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DESCRIPTION

BACKGROUND

[0001] Prosthetic heart valves are used to replace damaged or diseased heart valves. Prosthetic heart valves for human patients have been available since the 1950s. Today, there are three general types of prosthetic heart valves, including mechanical valves, tissue valves, and polymer valves. In some cases, a heart valve prosthesis is implanted into an annular opening in a patient's heart following surgical removal of a diseased or damaged natural valve. The valve can be secured in the annulus of the opening through the use of sutures or pins that penetrate the host tissue and an outside edge of the valve. Alternatively, the valve can be secured in the annulus by suturing the host tissue to a sewing ring. Heart valves function essentially as one-way check valves for blood flow through the beating heart.

[0002] The term "mechanical valve" refers to mono- or multi-leaflet (typically bi-leaflet) heart valves having a valve orifice fabricated at least in part of a rigid, biologically compatible material such as pyrolytic carbon, and comprising essentially no biological components. The term "bioprosthetic valve" refers to a multi-leaflet (e.g., bi-leaflet or tri-leaflet) heart valve having at least some biological components such as tissue or tissue components. The biological components of tissue valves are obtained from a donor animal (typically bovine or porcine), and the valve may comprise either biological materials alone or biological materials with man-made supports or stents. The term "polymeric valve" refers to a multi-leaflet (e.g., tri-leaflet or bi-leaflet) heart valve having at least some elastomeric polymer components, including at least elastomeric polymer valve leaflets.

[0003] A tri-leaflet heart valve prosthesis typically includes an annular valve body and three flexible leaflets attached thereto. The valve body includes an annular base and three leaflet support posts located at the circumference of the annulus. In some cases, a sewing ring annularly coupled to the periphery of the valve body may provide a place for sutures to be applied when the valve is implanted. The leaflets are attached to the three shaped posts along an attachment curve, and they also each have a free, unattached edge remote from the attachment curve. The place where two adjacent leaflets come together at one of the support posts is called the commissure, and the generally curved area on the leaflet between the free edge and the attachment curve is known as the belly of the leaflet. The free edges of the three leaflets come together at a "triple point" generally on the axis of the valve.

[0004] When blood flows in the forward direction, the energy of the blood flow deflects the three leaflets away from the center of the annulus and allows blood to flow through. When blood flows in the reverse direction, the three leaflets engage each other in a coaptive region, occlude the valve body annulus and prevent the flow of blood.

[0005] Heart valves may be may be implanted through open heart surgical procedures. More

recently, heart valves have been developed that are implanted percutaneously, e.g., using transcatheter procedures. Transcatheter percutaneous aortic replacement valve devices typically include a valve body mounted on a tubular expandable (e.g. balloon expandable or self-expanding) stent or frame. Examples include the SAPIEN device available from Edwards Lifesciences of Irvine, CA or the Core Valve device available from Medtronic of Minneapolis, MN.

[0006] Percutaneously implanted devices obviate the need for major open surgical procedures. However, implantation of these devices may be difficult. Replacement valves are typically sensitive devices, and care must be taken to avoid damage during implantation. In the case of aortic replacement valves, further difficulties may arise from the particular anatomy of the aortic region. The aortic region is characterized by high blood pressure subjecting tissue is in the area to high physical strains. Supporting stents for aortic replacement valves therefore must sufficiently be robust and rigid to operate in this environment. However, the introduction of such a stent in the region raises the risk that other vessels, such as the coronary arteries ostium dextra and ostium sinistra (referred to herein as the coronary ostia) descending on both sides of the aorta, may be disrupted in their function.

[0007] WO2007/081820 describes a replacement valve apparatus including a docking station, a self -expanding member, and a valve frame. The valve frame is adapted to be positioned within the docking station, whereas the self-expanding member is adapted to be associated with an outer wall of the docking station. The valve frame generally includes a substantially cylindrical body defining a lumen and a plurality of curved support structures attached to the substantially cylindrical body. The valve frame further can have a plurality of leaflets. Each leaflet can be attached to a respective inner curved support structure and can extend over a respective outer curved support structure, so as to position the body of the leaflet within the lumen of the valve frame.

[0008] AU2002212418 describes a support comprising a structure adapted to be radially contracted to enable the insertion of a support valve assembly into the patient's body, and to be unfolded to enable said structure to be supported against the wall of the site to be equipped with a cusp. The support structure comprises an axial portion supporting the cusp, having a thread or thread network structure adapted to be supported against the cardiac ring remaining after removal of the deficient native cusp, at least an axial wedging portion, having a thread or thread network structure separate from the structure of said axial portion of the cusp support, and with a diameter greater than the diameter of said axial portion enabling it to be supported against the wall bordering said remaining cardiac ring, and at least a thread linking point-to-point said portions.

[0009] US2006/0122693 describes a stent valve which includes a scaffold, the scaffold including interlinked struts, the scaffold having a scaffold passageway extending substantially longitudinally therethrough. The stent valve also includes a valve leaflet extending at least partially across the scaffold passageway, the valve leaflet defining a leaflet periphery. At least a portion of the leaflet periphery extends integrally from at least a portion of at least one of the

struts and at least a portion of the leaflet periphery is substantially parallel to the at least a portion of said at least one of said struts.

[0010] US2010/168839 describes a prosthetic heart valve designed to be circumferentially collapsible and then re-expandable. When the valve reaches the implant site in the patient, it re-expands to normal operating size, and also to engage surrounding tissue of the patient. The valve includes a stent portion and a ring portion that is substantially concentric with the stent portion but downstream from the stent portion in the direction of blood flow through the implanted valve. When the valve is implanted, the stent portion engages the patient's tissue at or near the native valve annulus, while the ring portion engages tissue downstream from the native valve site (e.g., the aorta).

SUMMARY

[0011] The invention relates to a prosthetic apparatus according to claim 1. The invention also relates to a method of making a prosthetic apparatus according to claim 11. Further advantageous embodiments are described in the dependent claims.

[0012] The inventors have realized that a percutaneously implantable aortic replacement valve device may be provided featuring, e.g., a polymeric tri-leaflet valve mounted in an expandable stent. As detailed herein, the stent may include one or more open regions adjacent the valve at positions corresponding to the coronary ostia. This allows the device to be implanted more easily, and reduces the risk of damaging, blocking, or otherwise disrupting the function of the ostia lowers the incidence of unwanted effects such as stenosis. Further, in cases where the device is an expandable device, positioning of the open regions adjacent the leaflets of the valve allows the device to be crimped down to a small size without damaging the sensitive valve leaflets.

[0013] The inventors have realized that a multi-leaflet polymeric heart valve (e.g. a tri-leaflet valve) may be mounted on the stent. In some embodiments, the valve features a partially open leaflet position which reduces forward flow pressure loss. In some embodiments, the valve features flexible valve posts with tips made of a soft flexible material. The flexibility of the posts allows the leaflets to properly close to block reverse blood flow without experiencing excessive stress or strain. These features act synergistically to provide a valve with advantageous durability, forward flow pressure loss and efficiency characteristics.

[0014] In one aspect, a prosthetic apparatus is disclosed including: a tubular stent disposed about a longitudinal axis and extending from a proximal end to a distal end, the stent defining a tubular passage between the ends. In some embodiments, the tubular stent has a proximal portion, a distal portion, and a middle portion located between the proximal and distal portions, hi some embodiments, the proximal and distal portions each include a mesh of support struts forming at least one ring of open elements disposed about the longitudinal axis. In some embodiments, the middle portion includes: a plurality of elongated posts extending along a

direction substantially parallel the longitudinal axis between the proximal and distal portions; and a crown shaped mounting ring attached to the posts and configured to mount a polymeric valve within the tubular passage; and a plurality of open regions. In some embodiments, the crown shaped ring may, additionally, or alternatively, be attached to the proximal portion of the stent.

[0015] In some embodiments, the open elements are open diamond shaped elements.

[0016] In some embodiments, the plurality of open regions each define an open area along the outer surface of the tubular support that is at least about 20 times the area of each of the open elements.

[0017] In some embodiments, the plurality of open regions each define an open area along the outer surface of the tubular support that is at least about 40 times the area of each of the open elements.

[0018] In some embodiments, the proximal and distal portions include a ring of N open elements, the plurality of stent posts consist of M posts extending between the rings, and the ratio of N to M is at least 4 to 1, at least 5 to 1, or is at least 6 to 1. In some embodiments, N=15 and M=3.

[0019] According to the invention, the apparatus includes a tubular polymeric sheath extending along the outer surface of the tubular support member from the proximal portion to the distal portion, but does not substantially cover the open regions in the middle portion. In some embodiments, the sheath encapsulates the elongated posts.

[0020] In some embodiments, the sheath includes regions of reinforced thickness corresponding to the elongated posts.

[0021] In some embodiments, the sheath includes regions of reinforced thickness corresponding to one or more of the support struts or the mounting ring.

[0022] Some embodiments include one or more sutures securing the sleeve to the stent.

[0023] Some embodiments include the polymeric heart valve. In some embodiments, the valve includes: a valve body having a central axis extending along the direction of the longitudinal axis of the tubular stent and having a body fluid pathway extending along the central axis from an inflow end to an outflow end; a flexible outer support disposed about an outer circumference of the body and including at least three flexible valve posts each extending in the axial direction to a tip and each attached to at least one of the elongated posts; and at least three flexible leaflets extending from the crown shaped mounting ring, each of the leaflets having an attached edge defining an attachment curve along the mounting ring extending between a respective pair of flexible valve posts, and where pairs of leaflets define a respective commissure at each of the at least three flexible valve posts; where the crown shape ring

includes a plurality of points each corresponding to a flexible valve post and attached to a respective one of the elongated posts of the stent.

[0024] In some embodiments, the flexible outer support of the valve encapsulates a portion of the tubular stent, hi some embodiments, the stents posts extend through the flexible outer support, e.g., extending through the valve posts.

[0025] In some embodiments, the at least three leaflets define a partially open position at rest, a fully open position deflecting away from the central axis during forward blood flow along a direction from the inflow end to the outflow end, and a closed position deflecting toward the central axis during reverse blood flow along a direction from the outflow end to the inflow end, and in the closed position, each of the flexible valve posts flexes inward toward the central axis.

[0026] In some embodiments, the tip of each valve post is formed of a material having a flexibility greater than the remainder of the valve post.

[0027] In some embodiments, the stent is configured to be crimped to reduce the outer diameter of the stent from an uncrimped diameter to a crimped diameter without damaging the valve. In some embodiments, the uncrimped diameter is at least about 20 mm and the crimped diameter is less than about 6 mm.

[0028] In some embodiments, the tubular stent includes a shape memory material. In some embodiments, the shape memory material includes Nitinol.

[0029] In some embodiments, stent is a self expanding stent.

[0030] In some embodiments, the stent is configured such that, when implanted in the human heart such that the valve is positioned proximal the location of the native aortic valve, the open regions are positioned proximal to the coronary ostia.

[0031] In some embodiments, the apparatus consists essentially of biocompatible materials.

[0032] A method is disclosed including: obtaining the apparatus of any of the types described above; and percutaneously implanting the apparatus in a human subject such that that the valve is positioned proximal the location of the native aortic valve, the open regions are positioned proximal to the coronary ostia.

[0033] The step of percutaneously implanting the apparatus includes: crimping the stent; using an introducer to position the stent in a desired location; and removing the introducer and expanding the stent to an uncrimped state.

[0034] Expanding the stent to an uncrimped state includes allowing the stent to self expand.

[0035] In another aspect, a method of making prosthetic apparatus is disclosed including:

obtaining a tubular stent of any of the types described above; placing the stent on a mandrel; forming a polymeric valve mounted on the mounting ring by a process including dip molding; forming a tubular polymeric sheath extending along the outer surface of the tubular support member from the proximal portion to the distal portion, but does not substantially cover the open regions in the middle portion.

[0036] According to the invention, the step of forming the tubular polymeric sheath includes a thermoforming process including: applying a polymer material to the outer surface of the tubular stent; disposing a heat shrink tube about the polymer material and the stent; applying heat to soften the polymer material and cause the heat shrink tube to shrink and apply force to mold the polymer material to form the sheath.

[0037] In some embodiments, forming the sheath includes encapsulating one or more of the support struts and the elongated posts.

[0038] Some embodiments include, during the thermoforming process, applying an air flow to valve to avoid thermal damage to the valve.

[0039] Some embodiments include applying strips of polymer material to reinforce the sheath at locations corresponding to the elongated posts or the mounting ring.

[0040] Some embodiments include applying additional polymer material to reinforce the sheath at locations corresponding to the struts.

BRIEF DESCRIPTION OF THE DRAWINGS

[0041]

Fig. 1 illustrates a prosthetic aortic valve replacement device in the aortic region following implantation.

Fig. 2A shows a perspective view of a tubular stent. For clarity, only one half of the tubular stent is shown. The remaining half of the stent may be obtained by reflection in a plane that slices through the tubular stent and includes the longitudinal axis A.

Fig. 2B shows a view of the tubular stent of Fig. 2A having been cut along its length and laid flat.

Fig. 2C is a photograph of a stent of the type illustrated in Figs. 2A and 2B.

Fig. 3 shows a stent of Figs. 2A-C in same view found in Fig. 2B, further including a sheath on the stent. The sheath is indicated by the gray area.

Fig. 4 is a photograph of a prosthetic aortic valve replacement device including the stent shown in Fig. 2C with a polymeric sheath and valve attached.

Fig. 5 is a detailed illustration of the valve of the prosthetic aortic valve replacement device shown in Fig. 4.

Fig. 6 is an illustration of a kit for crimping the prosthetic device of Fig. 4 onto a introducer.

Fig. 7 is a flow chart illustrating the steps for implanting a prosthetic device.

Fig. 8 is an illustration of a method of making the prosthetic device of Fig. 4.

Fig. 9 is a table showing forward pressure loss as a function of flow rate for embodiments of a valve with various leaflet thicknesses mounted on a stent featuring a crown shaped mounting ring of the type shown in Figs. 2A-2C.

Fig. 10 is a table showing backflow leakage for embodiments of a valve with various leaflet thicknesses mounted on a stent featuring a crown shaped mounting ring of the type shown in Figs. 2A-2C.

DETAILED DESCRIPTION

[0042] Generally, the present technology relates to a percutaneously implantable device that includes a polymeric heart valve. The device includes openings that prevent blockage or damage of anatomical features at the implantation site.

[0043] For example, Fig. 1 shows a prosthetic aortic valve replacement device 100 in the aortic region following implantation. The device lies between the heart 10 and the aorta 12 at about the position the aortic valve would normally be located. As detailed below, the device 100 includes a polymeric valve 101 mounted in a tubular stent 102. The left and right coronary vessels 13/14 or 14/13, depending on whether the depicted view is from above or from below are also shown. The tubular stent includes openings 104 positioned such that the coronary vessels 13, 14 are not blocked or occluded.

[0044] Figs. 2A, 2B and 2C show views of the tubular stent 102. Fig. 2A shows a perspective view. Fig. 2B shows a view of the tubular sent sliced along its length and rolled out flat. Fig. 2C is a photograph of an embodiment of the tubular stent 102.

[0045] Referring to Figs. 2A-2C, the tubular stent 102 is disposed about a longitudinal axis A. The stent 102 extends from proximal end (towards the bottom of the figures) to a distal end (towards the top of the figures) and defines a tubular passage between the two ends. The valve 101 (not shown) is mounted on the stent 102 in the tubular passage transverse to the axis A.

[0046] The stent 102 has a proximal portion 201, a distal portion 202 and a middle potion 203.

The middle portion 203 is located between the proximal and distal portions 201, 202. The proximal and distal portions each include a mesh of support struts 204. The support struts are arranged to form rings of open elements 210 (as shown, diamond elements) disposed about the axis A.

[0047] The middle portion 203 includes elongated posts 205 that extend along a direction substantially parallel to the axis A, connecting the proximal portion 201 to the distal portion 202. A mounting element for mounting the valve is attached to the posts 205. As shown, the mounting element is a crown shaped mounting ring 206 suitable for mounting a trileaflet polymeric valve of the type described in greater detail below. The points of the crown shaped mounting ring 206 are attached to the posts 205. In some embodiments, the crown shaped mounting ring 206 may, additionally or alternatively, be attached to the proximal portion 201 of the stent 102. For example, for the embodiment shown, an attachment may be made between the proximal pointing features on the ring 206 between the posts 205.

[0048] As shown the crown shaped mounting ring 206 includes three points extending towards the distal end of the stent 102. However, in other embodiments, any other number of points may be used, e.g., 1, 2, 3, 4, 5, etc. In some embodiments, the mounting element may have any other suitable shape, e.g. a circle, an oval, a ring with sinusoidal undulations towards and away from the distal end of the stent 102, a ring with sawtooth undulations towards and away from the distal end of the stent 102, etc.

[0049] The middle portion 203 also includes open regions 207 located distal the mounting ring 206 that are completely free of posts, struts, or any other structures. These open regions 207 correspond to the openings 104 described with reference to Fig. 1.

[0050] In typical embodiments, the area of each of the open regions 207 will be larger than the area of the open elements 210 that form the mesh found in the proximal and distal portions. For example, in various embodiments, the area of each of the open regions 207 may be at least 2, 3, 4, 5, 10, 20, 30, 40, 50, 60, 70, 80, 90, 100 or more times the area of each of the open elements 210. For example, in some embodiments, the area of each of the open regions 207 may be in the range of 2-100 times the area of the area of the open elements 210, or any subrange thereof. As shown, the ratio of areas is about 50. For example, in one embodiment, the area of the open region 207 is about 300 mm^2, while the area of the open diamond elements 210 is about 6 mm^2.

[0051] Accordingly, the relatively fine mesh of support struts 204 forming the rings of open elements 210 in the proximal and distal portions 201, 202 provide good mechanical support for the valve 101 and stent 102. Meanwhile, the larger open regions 207 in the middle portion 203 ensure that the portion of the device 100 located near the coronary ostia is free or substantially free from any obstructions (e.g., as shown in Fig. 1).

[0052] As shown, the proximal and distal portions 201 and 202 each include three rings of open diamond shaped elements 210 formed from the support struts 204. In other

embodiments, more or fewer rings may be used, e.g., 1, 2, 3, 4, 5, or more rings. In various embodiments the elements 210 may have other shapes including rectangular, square, polygonal, round, oval, etc. In some embodiments the struts 204 may form a mesh with an irregular or random pattern.

[0053] The number of posts 205 may also be chosen to ensure that the middle portion 203 remains suitably free of obstructions. In some embodiments, no more than, e.g., 6, 5, 4, 3, 2, or 1 posts may be used. In general, the number of posts 205 may be fewer than the number of open elements 210 found in each ring of elements in the proximal and distal portions 201 and 202. For example, in some embodiments there are N open elements 210 in each ring, and M posts 205, where M and N are integers. In some embodiments, the ratio of N to M is at least 2 to 1, 3 to 1, 4 to 1, 5 to 1 (as shown), 6 to 1, 7 to 1, 8 to 1, 9 to 1, 10 to 1 or more. For example, in the embodiment shown, the proximal and distal portions 201 and 202 each contain three rings of open diamond elements 210, with each ring having fifteen elements 210, therefore N=15. This embodiments has three posts 205, therefore M=3, giving a ration of N to M of 5 to 1.

[0054] The support struts 204 and posts 205 of the stent 102 may be made from any suitable material. In some embodiments, a shape memory material is used, e.g. a nickel titanium allow such as the material marketed under the trade name Nitinol. In various embodiments, other materials may be used, alone or in any suitable combination, including metallic, plastic, polymer, or other materials. In various embodiments, the materials may be biocompatible.

[0055] Referring to Fig. 3, according to the invention, a sheath 300 is formed that extends along the outer surface of the stent 102 from the proximal portion 201 to the distal portion 202, without substantially covering the open regions 207 of the middle portion 203. The sheath 300 may encapsulate the elongated posts 205 and some or all of the support struts 204 of the proximal and/or distal portions 201, 202 of the stent 102.

[0056] The sheath may be made of any suitable material, e.g., a polymer material such as silicone, polyurethane, polyether ether ketone (PEEK), etc. hi some embodiments, the polymer material may be the material produced under the trade name Angioflex by Abiomed, Inc. of Danvers, MA. In some embodiments, the sheath 300 includes regions of reinforced thickness at locations corresponding to the elongated posts 205 or the support struts 204. In some embodiments, the sheath 300 may be secured to the stent 102 using one or more sutures.

[0057] As shown in Fig. 4, in some embodiments, a polymeric trileaflet valve 101 is mounted on the crown shaped mounting ring 206. The sheath 300 may connect to an outer circumference of the body of the valve 101.

[0058] Fig. 5 shows a detailed view of the valve 101. The valve 101 includes an annular, generally cylindrical elastomeric valve body 1101 disposed about a central axis 1116, and having a sealable fluid passageway extending axially from an inflow end (as shown, the bottom) to an outflow end (as shown, the top). The valve 101 includes a flexible outer portion

1110 connected to the mounting ring 206 (not shown) and having at least three flexible valve posts 1112 each of which extends axially to a valve post tip 1120. As discussed in greater detail below, valve post tip 1120 may be made of a material having greater flexibility than the valve post 1112.

[0059] The valve 101 includes at least three flexible leaflets 1130 each having a free edge 1132, an attached edge 1133 and a belly 1134. The attached edge 1133 attaches to the outer portion 1110 to form an attachment curve running along the inner diameter of the outer portion between a pair of valve posts 1112. The free edge 1132 defines a free edge curve which extends from a first valve post tip 1120, towards the central axis 1116 and back to second valve post tip 1120. The free edges 1132 of adjacent leaflets 1130 define commissures 1135 at each of the valve post tips 1120. In some embodiments, the free edges 1132 curve upward in the region of the commissures 1135, such mat the leaflets 1130 have a homed shape in the region around each of the valve post tips 1120, as shown.

[0060] The outer portion 1110 of the valve body may be attached to the mounting ring 206. For example, in some embodiments, the material of the valve body may adhere to and/or encapsulate all or a portion of the ring 206.

[0061] Each of the valve posts 1112 may be attached to a respective one of the elongated posts 205 of the stent 102 (not shown). For example, in some embodiments, the material of the valve post 1112 may adhere to and/or encapsulate all or a portion of the post 205, e.g., as shown in Fig. 4. In some embodiments, the posts 205 may include one or more features that facilitate connection to the valve posts 1112. For example, as shown in Figs. 2A-4, the posts 205 may include holes that allow the material of the valve posts 1112 to extend through and around the post 205, to provide a stronger connection.

[0062] In operation, when blood flows in the forward direction, i.e., towards the top of the figure, the pressure of the blood flow causes the leaflets 1130 to deflect away from a central axis 1116 of the valve body 1101. In this "open" position, the leaflets 1130 define a large flow orifice (not shown) allowing the blood to flow freely in the forward direction. With the leaflets 1130 in the open position, the valve 101 presents little resistance to fluid flow. When blood flows in the reverse direction, i.e., towards the bottom of the figure, the pressure of the blood flow causes the valve post tips 1120 and the leaflets 1130 to deflect toward the central axis 1116. In this "closed" position, the leaflets 130 engage each other along the free edges 132, which help the valve 101 seal against reverse flow.

[0063] As shown, the leaflets 1130 are cast in a partially open position at rest (i.e. in the absence of forward or reverse fluid pressure against the valve). For example, in some embodiments the at rest opening of commissures in the region closest to their respective flexible valve post tip 1120 is in the range of 0.60 mm or less, e.g. about 0.25 mm.

[0064] For example, the open area of the valve 101 in the at-rest position (e.g., the open cross sectional area presented to fluid flow through the valve) may be a suitable fraction of the open

area of the valve in the absence of the leaflets 1130. In some embodiments the open area in the partially open at rest positions may be greater than 5%, 10%, 25% or more of the open area, e.g., in the range of 5-10%, 10-20%, 10-30%, or any other suitable range.

[0065] This configuration reduces the energy required to open the leaflets during forward blood flow relative to that required for opening an equivalent valve formed in a closed position at rest. The relative ease of opening of valve 101 when formed in the partially open rest position results in a decrease in forward flow pressure loss.

[0066] Furthermore, the partially open rest position leaflet geometry helps ensure a symmetric opening of the leaflets 1130 in response to forward flow, even in cases where the flow is not uniformly distributed (e.g. due to the specifics of the heart anatomy, or other factors). For example, by providing the leaflets 1130 in the partially open rest configuration, the valve can avoid unwanted adhesion of free edges of one or more pairs of adjacent leaflets 1130 to one another. This prevents low fluid velocities in the commissure 1135 between the leaflets 1130.

[0067] Moreover, this valve structure can reduce or prevent the occurrence a "lazy leaflet", i.e., a leaflet that does not properly and completely move between its intended open and closes positions.

[0068] Avoiding low fluid flow and/or asymmetric flow patterns allows the valve to be properly washed through by the flow of blood in both forward and reverse directions, reducing or eliminating the build up of unwanted materials in the valve. This can lead to a reduction or even elimination of deleterious effects, e.g., thrombosis.

[0069] When transitioning from the partially open rest position to the closed position, the valve posts 1112 flex inward toward the central axis to allow leaflets 1130 to close properly to seal the valve against reverse flow. This flexing beneficially reduces strain on the leaflets 1130, reducing or eliminating the occurrence of tears, and improving the reliability and durability of the valve 101. Moreover, in some embodiments, the tips 1120 of valve posts are formed of a material that is more flexible than the remainder of the valve posts 1112. This allows for increased flexing in the area near the commissures 1135 without compromising the overall structural integrity of posts 1112. Accordingly, force may be transferred from the leaflets 1130 to the valve posts 1112 through tips 1120 while reducing or eliminating unwanted stress concentrations in the leaflets 1130. In other words, the flexible post tips 1120 serve as a strain relief for the leaflet 1130 transition to the valve posts 1112 while reducing stress concentrations in the leaflets 1130 thereby increasing reliability of the polymeric valve 101. Note also that, due to the transition from stiff to soft material in the post tips 1120, relatively short, low profile posts 1112 may be used.

[0070] In some embodiments, each flexible valve post tip 1120 extends beyond the free edge 1132 of the leaflets 1130 where the leaflets attach to the posts 1112 (i.e. near commissures 1135). In some embodiments, each flexible tip 1120 extends beyond the free edge of the leaflets by 1 mm to 2 mm, e.g., by 1.5 mm. In some embodiments, this flexible tip configuration

acts to reduces stress concentrations between the softer leaflet 1130 material and the harder post 1112 in order to increase the valve reliability. Although not shown, in some embodiments, the posts 205 of the stent 102 extends through the valve posts 1112, and out through the tips 1120.

[0071] In some embodiments, a portion of the free edge 1132 of the leaflet 1130 is substantially straight, extending radially towards the central axis 1116. As noted above, in one embodiment, portions of the free edge 1132 of the leaflet 1130 curve upward slightly at the valve post tip 1120. In one embodiment, the belly 1134 of the leaflet 1130 has a thickness profile less than a thickness profile of the free edge 1132 of the leaflet 1130. The thickness profile of the free edge 1132 can be in the range of 1 to 2.5 times greater than the thickness profile of the belly 1134. The leaflets can be made from a biocompatible polymer, such as silicone and/or polyurethane.

[0072] In various embodiments any other suitable valve may be used for valve 101 including any suitable polymeric valve known in the art., however according to the invention, the valve is formed by dip molding.

[0073] In various embodiments any suitable dimensions for the device 100 may be used. For example, in some embodiments, the device 100 has an outer diameter of about 23 mm or about 27 mm. In some embodiments, the device 100 has an outer diameter in the range of 10-100 mm, or any subrange thereof. In some embodiments, the device has a total length of about 48mm. In some embodiments, the device has a total length of in the range of 10-100 mm, or any subrange thereof. In some embodiments, the wall thickness of the tubular stent 102 is about 0.5 mm. In some embodiments, the wall thickness of the tubular stent 102 is about 0.1-1.0 mm or any subrange thereof.

[0074] In some embodiments, the device 100 may be crimped to reduce its outer diameter to allow for percutaneous implantation, e.g., using transcatheter techniques known in the art. For example, Fig. 6 illustrates a kit used for crimping the device 100. The kit includes a cone 601, a cap 602, and an introducer sleeve 603. The device 100 is inserted into the wide end of the cone 601 and capped with the cap 602. The introducer sleeve 603 is attached to the device 100 (e.g. using one or more pins which attach to the stent 102). The cone 601 is pushed back while the sleeve 603 is advanced. The device 100 is crimped as it passes out through the narrow end of the cone and is inserted within the sleeve 100.

[0075] In various embodiments, the device 100 may be crimped to any suitable size. In some embodiments, e.g., where the device 100 has an outer diameter in the range of 20-30 mm, the device may be crimped to a reduced outer diameter in the range of 4-10 mm, e.g., to a sufficiently small outer diameter for use with a catheter introduction system with a catheter size in the range of 12-30 Fr (in the familiar French catheter size scale). Advantageously, in some embodiments, positioning of the open regions 207 adjacent the leaflets of the valve 101 allows the device to be crimped down to a small size without damaging the sensitive valve leaflets.

[0076] Fig. 7 is a flow diagram 700 illustrating the steps for implantation of the device 100. In step 701, the device is obtained. In step 702 the device is crimped to reduce its outer diameter. In step 703 the device is loaded on to an introducer (e.g. as described with reference to Fig. 6). In step 704 the device is positioned at a desired location in a subject, e.g., using a transcatheter method. In step, 705 the device is expanded back to its uncrimped size, e.g., by removing the introducer. In some embodiments the device 100 is self expanding (e.g., owing to shape memory properties of the stent 102). In some embodiments an expander, such as a balloon catheter expander may be used.

[0077] Fig. 8 illustrates a method 800 of making the device 100 shown in Fig. 4. In step 801, a mandrel is obtained having a portion with a shape corresponding to the shape of the valve 101. In step 802, the stent 102 is obtained and placed over the mandrel. The stent may be constructed using any suitable technique known in the art including molding, welding, brazing, etc.

[0078] In step 803, the valve 101 is formed on the mandrel, using a dip molding

[0079] For example, in some embodiments, the mandrel and the stent 102 may be cleaned with alcohol. Next, a polymer conduit is placed on the valve mandrel and the stent 102. Optionally, strips of flexible material (e.g., a polymer such as Angioflex) may be adhered the posts 205 of the stent 102 to form the to reinforce this area. The mandrel assembly is dipped in a polymer solution having a suitable viscosity, e.g., within the 730±50 cp range. In some embodiments, the polymer solution can be an Angioflex solution produced by Abiomed of Danvers, MA. At this step, the valve mandrel is cleaned, e.g. with alcohol. Next, the valve mandrel is placed upside down in a container of Dioxane, e.g., for 30 seconds so that the entire stent is covered. Next, the valve mandrel is dipped in the polymer solution. Once the valve mandrel is removed from the solution any excess solution is removed. The dipping process may be repeated to obtain a desired leaflet profile.

[0080] Although one valve fabrication process has been described above, it is to be understood that any suitable fabrication technique known in the art may be employed, however according to the invention the valve is formed by dip molding.

[0081] For example, the valve 101 may be fabricated using one or more of the techniques described in Labma NMK, Woodhouse KA, Cooper SL. Polyurethanes in Biomedical Applications. 1998 CRC Press LLC, Boca Raton, Florida, p.33.; Lyman DJ, Searl WJ, Albo D, Bergman S, Lamb J, Metcalf LC, and Richards K. Polyurethane elastomers in surgery. Int J Polym Mater, 5:211, 1977; Boretos JW. Procedures for the fabrication of segmented polyurethane polymers into useful biomedical prostheses. National Institutes of Health, 1968.; snf Kardos JL, Mehta BS, Apostolou SF, Thies C, and Clark RE. Design, fabrication and testing of prosthetic blood vessels. Biomater Med Dev Artif Organs, 2:387, 1974.

[0082] In step 804, after molding the valve, a heat shrink tube is placed over the conduit and stent 102 on the mandrel. The heat shrink tubing may be made of a thermoplastic material

such as poly olefin, fluoropolymer (such as fluorinated ethylene propylene, polytetrafluoroethylene or polyvinylidene fluoride), polyvinyl chloride, neoprene, silicone elastomer, Viton, etc.

[0083] In step 805, heat is applied, e.g., with a heat gun, to soften the conduit and cause the heat shrink tubing to contract around the mandrel. The contracting tubing applies a force which molds the softened material of the conduit, causing it to flow around and encapsulate at least a portion of the stent 102 to form the sheath 300. This molding process may be referred to as "thermoforming". In some embodiments, the valve 101 is cooled during the thermoforming process (e.g., by application of an air flow), to avoid thermal damage to the valve 101.

[0084] After cooling, the heat shrink tubing is removed (e.g. cut and peeled away). The valve 101 may be cut (e.g., using laser cutting) to free the valve leaflets.

[0085] In step 806, the assembly is removed from the mandrel, resulting in the device 100 as shown in Fig. 4. Some embodiments include an additional step (not shown) of securing the sheath 300 to the stent 102 using, e.g. sutures.

[0086] In some embodiments, the valve 101 is formed in the partially open position as described above, and may exhibit advantageous hemodynamic performance. Fig. 9 shows a table detailing forward pressure loss as a function of flow rate for embodiments of the valve 101 with various leaflet thicknesses. The pressure loss increases roughly linearly as a function of flow rate, from a loss of about 6-7 mmHg at a flow rate of 5 L/minute to a loss of about 22-25 mmHg at a flow rate of 25 L/minute. Other embodiments may exhibit even lower pressure drops, e.g., reduced by a factor of two or more from the values shown. For example, some embodiments may have a pressure drop of about 5 mmHg or less at a flow rate of 10 L/minute.

[0087] In some embodiments, this performance is comparable or superior to that of a comparable bioprosthetic valve or a comparable mechanical valve. Some embodiments feature the utilization of flexible and peripherally located leaflets which avoid blood flow disturbances such as cavitation and stagnation leading to cell damage and thrombosis. Additional performance benefits include the avoidance of reliability issues typically associated with bioprosthesis (i.e., problems with limited life from structural changes such as calcification and leaflet wear, leading to valve failure -- biological tissue fixation and methods used to mount the tissue to a supporting stent may account for this shortcoming).

[0088] Fig. 10 shows a plot of valve leakage detailing forward pressure loss as a function of flow rate for embodiments of the valve 101 with various leaflet thicknesses. The valve leakage rate at a reverse flow pressure of 85 mmHg is less than about 8 mL/second in some embodiments, and less than about 4 mL/second in another embodiment. Further embodiments may have even lower leakage rates. This performance is comparable or superior to that of a comparable mechanical valve or bioprosthesis valve.

[0089] The closing volume loss of for embodiments of the valve 101 may be, e.g., less than about 10 mL, 8 mL 6, mL, 4 mL, 2mL, 1 mL, or less, (e.g., corresponding to a hydraulic efficiency of at least 80%, at least 85%, or more). This performance is comparable or superior to that of a comparable mechanical valve or bioprosthesis valve.

REFERENCES CITED IN THE DESCRIPTION

Cited references

This list of references cited by the applicant is for the reader's convenience only. It does not form part of the European patent document. Even though great care has been taken in compiling the references, errors or omissions cannot be excluded and the EPO disclaims all liability in this regard.

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- **LYMAN DJSEARL WJALBO DBERGMAN SLAMB JMETCALF LCRICHARDS K**Polyurethane elastomers in surgeryInt J Polym Mater, 1977, vol. 5, 211- [0081]
- **BORETOS JW**Procedures for the fabrication of segmented polyurethane polymers into useful biomedical prosthesesNational Institutes of Health19680000 [0081]
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Patentkrav

1. Proteseapparat omfattende:

en polymerventil (101); og

en rørformet stent (102), som er anbragt omkring en langsgående akse (A) og strækker sig fra en proksimal ende til en distal ende, hvor stenten (120) definerer en rørformet passage mellem enderne;

hvor den rørformede stent (102) har en proksimal del (201), en distal del (202) og en midterste del (203) placeret mellem den proksimale (201) og distale (202) del;

hvor den proksimale (201) og distale (202) del hver omfatter et net af støttestivere (204), der danner mindst en ring af åbne elementer (210) anbragt omkring den langsgående akse (A);

hvor den midterste del (203) omfatter:

en flerhed af langstrakte stænger (205), der strækker sig langs en retning i alt væsentligt parallel med den langsgående akse (A) mellem den proksimale (201) og distale (202) del;

en kroneformet monteringsring (206) fastgjort til stængerne (205) og konfigureret til at montere polymerventilen (101) i den rørformede passage; og

en flerhed af åbne områder (104, 207) distalt for monteringsringen (206), som er fri for langstrakte stænger, støttestivere eller andre strukturer;

hvor:

apparatet omfatter yderligere:

en rørformet, polymerkappe (300), der strækker sig langs den ydre overflade af den rørformede stent (102) fra den proksimale del (201) til den distale del (202), men ikke i alt væsentligt dækker de åbne områder (104, 207) i den midterste del (203), hvor kappen (300) er varmekrympet på stenten (102),

kendetegnet ved, at kappen (300) er støbt ved at anbringe et varmekrymperør omkring polymermaterialet og stenten (102) og påføre varme for at blødgøre polymermaterialet og få varmekrymperøret til at krympe og påføre kraft til at formstøbe polymermaterialet for at få kappen (300) til at flyde rundt og indkapsle mindst en del af stenten (102) for at

forme kappen (300), og polymerventilen (101) er formet ved dyppestøbning.

2. Apparatet ifølge krav 1, hvor de åbne elementer (210) er åbne diamantformede elementer.

3. Apparatet ifølge krav 1 eller 2, hvor kappen (300) indkapsler de langstrakte stænger (205).

4. Apparatet ifølge krav 3, hvor kappen (300) omfatter områder med forstærket tykkelse svarende til de langstrakte stænger (205).

5. Apparatet ifølge krav 3 eller 4, hvor kappen (300) omfatter områder med forstærket tykkelse svarende til en eller flere af støttestiverne (204) eller monteringsringen (206).

6. Apparatet ifølge et hvilket som helst af de foregående krav, hvor polymerventilen (101) omfatter:

et ventillegeme (1101) med en central akse (1116), der strækker sig langs retningen af den rørformede stents (102) længdeakse (A) og har en kropsvæskebane, der strækker sig langs den centrale akse (1116) fra en indstrømningsende til en udstrømningsende;

en fleksibel ydre støtte (1110) anbragt omkring en ydre omkreds af legemet (1101) og forbundet med monteringsringen (206), idet den ydre støtte (1110) omfatter mindst tre fleksible ventilstænger (1112), der hver strækker sig i den aksiale retning til en spids (1120) og hver er fastgjort til mindst en af de langstrakte stænger (205); og

mindst tre fleksible fligklapper (1130), der strækker sig fra den kroneformede monteringsring (206), idet hver af fligklapperne (1130) har en fastgjort kant (1133) fastgjort til den ydre støtte (1110), der definerer en fastgørelseskurve langs monteringsringen (206), der strækker sig mellem et respektivt par af fleksible ventilstænger (1112), og

hvor par af fligklapper (1130) definerer en respektiv kommissur (1135) ved hver af de mindst tre fleksible ventilstænger (1112);

hvor den kroneformede monteringsring (206) omfatter en flerhed af punkter, der hver svarer til en fleksibel ventilstang (1112) og fastgjort til en respektiv en af de langstrakte stænger (205) af stenten (102).

7. Apparatet ifølge krav 6, hvor spidsen (1120) af hver ventilstang (1112) er dannet af et materiale med en fleksibilitet større end resten af ventilstangen (1112); og/eller eventuelt

hvor stenten (102) er konfigureret til at blive krympet for at reducere stentens ydre diameter fra en ikke-krympet diameter til en krympet diameter uden at beskadige polymerventilen (101); og/eller eventuelt hvor den ikke-krympede diameter er mindst ca. 20 mm, og den krympede diameter er mindre end ca. 6 mm.

8. Apparatet ifølge et hvilket som helst af de foregående krav, hvor den rørformede stent (102) omfatter et formhukommelsesmateriale, og eventuelt hvor formhukommelsesmaterialet omfatter Nitinol.

9. Apparatet ifølge et hvilket som helst af de foregående krav, hvor stenten (102) er en selvekspanderende stent.

10. Apparatet ifølge et hvilket som helst af de foregående krav, hvor stenten (102) er konfigureret, når den er implanteret i menneskehjertet, således at polymerklappen (101) er placeret proksimalt ved placeringen af den naturlige aortaklap, de åbne områder er anbragt proksimalt i forhold til den koronare åbning; og/eller eventuelt

hvor apparatet i alt væsentligt består af biokompatible materialer.

11. Fremgangsmåde til fremstilling af proteseapparat omfattende:

opnåelse af en rørformet stent (102), der er anbragt omkring en langsgående akse (A) og strækker sig fra en proksimal ende til en distal ende, hvor stenten (102) definerer en rørformet passage mellem enderne; hvor den rørformede stent (102) har en proksimal del (201), en distal del (202) og en midterste del (203) placeret mellem den proksimale (201) og distale (202) del;

hvor den proksimale (201) og distale (202) del hver omfatter et net af støttestivere (204), der danner mindst en ring af åbne elementer (210) anbragt omkring den langsgående akse (A);
hvor den midterste del (203) omfatter:
en flerhed af langstrakte stænger (205), der strækker sig langs en retning i alt væsentligt parallel med den langsgående akse (A) mellem den proksimale (201) og distale (202) del; og
en kroneformet monteringsring (206) fastgjort til stængerne (205) og konfigureret til at montere en polymerventil (101) inden i den rørformede passage; og
en flerhed af åbne områder (104, 207) distalt for monteringsringen (206), som er frie af langstrakte stænger, støttestivere eller andre strukturer;
anbringelse af stenten (102) på en dorn;
formning af en polymerventil (101) monteret på monteringsringen (206) ved en proces omfattende dyppestøbning; og
formning af en rørformet polymerkappe (300), der strækker sig langs den ydre overflade af den rørformede stent (102) fra den proksimale del (201) til den distale del (202), men ikke i alt væsentligt dækker de åbne områder (104, 207) i den midterste del (203),
hvor nævnte formning af den rørformede polymerkappe (300) inkluderer en termoformningsproces omfattende:
påføring af et polymermateriale på den ydre overflade af den rørformede stent (102);
anbringelse af et varmekrymperør omkring polymermaterialet og stenten (102);
og
påføring af varme for at blødgøre polymermaterialet og få varmekrymperøret til at krympe og påføre kraft for at formstøbe polymermaterialet til at forme kappen (300).

12. Fremgangsmåden ifølge krav 11, hvor formning af kappen (300) omfatter indkapsling af en eller flere af støttestiverne (204) og de langstrakte stænger (205).

13. Fremgangsmåden ifølge krav 11 eller 12, yderligere omfattende, under termoformningsprocessen, at påføre en luftstrøm til polymerventilen (101) for at undgå varmebeskadigelse af polymerventilen (101).

14. Fremgangsmåden ifølge et hvilket som helst af kravene 11 til 13, yderligere omfattende at påføre strimler af polymermateriale for at forstærke kappen (300) på steder svarende til de langstrakte stænger (205) eller monteringsringen (206).

15. Fremgangsmåden ifølge et hvilket som helst af kravene 11 til 13, yderligere omfattende at påføre yderligere polymermateriale for at forstærke kappen (300) på steder svarende til stiverne (204).

DRAWINGS

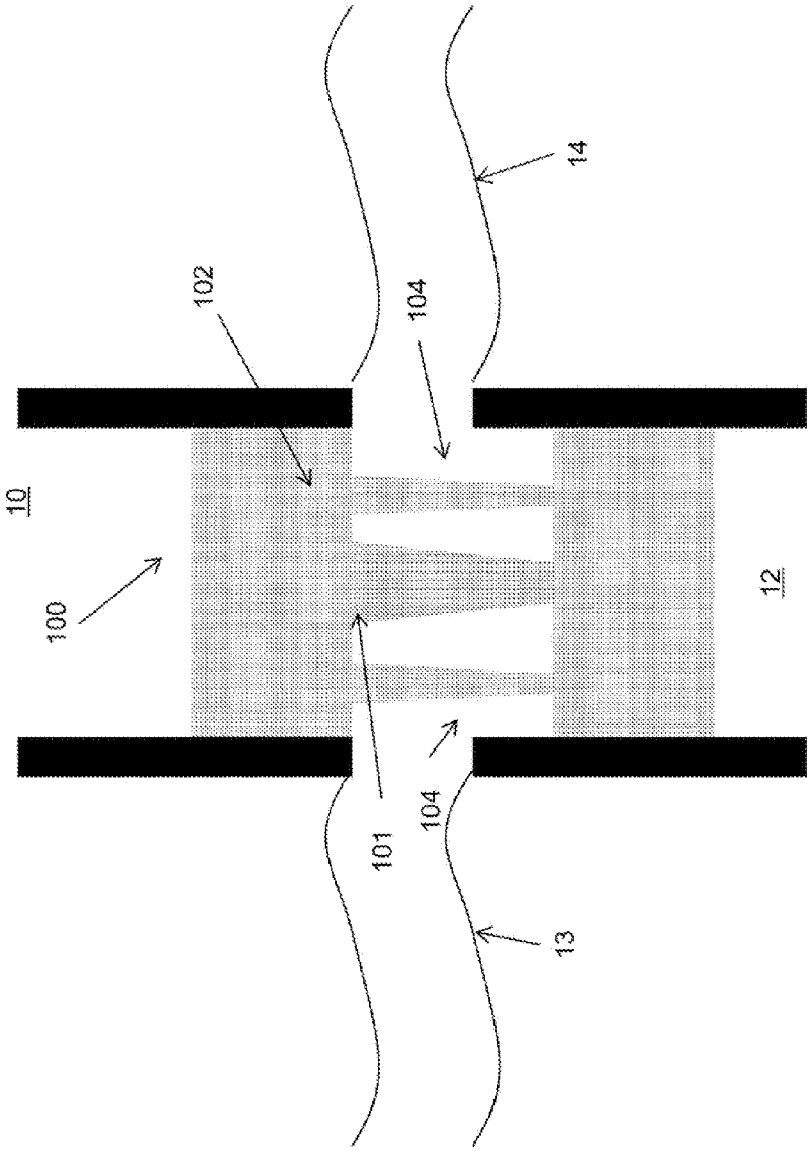

Fig. 1

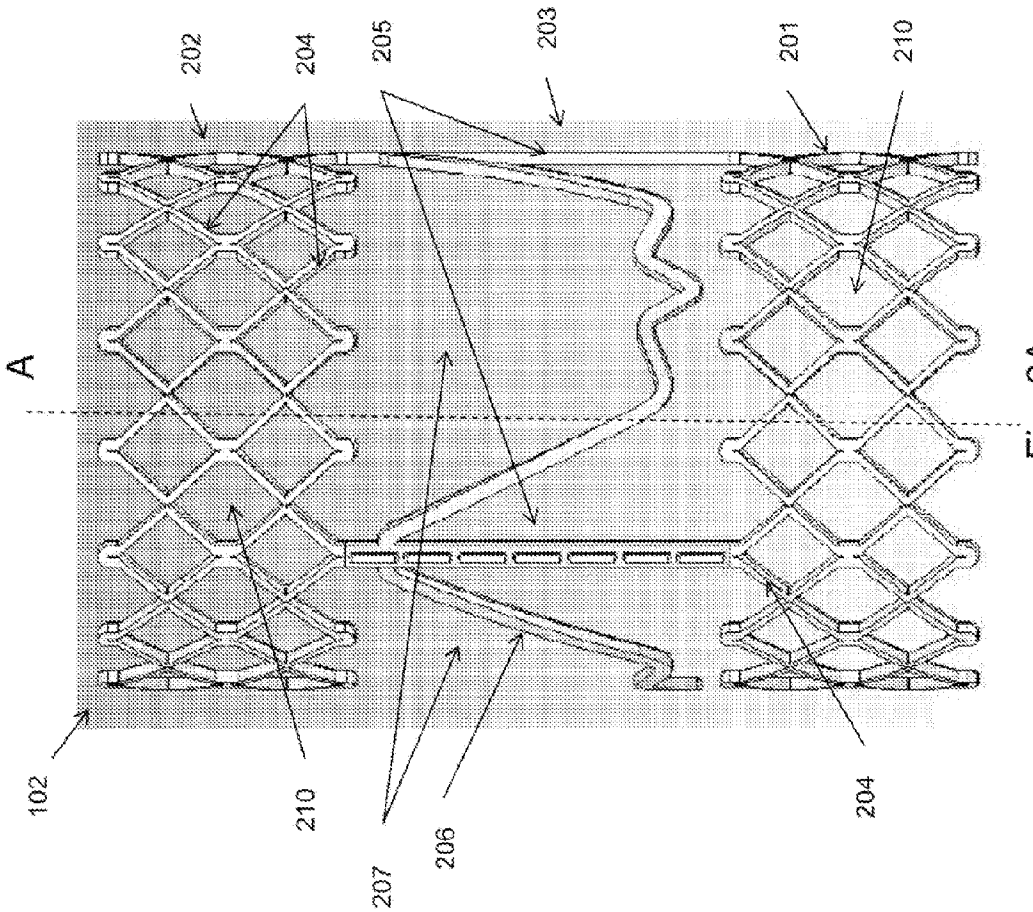

Fig. 2A

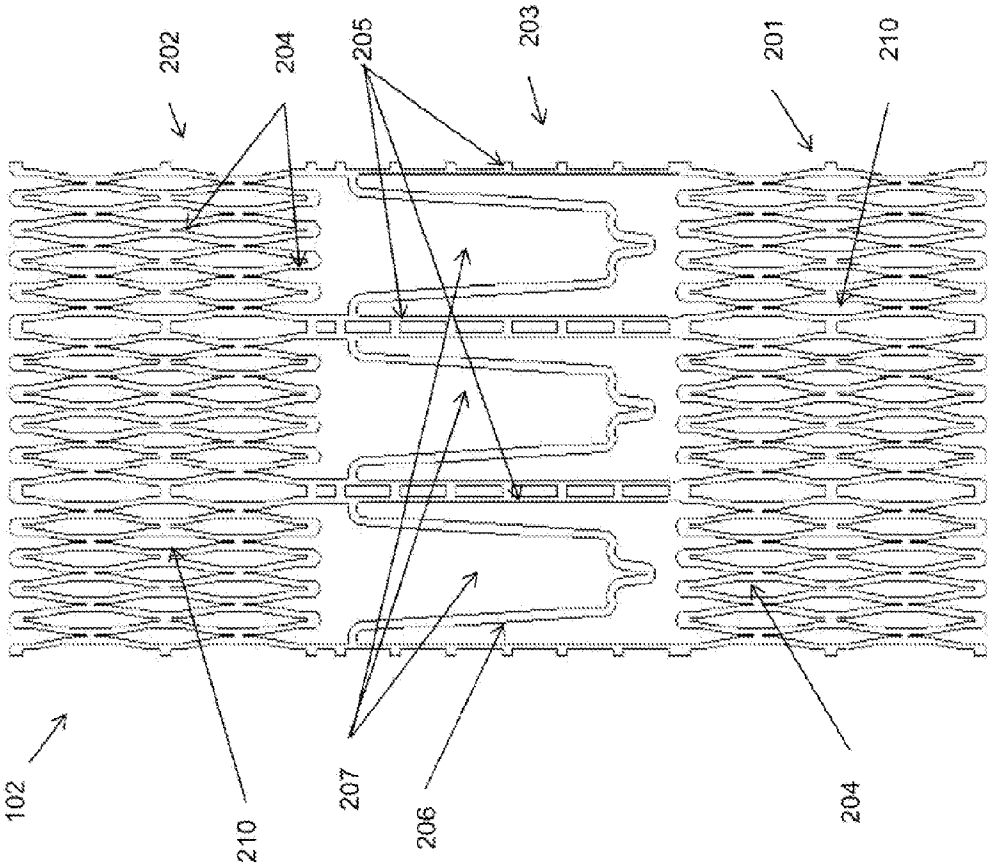

Fig. 2B

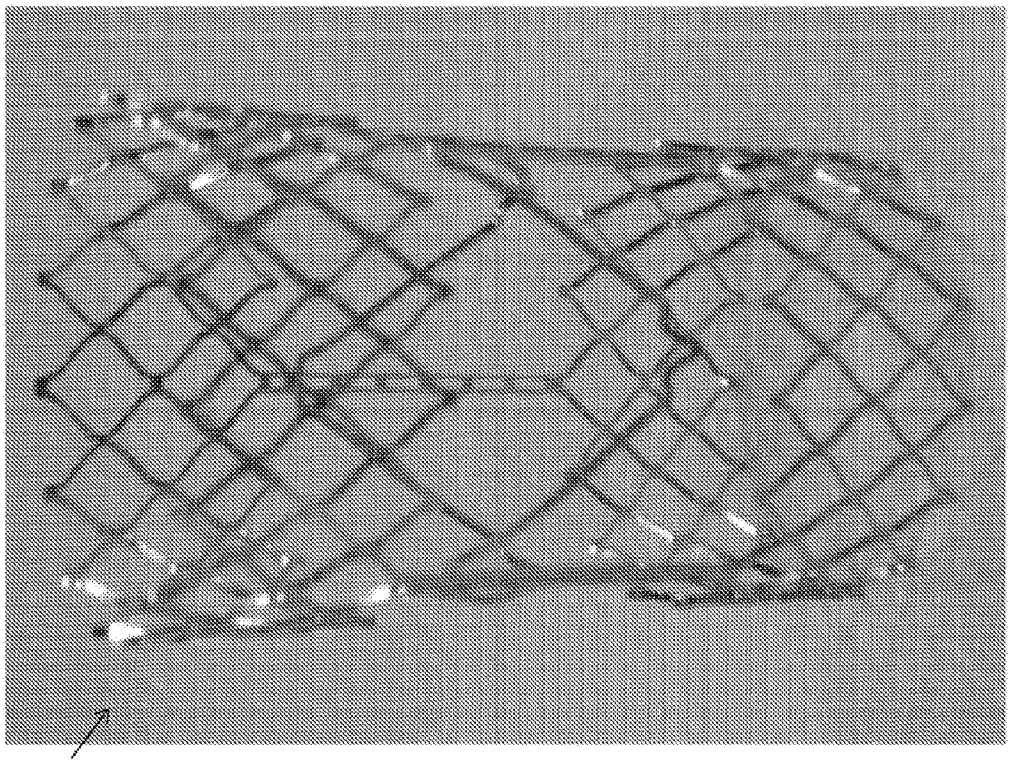

Fig. 2C

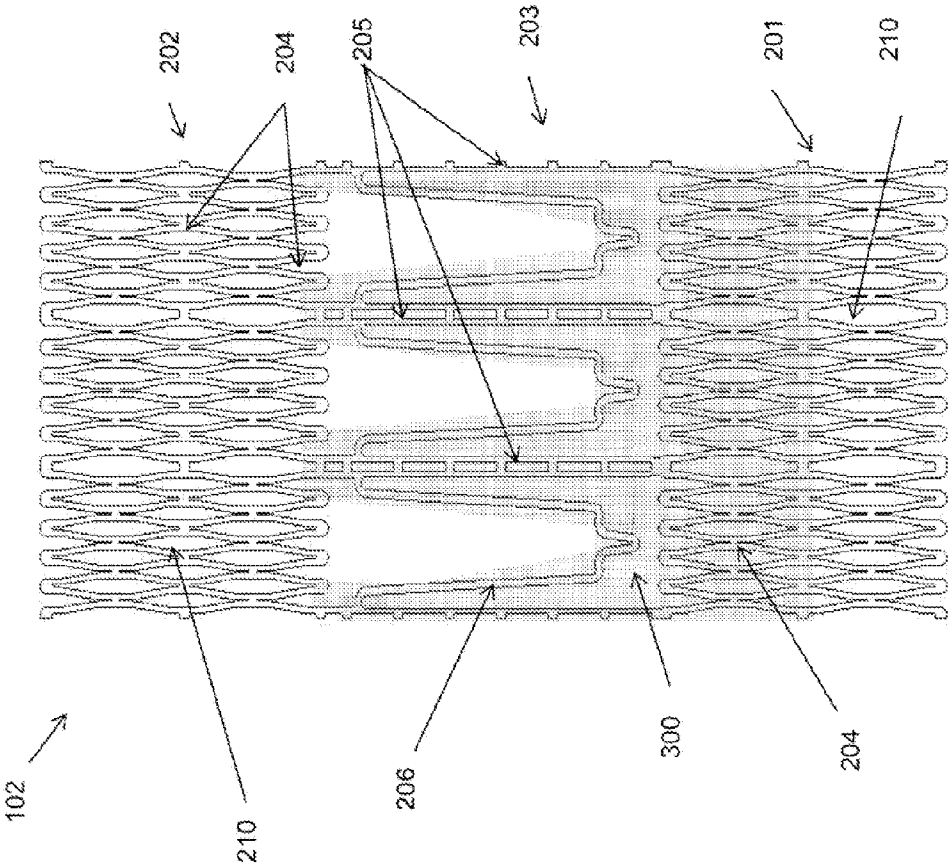

Fig. 3

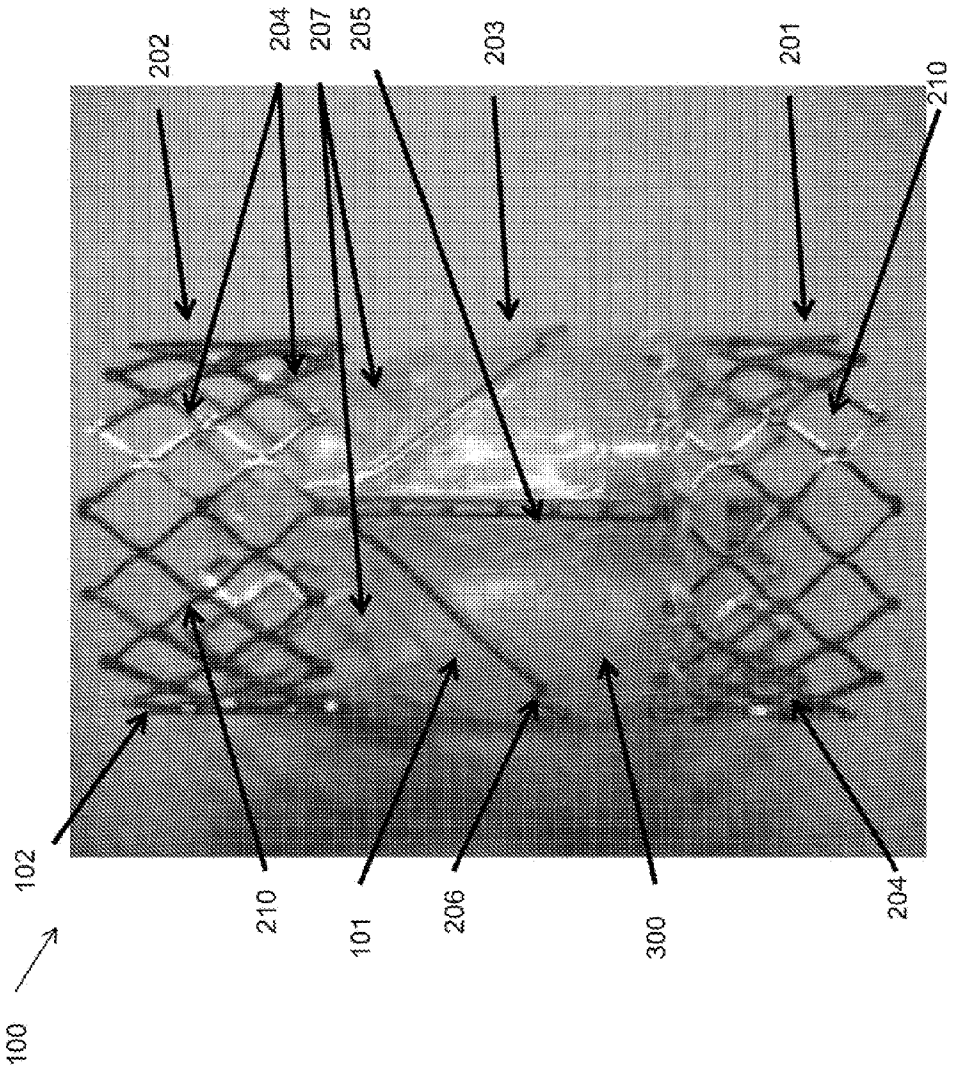

Fig. 4

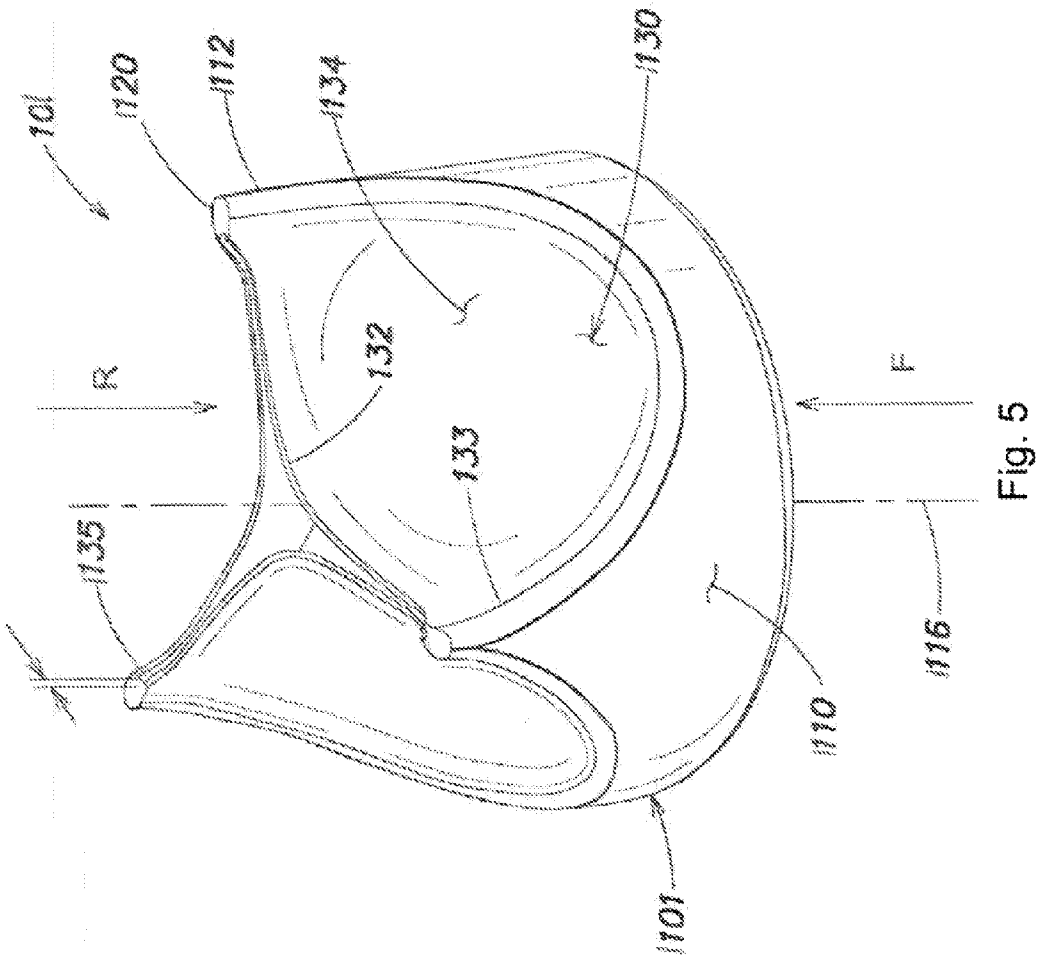

Fig. 5

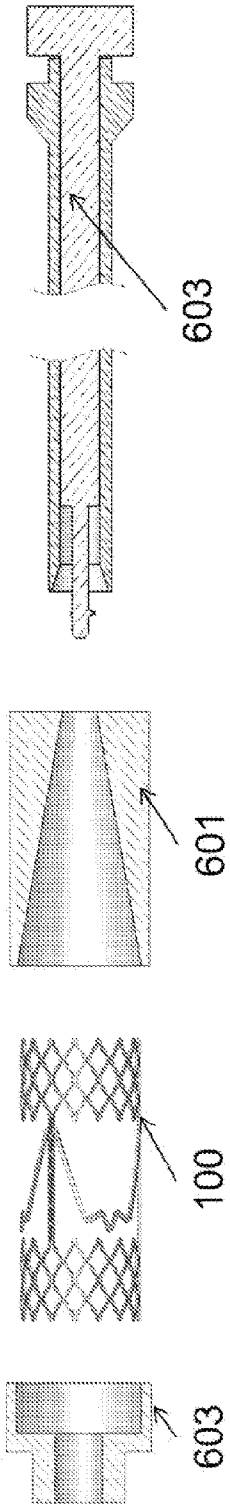

Fig. 6

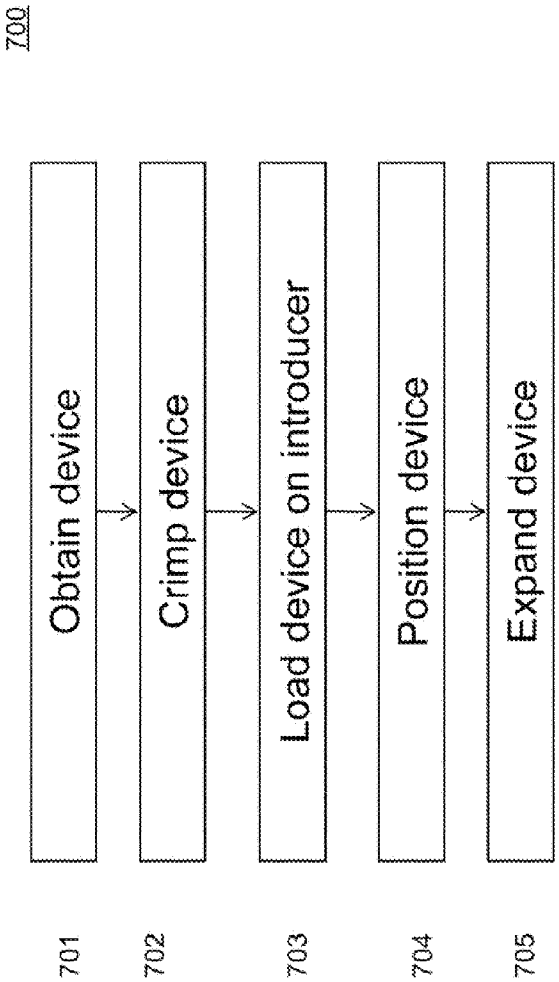
700
Obtain device
Crimp device
Load device on introducer
Position device
Expand device
701
702
703
704
705

Fig. 7

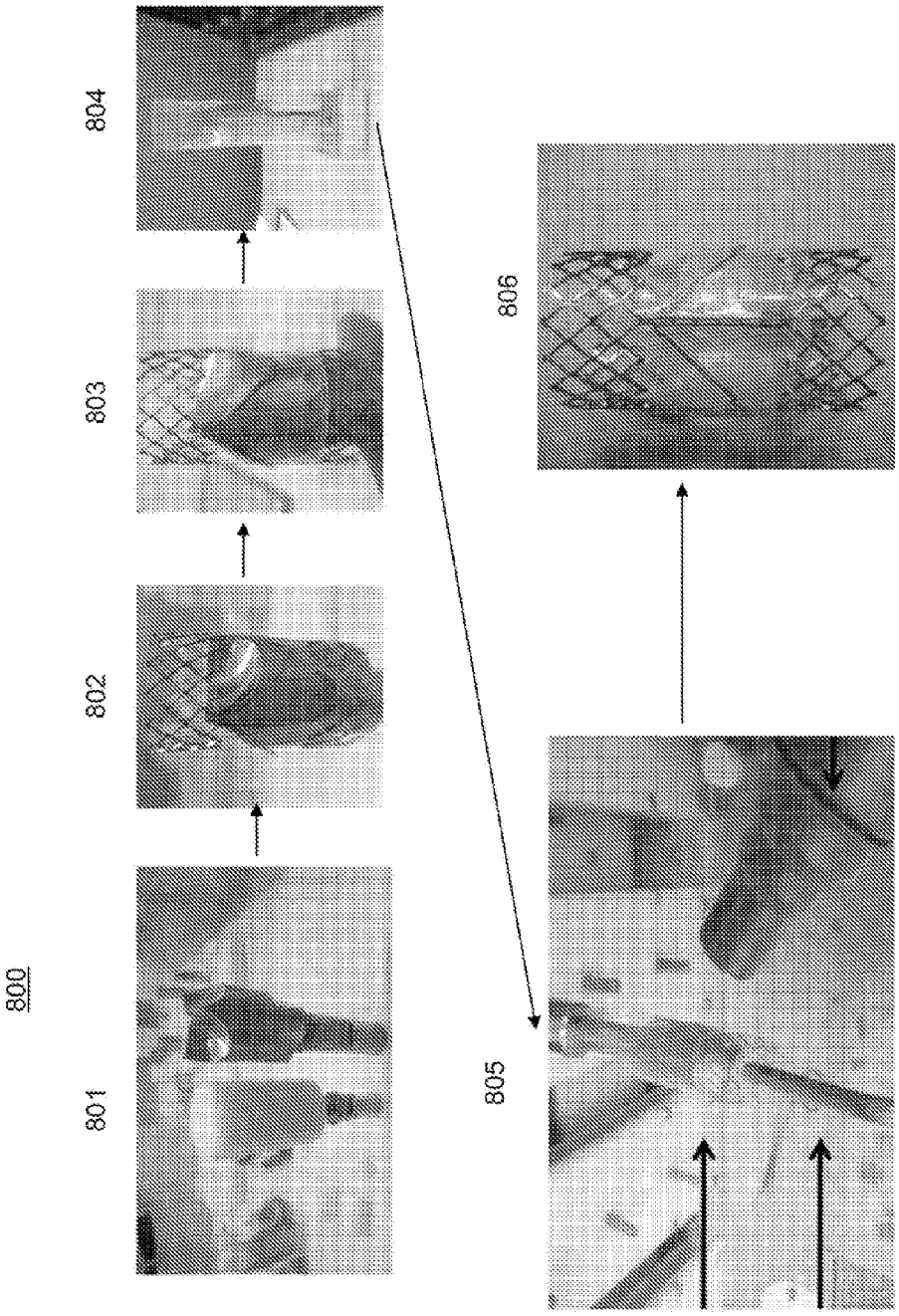

Fig. 8

Sample Name	Leaflet Thickness (in.)	Pressure Drop (mmHg) @ Various Flow Rates				
		5 L/min	10 L/min	15 L/min	20 L/min	24 L/min
Crown 1	0.0105	7.3	**9.7**	14.5	19.5	25.2
Crown 2	0.0085	6.5	**9.8**	13.2	17.8	22.7
Crown 3	0.0066	6.0	**9.3**	14.8	19.8	25.2

Fig. 9

In Vitro Backflow Leakage Rate

Sample Name	Avg. Leaflet Thickness (in.)	Leakage Rate (mL/sec)
Crown 1	0.0105	7.1
Crown 2	0.0085	3.6
Crown 3	0.0066	7.9

Fig. 10