(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
09 November 2017 (09.11.2017)

WIPO | PCT

(10) International Publication Number
WO 2017/192999 A1

(51) International Patent Classification:
A61B 17/3211 (2006.01) *A61B 17/00* (2006.01)
A61B 17/32 (2006.01)

(21) International Application Number:
PCT/US2017/031311

(22) International Filing Date:
05 May 2017 (05.05.2017)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
62/332,495 06 May 2016 (06.05.2016) US

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(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DJ, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KH, KN, KP, KR, KW, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(84) Designated States *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG).

(54) Title: INTERNAL CAROTID ARTERY THROMBECTOMY DEVICES AND METHODS

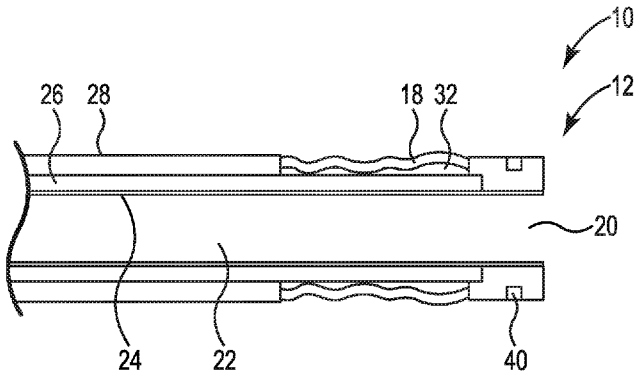

Fig. 4A

(57) Abstract: Embodiments of the invention include tools and methods for performing thrombectomy in patients' internal carotid arteries. A balloon guiding sheath in accordance with embodiments comprises an elongated 7-9 Fr sheath having a working section length of about ninety centimeters, an access port on a proximal end portion and a distal port on a distal end portion. A 6-8 Fr working lumen extends through the sheath between the access port and the distal port. An inflatable balloon is on the distal end portion of the sheath. An inflation lumen extends in the sheath between the balloon and an inflation port. The guiding sheath is configured with stiffness and other characteristics to enable direct insertion of the working length of the sheath into a patient's vasculature through an arteriotomy in the femoral artery, and to position the balloon in the internal carotid artery.

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Published:

— *with international search report (Art. 21(3))*

— *before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments (Rule 48.2(h))*

INTERNAL CAROTID ARTERY THROMBECTOMY DEVICES AND METHODS

CROSS REFERENCE TO RELATED APPLICATION

[0001] This application claims the benefit of U.S. Provisional Application Serial No. 62/332,495 filed on May 6, 2016 and entitled System and Method for Interventional Cardiac Device.

FIELD OF THE INVENTION

[0002] The invention relates generally to medical devices and methods of use. Embodiments of the invention include devices for performing thrombectomy or embolectomy in the internal carotid artery and other vessels of a patient.

BACKGROUND

[0003] Acute Ischemic Stroke (AIS) can be caused by thrombus, embolus or other occlusions in regions of the internal carotid artery (ICA) such as the Petrous part, Cavernous part or Cerebral part. Approaches for performing thrombectomy or embolectomy to treat AIS include positioning a balloon guiding catheter in the carotid artery at a location upstream from the occlusion, typically at a proximal location in the artery such as the Cervical part. After the balloon is inflated to provide antegrade blood flow cessation, suction can be applied to the catheter to retrieve the embolus. Thrombectomy tools such as stent retrievers can also be delivered directly to the embolus through the guiding catheter to break up the embolus and enhance the retrieval process.

[0004] These thrombectomy procedures may involve placing a sheath through an arteriotomy in the patient's common femoral artery, and delivering the guiding catheter to the ICA through the sheath. For example, an 8-9 French (Fr) inner diameter (ID) (0.015-0.118 inches) sheath having a length on the order of twenty-five centimeters can be used to provide the access to the arterial tree through the arteriotomy. A balloon guiding catheter having a 7-8 Fr outer diameter (OD) (0.092-0.105 inches), commonly about ninety centimeters in length, can then be delivered to the ICA through the sheath. A 10-11 Fr (0.131-0.144 inch) arteriotomy may be required for the sheath during procedures of these types. Unfortunately these relatively large arteriotomies can enhance the risk of bleeding, especially since patient's undergoing these procedures may be receiving thrombolytics that may increase the risks of hemorrhagic complications.

[0005] Relatively small diameter distal access aspiration catheters (e.g., up to about 0.087 inch OD) are sometimes used during thrombectomy in the ICA. Such distal aspiration

catheters include the ACE 68 from Penumbra, Inc. and the Sophia Plus from Microvention, Inc. For example, during these procedures the distal aspiration catheter can inserted with the end positioned at the distal middle cerebral artery. Other thrombecotomy tools such as stent retrievers are sometimes delivered to the intracranial vasculature through distal access catheters used in this manner. However, balloon guiding catheters have IDs that are too small to accommodate these distal aspiration catheters. Other known balloon guide catheters include the MO.MA Ultra and Cello devices from Medtronic, Inc., and the Flowgate2 device from Stryker Neurovascular. The relatively long period of time required to place a sheath and then a balloon guide catheter can detract from the benefits of this treatment.

[0006] Stents and other endovascular tools are sometimes placed in the ICA or other vasculature using guiding sheaths that do not have balloons. Guiding sheaths are typically about ninety centimeters in length. These devices act as a combination of access sheath and guiding catheter. The need for a separate sheath is obviated by the use of these guiding sheaths since they are sufficiently long to provide access to the target vessel. Although guiding sheaths do not provide arterial occlusion, they can be rapidly placed.

[0007] There is a continuing need for improved devices and methods for performing mechanical revascularization such as thrombectomy and embolectomy in the ICA and other vasculature. In particular, there is a need for such devices and methods that provide enhanced efficacy. Devices and methods of these types that can improve the efficiency of health care delivery would be especially desirable.

SUMMARY

[0008] Embodiments of the invention include tools and methods for performing thrombectomy, embolectomy and other procedures in patients' internal carotid arteries and other vasculature. A balloon guiding sheath in accordance with embodiments comprises an elongated sheath having a working section length of at least ninety centimeters, a proximal end portion and a distal end portion. The sheath has an access port is on the proximal end portion and a distal port on the distal end portion. A working lumen extends through the sheath between the access port and the distal port. An inflatable balloon is on the distal end portion of the sheath. An inflation port is on the proximal end portion of the sheath. An inflation lumen extends in the sheath between the inflation port and the balloon. The sheath is configured to enable direct insertion of the working length of the sheath into a patient's vasculature through an arteriotomy to position the balloon at a target site.

[0009] In embodiments, the balloon guiding sheath has an outer diameter between about 0.104 and 0.149 inches, and the working lumen has an inner diameter between about 0.087-0.126 inches. The sheath can include a recess at the distal end portion, with the balloon being located substantially within the recess when the balloon is in an uninflated state. Embodiments of the sheath have a working length sufficiently long to enable the distal end portion to reach a patient's internal carotid artery from a femoral artery arteriotomy.

[0010] A method for using the balloon guiding sheath in accordance with embodiments of the invention includes inserting the balloon guiding sheath directly into a patient's vasculature through an arteriotomy in the patient's femoral artery. The balloon guiding sheath is advanced through the patient's vasculature and positioned at the distal end portion in the patient's internal carotid artery. The balloon is inflated. Relatively low pressure is applied to the access port to suction an embolus. The balloon is deflated, and the balloon guiding sheath is withdrawn through the arteriotomy in the femoral artery.

BRIEF DESCRIPTION OF THE DRAWINGS

[0011] FIG. 1 is an isometric illustration of a balloon guiding sheath in accordance with embodiments of the invention.

[0012] FIG. 2 is a cross sectional illustration of the guiding sheath shown in FIG. 1, taken along line 2—2 in FIG. 1.

[0013] FIG. 3 is a cross sectional illustration of the guiding sheath shown in FIG. 1, taken along line 3—3 in FIG 1.

[0014] FIG. 4A is detailed cross sectional illustration of the distal end portion of the guiding sheath shown in FIG. 1, taken along ling 4A—4A in FIG. 1, showing the balloon in an uninflated state.

[0015] FIG. 4B is a detailed cross section illustration of the distal end portion of the guiding sheath shown in FIG. 4A, showing the balloon in an inflated state.

[0016] FIG. 5 is an illustration of a portion of an internal carotid artery (ICA) into which a guiding sheath has been positioned during a thrombectomy procedure in accordance with embodiments of the invention.

[0017] FIG. 6A is a detailed cross sectional illustration of the distal end portion of a guiding sheath in accordance with other embodiments of the invention, showing the balloon in an uninflated state.

[0018] FIG. 6B is a detailed cross section illustration of the distal end portion of the guiding sheath shown in FIG. 6A, showing the balloon in an inflated state.

[0019] FIG. 7 is an isometric illustration of an endovascular instrument set in accordance with embodiments of the invention.

[0020] FIG. 8 is an illustration of the distal end portion of the expansion tool shown in FIG. 7, with the balloon in the expanded state.

[0021] FIG. 9 is an illustration of the distal end of the expansion tool shown in FIG. 7 located in the sheath/guide catheter shown in FIG. 7, with the balloon of the expansion tool inflated to diametrically expand the distal end portion of the sheath/guide catheter.

[0022] FIG. 10 is an illustration of a distal end portion of an expansion tool in accordance with other embodiments of the invention, shown located in a sheath/guide catheter, and with the balloon of the expansion tool inflated to diametrically expand the distal end portion of the sheath/guide catheter.

[0023] FIG. 11 is an isometric illustration of an intermediate access aspiration catheter in accordance with embodiments of the invention.

[0024] FIG. 12 is an illustration of the intermediate access aspiration catheter shown in FIG. 11 following its insertion into the ICA of a patient.

[0025] FIG. 13 is an illustration of an intermediate access aspiration catheter having a tapered tip in accordance with other embodiments of the invention.

[0026] FIG. 14 is an illustration of the intermediate access aspiration catheter shown in FIG. 13 following its insertion into the ICA of a patient.

[0027] FIG. 15 is an illustration of a stent retriever in accordance with embodiments of the invention.

[0028] FIG 16 is a cross sectional illustration of the stent retriever shown in FIG. 15, taken along line 16—16 in FIG. 15.

[0029] FIG. 17 is an illustration of a stent retriever in accordance with other embodiments of the invention.

DETAILED DESCRIPTION

[0030] A balloon guiding sheath 10 in accordance with embodiments of the invention can be described generally with reference to FIG. 1. As shown, guiding sheath 10 includes an elongated sheath 12 having an access port 14 and inflation port 16 on its proximal end portion, and a balloon 18 and port 20 on the its distal end portion. FIG. 2 is a cross sectional view of an embodiment of the sheath 12 at a location between the access port 14 and balloon 18. The sheath 12 is a tubular structure that includes a primary or working lumen 22 extending between the access port 14 and port 20. Lumen 22 is defined by an inner layer 24, intermediate layer 26 and an outer layer 28 in the illustrated embodiment. The inner layer 24 can be formed from polymer such as PTFE (polytetrafluoroethylene). The intermediate layer 26 can be formed from coiled or braided strands of material such as stainless steel or polymer wire. The outer layer 28 can be formed from polymer material such as nylon. An inflation lumen 30, shown in the outer layer 28 in the illustrated embodiment, extends between the inflation port 16 and the balloon 18. In other embodiments (not shown) the inflation lumen is in other structures of the sheath 12, or a tubular structure within the lumen 22. Other embodiments (now shown) include more than one inflation lumen, and/or such lumens having different cross sectional shapes.

[0031] The primary structural components (e.g., layers 24, 26 and 28) of the sheath 12 are configured to provide the sheath with longitudinal and rotational stiffness characteristics (e.g., the capabilities of being able to be pushed and/or twisted between its proximal and distal ends) to enable the device to be relatively rapidly delivered to the desired or target location in the patient's vasculature. In embodiments (not shown), the sheath 12 can be formed from more or fewer and/or different types of structural layers. For example, a lubricious coating layer can be applied to all or portions of the exterior surface of the outer layer 28. Other embodiments do not have an outer friction-reducing coating. The outer layer 28 of the sheath 12 can be formed of low-friction material in embodiments. The composition of the sheath 12 along its length can be varied to provide graded longitudinal and rotational stiffness characteristics. These graded stiffness characteristics can be provided, for example, by varying the material properties and/or thicknesses of the layers such as 24, 26 and 28 along the length of the sheath 12, and/or by including more or fewer and/or different such structural layers. The guiding sheath 10 is sufficiently long to enable the device to be advanced from the arteriotomy through the

vasculature, and the distal end portion and port 20 positioned at the target site. In embodiments, the sheath has a working length that can be inserted into the patient of at least ninety centimeters. In embodiments, the guiding sheath can be longer or shorter.

[0032] The distal end portion of the sheath 12 including the balloon 18 can be described with reference to FIGs. 3, 4A and 4B. Balloon 18 is located in a recess 32 on the distal end portion, adjacent the port 20. In the illustrated embodiment the recess 32 is in the outer layer 28, but in other embodiments the recess is located in other or additional layers of the sheath 12. The recess 32 or other structure opening into the interior of the balloon 18 is coupled to the inflation lumen 30 so inflation fluid can be delivered to and withdrawn from the balloon through the inflation port 16. FIG. 4A shows the balloon 18 in the wrapped, undeployed and uninflated state. In the illustrated embodiment the uninflated balloon 18 is a low profile structure that has a diameter that is not, or not substantially, greater than the diameter of the adjacent portions of the sheath 12 to optimize the ability of the guiding sheath 10 to be inserted. In other embodiments (not shown), the balloon 18 can be mounted over the outer surface of the sheath. FIG. 4B shows the balloon in inflated, deployed and diametrically expanded state. Balloon 18 is sized and configured to occlude arteries or other vessels in which it is positioned. In embodiments, for example, the balloon 18 can be expanded to about ten millimeters in diameter, and can be about ten millimeters in length. The balloon 18 can also be rewrapped or deflated tight enough through the withdrawal of fluid through lumen 30 to optimize the ability of the guiding sheath 12 to be withdrawn.

[0033] Embodiments of sheath 12 also include a radiopaque marker 40. Marker 40 is shown on distal end portion of the sheath 12 in the embodiments of FIGs. 4A and 4B. Marker 40 can be imaged during procedures to identify the location of the sheath 12, and in particular the distal end of the sheath, in the patient's vasculature.

[0034] In embodiments, guiding sheath 10 has an outer diameter (OD) of about 6.2-9.2 Fr, or about 0.104-0.149 inches. Devices with these ODs can have inner diameters (IDs), for example, in the range of 6-9 Fr (0.087-0.126 inches). Other embodiments of the guiding sheath 10 have an OD of about 6.2-9.2 Fr. Devices of with these ODs can have IDs, for example, in the range of 7-9 Fr (0.079-0.118 inches). Still other embodiments of the guiding sheath 10 have ODs in the range of 7-8 Fr. Devices with these ODs can have IDs, for example, in the range of 6-9 Fr. A particularly useful embodiment of guiding sheath 10 has an OD of less than 0.150 inch (e.g., about 9.2 Fr) and an ID of greater than 0.087 inch (e.g., about 6 Fr). Other embodiments of guiding sheath 10 have larger ODs (e.g., 9-10 Fr (0.118-0.131 inches) or larger). These larger OD guiding sheaths 10 can have IDs, for example, in the range of 0.113-0.126 inches). Yet other embodiment have smaller ODs, (e.g., 4-6 Fr (0.053-0.079 inches) or smaller). In

embodiments, the sheath 12 has a generally constant diameter. In other embodiments the sheath 12 has a generally increasing diameter along its length in the direction from the distal end portion toward the proximal end portion, so that portions of the sheath entering the arteriotomy during the insertion of the guiding catheter 10 to the target site will not generally decrease in size, thereby minimizing bleeding at the arteriotomy. Any transitions along the outer surface of the sheath 12 are preferably smooth.

[0035] The use of a guiding sheath 10 in accordance with embodiments of the invention to perform a thrombectomy or embolectomy can be described with reference to FIG. 5, which shows a portion of an internal carotid artery (ICA) 50 including the Cervical part 52, Petrous part 54, Cavernous part 56 and Cerebral part 58. Guiding sheath 10 combines the functionality of a sheath and a balloon guide catheter. The guiding sheath 10 can be inserted directly (e.g., without the use of a sheath or other introducer) through an arteriotomy (e.g., in the femoral artery), and advanced through the patient's vasculature with the balloon 18 in its uninflated state. The surgeon can continue this insertion procedure to position the distal end portion and port 20 at the target site, upstream from the embolus to be removed. Fluid is then applied through the inflation port 16 to deploy or inflate the balloon 18 and occlude the ICA. By applying relatively low pressure or a vacuum to the access port 14, embolus downstream from the port 20 can be removed by suction. In embodiments such as that shown in FIG. 5, the distal end portion of the guiding sheath 10 is positioned with the balloon 18 and port 20 in the Cervical part 52 of the ICA (i.e., at a relatively proximal location in the ICA), enabling the removal of embolus (not shown) in the Petrous part 54, Cavernous part 56 and Cerebral part 58. In embodiments, guiding sheaths 10 having an OD between about 6 and 9 Fr can be efficaciously placed in the Cervical part 52 of many patients. In other embodiments, guiding sheaths 10 having these or smaller ODs such as 7-8 Fr can be inserted further (i.e., distally) into the ICA (e.g., to the Petrous part 54 or beyond). Imaging, using the marker 40, can be used by the surgeon during insertion of the guiding sheath 10 to position the end portion and port 20 at the desired location in the ICA. Following the removal of the embolus, the fluid can be removed through the inflation port 16 to uninflate the balloon. The guiding sheath 10 can then be withdrawn from the patient's vasculature.

[0036] In other embodiments, additional endovascular tools such as distal access aspiration or mechanical stent retriever tools can be used with guiding sheaths 10 that are positioned in accordance with methods described above. During these procedures, the additional endovascular tools can be inserted into the access port 14, fed through the lumen 22 and port 20, and delivered to the target site.

[0037] Guiding sheath 10 offers a number of important advantages. For example, the ability to place one device instead of two (i.e., a standard sheath and guide catheter), or a single

device in connection with certain procedures such as the thrombectomy procedure described above, shortens the procedure time and reduces the number of instruments used. Smaller arteriotomies can also be used since the diameters of the devices used for a given procedure are reduced. This advantage is particularly important in connection with thrombectomy procedures because patients undergoing procedures of these types may be receiving thrombolytics that can increase the risk of bleeding at the arteriotomy. Morbidity associated with embolus fragmentation can be reduced by the temporary antegrade flow cessation. The relatively large IDs of the devices markedly improve suction efficiency by providing flow rates that can be up to two or three, or even more times those of current devices. The stiffnesses and other characteristics of the sheath 12 can provide improved support for distal access devices and prevent "back out" that can result in loss of access during use. The relatively large balloon inflation lumens provided by the device enable the balloon to be rapidly deployed and uninflated, thereby reducing the time required for procedures. The efficiency and efficacy of healthcare services are thereby enhanced. Because of their enhanced size features, embodiments of guiding sheaths 10 are free from or do not have hydrophylic or other friction-reducing coatings that might be susceptible to separation from the guiding sheath during use.

[0038] FIGs. 6A and 6B illustrate the distal end portions of a guiding sheath 110 in accordance with embodiments of the invention. As shown in FIG. 6B, when the balloon 118 is in the deployed or expanded shape, it has a concave or funnel-shaped opening that in the illustrated embodiment extends distally from the distal ends of the inner, intermediate and outer layers 24, 26 and 28. In other embodiments the distal end of the inflated balloon 118 extends distally of one or more of the layers such as 24, 26 and 28 of the sheath 112. During use of the guiding sheath 110, the asymmetric and concave shape of the inflated balloon 118 can cause the retrieved thrombus to be preferentially drawn to the port 120, thereby reducing the possibility of the thrombus being trapped between the distal end of the guiding sheath and the vessel wall. By enhancing the collection of the thrombus, guiding sheath 110 can provide improved treatment efficacy. Other than the differences shown in FIGs. 6A and 6B and described above, guiding sheath 110 can be similar to or substantially the same as guiding sheath 10.

[0039] FIG. 7 is an illustration of an endovascular instrument set 200 in accordance with embodiments of the invention that includes a sheath/guide catheter 202 and an expansion tool 204. Sheath/guide catheter 202 includes an elongated tubular member 206 having an access port 208 on its proximal end and a diametrically expandable tip 210 with a distal port on its distal end. The tubular member 206 has a lumen 207 (e.g., FIG. 9), and can be a structure that is the same as or similar to that of the sheath 12 described above in connection with FIGs. 1-3, or other known or conventional sheaths or guide catheters. The structure of the tubular member 206 will

be configured to enable the sheath/guide catheter 202 to be inserted into and through a patient's vasculature, and to position the tip 210 at a target site while the tip is in a retracted or diametrically-reduced state. The tip 210 is diametrically expandable in response to a force applied from the inside of the tip, and capable of retaining its expanded shape. In embodiments, for example, the tip 210 can be formed from malleable metals or other materials. In other embodiments the tip 210 can be an expandable braided or coiled wire structure. In still other embodiments the tip 210 is formed from a plurality of petal members that open like a flower. Shape memory materials such as nitinol can be used in these and other embodiments of the tip 210.

[0040] Expansion tool 204 includes an elongated tubular member 220 having an inflation port 212 on its proximal end and a diametrically expandable balloon 214 on its distal end. A lumen (not shown) extends through the tubular member 220 between the inflation port 212 and the balloon 214. The outer diameter of the tubular member 220 is less than the inner diameter of the lumen 207 of the sheath/guide catheter 202. The balloon 214 is shown in its uninflated or diametrically retracted state in FIG. 7. As shown in FIG. 8, the balloon 214 can be inflated and diametrically expanded by the application of fluid though the inflation port 212.

[0041] The use of instrument set 200 can be described in connection with FIGs. 7-9. In embodiments, the sheath/guide catheter 202 is used to remove embolus from ICAs in a manner similar to that described above. Following the insertion of sheath/guide catheter 202 and the positioning of its tip 210 (in the retracted state) at the target site, as described above, the expansion tool 204 is inserted through the sheath/guide catheter with the balloon 214 in the uninflated state to position the balloon adjacent the sheath/guide catheter tip. The balloon 214 is then deployed or inflated and diametrically expanded. The expansion of the balloon 214 applies sufficient forces on the tip 210 of the sheath/guide catheter 202 to cause the tip to take its expanded diameter shape (e.g., a concave shape, as shown in FIG. 9). By this expansion the tip 210 can be urged into contact with the inner walls of the vessel. The balloon 214 can then be returned to its uninflated state by withdrawing the inflation fluid through the port 212, and the expansion tool 204 withdrawn from the sheath/guide catheter 202. The tip 210 will remain in the expanded diameter state following the withdrawal of the expansion tool 204. The sheath/guide catheter 202 can then be used in connection with an endovascular procedure. For example, suction can be applied to the access port 208 to remove embolus. Alternatively, a tool such as a distal access or other catheter or a stent removal tool can be inserted through the sheath/guide catheter 202 and delivered to the target site. Following the procedure, the sheath/guide catheter 202 is withdrawn from the patient. The tip 210 is sufficiently resilient that it will diametrically

retract or collapse during the removal. In other embodiments the tip 210 is configured to be retracted by the surgeon before removal of the sheath/guide catheter 202.

[0042] In embodiments, the tip 210 and/or balloon 214 can be configured to take other diametrically expanded shapes. FIG. 10, for example, illustrates a sheath/guide catheter 202' having a tip 210' and an expansion tool 204' with a balloon 214' that are configured and cooperate to symmetrically expand the tip of the sheath/guide catheter. Other features of the sheath/guide catheter 202' and expansion tool 204' can be the same as or similar to those of sheath/guide catheter 202 and expansion tool 204 described above. Similarly, the sheath/guide catheter and/or expansion tool can be configured to cooperate to provide tips that have other shapes when in the diametrically expanded state.

[0043] FIG. 11 is an illustration of an intermediate access aspiration catheter 300 in accordance with embodiments of the invention. As shown, catheter 300 includes an elongated tubular member 312 having an access port 314 on its proximal end portion, and a tip 316 on its distal end portion. Intermediate aspiration catheter 300 is configured to be inserted into intermediate locations of a patient's ICA. In embodiments, for example, the catheter 300 is configured to have its tip 316 positioned in the Petrous part or Cavernous part of the ICA. One embodiment of the intermediate aspiration catheter 300 has an OD of about 8 Fr (e.g., about 0.105 inch). The ID of such an 8 Fr catheter 300 can be between about 0.080-0.090 inches, in embodiments. Other embodiments of the catheter 300 have an OD between about 7 Fr and 8 Fr (e.g., about 0.092-0.105 inches). The IDs of such 7-8 Fr catheters 300 can range between about 0.080-0.090 inches. Yet other embodiments of the catheter 300 have an OD between about 8 Fr and 9 Fr (e.g., about 0.105-.0118 inches). The IDs of such 8-9 Fr catheters 300 can range between about 0.080-0.090 inches. The catheter 300 can be about ninety centimeters long in embodiments. Other embodiments can have other lengths, which can depend on factors such as the applications for which the device is used.

[0044] Tip 316, which can be between ten and twenty centimeters in length in embodiments (other embodiments have other lengths), is more flexible that the portions of the tubular member 312 between the tip and access port 314. In embodiments, the tip 316 is sufficiently long and flexible to enable the tip to be positioned in the Petrous part or Cavernous part of the ICA. FIG. 12, for example, shows the catheter 300 located with the tip 316 in the Petrous part 340 of an ICA. The portions of tubular member 312 proximal to the tip 312 are sufficiently stiff that they can be manipulated during the insertion of the catheter 300 to relatively quickly position the tip 312 at the desired location. In embodiments, the tubular member 312 can be the same as or similar to the structure of the sheath 12 of the guiding sheath 10 described above. In other embodiments the tubular member 312 has other structures that

provide the functional characteristics described above. For example, the tip 316 can have fewer component layers than that of the guiding sheath 10 to provide the appropriate flexibility of the tip.

[0045] In embodiments, the catheter 300 can be inserted directly through an arteriotomy and advanced to a target site. In other embodiments, the catheter 300 is used with other devices such as the guiding sheath 10 (i.e., the catheter is advanced to the target site though the guiding sheath after the guiding sheath has been inserted and positioned). After the catheter 300 is inserted and the tip 316 positioned (i.e., adjacent or upstream of an embolus), suction can be applied to the device through the access port 314 to collect the embolus.

[0046] FIG. 13 is an illustration of the distal end portion of another intermediate access aspiration catheter 300' in accordance with embodiments of the invention. As shown, catheter 300' has a tapered tip 316' that tapers to a smaller diameter than the diameter of the tubular member 312'. Other than the tapered shape of the tip 316', features of catheter 300' can be the same as or similar to those of catheter 300 described above in connection with FIG. 11. Embodiments of catheter 300' are configured to have its tip 316' positioned in the Cavernous part or Cerebral part of the ICA, for example adjacent or in the Middle Cerebral artery. FIG 14, for example, shows the catheter 300' located with the tip 316' in the Cerebral part 342 of the ICA. In embodiments, catheter 300' has a tubular member with an OD of about 8 Fr and a tip 316' that tapers to an OD of about 6-7 Fr. The ID of the distal end of the tip 316' in such embodiments can be, for example, in the range of 0.075-0.085 inches. Other embodiments of the catheter 300' have an OD between about 7 Fr and 8 Fr (e.g., about 0.092-0.105 inches), and a tip 316' that tapers to an OD of about 0.080-0.090 Fr. Yet other embodiments of the catheter 300' have an OD between about 8 Fr and 9 Fr (e.g., about 0.105-.0118 inches), and a tip 316' that tapers to an OD of about 7.5-8.5 Fr. Catheter 300' can be inserted, advanced and used in manners similar to or the same as those described above in connection with catheter 300, including in connection with a guiding sheath 10.

[0047] FIGs. 15 and 16 are illustrations of a stent retriever 400 in accordance with embodiments of the invention. Stent retriever 400, which is shown in its diametrically expanded or deployed state in FIG. 15, includes a body 410 having a proximal or first portion 412 and a distal tip 414. A wire 416 extends from the body 410. Both the first portion 412 and the distal tip 414 are formed from a mesh of wires 418. In embodiments, the wires 418 are metal such as stainless steel or nitinol, and can be braided. As shown, the mesh density of the wires 418 in the distal tip 414 is greater than the mesh density of the wires in the first portion 412 (i.e., the first portion is more porous than the distal tip). In embodiments, the mesh density of the wires 418 in the tip 414 is sufficiently high to cause the tip to be substantially closed (i.e., non-porous). In

embodiments, the distal tip 414 can be approximately one-fourth to one-third of the length of the body 410, although it has other lengths in other embodiments. As described in greater detail below, the tip 414 is configured to trap portions of emboli that are released and not trapped by the first portion 412 during thrombectomy procedures. In embodiments, the mesh density of the wires 418 in the first portion 412 is sufficiently low to enable the wires of the first portion to engage an embolus during thrombectomy procedures. In embodiments, the stent retriever 400 is configured as a self-expandable device. In other embodiments the stent retriever 400 is configured as a balloon-expandable device.

[0048] Stent retriever 400 is placed in a reduced-diameter or unexpanded state (not shown) for delivery. Conventional or otherwise known structures (e.g., a removable sheath; not shown) can be used to place the stent in the unexpanded state. While in the unexpanded state, the stent retriever 400 is inserted through the patient's vasculature to the target site in a conventional or otherwise known manner. For example, in embodiments the stent retriever 400 can be delivered though a guiding sheath 10 of the type described above. At the target site the stent retriever 400 is pushed through the embolus. In embodiments, at least the tip 414 is positioned beyond the embolus. After the stent retriever 400 is positioned, it is actuated or deployed to diametrically expand (e.g., by unsheathing a self-expanding embodiment). With the stent retriever 400 in its expanded state, the surgeon can manipulate the device, including the first portion 412, to engage the embolus and release the embolus from the vessel. The stent retriever 400 and embolus are then withdrawn from the vessel. In embodiments, much if not all of the embolus will be engaged by the relatively low density wire mesh of the first portion 412. Portions of the embolus that break free or are otherwise not engaged by the first portion 412 can be captured by the tip 414 during the withdrawal of the stent retriever 400. Stent retriever 400 thereby provides enhanced efficacy by allowing for less thromboembolic events.

[0049] FIG. 17 is an illustration of a stent retriever 500 in accordance with other embodiments of the invention. Stent retriever 500, which is shown in its diametrically expanded or deployed state in FIG. 17, includes a proximal or first stent member 502 and a distal or second stent member 504. The second stent member 504 is spaced from the first stent member 502 (e.g., by about 2-10 millimeters in embodiments). In other embodiments (not shown) the second stent member 504 is positioned immediately adjacent the first stent member 502. Both the first member 502 and the second member 504 are formed from a mesh of wires 506. In embodiments, the wires 506 are metal such as stainless steel or nitinol, and can be braided. In the illustrated embodiment the first stent member 502 is closed at both ends, and has a first, relatively low mesh density. In embodiments, the mesh density of the wires 506 of the first stent member 502 is sufficiently low to enable the wires to engage an embolus during thrombectomy

procedures. The second stent member 504 is located distally of the first member 502 and has a relatively high mesh density of the wires 506 that is greater than the mesh density of the first stent member 502. In embodiments, the mesh density of the wires 506 in the second stent member 504 is sufficiently high to cause the member to be substantially closed. The second stent member 504 is concave, with the opening facing the first stent member 502, in embodiments. As described in greater detail below, the second stent member 504 is configured to trap portions of emboli that are released and not engaged by the first stent member 502 during thrombectomy procedures. In embodiments, the stent retriever 500 is configured as a self-expandable device. In other embodiments the stent retriever 500 is configured as a balloon-expandable device.

[0050] Stent retriever 500 is placed in a reduced-diameter or unexpanded state (not shown) for delivery. Conventional or otherwise known structures (e.g., a removable sheath; not shown) can be used to place both the first and second stent members 502 and 504, respectfully in the unexpanded state. While in the unexpanded state, the stent retriever 500 is inserted through the patient's vasculature to the target site in a conventional or otherwise known manner. For example, in embodiments the stent retriever 500 can be delivered though a guiding sheath 10 of the type described above. At the target site the stent retriever 500 is pushed through the embolus. In embodiments, at least the second stent member 504 is positioned beyond the embolus. After the stent retriever 500 is positioned, it is actuated or deployed to diametrically expand both the first and second stent members 502 and 504 (e.g., by unsheathing a self-expanding embodiment). With the stent retriever 500 in its expanded state, the surgeon can manipulate the tool, including the first stent member 502, to engage the embolus and release the embolus from the vessel. The stent retriever 500 and engaged embolus are then withdrawn from the vessel. In embodiments, much if not all of the embolus will be engaged by the relatively low density wire mesh of the first stent member 502. Portions of the embolus that break free or are otherwise not engaged by the first stent member 502 can be captured by the second stent member 504 during the withdrawal of the stent retriever 500. Stent retriever 500 thereby provides enhanced efficacy by allowing for less thromboembolic events.

[0051] Although the invention has been described with reference to preferred embodiments, those of skill in the art will recognize that changes can be made in form and detail without departing from the spirit and scope of the invention. In particular, although described in connection with procedures involving the ICA, the devices and methods can be used in other vasculature of patients.

CLAIMS

What is claimed is:

1. A balloon guiding sheath, comprising:

an elongated sheath having a working section length of at least ninety centimeters, a proximal end portion and a distal end portion;

an access port on the proximal end portion of the sheath;

a distal port on the distal end portion of the sheath;

a working lumen extending through the sheath between the access port and the distal port;

an inflatable balloon on the distal end portion of the sheath;

an inflation port on the proximal end portion of the sheath;

an inflation lumen extending in the sheath between the inflation port and the balloon; and

wherein the sheath is configured to enable direct insertion of the working length of the sheath into a patient's vasculature through an arteriotomy to position the balloon at a target site.

2. The balloon guiding sheath of claim 1 wherein the sheath has an outer diameter between about 0.104 and 0.124 inches.

3. The balloon guiding sheath of claim 2 wherein the working lumen has an inner diameter between about 0.087-0.113 inches.

4. The balloon guiding sheath of claim 3 wherein the sheath has a generally constant outer diameter along its working length.

5. The balloon guiding sheath of claim 4 wherein:

the sheath includes a recess at the distal end portion; and

the balloon is located substantially within the recess when the balloon is in an uninflated state.

6. The balloon guiding sheath of claim 5 wherein the sheath has a working length sufficiently long to enable the distal end portion to reach a patient's internal carotid artery from a femoral artery arteriotomy.

7. A method for using the balloon guiding sheath of claim 6, including:

inserting the balloon guiding sheath directly into a patient's vasculature through an arteriotomy in the patient's femoral artery;

advancing the balloon guiding sheath through the patient's vasculature and positioning the distal end portion in the patient's internal carotid artery;

inflating the balloon;

applying relatively low pressure to the access port to suction an embolus;

deflating the balloon; and

withdrawing the balloon guiding sheath through the arteriotomy in the femoral artery.

8. A method for using the balloon guiding sheath of claim 6, including:

inserting the balloon guiding sheath directly into a patient's vasculature through an arteriotomy in the patient's femoral artery;

advancing the balloon guiding sheath through the patient's vasculature and positioning the distal end portion in the patient's internal carotid artery;

inflating the balloon;

inserting a tool into the balloon guiding sheath through the access port after positioning the distal end portion in the patient's internal carotid artery;

advancing the tool through the balloon guiding sheath, out of the distal port, and into the patient's carotid artery;

actuating the tool to retrieve an embolus;

withdrawing the tool from the balloon guiding sheath;

deflating the balloon; and

withdrawing the balloon guiding sheath through the arteriotomy in the femoral artery.

9. The method of claim 8 wherein:

inserting the tool into the balloon guiding sheath includes inserting an intermediate access aspiration catheter having a distal end portion, and positioning the distal end portion in the Petrous part, Cavernous part or Cerebral part of the patient's internal coronary artery; and

applying relatively low pressure to the intermediate access aspiration catheter to suction the embolus.

10. The method of claim 9 wherein inserting the intermediate access aspiration catheter includes inserting a catheter having a tapered tip.

11. The method of claim 9 wherein inserting an intermediate access aspiration catheter includes inserting a catheter having an outer diameter between about 7 and 9 Fr.

12. The method of claim 9 wherein inserting an intermediate access aspiration catheter includes inserting a catheter having an outer diameter of about 8 Fr.

13. The method of claim 8 wherein inserting a tool includes inserting a stent retriever having a proximal portion with first mesh density and a distal portion with a second mesh density that is greater than the first mesh density.

14. The balloon guiding sheath of claim 1 wherein:

the sheath includes a recess at the distal end portion; and

the balloon is located substantially within the recess when the balloon is in an uninflated state.

15. The balloon guiding sheath of claim 14 wherein the sheath has an outer diameter between about 0.104 and 0.120 inches.

16. The balloon guiding sheath of claim 15 wherein the working lumen has an inner diameter between about 0.087-0.113 inches.

17. The balloon guiding sheath of claim 16 wherein the balloon extends beyond the distal port and defines a funnel-shaped opening into the distal port when the balloon is in an inflated state.

18. The balloon guiding sheath of claim 1 wherein the balloon extends beyond the distal port and defines a funnel-shaped opening into the distal port when the balloon is in an inflated state.

19. An intermediate access aspiration catheter, comprising:

an elongated sheath having a proximal end portion, a distal end portion, and a working section length sufficiently long to enable the distal end portion to reach a patient's internal carotid artery from a femoral artery arteriotomy;

an access port on the proximal end portion of the sheath;

a distal port on the distal end portion of the sheath;

a flexible tip on the distal end portion of the sheath, wherein the flexible tip is more flexible than portions of the sheath between the tip and the access port;

a working lumen extending through the sheath between the access port and the distal port;

wherein the sheath is configured to have sufficient stiffness and tip flexibility to enable insertion of the working length of the sheath into a patient's vasculature through an arteriotomy in the patient's femoral artery to position the distal port at a target site in a Petrous part, Cavernous part or Cerebral part of the patient's internal carotid artery.

20. The intermediate access aspiration catheter of claim 19 wherein the sheath has an outer diameter of about 8 Fr.

21. The intermediate access aspiration catheter of claim 20 wherein the sheath has an inner diameter of about 0.080-0.090 inches.

22. The intermediate access aspiration catheter of claim 20 wherein the flexible tip is tapered to a reduced outer diameter.

23. The intermediate access aspiration catheter of claim 22 wherein the flexible tip tapers to an outer diameter of about 6-7 Fr at the distal port.

24. The intermediate access aspiration catheter of claim 19 wherein the flexible tip is tapered to a reduced outer diameter.

25. A method for using the intermediate access aspiration catheter of claim 19, comprising:

inserting the intermediate access aspiration catheter into a patient's vasculature through an arteriotomy in the patient's femoral artery;

advancing the intermediate access aspiration catheter through the patient's vasculature and positioning the flexible tip in a Petrous part, Cavernous part or Cerebral part of the patient's internal carotid artery;

applying relatively low pressure to the access port to suction an embolus; and

withdrawing the intermediate access aspiration catheter through the arteriotomy in the femoral artery.

26. An endovascular instrument set, comprising:

a sheath/guide tool, including:

an elongated tubular member having a proximal end portion and a distal end portion;

an access port on the proximal end portion;

a distal port on the distal end portion;

a diametrically expandable tip on the distal end portion; and

a lumen having an inner diameter extending between the access port and the distal port; and

an expanding tool, including:

an elongated tubular member having an outer diameter that is less than the inner diameter of the sheath/guide tool lumen inner diameter, a proximal end portion and a distal end portion;

an inflation port on the proximal end portion;

an inflatable balloon on the distal end portion; and

an inflation lumen extending between the inflation port and the balloon; and

wherein the expanding tool can be inserted into the sheath/guide tool and the balloon of the expanding tool positioned adjacent the expandable tip of the sheath/guide tool, and the balloon inflated to expand the tip.

27. The endovascular instrument set of claim 26 wherein the diametrically expandable tip of the sheath/guide tool is expandable to a concave shape.

28. A method for using the endovascular instrument set of claim 26, comprising:

inserting the sheath/guide tool into a patient's vasculature;

advancing the sheath/guide tool through the patient's vasculature and positioning the distal end portion at a target site;

inserting the expanding tool into the access port of the sheath/guide tool;

advancing the expanding tool through the sheath/guide tool and positioning the inflatable balloon in the expandable tip;

inflating the balloon to expand the expandable tip of the sheath/guide tool into engagement with walls of the patient's vasculature;

deflating the balloon and withdrawing the expanding tool from the sheath/guide tool;

performing a procedure in the patient's vasculature through the sheath/guide tool and expanded tip; and

withdrawing the sheath/guide tool from the patient's vasculature.

29. A stent retriever comprising a diametrically expandable tubular mesh including a proximal portion having a first mesh density and a concave distal portion having a second mesh density, wherein the second mesh density is greater than the first mesh density and is sufficiently high to trap embolus when the stent retriever is in its diametrically expanded state.

30. The stent retriever of claim 29 wherein the concave distal portion is substantially closed when the stent retriever is in its expanded state.

31. A stent retriever comprising:

a diametrically expandable proximal member having a first mesh density; and

a diametrically expandable distal member having a concave shape opening toward the proximal member and a second mesh density that is greater than the first mesh density and sufficiently high to trap embolus when the stent retriever is in its expanded state.

32. The stent retriever of claim 31 wherein the distal member is substantially closed when the stent retriever is in its expanded state.

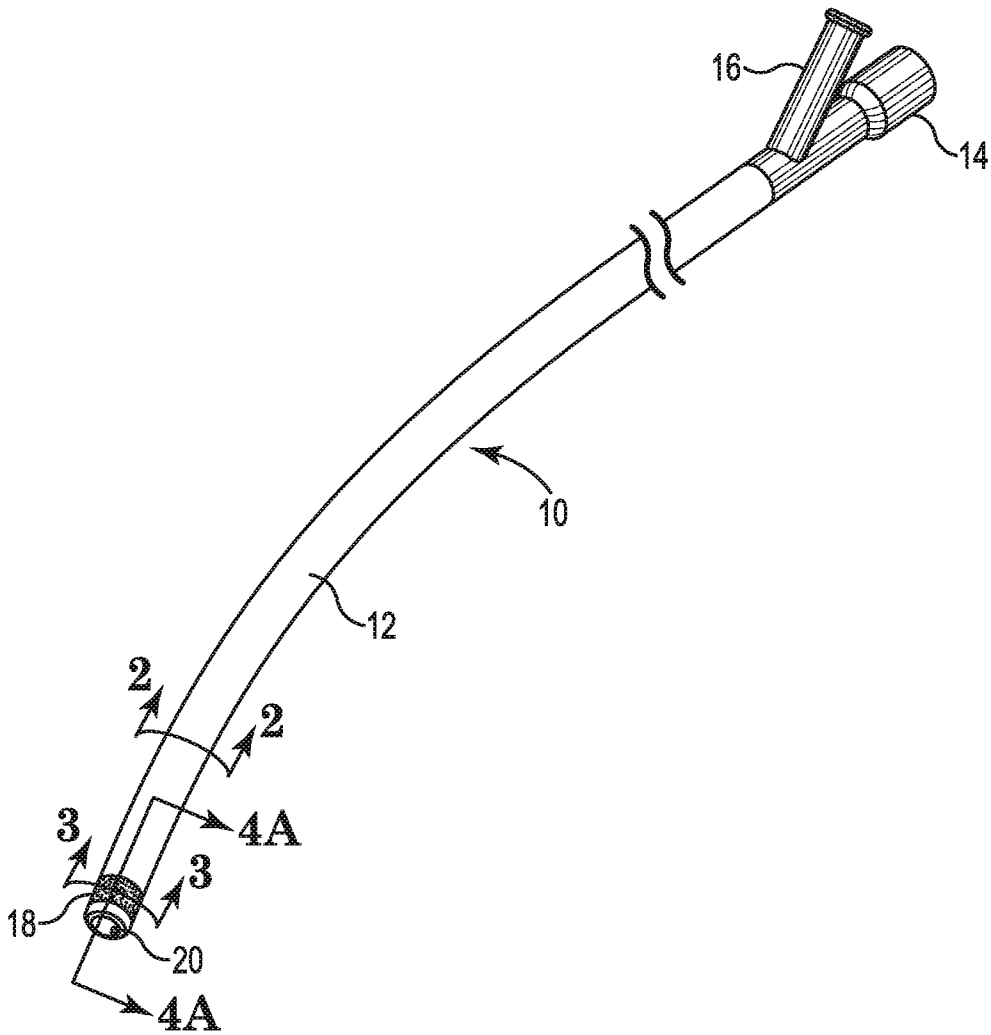

Fig. 1

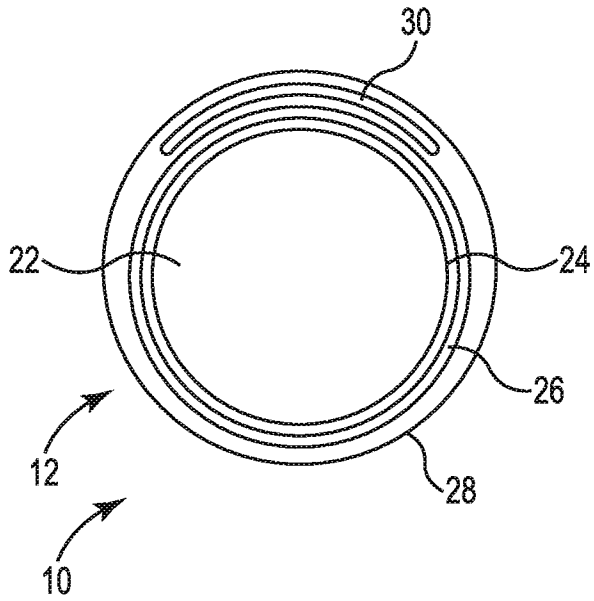

Fig. 2

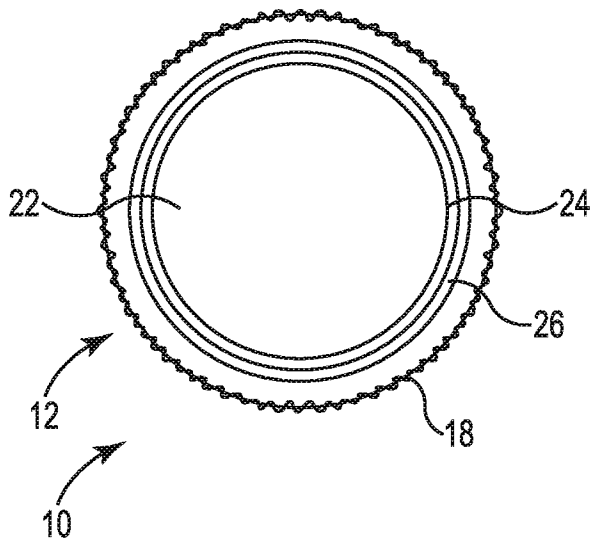

Fig. 3

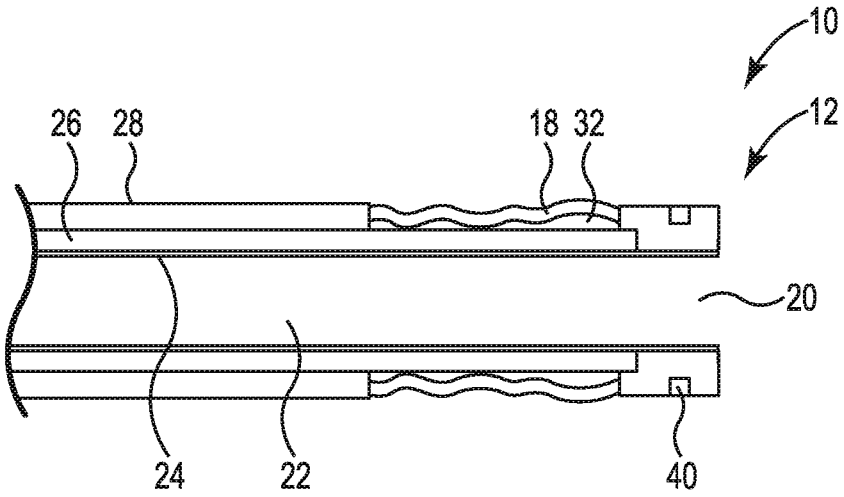

Fig. 4A

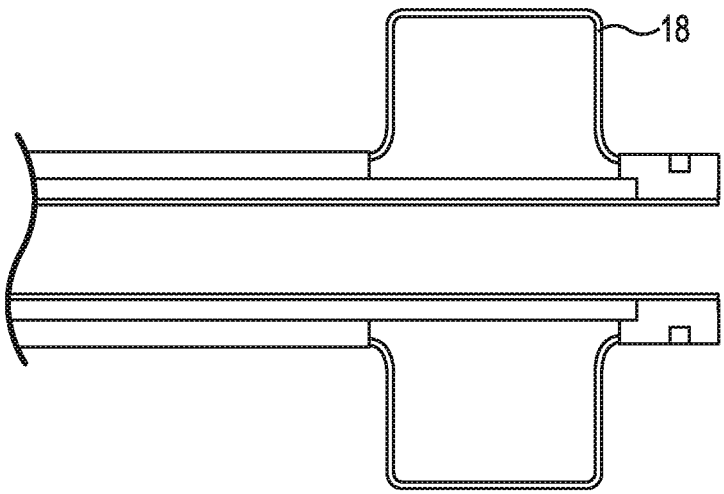

Fig. 4B

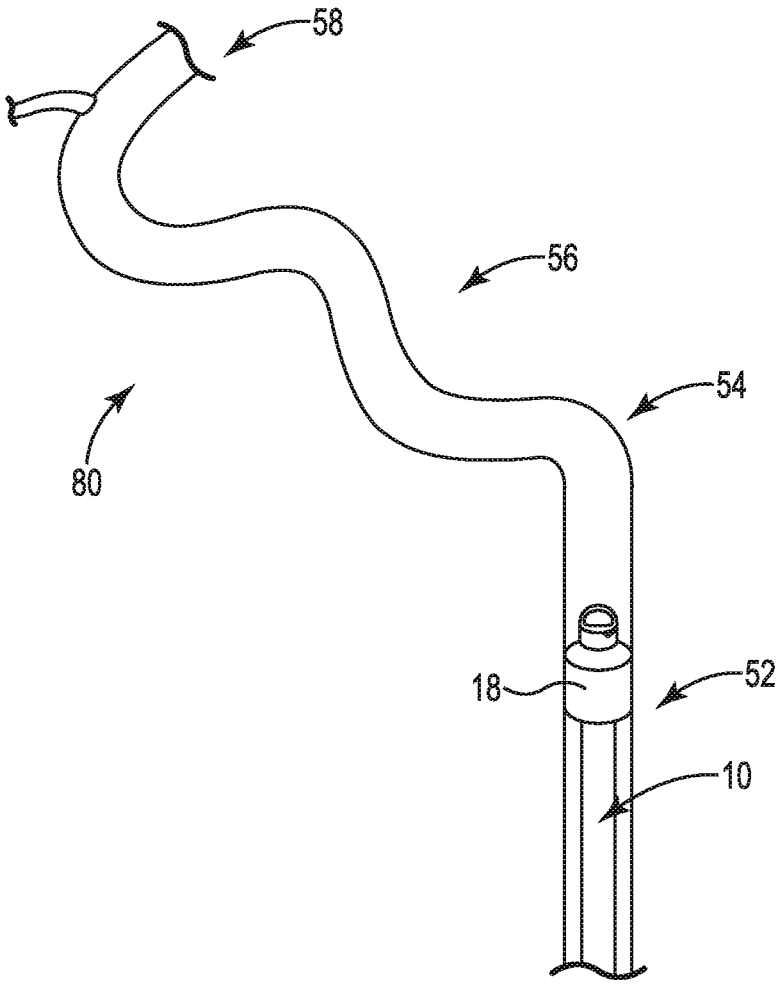

Fig. 5

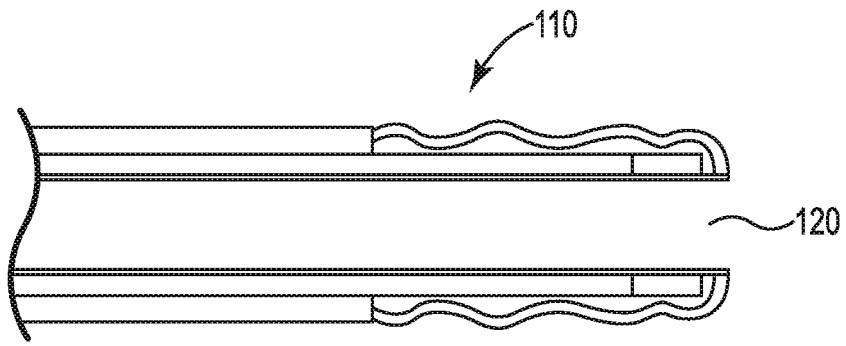

Fig. 6A

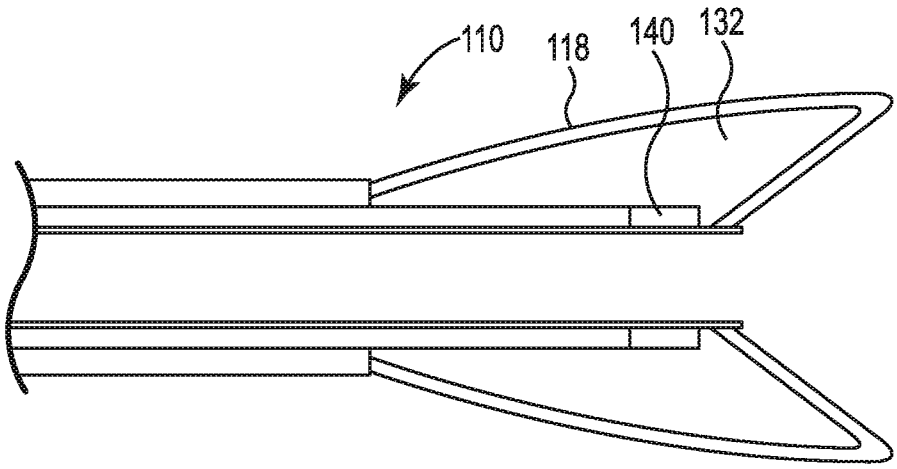

Fig. 6B

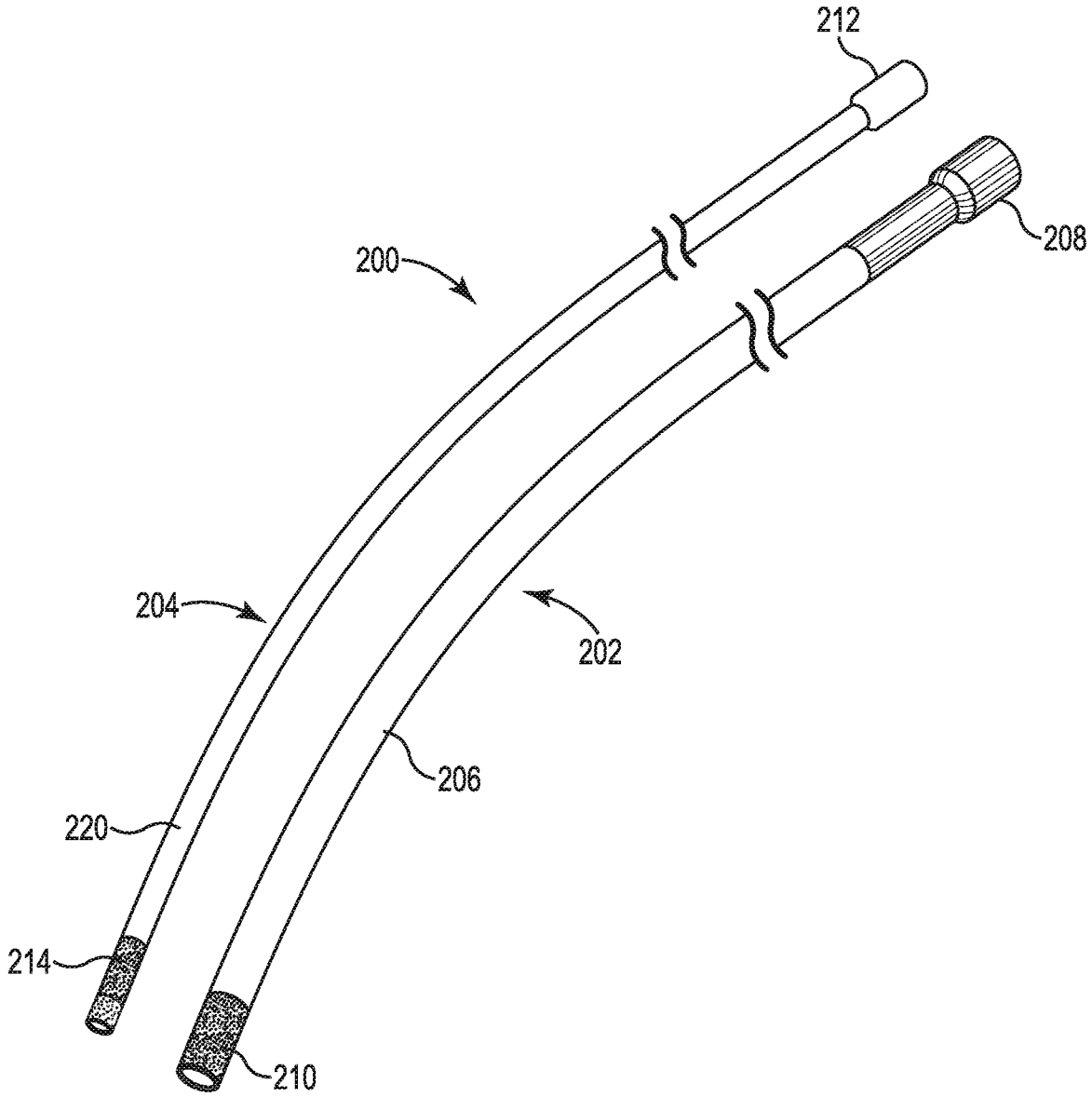

Fig. 7

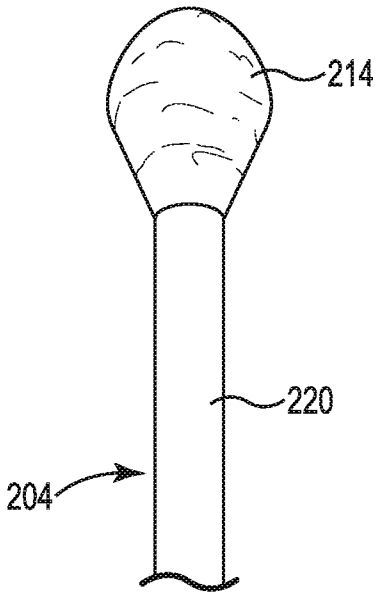

Fig. 8

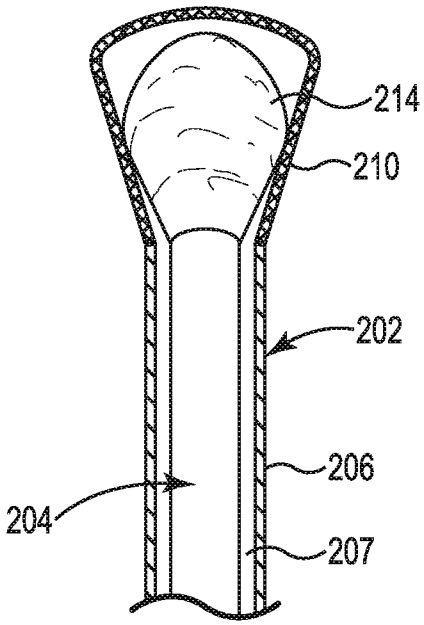

Fig. 9

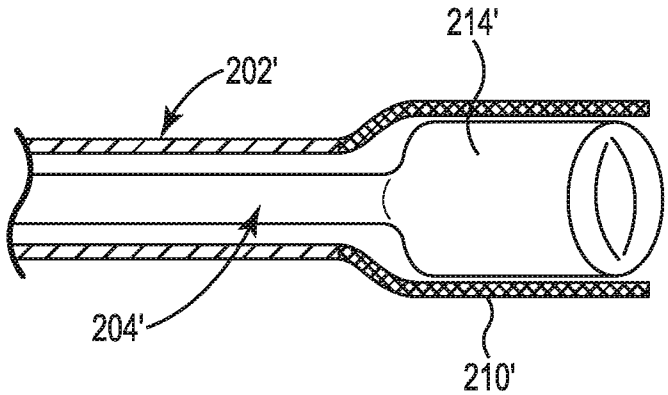

Fig. 10

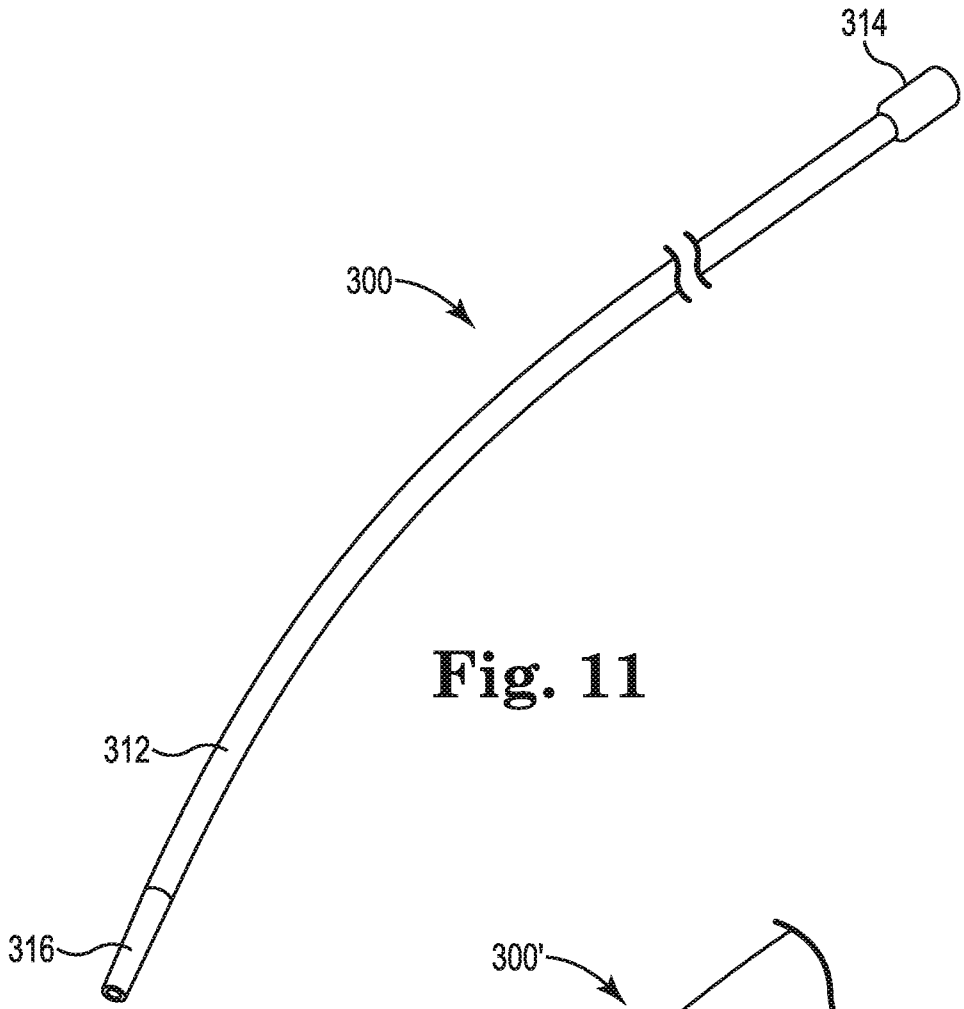

Fig. 11

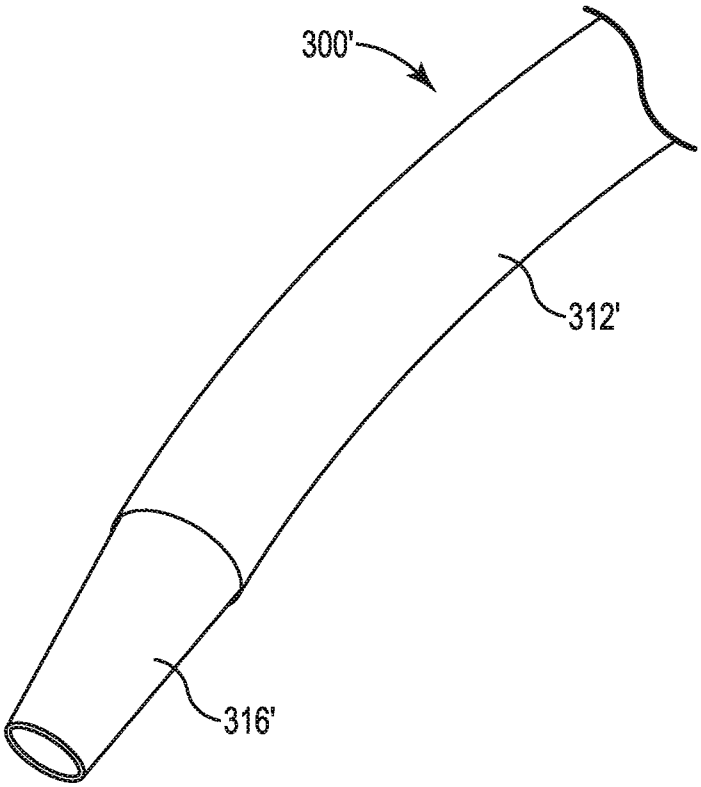

Fig. 13

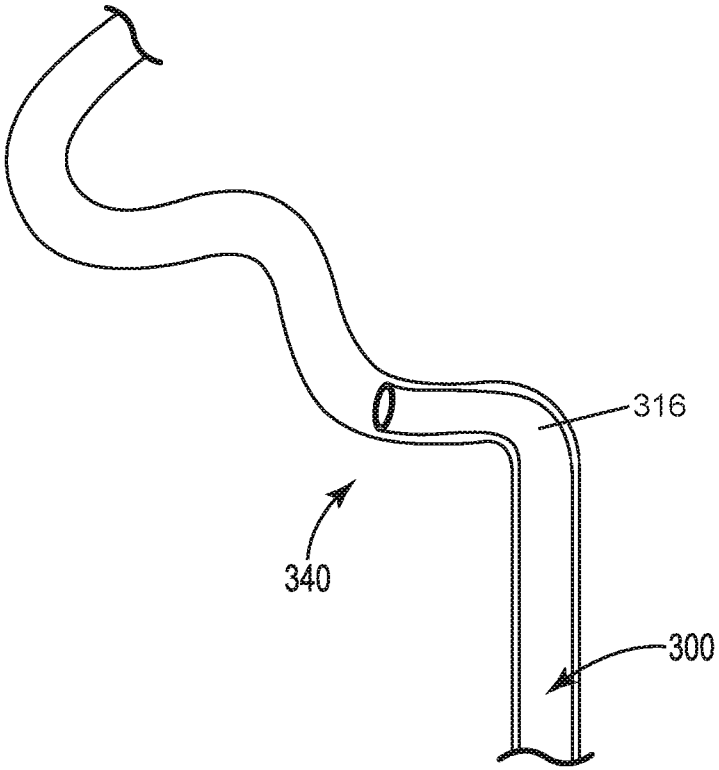

Fig. 12

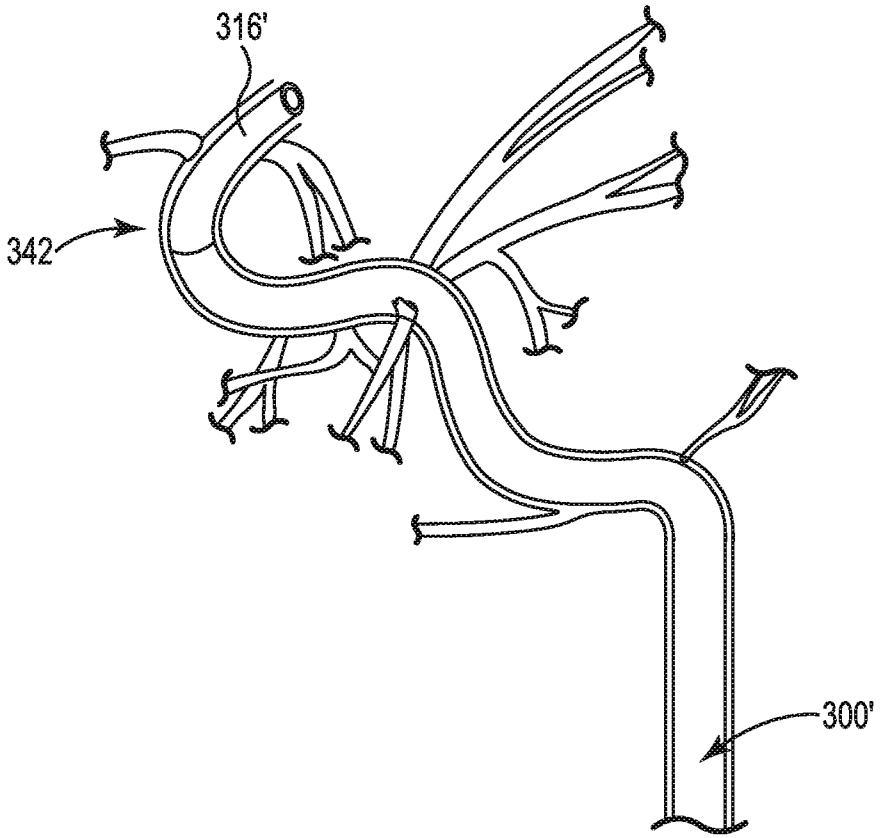

Fig. 14

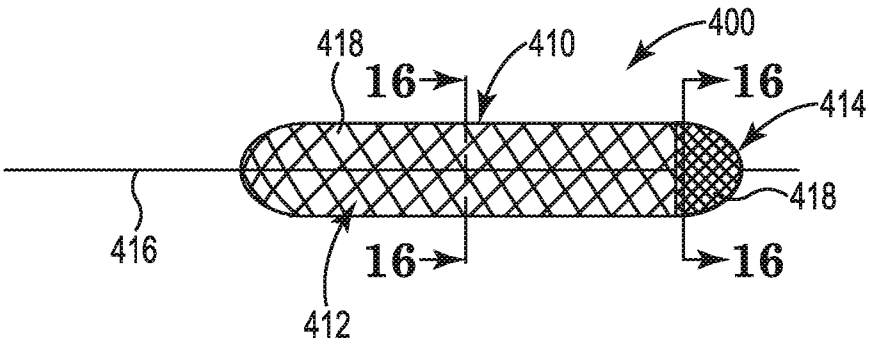

Fig. 15

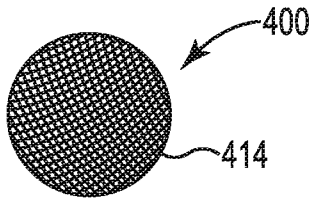

Fig. 16

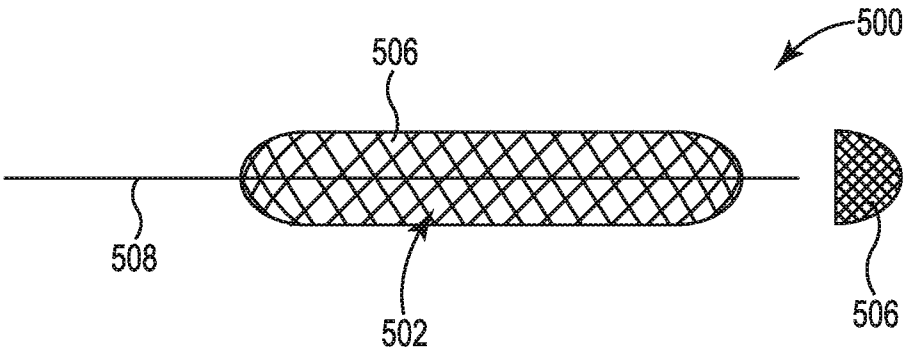

Fig. 17

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2017/031311

A. CLASSIFICATION OF SUBJECT MATTER

A61B 17/3211(2006.01)i, A61B 17/32(2006.01)i, A61B 17/00(2006.01)i

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)
A61B 17/3211; A61M 25/10; A61M 25/09; A61M 25/00; A61B 17/22; A61B 17/32; A61M 29/02; A61B 17/00

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
Korean utility models and applications for utility models
Japanese utility models and applications for utility models

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
eKOMPASS(KIPO internal) & Keywords: balloon guiding sheath, elongated sheath, access port, distal port, working lumen, inflatable balloon, inflation port, inflation lumen

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2014-0107575 A1 (CONCENTRIC MEDICAL, INC.) 17 April 2014 See paragraphs [0026], [0044]-[0046], [0056]-[0061]; and figures 1-2B.	1-6,14-18
X	US 2007-0270740 A1 (HOLMES, JR., D. R. et al.) 22 November 2007 See abstract; paragraph [0045]; and figures 1, 2.	1-4,18
X	US 2009-0306597 A1 (LUPTON, H. W. et al.) 10 December 2009 See paragraphs [0041]-[0046]; and figures 1-3.	1-4,18
X	US 5263959 A (FISCHELL, R. E.) 23 November 1993 See column 2, line 44 - column 3, line 54; and figure 1A.	1-4,18
X	US 5135482 A (NERACHER, A.) 04 August 1992 See column 2, lines 13-54; column 3, lines 1-21; and figures 1-3.	1-4,18

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

☒ See patent family annex.

* Special categories of cited documents:
"A" document defining the general state of the art which is not considered to be of particular relevance
"E" earlier application or patent but published on or after the international filing date
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
"O" document referring to an oral disclosure, use, exhibition or other means
"P" document published prior to the international filing date but later than the priority date claimed
"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents,such combination being obvious to a person skilled in the art
"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
17 October 2017 (17.10.2017)	**18 October 2017 (18.10.2017)**

Name and mailing address of the ISA/KR
International Application Division
Korean Intellectual Property Office
189 Cheongsa-ro, Seo-gu, Daejeon, 35208, Republic of Korea
Facsimile No. +82-42-481-8578

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INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2017/031311

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

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

1. ☒ Claims Nos.: 7-13, 25, 28
because they relate to subject matter not required to be searched by this Authority, namely:
Claims 7-13, 25 and 28 pertain to methods for treatment of the human body by surgery or therapy and thus relate to a subject-matter which this International Searching Authority is not required to search under PCT Article 17(2)(a)(i) and PCT Rule 39.1(iv).

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

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

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

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

Group I, claims 1-6 and 14-18, directed to a balloon guiding sheath comprising: an elongated sheath; an access port; a distal port; a working lumen; an inflatable balloon; an inflation port; and an inflation lumen.

Group II, claims 19-24, directed to an intermediate access aspiration catheter comprising: an elongated sheath; an access port; a distal port; a flexible tip; and a working lumen.

Group III, claims 26 and 27, directed to an endovascular instrument set comprising: a sheath/guide tool including an elongated tubular member, an access port, a distal port, a diametrically expandable tip, and a lumen; and an expanding tool including an elongated tubular member, an inflation port, an inflatable balloon, and an inflation lumen.

Group IV, claims 29-32, directed to a stent retriever comprising: a diametrically expandable proximal member(portion) having a first mesh density; and a diametrically expandable distal member(portion) having a second mesh density.

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

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

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

4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.: 1-6, 14-18

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.
☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.
☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No.

PCT/US2017/031311

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 2014-0107575 A1	17/04/2014	EP 1409064 A1	21/04/2004
		EP 1409064 B1	18/12/2013
		ES 2452291 T3	31/03/2014
		US 2002-0198491 A1	26/12/2002
		US 2002-0198492 A1	26/12/2002
		US 2004-0079429 A1	29/04/2004
		US 2011-0172699 A1	14/07/2011
		US 6638245 B2	28/10/2003
		US 6702782 B2	09/03/2004
		US 7766049 B2	03/08/2010
		WO 03-000334 A1	03/01/2003
US 2007-0270740 A1	22/11/2007	US 6569129 B1	27/05/2003
		US 7727184 B2	01/06/2010
US 2009-0306597 A1	10/12/2009	IE S20090239 A2	28/10/2009
		US 8133243 B2	13/03/2012
US 5263959 A	23/11/1993	EP 0657140 A1	14/06/1995
		US 5423846 A	13/06/1995
US 5135482 A	04/08/1992	CA 1281968 C	26/03/1991
		EP 0232678 A2	19/08/1987
		EP 0232678 B1	03/04/1991
		JP 62-170261 A	27/07/1987