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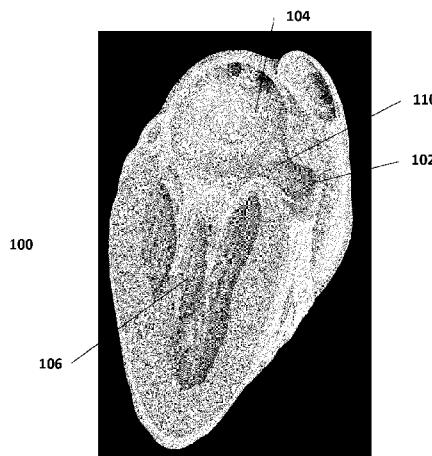
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FIG. 1



(57) Abstract: Devices and methods for occluding the left atrial appendage (LAA) to prevent blood from clotting within the LAA and subsequently embolizing, particularly in patients with atrial fibrillation. A foam implant encapsulated with a tough thromboresistant membrane is placed via transvascular means into the LAA and anchored with adhesives and/or mechanical anchors. Tissue over-and in-growth are optimized to anchor the implant in place and provide a permanent occlusion.

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DEVICES AND METHODS FOR EXCLUDING THE LEFT ATRIAL APPENDAGE

Cross-Reference to Related Applications

[0001] This application claims the priority benefit under 35 U.S.C. §119(e) of U.S. Provisional Application No. 61/779,802, filed March 13, 2013, the entirety of which is hereby incorporated by reference herein.

Field of the Invention

[0002] The embodiments disclosed herein relate to devices and methods for occluding the left atrial appendage (LAA) to prevent blood from clotting within the LAA and subsequently embolizing, particularly in patients with atrial fibrillation.

BACKGROUND OF THE INVENTION

[0003] Atrial fibrillation (Afib) is a condition in which the normal beating of the left atrium (LA) is chaotic and ineffective. The left atrial appendage (LAA) is a blind pouch off the LA. In patients with Afib blood stagnates in the LAA facilitating clot formation. These clots (or clot fragments) have a tendency to embolize or leave the LAA and enter the systemic circulation. A stroke occurs when clot/clot fragment embolizes and occludes one of the arteries perfusing the brain. Anticoagulants, e.g. Coumadin, have been shown to significantly reduce the stroke risk in Afib patients. These drugs reduce clot formation but also increased bleeding complications including hemorrhagic strokes, subdural hematoma and bleeding in the gastrointestinal tract.

[0004] There are about 8 million people in the US and EU with Afib. About 4.6 million of these patients are at a high risk for stroke and would benefit from anticoagulation. A large portion of these patients cannot take anticoagulants due to an increased bleeding risk leaving their stroke risk unaddressed. The prevalence of Afib increases with age.

[0005] Several devices for occluding the LAA are described in the prior art and each has limitations this invention improves upon. The prior art devices are metal structures which are circular in cross section and are made to expand to fill the LAA ostium. These devices are offered in many sizes and must be closely matched to the highly variable LAA anatomy. This is difficult to do using fluoroscopy and often

requires adjunctive imaging in the form of transesophageal echocardiography, cardiac CT and MRI, all with three dimensional reconstructions. If the device is significantly oversized, the LAA ostium may become overstretched leading to tearing resulting in bleeding into the pericardial space. If the device is too small, it will not adequately seal the ostium and may be prone to embolization. Even if sized correctly, the device forces the oval LAA ostium to take the round shape of the device, often resulting in residual leakage at the edges due to poor sealing.

[0006] Anchoring of these implants in the proper location is described in the prior art devices predominately using an array of radially disposed barbs or hooks which engage into the surrounding cardiac tissue upon expansion of the device. The device must therefore have sufficient spring force or stiffness for the barbs to engage the surrounding tissue. These barbs may lead to leaking of blood through the tissue into the pericardial space which may lead to cardiac tamponade. Furthermore, the geometry of these barbs and hooks prevent additional positioning once the implant is fully expanded.

[0007] For all of these reasons it would be desirable to have a device which did not require an excessive number of sizes requiring extensive pre-procedure imaging, could be repositioned when fully expanded and secured without an array of hooks or barbs.

SUMMARY OF THE INVENTION

[0008] Devices and methods for occluding the left atrial appendage (LAA) to prevent blood from clotting within the LAA and subsequently embolizing are disclosed herein. These concepts include the ability to deliver a device through a catheter that is tracked over a guide wire through the vascular system. Foams are described that are collapsed for delivery and then expand in place in the LAA. Anchoring of these plugs are made by tissue ingrowth from the LAA into the foams, adhesives, barbs or distal anchoring elements. Foam plugs are described that are encapsulated with jackets that are sufficiently strong to enable handling of the plugs without tearing and also to encourage the creation of a neointima on at least the proximal, LA facing side.

[0009] There is provided in accordance with one aspect of the present invention, a left atrial appendage occlusion device. The device comprises an expandable, open cell foam body having a proximal end, a distal end and a side wall. A skin covers at

least the proximal (atrial) end of the body, and an expandable lumen extends through the body. The lumen can support a portion of a delivery catheter and/or a guidewire, but collapses to a near zero cross sectional area when such components are removed. This feature reduces the likelihood of emboli forming within the central lumen and dislodging into the bloodstream. The body is compressible within a delivery catheter having an inside diameter of no more than about 20 F and can self expand to a diameter of at least about 25 mm when released from the delivery catheter.

[0010] In one implementation of the invention, the skin comprises ePTFE. The skin may extend throughout the length of the guidewire lumen, and may additionally cover at least a portion of the distal end as well as the proximal end of the body. In one embodiment, the skin comprises a tubular ePTFE sleeve, which extends through the guidewire lumen in the open cell foam body, and everts back over the outside of the body, for connection to itself to encase the open cell foam body and line the guidewire lumen.

[0011] Preferably, at least one tissue ingrowth surface is provided on the side wall of the body, such as by providing at least one aperture through the skin to place the open cell foam body in direct contact with adjacent tissue. The tissue ingrowth surface may comprise at least about 20%, 40%, 60%, 80% or more of the surface area of the side wall of the body.

[0012] At least one radiopaque marker may be provided, such as a radiopaque wire or thread, and/or the foam and/or skin can be loaded with or impregnated with a radiopaque filler such as barium sulfate, bismuth subcarbonate, or tungsten to permit fluoroscopic visualization. At least one or two or more tissue penetrating elements or other anchors may be provided.

[0013] In accordance with another aspect of the present invention, there is provided a left atrial appendage closure system. The system comprises a delivery catheter, comprising an elongate flexible tubular body, having a proximal end and a distal end and at least one lumen extending therethrough. A self-expandable open cell foam body compressed within the distal end of the delivery catheter carries a skin covering at least a portion of the body, and a guidewire extending through the body. An axially moveable deployment control such as a push wire extends through the lumen, for deploying the foam body from the distal end of the closure system.

[0014] The system may additionally comprise a guidewire, having an inflatable balloon thereon. Preferably, at least one tissue ingrowth area is provided on the body, such as by exposing the open cell foam body through at least one window in the skin.

BRIEF DESCRIPTION OF THE DRAWINGS

[0015] The presently disclosed embodiments will be further explained with reference to the attached drawings, wherein like structures are referred to by like numerals throughout the several views. The drawings shown are not necessarily to scale, with emphasis instead generally being placed upon illustrating the principles of the presently disclosed embodiments.

[0016] FIG. 1 shows the anatomy of the left atrium and left atrial appendage.

[0017] FIG. 2 shows a left atrial appendage with one foam plug embodiment in place that uses adhesive.

[0018] FIG. 3 shows an x-ray image of a foam plug.

[0019] FIG. 4 shows a left atrial appendage with foam embodiment and distal anchor in place.

[0020] FIG. 5 shows a screw anchor.

[0021] FIG. 6 shows a longitudinal cross section of a foam plug embodiment.

[0022] FIG. 7 shows an LAA cross section.

[0023] FIG. 8 is a schematic illustration of a guide catheter approaching the ostium to the left atrial appendage.

[0024] FIG. 9 is an illustration as in FIG. 8, with a guidewire placed within the left atrial appendage.

[0025] FIG. 10 is an illustration as in FIG. 9, with an inflatable balloon at the distal region of the guidewire positioned within the left atrial appendage.

[0026] FIG. 11 is an illustration as in FIG. 10, with the guide catheter advanced distally along the guidewire and into the left atrial appendage.

[0027] FIG. 12 is an illustration as in FIG. 11, showing the occlusion device and pusher positioned within the guide catheter.

[0028] FIG. 13 is an illustration as in FIG. 12, showing the occlusion device partially deployed exiting the guide catheter.

[0029] FIG. 14 is an illustration as in FIG. 13, with the occlusion device fully deployed within the left atrial appendage.

[0030] FIG. 15 is an illustration as in FIG. 14, showing the deployment of adhesives or other anchoring structures to retain the occlusion device within the left atrial appendage.

[0031] FIG. 16 shows a plug occlusive device in longitudinal cross section using metal and foam.

[0032] FIG. 17 shows a plug using metal coils and foam.

[0033] FIG. 18 shows a plug using a single metal coil.

[0034] FIG. 19 shows a plug with a dilating distal tip.

[0035] FIG. 20 shows a plug with proximal and distal caps.

[0036] FIG. 21 shows a plug adhesive delivery system.

[0037] FIG. 22 shows the delivery of an expanding foam system.

[0038] FIG. 23 shows a plug with barbs.

[0039] FIG. 24 shows a plug with a retrieval suture attachment.

[0040] FIGS. 25A and 25B show a distal anchoring system.

[0041] FIG. 26 shows an alternative distal anchoring system.

[0042] While the above-identified drawings set forth presently disclosed embodiments, other embodiments are also contemplated, as noted in the discussion. This disclosure presents illustrative embodiments by way of representation and not limitation. Numerous other modifications and embodiments can be devised by those skilled in the art which fall within the scope and spirit of the principles of the presently disclosed embodiments.

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENT

[0043] The heart 100 is shown in FIG. 1 with the left atrial appendage (LAA) 102 which is a cavity emanating from the left atrium (LA) 104. The LAA 102 is quite variable in shape in all dimensions. If the heart is not beating normally, a condition called atrial fibrillation, blood within the LAA becomes stagnant which promotes clot formation. If blood clots within the LAA, the clots may pass from the LAA 102 to the LA 104, to the left ventricle 106 and out of the heart 100 into the aorta. Vessels that bring blood to the brain branch off the aorta. If the clot passes to the brain via these

vessels, it may get stuck and occlude a small vessel in the brain which then causes an ischemic stroke. Strokes have severe morbidities associated with them.

[0044] The opening of the LAA 102 to the LA 104 is called an ostium 110. The object of this invention is to occlude the ostium 110 thereby sealing off the LA 104 from the LAA 102. The ostium 110, is oval, highly variable and dependent of loading conditions, i.e., left atrial pressure.

[0045] One embodiment of the LAA occlusion device is shown in FIG. 2. The occlusion device or plug 204 is placed within the LAA 200 at its opening to the LA 202. The plug 204 comprises an expandable media such as an open cell foam which enables collapse and expansion of the plug and also to enhance ingrowth of tissue into the foam. The foam plug 204 is at least partially encapsulated within a thin strong layer 206 such as ePTFE (expanded polytetrafluoroethylene), polyolefin or polyester. Alternatively bioabsorbable materials could be utilized such as PLA, PGA, PCL, PHA, or collagen. This thin encapsulating layer can be oriented or otherwise modified to be elastomeric in at least one direction, such as radially.

[0046] The plug may be made of polyurethane, polyolefin, PVA, collagen foams or blends thereof. One suitable material is a polycarbonate-polyurethane urea foam with a pore size of 100-250um and 90-95% void content. The foam could be non-degradable or use a degradable material such as PLA, PGA, PCL, PHA, and/or collagen. If degradable, the tissue from the LAA will grow into the foam plug and replace the foam over time. The plug 204 may be cylindrical in shape in an unconstrained expansion but may also be conical with its distal end smaller than the proximal end or reversed. It could also be oval in cross section to better match the opening of the LAA.

[0047] The foam plug 204 is oversized radially in an unconstrained expansion to fit snuggly into the LAA and may be 5-50 mm in diameter depending on the diameter of the target LAA. The length of the plug is similar to or greater than its diameter such that the L/D ratio is about or greater than about 1.0 or greater than about 1.5 or greater than about 2.0 to maximize its stability. The compliance of the material is designed such that it pushes on the walls of the LAA with sufficient force to maintain the plug in place but without overly stretching the LAA wall. The foam and/or skin also conforms to the irregular surfaces of the LAA as it expands, to provide a complementary surface structure to the native LAA wall to further enhance anchoring and promote sealing. Thus, while

some left atrial appendage occlusion devices in the prior art include a mechanical frame which forces at least some aspect of the left atrial appendage into a circular configuration, the expandable foam implant of the present invention conforms to the native configuration of the left atrial appendage. In one embodiment, the structure of the foam may be fabricated such that squeezing axially on the opposing ends of the foam causes the foam to increase in diameter.

[0048] The ePTFE or foam material may be provided with one or two or more radiopaque markers such as radiopaque threads 210 or be filled with or impregnated with a radiopaque filler such as barium sulfate, bismuth subcarbonate, or tungsten which permit the operator to see under x-ray the plug for proper positioning in the anatomy. An x-ray image is shown in FIG. 3 where one cannot see the foam plug 300 but can clearly see the threads 302 and the crimp 304 (discussed below). This thread or ribbon may be made from a radiopaque metallic wire such as platinum or tungsten or a polymer with a radiopaque filler such as barium, bismuth, tantalum, tungsten, titanium or platinum.

[0049] The outer ePTFE layer may be formed from a tube with a diameter about the same diameter of the foam plug and a wall thickness between about 0.0001" and about 0.001" thick and serves to allow one to collapse and pull on the plug without tearing the foam material. The ePTFE material also serves as the blood contacting surface facing the left atrium 206 and has pores or nodes such that blood components coagulate on the surface and an intimal or neointimal covering of tissue grows across it and anchors tightly to the material. Pore sizes within the range of from about 4 μ to about 110 μ , ideally 5-35 μ are useful for formation and adherence of a neointima.

[0050] The outer covering 206 may be constructed of materials other than ePTFE such as woven fabrics, meshes or perforated films made of FEP, polypropylene, polyethylene, polyester or nylon. The covering should have a low compliance (non-elastic), at least longitudinally, be sufficiently strong as to permit removal of the plug, a low coefficient of friction, and be thromboresistant. The outer covering serves as a matrix to permit plug removal as most foams are not sufficiently strong to resist tearing when pulled. The plug can also be coated with or contain materials to enhance its ultrasonic echogenic profile, thromboresistance, lubricity, and/or to facilitate echocardiographic visualization, promote cellular ingrowth and coverage.

[0051] The outer covering has holes in it to permit contact of the LAA tissue with the foam plug to encourage ingrowth of tissue into the foam plug pores. These holes may be 1 to 5 mm in diameter or may also be oval with their long axis aligned with the axis of the foam plug, the length of which may be 80% of the length of the foam plug and the width may be 1-5mm. The holes may be as large as possible such that the outer covering maintains sufficient strength to transmit the tensile forces required for removal. The holes may be preferentially placed along the device. In one embodiment, holes are placed distally to enhance tissue ingrowth from the LAA wall.

[0052] In one implementation of the invention, the implant is provided with proximal and distal end caps of ePTFE, joined together by two or three or four or more axially extending strips of ePTFE. The axially extending strips are spaced apart from each other circumferentially, to provide at least two or three or four or more laterally facing windows through which the open cell foam body will be in direct contact with the tissue wall of the left atrial appendage. This outer covering could be a mesh or netting as well. As shown in FIG. 20, the covering 2004 is only on the proximal and distal faces of the plug 2000. They may be glued to the foam plug and then crimped to the center tube 2002.

[0053] One means of adhering the foam plug in place within the LAA is to use an adhesive, such as a low viscosity cyanoacrylate (1-200 cps). The adhesive is injected into place along the sidewall near the distal end of the foam plug 208. Holes in the ePTFE covering permit the adhesive to interact between the foam plug 204 and the LAA wall 200. Injection of the adhesive may be accomplished with several means, one of which is to inject through the catheter into the center lumen 212. Passages 214 serve to guide the adhesive to the correct location. The distal end of the foam plug must be restricted at that time to prevent the adhesive from exiting the distal crimp 216. Alternatively, FIG. 21 shows tubes 2104 that are pre-placed through the guide catheter 2102, through the center lumen of the plug 2106 and bend backwards in the LAA to the distal end of the plug 2100. These tubes 2104 pass all the way to the proximal end of the guide catheter 2102 where a fitting is attached to permit injection of the adhesive which then exits the small tubes 2104 at the desired location of the plug. These tubes are made of polyethylene, polypropylene or FEP so that the adhesive will not adhere to the tubes. The tubes 2104 are withdrawn after injection through the guide catheter out of the patient.

[0054] Other one part adhesives including aqueous cross linking adhesives, polyurethane, PEG, PGA, PLA, polycaprolactone or a lycine-derived urethane may be used. In addition, these adhesives may be made in two components such that one component is adherent to the foam and the second injected in vivo. Also, these two component adhesives may be injected simultaneously to mix in vivo to prevent fouling of injection tubes.

[0055] An alternative anchoring means for plug 400 is one or two or more distal anchors as shown in FIG. 4. Wire 404 is passed through the center lumen 410 into the LAA and attached to the distal wall of the LAA. In this case, a screw wire 408 is threaded into the wall of the LAA 406. A closer detail of this is seen in FIG. 5 as screw 502 is shown embedded into the LAA wall 504 but not all the way through the epicardial surface 506.

[0056] Additional means of anchoring include the use of a plurality of hooks or barbs or graspers to grab the distal wall and baskets, mallecots, distal foam plugs and Nitinol wire birds nests that open within the LAA and push outward on the wall or engage the protrusions of the LAA. It may be desirable to place the plug then engage the anchor as a secondary step. One such embodiment could include a multitude of nitinol wires with a ball or catch welded proximal to the anchor tip. These could be gathered with the delivery catheter then released when the ideal plug position has been confirmed.

[0057] A cross section of one embodiment is shown in FIG. 6 with foam plug 600 and the left atrium face 602 and the LAA face 610. The ePTFE material 604 encapsulates the foam plug 600 and its open ends are connected with an attachment structure such as a wire, suture or tubular crimp 606 over an inner tube 608. The inner tube 608 may be made of an implant grade stainless steel such as 304 or 316 grades or a cobalt-chromium alloy such as MP35n and the crimp 606 may be made of annealed 304 or 316 stainless steel or a cobalt-chromium alloy such as MP35n. This crimp also serves as an element which can be snared should the device need to be removed.

[0058] Referring to FIG. 6, the tubular ePTFE layer 604 extends along an inner layer 612 which lines the guidewire lumen, and everts out around the left atrial face 602 to form outer layer 614. A first end 616 of inner layer 612 is disposed concentrically within a second end 618 of outer layer 614. The first end 616 and second end 618 are clamped between inner tube 608 and outer crimp 606. In this manner, the implant can be

encapsulated in a manner that presents a seamless left atrial face 602, and preserves the integrity of the guidewire lumen with inner tube 608.

[0059] Placement of the device is shown in FIG. 7 through 15. To close the left atrial appendage, the left atrium (LA) must first be accessed from the venous system. One approach is to use a Brockenbrough-style needle to puncture the atrial septum to access the LA from the right atrium (RA). The basic needle-puncture technique is performed obtaining venous access typically via the right femoral vein. A Mullins sheath and dilator are then tracked over a 0.025" or 0.032" guide wire previously placed in the superior vena cava (SVC). Fluoroscopic and echocardiographic imaging, such as transesophageal echo (TEE) or intracardiac echo (ICE), are typically utilized. If echo is not utilized, it is common to also place a pigtail catheter in the aortic root to define the location of the aortic valve, a step not necessary when using echo.

[0060] Once the Mullins sheath and dilator are in the SVC, the guide wire is removed and a trans-septal needle is placed through the dilator. The needle contains a stylette to prevent skiving off of polymeric material from the dilator lumen as it traverses to the tip. Once the needle is near the dilator tip, the stylette is removed and the needle is connected to a manifold and flushed. The Mullins sheath/dilator set and the needle (positioned within the dilator tip) are retracted into the SVC toward the RA as a unit. As the system is withdrawn down the wall of the SVC into the RA and positioned in the fossa ovale, the preferred puncture location.

[0061] Once proper position in the fossa ovale is observed, the needle is advanced across the fossa ovale into the LA. Successful trans-septal puncture can be confirmed by echo, pressure measurement, O₂ saturation and contrast injection. Once the needle position is confirmed to be positioned in the LA, the sheath and dilator can be advanced over it into the LA. In some cases, the user will first pass a guide wire through the needle into the LA and into an upper pulmonary vein (typically the left) prior to crossing. Alternative options include the use of radiofrequency trans-septal needles, which are useful for crossing very thick or hypertrophic septa, or the use of a safety wire placed through the needle and utilized for the initial puncture.

[0062] Referring to FIGURES 8 through 15, a guide catheter 802 is placed through the femoral vein into the right atrium of the heart and across the intra-atrial septum into the left atrium as described above and positioned near the LAA ostium 804.

A guidewire 902 usually of 0.035" diameter is placed through guide catheter 900 and into the LAA 904. This guidewire 1002 may have attached to its distal end a balloon 1006 which is inflated in the LAA and serves as a bumper to prevent guide catheter 1100 from perforating the wall of the LAA. The guide catheter 1100 is then advanced over the guide wire 1108 into the LAA 1104. A radiopaque marker 1102 is used to guide catheter placement under fluoroscopy. The foam plug 1204 is then pushed through the guide catheter 1200 with pusher 1202 and is shown exiting the guide catheter 1300 slowly in FIG. 13 until it is fully deployed as shown in FIG. 14. The foam plug 1404 position may then be adjusted in place using the distal balloon 1408 and the guide catheter 1400, sliding the foam plug proximally by pulling on the balloon 1408 through shaft 1412 or sliding it distally by pushing guide catheter 1400 distally. The guide wire may also contain a pressure sensor within it such that sealing of the LAA is monitored and confirmation of a sufficient seal is made. Once the user is happy with the placement, the adhesive 1514 may be injected and/or mechanical anchors be deployed anchoring the plug to the wall. The guide wire balloon 1508 is deflated, after which the guide wire. In an alternative embodiment, a binary adhesive system can be used where one component of the binary system is bonded to the outer surface of the skin covering the foam plug. The second component can be injected at the interface between foam plug and the wall of the LAA such that bonding happens only at the interface minimizing the risk of adhesive embolization.

[0063] An alternative to pushing the plug through the entire length of the guide catheter is that the plug 1204 may be initially located at the distal end of the guide catheter 1200 as shown in FIG. 12. The guidewire 1210 passes through the center of the plug 1204 and in this mode, the pusher 1202 only needs to push the plug a short ways to deploy it into the LAA.

[0064] For alternative anchors, they may be deployed, the shafts disconnected and removed. Disconnection mechanisms may be any of several types, such as threaded, electrolytic detachment, or others known in the art.

[0065] Alternative plug concepts include a combination of foam and metal implant as shown in FIG. 16. The foam 1600 is designed to provide ingrowth of tissue and also to provide a cushion of the metal stent 1602 onto the tissue of the LAA. The proximal face of the plug is covered in ePTFE, polyester or another thromboresistant

tissue scaffold material to facilitate sealing with the desired pore size to encourage overgrowth. Stent 1602 could be made of Nitinol to enable it to pack into a 10, 12, 14, 16, 18 or 20F delivery catheter and expand to its desired diameter. It could be braided, laser cut or wire formed. Any of a variety of stent wall patterns may be utilized, depending upon the desired performance. The stent may be a balloon expandable stent, or self-expandable stent as are understood in the art. In the illustrated embodiment, a self-expandable stent 1602 comprises a plurality of proximal apices 1608 and distal apices 1610 connected by a plurality of zig zag struts 1612. A hole 1606 allows passage of the guidewire for delivery. This design may be advantageous in that the expansion force exerted by the plug on the LAA can be controlled separately from the foam characteristics. Also, it may be easier to pack this concept into a smaller geometry.

[0066] Alternatively, the foam plug may be constructed of 2 foams. One denser core to provide force and an outer softer foam to engage the tissue irregularities. The softer foam could also be located on the proximal and/or distal ends to facilitate retrieval.

[0067] Another means of adding stiffness to the foam plug is shown in FIG. 17 where a cavity 1704 in the foam plug 1700 is made and a coil of wire 1702 may be advanced from the guide catheter at the proximal end 1706 into the cavity 1704. As the wire enters the cavity, it expands to its predetermined size and exerts force on the foam radially outwards. The type and amount of wire may be determined *in vivo* using x-ray guidance to examine the radial expansion of the foam into the LAA.

[0068] Instead of wires as shown in FIG. 17, a balloon may be passed into the foam and inflated to provide radial force while the outer foam serves to engage the tissue irregularities and tissue ingrowth. Following inflation, the balloon may be detached from a deployment catheter and the deployment catheter withdrawn. The balloon is preferably provided with a valve, to prevent the escape of inflation media. Inflation media may be any of a variety of media which is convertible between a first, flowable state and a second, hardened state such as by cross linking or polymerization *in situ*.

[0069] Another LAA plug is shown in FIG. 18 as a spring like implant wire 1800 that is covered with foam 1802 to encourage ingrowth. The proximal face of the implant is covered with a sheet of ePTFE or other tissue scaffolding material. This implant may be stretched out for delivery and released in place.

[0070] Rather than using a foam, a low porosity outer bag without perforations could be placed in the LAA and then filled with a substance to provide the radial expansion. This substance may be a hydrogel, cellulose or polyvinylacetate.

[0071] Rather than requiring the use of a separate dilation device to cross the septum, the distal crimp element 1902 may be formed in a tapered manner such that it extends from the distal end of the catheter 1200 and serves as a dilating tip to dilate the opening in the septum as the catheter is advanced. See Figure 19.

[0072] An alternative plug design uses a foam such as cellulose sponge material that is compacted and dehydrated such that it can be packed into the guide catheter. This foam material 2202 may be packed into the guide catheter as shown in FIG. 22. The foam plug 2202 is then advanced from the distal end of the guide catheter 2204 with a plunger 2206 into the LAA. The plug exits the guide catheter and opens to a disc shape 2210. As the foam absorbs fluid in the blood, its length expands to form a cylinder 2220 filling the LAA. Expansion ratios for compressed cellulose materials may be as high as 17:1, expanded to compressed length.

[0073] It may be advantageous to use small barbs 2302 in FIG. 23 to further engage the plug 2204 into the LAA. Barbs may be unidirectional or bidirectional to resist movement in either the proximal or distal direction. These barbs are embedded into the foam plug and may be .1 to 1 mm in height. It may be desirable to place the plug then engage the barbs as a secondary step. One such embodiment could include a multitude of nitinol barb wires with a ball or catch welded proximal to the barb tip. These could be gathered with the delivery catheter within a sleeve or suture then released when the ideal plug position has been confirmed.

[0074] One means of removing a device that is not functioning properly is to releasably attach a retrieval suture 2400 to the implant, such as to the proximal cap 2402 which also passes proximally throughout the entire length of the guide catheter 2404 in FIG. 24. If the device is to be removed, pulling on both ends of the suture 2400 will pull the outer covering into the guide catheter 2404 which can then be removed from the patient. If the device is properly placed, the suture 2400 may be cut and removed leaving the plug in place.

[0075] Deployment of the occlusion device has been discussed primarily in the context of a transvascular access. However, implants of the present invention may

alternatively be deployed via direct surgical access, or various minimally invasive access pathways (e.g. jugular vein). For example, the area overlying the xiphoid and adjacent costal cartilage may be prepared and draped using standard techniques. A local anesthetic may be administered and skin incision may made, typically about 2 cm in length. The percutaneous penetration passes beneath the costal cartilage, and a sheath may be introduced into the pericardial space. The pericardial space may be irrigated with saline, preferably with a saline-lidocaine solution to provide additional anesthesia and reduce the risk of irritating the heart. The occlusion device may thereafter be introduced through the sheath, and through an access pathway created through the wall of the LAA. Closure of the wall and access pathway may thereafter be accomplished using techniques understood in the art.

[0076] Depending upon the desired clinical performance, any of the LAA occlusion devices of the present invention may be provided with a drug or other bioactive agent, which may be injected via the deployment catheter, or impregnated within the open cell foam or coated on the implant. The bioactive agent may be eluted or otherwise released from the implant into the adjacent tissue over a delivery time period appropriate for the particular agent as is understood in the art.

[0077] Useful bioactive agents can include those that modulate thrombosis, those that encourage cellular ingrowth, throughgrowth, and endothelialization, and potentially those that resist infection. For example, agents that may promote endothelial, smooth muscle, fibroblast, and/or other cellular growth into the implant including collagen (Type I or II), heparin, a combination of collagen and heparin, extracellular matrix (ECM), fibronectin, laminin, vitronectin, peptides or other biological molecules that serve as chemoattractants, moleculesMCP- 1, VEGF, FGF-2 and TGF-beta, recombinant human growth factors, and/or plasma treatment with various gases.

[0078] Anti-thrombotics can typically be separated into anti-coagulants and anti-platelet agents. Anti-Coagulants include inhibitors of factor(s) within the coagulation cascade and include heparin, heparin fragments and fractions as well as inhibitors of thrombin including hirudin, hirudin derivatives, dabigatran, argatroban and bivalrudin and Factor X inhibitors such as low molecular weight heparin, rivaroxaban, apixaban.

[0079] Antiplatelet agents include GP 2b/3a inhibitors such as epifibitide, and abciximab, ADP Receptor agonists (P2/Y12) including thienopyridines such as

ticlopidine, clopidogrel, prasugrel and tacaagrelor and aspirin. Other agents include lytic agents, including urokinase and streptokinase, their homologs, analogs, fragments, derivatives and pharmaceutical salts thereof and prostaglandin inhibitors.

[0080] Antibiotic agents can include, but are not limited to penicillins, cephalosporins, vancomycins, aminoglycosides, quinolonges, polymyxins, erythromycins, tetracyclines, chloraphenicols, clindamycins, lincomycins, sulfonamides, their homologs, analogs, derivatives, pharmaceutical salts and combinations thereof.

[0081] Another means of anchoring is shown in FIG. 25A where the foam plug 2500 is placed in the LAA. The distal screw lead 2502 is advanced and screwed into the LAA wall. Guide 2506 is pulled proximally as shown in FIG. 25B. When this guide 2506 is pulled back, the screw lead wire, made of Nitinol, bunches up into a “birds nest” 2508 or forms a coil inside the foam plug 2500. The screw lead wire 2502 is pushed distally from the guide catheter 2504 with a pusher 2510 and continues to bunch up into the foam. The catheter system 2504, 2506 and 2510 are then removed.

[0082] Another means of anchoring the distal anchor element to the foam is shown in FIG. 26. Two barbed leads 2604 are attached to anchor 2602 such that when advanced into place in the foam plug 2600, the barbs 2604 dig into the foam plug.

[0083] Biologic agents as outlined above maybe be added to the implant 204 and may be injected through the delivery catheter into the space between the proximal cap 206 and the foam plug 204. This may serve as a reservoir to minimize thrombus formation during the initial implantation and reduce the need for systemic anticoagulation following device implantation.

[0084] An electronic pressure sensor may be embedded into the proximal end of the foam plug which may be used to transmit LA pressure to a remote receiver outside the body for the monitoring of LA pressure which is useful to monitor cardiac function. In addition, a cardiac pacer or defibrillator may be embedded into the foam plug and attached electrically to the distal anchor. A drug delivery reservoir may be embedded with connection to the LA for controlled delivery of biologic agents as outlined above.

[0085] All patents, patent applications, and published references cited herein are hereby incorporated by reference in their entirety. It should be emphasized that the above-described embodiments of the present disclosure are merely possible examples of implementations, merely set forth for a clear understanding of the principles of the

disclosure. Many variations and modifications may be made to the above-described embodiment(s) without departing substantially from the spirit and principles of the disclosure. It will be appreciated that several of the above-disclosed and other features and functions, or alternatives thereof, may be desirably combined into many other different systems or applications. All such modifications and variations are intended to be included herein within the scope of this disclosure, as fall within the scope of the appended claims.

WHAT IS CLAIMED IS:

1. A left atrial appendage occlusion device, comprising:
 - an expandable, open cell foam body having a proximal end for facing the left atrium following implantation in the left atrial appendage, a distal end for facing into the left atrial appendage following implantation, and a side wall;
 - a skin covering at least the proximal end of the body; and
 - a guidewire lumen extending through the body;

wherein the body can be compressed within a delivery catheter having an inside diameter of no more than about 20F and can self-expand to a diameter of at least about 25mm when released from the delivery catheter.
2. A left atrial appendage occlusion device as in Claim 1, wherein the skin comprises ePTFE.
3. A left atrial appendage occlusion device as in Claim 1, wherein the skin extends throughout the length of the guidewire lumen to the distal end.
4. A left atrial appendage occlusion device as in Claim 3, wherein the skin additionally covers at least a portion of the distal end of the body.
5. A left atrial appendage occlusion device as in Claim 1, comprising at least one tissue ingrowth surface on the sidewall of the body.
6. A left atrial appendage occlusion device as in Claim 5, wherein the tissue ingrowth surface comprises an exposed surface of the foam which is not covered by the skin.
7. A left atrial appendage occlusion device as in Claim 6, wherein the tissue ingrowth surface comprises at least about 20% of the surface area of the side wall of the body.
8. A left atrial appendage occlusion device as in Claim 1, wherein the skin comprises a tubular sleeve that has a first end and a second end, and the sleeve extends through the guidewire lumen and everts back over the body so that the first end and second end are connected to each other to enclose the foam body.
9. A left atrial appendage occlusion device as in Claim 8, wherein the first end and second end are connected to each other by a crimp.
10. A left atrial appendage occlusion device as in Claim 1, further comprising at least one radiopaque marker.

11. A left atrial appendage occlusion device as in Claim 10, wherein the radiopaque marker comprises a radiopaque thread.
12. A left atrial appendage occlusion device as in Claim 8, comprising a plurality of openings in the skin to permit tissue ingrowth into the foam.
13. A left atrial appendage occlusion device as in Claim 1, wherein the device comprises a substantially cylindrical configuration in an unconstrained expansion.
14. A left atrial appendage occlusion device as in Claim 1, further comprising at least one anchor.
15. A left atrial appendage occlusion device as in Claim 14, wherein the anchor comprises a tissue penetrating element.
16. A left atrial appendage occlusion device as in Claim 15, wherein the tissue penetrating element comprises a helical wire.
17. A left atrial appendage closure system, comprising:
 - a delivery catheter comprising an elongate flexible tubular body, having a proximal end and a distal end and at least one lumen extending therethrough;
 - a self-expandable open cell foam body compressed within the distal end of the delivery catheter; the body comprising a skin covering at least a portion of the body and a guidewire extending through the body; and
 - an axially movable deployment control extending through the lumen, for deploying the foam body from the distal end of the closure system.
18. A left atrial appendage closure system as in Claim 17, additionally comprising a guidewire having an inflatable balloon thereon.
19. A left atrial appendage closure system as in Claim 17, additionally comprising a skin covering at least a portion of the foam body.
20. A left atrial appendage closure system as in Claim 19, additionally comprising at least one opening through the skin to permit tissue ingrowth into the foam body.
21. A left atrial appendage closure system as in Claim 17, additionally comprising a second lumen extending through the tubular body.
22. A left atrial appendage closure system as in Claim 21, wherein the second lumen is configured to deliver a flowable media to a surface of the foam body.

23. A left atrial appendage closure system as in Claim 22, wherein the flowable media comprises an adhesive.

24. A method of excluding a left atrial appendage, comprising the steps of: providing a delivery catheter having an elongate tubular body with a proximal end and a distal end;

advancing a guidewire into the left atrial appendage;

advancing the distal end over the guidewire and into the left atrial appendage;

deploying an implant from the distal end,

wherein the implant comprises a self-expanding body having an open cell foam and an outer layer, and the implant conforms to the surface of the left atrial appendage.

25. A method of excluding a left atrial appendage as in Claim 24, further comprising the step of inflating a balloon on the wire prior to the deploying an implant step.

26. A method of excluding a left atrial appendage as in Claim 24, further comprising the step of anchoring the implant to adjacent tissue.

27. A method of excluding a left atrial appendage as in Claim 26, wherein the anchoring step comprises adhesively bonding the implant to adjacent tissue.

28. A method of excluding a left atrial appendage as in Claim 26, wherein the anchoring step comprises mechanically engaging the adjacent tissue.

FIG. 1

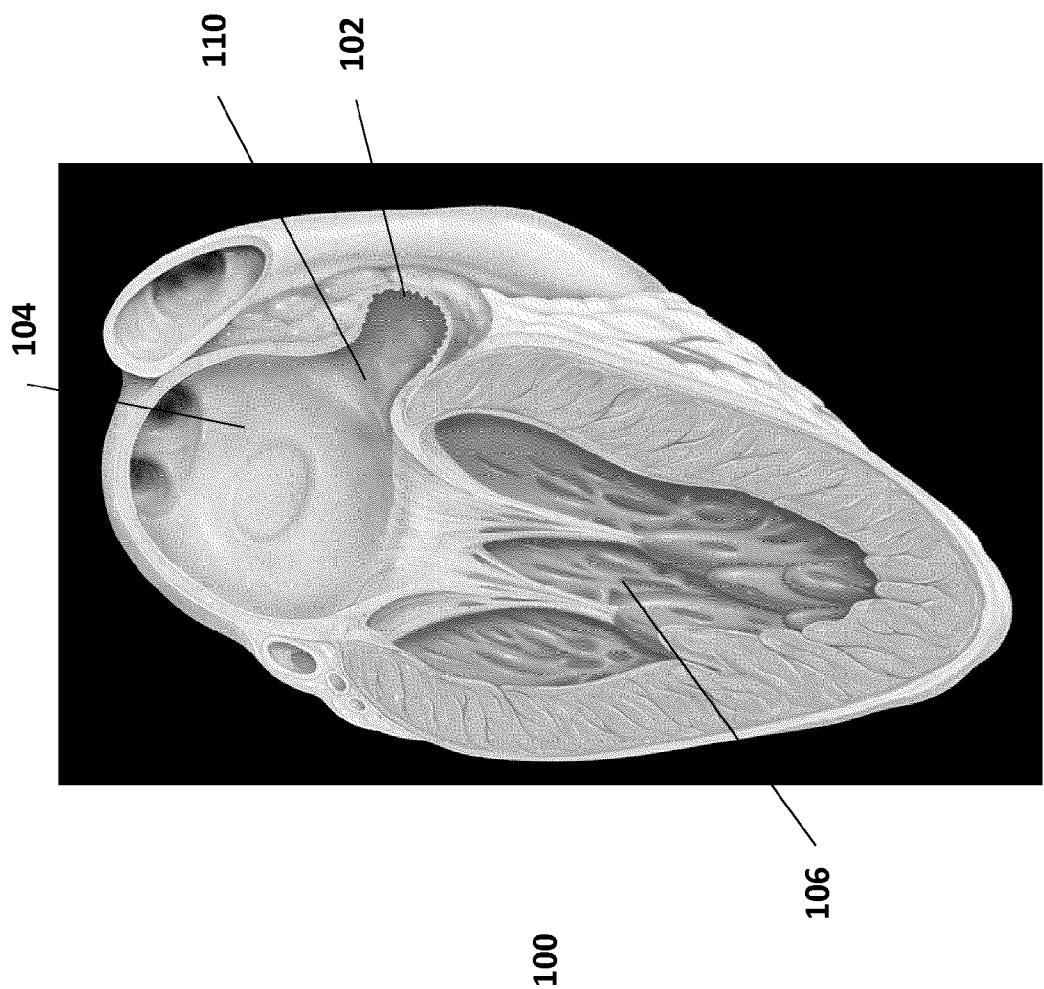


FIG. 2

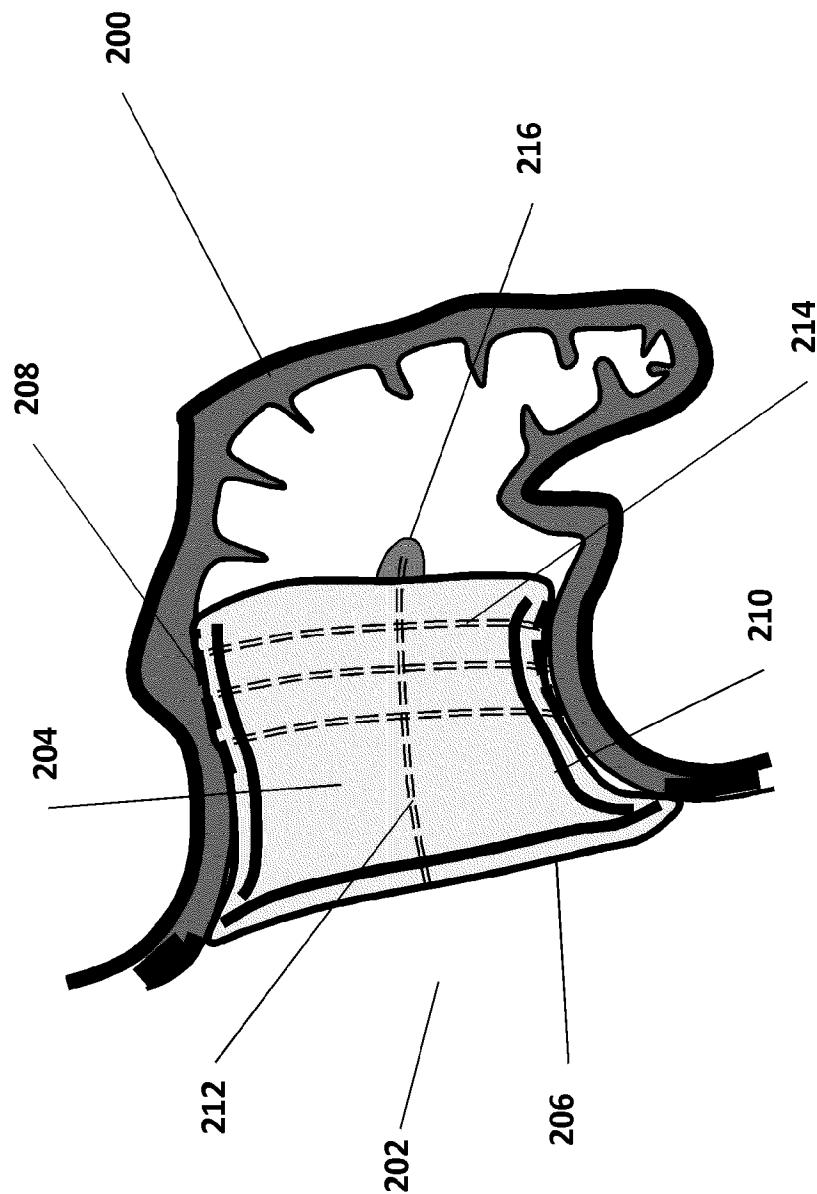


FIG. 3

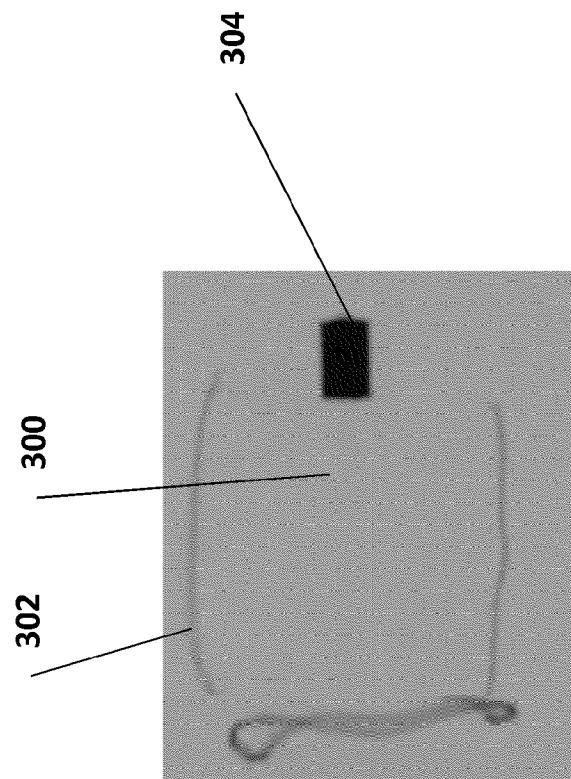


FIG. 4

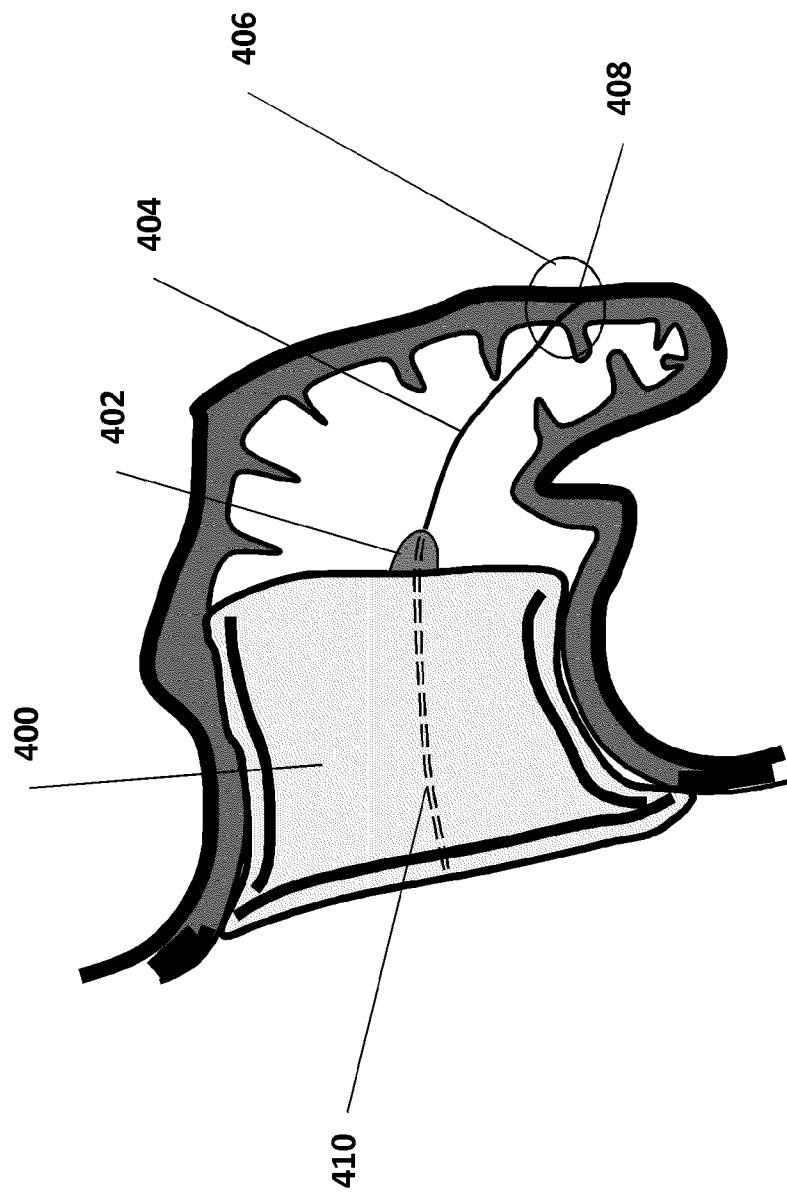
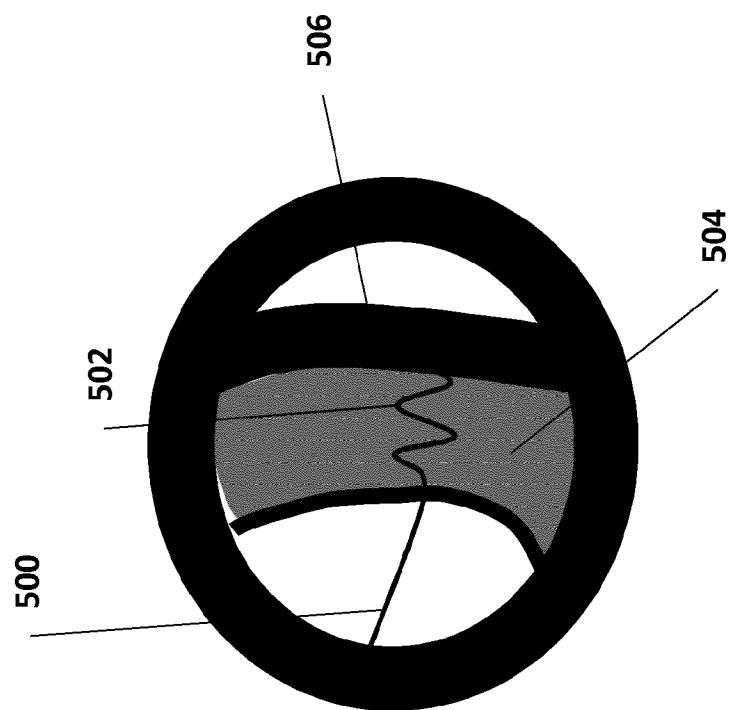


FIG. 5



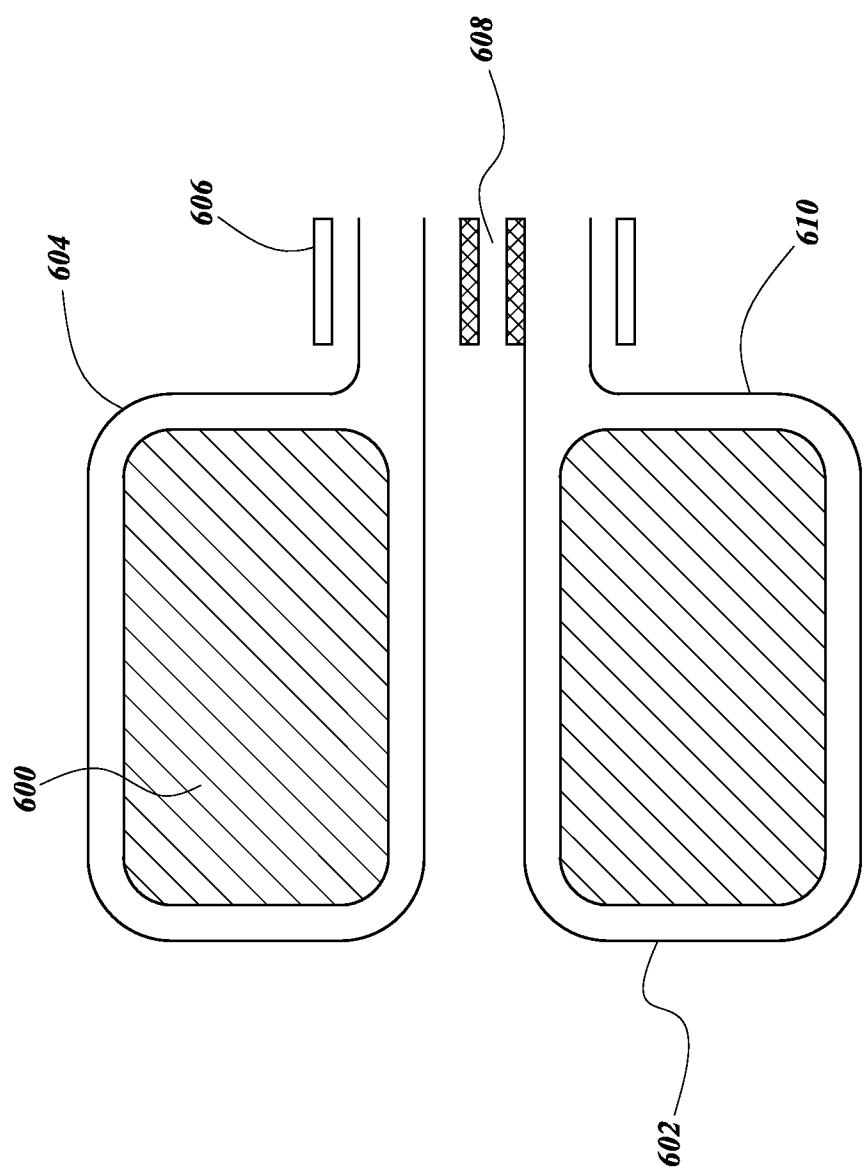


FIG. 6

FIG. 7

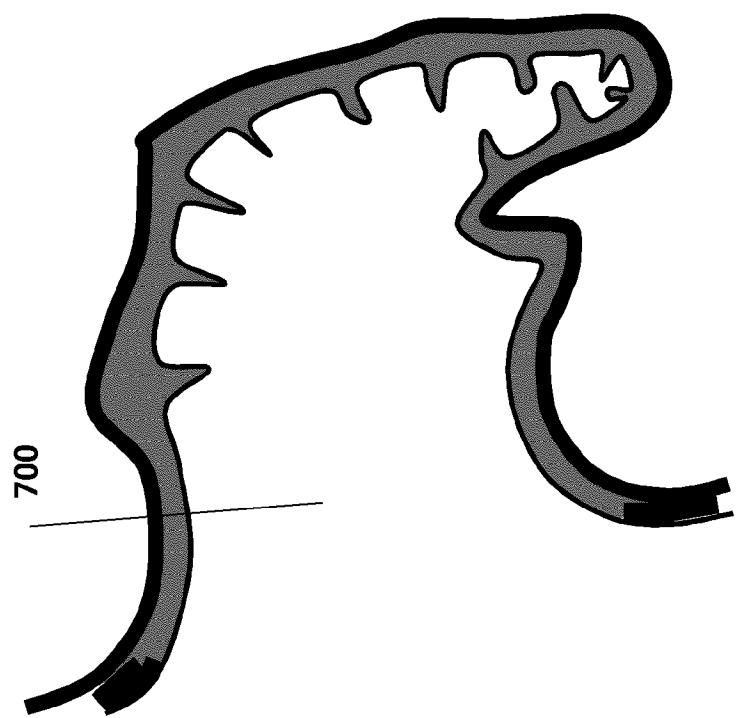
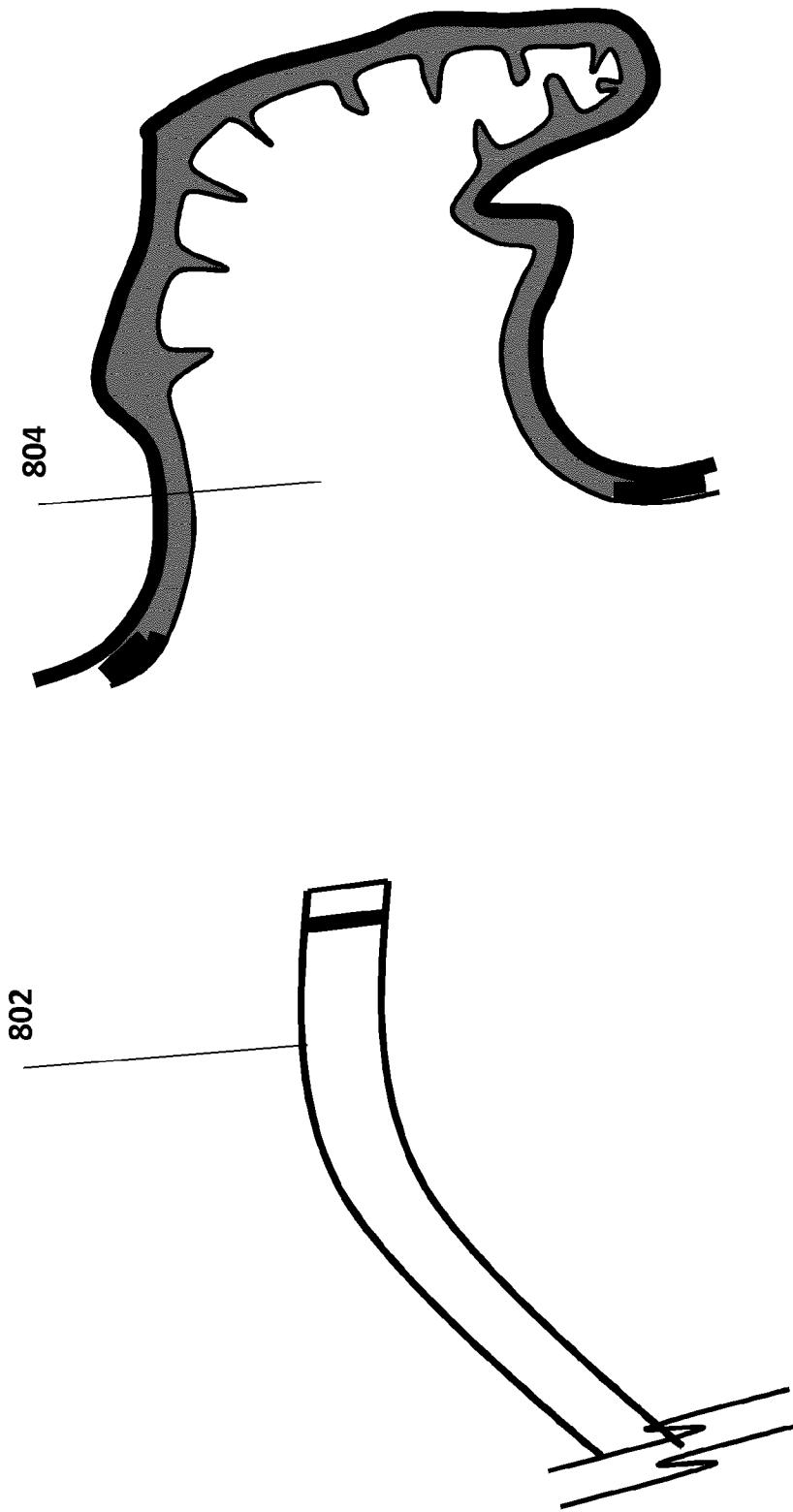
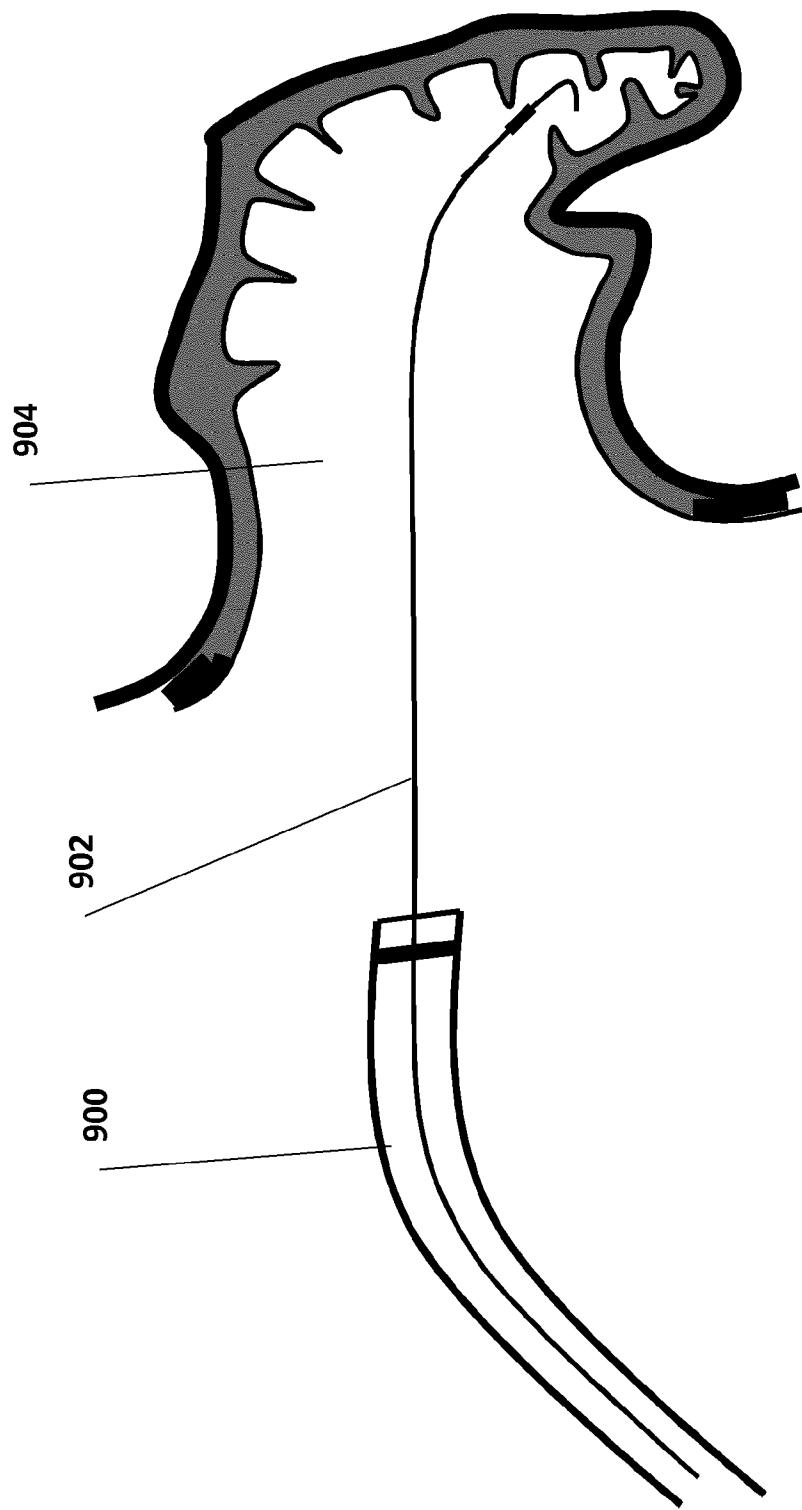


FIG. 8



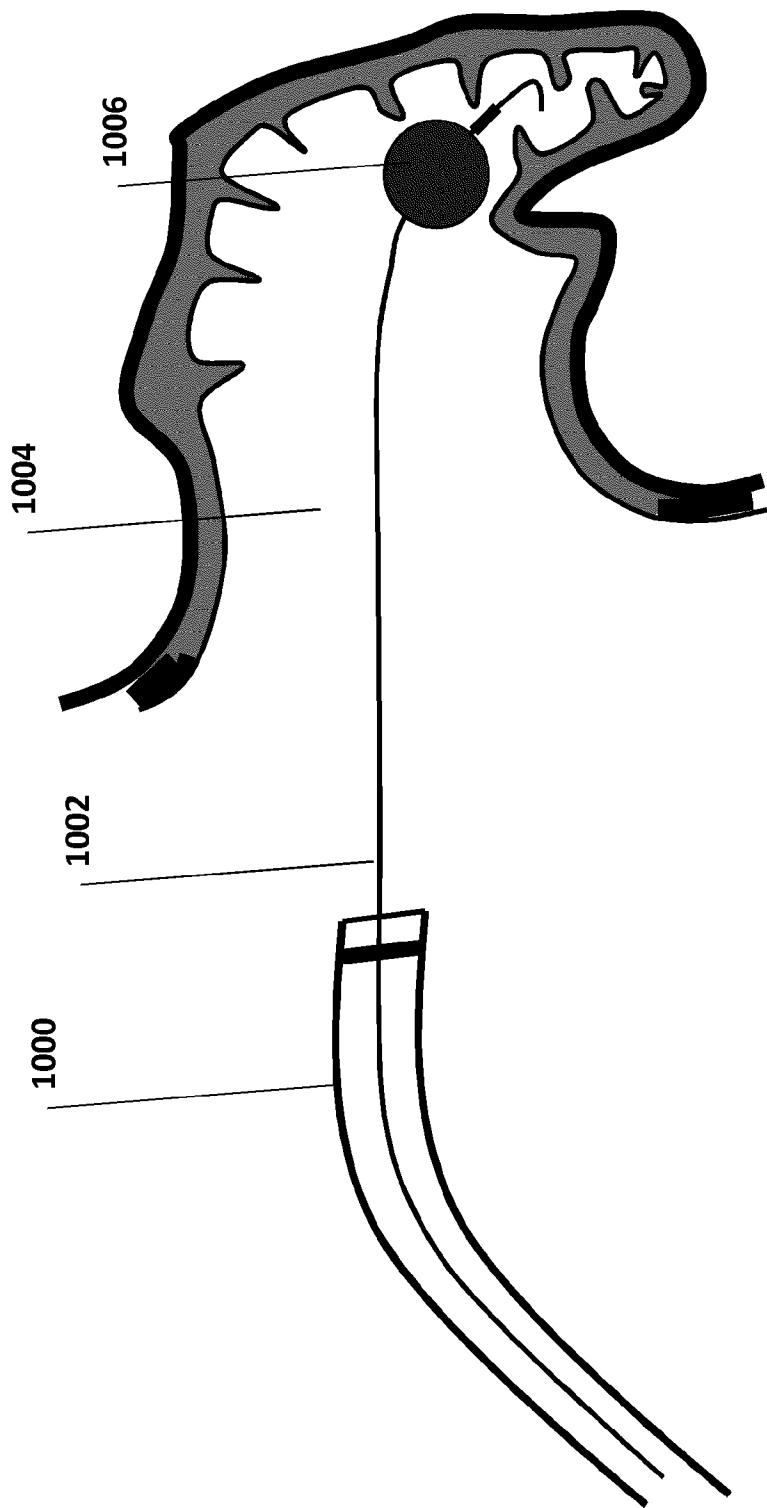
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FIG. 9



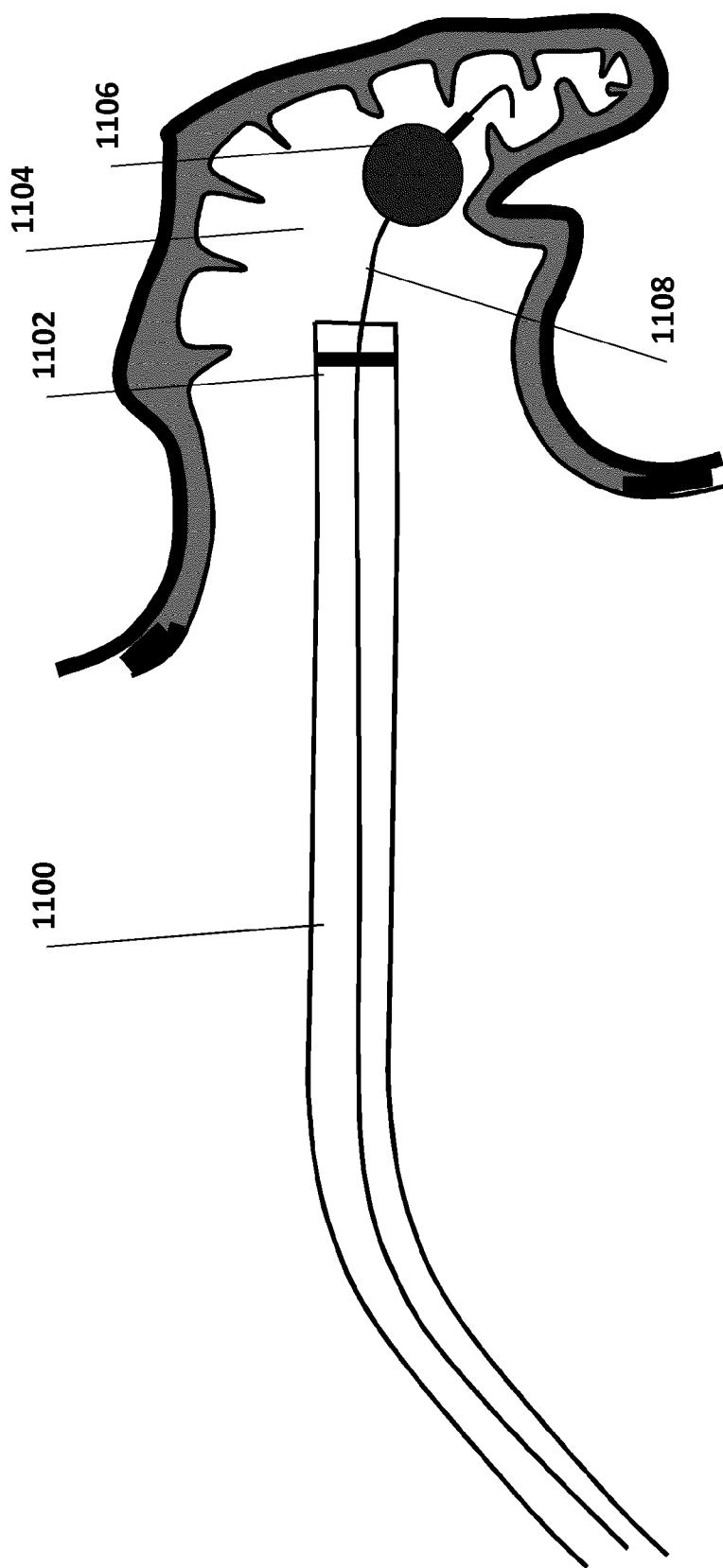
10/21

FIG. 10



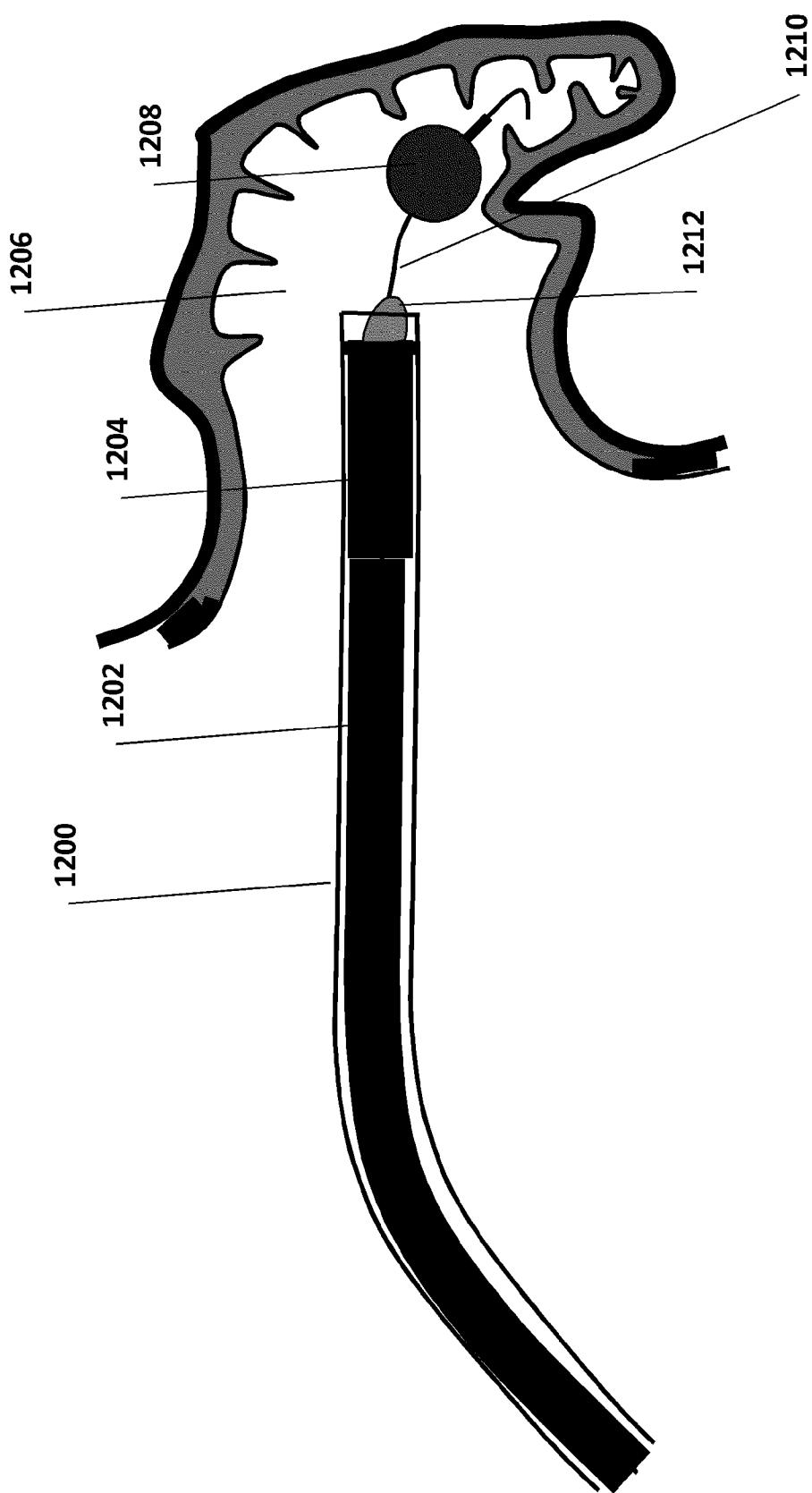
11/21

FIG. 11



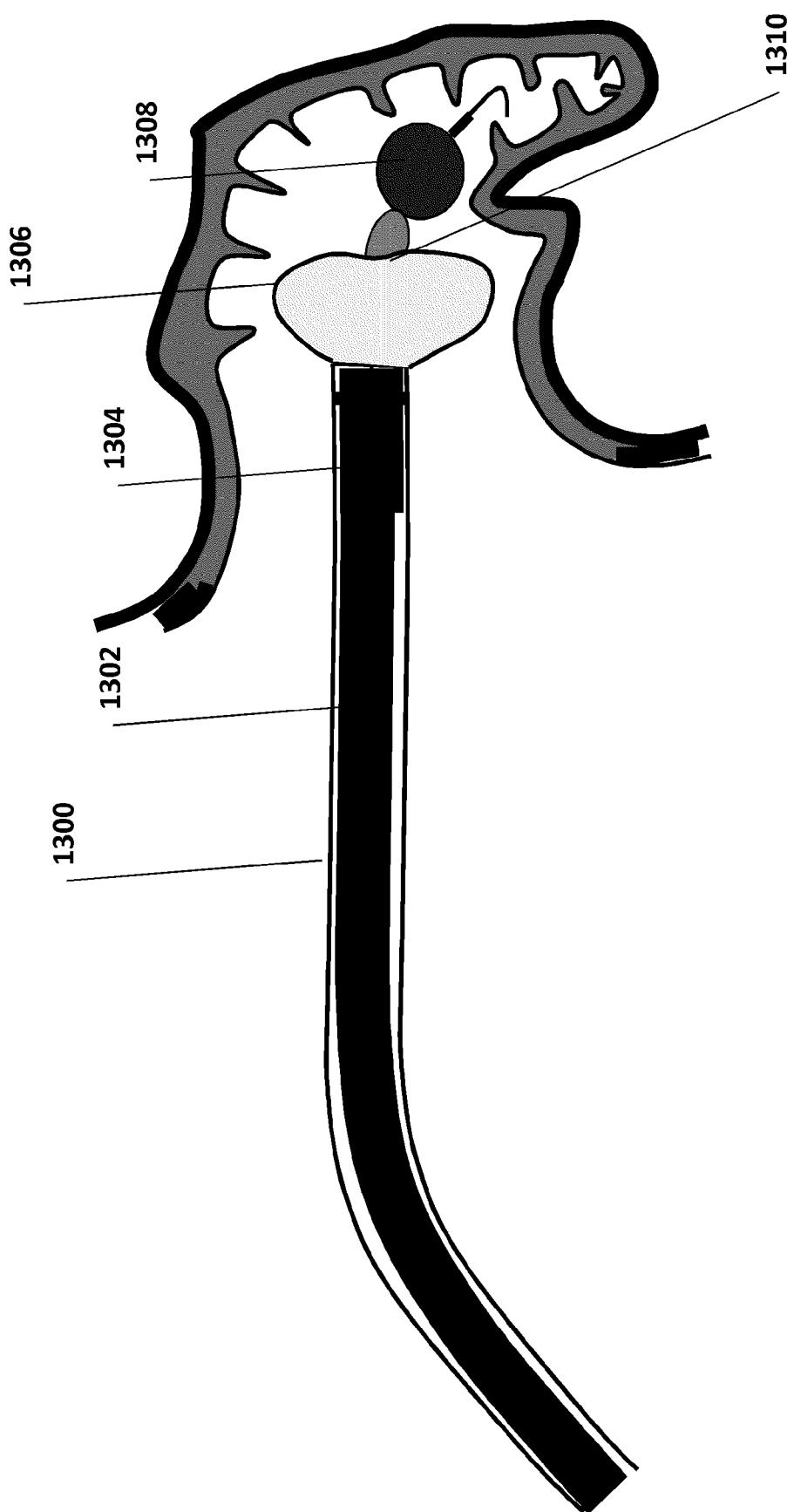
12/21

FIG. 12



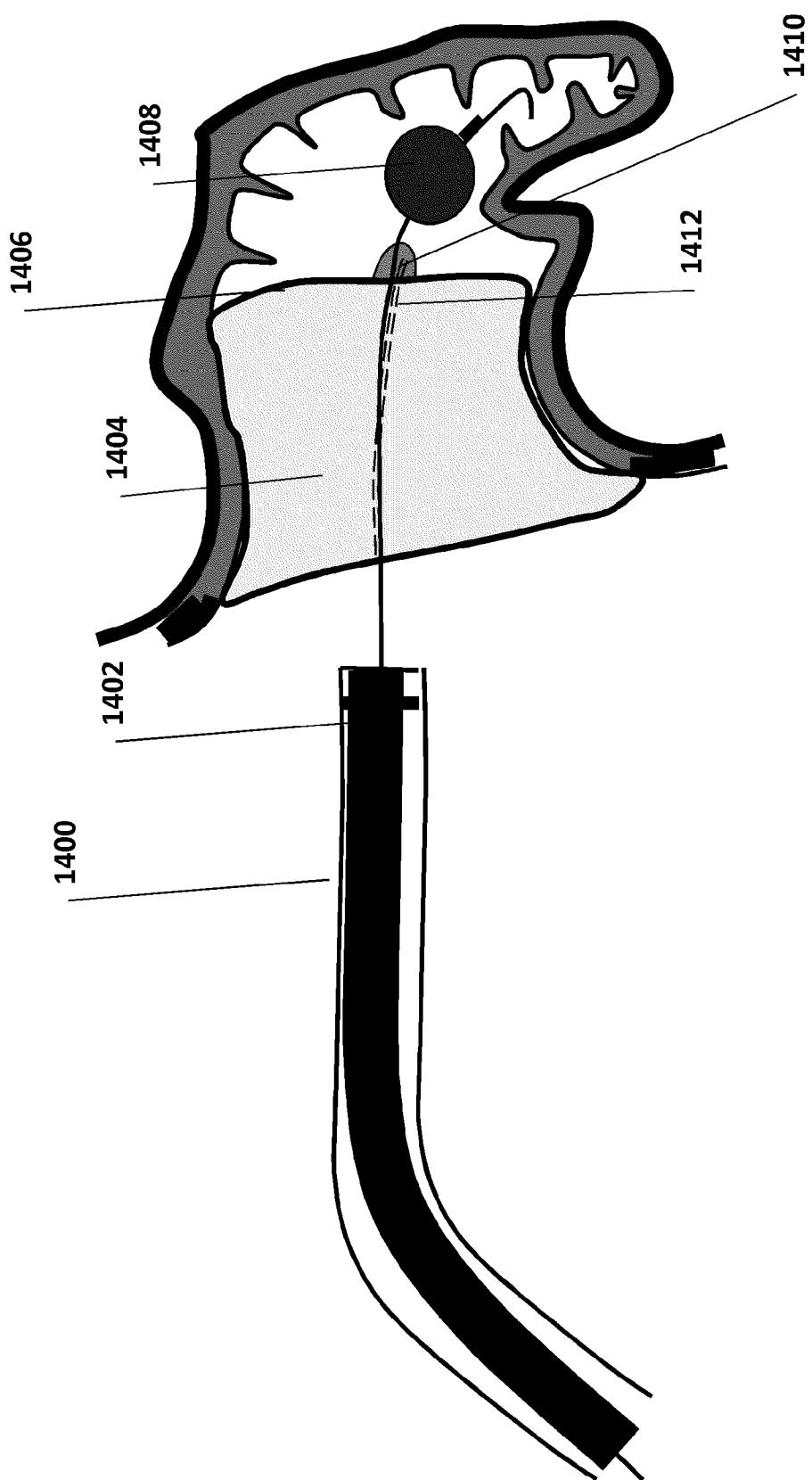
13/21

FIG. 13



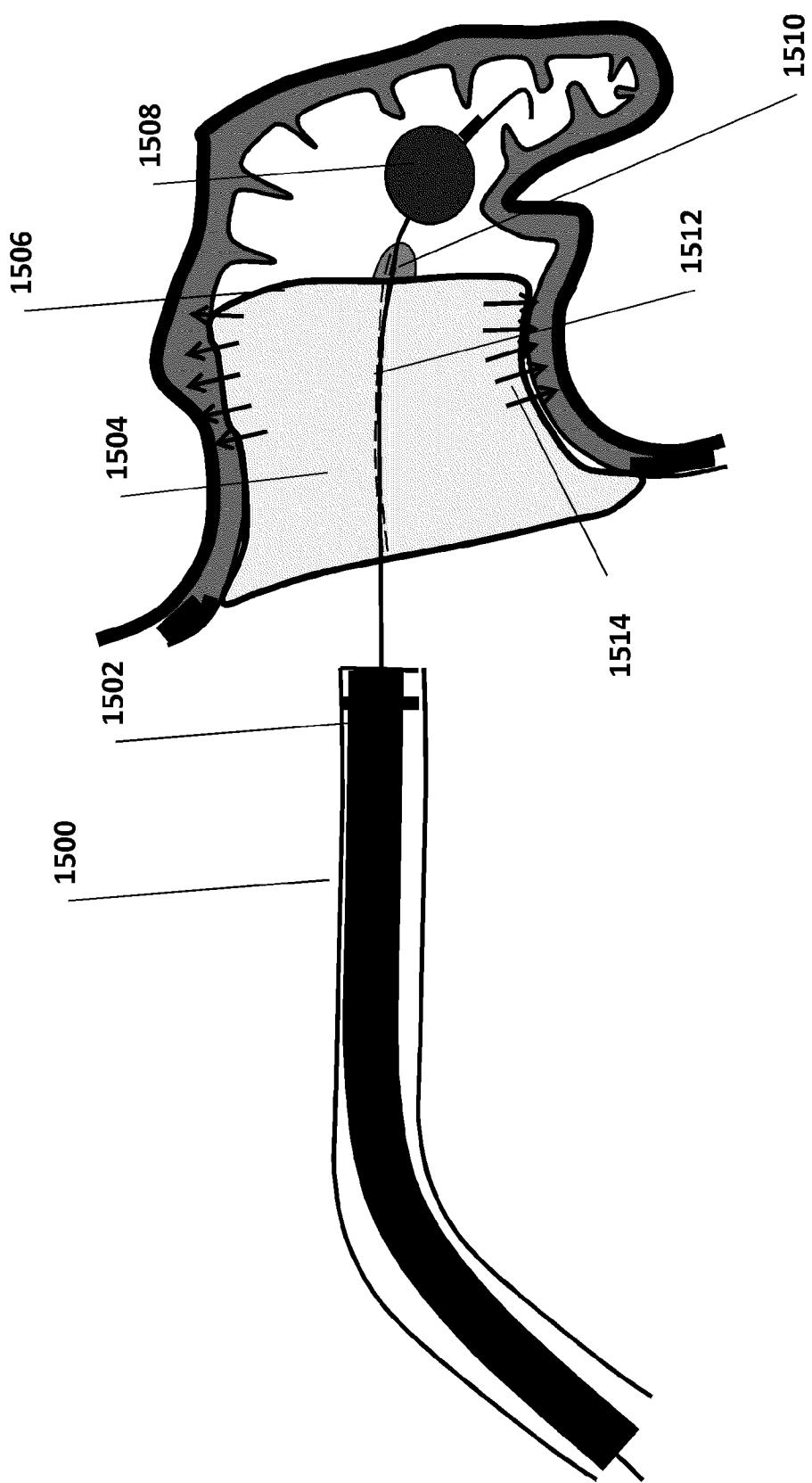
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FIG. 14



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FIG. 15



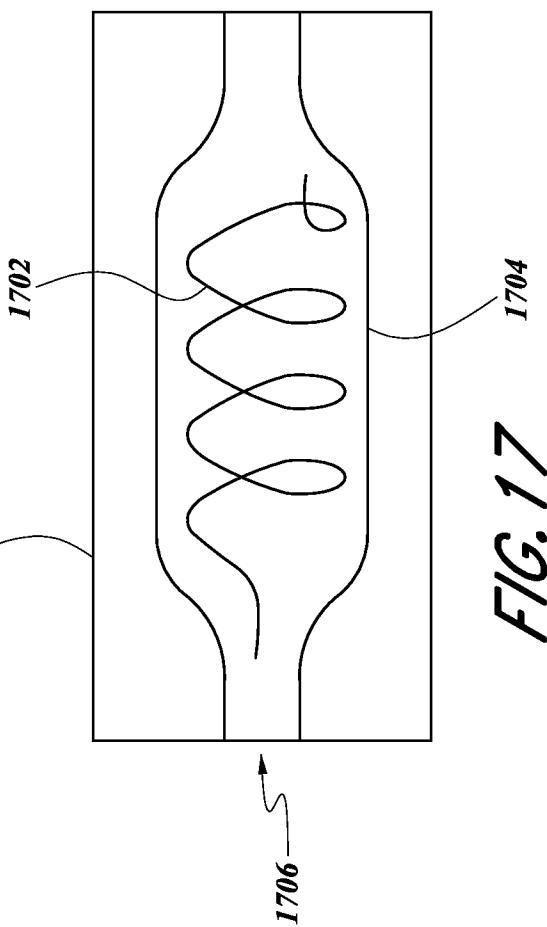


FIG. 17

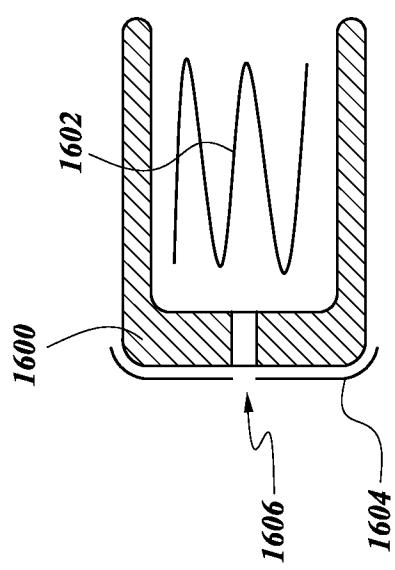


FIG. 16

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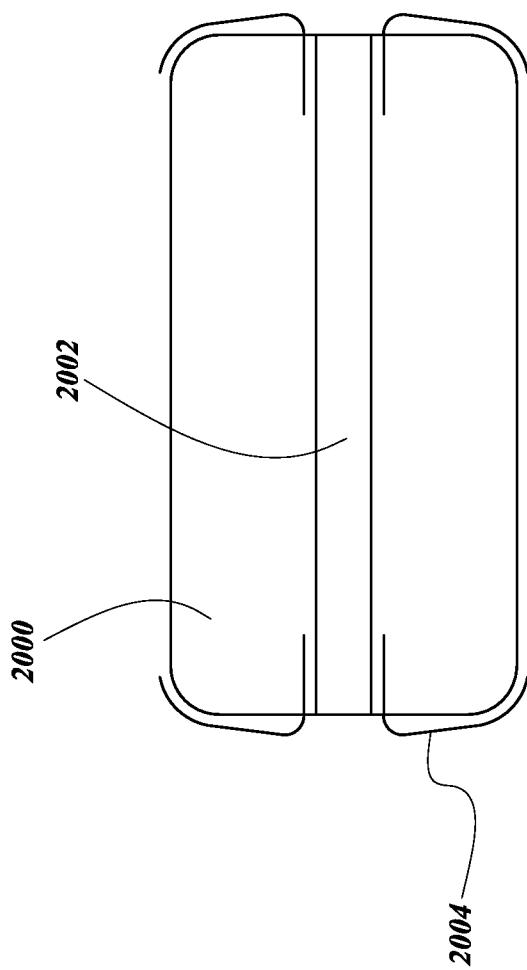


FIG. 20

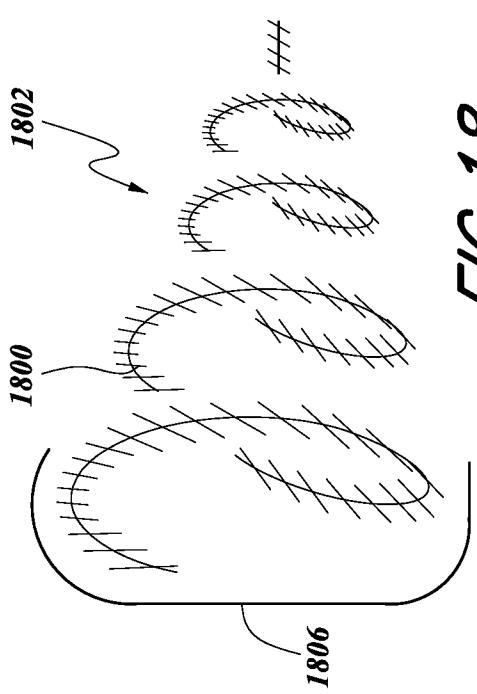


FIG. 18

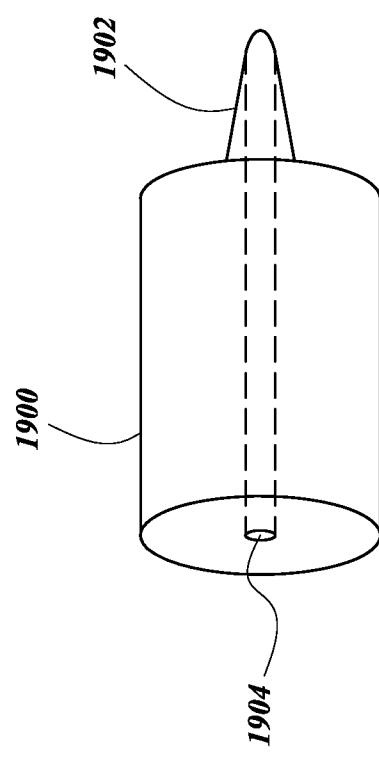


FIG. 19

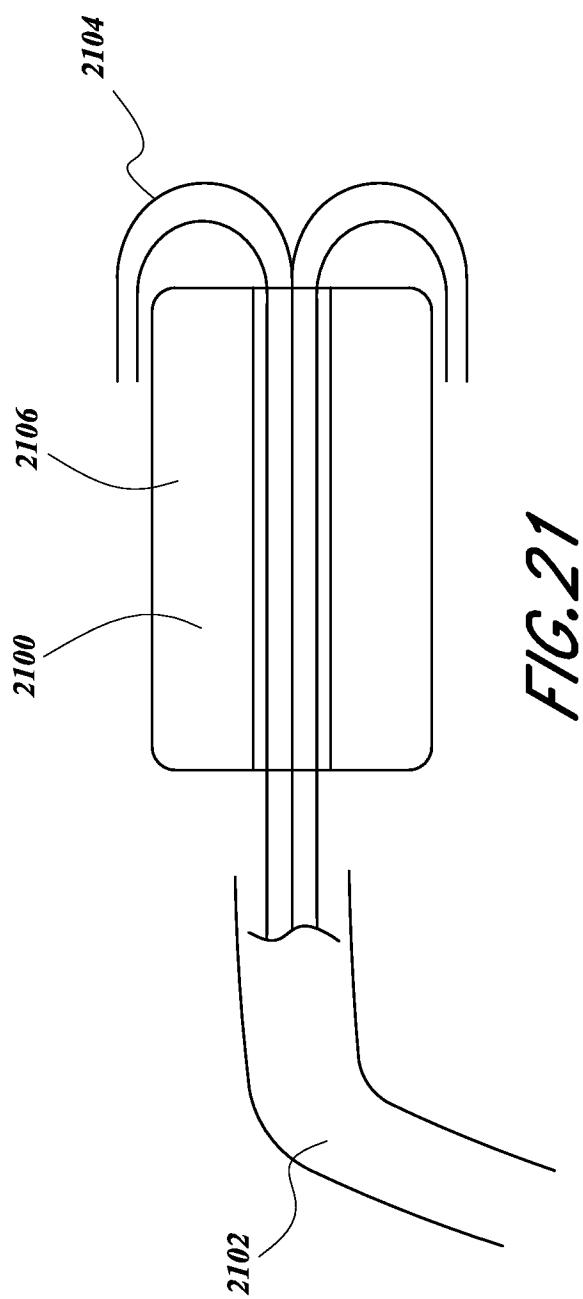
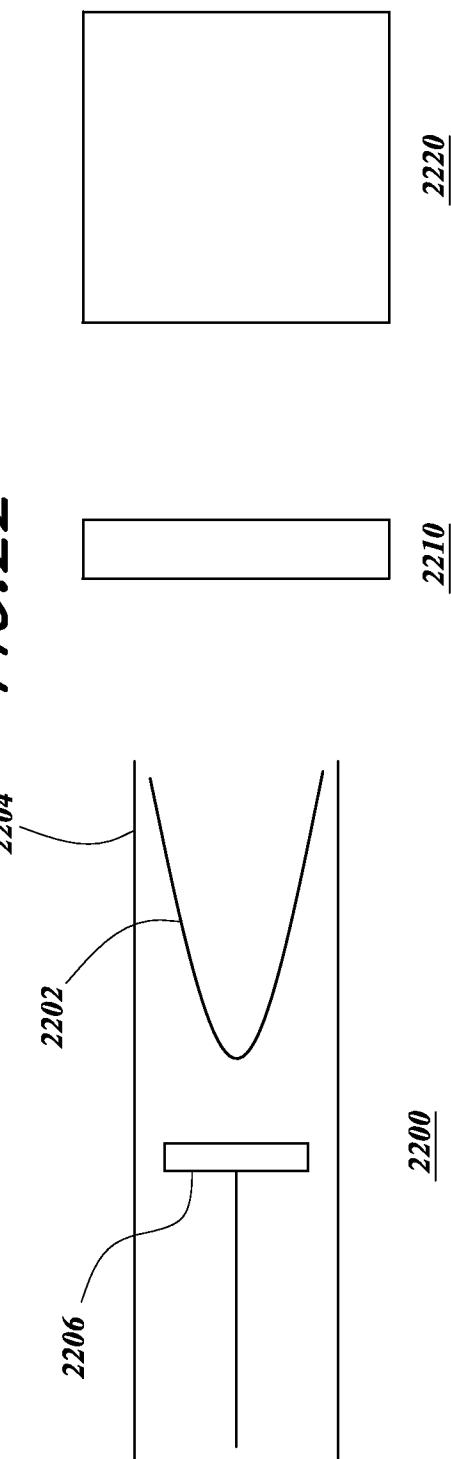


FIG. 22



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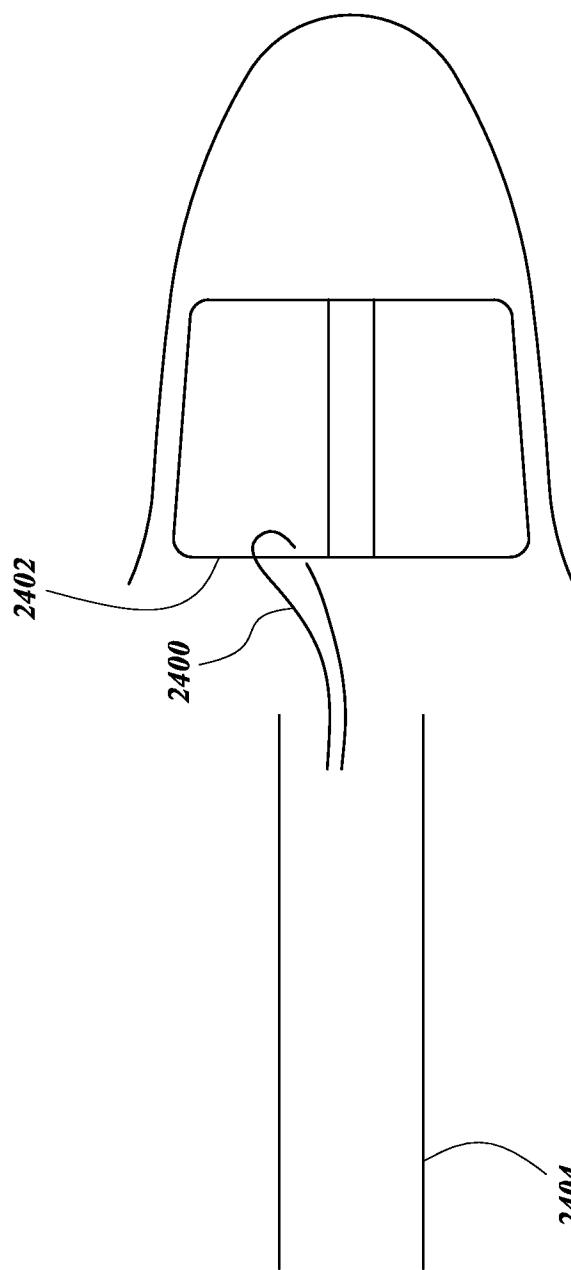


FIG. 24

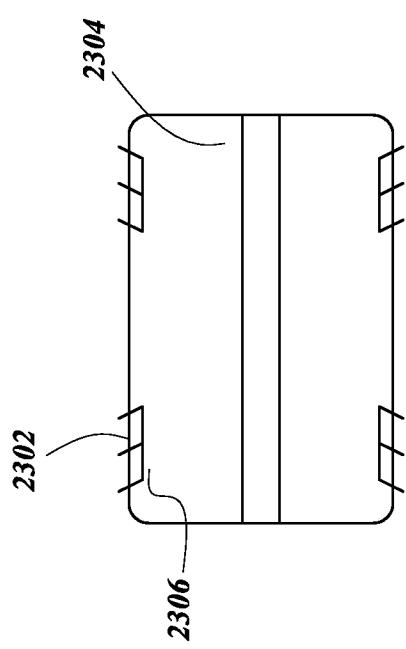
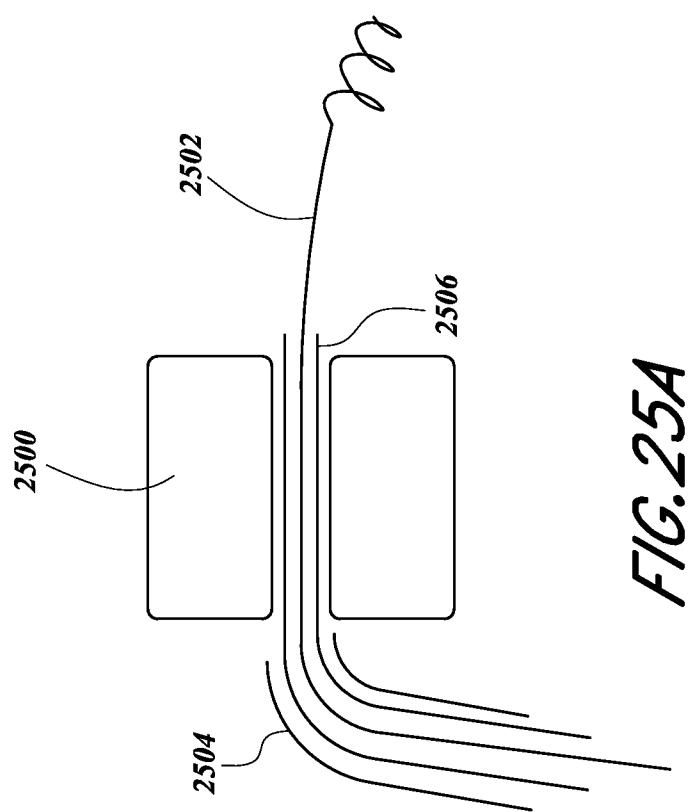
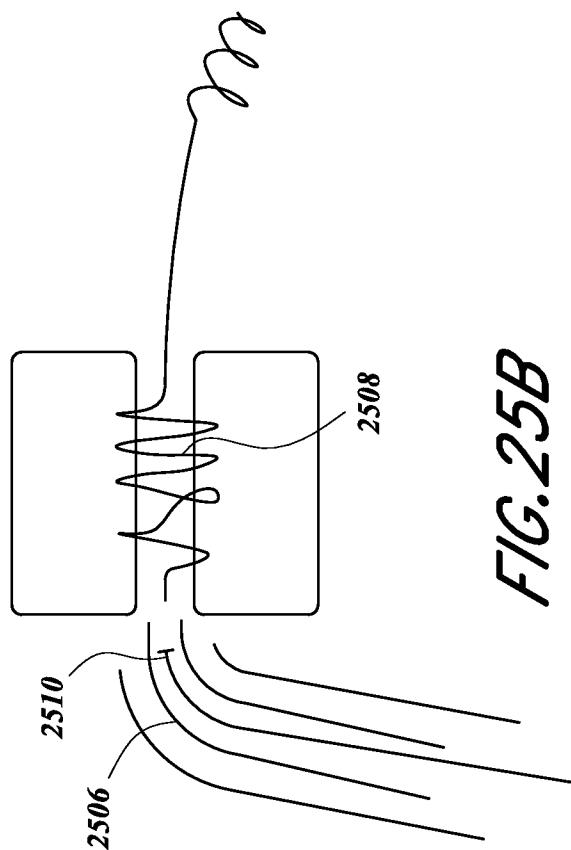


FIG. 23

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RECTIFIED SHEET (RULE 91)

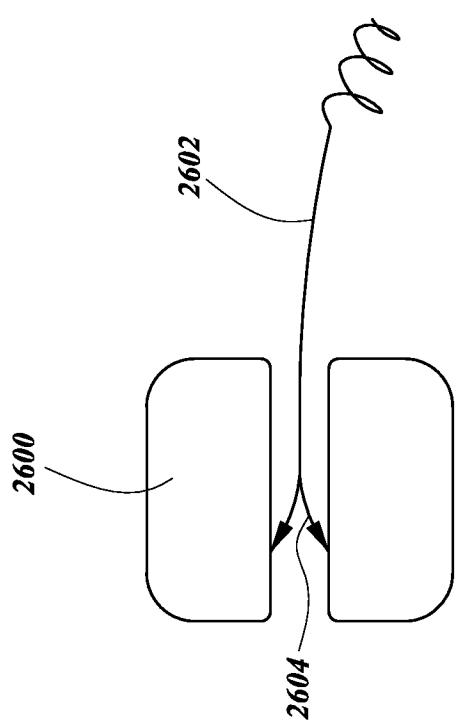


FIG. 26

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US2014/022865

A. CLASSIFICATION OF SUBJECT MATTER

IPC(8) - A61M 29/02 (2014.01)
USPC - 604/96.01

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)
IPC(8) - A61B 17/00, 17/068, 17/12, 17/122; A61F 2/00, 2/01, 2/04, 2/84, 2/958; A61M 29/00, 29/02 (2014.01)
USPC - 604/96.01; 606/157, 191, 194, 198, 200, 213; 623/1.11, 2.26, 23.64, 23.65

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
CPC - A61B 17/0057, 17/12022, 17/12027, 17/12122, 17/12136, 17/12159, 17/12172, 2017/00243, 2017/00592, 2017/00597, 2017/00867, 2017/12054; A61M 29/00 (2014.02)

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
Orbit, Google Patents, Google Scholar

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2010/0228279 A1 (MILES et al) 09 September 2010 (09.09.2010) entire document	1, 2, 5, 7, 10, 11, 13-15, 17, 19, 24, 26, 28
Y		3, 4, 6, 8, 9, 12, 16, 18, 20-23, 25, 27
Y	US 2009/0287145 A1 (CRAGG et al) 19 November 2009 (19.11.2009) entire document	3, 4, 8, 9, 12
Y	US 2009/0112249 A1 (MILES et al) 30 April 2009 (30.04.2009) entire document	4, 16
Y	US 2011/0178539 A1 (HOLMES JR et al) 21 July 2011 (21.07.2011) entire document	6, 7, 12, 18, 20-23, 25
Y	US 2012/0323267 A1 (REN) 20 December 2012 (20.12.2012) entire document	9
Y	US 2009/0264920 A1 (BERENSTEIN) 22 October 2009 (22.10.2009) entire document	22, 23
Y	US 2012/0283773 A1 (VAN TASSEL et al) 08 November 2012 (08.11.2012) entire document	27

Further documents are listed in the continuation of Box C.

* 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

06 June 2014

Date of mailing of the international search report

03 JUL 2014

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