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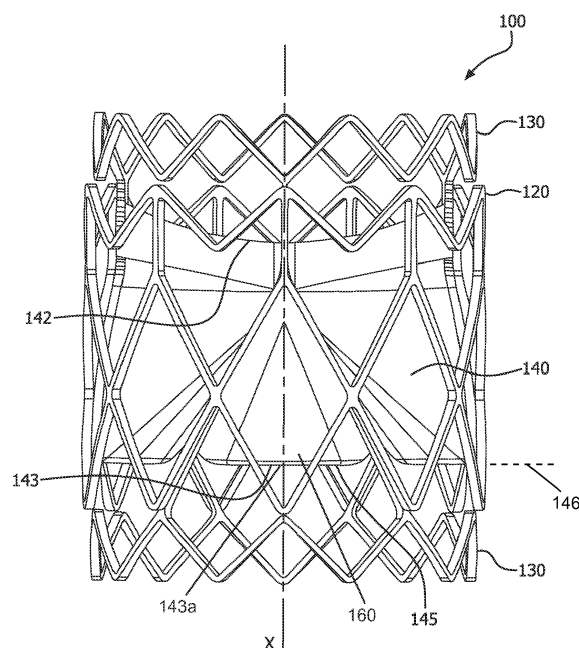
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(54) **MULTI-FRAME PROSTHETIC HEART VALVE**

(57) Described embodiments are directed toward prosthetic valves and systems and methods of making prosthetic valves. In accordance with an embodiment, a prosthetic valve comprises and leaflet frame, and outer frame and a film. The leaflet frame has a generally tubular shape defining a plurality of leaflet windows. The outer frame has a generally tubular shape. The leaflet frame is coaxially disposed at least partially within the outer frame. The leaflet frame and outer frame are coupled at least in part by a contiguous portion of the film. At least a portion of the contiguous portion of the film is contained between and couples the leaflet frame to the outer frame to inhibit relative movement therebetween. The film defines a leaflet extending from each of the leaflet windows.



**FIG. 1A**

## Description

### Field

**[0001]** The present disclosure relates generally to prosthetic valves and more specifically synthetic flexible leaflet-type prosthetic valve devices, systems and methods.

### Background

**[0002]** Bioprosthetic valves have been developed that attempt to mimic the function and performance of a native valve. Flexible leaflets are fabricated from biological tissue such as bovine pericardium. In some valve designs the biological tissue is sewn onto a relatively rigid frame that supports the leaflets and provides dimensional stability when implanted. Although bioprosthetic valves can provide excellent hemodynamic and biomechanical performance in the short term, they are prone to calcification and cusp tears, among other failure modes, requiring reoperation and replacement.

**[0003]** Attempts have been made to use synthetic materials, such as polyurethane, among others, as a substitute for the biological tissue, to provide a more durable flexible leaflet prosthetic valve, herein referred to as a synthetic leaflet valve (SLV). However, synthetic leaflet valves have not become a valid valve replacement option since they suffer premature failure, due to, among other things, suboptimal design and lack of a durable synthetic material.

**[0004]** A number of fabrication techniques have been used to couple the leaflets to a frame, including sewing individual leaflets to the frame (biological and synthetic), and for synthetic leaflets only, injection molding and dip coating a polymer onto the frame. In many cases, the resulting leaflet is supported on the frame and defines a flap having a mounting edge where the leaflet is coupled to the frame and a free edge that allows the flap to move.

**[0005]** The leaflet moves under the influence of fluid pressure. In operation, the leaflets open when the upstream fluid pressure exceeds the downstream fluid pressure and close when the downstream fluid pressure exceeds the upstream fluid pressure. The free edges of the leaflets coapt under the influence of downstream fluid pressure closing the valve to prevent downstream blood from flowing retrograde through the valve.

**[0006]** Valve durability under the repetitive loads of the leaflets opening and closing is dependent, in part, on the load distribution between the leaflet and the frame. Further, substantial load is encountered on the leaflet when in the closed position. Mechanical failure of the leaflet can arise, for example, at the mounting edge, where the flexible leaflet is supported by the relatively rigid frame. The repetitive loads of leaflet opening and closing leads to material failure by fatigue, creep or other mechanism, depending in part on the leaflet material. Mechanical failure at the mounting edge is especially prevalent with syn-

thetic leaflets.

**[0007]** The durability of the valve leaflets is also, but not limited to, a function of the character of bending by the leaflet during the opening-closing cycle. Small radius bends, creases and intersecting creases, can produce high stress zones in the leaflet. These high stress zones can cause the formation of holes and tears under repetitive loading.

**[0008]** Bioprosthetic valves may be delivered using surgical or transcatheter techniques. A surgical valve is implanted into a patient using open-heart surgical techniques. The surgical valve is usually manufactured to have a fixed diameter as opposed to a transcatheter valve which is required to attain a range of diameters for access and delivery. The surgical valve is usually provided with a sewing cuff about a perimeter of the valve to allow for suturing to the native tissue orifice. Sewing cuffs are well known in the art.

**[0009]** A transcatheter prosthetic valve is delivered endovascularly via a catheter which can help to minimize patient trauma as compared with an open-heart, surgical procedure. Open-heart surgery involves extensive trauma to the patient, with attendant morbidity and extended recovery. A valve delivered to the recipient site via a catheter avoids the trauma of open-heart surgery and may be performed on patients too ill or feeble to survive the open-heart surgery.

**[0010]** Some transcatheter valves comprise flexible leaflets mounted inside a tubular metal frame. The metal frame may be self expanding or balloon-expanded from a pre-deployed compressed diameter to the deployed functional diameter. The diameter of the delivery system is dependent, in part, on the resulting thickness of the compressed valve leaflets within the frame as it is mounted on the delivery catheter. In addition to the valve durability issues discussed above, the transcatheter valve must also be able to withstand the handling and deployment stresses associated with being compressed and expanded.

**[0011]** The transcatheter valve must be capable of being securely coupled to the tissue orifice of the implantation site after endovascular placement so as to avoid, for example, dislodgement or migration of the valve after placement. The coupling of the valve to the implantation site is commonly facilitated by relatively high hoop strength of the frame placed in urging engagement with the tissue orifice.

**[0012]** There exists a need for a durable prosthetic valve that may be delivered either surgically or endovascularly.

## SUMMARY

**[0013]** Described embodiments are directed to an apparatus, system, and methods for valve replacement, such as cardiac valve replacement. More specifically, described embodiments are directed toward flexible leaflet valve devices and systems having a multi-part support

member or frame, and methods of making and delivering the valve devices.

**[0014]** An aspect of the invention is recited in claim 1. Selected optional features are recited in the dependent claims.

**[0015]** In accordance with an embodiment, a prosthetic valve comprises a leaflet frame, an outer frame, and a film. The leaflet frame has a generally tubular shape defining a plurality of leaflet windows. The outer frame has a generally tubular shape. The leaflet frame is coaxially disposed at least partially within the outer frame. The leaflet frame and outer frame are coupled at least in part by a contiguous portion of the film. At least a portion of the contiguous portion of the film being contained between and coupling the leaflet frame and outer frame that inhibits relative movement and prevents contact between the leaflet frame and outer frame. The film defines a leaflet extending from each of the leaflet windows.

**[0016]** In accordance with an embodiment, a prosthetic valve comprises and leaflet frame, and outer frame and a film. The leaflet frame has a generally tubular shape defining a plurality of leaflet windows. The outer frame has a generally tubular shape. The leaflet frame is coaxially disposed at least partially within the outer frame. The outer frame includes frame elements that overlay the leaflet windows that are defined by the leaflet frame in cooperative arrangement so as to provide structural support over the leaflet windows. The film defines a leaflet extending from each of the leaflet windows.

**[0017]** In accordance with an embodiment, a method of making a prosthetic valve, comprises: wrapping a first layer of film into a tubular form about a mandrel;

**[0018]** providing a leaflet frame having a generally tubular shape, the leaflet frame having a leaflet frame leaflet surface and a leaflet frame outer surface, the leaflet frame defining a plurality of leaflet windows having a window top; providing an outer frame having a generally tubular shape, the outer frame having an outer frame leaflet surface and an outer frame outer surface; placing the leaflet frame and the outer frame over the first layer of film with the leaflet frame and outer frame spaced apart from each other defining a bridge portion therebetween, the leaflet frame inner surface and the outer frame inner surface in contact with the first layer of film;

**[0019]** forming a second layer of film over the leaflet frame and the outer frame in contact with the leaflet frame outer surface and the outer frame outer surface; coupling the first layer of film and the second layer of film to each other and to the leaflet frame and the outer frame; cutting the first layer of film and the second layer of film across the window top within the leaflet window so as to define a leaflet free edge; masking with release material a portion of the film disposed in the leaflet window that defines the leaflet to prevent further bonding of the leaflet during subsequent processing steps; wrapping a third layer of film into a tubular form over the second layer of film and over the release material that is over the leaflet window, overlapping the leaflet frame, the outer frame, and over

the bridge portion between the leaflet frame and outer frame; coupling the third layer of film and the second layer of film to each other;

**[0020]** removing the assembly from the mandrel; disposing coaxially and at least partially the leaflet frame into the outer frame, folding and overlapping at least partially the bridge portion so as to contain the bridge portion between the leaflet frame and the outer frame; placing the assembly back on the mandrel; coupling the bridge portion to itself and to the third layer of film adjacent the leaflet frame outer surface and the first layer adjacent the outer frame inner surface in nesting engagement.

## BRIEF DESCRIPTION OF THE DRAWINGS

**[0021]** The accompanying drawings are included to provide a further understanding of the present disclosure and are incorporated in and constitute a part of this specification, illustrate embodiments described herein, and together with the description serve to explain the principles discussed in this disclosure.

FIG. 1A is a side view of an embodiment of a valve; FIG. 1B is a side view of the embodiment of the valve of FIG. 1A;

FIG. 1C is a perspective view of the embodiment of the valve of FIG. 1A

FIG. 1D is a representation of a valve in an expanded configuration;

FIG. 1E is a representation of a valve in a compressed configuration;

FIG. 2A is a representation of the embodiment of the valve of FIG. 1A unrolled to a flat orientation;

FIG. 2B is an exploded representation of the embodiment of the valve of FIG. 1A unrolled to a flat orientation;

FIG. 3A is an axial or top view of the embodiment of the valve of FIG. 1A in an open configuration;

FIG. 3B is an axial or top view of the embodiment of the valve of FIG. 1A in a closed configuration;

FIG. 4A is a side view of an embodiment of a transcatheter delivery system within anatomy;

FIG. 4B is a side view of an embodiment of a surgical valve within anatomy;

FIG. 5A is a cross-sectional view of an embodiment of the valve during manufacture;

FIG. 5B is a cross-sectional view of an embodiment of the valve;

FIG. 6A is a representation of an embodiment of an outer frame unrolled to a flat orientation;

FIG. 6B is a representation of an embodiment of an outer frame unrolled to a flat orientation;

FIG. 7A is a representation of an embodiment of a leaflet frame unrolled to a flat orientation;

FIG. 7B is a representation of an embodiment of a leaflet frame unrolled to a flat orientation;

FIG. 8A is a representation of an embodiment of a leaflet frame unrolled to a flat orientation;

FIG. 8B is a representation of an embodiment of a leaflet frame unrolled to a flat orientation;  
 FIG. 8C is a representation of an embodiment of a leaflet frame unrolled to a flat orientation;  
 FIG. 8D is a representation of an embodiment of a leaflet frame unrolled to a flat orientation;  
 FIG. 8E is a representation of an embodiment of a leaflet frame unrolled to a flat orientation;  
 FIG. 9A is a side view of valve components on an assembly mandrel, in accordance with an embodiment;  
 FIG. 9B is a side view of valve components on an assembly mandrel, in accordance with an embodiment;  
 FIG. 10A is a side exploded view of a prosthetic valve comprising a leaflet frame having a generally tubular shape and an outer frame having a generally tubular shape that are coupled by a mechanic engagement member, in accordance with another embodiment;  
 FIG. 10B is an assembled view of the embodiment of FIG. 10A;  
 FIG. 11A is a side view of an embodiment of a valve;  
 FIG. 11B is a perspective view of the embodiment of the valve of FIG. 11 A;  
 FIG. 12 is a side view of a leaflet frame on an assembly mandrel, in accordance with an embodiment;  
 FIG. 13A is a side view of the leaflet frame on a cutting mandrel, in accordance with an embodiment; and  
 FIG. 13B is a perspective view of the leaflet frame on the cutting mandrel of FIG. 13A.

## DETAILED DESCRIPTION

**[0022]** Persons skilled in the art will readily appreciate that various aspects of the present disclosure can be realized by any number of methods and apparatus configured to perform the intended functions. Stated differently, other methods and apparatuses can be incorporated herein to perform the intended functions. It should also be noted that the accompanying drawing figures referred to herein are not necessarily drawn to scale, but may be exaggerated to illustrate various aspects of the present disclosure, and in that regard, the drawing figures should not be construed as limiting.

**[0023]** Although the embodiments herein may be described in connection with various principles and beliefs, the described embodiments should not be bound by theory. For example, embodiments are described herein in connection with prosthetic valves, more specifically cardiac prosthetic valves. However, embodiments within the scope of this disclosure can be applied toward any valve or mechanism of similar structure and/or function. Furthermore, embodiments within the scope of this disclosure can be applied in non-cardiac applications.

**[0024]** The term leaflet as used herein in the context of prosthetic valves is a component of a one-way valve wherein the leaflet is operable to move between an open

and closed position under the influence of a pressure differential. In an open position, the leaflet allows blood to flow through the valve. In a closed position, the leaflet substantially blocks retrograde flow through the valve. In embodiments comprising multiple leaflets, each leaflet cooperates with at least one neighboring leaflet to block the retrograde flow of blood. The pressure differential in the blood is caused, for example, by the contraction of a ventricle or atrium of the heart, such pressure differential typically resulting from a fluid pressure building up on one side of the leaflets when closed. As the pressure on an inflow side of the valve rises above the pressure on the outflow side of the valve, the leaflet opens and blood flows therethrough. As blood flows through the valve into a neighboring chamber or blood vessel, the pressure on the inflow side equalizes with the pressure on the outflow side. As the pressure on the outflow side of the valve rises above the blood pressure on the inflow side of the valve, the leaflet returns to the closed position generally preventing retrograde flow of blood through the valve.

**[0025]** The term membrane as used herein refers to a sheet of material comprising a single composition, such as, but not limited to, expanded fluoropolymer.

**[0026]** The term composite material as used herein refers to a combination of a membrane, such as, but not limited to, expanded fluoropolymer, and an elastomer, such as, but not limited to, a fluoroelastomer. The elastomer may be imbibed within a porous structure of the membrane, coated on one or both sides of the membrane, or a combination of coated on and imbibed within the membrane.

**[0027]** The term laminate as used herein refers to multiple layers of membrane, composite material, or other materials, such as elastomer, and combinations thereof.

**[0028]** The term film as used herein generically refers to one or more of the membrane, composite material, or laminate.

**[0029]** The term biocompatible material as used herein generically refers to a film or a biological material, such as, but not limited to, bovine pericardium.

**[0030]** The term leaflet window is defined as that space that a frame defines from which a leaflet extends. The leaflet may extend from frame elements or adjacent to frame elements and spaced apart therefrom.

**[0031]** The terms native valve orifice and tissue orifice refer to an anatomical structure into which a prosthetic valve may be placed. Such anatomical structure includes, but is not limited to, a location wherein a cardiac valve may or may not have been surgically removed. It is understood that other anatomical structures that may receive a prosthetic valve include, but are not limited to, veins, arteries, ducts and shunts. Although reference is made herein to replacing a native valve with a prosthetic valve, it is understood and appreciated that a valve orifice or implant site may also refer to a location in a synthetic or biological conduit that may receive a valve for a particular purpose, and therefore the scope of the embodiments provided herein is not limited to valve replacement.

**[0032]** As used herein, "couple" means to join, connect, attach, adhere, affix, or bond, whether directly or indirectly, and whether permanently or temporarily.

**[0033]** Embodiments herein include various apparatus, systems, and methods for a prosthetic valve suitable for surgical and transcatheter placement, such as, but not limited to, cardiac valve replacement. The valve is operable as a one-way valve wherein the valve defines a valve orifice into which leaflets open to permit flow and close so as to occlude the valve orifice and prevent flow in response to differential fluid pressure.

**[0034]** Embodiments provided herein present advancement in prosthetic valve technology related to, but not limited to, mechanical and biological performance advantages. In accordance with some embodiments presented herein, a prosthetic valve comprises two frames that are coupled together by a contiguous film in which a leaflet frame is nested into an outer frame in a telescoping manner, wherein there is no chance for the valve to leak between the leaflet frame and the outer frame.

**[0035]** Commonly, a prosthetic flexible leaflet heart valve will have the leaflets attached directly to the frame by suturing. An alternate form of construction can have the leaflet material attached to the inside of the frame, but this arrangement presents the possibility of the leaflet material peeling away if not sufficiently bonded. Another form of construction can have the leaflet material attached to the outside of the frame, but this arrangement often presents problems with abrasion of the leaflet on the frame. In the embodiments provided herein, the problems are avoided by using a pair of frames, between which the leaflet material is contained. In accordance with embodiments provided herein, a pair of frames can be compressed and reexpanded while maintaining the original geometry of the frames with respect to one another, such to provide for transcatheter delivery.

**[0036]** In accordance with some embodiments presented herein, a prosthetic valve comprises two frames; a leaflet frame and an outer frame. The film that comprises the leaflet may be coupled to the inner surface of the leaflet frame. In some other embodiments, the film that comprises the leaflet is contained between the leaflet frame and the outer frame and extends through a leaflet window defined by the leaflet frame. The leaflet, therefore, is significantly prevented from peeling or delaminating as it is contained between the leaflet frame and outer frame, as compared to where the leaflets are only coupled to the inner surface of the leaflet frame.

**[0037]** In accordance with some embodiments presented herein, a prosthetic valve comprises two frames; a leaflet frame and an outer frame. The leaflet frame and the outer frame are separated from each other by a film. In other words, there is a metal to polymer to metal interconnection, wherein there is no metal to metal contact between the two frames.

**[0038]** In accordance with some embodiments presented herein, a prosthetic valve comprises two frames; a leaflet frame and an outer frame. The leaflet frame is

nested within the outer frame, wherein the leaflet frame and outer frame cooperate to provide relatively high resistance to flat plate compression, among other things. In accordance with some embodiments, the outer frame provides frame elements that overlay the leaflet windows that are defined by the leaflet frame so as to provide structural support over the leaflet windows. In accordance with some embodiments, the outer frame provides frame elements that overlay the leaflet windows that are defined by the leaflet frame so as to prevent tissue from extending into the leaflet windows when implanted. In accordance with some embodiments, the outer frame provides frame elements that overlay the leaflet windows that are defined by the leaflet frame and act in concert so as to allow the frame assembly to compress and expand uniformly for transcatheter embodiments.

**[0039]** In accordance with some embodiments presented herein, a prosthetic valve comprises two frames; a leaflet frame and an outer frame. The leaflet frame defines leaflet windows that define, in part, the shape of the leaflets. In some embodiments the leaflet comprises a flat base, wherein the leaflet bends from the base towards the leaflet free edge with minimal creasing and fluttering. In some embodiments the leaflet comprises a flat base, that, among other things, provides for one or more of a shorter valve length, substantially prevents blood stagnation and pooling and encourages washing at the base, as compared to leaflets having a rounded base.

**[0040]** In accordance with some embodiments presented herein, a prosthetic valve comprises two frames; a leaflet frame and an outer frame. The leaflet frame defines leaflet windows from which the leaflets extend. The leaflets are defined by the intersection of films that form an overlapping zone so as to define, at least in part, the leaflet base and/or the leaflet sides.

#### The Valve

**[0041]** FIG. 1A is a side view of a valve 100, in accordance with an embodiment. FIG. 1B is also a side view of the valve 100 of FIG. 1A rotated 60 degrees about the longitudinal axis X. FIG. 1C is a perspective view of the valve 100 of FIG. 1A. FIG. 2A is a side view of the valve 100 of FIG. 1A, wherein the valve 100 has been longitudinally cut and laid open to better illustrate the elements of the generally tubular-shaped valve 100. FIG. 2B is an exploded view of the embodiment of FIG. 2A. FIGs. 3A and 3B are axial views of the valve 100 of FIG. 1A in an open and closed configuration, respectively. In FIG. 3B the leaflets 140 are shown slightly open to better show the features but it is understood that a fully closed valve 100 will have the leaflet free edges 142 of the leaflets 140 coming together to coapt under the influence of downstream fluid pressure which results in closing the valve to prevent downstream blood from flowing retrograde through the valve.

**[0042]** The valve 100 comprises an outer frame 120, a leaflet frame 130, and a film 160 covering the outer

frame 120 and leaflet frame 130, coupling the outer frame 120 to the leaflet frame 130, and defining leaflets 140. The embodiment of valve 100 is discussed further related to a transcatheter valve that may be compressed and re-expanded. It is understood that the embodiment of valve 100 is also applicable to a surgical valve by the addition of a sewing cuff 170, as shown in FIG. 4B. Leaflet frame and outer frame configurations related to surgical valve only embodiments where the valves have a fixed diameter, will be discussed in other embodiments later in this disclosure.

**[0043]** In accordance with an embodiment, a prosthetic valve comprises a leaflet frame 130 having a generally tubular shape, an outer frame 120 having a generally tubular shape, and film 160. The leaflet frame 130 is coaxially disposed at least partially within the outer frame 120. The outer frame 120 provides frame elements that overlay leaflet windows that are defined by the leaflet frame 130 so as to provide structural support over the leaflet windows, as shown in FIGs. 1A-1B. The leaflet frame 130 defines a plurality of leaflet windows, wherein the film 160 defines a leaflet extending from each of the leaflet windows.

#### The Outer Frame

**[0044]** The outer frame 120 is a generally tubular member defining a generally open pattern of apertures 122, in accordance with an embodiment. In accordance with transcatheter embodiments, the outer frame 120 is operable to allow the outer frame 120 to be compressed and expanded between different diameters. The outer frame 120 comprises an outer frame first end 121 a and an outer frame second end 121 b opposite the outer frame first end 121 a. The outer frame 120 comprises an outer frame outer surface 126a and an outer frame inner surface 126b opposite the outer frame outer surface 126a, as shown in FIG. 5A. The outer frame 120 may comprise a structure known in the art as a stent. A stent is a tubular member that may have a small diameter suitable for percutaneous transcatheter delivery into the anatomy, and may be expanded to a larger diameter when deployed into the anatomy. Stents having various designs and material properties are well known in the art.

**[0045]** By way of example, and as illustrated in the embodiments of FIGs. 1A-1C and 2A-2B, the valve 100 includes the outer frame 120 that defines a stent having apertures 122 having generally a diamond shape when in a large diameter configuration, as shown generally in FIG. 1D. Upon compression to a smaller diameter, the apertures 122 deform to generally define an elongated diamond shape, as shown generally in FIG. 1E. Upon re-expansion to a larger diameter, the apertures 122 re-expand to again define a generally diamond shape.

**[0046]** FIGs. 6A and 6B are side views of alternative embodiments of the outer frame 120a, 120b wherein the outer frame has been longitudinally cut and laid open to better illustrate the elements of the outer frame. It is ap-

preciated that there are many embodiments of the outer frame having configurations suitable for the particular purpose.

**[0047]** An open framework of the stent can define any number of features, repeatable or otherwise, such as geometric shapes and/or linear or meandering series of sinusoids. Geometric shapes can comprise any shape that facilitates substantially uniform circumferential compression and expansion. The outer frame 120 may comprise a cut tube, or any other element suitable for the particular purpose. The outer frame 120 may be etched, cut, laser cut, or stamped into a tube or a sheet of material, with the sheet then formed into a substantially cylindrical structure. Alternatively, an elongated material, such as a wire, bendable strip, or a series thereof, can be bent or braided and formed into a substantially cylindrical structure wherein the walls of the cylinder comprise an open framework that is compressible to a smaller diameter in a generally uniform and circumferential manner and expandable to a larger diameter.

**[0048]** It is known that stents of various designs may be elastically deformable so as to be self-expanding under spring loads. It is also known that stents of various designs may be plastically deformable so as to be mechanically expanded such as with a balloon. It is also known that stents of various designs may be plastically deformable as well as elastically deformable. The embodiments of the outer frame 120 presented herein are not to be limited to a specific stent design or mode of expansion.

**[0049]** The outer frame 120 can comprise any metallic or polymeric biocompatible material. For example, the outer frame 120 can comprise a material, such as, but not limited to nitinol, cobalt-nickel alloy, stainless steel, or polypropylene, acetyl homopolymer, acetyl copolymer, ePTFE, other alloys or polymers, or any other biocompatible material having adequate physical and mechanical properties to function as described herein.

**[0050]** In accordance with embodiments, the outer frame 120 and/or leaflet frame 130 can be configured to provide positive engagement with an implant site to firmly anchor the valve 100 to the site, as shown in FIG. 4A representing a transcatheter deployment of the valve 100. In accordance with an embodiment, the outer frame 120 can comprise a sufficiently rigid frame having small elastic recoil so as to maintain sufficient apposition against a tissue orifice 150 to maintain position. In accordance with another embodiment, the outer frame 120 and/or leaflet frame 130 can be configured to expand to a diameter that is larger than a tissue orifice 150 so that when valve 100 expands into the tissue orifice 150, it can be firmly seated therein. In accordance with another embodiment, the outer frame 120 can comprise one or more anchors (not shown) configured to engage the implant site, such as a tissue orifice 150, to secure the valve 100 to the implant site.

**[0051]** It is appreciated that other elements or means for coupling the valve 100 to an implant site are anti-

pated. By way of example, but not limited thereto, other means, such as mechanical and adhesive means may be used to couple the valve 100 to a synthetic or biological conduit.

#### Leaflet frame

**[0052]** Referring again to FIGs. 1C and 2B, the leaflet frame 130 is a generally tubular member defining a plurality of leaflet windows 137 that are coupled together by frame elements 139, in accordance with an embodiment. The leaflet frame 130 comprises a leaflet frame first end 138a and a leaflet frame second end 138b opposite the leaflet frame first end 138a. The leaflet frame 130 comprises a leaflet frame outer surface 132a and a leaflet frame inner surface 132b opposite the leaflet frame outer surface 132a, as shown in FIG. 5A, and as shown in FIG. 3A. The leaflet frame first end 138a and the leaflet frame second end 138b define a generally zigzag configuration to facilitate flexion about flex points 136 such as which facilitates compression and expansion between different diameters for compression onto a delivery device and expansion by a balloon for the transcatheter valve 100 embodiments, as generally explained for the outer frame 120. As will be discussed later, the surgical valve 100 embodiment may or may not have the zigzag configuration since the surgical valve 100 may be of a fixed diameter and need not be operable to compress and re-expand.

**[0053]** The leaflet frame 130 may be referred to in a general sense as a stent or a frame. The term frame elements 139 as used herein refers to any portion of the leaflet frame 130 or outer frame 120, such as, but not limited to, those individual portions that define a leaflet window 137 or aperture 122.

**[0054]** The leaflet frame 130 defines a predetermined repeating pattern as shown in FIG. 2B, in accordance with an embodiment. The leaflet frame 130 defines three interconnected leaflet windows 137 having a substantially triangular shape. Each of the leaflet windows 137 includes two leaflet window sides 133 including posts 131, a leaflet window base 134, and a leaflet window top 135. In this embodiment, the leaflet window base 134 defines a flex point 136 which will be described further below. A leaflet window side 133 and leaflet window top 135 of one leaflet window 137 is interconnected with a leaflet window side 133 of an adjacent leaflet window 137 at the posts 131.

**[0055]** The leaflet frame 130 defines any number of features and geometric shapes that facilitate substantially uniform circumferential compression and expansion. The leaflet frame 130 may comprise a cut tube, or any other element suitable for the particular purpose. The leaflet frame 130 may be etched, cut, laser cut, or stamped into a tube or a sheet of material, with the sheet then formed into a substantially cylindrical structure. Alternatively, an elongated material, such as a wire, bendable strip, or a series thereof, can be bent or braided and

formed into a substantially cylindrical structure wherein the walls of the cylinder comprise an open framework that is compressible to a smaller diameter in a generally uniform and circumferential manner and expandable to a larger diameter.

**[0056]** The leaflet frame 130 can comprise any metallic or polymeric biocompatible material. For example, the leaflet frame 130 can comprise a material, such as, but not limited to nitinol, cobalt-nickel alloy, stainless steel, or polypropylene, acetyl homopolymer, acetyl copolymer, ePTFE, other alloys or polymers, or any other biocompatible material having adequate physical and mechanical properties to function as described herein.

**[0057]** As will be described in more detail below, a film 160 is disposed over each of the three leaflet windows 137 to form a leaflet 140. Further embodiments will be described below wherein the leaflet window 137 defines shapes other than a substantially triangular shape, including, but not limited to a parabolic shape and a trapezoidal shape, with and without a leaflet window top 135, suitable for a particular purpose of an embodiment of a surgical and transcatheter valve 100.

**[0058]** FIGs. 7A and 7B are side views of alternative embodiments of the leaflet frame 130a, 130b wherein the leaflet frame has been longitudinally cut and laid open to better illustrate the elements of the leaflet frame. The leaflet frame 130a includes leaflet windows 137a having a substantially triangular shape defining a pointed leaflet window base 134a. The leaflet frame 130b includes leaflet windows 137b having a substantially triangular shape defining a flat leaflet window base 134b. The flat leaflet window base 134b may be used to define the leaflet base.

**[0059]** FIGs. 8A-8C are side views of alternative embodiments of the leaflet frame 130c-130e wherein the leaflet frame has been longitudinally cut and laid open to better illustrate the elements of the leaflet frame. The leaflet frame 130c includes leaflet windows 137c having a substantially triangular shape defining a pointed leaflet window base 134c. The leaflet frame 130d includes leaflet windows 137d having a substantially parabolic shape defining a rounded leaflet window base 134d. The flat leaflet window base 134b may be used to define the leaflet base. The leaflet frame 130e includes leaflet windows 137e having a substantially triangular shape defining a pointed leaflet window base 134e but not having a leaflet window top.

**[0060]** FIG. 8D is a side view of an alternative embodiment of the leaflet frame 130f wherein the leaflet frame 130f has been longitudinally cut and laid open to better illustrate the elements of the leaflet frame 130f, of a valve substantially shown as the valve 100 of FIGs. 11A and 11B. A leaflet 140f is shown in dotted line to represent where the leaflet 140f is located within the leaflet window 137f, the leaflet window 137f being defined by the leaflet window sides 133f and the leaflet window base 134f. The two leaflet sides 141f diverge from the leaflet base 143f, wherein the leaflet base 143f is substantially flat, with the leaflet free edge 142f opposite the leaflet base 143f, as

shown in dashed lines in FIG. 8D. The leaflet frame 130f further defines posts 1121 from which the leaflet free edge 142 f extends.

**[0061]** FIG. 8E is a side view of an alternative embodiment of the leaflet frame 130g wherein the leaflet frame 130g has been longitudinally cut and laid open to better illustrate the elements of the leaflet frame 130g. A leaflet 140g is shown in dotted line to represent where the leaflet 140g is located within the leaflet window 137g, the leaflet window 137g being defined by the leaflet window sides 133g and the leaflet window base 134g. Two leaflet sides 141g diverge from the leaflet base 143g, wherein the leaflet base 143g is substantially flat, with the leaflet free edge 142g opposite the leaflet base 143g, as shown in dashed lines in FIG. 8E. The leaflet frame 130g comprises a plurality of leaflet frame elements defining a plurality of isosceles triangles interconnected by a leaflet window base 134g defining leaflet windows 137g that define isosceles trapezoids. Each leaflet window side 133g is defined by a side of one triangle and a side of an adjacent triangle.

**[0062]** As previously discussed, the leaflet window base may be used to define the leaflet base in accordance with embodiments. Also as previously discussed, the leaflet base may be defined as a virtual leaflet base 143a by a fold line 146 in the film 160 in the fold region spaced apart from the leaflet window base 134, as shown in FIGs. 1A and 1B, and shown by the dashed lines in FIG. 2B. It is appreciated that there are many embodiments of the outer frame having configurations suitable for the particular purpose.

**[0063]** In transcatheter valve 100 embodiments, the leaflet frame 130 is elastically, plastically, or both, compressible to obtain a relatively small diameter to accommodate percutaneous transcatheter mounting and delivery. In accordance with an embodiment as shown in FIG. 2B, the leaflet frame 130 may comprise one or more flex points 136 so as to provide a preferential flexing location for the leaflet frame 130 to flex when compressed to a smaller diameter. A flex point 136 comprises a site on the leaflet frame 130 that undergoes the highest degree of bending when transitioning from an expanded state to collapsed state and vice versa. The flex point 136 can comprise a geometry, structural modification or material modification, among others, that biases the leaflet frame 130 to bend at the flex point 136 when compressed.

**[0064]** The leaflet frame 130 may comprise, such as, but not limited to, any elastically deformable metallic or polymeric biocompatible material, in accordance with embodiments. The leaflet frame 130 may comprise a shape-memory material, such as nitinol, a nickel-titanium alloy. Other materials suitable for the leaflet frame 130 include, but are not limited to, other titanium alloys, stainless steel, cobalt-nickel alloy, polypropylene, acetyl homopolymer, acetyl copolymer, other alloys or polymers, or any other biocompatible material having adequate physical and mechanical properties to function as a leaflet frame 130 as described herein.

**[0065]** In accordance with an embodiment, the leaflet frame 130 and the outer frame 120 comprise a shape memory material operable to flex under load and retain its original shape when the load is removed, thus allowing the leaflet frame 130 and the outer frame 120 to self-expand from a compressed shape to a predetermined shape. The leaflet frame 130 and the outer frame 120 may comprise the same or different materials. In accordance with an embodiment, the leaflet frame 130 and the outer frame 120 are plastically deformable to be expanded by a balloon. In another embodiment the outer frame 120 and the leaflet frame 130 are elastically deformable so as to be self-expanding.

## 15 The Film

**[0066]** The film 160 is generally any sheet-like material that is biologically compatible and configured to couple to the outer frame 120 and the leaflet frame 130, in accordance with embodiments. It is understood that the term "film" is used generically for one or more biocompatible materials suitable for a particular purpose. The leaflets 140 are also comprised of the film 160.

**[0067]** In accordance with an embodiment, the biocompatible material is a film 160 that is not of a biological source and that is sufficiently flexible and strong for the particular purpose, such as a biocompatible polymer. In an embodiment, the film 160 comprises a biocompatible polymer that is combined with an elastomer, referred to as a composite.

**[0068]** It is also understood that the film 160 is coupled to the outer frame 120 may not be the same film 160 that is coupled to the leaflet frame 130, in accordance with embodiments. Details of various types of film 160 are discussed below. In an embodiment, the film 160 may be formed from a generally tubular material to at least partially cover the outer frame 120 and the leaflet frame 130. The film 160 can comprise one or more of a membrane, composite material, or laminate. Details of various types of film 160 are discussed below.

## Leaflet

**[0069]** Each leaflet window 137 is provided with a biocompatible material, such as a film 160, which is coupled to a portion of the leaflet window sides 133 with the film 160 defining a leaflet 140. Each leaflet 140 defines a leaflet free edge 142 and a leaflet base 143, in accordance with an embodiment. As will be described below, it is anticipated that a plurality of embodiments of leaflet base configurations may be provided. In accordance with an embodiment, the film 160 is coupled to a portion of the leaflet window sides 133 and to the leaflet window base 134 where the leaflet 140 is defined by the portion of the leaflet window sides 133 and to the leaflet window base 134. In accordance with another embodiment, the film 160 is coupled to a portion of the leaflet window sides 133 but not the leaflet window base 134 of the leaflet



frame 130 where the leaflet 140 is defined by the portion of the leaflet window sides 133 and to a virtual leaflet base 143a defined by a fold region as will be described below.

**[0070]** The shape of the leaflets 140 are defined in part by the shape of the leaflet window 137 and the leaflet free edge 142. As will be discussed below in accordance with an embodiment, the shape of the leaflets 140 also depends in part on a process that induces a fold at the fold line 145 to define a virtual leaflet base 143a as will be described further below, so as to impart a predetermined shape to the leaflet 140. Since high bending stresses are located at the leaflet base, defining a virtual leaflet base 143a that is not bound by the leaflet window base 134 may reduce the chance of tearing of the leaflet 140 at the interface of the leaflet base 143 to the leaflet window base 134. It may also reduce blood pooling and stagnation at the leaflet base 143 as compared with a rounded leaflet base.

**[0071]** In accordance with an embodiment, substantially the entire leaflet frame 130 lies adjacent to the outer frame inner surface 126b, as shown in FIG. 3A. As such, when the leaflets 140 are in a fully open position, the valve 100 presents a substantially circular valve orifice 102 as shown in FIG. 3A. Fluid flow is permitted through the valve orifice 102 when the leaflets 140 are in an open position.

**[0072]** As the leaflets 140 cycle between the open and closed positions, the leaflets 140 generally flex about the leaflet base 143 and the portion of the leaflet window sides 133 to which the leaflets are coupled. When the valve 100 is closed, generally about half of each leaflet free edge 142 abuts an adjacent half of a leaflet free edge 142 of an adjacent leaflet 140, as shown in FIG. 3B. The three leaflets 140 of the embodiment of FIG. 3B meet at a triple point 148. The valve orifice 102 is occluded when the leaflets 140 are in the closed position stopping fluid flow.

**[0073]** Referring to FIG. 3B, in accordance with an embodiment, each leaflet 140 includes a central region 182 and two side regions 184 on opposite sides of the central region 182. The two central region sides 183 converge from the leaflet base 143 to the leaflet free edge 142. Each of the side regions 184 have a shape substantially that of a triangle and each are defined by one of the central region sides 183, one of the leaflet sides 141, and the leaflet free edge 142.

**[0074]** The leaflet 140 can be configured to actuate at a pressure differential in the blood caused, for example, by the contraction of a ventricle or atrium of the heart, such pressure differential typically resulting from a fluid pressure building up on one side of the valve 100 when closed. As the pressure on an inflow side of the valve 100 rises above the pressure on the outflow side of the valve 100, the leaflet 140 opens and blood flows there-through. As blood flows through the valve 100 into a neighboring chamber or blood vessel, the pressure equalizes. As the pressure on the outflow side of the valve

100 rises above the blood pressure on the inflow side of the valve 100, the leaflet 140 returns to the closed position generally preventing the retrograde flow of blood through the inflow side of the valve 100.

**[0075]** It is understood that the leaflet frame 130 may comprise any number of leaflet windows 137, and thus leaflets 140, suitable for a particular purpose, in accordance with embodiments. Leaflet frames 130 comprising one, two, three or more leaflet windows 137 and corresponding leaflets 140 are anticipated.

#### Valve Film

**[0076]** As shown in the exploded unwrapped view of FIG. 2B of the embodiment of FIG. 2A, the outer frame 120 is located substantially coplanar, laterally adjacent to and spaced apart from the leaflet frame 130. The leaflet window base 134 of the leaflet window 137 is located proximate to an outer frame first end 121 a of the outer frame 120 with the leaflet frame first end 138a of the leaflet frame 130 extending away from the outer frame 120. This placement is also used in the manufacture of the valve 100 as will be discussed below. While in this placement, the film 160 is coupled to the outer frame 120 and a portion of the leaflet frame 130 with the film 160 coupling the outer frame 120 to the leaflet frame 130.

**[0077]** The film 160 that spans the space between the outer frame 120 and the leaflet frame 130 defines at least in part a fold region 144 shown as dashed lines in FIG. 2B. As will be discussed further below, in accordance with an embodiment, the fold region 144 is provided to allow the leaflet frame 130 to be telescopically disposed within the outer frame 120, the outer frame 120 having an inner diameter that is larger than the outer diameter of the leaflet frame 130, in accordance with an embodiment of a method of making the valve 100, hence creating a fold within the fold region 144 along a generally circumferential line 146.

**[0078]** It is anticipated that the film 160 may be coupled to the leaflet frame 130 and the outer frame 120 in many ways suitable for a particular purpose, in accordance with embodiments. In accordance with an embodiment, the outer frame 120 may be wrapped with overlapping layers of a film 160 having a first composition. The leaflet frame 130 may be wrapped with overlapping layers of a film 160 having a second composition. The wrapped leaflet frame 130, the wrapped outer frame 120, and the space between the outer frame 120 and the leaflet frame 130 may be wrapped with overlapping layers of a film 160 having a third composition defining, at least in part, the fold region 144.

**[0079]** In another embodiment, the film 160 may be coupled to the inner or outer surface of the leaflet frame 130 and outer frame 120. In another embodiment, the film 160 may be coupled to the inner and outer surface of the leaflet frame 130 and outer frame 120 sandwiching the leaflet frame 130 and outer frame 120 between the film 160. As will be discussed below, coupling the film

160 to at least the leaflet frame outer surface 132a and the outer frame inner surface 126b, as shown in FIGs. 3A and 5A-5B may provide additional support to the leaflet 140 to prevent disengagement of the leaflet 140 from the leaflet frame 130 since a portion of the film 160 is contained between the leaflet frame 130 and the outer frame 120, as shown in FIG. 5B.

**[0080]** Wherever the film 160 is present it prevents blood from traveling through or across the valve 100 other than through the valve orifice 102 when the leaflets 140 are in an open position and uncovered portions of the leaflet frame 130 or outer frame 120. As such, the film 160 creates a barrier to blood flow in any interstitial space(s) or apertures 122 of the outer frame 120 and leaflet frame 130, and therebetween, that the film 160 covers.

**[0081]** The film 160 is fixedly secured or otherwise coupled at a single or a plurality of locations of the inner surface or outer surface of the outer frame 120 and leaflet frame 130, for example, using one or more of taping, heat shrinking, adhesion and other processes known in the art. In some embodiments, a plurality of membrane/composite layers, i.e., a laminate, are used and can be coupled to both the inner and outer surfaces of the outer frame 120 and the leaflet frame 130 to form at least a portion of the film 160.

**[0082]** The film 160 comprises any material(s) that have the suitable physical and mechanical properties to perform the functions described herein. The film 160 may comprise the same material that the leaflet 140 comprises, as described above, or a different material. Similarly, the film 160 may or may not be homogenous in material composition. Different portions of the film 160 can comprise different materials which can give it different physical and mechanical properties.

**[0083]** As shown in FIGs. 5A and 5B, both views showing the elements in cross-section, the leaflet frame 130 has a generally tubular shape defining a plurality of leaflet windows (not shown). The outer frame 120 has a generally tubular shape. The leaflet frame 130 is coaxially disposed at least partially within the outer frame 120. The leaflet frame 130 and outer frame 120 are coupled at least in part by a contiguous portion of the film 160. At least a portion of the contiguous portion of the film 160 is contained between and couples the leaflet frame 130 to the outer frame 120 to inhibit relative movement therebetween. The film defines a leaflet 140 extending from each of the leaflet windows. The leaflet base 143 is defined at a fold line 145 in the film 160. In accordance with an embodiment, at least a portion of the contiguous portion of the film 160 that is contained between and coupling the leaflet frame 130 and outer frame 120 prevents contact between the leaflet frame 130 and outer frame 120.

**[0084]** As previously discussed, in an embodiment of a method of making the valve 100, the leaflet frame 130 is disposed within the outer frame 120 in a telescoping manner whereby folding the film 160 in the fold region 144, as shown in FIGs. 5A and 5B. The leaflet frame 130

is therefore nested within the outer frame 120 while remaining coaxial therewith. The assembly is further processed to couple the fold region 144 to itself and to the wrapped leaflet frame 130 and outer frame 120 while preventing the film 160 defining the leaflets 140 from adhering to unintended parts of the valve 100 that would prevent leaflet function.

**[0085]** In accordance with another embodiment, the frame members defining the apertures of the leaflet frame 130 and outer frame 120 are preferentially aligned to provide overlapping and complimentary arrangement so as to provide structural rigidity to the assembly.

**[0086]** In accordance with an embodiment of a transcatheter valve 100, with reference to FIGs. 1D-1E, the valve 100 may be compressed into a collapsed configuration having a smaller diameter and expanded into an expanded configuration so that the valve 100 can be endovascularly delivered in the collapsed configuration and expanded upon deployment within the tissue orifice 150 as shown in FIG. 4A. The leaflet frame 130 and the outer frame 120 can be operable to recover circumferential uniformity when transitioning from the collapsed configuration to the expanded configuration.

**[0087]** The valve 100 may be mounted onto a delivery catheter, suitable for a particular purpose. The diameter of the valve 100 in the collapsed configuration is determined in part by the thickness of the leaflet frame 130 within the outer frame 120 and the leaflet thickness.

#### 30 Leaflet Film

**[0088]** The biocompatible material that makes up the leaflet 140 can comprise any biological tissue or synthetic, biocompatible materials sufficiently compliant and flexible, such as a biocompatible polymer. In an embodiment, the leaflet 140 comprises a biocompatible polymer that is combined with an elastomer, referred to as a composite. A material according to one embodiment includes a composite material comprising an expanded fluoropolymer membrane, which comprises a plurality of spaces within a matrix of fibrils, and an elastomeric material. It should be appreciated that multiple types of fluoropolymer membranes and multiple types of elastomeric materials can be combined to form a laminate while remaining within the scope of the present disclosure. It should also be appreciated that the elastomeric material can include multiple elastomers, multiple types of non-elastomeric components, such as inorganic fillers, therapeutic agents, radiopaque markers, and the like while remaining within the scope of the present disclosure.

**[0089]** In accordance with an embodiment, the composite material includes an expanded fluoropolymer material made from porous ePTFE membrane, for instance as generally described in U.S. Patent No. 7,306,729 to Bacino.

**[0090]** The expandable fluoropolymer, used to form the expanded fluoropolymer material described, may comprise PTFE homopolymer. In alternative embodi-

ments, blends of PTFE, expandable modified PTFE and/or expanded copolymers of PTFE may be used. Non-limiting examples of suitable fluoropolymer materials are described in, for example, U.S. Patent No. 5,708,044, to Branca, U.S. Patent No. 6,541,589, to Bailie, U.S. Patent No. 7,531,611, to Sabol et al., U.S. Patent Application No. 11/906,877, to Ford, and U.S. Patent Application No. 12/410,050, to Xu et al.

**[0091]** The expanded fluoropolymer membrane can comprise any suitable microstructure for achieving the desired leaflet performance. In accordance with an embodiment, the expanded fluoropolymer comprises a microstructure of nodes interconnected by fibrils, such as described in U.S. Patent No. 3,953,566 to Gore. The fibrils radially extend from the nodes in a plurality of directions, and the membrane has a generally homogeneous structure. Membranes having this microstructure may typically exhibit a ratio of matrix tensile strength in two orthogonal directions of less than 2, and possibly less than 1.5.

**[0092]** In another embodiment, the expanded fluoropolymer membrane has a microstructure of substantially only fibrils, as is generally taught by U.S. Patent No. 7,306,729, to Bacino. The expanded fluoropolymer membrane having substantially only fibrils, can possess a high surface area, such as greater than  $20\text{m}^2/\text{g}$ , or greater than  $25\text{m}^2/\text{g}$ , and in some embodiments can provide a highly balanced strength material having a product of matrix tensile strengths in two orthogonal directions of at least  $1.5 \times 10^5 \text{MPa}^2$ , and/or a ratio of matrix tensile strengths in two orthogonal directions of less than 4, and possibly less than 1.5.

**[0093]** The expanded fluoropolymer membrane can be tailored to have any suitable thickness and mass to achieve the desired leaflet performance. By way of example, but not limited thereto, the leaflet 140 comprises an expanded fluoropolymer membrane having a thickness of about  $0.1 \mu\text{m}$ . The expanded fluoropolymer membrane can possess a mass per area of about  $1.15 \text{g}/\text{m}^2$ . Membranes according to an embodiment of the invention can have matrix tensile strengths of about 411 MPa in the longitudinal direction and 315 MPa in the transverse direction.

**[0094]** Additional materials may be incorporated into the pores or within the material of the membranes or in between layers of membranes to enhance desired properties of the leaflet. Composite materials described herein can be tailored to have any suitable thickness and mass to achieve the desired leaflet performance. Composite materials according to embodiments can include fluoropolymer membranes and have a thickness of about  $1.9 \mu\text{m}$  and a mass per area of about  $4.1 \text{g}/\text{m}^2$ .

**[0095]** The expanded fluoropolymer membrane combined with elastomer to form a composite material provides the elements of the present disclosure with the performance attributes required for use in high-cycle flexural implant applications, such as heart valve leaflets, in various ways. For example, the addition of the elastomer

can improve the fatigue performance of the leaflet by eliminating or reducing the stiffening observed with ePTFE-only materials. In addition, it may reduce the likelihood that the material will undergo permanent set deformation, such as wrinkling or creasing, that could result in compromised performance. In one embodiment, the elastomer occupies substantially all of the pore volume or space within the porous structure of the expanded fluoropolymer membrane. In another embodiment the elastomer is present in substantially all of the pores of the at least one fluoropolymer layer. Having elastomer filling the pore volume or present in substantially all of the pores reduces the space in which foreign materials can be undesirably incorporated into the composite. An example of such foreign material is calcium that may be drawn into the membrane from contact with the blood. If calcium becomes incorporated into the composite material, as used in a heart valve leaflet, for example, mechanical damage can occur during cycling open and closed, thus leading to the formation of holes in the leaflet and degradation in hemodynamics.

**[0096]** In an embodiment, the elastomer that is combined with the ePTFE is a thermoplastic copolymer of tetrafluoroethylene (TFE) and perfluoromethyl vinyl ether (PMVE), such as described in U.S. Patent No. 7,462,675 to Chang et al. As discussed above, the elastomer is combined with the expanded fluoropolymer membrane such that the elastomer occupies substantially all of the void space or pores within the expanded fluoropolymer membrane to form a composite material. This filling of the pores of the expanded fluoropolymer membrane with elastomer can be performed by a variety of methods. In one embodiment, a method of filling the pores of the expanded fluoropolymer membrane includes the steps of dissolving the elastomer in a solvent suitable to create a solution with a viscosity and surface tension that is appropriate to partially or fully flow into the pores of the expanded fluoropolymer membrane and allow the solvent to evaporate, leaving the filler behind.

**[0097]** In one embodiment, the composite material comprises three layers: two outer layers of ePTFE and an inner layer of a fluoroelastomer disposed therebetween. Additional fluoroelastomers can be suitable and are described in U.S. Publication No. 2004/0024448 to Chang.

**[0098]** In another embodiment, a method of filling the pores of the expanded fluoropolymer membrane includes the steps of delivering the filler via a dispersion to partially or fully fill the pores of the expanded fluoropolymer membrane.

**[0099]** In another embodiment, a method of filling the pores of the expanded fluoropolymer membrane includes the steps of bringing the porous expanded fluoropolymer membrane into contact with a sheet of the elastomer under conditions of heat and/or pressure that allow elastomer to flow into the pores of the expanded fluoropolymer membrane.

**[0100]** In another embodiment, a method of filling the

pores of the expanded fluoropolymer membrane includes the steps of polymerizing the elastomer within the pores of the expanded fluoropolymer membrane by first filling the pores with a prepolymer of the elastomer and then at least partially curing the elastomer.

**[0101]** After reaching a minimum percent by weight of elastomer, the leaflets constructed from fluoropolymer materials or ePTFE generally performed better with increasing percentages of elastomer resulting in significantly increased cycle lives. In one embodiment, the elastomer combined with the ePTFE is a thermoplastic copolymer of tetrafluoroethylene and perfluoromethyl vinyl ether, such as described in U.S. Patent No. 7,462,675 to Chang et al., and other references that would be known to those of skill in the art. Other biocompatible polymers which can be suitable for use in leaflet 140 include but are not limited to the groups of urethanes, silicones (organopolysiloxanes), copolymers of silicon-urethane, styrene/isobutylene copolymers, polyisobutylene, polyethylene-co-poly(vinyl acetate), polyester copolymers, nylon copolymers, fluorinated hydrocarbon polymers and copolymers or mixtures of each of the foregoing.

#### Other Considerations

**[0102]** FIGs. 10A and 10B are side exploded and assembled views, respectively, of a prosthetic valve 1000 comprising a leaflet frame 1130 having a generally tubular shape and an outer frame 1120 having a generally tubular shape that are coupled by a mechanical engagement member 1110, in accordance with another embodiment. The leaflet frame 1130 comprises an engagement member 1110 operable to engage the outer frame 1120 to affect coupling in which the leaflet frame 1130 is nested into the outer frame 1120 in a telescoping manner. The leaflet frame 1130 defines a plurality of leaflet windows 137, wherein film defines a leaflet extending from each of the leaflet windows 137.

**[0103]** In accordance with an embodiment, the valve 100 can be configured to prevent interference with a heart conduction system by not covering a bundle branch in the left ventricle when implanted, such as might be encountered with an aortic valve replacement procedure. For example, the valve 100 can comprise a length of less than about 25 mm or less than about 18 mm. The valve 100 can also comprise an aspect ratio of less than one, wherein the ratio describes the relationship between the length of the valve 100 to the expanded, functional diameter. However, the valve 100 can be constructed at any length and, more generally, any desirable dimension.

**[0104]** In a transcatheter embodiment, in a collapsed state, the valve 100 can have a collapsed profile that is less than about 35% of the expanded profile. For example, the valve 100 comprising a 26 mm expanded diameter can have a collapsed diameter of less than about 8 mm, or less than about 6 mm. The percent difference in diameter is dependent on dimensions and materials of the valve 100 and its various applications, and therefore,

the actual percent difference is not limited by this disclosure.

**[0105]** The valve 100 can further comprise a bio-active agent. Bio-active agents can be coated onto a portion or the entirety of the film 160 for controlled release of the agents once the valve 100 is implanted. The bio-active agents can include, but are not limited to, vasodilator, anti-coagulants, anti-platelet, anti-thrombogenic agents such as, but not limited to, heparin. Other bio-active agents can also include, but are not limited to agents such as, for example, antiproliferative/antimitotic agents including natural products such as vinca alkaloids (i.e. vinblastine, vincristine, and vinorelbine), paclitaxel, epididodophyllotoxins (i.e. etoposide, teniposide), antibiotics (dactinomycin (actinomycin D) daunorubicin, doxorubicin and idarubicin), anthracyclines, mitoxantrone, bleomycins, plicamycin (mithramycin) and mitomycin, enzymes (L-asparaginase which systemically metabolizes L-asparagine and deprives cells which do not have the capacity to synthesize their own asparagine); antiplatelet agents such as G(GP) IIb/IIIa inhibitors and vitronectin receptor antagonists; anti-proliferative/antimitotic alkylating agents such as nitrogen mustards (mechlorethamine, cyclophosphamide and analogs, melphalan, chlorambucil), ethylenimines and methylmelamines (hexamethylmelamine and thiotepa), alkyl sulfonates-busulfan, nitrosoureas (carmustine (BCNU) and analogs, streptozocin), trazenes-dacarbazine (DTIC); anti-proliferative/antimitotic antimetabolites such as folic acid analogs (methotrexate), pyrimidine analogs (fluorouracil, floxuridine, and cytarabine), purine analogs and related inhibitors (mercaptopurine, thioguanine, pentostatin and 2-chlorodeoxyadenosine {cladribine}); platinum coordination complexes (cisplatin, carboplatin), procarbazine, hydroxyurea, mitotane, aminoglutethimide; hormones (i.e. estrogen); anti-coagulants (heparin, synthetic heparin salts and other inhibitors of thrombin); fibrinolytic agents (such as tissue plasminogen activator, streptokinase and urokinase), aspirin, dipyridamole, ticlopidine, clopidogrel, abciximab; antimigratory; antisecretory (breveldin); anti-inflammatory: such as adrenocortical steroids (cortisol, cortisone, fludrocortisone, prednisone, prednisolone, 6 $\alpha$ -methylprednisolone, triamcinolone, betamethasone, and dexamethasone), non-steroidal agents (salicylic acid derivatives i.e. aspirin; para-aminophenol derivatives i.e. acetaminophen; indole and indene acetic acids (indomethacin, sulindac, and etodolac), heteroaryl acetic acids (tolmetin, diclofenac, and ketorolac), arylpropionic acids (ibuprofen and derivatives), anthranilic acids (mefenamic acid, and meclofenamic acid), enolic acids (piroxicam, tenoxicam, phenylbutazone, and oxyphenbutazone), nabumetone, gold compounds (auranofin, aurothioglucose, gold sodium thiomalate); immunosuppressives: (cyclosporine, tacrolimus (FK-506), sirolimus (rapamycin), azathioprine, mycophenolate mofetil); angiogenic agents: vascular endothelial growth factor (VEGF), fibroblast growth factor (FGF); angiotensin receptor blockers; nitric oxide

donors; anti-sense oligonucleotides and combinations thereof; cell cycle inhibitors, mTOR inhibitors, and growth factor receptor signal transduction kinase inhibitors; retinoids; cyclin/CDK inhibitors; HMG co-enzyme reductase inhibitors (statins); and protease inhibitors.

#### Transcatheter Delivery System

**[0106]** In an embodiment, with reference to FIG. 4A, a valve delivery system 500 comprises a valve 100 having a collapsed configuration and an expanded configuration as previously described and an elongated flexible catheter 480, such as a balloon catheter, configured to deploy the valve 100 via endovascular access. The catheter 480 can comprise a balloon to expand the valve 100 and/or if required, to touch up the valve 100 to ensure proper seating. The valve 100 can be mounted to the distal section of the catheter 480 for delivery through the vasculature. In order to hold the valve in a collapsed configuration on the catheter 480, the valve delivery system may further comprise a removable sheath (not shown) to closely fit over the transcatheter valve 100.

**[0107]** A method of delivery can comprise the steps of radially compressing a valve into its collapsed configuration onto the distal end of an elongate flexible catheter having proximal and distal ends; delivering the valve to a tissue orifice, such as a native aortic valve orifice, via a transfemoral or transapical route, and expanding the valve into the tissue orifice. The valve can be expanded by inflating a balloon.

**[0108]** A method of delivery can comprise the steps of radially compressing a valve into its collapsed configuration, onto the distal section of an elongated flexible catheter having proximal and distal ends. A restraint, which can be connected to a tether that passes through the orifice of valve and the lumen of the catheter, is fitted around the posts of the valve. The valve is then delivered to a native valve orifice, such as a native aortic valve orifice, via a route of delivery and expanded into the native orifice. The route of delivery can comprise a transfemoral or transapical route. The valve can be expanded by inflating a balloon.

#### Method of Making

**[0109]** Embodiments described herein also pertain to a method of making the valve 100 embodiments as described herein. In order to make the various embodiments, a cylindrical mandrel 710 can be used. With reference to FIG. 9A, the mandrel 710 comprises a structural form operable to receive the leaflet frame 130 and outer frame 120 thereon.

**[0110]** With reference to FIGs. 9A-9B, an embodiment of a method of making a valve 100 comprises the steps of wrapping a first layer of film 160, e.g., a composite as described herein, into a tubular form about the mandrel 710; placing the leaflet frame 130 and outer frame 120 over the first layer of film 160, as shown in FIG. 9A; form-

ing a second layer of film 160 over the leaflet frame 130 and the outer frame 120; thermally setting the assembly; cutting the film 160 across the leaflet window top within the leaflet window 137, masking with release material 170 a portion of the film 160 in the leaflet window that defines the leaflet 140 to prevent further bonding of leaflet 140 during subsequent processing steps; wrapping a second layer of film 160 into a tubular form over the leaflet frame 130, the outer frame 120, and over the first layer of film 160; thermal setting the assembly; remove the assembly from the mandrel, telescopically insert the leaflet frame into the outer frame; placing the assembly back on the mandrel; thermal setting the assembly to couple the leaflet frame 130 to the outer frame 120 in nesting engagement.

**[0111]** With reference to FIG. 12, the mandrel 710 comprises a structural form operable to receive the leaflet frame 130 thereon. An embodiment of a method of making a valve 100 comprises the steps of wrapping a first layer of film 160, e.g., a composite as described herein, into a tubular form about the mandrel 710; placing the leaflet frame 130 over the first layer of film 160, as shown in FIG. 12; forming a second layer of film 160 over the leaflet frame 130; thermally setting the assembly; receiving the assembly over a cutting mandrel 712 as shown in FIGs. 13A and 13B; cutting the film 160 across the leaflet window top within the leaflet window 137, resulting in the valve 100 of FIGs. 11A and 11B. In FIGs. 11A and 11B the leaflets 140 are shown slightly open as held by the cutting mandrel 712. It is understood that a fully closed valve 100 will have the leaflet free edges 142 of the leaflets 140 coming together to coapt under the influence of downstream fluid pressure which results in closing the valve to prevent downstream blood from flowing retrograde through the valve.

#### EXAMPLES

##### Example 1

**[0112]** A heart valve was produced having polymeric leaflets formed from a composite material having an expanded fluoropolymer membrane and an elastomeric material and joined between two collapsible metallic frames.

**[0113]** The leaflet frame and outer frame was laser machined from a length of SS316LVM tube hard tempered with an outside diameter of 23.0 mm and a wall thickness of 0.65 mm in the shape shown illustratively and generally indicated in Figure 9A. The leaflet frame 130 and outer frame 120 were electro-polished resulting in 0.0127 mm material removal from each surface and leaving the edges rounded.

**[0114]** Fluorinated ethylene propylene (FEP) powder (Daikin America, Orangeburg N.Y.) was then applied to the leaflet frame 130 and outer frame 120. More specifically, the FEP powder was stirred to form an airborne "cloud" in an enclosed blending apparatus, such as a

standard kitchen type blender, while the frames were suspended in the cloud. The frames were exposed to the FEP powder cloud until a uniform layer of powder was adhered to the entire surface of the frames. The frames were then subjected to a thermal treatment by placing it in a forced air oven set to 320°C for approximately three minutes. This caused the powder to melt and adhere as a thin coating over the entire frame. The frames were removed from the oven and left to cool to room temperature.

#### Initial Assembly and Thermal Process Cycle

**[0115]** A 21 mm diameter vented metal cylindrical mandrel having a diameter corresponding to the inner diameter of the leaflet frame 130 and outer frame 120 was helically wrapped with sintered ePTFE fiber. A thin film of type 1 (ASTM D3368) FEP was constructed using melt extrusion and stretching. The type 1 (ASTM D3368) FEP film was about 40  $\mu\text{m}$  thick and was about 7.7 cm wide. The mandrel was helically wrapped with one layer of this type 1 FEP film over the sintered ePTFE fiber only in the region of outer frame.

**[0116]** The mandrel was radially wrapped with five layers of an ePTFE membrane with an FEP coating towards the mandrel. The ePTFE membrane was manufactured according to the general teachings described in US Patent 7,306,729. The ePTFE membrane had a mass per area of 2.3 g/m<sup>2</sup>, a bubble point of 101.5MPa, a thickness of about 356 nm, a matrix tensile strength of 319 MPa in the longitudinal direction and 407 MPa in the transverse direction.

**[0117]** The mandrel was helically wrapped with one layer of type 1 FEP film.

**[0118]** The diameter of the leaflet frame and outer frame were expanded slightly and received on the wrapped mandrel with approximately a 10mm space between them, rotational alignment was not necessary.

**[0119]** The leaflet frame, outer frame and the space therebetween were helically wrapped with 1 layer of type 1 FEP film.

**[0120]** The leaflet frame, outer frame and the space therebetween that will become the bridge portion 162 and the fold region 144, as shown in FIG. 2B, were circumferentially wrapped with 5 layers of the same ePTFE membrane with an FEP coating as described above with the coating toward the mandrel.

**[0121]** The wrapped leaflet frame, outer frame and the space therebetween were wrapped with several layers of an ePTFE membrane imbibed with a polyimide material referred to as a release liner.

**[0122]** A substantially nonporous ePTFE membrane was configured into a cylinder and placed over the assembly, referred to as sacrificial tube. Sintered ePTFE fiber was used to seal both ends of the sacrificial tube against the mandrel.

**[0123]** The assembly, including the mandrel, was heated in an oven capable of applying pneumatic pressure

external to the sacrificial tube described above and while maintaining a vacuum internal to the mandrel for 40 min such that the mandrel temperature reached approximately 360°C. The assembly was removed from the oven and allowed to cool to room temperature while still pressurized and under vacuum.

**[0124]** The sacrificial tube and release liner was removed. The sintered ePTFE fiber was removed to release the frame assembly from the mandrel.

**[0125]** The polymeric material was trimmed and removed from the leaflet windows of the leaflet frame. The ends of each frame were circumferentially trimmed by a scalpel.

#### Intermediate Assembly and Thermal Process Cycle

**[0126]** An unsintered 15 mm diameter ePTFE tube was disposed on a 21.5 mm vented metal mandrel. Two layers of a substantially nonporous ePTFE membrane with a FEP coating was circumferentially wrapped on the mandrel with the coating side towards the mandrel. The wrapped mandrel was placed in a convection oven set to 320°C and heated for 20 min. The ePTFE and substantially nonporous ePTFE membrane combined to serve as a release liner and was perforated to communicate pressure between the vent holes in the mandrel.

**[0127]** The leaflet frame was disposed onto the vented metal mandrel and vent holes were made in the apertures of the leaflet frame over the mandrel vent holes.

**[0128]** A leaflet material was then prepared. A membrane of ePTFE was manufactured according to the general teachings described in US Patent 7,306,729. The ePTFE membrane had a mass per area of 0.452 g/m<sup>2</sup>, a thickness of about 508 nm, a matrix tensile strength of 705 MPa in the longitudinal direction and 385 MPa in the transverse direction. This membrane was imbibed with a fluoroelastomer. The copolymer consists essentially of between about 65 and 70 weight percent perfluoromethyl vinyl ether and complementally about 35 and 30 weight percent tetrafluoroethylene.

**[0129]** The fluoroelastomer was dissolved in Novec HFE7500 (3M, St Paul, MN) in a 2.5% concentration. The solution was coated using a Mayer bar onto the ePTFE membrane (while being supported by a polypropylene release film) and dried in a convection oven set to 145°C for 30 seconds. After 2 coating steps, the final ePTFE/fluoroelastomer or composite had a mass per area of 1.75 g/m<sup>2</sup>, 29.3% fluoropolymer by weight, a dome burst strength of about 8.6 KPa, and thickness of 0.81  $\mu\text{m}$ .

**[0130]** The following test methods were used to characterize the ePTFE layers and the multi-layered composite. The thickness was measured with a Mitutoyo Snap Gage Absolute, 12.7 mm (0.50") diameter foot, Model ID-C112E, Serial # 10299, made in Japan. The density was determined by a weight/volume calculation using an Analytical Balance Mettler PM400 New Jersey, USA. The force to break and tensile strengths were measured using

an Instron Model #5500R Norwood, MA, load cell 50 kg, gage length = 25.4 cm, crosshead speed = 25 mm/minute (strain rate = 100% per minute) with flat faced jaws. Unless otherwise noted, these test methods were used to generate the data in subsequent examples.

**[0131]** Ten layers of the composite leaflet material was wrapped around the leaflet frame with an elastomer rich side of the composite facing towards the mandrel. In exemplary embodiments, the composite material is oriented to have a predetermined matrix tensile strength along a direction generally perpendicular with the longitudinal axis of the combined tool assembly. More specifically, the predetermined matrix tensile strength is about 705 MPa.

**[0132]** The mandrel was radially wrapped with one layer of a substantially nonporous ePTFE membrane with an FEP coating towards the mandrel with a spacing 8 mm from the base of the leaflet frame. The ePTFE membrane was manufactured according to the general teachings described in US Patent 7,306,729. The ePTFE membrane had a mass per area of about 11 g/m<sup>2</sup>, a thickness of about 5.5 μm, a matrix tensile strength of 310 MPa in the longitudinal direction and 103 MPa in the transverse direction.

**[0133]** A Kapton® (El DuPont de Nemours, Inc., Wilmington, DE) polyimide film acting as a mask was wrapped over the substantially nonporous ePTFE membrane with an FEP coating layer.

**[0134]** The outer frame was placed on the mandrel with 10 mm spacing between the leaflet frame and the outer frame. The leaflet frame and the outer frame were aligned such that the longitudinal outer frame posts were collinear with the leaflet frame posts.

**[0135]** The leaflet frame and outer frame were wrapped with 24 layers of the composite leaflet material described earlier with an elastomer rich side of the composite facing towards the mandrel. In exemplary embodiments, the composite material is oriented to have a predetermined matrix tensile strength along a direction generally perpendicular with the longitudinal axis of the combined tool assembly. More specifically, the predetermined matrix tensile strength is about 705 MPa.

**[0136]** The final leaflet was comprised of 29.3 % fluoropolymer by weight with a thickness of approximately 27 μm. Each leaflet had 34 layers of the composite and a ratio of thickness/number of layers of 0.8 μm.

**[0137]** The mandrel was again radially wrapped with one layer of a substantially nonporous ePTFE membrane with an FEP coating towards the mandrel with a spacing 8 mm from the base of the leaflet frame.

**[0138]** The assembly was wrapped with several layers of the sacrificial release liner. A sacrificial tube was placed over the assembly and sintered ePTFE fiber was used to seal both ends of the sacrificial tube against the mandrel.

**[0139]** The assembly was processed in an oven capable of applying pneumatic pressure external to the sacrificial material configured into a tube described above

and while maintaining a vacuum internal to the tube for 25 min such that the mandrel temperature reached approximately 330° C. The assembly was removed from the oven and allowed to cool to room temperature while still pressurized and under vacuum.

**[0140]** The sacrificial tube and liner were removed from the frame assembly and the frame assembly was removed from the mandrel. The Kapton® mask was removed.

**[0141]** A scalpel was used to circumferentially trim the free edge of each leaflet and the distal end of leaflet frame.

#### Final Assembly and Thermal Process Cycle

**[0142]** The outer frame was radially expanded to a 24 mm diameter using a tapered mandrel.

**[0143]** A release liner as described above was placed on a 21.5mm vented mandrel.

**[0144]** Three Kapton® masks were cut to the shape of leaflet window with a 30 mm tapered extension.

**[0145]** The frames with leaflet material were placed onto the mandrel and the tapered extensions of the Kapton® masks were inserted under the top ring of the leaflet frame from the trimmed end and were advanced axially until the masks aligned with the leaflet window.

**[0146]** The leaflet frame was wrapped with 2 layers of the type 1 FEP film.

**[0147]** A hot iron was used to remove the FEP film from the leaflet window region by melting it away from the perimeter and to tack the FEP film in all regions of leaflet frame outside the masks.

**[0148]** Vent holes were made within all the frame apertures and in the polymer tube region connecting the inner and outer frame.

**[0149]** While holding the leaflet frame in place, the outer frame was coaxially disposed over the leaflet frame by telescopically inverting the bridge portion of the contiguous tube.

**[0150]** The entire frame assembly was circumferentially wrapped with one substantially nonporous ePTFE membrane with an FEP coating towards the mandrel.

**[0151]** The assembly was wrapped with several layers of the sacrificial release liner. A sacrificial tube was placed over the assembly and sintered ePTFE fiber was used to seal both ends of the sacrificial tube against the mandrel.

**[0152]** The assembly was processed in an oven capable of applying pneumatic pressure external to the sacrificial material configured into a tube described above and while maintaining a vacuum internal to the tube for 25 min such that the mandrel temperature reached approximately 330° C. The assembly was removed from the oven and allowed to cool to room temperature while still pressurized and under vacuum.

**[0153]** The frame assembly was removed from the mandrel.

**[0154]** A scalpel was used to circumferentially trim

each end of leaflet frame.

**[0155]** The Kapton was rotationally peeled away from inside the outer frame and away from leaflets.

**[0156]** Using scissors, both ends of the leaflet frame were trimmed to follow frame contour.

**[0157]** The resulting valve 100 includes leaflets 140 formed from a composite material with more than one fluoropolymer layer having a plurality of pores and an elastomer present in substantially all of the pores of the more than one fluoropolymer layer. Each leaflet 140 is movable between a closed position, shown in FIGs. 3B, in which blood is substantially prevented from flowing through the valve assembly, and an open position, shown in FIG. 3A, in which blood is allowed to flow through the valve assembly. Thus, the leaflets 140 of the valve 100 cycle between the closed and open positions generally to regulate blood flow direction in a human patient.

**[0158]** The performance of the valve leaflets was characterized on a real-time pulse duplicator that measured typical anatomical pressures and flows across the valve. The flow performance was characterized by the following process:

**[0159]** The valve assembly was potted into a silicone annular ring (support structure) to allow the valve assembly to be subsequently evaluated in a real-time pulse duplicator. The potting process was performed according to the recommendations of the pulse duplicator manufacturer (ViVitro Laboratories Inc., Victoria BC, Canada)

**[0160]** The potted valve assembly was then placed into a real-time left heart flow pulse duplicator system. The flow pulse duplicator system included the following components supplied by VSI Vivitro Systems Inc., Victoria BC, Canada: a Super Pump, Servo Power Amplifier Part Number SPA 3891; a Super Pump Head, Part Number SPH 5891 B, 38.320 cm<sup>2</sup> cylinder area; a valve station/fixture; a Wave Form Generator, TriPack Part Number TP 2001; a Sensor Interface, Part Number VB 2004; a Sensor Amplifier Component, Part Number AM 9991; and a Square Wave Electro Magnetic Flow Meter, Carolina Medical Electronics Inc., East Bend, NC, USA.

**[0161]** In general, the flow pulse duplicator system uses a fixed displacement, piston pump to produce a desired fluid flow through the valve under test.

**[0162]** The heart flow pulse duplicator system was adjusted to produce the desired flow (5L/min), mean pressure (15mmHg), and simulated pulse rate (70 bpm). The valve under test was then cycled for about 5 to 20 minutes.

**[0163]** Pressure and flow data were measured and collected during the test period, including right ventricular pressures, pulmonary pressures, flow rates, and pump piston position.

**[0164]** Parameters used to characterize the valve are effective orifice area and regurgitant fraction. The effective orifice area (EOA), which can be calculated as follows:  $EOA(cm^2) = Q_{rms} / (51.6 * (\Delta P)^{1/2})$  where  $Q_{rms}$  is the root mean square systolic/diastolic flow rate (cm<sup>3</sup>/s) and  $\Delta P$  is the mean systolic/diastolic pressure drop (mm-

Hg).

**[0165]** Another measure of the hydrodynamic performance of a valve is the regurgitant fraction, which is the amount of fluid or blood regurgitated through the valve divided by the stroke volume.

**[0166]** The hydrodynamic performance measured values were; EOA = 2.06 cm<sup>2</sup>, and regurgitant fraction = 8.2 %.

## 10 Example 2

**[0167]** Another valve was made as described in Example 1 with the following exceptions.

## 15 Initial Assembly and Thermal Process Cycle

**[0168]** The diameter of the leaflet frame and outer frame were expanded slightly and received on the wrapped mandrel with 16mm space between them, rotational alignment if the leaflet frame and outer frame was made.

## Final Assembly and Thermal Process Cycle

**[0169]** A scalpel was used to cut above the mechanical linking tab. The tab was deformed to link inner and outer frames.

**[0170]** The resulting valve 100 includes leaflets 140 formed from a composite material with more than one fluoropolymer layer having a plurality of pores and an elastomer present in substantially all of the pores of the more than one fluoropolymer layer. Each leaflet 140 is movable between a closed position, shown in FIG. 3B, in which blood is substantially prevented from flowing through the valve assembly, and an open position, shown in FIG. 3A, in which blood is allowed to flow through the valve assembly. Thus, the leaflets 140 of the valve 100 cycle between the closed and open positions generally to regulate blood flow direction in a human patient.

**[0171]** The hydrodynamic performance was measured. The performance values were; EOA = 2.3 cm<sup>2</sup> and regurgitant fraction = 11.8 %.

**[0172]** The invention may also be understood with reference to the following numbered clauses 1 to 59:

## 45 Clause 1. A prosthetic valve comprising:

a leaflet frame having a generally tubular shape, the leaflet frame defining a plurality of leaflet windows;

an outer frame having a generally tubular shape; and a film, the leaflet frame being coaxially disposed at least partially within the outer frame, the leaflet frame and outer frame are coupled at least in part by a contiguous portion of the film, at least a portion of the contiguous portion of the film being contained between and coupling the leaflet frame and outer frame to inhibit relative



movement between the leaflet frame and outer frame, wherein the film defines a leaflet extending from each of the leaflet windows.

Clause 2. The prosthetic valve of Clause 1, wherein the film that defines the leaflet extends between the leaflet frame and the outer frame.

Clause 3. The prosthetic valve of Clause 1, wherein the leaflet includes a leaflet base comprising a fold in the film at an interface between portions of the film that are coupled with the leaflet frame and portions of the film that are not coupled with the leaflet frame.

Clause 4. The prosthetic valve of Clause 1, the leaflet frame including a leaflet frame inner surface and a leaflet frame outer surface opposite the leaflet frame inner surface, wherein the film defines at least one leaflet that is coupled to the leaflet frame outer surface, wherein the film defines a leaflet extending from each of the leaflet windows.

Clause 5. The prosthetic valve of Clause 1, the leaflet frame including a leaflet frame inner surface and a leaflet frame outer surface opposite the leaflet frame inner surface, the outer frame including an outer frame inner surface and an outer frame outer surface opposite the outer frame inner surface, wherein the film defines at least one leaflet that is coupled to the leaflet frame inner surface, wherein the film defines a leaflet extending from each of the leaflet windows.

6. The prosthetic valve of Clause 1, the leaflet frame including a leaflet frame inner surface and a leaflet frame outer surface opposite the leaflet frame inner surface, the outer frame including an outer frame inner surface and an outer frame outer surface opposite the outer frame inner surface, wherein the film defines at least one leaflet that is coupled to the leaflet frame inner surface and leaflet frame outer surface, wherein the film defines a leaflet extending from each of the leaflet windows.

7. The prosthetic valve of Clause 1, wherein the leaflet frame defines three interconnected leaflet windows having a substantially triangular shape.

8. The prosthetic valve of Clause 1, wherein each of the leaflet windows includes two leaflet window sides, a leaflet window base, and a leaflet window top, wherein the leaflet is coupled to the two leaflet window sides and the leaflet window base.

Clause 9. The prosthetic valve of Clause 1, wherein a leaflet window side of one leaflet window is interconnected with a leaflet window side of an adjacent leaflet window.

Clause 10. The prosthetic valve of Clause 1, wherein the leaflet window is defined at least in part by frame elements corresponding to leaflet sides, wherein the film is coupled to the window frame elements and extends across the leaflet window defining the leaflet.

Clause 11. The prosthetic valve of Clause 1, wherein the leaflet frame comprises a plurality of leaflet frame

elements defining a plurality of isosceles triangles interconnected by a leaflet window base, wherein each leaflet window side is defined by a side of one triangle and a side of an adjacent triangle, each leaflet window defining an isosceles trapezoid.

Clause 12. The prosthetic valve of Clause 1, wherein the prosthetic valve comprises a collapsed configuration and an expanded configuration for transcatheter delivery.

Clause 13. The prosthetic valve of Clause 1, wherein the leaflet is moveable between an open and closed position.

Clause 14. The prosthetic valve of Clause 1, wherein the leaflet comprises a polymeric material.

Clause 15. The prosthetic valve of Clause 1, wherein the leaflet comprises a laminate.

Clause 16. The prosthetic valve of Clause 15, wherein the laminate has more than one layer of a fluoropolymer membrane.

Clause 17. The prosthetic valve of Clause 1, wherein the leaflet comprises a film having at least one fluoropolymer membrane layer having a plurality of pores and an elastomer present in substantially all of the pores of at least one layer of fluoropolymer membrane.

Clause 18. The prosthetic valve of Clause 17, wherein the film comprises less than about 80% fluoropolymer membrane by weight.

Clause 19. The prosthetic valve of Clause 17, wherein the elastomer comprises (per)fluoroalkylvinylethers (PAVE).

Clause 20. The prosthetic valve of Clause 17, wherein the elastomer comprises a copolymer of tetrafluoroethylene and perfluoromethyl vinyl ether.

Clause 21. The prosthetic valve of Clause 17, wherein the fluoropolymer membrane comprises ePTFE.

Clause 22. The prosthetic valve of Clause 1, wherein either or both of the leaflet frame and outer frame defines a generally open pattern of apertures operable to allow the outer frame to be compressed and expanded between different diameters.

Clause 23. The prosthetic valve of Clause 1, wherein either or both of the leaflet frame and outer frame comprise a shape memory material.

Clause 24. The prosthetic valve of Clause 1, wherein the outer frame includes frame elements that overlay the leaflet windows that are defined by the leaflet frame in cooperative arrangement so as to provide structural support over the leaflet windows.

Clause 25. The prosthetic valve of Clause 1, the leaflet frame including a leaflet frame inner surface and a leaflet frame outer surface opposite the leaflet frame inner surface, the outer frame including an outer frame inner surface and an outer frame outer surface opposite the outer frame inner surface, wherein the film defines at least one leaflet that is coupled to the leaflet frame outer surface, the at least a portion of the contiguous portion of the film is coupled to a

portion of the leaflet frame outer surface and a portion of the outer frame inner surface between and coupling the leaflet frame to the outer frame.

Clause 26. The prosthetic valve of Clause 1, wherein the at least a portion of the contiguous portion of the film that is contained between and coupling the leaflet frame and outer frame prevents contact between the leaflet frame and outer frame.

Clause 27. The prosthetic valve of Clause 1, wherein the leaflet frame and outer frame are separated by the film and are not in contact with each other.

Clause 28. The prosthetic valve of Clause 1, wherein the leaflets are defined by a fold line and overlap of the film that defines, at least in part, a leaflet base of the leaflet.

Clause 29. The prosthetic valve of Clause 1, wherein each of the leaflet windows includes two leaflet window sides and a leaflet window base, wherein the leaflet is coupled to at least a portion of the two leaflet window sides.

Clause 30. A prosthetic valve comprising:

a leaflet frame having a generally tubular shape, the leaflet frame defining a plurality of leaflet windows;

an outer frame having a generally tubular shape; and

a film, the leaflet frame being coaxially disposed at least partially within the outer frame, wherein the outer frame includes frame elements that overlay the leaflet windows that are defined by the leaflet frame in cooperative arrangement so as to provide structural support over the leaflet windows, wherein the film defines a leaflet extending from each of the leaflet windows.

Clause 31. The prosthetic valve of Clause 30, wherein the film is disposed between the leaflet frame and the outer frame.

Clause 32. The prosthetic valve of Clause 30, wherein the leaflet frame and outer frame are separated by the film and are not in contact with each other.

Clause 33. The prosthetic valve of Clause 30, wherein the film that defines the leaflet extends between the leaflet frame and the outer frame.

Clause 34. The prosthetic valve of Clause 30, wherein the leaflet includes a leaflet base comprising a fold in the film at an interface between portions of the film that are coupled with the leaflet frame and portions of the film that are not coupled with the leaflet frame.

Clause 35. The prosthetic valve of Clause 30, the leaflet frame including a leaflet frame inner surface and a leaflet frame outer surface opposite the leaflet frame inner surface, wherein the film defines at least one leaflet that is coupled to the leaflet frame outer surface, wherein the film defines a leaflet extending from each of the leaflet windows.

Clause 36. The prosthetic valve of Clause 30, the

leaflet frame including a leaflet frame inner surface and a leaflet frame outer surface opposite the leaflet frame inner surface, the outer frame including an outer frame inner surface and an outer frame outer surface opposite the outer frame inner surface, wherein the film defines at least one leaflet that is coupled to the leaflet frame inner surface, wherein the film defines a leaflet extending from each of the leaflet windows.

Clause 37. The prosthetic valve of Clause 30, the leaflet frame including a leaflet frame inner surface and a leaflet frame outer surface opposite the leaflet frame inner surface, the outer frame including an outer frame inner surface and an outer frame outer surface opposite the outer frame inner surface, wherein the film defines at least one leaflet that is coupled to the leaflet frame inner surface and leaflet frame outer surface, wherein the film defines a leaflet extending from each of the leaflet windows.

Clause 38. The prosthetic valve of Clause 30, wherein the leaflet frame defines three interconnected leaflet windows having a substantially triangular shape.

Clause 39. The prosthetic valve of Clause 30, wherein each of the leaflet windows includes two leaflet window sides, a leaflet window base, and a leaflet window top, wherein the leaflet is coupled to the two leaflet window sides and the leaflet window base.

Clause 40. The prosthetic valve of Clause 30, wherein a leaflet window side of one leaflet window is interconnected with a leaflet window side of an adjacent leaflet window.

Clause 41. The prosthetic valve of Clause 30, wherein the leaflet window is defined at least in part by frame elements corresponding to leaflet sides, wherein the film is coupled to the window frame elements and extends across the leaflet window defining the leaflet.

Clause 42. The prosthetic valve of Clause 30, wherein the leaflet frame comprises a plurality of leaflet frame elements defining a plurality of isosceles triangles interconnected by a leaflet window base, wherein each leaflet window side is defined by a side of one triangle and a side of an adjacent triangle, each leaflet window defining an isosceles trapezoid.

Clause 43. The prosthetic valve of Clause 30, the leaflet frame including a leaflet frame inner surface and a leaflet frame outer surface opposite the leaflet frame inner surface, the outer frame including an outer frame inner surface and an outer frame outer surface opposite the outer frame inner surface, wherein the film defines at least one leaflet that is coupled to the leaflet frame outer surface, the at least a portion of a contiguous portion of the film is coupled to a portion of the leaflet frame outer surface and a portion of the outer frame inner surface between and coupling the leaflet frame to the outer frame.

Clause 44. The prosthetic valve of Clause 43, wherein the leaflets are defined by a fold line of the film

that defines, at least in part, a leaflet base of the leaflet.

Clause 45. The prosthetic valve of Clause 30, wherein the prosthetic valve comprises a collapsed configuration and an expanded configuration for transcatheter delivery.

Clause 46. The prosthetic valve of Clause 30, wherein the leaflet is moveable between an open and closed position.

Clause 47. The prosthetic valve of Clause 30, wherein the leaflet comprises a polymeric material.

Clause 48. The prosthetic valve of Clause 30, wherein the leaflet comprises a laminate.

Clause 49. The prosthetic valve of Clause 48, wherein the laminate has more than one layer of a fluoropolymer membrane.

Clause 50. The prosthetic valve of Clause 30, wherein the leaflet comprises a film having at least one fluoropolymer membrane layer having a plurality of pores and an elastomer present in substantially all of the pores of at least one layer of fluoropolymer membrane.

Clause 51. The prosthetic valve of Clause 50, wherein the film comprises less than about 80% fluoropolymer membrane by weight.

Clause 52. The prosthetic valve of Clause 50, wherein the elastomer comprises (per)fluoroalkylvinylethers (PAVE).

Clause 53. The prosthetic valve of Clause 50, wherein the elastomer comprises a copolymer of tetrafluoroethylene and perfluoromethyl vinyl ether.

Clause 54. The prosthetic valve of claim 50, wherein the fluoropolymer membrane comprises ePTFE.

Clause 55. The prosthetic valve of Clause 30, wherein either or both of the leaflet frame and outer frame defines a generally open pattern of apertures that allow the outer frame to be compressed and expanded between different diameters.

Clause 56. The prosthetic valve of Clause 30, wherein either or both of the leaflet frame and outer frame comprise a shape memory material.

Clause 57. The prosthetic valve of Clause 30, wherein the leaflets are defined by a fold line and overlap of the film that defines, at least in part, a leaflet base of the leaflet.

Clause 58. The prosthetic valve of Clause 30, wherein each of the leaflet windows includes two leaflet window sides and a leaflet window base, wherein the leaflet is coupled to at least a portion of the two leaflet window sides.

Clause 59. A method of making a valve, comprising:

wrapping a first layer of film into a tubular form about a mandrel;

providing a leaflet frame having a generally tubular shape, the leaflet frame having a leaflet frame inner surface and a leaflet frame outer surface, the leaflet frame defining a plurality of

leaflet windows having a window top; providing an outer frame having a generally tubular shape, the outer frame having an outer frame inner surface and an outer frame outer surface; placing the leaflet frame and the outer frame over the first layer of film with the leaflet frame and outer frame spaced apart from each other defining a bridge portion therebetween, the leaflet frame inner surface and the outer frame inner surface in contact with the first layer of film; forming a second layer of film over the leaflet frame and the outer frame in contact with the leaflet frame outer surface and the outer frame outer surface; coupling the first layer of film and the second layer of film to each other and to the leaflet frame and the outer frame; cutting the first layer of film and the second layer of film across the window top within the leaflet window so as to define a leaflet free edge; masking with release material a portion of the film disposed in the leaflet window that defines the leaflet to prevent further bonding of the leaflet during subsequent processing steps; wrapping a third layer of film into a tubular form over the second layer of film and over the release material that is over the leaflet window, overlapping the leaflet frame, the outer frame, and over the bridge portion between the leaflet frame and outer frame; coupling the third layer of film and the second layer of film to each other forming an assembly; removing the assembly from the mandrel; disposing coaxially and at least partially the leaflet frame into the outer frame, folding and overlapping the bridge portion defining a circumferential fold in the bridge portion and containing at least a portion of the bridge portion between the leaflet frame and the outer frame, a portion of the fold defining a leaflet base; placing the assembly back on the mandrel; and coupling the bridge portion to itself and to the third layer of film adjacent the leaflet frame outer surface and the first layer adjacent the outer frame inner surface in nesting engagement.

**[0173]** Numerous characteristics and advantages have been set forth in the preceding description, including various alternatives together with details of the structure and function of the devices and/or methods. The disclosure is intended as illustrative only and as such is not intended to be exhaustive. It will be evident to those skilled in the art that various modifications can be made, especially in matters of structure, materials, elements, components, shape, size and arrangement of parts including combinations within the principles of the disclosure, to the full extent indicated by the broad, general meaning of the terms in which the appended claims are expressed. To the extent that these various modifications

do not depart from the scope of the appended claims, they are intended to be encompassed therein.

## Claims

### 1. A prosthetic valve (100) comprising:

a leaflet frame (130) having a generally tubular shape, the leaflet frame defining a plurality of leaflet windows (137);  
 an outer frame (120) having a generally tubular shape; and  
 a film (160), the leaflet frame being coaxially disposed at least partially within the outer frame, wherein the outer frame includes frame elements that overlay the leaflet windows that are defined by the leaflet frame in cooperative arrangement so as to provide structural support over the leaflet windows, wherein the film defines a leaflet (140) extending from each of the leaflet windows.

2. The prosthetic valve (100) of claim 1, wherein the film (160) is disposed between the leaflet frame (130) and the outer frame (120); or  
 wherein the leaflet frame (130) and outer frame (120) are separated by the film (160) and are not in contact with each other; or  
 wherein the film (160) that defines the leaflet (140) extends between the leaflet frame (130) and the outer frame (120).

3. The prosthetic valve (100) of claim 1, wherein the leaflet (140) includes a leaflet base (143) comprising a fold (145) in the film (160) at an interface between portions of the film that are coupled with the leaflet frame (130) and portions of the film that are not coupled with the leaflet frame.

4. The prosthetic valve (100) of claim 1, the leaflet frame (130) including a leaflet frame inner surface and a leaflet frame outer surface (132) opposite the leaflet frame inner surface, wherein the film (160) defines at least one leaflet (140) that is coupled to the leaflet frame outer surface, wherein the film defines a leaflet extending from each of the leaflet windows (137).

5. The prosthetic valve (100) of claim 1, the leaflet frame (130) including a leaflet frame inner surface (132b) and a leaflet frame outer surface (132a) opposite the leaflet frame inner surface, the outer frame (120) including an outer frame inner surface (126b) and an outer frame outer surface (126a) opposite the outer frame inner surface, wherein the film (160) defines at least one leaflet (140) that is coupled to the leaflet frame inner surface, wherein the film de-

finer a leaflet extending from each of the leaflet windows; optionally wherein the at least one leaflet (140) is coupled to an inner surface (126b) of the outer frame; or

wherein the leaflet frame (130) defines three interconnected leaflet windows (137) having a substantially triangular shape.

6. The prosthetic valve (100) of claim 1, wherein each of the leaflet windows (137) includes two leaflet window sides (133), a leaflet window base (134), and a leaflet window top (135), wherein the leaflet (140) is coupled to the two leaflet window sides and the leaflet window base; or  
 wherein a leaflet window side (133) of one leaflet window (137) is interconnected with a leaflet window side of an adjacent leaflet window.

7. The prosthetic valve (100) of claim 1, wherein the leaflet window (137) is defined at least in part by frame elements (139) corresponding to leaflet sides (141), wherein the film (160) is coupled to the window frame elements and extends across the leaflet window (137) defining the leaflet (140); or  
 wherein the leaflet frame (130) comprises a plurality of leaflet frame elements defining a plurality of isosceles triangles interconnected by a leaflet window base (134), wherein each leaflet window side (133) is defined by a side of one triangle and a side of an adjacent triangle, each leaflet window defining an isosceles trapezoid.

8. The prosthetic valve (100) of claim 1, the leaflet frame (130) including a leaflet frame inner surface (132b) and a leaflet frame outer surface (132a) opposite the leaflet frame inner surface, the outer frame (120) including an outer frame inner (126b) surface and an outer frame outer surface (126a) opposite the outer frame inner surface, wherein the film (160) defines at least one leaflet (140) that is coupled to the leaflet frame outer surface, the at least a portion of a contiguous portion of the film is coupled to a portion of the leaflet frame outer surface and a portion of the outer frame inner surface between and coupling the leaflet frame to the outer frame; optionally wherein the leaflets (140) are defined by a fold line (145) of the film (160) that defines, at least in part, a leaflet base (143) of the leaflet.

9. The prosthetic valve (100) of claim 1, wherein the prosthetic valve comprises a collapsed configuration and an expanded configuration for transcatheter delivery; or wherein the leaflet (140) is moveable between an open and closed position.

10. The prosthetic valve (100) of claim 1, wherein the leaflet (140) comprises a polymeric material; or wherein the leaflet (140) comprises a laminate, op-

tionally the laminate having more than one layer of a fluoropolymer membrane;  
 or wherein the leaflet (140) comprises a film (160) having at least one fluoropolymer membrane layer having a plurality of pores and an elastomer present in substantially all of the pores of at least one layer of fluoropolymer membrane. 5

11. The prosthetic valve (100) of claim 10, wherein the film (160) comprises less than about 80% fluoropolymer membrane by weight; or wherein the fluoropolymer membrane comprises ePTFE. 10
12. The prosthetic valve (100) of claim 10, wherein the elastomer comprises (per)fluoroalkylvinylethers (PAVE) or a copolymer of tetrafluoroethylene and perfluoromethyl vinyl ether. 15
13. The prosthetic valve (100) of claim 1, wherein either or both of the leaflet frame (130) and outer frame (120) defines a generally open pattern of apertures (122) that allow the outer frame to be compressed and expanded between different diameters. 20
14. The prosthetic valve (100) of claim 13, wherein frame members defining the apertures (122) of the leaflet frame (130) and the outer frame (120) are aligned to provide overlapping and complimentary arrangement so as to provide structural rigidity to the assembly. 25  
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15. The prosthetic valve (100) of claim 1, wherein either or both of the leaflet frame (130) and outer frame (120) comprise a shape memory material or wherein the leaflets (140) are defined by a fold line (145) and overlap of the film that defines, at least in part, a leaflet base (143) of the leaflet; or wherein each of the leaflet windows (137) includes two leaflet window sides (137) and a leaflet window base (134), wherein the leaflet (140) is coupled to at least a portion of the two leaflet window sides. 35  
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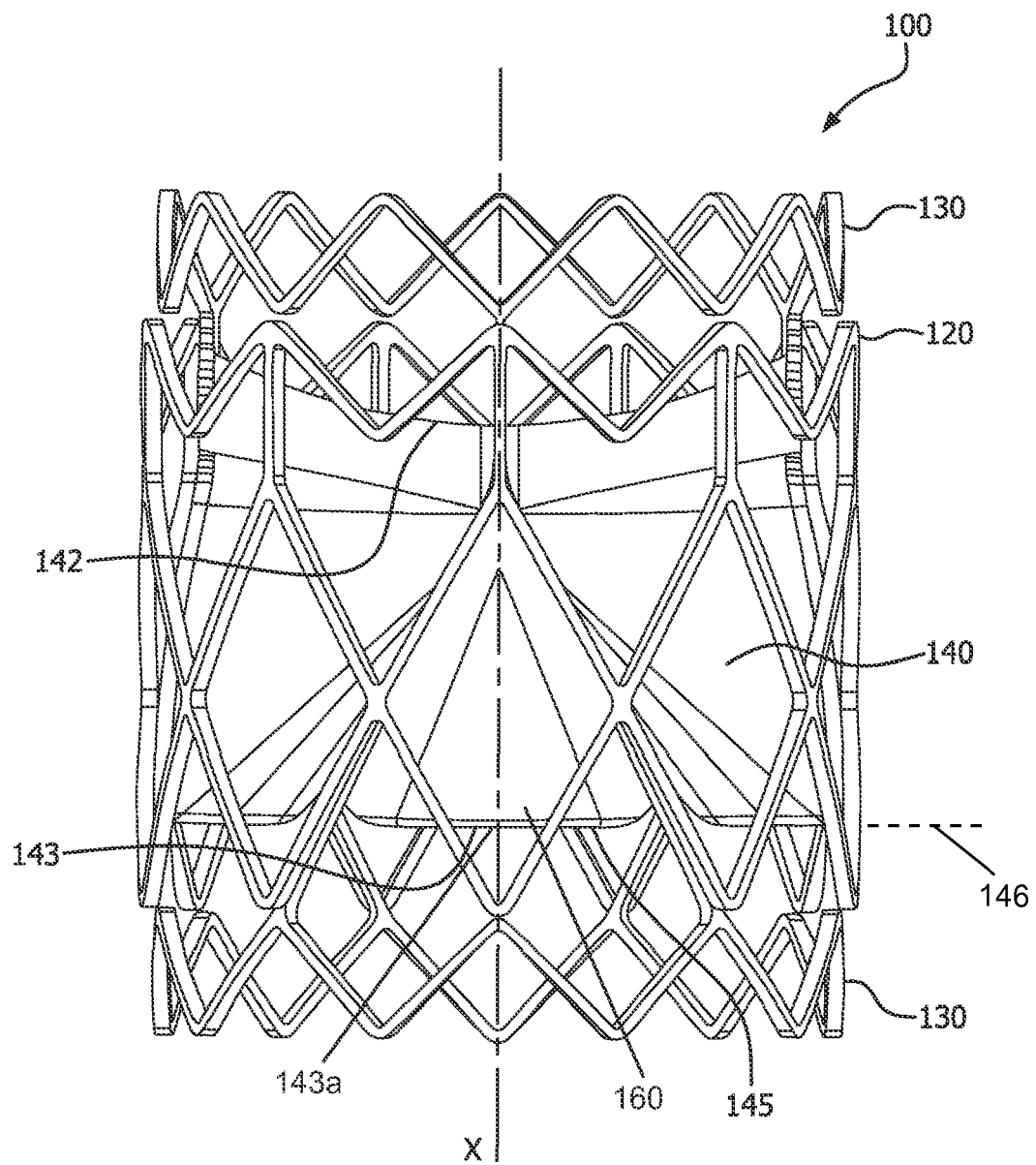


FIG. 1A

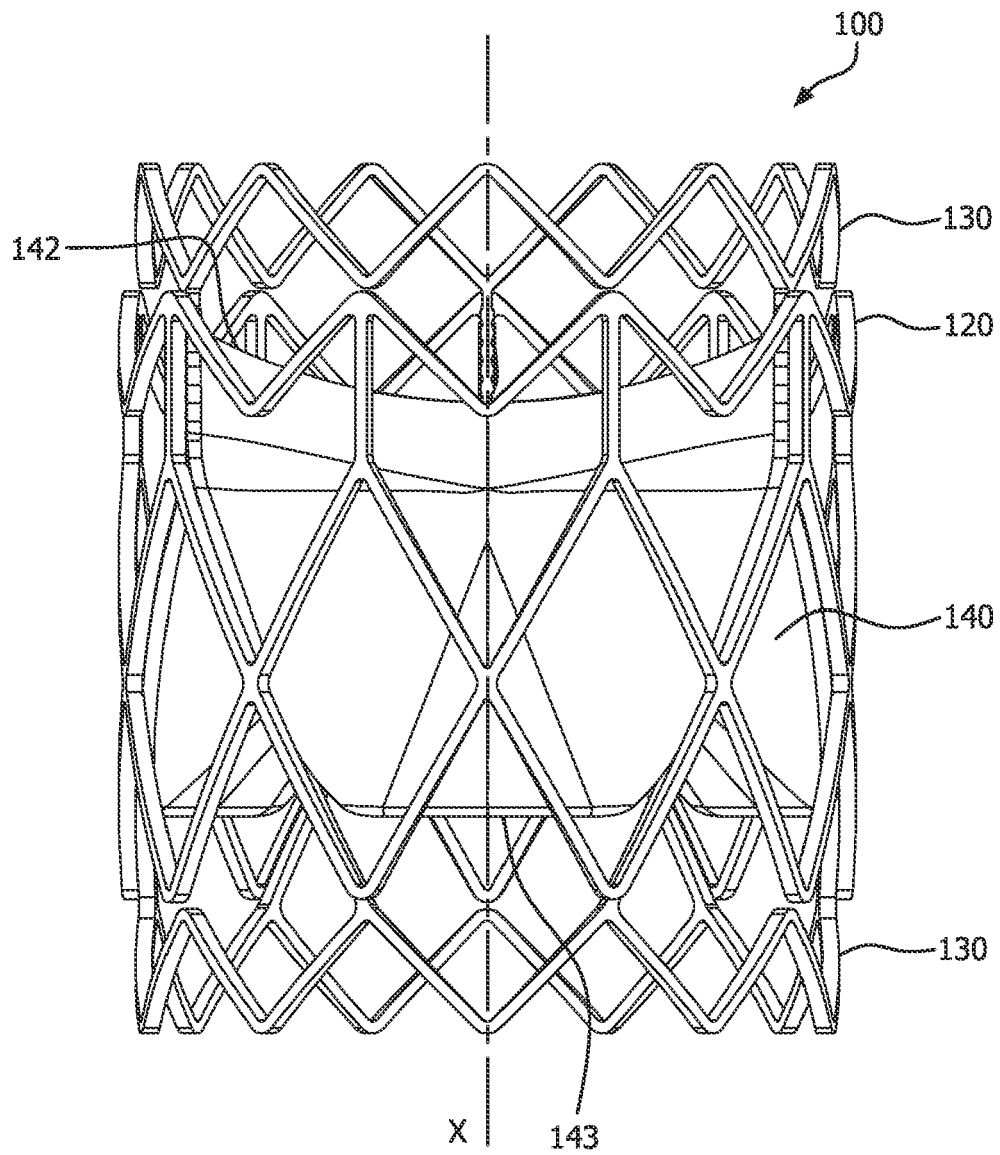


FIG. 1B

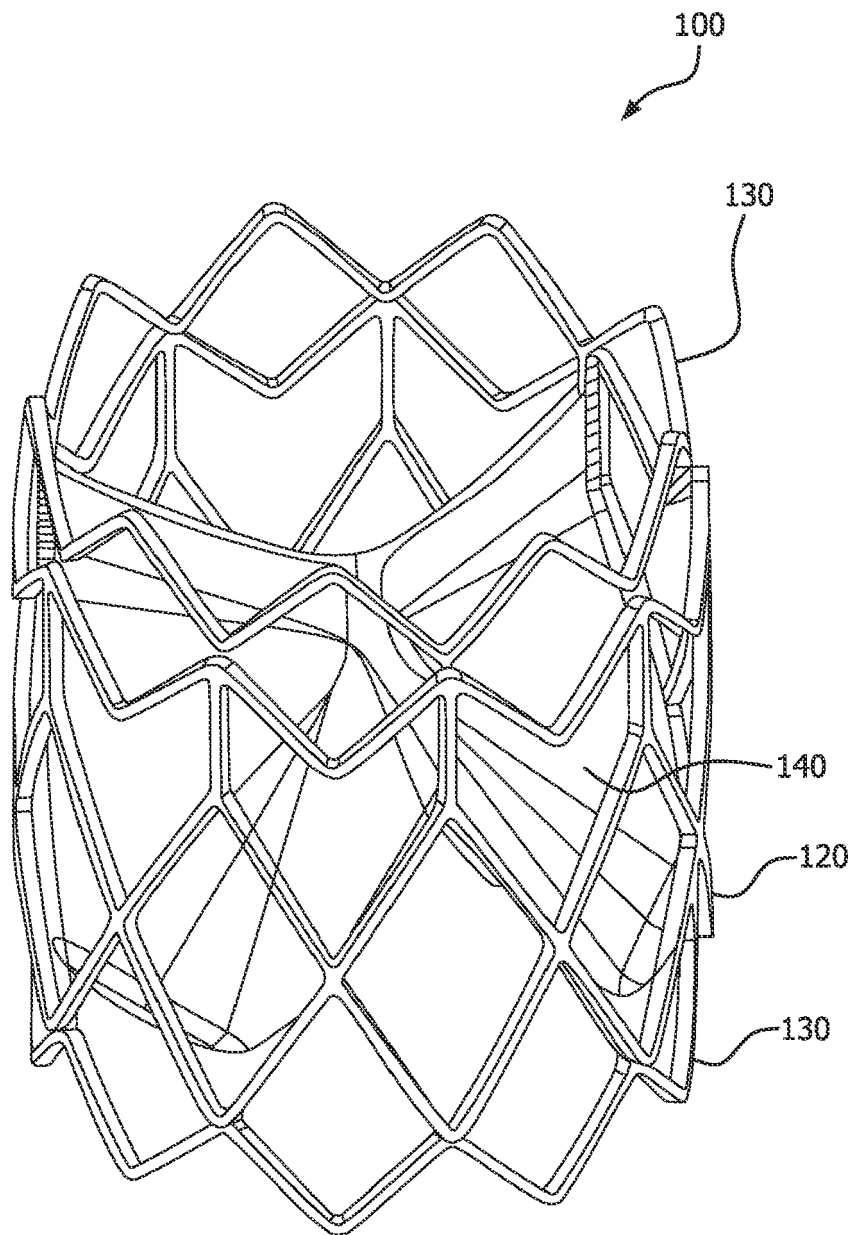


FIG. 1C



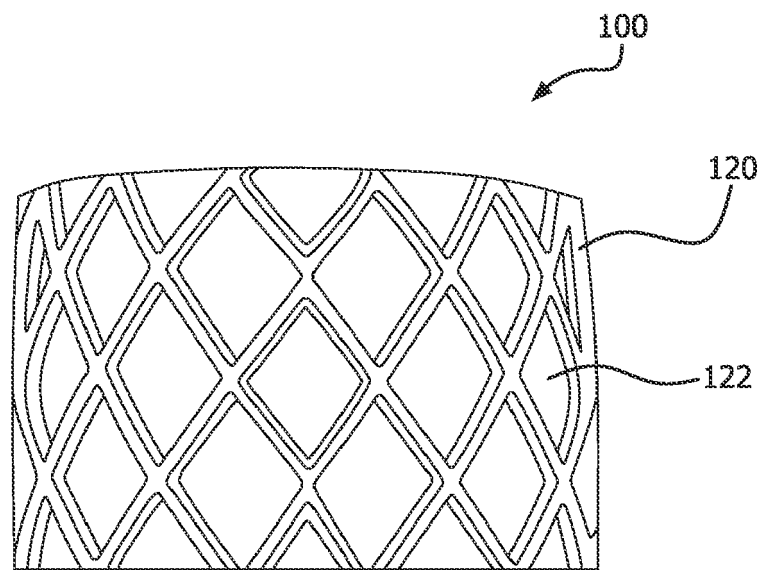


FIG. 1D

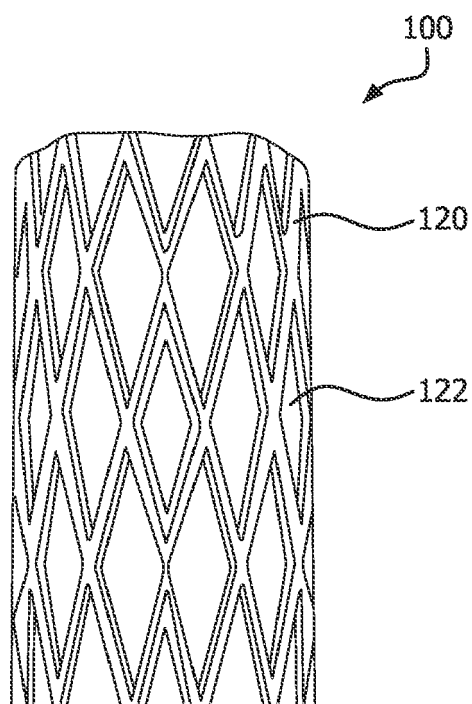


FIG. 1E

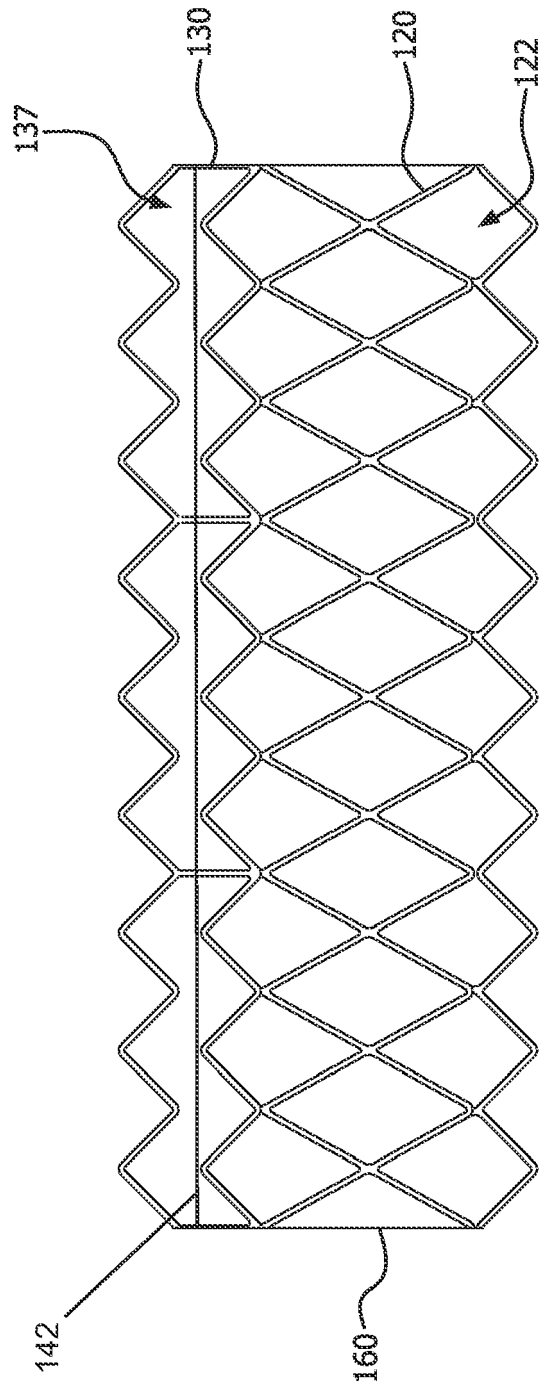


FIG. 2A

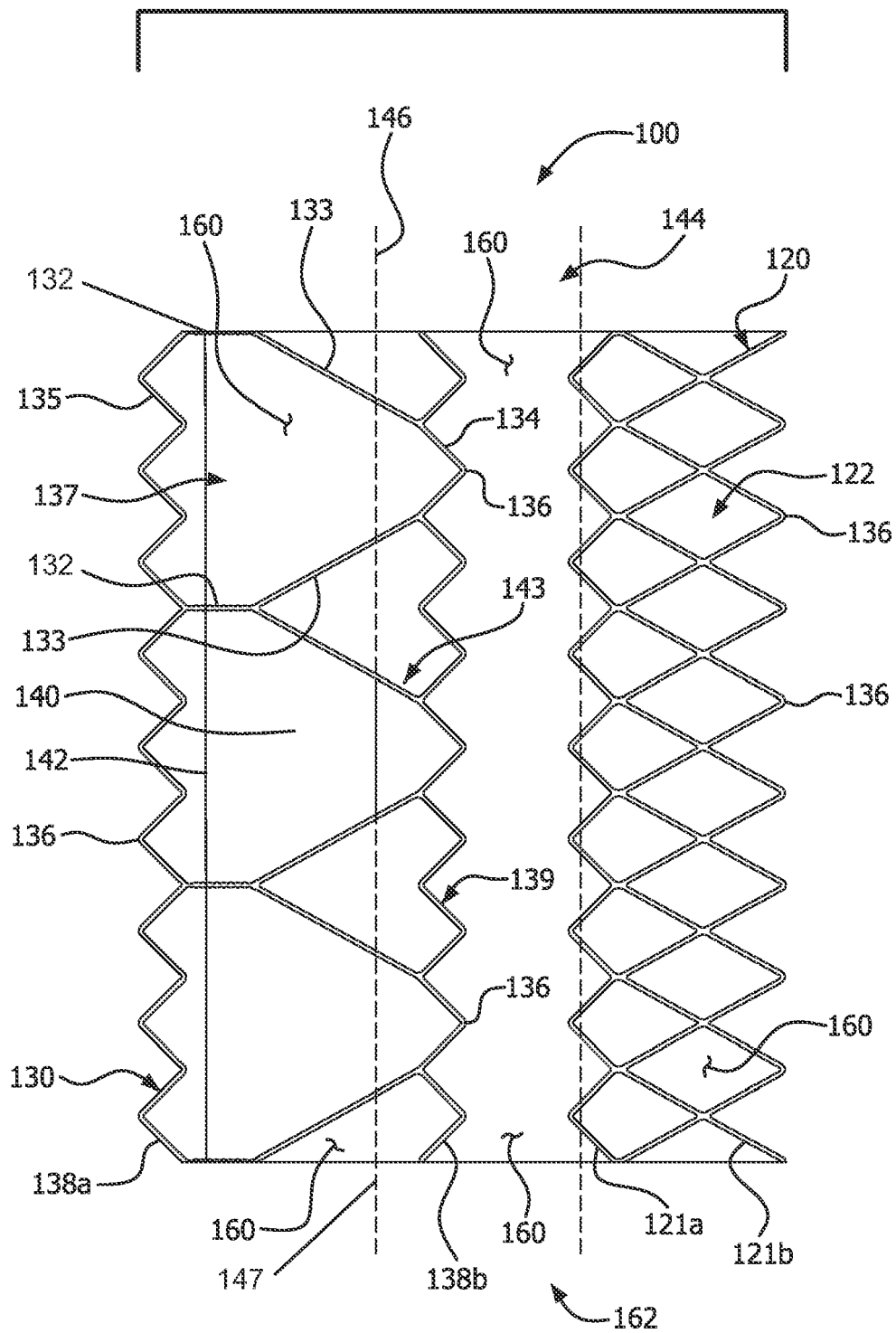


FIG. 2B

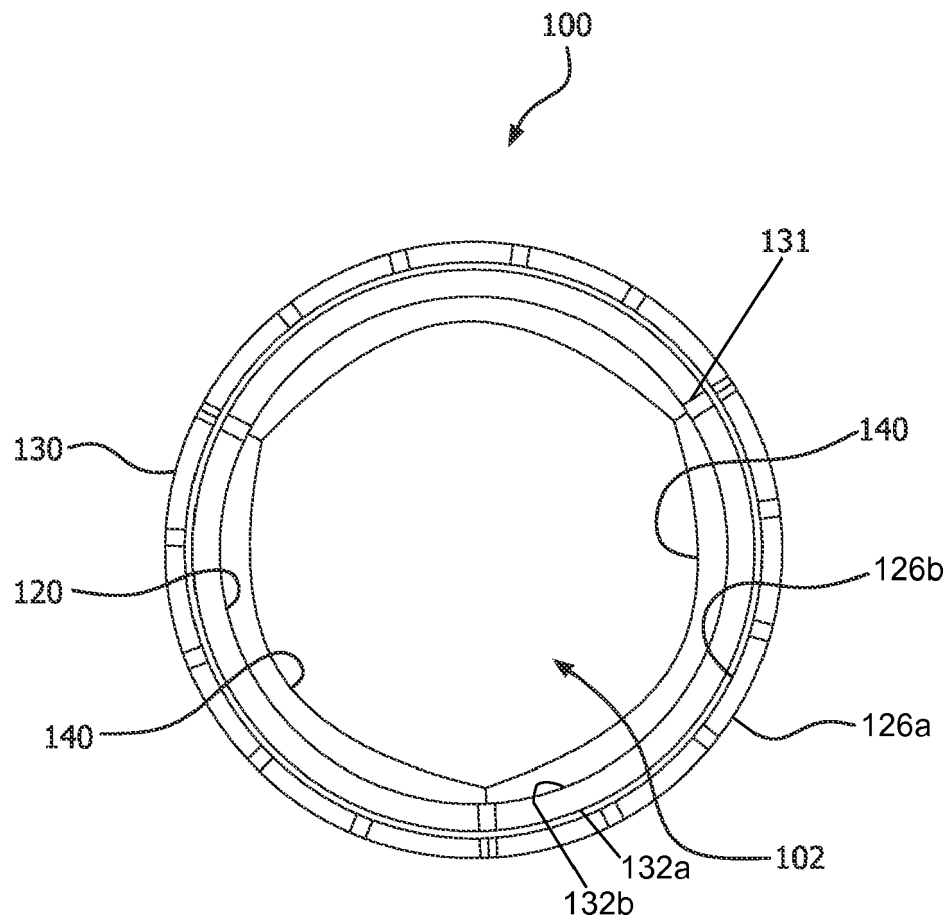


FIG. 3A

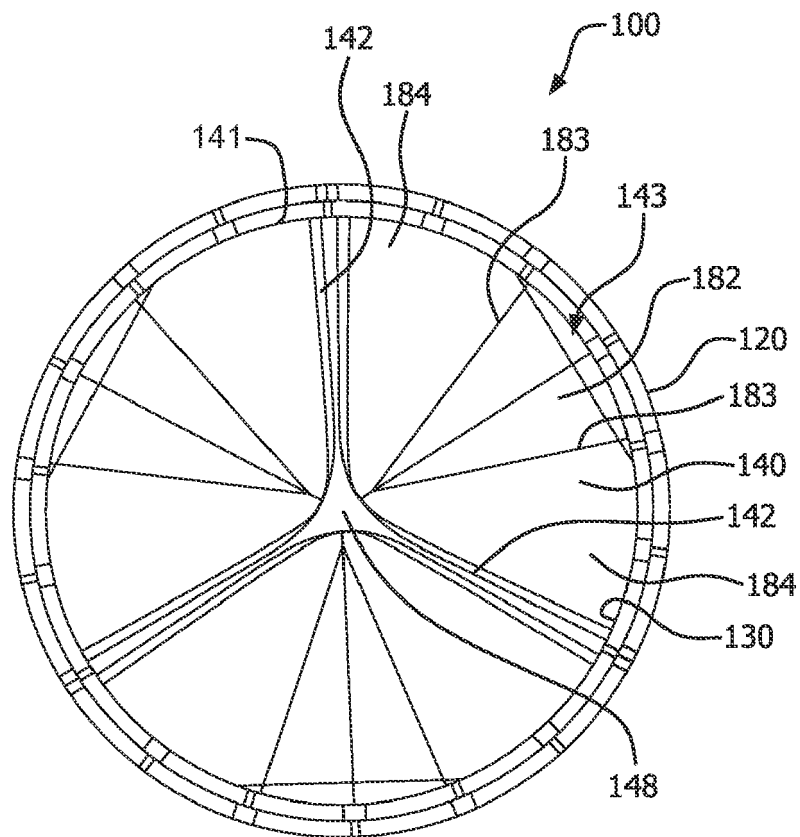


FIG. 3B

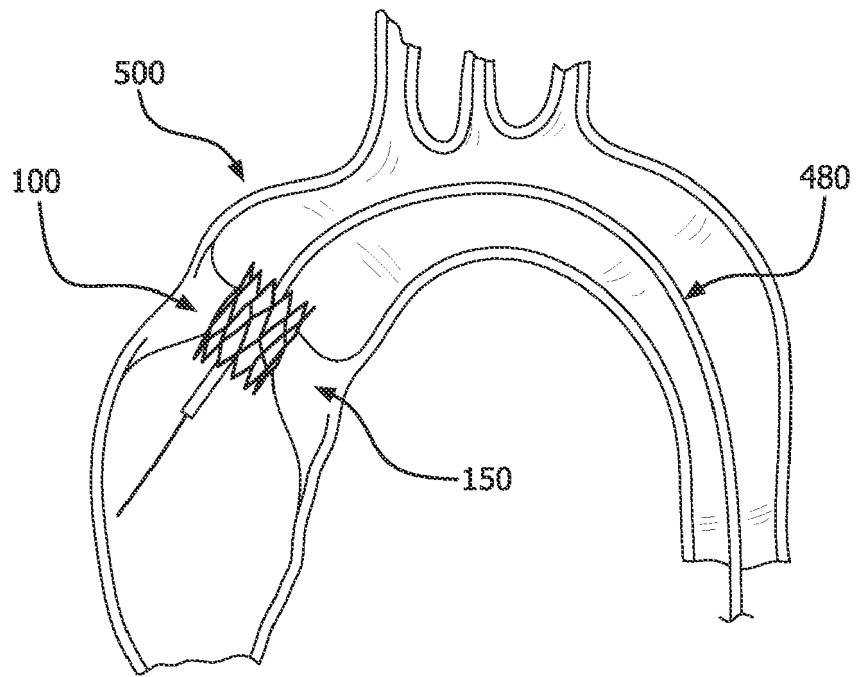


FIG. 4A

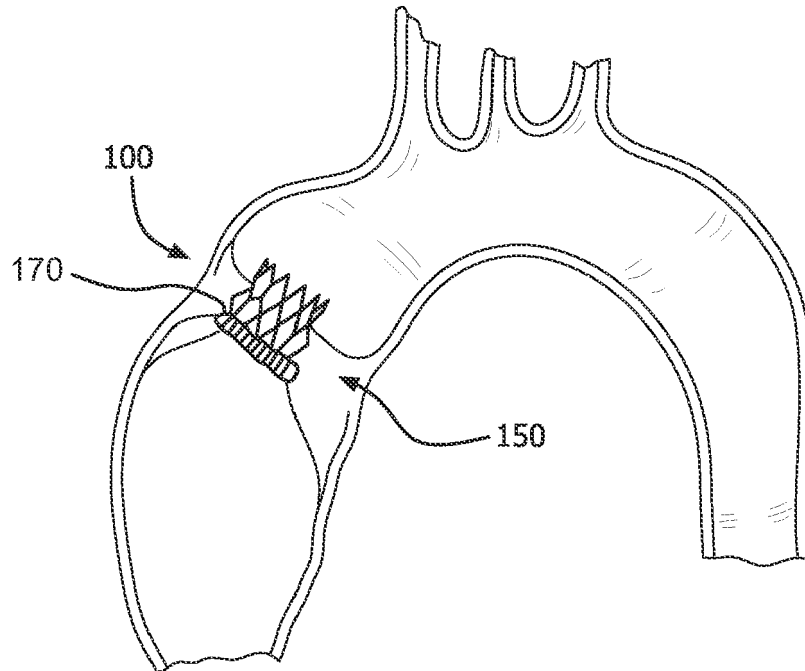


FIG. 4B

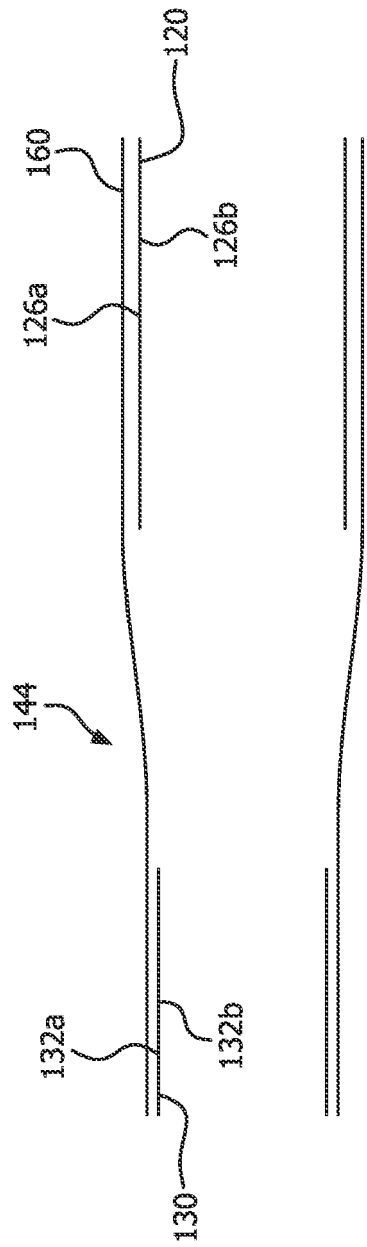


FIG. 5A

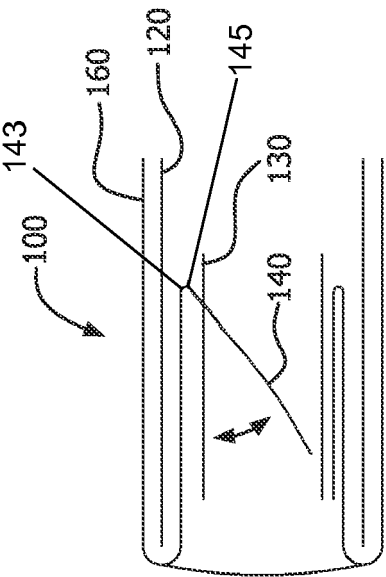


FIG. 5B

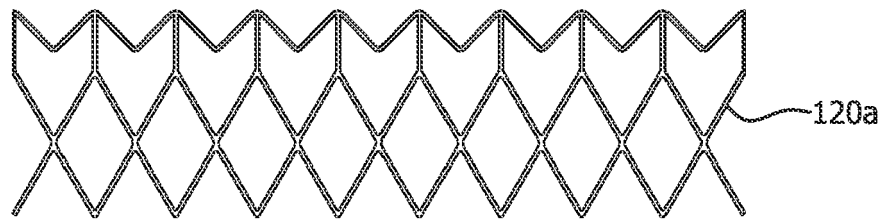


FIG. 6A

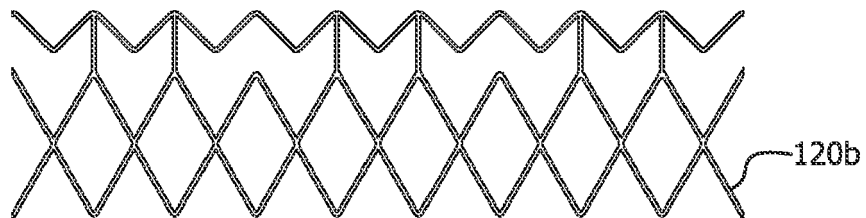


FIG. 6B



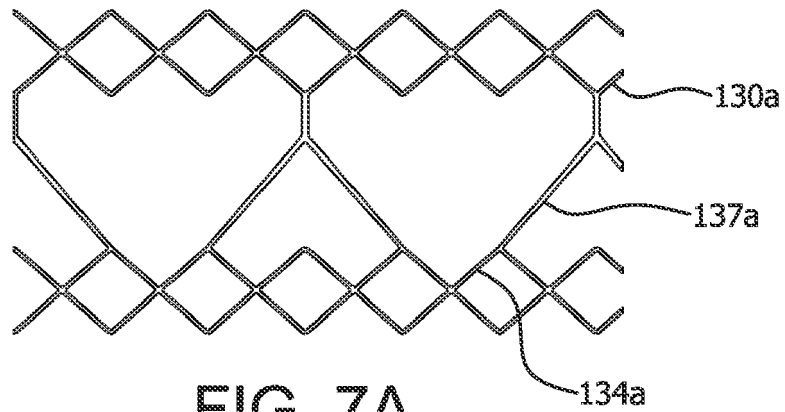


FIG. 7A

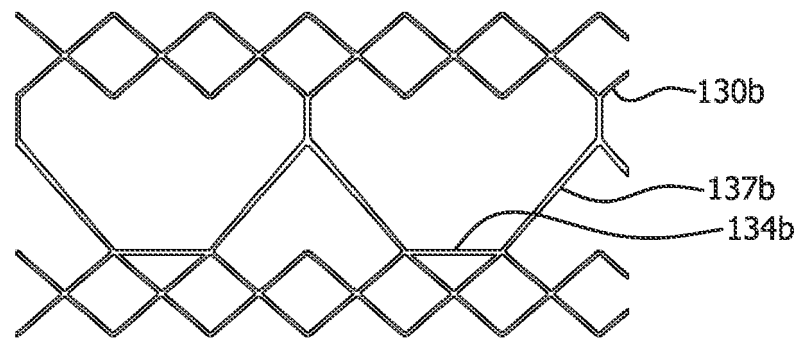


FIG. 7B

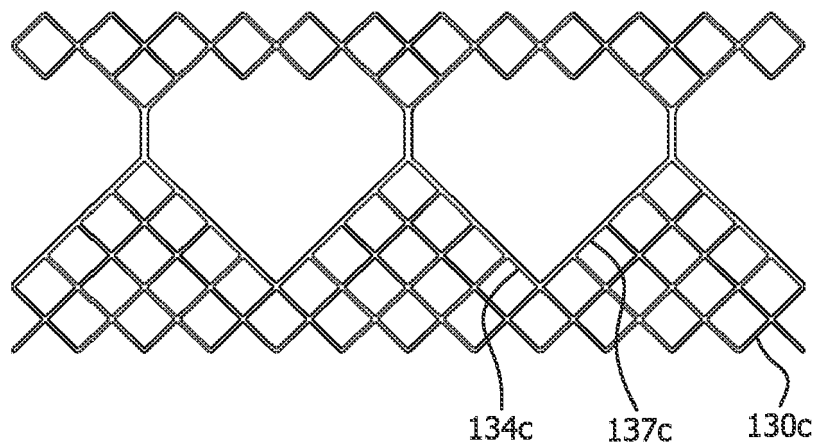


FIG. 8A

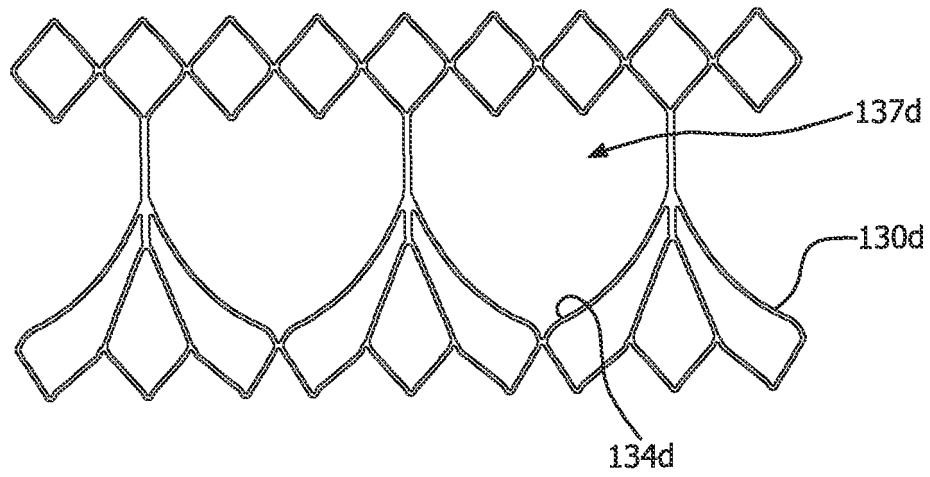


FIG. 8B

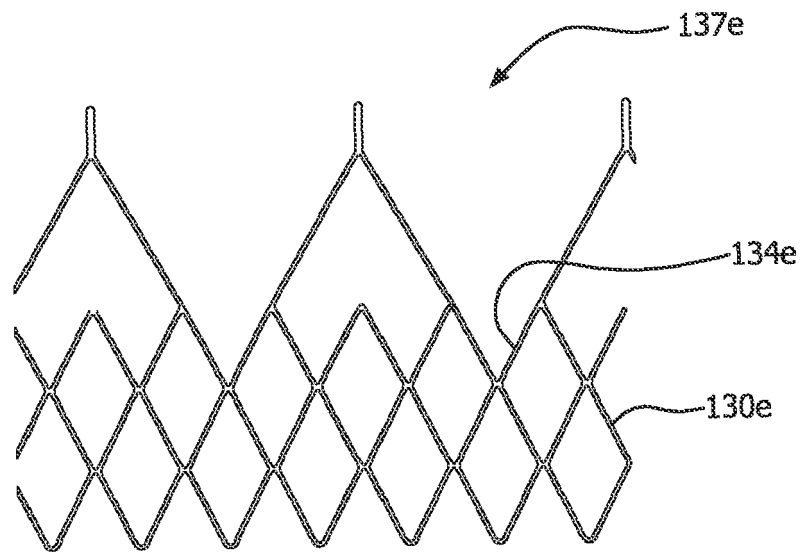


FIG. 8C

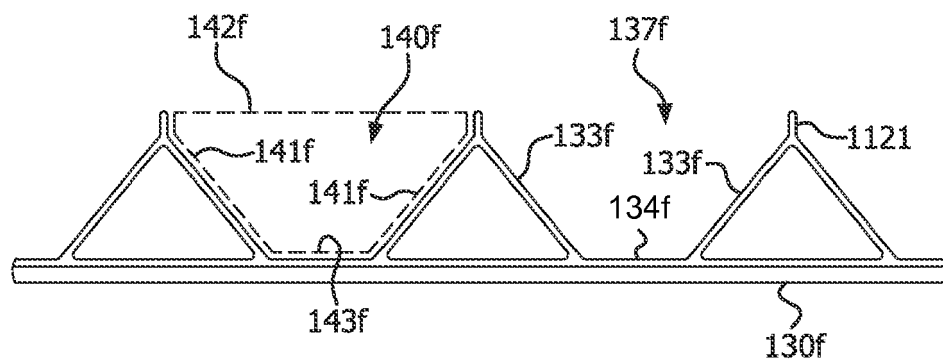


FIG. 8D

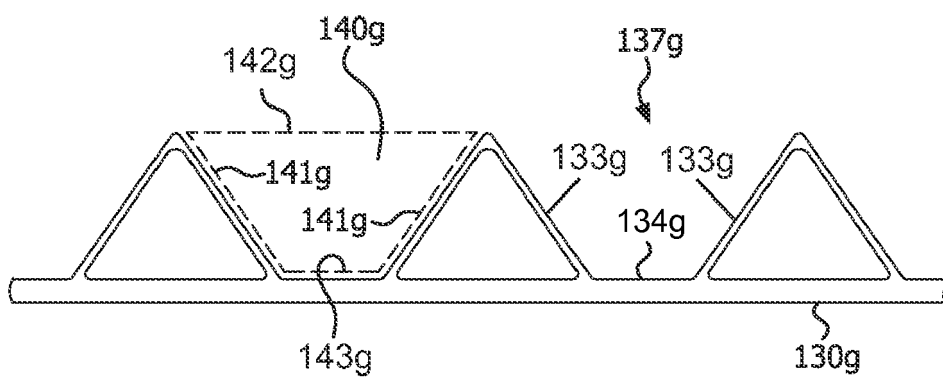


FIG. 8E

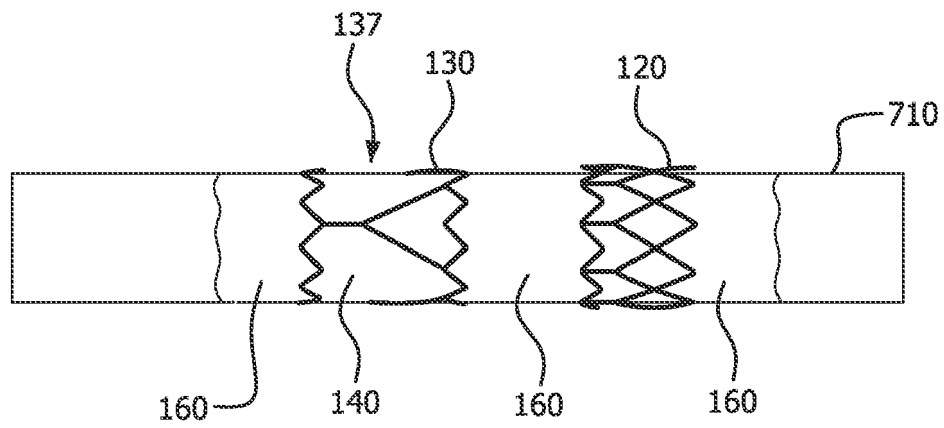


FIG. 9A

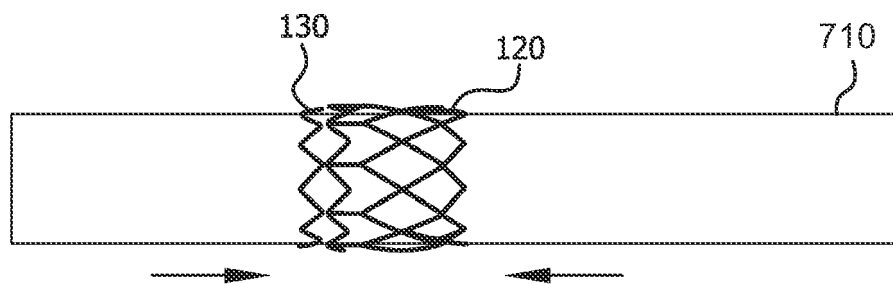


FIG. 9B

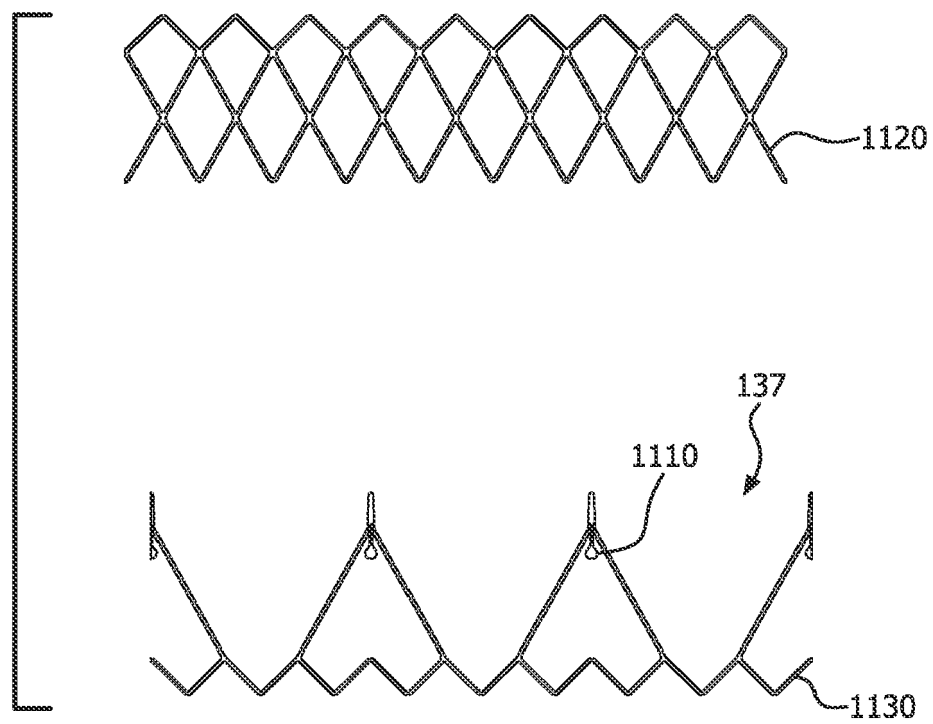


FIG. 10A

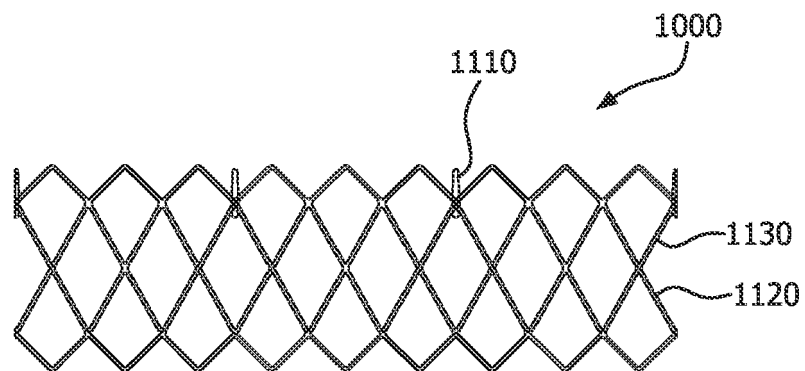


FIG. 10B

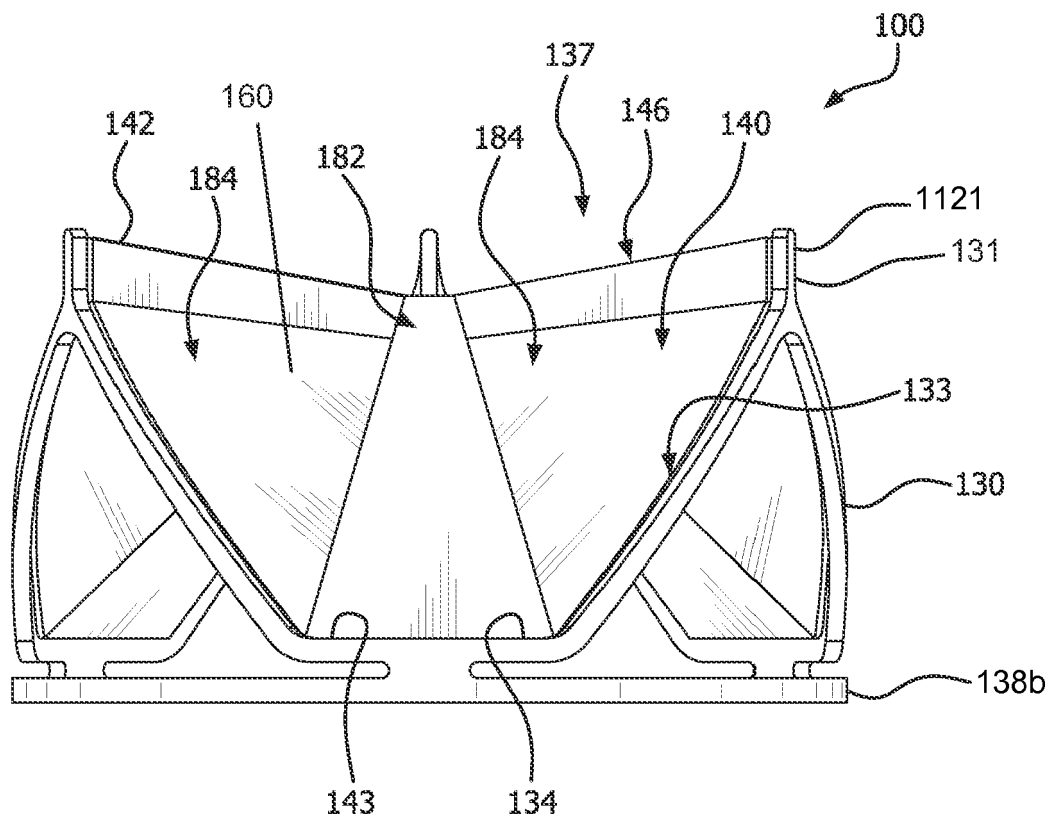


FIG. 11A

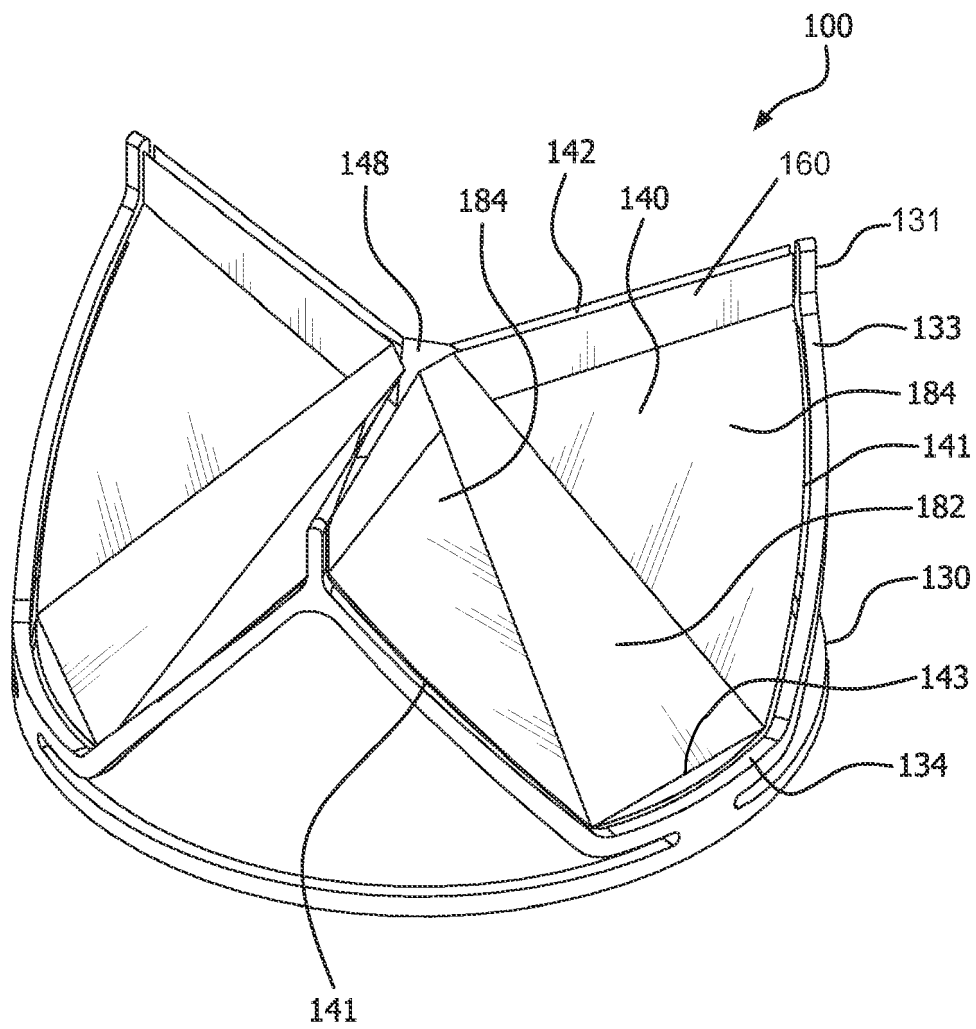


FIG. 11B

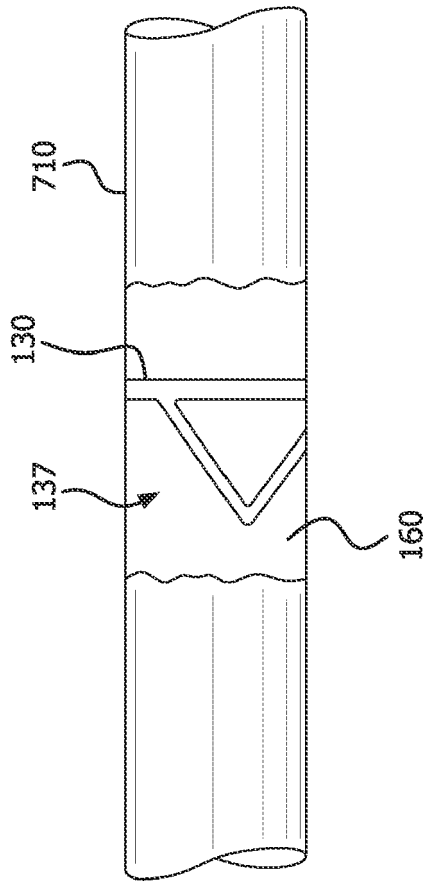


FIG. 12



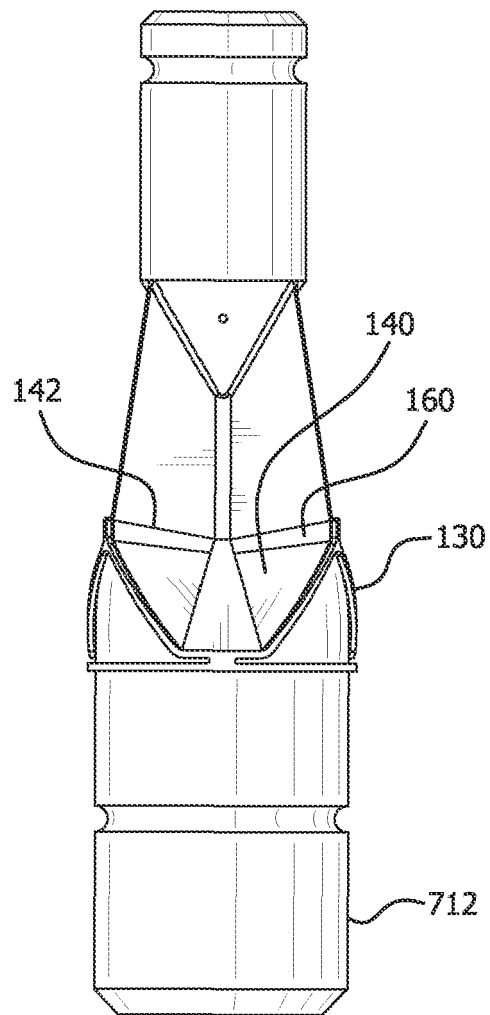


FIG. 13A

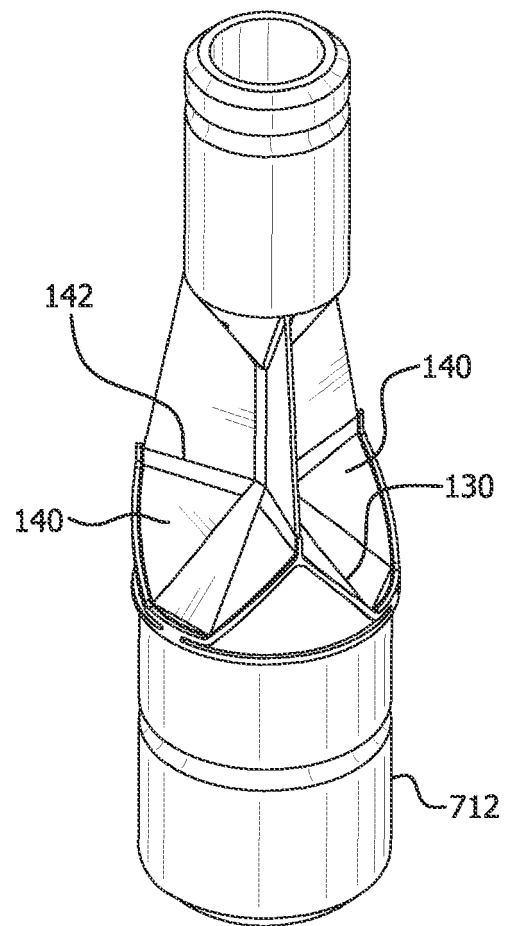


FIG. 13B



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Y	* paragraphs [0573] - [0583], [0595] - [0598]; figures 1-4E *	11,12	
Y	----- WO 2012/167131 A1 (GORE & ASS [US]; BRUCHMAN WILLIAM C [US]; HARTMAN CODY L [US]) 6 December 2012 (2012-12-06) * paragraphs [0067] - [0083], [0112] - [0120], [0141] - [0146], [0154] - [0159]; figures 1A-44 *	11,12	
E	----- WO 2014/018189 A2 (GORE & ASS [US]) 30 January 2014 (2014-01-30) * paragraphs [0058] - [0114]; figures 1A-3C *	1-15	
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			A61F
The present search report has been drawn up for all claims			
Place of search <b>The Hague</b>		Date of completion of the search <b>12 October 2017</b>	Examiner <b>Geuer, Melanie</b>
CATEGORY OF CITED DOCUMENTS X : particularly relevant if taken alone Y : particularly relevant if combined with another document of the same category A : technological background O : non-written disclosure P : intermediate document		T : theory or principle underlying the invention E : earlier patent document, but published on, or after the filing date D : document cited in the application L : document cited for other reasons ----- & : member of the same patent family, corresponding document	

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## 摘要

所描述的实施方式涉及人工瓣膜和系统以及制造人工瓣膜的方法。根据实施方式,人工瓣膜包括瓣叶框架、外框架和薄膜。瓣叶框架具有限定多个瓣叶窗口的大致管状的形状。外框架具有大致管状的形状。瓣叶框架以同轴的方式至少部分地设置在外框架内。瓣叶框架和外框架至少部分地由薄膜的连续部分联接。薄膜的连续部分的至少一部分容纳在瓣叶框架与外框架之间并且将瓣叶框架联接至外框架以阻止它们之间的相对运动。薄膜限定从瓣叶窗口中的每一者处延伸的瓣叶。