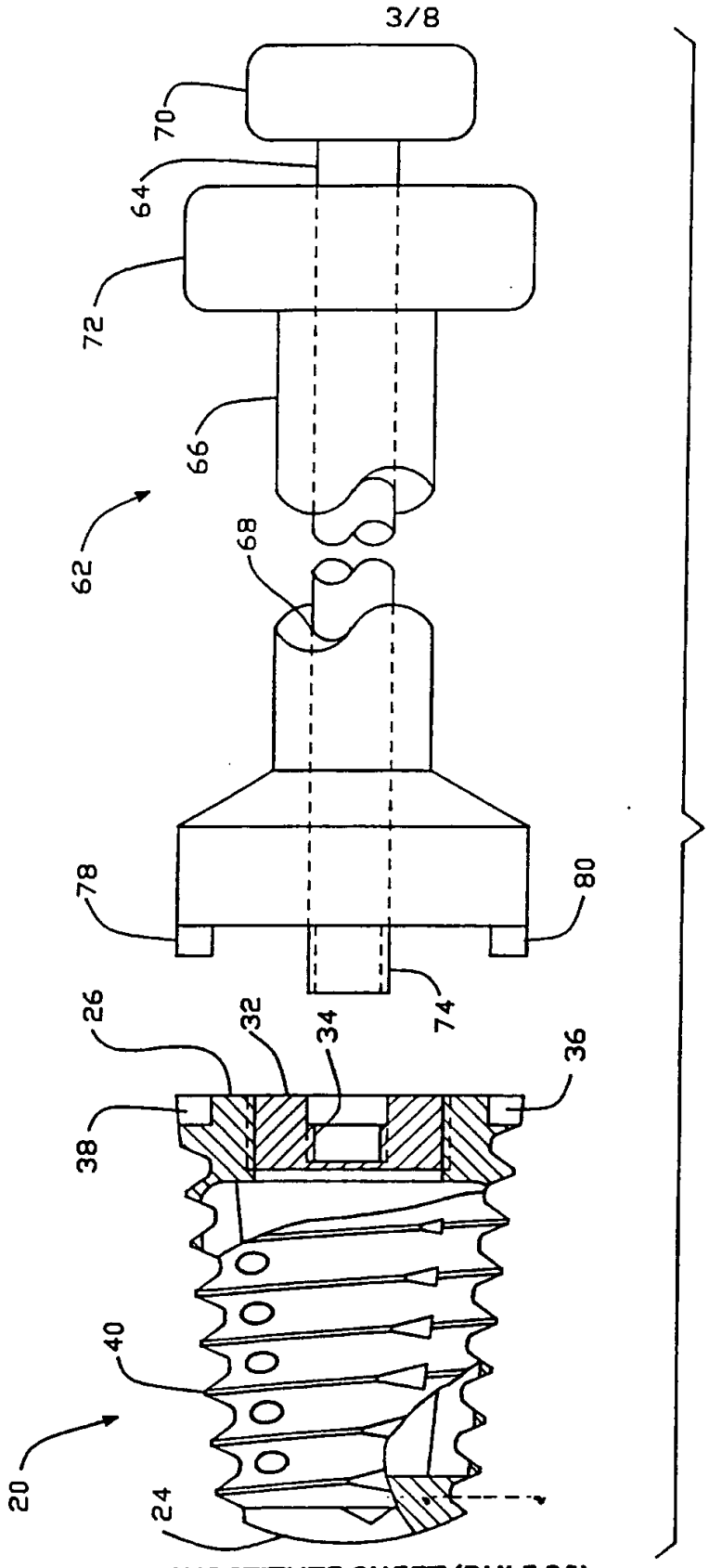

FIG.—5

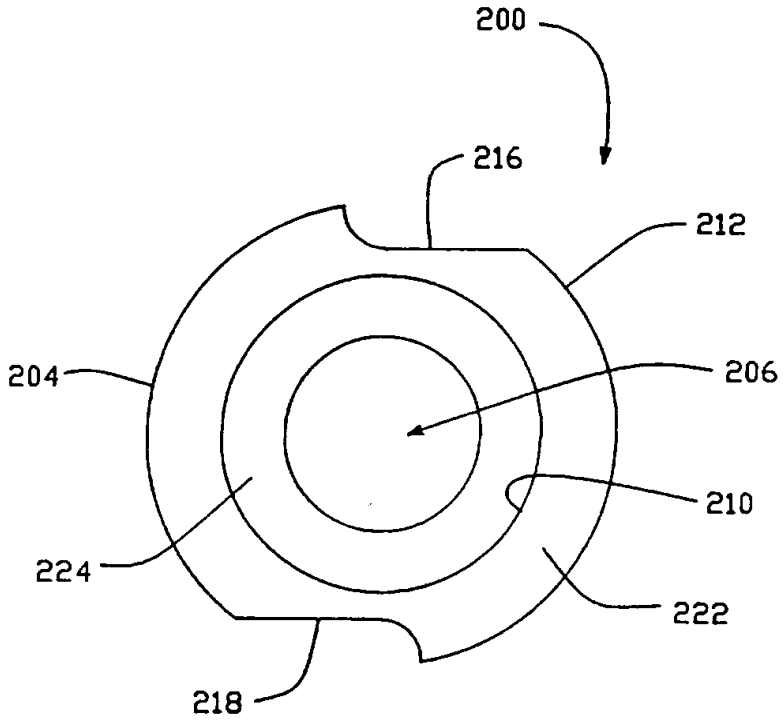

FIG.-12

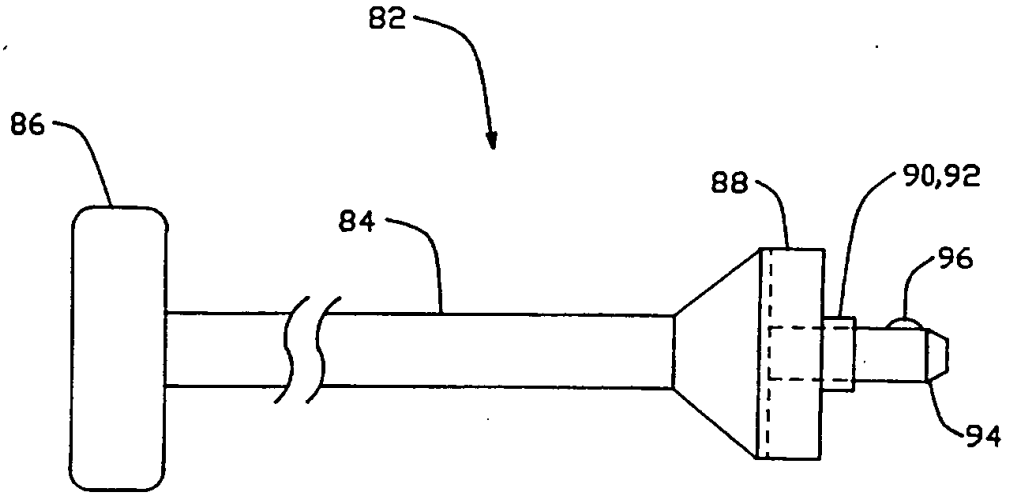

FIG.-6

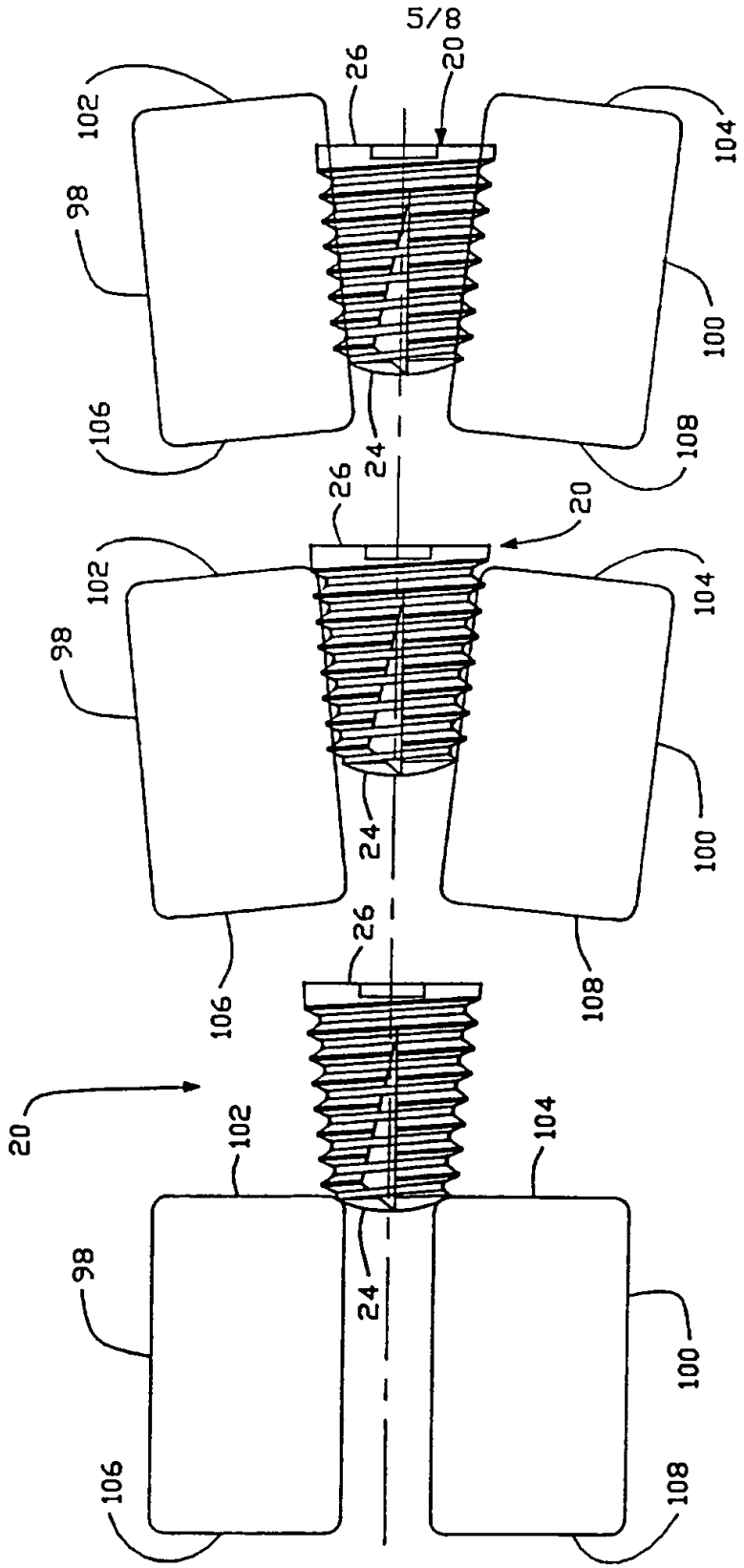
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FIG.—9
FIG.—8
FIG.—7

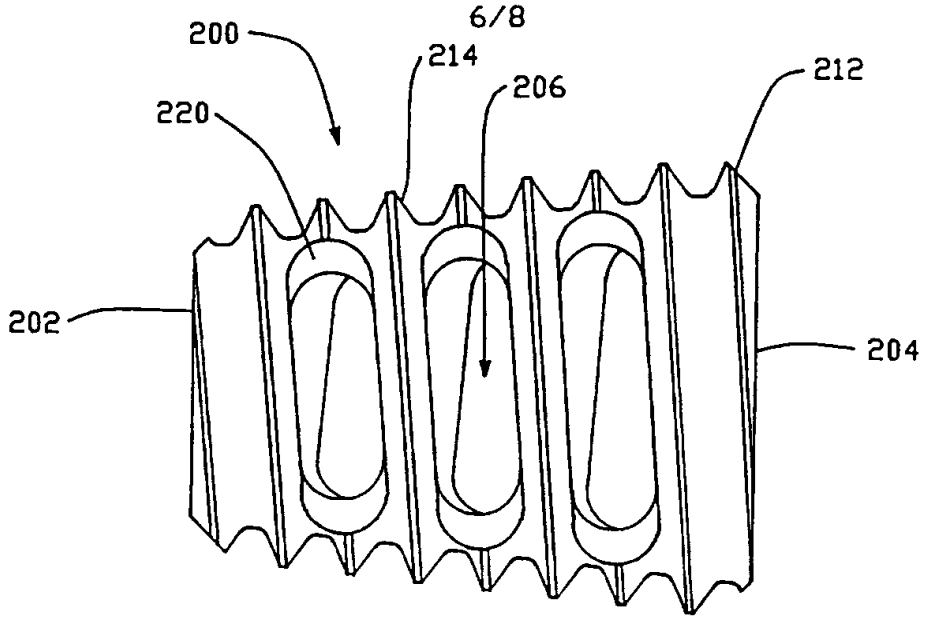

FIG.—10

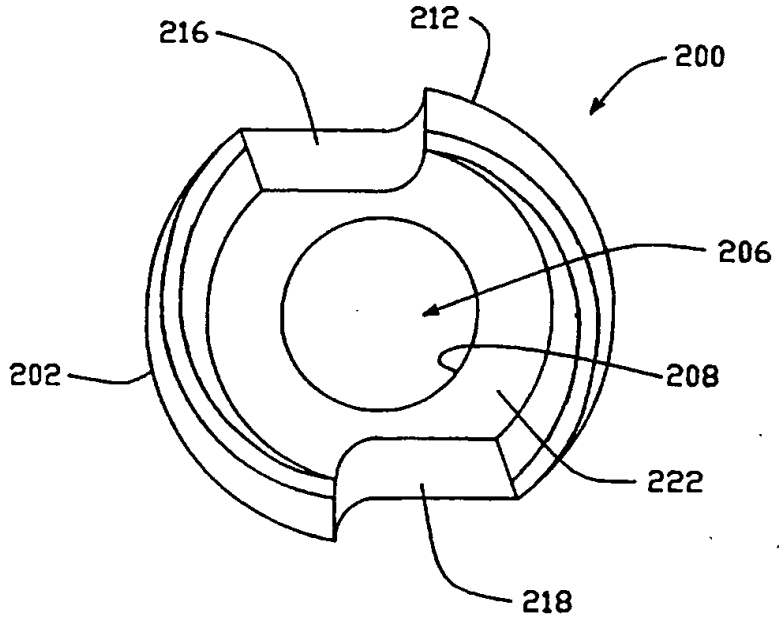

FIG.—11

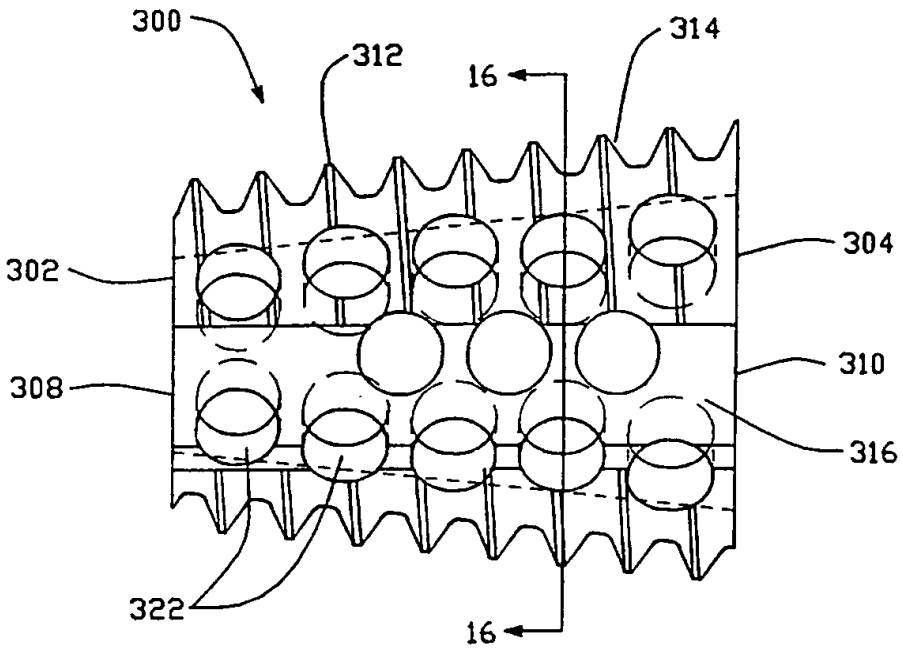

FIG.—13

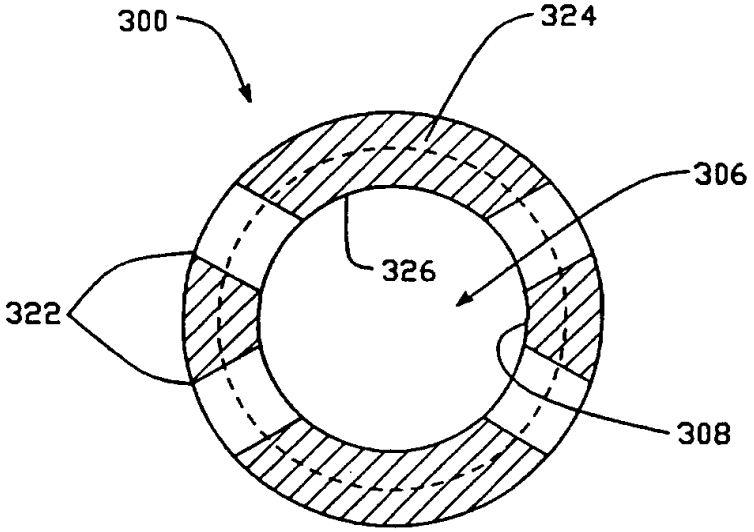

FIG.—16

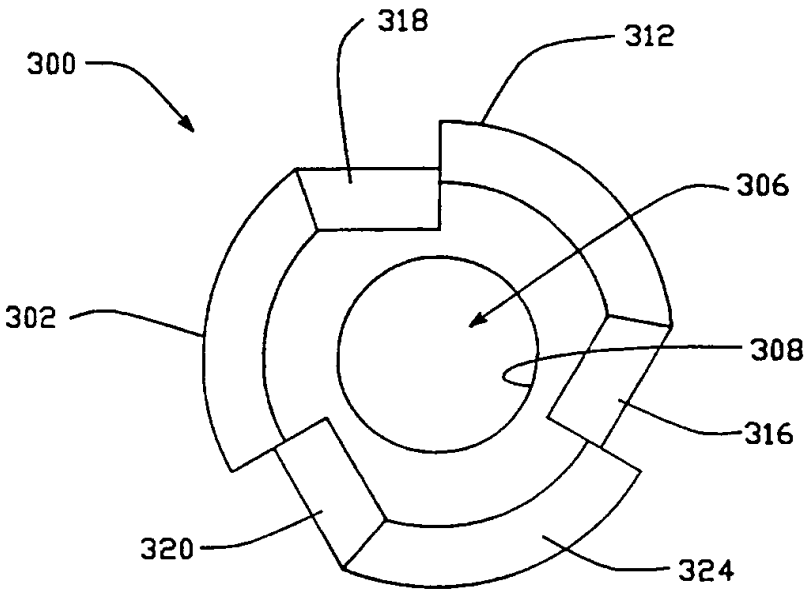
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FIG.—14

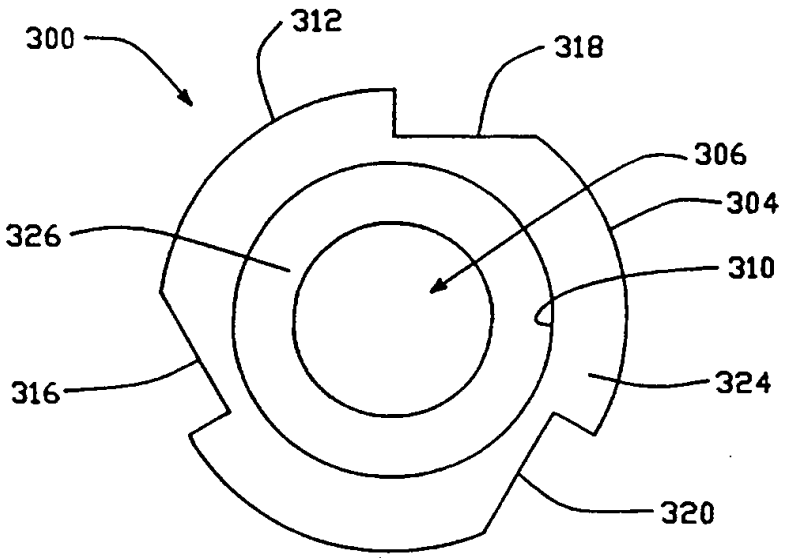
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FIG.—15

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US95/11281

A. CLASSIFICATION OF SUBJECT MATTER

IPC(6) :A61B 17/70
US CL :606/61

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. : 606/61, 65, 66, 72, 73, 76, 90, 104; 623/17, 16

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.
X --- Y	US, A, 4,950,270 (BOWMAN ET AL.) 21 August 1990, see Fig. 1.	1-3, 8, 9, 11-15, 18, 21-25, 27-30, 39-42, 45, 47-49, 52-54, 64-66, 71-73, 75, 77-82, 85-89, 91-93, 98 --- 4-7, 10, 16, 17, 19, 20, 26, 31-38, 43, 44, 46, 50, 51, 74, 76, 83, 84

[X] Further documents are listed in the continuation of Box C. [ ] See patent family annex.

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Date of the actual completion of the international search	Date of mailing of the international search report
16 OCTOBER 1995	05 DEC 1995
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 GUY TUCKER Telephone No. (703) 308-3271

Form PCT/ISA/210 (second sheet)(July 1992)*

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US95/11281

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, A, 4,537,185 (STEDNITZ) 27 August 1985, see Fig. 2.	4-7, 16, 17 19, 26, 35, 36, 38, 43, 44, 46, 50, 51, 74, 76
Y	US, A, 4,484,570 (SUTTER ET AL.) 27 November 1984, see Fig. 3.	10, 20, 31-38, 83, 84
X	US, A, 4,349,921 (KUNTZ) 21 September 1982, see Fig. 4.	60
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Y		61, 62, 69

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INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 6 : A61F 2/44 | A1

(11) International Publication Number: WO 96/17564

(43) International Publication Date: 13 June 1996 (13.06.96)

(21) International Application Number: PCT/US95/15654

(22) International Filing Date: 1 December 1995 (01.12.95)

(30) Priority Data:
08/353,566 9 December 1994 (09.12.94) US

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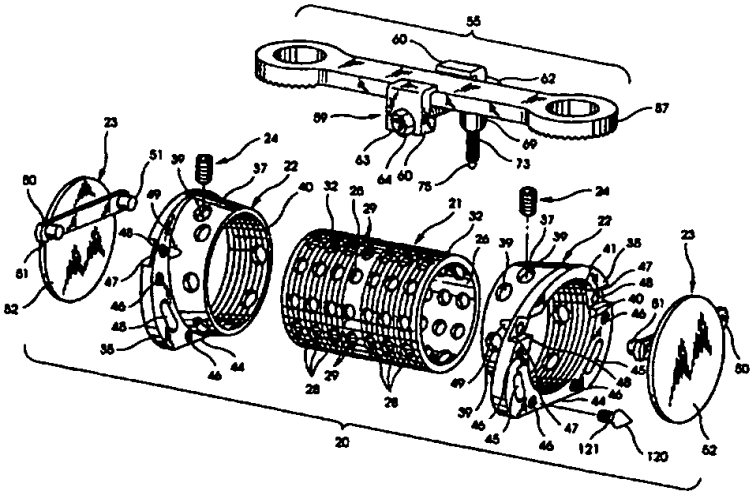
(81) Designated States: AU, CA, CN, JP, KR, European patent (AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE).

Published
With international search report.

(54) Title: ADJUSTABLE VERTEBRAL BODY REPLACEMENT



(57) Abstract

An adjustable vertebral boby replacement implant assembly (20) includes a thin-walled cylindrical body (21) configured to span over most of the length between intact vertebrae. The cylindrical body (21) defines a hollow interior (26) with a plurality of bone-ingrowth apertures (28, 29) communicating with the interior. The assembly further includes endplates (22) configured to contact the adjacent vertebra and to engage the cylindrical body therebetween. The cylindrical body and the endplates include mating threads (32, 40, 41) to permit adjustment of the overall height of the implant. In one embodiment is a set screw (24) for locking the cylindrical body to the endplates. In another embodiment, a crimping channel (100) and notch (101) are defined in the endplates to be crimped onto the cylindrical body. A means for connecting the replacement implant to a longitudinal member is provided, which is one embodiment contemplates a clamp and screw assembly (55) and another embodiment includes an arm (94) projecting from the endplates with an opening (95) to receive a longitudinal member (105) therethrough.

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ADJUSTABLE VERTEBRAL BODY REPLACEMENT

BACKGROUND OF THE INVENTION

The present invention concerns an implant for replacement of one or more vertebral bodies and their adjacent disks. More particularly, the vertebral body replacement is particularly well suited for implantation through an anterior approach.

The treatment of injuries to the spine has advanced significantly since the days of the first recorded surgical procedure for spinal cord injury in the late 7th Century. The techniques, instrumentation and implants have changed over the years and have been better adapted to address many forms of spinal injury and deformities that can occur due to trauma, disease or congenital effects. One type of spinal deformity, a kyphosis, involves a prolapse of the vertebral column towards the front of the body, often caused by the destruction of the vertebral body itself. This destruction can be in the form of a trauma type injury, such as a fracture or burst injury to the vertebral body, or a non-traumatic deformity caused by a tumor or a degeneration of the bone in the vertebral body.

Treatment of a kyphosis in the thoracic or lumbar spine appears now to be best achieved through an anterior approach, particularly in order to avoid some of the more severe complications associated with support or replacement of a damaged vertebral body. In most treatments of a kyphosis, a high degree of anterior reconstruction of the spine is required, most frequently involving total removal of the damaged vertebral body. In a typical anterior approach, partial or total ablation of the vertebral body and the two

adjacent vertebral disks is carried out. The remaining space is then distracted to manipulate the spine to its correct orientation.

In many cases, the space is filled with a polymerizable paste or a bone graft which is frequently modeled to give it the shape of the destroyed vertebral body. Frequently, autologous bone, such as that extracted from the ilium, is used to bridge the space. The polymerizable paste can include a PMMA bone cement. Once the cavity remaining after the removal of the original vertebral body has been filled, an osteosynthesis instrument is positioned between the adjacent unaffected vertebrae to prevent any relative movement therebetween. The osteosynthesis device is essential to restabilize the vertebral column, to support the loads to which the thoracic or lumbar spine is exposed, and to enhance the likelihood and quickness of union of the bone graft material with the adjacent vertebral bodies. Once the bone graft and material is sufficiently solid, the osteosynthesis device normally is not subjected to any further mechanical stresses.

A known osteosynthesis device is depicted in U.S. Patent No. 5,108,395 to Jean-Marie Laurain, the disclosure of which is incorporated herein by reference. This system is illustrated in FIGS. 1 and 2 of the present application. Referring first to FIG. 1, it can be seen that a damaged vertebra V_3 includes a destroyed vertebral body C_3. An interior implant 1 is provided for bridging between the two intact vertebrae V_2 and V_4 to permit removal of the damaged vertebra V_3 and its adjacent disks D_2 and D_3. The anterior implant 1 includes a pair of clamps 2 which are engaged to the intact vertebral bodies by way of a number of spikes 3. In addition, the clamps 2 are maintained in position by bone screws 5 extending through screw holes 11, lateral lugs 8 of the clamps. The implant 1 also includes a plate 6 which is configured to span between the intact

vertebrae and is strong enough to support the loads generated in the spinal column at that location.

Each clamp 2 includes a threaded post 12 projecting therefrom which is configured to pass through a corresponding opening 14 at each end of the plate 6. A nut 7 is adapted to engage the threaded post 12 to fix the plate 6 to each of the clamps 2. The surface of the clamps 2 include serrations 15 which mate with corresponding serrations 16 at each end of the plate 6, thereby permitting differing angular orientations of the plate relative to each of the clamps. An opening 9 is provided through the threaded post 12 of the clamps to receive another bone screw 5 for firm fixation of the clamp with the healthy vertebral bodies V_2 and V_4.

An important feature of the system described in the '395 patent is the provision of notches 18 in each of the clamps 2. The notches are configured to receive the tips of a forceps 19 which is used to provide a distraction force between the two vertebrae V_2 and V_4. As shown in FIG. 2, once the clamps 2 are fixed to the corresponding intact vertebrae, the forceps 19 are used to distract and permit room for placement of a bone graft G. Once the bone graft is in place, the anterior plate 6 can be attached to each of the clamps 2 in the manner previously described. Once the plate is in position, the distraction forceps 19 is removed and the nut 7 tightened to form a rigid construct.

The anterior construct shown in the '395 patent and in FIGS. 1 and 2 of this application is one system for providing anterior fixation with the use of autologous or allogenic bone graft material. Other implants have been devised which rely upon an additional element interposed between the adjacent vertebra, in lieu of or in addition to the traditional bone graft material. One such device is shown in the patent to Harms et al. no. 4,820,305, which is sold as the "Harms Cage" by the Biedermann-Motech Company. This device contemplates a hollow cylindrical mesh which is

inserted in the gap between adjacent vertebra, with bone graft material being disposed inside the hollow interior of the mesh.

The patent to Brantigan, No. 5,192,327, shows a device similar to the "Harms Cage" which is composed of a number of hollow oval-shaped implants within which bone graft material is disposed. European Patent No. 0 179 695 to Kehr shows a rigid inert body having a number of passageways extending between the intact vertebrae into which bone growth material can be implanted. In addition, the device shown in the Kehr European patent includes a plate spanning between the vertebrae having holes for receiving bone screws therethrough.

Another variety of implant devices particularly suited for replacement of vertebral bodies include components of generally solid construction which completely occupy the empty vertebral space. These devices are represented by the patents to Kapp et al., no. 4,554,914; Doty, no. 4,599,086; Ogilvie et al., no. 4,636,217; and Downey, no. 5,147,404. Each of these devices is provided with a spike or similar mechanism for engaging the end plates of the intact vertebrae to maintain the implant in position. A similar construction is followed in the U.S. Patent 5,062,850 to MacMillan et al., although this device includes open space between support columns of the axially fixed vertebral body prosthesis.

In each of the former patents, the implant device requires separate distraction of the intact vertebrae prior to insertion of the device. The following patents show vertebral prosthesis which include some feature for expansion of the device *in situ*. For example, the Main et al., no. 4,932,975, and Barber no. 5,236,460 show prostheses that telescope through the admission of a hydraulic fluid. The patents of Rezaian, no. 4,401,112; Wu, no. 4,553,273 and Daher, no. 4,657,550 show devices that expand *in situ* the manipulation of a threaded component. In addition, the

Rezaian patent shows a turnbuckle construct of this type with the addition of a spiked plate engaged in the opposite intact vertebrae to strengthen the construct.

In recent years, the application of anterior approaches to instrumenting the spine has become more prevalent. As these anterior approaches advance, it becomes of greater necessity to provide a vertebral body replacement that meets all of the benefits of anterior surgery without the detriments of the several prior devices. Each of the above-mentioned vertebral body replacements suffer from one or more disadvantages. For instance, some of the devices do not provide means for osteosynthesis between the intact vertebrae. These devices lack features that can either permit bone ingrowth or facilitate placement of bone graft between adjacent healthy vertebrae. It is recognized that a more permanent and stable correction of a kyphotic condition occurs with fusion of a bony mass in place of the replaced vertebra. Thus, any vertebral body replacement should accommodate this aspect. Other vertebral prosthesis offer no means for adjusting the size of the implant to accommodate the specific vertebral anatomy. Further, other of the devices do not contemplate some auxiliary fixation to help provide a stable construct. Each of these needs, and many others, are met by the vertebral body replacement according to the present invention.

SUMMARY OF INVENTION

The present invention contemplates a vertebral replacement implant and assembly for fixation of the implant in the space left by a removed vertebra between two intact vertebrae. In one aspect, the implant includes a thin-walled cylindrical body sized to occupy a substantial portion of the space between the intact vertebrae. The cylindrical body is hollow with a plurality of apertures through the wall of the body in communication with the interior, to permit bone ingrowth once the implant is implanted. The opposite ends of the cylindrical body carries continuous threads, preferably on the outer surface of the body.

The inventive implant further contemplates a pair of endplates having a surface directed against a corresponding one of the intact vertebrae when the prosthesis is implanted. The endplates each include a cylindrical portion extending from the end surface, which portion includes threads for mating with the threaded ends of the cylindrical body. Preferably, the threads of the endplates are internal to the cylindrical portion. In one aspect, the endplates are themselves hollow to provide communication between the hollow interior of the cylindrical body and the adjacent intact vertebrae. Alternatively, the invention contemplates the addition of an end cap to the implant to close the end surface of the endplates against the adjacent vertebrae in order to provide additional support for weak vertebrae.

Another feature of the invention resides in the provision of means for fixing the cylindrical body to each of the endplates to prevent unthreading of the mating threads of the three components of the implant. In one embodiment, the means for fixing includes apertures in the threaded portion of the endplates which are threaded to accept a set screw. Preferably, two set screws are threaded into two such apertures in the endplates to apply a clamping pressure

against the cylindrical body engaged with the endplate.

In another embodiment, the means for fixing contemplates a crimpable cylindrical portion of the endplates. In one aspect, the cylindrical portion includes an annular ring, dissected by a crimping notch. The application of a crimping force around the annular ring reduces the notch, and thereby reduces the circumference of the cylindrical portion so it is tightly engaged about the cylindrical body threaded therein.

Another inventive aspect resides in the provision of means for connecting the implant to a longitudinal member extending outside the space left by the removed vertebrae. The longitudinal member may be a plate or a rod that is fixed in a known manner to the adjacent intact vertebrae. Preferably, the longitudinal member can be used to assist in the distraction of the intact vertebrae for insertion of the vertebral replacement implant.

In one embodiment, the means for connecting includes a clamp configured to clamp onto the longitudinal member. The clamp supports a screw directed towards the replacement implant when it is interposed between the intact vertebrae. The cylindrical body of the implant includes a number of apertures threaded to receive the connecting screw. The clamp is preferably slidable along the length of the longitudinal implant to facilitate alignment of the screw with the number of threaded apertures of the cylindrical body. In addition, the clamp includes a spherical seat, and the screw includes a spherical head to permit varying angular orientations of the screw relative to the longitudinal member.

In another embodiment, the means for connecting includes an arm extending from a flange of the endplates. The free end of the arm defines an opening through which the longitudinal member extends. A set screw intersects the opening to provide fixation of the longitudinal member to the arm of the endplates.

One object of the present invention is to provide a

vertebral body replacement implant configured to support the space left by removal of a damaged or diseased vertebra. One objective is to provide an implant that can be easily adjusted to vary the overall length of the implant dependent upon the vertebral level into which the implant is interposed. A further objective of the inventive implant is to permit this length adjustment yet provide means for fixing the components to prevent disengagement or unthreading.

A further object is achieved by the present invention by the provision of means for connecting the vertebral replacement implant to a longitudinal member extending along the length of the spine between the adjacent intact vertebrae. The longitudinal member can be used for distracting the space left by the removed vertebra to facilitate insertion of the replacement implant. Yet another object is to provide an implant that can house bone growth material to facilitate fusion of the instrumented level.

One benefit of the vertebral body replacement of the present invention is that it provides a strong implant to support the spinal loads while awaiting fusion of bone growth material between the intact vertebrae. A further benefit is that the implant can be more easily adjusted to accommodate spaces at different vertebral levels.

Other objects and benefits of the invention can be gleaned from the following written description of the invention, considered together with the accompanying figures and claims.

DESCRIPTION OF THE FIGURES

FIG. 1 is an exploded perspective view of a spinal osteosynthesis implant according to the prior art patent 5,108,395.

FIG. 2 is a view showing a portion of the view of FIG. 1 with the addition of an instrument for permitting positioning of a graft between the vertebrae carrying the clamps associated with the prior device of the '395 patent.

FIG. 3 is an exploded perspective view of a vertebral body replacement assembly in accordance with one embodiment of the present invention.

FIG. 4 is an end elevational view of an endplate used in connection with the vertebral body replacement assembly shown in FIG. 3.

FIG. 5 is a side elevational view of an endplate used with the vertebral body replacement assembly of FIG. 3.

FIG. 6 is a perspective exploded view showing a component of the clamp assembly used with the vertebral body replacement assembly shown in FIG. 3.

FIG. 7 is a side elevational view of a vertebral body replacement assembly in accordance with another embodiment of the invention, particularly for use with an elongated rod spanning the vertebral sections.

FIG. 8 is an end elevational view of the vertebral body replacement assembly shown in FIG. 7, with the assembly shown in position on a intact vertebra.

FIG. 9 is a side elevational view of the assembly shown in FIG. 7 as engaged to an elongated rod.

FIG. 10 is a perspective view of the endplate used with the vertebral body replacement assembly shown in FIG. 7.

FIG. 11 is an end elevational view of one specific endplate used in connection with the vertebral body replacement assembly shown in FIG. 3 in the thoracic spine.

DESCRIPTION OF THE PREFERRED EMBODIMENTS

For the purposes of promoting an understanding of the principles of the invention, reference will now be made to the embodiments illustrated in the drawings and specific language will be used to describe the same. It will nevertheless be understood that no limitation of the scope of the invention is thereby intended, such alterations and further modifications in the illustrated device, and such further applications of the principles of the invention as illustrated therein being contemplated as would normally occur to one skilled in the art to which the invention relates.

Referring now to FIG. 3, a vertebral body replacement assembly 20 is shown in accordance with one embodiment of the present invention. The assembly 20 generally includes a threaded cylindrical body 21, threaded endplates 22 and end caps 23. A set screw 24 is also provided as one embodiment of a means for fixing each of the endplates 22 to a corresponding end of the cylindrical body 21. In one specific embodiment, the set screw 24 is a breakable locking screw in which the head of the screw shears off when the tightening torque limit is reached. Such a locking screw is disclosed in co-pending French patent application No. 94 10 377, filed on August 29, 1994.

The threaded cylindrical body 21 is formed from a cylindrical wall 25 which defines a hollow cavity 26 therein. The cavity is configured to receive bone osteosynthesis material, which may be in the form of autogenous or allograph material. The cylindrical wall 25 is provided with a plurality of apertures 28 in communication with the cavity 26. These apertures provide a path for bone or tissue ingrowth to further enhance the stability of the implant. The cylindrical wall 25 includes a second plurality of threaded apertures 29 generally in the middle of the

implant, which are configured to engage the support assembly 55 as described in more detail herein.

In one important feature of the cylindrical body 21, the opposite ends of the cylindrical wall 25 are formed into external threads 32. In one specific embodiment, the threads 32 extend from each opposite end over most of the total length of the threaded cylindrical body 21 and are configured to engage the threaded endplates 22. Each endplate includes a flange 35, which preferably assumes a shape to cover a substantial load-bearing area of the end plates of the adjacent intact vertebral bodies. A cylinder 37 is integrally formed with flange 35 to extend toward the threaded cylindrical body 21 when the endplates 22 are placed within the excised vertebral space. The cylinder 37 of each endplate includes a number of threaded openings 39 adapted to receive a set screw 24 therein.

The cylinder 37 and flange 35 of the endplates 22 define a bore 40 therethrough. The inside surface of the bore 40 is provided with internal threads 41 which are configured to mate with the external threads 32 of the cylindrical body 21. In the preferred embodiment, the threads 41 extend along at least the entire length of the cylinder 37 and preferably into the flange 35.

Further details of the endplates 22 can be seen in FIGS. 4 and 5. As shown in FIG. 5, the cylinder 37 is integrally formed with the flange 35 to define a lordosis angle 43. This angle is intended to permit use of the vertebral body replacement assembly 20 to replace a damaged vertebra, such as vertebra V_3 shown in FIG. 1, and still maintain the normal lordotic curvature of the spine at that level. The end face 36 of the flange 35 is provided with vascularization apertures 45 extending through the flange. These apertures 45 are intended to provide an avenue for vascularization of the space between the adjacent vertebrae. The end face 36 can be provided with four spikes, such as spikes 91 shown in

the embodiment of FIG. 7. Alternatively, spikes 120 (FIG. 3) can be provided that include a threaded stem 121 to be engaged in threaded apertures 46 defined in end face 36. In either case, the spikes (91, 120) are configured to penetrate the end plate of the adjacent vertebra to help maintain the position of the implant in situ.

The end face is further provided with a mounting slot 47 passing across the flange 35 and spanning along a chord of the internal bore 40. Within each mounting slot is an aperture 48 passing therethrough. The cylinder 37 of the endplate 22 is provided with a mounting notch 49 that is aligned with each aperture 48 in the mounting slot 47. This slot 47, aperture 48 and notch 49 are configured to support an end cap 23, as herein described. Referring back to FIG. 3, the end cap 23 includes a generally rectangular support bar 50 which is mounted to span across a chord of the flat circular plate 52 of the end cap. At each end of the support bar 50 is an outwardly projecting lug 51. Each lug 51 is sized to be received within a corresponding aperture 48, while the support bar 50 is itself configured to fit within the mounting slot 47 in the flange 35. Further, each lug 51 slides conveniently into a corresponding mounting notch 49 in the cylinder 37. In this manner, the end cap 23 is held in position, particularly when the replacement body assembly is disposed between the adjacent intact vertebrae V_2 and V_4.

The end cap 23 provides additional support for the implant between the adjacent intact vertebrae. The end cap can be eliminated if bone growth between the adjacent vertebrae and through the replacement body is preferred. Alternatively, the plate 52 of each end cap 23 can be perforated to permit bone ingrowth between the vertebral end plates and the bone growth material disposed within the threaded cylindrical body 21. In the preferred embodiment, the endplates are shown solid to provide the maximum load bearing capability for loads along the length of the vertebral column.

In the illustrated embodiment, the threads 32 on the cylindrical replacement body are external threads, while the threads 40 in the endplates are internal. Alternatively, the cylinder 37 of the endplates can carry external threads and the cylindrical replacement body carry internal threads in the cavity 26. In this latter instance, the inner diameter of the cylindrical body would naturally be slightly greater than the outer diameter of the cylinder of the endplates.

In the preferred embodiment, the cylindrical wall forming the implant 21 can be relatively thin, when compared against replacement bodies of the prior art. In one specific embodiment, the wall is one (1) mm. thick. Since the primary load endured by the implant will be axial compression, rather than bending, a thin-walled cylinder is appropriate and even desirable.

It is also preferred that the implant 21 include a large number of apertures 28, 29 to promote tissue ingrowth and vascularization, thereby enhancing the stability of the construct after fusion has occurred. In one specific embodiment, the total area of the plurality of apertures is at least twenty five percent (25%) of the surface area of the cylindrical body 21.

In use, the damaged vertebra, such as vertebra V_3 shown in FIG. 1, is removed. In one embodiment, the clamps 2 of the interior implant 1 shown in FIGS. 1 and 2 are engaged to the intact vertebral bodies in the manner shown in FIG. 2. Also shown in FIG. 2, the forceps 19 can be used to distract the intact vertebrae to permit implantation of a vertebral body replacement assembly 20. In the preferred method, the optimum vertebral height is determined and the threaded cylindrical body 21 and threaded endplates 22 are fitted together to achieve that proper height. Specifically, each of the end caps can be threaded onto the threaded cylindrical body 21 until the desired height is attained.

It is important that the bottom edge 44 of the flange 35

of each of the endplates be generally oriented in the same way between the two threaded endplates 22. This orientation is important because the replacement assembly 20 will be disposed between the two intact vertebrae, bearing against the end plates of those vertebrae. In order to maintain the maximum load bearing capability, the flanges 35, and particularly the end face 36, assume the shape of the vertebral body against which the endplates bear and are sized to occupy as much area of the intact vertebral body end plate as possible.

Preferably, three such shapes are provided to accommodate the anatomic variations of the vertebral bodies at the lumbar, thoraco-lumbar and thoracic levels. the configuration of the flange 35 shown in FIG. 4 is applicable to the thoraco-lumbar vertebrae. A smaller, more rounded, configuration can be provided for implantation at the thoracis level, such as the flange 35' shown in FIG. 11. The flange 35' is also shown as including a relief radius 38 to increase the clearance between the flange and the dural space housing the spinal cord. This relief radius 38 is preferably included in all three shapes of the endplate flanges.

In one specific embodiment, the external threads 32 on the threaded cylindrical body 21 are cut in opposite directions so that the endplates can be drawn together or apart by rotating only the cylinder. Thus, as the cylinder is rotated in one direction, the threads 32 at each of the ends engage the internal threads 41 of each of the end caps 23 in the right direction to draw the end caps together. Alternatively, the handedness of the threads 32 can be the same at each end so that it is necessary to individually thread each end cap in opposite directions onto the cylindrical body 21. The disadvantage of this arrangement is that it is more difficult to adjust the height of the total assembly 20 while maintaining the proper orientation of each of the lower edges 44 of the end face 36. An advantage is that *in situ* the assembly is unable to unthread itself.