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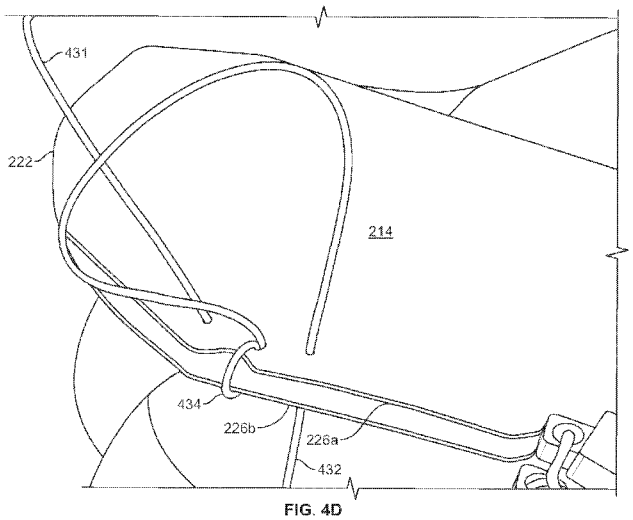


FIG. 4D

(57) Abstract: A prosthetic heart valve provided herein can include at least two leaflets being secured together along aligned edges thereof by a stitch of a single thread. The stitch includes at least one loop extending through a first aperture, around the aligned edges, and back through the first aperture.

WO 2016/123082 A1

PROSTHETIC HEART VALVE SQUARE LEAFLET-LEAFLET STITCH

RELATED APPLICATIONS

This application claims priority to U.S. Provisional Application Serial No. 62/107,605, filed January 26, 2015 and U.S. Utility Application Serial No. 15/005,081, filed January 25, 2016.

FIELD

This document provides prosthetic heart valves having square leaflet-leaflet stitches.

BACKGROUND

The human heart contains four valves: tricuspid valve, pulmonic valve, mitral valve and aortic valve. Their main purpose is to maintain unimpeded forward flow through the heart and from the heart into the major blood vessels connected to the heart, the pulmonary artery and the aorta. As a result of a number of disease processes, both acquired and congenital, any one of the four heart valves may malfunction and result in either stenosis (impeded forward flow) and/or backward flow (regurgitation). Either process burdens the heart and may lead to serious problems including heart failure. Various procedures for fixing or replacing defective heart valves are known in the art. In some cases, artificial heart valves can be implanted in the heart of a patient to replace a diseased or damaged heart valve with a prosthetic equivalent.

Prosthetic heart valves can have a variety of designs. Two major types of prosthetic heart valves include mechanical heart valves and bioprosthetic heart valves. Mechanical heart valves can be made of synthetic materials, such as plastics or metals, while bioprosthetic heart valves can be made of biologic tissue mounted on a fabric covered plastic or metal frame. Bioprosthetic heart valves can include animal tissue, such as porcine or bovine tissue, that has been chemically treated to make the valve suitable for implantation in a human. Bioprosthetic valves do not generally require a patient to undergo anticoagulant therapy, which is typically required when using mechanical valves. As such, there is a need to further improve the design of

bioprosthetic valves to retain its functionality during the life of the patient and minimize stenosis and regurgitation.

SUMMARY

Prosthetic heart valves provided herein can have a structure adapted to retain functionality during the life of the patient and to minimize stenosis and regurgitation by having an improved connection between different parts of the prosthetic heart valve. Prosthetic heart valves provided herein can additionally have a reduced unexpanded profile. In some cases, prosthetic heart valves provided herein include a plurality of anchor elements. In some cases, anchor elements can be secured to an expandable tubular member. In some cases, the expandable tubular member can be a braided stent. In some cases, prosthetic heart valves provided herein include three or more leaflets. In some cases, the leaflets can have a body portion and sleeve portions one or both sides. In some cases, sides of the body portions can be secured together and sleeve portions secured to anchor elements (e.g., anchor elements attached to a braided stent). In some cases, anchor elements can include post leg structures adapted to compress and support sleeve portions of leaflets. In some cases, prosthetic heart valves provided herein can include a tubular seal. In some cases, the tubular seal can be secured to bottom edges of body portions of the leaflets. In some cases, the seal can be secured to a blood inlet side of an expandable member.

In some aspects, prosthetic heart valves provided herein include a square stitch between leaflets.

In some aspects, a prosthetic heart valve can include at least two leaflets that are secured together along aligned edges thereof by a stitch of a single thread. The stitch can have at least one loop extending through a first aperture, around the aligned edges, and back through the first aperture.

In some cases, the stitch can have at least one segment of thread extending from the first aperture to a second aperture in a direction parallel to the aligned edges of the at least two leaflets. In some cases, the stitch can have a second loop extended through the second aperture, around the aligned edges, and back through the second aperture. In some cases, the stitch can have at least three loops each extending from an aperture, around the aligned edges, and back to that aperture. In some cases, the

stitch runs in a forward direction having thread pass through a set of apertures and back in a reverse direction having the thread again pass through the set of apertures. In some cases, each aperture has two loops extending from that aperture, around the aligned edges, and tack to that aperture, wherein one loop is from the stitch running in the forward direction and one loop is from the stitch running in the reverse direction. In some cases, segments of thread extending between adjacent apertures in the forward direction are on an opposite side of the two leaflets from the segments of thread extending between adjacent apertures in the reverse direction.

In some cases, each leaflet has a body portion and two opposite sleeve portions, the body portion being defined by a bottom edge and two side edges adjacent each sleeve portion, wherein each of the at least two leaflets are aligned and stitched along a first side edge. In some cases, the leaflets define notches between the two side edges and the adjacent sleeve portion. In some cases, the stitch runs along a side edge from a bottom edge to a notch. In some cases, the prosthetic heart valve further includes a plurality of support element each supporting sleeve portions each leaflet along a line approximately aligned the stitch.

In some aspects, a prosthetic heart valve includes at least three leaflets, a tubular expandable member and a tubular seal. The at least three leaflets can be secured together along side edges thereof by a stitch. The tubular expandable member can be secured to an out flow end of the at least three leaflets. The tubular seal can be secured to an inflow end bottom edge of the at least three leaflets and to an outer surface of the tubular expandable member.

In some cases, the tubular expandable member is a braided stent. In some cases, the tubular seal is secured to the braided stent by a plurality of cross stitches connecting the tubular seal to a pair of overlapping wire members of the braided stent. In some cases, the tubular seal includes a woven fabric. In some cases, the woven fabric can have a thickness range from about 0.002 inches to about 0.003 inches (about 40 microns to about 80 microns. In some cases, the tubular seal includes a woven fabric within a polymer matrix. In some cases, the at least three leaflets are secured to the tubular seal in a portion of the tubular seal comprising the woven fabric. In some cases, the at least one leaflet includes bovine or porcine pericardium tissue or a synthetic material. In some cases, the stitch is formed using between 3 and

20 apertures and includes between 3 and 40 loops each extending from an aperture, around the aligned side edges, and back to that aperture.

In some aspects, a prosthetic heart valve includes at least three leaflets, a tubular expandable member and a tubular seal. The at least three leaflets can be secured together along side edges thereof by a stitch. At least one leaflet can be secured to at least a second leaflet by a running stitch. The running stitch can be a square stitch. The tubular expandable member can be secured to an out flow end of the at least three leaflets. The tubular seal can be secured to an inflow end bottom edge of the at least three leaflets and to an outer surface of the tubular expandable member.

The details of one or more embodiments of the invention are set forth in the accompanying drawings and the description below. Other features, objects, and advantages of the invention will be apparent from the description and drawings, and from the claims.

DESCRIPTION OF DRAWINGS

FIGS. 1A-1H illustrate an exemplary prosthetic heart valve and an exemplary delivery system provided herein. FIG 1A is a perspective view of the heart valve connected to a deployment device. FIG 1B is a side view of the exemplary prosthetic heart valve. FIGS. 1C-1H illustrate how the exemplary heart valve provided herein can be delivered by the delivery system.

FIGS. 2A-2C illustrates an exemplary leaflet, which can be used in prosthetic heart valves provided herein. FIG 2A illustrates a rounded notch in a leaflet where a leaflet can be secured to an adjacent leaflet. FIGS. 2B and 2C illustrate a portion of an exemplary leaflet for prosthetic heart valves. FIG 2B depicts a rounded notch in an armpit of a leaflet. FIG 2C depicts attachment elements in the armpit of the leaflet.

FIG 3 illustrates another exemplary leaflet, which can be used in prosthetic heart valves provided herein.

FIGS. 4A-4G illustrate how adjacent leaflets can be stitched together in prosthetic heart valves provided herein.

FIGS. 5A-5C illustrate a cross stich provided herein for connecting a seal to a braided stent in an exemplary prosthetic heart valve provided herein. FIG 5A shows a

front view of showing apertures in a seal for securing the seal to the braided stent, apertures in a seal for securing the seal to bottom edges of one or more leaflets, circumferential stitch connecting the seal to bottom edges of one or more leaflets, and a stitch connecting the seal to the braided stent. FIG. 5B depicts a close up view of the cross stitch and a portion of the circumferential stitch. FIG. 5C depicts a cross-sectional view showing the cross stitch and a portion of the circumferential stitch.

FIG. 6 depicts an apparatus that can be used to form a tubular seal provided herein.

FIGS. 7A and 7B depict exemplary tubular seals having a fabric positioned within a matrix, which can be used in a prosthetic heart valve provided herein.

Like reference symbols in the various drawings indicate like elements.

DETAILED DESCRIPTION

Prosthetic heart valves provided herein can include an improved stitch pattern between adjacent leaflets. In some cases, aligned edges of adjacent leaflets can be connected by a stitch of a single continuous thread including at least one loop extending through a first aperture, around the aligned edges, and back through the first aperture. As the term is used herein, this loop from an aperture around the aligned edges, and back through the same aperture stitch can be considered a "square stitch." The single continuous thread stitch can additionally include a thread segments that extend from a first aperture to a second aperture in a stitch line extending generally parallel to the aligned edges. In some cases, each aperture in a stitch line can include at least one square stitch. In some cases, the continuous thread stitch can extend in a forward direction and a reverse direction through the same apertures. In some cases, square stitches are formed in each aperture in the forward direction and in the reverse direction such that each aperture includes at least two square stitches. In some cases, segments extending along a surface of a leaflet along the stitch line between adjacent apertures can be formed on opposite sides of the two leaflets in the forward and reverse direction, which can provide a continuous line of compression along the stitch line. The stitch pattern provided herein can provide a secure seal between adjacent leaflets while minimizing the number of apertures, the width of the sealed section, and with a single continuous thread.

FIGS. 1A and 1B illustrate an exemplary prosthetic heart valve 100 provided herein. FIGS. 1C-1D depict how prosthetic heart valve 100 is deployed. FIG. 1A is a perspective view of prosthetic heart valve 100 connected to a deployment device 190. FIG. 1B is a side view of prosthetic heart valve 100. As shown, prosthetic heart valve 100 includes an expandable member 110, three leaflets 200, three anchor elements 120 securing sleeve portions 216 of leaflets 200 to expandable member 110, a tubular seal 130 secured around a blood inflow end of prosthetic heart valve 100. Anchor elements 120 can include post leg compression elements 122 and clamping support structures 126 adapted to provide support along opposite sides of sleeve portions 216. Expandable member 110 in FIGS. 1A-1D is a braided stent, which is adapted to transition between a restricted state having a smaller diameter and an expanded state having a larger diameter. Expandable member 110 can be self-expanding, mechanically expanded, or a combination thereof.

FIGS. 1C-1H depict an example of how an exemplary heart valve delivery system can deliver the prosthetic heart valve provided herein. As shown in FIGS. 1C-1H, prosthetic heart valve 100 can be deployed using a heart valve delivery system 180. System 180 can include a sheath 182 for retaining the prosthetic heart valve 100 with the expandable member 110 in a restricted state. Within sheath 182, anchor elements 120 (FIGS. 1A and 1B) can be connected to pushing prongs 192 and a pull line 194 can be connected to a nose cap 196, or end cap, positioned at the end of the sheath. As shown in FIG. 1A, the pull line 194 can extend through the expandable member 110 and through the valve opening between leaflets 200. As shown by figures 1D-1H, once a distal end of sheath 182 is delivered through the circulatory system to an appropriate location (e.g., within the heart), prosthetic heart valve 100 can be deployed by advancing pushing prongs 192 and pull line 194 relative to sheath 182 to push prosthetic heart valve 100 out of the sheath 182. In some cases, expandable member 110 can self-expand upon exiting sheath 182. In some cases, expandable member 110 can self-expand to a first intermediate diameter, and system 180 can mechanically expand expandable member 110 to a larger deployment diameter. For example, anchor elements 120 can include a locking mechanism to clip a portion of expandable member when the expandable member 110 is expanded to a predetermined locking diameter. In some cases, system 180 can mechanically expand expandable member 110 to a predetermined locking diameter compressing

expandable member 110 between pushing prongs 192 and nose cap 196 by moving pull line 194 relative to pushing prongs 192. The predetermined locking diameter can be a diameter adapted for setting of prosthetic heart valve 100 into surrounding tissue. After prosthetic heart valve 100 is set, system 180 can move pull line 194 and nose cap 196 relative to pushing prongs 192 to move the end cap through the opening between leaflets 200 in prosthetic heart valve 100. Pushing prongs 192 can then be retracted from anchor elements 120 and retracted into sheath 182. In some cases, pushing prongs 192 can include a shape member material adapted to help radially expand expandable member 110 as the expandable member 110 exits sheath 182. A control handle 188 can be used to control the relative movements of sheath 182, pushing prongs 192, and pull wire 194. Prosthetic heart valves provided herein can be adapted to limit damage to the valves during the setting of the valve.

In some cases, one or more radiopaque markers can be secured to prosthetic heart valves provided herein. For example, as shown in FIGS. 1A and 1B, expandable member 110 including a radiopaque marker 112. Any suitable radiopaque material (such a platinum, palladium, gold, or alloys thereof) can be used as the radiopaque material in radiopaque marker 112. One or more radiopaque markers can be used with an imaging system to help a physician ensure that a valve is set in an appropriate location. In some cases, prosthetic heart valves provided herein include at least 3 radiopaque markers.

As shown in FIG. 1A, prosthetic heart valve 100 can include a plurality of leaflets 200. In some cases, such as that shown, prosthetic heart valve 100 includes three leaflets 200. In some cases, prosthetic heart valves provided herein can have any suitable number of leaflets, for example two, three, four, five, or more leaflets. In some cases, leaflets 200 are secured to one another. In some cases, leaflets 200 can be secured to one another via a plurality of sutures. Leaflets 200 can be sutured along side edges of a body portion of each leaflet. In some cases, prosthetic heart valves provide herein can include a single line of sutures, which can be adapted to minimize leaks, minimize an amount of a width of the seam, and/or minimize the profile of the replacement heart valve during percutaneous insertion. In some cases, prosthetic heart valves provide herein can include a multiple lines of sutures.

Expandable member 110 can have any suitable structure, arrangement, or material. In some cases, expandable member 110 can include a braided wire stent.

For example, US Publication Number 2005/0143809, titled, "Methods and Apparatus for Endovascularly Replacing a Heart Valve," and filed on Nov. 5, 2004, which is herein incorporated by reference for its disclosure of possible structures and materials for a braided wire stent, discloses a braided wire stent. In some cases, expandable member 110 includes a shape memory material (e.g., a nickel-titanium alloy or a cobalt-chromium alloy).

Referring to FIGS. 2A-2C, a leaflet 200 can include a body portion 214 and sleeve portions 216. In some cases, the body portion 214 has a bottom edge 222, a first side edge 226, a second side edge 228, and a free edge 224. Leaflet 200 further includes a front, a back, a first side adjacent to the first side edge 226, and a second side adjacent to the second side edge 228. In some cases, the front of the leaflet 200 has a different texture than the back. In some cases, this occurs where the leaflet 200 is made from pig, cow, or other natural animal tissue. In some cases, leaflet 200 is made from bovine pericardium. Leaflets 200 can also be made from a synthetic material. Leaflets 200 can be assembled by aligning two leaflets 200 to position side regions of opposite leaflets 200 adjacent to each other to stitch the leaflets 200 together along stitch line 246, as shown in FIG. 2C.

As shown in FIGS. 2A-2C, leaflet 200 can define notches 232 and 234 along the side edges 228 and 226 adjacent to sleeve portions 216. Notches 232 and 234 can allow for post leg compression elements 122, which can be a part of anchor elements 120 (shown in FIGS. 1A and 1B), to compress and restrain sleeve portions 216 along the same line as the stitch line 246 without having a suture 258 (FIG. 2C) connecting post leg compression element 122 from abrading leaflets 200 due to the pulsating movement of the leaflets due to the circulatory system. Suture 258 can be used apply an appropriate and consistent compressive force between the post leg compression elements 122 in order to prevent leakage through sleeve portions 216 of the leaflets 200. Positioning the compression line and the stitch line 246 at an offset or at an angle in order to avoid having suture 258 pass through leaflet material can create a stress concentrator, which can result in tears in the leaflet material. Accordingly, a notched leaflet 200 can improve valve opening capabilities and the reliability of prosthetic heart valves provided herein.

FIG. 3 illustrate another exemplary leaflet, which can be used in prosthetic heart valves provided herein. As shown in FIG. 3, leaflet 300 can include a body

portion 314 and sleeve portions 316. In some cases, the body portion 314 has a bottom edge 322, a first side edge 326, a second side edge 328, and a free edge 324. Leaflet 300 further includes a front, a back, a first side adjacent to the first side edge 326, and a second side adjacent to the second side edge 328. In some cases, the front of the leaflet 300 has a different texture than the back. In some cases, this occurs where the leaflet 300 is made from pig, cow, or other natural animal tissue. In some cases, leaflet 300 is made from bovine pericardium. Leaflets 300 can also be made from a synthetic material. Leaflets 300 can be assembled by aligning two leaflets 300 to position side regions of opposite leaflets 300 adjacent to each other to stitch the leaflets 300 together along a stitch line positioned in the same way that stitch line 246 is shown in FIG. 2C. Leaflet 300 can define apertures 332 and 334 adjacent the side edges 328 and 326 and adjacent the sleeve portions 316. Apertures 332 and 334 in the leaflets 300 can allow one leaflet to be secured to an adjacent leaflet. Similar to the notches discussed above, apertures 332 and 334 can allow for post leg compression elements, which can be a part of anchor elements 120, to compress and restrain sleeve portions 316 along the same line as a stitch line without having a suture connecting post leg compression element from abrading leaflets 300 due to the pulsating movement of the leaflets due to the circulatory system. Apertures 332 and 334 can have a diameter significantly larger than the diameter of the suture in order to minimize abrasion of the leaflets 300. Accordingly, leaflets 300 used in prosthetic heart valves provided herein can improve the reliability of prosthetic heart valves provided herein.

FIGS. 4A-4G depict an example of how leaflets 200 can be jointed and provide an improved stitch between leaflets. As shown, stitch 446 can be a single continuous line stitch traveling along the stitch line in a forward direction and back in a reverse direction. In some cases, stitch 446 can run along a leaflet from a bottom edge to a side edge of the leaflet, e.g., bottom edge 222 to side edge 226 of leaflet 200 shown in FIG. 2A-2B. In some cases, stitch 446 can run from a side edge to a notch of a leaflet, e.g., side edge 226 to notch 234 of leaflet 200.

As shown in FIGS. 4D-4G, stitch 446 can include a plurality of perpendicular loop segments 434 extending through an aperture in the two leaflets, around outer side edges of the two attached leaflets, and back through the aperture. Stitch 446 can include a plurality of parallel segments 436 extending between adjacent apertures

along the stitch line. Stitch 446 can include two perpendicular loop segments 434 extending through apertures formed in the stitch line. In some cases, a first perpendicular loop segment 434 for a first aperture in the stitch line is formed when the stitch is formed in the forward direction and a second perpendicular loop segment 434 for the first aperture is formed in the reverse direction. In some cases, parallel segments 436 made in a forward direction alternate between opposite sides of the two leaflets between each aperture in the stitch line. In some cases, parallel segments 436 made in a reverse direction are formed on an opposite side of the two leaflets from parallel segments 436 made in a forward direction. In some cases, opposite parallel segments 436 made in the forward and reverse directions can provide a continuous compressive force along the entire length of the stitch line. Perpendicular loop segments 434 can provide compressive force to reinforce the seal formed between the two leaflets along the stitch line.

Stitch 446 can include any appropriate number of perpendicular loop segments formed through any appropriate number of apertures. As shown, stitch 446 includes six perpendicular loop segments formed through six apertures (two perpendicular loop segments per aperture). In some cases, stitch 446 can include up to twelve perpendicular loop segments formed through six or more apertures. In some cases, a stitch connecting side edge segments of leaflets can be formed using between 3 and 20 apertures and include between 3 and 40 perpendicular loop segments. In some cases, apertures can be positioned between 0.2 mm and 10 mm apart. In some cases, apertures can be positioned between 0.2 mm and 10 mm away from a side edges of the leaflets.

Stitch 446 can be formed in a process depicted in FIGS. 4A-4G. As shown in FIG. 4A, a thread needle 410 can be passed through aligned leaflet side edges 226a and 226b to create a first aperture in a location near bottom edges 222 approximately 1 mm from the bottom edges 222. The leaflet side edges 226a and 226b can be retained is a desired configuration by clamping the leaflets between clamp sides 422 and 424. Needle 410 pulls a leading end 431 of a thread 432 through the first aperture. As shown in FIG. 4B, needle 410 can then form a second aperture adjacent to the first aperture along the stitch line (towards the leaflet sleeve portion) about 0.5 mm away from the first aperture to pull leading end 431 of thread 432 through the second aperture to form a first parallel segment. As shown in FIG. 4C, a

perpendicular loop segment 434 can be made by guiding needle 410 around the leaflet side edges and re-enter the second aperture from a backside. Thread 432 can be pulled through the second aperture until it sits firmly against the leaflet material (e.g., leaflet pericardium tissue). FIG. 4D shows a second parallel segment, which can be made by pushing needle 410 through leaflet tissue along the stitch line to form a third aperture approximately 1 mm from the second aperture (towards the sleeve segments of the leaflet). As shown in FIG. 4E, a second perpendicular loop segment 434 can be formed by again having needle 410 loop around the leaflet side edges and reenter the third aperture through the backside. This is repeated up to notch 234 to form a total of six parallel segments 436 and six perpendicular loop segments 434 in a forward direction, as shown in FIG. 4F. The stitch pattern can then be repeated in a reverse direction towards bottom edges 222 of the leaflets through the previously formed apertures to have each aperture include two perpendicular loop segments 434 and create parallel segments on opposite sides from the parallel segments created in the forward direction, as shown in FIG. 4G. The method and stitches depicted in FIGS. 4A-4G is also envisioned for leaflets 300.

Stitch 446 and other stitches provided herein can improve the reliability of a seal formed along a stitch line, create fewer apertures through the leaflets, and simplify the stitching operation. Fewer apertures can limit an opportunity for blood to leak through the apertures. The single continuous line of stitch 446 using a single row of apertures can minimize a width of a side edge portion needed to form a continuous seal along the side edges of the leaflets, which can allow for a reduce restricted profile for prosthetic heart valves provided herein. For example, U.S. Patent No. 8,778,020 describes a variety of ways that leaflets can be sutured together using combinations of whip stitches and running stitches, which require additional apertures and multiple lines. Perpendicular loop segments 434 can provide a function similar to the whip stitches discussed in U.S. Patent No. 8,778,020 and parallel segments 436 can provide a function similar to the running stitches discussed in U.S. Patent No. 8,778,020. Although stitch 446 can provide an improved attachment between side edges of leaflets in prosthetic heart valves provided herein, some embodiments of prosthetic heart valves provided herein can use other stitch patterns, such as those described in U.S. Patent No. 8,778,020, which is hereby incorporated by reference.

Several important characteristics of the thread can include, but are not limited to, a tensile strength, abrasion resistance and creep rupture resistance characteristics that can withstand device delivery and implantation. The thread used for suturing together portions of the heart valve, e.g., sides edges of the leaflets, can composed of biocompatible materials that include polyethylene, such as ultra high molecular weight polyethylene (UHMWPE), polyester (PET), and combinations thereof.

Referring back to FIGS. 1A and 1B, prosthetic heart valve 100 can include a tubular seal 130. Tubular seal 130 can be secured to bottom edges 222 (FIG. 2A) of leaflets 200 by a cross stitch 134 within prosthetic heart valve 100. Tubular seal 130 can be secured to expandable tubular member 110 by fasteners 136 and extend around the outside of expandable tubular member 110 to provide a seal to minimize blood leakage around the leaflets 200 when prosthetic heart valve 100 is implanted. The structure and materials of tubular seal 130 are discussed below in reference to FIGS. 6, 7a, and 7b.

Referring to FIGS. 5A-5C, an improved tubular seal stitching pattern can include a cross stitch 132 between tubular seal 130 and expandable member 110. As shown in FIGS. 1A, 1B, and 5A-5C, expandable member 110 can be a braided stent including one or more wires having a first set of segments 114 extending helically in a first direction and a second set of segments 116 extending helically in a second direction such that the first set of segments 114 cross the second set of segments 116 at intersection points 118. As shown, one or more wires can have inflow crows 115 at an end of the braided stent where the wires transition a first segment 114 to a second segment 116. In some cases, cross stitches 132 secure tubular seal 130 to two crossing segments 114 and 116 of the braided stent at an intersection 118. A separate circumferential running stitch 134 can inserted into preformed apertures 133 to secure the adaptive seal to bottom edges 222 of leaflets 200 shown in FIGS. 2A and 2C. Cross-stitches around intersections 118 can increase the strength of the attachment of tubular seal 130 to the expandable member 110 while also allowing for improved load transfer to the expandable member 110. In some cases, the cross stitches secure tubular seal 130 at intersections 118 immediately above (proximal) of the inflow crowns 115. Cross stitches 132 can be formed by passing two stitches 132a, 132b of suture in orthogonal directions over intersections 118, passing through the tubular seal 130. In some cases, preformed apertures 131 for cross stitch 132 can be formed in the

tubular seal 130. In some cases, a portion of the tubular seal 130 sutured by cross stitch 132 includes an internal fabric, such as those discussed below. Each cross stitch 132 can be knotted independently. As shown in FIG. 5C, cross stitches 132 each include a separate knot 137. Additionally, cross stitches 132 can be arranged to not pass through leaflets 200. Cross stitches 132 can be repeated at a plurality of intersections 118 (FIG. 5A) circumferentially around an inflow end of a prosthetic heart valve provided herein such that an entire circumference of tubular seal 130 is securely attached. In some cases, each intersection 118 immediately adjacent to inflow crowns 115 is sutured to tubular seal 130 via a cross stitch provided herein.

Tubular seal 130 can have any suitable structure. In some cases, tubular seal 130 can include an elastic material. In some cases, tubular seal 130 can include one or more layers of an elastomeric polymer. In some cases, tubular seal 130 can include polycarbonate, polyurethane, silicone, polytetrafluoroethylene (PTFE), or a combination thereof. In some cases, tubular seal 130 can include an aliphatic polycarbonate-based thermoplastic urethane. In some cases, tubular seal 130 can include an elastomeric polymer having harnesses ranging from 75 Shore A to 75 Shore D using ASTM standard D2240 in force on January 1, 2014. In some cases, tubular seal 130 can include a polymeric material having the mechanical properties shown in Table I below. Notably, all of the listed ASTM standards refers to the standard in force on January 1, 2014.

				ASTM Standard
Durometer Range Available	75 Shore A-75 Shore D			D2240
Specific Gravity	1.10-1.14			D792
Melt Flow	2-26g/10min(205°C/3.26kg)			D1238
MECHANICAL PROPERTY RANGES				**ASTM Standard**
Durometer	75A-B20	55D	75D	75D
Ultimate Tensile Strength (psi)	400-9000	5000-10000	3000-8000	D638
Tensile (psi)				
@50% elongation	350-650	1500-1800	3000-8000	D638
@100% elongation	550-850	1800-2200	3000-8000	D638
@200% elongation	600-1200	2800-4200		D638
@300% elongation	1200-2000	4200-10000		D630
Ultimate Elongation (%)	350-750	200-400	100-300	D638

Table I

In some cases, tubular seal 130 can include attachment structures to improve the attachment of the tubular seal 130 to leaflets 200 and/or expandable member 110.

In some cases, such as shown in FIG 7A a tubular seal 730 can include an inflow end section 740 an outflow end section 750 wherein the inflow end section 740 includes a fabric embedded within elastomeric material and outflow end section 750 includes a plurality of grommets 732. The fabric in inflow end section 740 can be a woven material. In some cases, the fabric can have warp threads and weft threads. In some cases, the fabric can include non-elastomeric fibers. For example, in some cases, the fabric can include polyester fibers, e.g., PES 38/31 manufactured by SaatiTech. In some cases, the fabric is composed of fibers having a thread diameter of about 0.0011 inches (about 27 microns). Because the fabric includes non-elastic fibers, inflow end section 740 and outflow end section 750 have different overall elastic properties. In some cases, tubular seal 730 can be used as tubular seal 130 of prosthetic heart valve 100. In some cases, tubular seal 730 can be used in other prosthetic heart valves provided herein.

As shown in FIG 7A, an interface between the inflow end section 740 and the outflow end section 750 is non-linear due to a non-linear edge of fabric within the inflow end section 740. As shown, the non-linear edge can be sinusoidal. In some

cases, not shown, the non-linear edge can be scalloped. In some cases, the non-linear edge can be zigzagged, sinusoidal, stepped, scalloped or pointed. Because of the presence of a fabric within inflow end section 740, inflow end section 740 can be thicker than outflow end section 750. For example, in some cases, an inflow end section 740 can have a thickness of about 0.003 inches (about 70 microns) and the outflow end section 750 can have a thickness of about 0.002 inches (about 50 microns). Other dimensions are also suitable. A non-linear edge providing an non-linear interface between the inflow end section 740 and the outflow end section 750 can result an overall diameter increase of a prosthetic heart valve provided herein that tapers more gradually than would be provided by an inflow end section 740 having a linear interface with the outflow end section 750. The non-linear edge of the fabric can also transition the change in elastic properties between outflow end section 750 to inflow end section 740 to mitigate the formation of stress concentrators along the interface with can result in tears of the tubular member. Additionally, the shape of non-linear interface can limit the propagation of tears.

In some cases, the fabric can be arranged in inflow end section 740 to allow for the fabric within inflow end section 740 to be stretched in axial and radial directions. For example, in the case of a woven fabric, the fabric can be arranged to have the warp and the waft extend in directions orthogonal to the axis of the tubular seal to allow for the fabric to flex in both radial and axial directions. In some cases, both the warp and the waft can extend at an angle of between 30 degrees and 60 degrees with the axis of the tubular seal. In some cases, both the warp and the waft can extend at an angle of between 5 degrees and 70 degrees with the axis of the tubular seal. For example, the warp and waft can be arranged within the tubular member 730 to form an angle of about 45 degrees with the axis of the tubular seal. In some cases, the fabric can be a knit fabric arranged to allow for a predetermined amount of stretch in the axial and radial directions.

Additional exemplary tubular seals including a fabric and grommets are described in US Patent Application No. 2013/0090729, which is hereby incorporated by reference in its entirety. In some cases, tubular seals described in US Patent Application No. 2013/0090729 can be modified to include a fabric arranged to allow for it to stretch in a radial direction.

Tubular seal 730 can be created by producing one or more layers of elastomeric polymer, applying the fabric and grommets 732 to the one or more layers of elastomeric polymer, and overcoating the fabric and grommets 732 with one or more additional layers of elastomeric material. In some cases, different layers can have different elastomeric properties. In some cases, tubular seals (e.g., 130, 730, or 760) can include a radially innermost layer including a polycarbonate and a polyurethane; a radially outermost layer including a polycarbonate and a polyurethane; and at least one inner layer disposed between the radially outermost layer and the radially innermost layer including a polycarbonate and a polyurethane. In some cases, the modulus of elasticity of the inner layer is less than the modulus of elasticity of the radially innermost outer layer and the modulus of elasticity of the radially outermost outer layer. In some cases, the elongation to break of the inner layer is greater than the elongation to break of the radially innermost outer layer and the elongation to break of the radially outermost outer layer. Although the radially innermost outer layer and the radially outermost outer layer have been depicted as comprising the same material, it will be appreciated that they may be compositionally the same or different.

The multilayer tubular seals provided herein (e.g., 130, 730, 760) may be formed in a variety of ways. For example, multilayer tubular seals provided herein may be formed by successive applications of a polymer solution to an appropriately shaped mandrel, such as that illustrated in FIG. 6. Following a careful cleaning of the mandrel 600, the mandrel may be mounted to an appropriate holding fixture in a spray booth. A first coating composition comprising a carrier and at least one polymer may be applied to the mandrel 600 and subsequently dried to form a first coated mandrel. In some cases, the first coating composition comprises a polycarbonate, a polyurethane, and a volatile carrier. The coating composition may be applied as a single layer or multiple layers to achieve the desired dried coating thickness. The grommets 732 and the fabric may be positioned on the first coated mandrel, for example by inserting locating pins 620 in apertures 610 in the tapered mandrel 600 which align with corresponding perforations 30 provided in the grommets 32, 34, 36 and fabric 40. In FIG. 6, only one pin 620 has been illustrated for clarity. In some instances, it may be desirable to secure the plurality of grommets 732 and the fabric to the mandrel or to an underlying coating layer by applying a drop of a first coating

composition, or other adhesive composition, to each item to ensure that it remains properly positioned during subsequent processing. The fabric can be cut to a suitable shape having a non-linear edge using any suitable method. In some cases, the fabric can be die cut. In some cases, the fabric can be cut using a femtosecond laser. In some cases, a femtosecond laser cut fabric mitigate the chances of forming stress concentrators along the edge of the fabric.

A second coating composition comprising a carrier and at least one polymer may be applied to the first coated mandrel, the fabric, and the plurality of grommets. In some cases, the second coating composition comprises a polycarbonate, a polyurethane, and a volatile carrier. The carrier of the second coating composition may be removed, thereby forming a second coated mandrel. The second coating composition may be applied as a single layer or as multiple layers to achieve the desired dried coating thickness. In some cases, the second coating composition may be different from the first coating composition. In some cases, the second coating composition may be the same as the first coating composition.

In some cases, a third coating composition comprising a carrier and at least one polymer may be applied to the second coated mandrel. In some cases, the third coating composition comprises a polycarbonate, a polyurethane, and a volatile carrier. The carrier of the third coating composition may be removed thereby forming a tubular seal precursor. The third coating composition may be applied as a single layer or multiple layers to achieve the desired dried coating thickness. In some cases, the third coating composition may be different from the first coating composition. In some cases, the third coating composition may be the same as the first coating composition. In some cases, the third coating composition may be different from the second coating composition. In some cases, the third coating composition may be the same as the second coating composition. Following removal of the carrier from the third coating composition, the tubular seal precursor may be inspected to ensure that it is fully formed and meets dimensional specifications, such as a thickness specification. For example, a suitable thickness for the tubular seal precursor can range from about 0.001 inches to about 0.0030 inches (about 30 microns to about 75 microns) or from about 0.002 inches to about 0.0047 inches (about 50 microns to about 120 microns). Other suitable thicknesses for the tubular seal precursor include a range from about 0.0008 inches to about 0.002 inches (about 20 microns to about 40

microns), about 0.001 inches to about 0.002 inches (about 30 microns to about 50 microns), about 0.002 inches to about 0.0029 inches (about 50 microns to about 75 microns), about 0.002 inches to about 0.004 inches (about 50 microns to about 100 microns), about 0.004 inches to about 0.0047 inches (about 100 microns to about 120 microns), about 0.004 inches to about 0.0059 inches (about 100 microns to about 150 microns), about 0.0059 inches to about 0.0079 inches (about 150 microns to about 200 microns), as well as any thickness value within any of the listed ranges. Also, the tubular seal precursor may be inspected to ensure that it meets certain functional specifications, e.g., tensile and frictional specifications. The tubular seal precursor may then be trimmed, for example by laser cutting or blade cutting, to conform to dimensional specifications; and removed from the tapered seal-forming mandrel thereby forming a tubular seal. In some cases, at least some preformed apertures for suturing tubular seal to expandable member 110 and/or leaflets 200 can be performed by laser cutting. In some cases, at least some of the grommets may be formed by a laser cutting operation performed on a tubular seal precursor. For example, grommets 732 may be added to the multilayer, generally cylindrical seal, in a step not illustrated, as a proximal band. Subsequent laser cutting of the tubular seal precursor would then simultaneously form grommets 732 by removing the portions of the proximal band located between the projections.

In some cases, coating compositions may be selected to provide a relatively stiff dried polymer such as a dried polymer having a Shore D hardness of about 55. In some cases, coating compositions may be selected to provide a relatively elastomeric dried polymer such as a dried polymer having a Shore A hardness of about 80. For example, the first and third dried polymer layers may have a Shore D hardness of 55 and the second layer may have a Shore A hardness of 80.

Although in the example above three polymer layers were employed, it will be appreciated that a greater or lesser number of layers may be employed and that each of the three or more layers may comprise two or more sublayers. Additionally, although the plurality of grommets and the fabric were positioned between the first and second coating layers in the example, they could have been positioned elsewhere within the tubular seal including within a layer, or on the radially innermost or radially outermost surface of the tubular seal.

The mandrel 600 of FIG. 6 includes a taper which results in a tubular seal having a slightly smaller diameter proximal end compared to the diameter of the distal end. The taper allows the tubular seal to be removed from the mandrel with relative ease upon completion of the fabrication process. The smaller proximal diameter of the tubular seal tends to cause the proximal projections to lie more firmly against the anchor element of the replacement heart valve. In some cases, the surface of the mandrel may be textured, for example by bead blasting, to create a tubular seal having a lower apparent contact area. In combination with the selection of a relatively hard outer layer, a textured seal surface is believed to result in a lower friction surface.

In some cases, as shown in FIG. 7B, a tubular seal 760 can include a woven or non-woven fabric embedded throughout a polymer or metal matrix structure. In some cases, the matrix structure can be made of elastomeric material. In some cases, tubular seal 760 can be made of the fabric alone. The fabric can include non-elastic fibers but be arranged to allow for the tubular seal to stretch in axial and radial directions. In some cases, the fabric can be a knit fabric arranged to allow for a predetermined amount of stretch in the axial and radial directions. In some cases, the fabric can be made of a polymer, for example, a polyester. In some cases, the fabric can have a thickness ranging from about 0.002 inches to about 0.003 inches (about 40 to about 80 microns). In some cases, the fabric can be woven such that spacings between individual fibers create openings in the fabric that together constitutes about 20% to about 40% of a fabric surface.

A number of embodiments of the invention have been described. Nevertheless, it will be understood that various modifications may be made without departing from the spirit and scope of the invention. Accordingly, other embodiments are within the scope of the following claims.

WHAT IS CLAIMED IS:

1. A prosthetic heart valve comprising at least two leaflets being secured together along aligned edges thereof by a stitch of a single thread, the stitch comprising at least one loop extending through a first aperture, around the aligned edges, and back through the first aperture.

2. The prosthetic heart valve of claim 1, wherein the stitch further comprises at least one segment of thread extending from the first aperture to a second aperture in a direction parallel to the aligned edges of the at least two leaflets.

3. The prosthetic heart valve of claim 2, wherein the stitch comprises a second loop extended through the second aperture, around the aligned edges, and back through the second aperture.

4. The prosthetic heart valve of one of claims 1-3, wherein the stitch comprises at least three loops each extending from an aperture, around the aligned edges, and back to that aperture.

5. The prosthetic heart valve of claim 4, wherein the stitch runs in a forward direction having thread pass through a set of apertures and back in a reverse direction having the thread again pass through the set of apertures.

6. The prosthetic heart valve of claim 5, wherein each aperture has two loops extending from that aperture, around the aligned edges, and tack to that aperture, wherein one loop is from the stitch running in the forward direction and one loop is from the stitch running in the reverse direction.

7. The prosthetic heart valve of claim 5 or claim 6, wherein segments of thread extending between adjacent apertures in the forward direction are on an opposite side of the two leaflets from the segments of thread extending between adjacent apertures in the reverse direction.

8. The prosthetic heart valve of one of the preceding claims, wherein each leaflet has a body portion and two opposite sleeve portions, the body portion being defined by a bottom edge and two side edges adjacent each sleeve portion, wherein each of the at least two leaflets are aligned and stitched along a first side edge.

9. The prosthetic heart valve of claim 8, wherein the leaflets define notches between the two side edges and the adjacent sleeve portion.

10. The prosthetic heart valve of claim 8, further comprising a plurality of support element each supporting sleeve portions each leaflet along a line approximately aligned the stitch.

11. The prosthetic heart valve of one of the preceding claims, further comprising:

at least three leaflets secured together along side edges thereof by the stitch of claim 1;

a tubular expandable member secured to an out flow end of the at least three leaflets; and

a tubular seal secured to an inflow end bottom edge of the at least three leaflets and to an outer surface of the tubular expandable member.

12. The prosthetic heart valve of claim 11, wherein the tubular expandable member is a braided stent and wherein tubular seal is secured to the braided stent by a plurality of cross stitches connecting the tubular seal to a pair of overlapping wire members of the braided stent.

13. The prosthetic heart valve of claim 11 or claim 12, wherein the tubular seal comprises a woven fabric within a polymer matrix, the at least three leaflets are secured to the tubular seal in a portion of the tubular seal comprising the woven fabric.

14. The prosthetic heart valve of one of the preceding claims, wherein the at least one leaflet comprises bovine or porcine pericardium tissue or a synthetic material.

15. The prosthetic heart valve of one of the preceding claims, wherein the stitch is formed using between 3 and 20 apertures and includes between 3 and 40 loops each extending from an aperture, around the aligned side edges, and back to that aperture.

16. A prosthetic heart valve comprising at least two leaflets being secured together along aligned edges thereof by a stitch of a single thread, the stitch comprising at least one loop extending through a first aperture, around the aligned edges, and back through the first aperture.

17. The prosthetic heart valve of claim 16, wherein the stitch further comprises at least one segment of thread extending from the first aperture to a second aperture in a direction parallel to the aligned edges of the at least two leaflets.

18. The prosthetic heart valve of claim 17, wherein the stitch comprises a second loop extended through the second aperture, around the aligned edges, and back through the second aperture.

19. The prosthetic heart valve of one of claims 16, wherein the stitch comprises at least three loops each extending from an aperture, around the aligned edges, and back to that aperture.

20. The prosthetic heart valve of claim 19, wherein the stitch runs in a forward direction having thread pass through a set of apertures and back in a reverse direction having the thread again pass through the set of apertures.

21. The prosthetic heart valve of claim 20, wherein each aperture has two loops extending from that aperture, around the aligned edges, and tack to that aperture, wherein one loop is from the stitch running in the forward direction and one loop is from the stitch running in the reverse direction.

22. The prosthetic heart valve of claim 20, wherein segments of thread extending between adjacent apertures in the forward direction are on an opposite side of the two leaflets from the segments of thread extending between adjacent apertures in the reverse direction.

23. The prosthetic heart valve of claim 16, wherein each leaflet has a body portion and two opposite sleeve portions, the body portion being defined by a bottom edge and two side edges adjacent each sleeve portion, wherein each of the at least two leaflets are aligned and stitched along a first side edge.

24. The prosthetic heart valve of claim 23, wherein the leaflets define notches between the two side edges and the adjacent sleeve portion.

25. The prosthetic heart valve of claim 23, wherein the stitch runs along a side edge from a bottom edge to a notch.

26. The prosthetic heart valve of claim 23, further comprising a plurality of support element each supporting sleeve portions each leaflet along a line approximately aligned the stitch.

27. A prosthetic heart valve comprising:

at least three leaflets secured together along side edges thereof by a stitch of a single thread;

a tubular expandable member secured to an out flow end of the at least three leaflets; and

a tubular seal secured to an inflow end bottom edge of the at least three leaflets and to an outer surface of the tubular expandable member.

28. The prosthetic heart valve of claim 27, wherein the tubular expandable member is a braided stent and wherein tubular seal is secured to the braided stent by a plurality of cross stitches connecting the tubular seal to a pair of overlapping wire members of the braided stent.

29. The prosthetic heart valve of claim 27, wherein the tubular seal comprises a woven fabric and the at least three leaflets are secured to the tubular seal in a portion of the tubular seal comprising the woven fabric.

30. The prosthetic heart valve of claim 29, wherein the woven fabric can have a thickness range from about 40 to about 80 microns.

31. The prosthetic heart valve of claim 29, wherein the woven fabric is disposed within a polymer matrix.

32. The prosthetic heart valve of claim 27, wherein the at least one leaflet comprises bovine or porcine pericardium tissue or a synthetic material.

33. The prosthetic heart valve of claim 27, wherein the stitch is formed using between 3 and 20 apertures and includes between 3 and 40 loops each extending from an aperture, around the aligned side edges, and back to that aperture.

34. The prosthetic heart valve of claim 27, wherein one or more stitches can be repeated at a plurality of intersections circumferentially around the inflow end bottom edge.

35. A prosthetic heart valve comprising:

at least three leaflets secured together along side edges thereof by a stitch of a single thread, at least one leaflet being secured to at least a second leaflet by a running stitch, the running stitch being a square stitch;

a tubular expandable member secured to an out flow end of the at least three leaflets; and

a tubular seal secured to an inflow end bottom edge of the at least three leaflets and to an outer surface of the tubular expandable member.

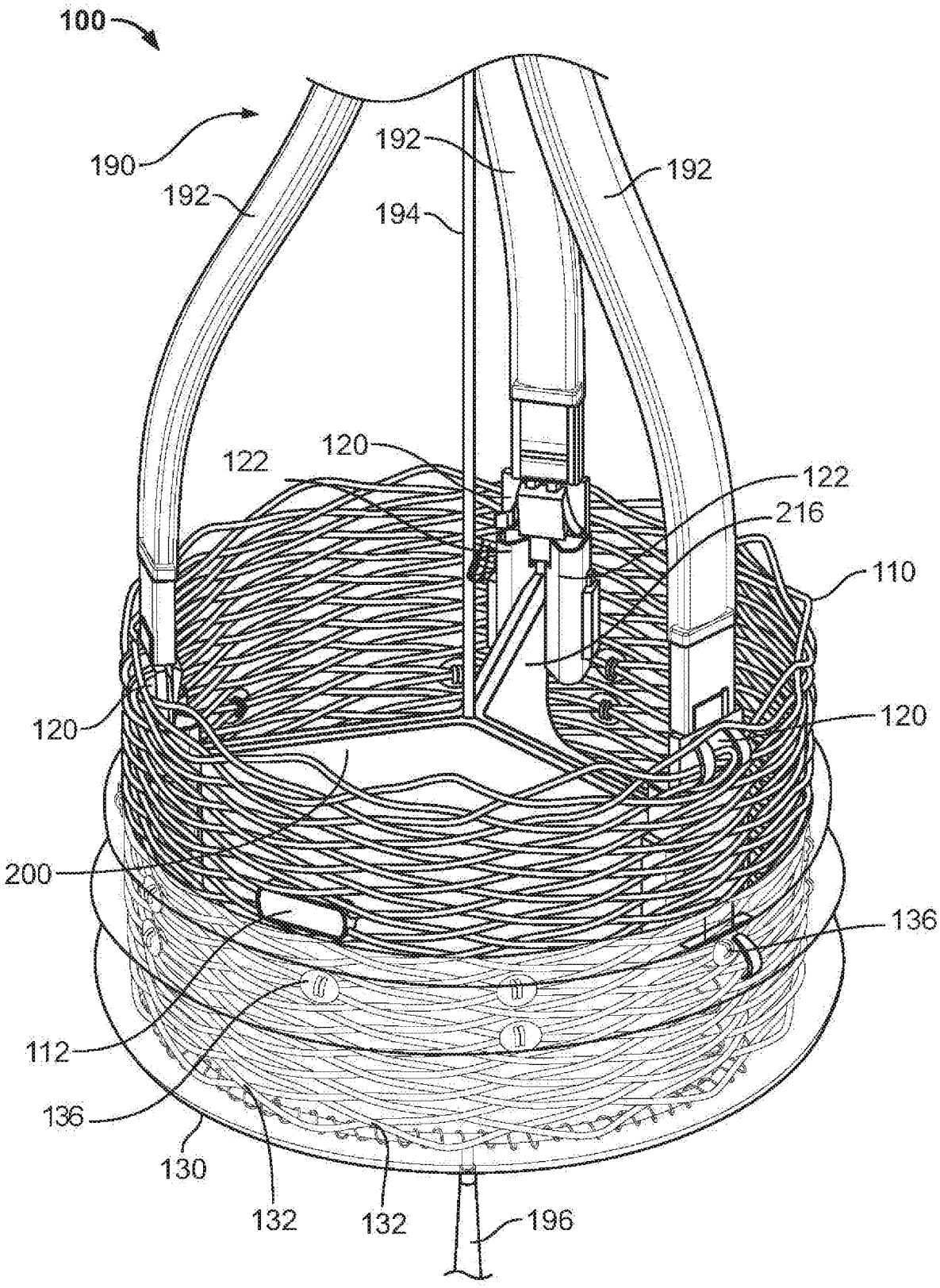

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FIG. 1A

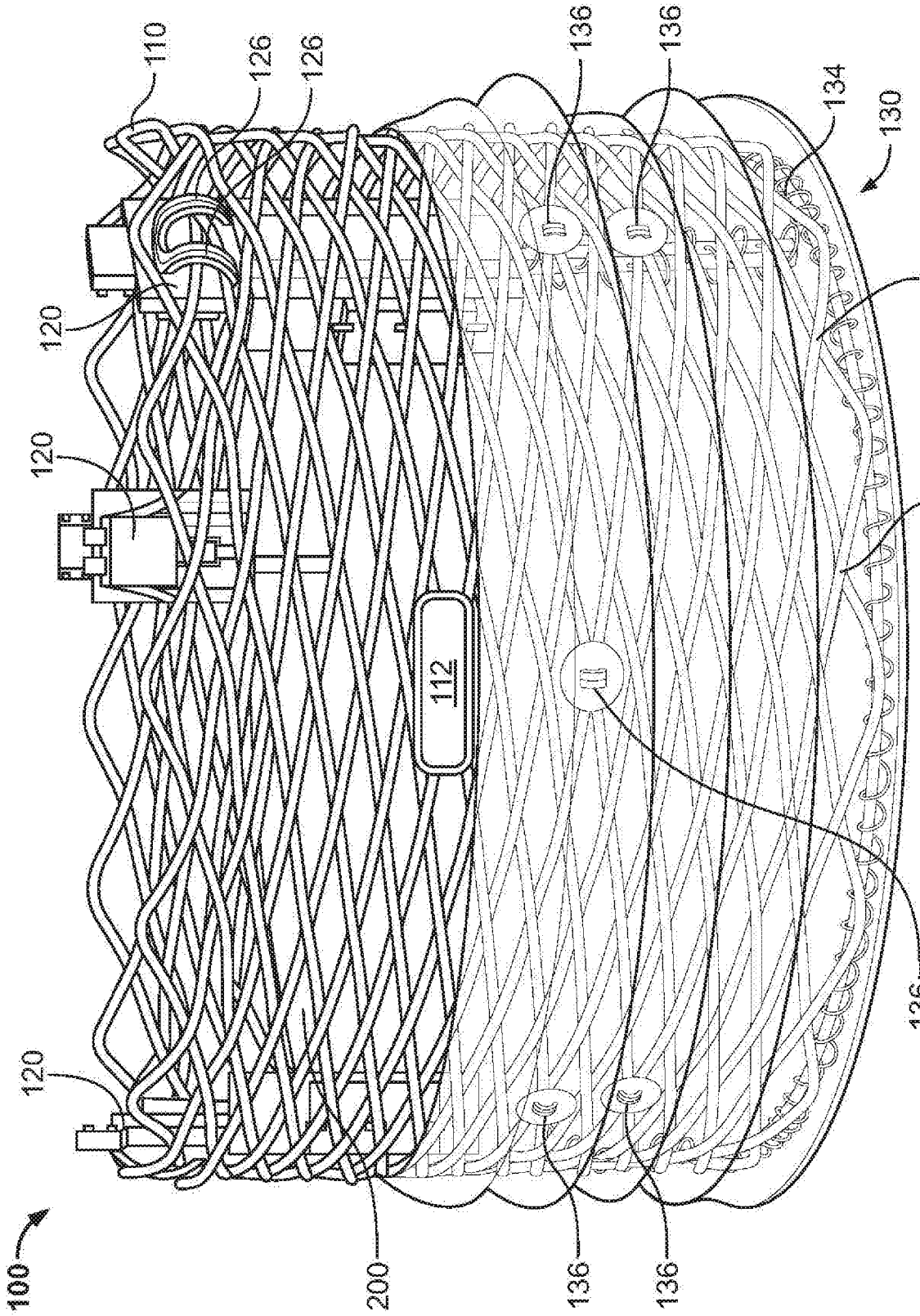

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FIG. 1B

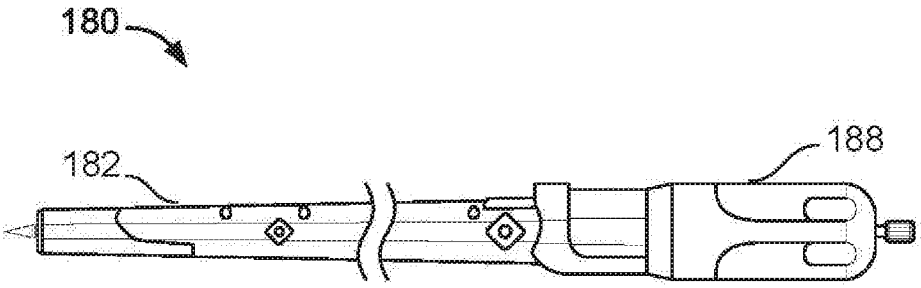


FIG. 1C

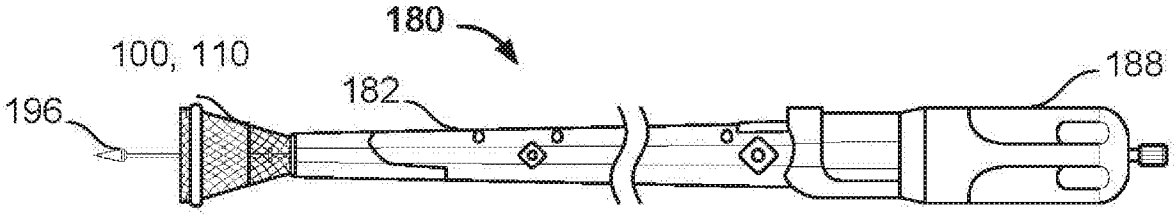


FIG. 1D

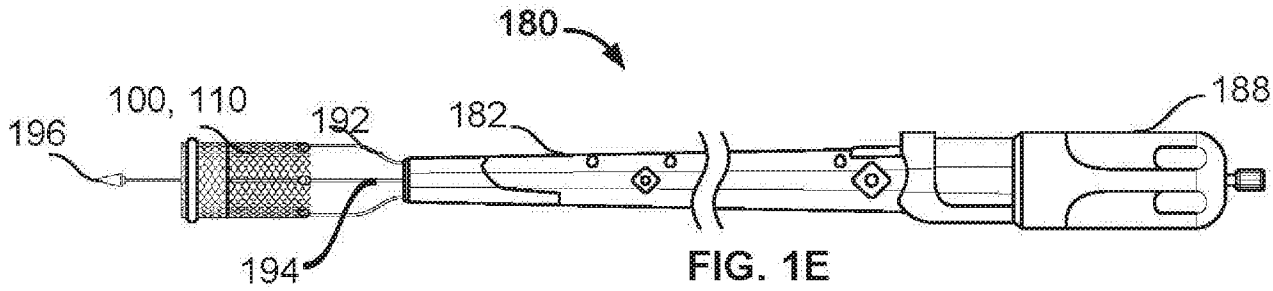


FIG. 1E

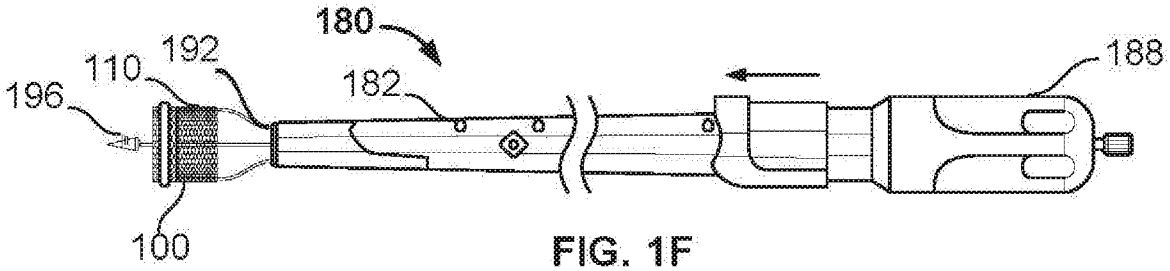


FIG. 1F

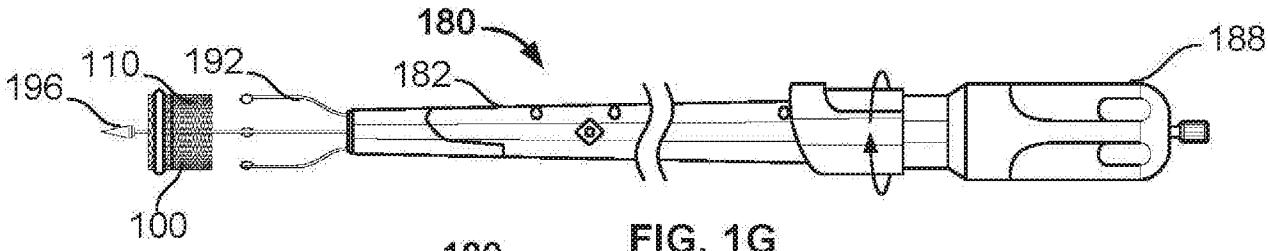


FIG. 1G

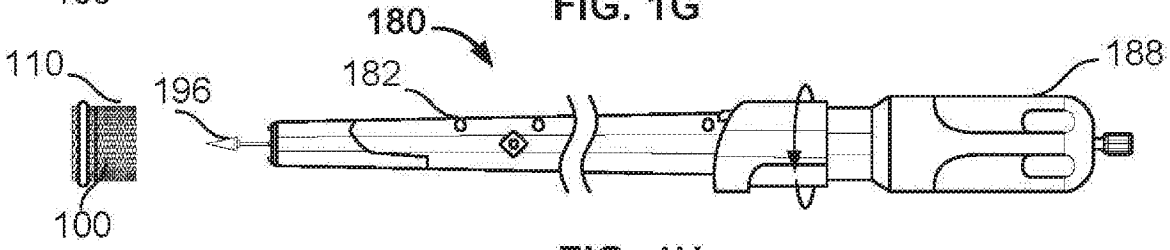


FIG. 1H

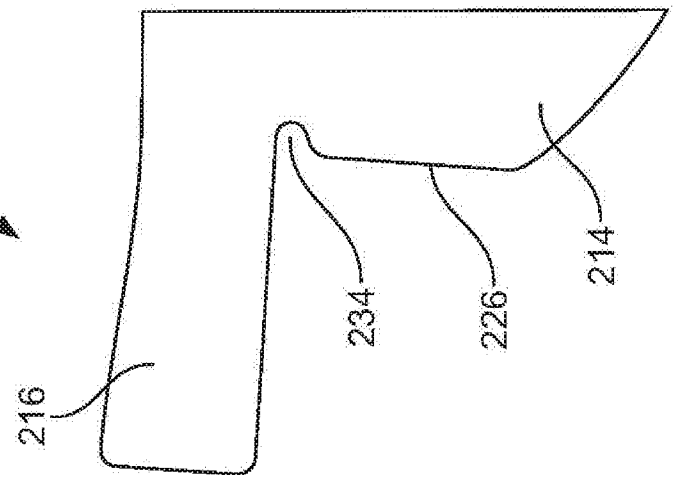


FIG. 2B

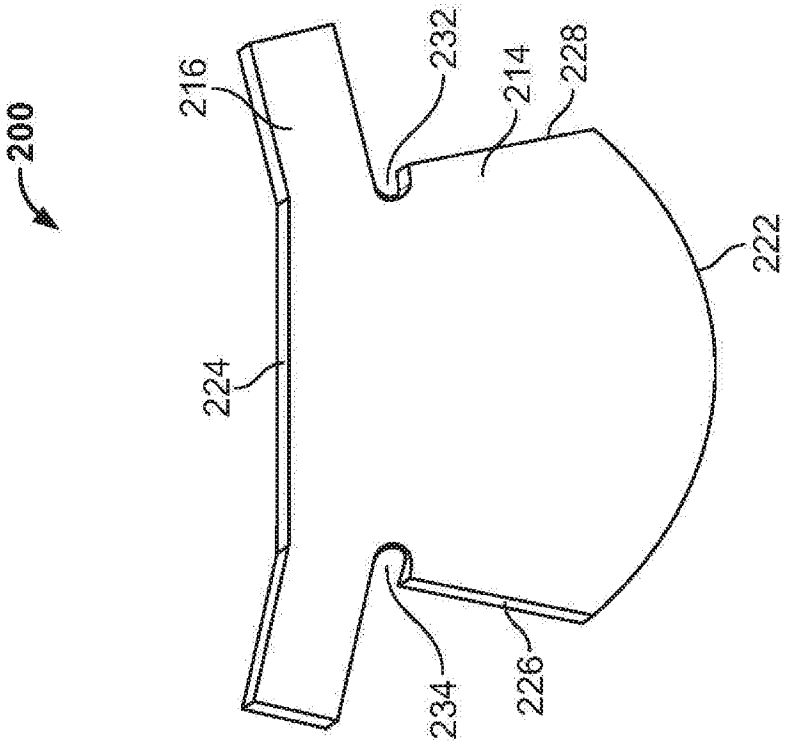


FIG. 2A

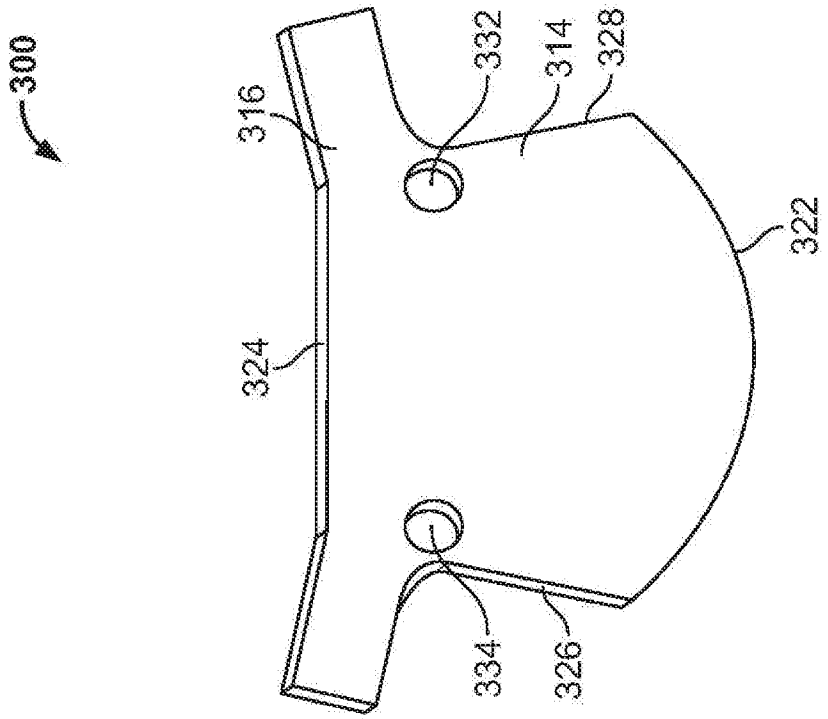

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FIG. 3

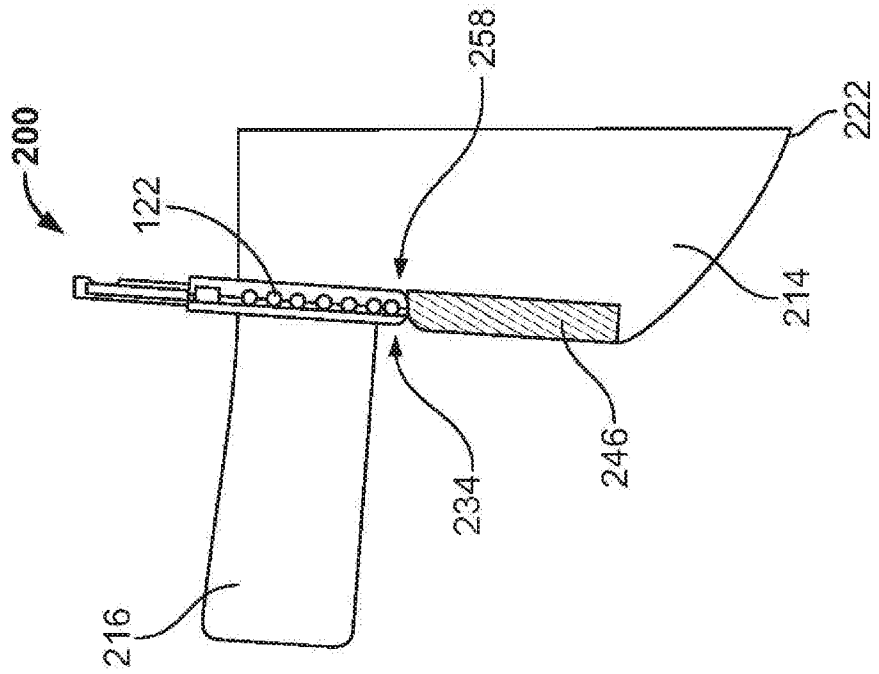

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FIG. 2C

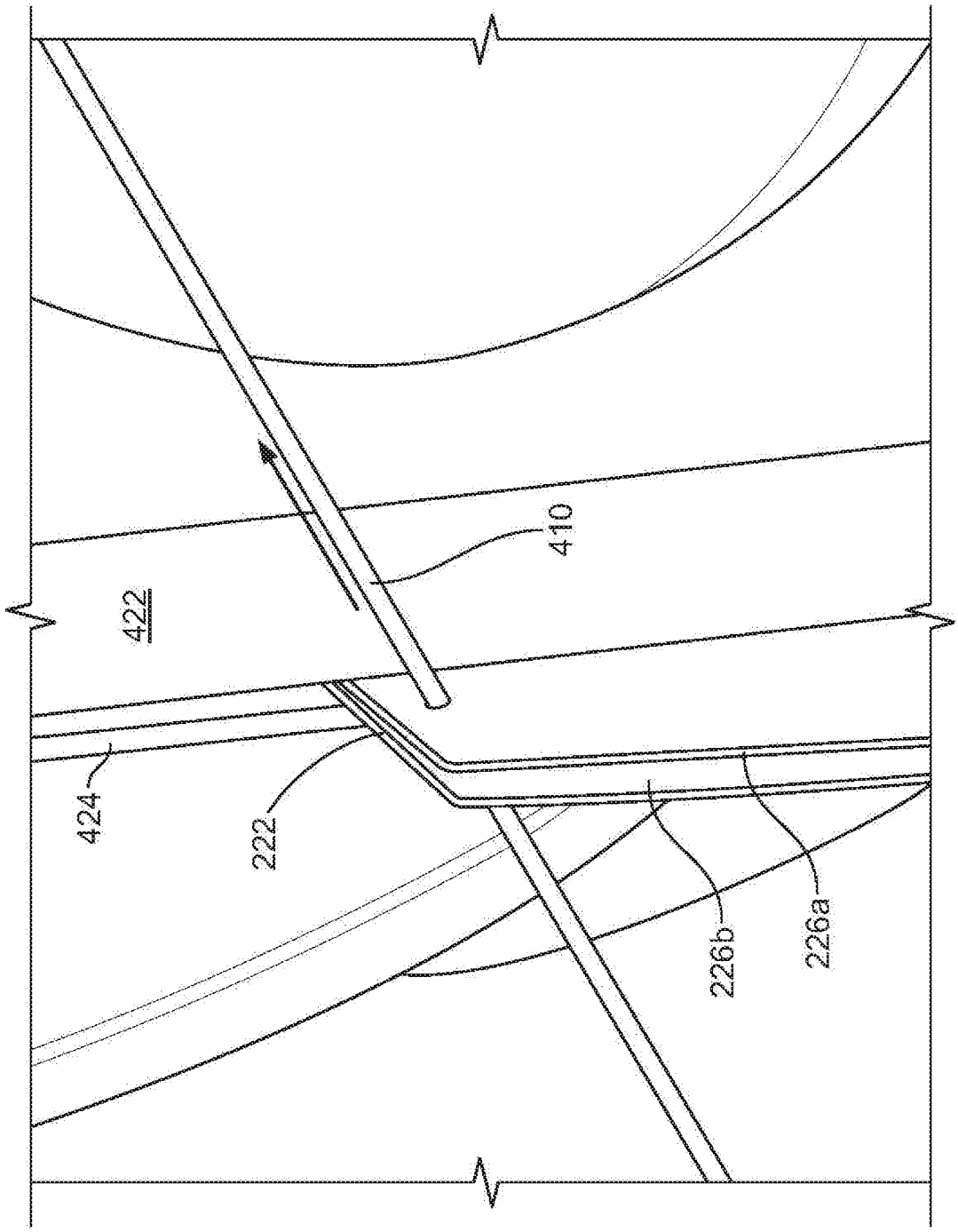


FIG. 4A

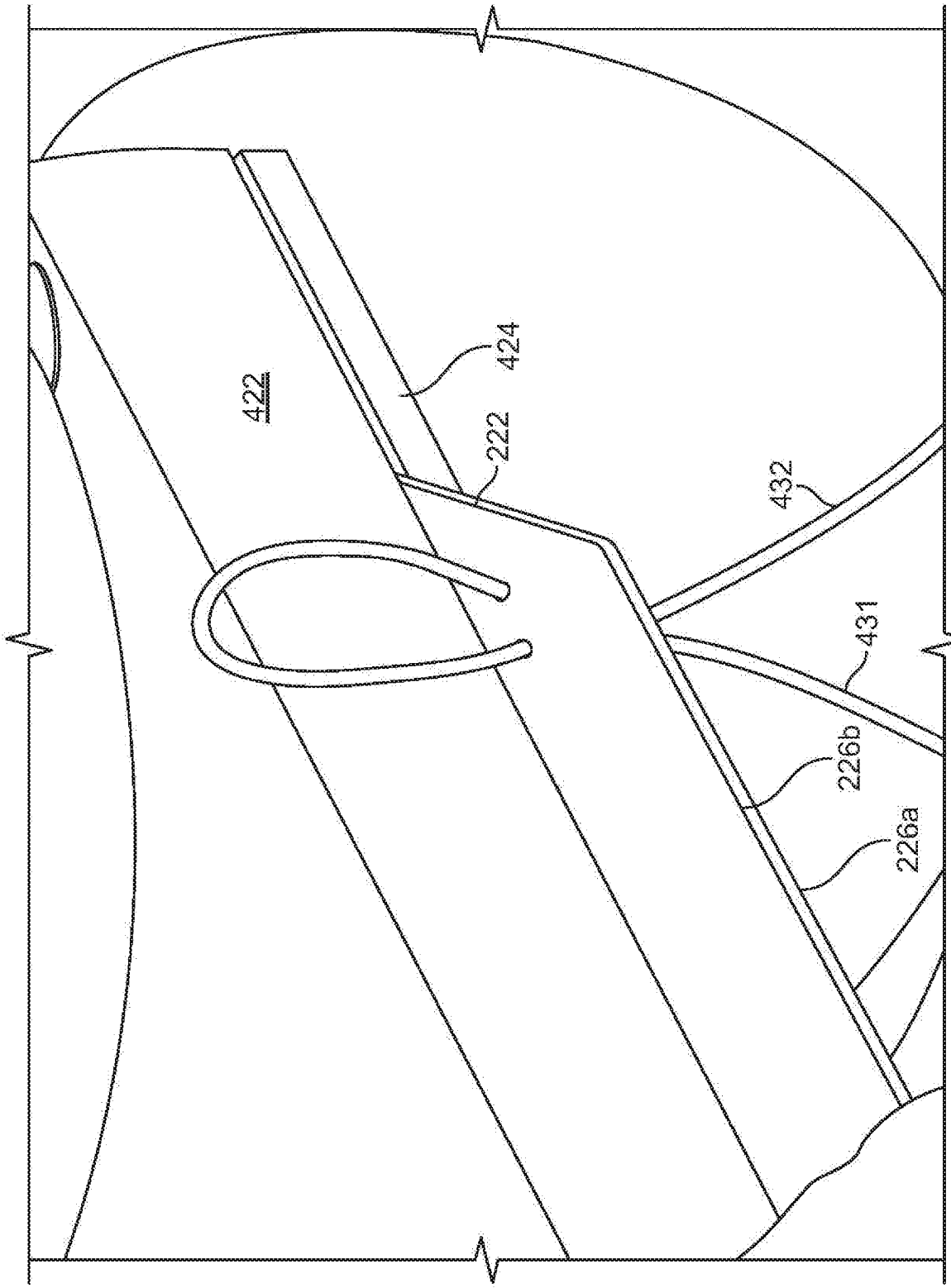


FIG. 4B

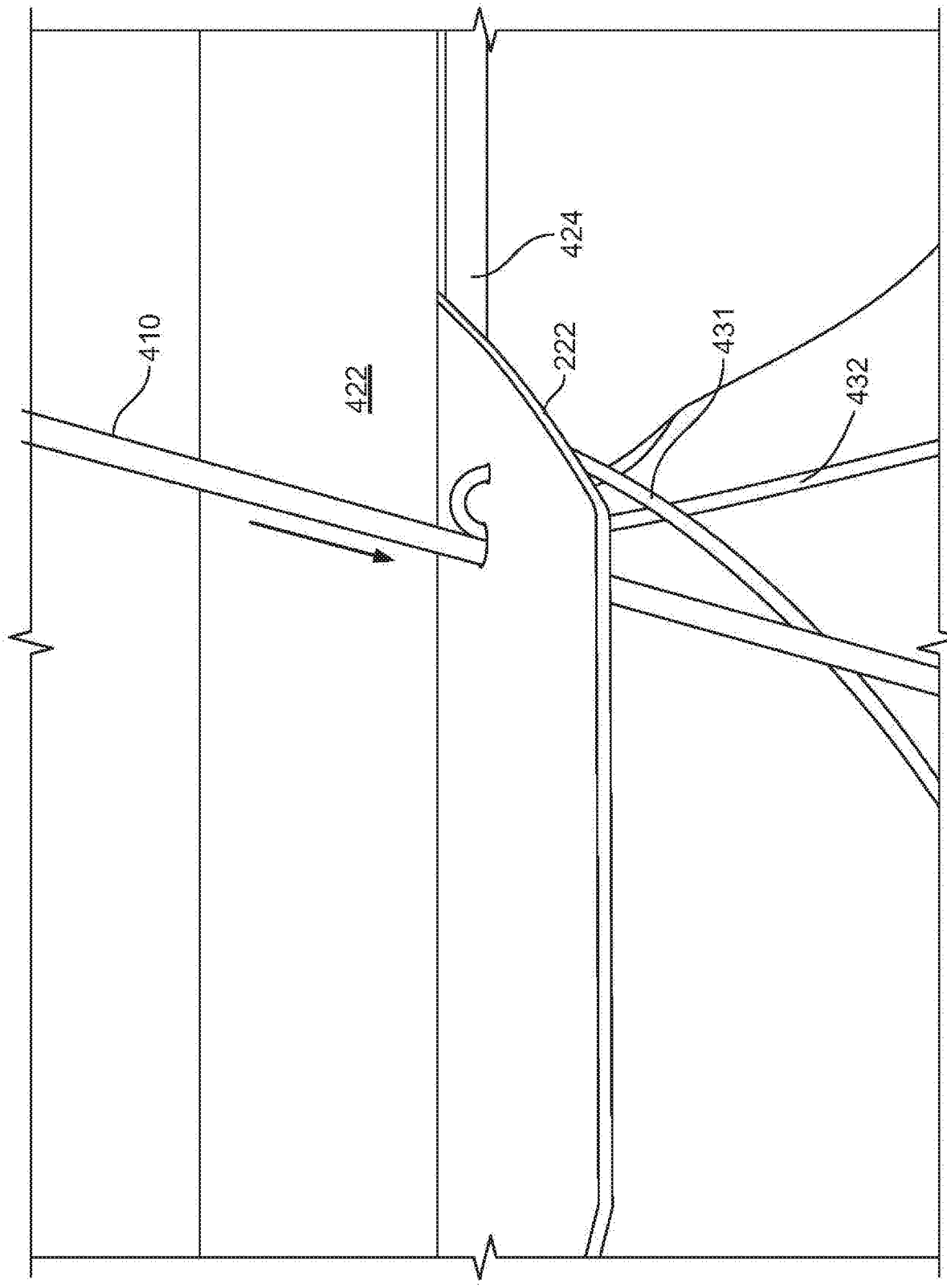


FIG. 4C

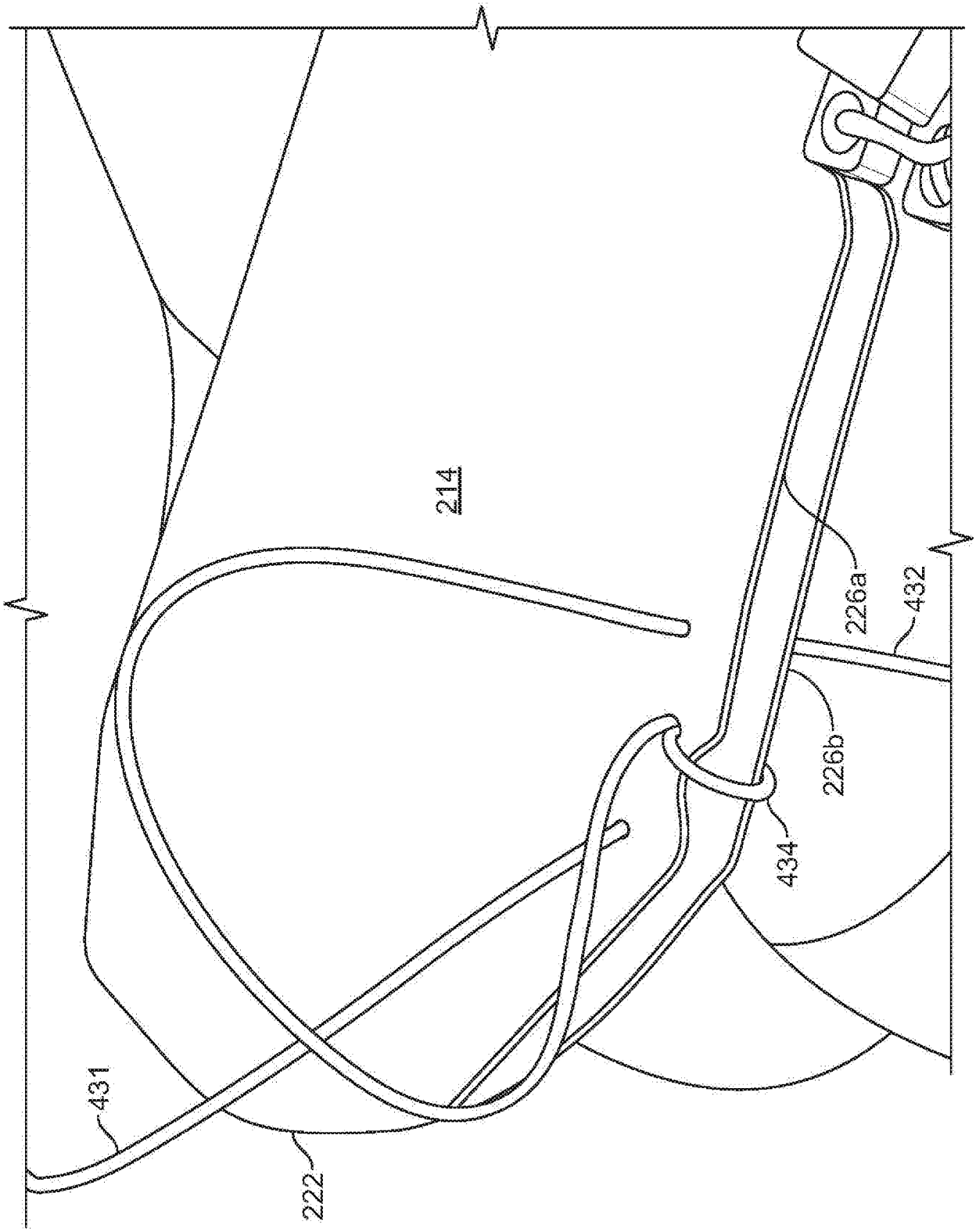


FIG. 4D

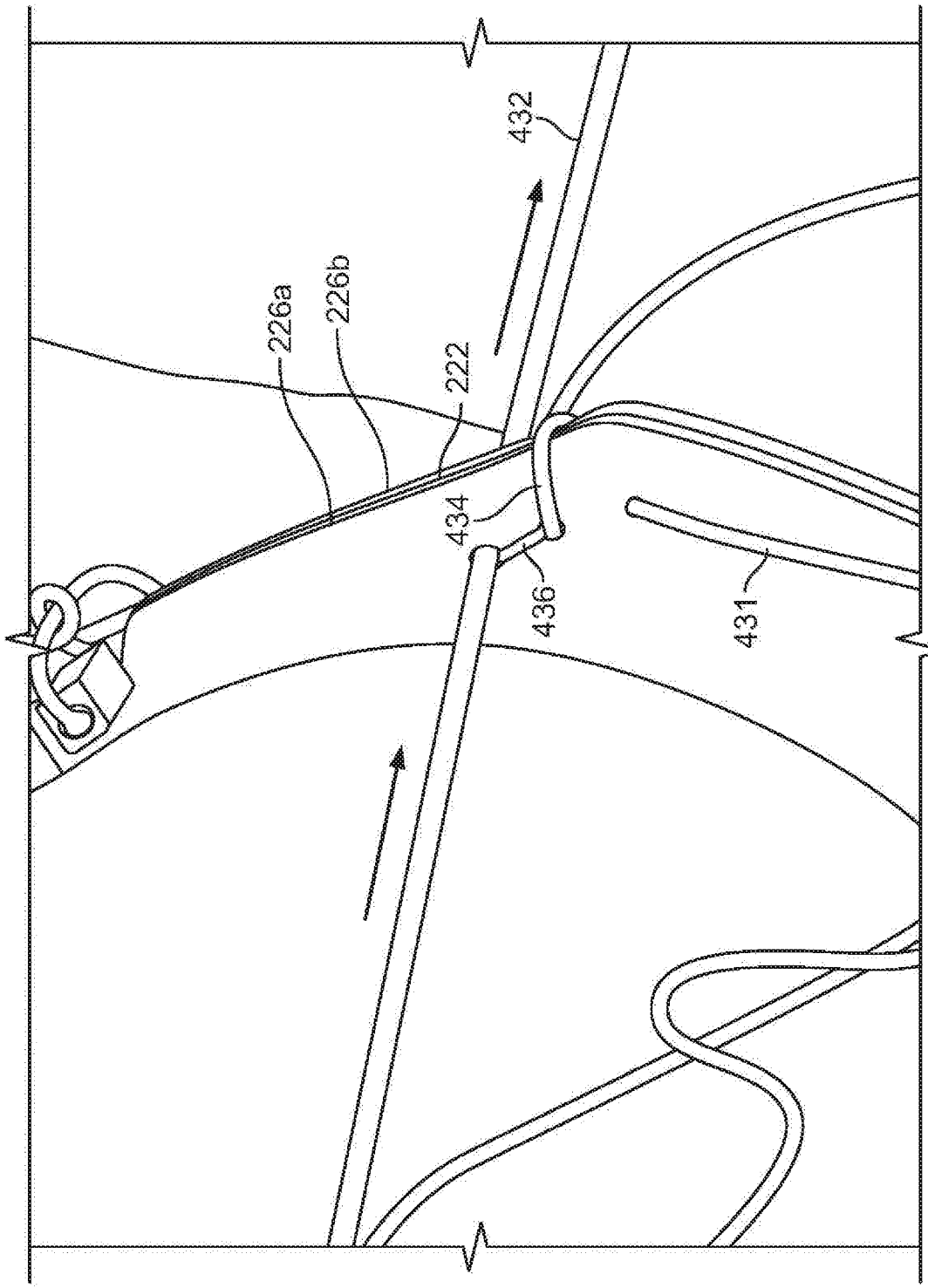


FIG. 4E

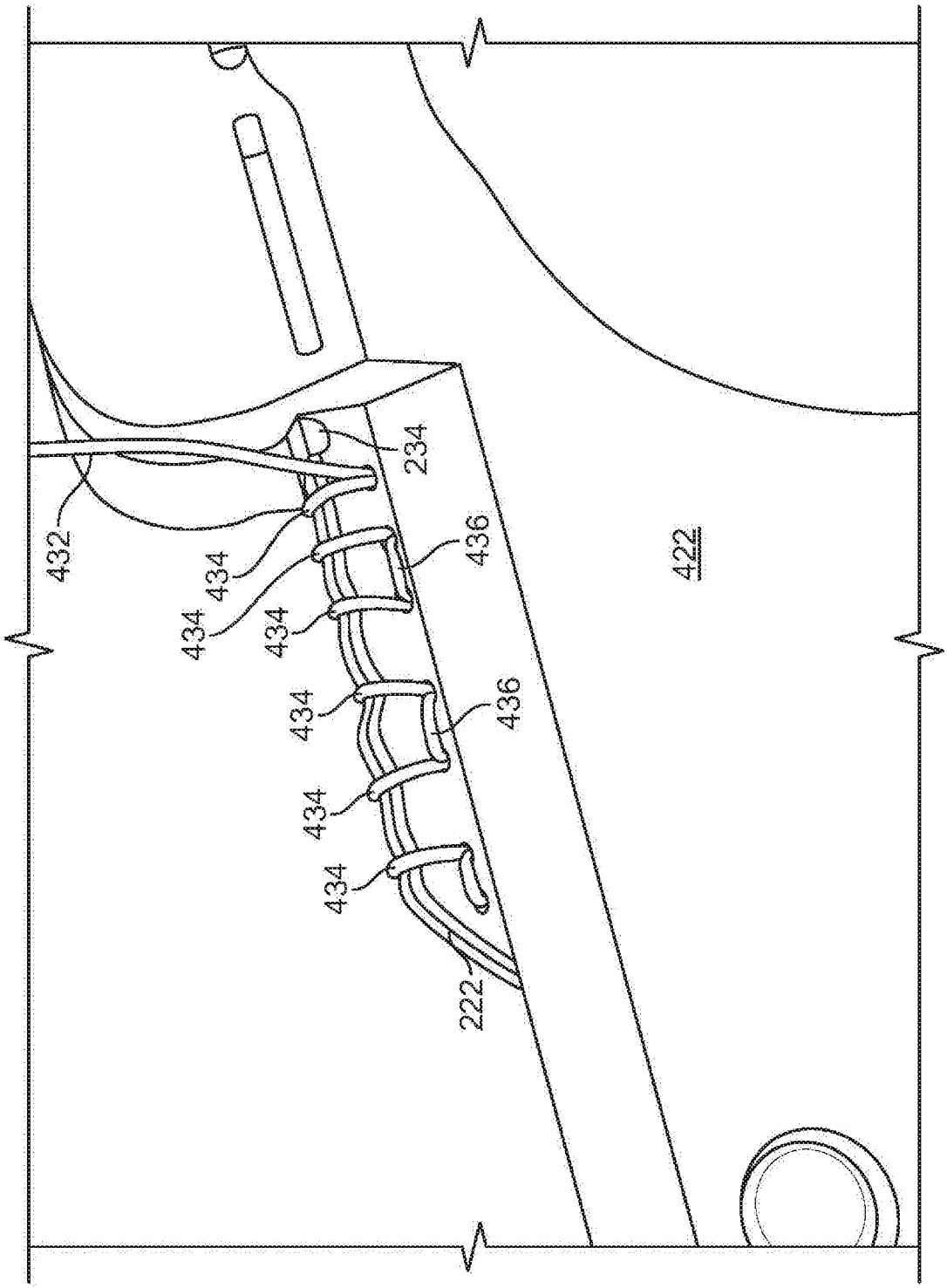


FIG. 4F

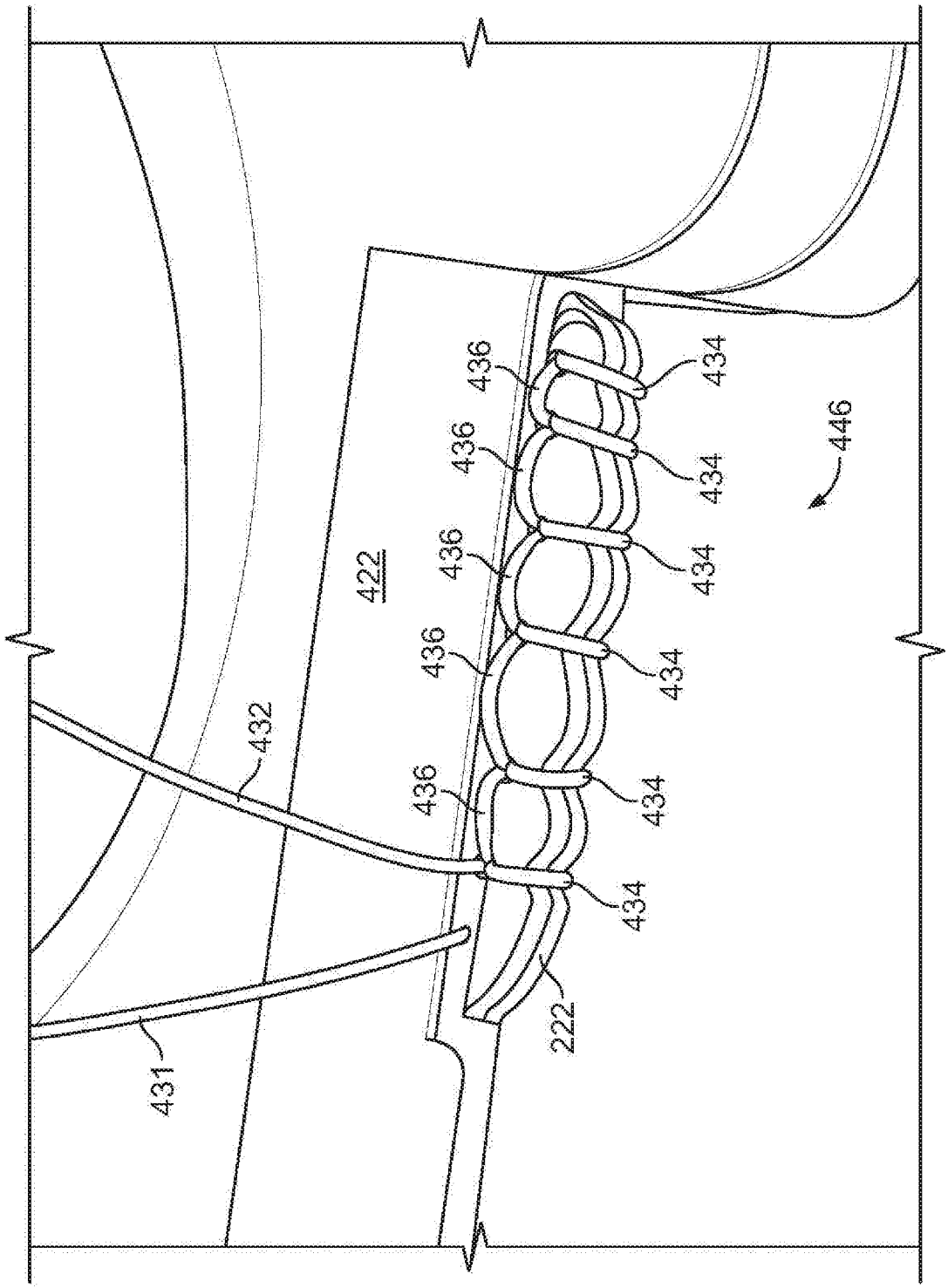


FIG. 4G

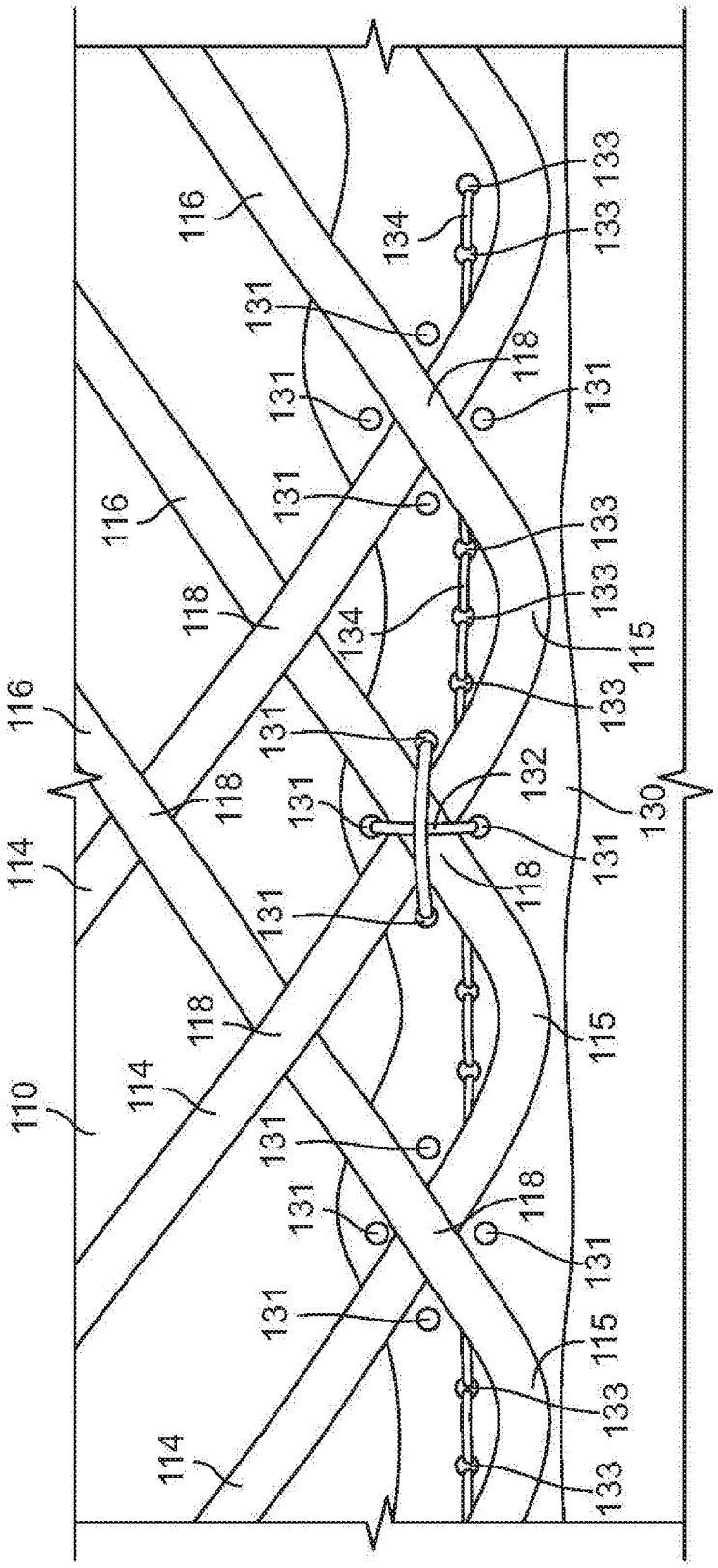


FIG. 5A

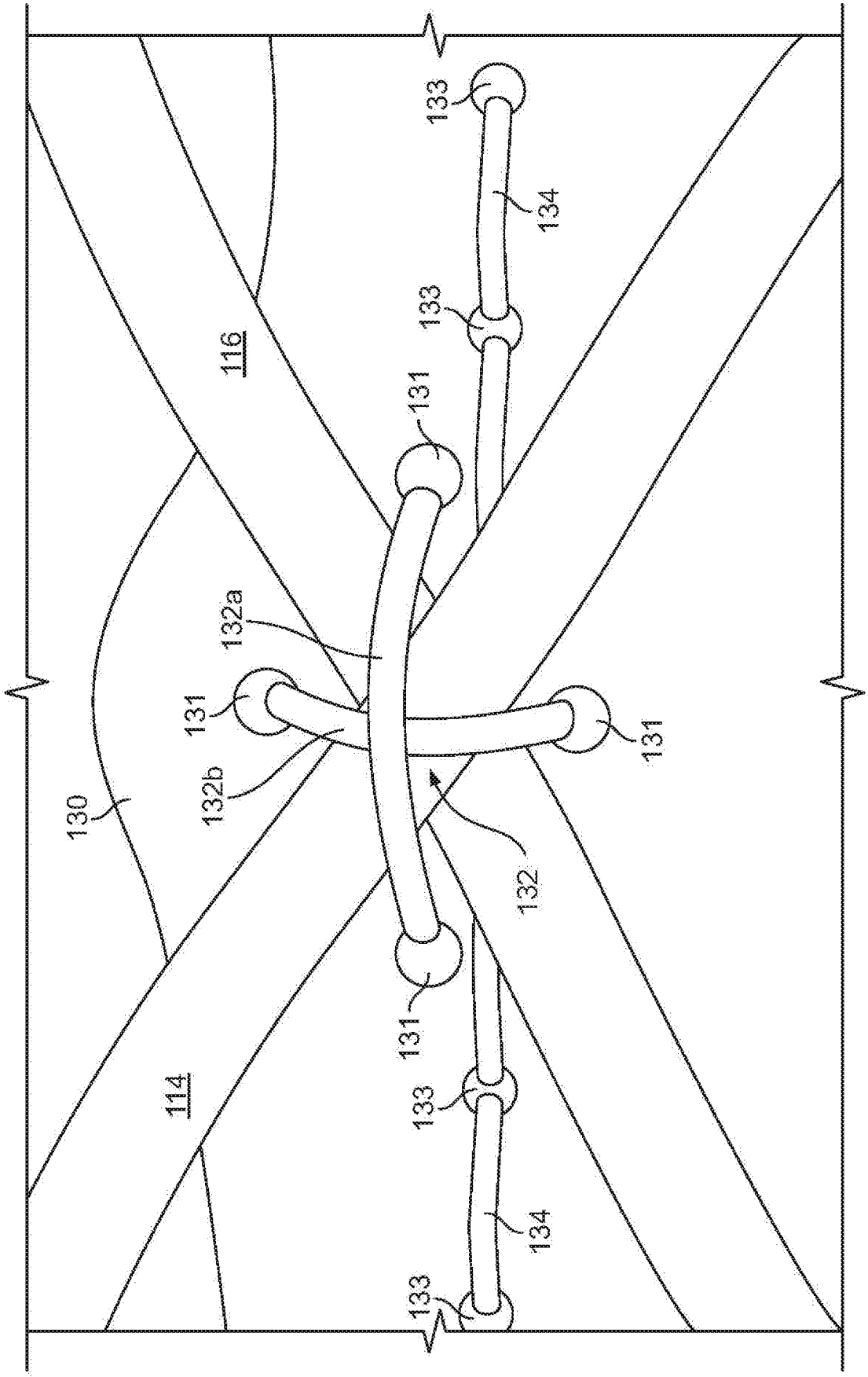

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FIG. 5B

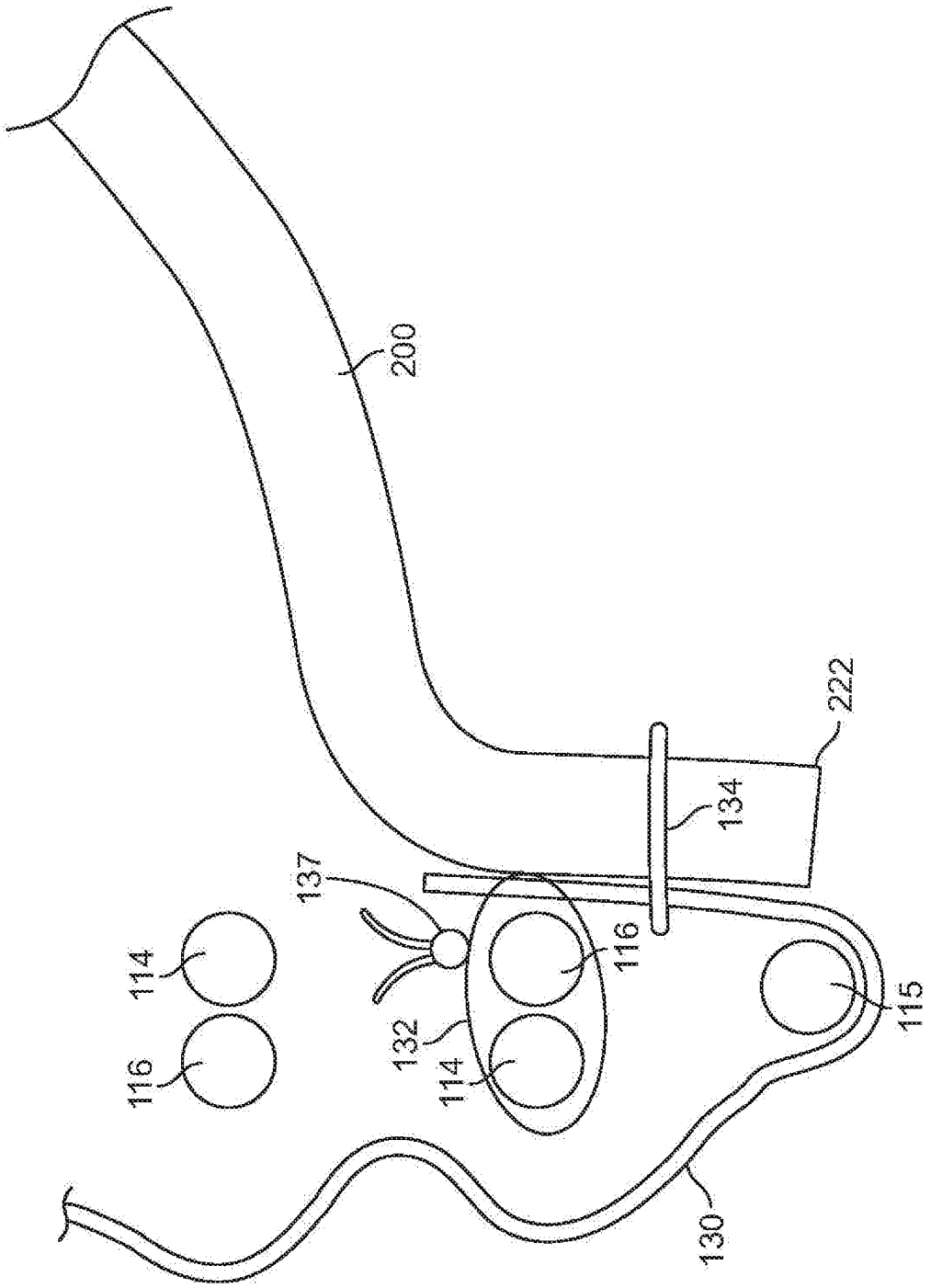


FIG. 5C

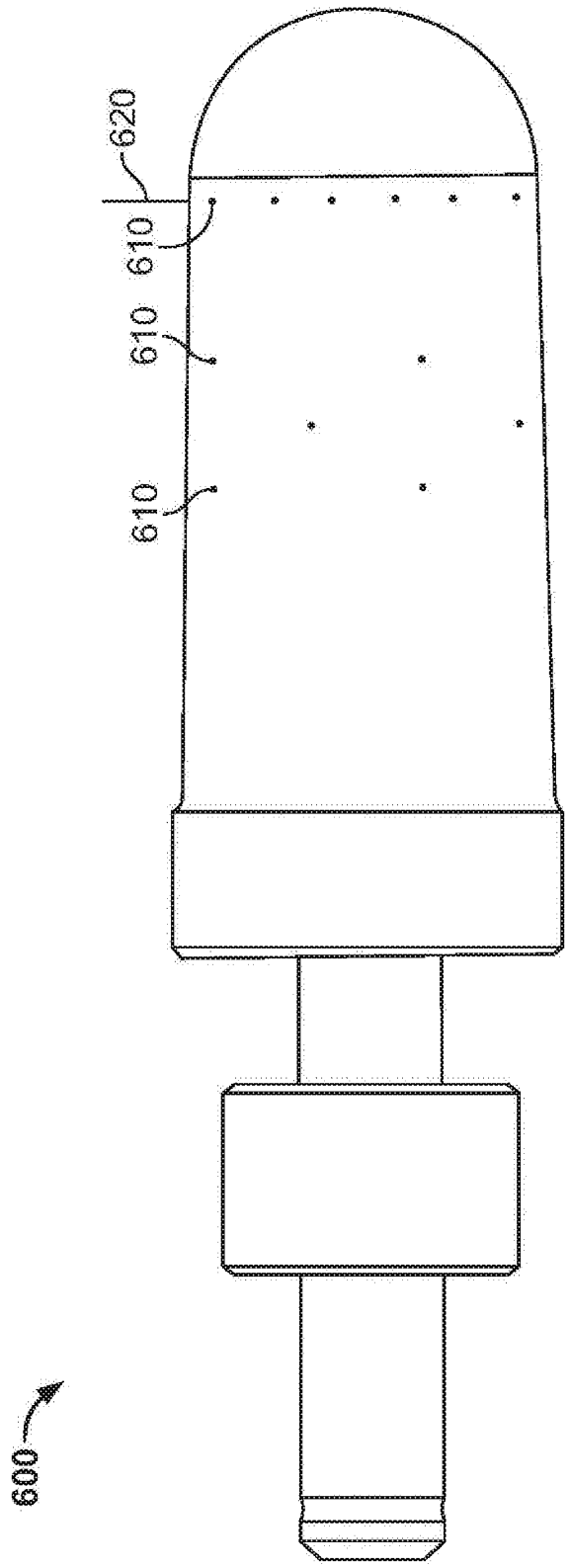


FIG. 6

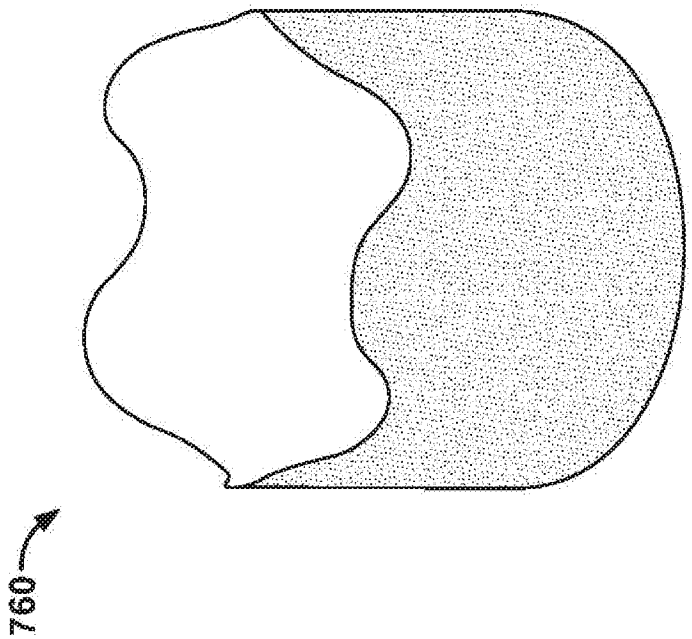


FIG. 7B

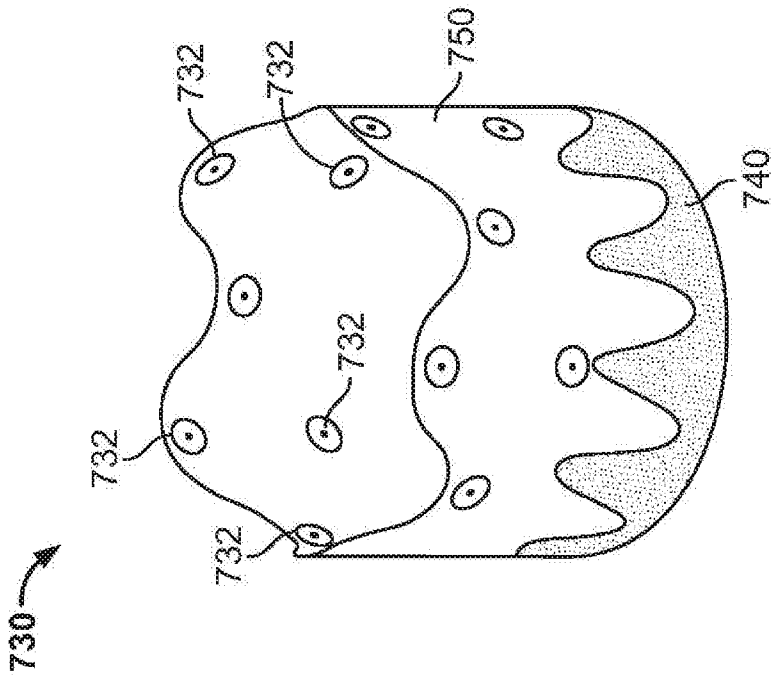


FIG. 7A

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2016/014878

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

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

B. FIELDS SEARCHED

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

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

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

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	WO 2013/070896 A1 (BOSTON SCIENT SCIMED INC [US]) 16 May 2013 (2013-05-16) page 3 - page 8; claims; figures	1-35
Y	WO 2014/203106 A1 (JENAVALVE TECHNOLOGY GMBH [DE]) 24 December 2014 (2014-12-24) the whole document	1-35
Y	WO 01/54624 A1 (3F THERAPEUTICS INC [US]) 2 August 2001 (2001-08-02) page 11 - page 13; figure 15	1-35
Y	US 2010/023120 A1 (HOLECEK ARIN N [US] ET AL) 28 January 2010 (2010-01-28) the whole document	1-35
Y	EP 0 051 451 A2 (SHILEY INC [US]) 12 May 1982 (1982-05-12) claims; figures	1-35

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

☒ See patent family annex.

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"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

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"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
14 April 2016	21/04/2016

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	Serra i Verdaguer, J

1

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/US2016/014878

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