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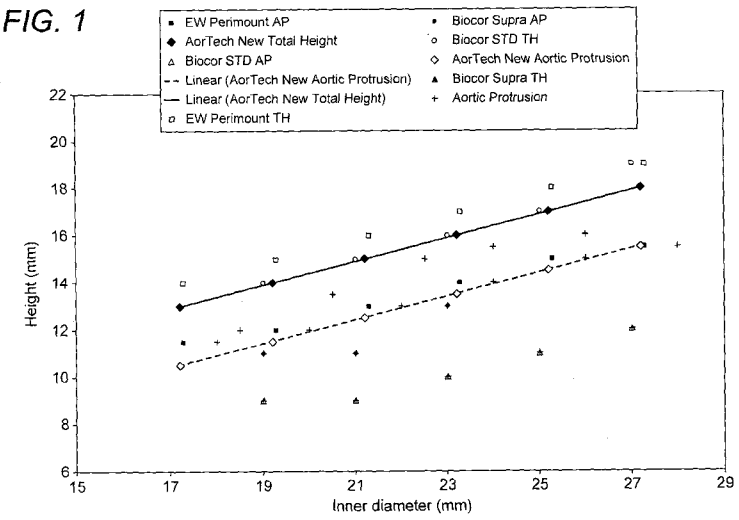
FIG. 1




(57) Abstract: There is provided a cardiac valve prosthesis used to replace natural valves of the heart wherein the prosthesis has a frame with an annular portion and at least two leaflets and the total height of the valve is correlated with the inner diameter of the valve and the effective orifice area. Scaling of the height of the frame with the diameter of the annular portion is considered advantageous as a reduced height of prosthesis can minimise the risk of abrasion of the aortic sinus and the coronary arteries following placement of the valve.

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**"Valve"**

## Field of Invention

The present invention relates to artificial cardiac or heart valves, more particularly to flexible leaflet heart valve prostheses which are used to replace natural aortic or pulmonary valves of the heart.

## Background

Ideally artificial cardiac valves should work in a similar fashion to natural heart valves in that when blood flows in a particular direction the valve adopts an open position to permit blood flow through the valve, whereas when blood tries to flow in the opposite direction the valve adopts a closed position preventing the flow of blood in the reverse direction through the valve (regurgitation).

Natural cardiac valves use thin flexible tissue leaflets as the closing members. Artificial heart valves can use flexible polymer leaflets as the closing members. In the closed position of the valve, the leaflets are arranged such that each leaflet contacts its neighbour. This arrangement serves to close the valve and prevent the back flow of blood through the valve. In the open position the leaflets separate from each other and move radially towards the inner walls of the blood vessel in which the valve is located. This open configuration of the valve permits the flow of blood through the valve.

Conventional cardiac valve prostheses typically comprise an annular frame disposed perpendicular to the blood flow. The annular frame generally has three posts extending from an annular stent portion in the downstream direction (blood outflow direction) defining three generally U-shaped openings or scallops between the posts to form a crown-like frame. Leaflets, which can adopt open and closed positions in a similar fashion to natural valve leaflets, are attached to the frame between the posts along the edges of the scallops. The leaflets are unattached to the frame at free edges of the leaflets adjacent to the downstream ends of the posts.

International Patent Application WO 98/32400 entitled "Heart Valve Prosthesis" discloses a cardiac valve design, using closed leaflet geometry, comprising

essentially a trileaflet valve with leaflets moulded in a geometry derived from a sphere towards the free edge and a cone towards the base of the leaflets.

International Patent Application WO 01/41679 discloses a cardiac valve wherein the leaflets have been designed to facilitate wash out of the whole leaflet orifice including the area close to the frame posts.

WO 2004/082536 discloses leaflets defined by a parabolic function and cardiac valves including such leaflets. It was discussed by WO 2004/082536 that by using leaflets with a parabolic configuration in cross section, stresses of the leaflets can be reduced and hence the lifespan of the valve may be improved.

To be suitable for implantation, advantageously synthetic or artificial cardiac valves should be sufficiently durable such that they are clinically functional for at least 20 years. Durability of the synthetic leaflets depends on the materials from which the leaflets are constructed and also the stresses to which the leaflets are subjected during use. Further, cardiac valves require to be properly positioned in the patient to optimize blood flow. Advantageously, a cardiac valve should aid proper positioning of the valve by a surgeon.

It is an aim of the present invention to provide an improved cardiac valve prosthesis.

According to a first aspect of the present invention, there is provided a cardiac valve prosthesis comprising:

a frame having an annular portion which, in use, is disposed substantially perpendicular to the blood flow, the frame having first and second ends, a first end being a blood inflow end and a second end defining at least two scalloped edge portions, separated and defined by at least two posts

and at least two leaflets, each leaflet being attached to the frame along a scalloped edge portion and being movable between an open and a closed position, each of the at least two leaflets having a blood inlet side, a blood outlet side and at least one free edge, the at least two leaflets being in a closed position when fluid pressure is applied to the blood outlet side of the at least two leaflets such that the at least one

free edge of a first leaflet is urged towards the at least one free edge of a second or further leaflet, and the at least two leaflets being in an open position when fluid pressure is applied to the blood inlet side of the at least two leaflets such that the at least one free edge of the first leaflet is urged away from the at least one free edge of the second or further leaflet;

wherein the total height of the valve is correlated with the inner diameter of the valve by

Inner diameter of valve = 2Total Height (mm) – 9mm +/- 0.2mm to the height value

wherein the Effective Orifice Area (EOA) ($mm^2$) varies relative to the inner diameter of the valve whereby EOA is at least

| **EOA ($mm^2$)** | 1.45 | 2.3 | 3.46 |
|---|---|---|---|

relative to an inner diameter of

| **Size (Inner Diameter) mm** | **19** | **23** | **27** |
|---|---|---|---|

The inventor has determined a cardiac valve frame that reduces the stresses to which the valve prosthesis is subjected during opening and closing of the valve. Further the frame promotes enhanced hydrodynamic properties of the valve.

Preferably the inner diameter of the valve = 2Total Height (mm) – 9mm +/- 0.1mm to the height value, and even more preferably the inner diameter of the valve = 2Total Height (mm) – 9mm to the height value

wherein the Effective Orifice Area (EOA) ($mm^2$) varies relative to the inner diameter of the valve whereby EOA is at least

| EOA ($mm^2$) | 1.45 | 2.3 | 3.46 |
|---|---|---|---|

relative to an inner diameter of

| Size (Inner Diameter) mm | 19 | 23 | 27 |
|---|---|---|---|

In embodiments of the valve the Effective Orifice Area (EOA) ($mm^2$) varies relative to the inner diameter of the valve whereby EOA is at least

| EOA ($mm^2$) | 1.45 | 2.3 | 3.46 |
|---|---|---|---|

relative to an inner diameter of

| Size (Inner Diameter) mm | 19 | 23 | 27 |
|---|---|---|---|

and the regurgitation provided by the valve relative to the inner diameter is less than or equal to

| Size (Inner Diameter) | 19 | 23 | 27 |
|---|---|---|---|
| Regurgitation | 1.2% | 3.3% | 5.0% |

By regurgitation is meant the backflow of blood across the valve from a blood outlet side of the leaflet of a valve towards a blood inlet side of a leaflet of the valve per cardiac cycle.

In further embodiments of the valve the Effective Orifice Area (EOA) ($mm^2$) varies relative to the inner diameter of the valve whereby EOA is at least

| EOA ($mm^2$) | 1.45 | 2.3 | 3.46 |
|---|---|---|---|

relative to an inner diameter of

| Size (Inner Diameter) mm | 19 | 23 | 27 |
|---|---|---|---|

the regurgitation provided by the valve relative to the inner diameter is less than or equal to

| Size (Inner Diameter) mm | 19 | 23 | 27 |
|---|---|---|---|
| Regurgitation | 1.2% | 3.3% | 5.0% |

and the pressure drop provided by the valve relative to the inner diameter is less than or equal to

| Size (Inner Diameter) | 19 | 23 | 27 |
|---|---|---|---|
| Pressure Drop (mmHg) | 10.0 | 5.2 | 2.4 |

The inner diameter of the frame is the measured internal diameter of the annular portion of the frame at the blood inflow end of the frame.

Pressure drop is defined herein as the pressure difference measured when the valve starts to open. Typically, there is a higher pressure drop in valves of small diameter in comparison to valves of larger diameter. It is indicative of resistance.

It is known that the internal diameter of a cardiac valve prosthesis relates to the EOA, for example a 10% decrease in diameter at the blood inflow portion of a annular portion of a cardiac valve from 20 mm to 18 mm roughly results in a 20% decrease in area.

As discussed, for example in Hans-Hinrich Sievers, Prosthetic Aortic Valve Replacement, *J Thorac Cardiovasc Surg* 2005;129:961-965, there is growing evidence that actual valve diameter dimensions vary considerably from the labeled diameters. In view of this, EOA cannot be compared merely on the basis of a labeled size of a valve, but requires measurement of the internal dimensions of a valve.

In embodiments the inner diameter of the frame can be further correlated with the aortic protrusion of the valve by

Inner diameter of valve = 2Aortic Protrusion (mm) – 4mm+/- 0.2 mm to the height value.

In embodiments the inner diameter of the frame can be further correlated with the aortic protrusion of the valve by

Inner diameter of valve = 2Aortic Protrusion (mm) – 4mm+/- 0.1 mm to the height value.

More preferably in embodiments the inner diameter of the frame can be further correlated with the aortic protrusion of the valve by

Inner diameter of valve = 2Aortic Protrusion (mm) – 4mm to the height value.

In embodiments of the frame the aortic projection and total height of the frame will vary as indicated according to Table 1.

Table 1

| **Size (Inner Diameter)** | **19** | **21** | **23** | **25** | **27** |
|---|---|---|---|---|---|
| **Aortic Projection (mm)** | 11.5 | 12.5 | 13.5 | 14.5 | 15.5 |
| **Total Height (mm)** | 14 | 15 | 16 | 17 | 18 |
| **ID (Inside Stent mm)** | 19.2 | 21.2 | 23.2 | 25.2 | 27.2 |

The ID (inside Stent mm) is the unfinished dimension of the annular portion prior to fixation of the leaflets onto the frame. The Inner Diameter is the measured internal diameter of the annular portion of a finished valve at the blood inflow end when the leaflets have been attached to the frame.

An advantage of scaling the aortic protrusion and total height of the frame with the diameter of the annular portion is that a reduced aortic protrusion of the valve ensures easier implantation of the valve. In particular, the reduced total height and aortic protrusion of the valve reduces the risk of abrasion on the aortic sinus and fouling of the coronary arteries. The shortened frame design can allow for better placement of the valve and can provide improved washing around the leaflets when, in use, the valve is located in the aortic sinus.

In embodiments the frame can be adapted such that peak stress is located at the outside diameter of the annular portion of the frame during the fully closed part of the cardiac cycle of the valve.

Advantageously a valve including the frame of the present invention can offer superior hydrodynamics and reduced regurgitation compared to leading tissue prostheses, resulting in greater net forward flow per cardiac cycle.

The annular portion of the valve may be provided such that all points of the annulus are not on the same plane, i.e. the annular portion is non-planar and the annular portion includes undulations at least at the blood inflow end of the annular portion wherein the peak of the undulations extend a short distance towards the tip of the posts. The annular portion which, in use, is substantially perpendicular to the blood flow axis thus has an undulating form wherein the undulations form a continuous wave around the annular portion such that a peak of the wave of an undulation corresponds to the position where a post extends from the blood outflow end of the annular portion and the trough of the wave corresponds to the scalloped end portion between the posts of the blood outflow portion.

This has the effect that the inflow end of the annular portion has alternating actuate portions which substantially correspond in direction with the scalloped ends between the posts. The undulating wave of the annular portion can therefore have a peak in the direction of the outflow end of the valve and a trough in the direction of the blood inflow end of the valve.

In embodiments the distance between the maximum of a peak of such arcuate portions on the annular portion and the minimum trough (peak to peak amplitude) can be in the range 2.3 to 2.7 mm, preferably 2.5 mm and have a frequency of 3 Hz. In embodiments the undulations at the blood inflow end of the annular portion can be defined by 1.25mm (peak amplitude) and a frequency of 3 Hz.

If too great or too small an amplitude is provided to the undulations at the blood inflow end of the annular portion, the annular portion will not conform to the natural anatomy to the body.

Where X and Y are defined as the radius of the annular portion and Z is orthogonal to X and Y, a total height (TH) of the valve can therefore be described as the distance in Z from the peak of a trough of an undulation at the blood inflow end to the tip of a post extending from the outflow end of the annular portion.

The aortic projection (AP) of the frame can be defined as the distance in Z from the peak of the undulating wave at the blood inflow end to the tip of a post extending from the outflow end.

The annular portion can include a sewing ring groove to allow the valve to be secured to an implantation site in a subject's body.

The frame and leaflets when not experiencing opening or closing loads adopt a neutral configuration. The neutral configuration is the configuration of the frame and leaflets when they are at rest i.e. free from externally applied loads such as blood flow pressure gradients or as exerted by valve delivery devices. When in a closed state both the leaflets and the frame experience load which causes the leaflets and frame to be stressed. In embodiments stresses can be distributed across the leaflets and frame such that, in use,

typically a peak stress of 3.0MPa ±10% is provided to any part of the leaflet.

In embodiments a typical peak stress of 15.0MPa ±10% can be
provided to any part of the frame.

In preferred embodiments a peak stress of 3.0MPa ±10%, yet more preferably 3.0MPa can be provided to any part of the leaflet, and a peak stress of 15.0MPa ±10%, yet more preferably 15.0MPa can be provided to any part of the frame.

As will be appreciated, in use, when experiencing loads in the open and closed positions, the posts of the frame may resiliently move to minimise the stress experienced by the leaflets; however, in the neutral configuration, generally, the frame is substantially cylindrical when considered from the blood inflow end of the annular portion to a lower portion of the posts. A lower portion of the posts can be considered to be the portion of the posts at the base of the scalloped portion of the frame at the blood outflow end of valve. In embodiments, the frame defines a substantially cylindrical shape from the blood inflow end of the annular portion to the tip of the posts.

In embodiments the posts may be outward leaning on opening of the leaflets to allow a larger outlet opening for blood during systole to reduce the pressure gradient across the valve.

**Scallop shape for leaflet attachment**

Suitably, the scalloped edge portion of the frame defined by at least two, preferably three posts, may be defined through intersecting the notional surface defined by the posts with a cylinder of radius R (where R is the internal diameter of the annular portion of the blood inflow portion of the valve). In embodiments the scallop shape may be provided as taught in the art, for example as discussed by WO 01/41679 or as discussed by Mackay et al. Biomaterials 17, 1996.

**Leaflet attachment**

In embodiments of the frame preferably three posts are provided which extend from the annular portion such that a crown-like frame is provided wherein three leaflets are hung on the frame between the posts. In embodiments, the crown-like frame or stent, provided by the annular portion and posts, can be manufactured with a frame scallop offset radially by 0.1mm to allow for the entire frame to be coated with a thin layer of leaflet material to aid adhesion of the leaflets. As noted

above, this means that the finished internal diameter of the blood inflow end of the annular portion is 0.2mm narrower than the unfinished blood inflow end of the frame. Leaflets may be added to the frame by a dip-moulding process. The frame may be formed from a biostable polymer, i.e. a polymer that is resistant to degradation when it is implanted in the body. The rigid fatigue- and creep-resistant frame material may be polyether etherketone PEEK, high modulus polyurethane, titanium, reinforced polyurethane, or polyacetal (Delrin).

Alternatively, a relatively low modulus polymer may be used, which may be fibre-reinforced, to more closely mimic the aortic wall. The frame can be machined or injection moulded.

Suitably, a first stage of valve manufacture may entail dipping the frame in a polyurethane solution (for example Elast-Eon™) in order to apply a coating of approximately 0.1mm thick. Having dried the frame with applied coating in an oven overnight, it can be placed on a dipping former and aligned with the former scallops. The combination of frame and three dimensional dipping mould can then be dipped into a polyurethane solution, which forms a coating of solution on frame and mould. This coating flows slowly over the entire mould surface ensuring a smooth coating. The new coating on the frame and dipping mould solvates the initial frame coating thus ensuring a good bond between leaflet and frame. The dipping mould with polyurethane covering can then be dried in an oven until all the solvent has been removed. One or more dips may be used. The shape of the former, and the viscosity and solvent interactive properties of the polyurethane solution, control the leaflet thickness and the distribution of thickness over the leaflet.

Once the leaflets have been provided, the valve can be removed from the dipping mould.

In such a method to form the leaflets on the frame, the stent posts, can be deflected by a taper on the former provided, such that on removal of the frame from the former, the posts recover to their original position. This can cause the shape of the

leaflets to change slightly as a result of the movement of the stent posts.

The dipping mould and frame can then be covered with an excess of polyurethane polymer and the polymer can be allowed to drain off onto the region of the mould known as the drain-off area. Leaflet free edges may be trimmed.

Alternatively, valve leaflets may be manufactured using injection moulding. In such an embodiment, a mould can be constructed with a cavity which allows the valve frame to be inserted in the mould. The cavity is also designed with the leaflet geometry, as defined herein, as the inner leaflet surface. A desired thickness distribution is defined for the leaflet and the outer leaflet surface of the mould is constructed by adding the leaflet thickness normally to the inner leaflet surface. This mould is inserted in a conventional injection moulding machine, the frame is inserted in the mould and the machine injects molten polymer into the cavity to form the leaflets and bond them to the frame. The polymer solidifies on cooling and the mould is opened to allow the complete valve to be removed.

The leaflets may also be formed using a reaction-moulding process (RIM) whereby the polymer is synthesised during the leaflet forming. In such embodiments, a mould is constructed as described above. This mould is inserted in a reaction-injection moulding machine, the frame is inserted in the mould and the machine injects a reactive mixture into the cavity. The polymer is produced by the reaction in the cavity to form the leaflets and bond them to the frame. When the reaction is complete, the mould is opened to allow the complete valve to be removed.

Yet a further option is to compression mould a valve initially dipped. In such an embodiment, this approach allows the leaflet thickness or thickness distribution to be adjusted from that initially produced. By varying the thickness of the leaflets the dynamics of the valve opening and closing can be modified. For example, the thickness of the leaflet along a cross-section defined by the intersection of a plane perpendicular to the blood flow axis and the leaflet can be varied so that the thickness changes gradually and substantially continuously from a first end of the

cross-section (i.e. first edge of the leaflet) to a second end of the cross-section (i.e. second edge of the leaflet) in such a way that the mean thickness of the first half of the leaflet is different from the mean thickness of the second half of the leaflet.

Suitably, a leaflet for use in the described valve may be of uniform thickness throughout, in the range 40 to 500 microns, preferably 50 to 200 microns, more preferably 80 to 150 microns.

In embodiments, the leaflet can be thickened towards its attachment to the frame. Alternatively the thickness of the leaflet, along a cross-section defined by the intersection of a plane perpendicular to the blood flow axis and the leaflet, can change gradually and substantially continuously from a first end of the cross-section (i.e. first edge of the leaflet) to a second end of the cross-section (i.e. second edge of the leaflet) in such a way that the mean thickness of the first half of the leaflet is different from the mean thickness of the second half of the leaflet.

Typically, the valves of the present invention may be manufactured in the neutral position or close to it and are therefore substantially free of bending stresses in this position.

According to a second aspect of the present invention, there is provided a cardiac valve prosthesis comprising:

a frame according to the first aspect and at least two flexible leaflets;

wherein the frame comprises an annular portion which, in use, is disposed substantially perpendicular to the blood flow, the frame having a first (blood inflow) and second (blood outflow) end, one of the ends defining at least two scalloped edge portions separated and defined by at least two posts extending toward the blood outflow end of the valve, each leaflet being attached to the frame along a scalloped edge portion and being movable between an open and a closed position,

each of the at least two leaflets having a blood inlet side, a blood outlet side and at least one free edge, the at least two leaflets being in a closed position when fluid pressure is applied to the outlet side of the at least two leaflets such that the at least one free edge of a first leaflet is urged towards the at least one free edge of a second or further leaflet, and the at least two leaflets being in an open position when fluid pressure is applied to the blood inlet side of the at least two leaflets such that the at least one free edge of the first leaflet is urged away from the at least one free edge of the second or further leaflet;

wherein, in a first plane perpendicular to the blood flow axis, the length of each leaflet in a circumferential direction (XY) between the posts at any position along the longitudinal axis (Z) of a post is defined by a parabolic function.

In the closed position, the leaflet can be substantially linear in relation to the lengths XY of the leaflet when provided according to a parabolic function or the like at each point in Z, such that the XY lengths in Z vary as a continuous function. This minimises localised stress concentrations and provides more uniform stress distribution across the leaflet.

It is understood that reference to a parabolic function includes reference to any pseudotrigonmetric, pseudoelliptical, smooth function or table of values that describe a geometry which is substantially parabolic.

The use of a pseudo function to describe a parabolic function will be clear to one skilled in the art.

Preferably the parabolic function defining the length of a leaflet in the circumferential direction (XY) between the posts at any position along the longitudinal axis (Z) of a post is defined by

$$Y_z = \left(\frac{4R}{L_z^2}\right) x.(L_z - x)$$

Wherein $Y_z$ = Y offset at a particular co-ordinate X and Z

R = parabolic maximum

$L_z$ = straight line distance between a first post and a second post of the frame at a height Z

x = distance from origin of post towards another post

wherein the length of the parabola can be determined by

Length = $\int_0^x \sqrt{1+\left(\frac{dy}{dx}\right)^2}\,dx$

Preferably at least one correction factor can be applied to the measured lengths of for example $L_2$ or R to take into account changes in the dimensions of the frame or material of the leaflet during the cycling of the cardiac valve between an open and closed position. For example, such changes, in the dimensions may be, but are not limited to, inward movement of the posts of the valve on closure of the valve, stretch in leaflet material on closure of the valve, or movement in the notional point of coincidence of the leaflets. It will be clear to the skilled man how to determine the correction factor required in view of the frame and leaflet material selected. Preferably the correction factor is positive, negative or zero.

The materials chosen to form the frame and the leaflets of the valve and the design of the frame will influence to what extent the valve, including both the frame and the leaflets, yields to the forces to which the valve is subjected during valve closure and opening. For example, typically, inward movement of the posts of the valve occurs on closure of the valve due to the force of the backward flow of blood on the leaflet. This typically occurs to a greater extent at the tips of the posts than where the posts meet the frame. A correction factor is preferably included in the determination of the XY lengths of the leaflet at each height in Z to compensate for this movement in the frame.

Preferably the cardiac valve prosthesis of the second aspect of the invention comprises three posts and three leaflets wherein the valve comprises three leaflets

with one end of the frame of the cardiac valve prosthesis defining at least three scalloped edge portions separated by at least three posts, wherein each leaflet is attached to the frame along a corresponding scalloped edge portion.

In such an embodiment, preferably the three posts are rotationally symmetrically distributed around the circumference of the frame.

In embodiments the frame can be a collapsible stent. This may be advantageous as a collapsible stent may be delivered to a patient by percutaneous delivery. In such embodiments of the valve wherein the frame is a collapsible stent, the collapsible stent may be moved from a collapsed to an erect position using an inflatable balloon when the stent is suitably located in the patient.

A leaflet of a cardiac valve of the present invention may be formed from any biostable and biocompatible material. The leaflets may be formed from Elasteon.

The leaflet may have different thicknesses along a cross section defined by the intersection of a plane perpendicular to the blood flow axis.

The thickness of the cross section of the leaflet in the XY plane, defined by the intersection of a plane perpendicular to the blood flow axis, may change gradually and substantially continuously from a thickest portion where the leaflet is conjoined to the frame to a thinnest portion at the midpoint of the XY plane of the leaflet.

A leaflet of a valve as described above has a top and bottom. The bottom of the leaflet is attached to the scalloped portion of the frame and the top of the leaflet defines the free edge.

The free edge of the leaflet may be shaped to increase the length of the free edge of the leaflet relative to the length of the leaflet in the XY direction.

The free edge of the leaflet may be shaped such that in the longitudinal direction (Z) the free edge of at least one leaflet is parabolic.

The parabola can be in either direction. However if the parabola of the free edge of the leaflet extends away from the frame, preferably the maximum height of the parabola is 0μm to 500μm more preferably 0μm to 100μm, even more preferably

0μm to 50μm higher than the notional straight line between the ends of the parabola.

In embodiments the free edge of at least one leaflet can be parabolic in the longitudinal direction toward the scalloped edge portion of the frame such that the maximum depth of the parabola can be between 50μm to 100μm, 50μm to 500μm, 50μm to 100μm lower than the notional straight line between the ends of the parabola.

By making the free edge of valve leaflets parabolic, the stress and strain characteristics of the leaflet at the free edge are improved.

In embodiments, during the manufacture of the valve, the leaflets can be provided to the frame such that the free edge of the leaflets extend 500 μm further than the tip of the posts. A parabolic cut from the free edge towards the frame of the valve with a distance from the previous free edge to the vertex of the parabola of 700 μm can then be made. This provides a parabola with a vertex spaced around 200 μm closer to the frame than the notional free edge of the leaflet that extends from the tip of the posts of the frame. In such an embodiment the coating to form the leaflets may be applied to the frame in any suitable way known in the art, for example using dip moulding, conventional injection moulding, reaction injection moulding or compression moulding.

Preferred aspects of the invention apply to each of the other aspects mutatis mutandis.

An embodiment of the present invention will now be described, by way of example only with reference to the accompanying drawings wherein;

Figure 1 illustrates the measured diameter of a cardiac valve against the height of the valve for valves according to the present invention and valves in the art;

Figure 2 illustrates a table comparing data for a valve of the present invention against data generated from an Edwards perimount valve;

Figure 3 shows a side elevation of a valve of the present invention;

Figure 4 shows a front elevation of a valve of the present invention and illustrates Total Height (TH) and Aortic Projection (AP);

Figure 5 illustrates an oblique view of a valve of the present invention;

Figure 6 illustrates the leaflet lengths XY in multiple planes in Z; and

Figure 7 illustrates a parabolic cut to the free edge of the leaflet.

As previously discussed, a number of leaflet designs have been suggested for use in cardiac valves to ensure that the cardiac valves have sufficient leaflet material such that the valve is capable of opening as wide as possible to the maximum orifice of the valve, and that such opening requires as little energy as possible and further that regurgitation of blood through the valve is minimised.

Previous valve designs have been largely based on tissue valves and have not taken account of the different material properties of synthetic material, particularly synthetic polymer material.

In an embodiment of a valve of the present invention, to reduce the sharp curvature, which promotes stress points at specific points along the free edge, the length of the free edge (XY) of the leaflet was determined using a parabolic function. The parabolic length of the free edge can be determined by using the distances between the posts of the frame where the free edge is conjoined to the posts and the parabolic maximum.

Use of a parabolic shape at the free edge results in a gentler curvature of the leaflets and enables the length of the material along the free edge to be determined from a knowledge of the frame dimensions. However, this design, contrary to previous teaching, does not necessarily allow close fitting to be achieved between the leaflets at all points along the free edge. However, the seal obtained between the leaflets using a parabolic or like function was found to be sufficient to minimise regurgitation of blood through the valve to the required degree for the valve to be effective.

The determination of the length XY at the free edge of the leaflet is important to ensure that closure of the leaflets is achieved and to minimise the excess material of

the leaflets at the free edge such that the free edges of the leaflets do not fold over each other in the closed position.

In addition to allowing determination of the length of XY at the free edge of the valve, the XY lengths of the leaflets at all points in Z can be determined by using a parabolic function.

In the closed position, the leaflet can be substantially linear in relation to the lengths XY of the leaflet when provided according to a parabolic function or the like at each point in Z, such that the XY lengths in Z vary as a continuous function. This minimises localised stress concentrations and provides more uniform stress distribution across the leaflet.

Additionally, the frame of the valve has been adapted to provide for easier implantation of the valve and allow for improved washing around the leaflets and advantageously provide superior hydrodynamics and reduced regurgitation.

As illustrated the heart valve prosthesis 8 of the present invention comprises a stent or frame 10 which is substantially cylindrical. The frame has a first end 12 and second end 14. The second end (blood outflow end) 14 comprises three scalloped edge portions 16a, 16b and 16c separated by three posts 18, each post having a tip 20.

The first end (blood inflow end) also comprises undulations 22 such that all parts of the blood inflow end of the annular portion of the frame are not provided on a first plane (a) which is substantially perpendicular to the longitudinal axis of the frame, but can be considered as extending from a first plane substantially perpendicular to the longitudinal axis of the frame to a second plane (b) substantially perpendicular to the longitudinal axis of the frame wherein the first and second planes ((a) and (b)) are spaced apart by 25 mm.

As will be appreciated in the art, different sizes of heart valve can be provided to suit different patients. In the present invention, embodiments of the frame are formed to provide valves of diameters 19 mm, 21 mm, 23 mm, 25 mm or 27 mm. In such diameters the Aortic Projection (AP) and Total Height (TH) of the valve is as indicated in Table 2.

**Table 2**

| **Size (Inner Diameter)** | **19** | **21** | **23** | **25** | **27** |
|---|---|---|---|---|---|
| **Scallop Depth (mm)** | 10.5 | 11.5 | 12.5 | 13.5 | 14.5 |
| **Aortic Projection (mm)** | 11.5 | 12.5 | 13.5 | 14.5 | 15.5 |
| **Total Height (mm)** | 14 | 15 | 16 | 17 | 18 |
| **ID (Inside Stent mm)** | 19.2 | 21.2 | 23.2 | 25.2 | 27.2 |
| **Wall thickness (Microns)** | 500 | 550 | 600 | 650 | 700 |

The cardiac valve further comprises three leaflets 30. Each leaflet 30 has a fixed edge 32 joined to a respective scalloped edge 16a, 16b or 16c of the frame 10 and a free edge 34 which extends substantially between the tips 20 of the posts 18.

The leaflets 30 are configured to be movable from an open to a closed position and from a closed to open position. In an aortic position (when the prosthesis is positioned at the site of the aortic valve), the leaflets 30 have a blood inlet side 36 and a blood outlet side 38 and are in the closed position when fluid pressure is applied to the outlet side 38 for example by the blood of the aortic artery and in the open position when fluid pressure is applied to the inlet side 36 for example by the blood of the ventricle. The leaflets are in a neutral position intermediate to the open and closed position in the absence of fluid pressure being applied to the leaflets.

Where the valve is being used in a mitral position, between the left atrium and left ventricle of the heart, the orientation of the valve is opposite to that described above such that blood flow from the left atrium moves the leaflets to an open position, the leaflets opening towards the left ventricle to allow blood to flow into the left ventricle. Back pressure from blood flow from the left ventricle towards the left atrium causes the mitral valve to close to minimise regurgitation.

This circumferential length (XY) can be mathematically defined using a parabolic function.

Function of a parabola

$$Y_z = \left(\frac{4R}{L_z^2}\right) x.(L_z\text{-}x)$$

Wherein $Y_z$ = Y offset at a particular co-ordinate X and Z

R = parabolic maximum

$L_z$ = straight line distance between a first post and a second post of the frame at a height Z

X = distance from origin of post towards another post

To calculate the circumferential length (XY) at a height point of the posts for a leaflet defined in the circumferential (XY) direction by a parabolic function the following function can be used:

length of parabolic curve = $\int_a^b \sqrt{1+\left(\frac{dy}{dx}\right)^2}\,dx$

This allows a circumferential length (XY) to be determined at each height point in Z.

Thus as shown in figure 6 the circumferential length (XY) can be determined at Z1, Z2, Z3 ...Zn.

The length of the leaflet in the circumferential direction (XY) is calculated and repeated in the radial direction (Z) to provide the complete geometry of the leaflet.

As the dimensions of the scallop edge 32 of the frame 10 as defined by the posts 18 of the frame can be determined by measuring the frame, then the straight line distance between a first post and a second post of the frame at a height Z ($L_z$) for a leaflet 30 can be determined by measuring the distance between the two posts 18 at several height points in Z (where Z is a particular height along the posts). This post to post distance can then be used in the equation detailed above to generate a parabola (P) at each height point. In the embodiment shown, due to the scallop

shape 32 defined by the posts 18 the circumferential length of the leaflet in XY will decrease moving from the first end at the tip 20 of the posts toward the second end of the frame 14 at the base of the posts. The more height points which are chosen, the more lengths (P) which can be calculated along Z. If a large number of height points are chosen the lengths determined by the parabolic function moving from the tip of the posts to the base will vary in a substantially linear fashion.

The leaflets 30 of a valve 8 which are of circumferential length (XY) as determined using the above parabolic function will meet at the free edge 34 of the leaflet 30, but will not meet significantly at points lower than the free edge 34. The meeting of the leaflets at the free edge allows regurgitation to be minimised without including excess material in the leaflets 30.

The circumferential length (XY) can be further adjusted to take account of factors which occur during cycling of the heart valve. These factors include inward movement of the posts 18 of the frame 10 due to pressure on the leaflets 30 during closing of the valve. The amount of inward movement of the posts 18 of the frame 10 is influenced by the rigidity of the frame 10 and the pressure exerted on the valve. The tips 20 of the posts 18 of the frame 10 move to a greater extent than the base of the posts and as the scallop geometry between the posts 18 of the frame 10 is accurately known this differential movement can be taken into account when determining the optimal circumferential length (P) of XY in the leaflet 30. In addition to the posts 18 of the frame 10 moving toward each other during closure, the posts 18 also move towards the centre point 42 where the leaflets meet or the point of coincidence. The circumferential length XY of the leaflet can be adjusted to account for this movement.

The material of the leaflet 30 typically has some degree of elasticity and will stretch in response to blood flow pressure. This stretching can again be taken into account in determining the lengths of the leaflet 30 to ensure that excess material of the leaflet of the valve is minimised.

Use of a parabolic function to determine the circumferential lengths XY of the leaflet at each height point in Z causes the vertical distribution of lengths of the leaflet to be substantially linear at the fully open and closed position.

As described above, it will be appreciated by those in the art that other functions with the addition of suitable modifying factors could be used to derive a function which substantially describes a parabola and which leads to the vertical distribution of lengths of the leaflet to be substantially linear at the fully open and closed position, but which is based on for instance an elliptical function.

As discussed, additional parameters may be included in the parabolic function used to determine the circumferential lengths XY of the leaflet. These additional factors may account for movement in the posts of the stent, elasticity of the leaflet material during movement of the leaflets from a closed to an open position or other factors which occur during cycling which influence the length of the leaflet require to allow closure.

The parabolic function described above explicitly determines lateral lengths of the parabolic curve at any height point in Z which is along a post of the frame. In view of this, the above function can be applied to any diameter of valve or valves with different heights of posts, without the need for geometric scaling. This means that different dimensions of valves can be manufactured with the same leaflet geometry without further undue experimentation.

In the embodiment described the surface contour of the leaflets 30 of the embodiment described are such that, in a fully open position, the intersection of the leaflets of the valve perpendicular to the blood flow axis, forms a substantially cylindrical shape.

Stress at the free edge of the leaflet can be further reduced by trimming the free edge 34 of the leaflet in the longitudinal direction (Z) such that the free edge is substantially parabolic 70, with the maximum depth of the parabola being furthest from the notional untrimmed free edge 74. The maximum depth of the parabola is generally located at the midpoint of the free edge 72

Ideally the notional free edge 74 is trimmed in a parabolic curve, wherein the maximum depth 72 of the parabola 70 in the longitudinal direction toward the second end of the frame is between 50μm to 1000μm, more preferably 50μm to

500μm, even more preferably 50μm to 100μm lower than the notional straight line 74 between the ends of the parabola.

It can be envisaged that a different shape of cut, trim or notch can be introduced in the free edge to decrease the stress at the free edge. Cuts, trims and notches which do not create bending stresses at localised points on the free edge are preferable. However, particular shapes of cuts, trims or notches may introduce defects into the leaflet which would decrease the leaflets durability to stress. A parabolic trim as described is therefore advantageous in that focal points of stress are not introduced to the free edge of the leaflet.

Leaflets of the geometry described herein can be produced using methods known in the art such as injection moulding, reaction injection moulding, compression moulding or dip moulding.

Modifications and improvements can be incorporated without departing from the scope of the invention.

**CLAIMS**

1. A cardiac valve prosthesis comprising:

a frame having an annular portion which, in use, is disposed substantially perpendicular to the blood flow, the frame having first and second ends, a first end being a blood inflow end and a second end defining at least two scalloped edge portions, separated and defined by at least two posts

and at least two leaflets, each leaflet being attached to the frame along a scalloped edge portion and being movable between an open and a closed position, each of the at least two leaflets having a blood inlet side, a blood outlet side and at least one free edge, the at least two leaflets being in a closed position when fluid pressure is applied to the blood outlet side of the at least two leaflets such that the at least one free edge of a first leaflet is urged towards the at least one free edge of a second or further leaflet, and the at least two leaflets being in an open position when fluid pressure is applied to the blood inlet side of the at least two leaflets such that the at least one free edge of the first leaflet is urged away from the at least one free edge of the second or further leaflet;

wherein the total height of the valve is correlated with the inner diameter of the valve by

Inner diameter of valve = 2Total Height (mm) – 9mm +/- 0.2mm to the height value

wherein the Effective Orifice Area (EOA) ($mm^2$) varies relative to the inner diameter of the valve whereby EOA relative to an inner diameter is at least or equal to

| **EOA ($mm^2$)** | **1.45** | **2.3** | **3.46** |
|---|---|---|---|
| **Size (Inner Diameter) mm** | **19** | **23** | **27** |

2. The cardiac valve prosthesis as claimed in claim 1 wherein the inner diameter of the valve = 2Total Height (mm) – 9mm +/- 0.1mm to the height value, wherein the

Effective Orifice Area (EOA) ($mm^2$) varies relative to the inner diameter of the valve whereby EOA is at least or equal to

| EOA ($mm^2$) | 1.45 | 2.3 | 3.46 |
|---|---|---|---|
| Size (Inner Diameter) mm | 19 | 23 | 27 |

3. The cardiac valve prosthesis as claimed in any one of claims 1 to 2 wherein the Effective Orifice Area (EOA) ($mm^2$) varies relative to the inner diameter of the valve whereby EOA is at least or equal to

| EOA ($mm^2$) | 1.45 | 2.3 | 3.46 |
|---|---|---|---|

relative to an inner diameter of

| Size (Inner Diameter) mm | 19 | 23 | 27 |
|---|---|---|---|

and the regurgitation provided by the valve relative to the inner diameter is less than or equal to

| Size (Inner Diameter) mm | 19 | 23 | 27 |
|---|---|---|---|
| Regurgitation | 1.2% | 3.3% | 5.0% |

4. The cardiac valve prosthesis as claimed in any one of claims 1 to 3 wherein the Effective Orifice Area (EOA) (mm2) varies relative to the inner diameter of the valve whereby EOA is at least or equal to

| EOA ($mm^2$) | 1.45 | 2.3 | 3.46 |
|---|---|---|---|

relative to an inner diameter of

| Size (Inner Diameter) mm | 19 | 23 | 27 |
|---|---|---|---|

the regurgitation provided by the valve relative to the inner diameter is less than or equal to

| Size (Inner Diameter) | 19 | 23 | 27 |
|---|---|---|---|
| Regurgitation | 1.2% | 3.3% | 5.0% |

and the pressure drop provided by the valve relative to the inner diameter is less than or equal to

| Size (Inner Diameter) | 19 | 23 | 27 |
|---|---|---|---|
| Pressure Drop (mmHg) | 10.0 | 5.2 | 2.4 |

5. The cardiac valve prosthesis as claimed in any one of claims 1 to 4 wherein the inner diameter of the frame is further correlated with the aortic protrusion of the valve wherein the inner diameter of valve = 2Aortic Protrusion (mm) – 4mm +/- 0.2 mm to the height valve.

6. The cardiac valve prosthesis as claimed in claim 5 wherein inner diameter of the frame, the aortic projection and total height of the frame are correlated as indicated according to Table 1.

Table 1

| **Size (Inner Diameter)** | **19** | **21** | **23** | **25** | **27** |
|---|---|---|---|---|---|
| **Aortic Projection (mm)** | 11.5 | 12.5 | 13.5 | 14.5 | 15.5 |
| **Total Height (mm)** | 14 | 15 | 16 | 17 | 18 |
| **ID (Inside Stent mm)** | 19.2 | 21.2 | 23.2 | 25.2 | 27.2 |

7. The cardiac valve prosthesis as claimed in any one of claims 1 to 6 wherein the annular portion includes undulations at least at the blood flow end of the annular portion wherein the peak of the undulation extend towards the tip of the posts.

8. The cardiac valve prosthesis as claimed in claim 7 wherein the undulations of the annular portion have a peak to peak amplitude in the range of 2.3 to 2.7mm, and have a frequency of 3Hz.

9. The cardiac valve prosthesis as claimed in any one of claims 1 to 8 wherein, in use, stresses experienced by the cardiac valve prosthesis are distributed across the

leaflets and frame such that a peak stress of 3.0MPa ±10% is provided to any part of the leaflet.

10. The cardiac valve prosthesis as claimed in any one of claims 1 to 9 wherein, in use, stresses experienced by the cardiac valve prosthesis are distributed across the leaflets and frame such that peak stress of 15.0MPa±10% is provided to any part of the frame.

11. The cardiac valve prosthesis as claimed in any one of claims 1 to 10 wherein a leaflet for use in the valve has a uniform thickness throughout, and is in the range 40 to 500 microns.

12. The cardiac valve prosthesis as claimed in any one of claims 1 to 11 wherein, in a first plane perpendicular to the blood flow axis, the length of each leaflet in a circumferential direction (XY) between the posts, at any position along the longitudinal axis (Z) of a post, is defined by a parabolic function.

13. The cardiac valve prosthesis as claimed in claim 12, wherein, in the closed position, the leaflet is substantially linear in relation to the lengths XY of the leaflet when provided according to a parabolic function at each point in Z, such that the XY lengths in Z vary as a continuous function.

14. The cardiac valve prosthesis as claimed in claim 12 and claim 13 wherein the parabolic function defining the length of a leaflet in the circumferential direction (XY) between the posts at any position along the longitudinal axis (Z) of a post is defined by

$$Y_z = \left(\frac{4R}{L_z^2}\right) x.(L_z - x)$$

Wherein $Y_z$ = Y offset at a particular co-ordinate X and Z

R = parabolic maximum

$L_z$ = straight line distance between a first post and a second post of the frame at a height Z

x = distance from origin of post towards another post

wherein the length of the parabola can be determined by

Length = $\int_0^x \sqrt{1+\left(\frac{dy}{dx}\right)^2}\,dx$

15. The cardiac valve prosthesis as claimed in any one of claims 12 to 14 wherein the prosthesis comprises three posts and three leaflets wherein the valve comprises three leaflets with one end of the frame of the cardiac valve prosthesis defining at least three scalloped edge portions separated by at least three posts, wherein each leaflet is attached to the frame along a corresponding scalloped edge portion.

16. The cardiac valve prosthesis as claimed in any one of claims 1 to 15 wherein a leaflet is formed from any biostable and biocompatible material, preferably Elasteon.

17. The cardiac valve prosthesis as claimed in any of claims 1 to 16 wherein the free edge of the leaflet is shaped to increase the length of the free edge of the leaflet relative to the length of the leaflet in the XY direction.

18. The cardiac valve prosthesis as claimed in any one of claims 1 to 17 wherein the free edge of the leaflet is shaped such that in the longitudinal direction (Z) the free edge of at least one leaflet is parabolic.

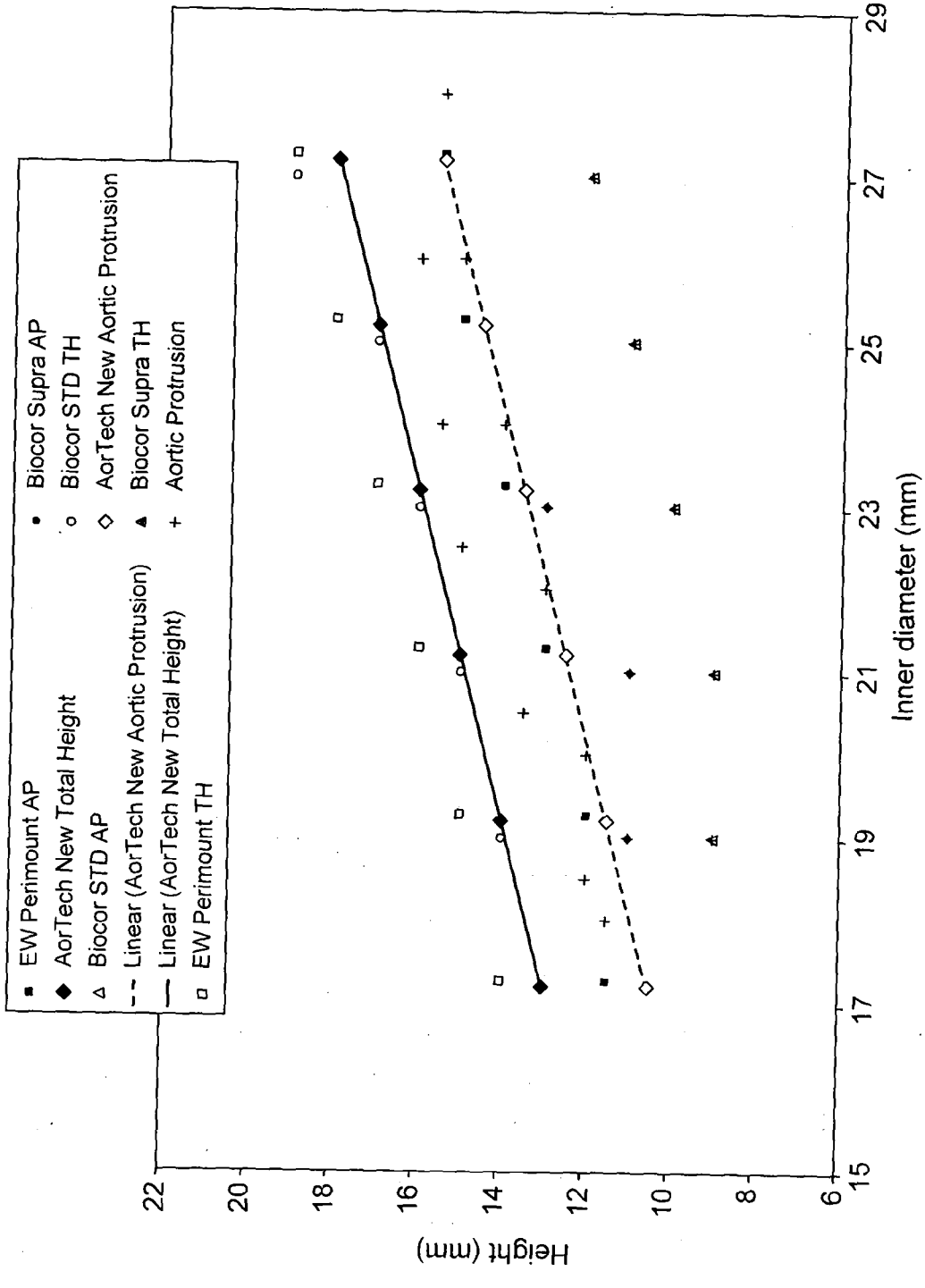
EW Perimount AP
AorTech New Total Height
Biocor STD AP
Linear (AorTech New Aortic Protrusion)
Linear (AorTech New Total Height)
EW Perimount TH
Biocor Supra AP
Biocor STD TH
AorTech New Aortic Protrusion
Biocor Supra TH
Aortic Protrusion
Height (mm)
Inner diameter (mm)
22
20
18
16
14
12
10
8
6
15
17
19
21
23
25
27
29

FIG. 1

| Size (inner diameter) | 19 | 23 | 27 |
|---|---|---|---|
| Pressure drop (mmHg) | 10.0 | 5.2 | 2.4 |
| EOA ($mm^2$) | 1.45 | 2.3 | 3.46 |
| Regurgitation | 1.2% | 3.3% | 5.0% |

AorTech polymer valve data

| Size (inner diameter) | 19 | 23 | 27 |
|---|---|---|---|
| Pressure drop (mmHg) | 12.5 | 7.8-9.2 | 3.7-4.0 |
| EOA ($mm^2$) | 1.22 | 2.1-2.3 | 3.1-3.56 |
| Regurgitation | | | |

Edwards Perimount data

FIG. 2

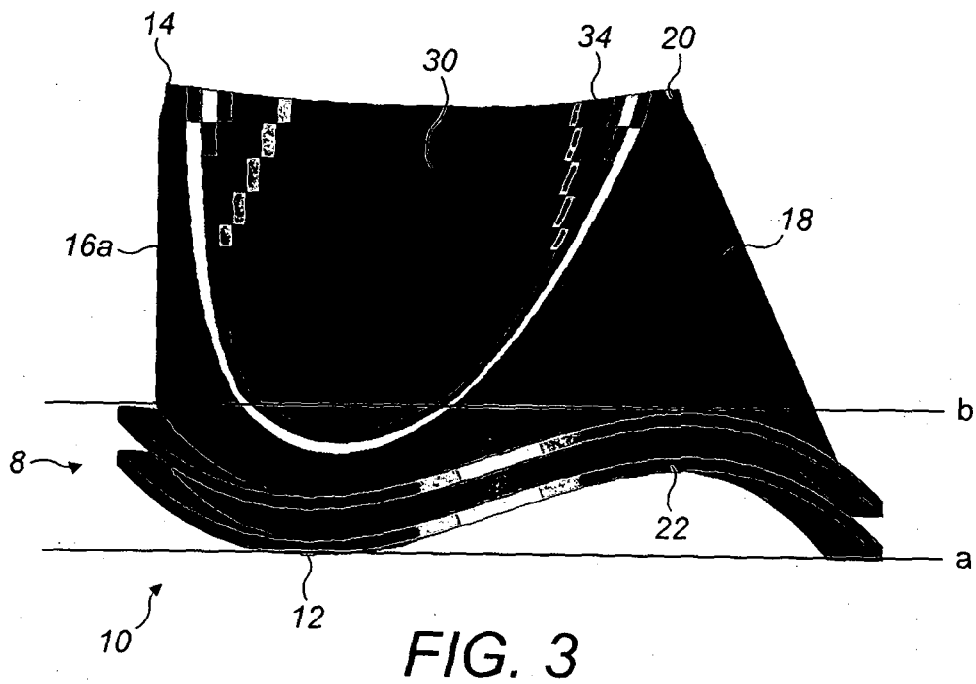


FIG. 3

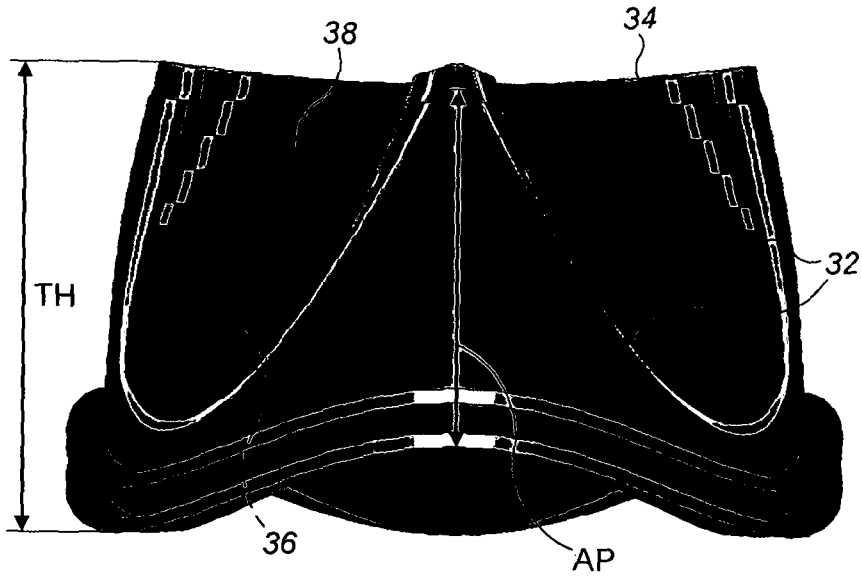


FIG. 4

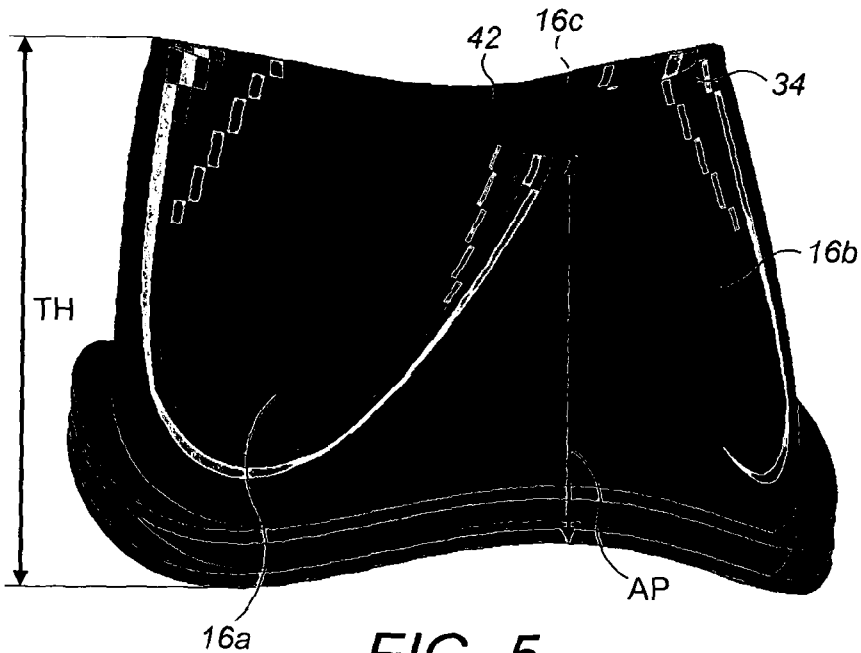


FIG. 5

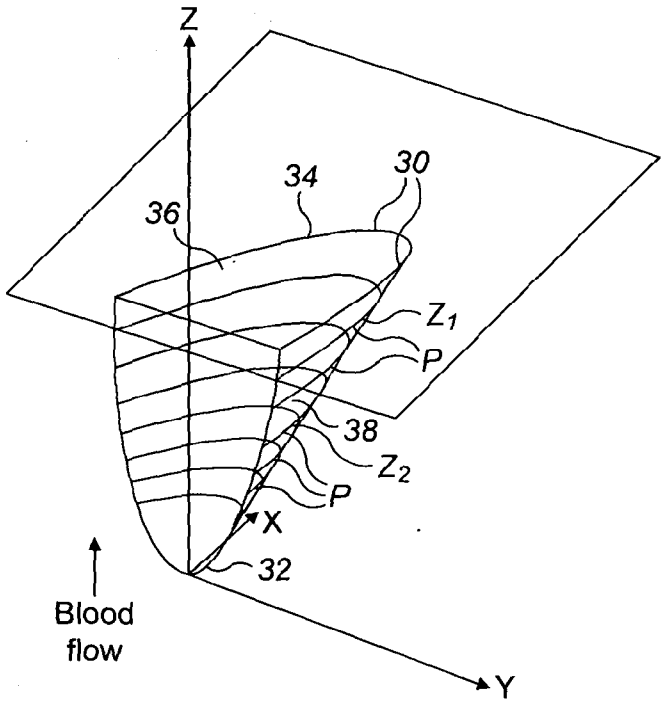


FIG. 6

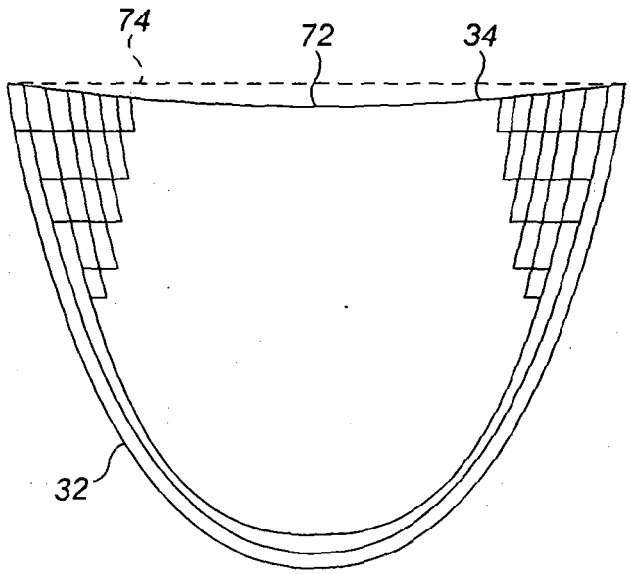


FIG. 7

# INTERNATIONAL SEARCH REPORT

International application No
PCT/GB2013/050641

A. CLASSIFICATION OF SUBJECT MATTER
INV. A61F2/24
ADD.

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

B. FIELDS SEARCHED

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

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

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

C. DOCUMENTS CONSIDERED TO BE RELEVANT

| Category* | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|---|---|---|
| Y | WO 01/97741 A2 (INTERNAT HEART INST OF MONTANA [US])<br>27 December 2001 (2001-12-27)<br>page 11, line 11 - page 30<br>figures 1-15 | 1-18 |
| Y | US 2005/075725 A1 (ROWE STANTON J [US])<br>7 April 2005 (2005-04-07)<br>figure 1 | 1-18 |

-/--

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

[X] See patent family annex.

* Special categories of cited documents :

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

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

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

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

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

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

| Date of the actual completion of the international search | Date of mailing of the international search report |
|---|---|
| 22 July 2013 | 30/07/2013 |

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

1

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

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

| Category* | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
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| A | SIEVERS ET AL: "Prosthetic aortic valve replacement", JOURNAL OF THORACIC AND CARDIOVASCULAR SURGERY, MOSBY-YEAR BOOK, INC., ST. LOUIS, MO, US, vol. 129, no. 5, 1 May 2005 (2005-05-01), pages 961-965, XP027240569, ISSN: 0022-5223 [retrieved on 2005-04-30] cited in the application the whole document ----- | 1-15 |

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Information on patent family members

International application No
PCT/GB2013/050641

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| | | WO 2005034812 A1 | 21-04-2005 |