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(54) Title: THROMBUS MANAGEMENT AND STRUCTURAL COMPLIANCE FEATURES FOR PROSTHETIC HEART VALVES

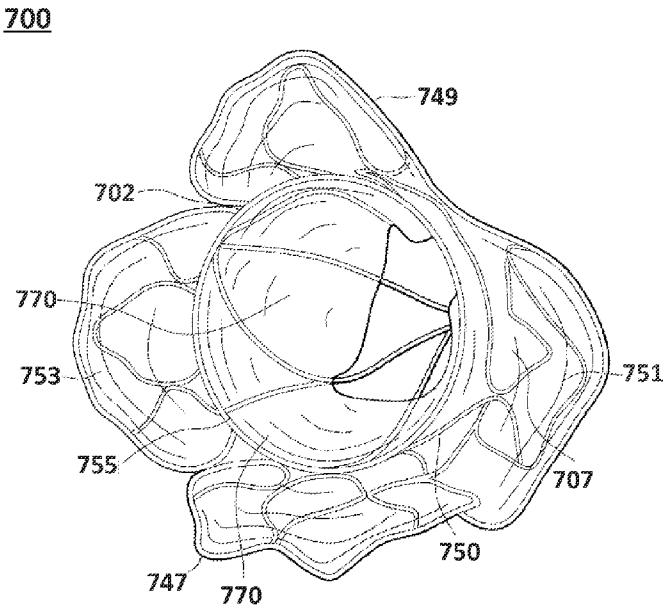

FIG. 24

(57) Abstract: A prosthetic heart valve can include an outer support assembly, an inner valve assembly, which define between them an annular space, and a pocket closure that bounds the annular space to form a pocket in which thrombus can be formed and retained. Alternatively, or additionally, the outer support assembly and the inner valve assembly can be coupled at the ventricle ends of the outer support assembly and the inner valve assembly, with the outer support assembly being relatively more compliant in hoop compression in a central, annulus portion than at the ventricle end, so that the prosthetic valve can seat securely in the annulus while imposing minimal loads on the inner valve assembly that could degrade the performance of the valve leaflets.

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THROMBUS MANAGEMENT AND STRUCTURAL COMPLIANCE FEATURES FOR PROSTHETIC HEART VALVES

Cross-Reference to Related Applications

[1001] This application is a continuation-in-part of U.S. Patent Application No. 14/155,535, filed January 15, 2014, and claims priority to and the benefit of U.S. Provisional Application No. 61/839,237, filed June 25, 2013 and U.S. Provisional Application No. 61/840,313, filed June 27, 2013. The disclosures of the foregoing applications are incorporated herein by reference in their entirety.

Background

[1002] Prosthetic heart valves, including those for insertion into atrioventricular valves (tricuspid and mitral valves) are susceptible to various problems, including problems with insufficient articulation and sealing of the valve within the native valve annulus, pulmonary edema due to poor atrial drainage, perivalvular leaking around the install prosthetic valve, lack of a good fit for the prosthetic valve within the native valve annulus, atrial tissue erosion, excess wear on the Nitinol structures, interference with the aorta at the posterior side of the mitral annulus, lack of customization, and thrombus formation, to name a few. Accordingly, there is still a need for a prosthetic heart valve that can address some or all of these problems.

Summary

[1003] A prosthetic heart valve can include an outer support assembly, an inner valve assembly, which define between them an annular space, and a pocket closure that bounds the annular space to form a pocket in which thrombus can be formed and retained. A prosthetic heart valve can alternatively, or additionally, include an outer support assembly and an inner valve assembly, coupled at the ventricle ends of the outer support assembly and the inner valve assembly, with the outer support assembly being relatively more compliant in hoop compression in a central, annulus portion than at the ventricle end, so that the prosthetic valve can seat securely in the annulus while imposing minimal loads on the inner valve assembly that could degrade the performance of the valve leaflets.

Brief Description of the Drawings

[1004] FIGs. 1A and 1B are schematic perspective and side cross sectional views of a prosthetic heart valve according to an embodiment.

[1005] FIGs. 2A-C are schematic views of an inner valve assembly of the prosthetic heart valve of FIGs. 1A and 1B.

[1006] FIG. 3 is a top view of a prosthetic heart valve according to another embodiment.

[1007] FIG. 4 is a top view of a prosthetic heart valve according to another embodiment.

[1008] FIG. 5 is a perspective side view of a portion of a prosthetic heart valve according to another embodiment.

[1009] FIG. 6 is an exploded view of a prosthetic heart valve system according to another embodiment.

[1010] FIGs. 7-9 are front, bottom, and top views of a prosthetic heart valve according to another embodiment.

[1011] FIG. 10 is an opened and flattened view of the inner frame of the valve of FIGs. 7-9, in an unexpanded configuration.

[1012] FIGs. 11 and 12 are side and bottom views, respectively, of the inner frame of FIG. 10 in an expanded configuration.

[1013] FIG. 13 is an opened and flattened view of the outer frame of the valve of FIGs. 7-9, in an unexpanded configuration.

[1014] FIGs. 14 and 15 are side and top views, respectively, of the outer frame of FIG. 13 in an expanded configuration.

[1015] FIGs. 16-18 are side, front, and top views of an assembly of the inner frame of FIGs. 10-12 and the outer frame of FIGs. 13-15.

[1016] FIG. 19 is a plan view of a fabric pattern for the inner and outer coverings of the outer frame assembly of the valve of FIGs. 7-9.

[1017] FIG. 20 is a plan view of a fabric pattern for the leaflets and outer covering of the inner valve assembly of the valve of FIGs. 7-9.

[1018] FIGs. 21 and 22 are schematic perspective and side cross sectional views of a prosthetic heart valve according to another embodiment.

[1019] FIGs. 23-25 are top and perspective views of a prosthetic heart valve according to another embodiment.

[1020] FIG. 26 is an exploded view of a prosthetic heart valve system according to another embodiment.

[1021] FIGs. 27 and 28 are schematic perspective and side cross sectional views of a prosthetic heart valve according to another embodiment.

[1022] FIGs. 29A-D are schematic illustrations of stiffness profiles of a prosthetic heart valve according to another embodiment.

Detailed Description

[1023] A schematic representation of a prosthetic heart valve 100 is shown in FIGs. 1A and 1B. Prosthetic heart valve 100 is designed to replace a damaged or diseased native heart valve such as a mitral valve. Valve 100 includes an outer frame assembly 110 and an inner valve assembly 140 coupled to the outer frame assembly.

[1024] Although not separately shown in the schematic illustration of outer frame assembly 110 in FIGs. 1A and 1B, outer fame assembly 110 may be formed of an outer frame 120, covered on all or a portion of its outer face with an outer covering 130, and covered on all or a portion of its inner face by an inner covering 132.

[1025] Outer frame 120 can provide several functions for prosthetic heart valve 100, including serving as the primary structure, as anchoring mechanism and/or an attachment point for a separate anchoring mechanism to anchor the valve to the native heart valve apparatus, a support to carry inner valve assembly 140, and/or a seal to inhibit paravalvular leakage between prosthetic heart valve 100 and the native heart valve apparatus.

[1026] Outer frame 120 is preferably formed so that it can be deformed (compressed and/or expanded) and, when released, return to its original (undeformed) shape. To achieve this, outer frame 120 is preferably formed of materials, such as metals or plastics, that have shape memory properties. With regards to metals, Nitinol® has been found to be especially useful since it can be processed to be austenitic, martensitic or super elastic. Other shape memory alloys, such as Cu-Zn-Al-Ni alloys, and Cu-Al-Ni alloys, may be used.

[1027] Outer frame 120 is preferably formed from a laser cut, thin-walled tube of Nitinol®. The laser cuts form regular cutouts in the thin Nitinol® tube. The tube can be expanded radially, placed on a mold or mandrel of the desired shape, heated to the martensitic temperature, and quenched. The treatment of the frame in this manner will form an open lattice frame structure, and may have a flared end or cuff at the atrium end portion 126 of outer frame 120. Outer frame 120 thus has shape memory properties and will readily revert to the memory shape at the calibrated temperature. Alternatively, outer frame 120 may be constructed from braided wire or other suitable material.

[1028] Inner valve assembly 140 is shown schematically in more detail in FIGs. 2A-2C. Inner valve assembly 140 can include an inner frame 150, an outer covering 160, and leaflets 170. In the simplified form shown schematically in FIG. 2A, inner frame 150 includes six axial posts or frame members that support outer covering 160 and leaflets 170. Leaflets 170 are attached along three of the posts, shown as commissure posts 152 in FIG. 2A, and outer covering 160 is attached to the other three posts, 154 in FIG. 2A, and optionally to commissure posts 152. In the simplified form illustrated schematically in FIG. 2A, each of outer covering 160 and leaflets 170 are formed of approximately rectangular sheets of material, which are joined together at their upper, or atrium end. The lower, ventricle end of outer covering 160 may be joined to inner covering 132 of outer frame assembly 110 (not shown in FIG. 2A), and the lower, ventricle end of leaflets 170 may form free edges, though coupled to the lower ends of commissure posts 152.

[1029] As shown in FIGs. 2B and 2C, leaflets 170 are movable between an open configuration (FIG. 2B) and a closed configuration (FIG. 2C) in which the leaflets coapt, or meet in sealing abutment.

[1030] At the lower, or ventricle end, leaflets 170 may have a smaller perimeter than outer covering 160. Thus, the free lower edges of the leaflets, between commissure posts 152

(each portion of leaflets 170 between adjacent commissure posts being referred to as a "belly" of leaflets 170) are spaced radially from the lower edge of outer covering 160. This radial spacing facilitates movement of the leaflets from the open position in FIG. 2B to the closed position in FIG. 2C, as the counter flow of blood from the ventricle to the atrium during systole can catch the free edges of the bellies and push the leaflets closed.

[1031] Outer covering 130 and inner covering 132 of outer frame 120, outer covering 160 and leaflets 170 may be formed of any suitable material, or combination of materials. In some embodiments, the tissue is optionally a biological tissue, such as a chemically stabilized tissue from a heart valve of an animal, such as a pig, or pericardial tissue of an animal, such as cow (bovine pericardium) or sheep (ovine pericardium) or pig (porcine pericardium) or horse (equine pericardium). Preferably, the tissue is bovine pericardial tissue. Examples of suitable tissue include that used in the products Duraguard®, Peri-Guard®, and Vascu-Guard®, all products currently used in surgical procedures, and which are marketed as being harvested generally from cattle less than 30 months old. Alternatively, valve leaflets 170 may optionally be made from pericardial tissue or small intestine submucosal tissue.

[1032] Synthetic materials, such as polyurethane or polytetrafluoroethylene, may also be used for valve leaflets 170. Where a thin, durable synthetic material is contemplated, e.g. for outer covering 130 or inner cover 132, synthetic polymer materials such expanded polytetrafluoroethylene or polyester may optionally be used. Other suitable materials may optionally include thermoplastic polycarbonate urethane, polyether urethane, segmented polyether urethane, silicone polyether urethane, silicone-polycarbonate urethane, and ultra-high molecular weight polyethylene. Additional biocompatible polymers may optionally include polyolefins, elastomers, polyethylene-glycols, polyethersulphones, polysulphones, polyvinylpyrrolidones, polyvinylchlorides, other fluoropolymers, silicone polyesters, siloxane polymers and/or oligomers, and/or polylactones, and block co-polymers using the same.

[1033] In another embodiment, valve leaflets 170 may optionally have a surface that has been treated with (or reacted with) an anti-coagulant, such as, without limitation, immobilized heparin. Such currently available heparinized polymers are known and available to a person of ordinary skill in the art.

[1034] As shown in FIGs. 1A, 1B, and 2A, inner valve assembly 140 may be substantially cylindrical, and outer frame assembly 110 may be tapered, extending from a

smaller diameter (slightly larger than the outer diameter of inner valve assembly 140) at a lower, ventricle portion 112 (where it is coupled to inner valve assembly 140) to a larger diameter, atrium portion 116, with an intermediate diameter, annulus portion 114 between the atrium and ventricle portions.

[1035] A tapered annular space or pocket 185 is thus formed between the outer surface of inner valve assembly 140 and the inner surface of outer frame assembly 110, open to the atrium end of valve assembly 100. When valve assembly 100 is disposed in the annulus of a native heart valve, blood from the atrium can move in and out of pocket 185. The blood can clot, forming thrombus, and the thrombus can be washed out by the flow of blood during the cyclic pumping of the heart, which is undesirable. To inhibit such washout of thrombus, and to enhance clotting, ingrowth of tissue into the surfaces of valve 100, and produce other benefits, the pocket can be covered, or enclosed, by a pocket closure 180.

[1036] Pocket closure 180 can be formed at least in part of any suitable material that is sufficiently porous to allow blood, including particularly red blood cells, to enter pocket 185, but is not so porous as to allow undesirably large thrombi to leave the pocket 185, or to allow washout of thrombus formed in the pocket 185. For example, pocket closure 180 may be formed at least in part from a woven or knit polyester fabric with apertures less than 160 μ, and preferably between 90 μ and 120 μ. It is not necessary for the entirety of pocket closure 180 to be formed of the same material, with the same porosity. For example, some portions of pocket closure 180 may be formed of a less porous, or blood impermeable, material and other portions formed of material of the porosity range noted above. It is also contemplated that a portion of the outer frame assembly 110 or the inner valve assembly 140 may be formed with an aperture that communicates with pocket 180, covered by a closure formed of material having the desired porosity, thus providing another path by which blood may enter, but thrombi are prevented from leaving, atrial pocket 185.

[1037] The outer surface of inner valve assembly 110, and/or the inner surface of outer frame assembly 140, need not by circular in cross-section as shown schematically in FIGs. 1A and 1B, but may be of non-constant radius at a given location along the central axis of valve 100. Thus, pocket 185 may not be of constant cross-section, and may not be continuous, but rather may be formed in two or more fluidically isolated, partially annular volumes. Similarly, pocket closure 180 need not be shaped as a ring with constant width as

shown schematically in FIGs. 1A and 1B, but rather than be a continues ring of varying with, a more complicated continuous shape, or may be formed in multiple, discrete sections.

[1038] Pocket closure 180 serves to trap and/or slow the flow of blood within pocket 185, reducing hemodynamic washout and increasing formation of thrombus in pocket 185. It also promotes active in-growth of native tissue into the several coverings of prosthetic heart valve 100, further stabilizing valve 100 in the native heart valve. The material forming the outer covering of inner valve assembly 140 can also be hardened or stiffened, providing better support for leaflets 170. Also, a mass of thrombus filling pocket 185 can serve as potting for inner valve assembly 140, further stabilizing the valve assembly. Greater stability for inner valve assembly 140 can provide more reliable coaption of valve leaflets 170, and thus more effective performance. The mass of thrombus can also stabilize the outer frame assembly 110 after it has been installed in, and flexibly conformed to, the native valve apparatus. This can provide a more effective seal between prosthetic heart valve 100 and the native valve apparatus, and reduce perivalvular leakage.

[1039] One possible implementation of the prosthetic heart valve shown schematically in FIGS. 1A-2C is prosthetic heart valve 200, shown in top view in FIG. 3. Prosthetic heart valve 200 includes an outer frame assembly 210 and an inner valve assembly 240 coupled to the outer frame assembly.

[1040] The outer frame assembly 210 includes an outer frame 220, covered on all or a portion of its outer face with an outer covering 230 (not visible), and covered on all or a portion of its inner face by an inner covering 232.

[1041] The inner valve assembly 240 includes an inner frame 250, an outer covering 260 (not visible), and leaflets 270. Inner frame 250 includes six axial posts or frame members that support outer covering 260 and leaflets 270. The inner valve assembly 240 may be substantially cylindrical, and outer frame assembly 210 may be tapered, extending from a smaller diameter (slightly larger than the outer diameter of inner valve assembly 240) at a lower, ventricle portion (where it is coupled to inner valve assembly 240) to a larger diameter, atrium portion, with an intermediate diameter, annulus portion between the atrium and ventricle portions.

[1042] A tapered annular space or pocket 285 (e.g., atrial thrombogenic sealing pocket) is thus formed between the outer surface of inner valve assembly 240 and the inner surface of

outer frame assembly 210, open to the atrium end of valve assembly 200. The pocket closure 280 can, for example, be formed from a circular piece of wire, or halo, with a permeable mesh fabric or tissue, that is sewn and thereby connected to the inner frame 250 and/or to the leaflets 170. The inner frame 250 has an inner wireframe structure (e.g., made of Nitinol wire) that supports the leaflets 270 sewn to the inner frame 250 and functions as a valve. The inner frame 250 in FIG. 3 includes three U-shaped wire components joined at their opened ends to form junctions. Leaflets 270 are sewn to these components to form articulating leaflets 170 creating and functioning as a prosthetic valve (e.g., prosthetic tricuspid valve; prosthetic mitral valve; prosthetic aortic valve, etc.).

[1043] Moreover, the inner frame 250 has (tether) attachment apertures 211 (not shown), for attaching tether assembly 290 (not shown). Tether assembly 290 is connected to epicardial securing pad 254 (not shown).

[1044] In operation, the inner valve assembly 240 is disposed within and secured within the outer frame assembly 210. Outer frame assembly 210 may also have in various embodiments an outer stent tissue material. Outer frame assembly 210 includes an articulating collar 246 which has a collar cover 248. Articulating collar 246 is specifically shaped to solve leakage issues arising from native structures. In particular, collar 246 is composed of an A2 segment 247, a P2 segment 249, and two commissural segments, the A1-P1 segment 251, and the A3-P3 segment 253. The collar 246 may also have in preferred embodiments a shortened or flattened or D-shaped section 262 of the A2 segment in order to accommodate and solve left ventricular outflow tract (LVOT) obstruction issues.

[1045] In operation, the prosthetic heart valve 200 may be deployed (e.g., as a prosthetic mitral valve) using catheter delivery techniques. The prosthetic heart valve 200 is compressed within a narrow catheter and delivered to the annular region of the native valve (e.g., the left atrium) with a pre-attached tether assembly 290. There, the valve 200 is pushed out of the catheter where it springs open into its pre-formed functional shape without the need for manual expansion (e.g., manual expansion using an inner balloon catheter). When the valve 200 is pulled into place, the outer frame assembly 210 is seated in the native mitral annulus, leaving the articulating collar 246 to engage the atrial floor and prevent pull-thru (where the valve 200 is pulled into the ventricle). In such embodiments, it is not necessary to cut-away the native leaflets, as has been taught in prior prosthetic efforts. Instead, the native leaflets can be used to provide a tensioning and/or sealing function around the outer frame

assembly 210. It is advantageous for the valve 200 to be asymmetrically deployed in order to address LVOT problems where non-accommodating prosthetic valves push against the A2 anterior segment of the valve (e.g., mitral valve) and close blood flow through the aorta, which anatomically sits immediately behind the A2 segment of the mitral annulus. Thus, D-shaped section 262 is deployed substantially immediately adjacent/contacting the A2 segment since the flattened D-shaped section 262 is structurally smaller and has a more vertical profile (closer to paralleling the longitudinal axis of the outer frame assembly 212) and thereby provides less pressure on the A2 segment. Once the valve 200 is properly seated, tether assembly 290 may be extended out through the apical region of the left ventricle and secured using an epicardial pad 254 or similar suture-locking attachment mechanism (not shown).

[1046] In an alternate embodiment, the tether assembly 290 is on the outer frame assembly 210, which would then have (tether) attachment apertures 213 for attaching tether assembly 290 to epicardial securing pad 254.

[1047] FIG. 4 is a top, or atrial, view of another embodiment of a prosthetic heart valve 300, illustrated without pocket closure 380. FIG. 4 shows the top of the junction tip 302 of the three U-shaped wire components of inner frame 350 joined at their opened ends to form junctions 302. Leaflets 370 are sewn to these components to form articulating leaflets 370 creating and functioning as a prosthetic valve (e.g., prosthetic tricuspid valve, prosthetic mitral valve, prosthetic aortic valve, etc.). Thrombogenic pocket 385 is shown below the plane of the collar. FIG. 4 shows vertical A2 segment 347, the P2 segment 349, and the commissural A1-P1 segment 351 and A3-P3 segment 353. FIG. 4 shows how upon deployment blood would fill the void or gap 385 between the inner valve assembly 340 and the outer frame assembly 310 of the valve 300. This blood creates a temporary fluid seal that pools in that space and provide a pressure buffer against the leakage inducing forces that accompany systolic and diastolic related intra-atrial and intra-ventricular pressure. Moreover, FIG. 4 provides an illustration of collar 346 that may, in some embodiments, include a shortened or flattened or D-shaped section 362 of the A2 segment in order to accommodate and solve left ventricular outflow tract (LVOT) obstruction issues.

[1048] FIG. 5 is a perspective side view of the P2 area 447 and A3-P3 area 453 of a self-expanding pre-configured compressible transcatheter prosthetic cardiovascular valve 400 contemplated herein, that contains as a sub-component, a self-expanding inner valve assembly 440. The valve 400 further includes as a sub-component, an outer frame assembly

410. The outer frame assembly 410 and the inner valve assembly 440 collectively define thrombogenic pockets 485. FIG. 5 shows one of the three U-shaped wire components of inner frame 450 joined at their opened ends to form junctions 402. Leaflets 470 are sewn to these components to form articulating leaflets 470 creating and functioning as a prosthetic valve. Thrombogenic pocket 485 is shown slightly below the plane of the majority of collar 446 except for the vertical A2 segment 447, the P2 segment 449, and the commissural A1-P1 segment 451 (not shown) and A3-P3 segment 453. FIG. 5 shows how upon deployment blood would fill the void or gap (i.e., pocket 485) between the inner valve assembly 440 and the outer frame assembly 410 at the A3-P3 segment 453 area of the valve 400. This blood creates a temporary fluid seal that would pool in that space and provide a pressure buffer against the leakage inducing forces that accompany systolic and diastolic related intra-atrial and intra-ventricular pressure.

[1049] FIG. 6 is an exploded view of an embodiment of the pre-configured compressible transcatheter prosthetic cardiovascular valve 400, which contains as a sub-component, a self-expanding inner frame 450. The valve 400 further includes as a sub-component, an outer frame assembly 410. The outer frame assembly 410 and the inner valve assembly 440 collectively define thrombogenic pockets 485 (not shown). The pocket 485 is formed between inner valve assembly 440, as the inside of the V-shaped or U-shaped pocket, and the outer frame assembly 410 with outer covering 430, as the outside of the V-shaped or U-shaped pocket. In this valve 400, the inner valve assembly 440 has an atrial thrombogenic sealing pocket closure 480 (not shown) (e.g., formed from a circular piece of wire, or halo), with a permeable mesh fabric or tissue, that is sewn and thereby connected to the inner frame 450 and/or to the leaflets 470. The inner frame 450 includes an inner wireframe structure made of Nitinol wire that supports leaflets 570 sewn to the inner frame 450 and functions as a valve. The inner frame 450 includes three main U-shaped wire components 407 joined at their opened ends to form junctions 402. Optionally, in some embodiments, the inner frame 450 can include additional wire cross-members or struts (e.g., more than three).

[1050] In this valve 400, the inner frame 450 is sewn with tissue and acts a cover to prevent valvular leakage. The inner valve assembly 440 includes the leaflets 470. The leaflets 470 include articulating leaflets that define a valve function. The leaflets 470 are sewn to the inner frame 450. The inner frame 450 also has (tether) attachment apertures 411 for attaching tether assembly 490. Tether assembly 490 is shown in this example as

connected to epicardial securing pad 454. In operation, the covered inner valve assembly 440 (with leaflets 470), is disposed within and secured within the outer frame assembly 410. Outer frame assembly 410 may also have in various embodiments an outer covering 460. Outer frame assembly 410 has an articulating collar 446 which has a collar cover 448. Articulating collar 446 may also have in preferred embodiments a flattened or D-shaped section 462 at the A2 area to accommodate and solve left ventricular outflow tract (LVOT) obstruction issues. Collar 446 may also have specially formed commissural segments to prevent commissural leakage at A1-P1 segment 451 and at A3-P3 segment 453

[1051] In operation, the valve 400 may be deployed as a prosthetic valve using catheter delivery techniques. The valve 400 is compressed within a narrow catheter and delivered to the annular region of the native valve (e.g., the left atrium) with a pre-attached tether assembly 490. There, the valve 400 is pushed out of the catheter where it springs open into its pre-formed functional shape without the need for manual expansion (e.g., manual expansion using an inner balloon catheter). When the valve 400 is pulled into place, the outer frame assembly 410 is seated in the native annulus (e.g., native mitral annulus), leaving the articulating collar 446 to engage the atrial floor and prevent pull-thru (where the valve is pulled into the ventricle). In such embodiments, it is not necessary to cut-away the native leaflets, as has been taught in prior prosthetic efforts. Instead, the native leaflets can be used to provide a tensioning and/or sealing function around the valve 400 (e.g., around the outer frame assembly 410). It is advantageous for the valve 400 to be asymmetrically deployed in order to address LVOT problems where non-accommodating prosthetic valves push against the A2 anterior segment of the valve (e.g., the mitral valve) and close blood flow through the aorta, which anatomically sits immediately behind the A2 segment of the annulus (e.g., mitral annulus).

[1052] Thus, D-shaped section 462 is deployed substantially immediately adjacent/contacting the A2 segment since the flattened D-shaped section 462 is structurally smaller and has a more vertical profile (closer to paralleling the longitudinal axis of the outer frame assembly 410) and thereby provides less pressure on the A2 segment. Once the valve 400 is properly seated, tether assembly 490 may be extended out through the apical region of the left ventricle and secured using an epicardial pad 454 or similar suture-locking attachment mechanism.

[1053] FIGs. 7-9 are front, bottom, and top views, respectively, of a prosthetic heart valve 500 according to an embodiment.

[1054] Prosthetic heart valve 500 is designed to replace a damaged or diseased native heart valve such as a mitral valve. Valve 500 includes an outer frame assembly 510 and an inner valve assembly 540 coupled to the outer frame assembly 510.

[1055] As shown, outer frame assembly 510 includes an outer frame 520, covered on all or a portion of its outer face with an outer covering 530, and covered on all or a portion of its inner face by an inner covering 532.

[1056] Outer frame 520 can provide several functions for prosthetic heart valve 500, including serving as the primary structure, as anchoring mechanism and/or an attachment point for a separate anchoring mechanism to anchor the valve to the native heart valve apparatus, a support to carry inner valve assembly 540, and/or a seal to inhibit paravalvular leakage between prosthetic heart valve 500 and the native heart valve apparatus.

[1057] Outer frame 520 is configured to be manipulated and/or deformed (e.g., compressed and/or expanded) and, when released, return to its original (undeformed) shape. To achieve this, outer frame 520 can be formed of materials, such as metals or plastics, that have shape memory properties. With regards to metals, Nitinol® has been found to be especially useful since it can be processed to be austenitic, martensitic or super elastic. Other shape memory alloys, such as Cu-Zn-Al-Ni alloys, and Cu-Al-Ni alloys, may be used.

[1058] As best shown in FIG. 7, outer frame assembly 510 has an upper end (e.g., at the atrium portion 516), a lower end (e.g., at the ventricle portion 512), and a medial portion (e.g., at the annulus portion 514) therebetween. The medial portion of the outer frame assembly 510 has a perimeter that is configured (e.g., sized, shaped) to fit into an annulus of a native atrioventricular valve. The upper end of the outer frame assembly 510 has a perimeter that is larger than the perimeter of the medial portion. In some embodiments, the perimeter of the upper end of the outer frame assembly 510 has a perimeter that is substantially larger than the perimeter of the medial portion. As shown best in FIG. 9, the upper end and the medial portion of the outer frame assembly 510 has a D-shaped cross-section. In this manner, the outer frame assembly 510 promotes a suitable fit into the annulus of the native atrioventricular valve.

[1059] Inner valve assembly 540 includes an inner frame 550, an outer covering 560, and leaflets 570. As shown, the inner valve assembly 540 includes an upper portion having a periphery formed with multiple arches. The inner frame 550 includes six axial posts or frame members that support outer covering 560 and leaflets 570. Leaflets 570 are attached along three of the posts, shown as commissure posts 552 (best illustrated in FIG. 8), and outer covering 560 is attached to the other three posts, 554 (best illustrated in FIG. 8), and optionally to commissure posts 552. Each of outer covering 560 and leaflets 570 are formed of approximately rectangular sheets of material, which are joined together at their upper, or atrium end. The lower, ventricle end of outer covering 560 may be joined to inner covering 532 of outer frame assembly 510, and the lower, ventricle end of leaflets 570 may form free edges 575, though coupled to the lower ends of commissure posts 552.

[1060] Although inner valve assembly 540 is shown as having three leaflets, in other embodiments, an inner valve assembly can include any suitable number of leaflets. The leaflets 570 are movable between an open configuration and a close configuration in which the leaflets 570 coapt, or meet in a sealing abutment.

[1061] At the lower, or ventricle end, leaflets 570 may have a smaller perimeter than outer covering 560. Thus, the free lower edges of the leaflets, between commissure posts 552 (each portion of leaflets 570 between adjacent commissure posts being referred to as a "belly" of leaflets 570) are spaced radially from the lower edge of outer covering 560 of the inner valve assembly 540. This radial spacing facilitates movement of the leaflets 570 from the open position to the closed position as the counterflow of blood from the ventricle to the atrium during systole can catch the free edges of the bellies and push the leaflets 570 closed (e.g., coapt).

[1062] Outer covering 530 of the outer frame assembly 510 and inner covering 532 of outer frame assembly 510, outer covering 560 of the inner valve assembly 540 and leaflets 570 of the inner valve assembly 540 may be formed of any suitable material, or combination of materials, such as those discussed above. In this embodiment, the inner covering 532 of the outer frame assembly 510, the outer covering 560 of the inner valve assembly 540, and the leaflets 570 of the inner valve assembly 540 are formed, at least in part, of porcine pericardium. Moreover, in this embodiment, the outer covering 530 of the outer frame assembly 510 is formed, at least in part, of polyester.

[1063] In another embodiment, valve leaflets 570 may optionally have a surface that has been treated with (or reacted with) an anti-coagulant, such as, without limitation, immobilized heparin. Such currently available heparinized polymers are known and available to a person of ordinary skill in the art.

[1064] Inner valve assembly 540 is be substantially cylindrical, and outer frame assembly 510 is be tapered, extending from a smaller diameter (slightly larger than the outer diameter of inner valve assembly 540) at a lower, ventricle portion 512 (where it is coupled to inner valve assembly 540) to a larger diameter, atrium portion 516, with an intermediate diameter, annulus portion 514 between the atrium and ventricle portions.

[1065] As shown, a tapered annular space or pocket 585 is thus formed between the outer surface of inner valve assembly 540 and the inner surface of outer frame assembly 510, open to the atrium end of valve assembly 500. As shown, pocket closure 580 is coupled along the periphery of the upper end of the inner valve assembly 540. In some embodiments, the pocket closure 580, or a portion thereof, can be coupled along any suitable portion of the inner valve assembly 540.

[1066] As discussed above, pocket closure 580 can be formed at least in part of any suitable material that is sufficiently porous to allow blood, including particularly red blood cells, to enter pocket 585, but is not so porous as to allow undesirably large thrombi to leave the pocket 585, or to allow washout of thrombus formed in the pocket 585. In this embodiment, pocket closure 580 is formed entirely of knit polyester (i.e., PET warp knit fabric) having apertures of about 90-120 microns. In some embodiments, a pocket closure can include apertures less than about 160 microns.

[1067] Inner frame 550 is shown in more detail in FIGs. 10-12. Specifically, FIGs. 10-12 show inner frame 550 in an undeformed, initial state (FIG. 10), a side view of the inner frame 550 in a deployed configuration (FIG. 11), and a bottom view of the inner frame 550 in a deployed configuration (FIG. 12), respectively, according to an embodiment.

[1068] In this embodiment, inner frame 550 is formed from a laser-cut tube of Nitinol®. Inner frame 550 is illustrated in FIG. 10 in an undeformed, initial state, i.e. as laser-cut, but cut and unrolled into a flat sheet for ease of illustration. Inner frame 550 can be divided into four portions, corresponding to functionally different portions of the inner frame 550 in final form: atrial portion 541, body portion 542, strut portion 543, and tether clamp portion 544.

Strut portion 543 includes six struts, such as strut 543A, which connect body portion 542 to tether clamp portion 544.

[1069] Connecting portion 544 includes longitudinal extensions of the struts, connected circumferentially by pairs of opposed, slightly V-shaped connecting members (or "micro-Vs"). Connecting portion 544 is configured to be radially collapsed by application of a compressive force, which causes the micro-Vs to become more deeply V-shaped, with the vertices moving closer together longitudinally and the open ends of the V shapes moving closer together circumferentially. Thus, connecting portion 544 can be configured to compressively clamp or grip one end of a tether, either connecting directly onto a tether line (e.g. braided filament line) or onto an intermediate structure, such as a polymer or metal piece that is in term firmly fixed to the tether line.

[1070] In contrast to connecting portion 544, atrial portion 541 and body portion 542 are configured to be expanded radially. Strut portion 543 forms a longitudinal connection, and radial transition, between the expanded body portion and the compressed connecting portion 544.

[1071] Body portion 542 includes six longitudinal posts, such as post 542A. The posts can be used to attach leaflets 570 to inner frame 540, and/or can be used to attach inner assembly 540 to outer assembly 510, such as by connecting inner frame 550 to outer frame 520. In the illustrated embodiment, the posts include openings through which connecting members (such as suture filaments and/or wires) can be passed to couple the posts to other structures.

[1072] Inner frame 550 is shown in a fully deformed, i.e. to the final, deployed configuration, in side view and bottom view in FIGs. 11 and 12, respectively.

[1073] Outer frame 520 of valve 500 is shown in more detail in FIGs. 13-15. In this embodiment, outer frame 520 is also formed from a laser-cut tube of Nitinol®. Outer frame 520 is illustrated in FIG. 13 in an undeformed, initial state, i.e. as laser-cut, but cut and unrolled into a flat sheet for ease of illustration. Outer frame 520 can be divided into a coupling portion 571, a body portion 572, and a cuff portion 573, as shown in FIG. 13.

[1074] Coupling portion 571 includes multiple openings or apertures, such as 571A, by which outer frame 520 can be coupled to inner frame 550, as discussed in more detail below.

[1075] Outer frame 520 is shown in a fully deformed, i.e. to the final, deployed configuration, in side view and top view in FIGs. 14 and 15, respectively. As best seen in FIG. 15, the lower end of coupling portion 571 forms a roughly circular opening (identified by "O" in FIG. 15). The diameter of this opening preferably corresponds approximately to the diameter of body portion 542 of inner frame 550, to facilitate coupling of the two components of valve 500.

[1076] Outer frame 520 and inner frame 550 are shown coupled together in FIGs. 16-18, in front, side, and top views, respectively. The two frames collectively form a structural support for a prosthetic valve such as valve 500. The frames support the valve leaflet structure (e.g., leaflets 570) in the desired relationship to the native valve annulus, support the coverings (e.g., outer covering 530, inner covering 532, outer covering 560) for the two frames to provide a barrier to blood leakage between the atrium and ventricle, and couple to the tether (e.g., tether assembly 590) (by the inner frame 550) to aid in holding the prosthetic valve in place in the native valve annulus by the tether connection to the ventricle wall. The outer frame 520 and the inner frame 550 are connected at six coupling points (representative points are identified as "C"). In this embodiment, the coupling points are implemented with a mechanical fastener, such as a short length of wire, passed through aperture (such as aperture 571A) in coupling portion 571 of outer frame 520 and corresponding openings in longitudinal posts (such as post 542A) in body portion 542 of inner frame 550. Inner frame 550 is thus disposed within the outer frame 520 and securely coupled to it.

[1077] A template 534 (or design pattern) for cutting, shaping, and sizing outer covering 530 of outer frame assembly 510 and/or inner covering 532 of outer frame assembly is illustrated in FIG. 19, according to an embodiment. Design pattern 534 includes attachment location indications 536a, 536b. To arrange outer covering 530 into an assembled configuration (i.e., either coupled to or ready to be coupled to outer frame 520), the two ends of the outer covering 530 are coupled together (e.g., sewn) in accordance with the attachment location indications 536a, 536b of the template 534. Similarly, inner covering 532 is arranged into an assembled configuration by coupling (e.g., sewing) its ends together in accordance with the attachment location indications 536a, 536b.

[1078] Figure 20 illustrates a design pattern of one leaflet 570 and associated portion of outer covering 560 of the inner valve assembly in its initial, pre-assembled state (i.e., not attached to inner frame 550), according to an embodiment. As discussed above, the portion

of leaflet 570 between adjacent commissure posts is referred to as a "belly" of the leaflet 570. The belly has a curved edge indicated with reference 'B' in FIG. 20. During assembly of inner valve assembly 540, the leaflet 570 is coupled to the inner frame 550 of the inner valve assembly 540. Specifically, the belly edge B of the leaflet 570, or a portion thereof, is coupled to the inner frame 550 at the arch portion of the inner frame 550. In addition, outer covering 560 is folded over a portion of the inner frame 550 (e.g., the arch portion) along the axis indicated with 'F', and coupled to a portion of the inner frame 550 (e.g., the commissure post 552) along attachment line A. As shown, a coupling area C (e.g., a stitching area), is disposed outside and adjacent to attachment line A. Coupling area C can facilitate the assembly process. Subsequently, excess leaflet material and/or excess outer covering material can be cut away and disposed of or reused. For example, material disposed between the belly edge B and the F-axis, or material in the coupling area C, may, in some embodiments, be unnecessary material and thus can be cut away from the leaflet 570 and/or outer covering 560. The assembly process can be repeated for each leaflet 570, each outer covering 560, and each commissure post 552.

[1079] The leaflets 570 and the outer covering 560 can have any suitable size, shape, material, and/or configuration. For example, in this embodiment, leaflets 570 and/or outer covering 560 is formed of fixed porcine pericardium, with a thickness of about 0.01 inches.

[1080] A schematic representation of another embodiment of a prosthetic heart valve is shown in FIGs. 21 and 22. Prosthetic heart valve 600 is designed to replace a damaged or diseased native heart valve such as a mitral valve. Valve 600 includes an outer frame assembly 610 and an inner valve assembly 640 coupled to the outer frame assembly 610.

[1081] Although not separately shown in the schematic illustration of outer frame assembly 610 in FIGs. 21 and 22, outer fame assembly 610 may be formed of an outer frame 620, covered on all or a portion of its outer face with an outer covering 630, and covered on all or a portion of its inner face by an inner covering 632. The materials and construction of the components of prosthetic heart valve 600 can be similar to those of the other embodiments described above. The following discussion focuses on the aspects of this embodiment that differ from the previous embodiments.

[1082] Inner valve assembly 640 includes an inner frame 650 (not shown), an outer covering 660 (not shown), leaflets 670 (not shown), and atrial structure 655 (e.g., halo). As

shown, the halo 655 is disposed at the atrium portion 616 of inner valve assembly 640. In such a configuration, when valve 600 is implanted into a heart of a patient, halo 655 will be disposed above the atrial floor and/or native valve annulus of the patient's heart. In this manner, the halo 655 provides extended functionality (e.g., above the native mitral valve annulus) of the inner frame 650. In some instances, for example, if prosthetic leaflets are seated too low relative to the native valve annulus, the leaflets may improperly coapt (e.g., incomplete coaptation) and/or hemodynamic leakage can occur. Thus, disposing halo 655 above the native valve annulus can provide for and/or promote complete coaptation.

[1083] Halo 655 can be formed from any suitable method and material. For example, in some embodiments, halo 655 can be formed from a substantially circular piece of wire. In such embodiments, halo 655 can be coupled to (e.g., sewn) to inner frame 650.

[1084] Outer covering 630 and inner covering 632 of outer frame 620, outer covering 660 and leaflets 670 may be formed of any suitable material, or combination of materials, such as those discussed above in connection with other embodiments.

[1085] As shown in FIGs. 21 and 22, inner valve assembly 640 may be substantially cylindrical, and outer frame assembly 610 may be tapered, extending from a smaller diameter (slightly larger than the outer diameter of inner valve assembly 640) at a lower, ventricle portion 612 (where it is coupled to inner valve assembly 640) to a larger diameter, atrium portion 616, with an intermediate diameter, annulus portion 614 between the atrium and ventricle portions.

[1086] In some embodiments, the outer surface of inner valve assembly 610, and/or the inner surface of outer frame assembly 640, need not by circular in cross-section as shown schematically in FIGs. 21 and 22, but may be of non-constant radius at a given location along the central axis of valve 600.

[1087] The atrial halo 655 functions by extending the inner frame of an inner valve assembly above the plane of atrial floor in an improved prosthetic heart valve that includes an inner frame that holds the leaflets and which is disposed within an outer frame for reducing or preventing leaking when the prosthetic heart valve is disposed within a heart valve (e.g., mitral valve, tricuspid valve).

[1088] A benefit to having leaflets within a raised leaflet silo or cylinder (e.g., halo 650) is improved blood flow and leaflet closure. It has been observed that where the leaflet cylinder is at the atrial floor, leaflet coaptation is incomplete and can result in hemodynamic leakage.

[1089] Accordingly, by providing an atrial halo or ring structure that is raised above the plane of the native annulus or atrial floor, complete leaflet coaptation is encouraged. During ventricular contraction or systole, the blood is ejected towards aortic valve to exit the heart but is also ejected towards the prosthetic mitral valve, which needs to remain closed during systole. Retrograde blood hitting the prosthetic valve leaflets cause the leaflets to close, preventing regurgitation into the left atrium. During diastole or ventricular filling, the blood needs to flow from the atrium into the ventricle without obstruction. However, when prosthetic leaflets are not properly placed or properly aligned, the leaflets can obstruct efficient filling of the ventricle or cause uneven ventricular output.

[1090] FIG. 23 is a top-view of a prosthetic heart valve 700 according to an embodiment that is one possible implementation of the prosthetic heart valve shown schematically in FIGs. 21 and 22. Prosthetic heart valve 700 includes an outer frame assembly 710, an inner valve assembly 740, and a tether assembly 790. The inner valve assembly 740 includes an inner frame 750, and outer covering 760 (not shown), leaflets 770, and atrial structure 755 (e.g., halo). Halo 755 can be formed from a circular piece of wire that can be connected to the inner frame 750 and sewn to the leaflets 770. The inner frame 750 can be made of Nitinol® wire that supports leaflets 770 sewn to the inner frame 750 and functions as a valve. The inner frame 750 shown in FIG. 23 includes three U-shaped wire components joined at their opened ends to form junctions 702. Leaflets 770 are sewn to these components to form articulating leaflets, creating and functioning as a prosthetic valve (e.g., prosthetic mitral valve, prosthetic tricuspid valve).

[1091] In some embodiments, the inner frame 750 has tether attachment apertures 711 (not shown) for attaching tether assembly 790. Tether assembly 790 is connected to epicardial securing pad 754 (not shown).

[1092] In operation, the inner frame 750 (with leaflets 770), is disposed within and secured within the outer frame 720 of the outer frame assembly 710. Outer frame 720 includes an outer covering 730 (not shown) (e.g., tissue material) and an inner covering 732

(e.g., tissue material). Outer frame 720 has an articulating collar 746 which has a collar cover 748. Articulating collar 746 is configured (e.g., shaped and sized) to solve leakage issues arising from native structures. In particular, collar 746 is composed of an A2 segment 747, a P2 segment 749, and two commissural segments, the A1-P1 segment 751, and the A3-P3 segment 753. The collar 746 may also have, in some embodiments a shortened or flattened or D-shaped section 762 of the A2 segment in order to accommodate and solve left ventricular outflow tract (LVOT) obstruction issues.

[1093] In operation, the valve 700 may be deployed as a prosthetic mitral valve using catheter delivery techniques. The entire valve 700 is compressed within a narrow catheter and delivered to the annular region of the native valve, preferably the left atrium, with a pre-attached tether apparatus. Upon delivery, the valve 700 is pushed out of the catheter where it springs open into its pre-formed functional shape without the need for manual expansion (e.g., manual expansion using an inner balloon catheter). When the valve 700 is pushed and/or pulled into place, the outer frame assembly 710 is seated in the native valve annulus (e.g., native mitral annulus), leaving the articulating collar 746 to engage the atrial floor and prevent pull-through (where the valve is pulled into the ventricle). In such embodiments, it is not necessary to cut-away the native leaflets, as has been taught in prior prosthetic efforts. Instead, the native leaflets can be used to provide a tensioning and/or sealing function around the outer frame assembly 710. It is advantageous for the valve 700 to be asymmetrically deployed in order to address LVOT problems where non-accommodating prosthetic valves push against the A2 anterior segment of the valve (e.g., mitral valve) and close blood flow through the aorta, which anatomically sits immediately behind the A2 segment of the mitral annulus. Thus, D-shaped section 762 is deployed substantially immediately adjacent/contacting the A2 segment since the flattened D-shaped section 762 is structurally smaller and has a more vertical profile (closer to paralleling the longitudinal axis of the outer stent) and thereby provides less pressure on the A2 segment. Once the valve 700 is properly seated, tether assembly 790 may be extended out through the apical region of the left ventricle and secured using an epicardial pad 754 or similar suture-locking attachment mechanism (not shown).

[1094] In an alternate embodiment, the tether assembly 790 is on the outer frame 720, which would then have tether attachment apertures 713 for attaching tether assembly 790 to epicardial securing pad 754.

[1095] FIG. 24 is a perspective view of the A1-P1 side of the prosthetic heart valve 700 according to an embodiment. FIG. 24 shows one of the three U-shaped wire components of inner frame 750 joined at their opened ends to form junctions 702. Although three U-shaped wire components are shown, in other embodiments, any suitable number of U-shaped wire components can be joined at their opened ends to form junctions. Similarly, in some embodiments, the wire components of inner frame 750 can by any suitable shape or size. Leaflets 770 are sewn to these components to form articulating leaflets 770 creating and functioning as a prosthetic heart valve (e.g., mitral valve, tricuspid valve). Atrial halo 755 is shown with the plane of the circular wire above the plane of the majority of collar except for the vertical A2 segment 747, the P2 segment 749, and the commissural A1-P1 segment 751 an A3-P3 segment 753. FIG. 26 shows how upon deployment blood would fill the void or gap 707 between the inner frame 750 and the outer frame 720 at the A1-P1 segment 751 of the valve 700. This blood creates a temporary fluid seal that would pool in that space and provide a pressure buffer against the leakage inducing forces that accompany systolic and diastolic related intra-atrial and intra-ventricular pressure.

[1096] FIG. 25 is a perspective view of the A3-P3 side 753 of prosthetic heart valve 700 according to an embodiment. FIG. 25 shows one of the three U-shaped wire components of inner frame 750 joined at their opened ends to form junctions 702. Leaflets 770 are sewn to these components to form articulating leaflets 770 creating and functioning as a prosthetic tricuspid valve. Atrial halo 755 is shown with the plane of the circular wire above the plane of the majority of collar except for the vertical A2 segment 747, the P2 segment 749, and the commissural A1-P1 segment 751 and A3-P3 segment 753. FIG. 25 shows how upon deployment blood would fill the void or gap 708 between the inner frame 750 and outer frame 720 at the A3-P3 segment 753 area of the valve 700. This blood creates a temporary fluid seal that would pool in that space and provide a pressure buffer against the leakage inducing forces that accompany systolic and diastolic related intra-atrial and intra-ventricular pressure.

[1097] FIG. 26 is an exploded view of prosthetic heart valve 700 according to an embodiment. In this valve 700, the inner frame 750 is sewn with tissue 706 and acts a cover to prevent valvular leakage. The inner frame 750 contains the leaflets 770 comprised of articulating leaflets that define a valve function. The leaflets 770 are sewn to the inner frame 750. The inner frame 750 also has tether attachment apertures 711 for attaching tether

assembly 790. Tether assembly 790 is shown in this example as connected to epicardial securing pad 754. In operation, the covered inner frame 750 (e.g., covered with outer covering 760) (with leaflets 770), is disposed within and secured within the outer frame 720 of the outer frame assembly 710. Outer frame 720 may also have in various embodiments a covering (e.g., outer covering 730). Outer frame 720 has an articulating collar 746 which has a collar cover 748. Articulating collar 746 may also have in some embodiments a D-shaped section 762 to accommodate and solve left ventricular outflow tract (LVOT) obstruction issues.

[1098] In operation, the valve 700 may be deployed as a prosthetic valve (e.g., mitral valve) using catheter delivery techniques. The entire valve 700 is compressed within a narrow catheter and delivered to the annular region of the native valve, such as, for example, with a pre-attached tether assembly 790. There, the valve 700 is pushed out of the catheter where it springs open into its pre-formed functional shape without the need for manual expansion (e.g., manual expansion using an inner balloon catheter). When the valve 700 is pushed and/or pulled into place, the outer frame assembly 710 is seated in the native mitral annulus, leaving the articulating collar 746 to engage the atrial floor and prevent pull-through (where the valve is pulled into the ventricle). In such embodiments, it is not necessary to cut-away the native leaflets, as has been taught in prior prosthetic efforts. Instead, the native leaflets can be used to provide a tensioning and/or sealing function around the outer frame assembly 710. It is advantageous for the valve 700 to be asymmetrically deployed in order to address LVOT problems where non-accommodating prosthetic valves push against the A2 anterior segment of the valve (e.g., the mitral valve) and close blood flow through the aorta, which anatomically sits immediately behind the A2 segment of the mitral annulus. Thus, D-shaped section 762 is deployed immediately adjacent/contacting the A2 segment since the flattened D-shaped section 762 is structurally smaller and has a more vertical profile (closer to paralleling the longitudinal axis of the outer stent) and thereby provides less pressure on the A2 segment. Once the valve 700 is properly seated, tether assembly 790 may be extended out through the apical region of the left ventricle and secured using an epicardial pad 754 or similar suture-locking attachment mechanism.

[1099] Any of the prosthetic heart valve embodiments described above can incorporate additional structural features to enhance their performance. The structural features are

discussed below with reference to prosthetic heart valve 800, illustrated schematically in perspective and side views in FIGs. 27 and 28, respectively.

[1100] As shown, the outer frame 820 has an atrium portion 826, a ventricle portion 822, and an annulus portion 824 disposed between the atrium portion 826 and the ventricle portion 822. The inner frame 850 of the inner valve assembly 840 has a first end and a second end. The inner valve assembly 840 can be coupled to the outer frame 820 by a connection between the first end of the inner frame 850 and the ventricle portion 812 of the outer frame assembly 810. The inner frame assembly 840 can extend from the connection towards the atrium portion 816 of the outer frame assembly 810. The inner frame assembly 840 and the outer frame assembly 810 can diverge from the connection towards the atrium portion 816 of the outer frame assembly 810. The annulus portion 814 of the outer frame assembly 810 can be spaced radially from the inner valve assembly 840 and radially inwardly deflectable towards the inner valve assembly 840 to accommodate a natural heart valve annulus in the annulus portion 814.

[1101] The outer frame assembly 810 can be shaped and sized in any suitable manner to facilitate a proper fit into a native heart valve. For example, as shown, the outer frame 820 can be shaped and sized to resemble, at least in part, an hourglass shape. Specifically, the annulus portion 814 of outer frame assembly 810 varies from an intermediate diameter (or perimeter) near ventricle portion 812 to a smaller diameter (or perimeter) near the middle of annulus portion 814, to a larger diameter (or perimeter) near atrium portion 816. Thus, annulus portion 814 has an hourglass shape. Ventricle portion 812 has a maximum diameter larger than a maximum diameter of annulus portion 816. The ventricle portion has a minimum diameter smaller than a minimum diameter of the annulus portion 814.

[1102] The diameters and/or perimeters for each portion of the outer frame 820 can be selected based on the size and/or shape of a native heart valve into which prosthetic heart valve 800 is to be implanted. For example, the minimum diameter of the annulus portion 824 of the outer frame 820 can be smaller than that of the native valve annulus. Thus, in such a configuration, the diameters of the ventricle portion 822, annulus portion 824, and atrium portion 826 can collectively promote a suitable fit (e.g., a snug, secure fit) of the prosthetic heart valve 800 in a native heart valve. In this manner, the outer frame 820 can be configured to optimize securement and sealing between the prosthetic heart valve 800 (particularly outer

frame assembly 810) and a native valve annulus of a native heart valve. Thus, such a configuration minimizes the likelihood of paravalvular leaks.

[1103] Although the outer frame 820 is shown to have a circular cross-section, in some embodiments, the outer frame 820 can by any suitable shape or size. For example, in some embodiments, the outer frame 820 can have a D-shape cross-section. In this manner, the outer frame 820 can have a shape configured to correspond to (e.g., mate with) a native heart valve annulus.

[1104] In addition to, or instead of, outer frame 820 and/or outer frame assembly 810 with the hourglass shape described above, valve 800, or in some instances, outer frame 820 and/or outer frame assembly 810, in particular, can be formed to provide stiffness, such as resistance to hoop compression, that is varied spatially, i.e., axially and/or circumferentially.

[1105] In this manner, a suitable stiffness profile can be arranged such that the valve 800 promotes a desirable shape and sealing region when disposed in a native heart valve, thus minimizing the likelihood of paravalvular leaks and undesired movement of the valve. Similarly stated, valve 800 can be configured to have a stiffness profile suitable to cause desirable deformation of the native heart valve annulus (i.e., the sealing region), and thus, proper implantation of valve 800.

[1106] A desired stiffness profile of prosthetic valve 800 can be achieved by varying properties, characteristics, and/or the arrangement of the outer frame assembly 810 and the inner valve assembly 840. For example, the outer frame 820 and/or the inner frame 850 can contain portions of varying material states. For example, a first portion of outer frame 820 can be in an elastic state, while a second portion of outer frame 820 is in a super-elastic state. Similarly, for example, portions of the outer frame 820 and/or the inner frame 850 can be in an austenitic state and/or a martensitic state (e.g., a stress induced martensitic state). In this manner, portions of valve 800 can be configured to suitably mate with a native valve annulus, thus improving sealing and limiting paravalvular leaks.

[1107] In addition, the outer frame assembly 810 and/or inner valve assembly 840 can have varying widths, thicknesses, shapes (e.g., longitudinal shape), angles (e.g., angle of attachment between inner valve assembly 840 and outer frame assembly 810), and the like. In some embodiments, the outer covering 830, inner covering 832, outer covering 860, and/or

pocket closure 880 can be configured to determine, at least in part, the stiffness profile and/or shape of valve 800 (e.g., based on sewing pattern).

[1108] FIGs. 29B, and 29C and 29D illustrate axial and circumferential stiffness profiles, respectively, of prosthetic heart valve 800 (shown in FIG. 29A) according to an embodiment. The stiffness of heart valve 800 can vary axially and/or circumferentially in any suitable manner. For example, FIG. 29B represents an axial stiffness profile of valve 800. Specifically, as shown, the Z-axis represents an axial location on valve 800 (e.g., a location of the stiffness value). The S-axis represents a range of stiffness (or range of stiffness values), increasing from left (starting at origin O) to right.

[1109] Further to this example, as illustrated in FIG. 29B, in some embodiments, locations near the ventricle portion 822 (e.g., indicated as B in FIG. 29A) of the outer frame 822 can have a larger stiffness value, locations near the annulus portion 824 of the outer frame 820 can have a smaller stiffness value relative to the ventricle portion 822 (e.g., to facilitate cooperation with the native valve annulus), and locations near the atrium portion 826 (e.g., indicated as A in FIG. 29A) of the outer frame 820 can have a smaller, the same, or larger stiffness value (illustrated by the dotted line) than the stiffness value near the annulus portion 824. In this manner, the outer frame assembly 810 can be relatively more compliant in hoop compression in a central, annulus portion 814, than at the ventricle portion 812. Thus, in use, the prosthetic valve 800 can seat securely in the annulus of the native heart valve while imposing minimal loads on the inner valve assembly 840 that could degrade the performance of the valve leaflets 870. Although, for ease of illustration, the stiffness profile shown in FIG. 29B includes linear portions, in some embodiments, the stiffness profile can include non-linear portions instead of or in addition to the linear portions as shown.

[1110] Similarly, the stiffness of heart valve 800, or portions of heart valve 800, can have varying degrees of stiffness circumferentially, as illustrated by the stiffness profiles shown in FIGs. 29C and 29 D. By way of example, FIG. 29C illustrates a circumferential stiffness profile at axial location A (as shown by reference 'A' in FIG. 29A). Similarly, FIG. 29D illustrates a circumferential stiffness profile at axial location B (as shown by reference 'B' in FIG. 29A). As the profile extends radially from the origin (indicated as 'O'), the stiffness value increases.

[1111] Thus, as shown in FIG. 29C, the stiffness at S1 (90 degrees) is greater than the stiffness at S2 (270 degrees). Further to this example, in some embodiments, the circumferential portion from zero to 180 degrees can represent a relatively flat portion of an outer frame 820 of the outer frame assembly 810 having a D-shape configuration, and 180 to 360 degrees can represent a relatively curved portion of the outer frame 820 having the D-shape configuration.

[1112] In a similar fashion, FIG. 29D illustrates a circumferential stiffness profile at axial location B (as shown by reference 'B' in FIG. 29A). As shown, axial location B has a different stiffness profile than axial location A. Such variability in design, as discussed above, can provide for advantageous customization of heart valve 800, and cooperation of heart valve 800 with a native heart valve. Similar to FIG. 29C, FIG. 29D illustrates the stiffness at one side of valve 800 being be greater than a stiffness at another side of the valve 800. In this manner, in some instances, a portion of valve 800 that will experience greater forces from the native heart valve annulus can have a smaller stiffness value (e.g., more compliant) than a portion of the valve 800 that will experience smaller or fewer forces, thus optimizing the cooperation of the prosthetic heart valve 800 with the native heart (particularly the native heart valve annular region).

[1113] While various embodiments have been described above, it should be understood that they have been presented by way of example only, and not limitation, and as such, various changes in form and/or detail may be made. Any portion of the apparatus and/or methods described herein may be combined in any suitable combination, unless explicitly expressed otherwise. Where methods and/or schematics described above indicate certain events occurring in certain order, the ordering of certain events and/or flow patterns may be modified. Additionally, certain events may be performed concurrently in parallel processes when possible, as well as performed sequentially.

What is claimed is:

1. A prosthetic heart valve comprising:

an outer frame assembly having an atrium end configured to be disposed in an atrium of a heart and an opposite, ventricle end;

an inner valve assembly,

the inner valve assembly disposed within and coupled to the outer frame, the inner valve assembly and the outer frame assembly defining therebetween an annular region, the inner valve assembly and the outer frame assembly configured to substantially prevent blood flow therebetween through the annular region;

a pocket closure coupled between the outer frame assembly and the inner valve assembly and enclosing therewith a portion of the annular space, forming a thrombus retaining pocket, at least a portion of the pocket closure formed of a material having a porosity that is sufficiently large to allow red blood cells to pass through the pocket closure into the pocket and that is sufficiently small to prevent thrombus formed from the red blood cells to pass through the pocket closure from the pocket.

2. The prosthetic heart valve of claim 1, wherein the inner valve assembly includes:

an inner frame;

a covering disposed about the periphery of the inner frame, defining in part the annular region, and formed of a material substantially impermeable to blood; and

a valve leaflet assembly supported on the inner frame.

3. The prosthetic heart valve of claim 1, wherein the outer valve assembly includes:

an outer frame; and

an inner covering disposed about the inner periphery of the outer frame, defining in part the annular region, and formed of a material substantially impermeable to blood.

4. The prosthetic heart valve of claim 1, wherein:

the inner valve assembly includes:

an inner frame;

a covering disposed about the periphery of the inner frame, defining in part the annular region, and formed of a material substantially impermeable to blood; and

a valve leaflet assembly supported on the inner frame; and

the outer valve assembly includes:

an outer frame; and

an inner covering disposed about the inner periphery of the outer frame, defining in part the annular region, and formed of a material substantially impermeable to blood,

the covering of the inner frame coupled to the inner covering of the outer frame to close the ventricle end of the annular region, opposite the pocket covering.

5. The prosthetic heart valve of claim 1, wherein the inner valve assembly includes an atrium end having a periphery formed with multiple arches and wherein the pocket closure is coupled along the periphery of the upper end.

6. The prosthetic heart valve of claim 1, wherein the outer frame assembly has an annulus portion between the atrium end and the ventricle end, the annulus portion having a perimeter that is sized to fit into an annulus of an atrioventricular valve, the atrium end of the outer frame assembly having a perimeter that is substantially larger than the perimeter of the medial portion, each of the atrium end and the annulus portion being D-shaped in cross section.

7. The prosthetic heart valve of claim 1, wherein the inner frame is formed of an expanded shape memory metal.

8. The prosthetic heart valve of claim 1, wherein the outer frame is formed of an expanded shape memory metal.

9. The prosthetic heart valve of claim 1, wherein the pocket closure is formed at least in part of a material having a pore size less than about 160 μ.

10. The prosthetic heart valve of claim 9, wherein the pocket closure is formed at least in part of a material having a pore size between about 90 μ and about 120 μ.

11. The prosthetic heart valve of claim 1, wherein the pocket closure is formed at least in part of a material that is one of a woven material, a knit material, or a non-woven material.

12. A prosthetic heart valve comprising:

an outer frame assembly having an atrium portion, a ventricle portion, and an annulus portion between the atrium portion and the ventricle portion,

the ventricle portion having a maximum perimeter larger than a maximum perimeter of the annulus portion,

the ventricle portion having a minimum perimeter smaller than a minimum perimeter of the annulus portion,

the annulus portion have an hourglass shape with a minimum perimeter disposed between a larger perimeter near the atrium portion and a larger perimeter near the ventricle portion;

an inner valve assembly including an inner frame having an atrium end and a ventricle end,

the inner valve assembly coupled to the outer frame assembly by a connection between the ventricle end of the inner frame and the ventricle portion of the outer frame assembly,

the inner frame assembly extending from the connection towards the atrium portion of the outer frame assembly,

the inner frame assembly and the outer frame assembly diverging from the connection towards the atrium portion of the outer frame assembly,

the annulus portion of the outer frame assembly being spaced radially from the inner valve assembly and radially inwardly deflectable towards the inner valve assembly to accommodate in the annulus portion a natural valve annulus having a perimeter smaller than the minimum perimeter of the annulus portion.

13. The prosthetic heart valve of claim 12, wherein each of the atrium portion and the annulus portion of the outer frame assembly is D-shaped in cross section.

14. The prosthetic heart valve of claim 12, wherein the inner frame is formed of an expanded shape memory metal.

15. The prosthetic heart valve of claim 12, wherein the outer frame is formed of an expanded shape memory metal.

16. A prosthetic heart valve comprising:

an outer frame assembly having an atrium portion, a ventricle portion, and an annulus portion

between the atrium portion and the ventricle portion;

an inner valve assembly including an inner frame having an atrium end and a ventricle end,

the inner valve assembly coupled to the outer frame assembly by a connection between the ventricle end of the inner frame and the ventricle portion of the outer frame assembly,

the inner frame assembly extending from the connection towards the atrium portion of the outer frame assembly,

the inner frame assembly and the outer frame assembly diverging from the connection towards the atrium portion of the outer frame assembly,

the annulus portion and the atrium portion of the outer frame assembly being spaced radially from the inner valve assembly and being radially inwardly deflectable towards the inner valve assembly,

each of the atrium portion, the ventricle portion, and the annulus portion of the outer frame assembly having a stiffness in resistance to radial compression, the stiffness of the annulus portion being less than the stiffness of the ventricle portion.

17. The prosthetic heart valve of claim 16, wherein each of the atrium portion and the annulus portion of the outer frame assembly is D-shaped in cross section.

18. The prosthetic heart valve of claim 16, wherein the inner frame is formed of an expanded shape memory metal.

19. The prosthetic heart valve of claim 16, wherein the outer frame is formed of an expanded shape memory metal.

20. The prosthetic heart valve of claim 16, wherein the stiffness of the ventricle portion of the outer frame assembly is greater than the stiffness of the annulus portion.

21. The prosthetic heart valve of claim 16, wherein the stiffness of the ventricle portion of the outer frame assembly is less than the stiffness of the annulus portion.

22. A self-expanding pre-configured compressible transcatheter prosthetic cardiovascular valve that comprises an atrial thrombogenic sealing pocket cover disposed between a self-expanding inner wire frame and a self-expanding annular tissue-covered outer wire frame, said inner wire frame having articulating tissue leaflets that define a valve function, said inner

wire frame is disposed within the outer wire frame, said outer wire frame having an articulating circumferential collar, forming a multi-component prosthetic valve assembly for anchoring within the mitral valve or tricuspid valve of the heart.

23. A method of treating a disease or disorder of a heart valve in a patient, which comprises the step of surgically deploying the prosthetic heart valve according to claim 22 into the native annulus of the heart valve of the patient.

24. The method of claim 22, wherein the native annulus is the mitral valve annulus or the tricuspid valve annulus.

25. A self-expanding pre-configured compressible transcatheter prosthetic cardiovascular valve that comprises an atrial halo fluid sealing device mounted on a self-expanding inner wire frame having a leaflet structure comprised of articulating leaflets that define a valve function, wherein said inner wire frame is disposed within a self-expanding annular tissue-covered outer wire frame, said outer wire frame having an articulating collar, together forming a multi-component prosthetic valve assembly for anchoring within the mitral valve or triscuspid valve of the heart.

26. A method of treating a disease or disorder of a heart valve in a patient, which comprises the step of surgically deploying the prosthetic heart valve according to claim 26 into the native annulus of the heart valve of the patient.

27. The method of claim 25, wherein the native annulus is the mitral valve annulus or the tricuspid valve annulus.

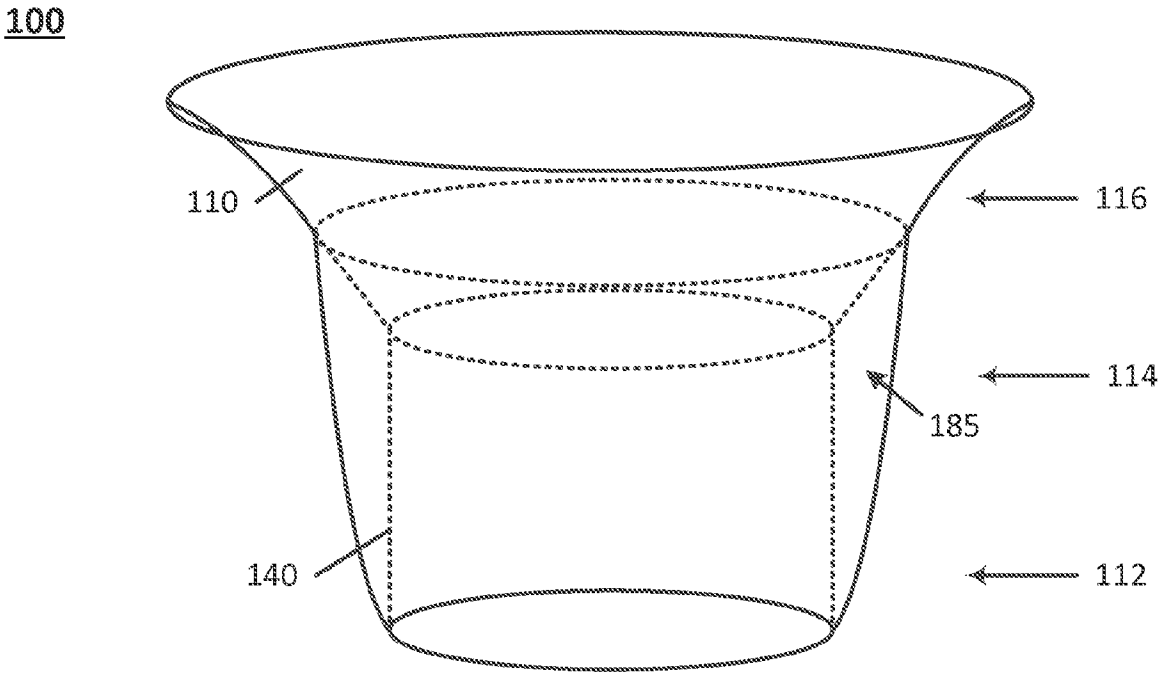

FIG. 1A

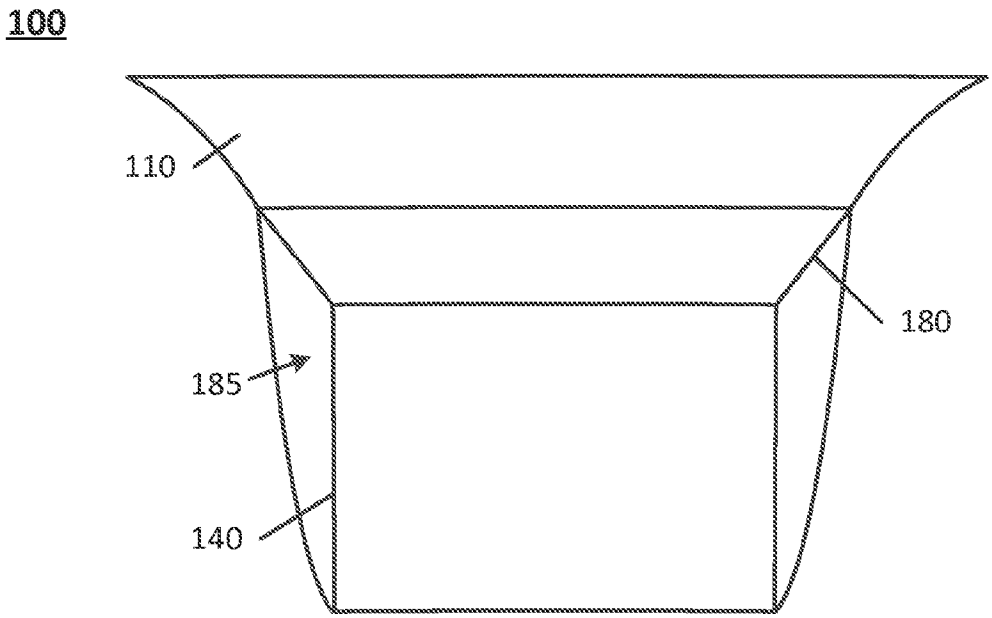

FIG. 1B

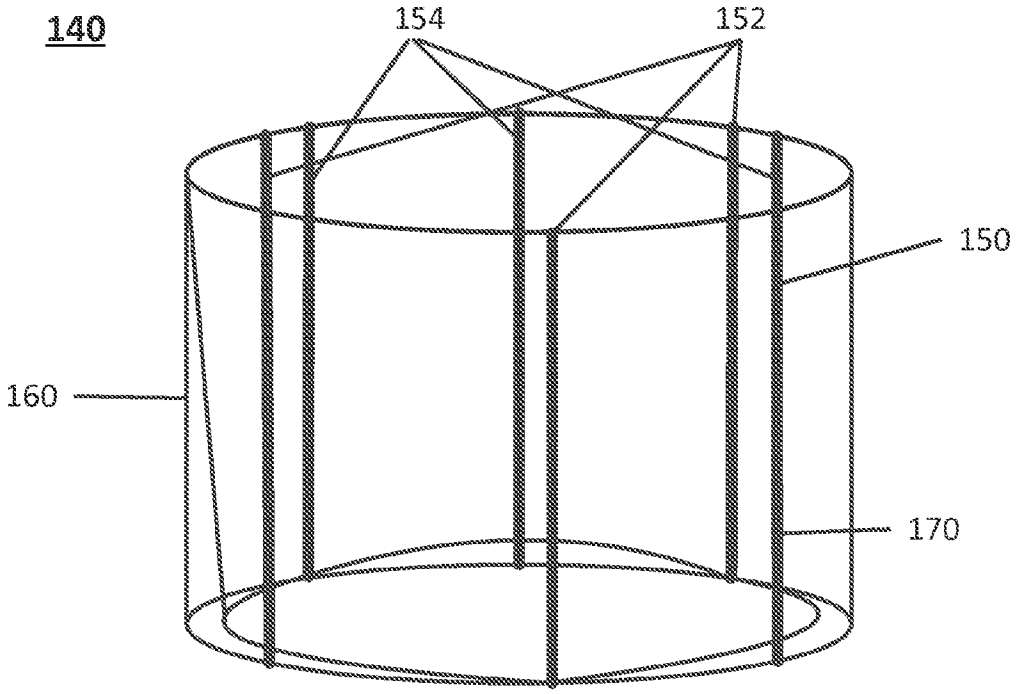

FIG. 2A

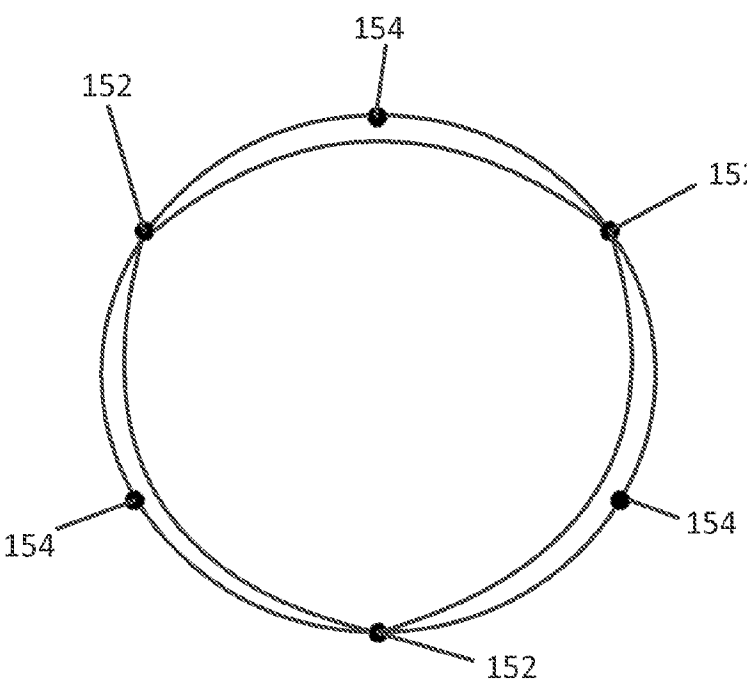

FIG. 2B

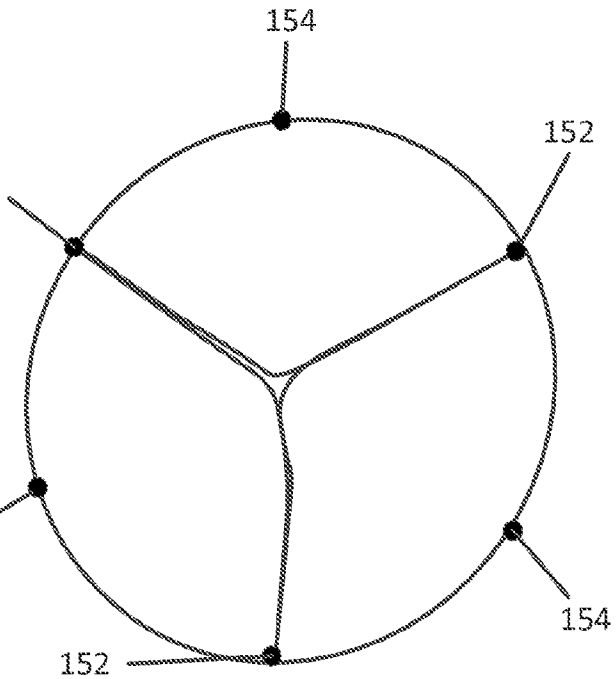

FIG. 2C

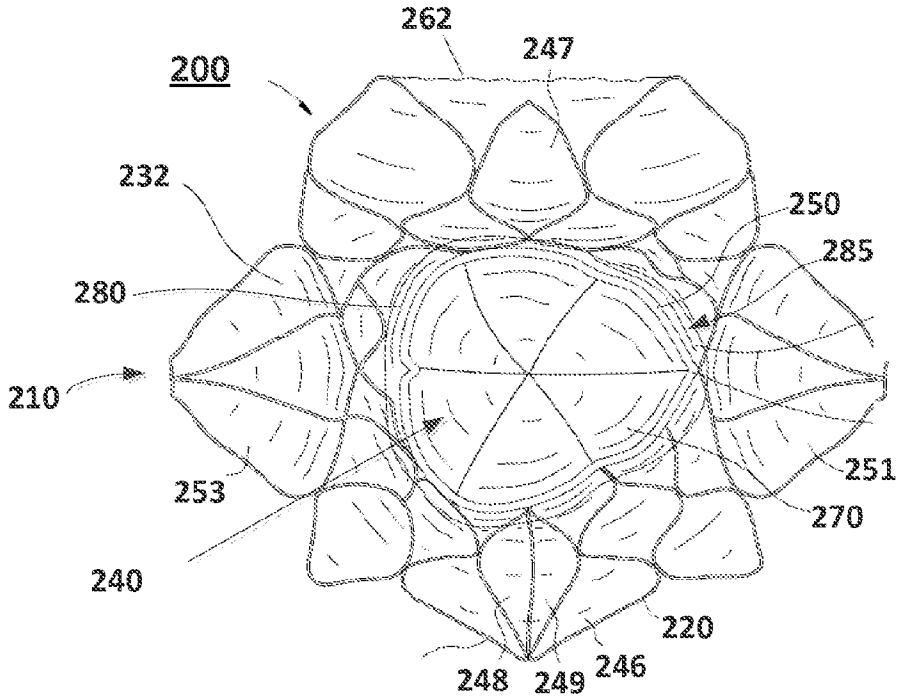
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FIG. 3

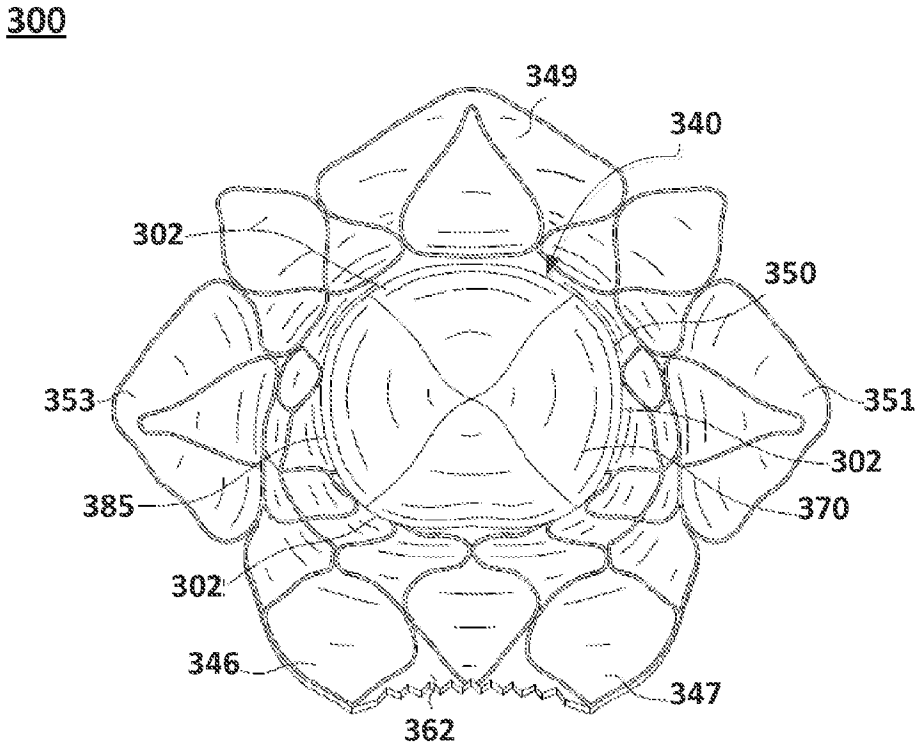
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FIG. 4

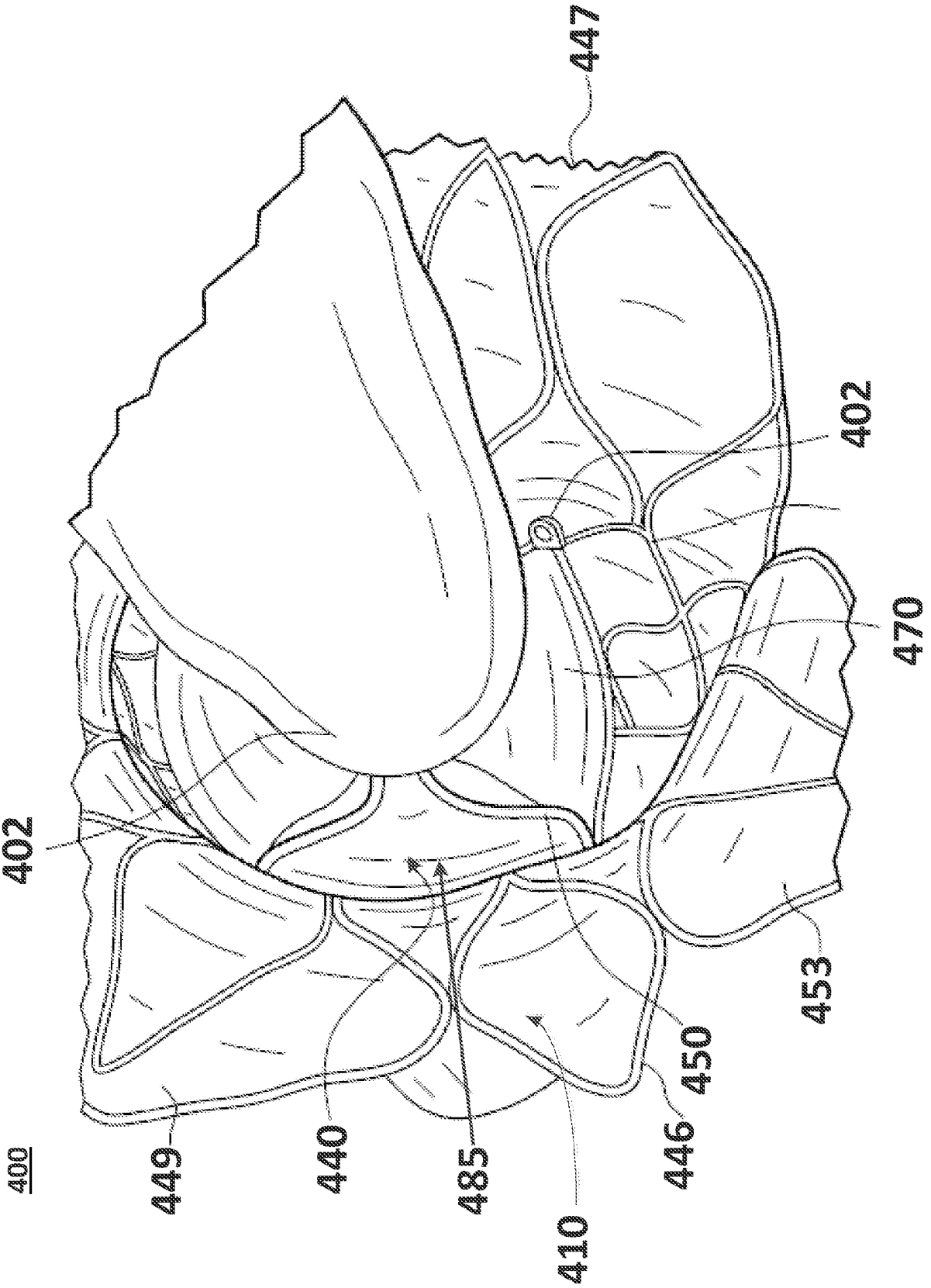

FIG. 5

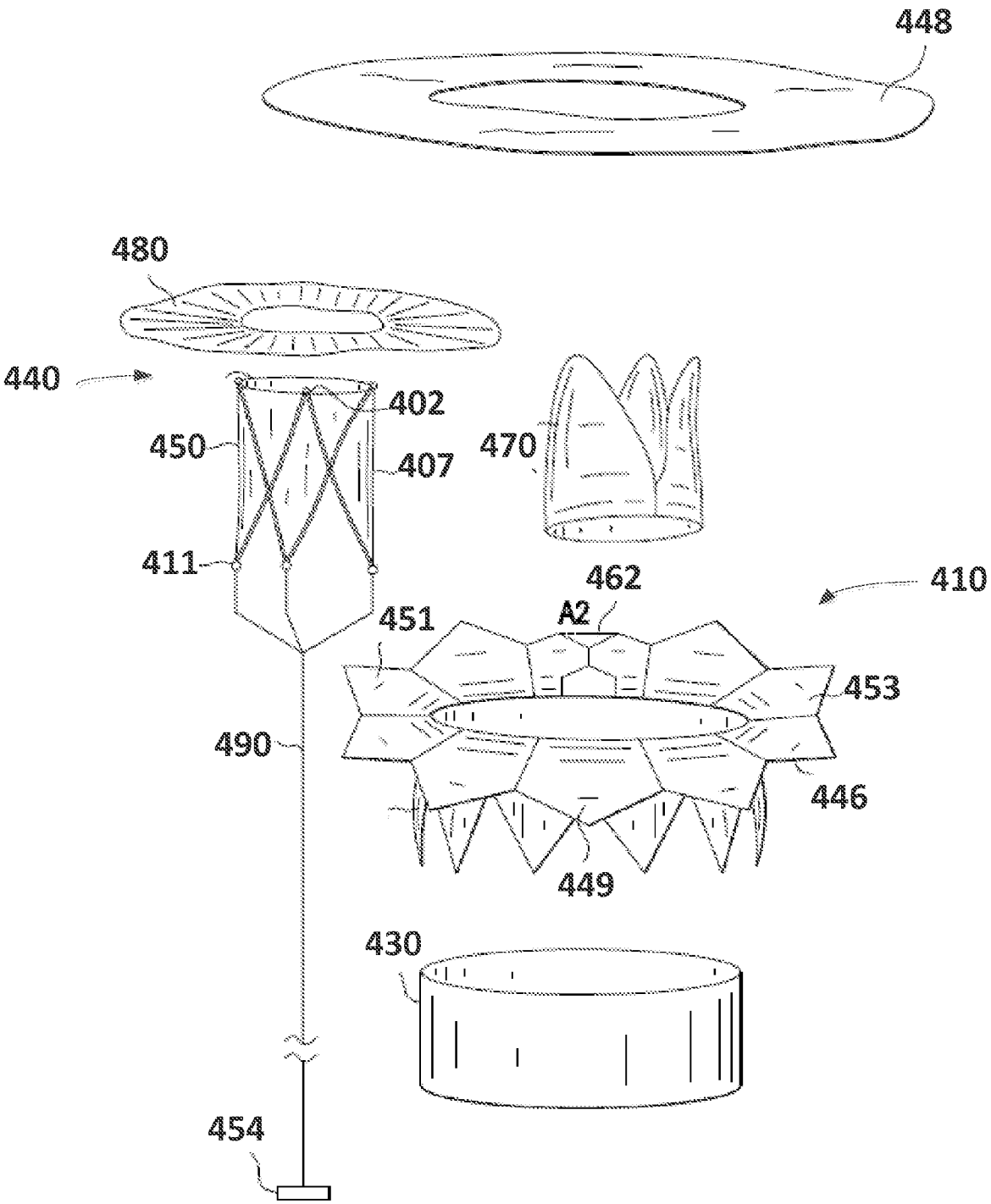
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FIG. 6

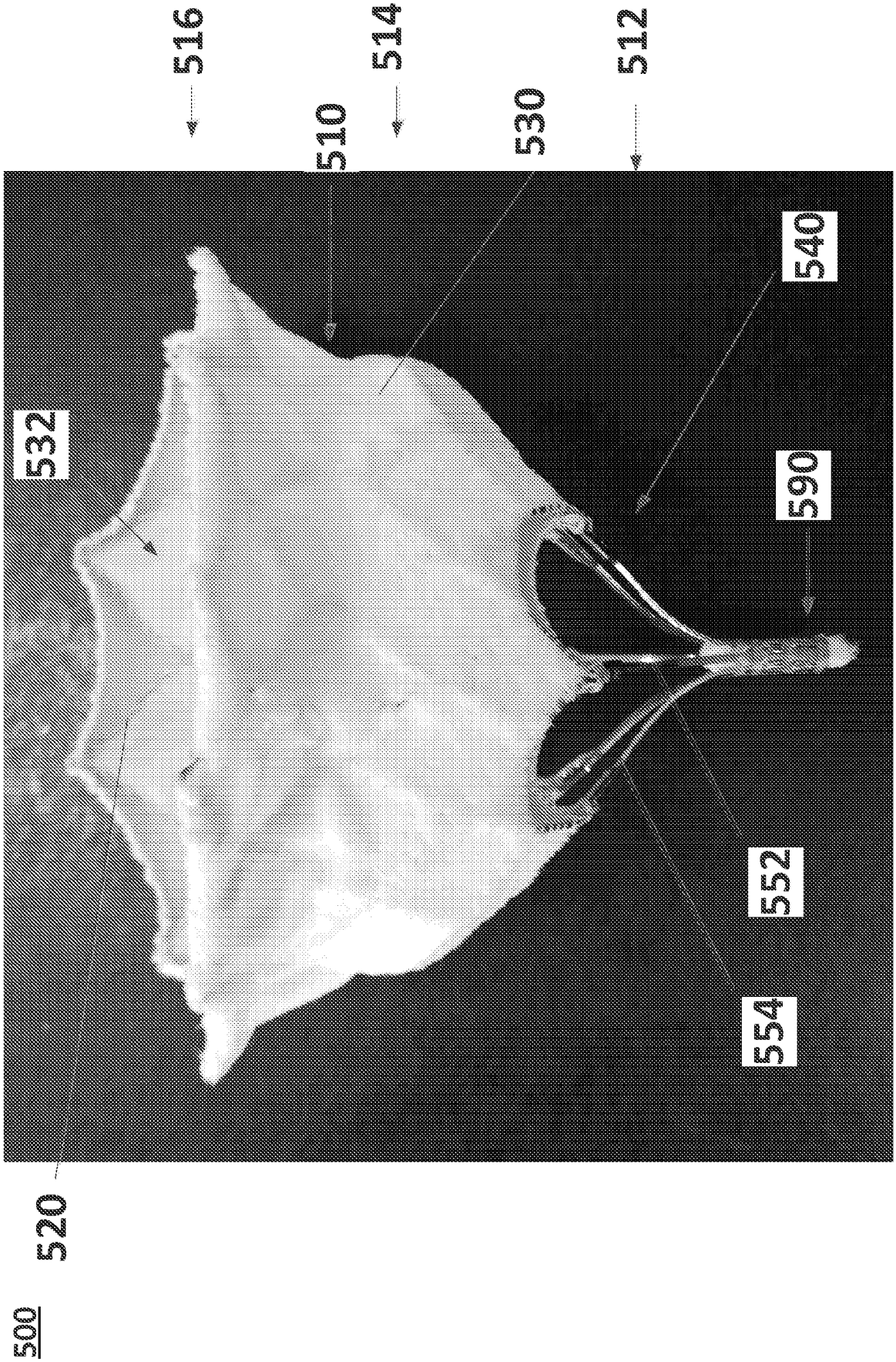


FIG. 7

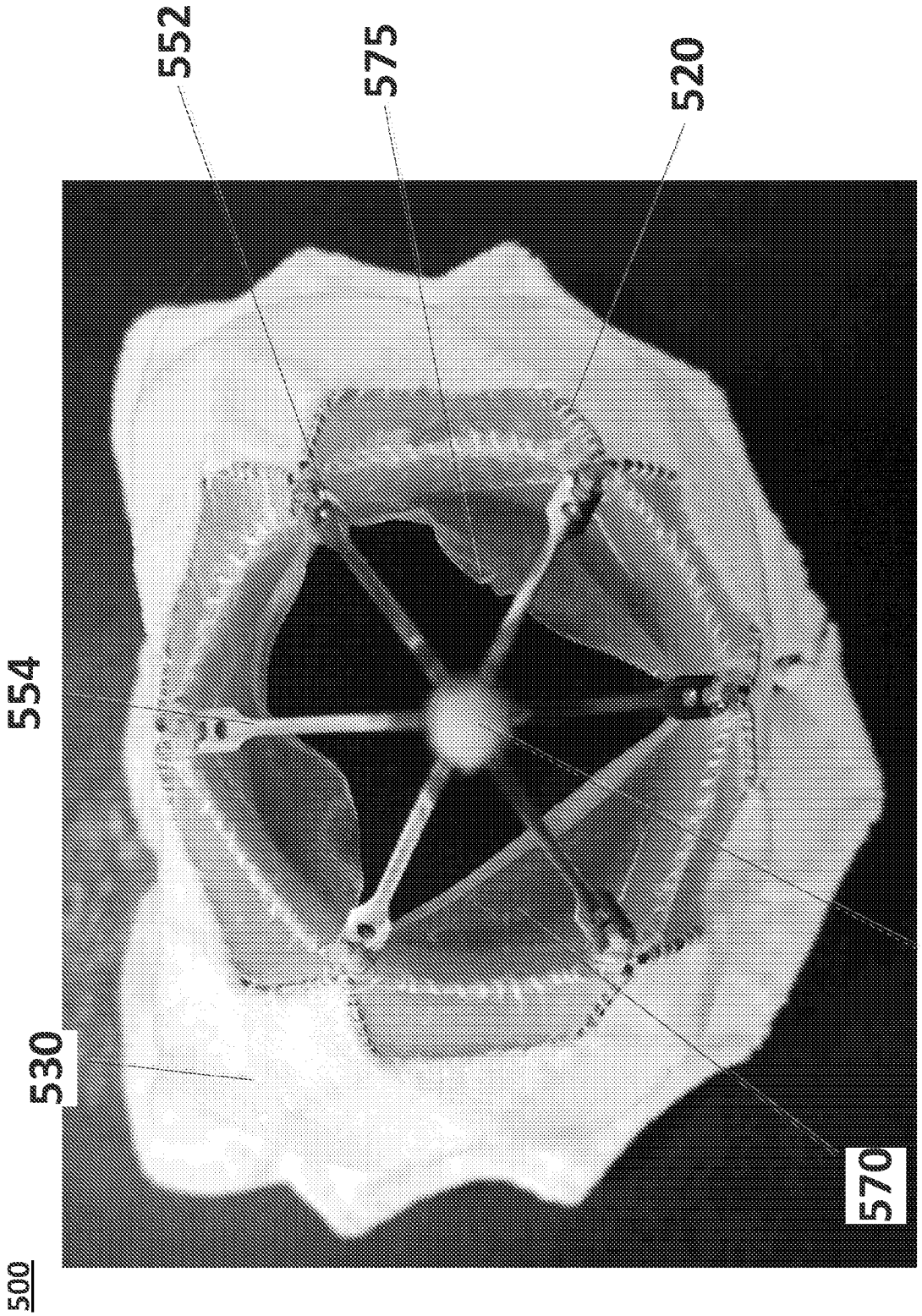


FIG. 8

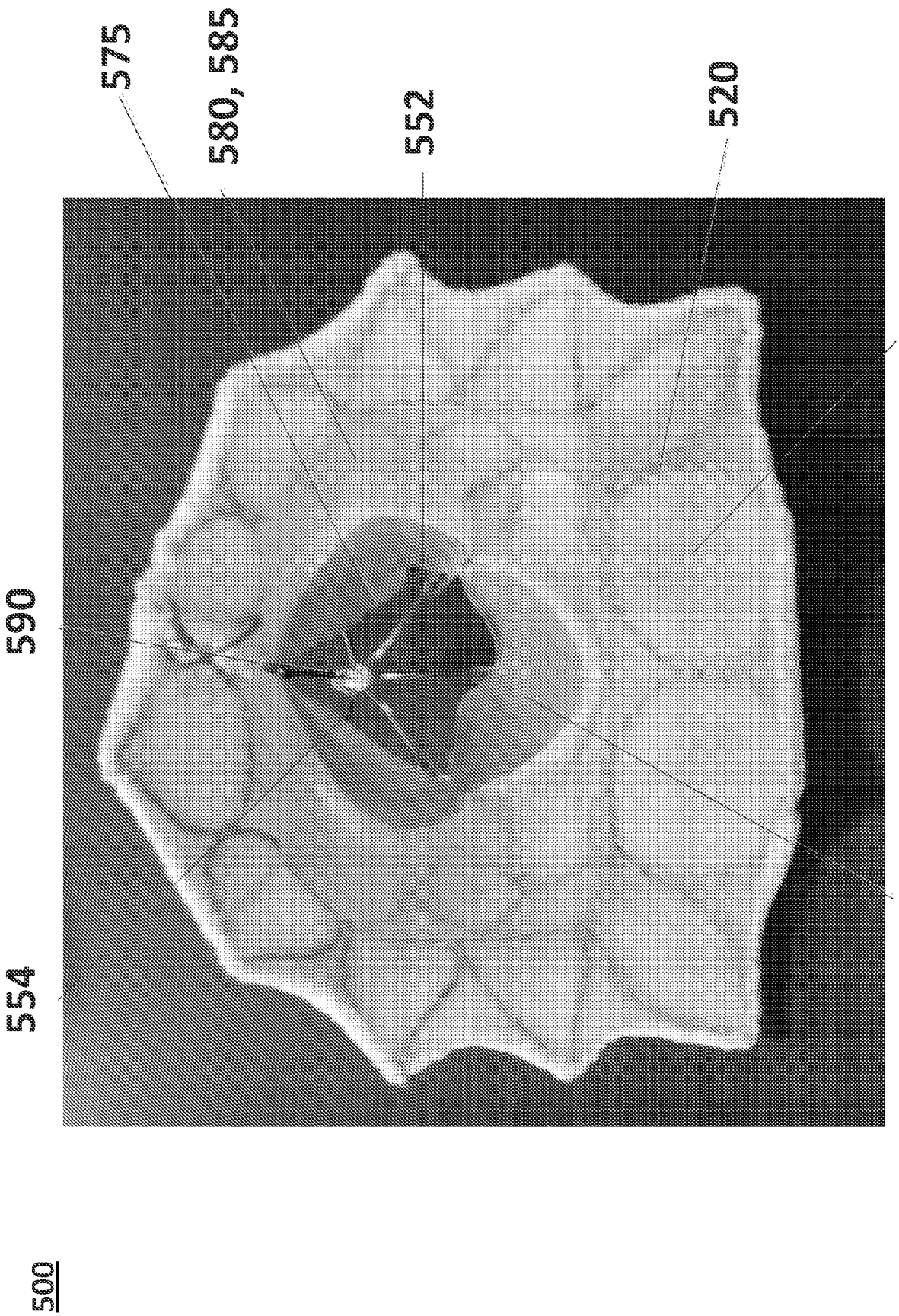
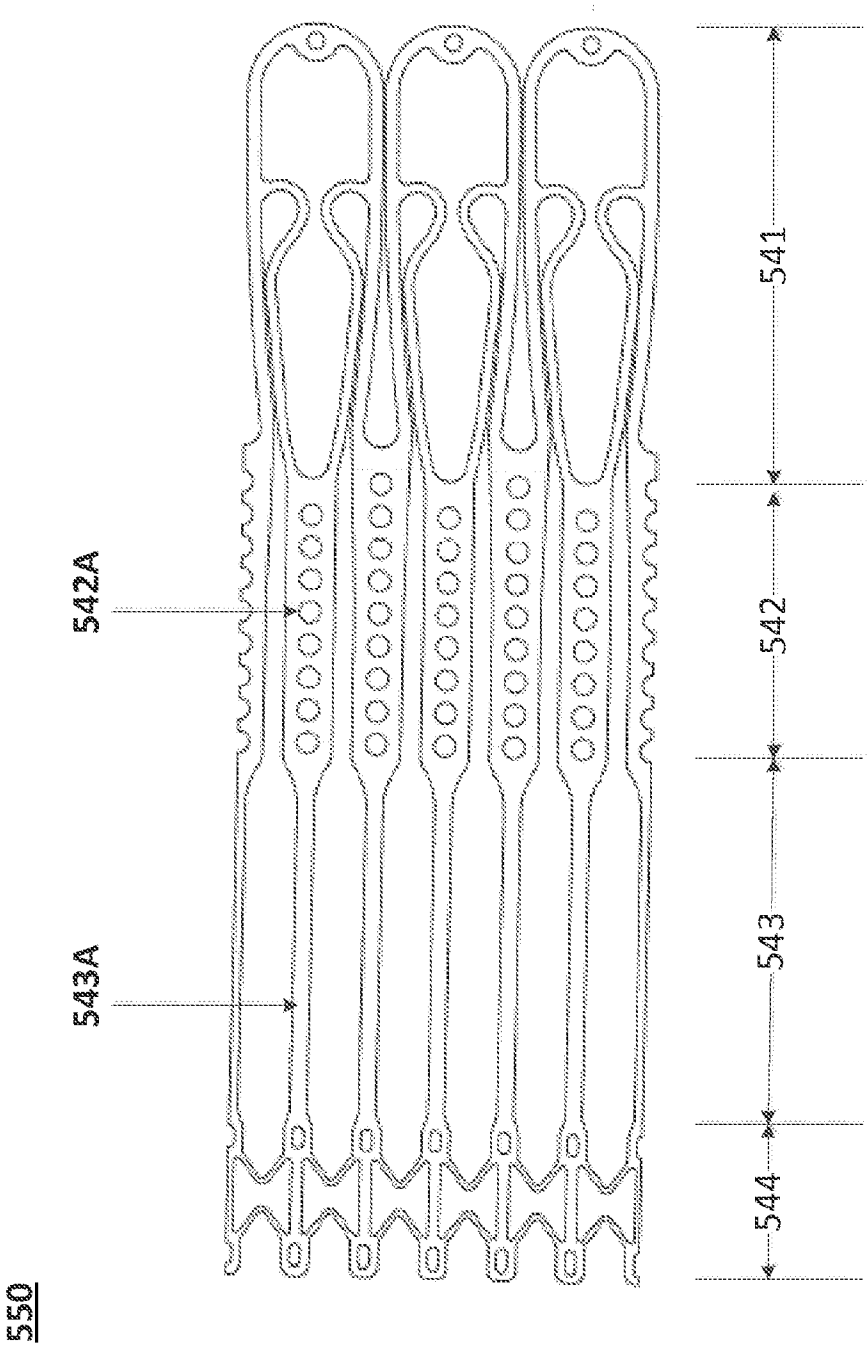


FIG. 9

FIG. 10



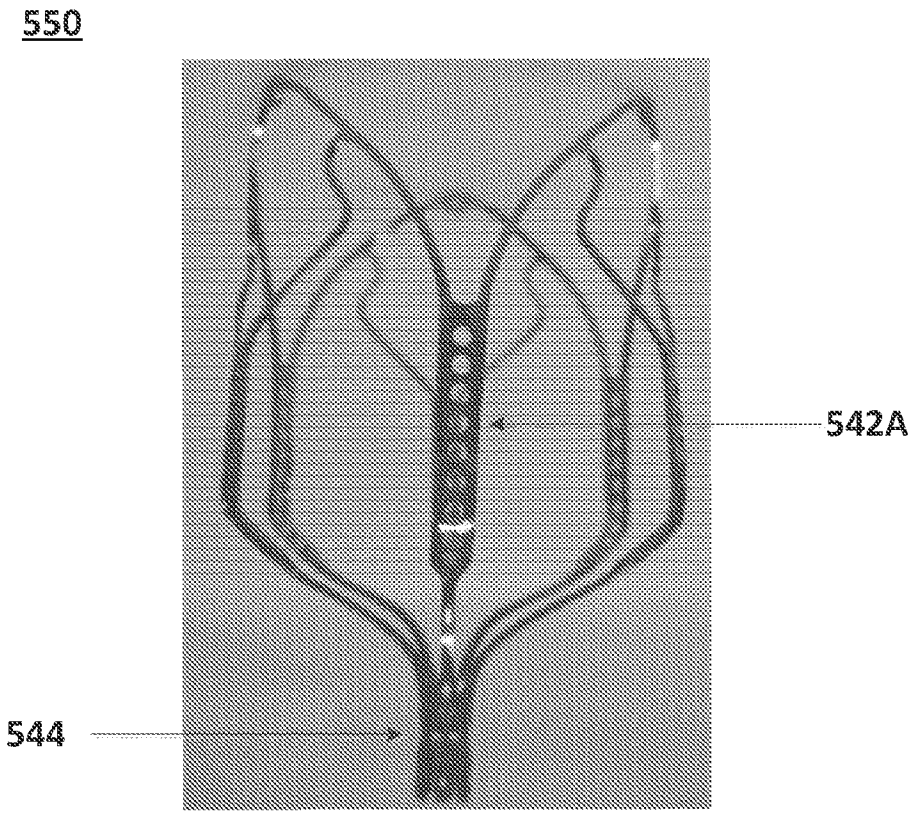


FIG. 11

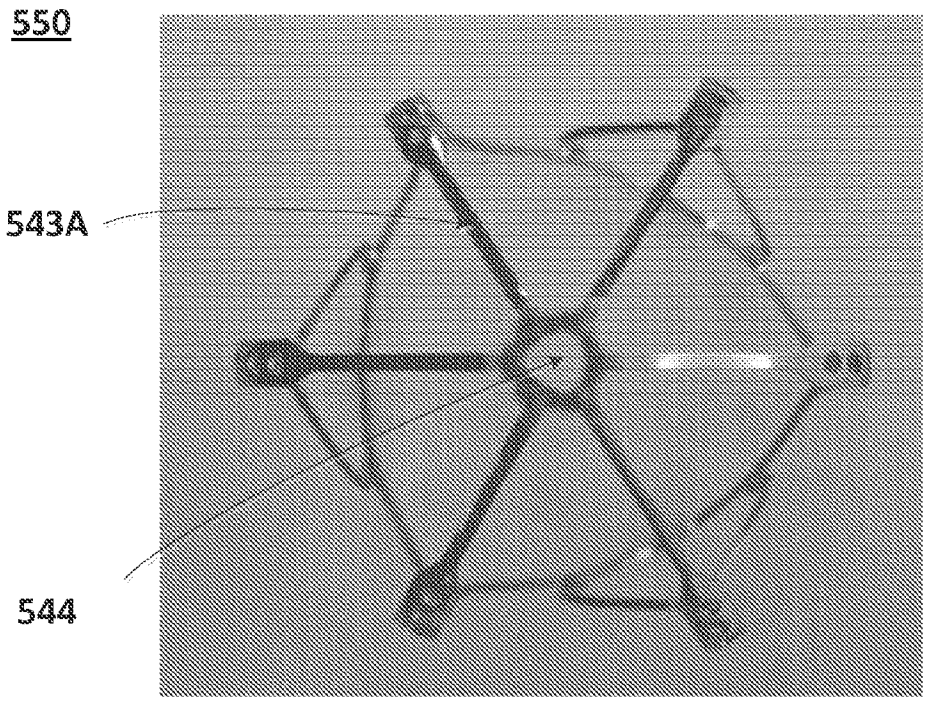


FIG. 12

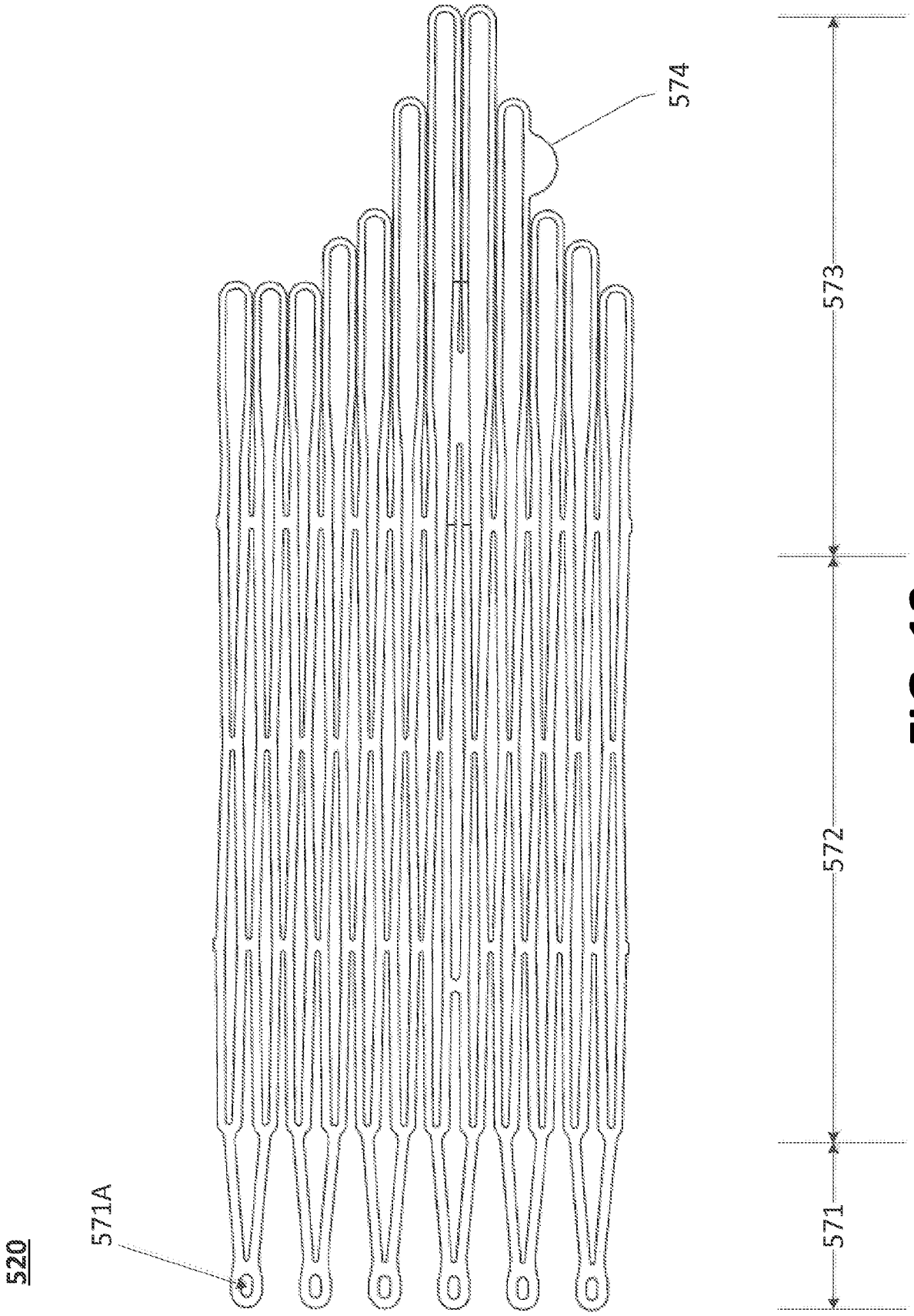


FIG. 13

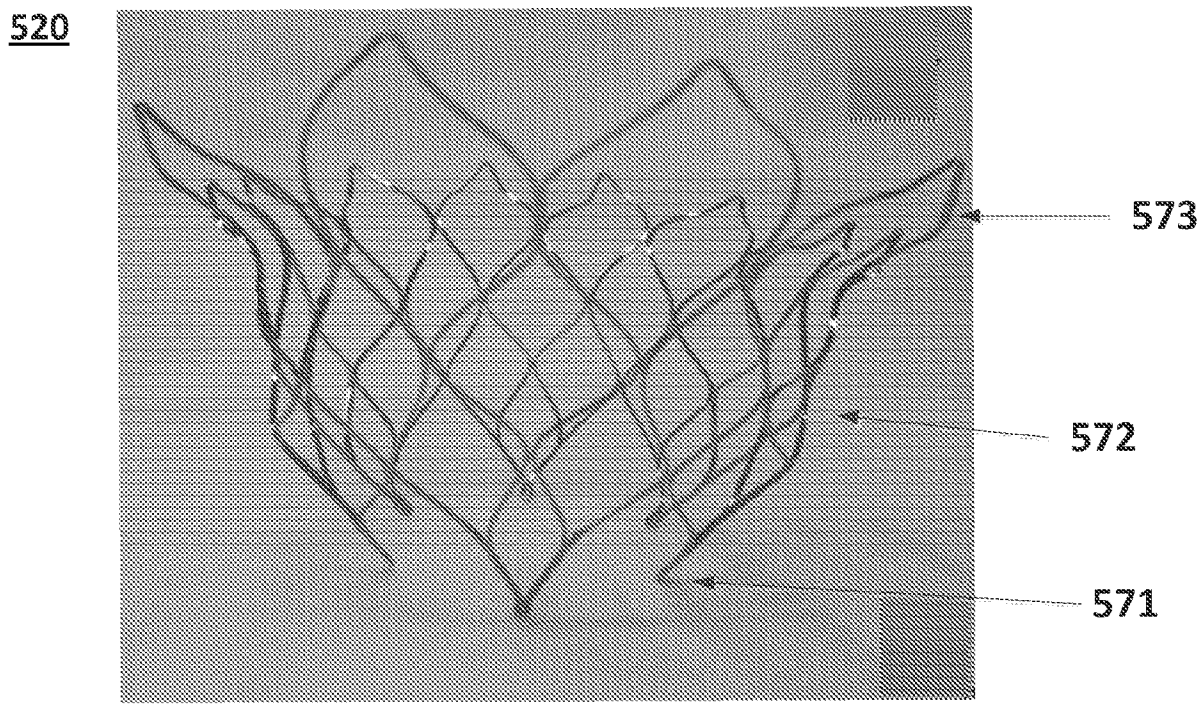


FIG. 14

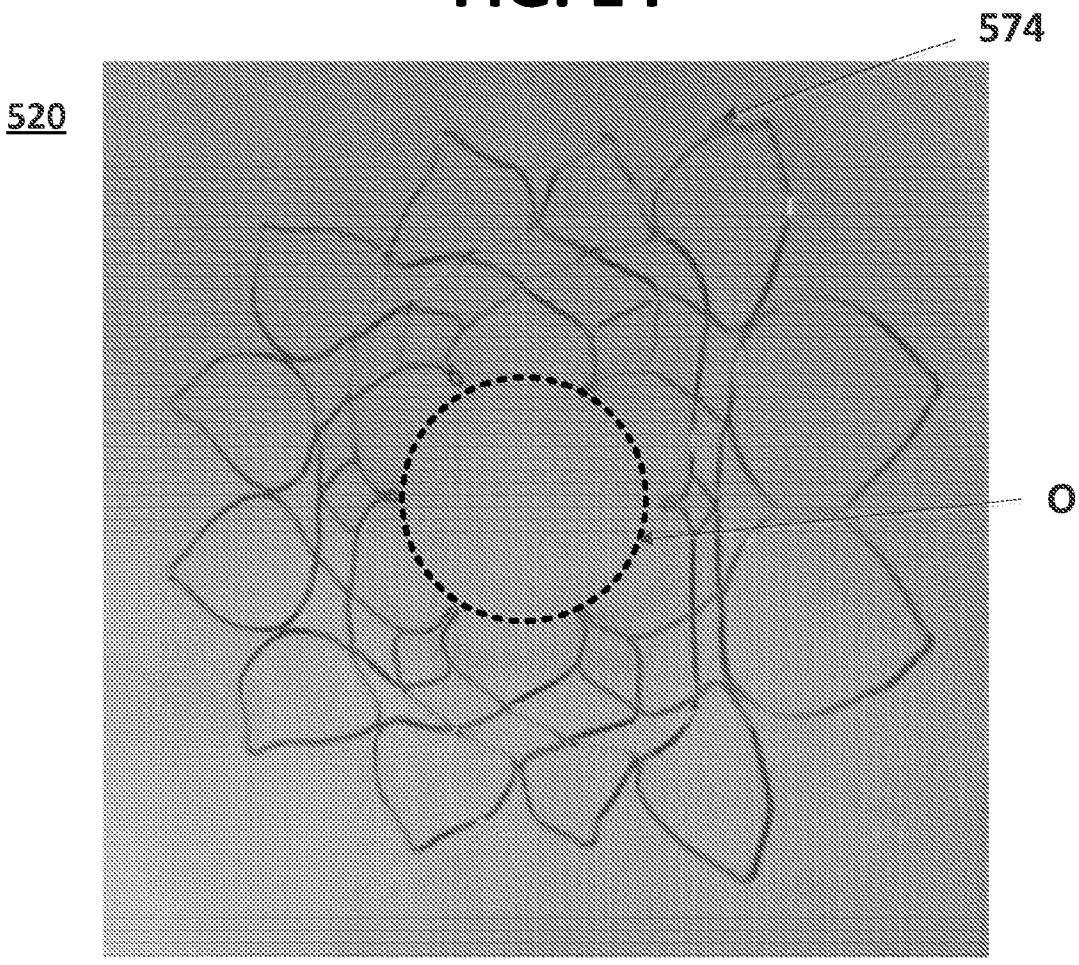


FIG. 15

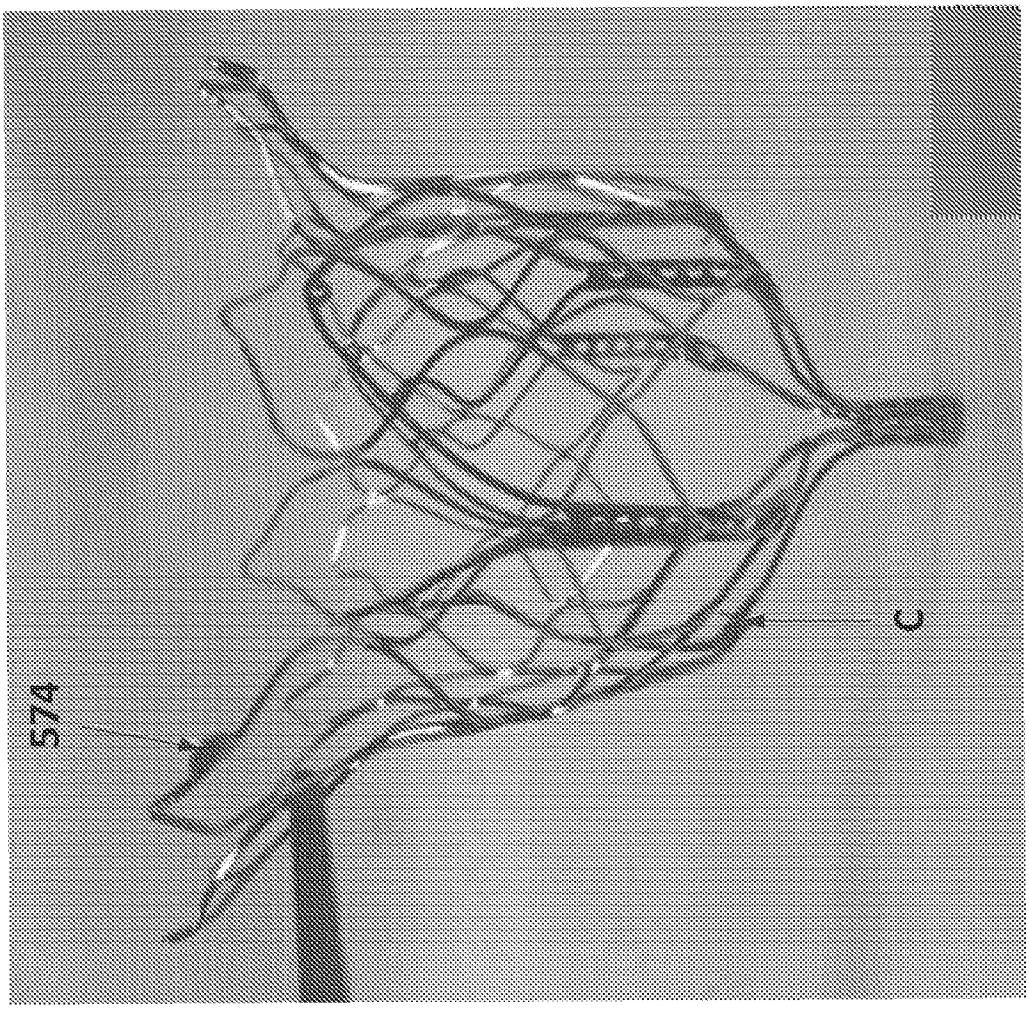


FIG. 16

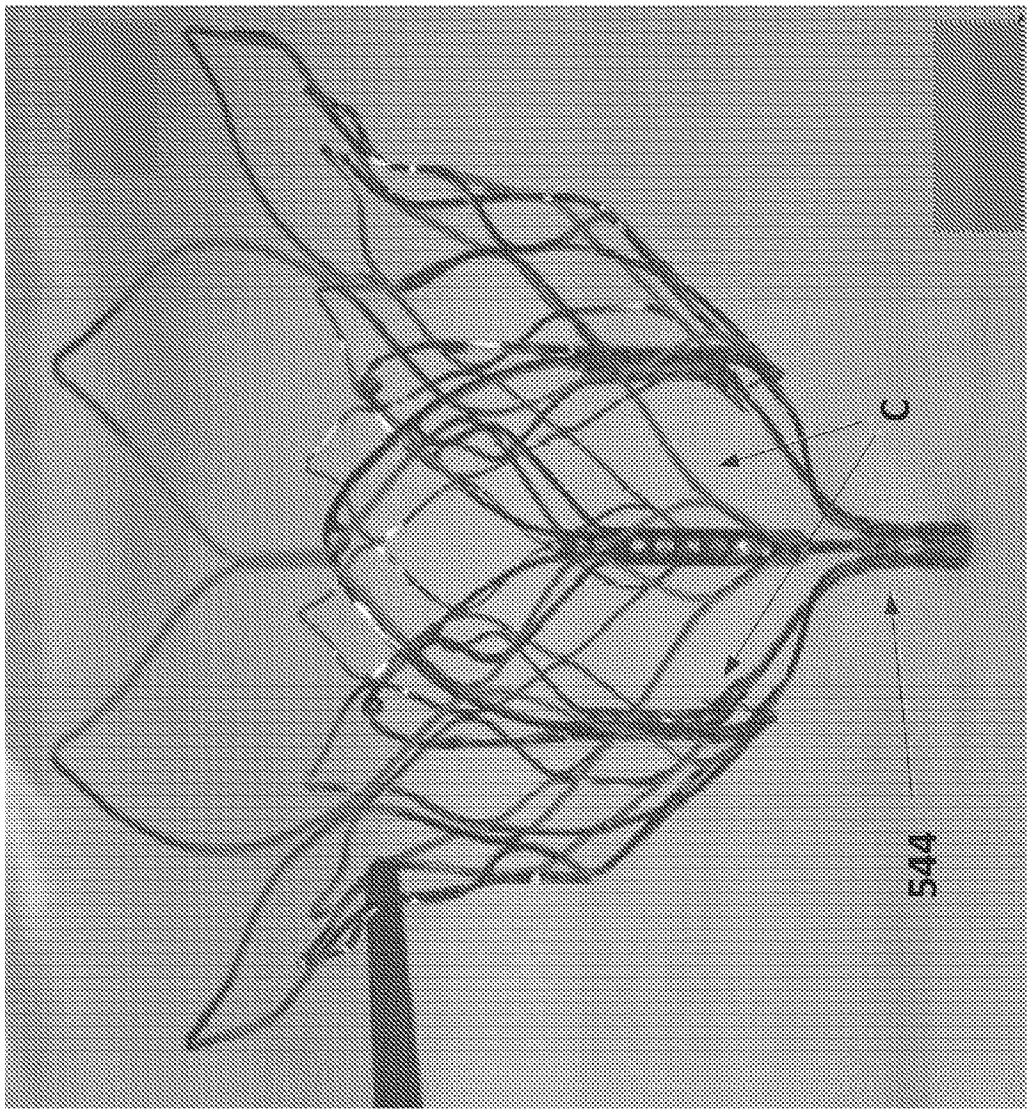


FIG. 17

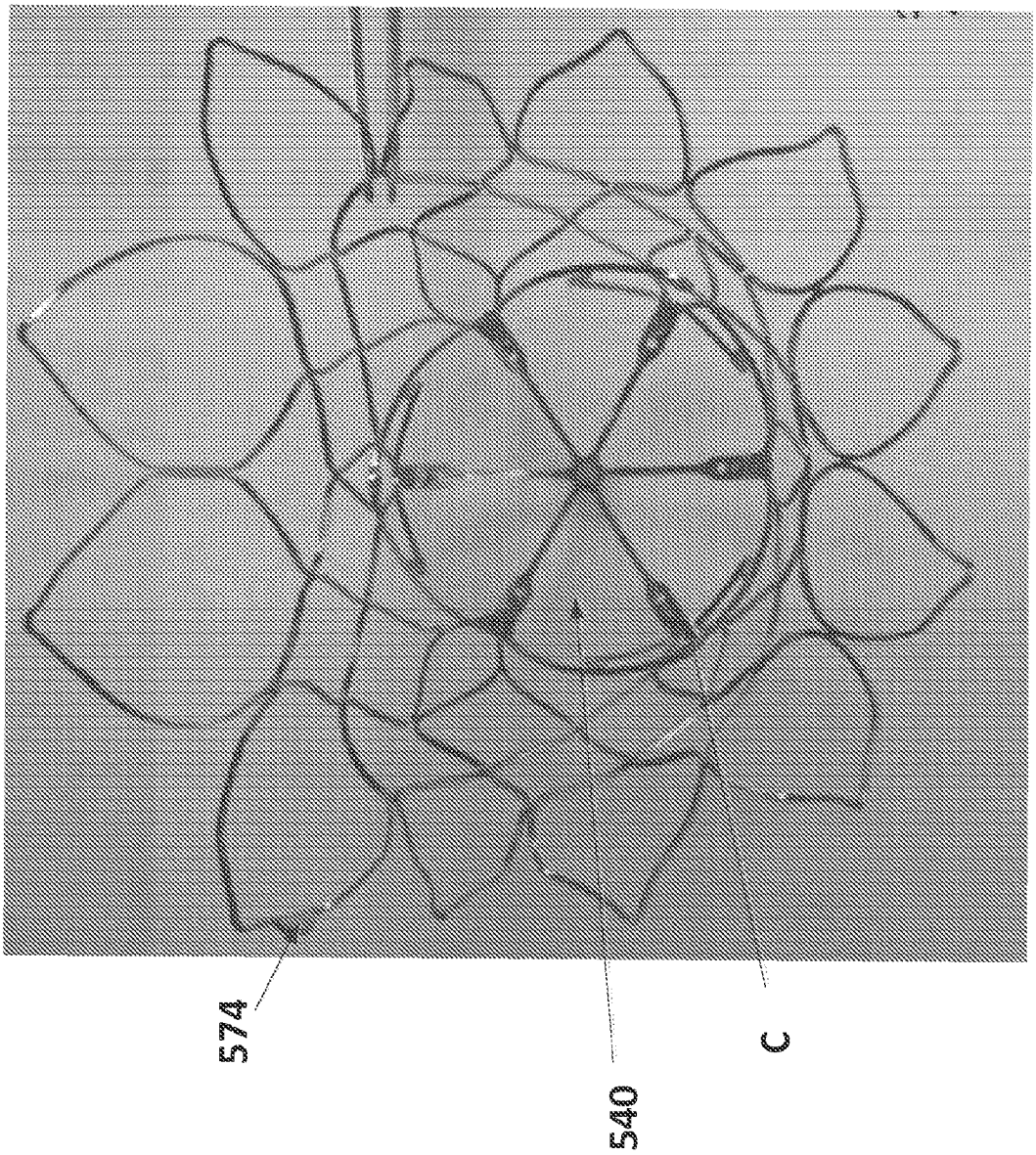


FIG. 18

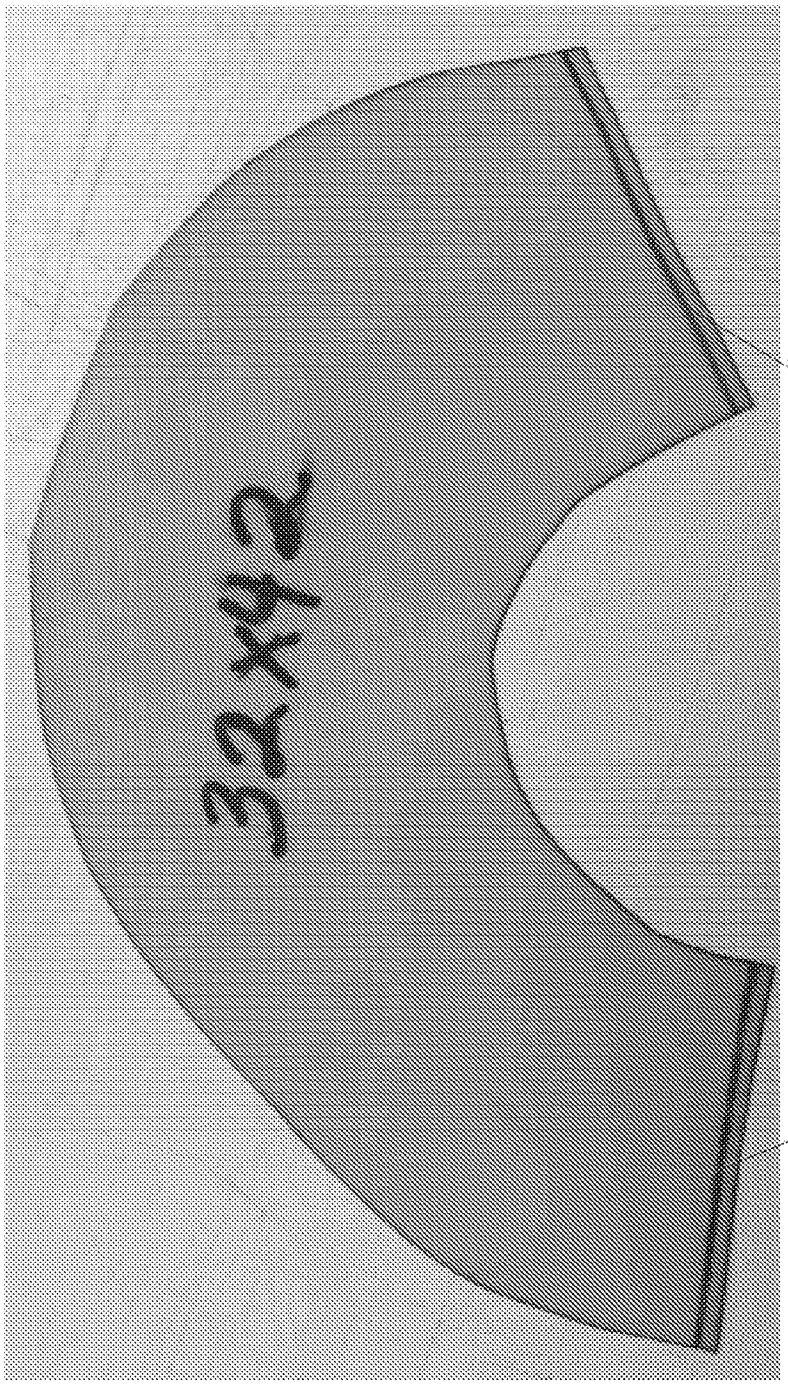


FIG. 19

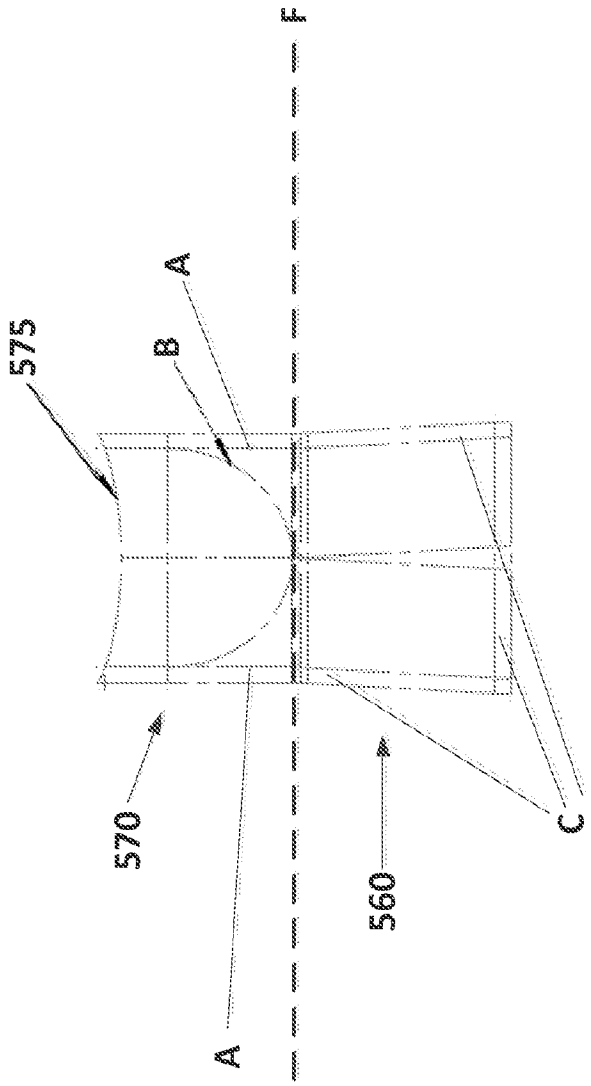


FIG. 20

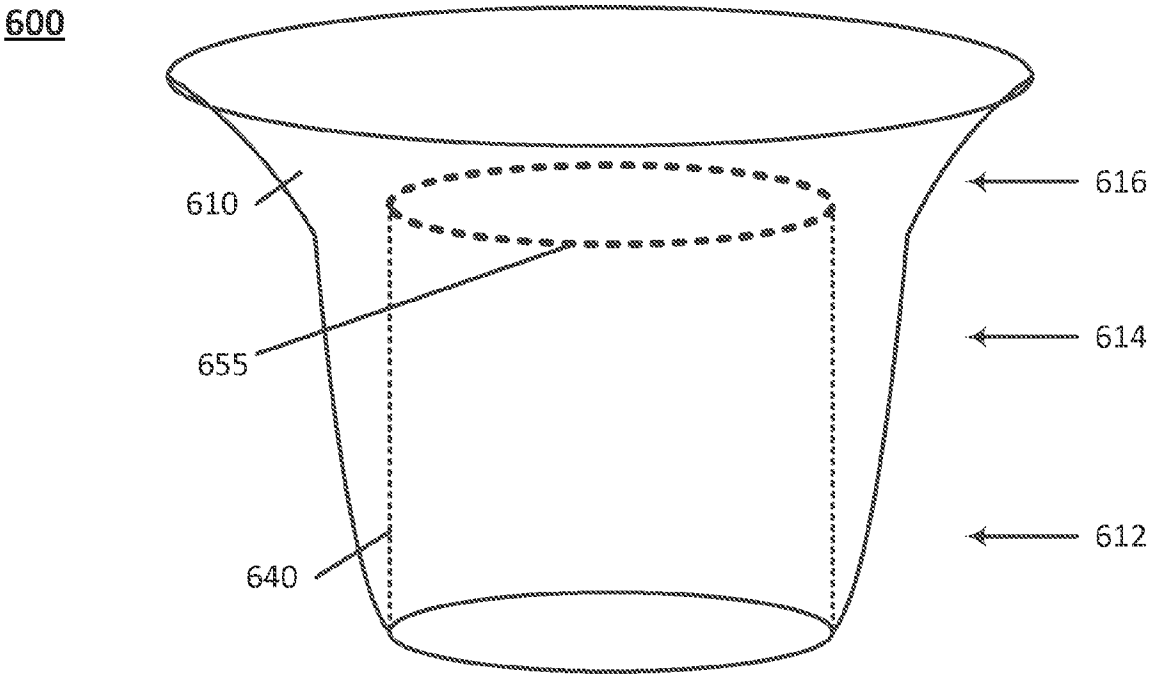


FIG. 21

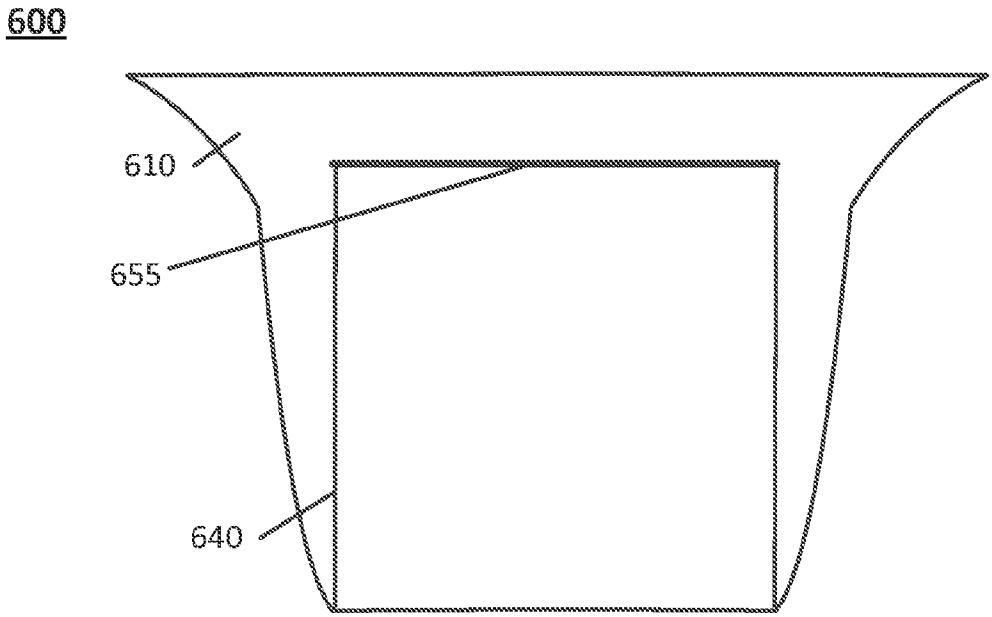


FIG. 22

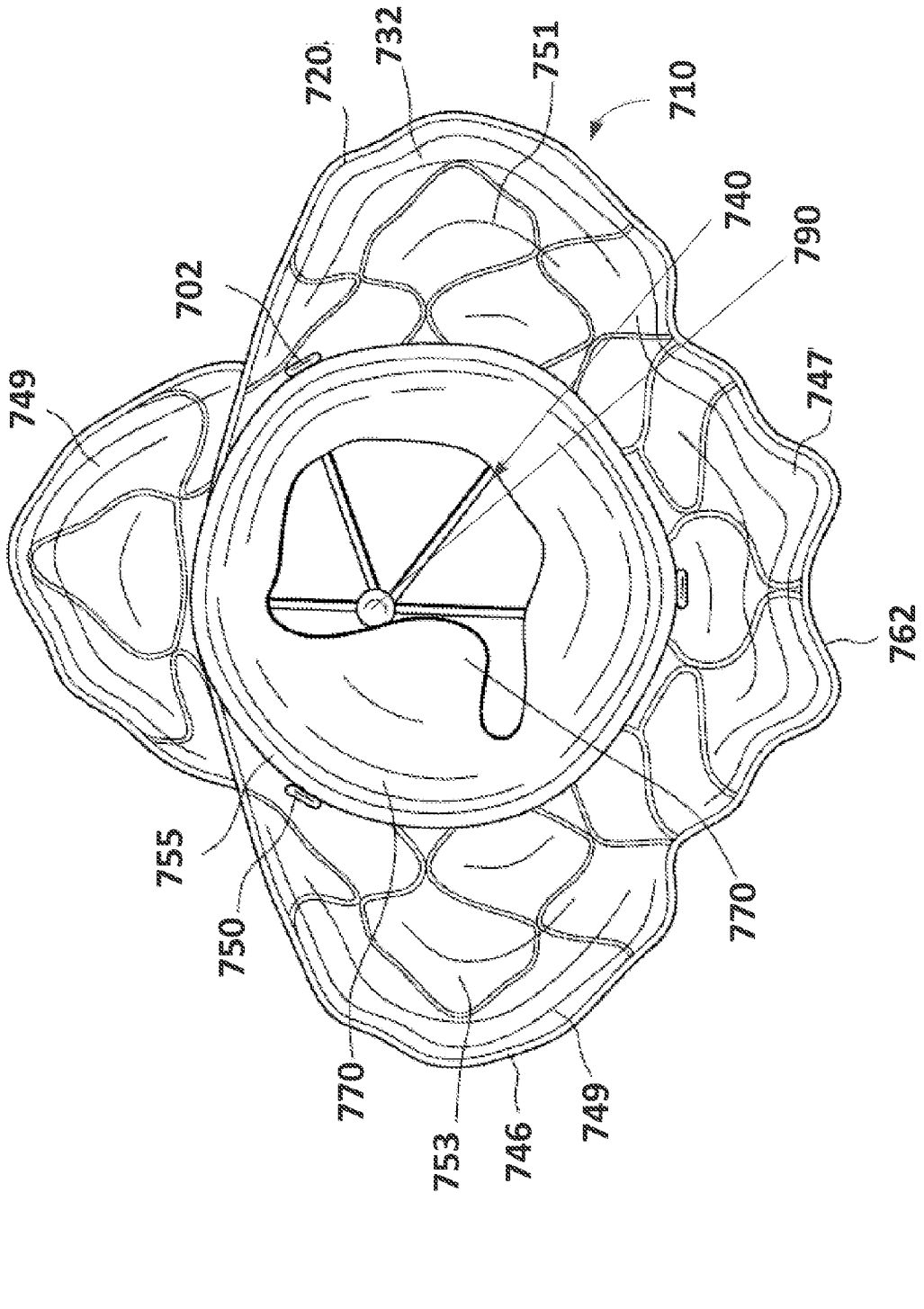

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FIG. 23

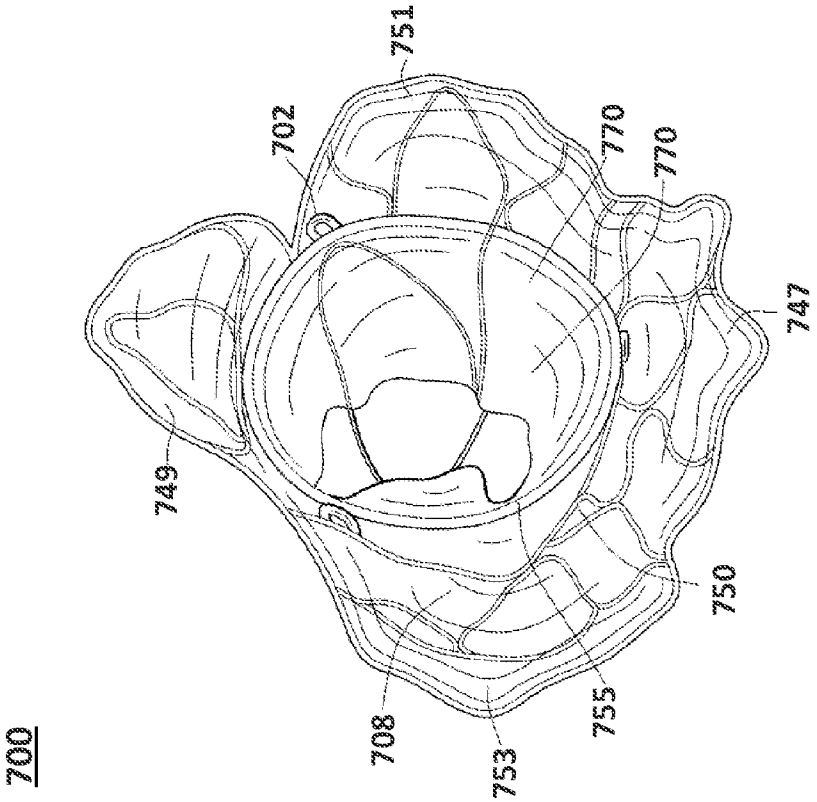
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FIG. 25

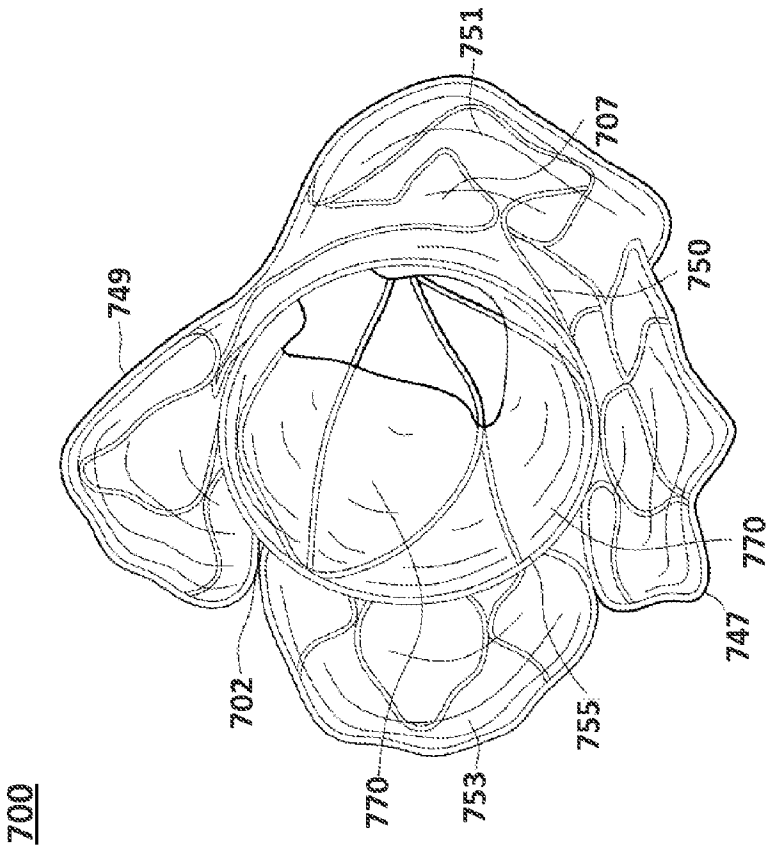
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FIG. 24

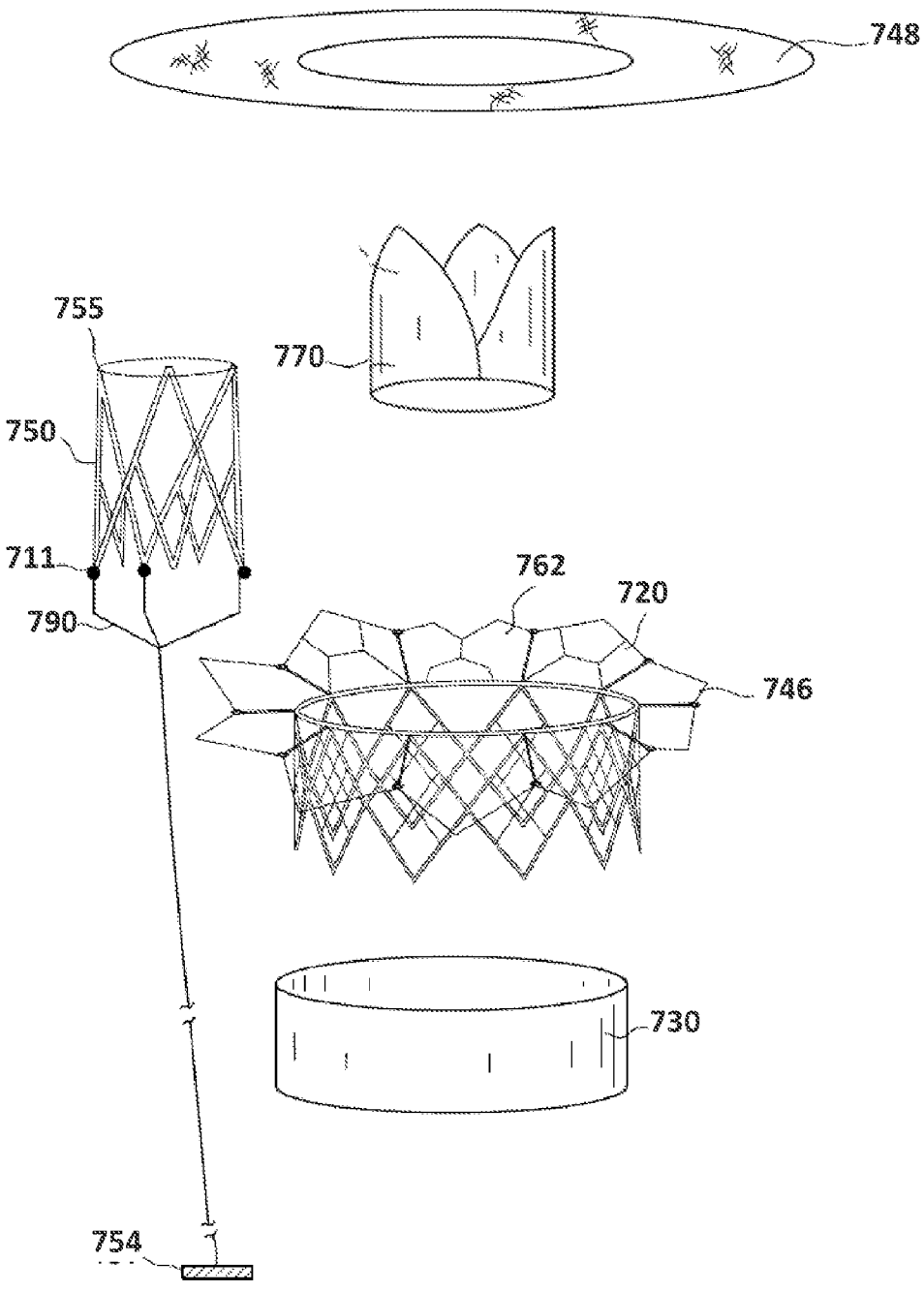

FIG. 26

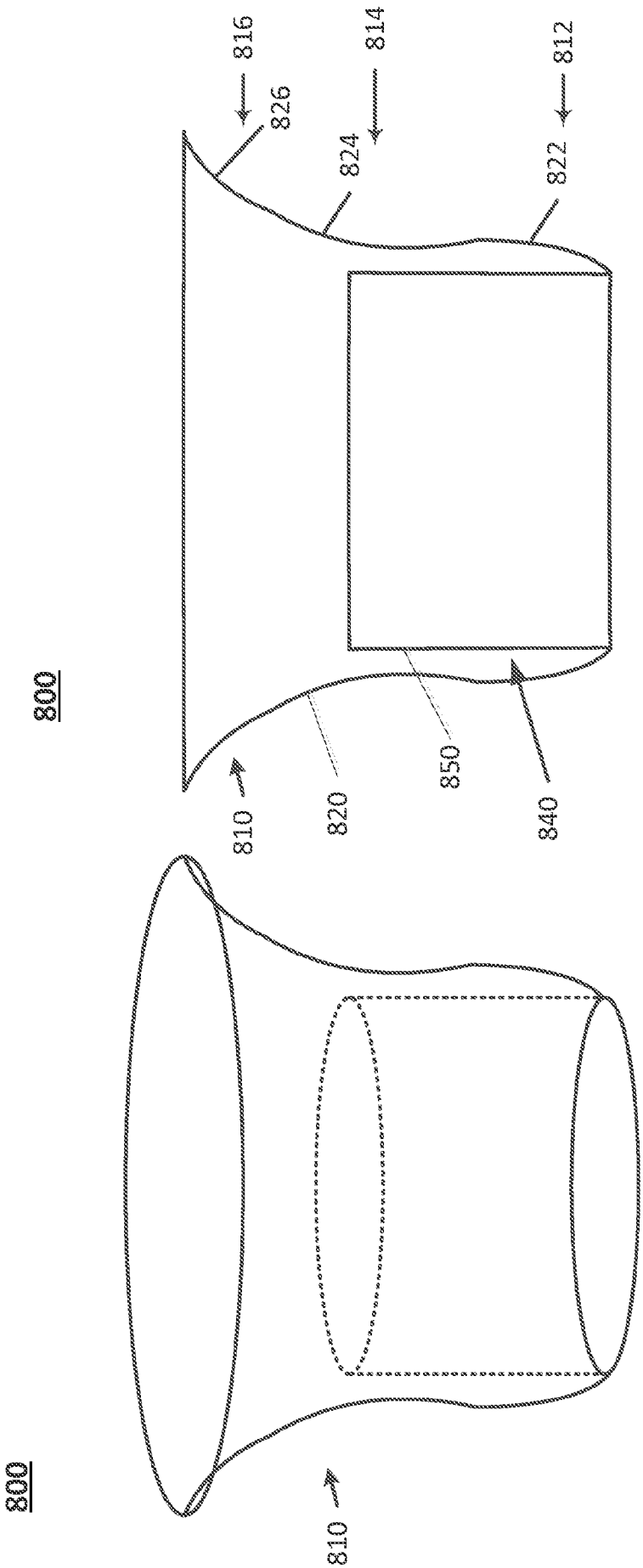

FIG. 28

FIG. 27

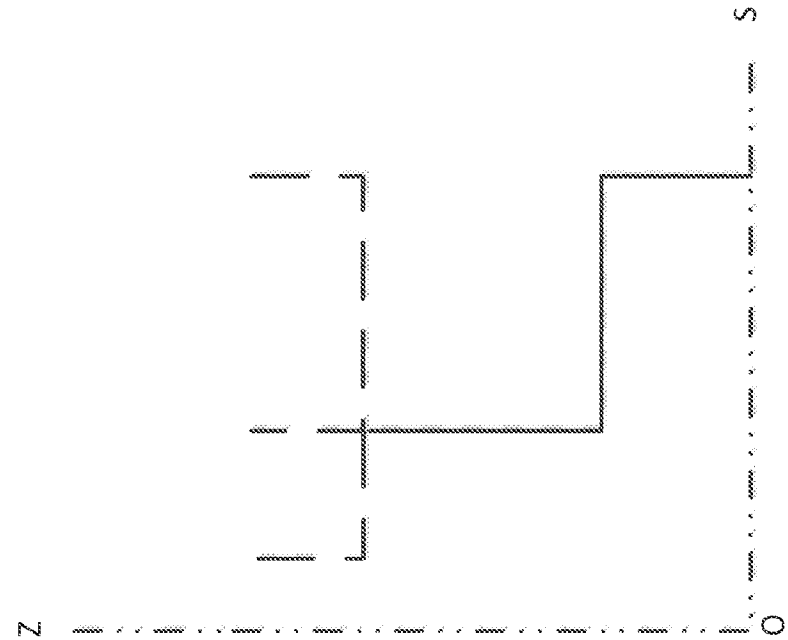

FIG. 29B

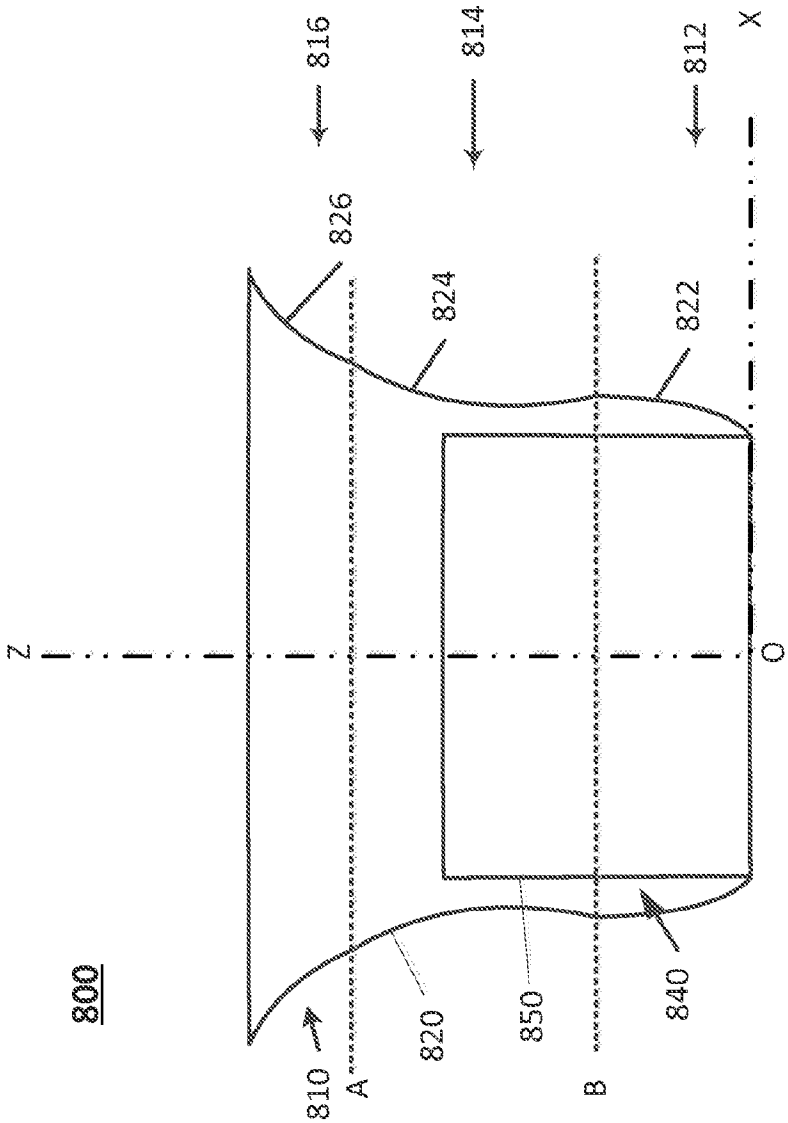

FIG. 29A

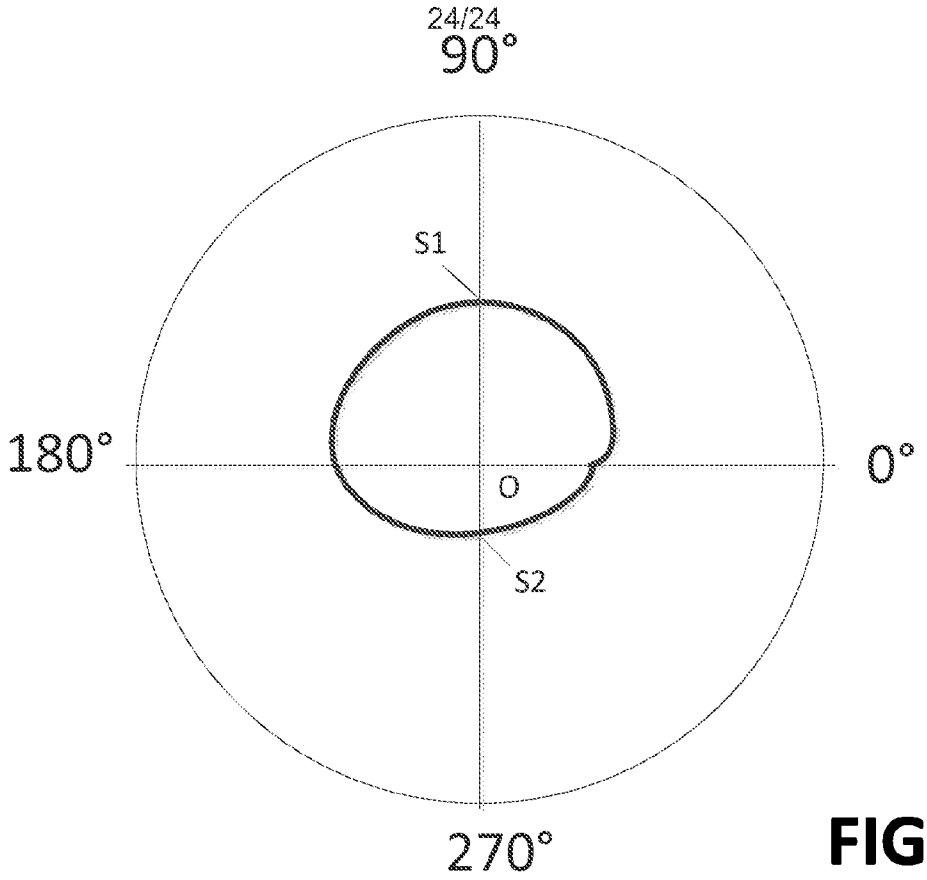

FIG. 29C

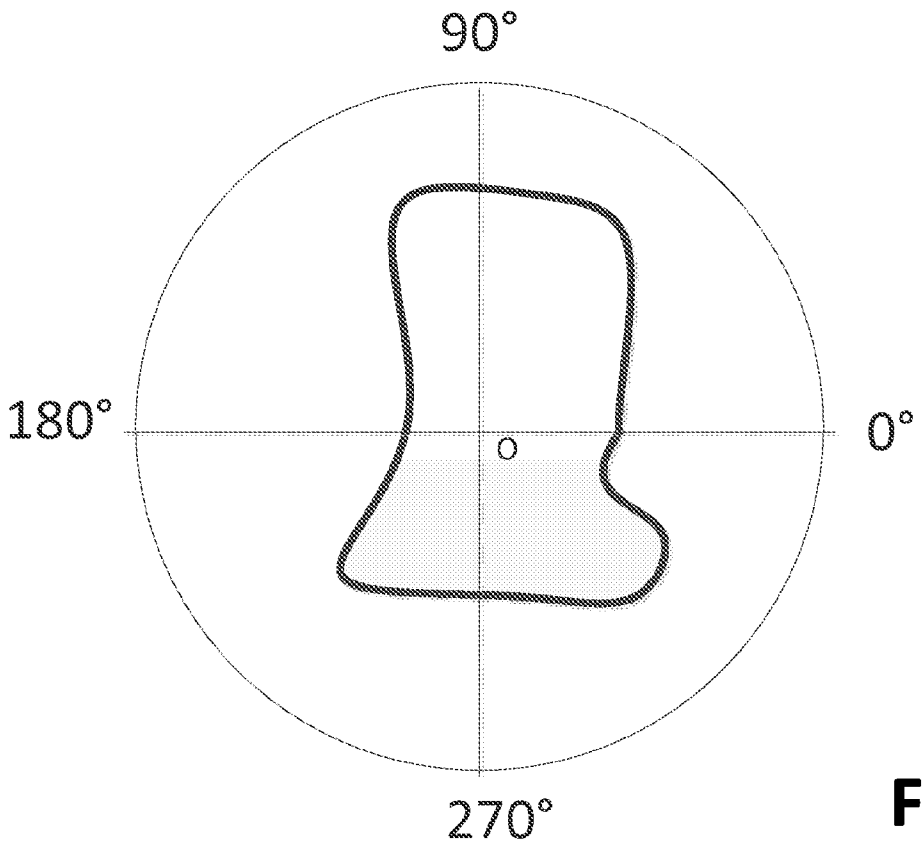

FIG. 29D

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2014/044047

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

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

B. FIELDS SEARCHED

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

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

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

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 2013/059747 A1 (FOUNDRY NEWCO XII INC [US]) 25 April 2013 (2013-04-25) paragraphs [0171] - [0183], [0229] - [0234]; figures 10A-10F, 16A-16E, 24C	1-11,22
A	WO 2013/028387 A2 (TENDYNE HOLDINGS INC [US]) 28 February 2013 (2013-02-28) paragraphs [0404] - [0424]; figures 12-20	1-8,22
A	CN 2 902 226 Y (WANG RONGZHEN [CN]) 23 May 2007 (2007-05-23) page 13, paragraph 3; figure 4	1,22

☐ Further documents are listed in the continuation of Box C.

☒ See patent family annex.

* Special categories of cited documents :

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

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

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

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

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

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

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

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

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
1 September 2014	17/11/2014

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

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2014/044047

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. [X] Claims Nos.: 23-27
because they relate to subject matter not required to be searched by this Authority, namely:

Claims 23 - 27 are considered a method for treatment of the human or animal body by surgery (Rule 39.1(iv) PCT) as they involve the step of surgically deploying of a prosthetic heart valve into the native annulus of the heart valve of a patient.

2. [ ] Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. [ ] Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

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

see additional sheet

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

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

3. [ ] As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. [X] No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

1-11, 22

Remark on Protest

[ ] The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.

[ ] The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.

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

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-11, 22

A prosthetic heart valve with an outer and an inner frame assembly. A thrombus retaining pocket is coupled between inner and outer frame assembly.

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2. claims: 12-21

A prosthetic heart valve with an outer and an inner frame assembly. The outer frame assembly has a deflectable annulus portion to accommodate in the annulus portion of the natural valve.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/US2014/044047

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