



(22) Date de dépôt/Filing Date: 2012/10/19

(41) Mise à la disp. pub./Open to Public Insp.: 2013/04/25

(45) Date de délivrance/Issue Date: 2023/08/01

(62) Demande originale/Original Application: 2 849 030

(30) Priorités/Priorities: 2011/10/19 (US61/549,044);
2012/03/01 (US61/605,699)

(51) Cl.Int./Int.Cl. *A61F 2/24* (2006.01)

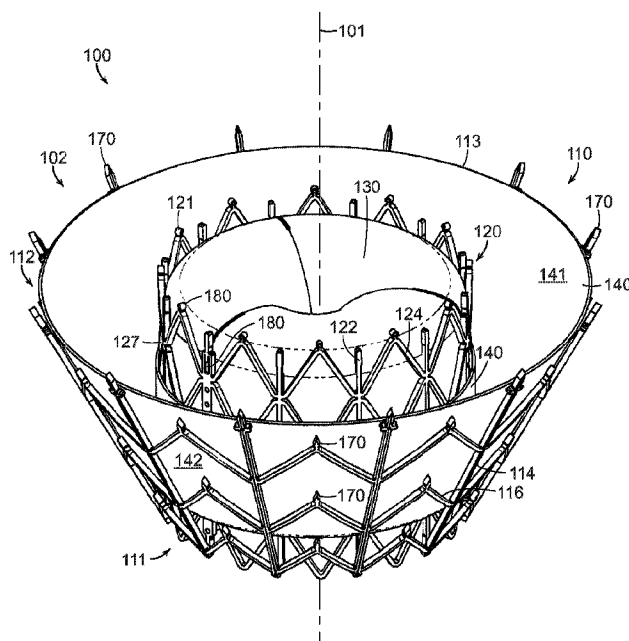
(72) Inventeurs/Inventors:
MORRISS, JOHN, US;
GIFFORD, HANSON, III, US;
FANN, JAMES L., US;
DUERI, JEAN-PIERRE, US;
MCLEAN, MATT, US;
GITTINGS, DARRIN, US;
LUNA, MICHAEL, US;
...

(73) Propriétaire/Owner:
TWELVE, INC., US

(74) Agent: SMART & BIGGAR LP

(54) Titre : DISPOSITIFS DE VALVULES CARDIAQUES PROTHETIQUES, VALVULES MITRALES PROTHETIQUES ET SYSTEMES ET PROCEDES ASSOCIES

(54) Title: PROSTHETIC HEART VALVE DEVICES, PROSTHETIC MITRAL VALVES AND ASSOCIATED SYSTEMS AND METHODS



(57) Abrégé/Abstract:

A prosthetic heart valve includes a flexible anchoring member at least partially surrounding and coupled to an inner valve support. The device can further include a prosthetic valve coupled to, mounted within, or otherwise carried by the valve support. The valve

(72) Inventeurs(suite)/Inventors(continued): DEEM, MARK, US; SUTTON, DOUGLAS, US; GRAINGER, JEFFREY J., US

(57) Abrégé(suite)/Abstract(continued):

support includes a plurality of posts connected circumferentially by a plurality of struts, where the posts extend along an axial direction generally parallel to the longitudinal axis and the struts extend circumferentially around and transverse to the longitudinal axis. The posts extend an entire longitudinal height H1 of the valve support 120. The device also includes one or more sealing members and tissue engaging elements like spikes.

ABSTRACT

A prosthetic heart valve includes a flexible anchoring member at least partially surrounding and coupled to an inner valve support. The device can further include a prosthetic valve coupled to, mounted within, or otherwise carried by the valve support. The valve support includes a plurality of posts connected circumferentially by a plurality of struts, where the posts extend along an axial direction generally parallel to the longitudinal axis and the struts extend circumferentially around and transverse to the longitudinal axis. The posts extend an entire longitudinal height HI of the valve support 120. The device also includes one or more sealing members and tissue engaging elements like spikes.

PROSTHETIC HEART VALVE DEVICES, PROSTHETIC MITRAL VALVES AND
ASSOCIATED SYSTEMS AND METHODS

CROSS-REFERENCES TO RELATED APPLICATIONS

[0000] This application is a divisional of Canadian Patent Application No. 2,849,030 filed October 19, 2012.

[0001] The present application claims priority to U.S. Provisional Patent Application No. 61/605,699, filed March 1, 2012, entitled "SYSTEM FOR MITRAL VALVE REPLACEMENT," to U.S. Provisional Patent Application No. 61/549,044, filed October 19, 2011, entitled "CONFORMABLE SYSTEM FOR MITRAL VALVE REPLACEMENT".

TECHNICAL FIELD

[0002] The present technology relates generally to prosthetic heart valve devices. In particular, several embodiments are directed to prosthetic mitral valves and devices for percutaneous repair and/or replacement of native mitral valves and associated systems and methods.

BACKGROUND

[0003] Conditions affecting the proper functioning of the mitral valve include, for example, mitral valve regurgitation, mitral valve prolapse and mitral valve stenosis. Mitral valve regurgitation is a disorder of the heart in which the leaflets of the mitral valve fail to coapt into apposition at peak contraction pressures, resulting in abnormal leaking of blood from the left ventricle into the left atrium. There are a number of structural factors that may affect the proper closure of the mitral valve leaflets. For example, many patients suffering

from heart disease experience dilation of the heart muscle, resulting in an enlarged mitral annulus. Enlargement of the mitral annulus makes it difficult for the leaflets to coapt during systole. A stretch or tear in the chordae tendineae, the tendons connecting the papillary muscles to the inferior side of the mitral valve leaflets, may also affect proper closure of the mitral annulus. A ruptured chordae tendineae, for example, may cause a valve leaflet to prolapse into the left atrium due to inadequate tension on the leaflet. Abnormal backflow can also occur when the functioning of the papillary muscles is compromised, for example, due to ischemia. As the left ventricle contracts during systole, the affected papillary muscles do not contract sufficiently to effect proper closure.

[0004] Mitral valve prolapse, or when the mitral leaflets bulge abnormally up in to the left atrium, causes irregular behavior of the mitral valve and may also lead to mitral valve regurgitation. Normal functioning of the mitral valve may also be affected by mitral valve stenosis, or a narrowing of the mitral valve orifice, which causes impedance of filling of the left ventricle in diastole.

[0005] Typically, treatment for mitral valve regurgitation has involved the application of diuretics and/or vasodilators to reduce the amount of blood flowing back into the left atrium. Other procedures have involved surgical approaches (open and intravascular) for either the repair or replacement of the valve. For example, typical repair approaches have involved cinching or resecting portions of the dilated annulus.

[0006] Cinching of the annulus has been accomplished by the implantation of annular or peri-annular rings which are generally secured to the annulus or surrounding tissue. Other repair procedures have also involved suturing or clipping of the valve leaflets into partial apposition with one another.

[0007] Alternatively, more invasive procedures have involved the replacement of the entire valve itself where mechanical valves or biological tissue are implanted into the heart in place of the mitral valve. These invasive procedures are conventionally done through large open thoracotomies and are thus very painful, have significant morbidity, and require long recovery periods.

[0008] However, with many repair and replacement procedures, the durability of the devices or improper sizing of annuloplasty rings or replacement valves may result in additional problems for the patient. Moreover, many of the repair procedures are highly

dependent upon the skill of the cardiac surgeon where poorly or inaccurately placed sutures may affect the success of procedures.

[0009] Less invasive approaches to aortic valve replacement have been developed in recent years. Examples of pre-assembled, percutaneous prosthetic valves include, e.g., the CoreValve Revalving[®] System from Medtronic/Corevalve Inc. (Irvine, CA, USA) and the Edwards-Sapien[®] Valve from Edwards Lifesciences (Irvine, CA, USA). Both valve systems include an expandable frame housing a tri-leaflet bioprosthetic valve. The frame is expanded to fit the substantially symmetric, circular and rigid aortic annulus. This gives the expandable frame in the delivery configuration a symmetric, circular shape at the aortic valve annulus, suitable to supporting a tri-leaflet prosthetic valve (which requires such symmetry for proper coaptation of the prosthetic leaflets). Thus, aortic valve anatomy lends itself to an expandable frame housing a replacement valve since the aortic valve anatomy is substantially uniform, symmetric, and fairly rigid.

[0010] Mitral valve replacement, compared with aortic valve replacement, poses unique anatomical obstacles, rendering percutaneous mitral valve replacement significantly more challenging than aortic valve replacement. First, unlike the relatively symmetric and uniform aortic valve, the mitral valve annulus has a non-circular D-shape or kidney-like shape, with a non-planar, saddle-like geometry often lacking symmetry. Such unpredictability makes it difficult to design a mitral valve prosthesis having the ability to conform to the mitral annulus. Lack of a snug fit between the prosthesis and the native leaflets and/or annulus may leave gaps therein, creating backflow of blood through these gaps. Placement of a cylindrical valve prosthesis, for example, may leave gaps in commissural regions of the native valve, potentially resulting in perivalvular leaks in those regions.

[0011] Current prosthetic valves developed for percutaneous aortic valve replacement are unsuitable for adaptation to the mitral valve. First, many of these devices require a direct, structural connection between the device structure which contacts the annulus and/or leaflets and the device structure which supports the prosthetic valve. In several devices, the same stent posts which support the prosthetic valve also contact the annulus or other surrounding tissue, directly transferring to the device many of the distorting forces exerted by the tissue and blood as the heart contracts during each cardiac cycle. Most cardiac replacement devices further utilize a tri-leaflet valve, which requires a substantially symmetric, cylindrical support around the prosthetic valve for proper opening and closing of the three leaflets over years of

life. If these devices are subject to movement and forces from the annulus and other surrounding tissues, the prostheses may be compressed and/or distorted causing the prosthetic leaflets to malfunction. Moreover, the typical diseased mitral annulus is much larger than any available prosthetic valve.

[0012] In addition to its irregular, unpredictable shape, the mitral valve annulus lacks a significant amount of radial support from surrounding tissue. The aortic valve, for example, is completely surrounded by fibro-elastic tissue, helping to anchor a prosthetic valve by providing native structural support. The mitral valve, on the other hand, is bound by muscular tissue on the outer wall only. The inner wall of the mitral valve is bound by a thin vessel wall separating the mitral valve annulus from the inferior portion of the aortic outflow tract. As a result, significant radial forces on the mitral annulus, such as those imparted by an expanding stent prostheses, could lead to collapse of the inferior portion of the aortic tract with potentially fatal consequences.

[0013] The chordae tendineae of the left ventricle may also present an obstacle in deploying a mitral valve prosthesis. This is unique to the mitral valve since aortic valve anatomy does not include chordae. The maze of chordae in the left ventricle makes navigating and positioning a deployment catheter that much more difficult in mitral valve replacement and repair. Deployment and positioning of a prosthetic valve or anchoring device on the ventricular side of the native mitral valve is further complicated by the presence of the chordae.

[0014] Given the difficulties associated with current procedures, there remains the need for simple, effective, and less invasive devices and methods for treating dysfunctional heart valves.

SUMMARY OF THE INVENTION

[0014a] According to one aspect of the present invention, there is provided a prosthetic heart valve device for repair or replacement of a native heart valve of a patient, the heart valve having an annulus and leaflets, comprising: an anchoring member having a first portion comprising an upstream portion having a first cross-sectional dimension and a second portion having a downstream portion having a second cross-sectional dimension less than the first

cross-sectional dimension, wherein the first portion is configured to engage cardiac tissue to retain the anchoring member in a fixed longitudinal position relative to the annulus; a valve support coupled to the second portion of the anchoring member and configured to support a prosthetic valve, wherein the valve support is radially separated from the first portion of the anchoring member such that the first portion of the anchoring member can deform inwardly without substantially deforming the valve support.

BRIEF DESCRIPTION OF THE DRAWINGS

[0015] Many aspects of the present disclosure can be better understood with reference to the following drawings. The components in the drawings are not necessarily to scale. Instead, emphasis is placed on illustrating clearly the principles of the present disclosure. Furthermore, components can be shown as transparent in certain views for clarity of illustration only and not to indicate that the illustrated component is necessarily transparent.

[0016] Figures 1 and 2 are schematic illustrations of a mammalian heart having native valve structures suitable for replacement with various prosthetic heart valve devices in accordance with embodiments of the present technology.

[0017] Figure 3 is a schematic cross-sectional side view of a native mitral valve showing the annulus and leaflets.

[0018] Figure 4A is a schematic illustration of the left ventricle of a heart having either i) prolapsed leaflets in the mitral valve, or ii) mitral valve regurgitation in the left ventricle of a heart having impaired papillary muscles, and which are suitable for combination with various prosthetic heart valve devices in accordance with embodiments of the present technology.

[0019] Figure 4B is a schematic illustration of a heart in a patient suffering from cardiomyopathy, and which is suitable for combination with various prosthetic heart valve devices in accordance with embodiments of the present technology.

[0020] Figures 5A is a schematic illustration of a native mitral valve of a heart showing normal closure of native mitral valve leaflets.

[0021] Figure 5B is a schematic illustration of a native mitral valve of a heart showing abnormal closure of native mitral valve leaflets in a dilated heart, and which is suitable for combination with various prosthetic heart valve devices in accordance with embodiments of the present technology.

[0022] Figure 5C is a schematic illustration of a mitral valve of a heart showing dimensions of the annulus, and which is suitable for combination with various prosthetic heart valve devices in accordance with embodiments of the present technology.

[0023] Figure 6A is a schematic, cross-sectional illustration of the heart showing an antegrade approach to the native mitral valve from the venous vasculature, in accordance with various embodiments of the present technology.

[0024] Figure 6B is a schematic, cross-sectional illustration of the heart showing access through the inter-atrial septum (IAS) maintained by the placement of a guide catheter over a guidewire, in accordance with various embodiments of the present technology.

[0025] Figures 7 and 8 are schematic, cross-sectional illustrations of the heart showing retrograde approaches to the native mitral valve through the aortic valve and arterial vasculature, in accordance with various embodiments of the present technology.

[0026] Figure 9 is a schematic, cross-sectional illustration of the heart showing an approach to the native mitral valve using a trans-apical puncture in accordance with various embodiments of the present technology.

[0027] Figure 10A shows an isometric view of a prosthetic heart valve device in accordance with an embodiment of the present technology.

[0028] Figure 10B illustrates a cut-away view of a heart showing the prosthetic treatment device of Figure 10A implanted at a native mitral valve in accordance with an embodiment of the present technology.

[0029] Figures 10C-10F are side, perspective cut-away, top, and bottom views, respectively, of a prosthetic heart valve device in accordance with an embodiment of the present technology.

[0030] Figure 11A is a side view of a valve support in an expanded configuration in accordance with an embodiment of the present technology.

[0031] Figures 11B-11D are isometric views of additional embodiments of valve supports with prosthetic valves mounted therein in accordance with the present technology.

[0032] Figure 11E shows an isometric view of a prosthetic heart valve device in accordance with another embodiment of the present technology.

[0033] Figures 12A-12C are side views of various longitudinal ribs flexing in response to a distorting force in accordance with further embodiments of the present technology.

[0034] Figures 13A is a schematic, cross-sectional view of a prosthetic heart valve device in accordance with another embodiment of the present technology.

[0035] Figures 13B-13F are partial side views of prosthetic heart valve devices illustrating a variety of longitudinal rib configurations in accordance with additional embodiments of the present technology.

[0036] Figure 14A is a schematic top view of a native mitral valve illustrating the major and minor axes.

[0037] Figures 14B-14C are schematic top views of an anchoring member in an expanded configuration and in a deployed configuration, respectively, in accordance with an embodiment of the present technology.

[0038] Figure 15 is an isometric view of a prosthetic heart valve device illustrated in a deployed configuration in accordance with an additional embodiment of the present technology.

[0039] Figure 16A is a top view of a prosthetic heart valve device illustrated in an expanded configuration in accordance with a further embodiment of the present technology.

[0040] Figures 16B-16C are a first side view and a second side view, respectively, of the prosthetic heart valve device of Figure 16A.

[0041] Figure 16D is a side view of a prosthetic heart valve device showing the longitudinal axis of the anchoring member off-set from the longitudinal axis of the valve support by a tilt angle in accordance with another embodiment of the present technology.

[0042] Figure 16E is a schematic top view of a native mitral valve in the heart viewed from the left atrium and showing the prosthetic treatment device of Figure 16A-16C implanted at the native mitral valve in accordance with an embodiment of the present technology.

[0043] Figures 17A-17C are schematic top and first and second side views of the prosthetic heart valve device of Figure 16A showing dimensions and taper angles of various aspects of the device in accordance with embodiments of the present technology.

[0044] Figure 18 is an isometric view of an anchoring member illustrated in an expanded configuration in accordance with yet another embodiment of the present technology.

[0045] Figures 19A-19C are isometric, side and top views, respectively, of a prosthetic heart valve device having a sealing member in accordance with a further embodiment of the present technology.

[0046] Figure 20A is an isometric view of a prosthetic heart valve device without a sealing member in accordance with an embodiment of the present technology.

[0047] Figures 20B-20E are isometric views of prosthetic heart valve devices having sealing members in accordance with additional embodiments of the present technology.

[0048] Figures 21A-21B are cross-sectional side and isometric views of a prosthetic heart valve device having a tubular valve support member in accordance with a further embodiment of the present technology.

[0049] Figures 21C-21F are partial cross-sectional side views and an isometric view of prosthetic heart valve devices having a tubular valve support member in accordance with other embodiments of the present technology.

[0050] Figures 22A-22G and 22I-22K are enlarged side views of various mechanisms of coupling a valve support to an anchoring member in accordance with additional embodiments of the present technology.

[0051] Figure 22H is a side view of a post in the prosthetic heart valve device of Figure 40G.

[0052] Figures 23A-23B are enlarged side views of a additional mechanisms for coupling an anchoring member to a valve support member in accordance with further embodiments of the present technology.

[0053] Figure 24A is a perspective view of an integral connection between a valve support and an anchoring member in accordance with an additional embodiment of the present technology.

[0054] Figures 24B-24D are enlarged views of additional embodiments of an integral connection between a valve support and an anchoring member in accordance with the present technology.

[0055] Figure 25A is a partial cross-sectional view of a prosthetic heart valve device having an anchoring member and a valve support in accordance with an embodiment of the present technology.

[0056] Figure 25B is an enlarged view of the designated box shown in Figure 25A

[0057] Figures 26A-26D are schematic cross-sectional views of prosthetic heart valve devices having atrial retainers and implanted at a native mitral valve in accordance with various embodiments of the present technology.

[0058] Figure 27 is a side view of an anchoring member having a vertical portion at the upstream end for engaging the annulus in accordance with another embodiment of the present technology.

[0059] Figure 28 is a side view of a prosthetic heart valve device in an expanded configuration and having a plurality of stabilizing elements in accordance with an embodiment of the present technology.

[0060] Figure 29 is an enlarged schematic, side view of a prosthetic heart valve device having an extended arm in accordance with an embodiment of the present technology.

[0061] Figures 30A-30C are enlarged partial side views of a prosthetic heart valve device having arms coupled to the device at various angles with respect to a longitudinal axis of the device in accordance with further embodiments of the present technology.

[0062] Figures 31A-31C are enlarged, partial side views of a prosthetic heart valve device having arms of various lengths coupled to the device in accordance with additional embodiments of the present technology.

[0063] Figures 32A, 32B, 32C, and 32D are cross-sectional views of a heart with an implanted prosthetic heart valve device having arms disposed on an inward-facing surface of the leaflets in accordance with various embodiments of the present technology.

[0064] Figures 32A-1, 32B-1, 32C-1 and 32D-1 are enlarged views of the arms engaging the inward-facing surface of the leaflets as shown in Figures 32A, 32B, 32C and 32D, respectively in accordance with various embodiments of the present technology.

[0065] Figures 33A-33C are schematic views illustrating various embodiments of tissue engaging elements for use with prosthetic heart valve devices in accordance with the present technology.

[0066] Figures 34A, 34B and 34C are cross-sectional views of a heart with an implanted prosthetic heart valve device having arms with tissue engaging elements disposed on an inward-facing surface of the leaflets in accordance with various embodiments of the present technology.

[0067] Figures 34A-1, 34B-1 and 34C-1 are enlarged views of the arms engaging the inward-facing surface of the leaflets as shown in Figures 34A, 34B and 34C, respectively in accordance with various embodiments of the present technology.

[0068] Figures 35A-35C are side views of prosthetic heart valve devices and shown implanted at a mitral valve (illustrated in cross-section), the devices having arms for engaging

an outward-facing surface of the native leaflets in accordance with further embodiments of the present technology.

[0069] Figure 35C-1 is an enlarged view of the arm engaging the inward-facing surface of the leaflets as shown in Figure 35C in accordance with various embodiments of the present technology.

[0070] Figure 36A is a side view of a prosthetic heart valve device and shown implanted at a mitral valve (illustrated in cross-section), the device having arms for engaging an outward-facing surface of the native leaflets and arms for engaging an inward-facing surface of the native leaflets in accordance with an additional embodiment of the present technology.

[0071] Figure 36B is an enlarged view of the arms engaging the inward-facing and outward-facing surfaces of the leaflets as shown in Figure 36A.

[0072] Figures 37A-37D are enlarged side views of additional embodiments of arms suitable for use with a prosthetic heart valve device in accordance with the present technology.

[0073] Figure 38A is a side view of a prosthetic heart valve device having a plurality of non-interconnected arms in accordance with a further embodiment of the present technology.

[0074] Figure 38B is a side view of a prosthetic heart valve device having a plurality of circumferentially connected arms in accordance with a further embodiment of the present technology.

[0075] Figures 39A-39D are schematic top views of arm location patterns in accordance with additional embodiments of the present technology.

[0076] Figures 40A-40D are side views of prosthetic heart valve devices having tissue engaging elements on varying structures of the device in accordance with additional embodiments of the present technology.

[0077] Figures 40E-40G are enlarged side views of tissue engaging elements suitable for use with prosthetic heart valve devices in accordance with other embodiments of the present technology.

[0078] Figures 40I-40T are enlarged side views of embodiments of tissue engaging elements suitable for use with prosthetic heart valve devices in accordance with additional embodiments of the present technology.

[0079] Figure 41 is an isometric view of a prosthetic heart valve device having a plurality of annulus engaging elements in accordance with a further embodiment of the present technology.

[0080] Figures 42A-42B are cross-sectional side and enlarged views of a prosthetic heart valve device having tissue engaging elements deployable from a plurality of tubular ribs in accordance with another embodiment of the present technology.

[0081] Figures 43A-43B are an isometric view and an enlarged detail view of a prosthetic heart valve device having a sealing member configured with tissue engaging elements in accordance with another embodiment of the present technology.

[0082] Figures 44A-44F are enlarged side views of embodiments of tissue engaging elements suitable for use with prosthetic heart valve devices in accordance with additional embodiments of the present technology.

[0083] Figure 45A is an isometric view of a prosthetic heart valve device having a plurality of tethers between the anchoring member 110 and the valve support 120 in accordance with an embodiment of the present technology.

[0084] Figure 45B is an isometric view of a prosthetic heart valve device having a plurality of septa between the anchoring member 110 and the valve support 120 in accordance with another embodiment of the present technology.

[0085] Figure 46A is side partial cut-away view of a delivery system in accordance with an embodiment of the present technology.

[0086] Figure 46B is an enlarged cross-sectional view of a distal end of a delivery system in accordance with an embodiment of the present technology.

[0087] Figures 46C-46D are enlarged partial side views of a valve support configured for use with the delivery system of Figure 46B in accordance with an embodiment of the present technology.

[0088] Figures 47A-47D are cross-sectional views of a heart showing an antegrade or trans-septal approach to the mitral valve in accordance with an embodiment of the present technology.

[0089] Figures 48A-48C are cross-sectional views of the heart illustrating a method of implanting a prosthetic heart valve device using a trans-septal approach in accordance with another embodiment of the present technology.

[0090] Figures 49A-49B are cross-sectional views of the heart showing a retrograde approach to the mitral valve via the aorta and left ventricle in accordance with a further embodiment of the present technology.

[0091] Figures 50A-50B are cross-sectional views of the heart illustrating a further embodiment of a method of implanting the prosthetic heart valve device using a trans-apical approach in accordance with aspects of the present technology.

[0092] Figures 51A-51B are partial side views of a delivery system wherein a prosthetic heart valve device is mounted on an expandable balloon of a delivery catheter in accordance with another embodiment of the present technology.

[0093] Figures 52A-52D are cross-sectional views of a heart showing a method of delivering a prosthetic heart valve device having a valve support movably coupled to an anchoring member in accordance with a further embodiment of the present technology.

[0094] Figures 53A-53D are partial side views showing various mechanisms for movably coupling the valve support to the anchoring member in accordance with additional embodiments of the present technology.

[0095] Figure 53E is a partial top view of the device of Figure 53D.

[0096] Figure 53F is a side view of an alternative mechanism for slideably coupling a valve support and anchoring member in accordance with another embodiment of the present technology.

[0097] Figures 53G-53H are schematic side views of a prosthetic heart valve device showing yet another mechanism for coupling the valve support to the anchoring member in accordance with a further embodiment of the present technology.

[0098] Figure 54A is a cross-sectional side view of another embodiment of a delivery system for the prosthetic heart valve device in accordance with other aspects of the present technology.

[0099] Figure 54B is a partial cross-sectional side view of a distal portion of the delivery system of Figure 54A.

[00100] Figures 55A-55C are perspective views of the delivery system of Figure 46 illustrating the steps of delivering the prosthetic treatment device of the invention.

[00101] Figure 56 is a side cross-sectional view of a further embodiment of a delivery system for the prosthetic treatment device of the invention.

[00102] Figures 57A-57D are isometric views of prosthetic treatment devices in accordance with additional embodiments of the present technology.

[00103] Figure 57E is a schematic cross-sectional view of the prosthetic heart valve device of Figure 57A implanted at a native mitral valve in accordance with an embodiment of the present technology.

[00104] Figures 58A-58D are cross-sectional views of a heart showing a method of delivering a prosthetic heart valve device to a native mitral valve in the heart using a trans-apical approach in accordance with another embodiment of the present technology.

[00105] Figures 59A-59C are isometric views of prosthetic treatment devices in accordance with additional embodiments of the present technology.

[00106] Figure 59D is a schematic cross-sectional view of a prosthetic heart valve device implanted at a native mitral valve in accordance with another embodiment of the present technology.

[00107] Figures 60A-60B are cross-sectional side views of a distal end of a delivery catheter for delivering the prosthetic heart valve device of Figure 59C to a native mitral valve in the heart in accordance with another embodiment of the present technology.

[00108] Figure 61 is a side view of a prosthetic heart valve device having first and second anchoring members for engaging supra-annular and subannular tissue of the mitral valve, respectively, in accordance with yet another embodiment of the present technology.

[00109] Figures 62A-62C are partial cross-sectional side views of a distal end of a delivery system showing delivery of the prosthetic heart valve device of Figure 61 at a mitral valve in accordance with another embodiment of the present technology.

[00110] Figure 63 is an isometric side view of a prosthetic heart valve device having an anchoring member with a supra-annular engaging rim and a subannular engaging ring in accordance with a further embodiment of the present technology.

[00111] Figures 64A-64D are side views of the prosthetic heart valve device of Figure 63 showing embodiments of methods for deploying the device at the mitral valve annulus in accordance with aspects of the present technology.

[00112] Figure 65A is a cross-sectional view of a prosthetic heart valve device having an inflatable anchoring member and shown implanted in a native mitral valve of a heart in accordance with another embodiment of the present disclosure.

[00113] Figure 65B is a partial cross-sectional side view of a distal end of a delivery system suitable for delivery of the prosthetic heart valve device of Figure 65A in accordance with another embodiment of the present technology.

[00114] Figures 66A-66D are cross-sectional views of prosthetic heart valve devices having fillable chambers in accordance with additional embodiments of the present technology.

[00115] Figures 67A-67B are isometric views of additional embodiments of prosthetic heart valve devices in accordance with aspects of the present technology.

[00116] Figures 68A-68B are side views of prosthetic heart valve devices having a positioning element in accordance with an additional embodiments of the present technology.

[00117] Figures 69A-69E are cross-sectional and side views of prosthetic heart valve devices shown in an expanded configuration and configured in accordance with an additional embodiment of the present technology.

[00118] Figure 70 is a cross-sectional side view of another prosthetic heart valve device configured in accordance with an embodiment of the present technology.

[00119] Figure 71 is a cross-sectional side view of yet another prosthetic heart valve device configured in accordance with an embodiment of the present technology.

DETAILED DESCRIPTION

[00120] Specific details of several embodiments of the technology are described below with reference to Figures 1-71. Although many of the embodiments are described below with respect to devices, systems, and methods for percutaneous replacement of a native mitral valve using prosthetic valve devices, other applications and other embodiments in addition to those described herein are within the scope of the technology. Additionally, several other embodiments of the technology can have different configurations, components, or procedures than those described herein. A person of ordinary skill in the art, therefore, will accordingly understand that the technology can have other embodiments with additional elements, or the technology can have other embodiments without several of the features shown and described below with reference to Figures 1-71.

[00121] With regard to the terms "distal" and "proximal" within this description, unless otherwise specified, the terms can reference a relative position of the portions of a prosthetic valve device and/or an associated delivery device with reference to an operator and/or a location in the vasculature or heart. For example, in referring to a delivery catheter suitable to deliver and position various prosthetic valve devices described herein, "proximal" can refer to a position closer to the operator of the device or an incision into the vasculature, and "distal" can refer to a position that is more distant from the operator of the device or further from the incision along the vasculature (e.g., the end of the catheter). With respect to a prosthetic heart valve device, the terms "proximal" and "distal" can refer to the location of portions of the device with respect to the direction of blood flow. For example, proximal can refer to an upstream position or a position of blood inflow, and distal can refer to a downstream position or a position of blood outflow. For ease of reference, throughout this disclosure identical reference numbers and/or letters are used to identify similar or analogous components or features, but the use of the same reference number does not imply that the parts should be construed to be identical. Indeed, in many examples described herein, the identically numbered parts are distinct in structure and/or function. The headings provided herein are for convenience only.

Overview

[00122] Systems, devices and methods are provided herein for percutaneous replacement of native heart valves, such as mitral valves. Several of the details set forth below are provided to describe the following examples and methods in a manner sufficient to enable a person skilled in the relevant art to practice, make and use them. Several of the details and advantages described below, however, may not be necessary to practice certain examples and methods of the technology. Additionally, the technology may include other examples and methods that are within the scope of the disclosure but are not described in detail.

[00123] Embodiments of the present technology provide systems, methods and apparatus to treat valves of the body, such as heart valves including the mitral valve. The apparatus and methods enable a percutaneous approach using a catheter delivered intravascularly through a vein or artery into the heart. Additionally, the apparatus and methods enable other less-invasive approaches including trans-apical, trans-atrial, and direct aortic delivery of a prosthetic replacement valve to a target location in the heart. The apparatus and methods enable a prosthetic device to be anchored at a native valve location by engagement with a subannular surface of the valve annulus and/or valve leaflets. Additionally, the embodiments of the devices and methods as described herein can be combined with many known surgeries and procedures, such as known methods of accessing the valves of the heart (e.g., the mitral valve or tricuspid valve) with antegrade or retrograde approaches, and combinations thereof.

[00124] The devices and methods described herein provide a valve replacement device that has the flexibility to adapt and conform to the variably-shaped native mitral valve anatomy while mechanically isolating the prosthetic valve from the anchoring portion of the device. Several embodiments of the device effectively absorb the distorting forces applied by the native anatomy. The device has the structural strength and integrity necessary to withstand the dynamic conditions of the heart over time, thus permanently anchoring a replacement valve and making it possible for the patient to resume a substantially normal life. The devices and methods further deliver such a device in a less-invasive manner, providing a patient with a new, permanent replacement valve but also with a lower-risk procedure and a faster recovery.

[00125] In accordance with various embodiments of the present technology, a device for repair or replacement of a native valve of a heart is disclosed. The native valve has an annulus and leaflets, and the device includes an anchoring member having a first portion

configured to engage tissue on or under the annulus and to deform in a non-circular shape to conform to the tissue. The anchoring member also can include a second portion. The device also includes a valve support coupled to the second portion of the anchoring member and configured to support a prosthetic valve and having a cross-sectional shape. In various embodiments, the first portion of the anchoring member is mechanically isolated from the valve support such that the cross-sectional shape of the valve support remains sufficiently stable so that the prosthetic valve remains competent when the anchoring member is deformed in the non-circular shape.

[00126] Some embodiments of the disclosure are directed to prosthetic heart valve devices for implantation at a native mitral valve wherein the mitral valve has an annulus and leaflets. In one embodiment, the device can have an anchoring member positionable in a location between the leaflets, wherein a first portion of the anchoring member is expandable to a dimension larger than a corresponding dimension of the annulus. In this embodiment, upstream movement of the anchoring member is blocked by engagement of the upstream portion with tissue on or near the annulus. The anchoring member can also include a second portion. The device can also include a valve support coupled to the second portion of the anchoring member, wherein an upstream region of the valve support is spaced radially inward from at least the first portion of the anchoring member. The valve support can be configured to support a prosthetic valve.

[00127] In another arrangement, a device for implantation at a native valve having an annulus and leaflets can include a hyperboloidic anchoring member having an upstream end configured to engage an inward facing surface of the leaflets downstream of the annulus and a downstream end, wherein the upstream end has a larger cross-sectional area than the downstream end. The device can also include a valve support positioned in the anchoring member and configured to support a prosthetic valve. The valve support is coupled to the anchoring member at a location spaced substantially downstream from the upstream end and is uncoupled to the anchoring member at the upstream end.

[00128] Other aspects of the disclosure are directed to prosthetic heart valve devices for repair or replacement of a native heart valve of a patient, wherein the heart valve has an annulus and leaflets. In one embodiment, the device includes an anchoring member having a first portion having a first cross-sectional dimension and second portion having a second cross-sectional dimension less than the first cross-sectional dimension. The first portion is

configured to engage cardiac tissue to retain the anchoring member in a fixed longitudinal position relative to the annulus. The device can also include a valve support coupled to the second portion of the anchoring member and configured to support a prosthetic valve. The valve support can be radially separated from the first portion of the anchoring member such that the first portion can deform inwardly without substantially deforming the valve support.

[00129] In a further arrangement, the present disclosure also is directed to a device for implantation at a native heart valve. The device can include an anchoring member having an upstream end configured to engage tissue on or downstream of a native annulus of the heart valve, and a valve support configured to support a prosthetic valve. The valve support can be coupled to the anchoring member. In some arrangements, the anchoring member can resist upstream migration of the device without an element of the device extending behind native valve leaflets.

[00130] In another embodiment, the device can include an anchoring member positionable between the leaflets of the native valve. The anchoring member can have a plurality of tissue engaging elements on an upstream end and/or on an exterior surface which are configured to engage cardiac tissue on or near the annulus so as to prevent migration of the device in the upstream direction. The device can also include a valve support positioned within an interior of the anchoring member and coupled to a downstream portion of the anchoring member, wherein the valve support is radially separated from at least an upstream portion of the anchoring member.

[00131] Further embodiments of the disclosure are directed to a device for repair or replacement of a native mitral valve having an annulus and a pair of leaflets that include a support structure having an upper region, a lower region, and an interior to retain a prosthetic valve. The device can also include an anchoring member surrounding at least a portion of the support structure, wherein the anchoring member is positionable between the leaflets and has a plurality of flexible elements (e.g., wires, laser cut metal elements, etc.) arranged in a diamond pattern, an upper portion, and a lower portion. The upper portion of the anchoring member can be flared outwardly in a proximal direction such that proximal ends of the flexible elements point radially outward so as to engage cardiac tissue on or near the annulus and inhibit migration of the device in the upstream direction. The lower region of the support structure can be coupled to the lower portion of the anchoring member, and the lower region

of the support structure can be mechanically isolated from at least deformation of the flared upper portion of the anchoring member.

[00132] Other embodiments of the disclosure are directed to prosthetic heart valve devices having a cylindrical support and an anchor defined by a structure separate from the cylindrical support. The cylindrical support can have a longitudinal axis and an interior along the longitudinal axis through which blood may flow. The anchor can have a non-circular cross-section with an outwardly flared upstream end configured to engage subannular tissue of a mitral valve. The anchor can also surround the cylindrical support and be coupled to the support at a downstream end opposite the upstream end.

[00133] In a further embodiment, the device can include an expandable valve support configured for placement between the two leaflets. The support can have a first region, a second region and an interior in which a valve may be coupled. The device can also include an anchoring member having a first portion and a second portion, the second portion coupled to the second region of the valve support. The first portion of the anchoring member can extend outwardly away from the second portion. The anchoring member can have a first perimeter at the first portion configured to engage tissue on or near the annulus. The anchoring member can be mechanically isolated from the valve support such that a force exerted radially at or near the first perimeter will not substantially alter a shape of the valve support.

[00134] Additional embodiments are directed to devices to treat a heart valve of a patient that include an inner frame and an outer frame coupled to the inner frame. The inner frame can have an outer surface and an inner surface that is configured to support a prosthetic valve. The outer frame can have an upper portion with a cross-sectional dimension greater than a corresponding cross-sectional dimension of an annulus of the mitral valve, wherein the upper portion is configured to engage tissue at or below the annulus of the mitral valve. The upper portion can also prevent migration of the device in an upward or upstream direction during ventricular systole. Further, the upper portion of the outer frame can be mechanically isolated from the inner frame.

[00135] In a further embodiment, the device can include a cylindrical inner skeleton and an outer skeleton coupled to the inner skeleton and positionable between the leaflets downstream of the annulus. The outer skeleton can be deformable to a non-circular cross-section while the inner skeleton remains substantially circular in cross-section. The inner

skeleton can have an interior to which a prosthetic valve may be coupled. The outer skeleton can have a plurality of flexible elements (e.g., wires, laser cut metal elements, etc.), wherein at least a portion of the flexible elements can be configured to engage native subannular tissue so as to prevent migration of the device in an upstream direction. In one embodiment, the plurality of flexible wires are arranged in a diamond configuration.

[00136] In yet a further embodiment, a prosthetic mitral valve device can include a valve support having upstream and downstream ends, an interior in which a valve may be coupled, and a perimeter. The device can also include an anchoring member having a flared upstream portion and a downstream portion coupled to the perimeter of the valve support. The upstream portion can be mechanically isolated from the valve support and can be configured to engage subannular tissue of a native mitral valve. Additionally, the device can be moveable into a plurality of configurations including a first configuration in which the valve support and the anchoring member are radially contracted, and wherein the valve support has a first cross-sectional shape. The device can also move into a second configuration in which the valve support and the anchoring member are radially expanded and in which the valve support has a second cross-sectional shape. Additionally, the device can move into a third configuration in which the anchoring member is engaged with and deformed by the subannular tissue while the valve support remains in the second cross-sectional shape.

[00137] In some embodiments, the device may comprise an atrial retainer extending from the anchoring member or the valve support to a position at least partially upstream of the native mitral annulus. The atrial extension member may comprise an atrial engagement structure adapted to engage an upstream surface (e.g., supra-annular surface) of the annulus and/or an interior wall of the atrium for further stabilizing or anchoring the device. For example, the atrial retainer can block downstream movement of the device.

[00138] Some embodiments of the device may further comprise one or more stabilizing members to inhibit the device from tilting or being displaced laterally. The stabilizing members may comprise a plurality of arms extending radially outwardly from the valve support and/or the anchoring member. The arms may be configured to extend behind the native leaflets and/or into engagement with the ventricular wall or papillary muscles.

[00139] A further embodiment, in accordance with another aspect of the present disclosure, is directed to a device for implantation at a native mitral valve, wherein the native mitral valve has an annulus and leaflets. The device can include a valve support having

upstream and downstream ends, an interior in which a valve may be coupled, and an outer surface, and include a first anchoring member having a first flared upstream portion and a first downstream portion coupled to the outer surface of the valve support. In other embodiments, the first downstream portion can be coupled to inner surface of the valve support, or in some embodiments, to an end of the valve support. The device can also include a second anchoring member at least partially surrounding the first anchoring member. The first upstream portion of the first anchoring member can be mechanically isolated from the valve support and configured to engage supra-annular tissue of the native mitral valve. The second anchoring member can have a second flared upstream portion and a second downstream portion coupled to the outer surface of the valve support, wherein the second upstream portion can be mechanically isolated from the valve support and is configured to engage subannular tissue of the native mitral valve.

[00140] In yet a further embodiment, the device for implantation can include a radially expandable anchoring member configured to engage native tissue on or downstream of the annulus. The anchoring member can have a first longitudinal length on a posterior leaflet-facing side and a second length on an anterior leaflet-facing side. In certain embodiments, the first length can be greater than the second length such that occlusion of a left ventricle outflow tract (LVOT) is limited. The device can also include a valve support, or alternatively a prosthetic valve, coupled to an interior or to an end of the anchoring member.

[00141] Other embodiments of the present technology provide a device for implantation at a native mitral valve having an annulus and leaflets, wherein the device includes a valve support having upstream and downstream ends, an interior in which a valve may be coupled, and an outer surface. The device can also include an anchoring member having a flared upstream portion and a downstream portion coupled to the outer surface of the valve support, wherein the upstream portion can have an upper ring and a lower ring coupled to the upper ring. The device can further include a plurality of flexible annulus engaging elements distributed around a circumference of the anchoring member and coupling the upper ring to the lower ring. The lower ring is configured to move in an upstream direction toward the upper ring such that the annulus is received between the upper and lower rings and within the annulus engaging elements.

[00142] The disclosure further provides systems for delivery of prosthetic valves and other devices using endovascular or other minimally invasive forms of access. For example,

embodiments of the present technology provide a system to treat a mitral valve of a patient, in which the mitral valve has an annulus. The system comprises a device to treat the mitral valve as described herein and a catheter having a lumen configured to retain the device within the catheter.

[00143] In other aspects, a system for replacing a native valve in a patient is provided. The system can include an elongated catheter body having a distal end and a proximal end, and a housing coupled to the distal end of the catheter body and having a closed end and an open end. The system can also include a plunger within the housing which is axially movable relative to the housing, and an actuator at the proximal end of the catheter body and coupled to the plunger such that moving the actuator moves the housing axially relative to the plunger. The system can further include a prosthetic valve device having a collapsed configuration and an expanded configuration. The prosthetic valve device can be positionable in the housing in the collapsed configuration and can be releasable proximally from the housing by moving the actuator.

[00144] In yet another aspect, embodiments of the present technology provide a method of treating a heart valve of a patient. The mitral valve has an annulus and leaflets coupled to the annulus. The method can include implanting a device as described herein within or adjacent to the annulus. The device, in some embodiments, can include a valve support coupled to and at least partially surrounded by an anchoring member. The anchoring member can be disposed between the leaflets and an upstream portion of the anchoring member can be configured to engage tissue on or downstream of the annulus to prevent migration of the device in an upstream direction. Further, the valve support can be mechanically isolated from the anchoring member at least at the upstream portion.

[00145] In yet a further aspect, embodiments of the present technology provide a method for replacement of a native mitral valve having an annulus and leaflets. The method can include positioning a device as described herein between the leaflets, while the device is in a collapsed configuration. The method can also include allowing the prosthetic device to expand such that an anchoring member of the prosthetic device is in a subannular position in which it engages tissue on or downstream of the annulus. The anchoring member can have a diameter larger than a corresponding diameter of the annulus in the subannular position. The method can further include allowing a valve support to expand within the anchoring member, wherein the valve support is coupled to the anchoring member. In various embodiments, the

valve support can be mechanically isolated from the anchoring member such that deformation of the anchoring member when the anchoring member engages the tissue does not substantially deform the valve support. In some arrangements, certain regions of the valve support may deform, but a support region suitable for retaining a prosthetic valve does not substantially deform such that leaflet coaptation of the prosthetic valve would not be compromised.

[00146] The devices and methods disclosed herein can be configured for treating non-circular, asymmetrically shaped valves and bileaflet or bicuspid valves, such as the mitral valve. Many of the devices and methods disclosed herein can further provide for long-term (e.g., permanent) and reliable anchoring of the prosthetic device even in conditions where the heart or native valve may experience gradual enlargement or distortion.

Cardiac and Mitral Valve Physiology

[00147] Figures 1 and 2 show a normal heart H. The heart comprises a left atrium that receives oxygenated blood from the lungs via the pulmonary veins PV and pumps this oxygenated blood through the mitral valve MV into the left ventricle LV. The left ventricle LV of a normal heart H in systole is illustrated in Figure 2. The left ventricle LV is contracting and blood flows outwardly through the aortic valve AV in the direction of the arrows. Back flow of blood or "regurgitation" through the mitral valve MV is prevented since the mitral valve is configured as a "check valve" which prevents back flow when pressure in the left ventricle is higher than that in the left atrium LA.

[00148] The mitral valve MV comprises a pair of leaflets having free edges FE which meet evenly, or "coapt" to close, as illustrated in Figure 2. The opposite ends of the leaflets LF are attached to the surrounding heart structure via an annular region of tissue referred to as the annulus AN. Figure 3 is a schematic cross-sectional side view of an annulus and leaflets of a mitral valve. As illustrated, the opposite ends of the leaflets LF are attached to the surrounding heart structure via a fibrous ring of dense connective tissue referred to as the annulus AN, which is distinct from both the leaflet tissue LF as well as the adjoining muscular tissue of the heart wall. The leaflets LF and annulus AN are comprised of different types of cardiac tissue having varying strength, toughness, fibrosity, and flexibility. Furthermore, the mitral valve MV may also comprise a unique region of tissue interconnecting each leaflet LF to the annulus AN, referred to herein as leaflet/annulus

connecting tissue LAC (indicated by overlapping cross-hatching). In general, annular tissue AN is tougher, more fibrous, and stronger than leaflet tissue LF.

[00149] Referring to Figure 2, the free edges FE of the mitral leaflets LF are secured to the lower portions of the left ventricle LV through chordae tendineae CT (referred to hereinafter "chordae") which include a plurality of branching tendons secured over the lower surfaces of each of the valve leaflets LF. The chordae CT in turn, are attached to the papillary muscles PM, which extend upwardly from the lower wall of the left ventricle LV and interventricular septum IVS.

[00150] Referring now to Figures 4A to 4B, a number of structural defects in the heart can cause mitral valve regurgitation. Ruptured chordae RCT, as shown in Figure 4A, can cause a valve leaflet LF2 to prolapse since inadequate tension is transmitted to the leaflet via the chordae. While the other leaflet LF1 maintains a normal profile, the two valve leaflets do not properly meet and leakage from the left ventricle LV into the left atrium LA will occur, as shown by the arrow.

[00151] Regurgitation also occurs in the patients suffering from cardiomyopathy where the heart is dilated and the increased size prevents the valve leaflets LF from meeting properly, as shown in Figure 4B. The enlargement of the heart causes the mitral annulus to become enlarged, making it impossible for the free edges FE to meet during systole. The free edges of the anterior and posterior leaflets normally meet along a line of coaptation C as shown in Figure 5A, but a significant gap G can be left in patients suffering from cardiomyopathy, as shown in Figure 5B.

[00152] Mitral valve regurgitation can also occur in patients who have suffered ischemic heart disease where the functioning of the papillary muscles PM is impaired, as illustrated in Figure 4A. As the left ventricle LV contracts during systole, the papillary muscles PM do not contract sufficiently to effect proper closure. One or both of the leaflets LF1 and LF2 then prolapse. Leakage again occurs from the left ventricle LV to the left atrium LA.

[00153] Figures 5A-5C further illustrate the shape and relative sizes of the leaflets L of the mitral valve. Referring to Figure 5C, it may be seen that the overall valve has a generally "D"-shape or kidney-like shape, with a long axis MVA1 and a short axis MVA2. In healthy humans the long axis MVA1 is typically within a range from about 33.3 mm to about 42.5 mm in length (37.9 +/- 4.6 mm), and the short axis MVA2 is within a range from about 26.9

to about 38.1 mm in length (32.5 +/- 5.6 mm). However, with patients having decreased cardiac function these values can be larger, for example MVA1 can be within a range from about 45 mm to 55 mm and MVA2 can be within a range from about 35 mm to about 40 mm. The line of coaptation C is curved or C-shaped, thereby defining a relatively large anterior leaflet AL and substantially smaller posterior leaflet PL (Figure 5A). Both leaflets appear generally crescent-shaped from the superior or atrial side, with the anterior leaflet AL being substantially wider in the middle of the valve than the posterior leaflet. As illustrated in Figure 5A, at the opposing ends of the line of coaptation C the leaflets join together at corners called the anterolateral commissure AC and posteromedial commissure PC, respectively.

[00154] Figure 5C shows the shape and dimensions of the annulus of the mitral valve. The annulus is an annular area around the circumference of the valve comprised of fibrous tissue which is thicker and tougher than that of the leaflets LF and distinct from the muscular tissue of the ventricular and atrial walls. The annulus may comprise a saddle-like shape with a first peak portion PP1 and a second peak portion PP2 located along an interpeak axis IPD, and a first valley portion VP1 and a second valley portion VP2 located along an intervalley axis IVD. The first and second peak portion PP1 and PP2 are higher in elevation relative to a plane containing the nadirs of the two valley portions VP1, VP2, typically being about 8-19 mm higher in humans, thus giving the valve an overall saddle-like shape. The distance between the first and second peak portions PP1, PP2, referred to as interpeak span IPD, is substantially shorter than the intervalley span IVD, the distance between first and second valley portions VP1, VP2.

[00155] A person of ordinary skill in the art will recognize that the dimensions and physiology of the patient may vary among patients, and although some patients may comprise differing physiology, the teachings as described herein can be adapted for use by many patients having various conditions, dimensions and shapes of the mitral valve. For example, work in relation to embodiments suggests that some patients may have a long dimension across the annulus and a short dimension across the annulus without well-defined peak and valley portions, and the methods and device as described herein can be configured accordingly.

Access to the Mitral Valve

[00156] Access to the mitral valve or other atrioventricular valve can be accomplished through the patient's vasculature in a percutaneous manner. By percutaneous it is meant that a location of the vasculature remote from the heart is accessed through the skin, typically using a surgical cut down procedure or a minimally invasive procedure, such as using needle access through, for example, the Seldinger technique. The ability to percutaneously access the remote vasculature is well-known and described in the patent and medical literature. Depending on the point of vascular access, the approach to the mitral valve may be antegrade and may rely on entry into the left atrium by crossing the inter-atrial septum. Alternatively, approach to the mitral valve can be retrograde where the left ventricle is entered through the aortic valve. Once percutaneous access is achieved, the interventional tools and supporting catheter(s) may be advanced to the heart intravascularly and positioned adjacent the target cardiac valve in a variety of manners, as described herein.

[00157] Using a trans-septal approach, access is obtained via the inferior vena cava IVC or superior vena cava SVC, through the right atrium RA, across the inter-atrial septum IAS and into the left atrium LA above the mitral valve MV.

[00158] As shown in Figure 6A, a catheter 1 having a needle 2 may be advanced from the inferior vena cava IVC into the right atrium RA. Once the catheter 1 reaches the anterior side of the inter-atrial septum IAS, the needle 2 may be advanced so that it penetrates through the septum, for example at the fossa ovalis FO or the foramen ovate into the left atrium LA. At this point, a guidewire may be exchanged for the needle 2 and the catheter 1 withdrawn.

[00159] As shown in Figure 6B, access through the inter-atrial septum IAS may usually be maintained by the placement of a guide catheter 4, typically over a guidewire 6 which has been placed as described above. The guide catheter 4 affords subsequent access to permit introduction of the device to replace the mitral valve, as described in more detail herein.

[00160] In an alternative antegrade approach (not shown), surgical access may be obtained through an intercostal incision, preferably without removing ribs, and a small puncture or incision may be made in the left atrial wall. A guide catheter may then be placed through this puncture or incision directly into the left atrium, sealed by a purse string-suture.

[00161] The antegrade or trans-septal approach to the mitral valve, as described above, can be advantageous in many respects. For example, the use of the antegrade approach will

usually allow for more precise and effective centering and stabilization of the guide catheter and/or prosthetic valve device. Precise positioning facilitates accuracy in the placement of the prosthetic valve device. The antegrade approach may also reduce the risk of damaging the subvalvular device during catheter and interventional tool introduction and manipulation. Additionally, the antegrade approach may decrease risks associated with crossing the aortic valve as in retrograde approaches. This can be particularly relevant to patients with prosthetic aortic valves, which cannot be crossed at all or without substantial risk of damage.

[00162] An example of a retrograde approach to the mitral valve is illustrated in Figures 7 and 8. The mitral valve MV may be accessed by an approach from the aortic arch AA, across the aortic valve AV, and into the left ventricle LV below the mitral valve MV. The aortic arch AA may be accessed through a conventional femoral artery access route, as well as through more direct approaches via the brachial artery, axillary artery, radial artery, or carotid artery. Such access may be achieved with the use of a guidewire 6. Once in place, a guide catheter 4 may be tracked over the guidewire 6. Alternatively, a surgical approach may be taken through an incision in the chest, preferably intercostally without removing ribs, and placing a guide catheter through a puncture in the aorta itself. The guide catheter 4 affords subsequent access to permit placement of the prosthetic valve device, as described in more detail herein.

[00163] In some specific instances, a retrograde arterial approach to the mitral valve may be chosen due to certain advantages. For example, use of the retrograde approach can eliminate the need for a trans-septal puncture. The retrograde approach is also more commonly used by cardiologists and thus has the advantage of familiarity.

[00164] An additional approach to the mitral valve is via trans-apical puncture, as shown in Figure 9. In this approach, access to the heart is gained via thoracic incision, which can be a conventional open thoracotomy or sternotomy, or a smaller intercostal or sub-xyphoid incision or puncture. An access cannula is then placed through a puncture, sealed by a purse-string suture, in the wall of the left ventricle at or near the apex of the heart. The catheters and prosthetic devices of the invention may then be introduced into the left ventricle through this access cannula.

[00165] The trans-apical approach has the feature of providing a shorter, straighter, and more direct path to the mitral or aortic valve. Further, because it does not involve intravascular access, the trans-apical procedure can be performed by surgeons who may not

have the necessary training in interventional cardiology to perform the catheterizations required in other percutaneous approaches.

[00166] The prosthetic treatment device may be specifically designed for the approach or interchangeable among approaches. A person of ordinary skill in the art can identify an appropriate approach for an individual patient and design the treatment apparatus for the identified approach in accordance with embodiments described herein.

[00167] Orientation and steering of the prosthetic valve device can be combined with many known catheters, tools and devices. Such orientation may be accomplished by gross steering of the device to the desired location and then refined steering of the device components to achieve a desired result.

[00168] Gross steering may be accomplished by a number of methods. A steerable guidewire may be used to introduce a guide catheter and the prosthetic treatment device into the proper position. The guide catheter may be introduced, for example, using a surgical cut down or Seldinger access to the femoral artery in the patient's groin. After placing a guidewire, the guide catheter may be introduced over the guidewire to the desired position. Alternatively, a shorter and differently shaped guide catheter could be introduced through the other routes described above.

[00169] A guide catheter may be pre-shaped to provide a desired orientation relative to the mitral valve. For access via the trans-septal approach, the guide catheter may have a curved, angled or other suitable shape at its tip to orient the distal end toward the mitral valve from the location of the septal puncture through which the guide catheter extends. For the retrograde approach, as shown in Figures 7 and 8, guide catheter 4 may have a pre-shaped J-tip which is configured so that it turns toward the mitral valve MV after it is placed over the aortic arch AA and through the aortic valve AV. As shown in Figure 7, the guide catheter 4 may be configured to extend down into the left ventricle LV and to assume a J-shaped configuration so that the orientation of an interventional tool or catheter is more closely aligned with the axis of the mitral valve MV. In either case, a pre-shaped guide catheter may be configured to be straightened for endovascular delivery by means of a stylet or stiff guidewire which is passed through a lumen of the guide catheter. The guide catheter might also have pull-wires or other means to adjust its shape for more fine steering adjustment.

Selected Embodiments of Prosthetic Heart Valve Devices and Methods

[00170] Embodiments of the present technology as described herein can be used to treat one or more of the valves of the heart as described herein, and in particular embodiments, can be used for treatment of the mitral valve. Introductory examples of prosthetic heart valve devices, system components and associated methods in accordance with embodiments of the present technology are described in this section with reference to Figures 10A-56. It will be appreciated that specific elements, substructures, advantages, uses, and/or other features of the embodiments described with reference to Figures 10A-56 can be suitably interchanged, substituted or otherwise configured with one another and/or with the embodiments described with reference to Figures 57A-71 in accordance with additional embodiments of the present technology. Furthermore, suitable elements of the embodiments described with reference to figures 10A-71 can be used as stand-alone and/or self-contained devices.

[00171] Systems, devices and methods are provided herein for percutaneous implantation of prosthetic heart valves in a heart of a patient. In some embodiments, methods and devices are presented for the treatment of valve disease by minimally invasive implantation of artificial replacement heart valves. In one embodiment, the artificial replacement valve can be a prosthetic valve device suitable for implantation and replacement of a mitral valve between the left atrium and left ventricle in the heart of a patient. In another embodiment, the prosthetic valve device can be suitable for implantation and replacement of another valve (e.g., a bicuspid or tricuspid valve) in the heart of the patient. Figure 10A shows an isometric view of a prosthetic heart valve device 100 in an expanded configuration 102 in accordance with an embodiment of the present technology, and Figure 10B is a schematic illustration of a cross-sectional view of a heart depicting the left atrium, left ventricle, and native mitral valve of the heart. Figure 10B also shows an embodiment of the expandable prosthetic valve device 100 implanted in the native mitral valve region of the heart.

[00172] As shown in Figure 10A, the device 100 can include a flexible anchoring member 110 at least partially surrounding and coupled to an inner valve support 120. The device 100 can further include a prosthetic valve 130 coupled to, mounted within, or otherwise carried by the valve support 120. Figures 10C-10F are side, perspective cut-away, top, and bottom views, respectively, of the prosthetic heart valve device 100 in accordance with the present technology. The device 100 can also include one or more sealing members

140 and tissue engaging elements 170. For example, the sealing member 140 can, in one embodiment, extend around an inner wall 141 of the anchoring member 110 and/or around an exterior surface 127 of the valve support 120 to prevent paravalvular (e.g., paraprosthetic) leaks between the device 100 and the native tissue and/or between the anchoring member 110 and the valve support 120. In another specific embodiment, and as shown in Figure 10A, the tissue engaging elements 170 can be spikes disposed on an upstream perimeter 113 of the anchoring member 110 and extend in an upward and/or radially outward direction to engage, and in some embodiments, penetrate the native tissue to facilitate retention or maintain position of the device in a desired implanted location. The tissue engaging elements 170 may also be included around an outer wall 142 of the anchoring member 110 and can extend outwardly to engage and, in some embodiments, penetrate the native valve leaflets or other adjacent tissue. Additionally, the valve support 120 can have a plurality of coupling features 180, such as eyelets, around an upstream end 121 to facilitate loading, retention and deployment of the device 100 within and from a delivery catheter (not shown), as further described herein.

[00173] The prosthetic heart valve device 100 can be movable between a delivery configuration (not shown), an expanded configuration 102 (Figure 10A), and a deployed configuration 104 (Figure 10B). In the delivery configuration, the prosthetic heart valve device 100 has a low profile suitable for delivery through small-diameter guide catheters positioned in the heart via the trans-septal, retrograde, or trans-apical approaches described herein. In some embodiments, the delivery configuration of the prosthetic heart valve device 100 will preferably have an outer diameter no larger than about 8-10 mm for trans-septal approaches, about 8-10 mm for retrograde approaches, or about 8-12 mm for trans-apical approaches to the mitral valve MV. As used herein, "expanded configuration" refers to the configuration of the device when allowed to freely expand to an unrestrained size without the presence of constraining or distorting forces. "Deployed configuration," as used herein, refers to the device once expanded at the native valve site and subject to the constraining and distorting forces exerted by the native anatomy.

[00174] Referring back to Figure 3, "subannular," as used herein, refers to a portion of the mitral valve MV that lies on or downstream DN of the plane PO of the native orifice. As used herein, the plane PO of the native valve orifice is a plane generally perpendicular to the direction of blood flow through the valve and which contains either or both the major axis

MVA1 or the minor axis MVA2 (Figure 5C). Thus, a subannular surface of the mitral valve MV is a tissue surface lying on the ventricular side of the plane PO, and preferably one that faces generally downstream, toward the left ventricle LV. The subannular surface may be disposed on the annulus AN itself or the ventricular wall behind the native leaflets LF, or it may comprise a surface of the native leaflets LF, either inward-facing IF or outward-facing OF, which lies below the plane PO. The subannular surface or subannular tissue may thus comprise the annulus AN itself, the native leaflets LF, leaflet/annulus connective tissue, the ventricular wall or combinations thereof.

[00175] In operation, the prosthetic heart valve device 100 can be intravascularly delivered to a desired location in the heart, such as an intracardiac location near the mitral valve MV, while in the delivery (e.g., collapsed) configuration within a delivery catheter (not shown). Referring to Figure 10B, the device 100 can be advanced to a position within or downstream of the native annulus AN where the device 100 can be released from the delivery catheter to enlarge toward the expanded configuration 102 (Figure 10A). The device 100 will engage the native tissue at the desired location, which will deform or otherwise alter the shape of the device 100 into the deployed configuration 104 (Figure 10B). Once released from the catheter, the device 100 can be positioned such that at least a portion of the flexible anchoring member 110 engages a subannular surface of the native valve so as to resist systolic forces and prevent upstream migration of the device 100 (Figure 10B). In the embodiment illustrated in Figure 10B, the upstream perimeter 113 of the anchoring member 110 engages the inward-facing surfaces IF (Figure 3) of the native leaflets LF, which are pushed outwardly and folded under the native annulus AN. The leaflets LF engage a ventricular side of the annulus AN and are prevented from being pushed further in the upstream direction, thus maintaining the anchoring member 110 below the plane of the native valve annulus. The tissue engaging elements 170 can penetrate the tissue of the leaflets LF and/or the annulus AN to stabilize and firmly anchor the device 100. In some embodiments, however, some portions of the anchoring member 110 may extend above the annulus AN, with at least some portions of the anchoring member 110 engaging tissue in a subannular location to prevent migration of the device 100 toward the left atrium LA. As shown in Figure 10B, the leaflets LF can lie in apposition against the outer wall 142 of the anchoring member 110 forming a blood-tight seal with the sealing member 140. The tissue engaging elements 170 can apply pressure against or, in another embodiment, penetrate the annulus AN

or leaflets LF along the outer wall 142 of the anchoring member 110 to further stabilize the device 100 and prevent migration.

[00176] In accordance with aspects of the present technology, the proximal or upper end of the anchoring member 110, while in a deployed configuration 104, conforms to the irregularly-shaped mitral annulus AN, effectively sealing the device 100 against the native annulus AN to anchor the device and to prevent paravalvular leaks. As described further herein, the anchoring member 110 mechanically isolates the valve support 120 from distorting forces present in the heart such that the anchoring member 110 may adapt and/or conform to native forces while the valve support 120 maintains its structural integrity. Accordingly, the anchoring member 110 can be sufficiently flexible and resilient and/or coupled to the valve support 120 in such a manner as to mechanically isolate the valve support 120 from the forces exerted upon the anchoring member 110 by the native anatomy. Alternatively, or in addition to the above features, the valve support 120 may be more rigid and/or have greater radial strength than the radial strength of the anchoring member 110 so as to maintain its cylindrical or other desired shape and to ensure proper opening and closing of the prosthetic valve 130 housed within the valve support structure 120. In some embodiments, the valve support 120 has a radial strength of at least 100%, or in other embodiments at least 200%, and in further embodiments at least 300%, greater than a radial strength of the anchoring member 110. In one embodiment, the valve support 120 can have a radial strength of approximately 10 N to about 12 N. Thus, if deformed from its unbiased shape by exerting a radially compressive force against its circumference, the valve support 120 can exhibit a hoop force which is about 2 to about 20 times greater for a given degree of deformation than will be exhibited by the anchoring member 110.

[00177] As illustrated in Figures 10A-10F, the anchoring member 110 has a downstream portion 111 and an upstream portion 112 opposite the downstream portion 111 relative to a longitudinal axis 101 of the device 100. The upstream portion 112 of the anchoring member 110 can be a generally outward oriented portion of the device 100, as shown in Figure 10D. In one embodiment the anchoring member 110 has a generally hyperboloidic shape, such as the shape of a two-sheet hyperboloid. In another example, the downstream portion 111 can be substantially circular in cross-section while the upstream portion 112 can be generally non-circular. In some embodiments, the anchoring member 110 can include a series of circumferentially positioned, resiliently deformable and flexible longitudinal ribs 114 which,

in some embodiments, are connected circumferentially by deformable and/or flexible connectors 116. Once deployed, at least a portion of the upstream ends of the longitudinal ribs 114 engage a subannular surface of the native valve (e.g., mitral valve). As described in more detail below, certain embodiments of longitudinal ribs 114 are configured to penetrate subannular tissue to anchor and further stabilize the device 100.

[00178] Additionally, Figures 10A-10F also illustrate that the longitudinal ribs 114 and/or circumferential connectors 116 may be arranged in a variety of geometrical patterns. In the examples shown in Figures 10A-10F, the connectors 116 are formed in a chevron configuration. One of ordinary skill will recognize that diamond-shaped patterns, sinusoidal configurations, closed cells, open cells, or other circumferentially expandable configurations are also possible. In some embodiments, the longitudinal ribs 114 may be divided along their length into multiple, separated segments (not shown), e.g. where the connectors 116 interconnect with the longitudinal ribs 114. The plurality of connectors 116 and ribs 114 can be formed from a deformable material or from a resilient or shape memory material (e.g., nitinol). In other embodiments, the anchoring member 110 can comprise a mesh or woven construction in addition to or in place of the longitudinal ribs 114 and/or circumferential connectors 116. For example, the anchoring member 110 could include a tube or braided mesh formed from a plurality of flexible wires or filaments arranged in a diamond pattern or other configuration. In another example, a metal tube can be laser cut to provide a desired rib or strut geometry. The diamond configuration can, in some embodiments, provide column strength sufficient to inhibit movement of the device 100 relative the annulus under the force of systolic blood pressure against the valve 130 mounted in the valve support 120. In a particular example, the anchoring member 120 can be formed of a preshaped nitinol tube having, for example, a wall thickness of approximately 0.010 inches to about 0.030 inches.

[00179] Figures 11A-11E show several embodiments of valve supports 120 that can be used in embodiments of the prosthetic heart valve device 100 shown in Figures 10A-10F. Figures 11A-11D are side and isometric views of the valve support 120 shown in an expanded configuration 102, and Figure 11E is an isometric view of another embodiment of a prosthetic heart valve device 100 disposed in an expanded configuration 102 in accordance with the present technology. Referring to Figures 10A-10F and 11A-11E together, several embodiments of the valve support 120 can be generally cylindrical having an upstream end 121 and a downstream end 123 formed around a longitudinal axis 101 with a circular, oval,

elliptical, kidney-shaped, D-shaped, or other suitable cross-sectional shape configured to support a tricuspid or other prosthetic valve 130. In some embodiments, the valve support 120 includes a plurality of posts 122 connected circumferentially by a plurality of struts 124. The posts 122 and struts 124 can be arranged in a variety of geometrical patterns that can expand and provide sufficient resilience and column strength for maintaining the integrity of the prosthetic valve 130. For example, the plurality of posts 122 can extend longitudinally across multiple rows of struts 124 to provide column strength to the valve support 120. However, in other embodiments, the valve support 120 can include a metallic, polymeric, or fabric mesh or a woven construction.

[00180] Generally, the plurality of posts 122 can extend along an axial direction generally parallel to the longitudinal axis 101 and the struts 124 can extend circumferentially around and transverse to the longitudinal axis 101. The posts 122 can extend an entire longitudinal height H_1 of the valve support 120 (Figure 11A), or in another embodiment, the posts 122 can include a plurality of independent and separate post segments (not shown) along the valve support height H_1 . In one embodiment the height H_1 can be approximately 14 mm to about 17 mm. The struts 124 can form a series of rings around the longitudinal axis 101, wherein each ring has a circumferentially expandable geometry. In the example shown in Figures 11A, 11D and 11E, the struts 124 are formed in a series of zig-zags and arranged in pairs 180 degrees out of phase with each other so as to form a series of diamonds. Alternative expandable geometries can include sinusoidal patterns, chevron configurations (Figure 11B), closed cells (Figure 11C), open cells, or other expandable configurations. The plurality of struts 124 can attach to the plurality of posts 122 so as to define a plurality of nodes 125 where the struts and posts intersect. The plurality of struts 124 and the plurality of posts 122 can be formed from a deformable material or a resilient or shape memory material (e.g., nitinol).

[00181] The anchoring member 110 and the valve support 120 may be made of the same or, in some embodiments, different materials. In some embodiments, both the anchoring member 110 and the valve support 120 include a resilient biocompatible metal, such as stainless steel, nickel cobalt or cobalt chromium alloys such as MP35N, or nickel titanium alloys such as nitinol. Superelastic shape memory materials such as nitinol can allow the device to be collapsed into a very low profile delivery configuration suitable for delivery through the vasculature via catheter, and allow self-expansion to a deployed configuration

suitably sized to replace the target valve. In some embodiments, the anchoring member 110 and/or the valve support 120 can be laser cut from a single metal tube into the desired geometry, creating a tubular scaffold of interconnected struts. Anchoring member 110 may then be shaped into a desired configuration, e.g. a flared, funnel-like or hyperboloid shape, using known shape-setting techniques for such materials.

[00182] As shown in Figures 11B-11E, the valve support 120 has an interior surface 126 and an exterior surface 127, and the valve support 120 is configured to receive or support the prosthetic valve 130 within an interior lumen of the valve support 120 to inhibit retrograde blood flow (e.g., blood flow from the left ventricle into the left atrium). Accordingly, the valve support 120 can provide a scaffold to which prosthetic valve tissue can be secured and provide a scaffold that has sufficient axial rigidity to maintain a longitudinal position of the prosthetic valve 130 relative to the anchoring member 110. The valve support 120 can further provide such a scaffold having radial rigidity to maintain circularity (or other desired cross-sectional shape) to ensure that leaflets 132 of the prosthetic valve 130 coapt or otherwise seal when the device 100 is subject to external radial pressure. In one embodiment, the valve support 120 can have a support region 145 along the longitudinal axis 101 that is configured to attach to the prosthetic valve, or in other embodiments, be aligned with the coaptation portion of the leaflets 132 (shown in Figure 11B).

[00183] The valve 130 may comprise a temporary or permanent valve adapted to block blood flow in the upstream direction and allow blood flow in the downstream direction through the valve support 120. The valve 130 may also be a replacement valve configured to be disposed in the valve support 120 after the device 100 is implanted at the native mitral valve. The valve 130 can have a plurality of leaflets 132, and may be formed of various flexible and impermeable materials including PTFE, Dacron[®], pyrolytic carbon, or other biocompatible materials or biologic tissue such as pericardial tissue or xenograft valve tissue such as porcine heart tissue or bovine pericardium. Other aspects of valve 130 are described further below. The interior surface 126 within the lumen of the valve support 120 can be covered at least partially by an impermeable sealing member 140 to prevent blood flow from inside the valve support 120 to the outside of the valve support 120, where it could leak around the exterior of the valve support 120. In another embodiment, the sealing member 140 may be affixed to the exterior surface 127 of the valve support 120 and, in either embodiment, may be integrally formed with or attached directly to valve 130. In an

additional embodiment, the sealing member 140 can be applied on at least portions of both the interior surface 126 and the exterior surface 127 of the valve support 120.

[00184] As shown in Figures 11B-11E, the prosthetic valve 130 can be sutured, riveted, glued, bonded, mechanically interlocked, or otherwise fastened to posts 122 or commissural attachment structures 128, which are configured to align with valve commissures C. The posts 122 or commissural attachment structures 128 can include eyelets 129, loops, or other features formed thereon to facilitate attachment of sutures or other fastening means to facilitate attachment of the prosthetic valve 130. In one embodiment, shown in Figure 11B, the attachment structures 128 can be integrated into the structural frame of the valve support 120 such that the attachment structures 128 are distributed around the circumference of the valve support 120 and function as posts 122. In another embodiment, shown in Figure 11D, the attachment structures 128 can be attachment pads formed on parts of the posts 122 (e.g., along an upper end of the posts 122). In a further embodiment, shown in Figure 11E, the attachment structures 128 can be separate structures that can be coupled to posts 122, struts 124 or other components along the interior surface 126 of the valve support 120.

[00185] As illustrated in Figure 11C, the prosthetic valve 130 may also be attached to the sealing member 140 or sleeve which is attached to the interior surface 126 of the valve support 120, as described above. Once attached, the prosthetic valve 130 can be suitable to collapse or compress with the device 100 for loading into a delivery catheter (not shown). In one embodiment, the prosthetic valve 130 has a tri-leaflet configuration, although various alternative valve configurations may be used, such as a bi-leaflet configuration. The design of the prosthetic valve 130, such as the selection of tri-leaflet vs. bi-leaflet configurations, can be used to determine the suitable shape of the valve support 120. For example, for a tri-leaflet valve, the valve support 120 can have a circular cross-section, while for a bi-leaflet valve, alternative cross-sectional shapes are possible such as oval or D-shaped cross-sections. In particular examples, the valve support can have a circular cross-sectional diameter of approximately 25 mm to about 32 mm, such as 27 mm.

[00186] In some arrangements, the valve support 120 can have a permanent prosthetic valve pre-mounted therein, or the valve support 120 may be configured to receive a separate catheter-delivered valve following implantation of the device 100 at the native mitral valve. In arrangements where a permanent or replacement valve is desirable, the valve support 120 can further include a temporary valve pre-mounted within the interior lumen. If a period of

time between placement of the device 100 and further implantation of the permanent prosthetic valve is desirable, a temporary valve sewn into or otherwise secured within the valve support 120 can assure regulation of blood flow in the interim. For example, temporary valves may be used for a period of about 15 minutes to several hours or up to a several days. Permanent or replacement prosthetic valves may be implanted within a temporary valve or may be implanted after the temporary valve has been removed. Examples of pre-assembled, percutaneous prosthetic valves include, e.g., the CoreValve ReValving® System from Medtronic/Corevalve Inc. (Irvine, CA, USA), or the Edwards-Sapien® valve from Edwards Lifesciences (Irvine, CA, USA). If adapted to receive a separate catheter-delivered valve, the valve support 120 may have features within its interior lumen or on its upper or lower ends to engage and retain the catheter-delivered valve therein, such as inwardly extending ridges, bumps, prongs, or flaps. Additional details and embodiments regarding the structure, delivery and attachment of prosthetic valves, temporary valves and replacement valves suitable for use with the prosthetic heart valve devices disclosed herein can be found in International PCT Patent Application No. PCT/US2012/043636, entitled "PROSTHETIC HEART VALVE DEVICES AND ASSOCIATED SYSTEMS AND METHODS," filed June 21, 2012.

[00187] In some arrangements, the anchoring member 110 is defined by a structure separate from the valve support 120. For example, the anchoring member 110 can be a first or outer frame or skeleton and the valve support 120 can be a second or inner frame or skeleton. As such, the anchoring member 110 can at least partially surround the valve support 120. In some embodiments, the downstream portion 111 of the anchoring member 110 can be coupled to the valve support 120 while the upstream portion 112 is not connected or coupled to the valve support 120 in a manner that unduly influences the shape of the valve support 120. For example, in some embodiments, the upstream portion 112 of the anchoring member 110 can be configured to engage and deform to the shape of the native tissue on or under the annulus while the cross-sectional shape of the valve support 120 remains sufficiently stable. For example, the valve support 120 (e.g., at least at the upstream end 121) can be spaced radially inward from the upstream portion 112 of the anchoring member 110 such that if the anchoring member 110 is deformed inwardly, at least the upstream end 121 of the valve support 120 remains substantially undeformed. As used herein, "substantially undeformed" can refer to situations in which the valve support 120 is not engaged or

deformed, or can refer to scenarios in which the valve support 120 can deform slightly but the prosthetic valve 130 remains intact and competent (e.g., the leaflets 132 coapt sufficiently to prevent retrograde blood flow). In such arrangements, leaflets 132 of the prosthetic valve 130 can close sufficiently even when the device 100 is under systolic pressures or forces from the pumping action of the heart.

[00188] The longitudinal ribs 114 and/or circumferential connectors 116 can be less rigid than the posts 122 and/or struts 124 of the valve support 120, allowing greater flexibility in the anchoring member 110 and/or more stability to the shape and position of the valve support 120. In some embodiments, the flexibility of the anchoring member 110 can allow the anchoring member 110 to absorb distorting forces as well as allow the device 100 to conform to the irregular, non-circular shape of the native annulus (while leaving the valve support 120 substantially unaffected), encouraging tissue ingrowth and creating a seal to prevent leaks between the device 100 and the native tissue. In addition, the longitudinal ribs 114 and/or connectors 116 can be configured to press radially outward against the native valve, ventricular and/or aortic structures so as to anchor the device 100 in a desired position, as well as maintain an upstream deployed circumference 150' larger than that of the native annulus such that subannular positioning effectively prevents upstream migration of the device 100 (described further below in Figure 14C). Furthermore, the longitudinal ribs 114 can have sufficient resilience and column strength (e.g., axial stiffness) to prevent longitudinal collapse or eversion of the anchoring member 110 and/or the device 100 and to resist movement of the device in an upstream direction.

[00189] By structurally separating the anchoring member 110 from the valve support 120, the valve 130 and valve support 120 are effectively mechanically isolated from the distorting forces exerted on the anchoring member 110 by the native tissue, e.g., radially compressive forces exerted by the native annulus and/or leaflets, longitudinal diastolic and systolic forces, hoop stress, etc. For example, deformation of the anchoring member 110 by the native tissue can change a cross-section of the anchoring member 110 (e.g., to a non-circular or non-symmetrical cross-section), while the valve support 120 may be substantially undeformed. In one embodiment, at least a portion of the valve support 120 can be deformed by the radially compressive forces, for example, where the anchoring member 110 is coupled to the valve support 120 (e.g., the downstream end 123). However, the upstream end 121 of the valve support 120 and/or the valve support region 145 (Figure 11B) is mechanically

isolated from the anchoring member 110 and the compressive forces such that at least the valve support region 145 can be substantially undeformed. Thus the valve support 120, and at least the valve support region 145, can maintain a circular or other desirable cross-section so that the valve remains stable and/or competent. The flexibility of the longitudinal ribs 114 can contribute to the absorption of the distorting forces, and also aid in mechanically isolating the valve support 120 and valve 130 from the anchoring member 110.

[00190] At an upstream end of the device 100 oriented toward the left atrium, the valve support 120 can be configured to sit below, even with, or above the uppermost terminal of the upstream portion 112 of the anchoring member 110. At a downstream end of the device 100 oriented toward and residing within the left ventricle, the anchoring member 110 can be coupled to the valve support 120. Alternatively, the anchoring member 110 can be coupled to the valve support 120 anywhere along a length of the valve support 120. The valve support 120 and anchoring member 110 may be coupled by a variety of methods known in the art, e.g., suturing, soldering, welding, staples, rivets or other fasteners, mechanical interlocking, friction, interference fit, or any combination thereof. In other embodiments, the valve support 120 and the anchoring member 110 can be integrally formed with one another. In yet another embodiment, a sleeve or other overlaying structure (not shown) may be attached to both the anchoring member 110 and the valve support 120 to interconnect the two structures.

[00191] Figures 12A-12C are side views of various longitudinal ribs 114 flexing in response to a distorting force F in accordance with further embodiments of the present technology. The degree of flexibility of individual longitudinal ribs 114 (and thus the anchoring member 110) may be consistent among all ribs of an anchoring member 110, or, alternatively, some ribs 114 may be more flexible than other ribs 114 within the same anchoring member 110. Likewise, a degree of flexibility of individual ribs 114 may be consistent throughout an entire length of the rib 114 or the degree of flexibility can vary along the length of each rib 114.

[00192] As shown Figures 12A-12C, the longitudinal ribs 114 (shown individually as 114A-114C) may flex along their respective lengths in response to distorting forces F that can be applied by the surrounding tissue during or after implantation of the device 100. In Figure 12A, the rib 114A may flex downward to a position 75' or upward to a position 75" in response to an upward or downward force F_1 , respectively. Similarly, in Figure 12B, a rib 114B with multiple distinct segments 85A, 85B, 85C may flex and/or rotate

inwardly/outwardly or side-to-side in response to a laterally-directed force F_2 . The distinct segment 85A at the end of the rib 114B may flex and/or rotate inwardly/outwardly or side-to-side (e.g., to position 85A') in response to the laterally directed force F_2 separate from lower distinct segments 85B and 85C. In other arrangements, the segment 85A may flex and/or rotate (e.g., to position 85AB') with the distinct segment 85B or with both segments 85B and 85C together (not shown). As shown in Figure 12C, the rib 114C having a generally linear shape when in a relaxed state, may also flex and/or rotate inwardly/outwardly or side-to-side (e.g., to positions 95' or 95'') in response to a laterally-directed force F_3 , by bending to create a curved shape, or in another embodiment not shown, by bending so as to create two substantially linear segments.

[00193] Individual ribs 114 can also have a variety of shapes and be placed in a variety of positions around a circumference of the anchoring member 110. In some embodiments, the device 100 can include a first and second plurality of ribs wherein the first plurality of ribs have a characteristic different than the second plurality of ribs. Various characteristics could include size of the rib, rib shape, rib stiffness, extension angle and the number of ribs within a given area of the anchoring member. In other embodiments, the longitudinal ribs can be unevenly or evenly spaced around an outer perimeter of the anchoring member,

[00194] The ribs 114 can be positioned around a circumference oriented along the longitudinal axis 101 of the anchoring member 110 to create any number of overall cross-sectional geometries for the anchoring member 110, e.g., circular, D-shaped, oval, kidney, irregular, etc. Figure 13A is a schematic, cross-sectional view of a prosthetic heart valve device in accordance with another embodiment of the present technology, and Figures 13B-13F are partial side views of prosthetic heart valve devices illustrating a variety of longitudinal rib configurations in accordance with additional embodiments of the present technology. Referring to Figure 13A, an individual rib 114 can comprise a plurality of linear segments, such as segments 85A and 85B. In the illustrated example, the rib segment 85B is angled radially outwardly (e.g., angled away from the longitudinal axis 101) by a first angle A_1 . The rib segment 85B extends in an upstream direction from its point of attachment to the valve support 120 at the downstream end of the segment 85B, thereby giving the anchoring member 110 a conical or flared shape, with a larger diameter D_2 at the upstream portion 112 and a smaller diameter D_3 at the downstream portion 112 of the anchoring member 110. In one embodiment, the upper rib segment 85A can be angled at a steeper second angle A_2

relative to the longitudinal axis 101 than lower rib segment 85B, resulting in a wider flared upstream portion 112A at the upstream portion 112 of the anchoring member 110. In some arrangements, the wider flared upstream portion 112A may enhance sealing between the anchoring member 110 and the native tissue, while the downstream portion 111 can provide a more rigid geometry for resisting upstream movement of the device 100 when systolic forces are exerted on the device 100. Alternatively, the rib 114 can be arcuate over all or a portion of its length, as shown in the partial side view of Figure 13B.

[00195] In yet other embodiments, as illustrated by Figures 13C-13F, the rib 114 can have a more complex shape defined by multiple distinct segments 85A, 85B, 85C, etc. For example, as shown in Figure 13C, the rib 114 includes a linear rib segment 85C generally parallel to the longitudinal axis 101 connected at its upstream end to a linear and radially outwardly extending rib segment 85B, where rib segment 85B is connected at its upstream end to a more vertical rib segment 85A which is about parallel with the longitudinal axis 101. Referring to Figure 13D, the rib 114 can include a linear rib segment 85B generally parallel to longitudinal axis 101 and connected at its upstream end to a linear and radially outwardly extending rib segment 85A, which is generally perpendicular to longitudinal axis 101. Referring to Figure 13E, the rib 114 can include a linear rib segment 85C generally parallel to the longitudinal axis 101 and connected at its upstream end to a linear and radially outwardly extending rib segment 85B which is generally perpendicular to the longitudinal axis 101. The rib segment 85B can further be connected at its most radially outward end to a vertical rib segment 85C generally parallel with the longitudinal axis 101. In reference to Figure 13F, the rib 114 includes a linear segment 85D generally parallel with the longitudinal axis 101 and connected at its upstream end to a radially outwardly extending segment 85C which is generally perpendicular to the longitudinal axis 101. The rib segment 85C can further be connected at its most radially outward end to a linear, vertical segment 85B generally parallel with the longitudinal axis 101, and where 85B is connected at its most radially outward end to a linear and radially inward extending segment 85A.

[00196] In the embodiments illustrated in Figures 13C-13F, the ribs 114 can be coupled to the valve support 120 (e.g., coupled to posts 122) in a manner to enhance mechanical isolation of the valve support 120. For example, the ribs 114 may be attached to the valve support 120 near the downstream end of the ribs 114 such that a substantial portion of each rib 114 upstream of the attachment point is movable and deformable relative to the valve

support 120, thereby allowing the rib 120 to flex radially outward or circumferentially back and forth relative to the valve support 120. Additionally, one of ordinary skill in the art will recognize that in any of the embodiments illustrated in Figures 13A-13F, any or all of the rib segments may have a curvature, and any interconnections of segments shown as angled may instead be curved. Accordingly, any of these various geometries may be configured to allow the anchoring member 110 to conform to the native anatomy, resist migration of the device 100, and mechanically isolate the valve support 120 and/or the prosthetic valve 130 contained therein from forces exerted on the anchoring member 110 by the native tissue.

[00197] The flexible characteristics of the individual ribs 114 can allow for the flexibility and conformability of the anchoring member 110 to engage and seal the device 100 against uneven and uniquely-shaped native tissue. Additionally, the flexibility can assist in creating a seal between the device 100 and the surrounding anatomy. Figure 14A is a schematic top view of a native mitral valve MV illustrating the minor axis 50 and major axis 55, and Figures 14B-14C are schematic top views of an anchoring member 110 in an expanded configuration 102 and in a deployed configuration 104, respectively, overlaying the schematic of the native mitral valve MV in accordance with an embodiment of the present technology.

[00198] Referring to Figure 14B, the upstream portion 112 (Figure 10A) of the anchoring member 110 can have an outer circumference 150 with a diameter D_1 that is greater than the minor axis 50 (Figure 14A) of the native annulus, and usually less than the major axis 55 of the annulus, when the anchoring member 110 is in an expanded configuration 102 (shown as dashed lines). In other embodiments, the anchoring member 110 may have a diameter D_1 at least as large as the distance between the native commissures C, and may be as large as or even larger than the major axis 55 of the native annulus. In some embodiments, the outer circumference 150 of the anchoring member 110 has the diameter D_1 which is approximately 1.2 to 1.5 times the diameter (not shown) of the valve support 120 (or the prosthetic valve 130), and can be as large as 2.5 times the diameter of the valve support 120 (or the prosthetic valve 130). While conventional valves must be manufactured in multiple sizes to treat diseased valves of various sizes, the valve support 120 and the prosthetic valve 130, in accordance with aspects of the present technology, may be manufactured in just a single diameter to fit a multitude of native valve sizes. For example, the valve support 120 and the prosthetic valve 130 do not need to engage and fit the native anatomy precisely. In a specific example, the valve support 120 may have a diameter (not shown) in the range of about 25mm

to about 32 mm for adult human patients. Also in accordance with aspects of the present technology, the anchoring member 110 may be provided in multiple diameters to fit various native valve sizes, and may range in diameter at an upstream end from about 28 mm to about 80 mm, or in other embodiments, greater than 80 mm.

[00199] The top view of the anchoring member 110 shown in Figure 14C illustrates how flexibility and/or deformation of one or more longitudinal ribs 114 and/or rib segments allows the anchoring member 110 to distort relative to the expanded configuration 102, as shown by the dashed lines, into a deployed configuration 104, as shown by the bolded lines. As shown in Figure 14C, the anchoring member 110, when deployed or implanted at or under the mitral valve annulus, can conform to the highly variable native mitral valve tissue shape MV, as shown in the dotted lines, while the ribs 114 bend, twist, and stretch such that the overall shape of the anchoring member 110 has a deployed (e.g., a generally more oval or D-shaped, or other irregular shape) configuration 104 instead of a fully expanded configuration 102. Referring to Figures 14B-14C together, the anchoring member 110 covers the mitral valve commissures C in the deployed configuration 104, whereas the commissures C would be left unsealed or exposed in the more circular expanded configuration 102, potentially allowing paravalvular leaks. The anchoring member 110 could also be pre-shaped to be in a generally oval or D-shape, or other shape, when in an unbiased condition.

[00200] Figure 15 is an isometric view of an embodiment of the prosthetic heart valve device 100 illustrated in a deployed configuration 104 in accordance with an embodiment of the present technology. Figure 15 illustrates the device 100 having a plurality of ribs 114, wherein a first set of ribs 160 can be configured to bend inwards or compress toward the center longitudinal axis 101 of the device 100 and a second set of ribs 162 can be configured to bend outwards or flex in response to an distorting forces present in a subannular space of the native valve. As a result, the outer circumference 150 of the anchoring member 110 may distort from a more circular shape in the expanded configuration 102, as shown by the dashed line, to a generally more oval or D-shape in the expanded configuration 104, as shown by the solid line, thus conforming to the shape of the native anatomy. In a further arrangement, the upstream portion 112 of the anchoring member 110 may be sized slightly larger than the subannular space into which it is deployed, such that the anchoring member 110 is compressed to a slightly smaller diameter in its deployed configuration 104. This may cause a slight relaxation of the sealing member 142, such that sealing member sections between

adjacent ribs 114 are sufficiently slack to billow or curve inwards or outwards to form a slack section Bi, as shown in Figure 15. Such billowing can be desirable in some arrangements because the curvature of the relaxed sleeve segment Bi can engage and conform to the mitral leaflet tissue, thereby enhancing a seal formed between the device 100 and the native tissue.

[00201] As shown in Figure 15, the unbiased, expanded configuration of the valve support 120, which in the illustrated embodiment is circular in cross-section, remains substantially unaffected while the anchoring member 110 conforms to the non-circular shape of the native mitral valve annulus MV. Accordingly, the valve support 120 is mechanically isolated from these forces and maintains its structural shape and integrity. The mechanical isolation of the valve support 120 from the anchoring member 110 may be attributed to several aspects of the prosthetic heart valve device 100. For example, the relative high flexibility of the anchoring member 110 compared with the lower flexibility of the valve support 120 allows the anchoring member 110 to deform significantly when deployed and when in operation (e.g., conform to the shape and motion of the anatomy under ventricular systole forces) while the valve support 120 remains substantially undeformed (e.g., generally circular) in these same conditions. Additionally, radial spacing between the anchoring member 110 and the valve support 120, particularly at the upstream portion/upstream end where the anchoring member 110 engages the native annulus and/or subannular tissue, allows the anchoring member 110 to be deformed inwardly a substantial amount without engaging the valve support 110. Further, the anchoring member 110 can be coupled to the valve support 120 at a location (e.g. the downstream portion 111 of the anchoring member 110) which is spaced apart longitudinally a substantial distance from the location (e.g., the upstream portion 112 of the anchoring member 110) at which the anchoring member 110 engages the native annulus, allowing the ribs 114 of the anchoring member 110 to absorb much of the distorting forces exerted upon it rather than transmitting those forces directly to the valve support 120. Moreover, the coupling mechanisms employed to attach the anchoring member 110 to the valve support 120 can be configured (e.g., to be flexible or moveable) so as to reduce the transmission of forces from the anchoring member 110 to the valve support 120 (discussed in more detail herein).

[00202] In many embodiments, the anchoring member 110 can have sufficient flexibility such that the anchoring member 110 conforms to the native mitral annulus when in the deployed configuration 104 (Figures 14C and 15); however, the anchoring member 110 can

be configured to remain biased towards its expanded configuration 102 (e.g., Figures 10A and 14B) such that, when in the deployed configuration 104, the anchoring member 110 pushes radially outwards against the native annulus, leaflets, and/or ventricular walls just below the annulus. In some arrangements, the radial force generated by the biased anchoring member shape may be sufficient to deform the native anatomy such that the minor axis 50 (Figure 14A) of the native valve is increased slightly, and/or the shape of the annulus is otherwise altered. Such radial force can enhance anchoring of the device 100 to resist movement toward the atrium when the valve 130 is closed during ventricular systole as well as movement toward the ventricle when the valve 130 is open. Furthermore, the resulting compression fit between the anchoring member 110 and leaflets and/or ventricular walls or other structures helps create a long-term bond between the tissue and the device 100 by encouraging tissue ingrowth and encapsulation.

[00203] Figures 16A-17C illustrate a prosthetic heart valve device 100 configured in accordance with additional embodiments of the present disclosure. Figures 16A-16C include a top view and first and second side views of a prosthetic heart valve device 100 illustrated in an expanded configuration 102 that includes features generally similar to the features of the prosthetic heart valve device 100 described above with reference Figures 10A-15. For example, the device 100 includes the valve support 120 and the prosthetic valve 130 housed within an interior lumen of the valve support 120. However, in the embodiment shown in Figures 16A-16C, the device 100 includes an anchoring member 210 having an oval or D-shaped upstream perimeter 213 and a plurality of elevations around a circumference 250 of the anchoring member 210 such that the anchoring member 210 is suitable for engaging and conforming with tissue in the subannular region of the mitral valve.

[00204] Referring to Figures 16A-16C together, the device 100 can include the flexible anchoring member 210 at least partially surrounding and coupled to the valve support 120 at a downstream portion 211 of the anchoring member 210. The device 100 can also include one or more sealing members 140 extending around an inner wall 241 of the anchoring member 210 and/or around the exterior surface 127 or the interior surface 126 of the valve support 120 to prevent paravalvular leaks between the device 100 and the native tissue and/or between the anchoring member 210 and the valve support 120. In one embodiment, the sealing member 140 can wrap around and/or cover the upstream perimeter 213 of the anchoring member 210. For example, the sealing member 140 can be sewn, sutured, or adhered to a wall 241, 242 and

have an extended portion (not shown) that folds over the upstream perimeter 213. In one embodiment, the sealing member 140 can be adhered to an opposite wall (e.g., extend from the inner wall 241 to cover the upstream perimeter 213 and attached to an upper portion of the outer wall 242). However, in other embodiments, the sealing member 140 can have a longer free edge (not shown) left unattached. The free edge of the sealing member 140 can be suitable in some arrangements to inhibit blood flow between the upper perimeter 213 and the native tissue.

[00205] As illustrated in Figures 16B-16C, the anchoring member 210 has the downstream portion 211 and an upstream portion 212 opposite the downstream portion 111 along a longitudinal axis 201 of the device 100. Similar to the anchoring member 110 of device 100 (Figure 10A), the upstream portion 212 of the anchoring member 210 can be a generally outward oriented portion of the device 100. In some embodiments, the anchoring member 110 can include of a series of circumferentially positioned, resiliently deformable and flexible ribs 214 which can be in a crisscross pattern around the circumference 250 of the anchoring member 210 to form a diamond pattern. In one embodiment, the ribs 214 can be flexible wires or filaments arranged in a diamond pattern or configuration. The diamond configuration can, in some embodiments, provide column strength sufficient to inhibit movement of the device 100 relative the annulus under the force of systolic blood pressure against the valve 130 mounted in the valve support 120. In a particular example, the anchoring member 120 can be formed of a preshaped nitinol tube having, for example, a wall thickness of approximately 0.010 inches to about 0.030 inches. The diamond pattern or configuration can, for example, include one or more rows of diamonds, and in some embodiments, between approximately 12 and approximately 36 columns of diamonds around the circumference 250 of the anchoring member 210.

[00206] In some embodiments, the upstream perimeter 213 of the anchoring member 210 does not lie in a single plane. For example, the ribs 214 can have variable lengths and/or be off-set from each other at variable angles such that a distance (e.g., elevation) between a downstream perimeter 215 and the upstream perimeter 213 can vary around the circumference 250. For example, the upstream perimeter 213 can form a rim having a plurality of peaks 251 and valleys 252 (Figure 16B) for adapting to the shape of the native mitral valve (see Figure 5C). As used herein, “peaks” and “valleys” do not refer to diamond peaks and diamond valleys of a diamond pattern formed by the plurality of ribs 214, but refers

to portions of the upstream perimeter 213 having an undulating shape formed by changes in elevation with respect to the downstream perimeter 215. In one embodiment, the distance between the downstream perimeter 215 and the upstream perimeter (e.g., elevation) can vary from about 6 mm to about 20 mm, and in another embodiment, between about 9 mm and about 12 mm.

[00207] In one embodiment, the upstream perimeter 213 of the anchoring member 210 can have two peaks 251 that are separated by two valleys 252. In some embodiments, a first peak can have a different shape or elevation than that of a second peak. In other embodiments, the shape of a valley 252 can be different than a shape of an inverted peak 251. Accordingly, the peaks 251 and valleys 252 can be asymmetrically positioned and shaped around the circumference 250 of the anchoring member 210. In various arrangements, the valleys 252 can be configured for positioning along commissural regions of the native annulus, and the peaks 251 can be configured for positioning along leaflet regions of the native annulus. In one embodiment, the peaks 251 can have apices configured to be positioned near midpoint regions of the leaflets.

[00208] Referring to Figures 17A-17C, one specific example of the anchoring member 210 can have a first elevation E_1 between the downstream perimeter 215 and the upstream perimeter 213 of approximately 7 mm to about 8 mm at first and second regions 253, 254 of the anchoring member. The first and second regions 253, 254 are configured to align with the first and second commissures (e.g., anterolateral commissure AC and posteromedial commissure PC, Figure 5A) of the native mitral valve. The anchoring member 210 can also have a second elevation E_2 between the downstream perimeter 215 and the upstream perimeter 213 of approximately 9 mm to about 11 mm at a third region 255 of the anchoring member 210, wherein the third region 255 is configured to align with an anterior leaflet AL (Figure 5A) of the native mitral valve. The anchoring member 210 can further have a third elevation E_3 between the downstream perimeter 215 and the upstream perimeter 213 of approximately 12 mm to about 13 mm at a fourth region 256 of the anchoring member 210 opposite the third region 255, wherein the fourth region 256 is configured to align with a posterior leaflet PL (Figure 5A) of the native mitral valve. One of ordinary skill in the art will recognize that the elevations E_1 , E_2 and E_3 can have other measurements, and in some embodiments, the elevations E_1 , E_2 and E_3 can be different from one another or the same.

[00209] Additionally, the upstream perimeter 213 can form a rim having a generally oval or D-shape, or other irregular shape for adapting to the shape of the native mitral valve. For example, and referring to Figure 17A, the upstream perimeter 213 of the anchoring member 210 can have a major perimeter diameter D_{m1} and a minor perimeter diameter D_{m2} perpendicular to the major perimeter diameter D_{m1} . In one embodiment, the major perimeter diameter D_{m1} is greater than the long axis MVA1 of the native mitral valve (shown in Figure 5C) when the device 100 is in the expanded configuration 102 (Figure 17A). In another embodiment, the major perimeter diameter D_{m1} is less than the long axis MVA1 when the device 100 is in the expanded configuration 102. In such embodiments, the device 100 can be configured to have a major perimeter diameter D_{m1} that is greater than the long axis MVA1 when the device is in the deployed configuration (e.g., when engaging the tissue on or under the native annulus, see Figure 16E). Further, the minor perimeter diameter D_{m2} can be greater than the short axis MVA2 of the native mitral valve (shown in Figure 5C) when the device 100 is in the expanded configuration 102 (Figure 17A), or alternatively in the deployed configuration (Figure 16E). In one embodiment, the major perimeter diameter D_{m1} and/or minor perimeter diameter D_{m2} can be approximately 2 mm to approximately 22 mm, or in another embodiment, approximately 8 mm to approximately 15 mm greater than the long axis MVA1 and/or the short axis MVA2, respectively, of the native mitral valve. In some embodiments, the major perimeter diameter can be approximately 45 mm to about 60 mm and the minor perimeter diameter can be approximately 40 mm to about 55 mm.

[00210] Again referring to Figure 16C, the upstream portion 212 of the anchoring member 210 can be radially separated from the valve support 120 by a gap 257. In one embodiment, the gap 257 is greater on an anterior leaflet facing side of the device 100 (e.g., along the third region 255) than on a posterior leaflet-facing side of the device 100 (e.g., along the fourth region 256).

[00211] Referring back to Figures 16A and 16C, the valve support 120 can be oriented along the first longitudinal axis 101 and the anchoring member 210 can be oriented along the second longitudinal axis 201. The second longitudinal axis 201 can be off-set from the first longitudinal axis 101. “Off-set” can refer to an arrangement where the axes 101, 201 are parallel but separated such that the gap 257 can vary around the circumference 250 (Figure 16C). Figure 16D shows another embodiment in which “off-set” can refer to an arrangement wherein the second axis 201 can be angled from the first axis 101 (e.g., the first and second

101, 201 axes are non-collinear or non-parallel) such that the anchoring member 210 is generally tilted with respect to the valve support 120. In one embodiment, the second longitudinal axis 201 is disposed at a tilt angle A_{TL} between 15° and 45° relative to the first longitudinal axis 101.

[00212] In additional embodiments, and as shown in more detail in Figure 18, the first and second regions 253 and 254 of the upstream perimeter 213 can extend further from the longitudinal axis 201 than the third 255 and fourth regions 256. For example, the anchoring member 210 can have a generally conical body (shown in dotted lines) and have upstream rim extensions 258 in the first and second regions 253 and 254. In some embodiments, the third region 255 of the upstream perimeter 213 can extend further from the longitudinal axis 201 than the fourth region 256. In some arrangements, the third region 255 can have a size and shape that allows the anchoring member 210 to engage the inward facing surface of the anterior leaflet without substantially obstructing the left ventricular outflow tract (LVOT).

[00213] Referring to Figures 17A-17C together, the valve support 120 can be oriented along the longitudinal axis 101, and the upstream portion 212 of the anchoring member 210 can flare outward from the longitudinal axis 101 by a taper angle A_T . In embodiments where the ribs 214 are generally curved outward from the downstream portion 211 to the upstream portion 212 (rather than linear), the taper angle A_T can continuously change between the downstream portion and the upstream portion. In some embodiments, the taper angle A_T can be the same around the circumference 250 of the upstream portion 212 of the anchoring member 210; however, in other embodiments, the taper angle A_T can vary around the circumference 250. For example, the anchoring member 210 can have a first taper angle A_{T1} at the first and second regions 253 and 254 (Figure 17B) which can be configured to align with the anterolateral commissure AC and posteromedial commissure PC (see Figure 5C), respectively. The anchoring member 210 can further have a second taper angle A_{T2} at the third region 255 which can be configured to align with the anterior leaflet, and a third taper angle A_{T3} at the fourth region 256 which can be configured to align with the posterior leaflet (Figure 17C). In one embodiment, the taper angle can be approximately 30° to about 75° , and in another embodiment, between approximately 40° and about 60° .

[00214] Figure 16E is a schematic top view of a native mitral valve in the heart viewed from the left atrium and showing the prosthetic treatment device 100 of Figure 16A-16C implanted at the native mitral valve MV in accordance with an embodiment of the present

technology. Once deployed, and as illustrated in Figure 16E, at least a portion of the upstream ends of the ribs 214 (shown in Figures 16B-16C) engage a subannular surface of the native valve (e.g., mitral valve). As described in more detail below, certain embodiments of ribs 114 or 214 are configured to penetrate subannular tissue to anchor and further stabilize the devices 100.

[00215] Although the anchoring member 210 is deformable in response to distorting forces exerted by the native anatomy, the valve support 120 can have sufficient rigidity to maintain a circular or other original cross-sectional shape, thus ensuring proper functioning of the prosthetic valve leaflets 132 when opening and closing. Such mechanical isolation from the anchoring member 210 may be achieved by the valve support 120 having sufficient rigidity to resist deformation while anchoring member 210 is deformed, and by selecting a location and means for coupling the valve support 120 to the anchoring member 210 so as to mitigate the transmission of forces through the anchoring member 210 to the valve support 120 or the prosthetic valve 130 contained therein. For example, the valve support 120 may be coupled to the anchoring member 210 only at the downstream end 123 of the valve support 120, which is separated from the upstream end 121 where the anchoring member 210 engages the annulus. On the upstream end 121 of the anchoring member 210, the valve support 120 may be completely unconnected to and spaced radially apart from the anchoring member 210 by the gap 257 to allow deformation of the anchoring member 210 without impacting the shape of valve support 120 (see Figures 16A-16C where the prosthetic valve 130 is located). Thus, forces exerted on the anchoring member 210 by the annulus can be absorbed by the flexible ribs 214 of the anchoring member 210 to mitigate transmission of such forces to the downstream end 123 of valve support 120.

[00216] In some embodiments, it may be desirable to limit a distance the device 100 extends downstream of the annulus into the left ventricle (e.g., to limit obstruction of the left ventricle outflow tract (LVOT)). Accordingly, some embodiments of the device 100 can include anchoring members 210 having a relatively low overall elevation (e.g., elevations E_1 , E_2 and E_3 , Figures 17B-17C), such that the anchoring member 210 does not extend into or obstruct the LVOT. As shown in the side view of Figure 16B, for example, the anchoring member 110 can have a low overall elevation E_L (e.g., the distance between the upstream perimeter 213 and the downstream perimeter 215 of the anchoring member 210) with respect to a height H_V of the valve support 120. In such embodiments, the upstream perimeter 213 of

the anchoring member 110 may be just below, adjacent to, or positioned within the annulus of the native mitral valve while the downstream perimeter 215 of the anchoring member 210 is configured to extend minimally into the left ventricle below the native mitral valve annulus when the device 100 is implanted. In some arrangements, the valve support 120 can be coupled to anchoring member 210 so as to also minimize protrusion into the left ventricle, and in some embodiments, may extend upwardly through the plane of the native annulus into the left atrium.

Additional Components and Features Suitable for Use with the Prosthetic Heart Valve Devices

[00217] Additional components and features that are suitable for use with the prosthetic heart valve devices (e.g., devices 100 described above) are described herein. It will be recognized by one of ordinary skill in the art that while certain components and features are described with respect to a particular device (e.g., device 100), the components and features can also be suitable for use with or incorporated with other devices as described further herein.

[00218] As discussed above with respect to Figure 10A, some embodiments of the prosthetic heart valve device 100 can include a sealing member 140 that extends around portions of the anchoring member 110 and/or the valve support 120. For example, the embodiment illustrated in Figure 10A has a sealing member 140 around the inner wall 141 of the anchoring member 110 and around an exterior surface 127 of the valve support 120 to prevent paravalvular leaks both between the device 100 and the anatomy but also through components of the device 100.

[00219] Figures 19A-19C are isometric, side and top views, respectively, of a prosthetic heart valve device 100 having a sealing member 140 in accordance with a further embodiment of the present technology. Referring to Figures 19A-19C together, the device 100 includes a sealing member 140, such as a skirt 144. The skirt 144 can be disposed on the outer wall 142 or disposed on the inner wall 141 and at least partially over the upstream perimeter 113 of the anchoring member 110. Accordingly, the skirt 144 can be fixed and/or coupled to any surface of the anchoring member 110. The skirt 144 can also overlay an interior surface 126 (shown in Figure 19A) and/or exterior surface 127 of the valve support 120. Variations of the skirt 144 and/or other sealing members 140 can be configured to (1) create a blood flow-inhibiting seal between the anchoring member 110 and the native tissue,

(2) block blood flow through the walls 141, 142 of the anchoring member 110 and/or through the surfaces 126, 127 of the valve support 120, and (3) block blood flow through the space between the valve support 120 and the anchoring member 110. In some embodiments, the sealing member 140 can be configured to promote in-growth of adjacent tissue. The sealing member 140 can help to seal between the anchoring member 110 and the valve support 120, as well as between the device 100 and the surrounding anatomy such that blood flow is restricted to flowing through the prosthetic valve 130 from the left atrium to the left ventricle. Additionally, the sealing member 140 can provide circumferential support for the anchoring member 110 when in the expanded configuration 102 (Figures 10A, 16A and 19A) or deployed configuration 104 (Figures 10B and 16B). In some embodiments, the sealing member 140 may further serve to attach the anchoring member 110 to the valve support 120. For example, the skirt 144 can be coupled to the inner wall 141 of the anchoring member 110 and integrally formed with or otherwise attached to the sealing member 140 that is coupled to the valve support 120. In other embodiments, the sealing member 140 can be used to couple the valve support 120 to the prosthetic valve 130 housed in the interior of the valve support 120. Sealing members 140, such as skirts 144, can be coupled to the anchoring member 110 and/or valve support 120 with sutures, rivets or other known mechanical fasteners. In other embodiments, adhesives, glues and other bonding materials can be used to couple the sealing members to components of the device 100.

[00220] Figure 20A is an isometric view of a prosthetic heart valve device 100 without a sealing member 140, and Figures 20B-20E are isometric views of prosthetic heart valve devices 100 having sealing members 140 in accordance with additional embodiments of the present technology. For example, Figures 20B-20C show embodiments of the device 100 in which the sealing member 140 is a sleeve 146. The sleeve 146 can include an impermeable sealing material that is cylindrical and configured to fit within or over various frame or skeleton structures of the device 100 as further described below. In Figure 20B the sleeve 146 is on the exterior surface 127 of the valve support 120, whereas in Figure 20C, the sleeve 146 is also disposed on the inner wall 141 of the anchoring member 110 and on the exterior surface 127 of the valve support 120. Figure 20D illustrates an embodiment of the device 100 in which the sleeve 146 is disposed on the outer wall 142 of the anchoring member 110 and on the exterior surface 127 of the valve support 120. Referring to Figure 20E, the device 100

can also incorporate the sleeve 146 on both the outer wall 142 and inner wall 141 of the anchoring member 110 as well as on the exterior surface 127 of the valve support 120.

[00221] One of ordinary skill in the art will recognize that the sealing members 140, such as the skirts 144 and sleeves 146 shown in Figures 19A-20E, can fully cover the walls 141, 142 or surfaces 126, 127, or in other embodiments, at least partially cover the walls 141, 142, and/or the surfaces 126, 127 of the anchoring member 110 and the valve support 120, respectively. Any combination of sealing members 140 is contemplated. Additionally, the sealing member 140 can comprise a single continuous sheet of fluid impervious material (e.g., for covering the inner surface 141 of the anchoring member 110 and the exterior surface 127 of the valve support 120), which could create a seal between the anchoring member 110 and the valve support 120. In various embodiments, the sealing member 140, such as the skirt 144 or sleeve 146, can comprise a fabric or other flexible and biocompatible material such as Dacron[®], ePTFE, bovine pericardium, or other suitable flexible material to integrate with tissue and minimize paravalvular leaks. In other embodiments, the sealing member 140 can include a polymer, thermoplastic polymer, polyester, Gore-tex[®], a synthetic fiber, a natural fiber or polyethylene terephthalate (PET). The valve 130 may also be attached to the sealing member 140 or integrally formed with the sealing member 140.

[00222] In a further embodiment, shown in Figures 21A-21F, the valve support 120 may comprise a tubular member 148 of fabric, polymer, or pericardium with little or no metallic or other structural support. Referring to Figures 21A-21B, the tubular member 148 may be a thicker and more rigid portion of a sleeve 146 which is capable of retaining its shape and has sufficient strength to resist radial and axially tensile forces during systole, and axial compressive forces during diastole. The leaflets 132 of the prosthetic valve 130 may be integrally formed with, sewn or otherwise attached to the tubular member 148. In one embodiment, the tubular member 148 can be integrally formed with an outer portion 146A of the sleeve 146 that extends around the anchoring member 110 (shown in Figure 21A), or in another embodiment, the tubular member 148 can be a separate and/or thicker member which is sewn, bonded, or otherwise fastened to the sleeve 146 in a blood-tight manner. The tubular member 148 can optionally include reinforcing members to give it greater strength and to help it retain a desirable shape suitable for operating the valve 130. For example, a series of relatively stiff longitudinal struts 190 of metal or polymer can be coupled to or embedded within the walls of tubular member 148 (Figure 21C), and/or a wire coil 192 may extend

around or be embedded within walls of the tubular member 148 (Figure 21D). In a further embodiment, a series of tethers 194 can be coupled between the outer portion 146A of the sleeve 146 and tubular member 148 (Figure 21E). In one arrangement, the tethers 194 can extend at a downstream angle from the upstream portion 112 of the anchoring member 110 so as to inhibit collapse or structural compromise of the tubular member 148 during atrial systole. In yet another embodiment, a plurality of vertical septa 196 may be interconnected between the anchoring member 110 (and/or a sealing member 140 coupled to the inner wall 141 of the anchoring member 110) and the tubular member 148 (Figure 21F). The plurality of vertical septa 196 coupled between the anchoring member 110 and the valve support 120 can be a flexible fabric or polymer, and in some embodiments, can be the same material used for the sleeve 146. The septa 196, which can be collapsed with the anchoring member 110 to a low profile delivery configuration (not shown) can also constrain the outward deflection of the ribs 114 when the device 100 is in the expanded configuration 102.

[00223] As described herein, the anchoring member 110 can be a structure or component separate from the valve support 120. In one embodiment, the anchoring member 110 can be coupled to the valve support 120 at, for example, a downstream end 123 of the valve support 120, while the upstream portion of the anchoring member 110 can remain uncoupled to the valve support 120 and/or otherwise be mechanically isolated from the valve support 120. The anchoring member 110 can be coupled to the valve support 120 using a variety of mechanisms, including flexible, or non-rigid, coupling mechanisms. Figures 22A-22G and 22I-22K are enlarged side views of various mechanisms of coupling the valve support 120 to the anchoring member 110 that allow relative movement between the downstream portions of the anchoring member 110 and the valve support 120 or otherwise provide mechanical isolation of the valve support 120 from the anchoring member 110 in accordance with additional embodiments of the present technology.

[00224] Figures 22A-22B illustrate a downstream end 326 of a rib 114 of the anchoring member 110 coupled to a post 122 of the valve support 120. In a first embodiment, the rib 114 can be coupled to the post 122 by a suture, wire or other suitable filament 310 which is wrapped around the adjacent elements and tied (Figure 22B). In some embodiments, either or both the rib 114 and the post 122 may have a feature to which the filament 310 may be secured, such as a through-hole 312 (Figure 22C), a loop or eyelet 314 (Figure 22D), or a

groove 316 configured to retain the filament 310 therein and inhibit sliding along the rib 114 or post 122.

[00225] In another embodiment shown in Figure 22F, the rib 114 can be coupled to the post 122 by a rivet, screw, pin, or other fastener 318 which passes through aligned holes 319 in the rib 114 and the post 122. Alternatively, and as shown in Figures 22G-22H, the post 122 may have a cavity 320 in its outer wall configured to receive a downstream end 326 of rib 144, and the two elements 114, 122 can be fastened together by a filament or fastener 322. In this arrangement, a substantial portion of the systolic force exerted on the valve support 110 can be translated directly to the rib 114 because the downstream end of the rib 114 engages the floor of the cavity 320, thereby relieving the suture or fastener 322 from having to resist such force.

[00226] In further embodiments shown in Figures 22I-22J, a downstream end 326 of the rib 114 passes through a passage 324 formed through the post 122. The downstream end 326 is then secured to post 122 by a fastener 328 or a filament like those described above. Additionally, because the rib 114 is held within the passage 324, the systolic loads exerted on the valve support 120 can be translated directly to the ribs 114 rather than to the fastener 328. In yet another embodiment shown in Figure 22K, a downstream end 330 of the post 122 is formed radially outward in a hook or J-shape, forming a channel 332 in which a downstream end 326 of the rib 114 can be received. The ends 330, 326 of the two elements may be secured by a fastener 334 passing through holes 319 in the rib 114 and the post 122. Systolic loads applied to the post 122 can be translated directly to the rib 114 via channel 332, relieving fastener 334 from bearing a substantial portion of the load.

[00227] Figures 23A-23B illustrate further embodiments of mechanisms suitable for coupling the anchoring member 110 to the valve support 120. In the embodiments shown in Figures 23A-23B, circumferential connectors 116 of the anchoring member 110 are coupled to the struts 124 of the valve support 120. For example, in Figure 23A, the connectors 116 are formed so as to have an hourglass-shaped portion 336 forming a waist 338 and an enlarged connector head 340 forming a connector cell 341. Struts 124 similarly have an enlarged strut head 346 forming a strut cell 347. The hourglass portion 336 of the connector 116 can be configured to pass through the strut cell 347 such that the strut head 346 extends around the waist 338 of the connector 116. The connector head 340 can be sufficiently large that it is prevented from being released from the strut cell 347. Further, due to the diverging

angles of connector segments 116A, 116B, the strut head 346 can be prevented from sliding upward relative to the connector head 340. In such arrangements, systolic loads exerted in the upward direction on the valve support 120 can be translated through the struts 124 to the connectors 116, which in turn translate these forces to the ribs 114 which are driven into the native anatomy to anchor the device 100 in place.

[00228] In Figure 23B, the connectors 116 can be formed so as to have a loop portion 348 extending downwardly which is nested in a concave portion 350 formed in the strut 124. The loop portion 348 can be fastened to the concave portion 350 in various ways, e.g. by a suture 352 wrapped around each member 348, 350. In this arrangement, systolic loads applied to valve support 120 in the upstream direction can be transferred through the concave portion 350 to loop portions 348 of the anchoring member 110.

[00229] In other embodiments, the anchoring member 110, or selected components thereof, can be integrally formed with the valve support 120. As shown in Figure 24A, the ribs 114 of the anchoring member 110 can be integrally formed with posts 122 of the valve support 120 with a U-shaped bridge member 356 interconnecting each rib 114 to respectively aligned posts 122. The ribs 114 may be circumferentially interconnected by expandable connectors 116 formed integrally therewith. Alternatively, in the embodiment shown in Figure 24A, a plurality of separate bands or wires 358 extend around the circumference 150 of the anchoring member 110 and are each slideably coupled to the ribs 114, e.g. by extending through a hole 360 formed in each individual rib 114. The flexible bands or wires 358 permit ribs 114 to be collapsed inwardly to a low-profile delivery configuration (not shown), while limiting the outward deflection of the ribs 114 when in the expanded configuration 102. Alternatively, a tether 361 of wire or suture may be coupled between the individual ribs 114 and the posts 122 (shown in Figure 24B) to limit the outward deflection of the ribs 114 when in the expanded configuration 102.

[00230] In further embodiments, a sleeve 146 may be secured to the ribs 114 in a manner which limits the outward deflection of the ribs 114 when the device 100 is in the expanded configuration (shown in Figure 24C). The sleeve 146 may, for example, extend around the outer side of each rib 114 as shown in Figure 24C to constrain it from expanding outwardly beyond a predetermined limit. Optionally, the sleeve 146 may further include a horizontal septum 359 extending between an inner portion 146B of the sleeve 146 that extends around the valve support 120 and an outer portion 146A of the sleeve 146 that extends around the

anchoring member 110. The horizontal septum 359 can more rigidly constrain the outward flexion of the ribs 114. In some embodiments, the septum 359 can also seal the annular cavity 163 formed by the septum 359 between the inner portion 146B and the outer portion 146A to limit blood flow into this cavity 163 and minimizing clot formation therein. Alternatively, openings (not shown) may be formed in the sleeve 146 downstream of the septum 359 which can permit blood to flow into the enclosed cavity 163 to form a region of clot, thereby limiting the deflection of the ribs 114 and making the device more rigid and securely anchored. The septum 359, which can be a flexible fabric, polymeric, or pericardial material, can be located at the upstream end of the device 100 as shown, or at a location spaced further downstream from the upstream end 121 of the valve support 120. In a further embodiment shown in Figure 24D, each individual rib 114 can be constrained within a passage 364 formed in the sleeve 146 by suturing or bonding two layers of sleeve fabric together. In the expanded configuration 102, the movement of the ribs 114 can be limited relative to the sleeve 146.

[00231] Figure 25A is a partial cross-sectional view of a prosthetic heart valve device 100 having an anchoring member 110 and a valve support 120, and Figure 25B is an enlarged view of the designated box shown in Figure 25A in accordance with an embodiment of the present technology. As shown in Figures 25A and 25B, there can be a gap 108 between the valve support 120 and lower portion 111 of the anchoring member 110. If the gap 108 exists, the gap 108 can be protected by a sleeve 146 to prevent blood from leaking between the anchoring member 110 and the valve support 120 in either an upstream or downstream direction.

[00232] Figures 26A-26D are schematic cross-sectional views of prosthetic heart valve devices 100 having atrial retainers 410 and implanted at a native mitral valve MV in accordance with various embodiments of the present technology. Figures 26A-26C show several embodiments of the device 100 in which the device 100 includes an atrial retainer 410 configured to engage a supra-annular surface of the annulus AN or other tissue within the left atrium to assist the native leaflets in preventing downstream migration of the device 100 into the left ventricle. In these arrangements, the annulus AN can be sandwiched between a top circumference 150 of the anchoring member 110 and a bottom surface of the atrial retainer 410.

[00233] As shown in Figure 26A, one embodiment of the device 100 can include the atrial retainer 410 coupled to or integrally formed with the inner valve support 120. The atrial retainer 410 can extend upstream through the annulus AN and into a supra-annular space within the atrium and engage the supra-annular surface or other atrial tissue with an outwardly extending flange 420. In another embodiment shown in Figure 26B, the atrial retainer 410 can comprise a plurality of fingers 412 which may be formed integrally with or otherwise coupled to the valve support 120 (e.g. comprising upward extensions of posts 122 or upward extensions of the anchoring member 110). The fingers 212 can be generally uncovered or exposed within the left atrium as illustrated in Figure 26B; however, in another embodiment, the fingers 412 can be covered with a sealing member (not shown) or other covering of fabric, polymeric sheet, or pericardial tissue extending around the outside or inside surfaces of the fingers 412 to form a conical shape to help seal the device 100 with the native tissue on the atrial side of the annulus AN and to help funnel blood into the prosthetic valve 130 (Figure 10A). The fingers 412 may also include circumferential struts (not shown) interconnecting the fingers 412 to limit lateral deflection and enhance the stiffness of the fingers. The fingers 412 can include a resilient shape memory material (e.g., nitinol) such that the fingers can be straightened and deflected inwardly for delivery and be released to an unbiased, radially projecting outward position in the expanded configuration 102 as shown. For example, the fingers 412 can have finger tips 414 biased outwardly and, in some arrangements, in the downstream direction in the expanded configuration 102. During delivery to a desired position within the native mitral valve MV, the device 100 can be unsheathed in the distal or downstream direction (discussed in more detail below), such that the fingers 412 are first released to engage the atrial side of the valve annulus AN. This indexes the position of the device 100 relative to the native valve to ensure that the anchoring member 110 is positioned on the ventricular side of the native annulus AN but not overextended into the ventricle when it is unsheathed and expanded.

[00234] The atrial retainer 410 may alternatively be an extension of the anchoring member 110. In one embodiment shown in Figure 26C, the atrial retainer 410 can include a plurality of atrial loops 416, which, although depicted in a more vertical plane, may alternatively lie in a plane more parallel to the plane of the native annulus AN, and which extend upstream through the annulus AN, then extend radially outwardly to engage a supra-annular surface. The loops 416, which may comprise extensions of one or more ribs 114 of

the anchoring member 110, can include a resilient shape-memory metal (e.g., nitinol) or other material that may be compressed into a low profile shape for delivery then released to expand to the radially-extended configuration shown in Figure 26C. Similar to the device 100 of Figure 26C, Figure 26D is also a cross-sectional view of a prosthetic heart valve device 100 that includes an atrial retainer 410 formed by an extension of the anchoring member 110. As shown in Figure 26D, the atrial retainer 410 can include a cylindrical portion 418 which extends upwardly from the anchoring member 110 through the native annulus AN, with a flange 420 at the proximal region which extends over the atrial side of the native annulus AN to engage the supra-annular surface. The flange 420 can include a resilient shape memory material (e.g., nitinol) that can be collapsed for delivery and expand when deployed at the native mitral valve MV. The cylindrical portion 418 and flange 420 may be integrally formed with the anchoring member 110, e.g. comprised of extensions of the ribs 114, or in another embodiment, can be coupled to one or more portions of the anchoring member 110 and/or the valve support 120.

[00235] In other embodiments, the prosthetic heart valve device 100 can include atrial extending features that assist in retaining the device 100 in a desired location within the native mitral valve, but do not substantially engage atrial or supra-annular tissue. For example, Figure 27 is a side view of an anchoring member 110 having a vertical portion 422 at the upstream end 424 for engaging the annulus AN in accordance with another embodiment of the present technology. The anchoring member 110 can include the lower portion 111 and the upper flared portion 112 which is positionable in a subannular location between the leaflets LF and downstream of the annulus AN. The upstream portion 112 can be expandable to a dimension that is larger than a corresponding dimension of the subannular tissue and/or inward facing leaflets LF. The vertical portion 422 can be fitted within the annulus orifice so as to engage the annulus AN around an entire upstream circumference 150 of the anchoring member 110. The vertical portion 422 can be expandable to a dimension that is larger than a corresponding dimension of the annulus AN such that radial expansion of the vertical portion 422 presses outwardly against the native tissue to assist retaining the device in the desired location with the native mitral valve. Optionally, the anchoring member 110 can also include a plurality of tissue engaging elements 170, such as spikes. In one embodiment, the spikes (shown here as tissue engaging elements 170) can be distributed around the circumference 150 of the upper portion 112 of the anchoring member 110 and oriented such that the spikes

can penetrate tissue in a subannular location and can be configured to help the anchoring member 110 resist movement in either an upstream or downstream direction.

Prosthetic Heart Valve Devices Having Stabilizing Members

[00236] Figure 28 illustrates one embodiment of the prosthetic heart valve device 100 in an expanded configuration 102 that further comprises one or more stabilizing members 501 to help stabilize the device 100 at the native valve site and, in some embodiments, prevent tilting or lateral migration, or to inhibit upstream or downstream migration of the device 100. In some embodiments, the stabilizing members 501 may comprise one or more arms 510 extending from a lower or downstream portion 111 of the anchoring member 110. The arms 510 are configured to engage the native tissue, e.g. the valve leaflets, subannular tissue, or ventricular wall, either inside or outside the native leaflets, depending on the configuration.

[00237] Figure 29 is an enlarged schematic, side view of a prosthetic heart valve device having an extended arm in accordance with an embodiment of the present technology. As shown in Figure 29, an individual arm 510 may comprise an arm body 512, an arm extension 514, and an arm tip 516. The arm body 512 has an arm body length L_1 and may connect to a post 511 at a first joint 508. The post 511 can be a valve support post 122, an anchoring member rib 114, and/or another feature of the device 100 (e.g., strut 124 or connector 116). A first arm angle A_{A1} is formed by the intersection of the axes of post 511 and the arm body 512; the first arm angle A_{A1} selected such that the arm 512 is positionable so that the tip 516 can engage the native tissue at a desired location, e.g. the subannular tissue or ventricular wall behind the native leaflets. Figures 30A-30C are enlarged partial side views of a prosthetic heart valve device 100 having arms 510 coupled to the device at various angles with respect to a longitudinal axis 101 of the device in accordance with further embodiments of the present technology. In one embodiment, the first arm angle A_{A1} can be about 10° to about 45° . In other embodiments, the first arm angle A_{A1} can be an obtuse angle (Figures 30A), generally perpendicular or approximately a 90° angle (Figure 30B), or an acute angle (Figure 30C).

[00238] Referring back to Figure 29, the arm body 512 can connect to the arm extension 514 at a distal end of the arm body 512. The arm extension 514 can have an arm extension length L_2 which can be selected or optimized for penetrating a desired distance into the native tissue, such as about 0.5-2 mm. The arm extension 514 can extend from the arm body 212 at

second arm angle A_{A2} . The second arm angle A_{A2} can be formed by the intersection between the arm extension 514 and arm body 512 and be selected to provide the desired angle of engagement with the native tissue, such as about 100° to about 135° . In other embodiments, the arm extension 514 may be parallel or collinear with the arm body 512 (not shown), or may be eliminated entirely. The arm extension 514 terminates at the arm tip 516. In embodiments without an arm extension 514, the arm tip 516 can be the most distal portion of the arm body 512 (not shown).

[00239] The arm 510 may have an arm height H_{A1} extending from the first joint 508 to the most distal reaching point of the arm, which could be the arm tip 516 (shown in Figure 29) along an axis parallel to the longitudinal axis 101 of the device 100. The arm height H_{A1} can be selected or optimized such that the arm tip 516 engages a desired location in the subannular anatomy when the device 100 is in a desired longitudinal position relative to the native mitral valve (e.g., when the anchoring member 110 is in engagement with the subannular tissue). The arm height H_{A1} will depend upon of the overall height of the anchoring member 110 and/or valve support 120 as well as the location of the joint 508. Figures 31A-31C are enlarged, partial side views of prosthetic heart valve devices having arms 510 of various lengths ($L_1 + L_2$), and accordingly having variable heights H_{A1} . As shown, the arm height H_{A1} may be greater than the overall height H_{D1} of the anchoring member 110 (represented by rib 114) or valve support (Figure 31A), be intermediate between the respective heights H_{D1} , H_{V1} of the anchoring member 110 (represented by rib 114) and the valve support 120 (represented by post 122) (Figure 31B), or be less than the overall height H_{D1} of both the anchoring member 110 (represented by rib 114) and the valve support 120 (Figure 31C).

[00240] Additional details and embodiments regarding the structure and attachment of arms or other stabilizing members suitable for use with the device 100 can be found in International PCT Patent Application No. PCT/US2012/043636, entitled "PROSTHETIC HEART VALVE DEVICES AND ASSOCIATED SYSTEMS AND METHODS," filed June 21, 2012.

[00241] Figures 32A, 32B, 32C, and 32D are cross-sectional views of a heart with an implanted prosthetic heart valve device 100 having arms 510a disposed on an inward-facing surface of the leaflets LF, and Figures 32A-1, 32B-1, 32C-1 and 32D-1 are enlarged views of the arms 510a engaging the inward-facing surface of the leaflets as shown in Figures 32A,

32B, 32C and 32D, respectively. The embodiments of prosthetic heart valve devices 100 illustrated in Figures 32A-32D-1 have arms 510a configured to expand to a position radially inside the leaflets LF, radially outside the leaflets LF, or a combination of inside and outside the leaflets LF. For example, Figures 32A and 32A-1, show arms 510a expanding and engaging an inward surface of the leaflets LF and show the arms 510a partially piercing the leaflets LF. In another example illustrated in Figures 32B and 32B-1, the arms 510a may fully penetrate the leaflets LF. In a further example, the device 100 can incorporate arms 510a that 1) completely penetrate the leaflets LF and 2) partially pierce subannular tissue (Figures 32C and 32C-1). Referring to Figures 32D and 32D-1, the device 100 can be configured to incorporate arms 510a that fully penetrate both the leaflets LF and the annular tissue of the mitral valve MV.

[00242] Figures 33A-33C are schematic views illustrating various embodiments of tissue engaging elements 170 for use with prosthetic heart valve devices 100 in accordance with the present technology. Tissue engaging elements 170 can include any feature that engaged tissue in an atraumatic manner, such as a blunt element, or which partially pierces or fully penetrates cardiac tissue, such as a barb or spike. As used herein, "tissue engaging" refers to an element 170 which exerts a force on the tissue T but does not necessarily pierce the tissue T, such as being atraumatic to the tissue T, as shown in Figure 33A. As used herein, "partially piercing" refers to a tissue engaging feature 170 which at least partially penetrates the tissue T but does not break through an opposite surface S, as shown in Figure 33B. As used herein, "fully piercing" refers to a tissue engaging feature 170 which can both enter and exit the tissue T, as shown in Figure 33C. "Piercing" alone may refer to either partial or full piercing. Tissue engaging elements 170 may take the form of spikes, barbs, or any structure known in art capable of piercing cardiac tissue, or alternatively, any blunt or atraumatic feature configured to apply pressure on the cardiac tissue without piercing the tissue. Further details on positioning of such elements is described herein.

[00243] Figures 34A, 34B and 34C are cross-sectional views of a heart with an implanted prosthetic heart valve device 100 having arms 510a with tissue engaging elements 170 disposed on an inward-facing surface of the leaflets LF, and Figures 34A-1, 34B-1 and 34C-1 are enlarged views of the arms 510a engaging the inward-facing surface of the leaflets LF as shown in Figures 34A, 34B and 34C, respectively. As illustrated in Figures 34A-34C-1, tissue engaging elements 170 can be incorporated on and extend from the arms 510a in

either a downstream direction (Figures 34A and 34A-1), upstream direction (Figures 34B and 34B-1), or in both the downstream and upstream directions (Figures 34C and 34C-1). In other embodiments, the tissue engaging elements 170 can be incorporated on and extend from the components of the anchoring member 110 and/or the valve support 120 in either or both the upstream and downstream directions.

[00244] Figures 35A-35C are side views showing prosthetic heart valve devices 100 implanted at a mitral valve MV (illustrated in cross-section) in a deployed configuration 104, wherein the devices have arms 510b for engaging an outward-facing surface of the native leaflets LF in accordance with various embodiments of the present technology. Figure 35A shows an embodiment of the device 100 that includes arms 510b configured to extend from the downstream end of the device 100 (e.g., the ventricular end of a device implanted at a native mitral valve downstream of the leaflets) to reach behind the leaflets LF such that the leaflets LF are effectively sandwiched between the arms 510b and the outer wall 142 of the anchoring member 110. In another embodiment, and as shown in Figure 35B, the arms 510b may cause leaflets LF to fold upon themselves in the space between the arms 510b and the outer wall 142 of the anchoring member 110. In a further embodiment illustrated in Figure 35C, the arms 510b can also include the tissue engaging elements 170. Figure 35C-1 is an enlarged view of the arm 510b having tissue engaging elements 170 for engaging the outward-facing surface of the leaflets LF as shown in Figure 35C. As shown in Figure 35C-1, the arms 510b configured to engage an outside-facing surface of the native leaflets LF may include tissue engaging elements 170 on an inside surface of the arms 510b such that they are oriented toward the leaflet tissue.

[00245] In accordance with another embodiment of the present technology, Figure 36A is a side view showing a prosthetic heart valve device 100 implanted at a mitral valve MV (illustrated in cross-section). The device shown in Figure 36A has arms 510b for engaging an outward-facing surface of the native leaflets LF and arms 510a for engaging an inward-facing surface of the native leaflets LF. Inside/outside arms 510a, 510b may further comprise tissue engaging elements 170 on a radially inside surface or radially outside surface of the arms 510a, 510b, respectively, for engaging or piercing the leaflet tissue. The arrangement of inside/outside arms 510a, 510b around a circumference of the device 100 can alternate in a pre-designed pattern. For example, inside arms 510a can alternate with outside arms 510b as shown in Figure 36B, or alternatively, arms 510a, 510b may extend radially outward and/or

radially inward randomly or at irregular intervals, depending on placement of the device 100 and with respect to alignment with the native posterior and anterior leaflets.

[00246] Figures 37A-37D are enlarged side views of additional embodiments of arms 510 suitable for use with a prosthetic heart valve device 100 in accordance with the present technology. For example, in Figures 37A-37D, the arms 510 can have a similar overall profile as a profile of the anchoring member 110. The anchoring member 110 can include ribs having varying shapes, sizes and/or outwardly or inwardly oriented rib segments 85 for forming the overall anchoring member profile. Accordingly, the arms 510 can also have varying shapes, sizes and/or outwardly or inwardly oriented arm segments that mimic the anchoring member 110 profile. In some arrangements, the embodiments shown in Figures 37A-37D are configured to clamp leaflets LF and/or the annulus AN tissue between the arms 510 and the ribs 114 so as to conform the leaflet tissue to the shape of the anchoring device 110 for enhanced sealing and anchoring of the device. For example, Figure 37A illustrates one embodiment in which arm extensions 514 and/or arm bodies 512 may partially mimic the shape of the ribs 114 and/or rib segments 85, and Figure 37B illustrates another embodiment in which arm extensions 514 and/or arm bodies 512 more closely follow the shape of the ribs 114. Embodiments encompassed by Figures 37A-37B can apply to outward surface engaging arms 510b and/or inward surface engaging arms 510a. Additionally, as shown in Figures 37A-37B, the arm extensions 514 can extend radially outwardly so as to be generally parallel with an upstream segment 85A of the rib 114. The arm extension 514 can be configured to extend partially along the length of the rib 114 and/or rib segments 85 (Figures 37A and 37C) or fully along the length of the rib 114 and/or rib segments 85. In Figure 37D, the arms 510 have second arm extensions 518 connected to an upstream portion of the first arm extension 514 and extending outwardly so as to be generally parallel to a second rib segment 85B and third rib segment 85A.

[00247] In some embodiments, the prosthetic heart valve device 100 may incorporate a plurality of arms 510 around a circumference of the device 100; however, in other embodiments, the device may include the plurality of arms in groupings (e.g., first and second groupings so as to engage the posterior and anterior leaflets, respectively). Additionally, the arms 510 may extend from the anchoring member 110 and/or valve support 120 independently of other components including other arms 510, such as shown in Figure 38A. In other embodiments and as shown in Figure 38B, the device 100 may further include at least

one first arm 510x interconnected with at least one second arm 510y by interconnecting arm struts 520. The arm struts 520 can be configured to be circumferentially expandable and may connect all arms 510 (e.g., arm 510x and 510y) or one or more groups of arms 510. In some embodiments, the arm struts 520 can limit the outward extension of the arms 510x, 510y away from the device 100.

[00248] In accordance with aspects of the present technology, the arms 510 can be coupled to and/or extend from components of the device 100 symmetrically and/or asymmetrically around the circumference 150 of the device 100. Figures 39A-39D are schematic top views of arm location patterns with respect to the ribs 114 of the anchoring member 110 (e.g., as shown in Figure 38A). The arms 510 can be interspersed with ribs 114 (Figures 39A and 39C), in the same radial plane as the ribs 114 of the anchoring member 110 (Figure 39B), or both interspersed and in plane with the ribs 114 (Figure 39D). Further, the arms 510 may be configured to extend outside the expanded outer circumference 150 of the anchoring member 110 (Figure 39B), inside the expanded outer circumference 150 of the anchoring member 110 (Figure 39A), extend to the same outer circumference 150 of the anchoring member 110 (Figure 39C), or a combination of these configurations (Figure 39D).

[00249] In the above-described embodiments, the arms 510 may be configured to engage tissue independently of the deployment of anchoring member 110. For example, delivery catheters suitable for the delivery of the prosthetic heart valve devices 100 may be equipped with separate mechanisms operable to deploy the arms 510 and the anchoring members 110 individually or otherwise independently of each other. In this way, the anchoring member 110 may be first released into engagement with the native tissue so that the position of device 100 may be assessed and adjusted by the operator until the desired final position has been attained. Following deployment and positioning of the anchoring member 110, the arms 510 can be released to engage the tissue. Such deployment systems and methods are useful when the arms 510 are equipped with tissue engaging elements 170 which, once deployed, may prohibit any repositioning of the device 100. In some embodiments, the anchoring member 110 will be equipped with atraumatic tissue engagement elements 170 which do not penetrate tissue or inhibit device relocation once the anchoring member 110 has been deployed. Accordingly, some embodiments of the device 100 may be repositionable even with the anchoring member 110 expanded so long as the arms 510 are constrained in an undeployed

configuration, with the device 100 becoming permanently anchored only when the arms 510 are released.

[00250] Alternatively or in addition to tissue engaging elements 170 present on the arms 510 as described above, tissue engaging elements 170 may be present on other components of the device 100. Figures 40A-40E are side views of prosthetic heart valve devices 100 having tissue engaging elements 170 on varying structures of the device 100 in accordance with additional embodiments of the present technology. For example, tissue engaging elements 170 can be incorporated on the ribs 114 of the anchoring member 110. Figure 40A shows tissue engaging elements 170 incorporated on the upper rib segment 85A, and Figure 40B shows the tissue engaging elements 170 incorporated on lower rib segment 85B. Figure 40C illustrates an embodiment of the device having the tissue engaging elements 170 along the entire rib 114. The tissue engaging elements 170 are shown in Figures 40A-40C schematically, but one of ordinary skill in the art will recognize that the elements can be any of a variety of tissue engaging elements 170 described herein (e.g., atraumatic, partially piercing, fully penetrating, etc.), or in other embodiments, a combination of different types of tissue engaging elements 170. Additionally, the tissue engaging elements 170 are shown oriented in an upstream direction (e.g., to inhibit upstream migration of the device 100); however, in other embodiments, the tissue engaging elements 170 can be oriented in a downstream direction (e.g., to inhibit downstream migration of the device 100), or in a combination of downstream and upstream oriented directions. The tissue engaging elements 170 can be incorporated symmetrically around a circumference of the device 100, or in other embodiments, the tissue engaging elements 170 can be incorporated asymmetrically. For example, in some embodiments, the tissue engaging elements 170 can be present on a side of the device 100 aligned with the posterior leaflet, but be absent or have a different arrangement on a side of the device 100 aligned with the anterior leaflet such that the wall separating the aortic valve from the left ventricle will not be affected by the tissue engaging elements 170.

[00251] Figure 40D illustrates an embodiment of the device 100 having tissue engaging elements 170, such as spikes on an upstream tip 175 of the rib 114, wherein the spikes can be configured to fully or partially penetrate subannular tissue when the device 100 is deployed on or under the annulus of the mitral valve. In some embodiments, the tissue engaging elements 170 (e.g., spikes) can include barbs 176 or other features for retaining the tissue engaging elements 170 (e.g., spikes) in the tissue. In other embodiments, the tissue engaging

elements 170 (e.g., spikes) can be blunt so as to engage but not penetrate the subannular tissue. Figures 40E-40G are enlarged side views of tissue engaging elements 170 (e.g., spikes) suitable for use on upstream tips 175 of the ribs 114. Devices 100 having tissue engaging elements 170 on the upstream tips 175 can also incorporate features for limiting the distance of penetration into the tissue. For example, the upstream tip 175 can have a hilt 177 formed a short distance, e.g. 1-5 mm, proximal to the tip of each tissue engaging element 170 to limit the distance to which the tissue engaging element 170 can penetrate the subannular tissue (Figure 40E). Alternatively, as shown in Figure 40F, the depth penetration of the tissue engaging element 170 into the tissue can be limited by positioning connectors 116 a desired distance from the tips of the tissue engaging element 170. In a further embodiment shown in Figure 40G, a sealing member 140 may be attached to the ribs 114 such that the upstream edge 178 of the sealing member 140 can limit the depth of penetration of the tissue engaging element 170. In order to prevent slippage of the sealing member 140 downward, an attachment feature such as a hole 173 configured to receive a suture may be formed in the rib 114 at the desired distance from its upstream tip 175 to which the sealing member 140 can be firmly secured.

[00252] Alternatively, tissue engaging elements 170, such as bumps, ridges, or other protrusions configured to exert frictional forces on cardiac tissue, may be also present on one or more valve support struts 124, valve support posts 122, and/or other components (e.g., sealing members 140). These tissue engaging elements 170 can be disposed on an outer portion of these features and can be configured to extend outwardly to engage the native leaflets and to stabilize and firmly anchor the device 100 in the desired location. Alternatively, ridges, scales, bristles, or other features having directionality may be formed on the surface of the ribs 114, connectors 116, or sealing member 140 to allow movement relative to native tissue in one direction, while limiting movement in the opposite direction.

[00253] The tissue engaging elements 170 on the anchoring member 110 can be barbs, spikes, or other retention features configured to have a delayed deployment so as to allow the device to be repositioned or removed for a period of time until these elements become fully deployed. For example, the tissue engaging element 170 may be constructed of a shape memory material (e.g., nitinol) which is preshaped in a deployed configuration and adapted to retain the tissue engaging element 170 in the native tissue. The tissue engaging element 170 may be deformed into a contracted configuration which permits removal from tissue, and

retained in this shape by a bioerodable material or adhesive. Once immersed in tissue, this material can erode over a period of time (e.g., 10 minutes-2 hours) allowing the tissue engaging element 170 to return to its unbiased deployed shape which will assist in retaining the tissue engaging element 170 in the tissue.

[00254] Several examples of such delayed, deployable tissue engaging elements 170 are shown in Figures 40I-40T. In the embodiment of Figure 40I, the tissue engaging element 170 comprises a shape memory alloy shaft 450 laser cut so as to have a diamond-shaped window 451 near its distal tip 452, which can be sharp enough to penetrate tissue. The shape set so that window 451 is biased toward being open in an expanded configuration as shown in Figure 40I. Prior to delivery of the device, window 451 may be pinched closed and a bioerodable glue 455 may be injected into window 451 to hold it in a closed configuration as shown in Figure 40J. Upon deployment of the device, the distal tip 452 can penetrate the native tissue, e.g. valve leaflet or annulus, as shown in Figure 40K. The glue 455 within window 451 maintains it in a closed configuration for a period of time to allow the operator to reposition or remove the device if necessary. If left in position, the glue 455 erodes, allowing the window 451 to reopen into the expanded configuration which will retain the tissue engaging element 170 in the tissue as shown in Figure 40L.

[00255] In the embodiment shown in Figures 40M-40P, the tissue engaging element 170 comprises an arrowhead-shaped tip 453 having two or more wings 454 biased to be angled radially outward and pointing in a proximal direction as shown in Figure 40M. A bioerodable glue or coating 455 is applied over the arrowhead tip 453 to hold the wings 454 in a radially contracted configuration as shown in Figure 40N. In the contracted configuration, the device 100 is deployed such that the tissue engaging element 170 pierces the native tissue as shown in Figure 40O. The bioerodable coating 455 then erodes gradually until it allows the wings 454 to return to the laterally expanded configuration shown in Figure 40P, thus retaining the tissue engaging element 170 in the tissue.

[00256] A further embodiment is shown in Figures 40Q-40T. In this embodiment, the tissue engaging element 170 comprises a helical tip 456 in an unbiased state. A bioerodable coating 455 may be used to retain the helical tip 456 in a straightened configuration as shown in Figure 40R. The tissue engaging element 170 can penetrate the tissue in the contracted configuration, and when the bioerodable coating 455 erodes sufficiently to allow the helical

tip 456 to return to its deployed configuration, the tissue engaging element 170 can be retained in the tissue.

[00257] The prosthetic heart valve device 100 can also be configured to have additional tissue engaging elements 170 for engaging the annulus. For example, Figure 41 is an isometric view of a prosthetic heart valve device 100 having a plurality of annulus engaging elements 179 in accordance with a further embodiment of the present technology. The annulus engaging elements 179 can be a C-shaped hook feature or other shape that allows the element 179 to engage tissue on the annulus, as well as a portion of supra-annular tissue and subannular tissue. As shown, the annulus engaging elements 179 can be symmetrically (shown in Figure 41) or asymmetrically interspersed around the upstream perimeter of the anchoring member 110 and coupled to ribs 114, connectors 116 (not shown), or to a sealing member 140. The annulus engaging elements 179 may also be coupled to the anchoring member 110 at other locations downstream of the upstream perimeter 113, or in other embodiments to a portion of the valve support 120 that extends through at least the annulus plane PO (Figure 3). Additionally, the annulus engaging elements 179 may be blunt (e.g., for pressing but not penetrating into the annular tissue), or they may be sharp for penetrating the annulus tissue on either or both of the supra-annular or subannular surfaces. The annulus engaging element 179 can be suitable for both positioning the device 100 in the desired location (e.g., with anchoring member 110 below the annulus), as well as to inhibit movement of the device in either an upstream or downstream direction.

[00258] In another embodiment shown in Figures 42A-42B, a prosthetic heart valve device 100 can have tissue engaging elements 372 deployable from a plurality of tubular ribs 314. Referring to Figure 42A, the prosthetic heart valve device 100 can have an anchoring member 110 having a plurality of tubular ribs 314 configured to retain a plurality of deployable tissue engaging elements 372. Figure 42B is an enlarged view of the tubular rib 314 and a deployable tissue engaging element 372 retained within a lumen 316 of the rib 314 and shown before deployment of the element 372. The tissue engaging element 372 can comprise a shape memory material (e.g., nitinol) configured to deploy to a preformed shape upon release of the tissue engaging element 372 from the inner lumen 316 of the rib 314. Release of the tissue engaging element 372 can be achieved by engaging a proximal end 374 of the tissue engaging element 372. For example, the proximal end 374 can be engaged during the deployment of the device 100 to release the tissue engaging element 372 after the

anchoring member 110 is positioned at the desired location below the annulus AN. The tubular rib 314 can include a U-shaped deflector 318 and a pivot point 320 configured to guide the tissue engaging element 372 distally through a distal opening 315 of the rib 314. As illustrated in dotted lines in Figure 42B, engagement of the proximal end 374 of element 372 will encourage a distal end 376 of the tissue engaging element 372 from the distal opening 315 of the tubular rib 314 to penetrate adjacent subannular tissue. Once deployed and after exiting an opposing surface S, such as the supra-annular surface, the tissue engaging element 372 can transition into its preformed shape, such as a curled shape 378 that can resist retraction of the distal end 376 from the tissue.

[00259] In accordance with another embodiment of the prosthetic treatment device 100, tissue engaging elements 170 can be incorporated into sealing members 140 (e.g., sleeve 146). Figures 43A-43B are an isometric view and an enlarged detail view of a prosthetic heart valve device 100 having a sealing member 140 configured with tissue engaging elements 170. Referring to Figures 43A-43B together, the tissue engaging elements 170 can comprise metallic or polymeric wires 274 or fibers, rigid and sharp enough to penetrate tissue, which are woven into or otherwise coupled to sealing member 140 materials. The sealing member 140 can then be attached to outer and/or inner walls 141, 142 of the anchoring member 110 and/or interior and/or exterior surfaces 126, 127 of the valve support 120 such that tissue engaging elements 170 extend radially outward from the sealing member 140 to engage the adjacent leaflets or other tissue.

[00260] Figures 44A-44F are enlarged side views of embodiments of additional tissue engaging elements that can be incorporated on various device structures (referred collectively as “ST”), such struts, connectors, posts, arms, and/or ribs which may be incorporated into device features, such as the anchoring member 110 or valve support 120. For example, the additional tissue engaging elements may comprise one or more cut-out protrusions 350 (Figures 44A and 44B) in place of or in addition to tissue engaging elements 170. In a collapsed or straightened configuration, as shown by the side view of Figure 44C, cut-out protrusion 350 maintains low relief relative to the surface of structure ST to maintain a low profile during delivery. As the device 100 expands and structure ST changes to its deployed configuration (e.g. a curvature as shown in Figure 44D), the protrusion separates from the ST to a higher relief. The protrusion 350 may also be configured to grab subannular tissue, pulling the cut-out protrusions even farther away from structure ST. The device structures ST

may also be shaped to include sharp protrusions 352 along one or more of its edges or faces, as illustrated in Figure 44E, or may also include pointed scale-like protrusions 354, as shown in Figure 44F.

[00261] In addition to the stabilizing members 501 described above, the prosthetic heart valve devices described herein (e.g., devices 100) may also include support features such as tethers 360 and sealing member septa 370 for stabilizing the anchoring member 110 and/or the valve support 120, and/or for spreading pressure gradient loads evenly over a greater area of the device 100 (e.g., during ventricular systole). Referring to Figure 45A, one example of the device 100 can incorporate a plurality of tethers 360 at least loosely coupling the upper portion 112 of the anchoring member 110 to the upstream end 121 of the valve support 120. In one embodiment, the tethers 360 can include a single suture that is run continuously around the circumference 150 of the anchoring member 110. In another embodiment, the device 100 can include several sutures of discreet lengths tied between the anchoring member 110 and the valve support 120. In one embodiment the tethers can be a suture comprising polytetrafluoroethylene (PTFE). Generally, the tethers 360 assist in distributing forces evenly along the anchoring member 110 without deforming the valve support 120 or compromising the closure of the prosthetic valve 130. In some arrangements, the tethers 360 can assist in limiting radial expansion of the upstream portion. Accordingly, even with the incorporation of the tethers 360, the valve support 120 remains mechanically isolated from at least the upstream portion of the anchoring member 110.

[00262] Figure 45B shows another example of a stabilizing member 501 suitable to stabilize the anchoring member 110 and/or the valve support 120, and/or for spreading pressure gradient loads evenly over a greater area of the device 100 (e.g., during ventricular systole). As shown in Figure 45B, the device 100 can include a plurality of sealing member septa 370 extending between the anchoring member 110 and the valve support 120. In the illustrated embodiment, the septa 370 can be extensions of the sealing member material configured to span between a sealing member 140, such as a skirt 144, coupled to the inner wall 141 of the anchoring member 110 and a sealing member 140, such as a sleeve 146, coupled to an interior or exterior surface 126, 127 of the valve support 120. Accordingly, the septa 370 can be formed of fabric or other flexible and biocompatible materials such as Dacron[®], ePTFE, bovine pericardium, or other suitable materials. Similar to the embodiment illustrated in Figure 45A, the septa 370 can assist in distributing forces evenly along the

anchoring member 110 without deforming the valve support 120 or otherwise compromising the closure of the prosthetic valve 130. In some arrangements, the septa 370 can assist in preventing the device 100 from everting during ventricular systole. Accordingly, even with the incorporation of the septa 370, the valve support 120 is mechanically isolated from at least the upstream portion of the anchoring member 110.

[00263] Each of the elements and members of the device 100 may be made from any number of suitable biocompatible materials, e.g., stainless steel, nickel titanium alloys such as NitinolTM, cobalt chromium alloys such as MP35N, other alloys such as ELGILOY[®] (Elgin, IL), various polymers, pyrolytic carbon, silicone, polytetrafluoroethylene (PTFE), or any number of other materials or combination of materials depending upon the desired results. The arm members 510, sealing member 140, sleeves 146, anchoring member 110 and/or valve support 120 or other elements of device 100 may also be coated or covered with a material that promotes tissue in-growth (e.g., Dacron[®], PTFE, etc.)

Delivery Systems

[00264] Figures 46A-46D illustrate one embodiment of a delivery system 10 suitable for delivery of the prosthetic heart valve devices disclosed herein. As used in reference to the delivery system, "distal" refers to a position having a distance farther from a handle of the delivery system 10 along the longitudinal axis of the system 10, and "proximal" refers to a position having a distance closer to the handle of the delivery system 10 along the longitudinal axis of the system 10.

[00265] Figure 46A illustrates one embodiment of the delivery system 10 which may be used to deliver and deploy the embodiments of the prosthetic heart valve device 100 disclosed herein through the vasculature and to the heart of a patient. The delivery system 10 may optionally include a guiding catheter GC having a handle 12 coupled to a delivery shaft 16, which in one embodiment is 34F or less, and in another embodiment, 28F or less in diameter. The guiding catheter GC may be steerable or preshaped in a configuration suitable for the particular approach to the target valve. The delivery catheter 18 is placed through a hemostasis valve HV on the proximal end of guiding catheter GC and includes a flexible tubular outer shaft 19 extending to a delivery sheath 20 in which the device 100 is positioned in a collapsed or delivery configuration 106. A flexible inner shaft 28 is positioned slideably within outer shaft 19 and extends through the device 100 to a nosecone 21 at the distal end.

The inner shaft 28 has a guidewire lumen through which a guidewire 24 may be slideably positioned. The device 100 is coupled to the inner shaft 28 and is releasable from the inner shaft 28 by release wires 30, as more fully described below. The delivery sheath 20 can protect and secure the device 100 in its collapsed configuration 106 during delivery. The outer shaft 20 is coupled to a retraction mechanism 23 on the handle 14 of the delivery catheter 18. Various retraction mechanisms 23 may be used, such as an axially-slidable lever, a rotatable rack and pinion gear, or other known mechanisms. In this way, the outer shaft 20 may be retracted relative to the inner shaft 28 to release (e.g., deploy) the device 100 from the sheath 20.

[00266] Figure 46B shows the distal end of the delivery catheter 18 with the sheath 20 cut away to illustrate the coupling of the device 100 to the inner shaft 28. A plurality of locking fingers 32 are coupled to the nose cone 21 and extend proximally through the interior of the valve support 120 of the device 100. As shown in Figure 46C, a selected number of posts 122 of the valve support 120 have a coupling element 61 comprising a tab 34 cut out from each post 122 at a proximal end thereof. The tab 34 may be deflected inwardly from the post 122 as shown in Figure 46B and is configured to extend through a window 42 in the locking finger 32 as shown in Figure 46D. The release wires 30 pass through the holes 40 in the tabs 34, which prevents the tabs 34 from being withdrawn from the windows 42 to secure the device 100 to the inner shaft 28. The pull-wires 30 can be sandwiched tightly between the tabs 34 and the locking fingers 32, such that friction temporarily prevents the pull-wire 30 from slipping in a proximal or distal direction. In this way, the sheath 20 may be retracted relative to the device 100 to permit expansion of the device 100 while the inner shaft 28 maintains the longitudinal position of the device 100 relative to the anatomy. The pull-wires 30 may extend proximally to the handle 14, for example, in between the inner shaft 28 and the outer shaft 19 or within one or more designated lumens. A suitable mechanism (not shown) on the handle 14 can allow the operator to retract the release wires 30 in a proximal direction until they are disengaged from the tabs 34. Accordingly, the device 100 can be released from the locking fingers 32 and expand for deployment at the target site.

[00267] Figures 47A-47D are schematic, cross-sectional side views of a heart H showing a trans-septal or antegrade approach for delivering and deploying a prosthetic heart valve device 100. As shown in Figure 47A, a guidewire 24 may be advanced intravascularly using any number of techniques, e.g., through the inferior vena cava IVC or superior vena cava

SVC, through the inter-atrial septum IAS and into the right atrium RA. The guiding catheter GC may be advanced along the guidewire 24 and into the right atrium RA until reaching the anterior side of the atrial septum AS, as shown in Figure 47B. At this point, the guidewire 24 may be exchanged for the needle 25, which is used to penetrate through the inter-atrial septum IAS (Figure 47C). The guiding catheter GC may then be advanced over the needle 25 into the left atrium LA, as shown in Figure 47D. The guiding catheter GC may have a pre-shaped or steerable distal end to shape or steer the guiding catheter GC such that it will direct the delivery catheter 18 (Figure 46A) toward the mitral valve.

[00268] As an alternative to the trans-septal approach, the mitral valve may also be accessed directly through an incision in the left atrium. Access to the heart may be obtained through an intercostal incision in the chest without removing ribs, and a guiding catheter may be placed into the left atrium through an atrial incision sealed with a purse-string suture. A delivery catheter may then be advanced through the guiding catheter to the mitral valve. Alternatively, the delivery catheter may be placed directly through an atrial incision without the use of a guiding catheter.

[00269] Figures 48A-48C are cross-sectional views of the heart illustrating a method of implanting a prosthetic heart valve device 100 using a trans-septal approach. Referring to Figures 48A-48C together, the distal end 21 of the delivery catheter 18 may be advanced into proximity to the mitral valve MV. Optionally, and as shown in Figure 48A, a guidewire GW may be used over which catheter 18 may be slideably advanced over a guidewire GW. The sheath 20 of the delivery catheter 18, which contains the device 100 in a collapsed configuration 106, is advanced through the mitral valve annulus AN between native leaflets LF, as shown in Figure 48A. Referring to Figure 48B, the sheath 20 is then pulled back proximally relative to the distal nose cone 27 allowing the device 100 to expand such that anchoring member 110 pushes the leaflets LF outwardly to fold beneath the mitral valve annulus AN. The tips of the ribs 114 engage and may penetrate into or through the leaflet tissue to further engage the tissue of the annulus AN. After the sheath 20 has been removed and the device 100 allowed to expand, the delivery system can still be connected to the device 100 (e.g., system eyelets, not shown, are connected to the device eyelets 180, shown in Figure 10A) so that the operator can further control the placement of the device 100 in the expanded configuration 102. For example, the device 100 may be expanded upstream or downstream of the target location then pushed downstream or upstream, respectively, into the desired target

location before releasing the device 100 from delivery system 10. Once the device 100 is positioned at the target site, the pull-wires 30 (Figures 46A-46B) may be retracted in a proximal direction, to detach the device 100 in the deployed configuration 104 from the delivery catheter 18. The delivery catheter 18 can then be removed as shown in Figure 48C. Alternatively, the device 100 may not be connected to the delivery system 10 such that the device 100 deploys and is fully released from the delivery system 10.

[00270] Figures 49A and 49B illustrate another variation for delivering and deploying one or more prosthetic heart valve devices 100 using a retrograde approach to the mitral valve via the aorta and left ventricle. In this example, the guidewire GW may be advanced intravascularly from a femoral or radial artery or through direct aortic puncture through the aorta AO and aortic valve AV, and into the left ventricle LV of the heart H (Figure 49A). A guiding catheter GC, or alternatively, the delivery catheter 18, may be advanced along the guidewire GW until the distal end is positioned within the left ventricle in proximity to the mitral valve MV, as shown in Figures 49A and 49B. In many arrangements, the guiding catheter GC and/or the delivery catheter 18 will have a steering mechanism or a pre-shaped distal tip allowing it to be steered around the 180° turn from the aortic valve AV to the mitral valve MV. The distal end of the delivery catheter 18 may optionally be advanced at least partially through the mitral valve MV into the left atrium LA.

[00271] Figures 50A-50B illustrate delivery of the device 100 in the collapsed configuration 106 to the mitral valve MV in a trans-apical approach. Referring to Figure 50A, the delivery catheter 18 is advanced through a guiding catheter GC that has been inserted into the left ventricle of the heart through a puncture in the left ventricle wall at or near the apex of the heart. The catheter can be sealed by a purse-string suture. Alternatively, the delivery catheter 18 may be placed directly through a purse-string-sealed trans-apical incision without a guiding catheter. The sheath 20 and the device 100 (e.g., in the collapsed configuration 106) within the sheath 20 are advanced through the mitral annulus AN between native leaflets LF as shown in Figure 50A. Referring to Figure 50B, the sheath 20 is pulled proximally such that the device 100 expands to the expanded and/or deployed configurations 102, 104. The delivery system 10 can remain connected to the device 100 (e.g., system eyelets, not shown, are connected to the device eyelets 180, Figure 10A) after removing the sheath 20 so that the operator can control the placement of the device 100 while in the expanded configuration 102. The pull-wires 30 may be retracted in a proximal direction to

release the device 100 from the delivery system 10, allowing the delivery system 10 to be removed and the device to be fully implanted at the mitral valve MV in the deployed configuration 104. In one embodiment, the device 100 may be expanded upstream or downstream of the desired target location then pulled or pushed downstream or upstream, respectively, into the target location before releasing the device 100 from delivery system 10. Alternatively, the device 100 may not be connected to the delivery system 10 such that the device 100 deploys and is fully released from the delivery system 10.

[00272] Figures 51A-51B are partial side views of a delivery system 10 wherein a prosthetic heart valve device 100 is mounted on an expandable balloon 300 of a delivery catheter 18 in accordance with another embodiment of the present technology. Referring to Figures 51A and 51B together, the device 100 can be mounted on an expandable balloon 300 of a delivery catheter while in a collapsed configuration 106 and delivered to the desired location at or near a native mitral valve (Figure 51A). When the device 100 is released from the sheath 20 (Figures 46A-46B), the device 100 can be expanded to its expanded configuration 102 by inflation of the balloon 300 (Figure 51B). When using a balloon 300 with the delivery system 10, the device 100 can be advanced from the delivery shaft 16 to initially position the device 100 in a target location. The balloon 300 can be inflated to fully expand the device 100. The position of the device 100 relative to the mitral valve may then be adjusted using the device locking hub to position the device into desired implantation site (e.g., just below the annulus of the native mitral valve). In another embodiment, the balloon 300 can initially be partially inflated to partially expand the device 100 in the left atrium. The delivery system 10 can then be adjusted to push or pull (depending on the approach) the partially expanded heart valve device 100 into the implantation site, after which the device 100 can be fully expanded to its functional size. In other alternative methods, the anchoring member 110 is a self-expanding construct which is first released from a sheath 20 (Figures 46A-46B) at the target site to engage the native anatomy, while the valve support 120 is a balloon-expandable element mounted on a balloon 300 which is then expanded to fully deploy the valve support 120 after the anchoring member 110 has been released.

[00273] In still further embodiments, the valve support 120 of device 100 may be configured to be axially movable or detachable from the anchoring member 110. In such arrangements, the two components 110, 120 may be loaded in an axially separated configuration within the delivery system 10, thereby reducing the overall profile of the system

10. After delivery to the target valve site, the components 110, 120 can be assembled together. Figures 52A-52D show an embodiment of assembling the valve support 120 and anchoring member 110 in the heart. As shown in Figure 52A, the delivery catheter 380 is advanced into the left atrium via a guiding catheter GC placed through the inter-atrial septum or the atrial wall. The delivery catheter 380 has a split sheath 382, 384 comprising a distal nose cone 382 and a proximal capsule 384. The delivery catheter 380 is advanced through the native valve MV until the nose cone 382 is positioned distally of the native annulus AN (Figure 52A). The nose cone 382 is then advanced further distally while maintaining the position of the remainder of the delivery catheter 380 thereby releasing the anchoring member 110 from the nose cone 382 (Figure 52B). The anchoring member 110 self-expands outward, engaging the native leaflets LF and folding them outward beneath the native annulus AN, as shown in Figure 52B. The upstream tips of ribs 114 (Figure 52B) engage the subannular tissue to anchor the device 100 in position. The sealing member 140 is fixed around the perimeter 113 of the anchoring member 110 and has a connecting portion 386 extending into the proximal capsule 384 where it is fixed to the valve support 120, which is still constrained within the proximal capsule 384. The delivery catheter 380 is then advanced so as to position the proximal capsule 384 within the anchoring member 110 as shown in Figure 52C. By advancing the catheter 380 until the sealing member 140 becomes taught, the proper positioning may be attained. The proximal capsule 384 is then retracted relative to the nose cone 382 to release the valve support 120 from the proximal capsule 384. The valve support 120 can self-expand into engagement with the downstream end of anchoring member 110 to couple the two components together. The delivery catheter 380 may then be withdrawn from the patient.

[00274] Figures 53A-53H show various mechanisms that may be used for coupling the valve support 120 to the anchoring member 110 in the process shown in Figures 52A-52D. For example, as shown in Figure 53A, the valve support 120 may include a circumferential ridge or detent 388 near its downstream end that engages in a groove 390 in the anchoring member 110 to inhibit detachment of the two components. Alternatively, valve support 120 may have a hook 392 formed at the downstream end of each post 122 which is configured to extend around a downstream end of anchoring member 110, e.g. around either the downstream tip of rib 114 or connectors 116, as shown in Figures 53B-53C. For example, the hook 392 may be configured to flex inwardly when it engages the inner surface of the rib

114 as the valve support 120 is advanced, and be configured to resiliently recoil to its outward configuration when extended beyond the downstream end of the rib 114, as shown in Figure 53C. Optionally, a depth-limiting feature such as a stub 394 may extend outwardly from the valve support 120 which is configured to engage a complementary feature such as a bump or ridge 396 on the anchoring member 110 to prevent insertion of the valve support 120 beyond a predetermined depth.

[00275] In a further embodiment shown in Figures 53D-53F, the valve support 120 may have a coupling element 398 on its outer surface configured to slideably couple to the anchoring member 110. In a first configuration, the coupling element 398 comprises a loop 400, shown in Figure 53E, through which a vertical guide member 402 on the anchoring member 110 may slide. The anchoring member 110 may have a plurality of such guide members 402 extending upwardly from its downstream end at locations spaced around its circumference. A bump 404 may be formed near the downstream end of each guide member 402 over which the loop 400 may slide to inhibit the valve support 120 from sliding back in the upstream direction (Figure 53D). In an alternative configuration, shown in Figure 53F, the guide member 402 has a vertical slot 406 into which a radially extending pin 408 on the valve support 120 can extend. The pin 408 may slide to the downstream end of the slot 406 where it may be urged through a waist 411, which prevents the pin 408 from sliding back in the upstream direction.

[00276] In a further embodiment shown in Figures 53G-53H, coupling elements 398 on the valve support 120 are configured to slideably receive the ribs 114, which themselves perform a similar function as the guide members 402 (described with respect to Figures 53D-53F). As shown in Figure 53G, coupling of the ribs 114 to the valve support 120 helps restrain the ribs 114 in a radially compact configuration when the valve support 120 slides axially upward relative to the anchoring member 110. In the arrangement shown in Figures 53GG-53H, the delivery of the device 100 may not require the need for a separate sheath to constrain the ribs 114 during the delivery. As shown in Figure 53H, the valve support 120 may slide in the downstream direction relative to the anchoring member 110 until the ribs 114 assume their radially outward configuration. As with guide members 402, each rib 114 may have a bump 412 formed near its downstream end past which coupling element 398 may be urged, but which then inhibits valve support 120 from sliding in the upstream direction (Figure 53H).

[00277] Figures 54A-55C illustrate a delivery catheter 400 of a delivery system 40 in accordance with additional embodiments of the present technology. Figure 54A is a cross-sectional side view of the delivery system 40 for the prosthetic heart valve device 100 and Figure 54B is a partial cross-sectional side view of a distal portion of the delivery system 40 shown in Figure 54A. As shown in Figures 54A and 54B, the delivery catheter 400 comprises a sheath 402 having an outer wall 403 and a closed distal nose 406 defining a blind annular cavity 408. An inner wall 405 extends proximally to the proximal end of the catheter (not shown), thus forming a tubular catheter shaft 407 defining an inner lumen extending axially therethrough in which a guidewire GW may be slideably positioned. A piston 412 is slideably disposed in the cavity 408 and has an O-ring 413 around its circumference to create a fluid seal with the wall of the cavity 408. A tubular piston shaft 414 extends proximally from piston 412 and is slideably mounted over the catheter shaft 407. The piston shaft 414 is oversized relative to the catheter shaft 407 so as to define a fluid lumen 416 which is in communication with the cavity 408. The device 26 is retained in its radially collapsed delivery configuration within cavity 408, with piston shaft 414 and catheter shaft 407 extending through the interior of the valve support 120 (shown in Figures 55A-55C). Preferably, the device 100 is releasably coupled to piston 412 by, for example, pins (not shown) extending radially outwardly from piston shaft 414.

[00278] The sheath 402 may have features that limit its travel. For example, a wire (not shown) may tether the protective sheath to a handle on the proximal end of catheter 400. The wire may be attached to an adjustable stop on the handle, allowing the length of piston travel to be adjusted. When fluid is injected into cavity 408, piston 412 will travel until this stop is reached. In this manner, the deployment progression can be controlled.

[00279] To ease the retraction of sheath 402 through the valve of the device 100 following deployment, a tapered feature may advance to abut the proximal end of the sheath 402 (see Figure 56). Alternatively, piston 412 may have a taper or soft bumper material affixed directly to the back of piston 412 facing in the proximal direction. In this way the proximal side of the piston would itself provide an atraumatic leading surface to ease retraction of the sheath 402 through the valve support 120.

[00280] Features intended to control and smooth the deployment of device 100 can be incorporated. For example, a common problem during deployment of self-expanding stents is a tendency of the deployed device to "pop" or jump forward or backward as the final elements

exit the deployment device. Features to prevent the sheath 402 from being thrust forward by the expanding skeletons of the device 100 may be important in order to prevent accidental damage to the ventricle or other tissue. Such features may incorporate stops or tethers within the deployment system designed to retain the position of the sheath 402 relative to the deployed device 100. For example, the proximal edge of the sheath 402 could be swaged slightly inward to prevent the piston from exiting the sheath and to precisely locate the taper or bumper features described above to ease withdrawal of the system through the deployed valve. Alternatively or additionally, a spring mechanism (not shown) could be built into the delivery system 40 so that when the last features of the device 100 leave the sheath 402, the sheath actively retracts slightly into the downstream end of the newly deployed device 100.

[00281] The operation of the delivery catheter 400 is illustrated in Figures 55A-55C. The delivery catheter 400 is positioned at the target valve site using one of the approaches described elsewhere herein. The delivery catheter 400 is particularly well suited to placement through the native valve from the upstream direction. The catheter 400 is advanced until the sheath 402 is positioned downstream of the native annulus (Figure 55A). Fluid can then be injected through fluid lumen 416 into the cavity 408, distal to the piston 412 (Figure 55B). This drives the sheath 402 distally, releasing the device 100 from the cavity 408 (Figure 55C). The delivery catheter 400 and the device 100 may remain in a stationary longitudinal position relative to the native valve while the device 100 is deployed, thereby increasing the precision of deployment. In addition, the device 100 may be deployed in a slow and controlled manner, avoiding sudden and uncontrolled jumps of the device 100. Further, such hydraulic actuation allows the sheath 402 to be moved in incremental steps to only partially deploy the device 100, allowing the operator to assess its position relative to the native valve and reposition as needed before complete deployment.

[00282] In one embodiment, the piston 412 can be hydraulically actuated, however, in another embodiment, the piston 412 could be operated by manual retraction of the piston shaft 414 or advancement of the sheath 402. The delivery catheter 400 may be equipped with a handle on its proximal end having a retraction mechanism coupled to the piston shaft 414 and/or catheter shaft 407. Such a mechanism may use gears or pulleys to provide a mechanical advantage to reduce the force required to retract the piston or advance the sheath.

[00283] The delivery catheters in accordance with aspects of the present technology may further be configured to be reversible, to allow the device 100 to be retracted back in to the

catheter 400 after a full or partial deployment. One embodiment of such a catheter is illustrated in Figure 56, wherein the delivery catheter 400 of Figures 54A-55C is adapted to retract the device 100 back into the sheath 402 after being fully or partially deployed therefrom. The piston 412 has at least a first pulley 420 coupled thereto, while distal nose 406 has at least a second pulley 422 coupled thereto. A plurality of additional pulleys 423 may also be provided at locations around the circumference of the piston 412 for additional mechanical assistance. A cable 424, which may comprise a length of wire or suture, extends through the fluid lumen 416 and cavity 408, passes around first and second pulleys 420, 422 and any additional pulleys 423, and is secured to piston 412. The device 100 can be releasably coupled to the piston shaft 414 by a plurality of pins 426 extending radially from the piston shaft 414 into engagement with the device 100, preferably near a downstream end 428 thereof.

[00284] To deploy the device 100, the delivery catheter 400 of Figure 56 operates similarly as described above in connection with Figures 55A-55C; however, in an additional embodiment and before the downstream end 428 has been fully released from the sheath 402, the operator can check the location of the device 100. Upon deployment, the upstream end 430 of the device 100 will expand toward its expanded configuration. An operator can view, using ultrasound, fluoroscopy, MRI, or other means, the position and shape of the deployed device 100 in the native tissue. Following positioning, the sheath 402 may be further advanced relative to the piston 412 to fully deploy the device 100 from the sheath 402, whereupon the downstream end 428 fully expands and pins 426 are disengaged from device 100. In situations where the operator desires to recover the device 100 back into the sheath 402 for repositioning or other reasons, the cable 424 is pulled so as to move the piston 412 in the distal direction relative to the sheath 402. The pins 426 pull the device 100 with the piston 412 back into the sheath 402 and the device 100 is collapsed as it is pulled in the sheath 402. The delivery catheter 400 may then be repositioned and the device redeployed.

[00285] In one embodiment, the prosthetic heart valve device 100 may be specifically designed for a specific approach or delivery method to reach the mitral valve, or in another embodiment, the device 100 may be designed to be interchangeable among the approaches or delivery methods.

Additional Embodiments of Prosthetic Heart Valve Devices, Delivery Systems and Methods

[00286] Figures 57A-57E are isometric views of prosthetic heart valve devices 600 shown in an expanded configuration 602 and configured in accordance with additional embodiments of the present technology. The prosthetic heart valve devices 600 include features generally similar to the features of the prosthetic heart valve device 100 described above with reference to Figures 10A-56. For example, the prosthetic heart valve device 600 includes the valve support 120 configured to support a prosthetic valve 130 and an anchoring member 610 coupled to the valve support 120 in a manner that mechanically isolates the valve support 120 from forces exerted upon the anchoring member 610 when implanted at the native mitral valve. However, in the embodiments shown in Figures 57A-57E, an upstream region 612 of the anchoring member 610 is coupled to the valve support 120 such that a downstream region 611 of the anchoring member 610 is configured to engage native tissue on or downstream of the annulus so as to prevent migration of the device 600 in the upstream direction.

[00287] Figures 57A and 57B illustrate embodiments of the device 600 wherein the anchoring member 610 includes a plurality of longitudinal ribs 614 coupled to the upstream end 121 of the valve support 120 and extending in a downstream to distal direction. As shown in Figure 57A, the ribs 614 can project radially outward away from the longitudinal axis 101 at the downstream region 611 of the anchoring member 610 such that the downstream region 611 is flared outward for engaging subannular tissue below the mitral annulus. Figure 57B illustrates an embodiment of the device 600 having an anchoring member 610 with an upward-facing lip 617 at the downstream region. In this embodiment, the ribs 614 can be formed such that the downstream region is generally flared outwardly from the longitudinal axis 101 but the tips 615 of the ribs 614 reorient to point in an upstream direction at the lip 617. The lip 617 may assist the anchoring member 610 in engaging subannular tissue and can be configured to include tissue engaging elements (not shown) as described above with respect to device 100. The anchoring member 610 can also be coupled to the valve support 120 at a position desirable for positioning the valve support 120 and prosthetic valve 130 within the native valve. For example, Figure 57C illustrates an embodiment of the device 600 in which the anchoring member 610 can be coupled to the valve support 120 at a location downstream from the upstream end 121.

[00288] Referring to Figures 57A-57C together, the anchoring member 610 can have a first cross-sectional dimension D_{C1} at the upstream region 612 that is less than a second cross-sectional dimension D_{C2} at the downstream region 611. Additionally, the valve support 120 is radially separated from the downstream region 611 of the anchoring member 610 such that when the device 600 is deployed, the downstream region 611 can deform inwardly without deforming the upstream portion of the valve support 120. Additionally, the anchoring member 610 can have a generally oval or D-shape, or other irregular shape such as those described above with respect to Figures 16A-17C, while the valve support 120 can be generally cylindrical in shape. In such embodiments, the second cross-sectional dimension D_{C2} can be greater than a corresponding cross-sectional dimension (e.g., MVA1 or MVA2) of the annulus of the native mitral valve (Figure 5C).

[00289] Figure 57D illustrates yet another embodiment of the device 600 in an expanded configuration 602. As shown, the valve support 120 can include a flange 620 at the downstream end 123 of the valve support 120. The flange 620 can extend radially outward from the longitudinal axis 101 at the downstream end 123 to radially engage subannular tissue. The anchoring member 610 can include a plurality of ribs 614 coupled to the upstream end 121 of the valve support 120 and extending radially outward in the downstream direction to attach to an outer rim 622 of the flange 620. The anchoring member 610 can be configured to engage subannular tissue, such as inward-facing surfaces of the leaflets. In this embodiment, the ribs 614 can be flexible such that deformation of the anchoring member 610 between the coupling at the upstream region 612 and the coupling to the flange 620 at the lower region 611 will not substantially deform the valve support 120 wherein a prosthetic valve is connected.

[00290] Figure 57E is a schematic cross-sectional view of the prosthetic heart valve device 600 of Figure 57A implanted at a native mitral valve MV in accordance with an embodiment of the present technology. As shown, the flared downstream region 611 of the anchoring member 610 can engage the subannular tissue, e.g., inward-facing surfaces of the leaflets LF, a subannular surface, etc. The ribs 614 can incorporate tissue engaging elements 170 on the rib tips 615 for penetrating and/or partially penetrating the tissue. Further, the anchoring member 610 can expand radially outward to seal (not shown) against the tissue to prevent migration of the device 600 in the upstream or downstream direction and/or to prevent paravalvular leaks between the tissue and the device 600. Accordingly, the device

600 can incorporate one or more sealing members 140 as described above with respect to device 100. Additionally, the device 600 can also include an atrial extension member or atrial retainer 410 (shown in dotted lines) as described above with respect to the device 100. The atrial retainer, if present, can be configured to engage tissue above the annulus AN such as a supra-annular surface or some other tissue in the left atrium LA to inhibit downstream migration of the device (e.g., during atrial systole).

[00291] Figures 58A-58D are cross-sectional views of a heart showing a method of delivering a prosthetic heart valve device 600 to a native mitral valve MV in the heart using a trans-apical approach in accordance with another embodiment of the present technology. Referring to Figure 58A, the delivery catheter 18 is advanced through guiding catheter (not shown) which enters the left ventricle LV of the heart through a puncture in the left ventricle wall at or near the apex of the heart and is sealed by a purse-string suture. Alternatively, the delivery catheter 18 may be placed directly through a purse-string-sealed trans-apical incision without a guiding catheter. The sheath 20, containing a collapsed device 600, 606 (shown in Figure 58B), is advanced through the mitral annulus AN between native leaflets LF as shown in Figure 58A. Referring to Figures 58B- 58D together, the sheath 20 is pulled proximally to allow the device 600 to expand to the expanded and/or deployed configurations 602, 604 (Figures 58C and 58D).

[00292] Although the sheath 20 can be retracted and the device 600 allowed to expand, the delivery system can remain connected to the device 600 (e.g., system eyelets, not shown, are connected to the device eyelets, not shown) such that the operator can control the placement of the device 600 while in the expanded configuration 602 (Figures 58C and 58D). For example, as the sheath 20 is disengaged from the device 600, the upstream region 612 of the anchoring member 610 can remain collapsed within the sheath preventing the anchoring member 610 from fully expanding (Figure 58C). During this phase of the delivery, the position of the device 600 within the mitral valve area can be adjusted or altered. After the device 600 is located at the target site, the sheath 20 can be fully removed from the device 600 and the anchoring member 610 of the device 600 can expand outwardly at the downstream region 611 to engage subannular tissue, such as the leaflets LF, and to retain the device 600 in the desired target location. The pull-wires (not shown) may be retracted in a proximal direction to release the device 600 from the delivery system, allowing the delivery system to be removed and the device to be fully implanted at the mitral valve MV in the

deployed configuration 104. Alternatively, the device 600 may be expanded upstream or downstream of the desired target location then pulled or pushed downstream or upstream, respectively, into the target location before releasing the device 600 from delivery system.

[00293] Figures 59A-59C are isometric views of prosthetic heart valve devices 700 shown in an expanded configuration 702, and Figure 59D is a schematic cross-sectional view of the prosthetic heart valve device 700 implanted at a native mitral valve configured in accordance with further embodiments of the present technology. The prosthetic heart valve devices 700 include features generally similar to the features of the prosthetic heart valve devices 100 and 600 described above with reference to Figures 10A-58D. For example, the prosthetic heart valve device 700 includes the valve support 120 configured to support a prosthetic valve 130 and a first anchoring member 610 coupled to the valve support 120 in a manner that mechanically isolates the valve support 120 from forces exerted upon the first anchoring member 610 when implanted at the native mitral valve. Particularly, the upstream region 612 of the first anchoring member 610 is coupled to the valve support 120 and the downstream region 611 of the first anchoring member 610 is configured to flare outwardly to engage native tissue on or downstream of the annulus so as to prevent migration of the device 600 in the upstream direction. However, in the embodiments shown in Figures 59A-59D, the device 700 also includes a second anchoring member 710 having a downstream region 711 coupled to the valve support 120, and an upstream region 712 extending radially outward in the upstream direction. Accordingly, the device 700 includes both the first and second anchoring members 610 and 710 for engaging tissue on or under the annulus of the mitral valve.

[00294] Referring to Figures 59A-59D together, the first anchoring member 610 can have the first cross-sectional dimension D_{C1} at the upstream region 612 that is less than the second cross-sectional dimension D_{C2} at the downstream region 611. The second anchoring member 710 can have a third cross-sectional dimension D_{C3} at the upstream region 712 that is greater than a fourth cross-sectional dimension D_{C4} at the downstream region 711. In some embodiments, the third cross-sectional dimension D_{C3} is less than the second cross-sectional dimension D_{C2} such that the second anchoring member 710 can be partially surrounded by the first anchoring member 610 (Figure 59A). In such an embodiment, the upstream region 712 can apply radial outward pressure against an inner wall (not shown) of the first anchoring member 610 and further support the fixation of the first anchoring member 610 to the tissue

on or under the annulus. In another embodiment shown in Figure 59B, the third cross-sectional dimension D_{C3} can be approximately the same as the second cross-sectional dimension D_{C2} such that the first and second anchoring members 610, 710 meet at a flared junction 740. In one embodiment, the first and second anchoring members 610 and 710 can be coupled at the flared junction 740; however, in other embodiments, the first and second anchoring members 610 and 710 are not coupled. Figure 59C shows another embodiment of the device 700 wherein the downstream region 615 of the first anchoring member 610 is separated from the upstream region 713 of the second anchoring member 710 by a gap 750. In one embodiment, the device 700 shown in Figure 59C can be implanted at the native heart valve such that the first anchoring member 610 can engage supra-annular tissue or other cardiac tissue upstream of the annulus and the second anchoring member 710 can engage subannular tissue or other cardiac tissue downstream of the annulus such that the annulus is retained or captured within the gap 750.

[00295] In a further embodiment illustrated in Figure 59D, the third cross-sectional dimension D_{C3} is greater than the second cross-sectional dimension D_{C2} such that the second anchoring member 710 can partially surround the first anchoring member 610. In such an embodiment, the downstream region 611 of the first anchoring member 610 can apply radial outward pressure against an inner wall 741 of the second anchoring member 710 and further support the fixation of the second anchoring member 710 to the tissue on or under the annulus AN.

[00296] Additionally, the valve support 120 can be radially separated from the downstream region 611 of the first anchoring member 610 as well as the upstream region 712 of the second anchoring member 710 such that when the device 700 is deployed, the downstream region 611 and/or the upstream region 712 can deform inwardly without substantially deforming the valve support 120 or without deforming a support region 734 of the valve support 120 supporting the prosthetic valve 130. Additionally, the first and second anchoring members 610, 710 can have a generally oval or D-shape, or other irregular shape such as those described above with respect to Figures 16A-17C, while the valve support 120 can be generally cylindrical in shape. Moreover, additional features may be incorporated on the device 700, such as sealing membranes 140 and tissue engaging elements 170 as described above with respect to the device 100.

[00297] Figures 60A-60B are cross-sectional side views of a distal end of a delivery catheter 18 for delivering the prosthetic heart valve device 700 of Figure 59C to a native mitral valve in the heart in accordance with another embodiment of the present technology. As shown in Figures 60A-60B the prosthetic heart valve device 700 is collapsed into a delivery configuration 706 and retained within a two portion delivery sheath 70 at the distal end of the catheter 18 (Figure 60A). Upon delivery of the distal end of the catheter 18 to the desired location at or near a native mitral valve, the device 700 can be released from the two portion sheath 70 by retracting an upper portion 72 in a distal direction and/or retracting a lower portion 74 in a proximal direction (shown with arrows in Figure 60A) thereby separating the sheath and exposing the collapsed device 700 from within the sheath 70. In one embodiment, the device 700 can self-expand to its expanded configuration 702 following retraction of the sheath 70 (Figure 60B). As illustrated in Figure 60B, when the sheath 70 is retracted in both the proximal and distal directions, the first and second anchoring members 610, 710 can self-expand outwardly to engage the native tissue. When using a balloon 300 to expand the support valve 120, the balloon 300 can be inflated to fully expand the device 700.

[00298] Figure 61 illustrates a prosthetic heart valve device 800 configured in accordance with another embodiment of the present technology. Figure 61 is a side view of the device 800 that includes features generally similar to the features of the prosthetic heart valve devices 100, 600, 700 described above with reference to Figures 10A-60B. For example, the device 800 includes a support valve 120 having upstream and downstream ends 121, 123 and an interior in which a valve (not shown) may be coupled. The device also includes first and second anchoring members 810 and 850. The first anchoring member 810 has a first flared upstream portion 812 and a first downstream portion 811 that is coupled to an outer or exterior surface 127 of the valve support 120. The first flared upstream portion 812 can be mechanically isolated from the valve support 120. Additionally, the first flared upstream portion 812 can be configured to engage supra-annular tissue of the native mitral valve. The second anchoring member 850 can be configured to at least partially surround the first anchoring member 810 and to have a second flared upstream portion 852 for engaging the subannular tissue of the native mitral valve. The second anchoring member 850 can also have a second downstream portion 851 coupled to the outer surface 127 of the valve support 120 in a manner that mechanically isolates the valve support 120 from at least the second upstream portion 852.

[00299] As shown in Figure 61, the first anchoring member 810 can have a plurality of first longitudinal ribs 814 and the second anchoring member 850 can have a plurality of second longitudinal ribs 854. In one embodiment, each of the individual first ribs 814 are longer than each of the individual second ribs 854 such that the first anchoring member 810 has a height H_{AM1} greater than a height H_{AM2} of the second anchoring member 850. Accordingly, the height H_{AM2} can be selected to orient the second anchoring member 850 to engage subannular tissue, while the height H_{AM1} can be selected to orient the first anchoring member 810 to extend through the mitral valve from the left ventricle to engage supra-annular tissue in the left atrium.

[00300] Figure 61 illustrates one embodiment of the device 800 that can include a lower ring 808 on which the ribs 814, 854 can be interconnected. The lower ring 808 can allow the ribs 814, 854 to expand radially outward away from the valve support 120 at the upstream portions 812, 852. The device 800 can also include a first upper ring member 816 coupled to the plurality of first longitudinal ribs 814. The first upper ring member 816 can be shaped and or patterned to have a downward oriented rim 818 for engaging supra-annular tissue. The device can further include a second upper ring member 856 coupled to the plurality of second longitudinal ribs 854. The second upper ring member 856 can be shaped and or patterned to have an upward oriented rim 858 for engaging subannular tissue.

[00301] Figures 62A-62C are partial cross-sectional side views of a distal end of a delivery system 10 showing delivery of the prosthetic heart valve device 800 of Figure 61 at a mitral valve MV in accordance with another embodiment of the present technology. The device 800 can be retained in a collapsed configuration 806 within a sheath 20 of the delivery system (Figure 62A). When the distal end of the delivery system engages the target location, the sheath 20 can be retracted proximally from the device 800, thereby releasing the features of the device 800 to expand into the expanded configuration 102 (Figures 62B-62C). As shown in Figure 62B, the second anchoring member 850 can be released first from the retracting sheath 20 and the upward oriented rim 858 of the second upper ring member 856 can be positioned to engage the subannular tissue. The sheath 20 can prevent the first anchoring member 810 from disengaging from the delivery system 10 and/or moving outside the sheath 20 until the rim 858 of the second anchoring member 850 is moved into position to engage the subannular tissue. Referring to Figure 62C, a plunger 11 can engage the first anchoring member 810 (as shown by downward arrow in Figure 62B) and/or the sheath 20

can be disengaged/retracted (shown by upward arrow in Figure 62C) from the first anchoring member 810 thereby allowing the second anchoring member 850 to move radially outward to the expanded configuration 802. The downward oriented rim 818 of the first upper ring member 816 can be positioned to engage the supra-annular tissue (Figure 62C). Once deployed, the rings 816, 856 can sandwich the annulus AN of the mitral valve and inhibit movement of the device 800 in both upstream and downstream directions.

[00302] Figure 63 is an isometric side view of a prosthetic heart valve device 900 in accordance with a further embodiment of the present technology. The device 900 includes features generally similar to the features of the prosthetic heart valve devices 100, 600, 700 and 800 described above with reference to Figures 10A-62C. For example, the device 900 includes a support valve 120 having upstream and downstream ends 121, 123 and an interior in which a valve (not shown) may be coupled. The device 900 includes an anchoring member 910 that has a flared upstream portion 912 and a downstream portion 911 coupled to the valve support 120. However, the device 900 also includes upper and lower rings 950, 952 and a plurality of flexible annulus engaging elements 970 distributed around a circumference 980 of the anchoring member 910 and configured to couple the upper ring 950 to the lower ring 952. The flexible annulus engaging elements 970 can have a shape such as a C-shape or U-shape that is oriented to have an open portion outward from the device 900 such that the native annulus AN can be engaged in recesses 971 of the annulus engaging elements 970. The annulus engaging elements 970 can also include points 972, 973 for engaging and potentially piercing supra-annular and subannular tissue, respectively. The annulus engaging elements 970 can be suitably flexible to bend in a manner that brings the points 972, 973 close together for securing the device 900 to the annulus AN when the device 900 is deployed.

[00303] Figures 64A-64B illustrate a method for deploying the device 900 at the native mitral valve. Referring to Figures 63 and 64A-64B together, the annulus engaging elements 970 can be generally relaxed or have a wide recess 971 in an open state 903. As such, the upper ring 950 can rest above the lower ring 952 a first distance D_{R1} when the elements 970 are in the open state 903. The device 900 can also include a plurality of pull-wires 974 that are slideably engaged with the upper ring 950 (e.g., through holes 975) and secured to the lower ring 952. When the wires 974 are pulled in an upward or upstream direction, the lower ring 952 moves in an upward/upstream direction toward the upper ring 950. As the lower ring 952 approaches the upper ring 950, the annulus engaging elements 970 can bend such

that the points 972, 973 are brought closer together and/or engage or pierce the annulus tissue (Figure 64B). Accordingly, when the device 900 is in the deployed state 904, the upper ring 950 can be held by the pull-wires 974 at a second distance D_{R2} above the lower ring 952, wherein the second distance D_{R2} is less than the first distance D_{R1} .

[00304] Figures 64C-64D show an alternative arrangement of the pull-wires 974 in which the wires 974 are secured to the upper ring 950 and are slideably engaged with the lower ring 952 (e.g., through holes 976). The pull-wires 974 can also be slideably engaged with the upper ring 950 (e.g., such as through holes 975) such that the pull-wires can be pulled in an upward direction to bring the rings 950, 952 closer together in the deployed state 904.

[00305] Figure 65A is an isometric side view of a prosthetic heart valve device 1000 in accordance with a further embodiment of the present technology. The device 1000 includes features generally similar to the features of the prosthetic heart valve devices 100, 600, 700, 800 and 900 described above with reference to Figures 10A-64D. For example, the device 1000 includes a support valve 120 having upstream and downstream ends 121, 123 and an interior 134 in which a valve 130 may be coupled. However, the device 1000 includes an inflatable anchoring member 1010 coupled to and at least partially surrounding the valve support 120. The inflatable anchoring member 1010 can be configured to inflate/expand upon deployment and engage native tissue at the desired target location. As shown in Figure 65A, the inflatable anchoring member 1010 can have one or more fillable chambers 1014 for receiving a fill substance such as a solution (e.g., saline or other liquid) or gas (e.g., helium, CO₂ or other gas) following implantation of the device 1000. In other embodiments, the fillable chambers 1014 can be filled with a hardening material (e.g., epoxy, cement, or other resin).

[00306] In one embodiment, the fillable chambers 1014 and/or the anchoring member 1010 can be formed of polytetrafluoroethylene (PTFE), urethane, or other expandable polymer or biocompatible material. The fillable chambers 1014 can have a predetermined shape such that the fillable chambers 1014, when inflated, form fixation elements 1015 for engaging the native anatomy. For example, the fixation elements 1015 can include a supra-annular flange 1016 for engaging a surface of the annulus AN within the left atrium LA. The elements 1015 may also include subannular flanges 1018 for engaging subannular tissue and/or arms 1020 for engaging leaflets LF (e.g., behind leaflets). Accordingly, the chambers

1014 can be incorporated or shaped such that the anchoring member 1010 engages supra-annular tissue, subannular tissue, leaflets or other tissue at or near the mitral valve MV while mechanically isolating the valve support 120 from distorting diastolic and systolic forces generated in the heart and particularly radial forces exerted on the device 1000 at or near the native mitral valve. For example, following deployment, the inflatable anchoring member 1010 can absorb pulsatile loading and other forces generated against the device 1000 such that deformation of the anchoring member 1010 does not substantially deform the valve support 120.

[00307] Figure 65B is a partial cross-sectional side view of a distal end of a delivery system 10 suitable for delivery of the prosthetic heart valve device 1000 of Figure 65A in accordance with another embodiment of the present technology. As shown in Figure 65B, the delivery system 10 can include a delivery catheter 18 configured to retain the device 1000 in a collapsed configuration 1006. In the collapsed configuration 1006, the inflatable anchoring member 1010 is deflated. The delivery system 10 can also include a fill tube 90 suitable to deliver the fill substance when the device 1000 is in position and ready for deployment. Referring to Figures 65A-65B together, and in one embodiment, the inflatable anchoring member 1010 can be partially filled with the fill substance such that the position of the device 1000 at the implant site can be adjusted to align the fixation elements 1015 with the native tissue features before fully expanding and/or inflating the anchoring member 1010 to hold the device 1000 in place at the target location.

[00308] Figures 66A-66D are cross-sectional views of prosthetic heart valve devices 1100 having fillable chambers 1114 in accordance with additional embodiments of the present technology. Similar to the device 1000 discussed with respect to Figures 65A-65B, the devices 1100 include features such as the valve support 120 having an interior 134 in which a valve 130 is coupled and include an expandable anchoring member 1110 coupled to the valve support 120 in a manner that mechanically isolates the valve support 120 from forces exerted upon the anchoring member 1110 when implanted at the native mitral valve. The anchoring member 1110 can be coupled to the valve support 120 such that an upstream region 1112 of the anchoring member 1110 is configured to engage native tissue on or downstream of the annulus so as to prevent migration of the device 1100 in the upstream direction. In the embodiments shown in Figures 66A-66D, the devices 1100 can also include one or more fillable chambers 1114 configured to expand and/or inflate in an outward

direction to support an outward expansion of the anchoring member 1100 (Figures 66A, 66C-66D), or to engage native tissue (Figures 66B). In one embodiment, the fillable chambers 1114 and/or the anchoring member 1010 can be formed of polytetrafluoroethylene (PTFE), urethane, or other expandable polymer or biocompatible material. The fillable chambers 1114 can have a predetermined shape such that the fillable chambers 1114, when inflated, form fixation elements for engaging the native anatomy (as shown in Figure 66B) or for engaging the anchoring member 1110 (as shown in Figures 66A, 66C and 66D).

[00309] Referring to Figure 66A, the fillable chamber 1114 can be chambers 1114 created with a space between the valve support 120 and the anchoring member 1110. Following expansion of the device 1100, the fillable chambers 1114 can be filled with a fill substance such as a solution (e.g., saline or other liquid) or gas (e.g., helium, CO₂ or other gas). In other embodiments, the fillable chambers 1114 can be filled with a hardening material (e.g., epoxy, cement, or other resin). In other embodiments, the fillable chambers 1114 can be a separate component of the device 1100, such a ring-shaped chamber 1150 coupled to an outer surface 1142 of the anchoring member 1110 (Figure 66B) or to an inner surface 1141 of the anchoring member 1110 or to an exterior surface 127 of the support valve 120. In Figures 66C-66D, for example, the ring-shaped chamber 1150 can provide additional support to the anchoring member 1110 such that inward deformation is counteracted by the presence of the ring-shaped chamber 1150. Additionally, as shown in Figure 66D, the fillable chamber 114 can be a ring-shaped chamber 1150 that deforms the anchoring member 1110 in an outward direction against the native tissue.

[00310] In accordance with another aspect of the present technology, Figures 67A-67B illustrates other embodiments of a prosthetic heart valve device 1200. Referring to Figures 67A-67B together, the device 1200 can include a radially expandable anchoring member 1210 configured to engage native tissue on or downstream of the annulus, and a support valve 120 and/or a prosthetic valve 130 coupled to an interior portion 1234 of the anchoring member 1210. The anchoring member 1210 can have a first longitudinal length L_{L1} on a posterior leaflet-facing side 1222 of the anchoring member 1210 and have a second longitudinal length L_{L2} on an anterior leaflet-facing side 1224 of the anchoring member 1210. As shown in Figure 67A, the first length L_{L1} is greater than the second length L_{L2} such that occlusion of a left ventricle outflow tract (LVOT) is limited. Accordingly, in one embodiment, the posterior leaflet-facing side 1222 can provide suitable fixation and support for the anchoring member

1210 by engaging the thicker ventricular wall and tissue on the posterior leaflet side of the mitral valve. Concurrently, the shorter anterior leaflet-facing side 1224 of the anchoring member 1210 can have sufficient sealing and conformability to engage the anterior leaflet and/or subannular tissue aligned with the anterior leaflet of the native valve.

[00311] Optionally, the device 1200 can also include one or more stabilizing elements such as an arm 1250 coupled to the anchoring member 1210 for engaging a leaflet and/or a subannular surface. In Figure 67A, the arm 1250 can be coupled to a downstream end 1223 of the anchoring member 1210 on the posterior leaflet-facing side 1222 of the anchoring member 1210 and be configured to extend behind the posterior leaflet. In one embodiment, the arm 1250 can be configured to sandwich the posterior leaflet between the arm 1250 and the anchoring member 1210.

[00312] In Figure 67B, the device 1200 can include first and second arms (individually identified as 1250a and 1250b) coupled to the anchoring member 1210 for engaging leaflets and/or subannular surfaces. For example, the first arm 1250a can be coupled to the downstream end 1223 at the anterior leaflet-facing side 1224 of the anchoring member 1210 with extension 1251a and can be configured to further extend behind the anterior leaflet. The second arm 1250b can be coupled to the downstream end 1223 of the posterior leaflet-facing side 1222 of the anchoring member 1210 with extension 1251b and be configured to extend behind the posterior leaflet. In the illustrated embodiment, the extensions 1251a and 1251b can vary with respect to each other and be selected based on the anatomy of the target tissue. In other embodiments, not shown, the arm 1250 and or the anchoring member 1210 can include tissue engaging elements as described above with respect to device 100 for further positioning and stabilizing of the device 1200 at the desired target location. One of ordinary skill will recognize that the valve support 120 can also be uneven or have sides having different lengths such that the valve support will not substantially occlude the left ventricle outflow tract (LVOT).

[00313] Figures 68A-68B are side views of prosthetic heart valve devices 1300 shown in an expanded configuration 1302 and configured in accordance with an additional embodiment of the present technology. The prosthetic heart valve devices 1300 include features generally similar to the features of the prosthetic heart valve device 100 described above with reference to Figures 10A-56. For example, the prosthetic heart valve device 1300 includes the valve support 120 configured to support a prosthetic valve 130 and an anchoring member 110

coupled to the valve support 120 in a manner that mechanically isolates the valve support 120 from forces exerted upon the anchoring member 110 when implanted at the native mitral valve. However, in the embodiments shown in Figures 68A-68B, the device 1300 also includes a positioning element 1350 configured to adjust or maintain a desired position of the device 1300 within or near the native mitral valve (e.g., away from the LVOT). The positioning element 1350 can be coupled to the downstream portion 111 of the anchoring member 110 (as shown in Figures 68A-68B), the upstream portion 112 of the anchoring member 110, or to the valve support 120, at an element connection point 1352 and extend outward from the element connection point 1352 to engage ventricular tissue at a desired location. In one embodiment, the positioning element 1350 can extend outward from the device 1300 in a direction approximately transverse to the longitudinal axis 101. In other embodiments, not shown, the positioning element 1350 can extend outwardly from the device 1300 at an obtuse or an acute angle relative to the longitudinal axis 101 for engaging the ventricular tissue at the desired location.

[00314] In the embodiment shown in Figure 68A, the positioning element 1350 can include a positioning arm 1354 and a tissue engaging portion 1356 coupled to the distal arm end 1358 of the positioning arm 1354. The positioning arm 1354 and tissue engaging portion 1356 together can extend a desired positioning distance D_{PI} away from the element connection point 1352 on the device 1300 (e.g., from the anchoring member 110) such that the distal end 1360 of the positioning element 1350 can engage ventricular tissue, such as a ventricular wall. In some embodiments, the positioning distance D_{PI} can be selected to be greater than a distance between the implanted device 1300 and the ventricular tissue such that the positioning element 1350, after engaging the ventricular tissue, extends the distance between the implant device 1300 and the ventricular tissue. In this way, the device 1300 can be positioned, aligned and maintained in an alternate position within or near the mitral valve.

[00315] The tissue engaging portion 1356 can be configured to contact the ventricular tissue, or other tissue (e.g., annular tissue, leaflet tissue, etc.), in an atraumatic manner such that the tissue engaging portion 1356 does not penetrate or pierce the tissue. In one embodiment, the tissue engaging portion 1356 can be resilient and/or be formed of a shape memory material (e.g., nitinol) that can be partially deformed when engaging tissue. For example, the tissue engaging portion 1356 can be configured to absorb forces generated by the ventricular tissue (e.g., ventricular wall) during e.g., systole, without translating

movement or altering a desired position of the device 1300 with respect to the native mitral valve. In other embodiments, the distal end 1360 of the positioning element 1350 can have other shapes or configurations that penetrate the ventricular tissue. The device 1300 can include one or more positioning elements 1350 disposed around the device 1300 for positioning and/or maintaining a desired position of the device 1300 with respect to native anatomy. For example, it may be desirable to increase the distance between the device 1300 and the left ventricular outflow tract (LVOT), and a positioning element 1350 can be configured to engage ventricular tissue to push or encourage the device 1300 a selected distance away from the LVOT.

[00316] In the embodiment shown in Figure 68B, the positioning element 1350 can include a looped tissue engaging portion 1358 coupled to the device 1300 at the connection point 1352. The looped tissue engaging portion 1358 can extend the desired positioning distance D_{PI} away from the element connection point 1352 on the device 1300 (e.g., from the anchoring member 110) such that the distal end 1360 of the looped tissue engaging portion 1358 can engage ventricular tissue, such as a ventricular wall. The looped tissue engaging portion 1358 can be configured to absorb radially contracting forces or other forces generated and transmitted by the ventricular tissue (e.g., within the left ventricle) such that they are not transmitted to or can change the position of the device 1300 with respect to the native heart valve. Accordingly, the device 1300 can be positioned, aligned and maintained in an alternate position within or near the mitral valve.

[00317] In another embodiment, not shown, a positioning structure, separate from the prosthetic heart valve device 100, can be implanted or otherwise positioned in the left ventricle (e.g., at or near the LVOT) and which can be configured to engage portions of the device 100, such as the anchoring member 110. Accordingly, such a positioning structure can be provided to prevent the device 100 from obstructing or partially obstructing the LVOT. In one embodiment, not shown, the positioning structure could be a stent-like cylinder or cage that expands into engagement with the ventricular wall and keeps the LVOT clear to allow blood to flow freely from the left ventricle through the aortic valve. In one example, the positioning structure could be delivered by catheter that is inserted through the aorta and the aortic valve into the left ventricle, or through the apex or the left atrium via the same delivery catheter used for delivering and implanting the device 100.

[00318] Figures 69A-69E are cross-sectional and side views of prosthetic heart valve devices 1400 shown in an expanded configuration 1402 and configured in accordance with an additional embodiment of the present technology. The prosthetic heart valve devices 1400 include features generally similar to the features of the prosthetic heart valve devices 100, 600 described above with reference to Figures 10A-57E. For example, the prosthetic heart valve devices 1400 include the valve support 120 configured to support a prosthetic valve 130 and an anchoring member 110 or 610 coupled to the valve support 120 in a manner that mechanically isolates the valve support 120 from forces exerted upon the anchoring member 110 when implanted at the native mitral valve. However, in the embodiments shown in Figures 69A-69E, the devices 1400 also includes a an expandable tissue-engaging ring 1450 coupled to a tissue engaging portion of the anchoring member 110 and configured to provide additional contact surface for engaging native tissue at or near the annulus of the heart valve.

[00319] In one embodiment, shown in Figures 69A-69B, the expandable tissue-engaging ring 1450 can be coupled to an upstream perimeter 113 of the anchoring member 110 and have a tissue-engaging surface 1452 facing in an outward direction relative to the device 1400. In some embodiments, the tissue-engaging surface 1452 can have tissue-engaging elements 170 for engaging and/or piercing the tissue. In another embodiment, shown in Figure 69C, the expandable tissue-engaging ring 1450 can be coupled to a downstream perimeter 115 of the anchoring member 1410 and have a tissue-engaging surface 1452 facing in an outward direction relative to the device 1400. In another embodiment shown in Figure 69D, the expandable tissue-engaging ring 1450 may include a plurality of fibrous elements 1454 (e.g., fiber elements) that can be configured to encourage tissue ingrowth, thrombus and/or be configured to provide a seal between the anchoring member 110 and the tissue. In various arrangements, the expandable tissue-engaging ring 1450 can expand and contract between various deployment and delivery configurations.

[00320] Figure 69E shows another embodiment of the prosthetic heart valve device 1400 having the expandable tissue-engaging ring 1450. In this embodiment, the device 1400 can have a valve support 120 coupled to a first anchoring member 110 and a second anchoring member. In one embodiment, the first anchoring member 110 can be coupled to the valve support 120 at the downstream end 123 and extends outward and in an upstream direction. The second anchoring member 1410 can be coupled to the valve support 120 at the upstream end 121 and extend outward and in a downstream direction. The expandable tissue-engaging

ring 1450 can be coupled to the distal portions of the first and second anchoring members 110, 1410 and have the tissue-engaging surface 1452 facing in an outward direction relative to the device 1500 for engaging tissue at or near the annulus AN or leaflets LF. In a particular example, the expandable tissue-engaging ring 1450 can have a first end 1460 coupled to an upstream end 1461 of the first anchoring member 110. The expandable tissue-engaging ring 1450 can also have a second end 1470 coupled to a downstream end 1471 of the second anchoring member 1410. The tissue-engaging surface 1452 may also include tissue engaging elements 170 for engaging and/or piercing the tissue at the target location.

[00321] Referring to Figures 69A-69E together, the outward radial force of the expandable tissue-engaging ring 1450 against the tissue and supported by the anchoring members 110 and/or 1410 can prevent the device 1400 from migrating in an upstream direction. Additionally, the expandable tissue-engaging ring 1450 along with at least the portions of the anchoring members 110 and/or 1410 that are uncoupled from the valve support 120 can effectively mechanically isolate the valve support 120 and the valve 130 from compromising radially compressive forces exerted on the device 1400 from the heart valve tissue.

[00322] Figure 70 is a cross-sectional side view of another prosthetic heart valve device 1500 configured in accordance with an embodiment of the present technology. The device 1500 can also include features as described above including a valve support 120 and a prosthetic valve 130 retained within the valve support 120. The device 1500 can also include a plurality of anchoring members (individually identified as 110a-c). The anchoring members 110a-c can be coupled at respective downstream perimeters 115a-c to the valve support 120 and be separated by gaps 1515 such that respective upstream perimeter 113a-c can engage cardiac tissue at variable target locations at the native valve. Optionally, the device 1500 can also include the expandable tissue-engaging ring 1450 (Figures 69A-D) such as those having tissue engaging features 170 for further engaging tissue at the native valve. In one embodiment, the expandable tissue-engaging ring 1450 can be coupled to the upstream perimeter of more than one anchoring member (e.g., the upstream perimeters 113b and 113c of anchoring members 110b and 110c). However, in other arrangements, the device 1500 will not have the expandable tissue-engaging ring 1450.

[00323] Figure 71 is a cross-sectional side view of yet another prosthetic heart valve device 1600 configured in accordance with an embodiment of the present technology. The

device 1600 can also include features as described above including a valve support 120 and a prosthetic valve 130 retained within the valve support 120. The device 1500 can also include the anchoring member 110. However, the device 1600 can also include an expandable retainer 1610 for further engaging tissue at or near the native valve annulus. In one embodiment, the retainer 1610 can be an extension of upstream end 121 of the valve support 120, however, in another embodiment, the retainer 1610 can include a separate expandable feature coupled to the upstream end 121 of the valve support. In some arrangements, the retainer 1610 can be mechanically isolated from the valve support 120 such that forces generated at the native valve are absorbed or otherwise translated by the retainer 1610. In this manner, the retainer 1610 may be deformed by radial forces exerted on the retainer 1610 while the valve support remains substantially undeformed.

[00324] In one embodiment, as shown, the anchoring member 110 can be configured to engage the retainer 1610; however, in other embodiments, the anchoring member 110 can be positioned differently such that the anchoring member 110 contacts tissue different than that of the retainer 1610. For example, the anchoring member 110 may extend outside a radius (not shown) of the retainer to contact subannular tissue. Additional details and embodiments regarding the structure, delivery and attachment of retainers 1610 suitable for use with the prosthetic heart valve devices disclosed herein can be found in International PCT Patent Publication No. WO/2013/059743, entitled "DEVICES, SYSTEMS AND METHODS FOR HEART VALVE REPLACEMENT," filed October 19, 2012.

Additional Embodiments

[00325] Features of the prosthetic heart valve device components described above and illustrated in Figures 10A-71 can be modified to form additional embodiments configured in accordance with the present technology. For example, the prosthetic heart valve device 1100 illustrated in Figures 65A-65B without flared anchoring members can include anchoring members that are coupled to the valve support or other feature and are configured to extend radially outward to engage subannular tissue. Similarly, the prosthetic heart valve devices described above and illustrated in Figures 57A-71 can include features such as sealing members as well as stabilizing features such as arms and tissue engaging elements.

[00326] Features of the prosthetic heart valve device components described above also can be interchanged to form additional embodiments of the present technology. For example, the anchoring member 1210 of the prosthetic heart valve device 1200 illustrated in Figures 67A can be incorporated into the prosthetic heart valve device 600 shown in Figures 57A-57C.

[00327] The following Examples are illustrative of several embodiments of the present technology.

Examples

1. A device for repair or replacement of a native valve of a heart, the native valve having an annulus and leaflets coupled to the annulus, comprising:

an anchoring member having an upstream portion or a first portion configured to engage with tissue on or under the annulus and to deform in a non-circular shape to conform to the tissue and a downstream portion or second portion; and

a valve support coupled to the downstream portion of the anchoring member and configured to support a prosthetic valve, wherein the valve support has a cross-sectional shape;

wherein the upstream portion of the anchoring member is mechanically isolated from the valve support such that the cross-sectional shape of the valve support remains sufficiently stable that the prosthetic valve remains competent when the anchoring member is deformed in the non-circular shape.

2. The device of example 1 wherein the valve support has an upstream region spaced radially inward from the upstream portion of the anchoring member such that if the anchoring member is deformed inwardly the upstream region remains substantially undeformed.

3. The device of example 1 wherein the upstream portion is configured to engage valve tissue selected from an inward-facing surface of the annulus and an inward facing surface of the leaflets under the annulus.

4. The device of example 3 wherein the anchoring member is configured to apply outward force against the valve tissue so as to resist movement of the device when blood flows through the valve support in a downstream direction when the valve is open and when blood pushes in an upstream direction against the valve when the valve is closed.
5. The device of example 1 wherein the anchoring member is self-expanding.
6. The device of example 5 wherein the anchoring member comprises Nitinol.
7. The device of example 5 wherein the valve support is self-expanding.
8. The device of example 1 wherein both the anchoring member and the valve support comprise a metal.
9. The device of example 1 wherein the anchoring member is formed of a nitinol tube having a wall thickness of approximately 0.010 inches to about 0.130 inches.
10. The device of example 1 wherein the anchoring member includes a plurality of longitudinal ribs having axial stiffness to resist movement of the device in an upstream direction.
11. The device of example 1 wherein the anchoring member includes a plurality of interconnected struts.
12. The device of example 11 wherein the plurality of interconnected struts are arranged in a diamond configuration.
13. The device of example 1 wherein the anchoring member comprises a plurality of wires.
14. The device of example 13 wherein the plurality of wires are woven and/or welded together.

15. The device of example 1 wherein the anchoring member includes a plurality of flexible filaments arranged in a diamond configuration around a circumference of the anchoring member, and wherein the diamond configuration includes one or more rows of diamonds and between approximately 12 and approximately 36 columns of diamonds around the circumference.

16. The device of example 1 wherein the valve support includes an upstream end and a downstream end, and wherein the upstream end extends a distance in an upstream direction beyond the upstream portion of the anchoring member.

17. The device of example 1 wherein the valve support includes an upstream end and a downstream end, and wherein the upstream portion of the anchoring member extends a distance in an upstream direction beyond the upstream end of the valve support.

18. The device of example 1 wherein the anchoring member includes a rim at a proximal end of the upstream portion, the rim having an undeformed configuration, the undeformed configuration having a generally oval shape or a D-shape

19. The device of example 14 wherein the rim includes a plurality of peaks and a plurality of valleys.

20. The device of example 1 wherein:
the anchoring member includes a rim at a proximal end of the upstream portion, the rim having a generally oval shape or D-shape; and
the anchoring member includes a downstream end, and wherein a distance between the downstream end and the rim varies around a circumference of the anchoring member.

21. The device of example 20 wherein the distance varies from about 6 mm to about 20 mm.

22. The device of example 20 wherein the distance varies from about 9 mm to about 12 mm

23. The device of example 20 wherein the distance includes a plurality of distances including:

- a first distance between the downstream end and the rim being approximately 7 mm to about 8 mm at first and second regions of the anchoring member, first and second regions configured to align with first and second commissures of the native mitral valve;
- a second distance between the downstream end and the rim being approximately 9 mm to about 11 mm at a third region of the anchoring member, the third region configured to align with an anterior leaflet of the native mitral valve; and
- a third distance between the downstream end and the rim being approximately 12 mm to about 13 mm at a fourth region of the anchoring member opposite the third region, the fourth region configured to align with a posterior leaflet of the native mitral valve.

24. The device of example 1 wherein:

- the anchoring member includes a rim at a proximal end of the upstream portion, the rim having a generally oval shape or D-shape;
- the tissue on or under the annulus has a non-circular shape having a minor diameter and a major diameter generally perpendicular to the minor diameter;
- the upstream portion of the anchoring member has an outer perimeter having a major perimeter diameter and a minor perimeter diameter generally perpendicular to the major perimeter diameter;
- the major perimeter diameter is greater than the major diameter; and
- the minor perimeter diameter is greater than the minor diameter.

25. The device of example 24 wherein the major perimeter diameter is approximately 2 mm to approximately 22 mm greater than the major diameter.

26. The device of example 24 wherein the major perimeter diameter is approximately 8 mm to approximately 15 mm greater than the major diameter.

27. The device of example 24 wherein the major perimeter diameter is approximately 45 mm to about 60 mm.

28. The device of example 24 wherein the minor perimeter diameter is approximately 40 mm to about 55 mm.

29. The device of example 1 wherein the valve support is a generally circular cylinder.

30. The device of example 29 wherein the valve support has a diameter of approximately 25 mm to about 30 mm.

31. The device of example 1 wherein the valve support is a cylindrical valve support having a diameter of approximately 27 mm.

32. The device of example 1 wherein the valve support is a cylindrical valve support having a longitudinal height of approximately 14 mm to about 17 mm.

33. The device of example 1 wherein:

the upstream portion of the anchoring member has a proximal end perimeter having peak portions and valley portions corresponding to native peak and valley portions of the annulus, respectively; and

the corresponding peak portions are configured to align with the native valley portion and the corresponding valley portions are configured to align with the native peak portions.

34. The device of example 1 wherein the valve support is extends around a longitudinal axis, and wherein the upstream portion of the anchoring member flares outward from the longitudinal axis by a taper angle.

35. The device of example 34 wherein the taper angle continuously changes between the downstream portion and the upstream portion.

36. The device of example 34 wherein the taper angle varies around a circumference of the upstream portion.

37. The device of example 34 wherein the taper angle is between approximately 30° to about 75°.

38. The device of example 34 wherein the taper angle is between approximately 40° to about 60°.

39. The device of example 1 wherein the valve support is oriented along a first longitudinal axis and the anchoring member is oriented along a second longitudinal axis, and wherein the first and second longitudinal axes are non-collinear.

40. The device of example 39 wherein the second longitudinal axis is off-set from the first longitudinal axis.

41. The device of example 39 wherein the second longitudinal axis is non-parallel to the first longitudinal axis.

42. The device of example 41 wherein the second longitudinal axis is disposed at an angle between 15° and 45° relative to the first longitudinal axis.

43. The device of example 1 wherein the upstream portion of the anchoring member includes a flared portion and a vertical portion, the vertical portion configured to radially expand and engage the annulus.

44. The device of example 43 wherein the flared portion includes tissue engaging elements configured to engage subannular tissue.

45. The device of example 1 wherein the upstream portion is radially separated from the valve support by a gap.

46. The device of example 45 wherein:

the anchoring member includes a rim at a proximal end of the upstream portion, the rim having an oval shape;
the valve support is a cylindrical valve support at least partially surrounded by the anchoring member; and
the gap varies around a circumference of the cylindrical valve support.

47. The device of example 46 wherein the gap is greater on an anterior leaflet facing side of the device than on a posterior leaflet-facing side of the device.

48. The device of example 1 wherein the device is configured so as to avoid obstruction of a left ventricular outflow tract (LVOT) of the heart.

49. The device of example 1, further comprising a skirt overlying a surface of the anchoring member, the skirt configured to inhibit blood flow between the anchoring member and the valve support.

50. The device of example 49 wherein the skirt is further configured to inhibit blood flow between the anchoring member and the tissue.

51. The device of example 49 wherein the skirt comprises at least one of Dacron[®], ePTFE, bovine pericardium, a polymer, thermoplastic polymer, polyester, Gore-tex[®], a synthetic fiber, a natural fiber or polyethylene terephthalate (PET).

52. The device of example 1 wherein the valve support is coupled to the anchoring member with one or more of a plurality of rivets and a plurality of sutures.

53. The device of example 1 wherein the valve support has a radial strength of approximately 42 mm Hg to about 47 mm Hg.

54. The device of example 1 wherein the valve support has a radial strength at least 100% greater than a radial strength of the anchoring member.

55. The device of example 1, further comprising a valve coupled to the valve support to inhibit retrograde blood flow.

56. The device of example 55 wherein the valve is a tri-leaflet valve.

57. The device of example 55 wherein the valve comprises bovine pericardium.

58. The device of example 55 wherein the valve has a plurality of commissural attachment structures, the valve being coupled to the valve support at the commissural attachment structures.

59. The device of example 58 wherein the commissural attachment structures are permanently fixed to the valve support.

60. The device of example 58 wherein the commissural attachment structures are integral with an interior wall of the valve support.

61. The device of example 58 wherein the valve support has a first height and the commissural attachment structures have a second height less than the first height.

62. The device of example 1, wherein the valve support is further configured to receive a replacement valve after the device is implanted at a native valve location.

63. The device of example 62 further comprising a temporary valve coupled to the valve support.

64. The device of example 63 wherein the temporary valve is adapted to be displaced against an inner wall of the valve support when the replacement valve is received in the valve support.

65. The device of example 63 wherein the temporary valve comprises a removable valve, and wherein the replacement valve is secured within the valve support after the temporary valve has been removed.

66. A prosthetic heart valve device for implantation at a native mitral valve, the native mitral valve having an annulus and leaflets, comprising:

an anchoring member positionable in a location between the leaflets, wherein an upstream portion or first portion of the anchoring member is expandable to a dimension larger than a corresponding dimension of the annulus such that upstream movement of the anchoring member is blocked by engagement of the upstream portion with tissue on or near the annulus, and the anchoring member has a downstream portion or a second portion; and

a valve support coupled to the downstream portion of the anchoring member, wherein the valve support is spaced radially inward from at least the upstream portion of the anchoring member, and wherein the valve support is configured to support a prosthetic valve.

67. The device of example 66 wherein the valve support is mechanically isolated from at least the upstream portion of the anchoring member.

68. The device of example 66 wherein the upstream portion of the anchoring member has a first flexibility and the valve support has a second flexibility less than the first flexibility such that if the upstream portion of the anchoring member is distorted the valve support remains substantially undistorted.

69. The device of example 66 wherein the upstream region of the valve support is spaced radially inward from the upstream portion of the anchoring member such that if the anchoring member is deformed inwardly the valve support is not engaged.

70. The device of example 66 wherein:

the anchoring member is defined by a structure separate from the valve support;

the valve support is coupled to the anchoring member at the downstream portion of the anchoring member; and

the downstream portion is longitudinally spaced apart from the upstream portion.

71. The device of example 66, further comprising a plurality of flexible coupling mechanisms configured to flexibly couple the valve support to the downstream portion of the anchoring member.

72. The device of example 71 wherein the flexible coupling mechanism can include at least one of a suture, a wire, or a flexible filament.

73. The device of example 71 wherein the flexible coupling mechanism can include at least one of a rivet, a screw, or a pin.

74. The device of example 66 wherein the device is moveable into a plurality of configurations including:

- a first configuration in which the valve support and the anchoring member are radially contracted;
- a second configuration in which the valve support and the anchoring member are radially expanded; and
- a third configuration in which the anchoring member is engaged with and at least partially deformed by tissue on or near the annulus.

75. The device of claim 74 wherein the valve support has an expanded shape in the second configuration, and wherein the valve support remains substantially in the expanded shape in the third configuration.

76. The device of example 74 wherein the anchoring member assumes the second configuration in an unbiased condition.

77. The device of example 74 wherein the anchoring member is deformable from the second configuration to the third configuration.

78. The device of example 74 wherein the device in the first configuration has a low profile configured for delivery through a guide catheter positioned at or near the native mitral valve.

79. The device of example 76 wherein the upstream portion of the anchoring member has a first diameter in the second configuration, and wherein the first diameter spans at least the distance between native commissures of the native mitral valve.

80. The device of example 76 wherein the upstream portion of the anchoring member has a first diameter and the valve support has a second diameter in the second configuration, and wherein the first diameter is approximately between 1.2 to 1.5 times the second diameter.

81. The device of example 66 wherein the upstream portion of the anchoring member has a first expanded diameter of approximately 28 mm to about 80 mm.

82. The device of example 66 wherein the valve support has an expanded diameter of approximately 25 mm to about 32 mm.

83. The device of example 66 wherein the downstream portion is longitudinally spaced apart from the upstream portion, and wherein the upstream portion has a first cross-sectional dimension and the downstream portion has a second cross-sectional dimension less than the first cross-sectional dimension.

84. The device of example 66 wherein the upstream portion is configured to engage an inward facing surface of the leaflets downstream of the annulus.

85. The device of example 66 wherein the anchoring member resists upstream migration of the device without any element of the device extending behind the leaflets of the native mitral valve.

86. The device of example 66 wherein the device does not engage supra-annular tissue or tissue upstream of the annulus.

87. The device of example 66, further comprising a sealing member extending around the upstream portion of the anchoring member and configured to seal against the

tissue on or downstream of the annulus to inhibit blood flow between the anchoring member and the tissue.

89. The device of example 87 wherein the sealing member promotes tissue ingrowth into the sealing member.

89. The device of example 87 wherein the sealing member comprises one or more of a polymer, thermoplastic polymer, a polyester, a synthetic fiber, a fiber, polyethylene terephthalate (PET), PTFE, Gore-Tex[®] or Dacron[®].

90. The device of example 87 wherein the sealing member includes a plurality of tissue engaging elements on an outer surface of the sealing member.

91. The device of example 87 wherein the anchoring member has a plurality of points on an upstream end, and wherein the points are configured to penetrate tissue on or downstream of the annulus so as to prevent upstream movement of the device.

92. The device of example 91 wherein the anchoring member includes a delivery mechanism for transitioning the plurality of points from a retracted position to an engagement position, and wherein the engagement position includes penetration of the annulus tissue with the points.

93. The device of example 66 further comprising a plurality of anchoring clips on an upstream end of the anchoring member, wherein the anchoring clips are configured to engage the annulus.

94. The device of example 66 wherein the anchoring member includes —
a plurality of longitudinal ribs; and
a plurality of circumferential connectors interconnecting the plurality of ribs;
wherein the anchoring member is flared in a proximal direction such that proximal ends of the ribs orient radially outward for engaging tissue on or downstream of the annulus so as to prevent migration of the device in an upstream direction.

95. The device of example 94 wherein the anchoring member has a central longitudinal axis, and wherein each individual rib has a plurality of segments having varying extension angles relative to the longitudinal axis.

96. The device of example 94 wherein the plurality of longitudinal ribs includes a first and second plurality of ribs, and wherein the first plurality of ribs have a characteristic different than the second plurality of ribs, the characteristic selected from the group of size, shape, stiffness, extension angle and the number of ribs within a given area of the anchoring member.

97. The device of example 94 wherein the longitudinal ribs are unevenly spaced around an outer perimeter of the anchoring member.

98. The device of example 94 wherein the valve support includes a plurality of posts connected circumferentially by a plurality of struts, and wherein each individual longitudinal rib is integrally formed with a corresponding post on the valve support.

99. The device of example 98 wherein each of the plurality of longitudinal ribs comprises a curved elbow portion integrally formed with the corresponding posts, the elbow portion configured to urge individual ribs radially outward from an inward configuration to an outward configuration.

100. The device of example 98, further comprising a tether coupling each individual rib with the corresponding post, wherein the tether is configured to limit an outward deflection of the rib when the rib is in an expanded configuration.

101. The device of example 98 wherein one or more individual circumferential connectors include a looped connector head, and wherein one or more individual struts include a looped strut head, and wherein the looped connector heads are coupled to the looped strut heads to form a flexible coupling mechanism.

102. The device of example 101 wherein the looped connector head is passed through the looped strut head to form the flexible coupling mechanism.

103. The device of example 101 wherein one or more flexible filaments couple the looped connector head to the looped strut head to form the flexible coupling mechanism.

104. The device of example 94 wherein the plurality of circumferential connectors include a plurality of bands extending around a circumference of the anchoring member, and wherein the bands are slideably coupled to each individual rib.

105. The device of example 66 wherein the anchoring member includes a plurality of longitudinal ribs arranged in a crisscross pattern to form a diamond configuration, and wherein the anchoring member is flared in a proximal direction such that proximal ends of the ribs orient radially outward for engaging tissue on or near the annulus so as to prevent migration of the device in an upstream direction.

106. The device of example 66 wherein the valve support is generally cylindrical and at least the upstream portion of the anchoring member is generally non-circular.

107. The device of example 106 wherein the upstream portion of the anchoring member is D-shaped.

108. The device of example 66 wherein the upstream portion has a proximal end having a rim, and wherein the rim does not lie in a single plane.

109. The device of example 108 wherein the rim has an undulating shape with peaks extending in an upstream direction and valleys extending in a downstream direction.

110. The device of example 109 wherein at least one peak has a different shape or dimension than at least one other peak.

111. The device of example 109 wherein at least one peak, if inverted longitudinally, has a different shape or dimension than at least one valley.

112. The device of example 109 wherein the rim has two peaks which are separated by two valleys.

113. The device of example 109 wherein the valleys are configured for positioning along commissural regions of the annulus.

114. The device of example 109 wherein the peaks have apices configured to be positioned near midpoint regions of the leaflets.

115. The device of example 66 wherein:

the annulus comprises native peak portions and native valley portions;

the upstream portion of the anchoring member has a proximal end perimeter having corresponding peak portions and corresponding valley portion; and

the corresponding peak portions are configured to align with the native valley portion and the corresponding valley portions are configured to align with the native peak portions.

116. The device of example 66 wherein:

the upstream portion of the anchoring member has a cross-sectional dimension greater than a corresponding cross-sectional dimension of the annulus of the native mitral valve; and

the valve support has a support cross-sectional dimension less than the corresponding cross-sectional dimension of the annulus.

117. The device of example 66 wherein at least the upstream portion is mechanically isolated from the valve support.

118. The device of example 66 wherein the downstream portion is substantially tubular, and wherein the upstream portion of the anchoring member is deformable to a non-circular cross-section while the valve support remains substantially circular in cross-section.

119. The device of example 66 wherein:

the valve support includes a plurality of first struts interconnected around a circumference of the valve support;

the anchoring member includes a plurality of second struts interconnected around a circumference of the anchoring member; and

the first struts are more rigid than the second struts.

120. The device of example 94 wherein the longitudinal ribs are configured to absorb distorting diastolic and systolic forces generated in a heart having the native mitral valve.

121. The device of example 94 wherein the ribs and connectors are formed in a chevron configuration.

122. The device of example 119 wherein the plurality of second struts are interconnected in a chevron configuration.

123. The device of example 94 wherein the plurality of second struts are interconnected in a diamond configuration.

124. The device of example 119 wherein the posts and struts are formed in a chevron configuration.

125. The device of example 94 wherein the ribs and connectors are formed of a shape memory material.

126. The device of example 125 wherein the shape memory material comprises nitinol.

127. The device of example 94, further comprising a plurality of tissue engaging elements on at least one of the ribs or the circumferential connectors, wherein the tissue engaging elements are configured to engage tissue of the annulus or leaflets.

128. The device of example 119, further comprising a plurality of tissue engaging elements on at least the second struts, wherein the tissue engaging elements are configured to engage tissue of the annulus or leaflets.

129. The device of example 127 wherein the tissue engaging elements are one of barbs, hooks or spikes.

130. The device of example 127 wherein one or more tissue engaging elements are oriented in an upstream direction, the one or more tissue engaging elements configured to limit movement of the device in the upstream direction during ventricular systole.

131. The device of example 127 wherein one or more tissue engaging elements are oriented in a downstream direction, the one or more tissue engaging elements configured to limit movement of the device in the downstream direction.

132. The device of example 127 wherein the tissue engaging elements have:
a piercing configuration in which the tissue engaging elements have a low profile for penetrating the tissue; and
a retaining configuration in which the tissue engaging elements have an expanded profile for maintaining the tissue engaging element within the tissue.

133. The device of example 132 wherein the tissue engaging elements are held in the piercing configuration with one or more of a biodegradable glue or a biodegradable coating.

134. The device of example 132 wherein the tissue engaging elements expand to one of a diamond shape, an arrowhead shape or a helical shape when in the retaining configuration.

135. The device of example 66 wherein the anchoring member is coupled to a sleeve, and wherein the sleeve is configured to limit radial expansion of the anchoring member when the anchoring member is in an expanded configuration.

136. The device of example 135 wherein the sleeve includes an outer portion configured to cover the anchoring member and an inner portion configured to at least partially surround the valve support.

137. The device of example 136 wherein the sleeve includes a plurality of horizontal septums extending between the outer portion and the inner portion of the sleeve.

138. The device of example 84 wherein each individual rib has a flexibility independent of the flexibility of other ribs.

139. The device of example 94 wherein each individual rib has variable flexibility along a length of the rib.

140. The device of example 66 wherein the upstream portion of the anchoring member conforms to a shape of the annulus of the native mitral valve while in a deployed configuration.

141. A device for treating a native mitral valve having an annulus and leaflets, comprising:

an anchor having an upstream portion configured to engage an upstream-facing surface of the leaflets downstream of the annulus; and

a valve support at least partially within the anchor, wherein the valve support is configured to support a prosthetic valve;

wherein the anchor is deformable to a non-circular cross-section while the valve support remains substantially circular in cross-section.

142. The device of example 141, further comprising a sleeve at least partially surrounding the valve support, wherein the sleeve provides a fluid barrier.

143. The device of example 141, further comprising a sealing member extending around the upstream portion of the anchor and configured to seal against at least the upstream-facing surface of the leaflets to inhibit blood flow between the anchor and the leaflets.

144. The device of example 143 wherein the sealing member further extends around the valve support, and wherein the sealing member is configured to inhibit blood flow in a space between the valve support and the anchor.

145. The device of example 141 wherein the anchor has a downstream portion longitudinally separated from the upstream portion, and wherein the downstream portion is coupled to a downstream end of the valve support.

146. The device of example 145 wherein the upstream portion is not directly coupled to the valve support.

147. The device of example 141 wherein the valve support has an upstream end and a downstream end oriented along a longitudinal axis, and wherein the anchor is coupled to the valve support at an intermediate position between the upstream and downstream ends.

148. The device of example 141, further comprising a plurality of tethers coupling the upstream portion of the anchor to the valve support, the tethers configured to limit radial expansion of the upstream portion.

150. A device for implantation at a native valve having an annulus and leaflets, comprising:

- a hyperboloidic anchoring member having an upstream end configured to engage an inward facing surface of the leaflets downstream of the annulus and a downstream end, wherein the upstream end has a different cross-sectional area than the downstream end;

- a valve support positioned in the anchoring member and configured to support a prosthetic valve, wherein the valve support is coupled to the anchoring member at a location spaced substantially downstream from the upstream end and is uncoupled to the anchoring member at the upstream end.

151. The device of example 150 wherein the anchoring member is formed of a flexible and shape memory material formed in a diamond pattern and configured to self-expand radially outward.

152. The device of example 150 wherein the flared anchoring member has the shape of a two-sheet hyperboloid.

153. The device of example 150, further comprising an atrial retainer configured to engage supra-annular tissue such that downstream movement of the device is blocked by engagement of the atrial retainer with the supra-annular tissue.

154. The device of example 153 wherein the atrial retainer includes outward-facing extensions of the valve support.

155. The device of example 153 wherein the atrial retainer includes extensions of the anchoring member configured to pass through the native valve to engage the supra-annular tissue.

156. The device of example 150, further comprising a sealing member disposed on the anchoring member and the valve support, the sealing member configured to block blood flow between the valve support and the anchoring member.

157. The device of example 156 wherein the sealing member surrounds an outer surface of the valve support and an inner surface of the anchoring member.

158. The device of example 156 wherein the sealing member includes a sleeve configured to cover at least a portion of the upstream end of the anchoring member and configured to seal against at least the inward facing surface of the leaflets to inhibit blood flow between the anchoring member and the leaflets.

159. The device of example 156 wherein the sealing member comprises a flexible and biocompatible material.

160. The device of example 159 wherein the material comprises one or more of Dacron[®], ePTFE, or bovine pericardium.

160. The device of example 150 wherein the upstream end is configured with a plurality of atraumatic nodes such that the upstream end resists penetration of the inward facing surface of the leaflets downstream of the annulus.

170. The device of example 150 wherein the upstream end is configured with a plurality of atraumatic nodes, and wherein the atraumatic nodes are unevenly space circumferentially around the upstream end.

171. The device of example 170 wherein the anchoring member includes a posterior facing side and an anterior facing side, and wherein a first atraumatic node configuration on the posterior facing side is different than a second atraumatic node configuration on the anterior facing side.

172. A prosthetic heart valve device for repair or replacement of a native heart valve of a patient, the heart valve having an annulus and leaflets, comprising:

- an anchoring member having an upstream portion or a first portion having a first cross-sectional dimension and a downstream portion or a second portion having a second cross-sectional dimension less than the first cross-sectional dimension, wherein the upstream portion is configured to engage cardiac tissue to retain the anchoring member in a fixed longitudinal position relative to the annulus; and
- a valve support coupled to the downstream portion of the anchoring member and configured to support a prosthetic valve, wherein the valve support is radially separated from the upstream portion of the anchoring member such that the upstream portion can deform inwardly without substantially deforming the valve support.

173. The device of example 172 wherein the anchoring member is moveable from a collapsed configuration for delivery of the device through vasculature of the patient to an expanded configuration for engagement of the cardiac tissue.

174. The device of example 172 wherein the valve support comprises an interior sized to receive a balloon, and wherein the balloon expands the valve support from a delivery configuration to an expanded configuration.

175. The device of example 172 wherein at least one of the anchoring member or the valve support comprises one or more of a resilient material, shape memory material, super

elastic material, or a nickel titanium alloy, and wherein the at least one of the valve support or the anchoring member is configured to self-expand from a delivery configuration to an expanded configuration when released from a constraint.

176. The device of example 172, further comprising one or more positioning elements coupled to the anchoring member, the positioning elements configured to engage ventricular tissue to position the device away from the left ventricle outflow tract (LVOT).

177. The device of example 176 wherein the position element comprises:

- a positioning arm configured to extend from the anchoring member to the ventricular tissue; and
- a tissue engaging portion at a distal end of the positioning arm, wherein the tissue engaging portion is configured to engage the ventricular tissue atraumatically.

178. A device for implantation at a native valve having an annulus and a plurality of leaflets, the device comprising:

- an anchoring member positionable between the leaflets and having a plurality of tissue engaging elements on an upstream end configured to engage cardiac tissue on or near the annulus so as to prevent migration of the device in the upstream direction; and
- a valve support positioned within an interior of the anchoring member and coupled to a downstream portion of the anchoring member, wherein the valve support is radially separated from at least an upstream portion of the anchoring member.

179. A device for repair or replacement of a native mitral valve having an annulus and a pair of leaflets, the device comprising:

- a support structure having an upper region, a lower region, and an interior to retain a prosthetic valve; and
 - an anchoring member surrounding at least a portion of the support structure, wherein the anchoring member is positionable between the leaflets and has a plurality of interconnected struts, an upper portion, and a lower portion;
- wherein the upper portion of the anchoring member is flared outwardly in a proximal direction and includes a plurality of tissue engaging elements extending

radially outward so as to engage cardiac tissue on or near the annulus and inhibit migration of the device in the upstream direction; and

wherein the lower region of the support structure is coupled to the lower portion of the anchoring member, and wherein the lower region of the support structure is mechanically isolated from at least deformation of the flared upper portion of the anchoring member.

180. The device of example 179 wherein the anchoring member has a central longitudinal axis, and wherein the interconnected struts include an arcuate region extending outwardly away from the longitudinal axis.

181. The device of example 179 wherein the device further comprises a plurality of flexible coupling mechanisms configured to flexibly couple the support structure to the anchoring member.

182. The device of example 181 wherein the flexible coupling mechanism can include at least one of a suture, a wire, a flexible filament, a rivet, a screw, or a pin.

182. The device of example 179 wherein the plurality of interconnected struts comprises a resilient material.

183. The device of example 179 wherein the anchoring member comprises a material sufficiently resilient to self-expand from an inward configuration to an outward configuration when released from a constrained condition.

184. The device of example 179 further comprising a covering extending over the plurality of interconnected struts, the covering comprising a material to encourage tissue in-growth.

185. The device of example 179 wherein the covering comprises a skirt extending over at least a portion of the anchoring member.

186. A prosthetic heart valve device, comprising:
a cylindrical support having a longitudinal axis and an interior along the longitudinal axis through which blood may flow; and
an anchor defined by a structure separate from the cylindrical support, the anchor having a non-circular cross-section, wherein the anchor has an outwardly flared upstream end configured to engage subannular tissue of a mitral valve, and wherein the anchor surrounds the cylindrical support and is coupled to the cylindrical support at a downstream end opposite the upstream end.

187. The device of example 186, further comprising a valve coupled within the interior of the support and configured to block blood flow through the support in an upstream direction and allow blood flow through the support in a downstream direction.

188. The device of example 186, further comprising a stabilizing member extending outward from the downstream end of the anchor, the stabilizing member configured to engage native tissue downstream of an annulus of the mitral valve.

189. The device of example 188 wherein the stabilizing member includes a plurality of arms extending from the downstream end, the arm configured to engage one or more of the subannular tissue, native leaflets, or a ventricular wall.

190. The device of example 189 wherein the arms extend behind the native leaflets.

191. The device of example 189 wherein each individual arm includes an arm body and a tip at a distal end of the arm body, the tip configured to engage native tissue.

192. The device of example 191 wherein the tip exerts force on the native tissue without penetrating the native tissue.

193. The device of example 191 wherein the tip includes a tissue engaging element for piercing through at least a portion of the native tissue.

194. The device of example 193 wherein the tissue engaging element includes at least one of a spike and a barb.

195. The device of example 191 wherein each individual arm includes an arm body extending away from the longitudinal axis at a first angle, and wherein each arm also includes an arm extension extending away from the longitudinal axis at a second angle greater than the first angle.

196. The device of example 186 wherein the anchor has a second longitudinal axis, and wherein the second longitudinal axis is off-set from the longitudinal axis of the cylindrical support.

197. A device for repair or replacement of a native valve having an annulus and a plurality of leaflets, the device comprising:

- an expandable cylindrical support configured for placement between the leaflets, the support having an upstream region or a first region, a downstream region or a second region and an interior in which a valve may be coupled; and

- an anchoring structure having a first portion and a second portion, wherein the second portion of the anchoring structure is coupled to the downstream region of the cylindrical support, and wherein the first portion of the anchoring structure extends outwardly away from the second portion, the anchoring structure having an upstream or first perimeter configured to engage tissue on or near the annulus;

- wherein the anchoring structure is mechanically isolated from the cylindrical support such that a force exerted radially at or near the upstream perimeter will not substantially alter a shape of the cylindrical support.

198. The device of example 197 wherein the device is implantable at a native mitral valve.

199. The device of example 198 wherein the anchoring structure is configured to inhibit movement of the device in an upstream direction by engagement of the tissue on or near the annulus.

200. The device of example 197 wherein the expandable cylindrical support and the anchoring structure are moveable between a delivery configuration for placement of the device in a lumen of a delivery catheter, and an expanded configuration for placement within the native valve.

201. The device of example 197 wherein the upstream perimeter includes a tissue engaging element configured to at least partially penetrate the tissue on or near the annulus.

202. The device of example 197, further comprising a second anchoring structure coupled to the upstream region of the cylindrical support and extending outwardly ,so as to engage at least one of the anchoring structure or the tissue on or near the annulus.

203. The device of example 197, further comprising a second anchoring structure coupled to the upstream perimeter, the second anchoring structure extending outwardly in a downstream direction.

204. The device of any one of examples 202 or 203 wherein the second anchoring structure is mechanically isolated from the cylindrical support.

205. A device to treat a heart mitral valve of a patient, the device comprising:
an inner frame having an outer surface and an inner surface, the inner surface configured to support a prosthetic valve; and
an outer frame coupled to the inner frame, the outer frame having an upper portion with a cross-sectional dimension greater than a corresponding cross-sectional dimension of an annulus of the mitral valve, wherein the upper portion is configured to engage tissue at or below the annulus of the mitral valve and prevent migration of the device in an upward direction during ventricular systole, and wherein at least the upper portion is mechanically isolated from the inner frame.

206. The device of example 205 wherein:
the inner frame comprises a longitudinal axis; and

the inner frame comprises a delivery configuration and an expanded configuration, wherein the outer surface is further from the longitudinal axis in the expanded configuration than in the delivery configuration.

207. The device of example 205 wherein:
inner frame comprises a longitudinal axis;
the outer surface is separated from the longitudinal axis by a first distance; and
the upper portion of the outer frame is separated from the longitudinal axis by a second distance greater than the first distance.

207. The device of example 205 wherein the outer frame is conical or tapered between the upper portion and a lower portion.

208. The device of example 205 wherein the inner frame has a first longitudinal length on a posterior leaflet-facing side and a second length on an anterior leaflet facing side, and wherein the first length is greater than the second length.

209. The device of example 208 wherein the posterior leaflet facing side further includes an arm configured to receive a posterior leaflet between the arm and the outer frame.

210. A prosthetic heart valve device for treating a native mitral valve having an annulus and a pair of leaflets, the device comprising:

a cylindrical inner skeleton having an interior to which a prosthetic valve may be coupled;

an outer skeleton coupled to the inner skeleton and positionable between the leaflets downstream of the annulus, the outer skeleton having a plurality of interconnected struts, wherein at least a portion of the struts are configured to engage native subannular tissue so as to prevent migration of the device in an upstream direction; and

wherein the outer skeleton is deformable to a non-circular cross-section while the inner skeleton remains substantially circular in cross-section.

211. The device of example 210 wherein each of the interconnected struts are inclined away from the inner skeleton.

212. The device of example 210 wherein the outer skeleton has a downstream portion and an upstream portion, wherein the downstream portion is coupled to the inner skeleton, and wherein the struts extend outwardly at the upstream portion to engage native subannular tissue.

213. The device of example 210 wherein the outer skeleton has a downstream portion and an upstream portion, wherein the upstream portion is coupled to the inner skeleton, and wherein the struts extend outwardly at the downstream portion to engage native subannular tissue.

214. The device of example 210 wherein each of the interconnected struts provides a column strength sufficient to inhibit movement of the device relative to the annulus under the force of systolic blood pressure against a valve mounted in the inner skeleton.

215. The device of example 210 wherein at least some of the struts include upstream extensions configured to engage supra-annular tissue in a left atrium.

216. The device of example 210 wherein the inner skeleton includes atrial extending members to engage supra-annular tissue such that downstream movement of the device is blocked by the atrial extending members.

217. The device of example 210 wherein the interconnected struts comprise ribs interconnected by a plurality of circumferential connectors.

218. The device of example 210 wherein the interconnected struts are arranged in a diamond configuration.

219. A prosthetic mitral valve device, comprising
a valve support having upstream and downstream ends, an interior in which a valve
may be coupled, and a perimeter; and

an anchoring member having a flared upstream portion and a downstream portion coupled to the perimeter of the valve support, wherein the upstream portion is mechanically isolated from the valve support and is configured to engage subannular tissue of a native mitral valve;

wherein the device is moveable into a plurality of configurations including:

a first configuration in which the valve support and the anchoring member are radially contracted, and wherein the valve support has a first cross-sectional shape;

a second configuration in which the valve support and the anchoring member are radially expanded, and wherein the valve support has a second cross-sectional shape; and

a third configuration in which the anchoring member is engaged with and deformed by the subannular tissue while the valve support remains in the second cross-sectional shape.

220. The device of example 219 wherein the upstream portion of the anchoring member is oval or D-shaped in the third configuration.

221. The device of example 219 wherein the upstream portion of the anchoring member is oval or D-shaped in the second configuration.

222. The device of example 219 wherein the upstream portion of the anchoring member provides a seal over native mitral valve commissures in the third configuration.

223. The device of example 219 wherein the upstream portion of the anchoring member substantially conforms to the shape of the subannular tissue.

224. The device of example 219 wherein the upstream portion of the anchoring member is substantially circular in the second configuration.

225. The device of example 219 wherein the valve support is substantially circular in cross-section in the third configuration.

226. The device of example 219 wherein the upstream portion of the anchoring member has a first dimension in the second configuration, the first dimension larger than a corresponding dimension of the subannular tissue such that the upstream portion is compressed to a second dimension less than the first dimension and substantially the same as the corresponding dimension when the device is in the third configuration.

227. The device of example 226 wherein the upstream portion remains biased toward expanding toward the first dimension such that the anchoring member provides radial outward force against the subannular tissue.

228. A device for treating a native mitral valve of a patient, the native mitral valve having an annulus and a pair of leaflets, the device comprising:

- an anchoring member positionable between the leaflets and having a downstream end configured to engage native tissue on or downstream of the annulus so as to prevent migration of the device in the upstream direction; and
- a valve support configured to support a prosthetic valve, wherein the valve support is coupled to the anchoring member, and wherein the valve support is mechanically isolated from the anchoring member.

229. The device of example 228 wherein:

- the anchoring member surrounds at least a portion of the support structure;
- the anchoring member has a plurality of flexible wires arranged in a diamond pattern, wherein the anchoring member is flared in a distal direction such that distal ends of the wires point radially outward so as to engage native tissue on or near the annulus and to inhibit migration of the device in the upstream direction; and
- the valve support is mechanically isolated from at least a flared portion of the anchoring member.

230. The device of example 228 wherein the anchoring member has an upstream end having a first cross-sectional dimension and the downstream end having a second cross-sectional dimension greater than the first cross-sectional dimension, and wherein the

downstream end is configured to engage an inward facing surface of the leaflets downstream of the annulus.

231. The device of example 228 wherein the valve support is radially separated from the downstream end of the anchoring member such that the downstream end can deform inwardly without deforming the valve support.

232. The device of example 228 wherein:
the downstream end of the anchoring member is non-cylindrical;
the valve support is cylindrical and at least partially surrounded by the anchoring member; and
the anchoring member is coupled to the valve support at an upstream end opposite the downstream end.

233. The device of example 228 wherein the anchoring member has a downstream portion with a cross-sectional dimension greater than a corresponding cross-sectional dimension of the annulus of the native mitral valve.

234. The device of example 228, further comprising a sealing member extending around the downstream end of the anchoring member and configured to seal against the native tissue to inhibit blood flow between the anchoring member and the native tissue.

235. The device of example 228 wherein the valve support has a proximal end and a distal end, and wherein the anchoring member is coupled to the valve support at a position intermediate the proximal and distal ends.

236. The device of example 228 wherein the valve support includes a downstream portion, and wherein the downstream portion includes an outward extending flange configured to radially engage subannular tissue.

237. The device of example 228 wherein the downstream end is flared in an upstream direction.

238. The device of example 228, further comprising a second anchoring member, the second anchoring member having a second upstream end configured to engage tissue on or downstream of the annulus and having a second downstream end coupled to the valve support.

239. The device of example 228, further comprising tissue engaging elements on the anchoring member.

240. A device for implantation at a native mitral valve, the native mitral valve having an annulus and leaflets, comprising:

- a valve support having upstream and downstream ends, an interior in which a valve may be coupled, and an outer surface;
- a first anchoring member having a first flared upstream portion and a first downstream portion coupled to the outer surface of the valve support, the first upstream portion mechanically isolated from the valve support and configured to engage supra-annular tissue of the native mitral valve; and
- a second anchoring member at least partially surrounding the first anchoring member, the second anchoring member having a second flared upstream portion and a second downstream portion coupled to the outer surface of the valve support, wherein the second upstream portion is mechanically isolated from the valve support and is configured to engage subannular tissue of the native mitral valve.

241. The device of example 240 wherein:

- the first anchoring member has a plurality of first flexible filaments arranged in a diamond configuration, wherein at least a portion of the first filaments are configured to engage native supra-annular tissue so as to prevent migration of the device in the downstream direction; and
- the second anchoring member has a plurality of second flexible filaments arranged in the diamond configuration, wherein at least a portion of the second filaments are configured to engage native subannular tissue so as to prevent migration of the device in the upstream direction.

242. The device of example 241 wherein the first anchoring member has a first height and the second anchoring member has a second plurality height, and wherein the first height is different than the second height.

243. The device of example 240 wherein the first upstream portion includes a first ring member for engaging the supra-annular tissue, and wherein the second upstream portion includes a second ring member for engaging the subannular tissue.

exampleexample244. A device for implantation at a native mitral valve, the native mitral valve having an annulus and leaflets, comprising:

a valve support having upstream and downstream ends, an interior in which a valve may be coupled, and an outer surface; and

an expandable fixation element coupled to the outer surface, wherein the fixation element is configured to engage tissue above, on and below the annulus;

wherein the fixation element includes one or more inflatable chambers coupled to and mechanically isolated from the outer surface of the valve support between the upstream and downstream ends.

245. The device of example 244 wherein the inflatable chambers are filled with saline.

246. The device of example 244 wherein the inflatable chambers are filled with gas.

247. The device of example 244 wherein the inflatable chambers are formed of Polytetrafluoroethylene (PTFE) or urethane.

248. The device of example 244 wherein the inflatable chambers form a U-shaped structure for engaging the annulus and the leaflets.

249. A device for implantation at a native mitral valve, the native mitral valve having an annulus and leaflets, comprising:

a radially expandable valve support configured to engage native tissue on or downstream of the annulus, wherein the valve support has a first longitudinal

length on a posterior leaflet-facing side and a second length on an anterior leaflet facing side; and
a valve coupled to an interior of the valve support;
wherein the first length is greater than the second length such that occlusion of a left ventricle outflow tract (LVOT) is limited.

250. The device of example 249 wherein the posterior leaflet facing side further includes an arm configured to receive a posterior leaflet between the arm and the valve support.

251. A device for implantation at a native mitral valve, the native mitral valve having an annulus and leaflets, comprising:

a valve support having upstream and downstream ends, an interior in which a valve may be coupled, and an outer surface; and
an anchoring member having a flared upstream portion and a downstream portion coupled to the outer surface of the valve support, wherein the upstream portion has an upper ring and a lower ring coupled to the upper ring; and
a plurality of flexible coupling elements coupling the upper ring to the lower ring and configured to draw the lower and upper rings together;
wherein the lower ring is configured to move in an upstream direction toward the upper ring such that the annulus is received between the upper and lower rings.

252. The device of example 251 wherein the anchoring member is mechanically isolated from the valve support.

253. The device of example 251 wherein the lower ring is moved in an upstream direction with wires attached to the lower ring.

254. A method for replacement of a native heart valve having an annulus and leaflets coupled to the annulus, the method comprising:

positioning a prosthetic device between the leaflets in a collapsed configuration;
allowing the prosthetic device to expand such that an anchoring member of the prosthetic device is in a subannular position in which it engages tissue on or

downstream of the annulus, the anchoring member having a diameter larger than a corresponding diameter of the annulus in the subannular position; and allowing a valve support to expand within the anchoring member, wherein the valve support is coupled to the anchoring member, the valve support having a support region configured to support a prosthetic valve; wherein the support region of valve support is mechanically isolated from the anchoring member such that deformation of the anchoring member when engaging the tissue does not substantially deform the support region.

255. The method of example 254 wherein the prosthetic device comprises the device of any one of examples 1-140, 150-178, 219-227 and 251-253.

256. The method of example 254, further comprising delivering the prosthetic device by catheter prior to positioning the prosthetic device between the leaflets.

257. The method of example 256, further comprising retracting a sheath on the catheter to expose the prosthetic device in an expanded configuration, and moving the prosthetic device in an upstream direction such that the upstream portion of the anchoring member engages tissue.

258. The method of example 256, further comprising navigating the catheter configured to retain the prosthetic device in a delivery configuration by one or more of a trans-septal approach from a right atrium, a trans-apical approach via a left ventricular incision or puncture, or a trans-aortic approach through the aorta.

259. A method of treating a mitral valve of a patient, the mitral valve having an annulus and leaflets, the method comprising:

implanting a device within or adjacent to the annulus, the device comprising a valve support and an anchoring member coupled to and at least partially surrounding the valve support, wherein the anchoring member is disposed between the leaflets, and wherein an upstream portion of the anchoring member engages tissue on or downstream of the annulus to prevent migration of the device in an upstream direction; and

wherein the valve support has a support region for supporting a prosthetic valve, and the support region is mechanically isolated from the anchoring member at least at the upstream portion such that deformation of the upstream portion does not substantially deform the support region.

260. The method of example 259, wherein the implanting step includes: positioning the device between the leaflets and downstream of the annulus when the device is in a delivery configuration; expanding the device from the delivery configuration to an expanded configuration with the anchoring member extending between the leaflets; and moving the device in an upstream direction to engage the tissue on or downstream of the annulus with the upstream portion.

261. The method of example 259 wherein the upstream portion of the anchoring member has an oval shape when in a deployed configuration and the tissue at or below the annulus has a corresponding oval shape, and wherein the method further comprises: viewing the anchoring member and the mitral valve with echocardiography or fluoroscopy; and aligning the upstream portion of the anchoring member to engage with the tissue on or downstream of the annulus based on the echocardiography or fluoroscopy.

262. The method of example 259 wherein the prosthetic valve is coupled to the valve support, and wherein the prosthetic valve configured to allow blood to flow from a left atrium to a left ventricle and to inhibit blood flow from the left ventricle to the left atrium.

263. The method of example 262 wherein the anchoring member inhibits movement of the device toward the left atrium by engaging subannular tissue when the left ventricle contracts and the valve inhibits blood flow from the left ventricle to the left atrium.

264. The method of example 259, further comprising delivering the device by catheter prior to implantation at the mitral valve.

265. The method of example 259, further comprising retracting a sheath on the catheter to expose the device in an expanded configuration, and moving the device in an upstream direction such that the upstream portion of the anchoring member engages subannular tissue.

266. The method of example 259, further comprising navigating a catheter configured to retain the device in a delivery configuration by one or more of a trans-septal approach from a right atrium, a trans-apical approach via a left ventricular incision or puncture, or a trans-aortic approach through the aorta.

267. The method of example 259 wherein a temporary valve coupled to the valve support is activated after the device is implanted.

268. The method of example 267, further comprising positioning a replacement valve in an interior of the valve support and expanding the replacement valve into engagement with the valve support after the device has been implanted.

269. The method of example 259, further comprising coupling the prosthetic valve to the valve support after the device has been implanted at the mitral valve.

270. The method of example 259 wherein the device further comprises the prosthetic valve mounted to the support region of the valve support before the device is implanted.

271. The method of example 270 wherein prosthetic valve comprises a tissue valve.

272. The method of example 270 wherein the prosthetic valve comprises a plurality of leaflets which coapt to block blood flow through the valve support in the upstream direction.

273. The method of example 272 wherein the support region is mechanically isolated from the anchor member such that when the upstream portion is deformed in a non-circular shape the leaflets remain coapted sufficiently to block blood flow.

274. The method of example 259 wherein the anchor member has a plurality of tissue engaging elements around the upstream portion, and wherein the method further comprises engaging the tissue with the tissue engaging elements.

275. The method of example 274 wherein the engaging the tissue comprises penetrating the tissue with the tissue engaging elements.

276. The method of example 259, further comprising sealing blood flow paths between the anchor member and the tissue.

277. The method of example 276 wherein sealing blood flow paths comprises positioning a flexible sealing member between the anchor member and the tissue.

278. The method of example 277 wherein the flexible sealing member comprises a skirt extending around a circumference of the anchor member.

279. The method of example 278 wherein the skirt is configured to block blood flow between the anchor member and the support member.

280. The method of example 259, further comprising inhibiting downstream movement of the device relative to the annulus of the mitral valve.

281. The method of example 280 wherein inhibiting downstream movement of the device relative to the annulus of the mitral valve comprises engaging supra-annular tissue with an atrial element coupled to the device.

282. The method of example 280 wherein inhibiting downstream movement of the device relative to the annulus of the mitral valve comprises penetrating tissue on or near the annulus with a plurality of tissue engaging elements coupled to the anchor member.

283. The method of example 282, further comprising penetrating the tissue with the tissue engaging elements, wherein the tissue engaging elements comprise retention elements configured to resist pull-out from the tissue after penetration.

284. The method of example 283 wherein penetrating the tissue with the tissue engaging elements comprises:

inserting the retention elements into the tissue in a compact configuration; and
allowing the retention elements to expand into an expanded configuration after penetration of the tissue.

285. The method of example 260 wherein expanding the device from the delivery configuration comprises allowing the valve support to resiliently self-expand from a collapsed configuration to a deployed configuration.

286. The method of example 260 wherein expanding the device from the delivery configuration comprises allowing the anchor member to resiliently self-expand from a delivery configuration to an expanded configuration.

287. The method of example 259, further comprising radially expanding the valve support after the anchoring member engages the tissue on or downstream of the annulus.

288. The method of example 259 wherein the device is the device of any one of examples 1-140, 150-178, 219-227 and 251-253.

289. The method of example 259 wherein implanting a device within or adjacent to the annulus includes moving the device through a plurality of configurations including:

- a first configuration in which the valve support and the anchoring member are radially contracted, and wherein the valve support has a first cross-sectional shape;
- a second configuration in which the valve support and the anchoring member are radially expanded and the valve support has a second cross-sectional shape greater than the first cross-sectional shape; and
- a third configuration in which the anchoring member is engaged with and at least partially deformed by tissue on or downstream of the annulus while the valve support remains in the second cross-sectional shape.

290. The method of example 259, further comprising engaging one or more stabilizing members coupled to the anchoring member with native tissue.

291. A system for replacing a native valve in a patient, the system comprising:
an elongated catheter body having a distal end and a proximal end;
a housing coupled to the distal end of the catheter body and having a closed end and an open end;
a plunger within the housing axially movable relative thereto;
an actuator at the proximal end of the catheter body and coupled to the plunger such that moving the actuator moves the housing axially relative to the plunger; and
a prosthetic valve device having a collapsed configuration and an expanded configuration, wherein the prosthetic valve device is positionable in the housing in the collapsed configuration and is releasable proximally from the housing by moving the actuator.

292. The system of example 291 wherein the prosthetic valve device comprises the device of any one of examples 1-253.

293. A system to treat a mitral valve of a patient, the mitral valve having an annulus, the system comprising:

a device comprising the device of any one of examples 1-253; and
a catheter having a lumen configured to retain the device therein.

294. The system of example 293, further comprising a replacement valve configured to couple to the device after placement of the device at a native mitral valve location.

295. The system of example 294, further comprising a delivery catheter coupled to the replacement valve.

296. The system of example 293 wherein the catheter comprises an expandable member configured to radially expand portions of the device.

297. The system of example 293 wherein the catheter comprises a retractable sheath and the device is contained within the sheath, and wherein the device is configured to resiliently expand when the sheath is retracted.

298. The system of example 293 wherein the catheter comprises a guidewire lumen adapted to slideably receive a guidewire, the guidewire lumen having proximal and distal ports through which the guidewire may be slideably inserted.

Conclusion

[00328] The above detailed descriptions of embodiments of the technology are not intended to be exhaustive or to limit the technology to the precise form disclosed above. Although specific embodiments of, and examples for, the technology are described above for illustrative purposes, various equivalent modifications are possible within the scope of the technology as those skilled in the relevant art will recognize. For example, while steps are presented in a given order, alternative embodiments may perform steps in a different order. The various embodiments described herein may also be combined to provide further embodiments.

[00329] From the foregoing, it will be appreciated that specific embodiments of the technology have been described herein for purposes of illustration, but well-known structures and functions have not been shown or described in detail to avoid unnecessarily obscuring the description of the embodiments of the technology. Where the context permits, singular or plural terms may also include the plural or singular term, respectively.

[00330] Moreover, unless the word "or" is expressly limited to mean only a single item exclusive from the other items in reference to a list of two or more items, then the use of "or" in such a list is to be interpreted as including (a) any single item in the list, (b) all of the items in the list, or (c) any combination of the items in the list. Additionally, the term "comprising" is used throughout to mean including at least the recited feature(s) such that any greater number of the same feature and/or additional types of other features are not precluded. It will also be appreciated that specific embodiments have been described herein for purposes of illustration, but that various modifications may be made without deviating from the technology. Further, while advantages associated with certain embodiments of the technology have been described in the context of those embodiments, other embodiments

may also exhibit such advantages, and not all embodiments need necessarily exhibit such advantages to fall within the scope of the technology. Accordingly, the disclosure and associated technology can encompass other embodiments not expressly shown or described herein.

CLAIMS:

1. A prosthetic heart valve device for repair or replacement of a native heart valve of a patient, the heart valve having an annulus and leaflets, comprising:

an anchoring member having a first portion comprising an upstream portion having a first cross-sectional dimension and a second portion comprising a downstream portion having a second cross-sectional dimension less than the first cross-sectional dimension, wherein the first portion is configured to engage cardiac tissue to retain the anchoring member in a fixed longitudinal position relative to the annulus;

a valve support coupled to the second portion of the anchoring member and configured to support a prosthetic valve, wherein the valve support is radially separated from the first portion of the anchoring member such that the first portion of the anchoring member can deform inwardly without substantially deforming the valve support.

2. The device of claim 1 wherein the valve support has an upstream region spaced radially inward from the first portion of the anchoring member such that if the anchoring member is deformed inwardly the upstream region of the valve support remains substantially undeformed.

3. The device of claim 1 wherein the first portion of the anchoring member is configured to engage valve tissue selected from an inward-facing surface of the annulus and an inward facing surface of the leaflets under the annulus.

4. The device of claim 3 wherein the first portion of the anchoring member is configured to apply outward force against the valve tissue so as to resist movement of the device when blood flows through the valve support in a downstream direction when the valve is open and when blood pushes in an upstream direction against the valve when the valve is closed.

5. The device of claim 1 wherein the anchoring member is self-expanding.

6. The device of claim 5 wherein the anchoring member comprises Nitinol.

7. The device of claim 1 wherein the anchoring member is formed of a nitinol tube having a wall thickness of approximately 0.010 inches to about 0.130 inches.

8. The device of claim 1 wherein the anchoring member includes a plurality of longitudinal ribs having axial stiffness to resist movement of the device in an upstream direction toward a left atrium of the heart.

9. The device of claim 1 wherein the anchoring member includes a plurality of longitudinal ribs.

10. The device of claim 9 wherein the plurality of ribs are arranged in a diamond configuration.

11. The device of claim 1 wherein the anchoring member includes a plurality of flexible filaments arranged in a diamond configuration around a circumference of the anchoring member, and wherein the diamond configuration includes one or more rows of diamonds and between approximately 12 and approximately 36 columns of diamonds around the circumference.

12. The device of claim 1 wherein the valve support includes an upstream end and a downstream end, and wherein the upstream end extends a distance in an upstream direction beyond the upstream portion of the anchoring member.

13. The device of claim 1 wherein the valve support includes an upstream end and a downstream end, and wherein the first portion of the anchoring member extends a distance in an upstream direction beyond the upstream end of the valve support.

14. The device of claim 1 wherein the anchoring member includes a rim at a proximal end of the first portion, the rim having an undeformed configuration, the undeformed configuration having a generally oval shape or a D-shape.

15. The device of claim 14 wherein the rim includes a plurality of peaks and a plurality of valleys.

16. The device of claim 1 wherein:
the anchoring member includes a rim at a proximal end of the first portion, the rim having a generally oval shape or D-shape; and

the anchoring member includes a distal end of the second portion, and wherein a distance between the distal end and the rim varies around a circumference of the anchoring member.

17. The device of claim 16 wherein the distance varies from about 6 mm to about 20 mm.

18. The device of claim 16 wherein the distance varies from about 9 mm to about 12 mm.

19. The device of claim 16 wherein the distance includes a plurality of distances including:

a first distance between the distal end and the rim being approximately 7 mm to about 8 mm at first and second regions of the anchoring member, the first and second regions being configured to align with first and second commissures of the native mitral valve, respectively;

a second distance between the distal end and the rim being approximately 9 mm to about 11 mm at a third region of the anchoring member, the third region being configured to align with an anterior leaflet of the native mitral valve; and

a third distance between the distal end and the rim being approximately 12 mm to about 13 mm at a fourth region of the anchoring member opposite the third region, the fourth region being configured to align with a posterior leaflet of the native mitral valve.

20. The device of claim 1 wherein:

the anchoring member includes a rim at a proximal end of the first portion, the rim having a generally oval shape or D-shape;

the tissue on or under the annulus has a non-circular shape having a minor diameter and a major diameter generally perpendicular to the minor diameter;

the upstream portion of the anchoring member has an outer perimeter having a major perimeter diameter and a minor perimeter diameter generally perpendicular to the major perimeter diameter;

the major perimeter diameter is greater than the major diameter; and

the minor perimeter diameter is greater than the minor diameter.

21. The device of claim 20 wherein the major perimeter diameter is approximately 2 mm to approximately 22 mm greater than the major diameter.

22. The device of claim 20 wherein the major perimeter diameter is approximately 8 mm to approximately 15 mm greater than the major diameter.

23. The device of claim 20 wherein the major perimeter diameter is approximately 45 mm to about 60 mm.

24. The device of claim 20 wherein the minor perimeter diameter is approximately 40 mm to about 55 mm.

25. The device of claim 1 wherein the valve support is a generally circular cylinder.

26. The device of claim 25 wherein the valve support has a diameter of approximately 25 mm to about 30 mm.

27. The device of claim 1 wherein the valve support is a cylindrical valve support having a diameter of approximately 27 mm.

28. The device of claim 1 wherein the valve support is a cylindrical valve support having a longitudinal height of approximately 14 mm to about 17 mm.

29. The device of claim 1 wherein:

the first portion of the anchoring member has a proximal end perimeter having peak portions and valley portions corresponding to native peak and valley portions of the annulus, respectively; and

the corresponding peak portions are configured to align with the native valley portion and the corresponding valley portions are configured to align with the native peak portions.

30. The device of claim 1 wherein the valve support extends around a longitudinal axis, and wherein the first portion of the anchoring member flares outward from the longitudinal axis by a taper angle.

31. The device of claim 30 wherein the taper angle continuously changes between the first portion and the second portion.

32. The device of claim 30 wherein the taper angle varies around a circumference of the first portion.

33. The device of claim 30 wherein the taper angle is between approximately 30° to about 75°.

34. The device of claim 30 wherein the taper angle is between approximately 40° to about 60°.

35. The device of claim 1 wherein the valve support is oriented along a first longitudinal axis and the anchoring member is oriented along a second longitudinal axis, and wherein the first and second longitudinal axes are non-collinear.

36. The device of claim 35 wherein the second longitudinal axis is off-set from the first longitudinal axis.

37. The device of claim 35 wherein the second longitudinal axis is non-parallel to the first longitudinal axis.

38. The device of claim 1 wherein the first portion of the anchoring member includes a flared portion and a vertical portion, the vertical portion configured to radially expand and engage the annulus.

39. The device of claim 38 wherein the flared portion includes tissue engaging elements configured to engage subannular tissue.

40. The device of claim 1 wherein the first portion is radially separated from the valve support by a gap.

41. The device of claim 40 wherein:
the anchoring member includes a rim at a proximal end of the first portion, the rim having an oval shape;

the valve support is a cylindrical valve support at least partially surrounded by the anchoring member; and

the gap varies around a circumference of the cylindrical valve support.

42. The device of claim 41 wherein the gap is greater on an anterior leaflet facing side of the device than on a posterior leaflet-facing side of the device.

43. The device of claim 1 wherein the device is configured so as to avoid obstruction of a left ventricular outflow tract (LVOT) of the heart.

44. The device of claim 1, further comprising a skirt overlying a surface of the anchoring member, the skirt configured to inhibit blood flow between the anchoring member and the valve support.

45. The device of claim 44 wherein the skirt is further configured to inhibit blood flow between the anchoring member and the tissue.

46. The device of claim 44 wherein the skirt comprises at least one of Dacron®, ePTFE, bovine pericardium, a polymer, thermoplastic polymer, polyester, Gore-tex®, a synthetic fiber, a natural fiber or polyethylene terephthalate (PET).

47. The device of claim 1 wherein the valve support is coupled to the anchoring member with one or more of a plurality of rivets and a plurality of sutures.

48. The device of claim 1 wherein the valve support has a radial strength of approximately 42 mm Hg to about 47 mm Hg.

49. The device of claim 1, further comprising a valve coupled to the valve support to inhibit retrograde blood flow.

50. The device of claim 49 wherein the valve is a tri-leaflet valve.

51. The device of claim 49 wherein the valve comprises bovine pericardium.

52. The device of claim 49 wherein the valve support has a plurality of commissural attachment structures, the valve being coupled to the valve support at the commissural attachment structures.

53. The device of claim 52 wherein the commissural attachment structures are permanently fixed to the valve support.

54. The device of claim 52 wherein the commissural attachment structures are integral with an interior wall of the valve support.

55. The device of claim 52 wherein the valve support has a first height and the commissural attachment structures have a second height less than the first height.

56. The device of claim 1, wherein the valve support is further configured to receive a replacement valve after the device is implanted at a native valve location.

57. The device of claim 56 further comprising a temporary valve coupled to the valve support.

58. The device of claim 57 wherein the temporary valve is adapted to be displaced against an inner wall of the valve support when the replacement valve is received in the valve support.

59. The device of claim 57 wherein the temporary valve comprises a removable valve, and wherein the replacement valve is secured within the valve support after the temporary valve has been removed.

60. The device of claim 1, further comprising a prosthetic valve coupled to the valve support at a region where the valve support is mechanically isolated from at least the first portion of the anchoring member.

61. The device of claim 1 wherein the first portion of the anchoring member has a first flexibility and the valve support has a second flexibility less than the first flexibility such that a region of the valve support remains substantially undistorted when the first portion of the anchoring member distorts to the native mitral valve.

62. The device of claim 1 wherein:
the anchoring member is defined by a structure separate from the valve support;
the valve support is coupled to the anchoring member at the second portion of the anchoring member; and
the second portion of the anchoring member is longitudinally spaced apart from the first portion of the anchoring member.

63. The device of claim 1, further comprising a plurality of flexible coupling mechanisms configured to flexibly couple the valve support to the anchoring member.

64. The device of claim 63 wherein the plurality of flexible coupling mechanisms include at least one of a suture, a wire, a flexible filament, a rivet, a screw, or a pin.

65. The device of claim 1 wherein the device is moveable into a plurality of configurations including:

a first configuration in which the valve support and the anchoring member are radially contracted;

a second configuration in which the valve support and the anchoring member are radially expanded; and

a third configuration in which the anchoring member is engaged with and at least partially deformed by tissue on or near the annulus.

66. The device of claim 65 wherein the valve support has an expanded shape in the second configuration, and wherein the valve support remains substantially in the expanded shape in the third configuration.

67. The device of claim 65 wherein the anchoring member assumes the second configuration in an unbiased condition.

68. The device of claim 65 wherein the anchoring member is deformable from the second configuration to the third configuration.

69. The device of claim 65 wherein the device in the first configuration has a low profile configured for delivery through a guide catheter positioned at or near the native mitral valve.

70. The device of claim 65 wherein the first portion of the anchoring member has a first diameter in the second configuration, and wherein the first diameter spans at least a distance between native commissures of the native mitral valve.

71. The device of claim 65 wherein the first portion of the anchoring member has a first diameter and the valve support has a second diameter in the second configuration, and wherein the first diameter is approximately between 1.2 to 1.5 times the second diameter.

72. The device of claim 1 wherein the first portion of the anchoring member has a first expanded diameter of approximately 28 mm to about 80 mm.

73. The device of claim 1 or claim 72 wherein the valve support has an expanded diameter of approximately 25 mm to about 32 mm.

74. The device of claim 1 wherein the first portion of the anchoring member is a downstream portion longitudinally spaced apart from the second portion of the anchoring member that defines an upstream portion, and wherein the upstream portion has a first cross-sectional dimension and the downstream portion has a second cross-sectional dimension less than the first cross-sectional dimension.

75. The device of claim 1 wherein the anchoring member resists upstream migration of the device without any element of the device extending behind the leaflets of the native mitral valve.

76. The device of claim 1 wherein the device does not engage supra-annular tissue or tissue upstream of the annulus.

77. The device of claim 1, further comprising a sealing member extending around the first portion of the anchoring member and configured to seal against the tissue on or downstream of the annulus to inhibit blood flow between the anchoring member and the tissue.

78. The device of claim 77 wherein the sealing member promotes tissue ingrowth into the sealing member.

79. The device of claim 77 wherein the sealing member includes a plurality of tissue engaging elements on an outer surface of the sealing member.

80. The device of claim 1 wherein the anchoring member has a plurality of points on an upstream end, and wherein the points are configured to penetrate tissue on or downstream of the annulus so as to prevent upstream movement of the device.

81. The device of claim 80 wherein the anchoring member includes a delivery mechanism for transitioning the plurality of points from a retracted position to an engagement position, and wherein the engagement position includes penetration of the annulus tissue with the points.

82. The device of claim 1 further comprising a plurality of anchoring clips on an end of the anchoring member, wherein the anchoring clips are configured to engage the annulus.

83. The device of claim 1 wherein the anchoring member includes
a plurality of longitudinal ribs; and
a plurality of circumferential connectors interconnecting the plurality of ribs;
wherein the anchoring member is flared such that ends of the ribs orient radially outward for engaging tissue on or downstream of the annulus so as to prevent migration of the device in an upstream direction.

84. The device of claim 83 wherein the anchoring member has a central longitudinal axis, and wherein each individual rib has a plurality of segments having varying extension angles relative to the longitudinal axis.

85. The device of claim 83 wherein the plurality of longitudinal ribs includes a first and second plurality of ribs, and wherein the first plurality of ribs have a characteristic different than the second plurality of ribs, the characteristic selected from size, shape, stiffness, extension angle and number of ribs within a given area of the anchoring member.

86. The device of claim 83 wherein the longitudinal ribs are unevenly spaced around an outer perimeter of the anchoring member.

87. The device of claim 83 wherein the valve support includes a plurality of posts connected circumferentially by a plurality of struts, and wherein each individual longitudinal rib is integrally formed with a corresponding post on the valve support.

88. The device of claim 87 wherein each of the plurality of longitudinal ribs comprises a curved elbow portion integrally formed with the corresponding posts, the elbow portion configured to urge individual ribs radially outward from an inward configuration to an outward configuration.

89. The device of claim 87, further comprising a tether coupling each individual rib with the corresponding post, wherein the tether is configured to limit an outward deflection of the rib when the rib is in an expanded configuration.

90. The device of claim 87 wherein one or more individual circumferential connectors include a looped connector head, and wherein one or more individual struts include a looped strut head, and wherein the looped connector heads are coupled to the looped strut heads to form a flexible coupling mechanism.

91. The device of claim 90 wherein the looped connector head is passed through the looped strut head to form the flexible coupling mechanism.

92. The device of claim 90 wherein one or more flexible filaments couple the looped connector head to the looped strut head to form the flexible coupling mechanism.

93. The device of claim 83 wherein the plurality of circumferential connectors include a plurality of bands extending around a circumference of the anchoring member, and wherein the bands are slideably coupled to each individual rib.

94. The device of claim 1 wherein the anchoring member has a downstream portion that is substantially tubular, and wherein the upstream portion of the anchoring member is

deformable to a non-circular cross-section while the valve support remains substantially circular in cross-section.

95. The device of claim 1 wherein:

the valve support includes a plurality of first struts interconnected around a circumference of the valve support;

the anchoring member includes a plurality of second struts interconnected around a circumference of the anchoring member; and

the first struts are more rigid than the second struts.

96. The device of claim 1, further comprising a plurality of tissue engaging elements configured to engage tissue of the annulus or leaflets.

97. The device of claim 96 wherein the tissue engaging elements have:

a piercing configuration in which the tissue engaging elements have a low profile for penetrating the tissue; and

a retaining configuration in which the tissue engaging elements have an expanded profile for maintaining the tissue engaging element within the tissue.

98. The device of claim 1 wherein the anchoring member is coupled to a sleeve, and wherein the sleeve is configured to limit radial expansion of the anchoring member when the anchoring member is in an expanded configuration.

99. The device of claim 98 wherein the sleeve includes an outer portion configured to cover the anchoring member and an inner portion configured to at least partially surround the valve support.

100. The device of claim 99 wherein the sleeve includes a plurality of horizontal septums extending between the outer portion and the inner portion of the sleeve.

101. The device of claim 1 wherein:

the anchoring member has an upstream portion configured to engage an upstream-facing surface of the leaflets downstream of the annulus;

the valve support is at least partially within the anchor, and the valve support is configured to support a prosthetic valve; and

the anchor is deformable to a non-circular cross-section while the valve support remains substantially circular in cross-section.

102. The device of claim 101 wherein the second portion of the anchoring member has defines a downstream portion and the first portion of the anchoring member defines an upstream portion, and wherein the downstream portion is longitudinally separated from the upstream portion, and wherein the downstream portion is coupled to a downstream region of the valve support.

103. The device of claim 102, further comprising a plurality of tethers coupling the upstream portion of the anchor to the valve support, the tethers configured to limit radial expansion of the upstream portion.

104. The device of claim 1 wherein:

the anchoring member has a hyperboloidic shape including a first end at the first portion configured to engage an inward facing surface of the leaflets downstream of the annulus and a second end at the second portion, wherein the first end has a larger cross-sectional area than the second end;

the valve support positioned in the anchoring member, wherein the valve support is coupled to the anchoring member at a location spaced substantially apart from the first end and is uncoupled to the anchoring member at the first end.

105. The device of claim 1, further comprising an atrial retainer configured to engage supra-annular tissue such that downstream movement of the device is blocked by engagement of the atrial retainer with the supra-annular tissue.

106. The device of claim 105 wherein the atrial retainer includes outward-facing extensions of the valve support.

107. The device of claim 105 wherein the atrial retainer includes extensions of the anchoring member configured to pass through the native valve to engage the supra-annular tissue.

108. The device of claim 1 wherein the anchoring member includes a plurality of atraumatic nodes such that resist penetration of the inward facing surface of the leaflets downstream of the annulus.

109. The device of claim 1, further comprising one or more positioning elements coupled to the anchoring member, the positioning elements configured to engage ventricular tissue to position the device away from a left ventricle outflow tract (LVOT).

110. The device of claim 109 wherein the position element comprises:
a positioning arm configured to extend from the anchoring member to the ventricular tissue; and

a tissue engaging portion at a distal end of the positioning arm, wherein the tissue engaging portion is configured to engage the ventricular tissue atraumatically.

111. The device of claim 1 wherein the anchoring member resists upstream migration of the device without an element of the device extending behind the native valve leaflets.

112. The device of claim 1 wherein:
the valve support includes an upper region, a lower region, and an interior to retain a prosthetic valve; and

the anchoring member surrounds at least a portion of the valve support, wherein the anchoring member is positionable between the leaflets and has a plurality of flexible wires arranged in a diamond pattern, an upper portion, and a lower portion;

wherein the upper portion of the anchoring member is flared outwardly in a proximal direction such that proximal ends of the wires point radially outward so as to engage cardiac tissue on or near the annulus and inhibit migration of the device in the upstream direction; and

wherein the lower region of the support structure is coupled to the lower portion of the anchoring member, and wherein the upper region of the support structure is mechanically isolated from at least deformation of the flared upper portion of the anchoring member.

113. The device of claim 1 wherein:

the valve support comprises a cylindrical support having a longitudinal axis and an interior along the longitudinal axis through which blood may flow; and

the anchoring member is defined by a structure separate from the cylindrical support, the anchoring member having a non-circular cross-section, wherein the anchoring member has an outwardly flared upstream end configured to engage subannular tissue of a mitral valve, and wherein the anchoring member surrounds the cylindrical support and is coupled to the cylindrical support at a downstream end opposite the upstream end.

114. The device of claim 113, further comprising a valve coupled within the interior of the support and configured to block blood flow through the support in an upstream direction and allow blood flow through the support in a downstream direction.

115. The device of claim 114, further comprising a stabilizing member extending outward from the downstream end of the anchor, the stabilizing member configured to engage native tissue downstream of an annulus of the mitral valve.

116. The device of claim 115 wherein the stabilizing member includes a plurality of arms extending from the downstream end, the arm configured to engage one or more of the subannular tissue, native leaflets, or a ventricular wall.

117. The device of claim 116 wherein the arms extend behind the native leaflets.

118. The device of claim 116 wherein each individual arm includes an arm body and a tip at a distal end of the arm body, the tip configured to engage native tissue.

119. The device of claim 118 wherein the tip exerts force on the native tissue without penetrating the native tissue.

120. The device of claim 118 wherein the tip includes a tissue engaging element for piercing through at least a portion of the native tissue.

121. The device of claim 1, further comprising a second anchoring structure coupled to the first portion of the anchoring member and extending outwardly so as to engage tissue on or near the annulus.

122. The device of claim 121 wherein the second anchoring structure is coupled to an upstream perimeter of the anchoring member and the second anchoring structure extends outwardly in a downstream direction.

123. The device of claim 1 wherein:

the valve support comprises an inner frame having an outer surface and an inner surface, the inner surface configured to support a prosthetic valve; and

the anchoring member comprises an outer frame coupled to the inner frame, the outer frame having a first portion with a cross-sectional dimension greater than a corresponding cross-sectional dimension of an annulus of a native mitral valve, wherein the first portion is configured to engage tissue at or below the annulus of the native mitral valve and prevent migration of the device in an upward direction during ventricular systole, and wherein at least the first portion of the frame is mechanically isolated from the inner frame.

124. The device of claim 123 wherein the anchoring member has a first longitudinal length on a posterior leaflet-facing side and a second length on an anterior leaflet facing side, and wherein the first length is greater than the second length.

125. The device of claim 124 wherein the posterior leaflet facing side further includes an arm configured to receive a posterior leaflet between the arm and the outer frame.

126. The device of claim 1 wherein:

the valve support comprises a cylindrical inner skeleton having an interior to which a prosthetic valve may be coupled;

the anchoring member comprises an outer skeleton coupled to the inner skeleton and positionable between the leaflets downstream of the annulus, the outer skeleton having a plurality of flexible wires arranged in a diamond configuration, wherein at least a portion of the wires are configured to engage native subannular tissue so as to prevent migration of the device in the upstream direction; and

wherein the outer skeleton is deformable to a non-circular cross-section while the inner skeleton remains substantially circular in cross-section.

127. The device of claim 1 wherein the valve support has a proximal end and a distal end, and wherein the anchoring member is coupled to the valve support at a position intermediate the proximal and distal ends.

128. The device of claim 1, further comprising a second anchoring member, the second anchoring member having a second upstream end configured to engage tissue on or downstream of the annulus and having a second downstream end coupled to the valve support.

129. The device of claim 1, further comprising a second anchoring member at least partially surrounding the anchoring member, the second anchoring member having a second flared upstream portion and a second downstream portion coupled to an outer surface of the valve support, wherein the second upstream portion is mechanically isolated from the valve support and is configured to engage subannular tissue of the native valve.

130. The device of claim 129 wherein the anchoring member has a first height and the second anchoring member has a second height, and wherein the first height is different than the second height.

131. The device of claim 1, further comprising an expandable fixation element configured to engage on or near the annulus, wherein the fixation element includes one or more inflatable chambers coupled to at least one of the valve support and the anchoring member.

132. The device of claim 1 wherein the anchoring member has a first longitudinal length on a posterior leaflet-facing side and a second length on an anterior leaflet facing side, and wherein the first length is greater than the second length such that occlusion of a left ventricle outflow tract (LVOT) is limited.

133. The device of claim 132 wherein the posterior leaflet facing side further includes an arm configured to receive a posterior leaflet between the arm and the anchoring member.

134. The device of claim 1 wherein the anchoring member has a flared upstream portion having an upper ring and a lower ring coupled to the upper ring, and wherein the device further includes a plurality of flexible annulus engaging elements distributed around a circumference of the anchoring member and coupling the upper ring to the lower ring, and wherein the lower ring is configured to move in an upstream direction toward the upper ring such that the annulus is received between the upper and lower rings and within the annulus engaging elements.

1/85

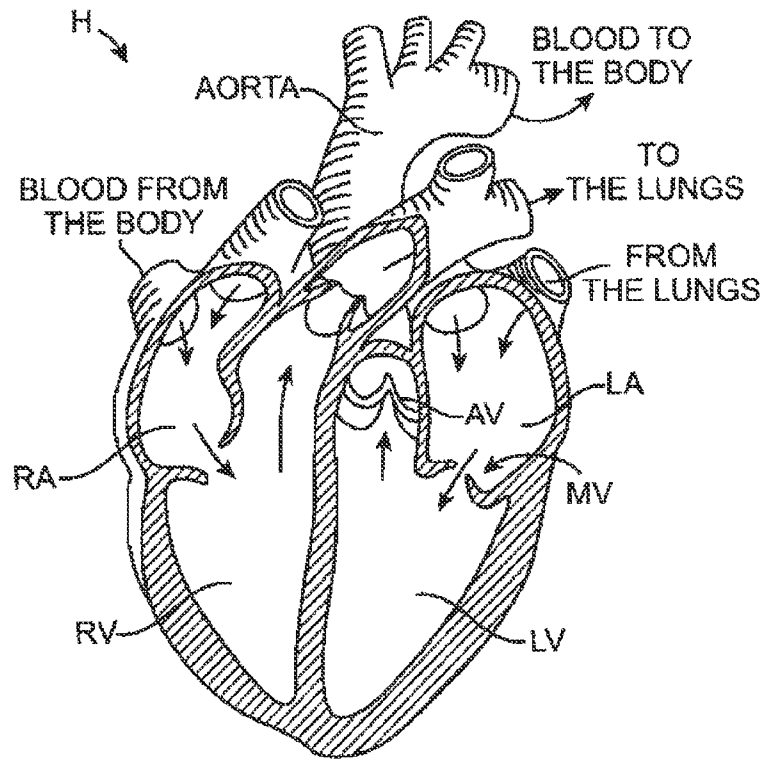


FIG. 1

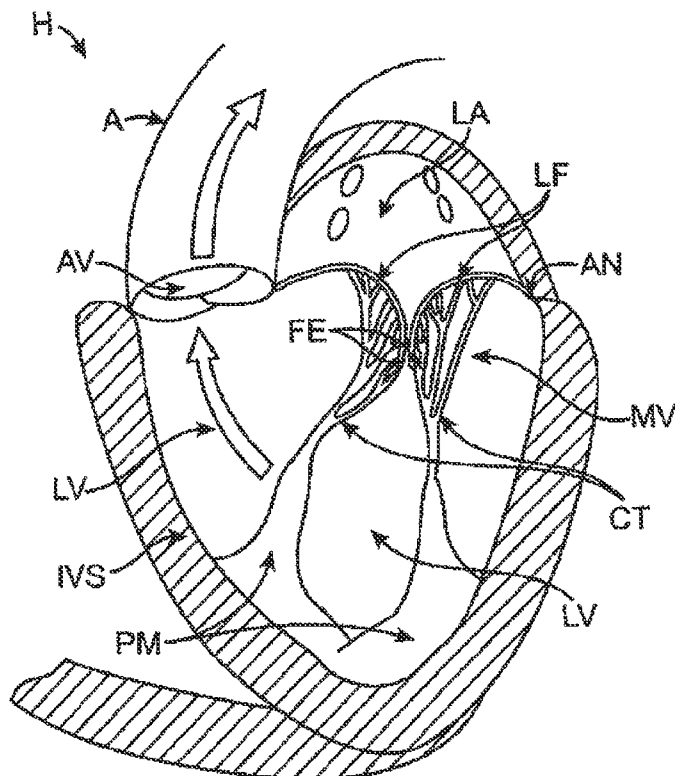


FIG. 2

2/85

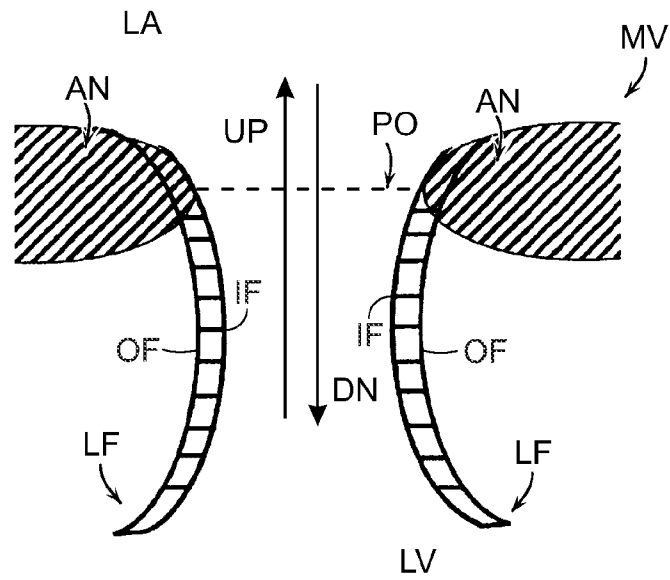


FIG. 3

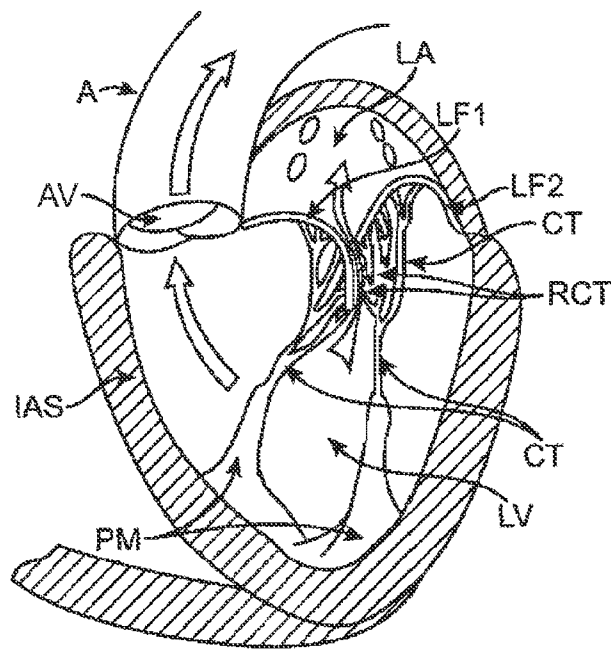


FIG. 4A

3/85

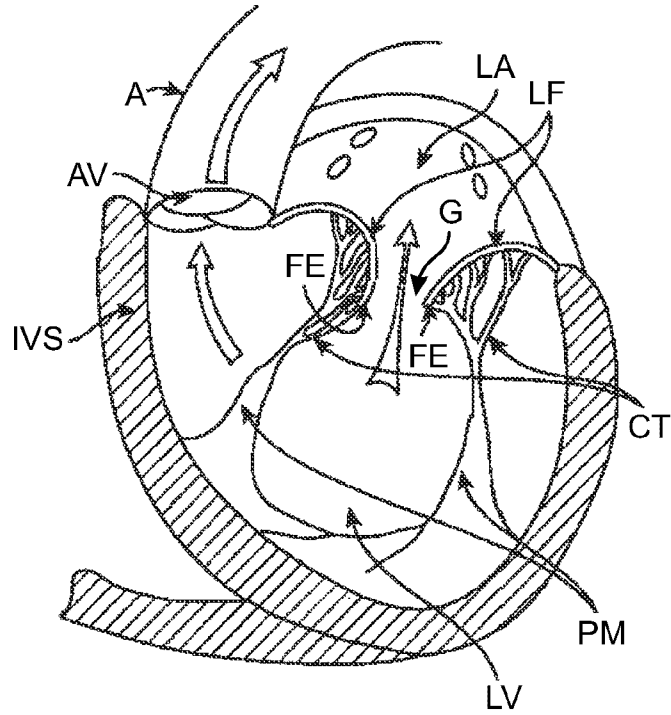


FIG. 4B

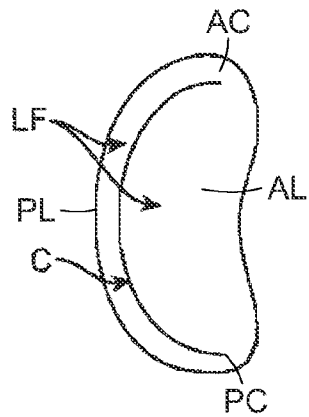


FIG. 5A

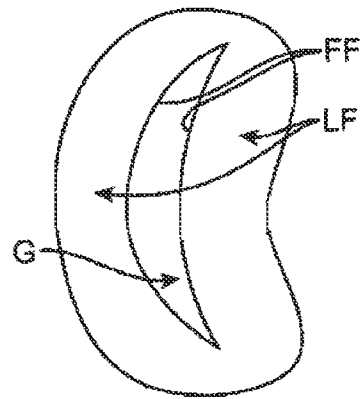


FIG. 5B

4/85

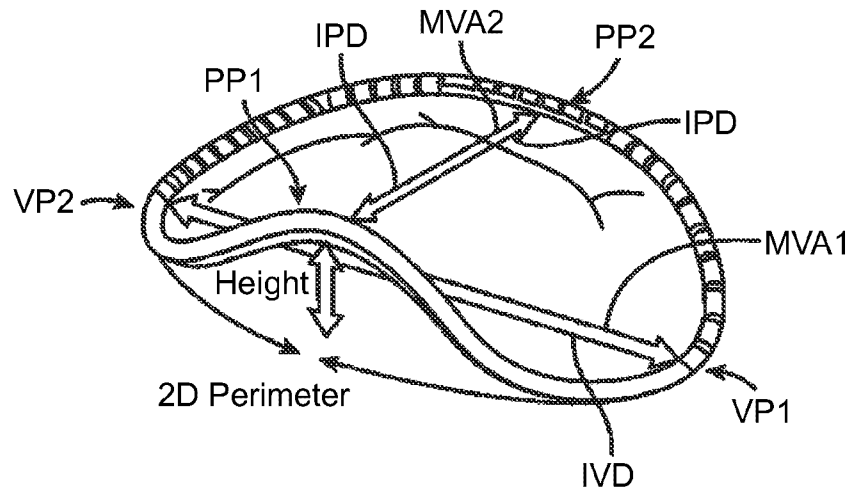


FIG. 5C

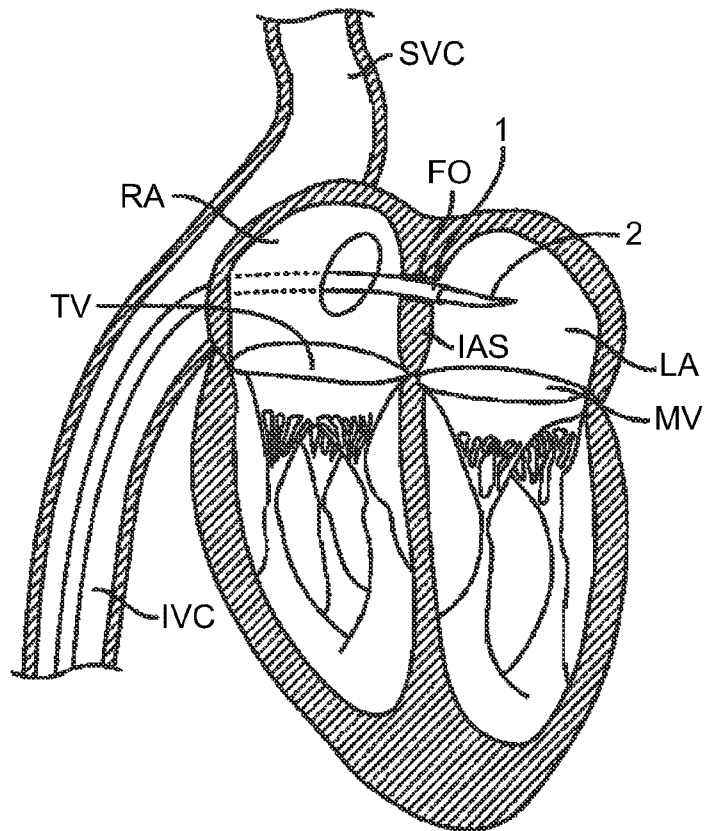


FIG. 6A

5/85

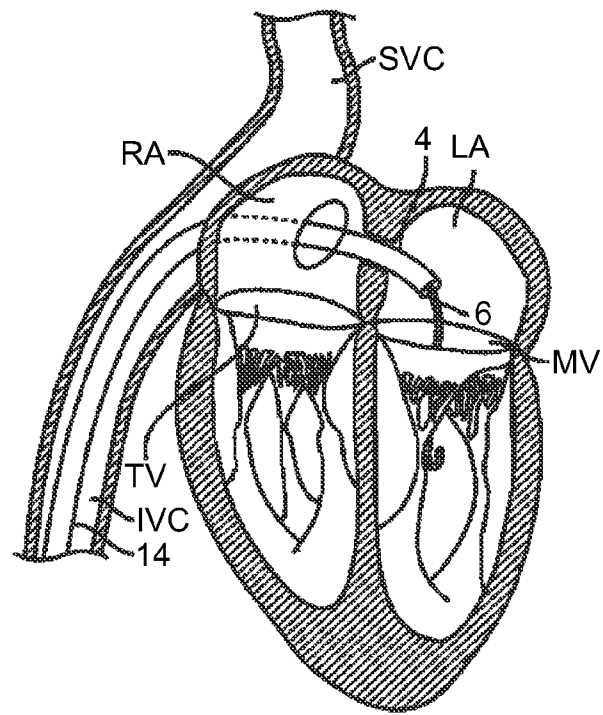


FIG. 6B

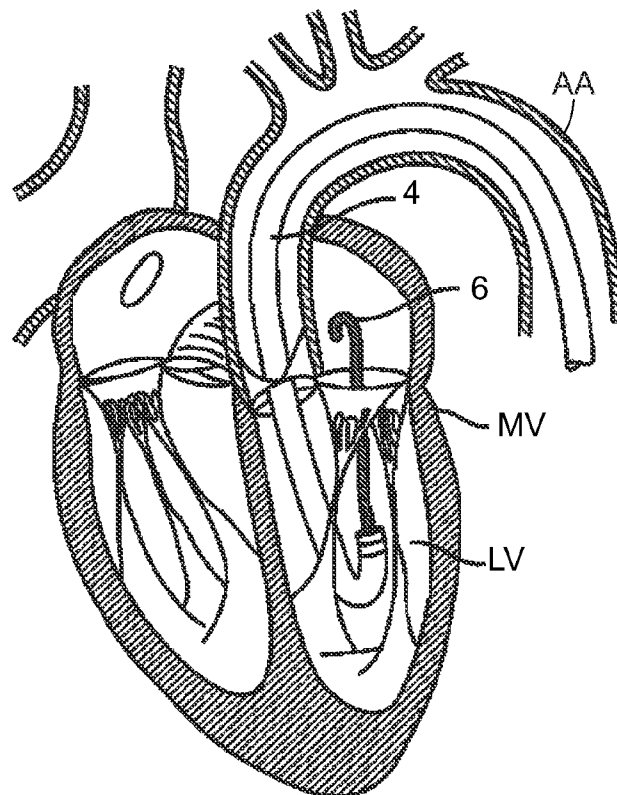


FIG. 7

6/85

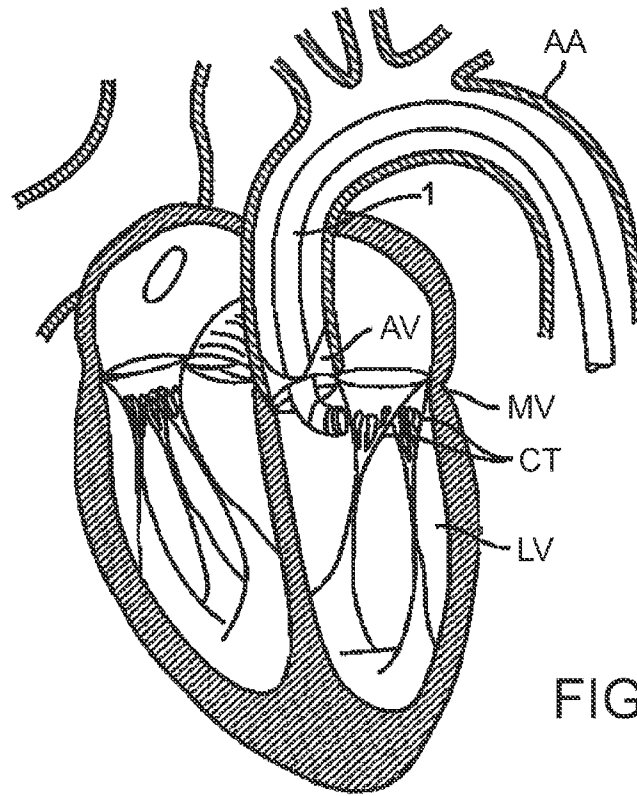


FIG. 8

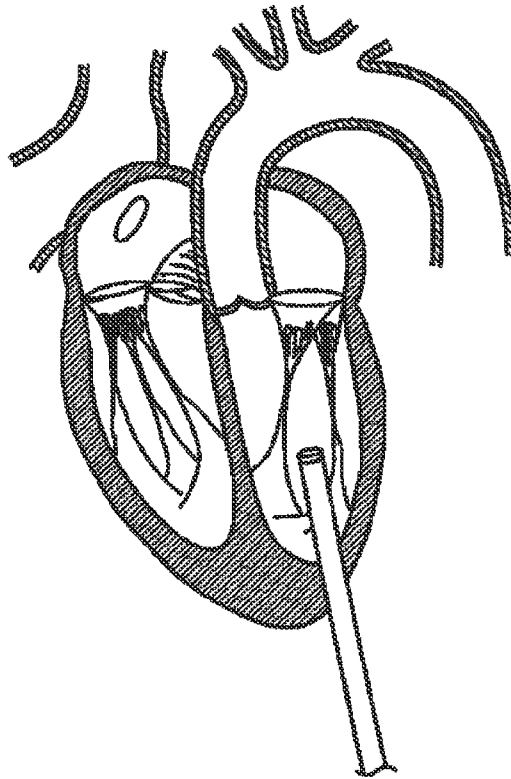


FIG. 9

7/85

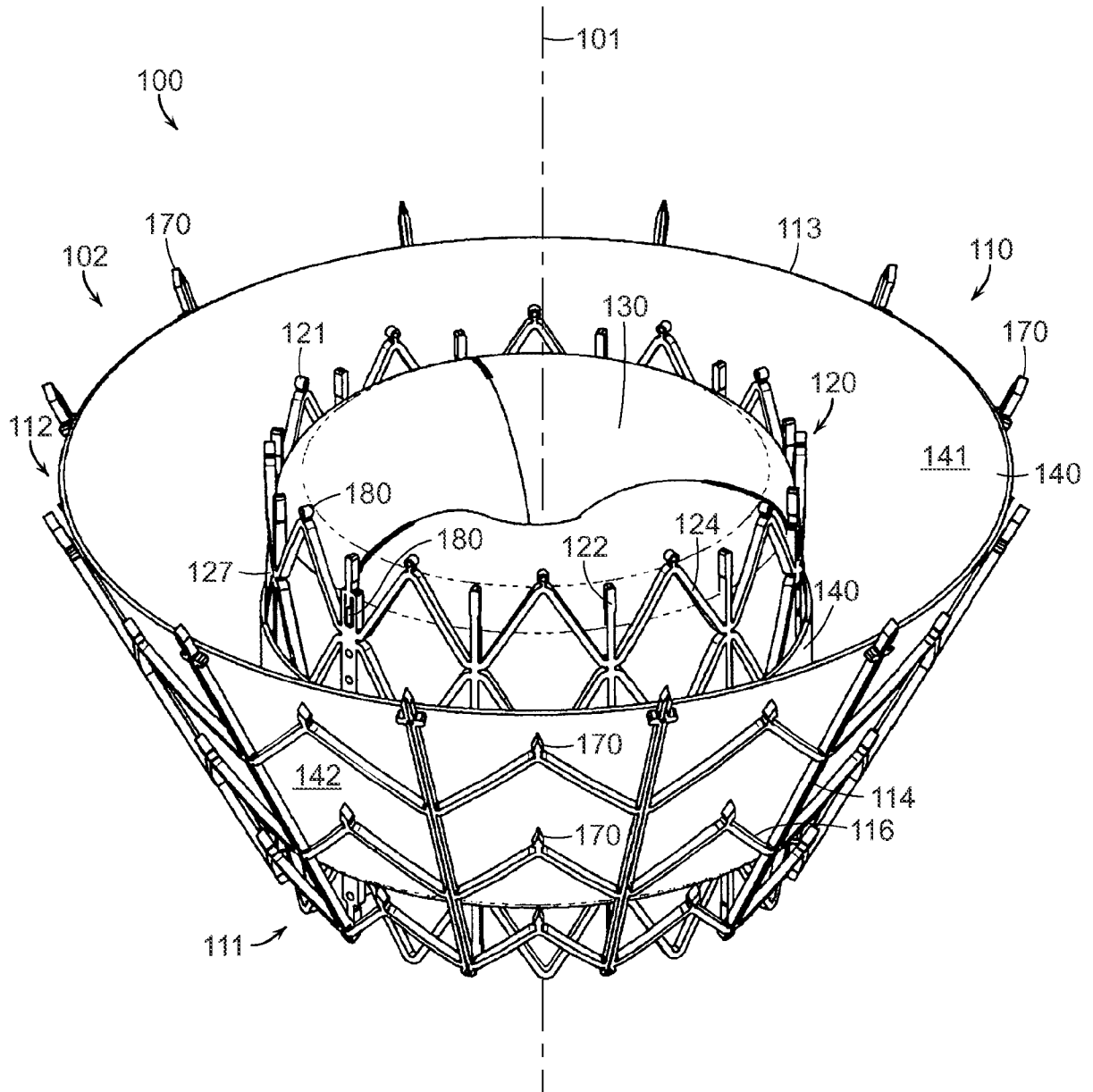


FIG. 10A

8/85

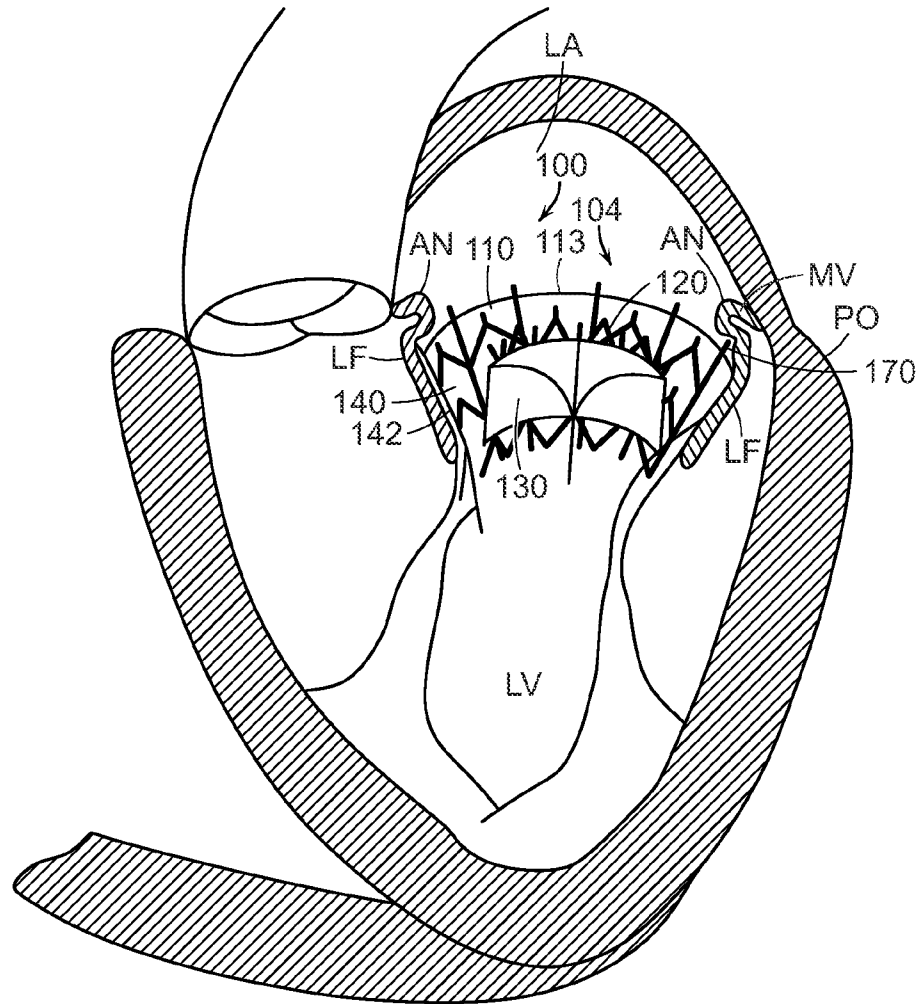


FIG. 10B

9/85

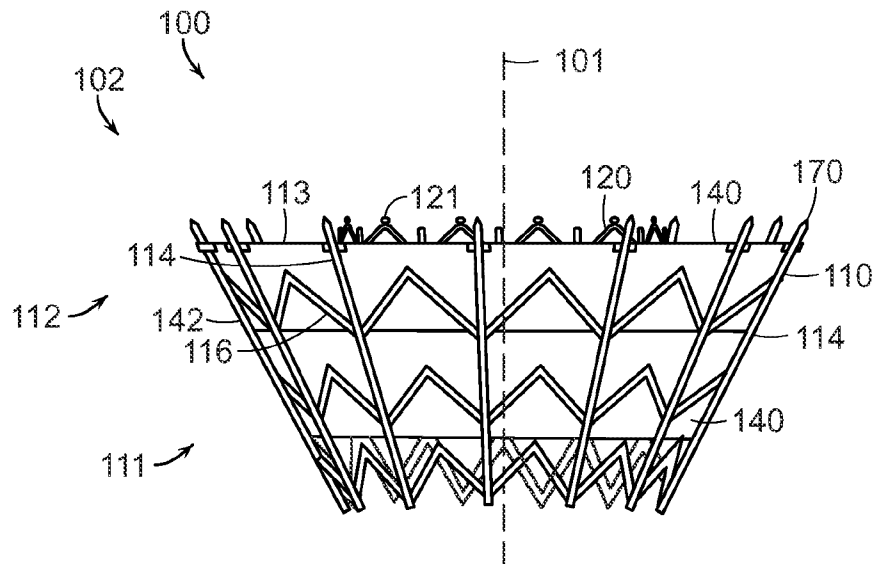


FIG. 10C

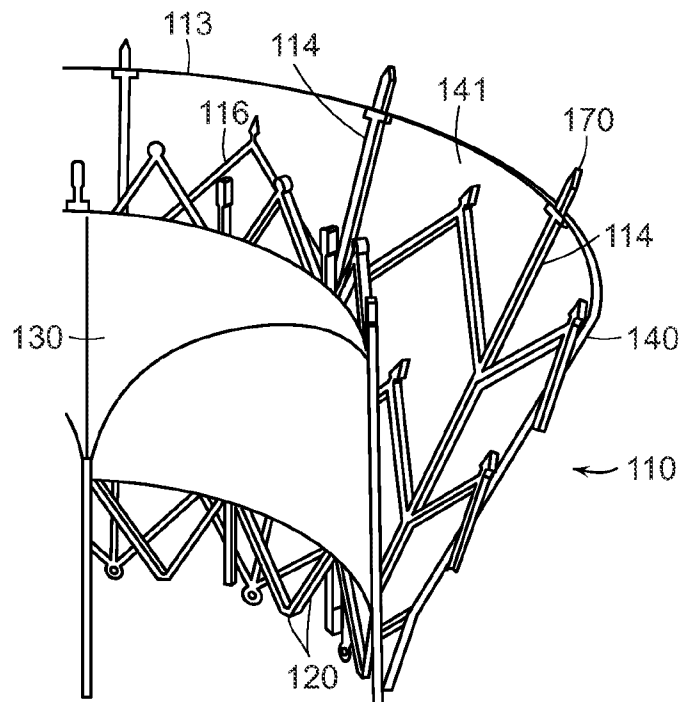


FIG. 10D

10/85

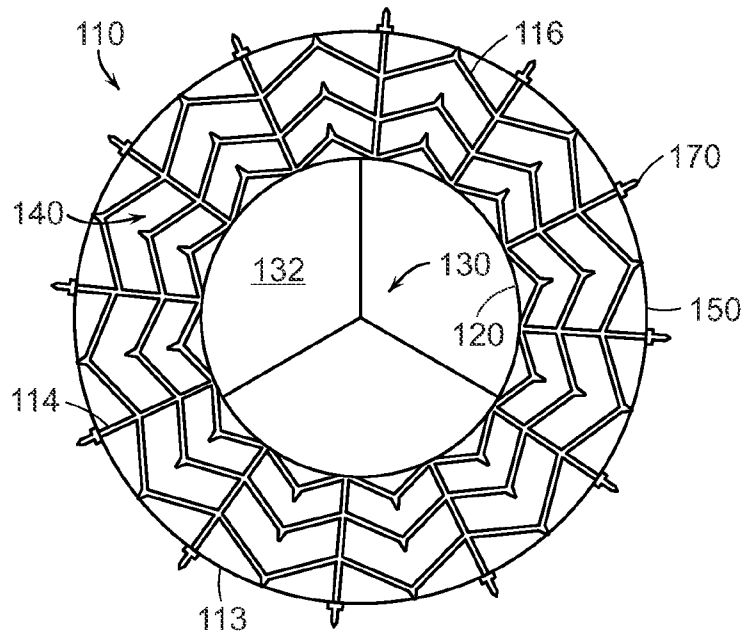


FIG. 10E

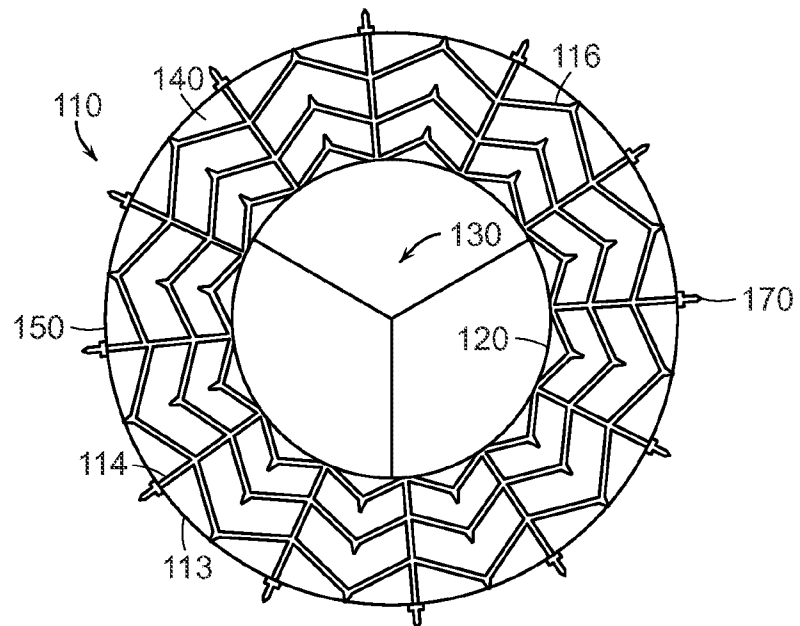


FIG. 10F

11/85

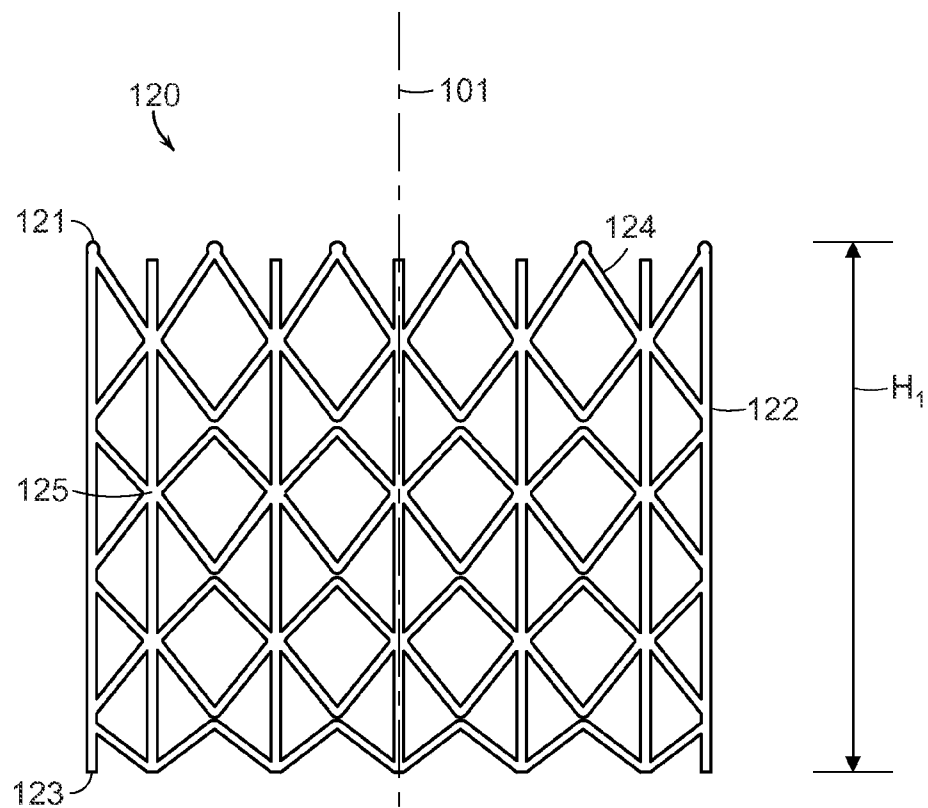


FIG. 11A

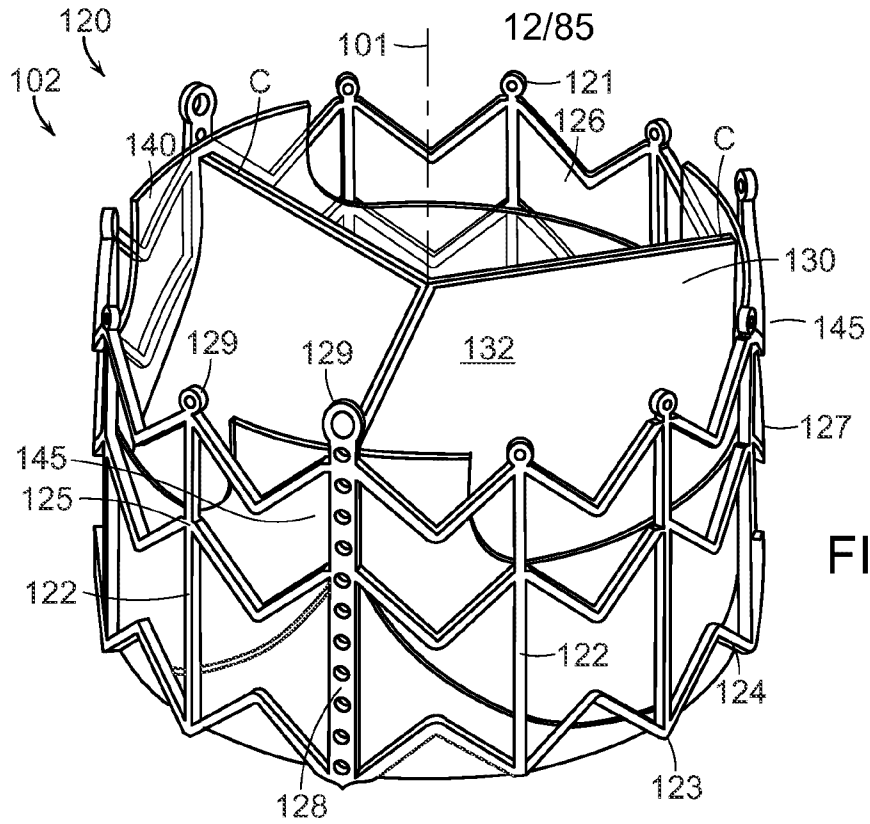


FIG. 11B

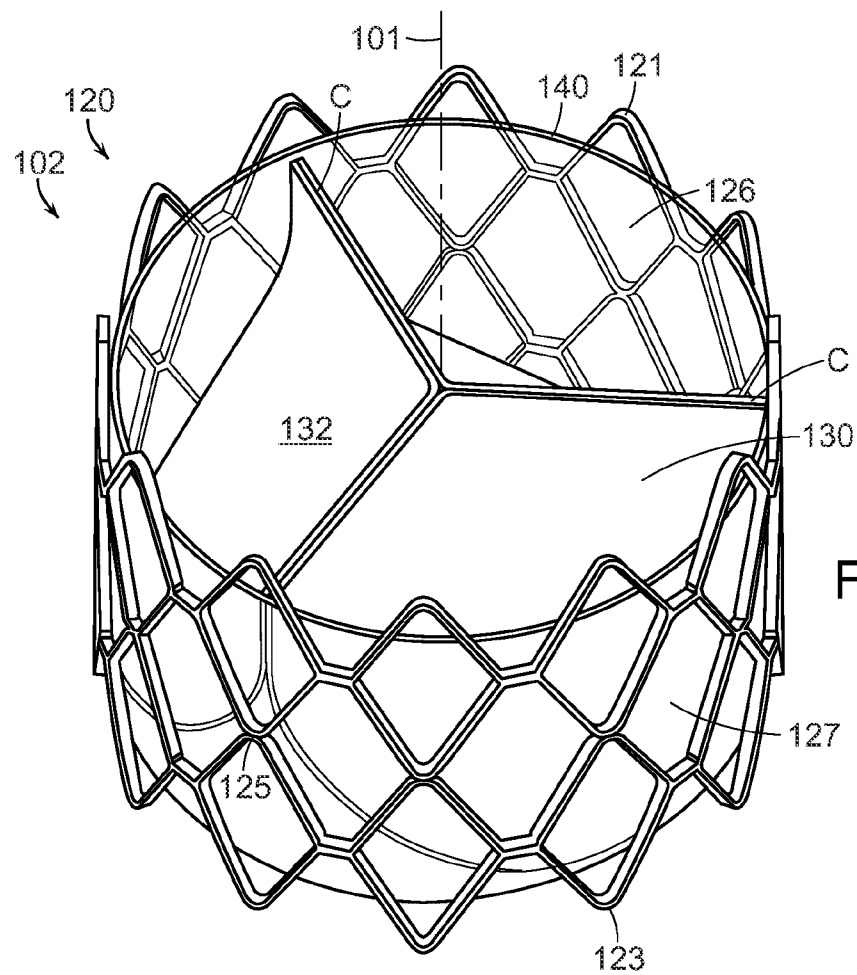


FIG. 11C

13/85

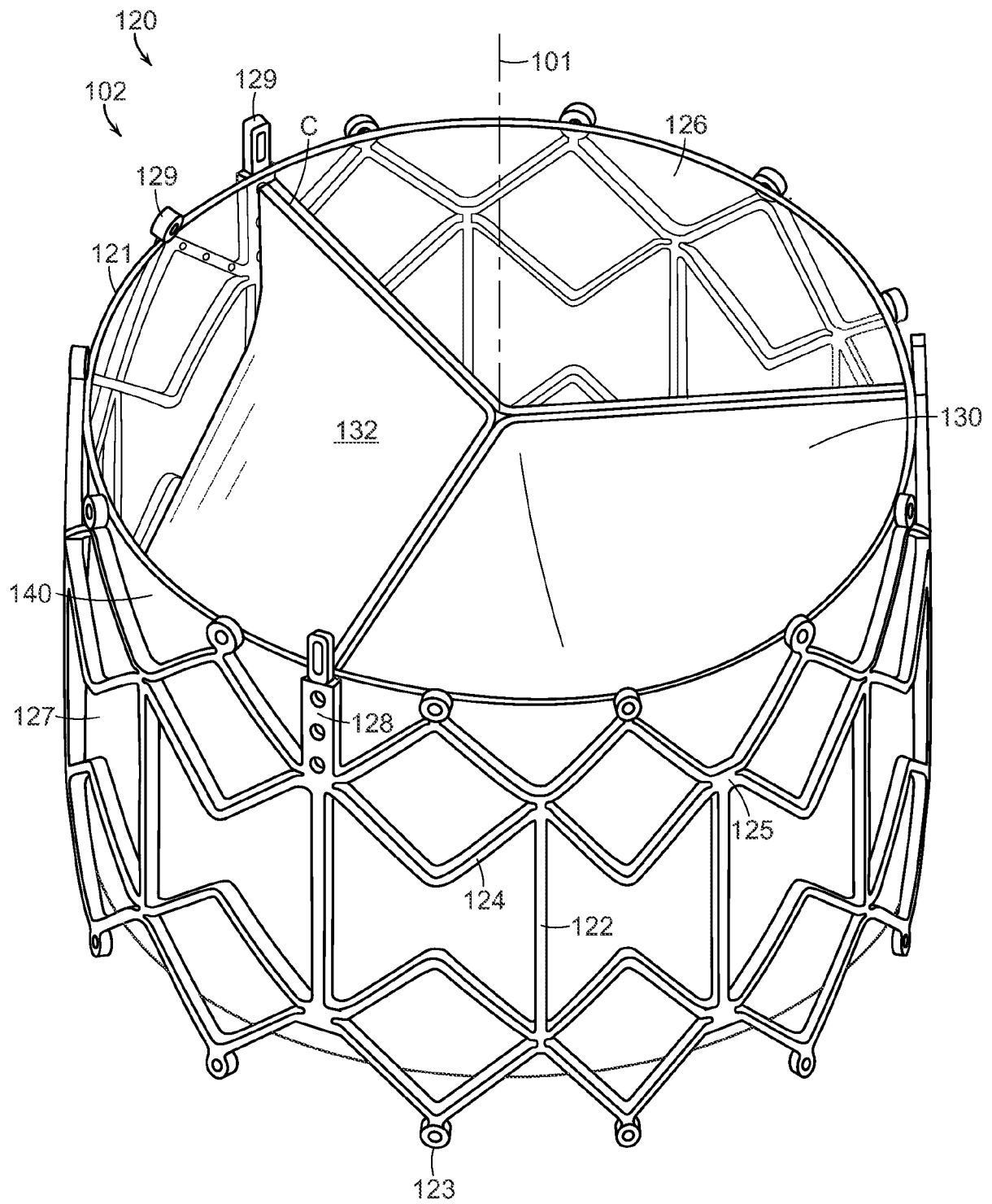


FIG. 11D

14/85

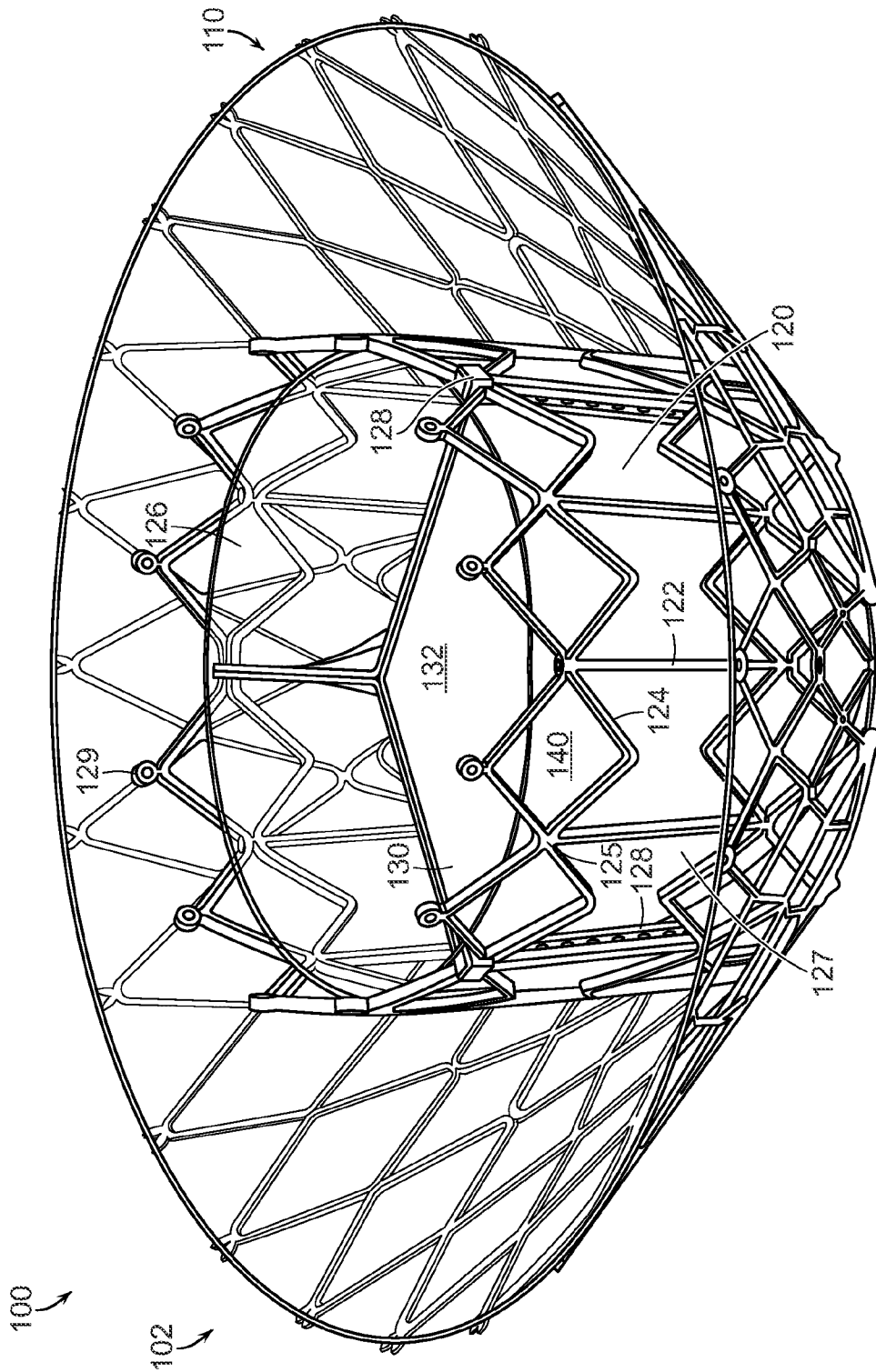


FIG. 11E

15/85

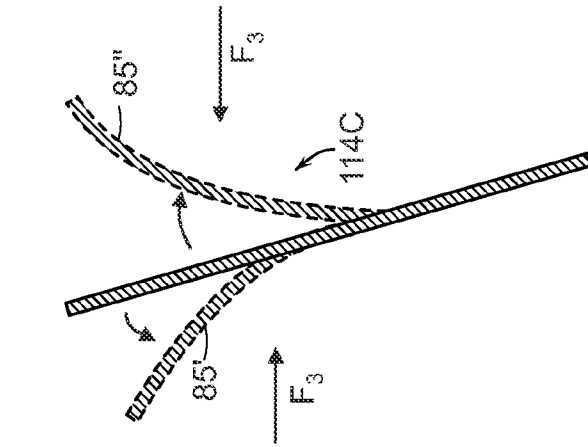


FIG. 12C

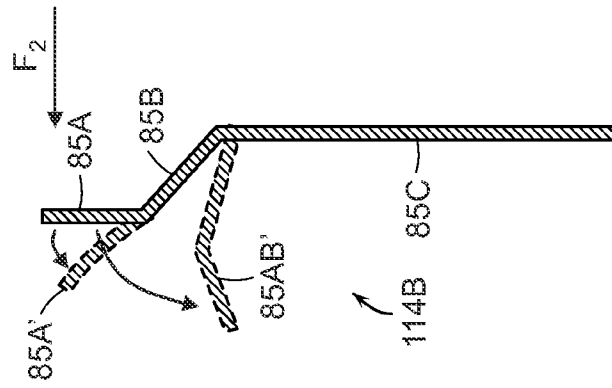


FIG. 12B

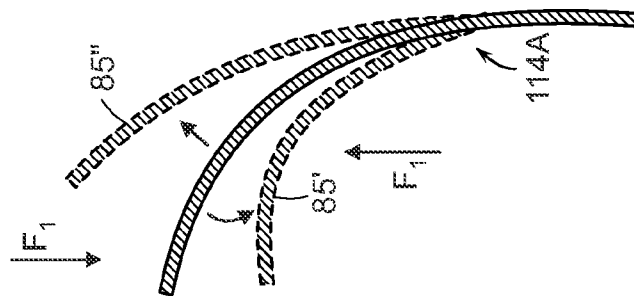


FIG. 12A

16/85

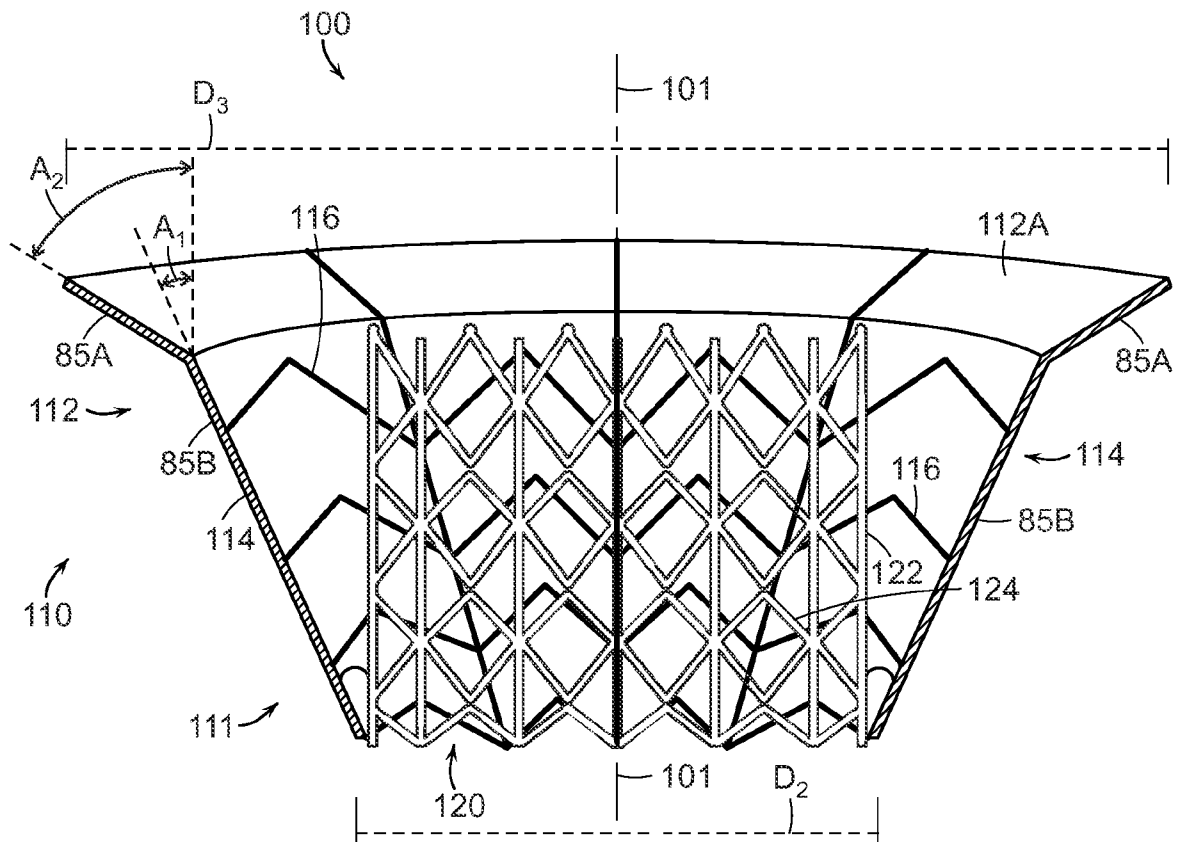


FIG. 13A

17/85

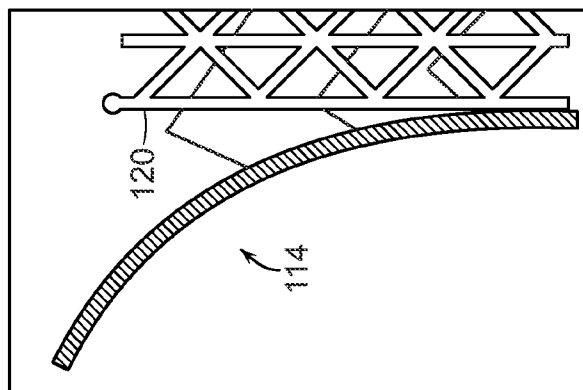


FIG. 13B

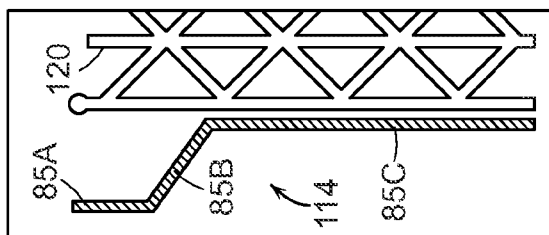


FIG. 13C

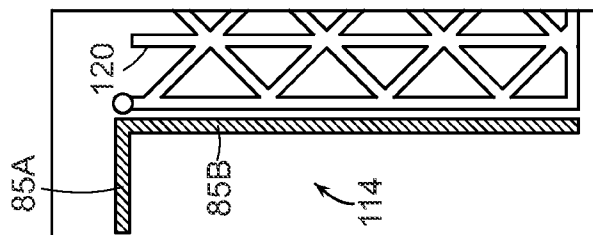


FIG. 13D

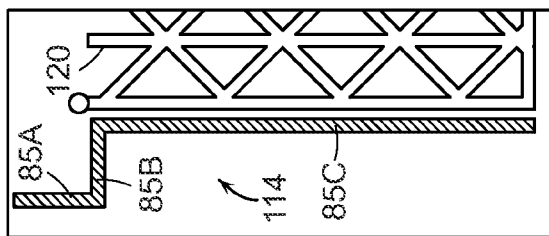


FIG. 13E

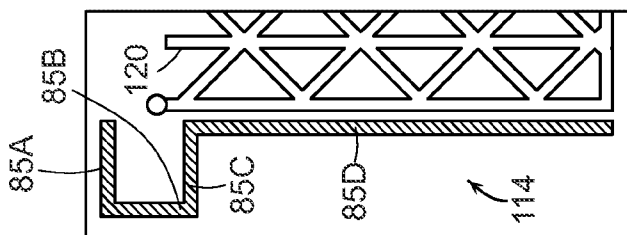


FIG. 13F

18/85

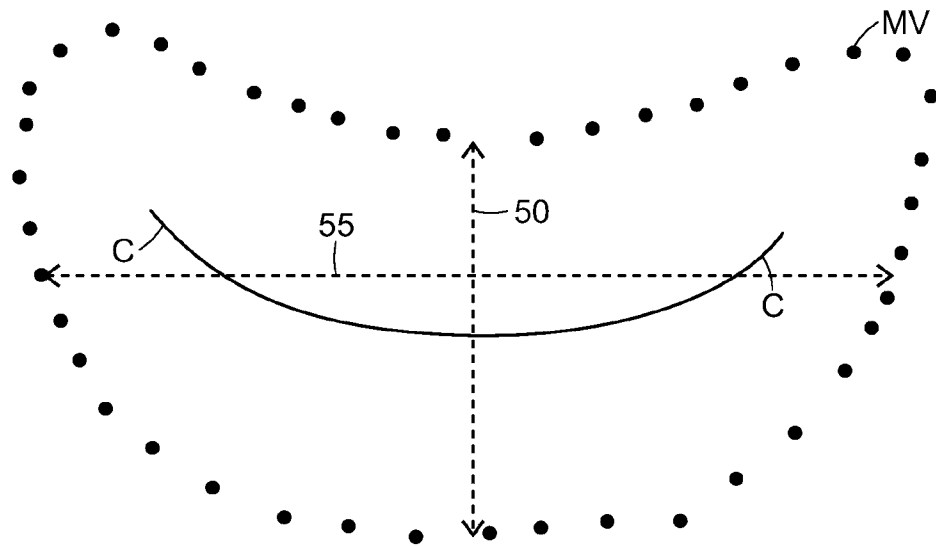


FIG. 14A

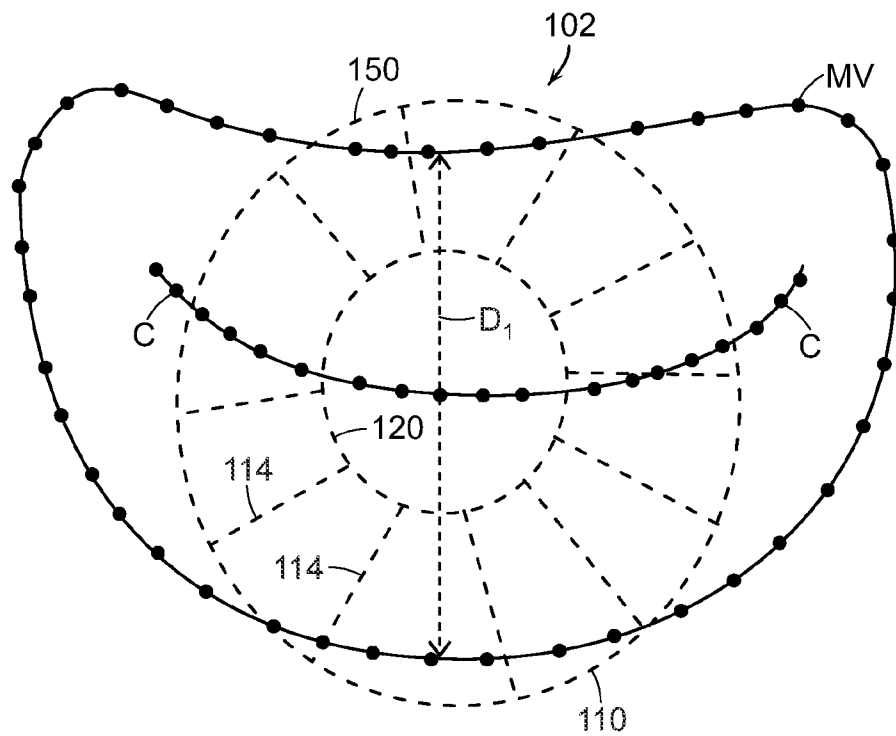


FIG. 14B

19/85

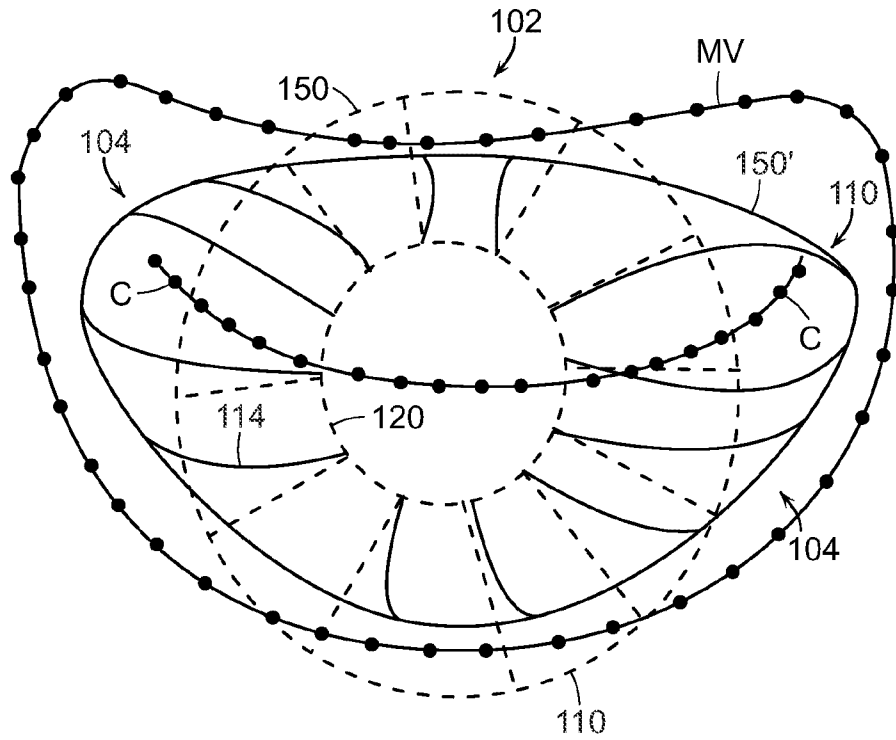


FIG. 14C

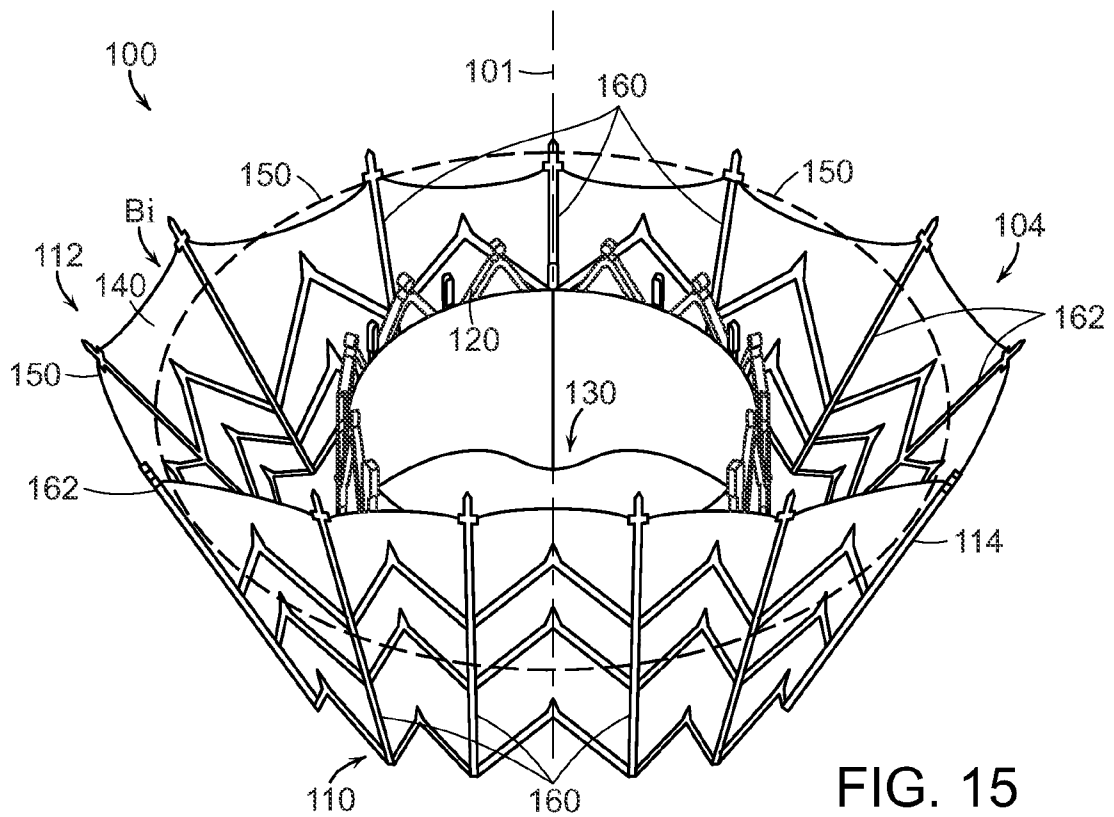


FIG. 15

20/85

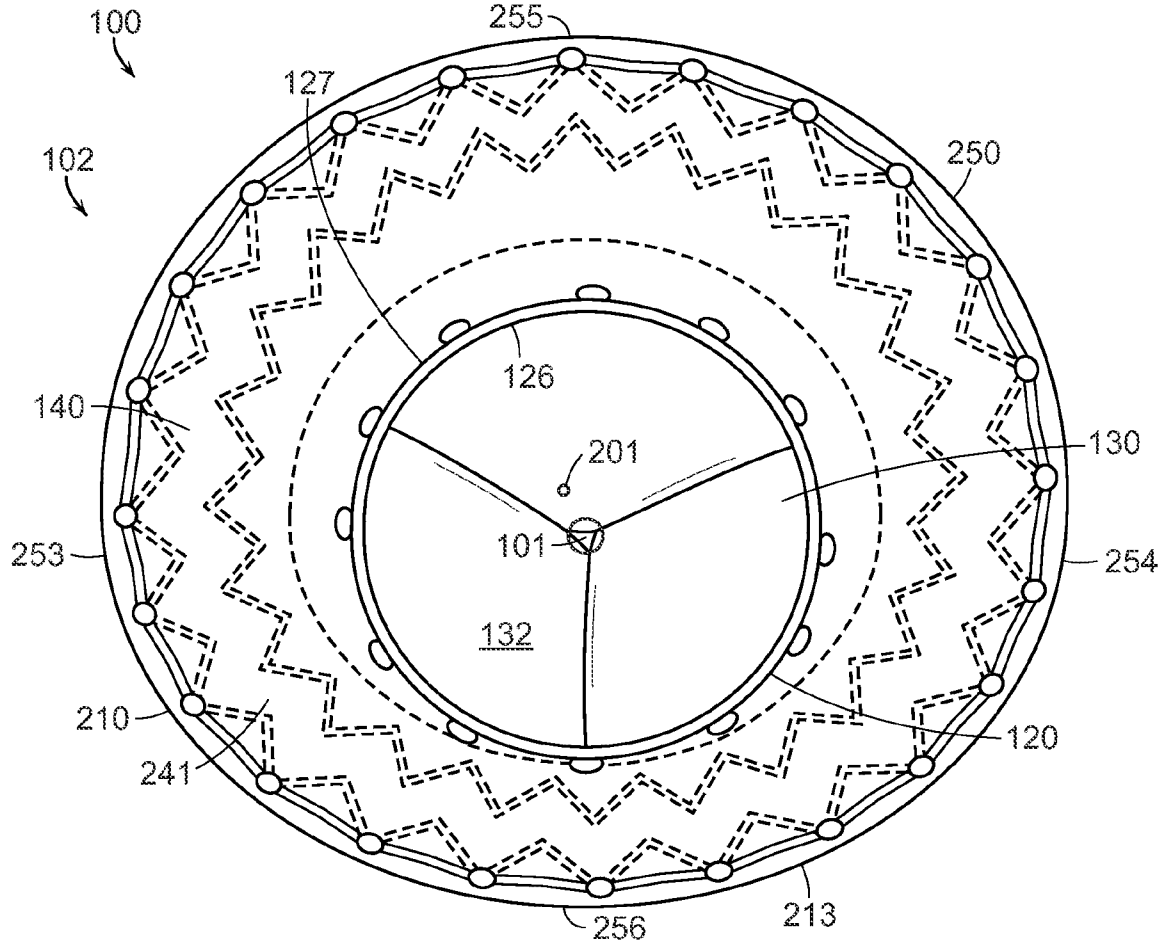


FIG. 16A

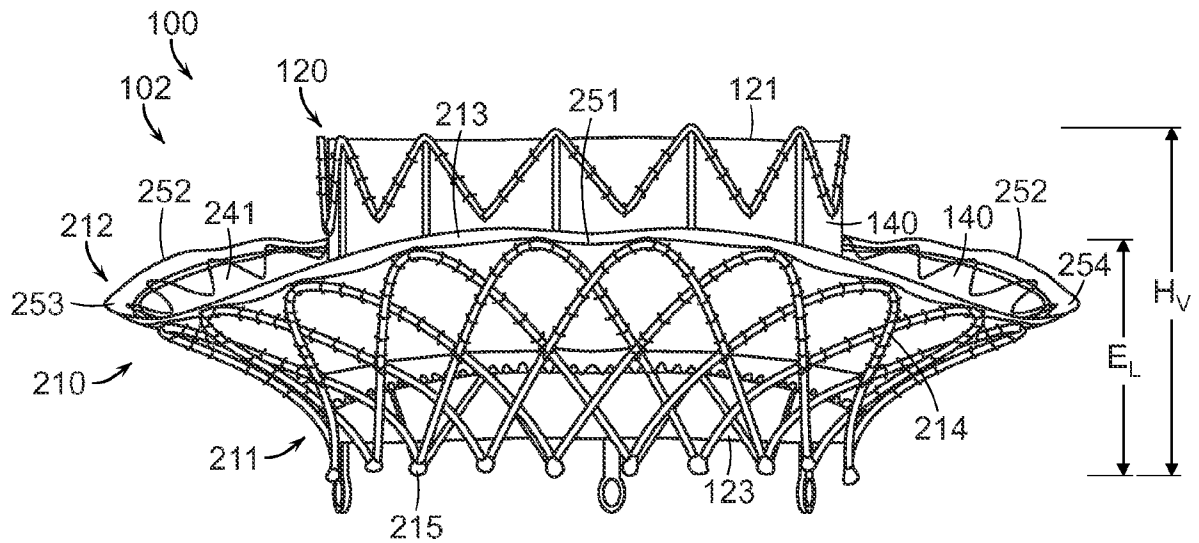


FIG. 16B

21/85

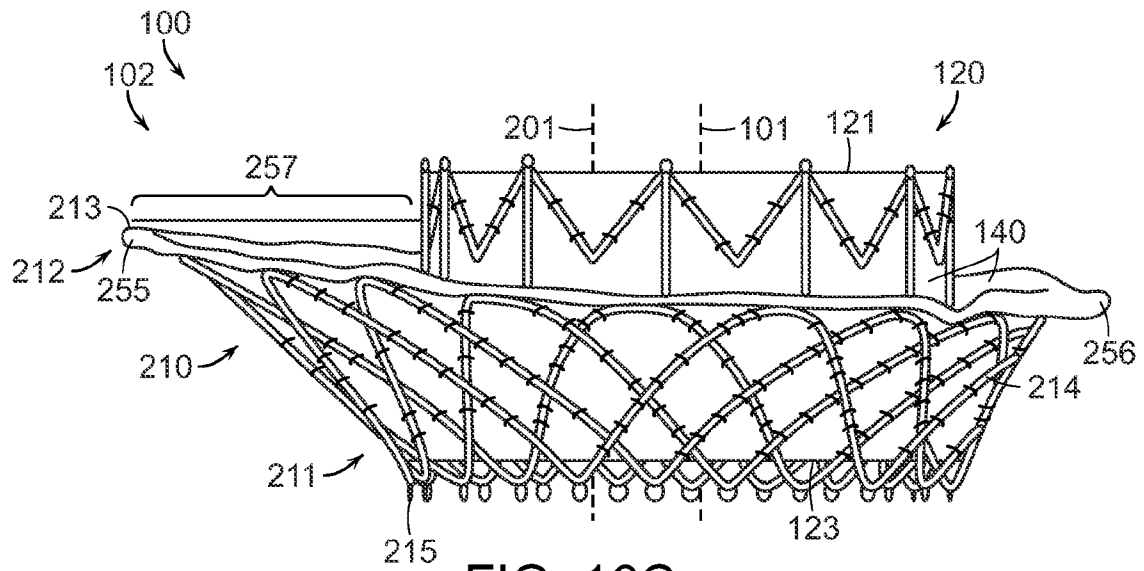


FIG. 16C

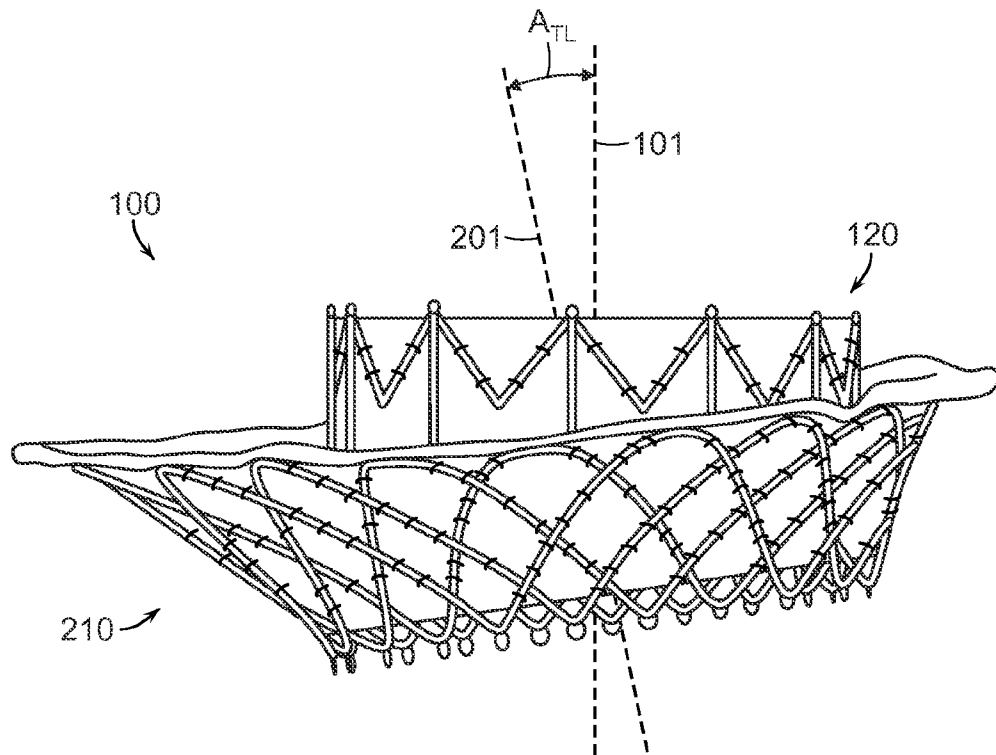


FIG. 16D

22/85

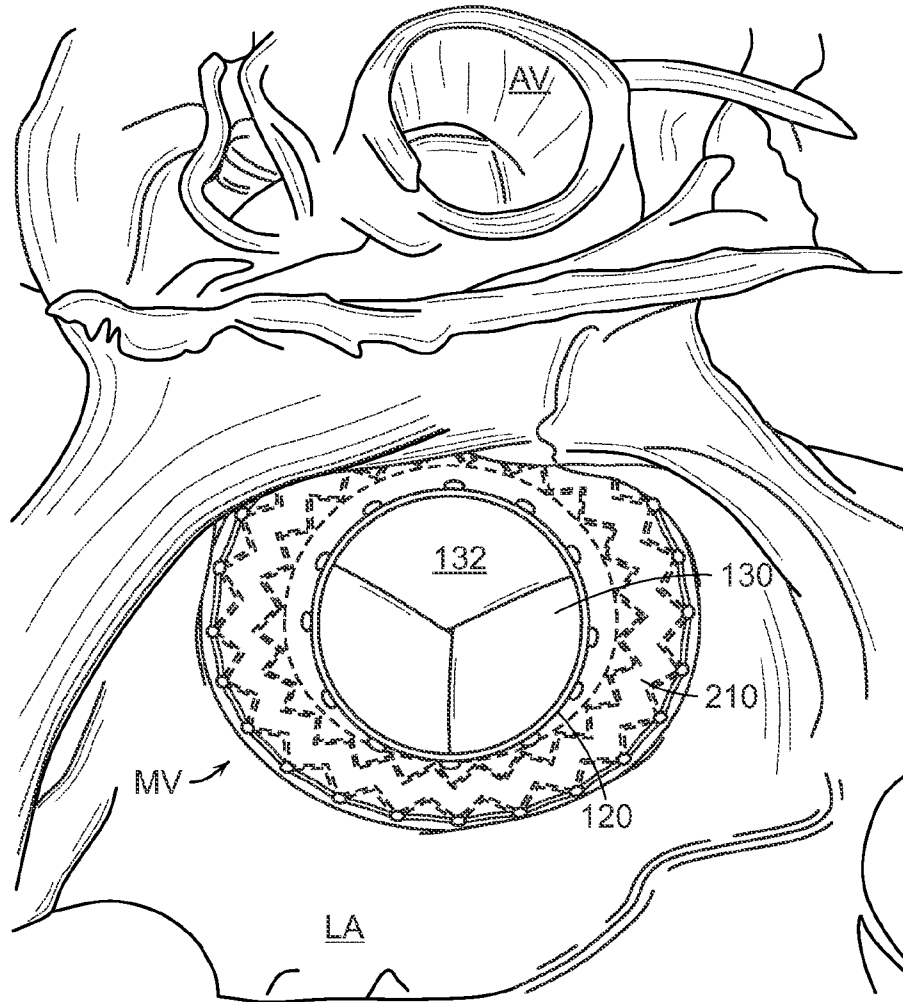


FIG. 16E

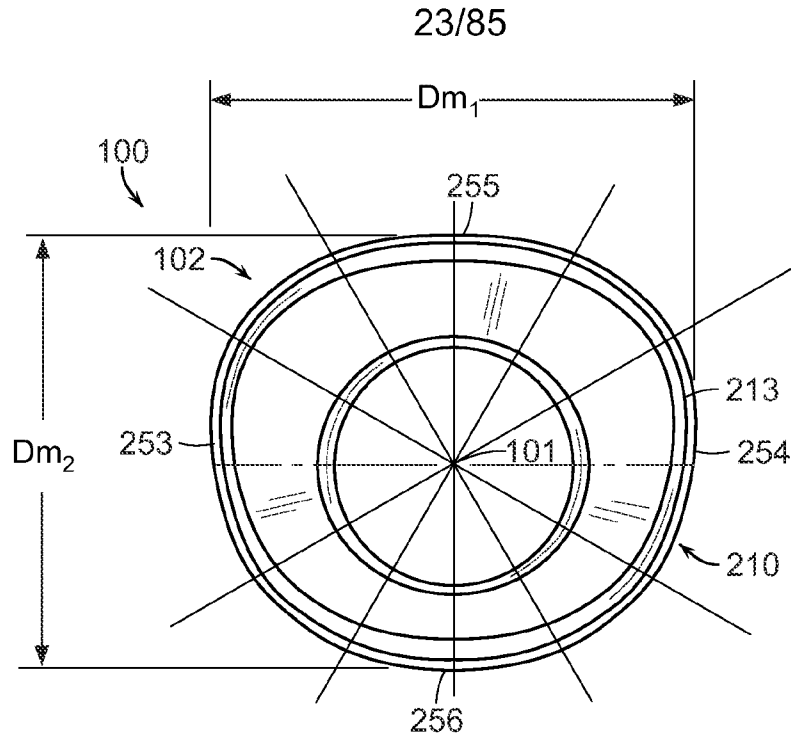


FIG. 17A

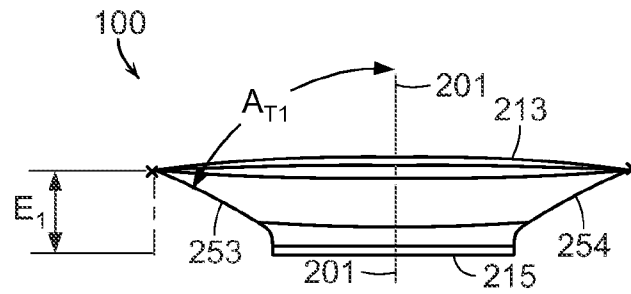


FIG. 17B

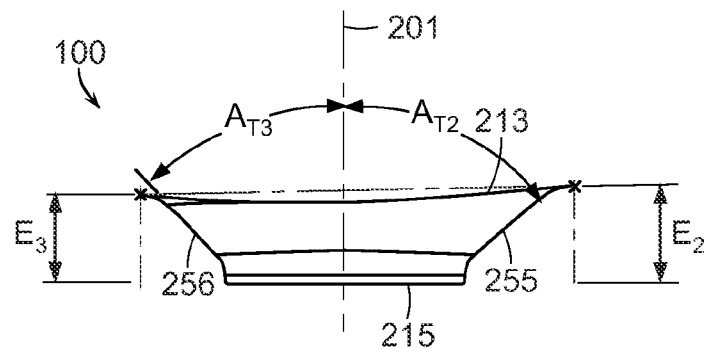


FIG. 17C

24/85

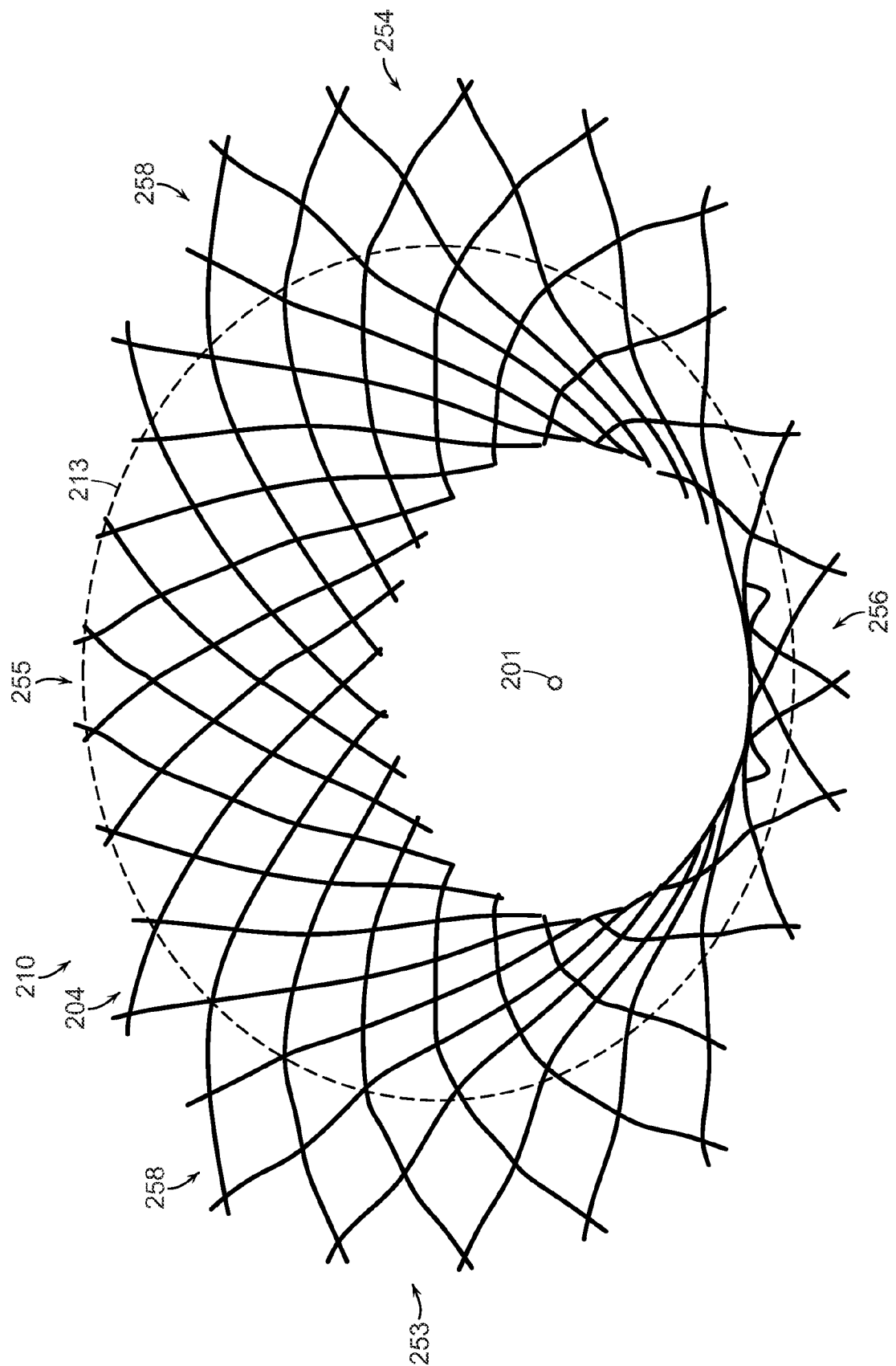


FIG. 18

25/85

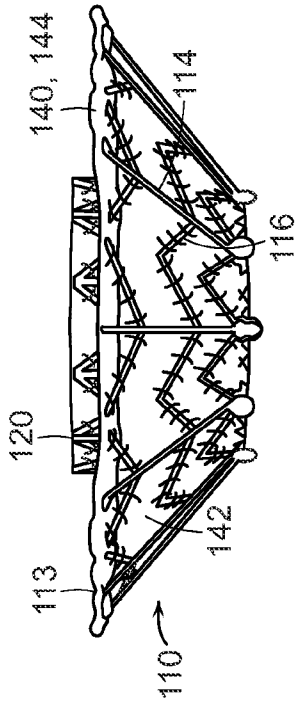


FIG. 19B

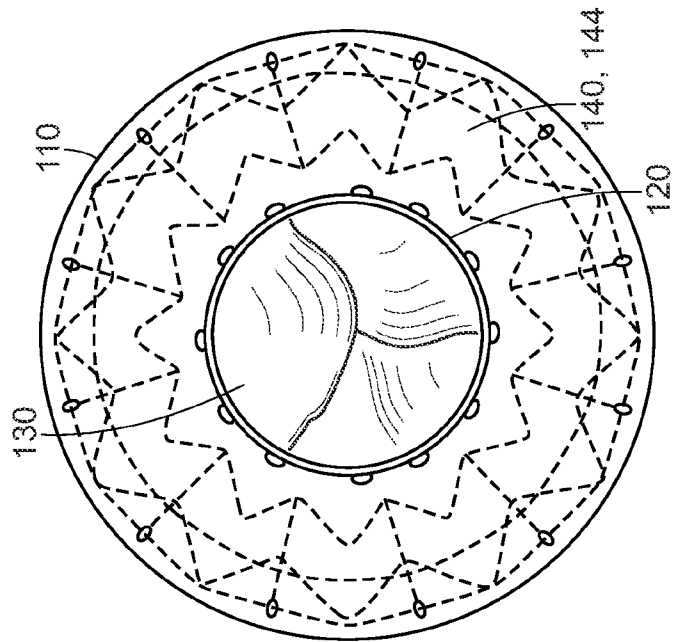


FIG. 19C

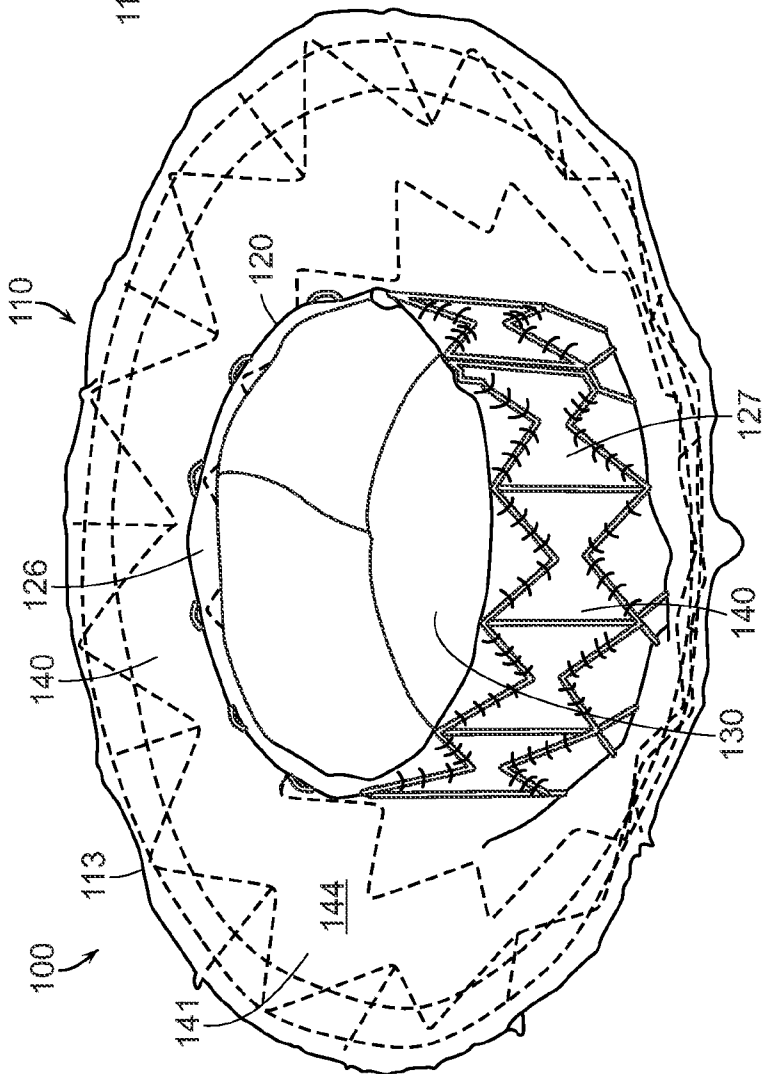


FIG. 19A

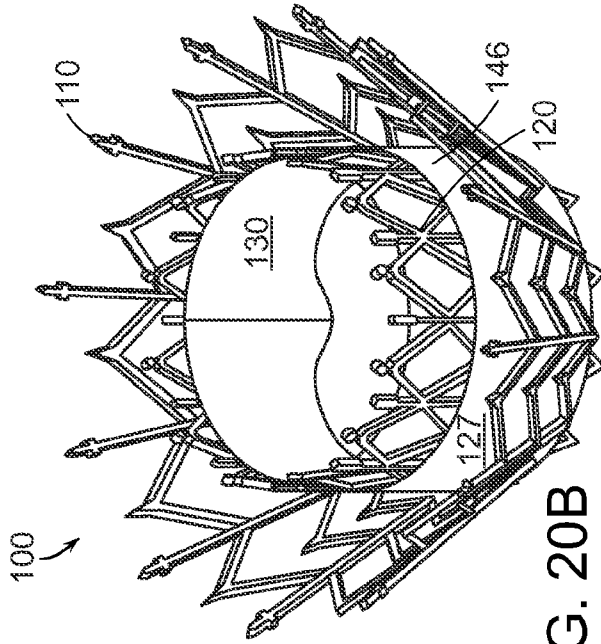


FIG. 20B

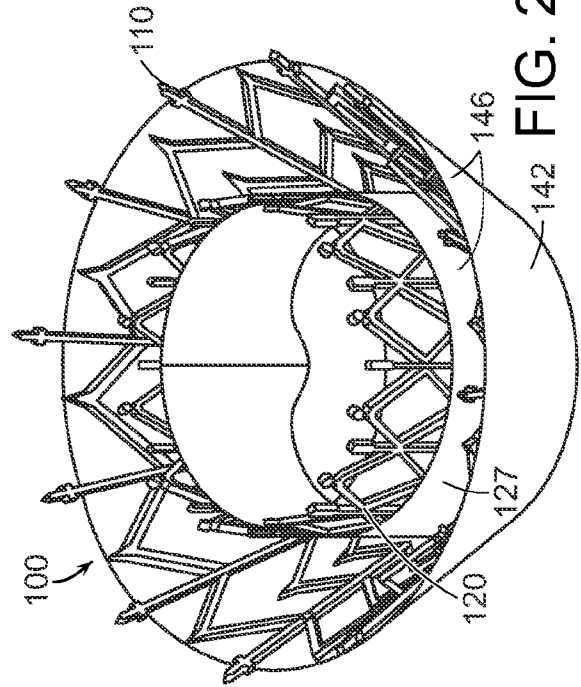


FIG. 20D

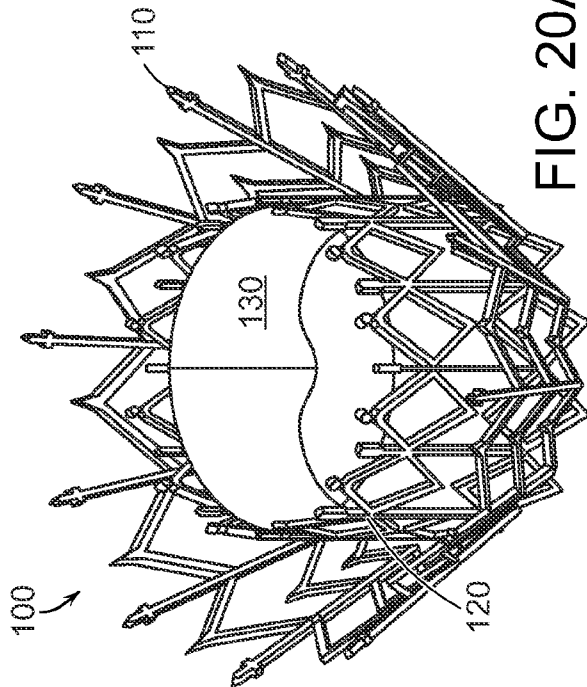


FIG. 20A

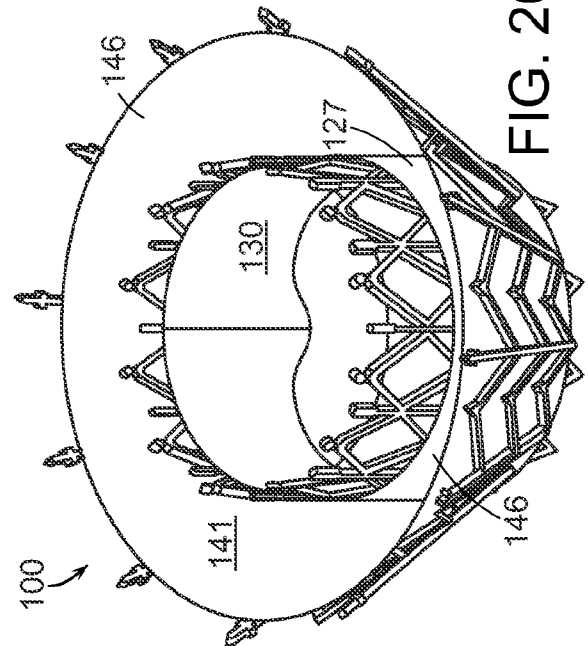


FIG. 20C

27/85

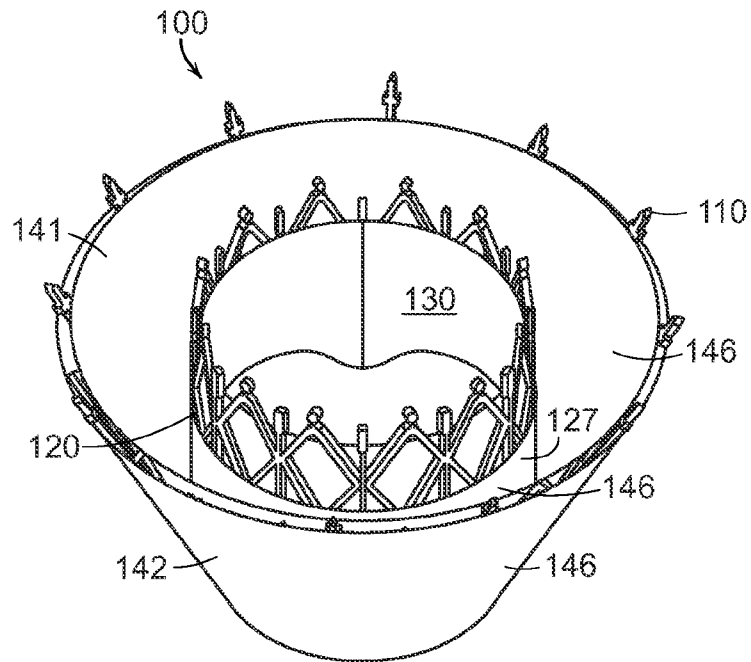


FIG. 20E

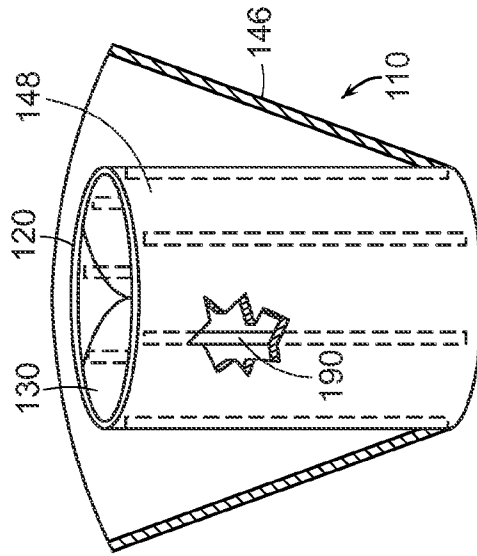


FIG. 21C

28/85

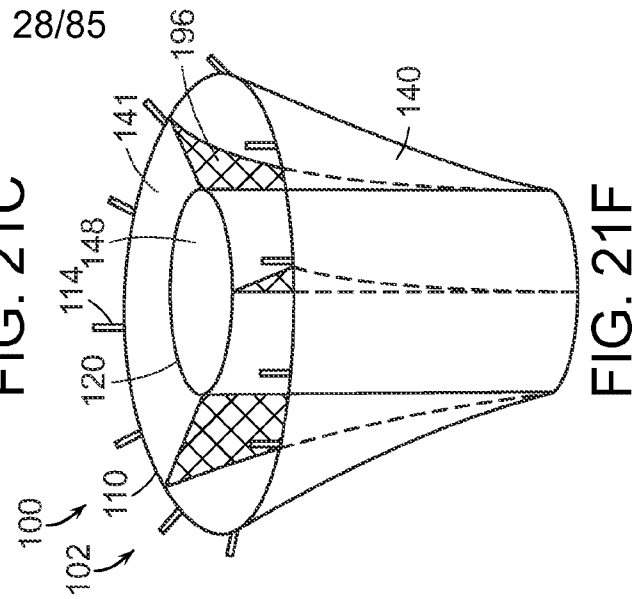


FIG. 21F

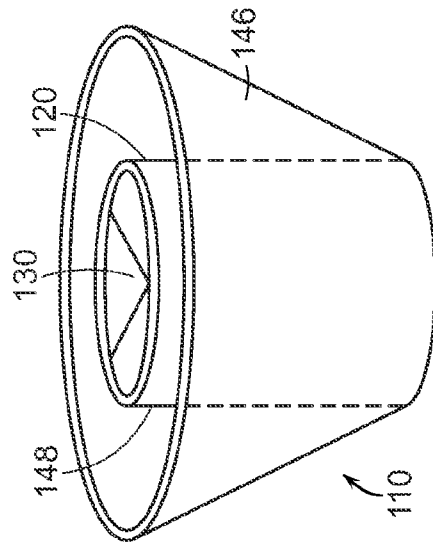


FIG. 21B

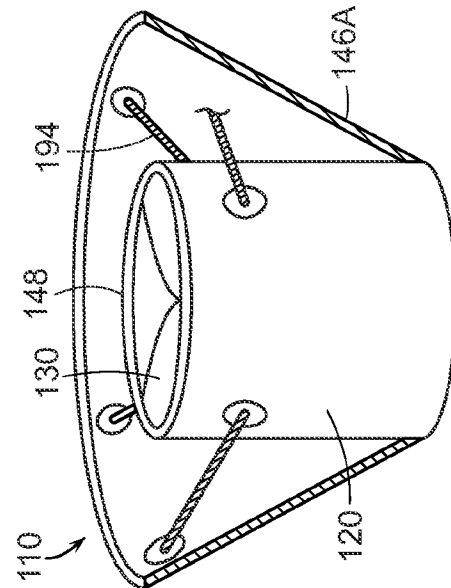


FIG. 21E

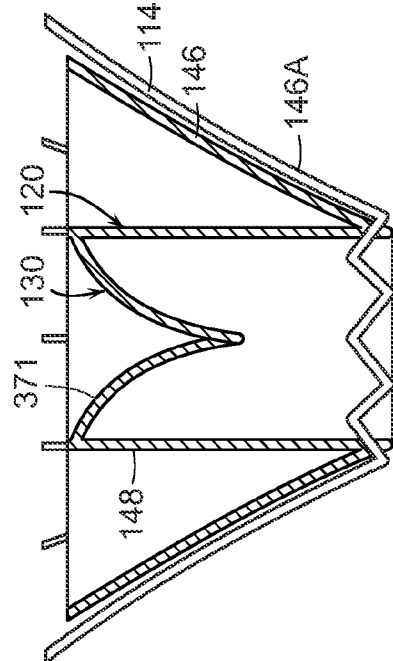


FIG. 21A

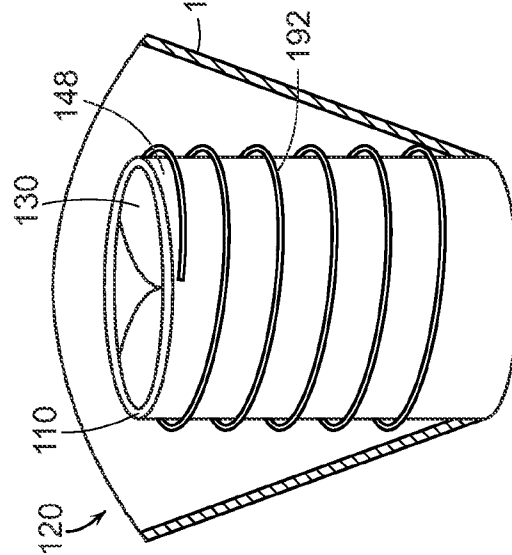


FIG. 21D

29/85

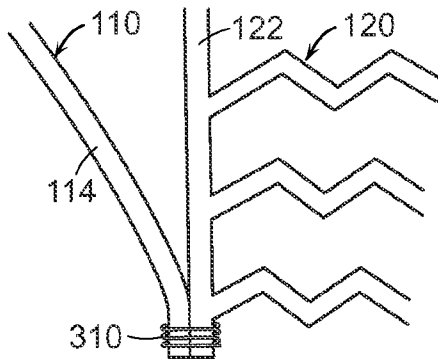


FIG. 22A

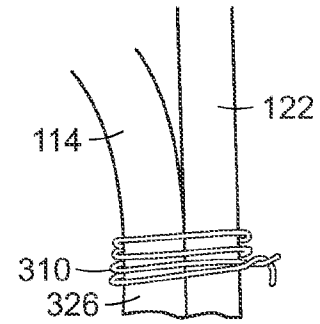


FIG. 22B

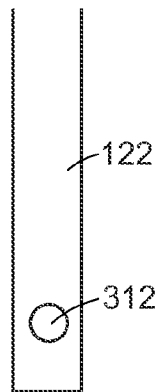


FIG. 22C

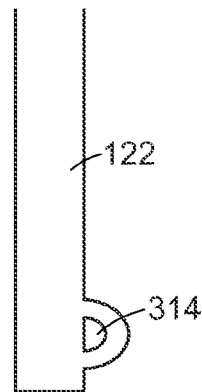


FIG. 22D

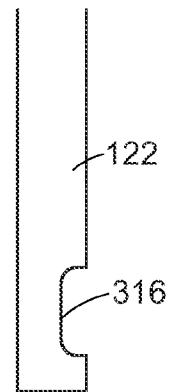


FIG. 22E

30/85

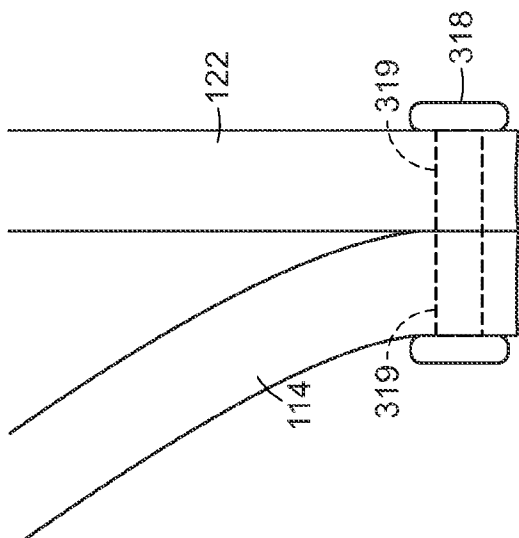


FIG. 22F

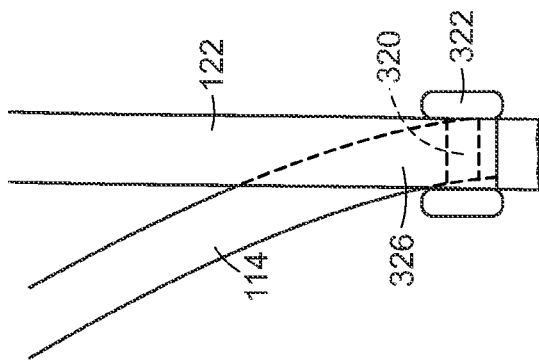


FIG. 22G

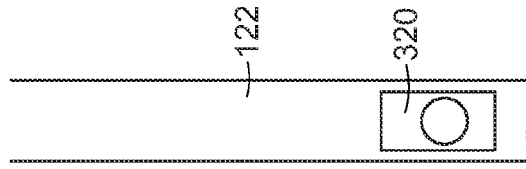


FIG. 22H

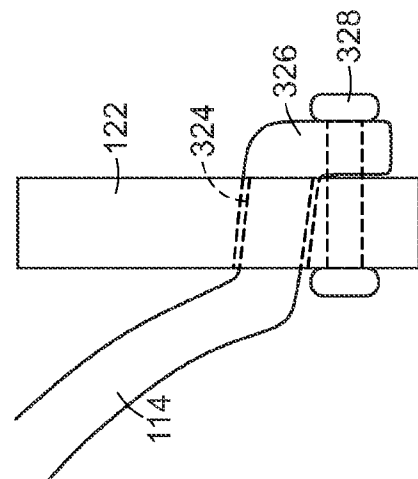


FIG. 22I

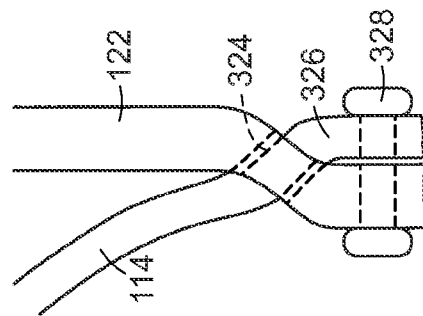


FIG. 22J

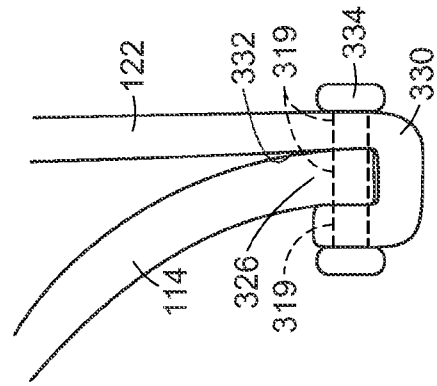


FIG. 22K

31/85

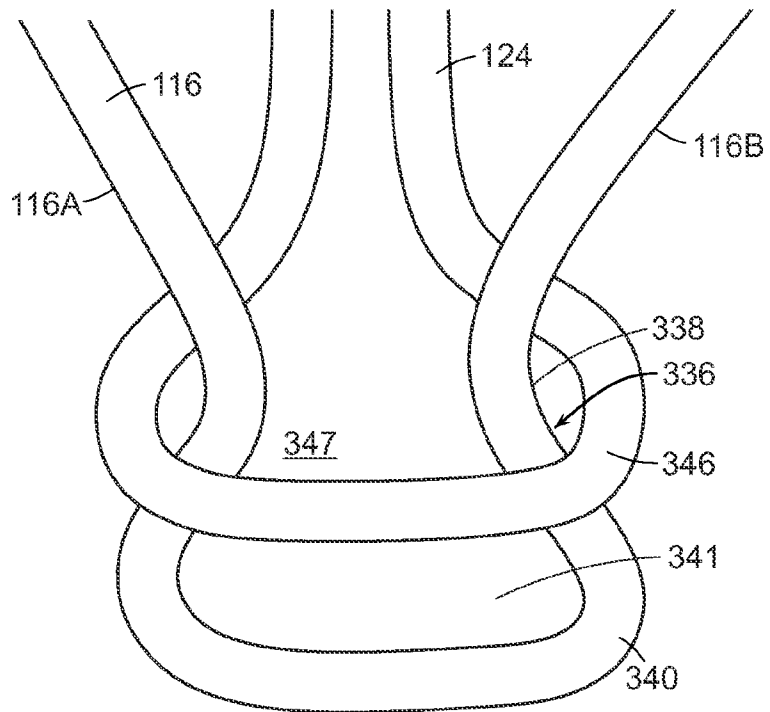


FIG. 23A

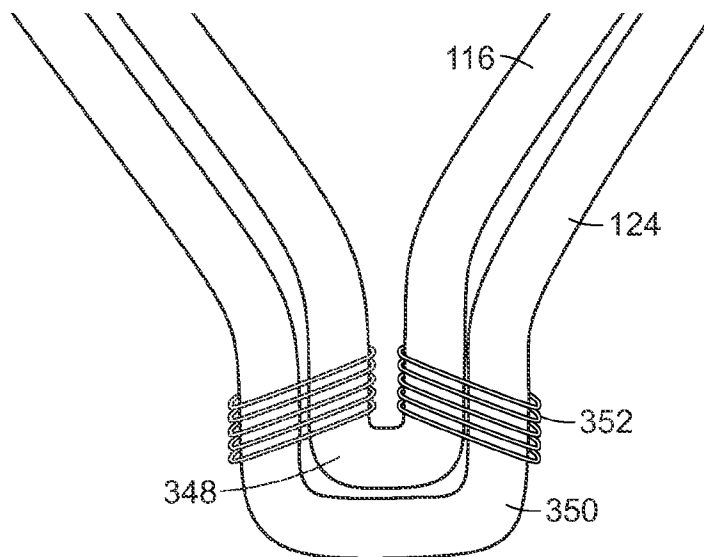


FIG. 23B

32/85

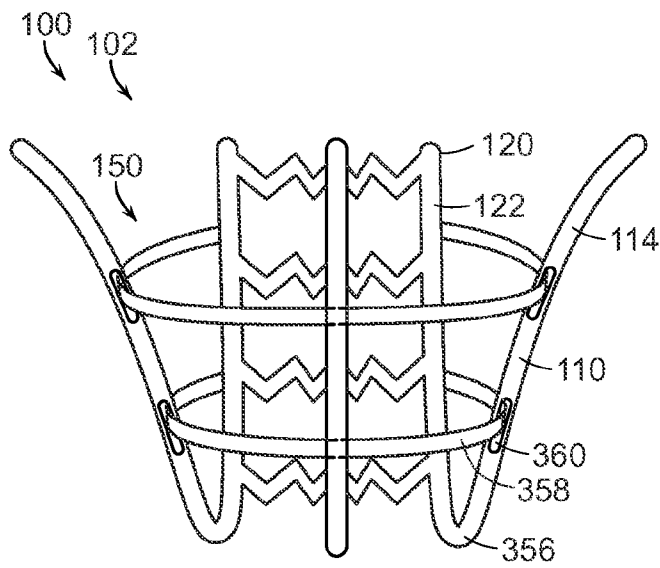


FIG. 24A

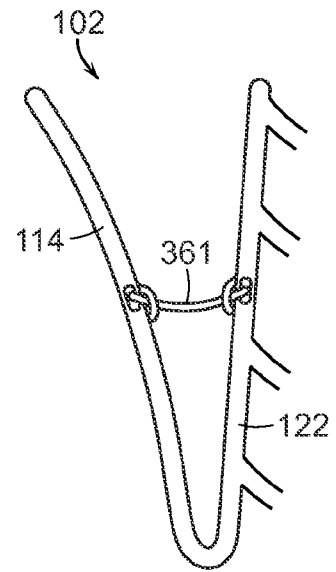


FIG. 24B

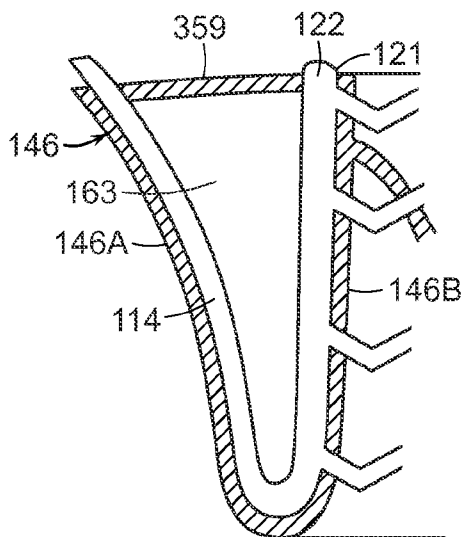


FIG. 24C

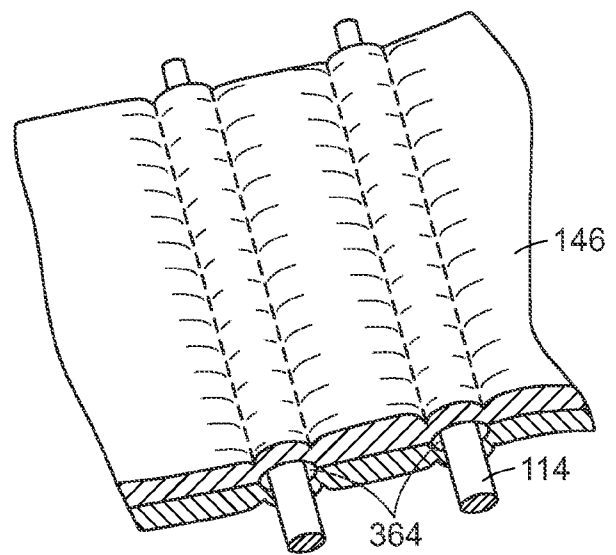


FIG. 24D

33/85

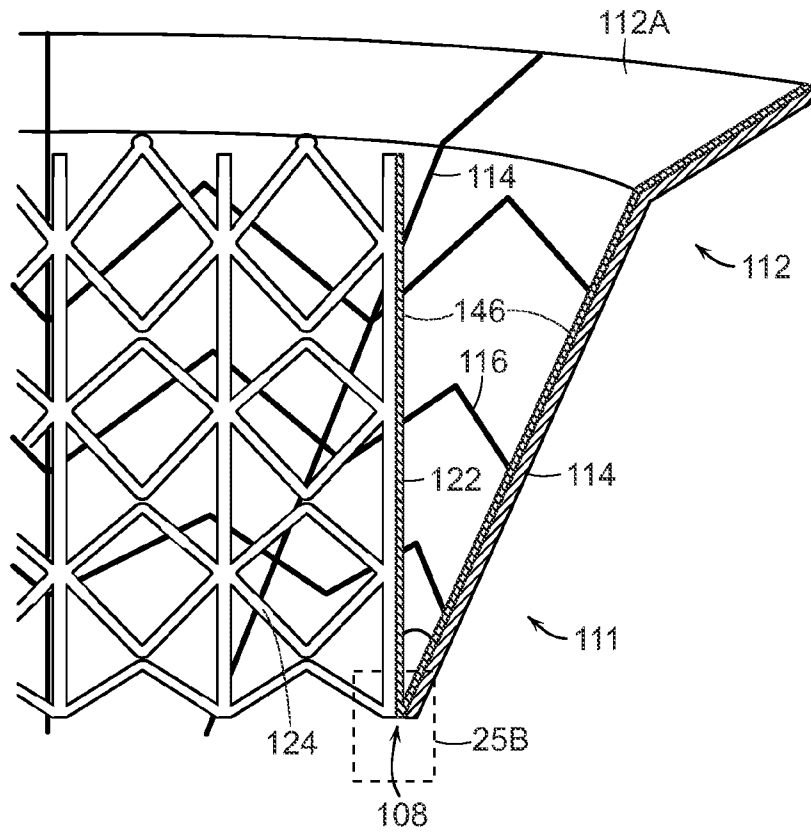


FIG. 25A

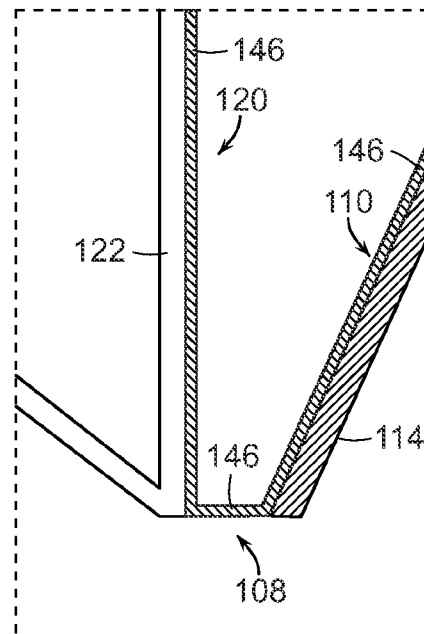


FIG. 25B

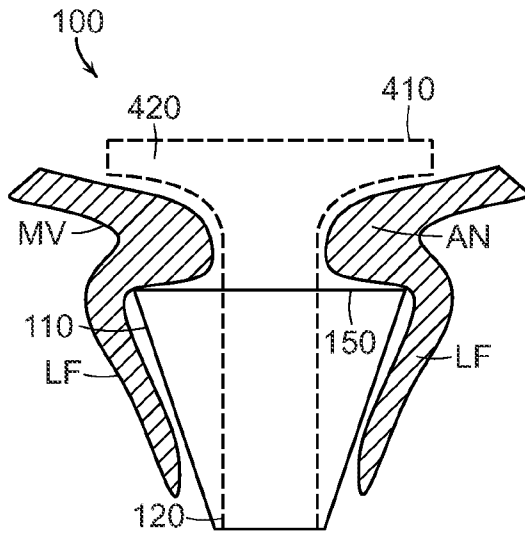


FIG. 26A

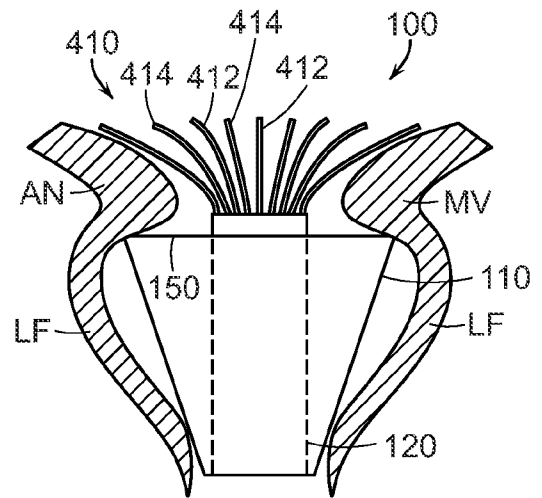


FIG. 26B

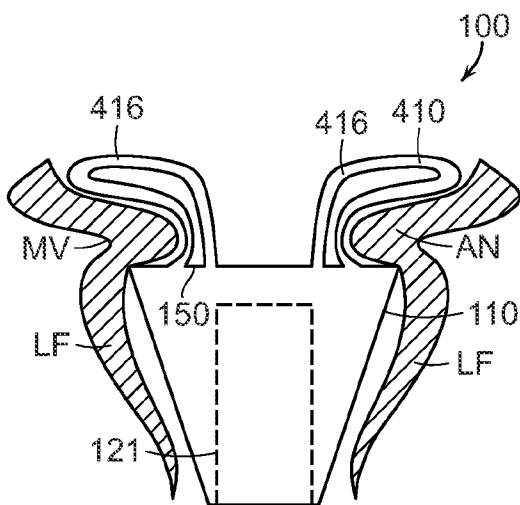


FIG. 26C

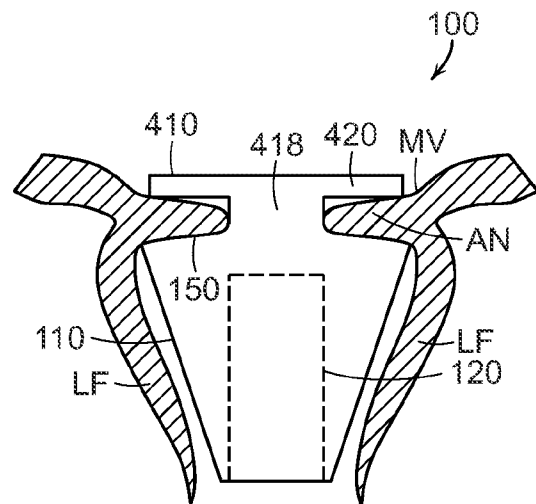


FIG. 26D

35/85

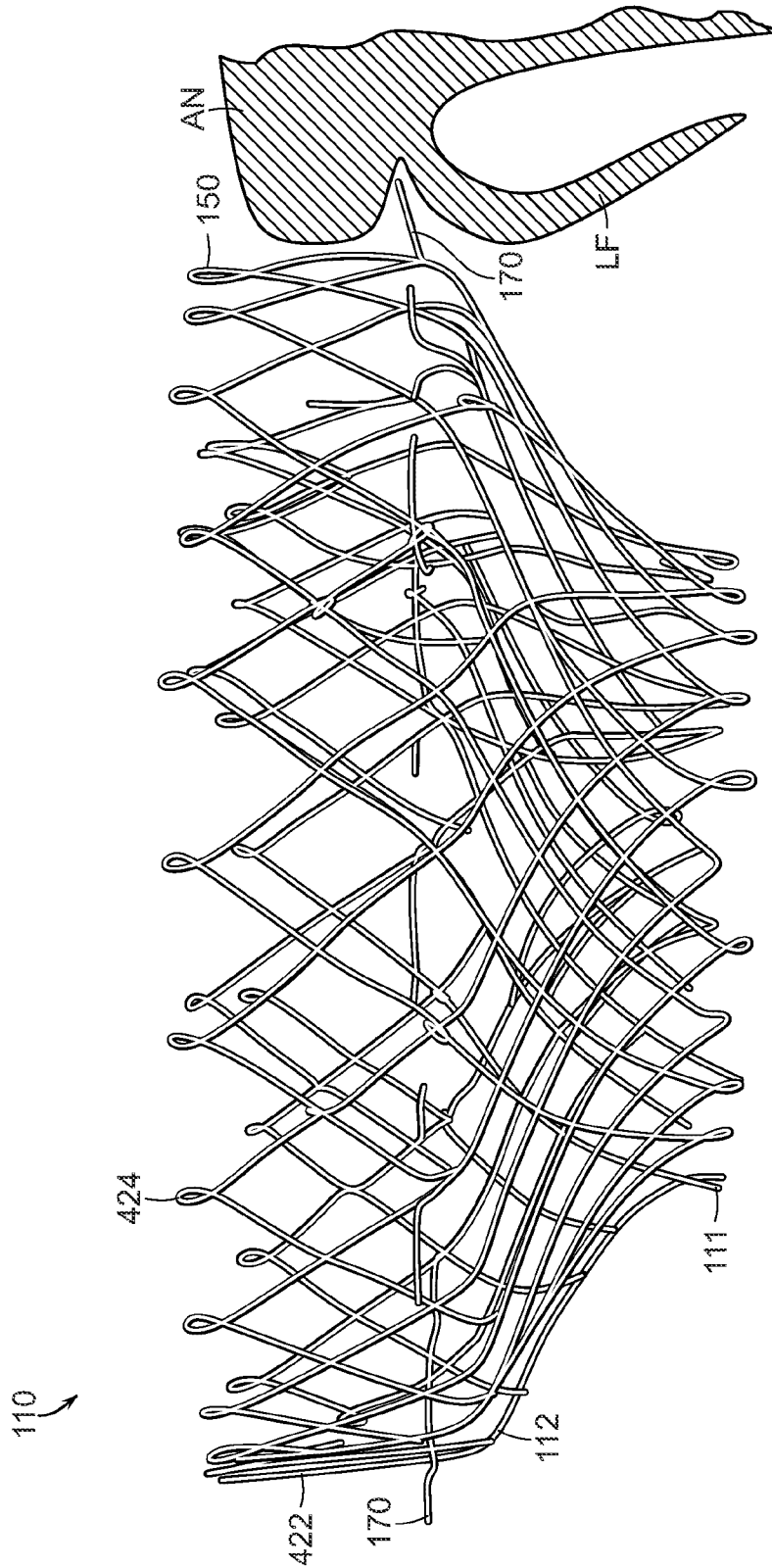


FIG. 27

36/85

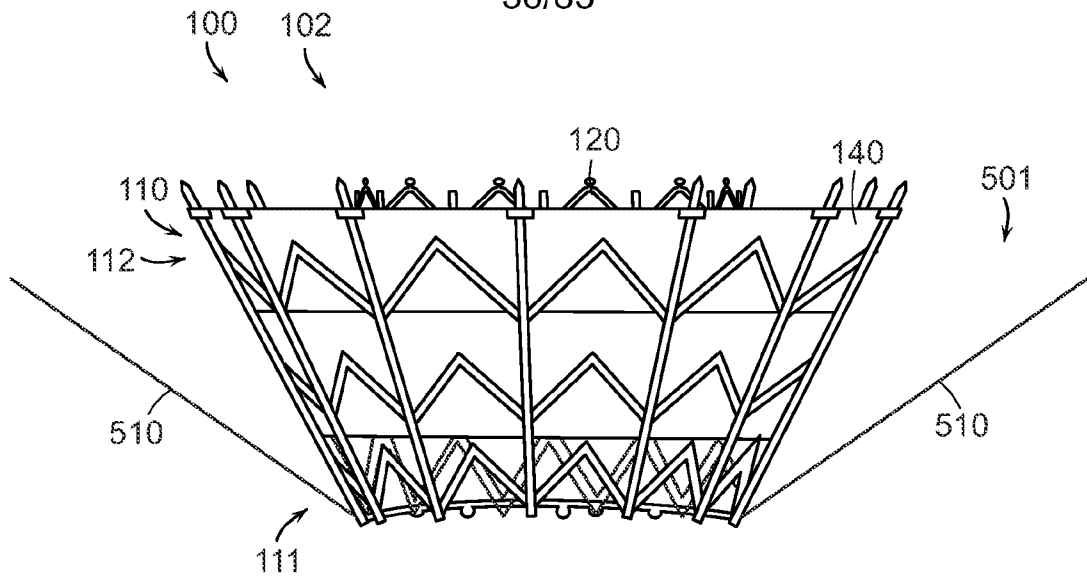


FIG. 28

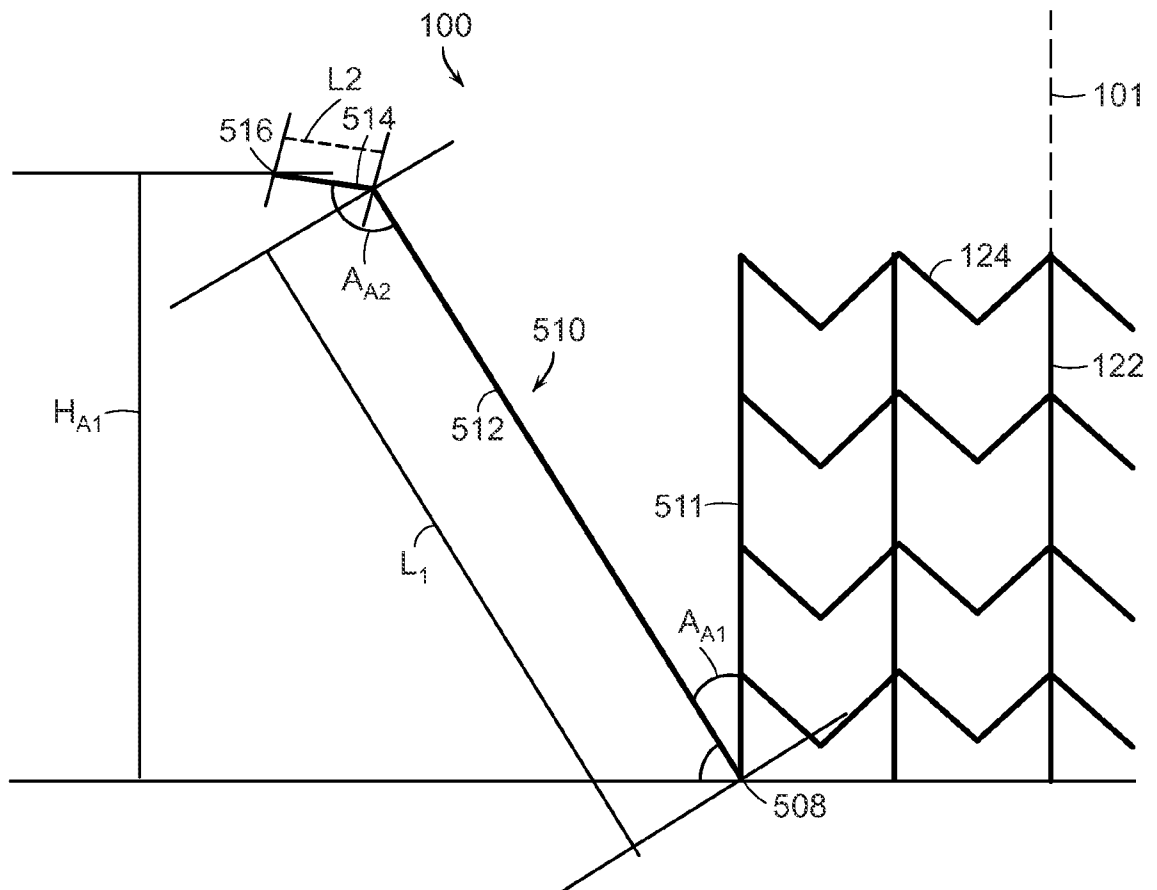


FIG. 29

37/85

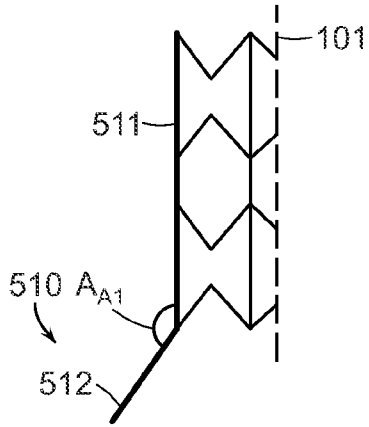


FIG. 30A

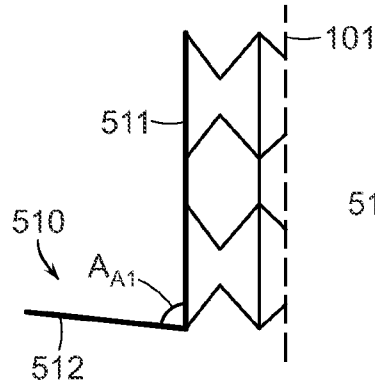


FIG. 30B

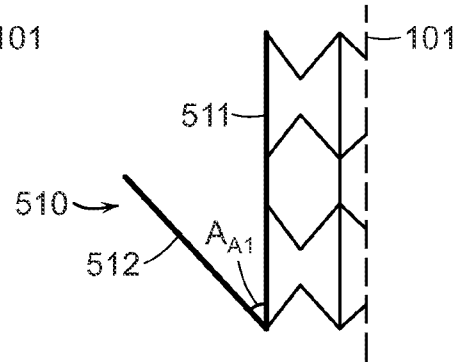


FIG. 30C

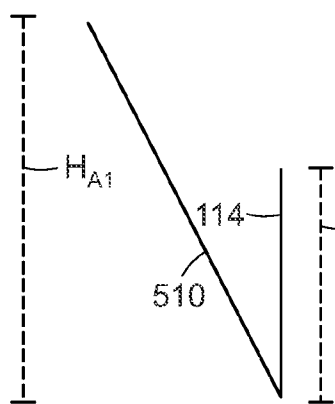


FIG. 31A

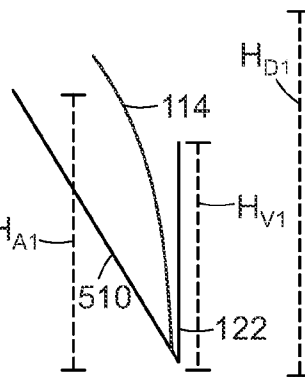


FIG. 31B

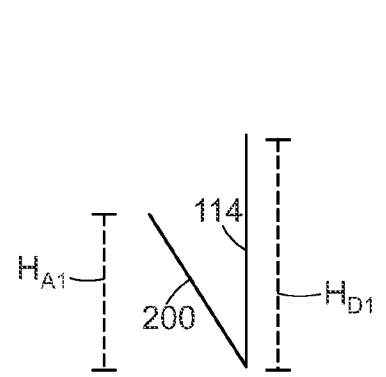


FIG. 31C

38/85

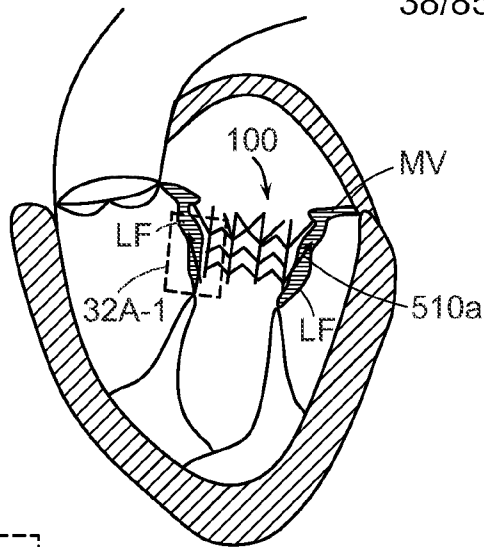


FIG. 32A



FIG. 32A-1

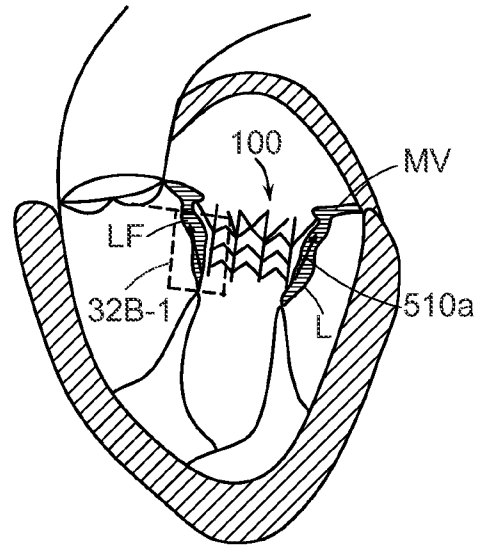


FIG. 32B

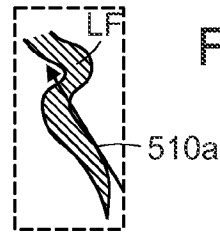


FIG. 32B-1

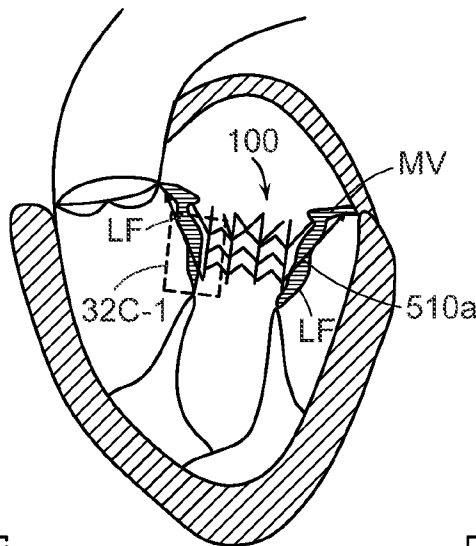


FIG. 32C

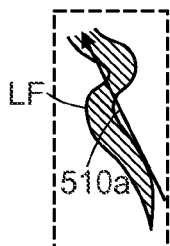


FIG. 32C-1

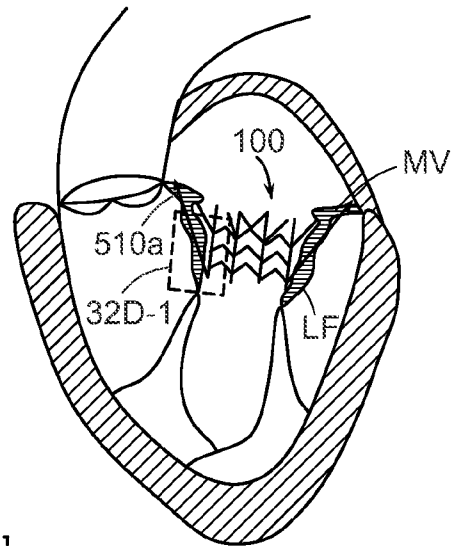


FIG. 32D

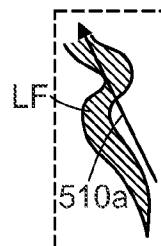


FIG. 32D-1

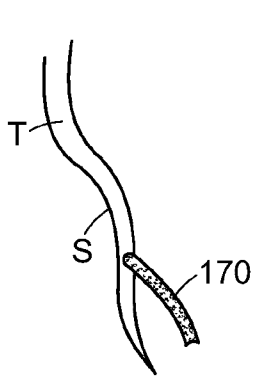


FIG. 33A

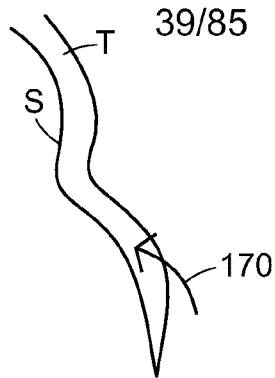


FIG. 33B

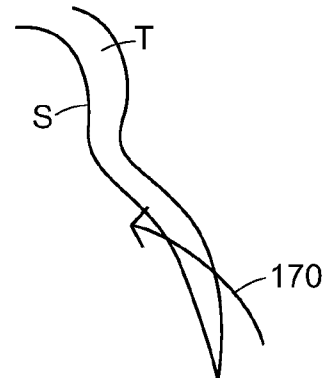


FIG. 33C

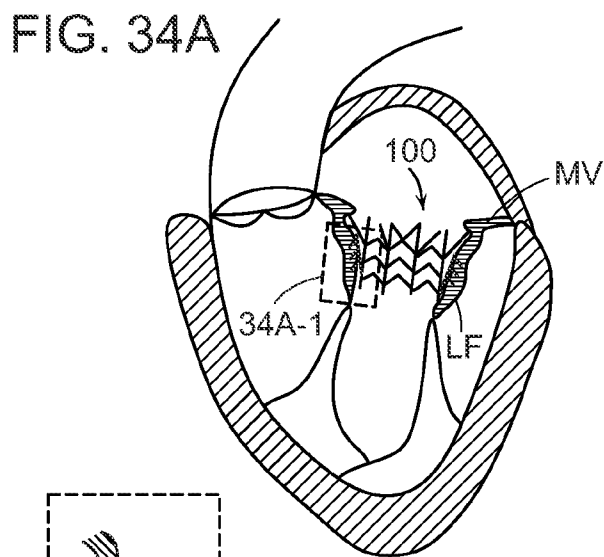


FIG. 34A-1

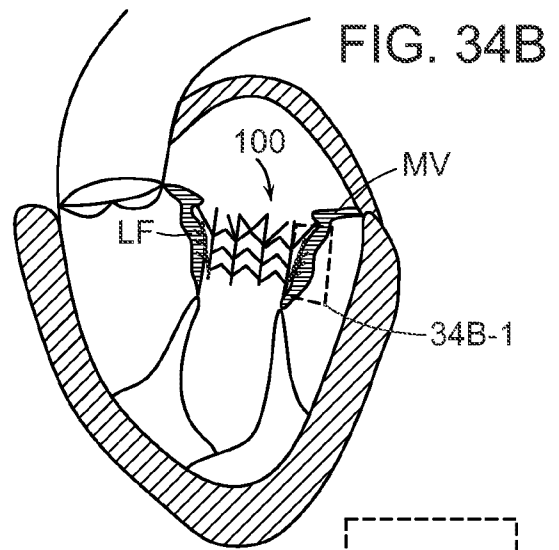
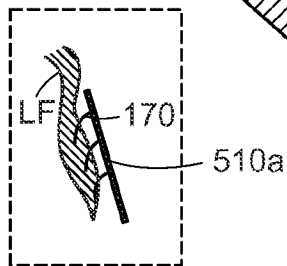


FIG. 34B-1

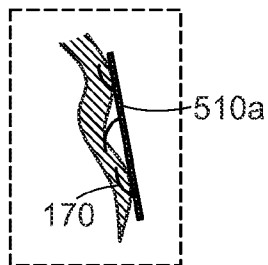
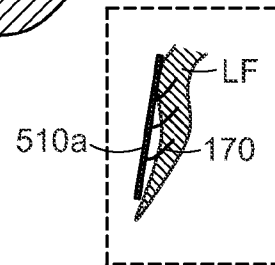


FIG. 34C-1

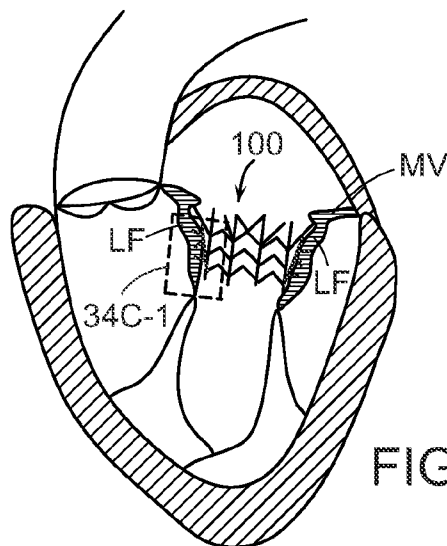


FIG. 34C

40/85

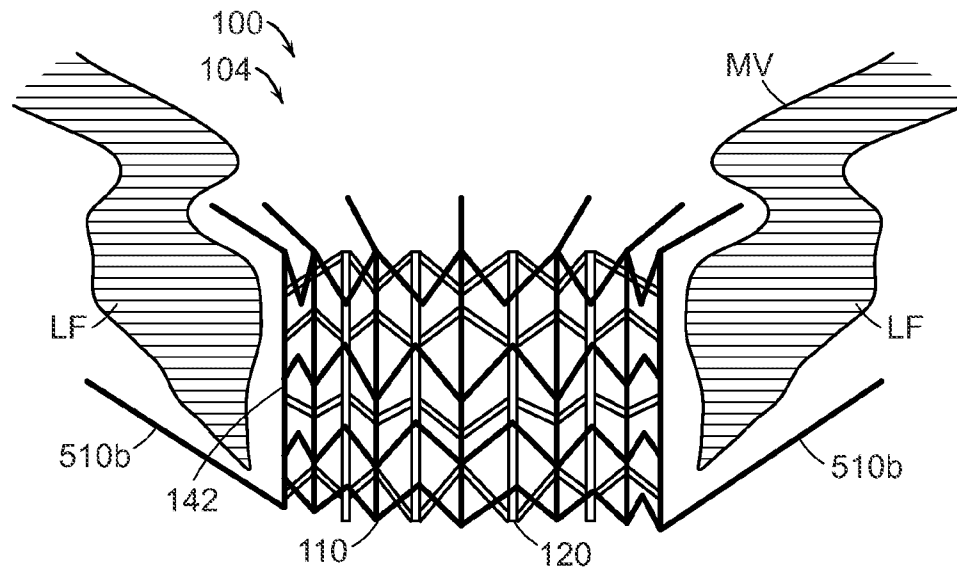


FIG. 35A

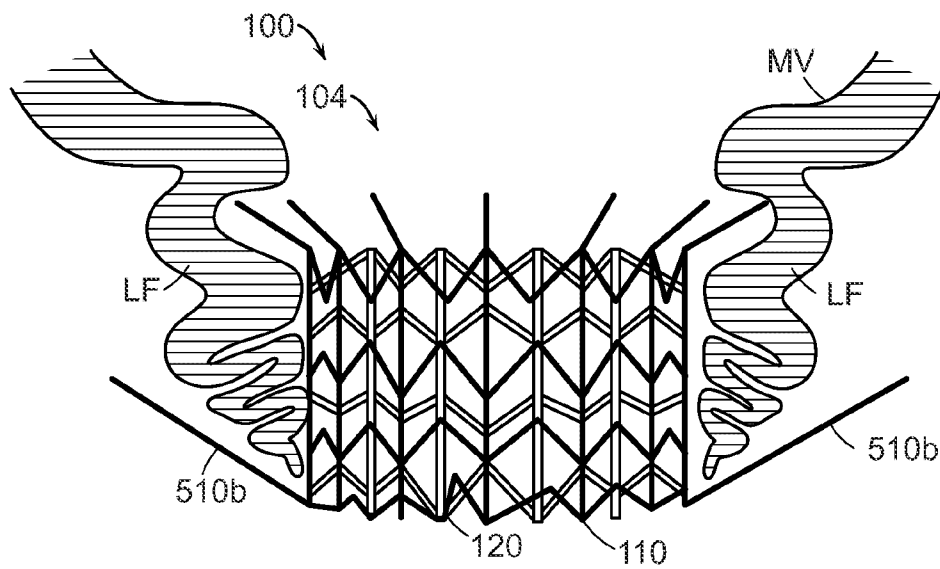


FIG. 35B

41/85

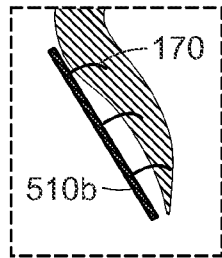


FIG. 35C-1

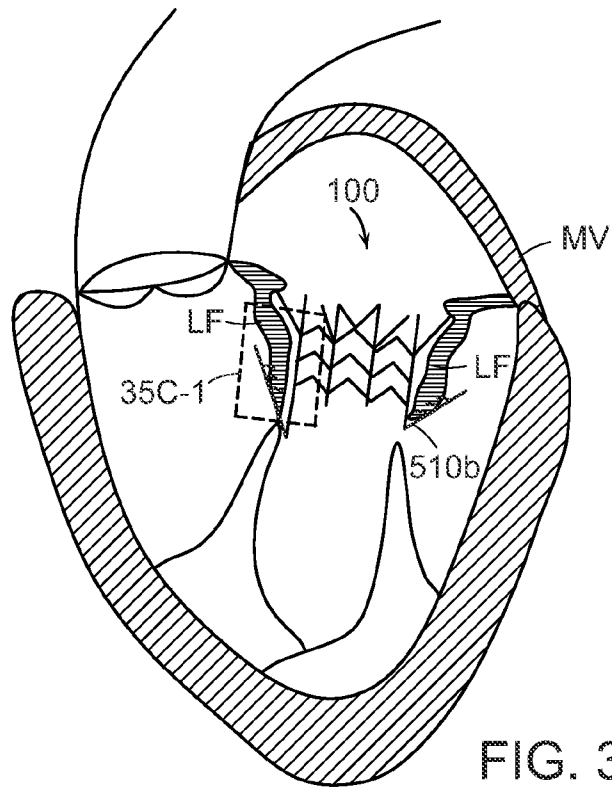


FIG. 35C

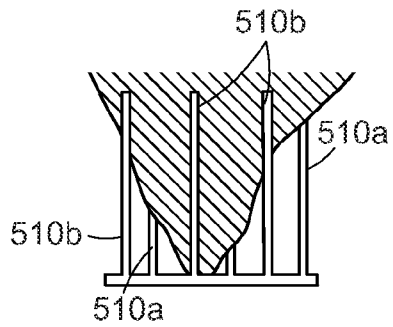


FIG. 36B

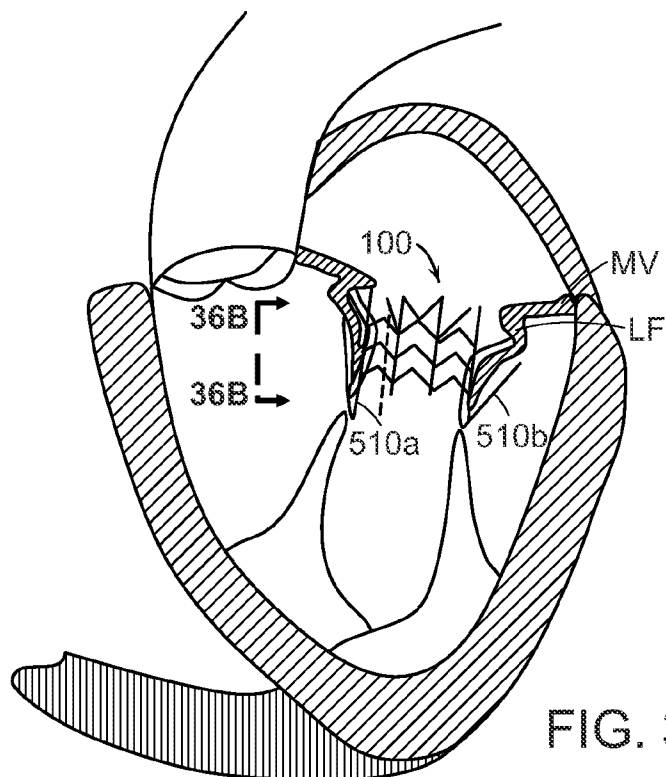


FIG. 36A

42/85

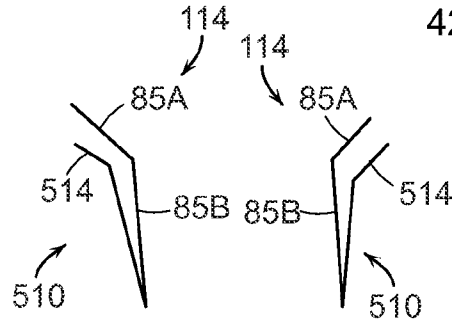


FIG. 37A

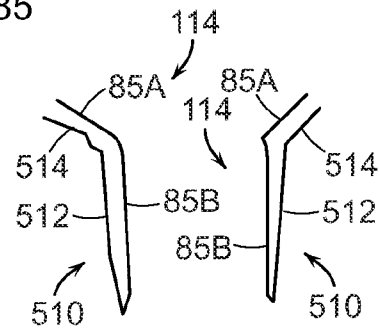


FIG. 37B

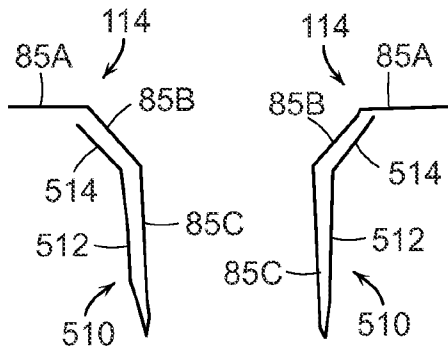


FIG. 37C

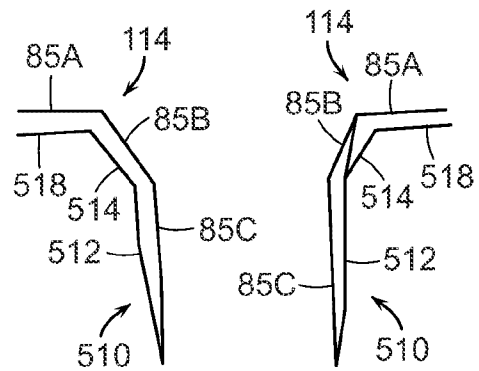


FIG. 37D

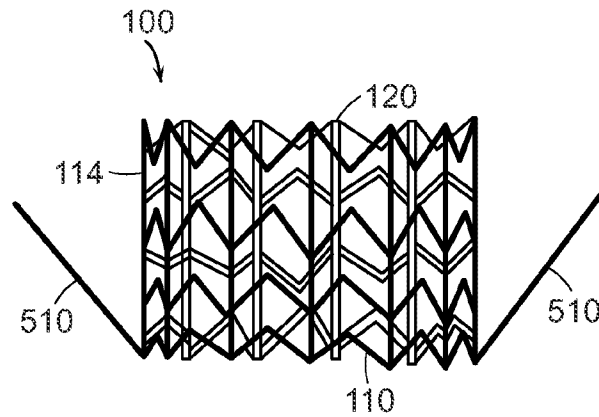


FIG. 38A

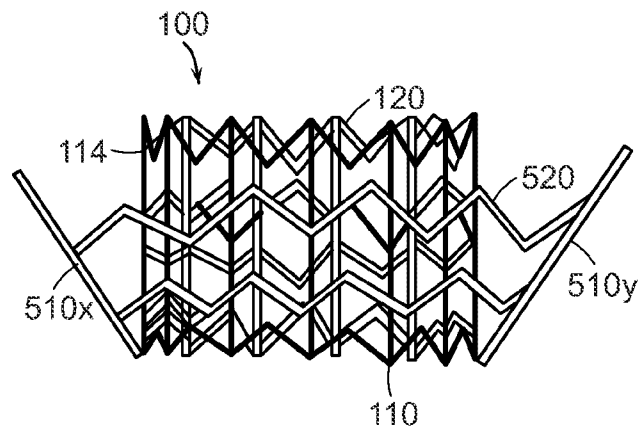


FIG. 38B

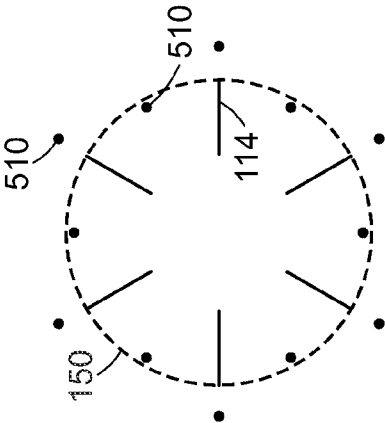


FIG. 39D

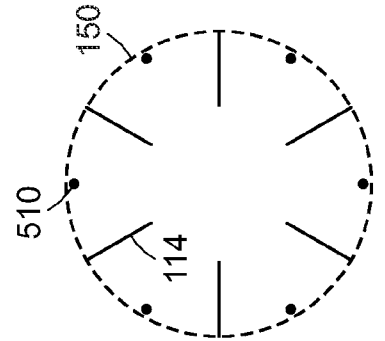


FIG. 39C

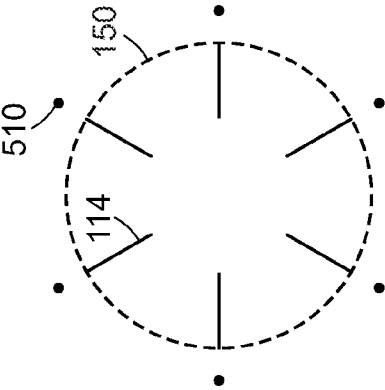


FIG. 39B

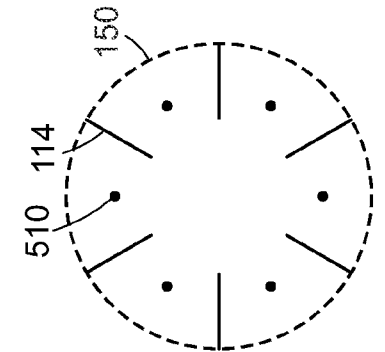


FIG. 39A

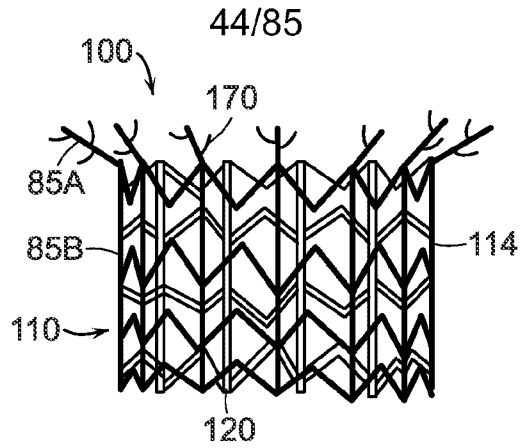


FIG. 40A

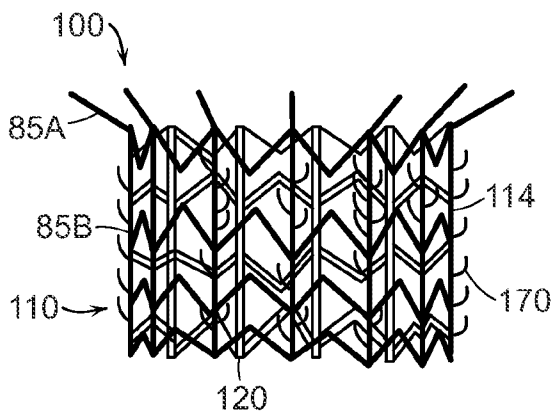


FIG. 40B

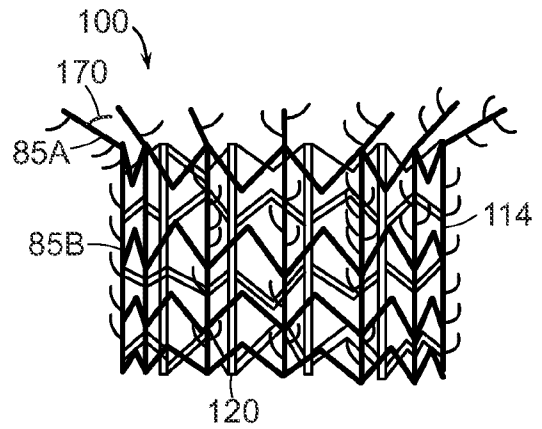


FIG. 40C

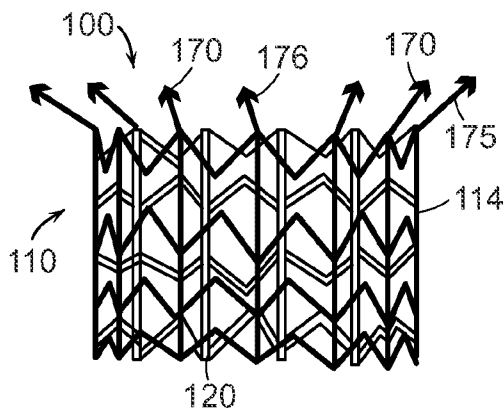


FIG. 40D

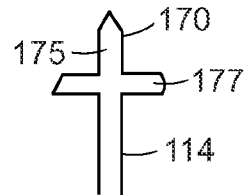


FIG. 40E

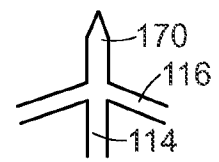


FIG. 40F

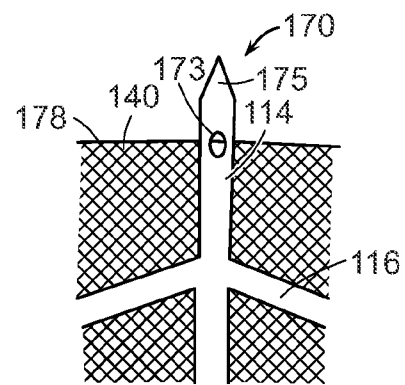


FIG. 40G

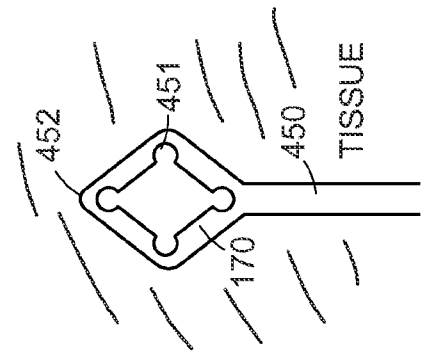


FIG. 40L

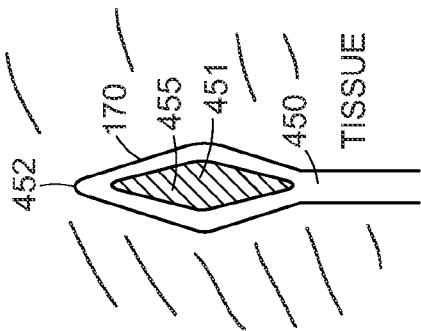


FIG. 40K

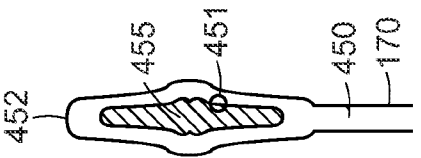


FIG. 40J

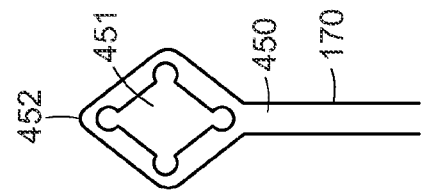


FIG. 40I

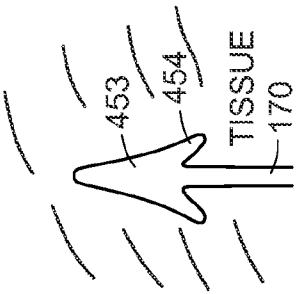


FIG. 40P

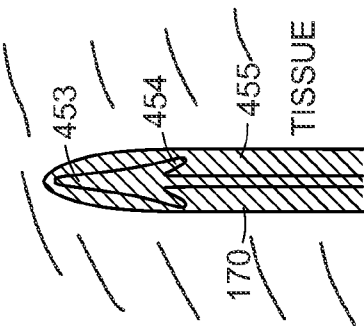


FIG. 400

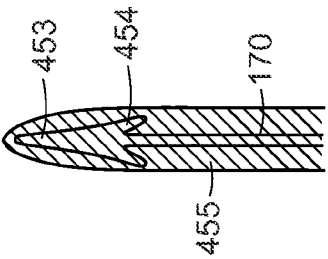


FIG. 40N

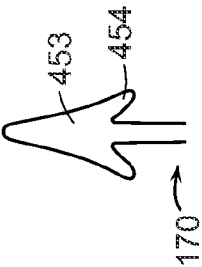


FIG. 40M

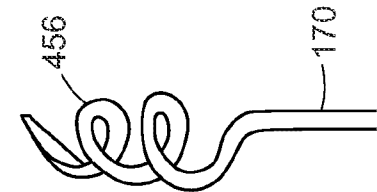


FIG. 40Q

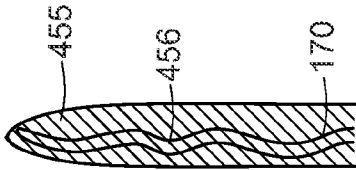


FIG. 40R

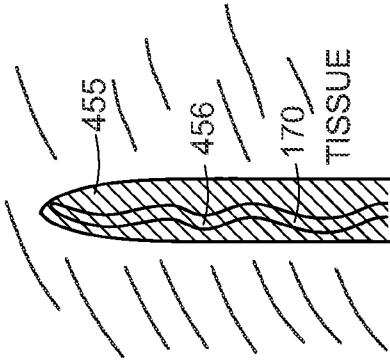


FIG. 40S

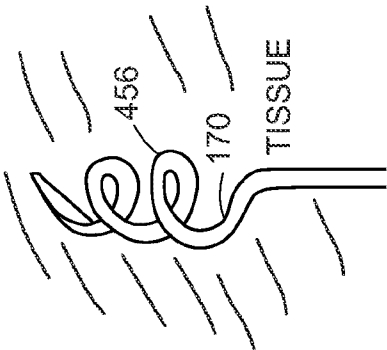


FIG. 40T

47/85

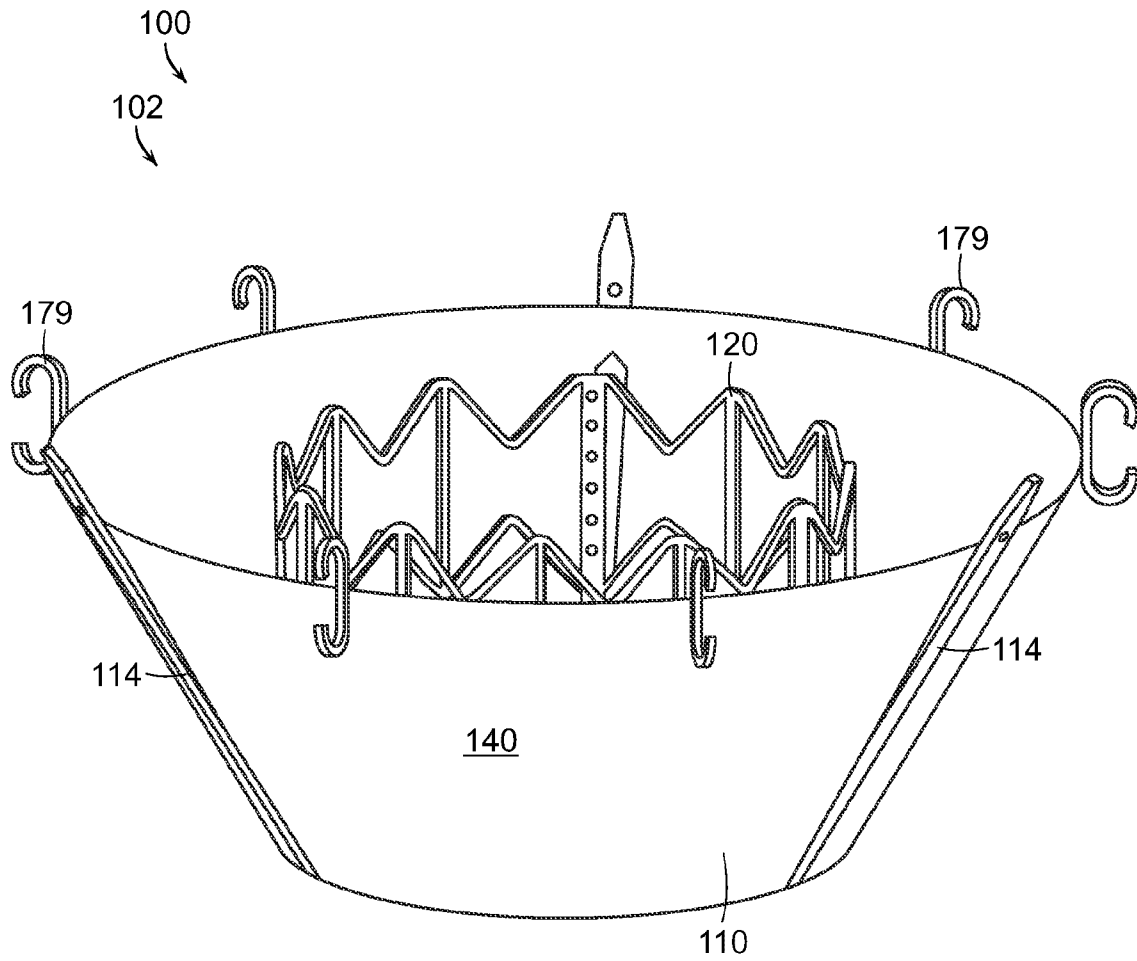


FIG. 41

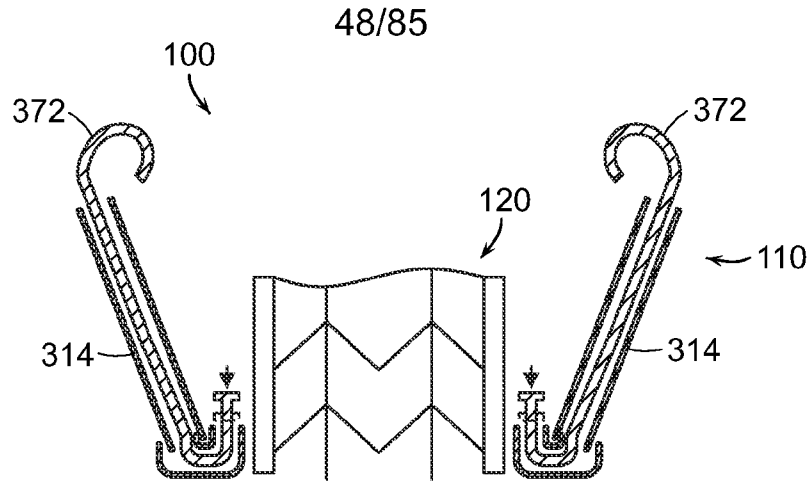


FIG. 42A

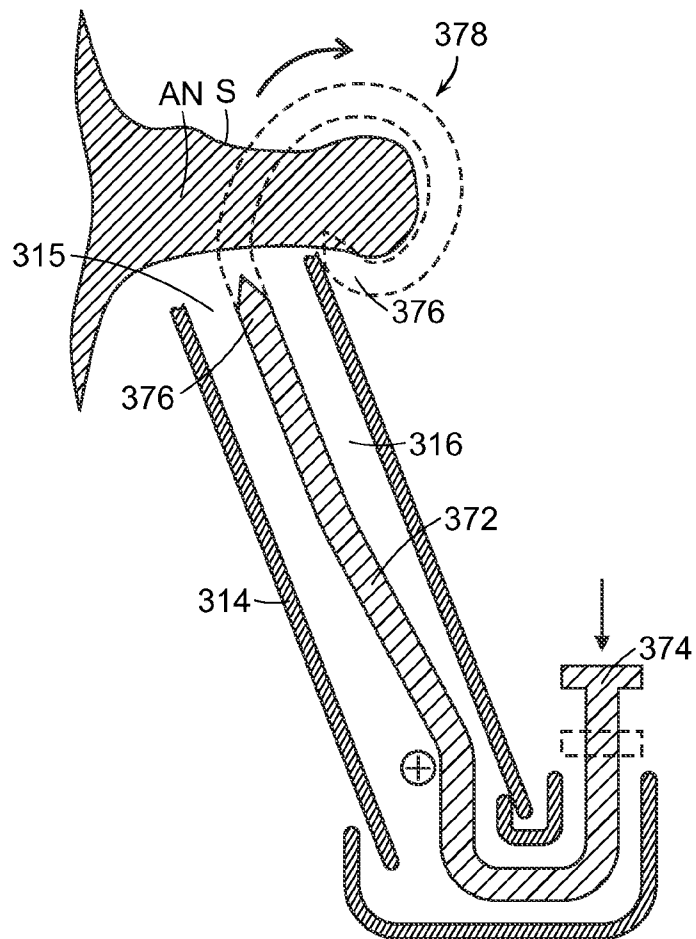


FIG. 42B

49/85

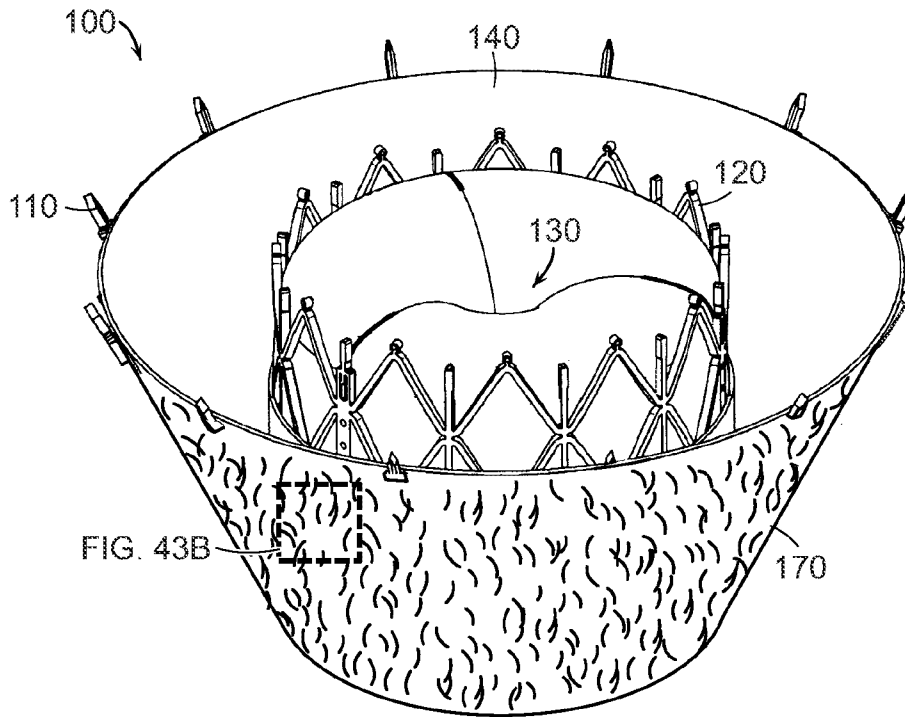


FIG. 43A

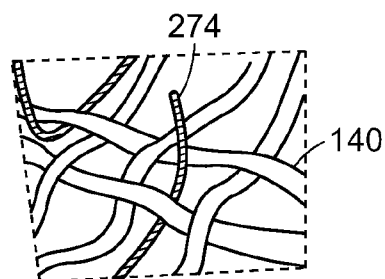


FIG. 43B

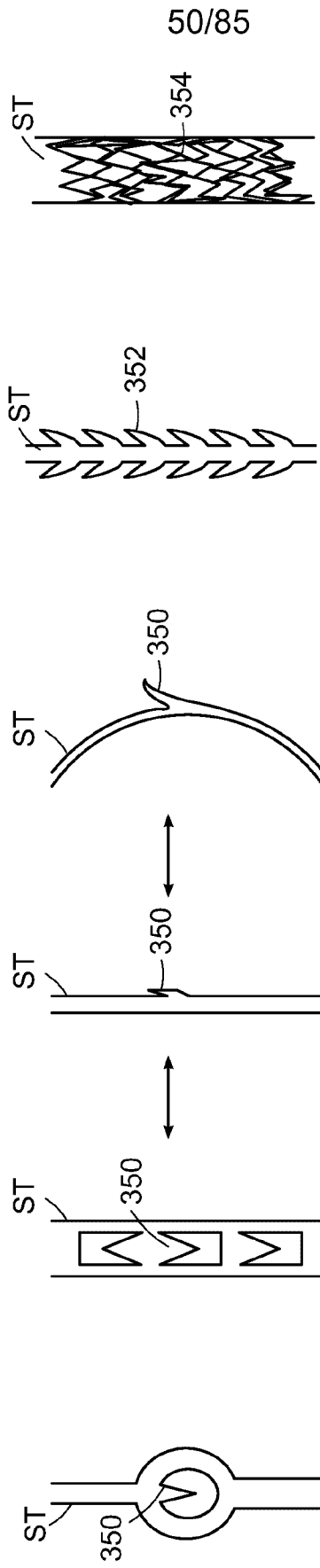


FIG. 44A FIG. 44B FIG. 44C FIG. 44D FIG. 44E FIG. 44F

51/85

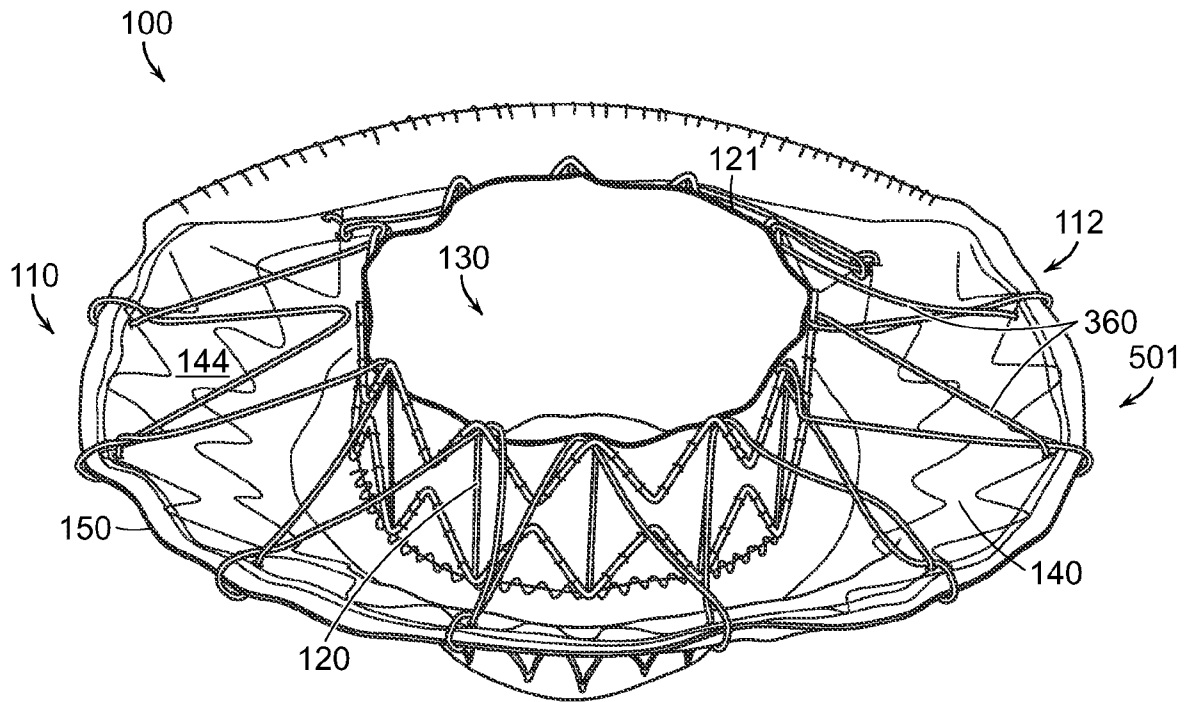


FIG. 45A

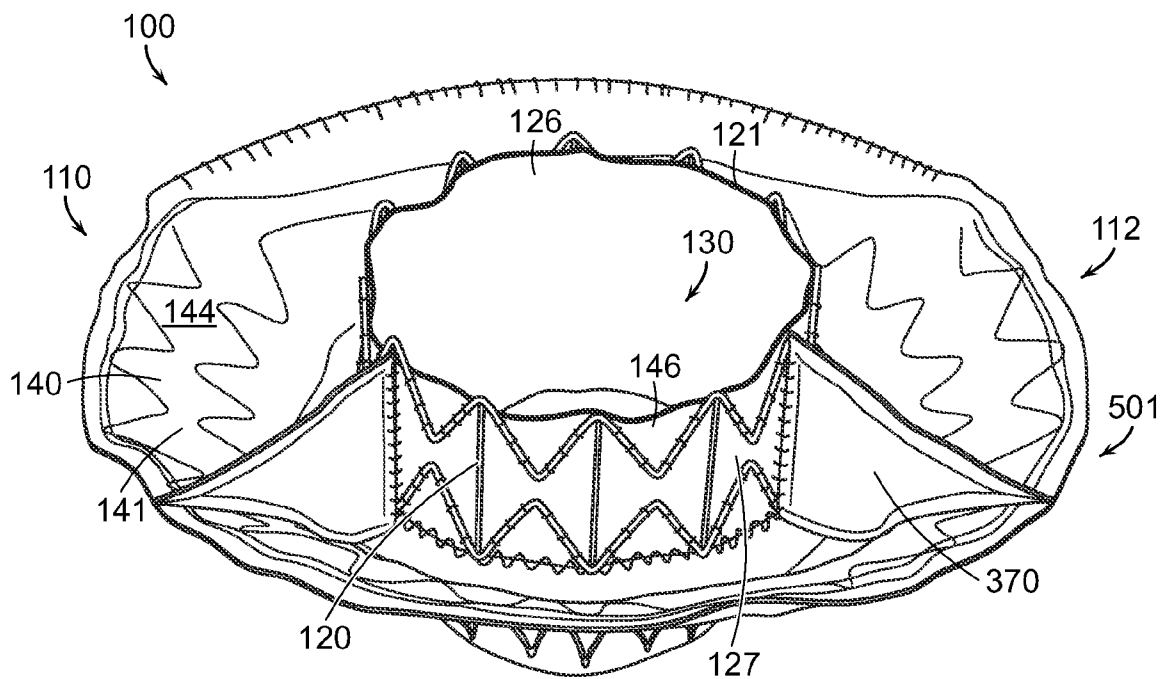


FIG. 45B

52/85

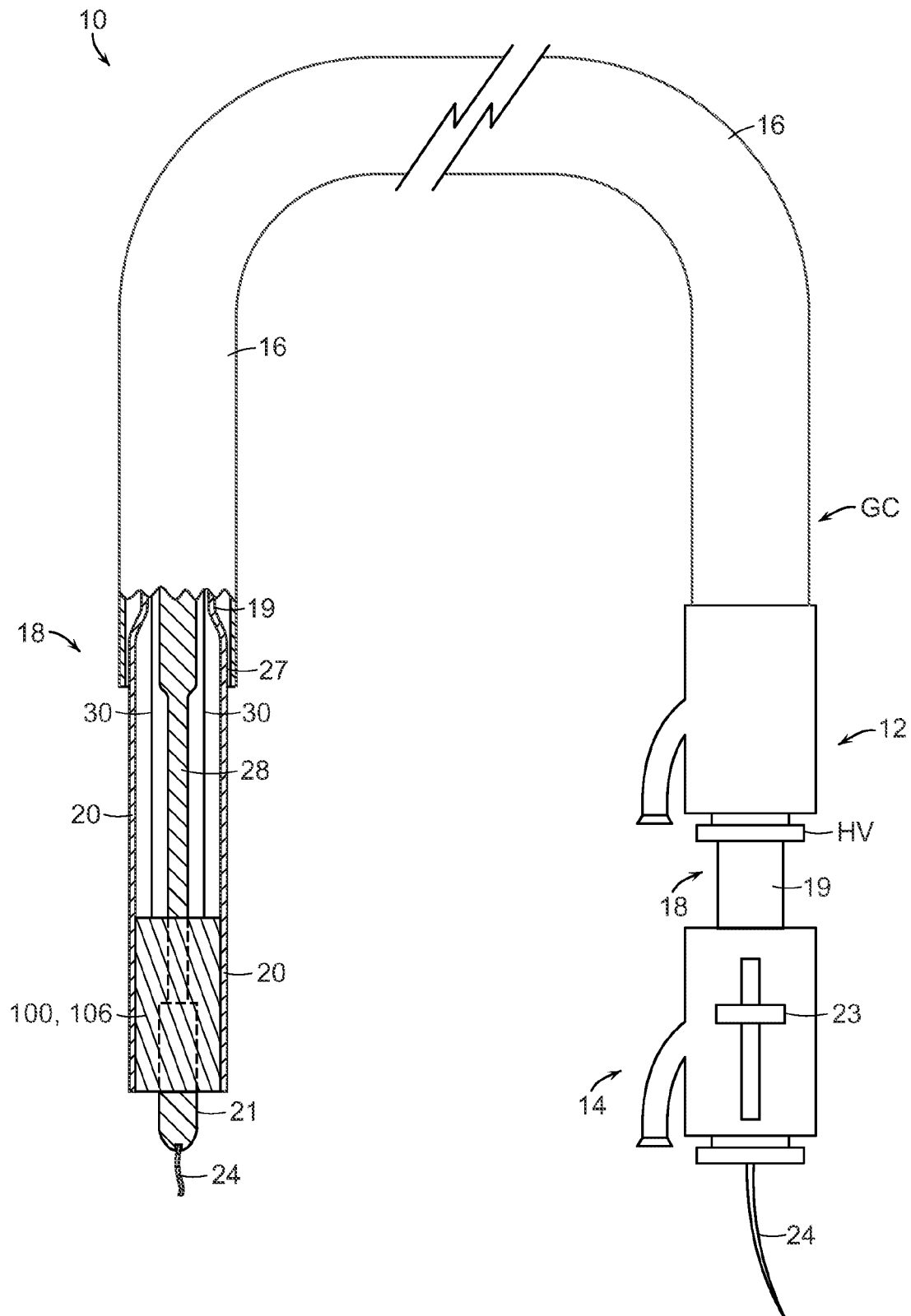


FIG. 46A

53/85

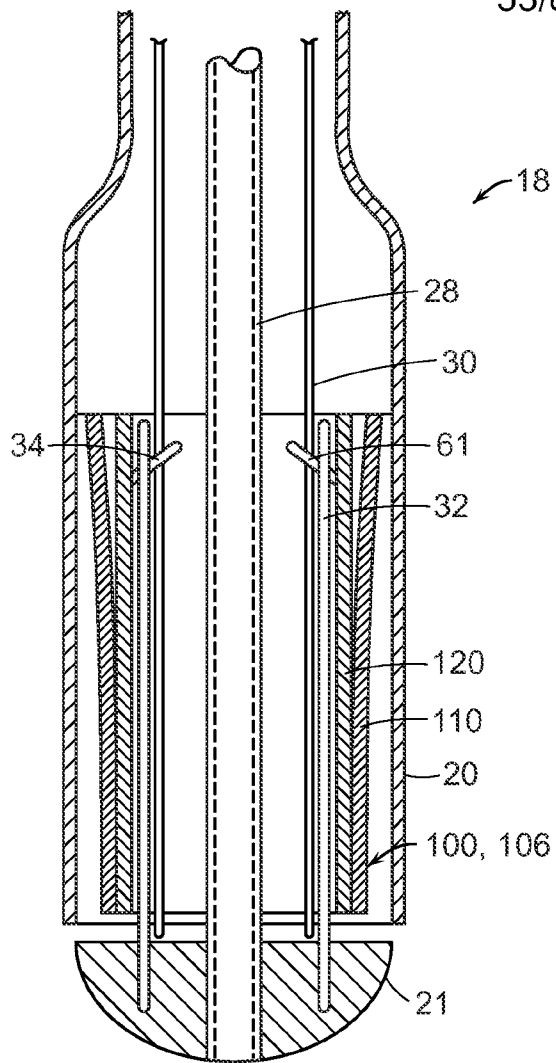


FIG. 46B

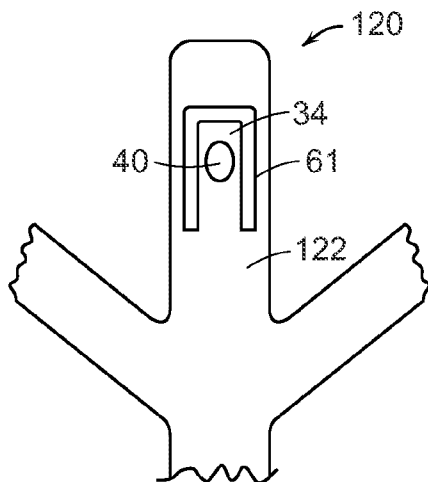


FIG. 46C

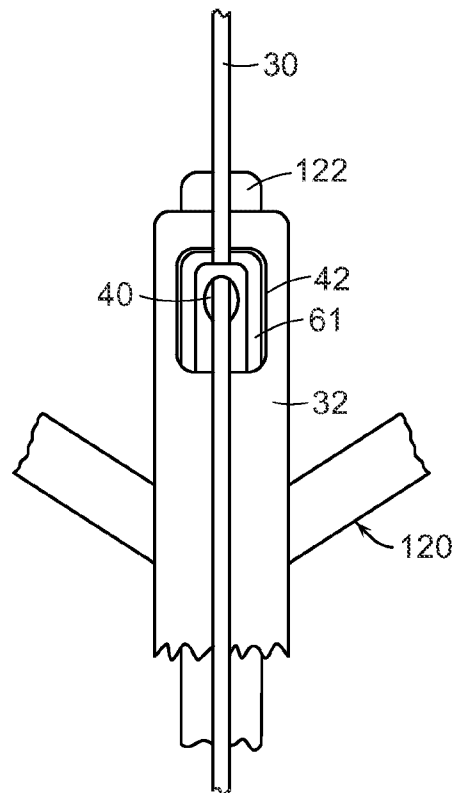


FIG. 46D

54/85

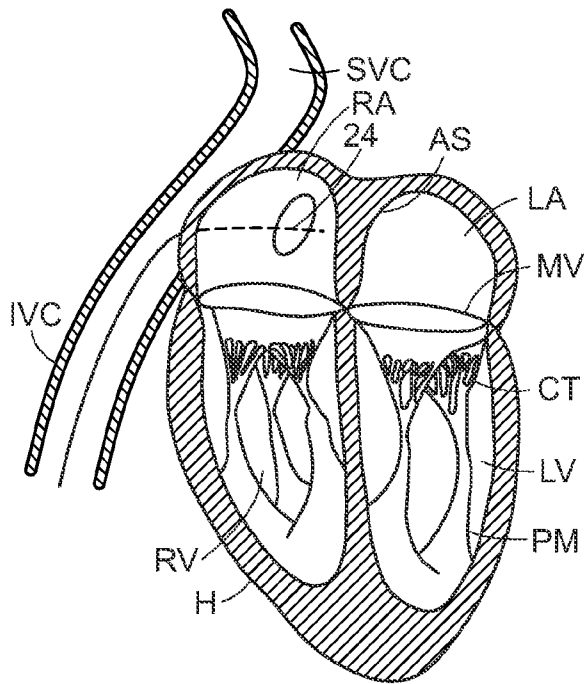


FIG. 47A

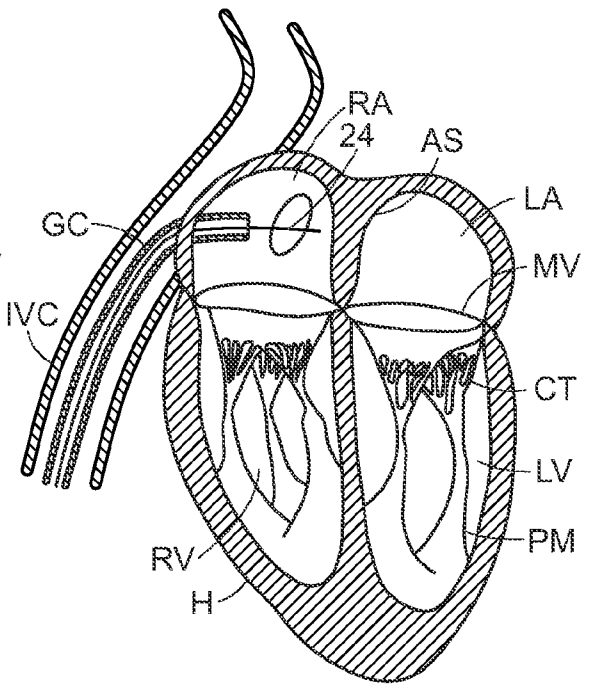


FIG. 47B

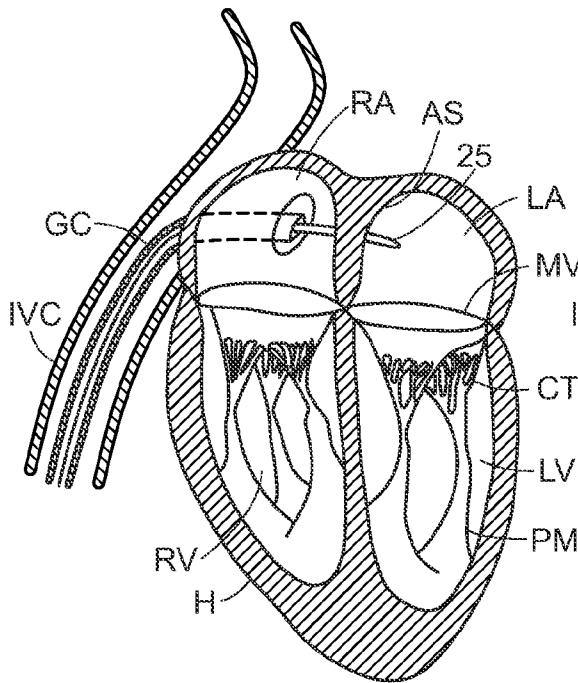


FIG. 47C

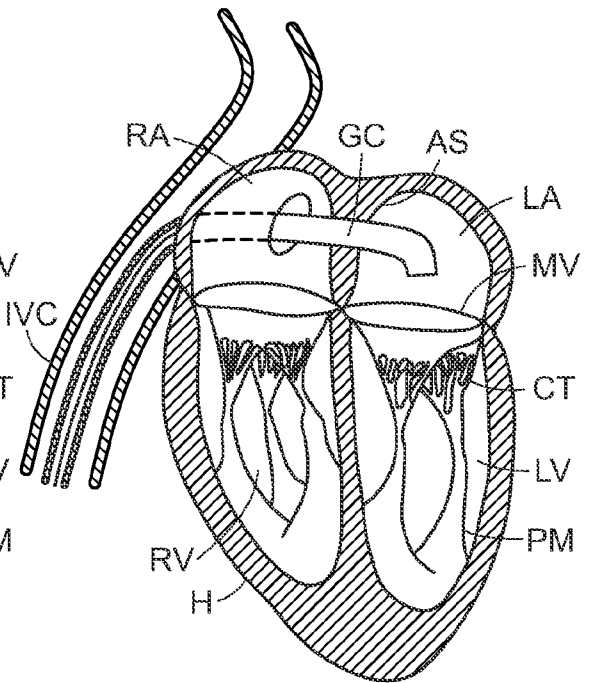


FIG. 47D

55/85

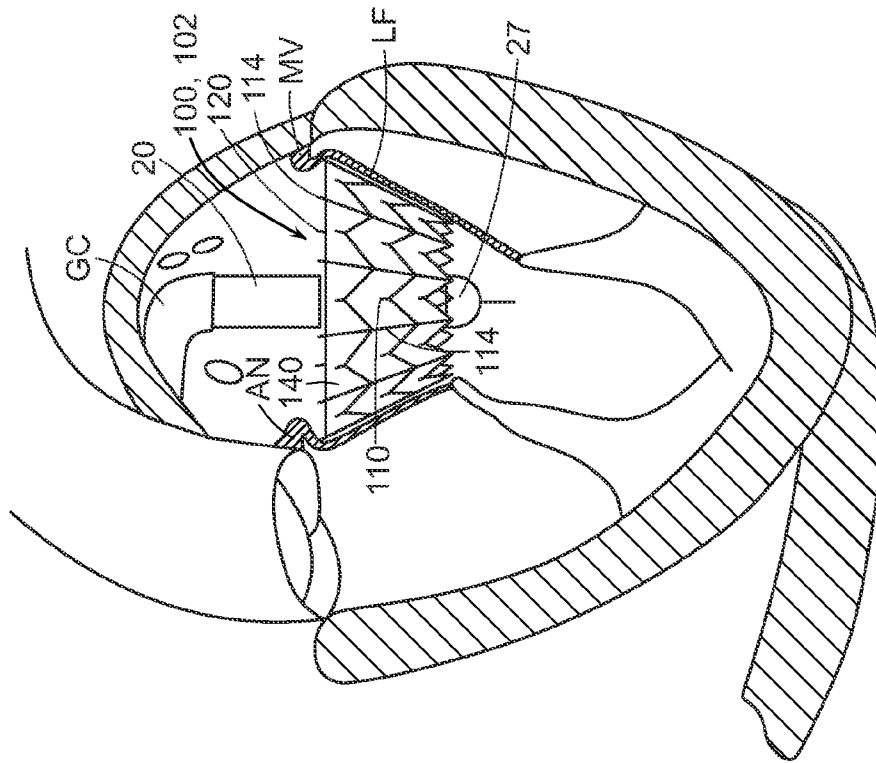


FIG. 48B

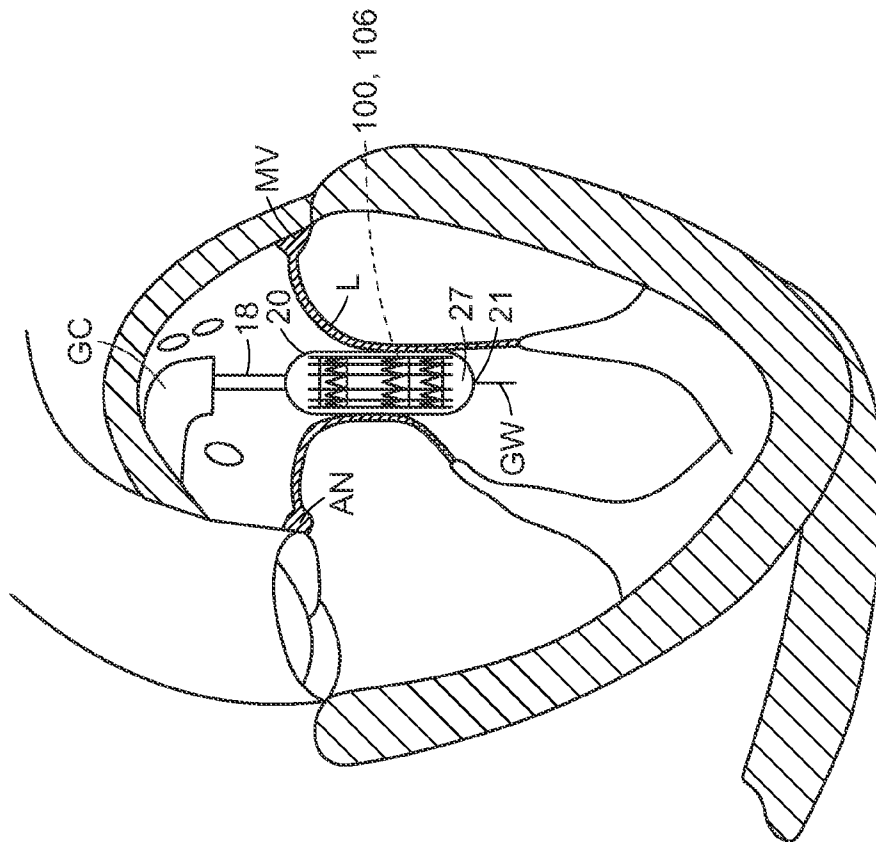


FIG. 48A

56/85

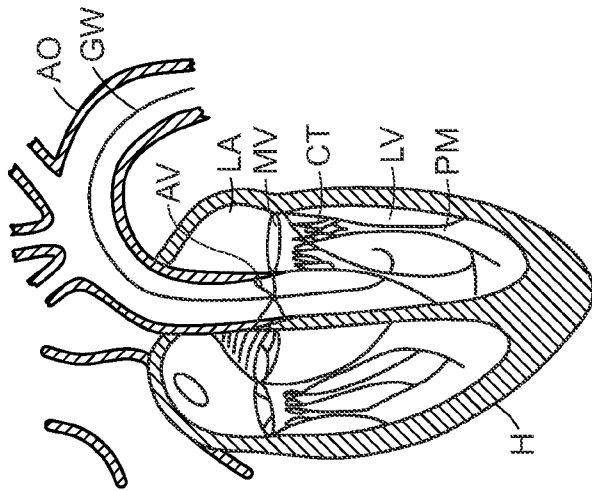


FIG. 49A

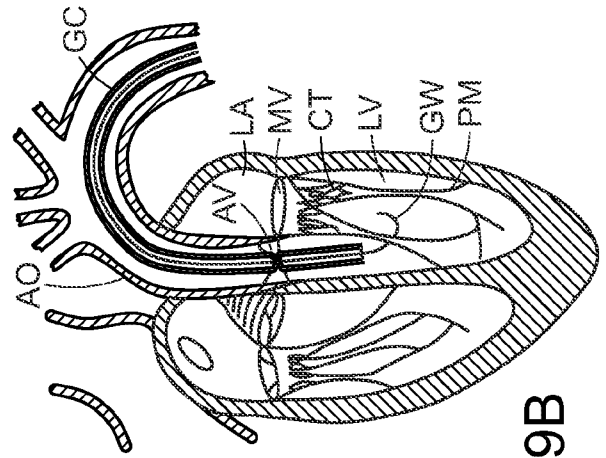


FIG. 49B

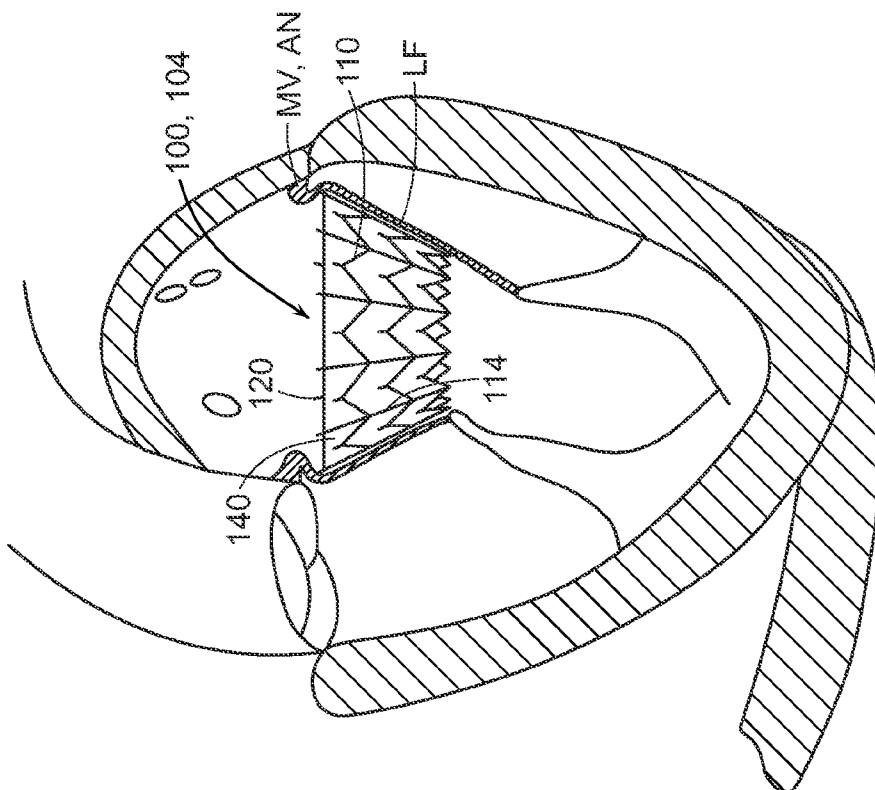


FIG. 48C

57/85

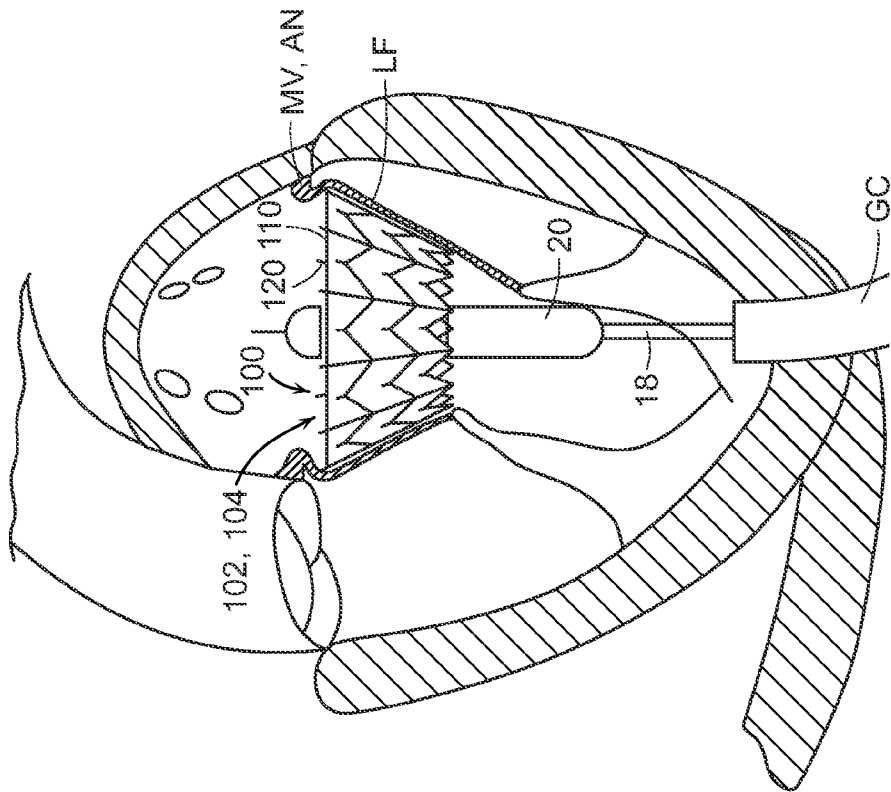


FIG. 50B

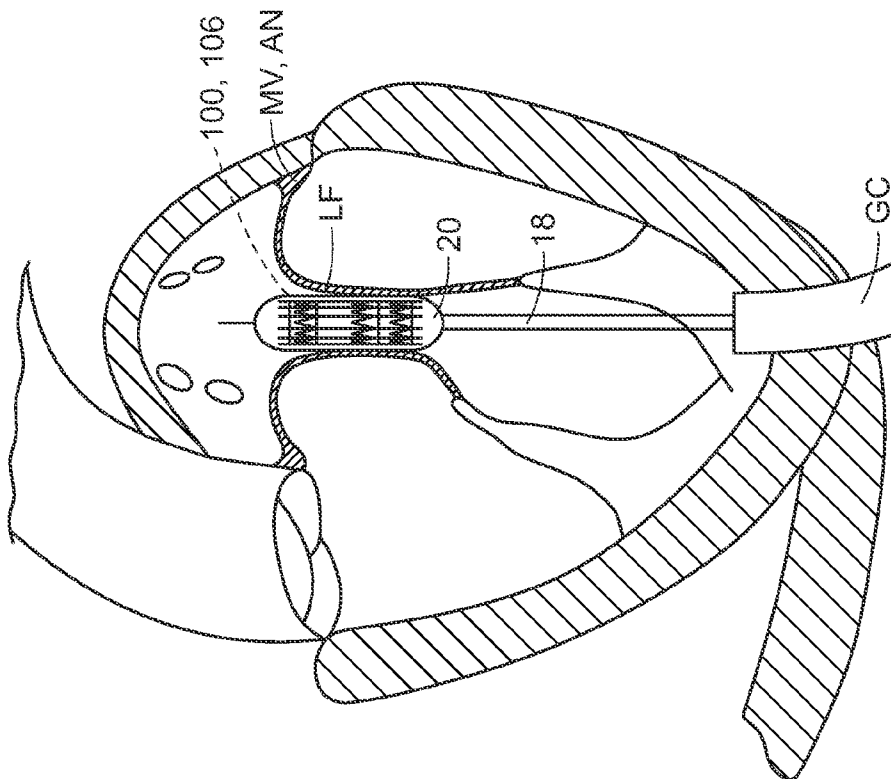


FIG. 50A

58/85

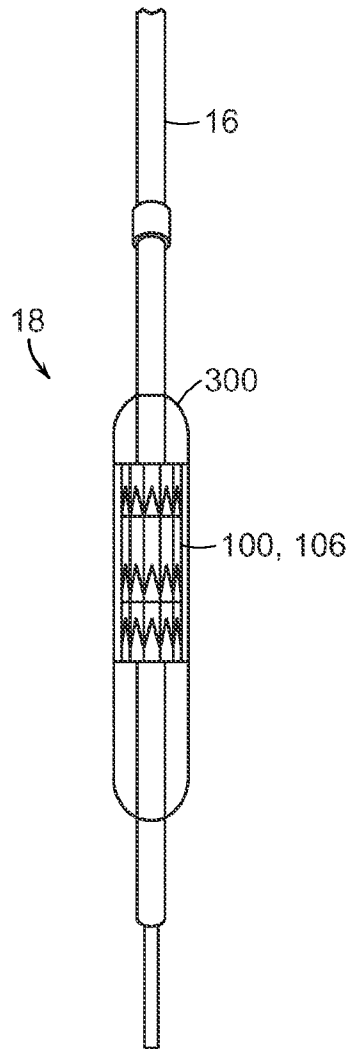


FIG. 51A

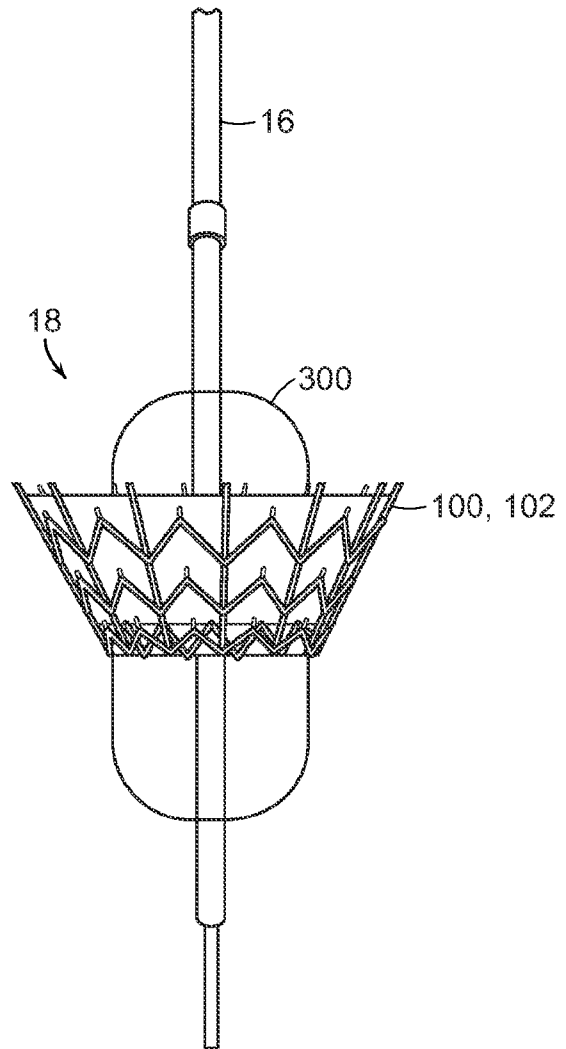


FIG. 51B

59/85

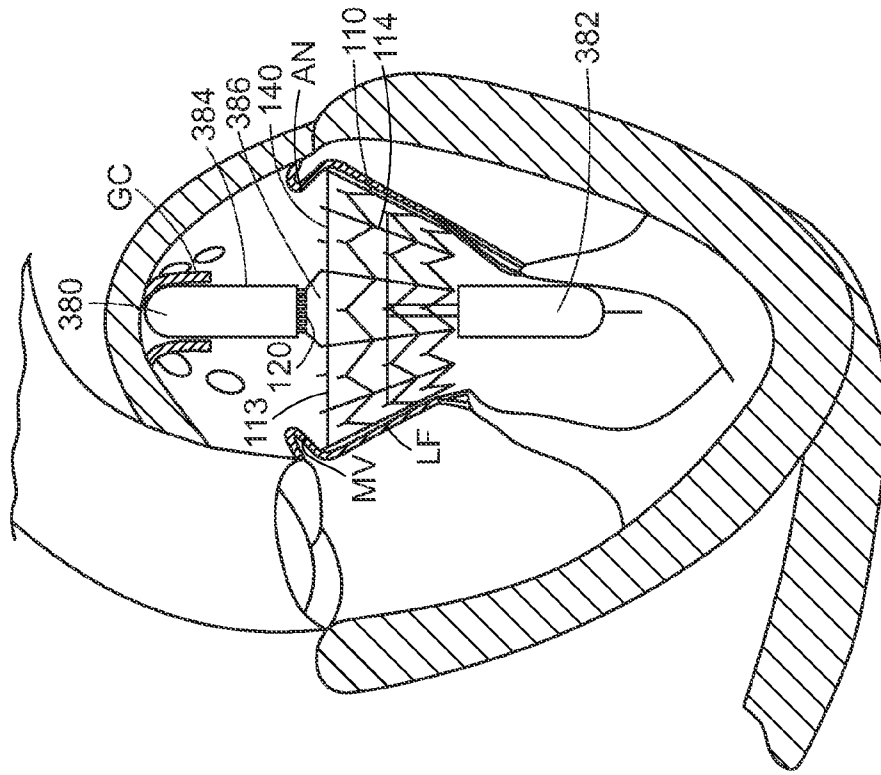


FIG. 52B

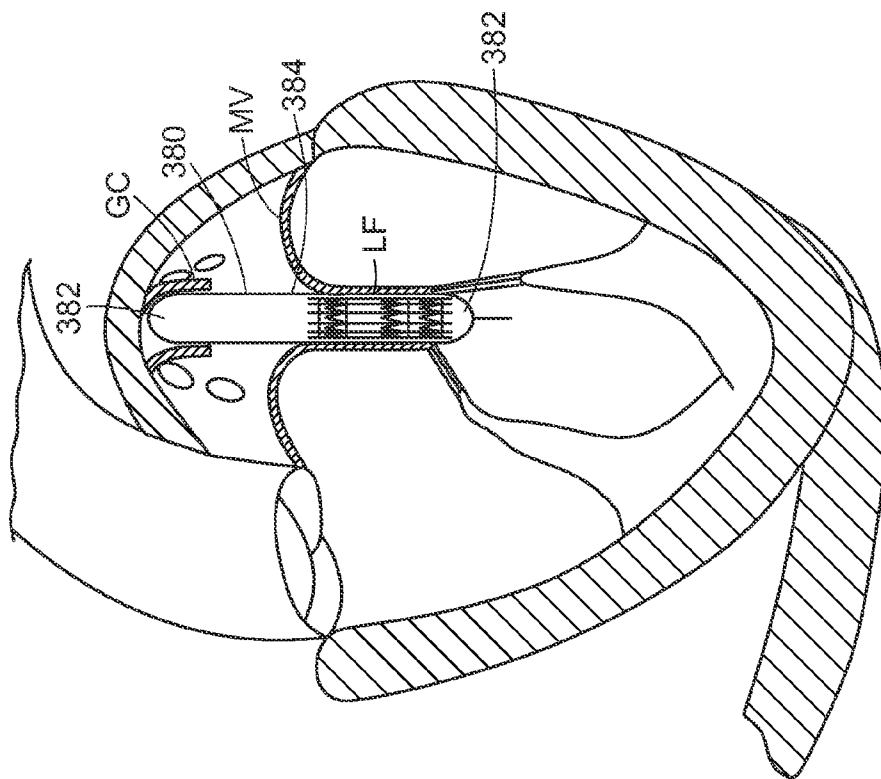


FIG. 52A

60/85

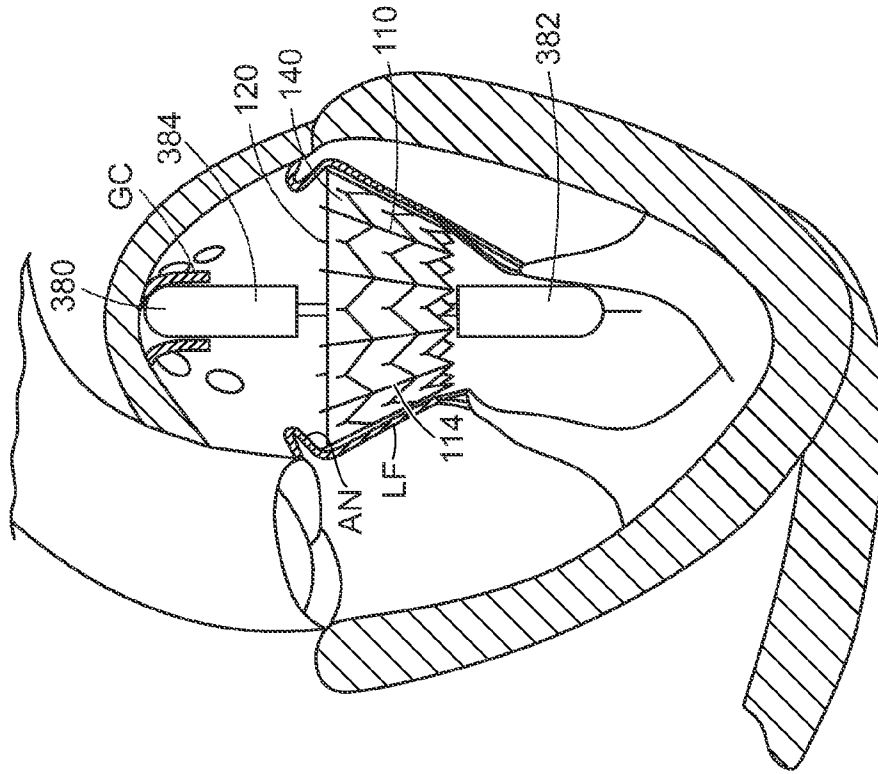


FIG. 52D

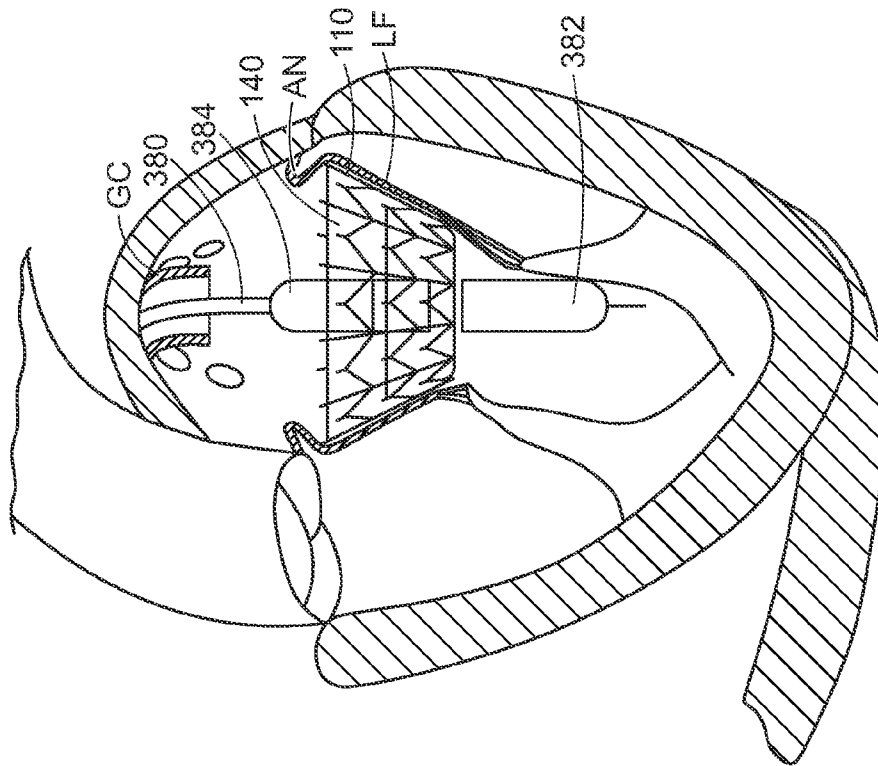


FIG. 52C

61/85

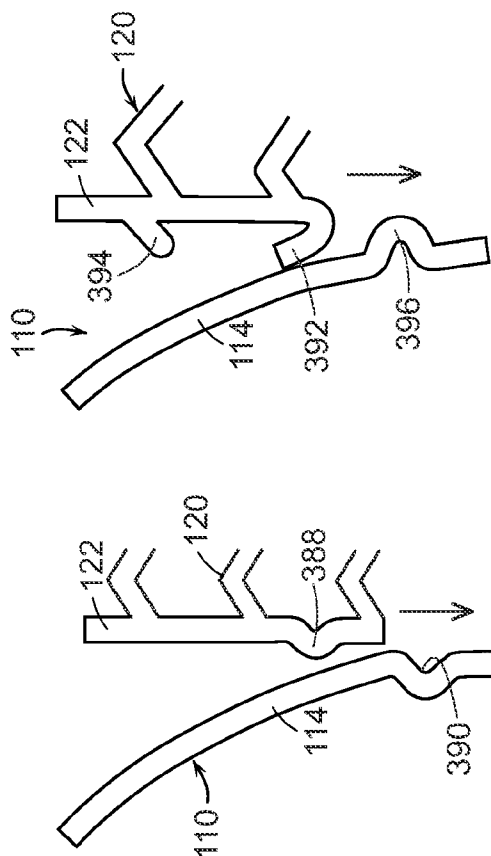


FIG. 53A

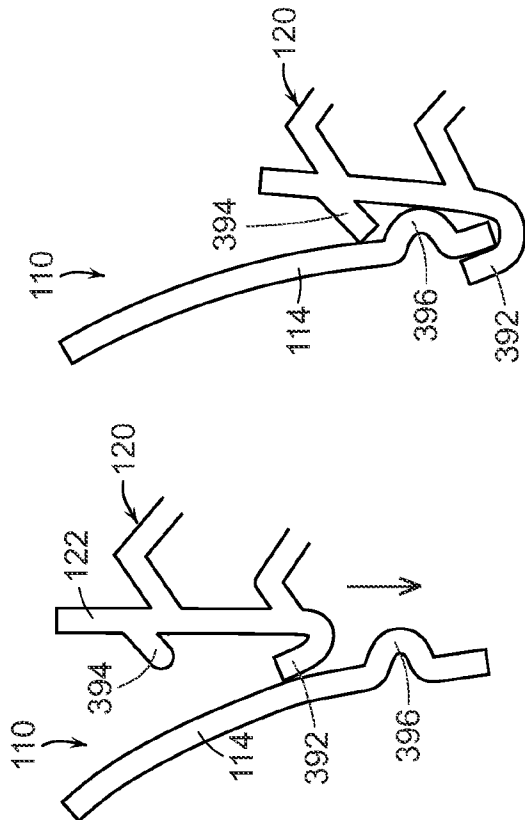


FIG. 53B

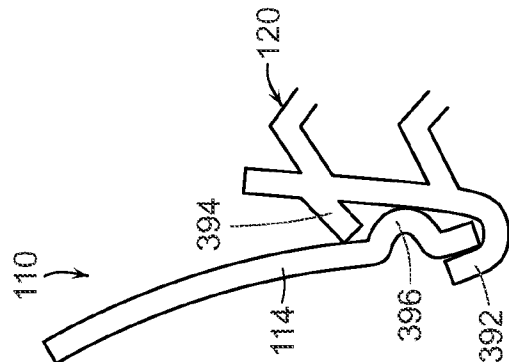


FIG. 53C

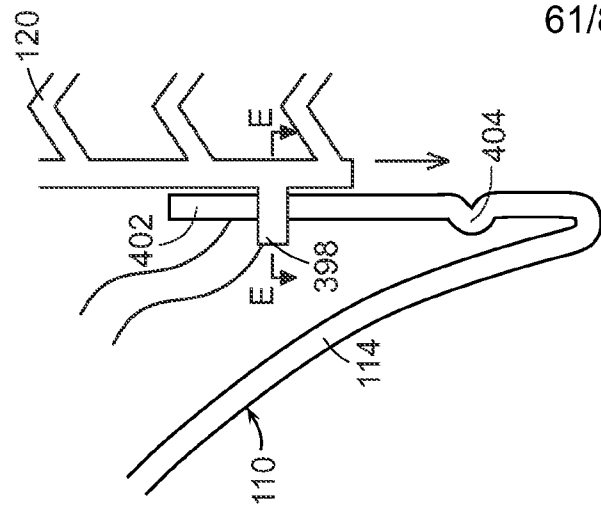


FIG. 53D

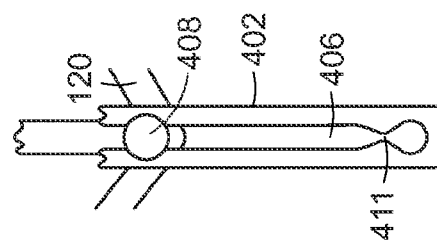


FIG. 53E

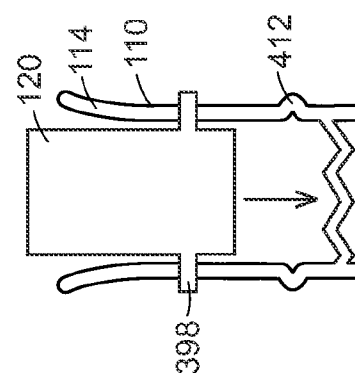


FIG. 53F

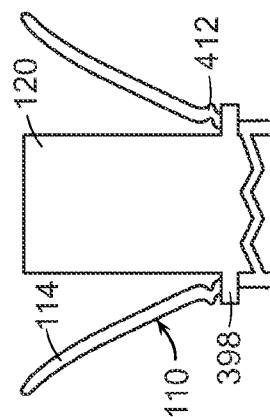
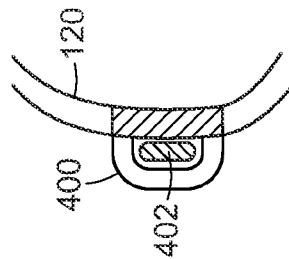


FIG. 53G



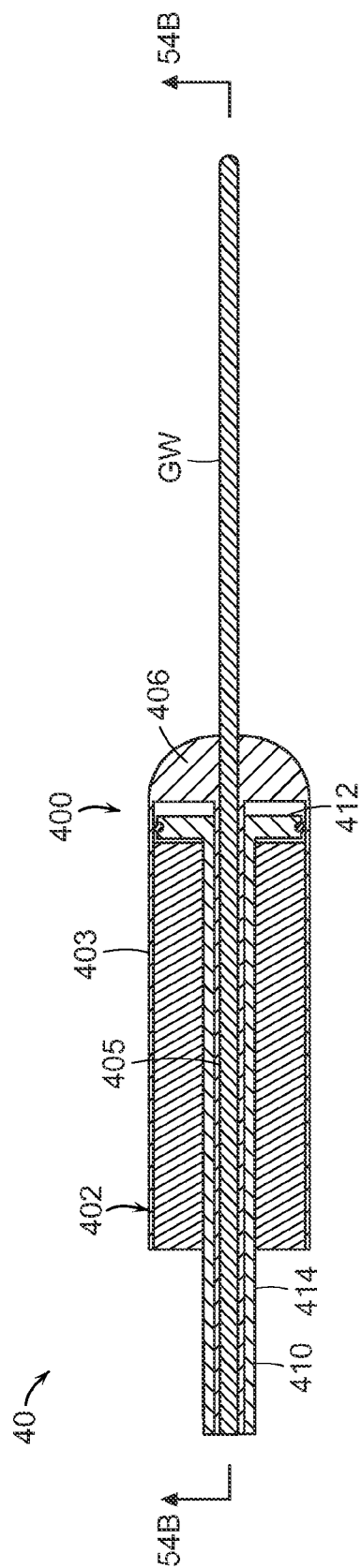


FIG. 54A

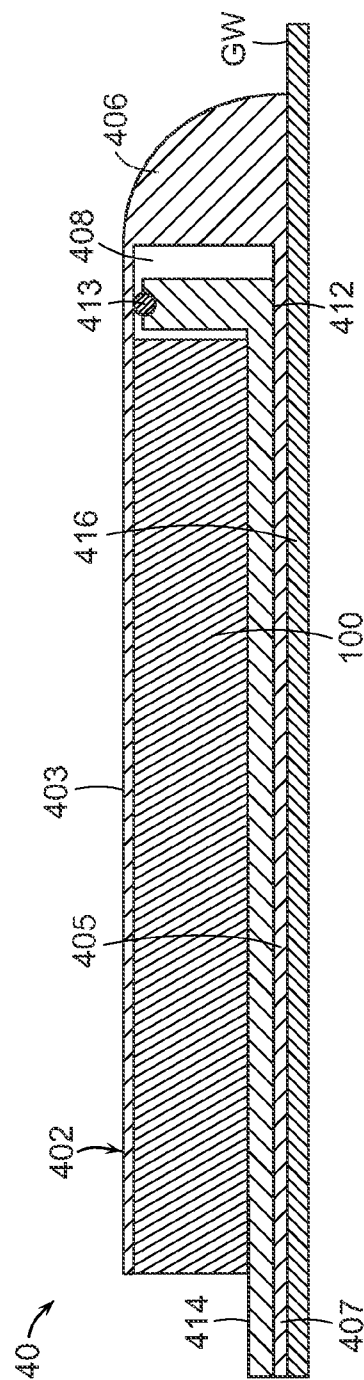


FIG. 54B

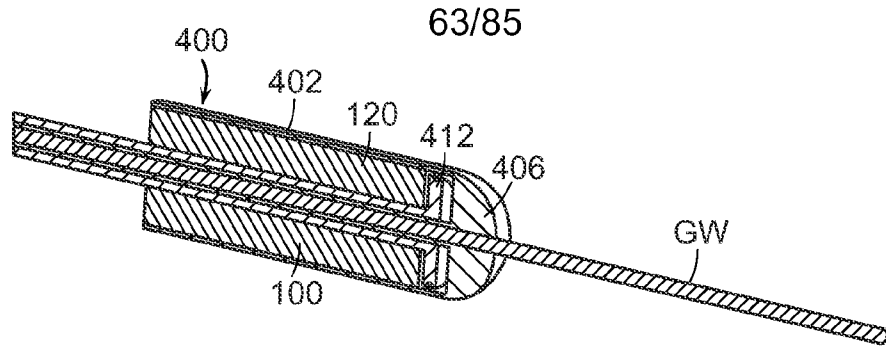


FIG. 55A

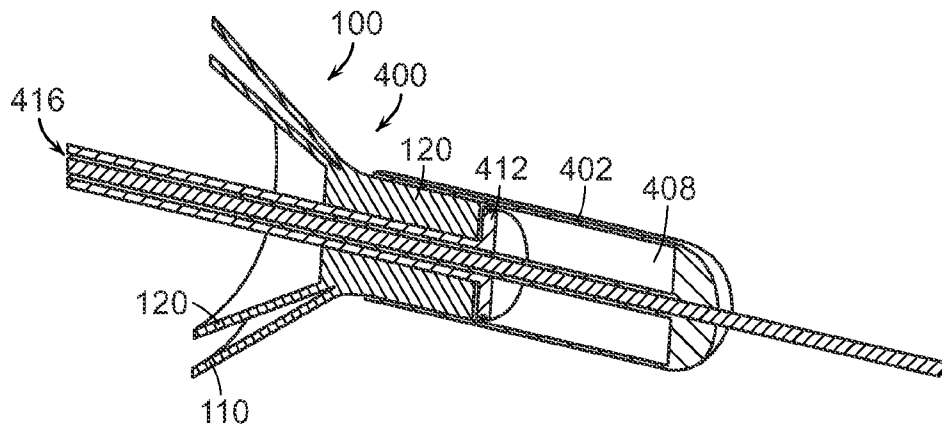


FIG. 55B

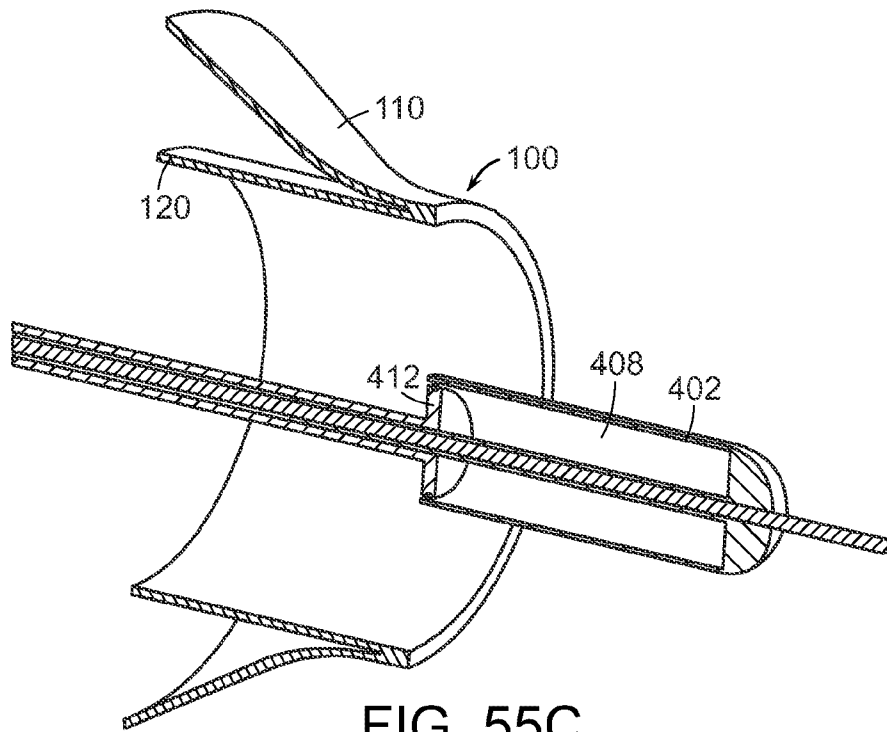


FIG. 55C

64/85

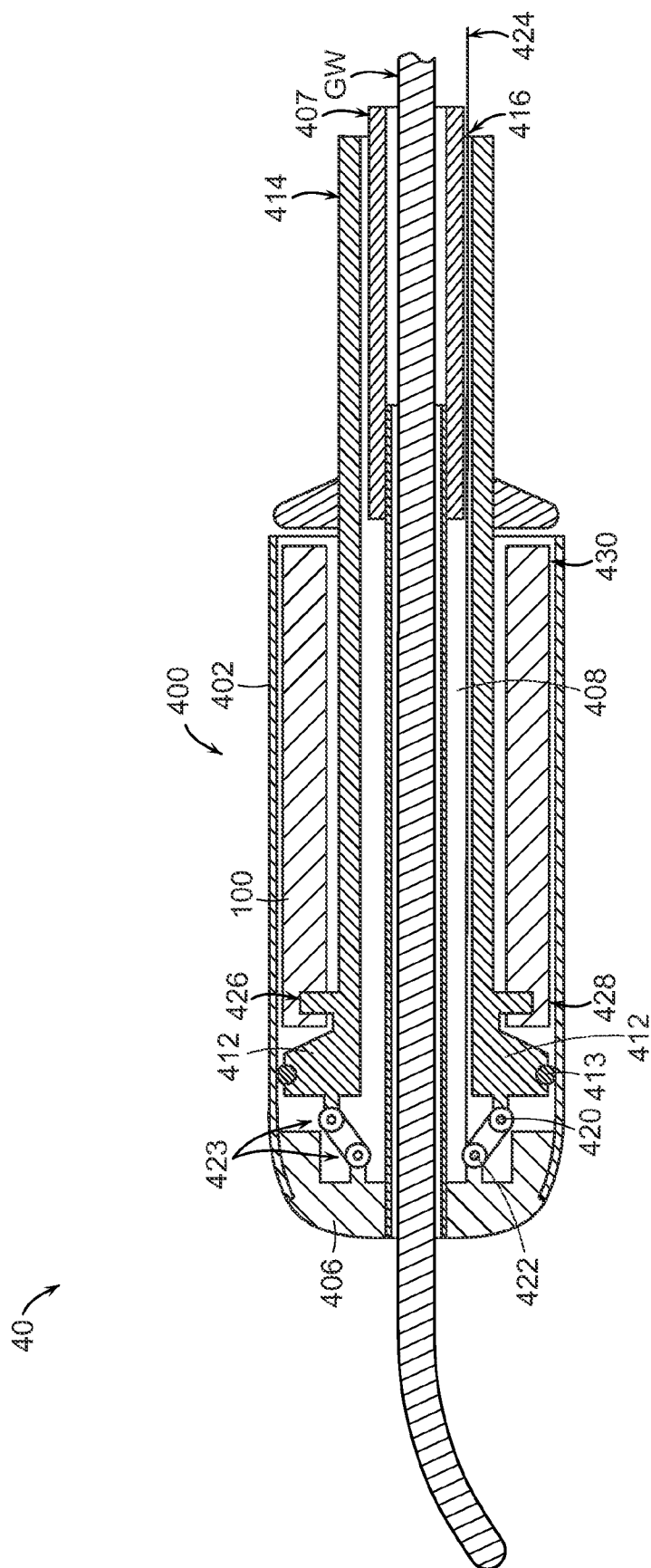
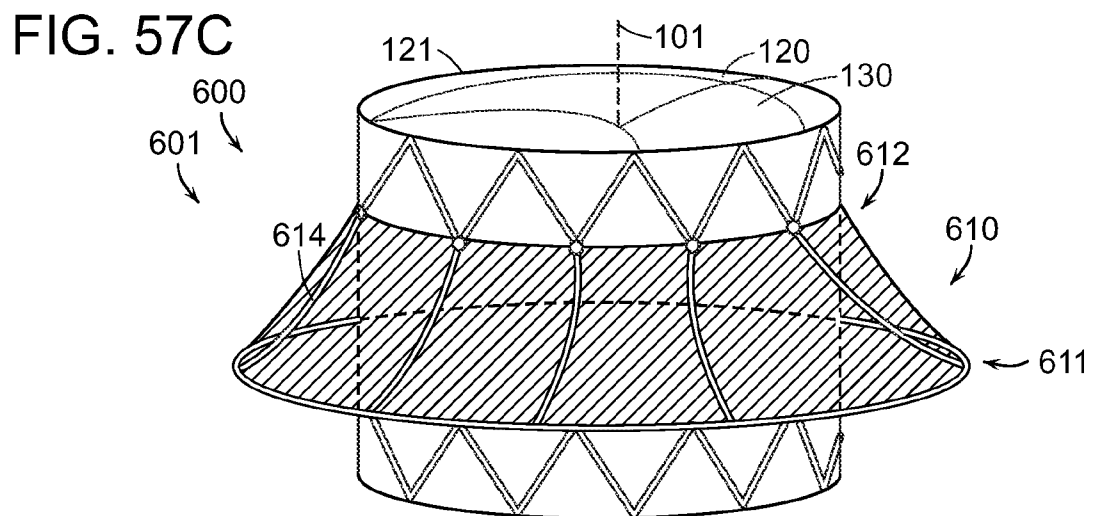
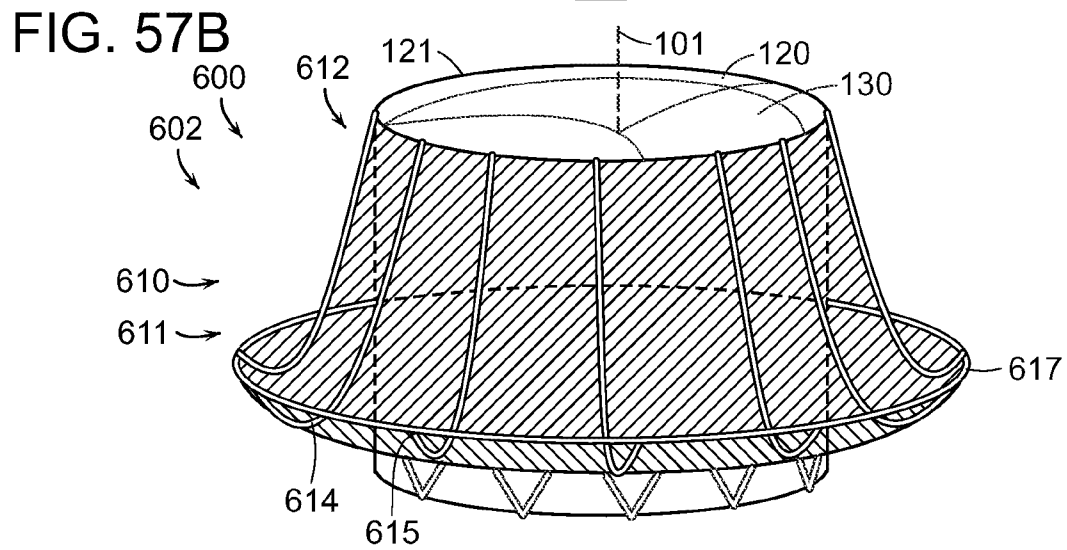
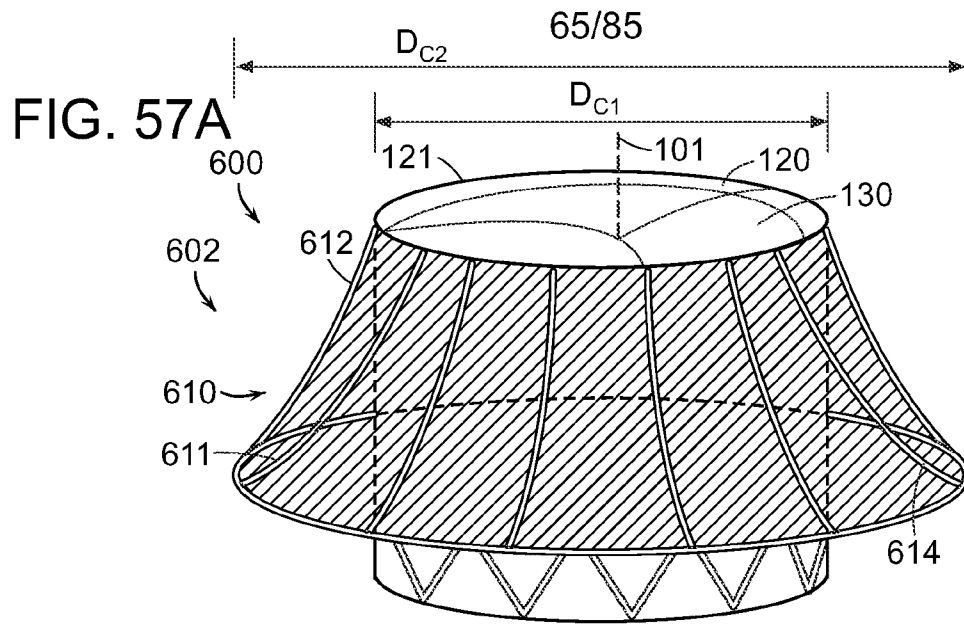


FIG. 56



66/85

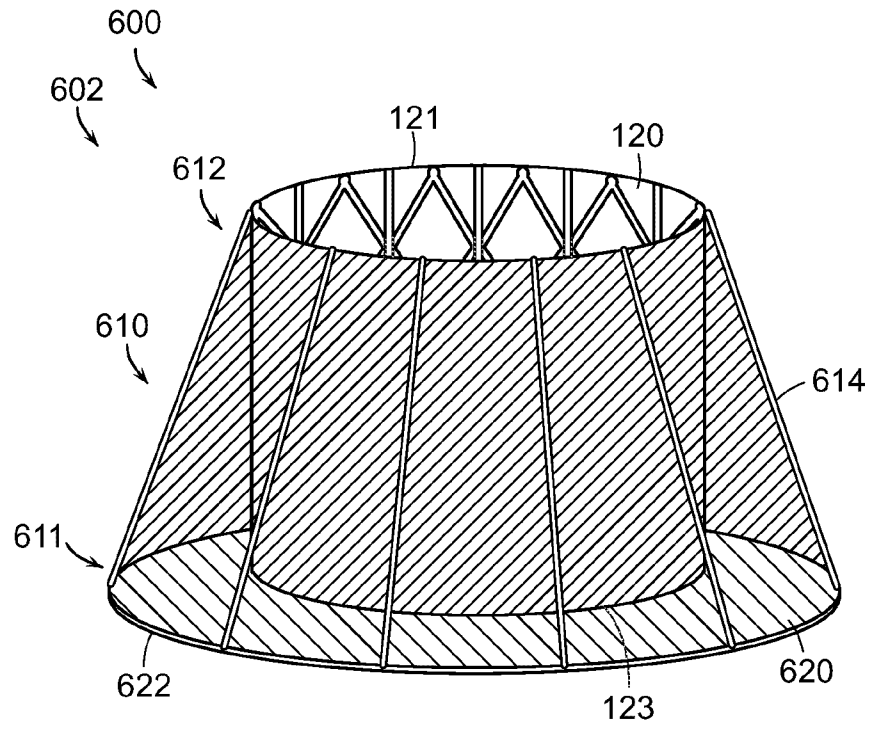


FIG. 57D

67/85

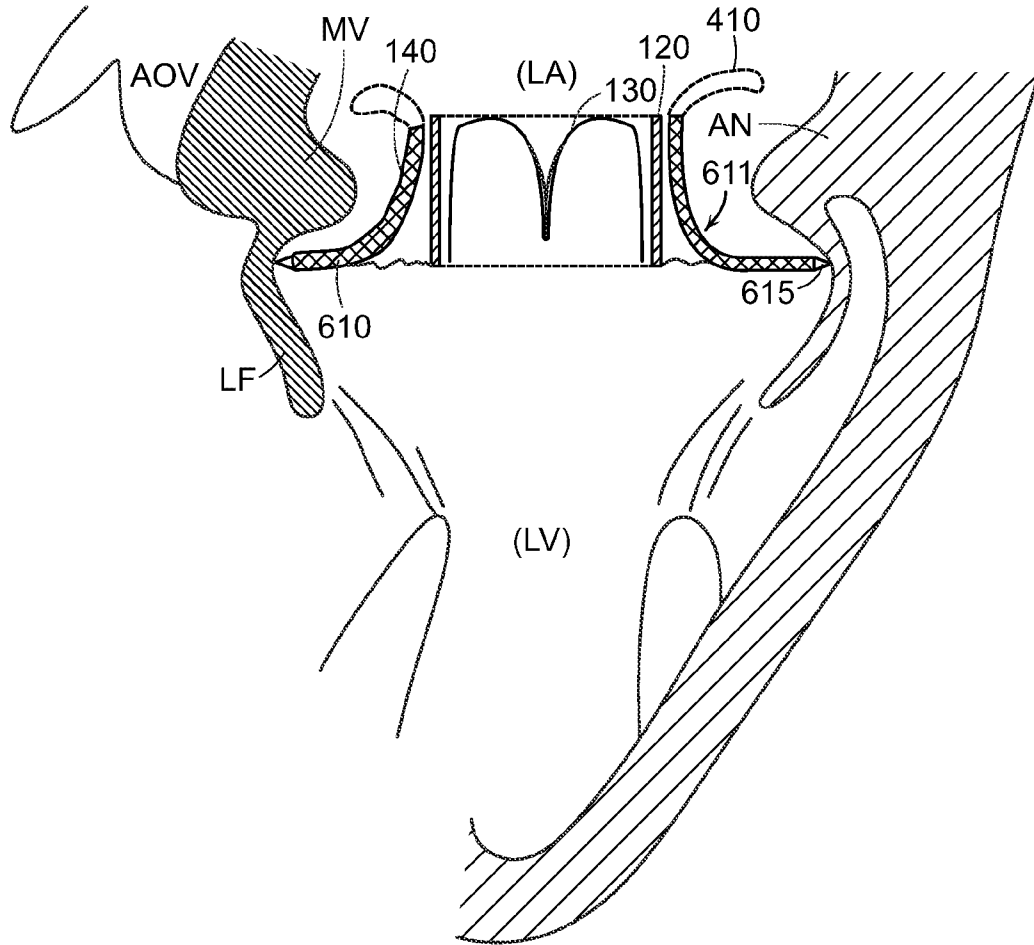


FIG. 57E

68/85

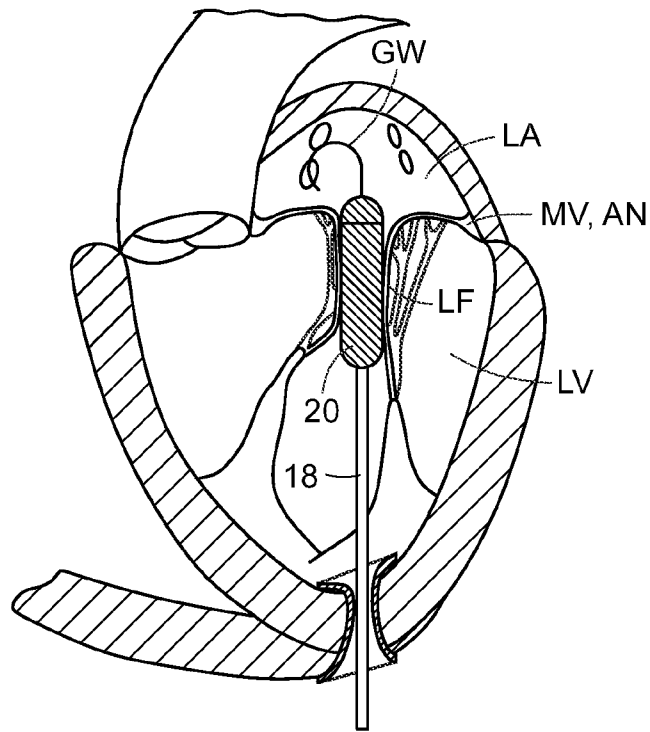


FIG. 58A

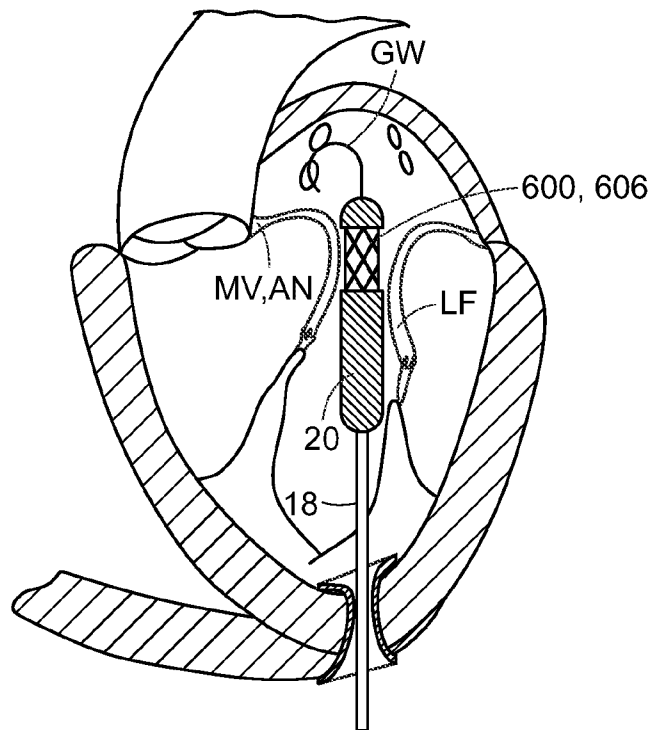


FIG. 58B

69/85

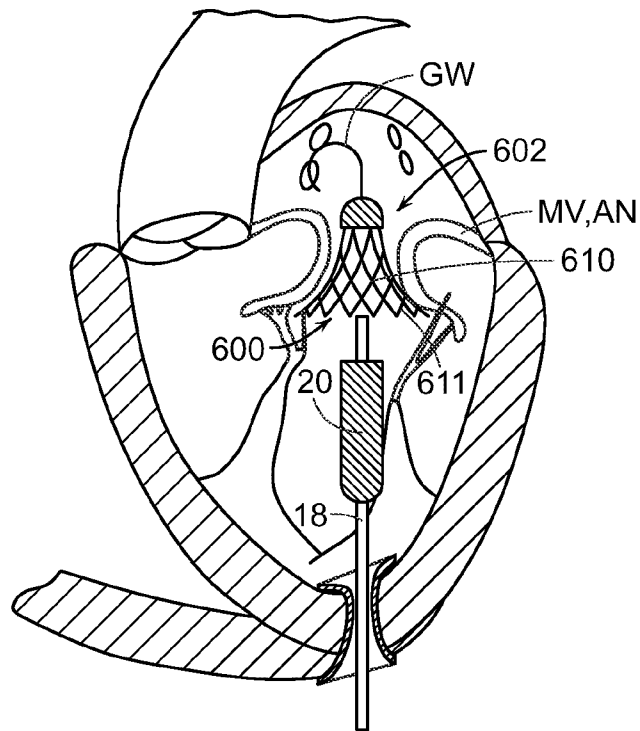


FIG. 58C

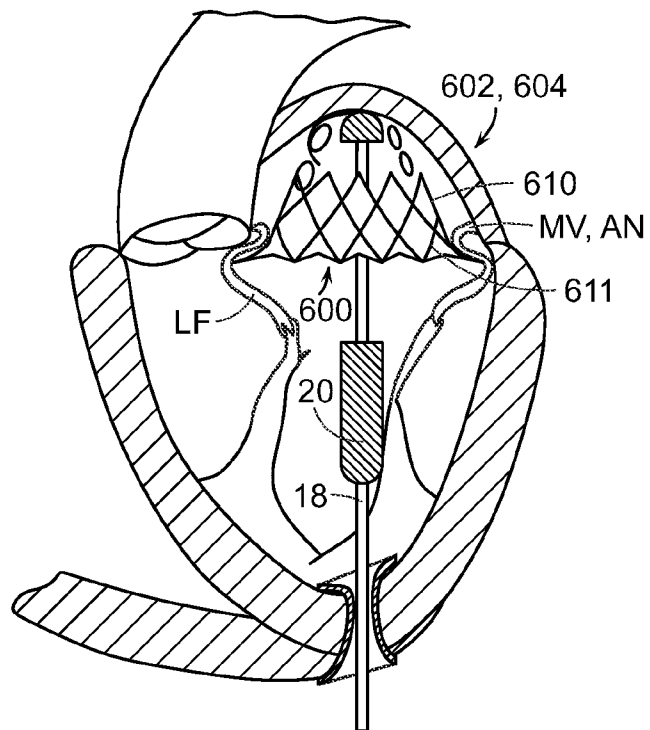


FIG. 58D

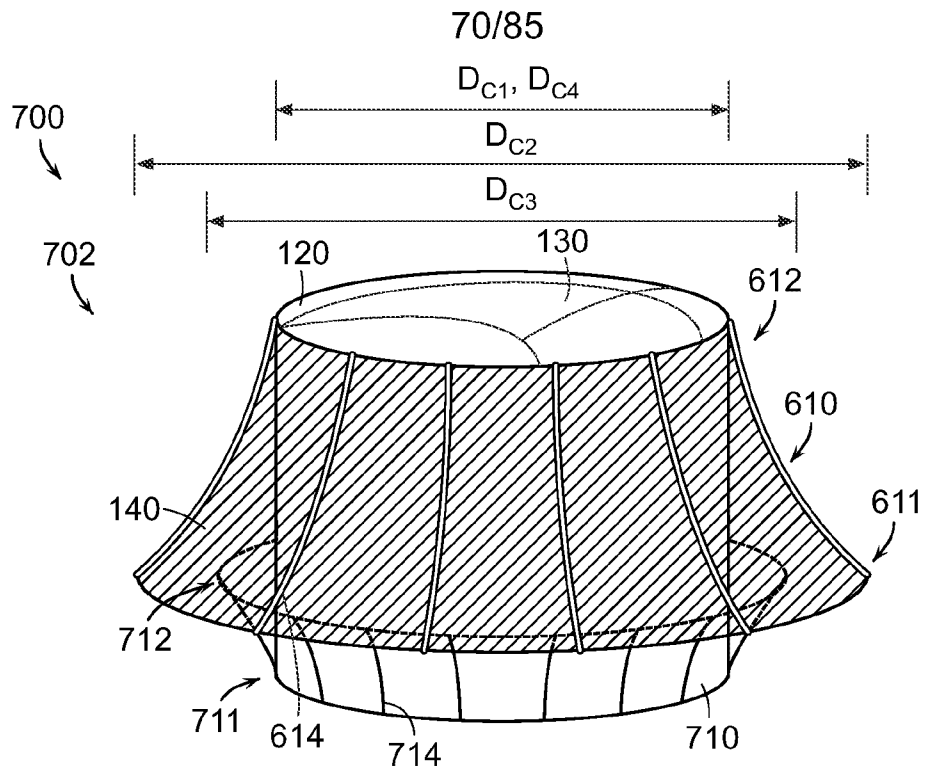


FIG. 59A

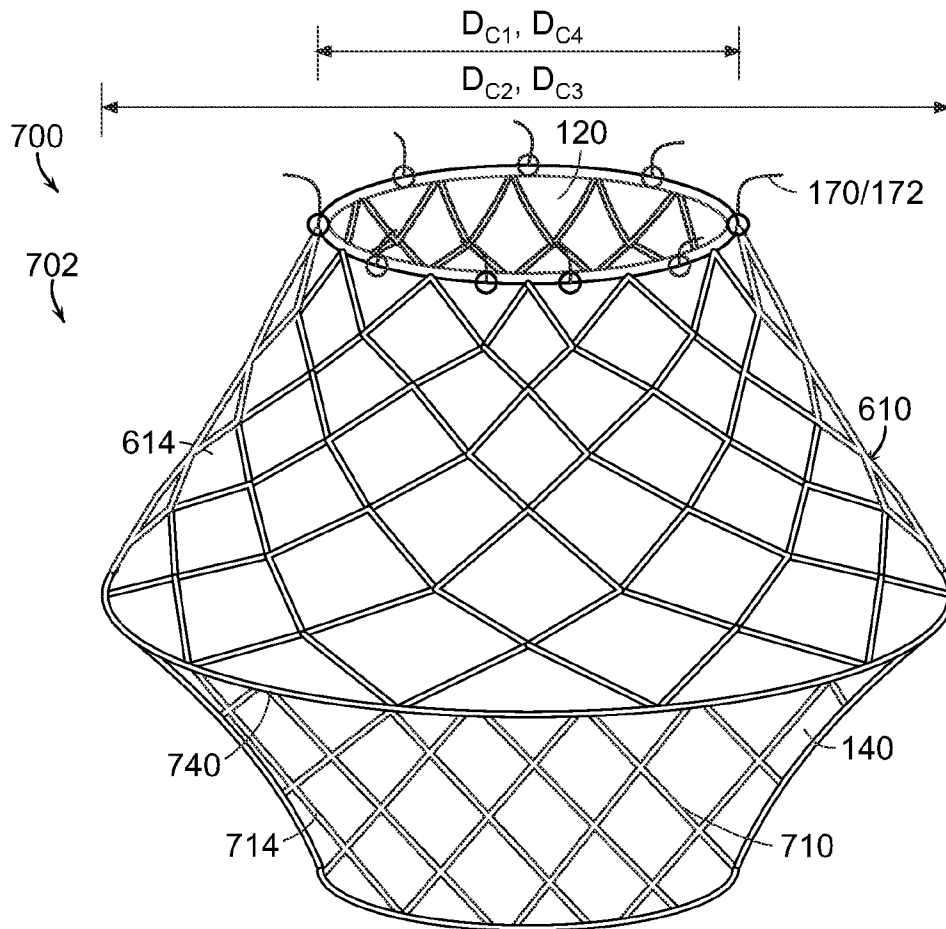


FIG. 59B

71/85

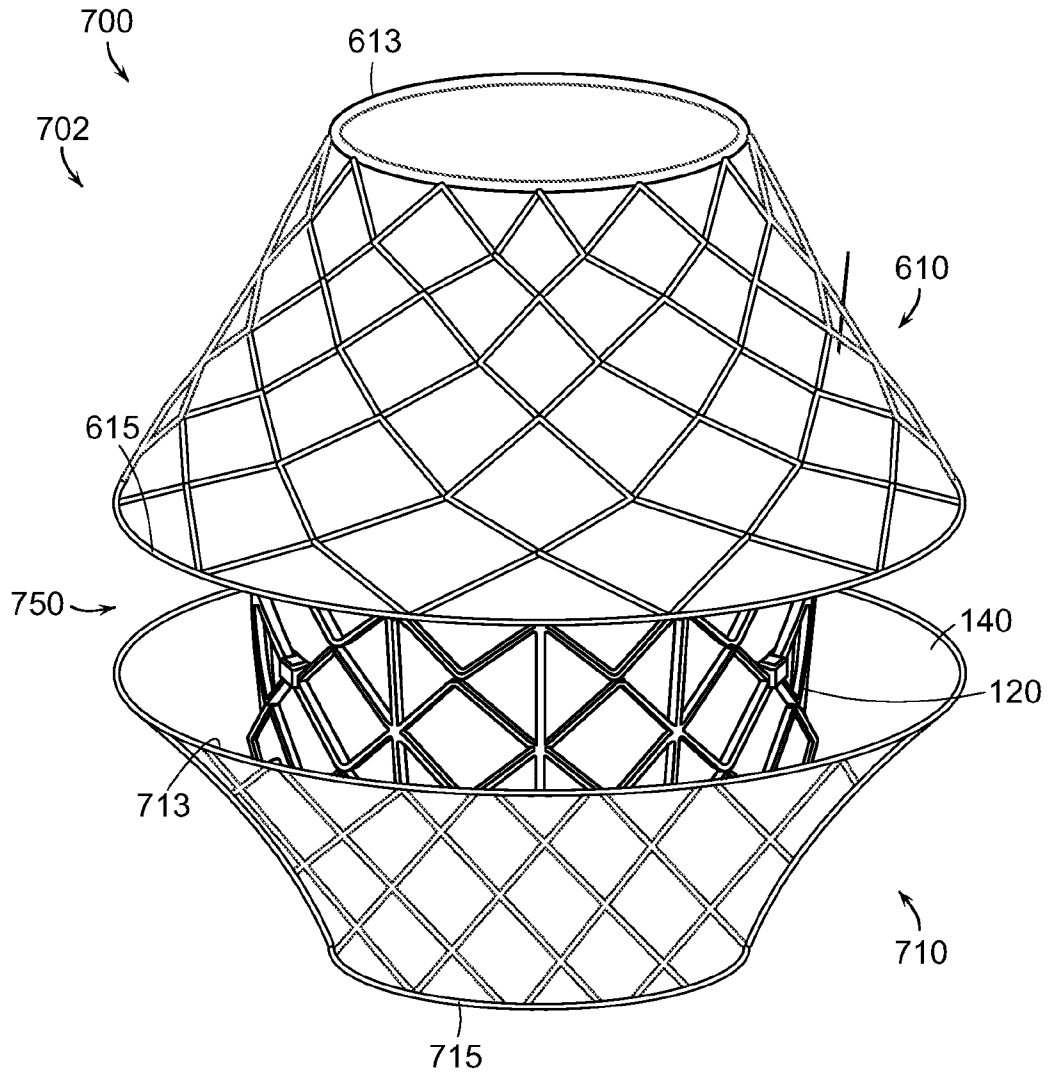


FIG. 59C

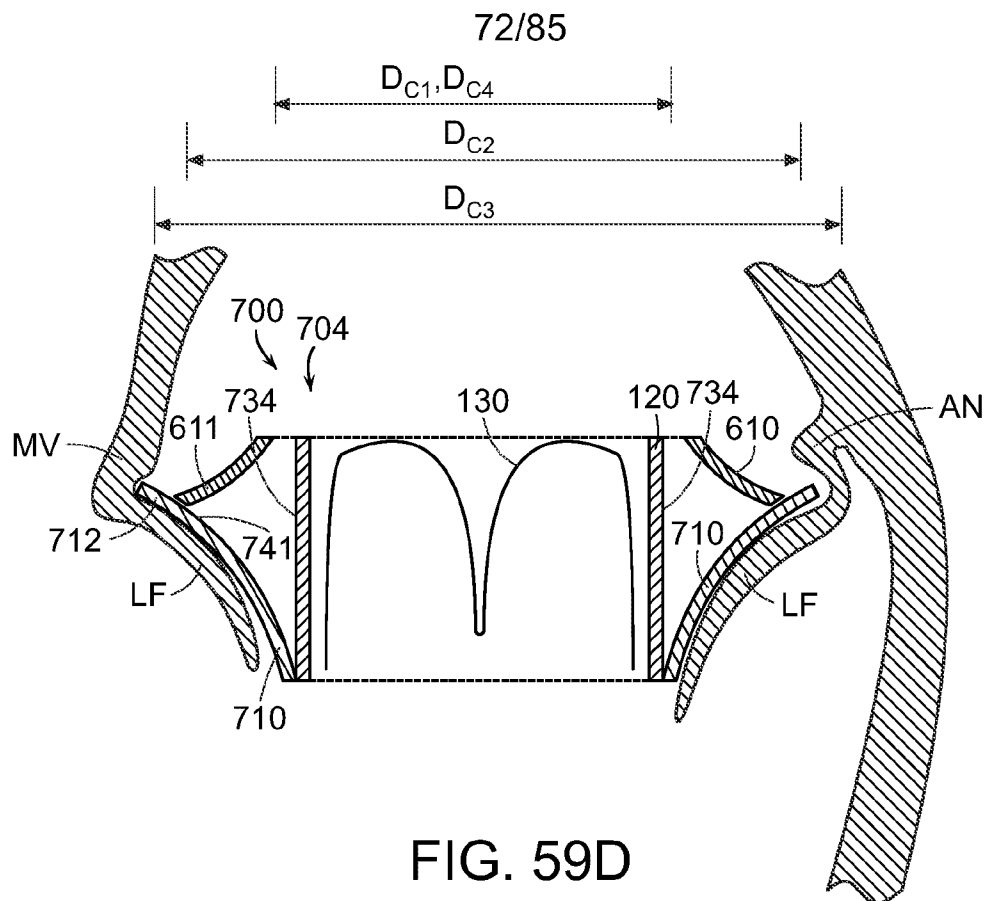


FIG. 59D

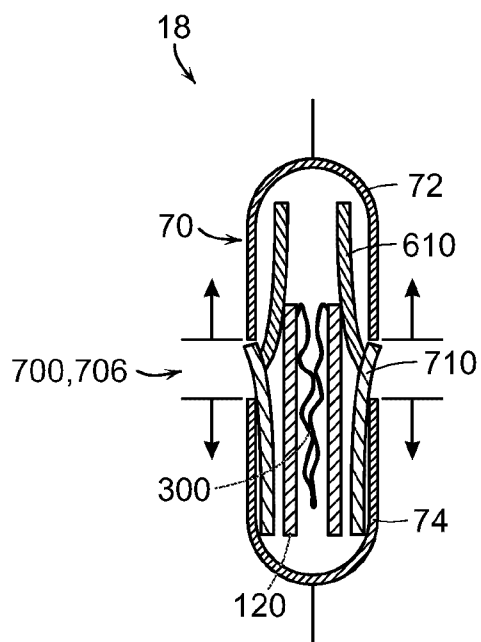


FIG. 60A

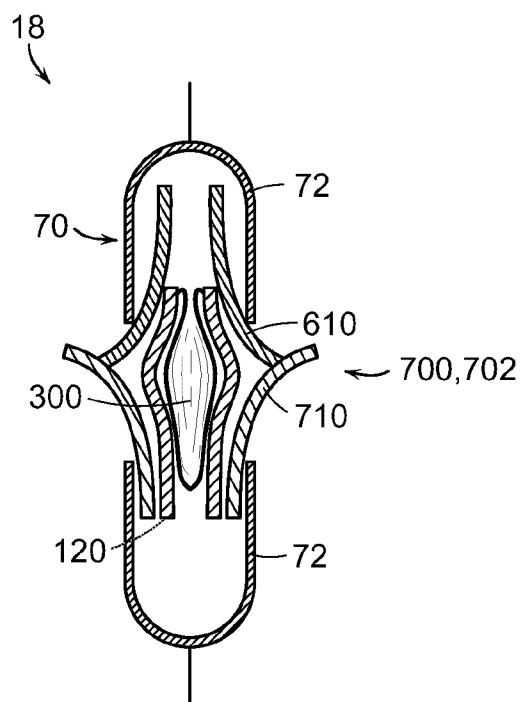


FIG. 60B

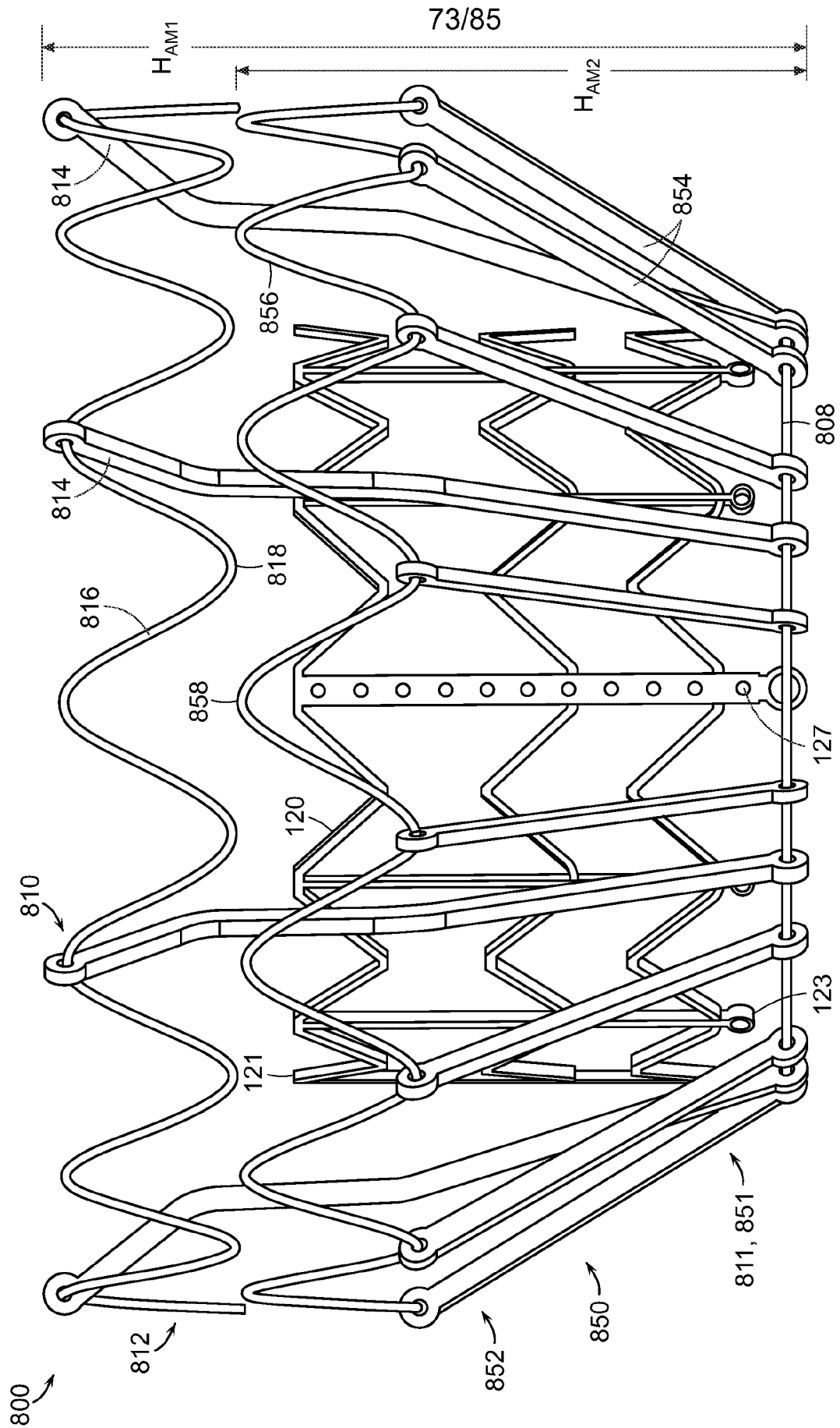


FIG. 61

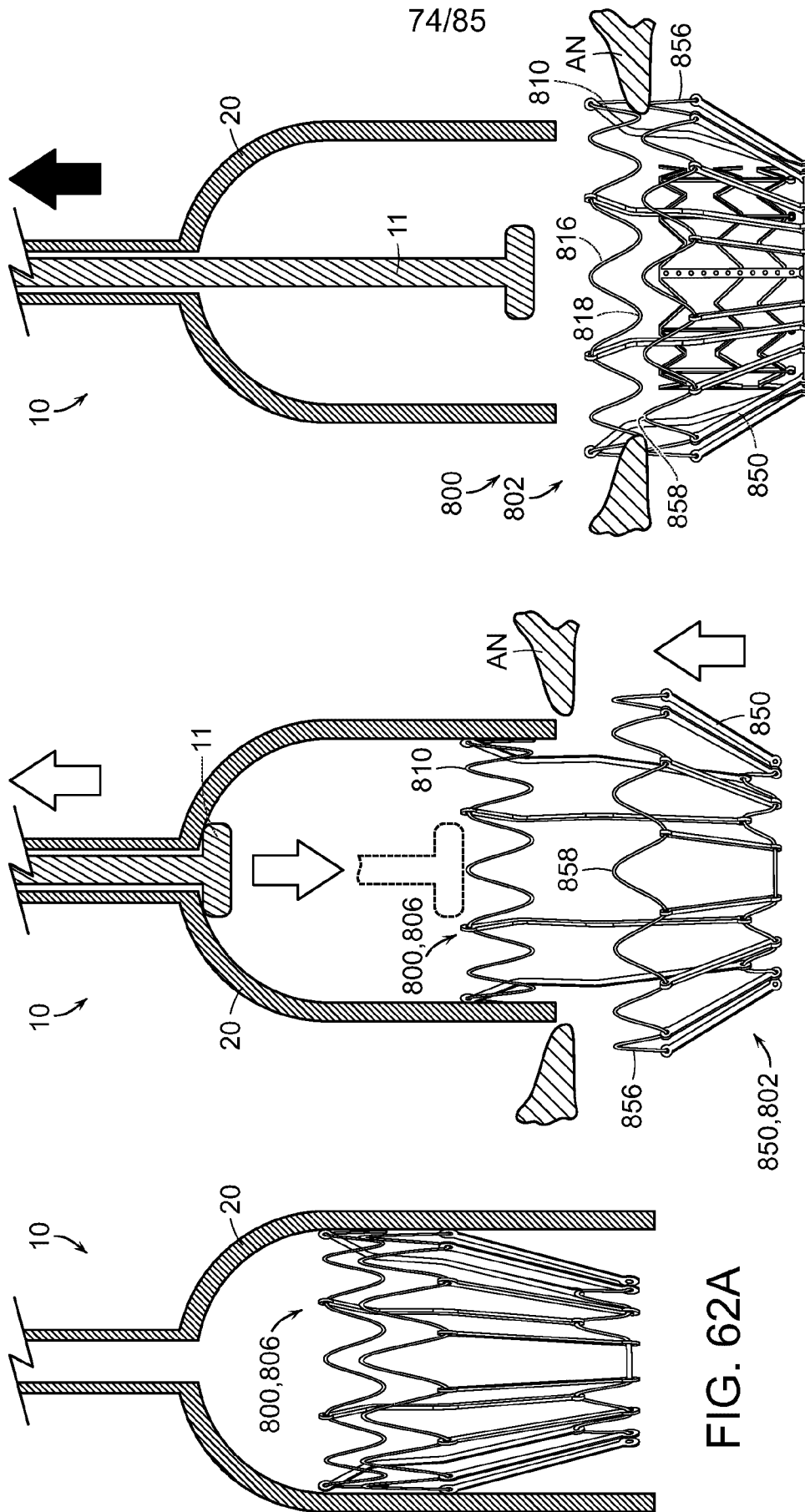


FIG. 62C

FIG. 62B

FIG. 62A

75/85

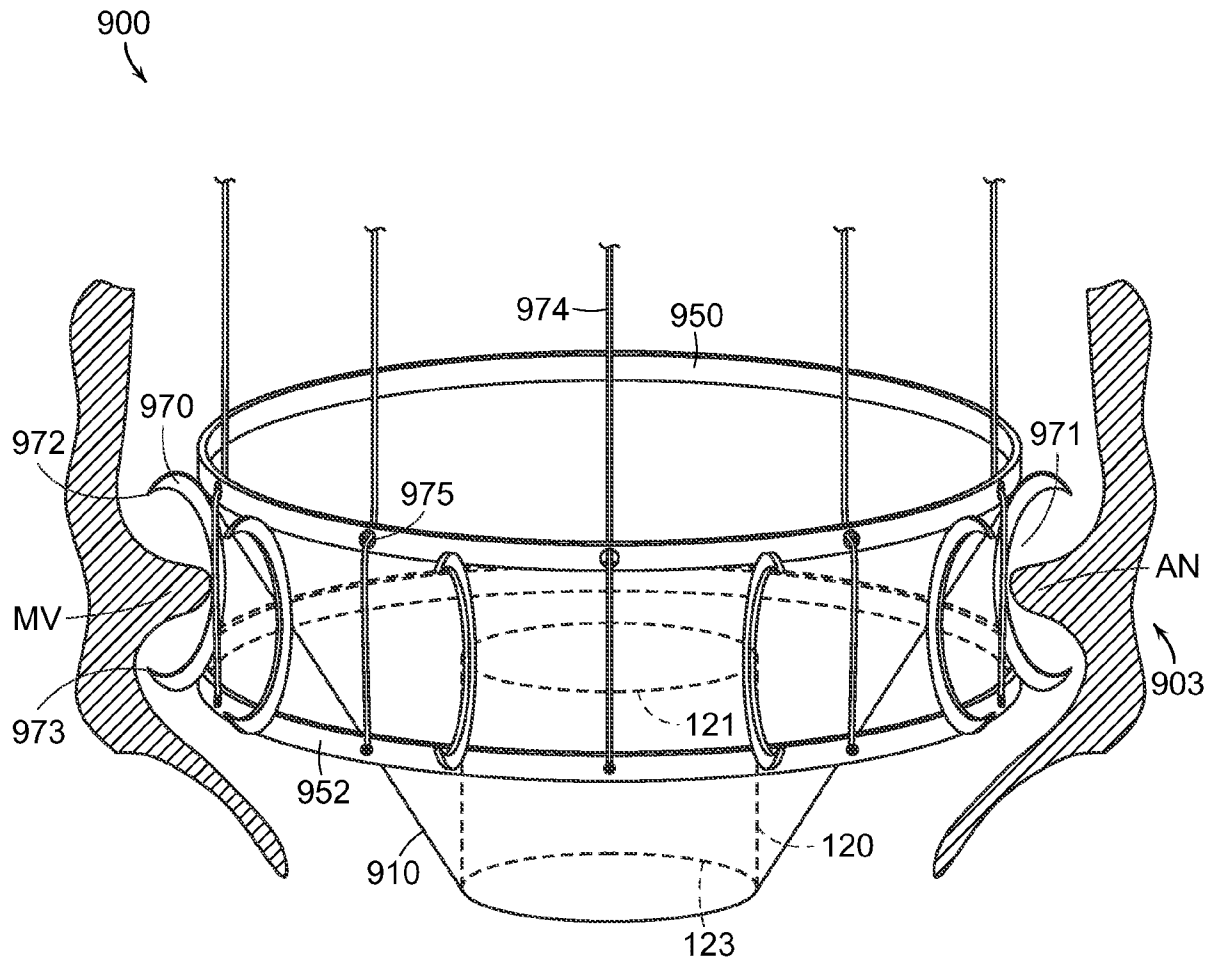


FIG. 63

76/85

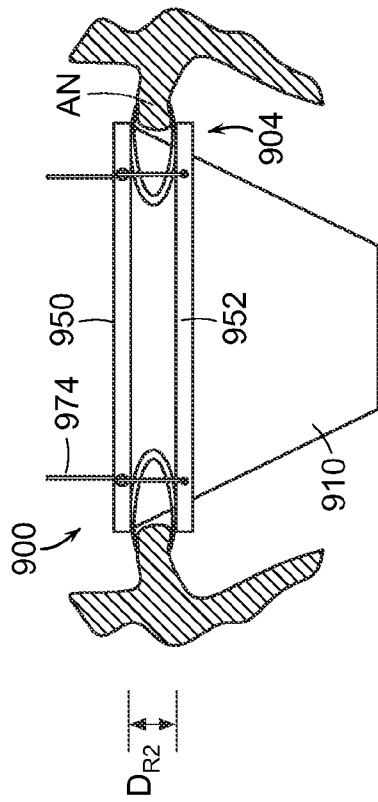


FIG. 64B

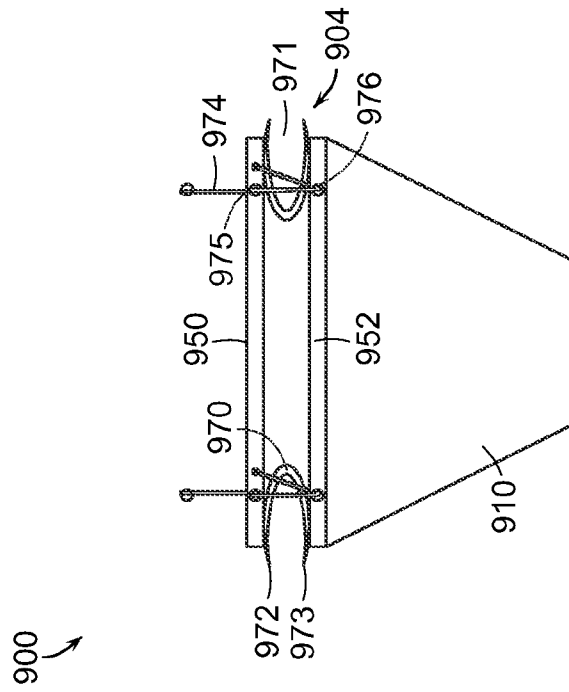


FIG. 64D

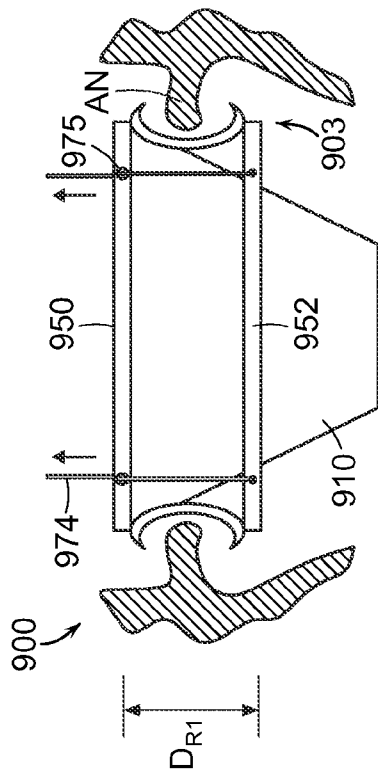


FIG. 64A

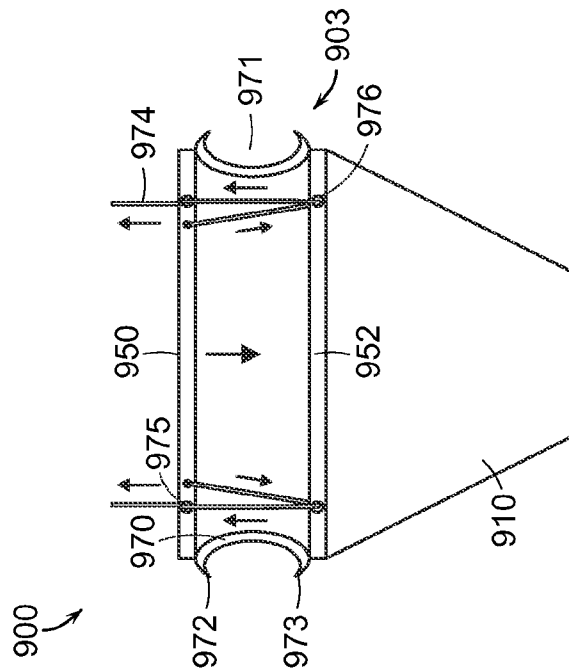


FIG. 64C

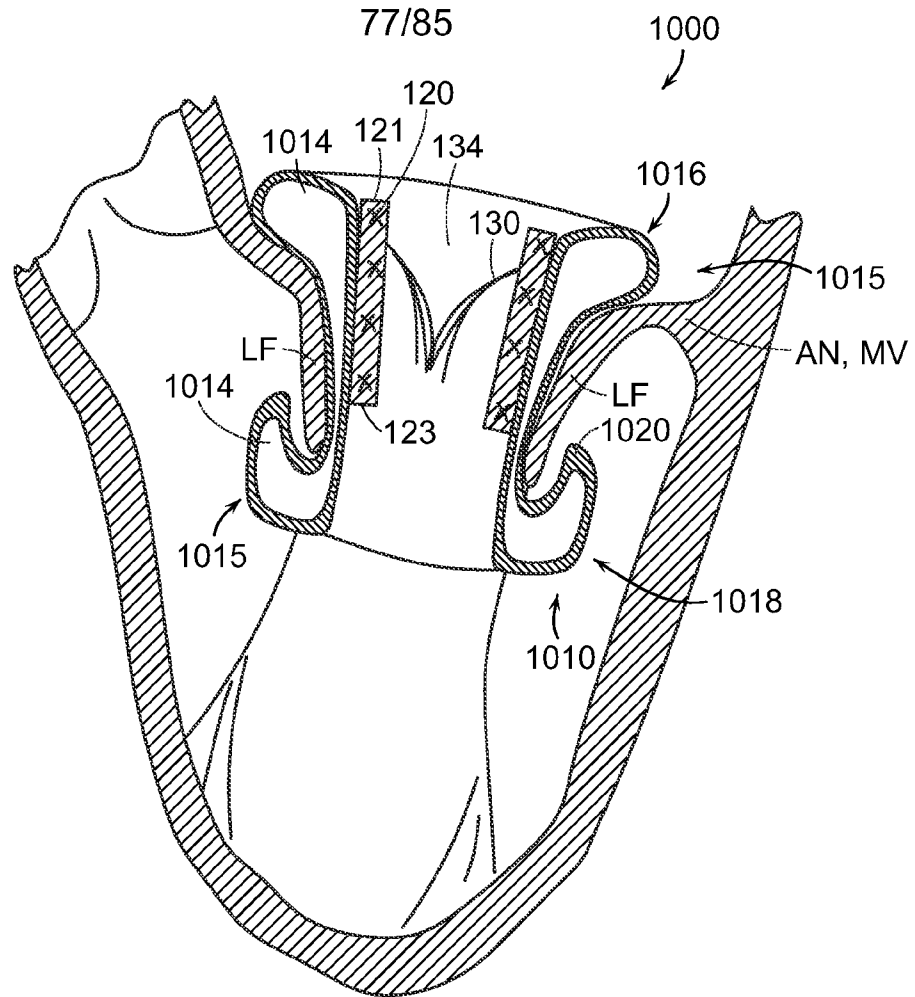


FIG. 65A

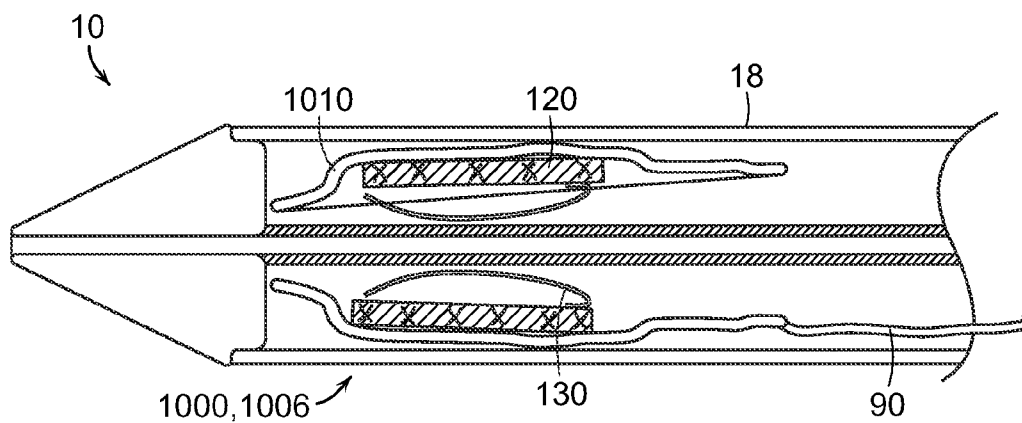


FIG. 65B

78/85

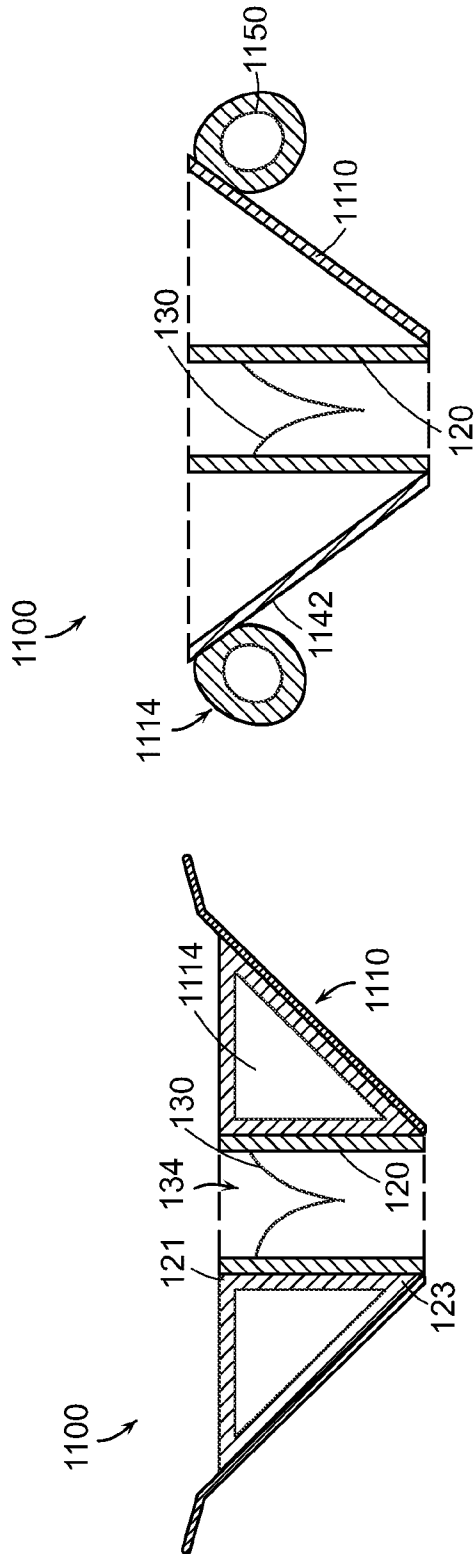


FIG. 66B

FIG. 66A

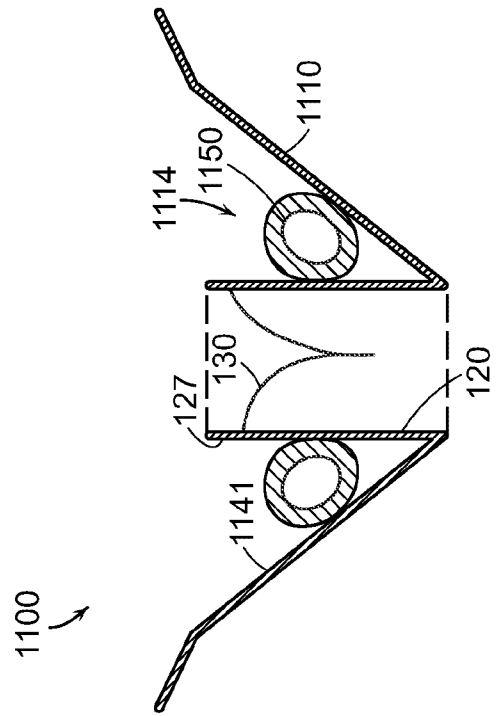


FIG. 66C

79/85

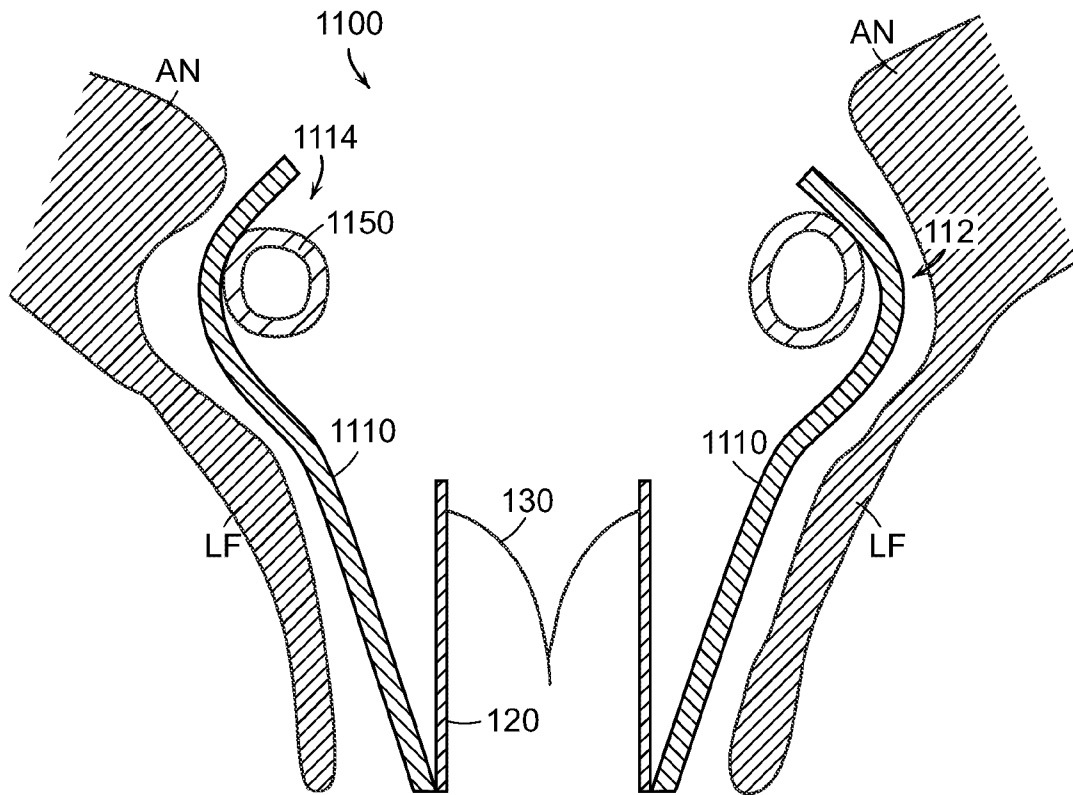


FIG. 66D

80/85

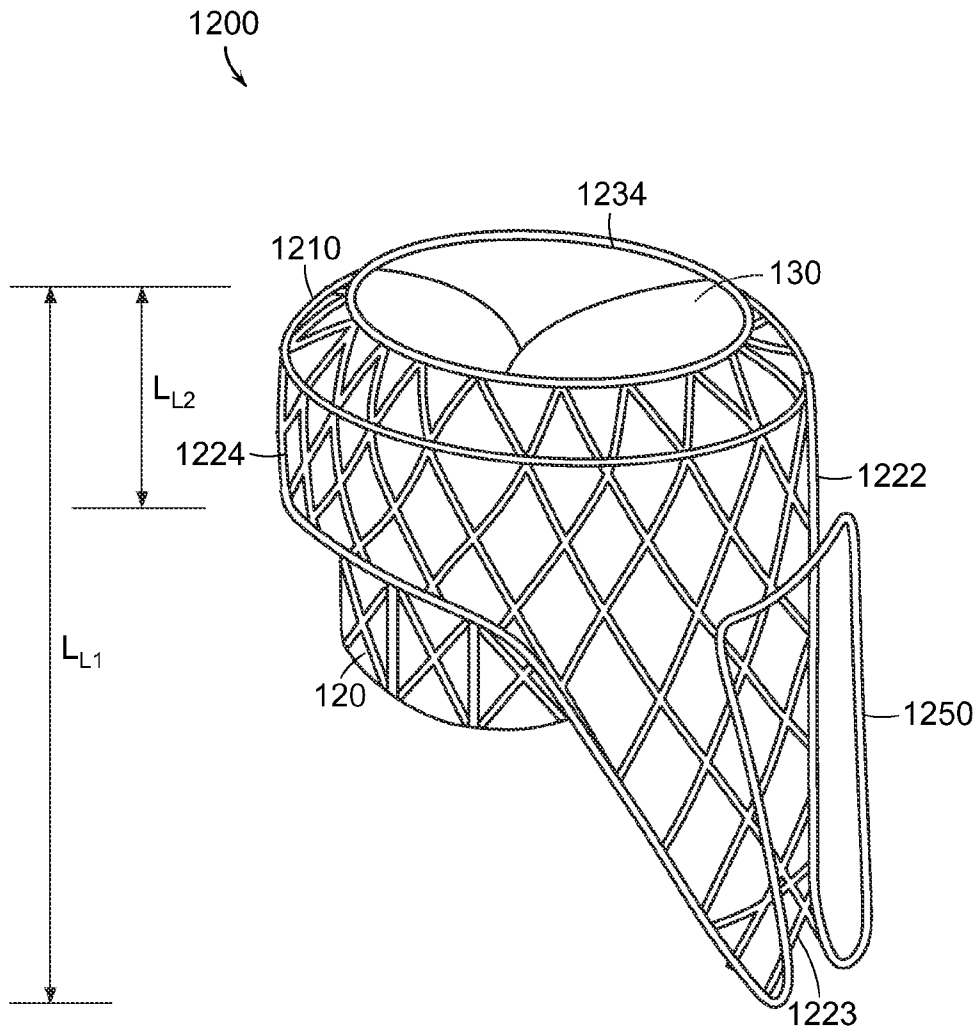


FIG. 67A

81/85

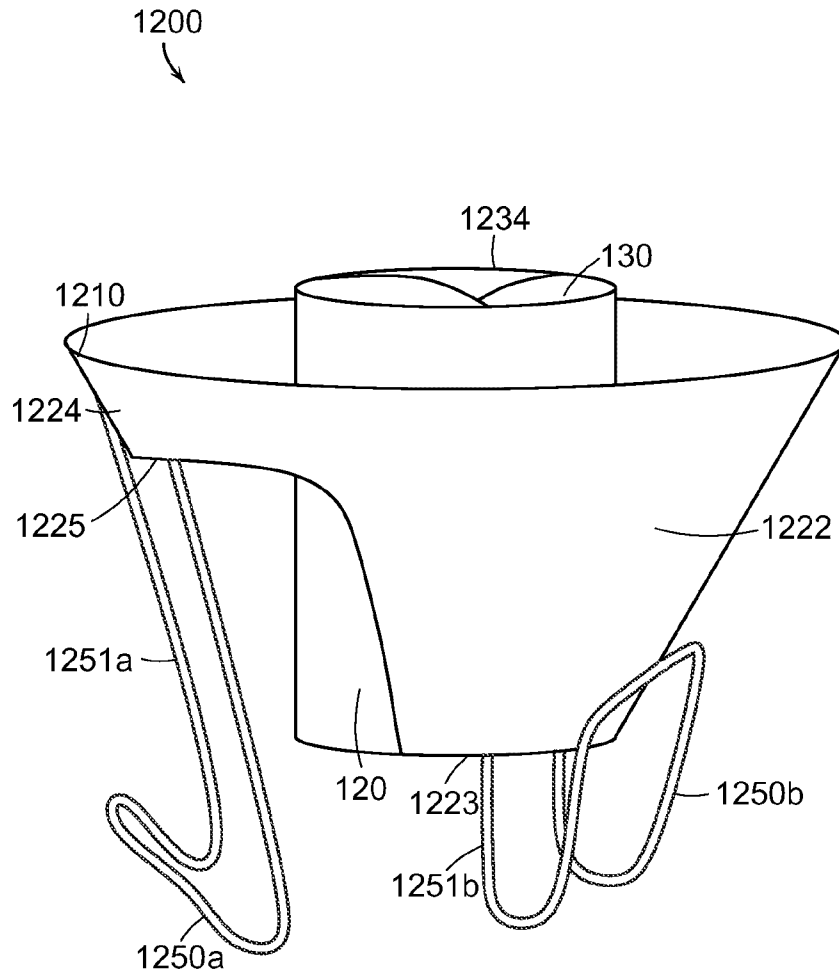
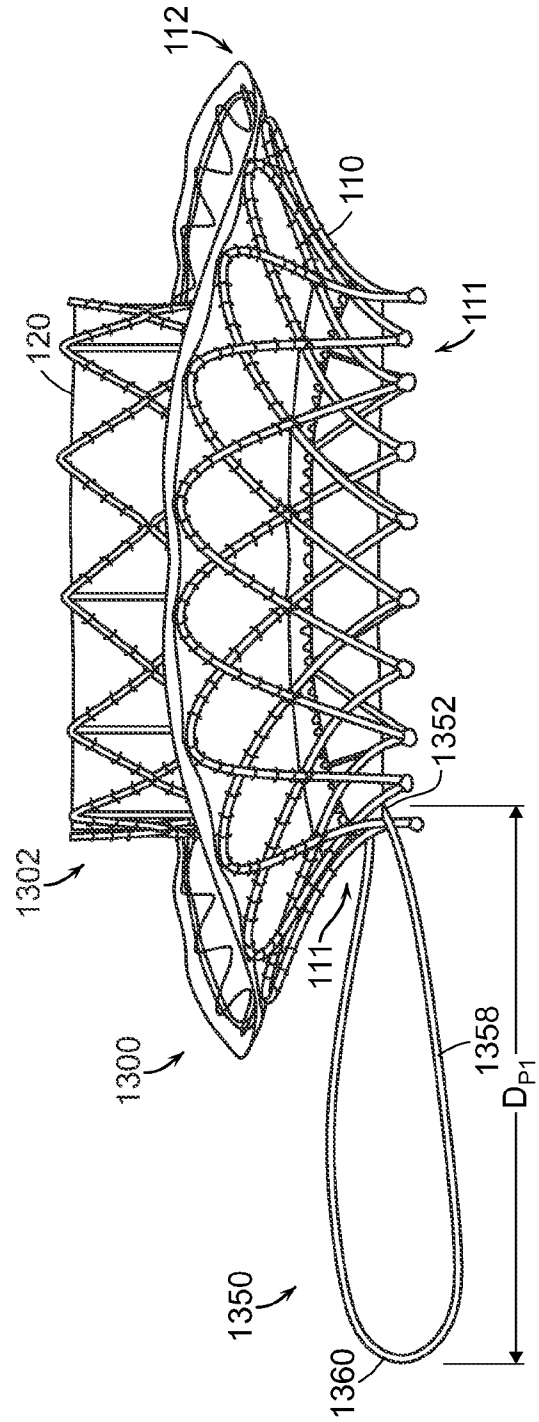
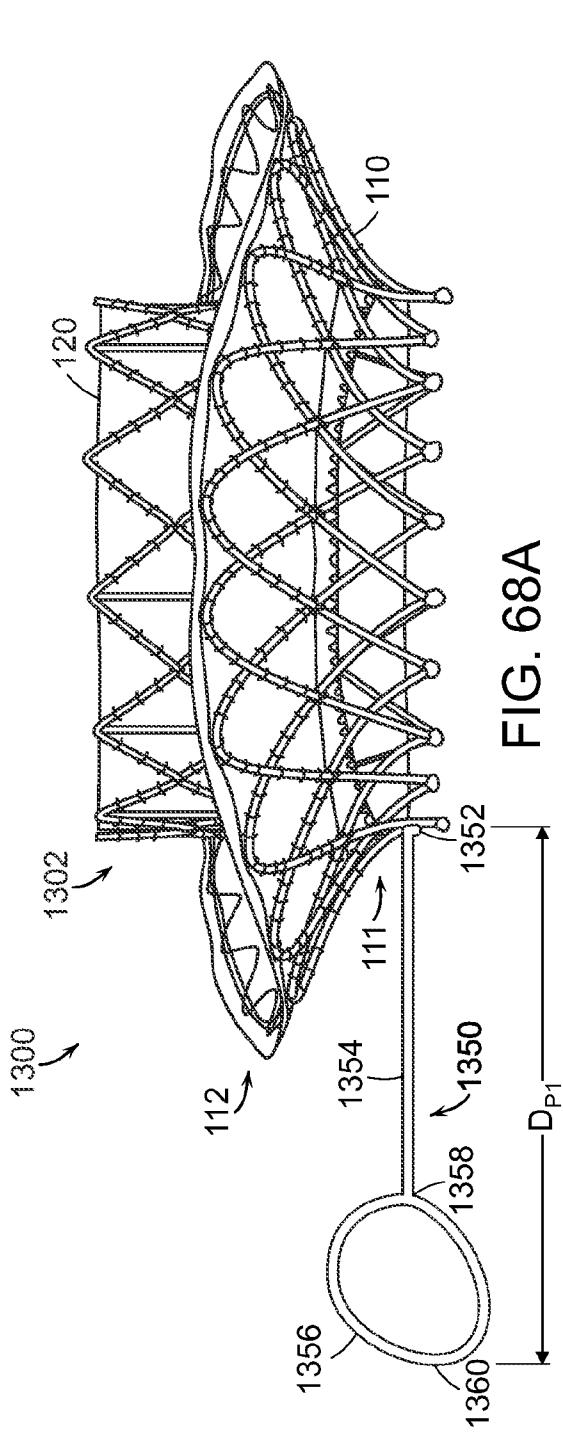


FIG. 67B



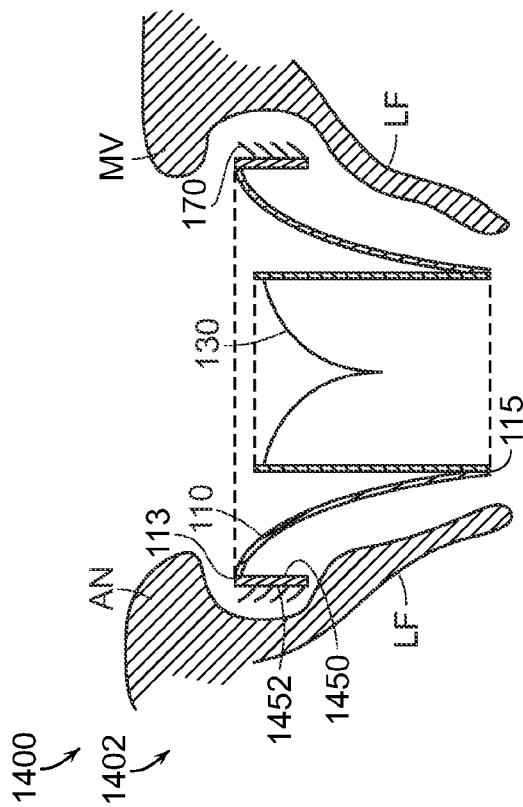


FIG. 69A

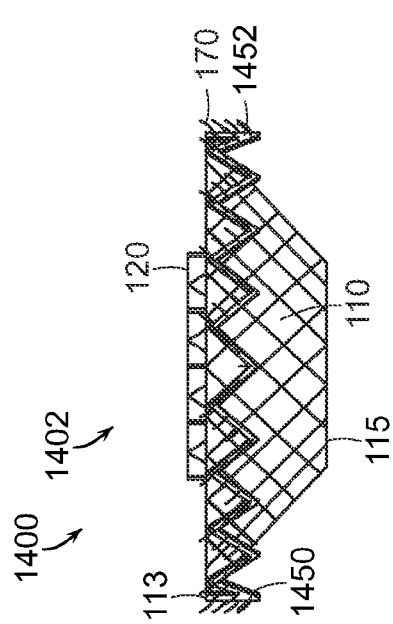


FIG. 69B

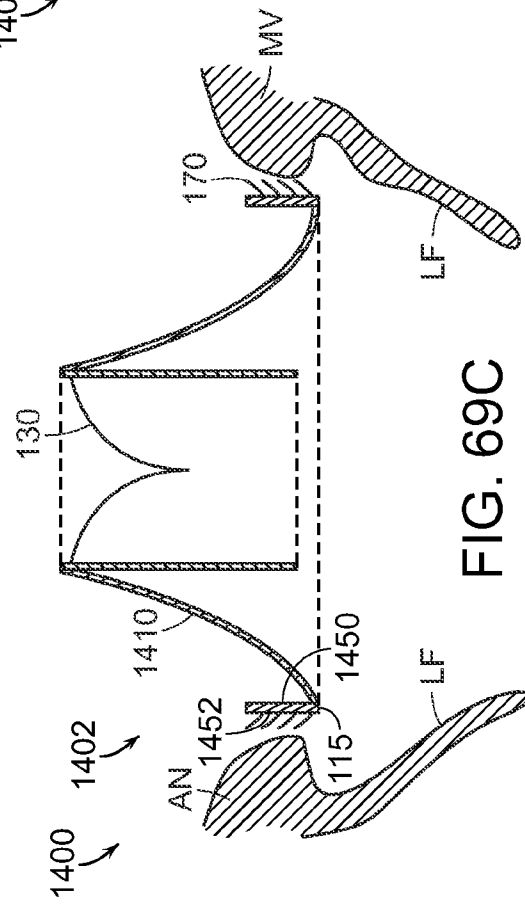


FIG. 69C

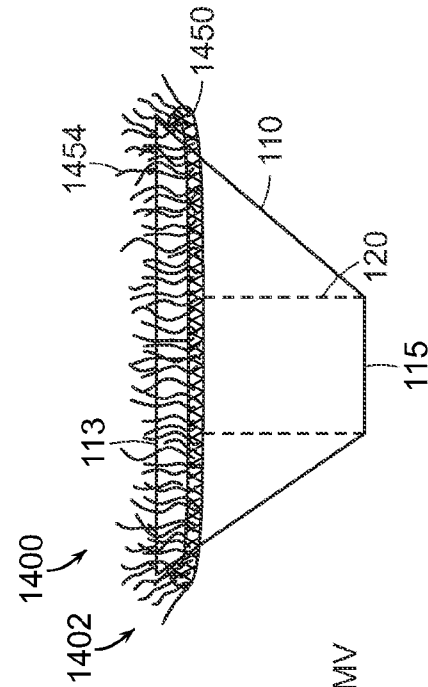


FIG. 69D

84/85

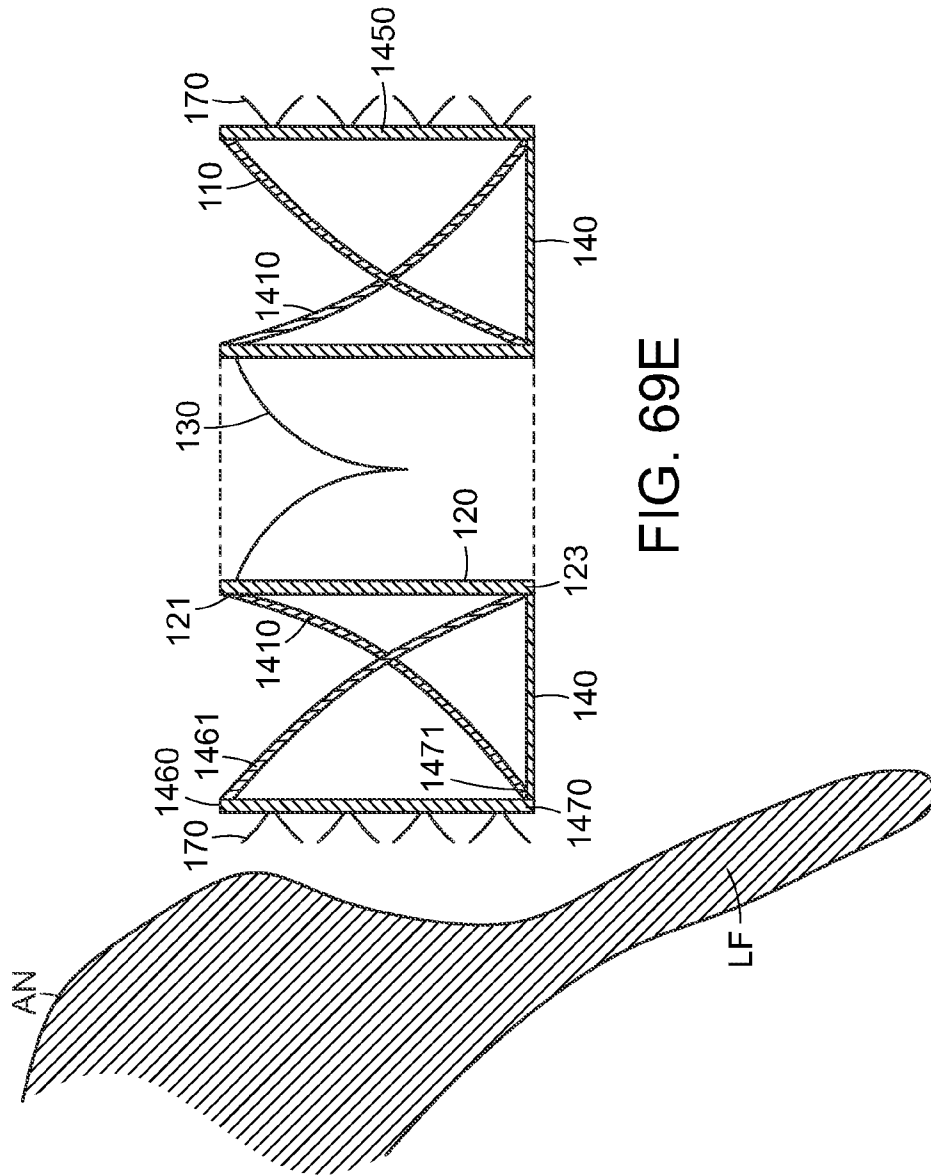


FIG. 69E

85/85

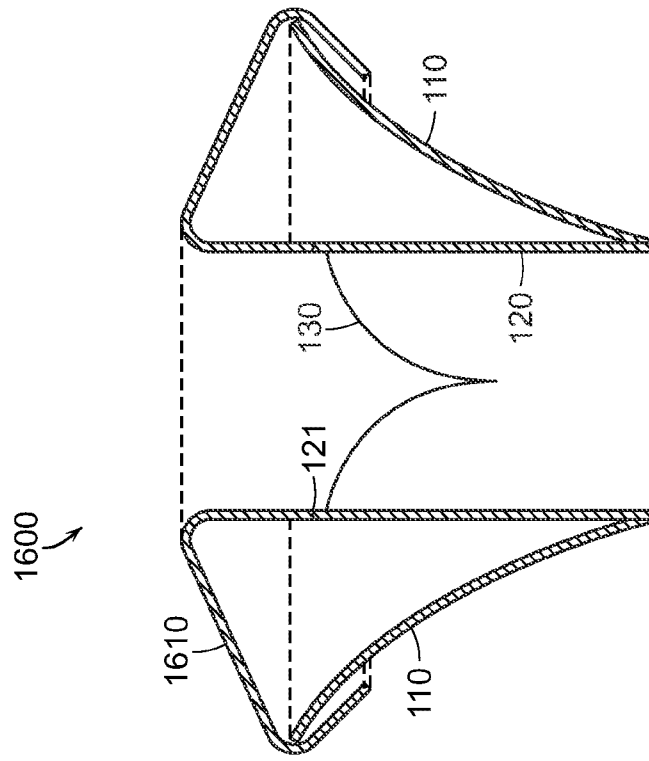


FIG. 71

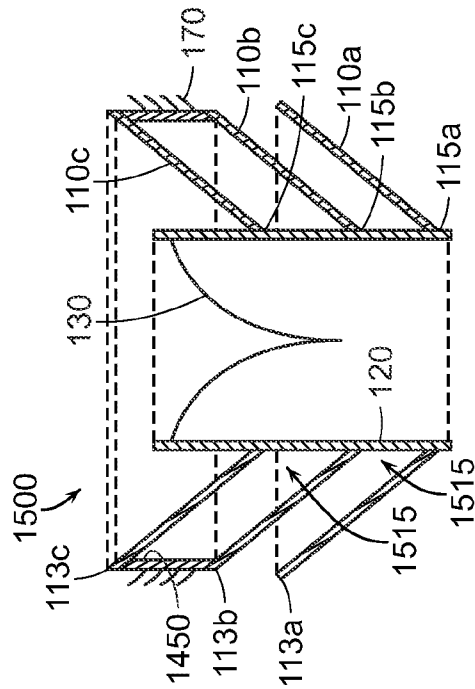


FIG. 70

