

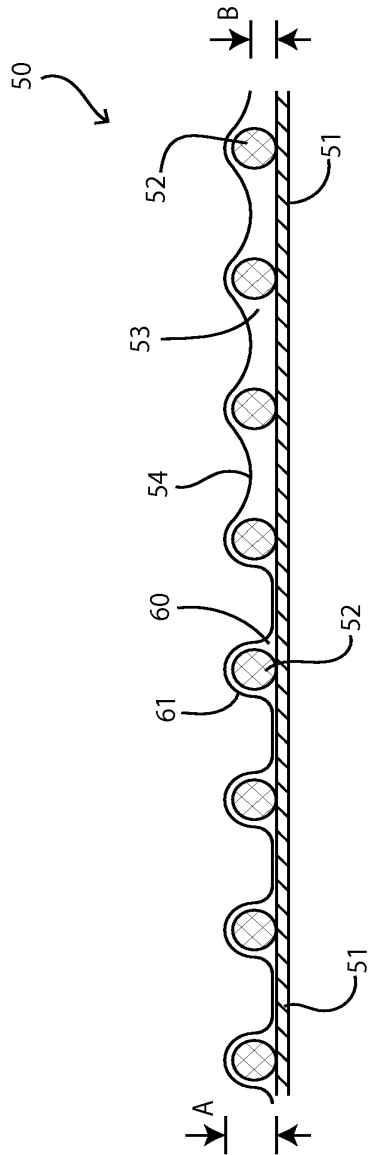


Fig.2

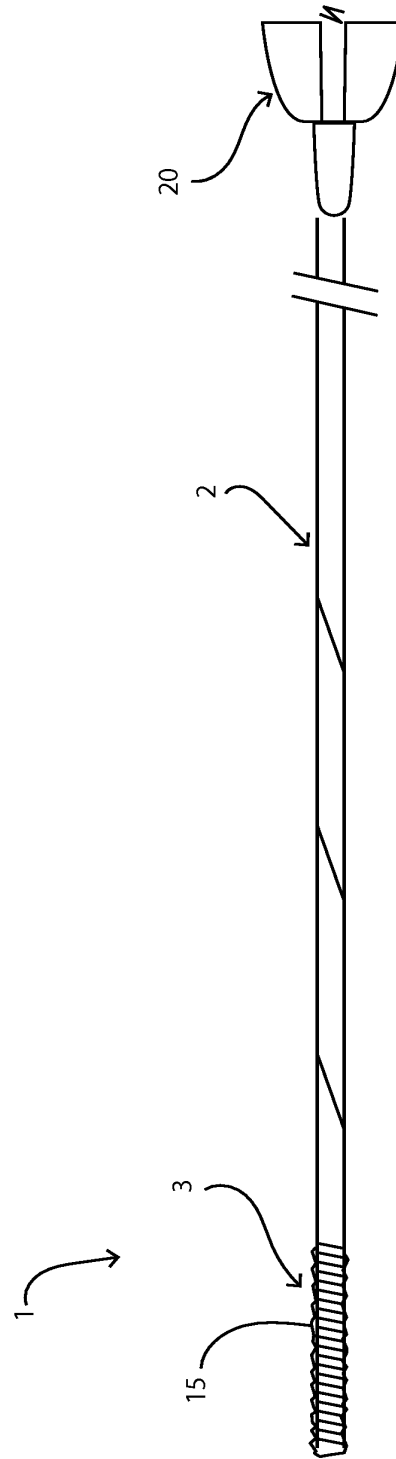


Fig.3

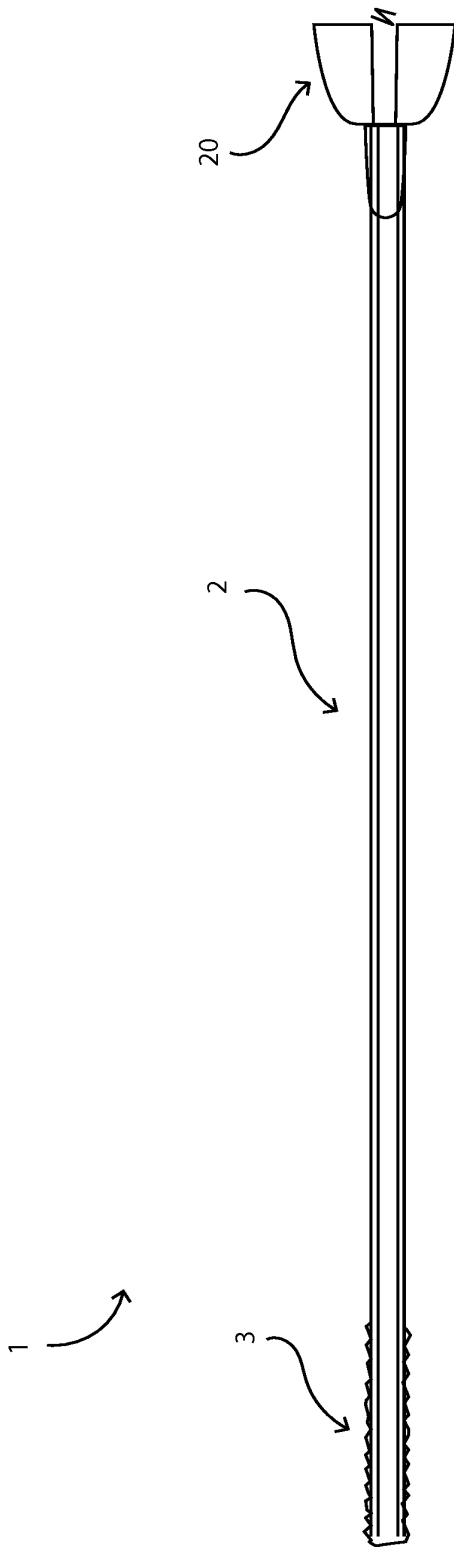


Fig.4

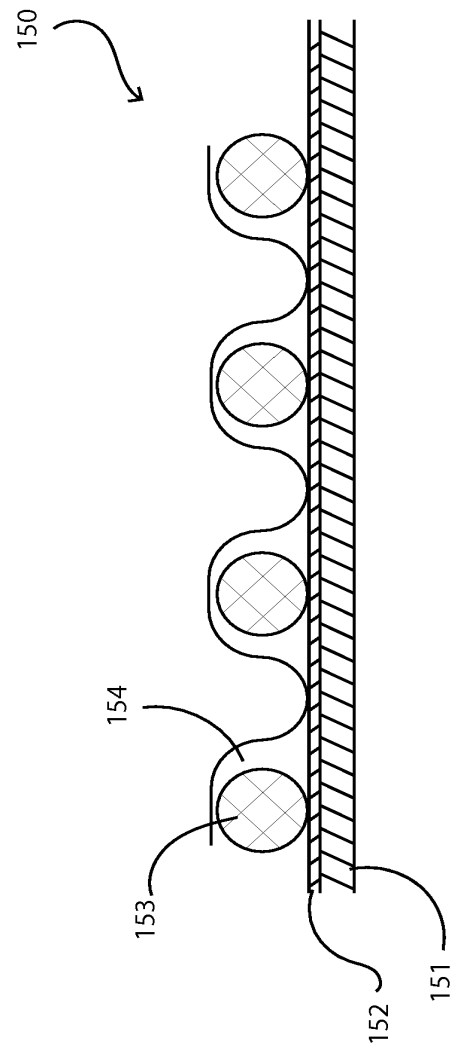


Fig.5

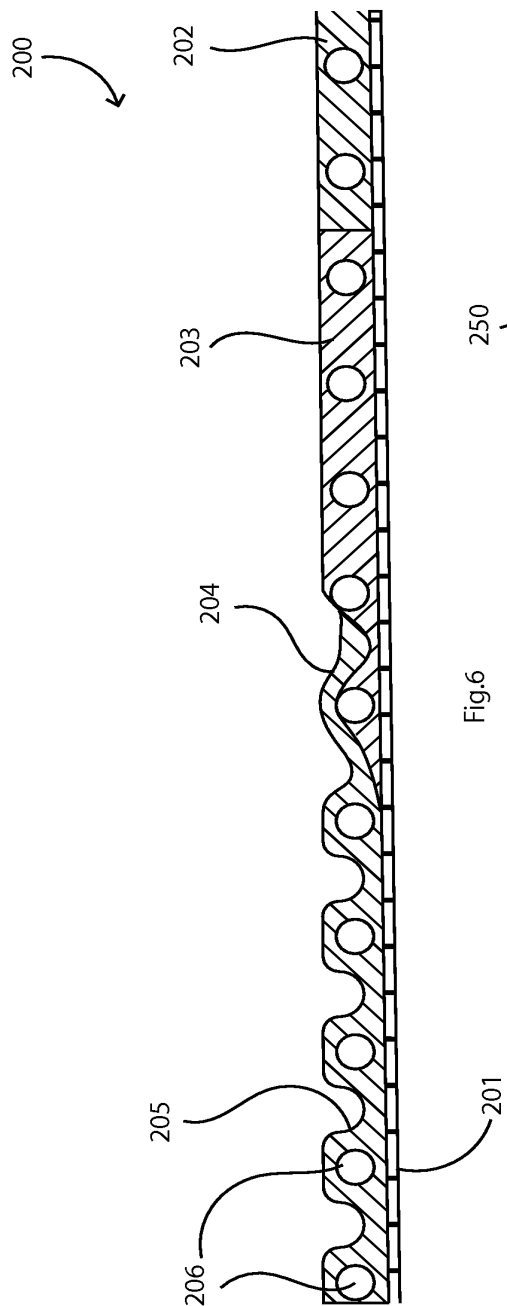


Fig. 6

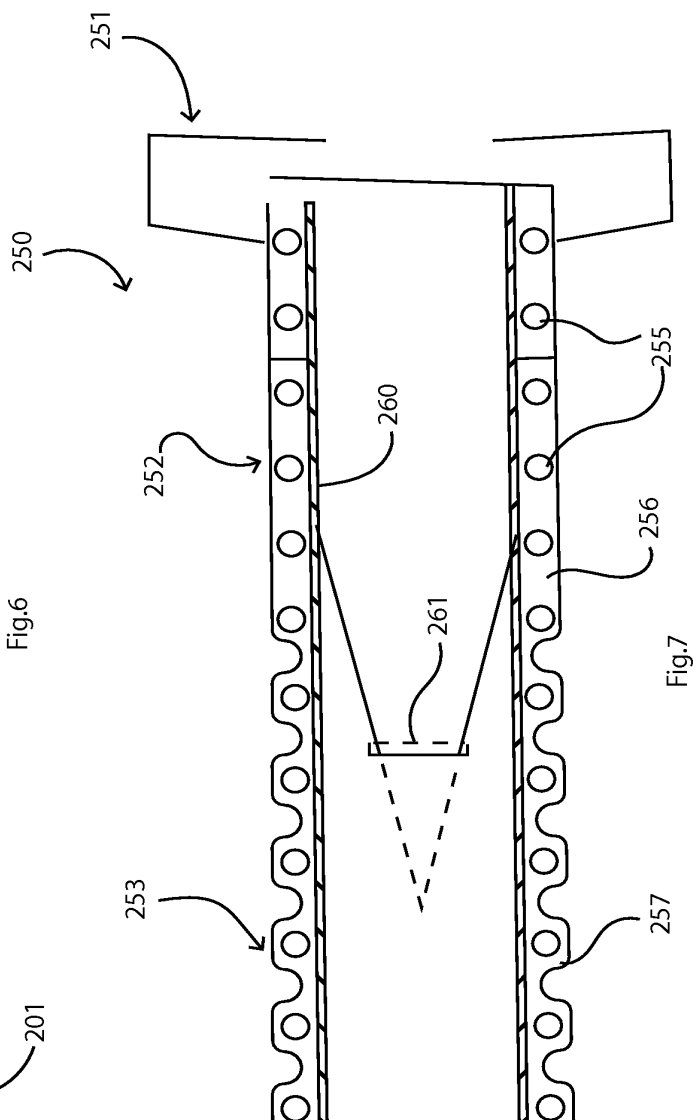


Fig. 7

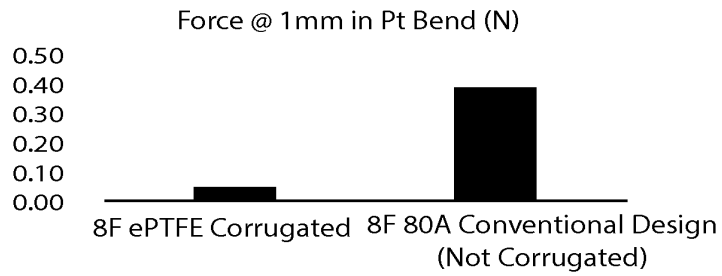


Fig.8

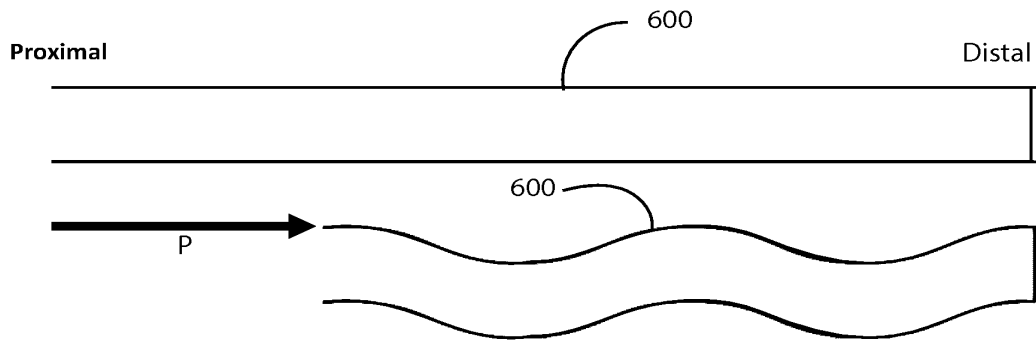


Fig.9

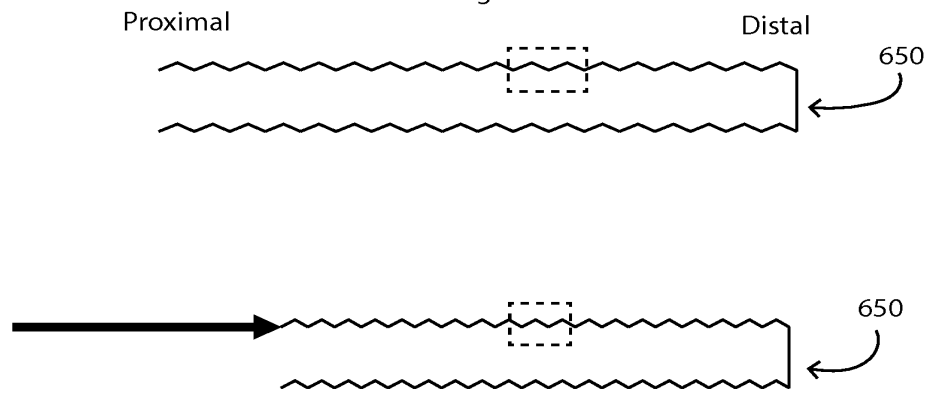
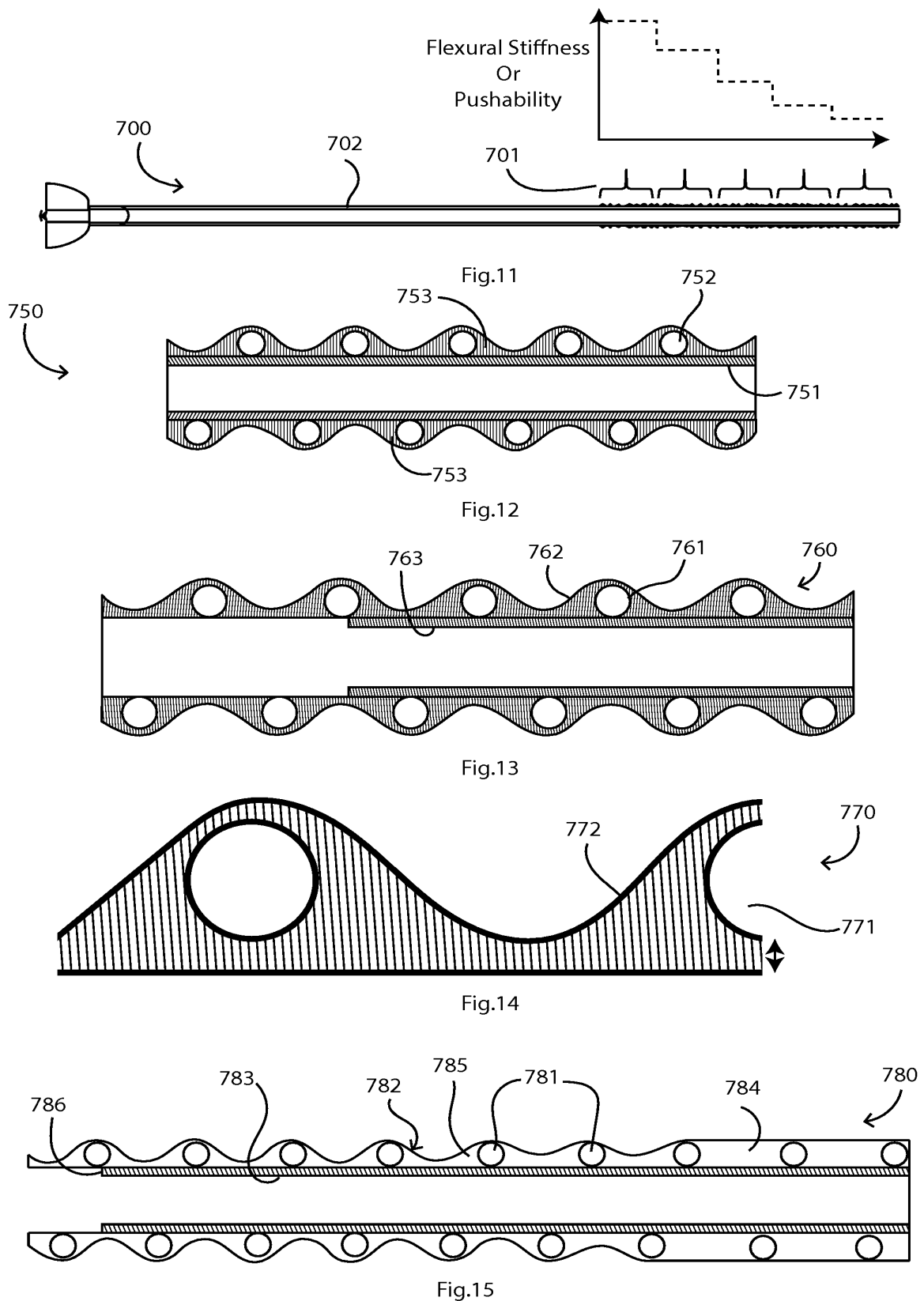


Fig.10



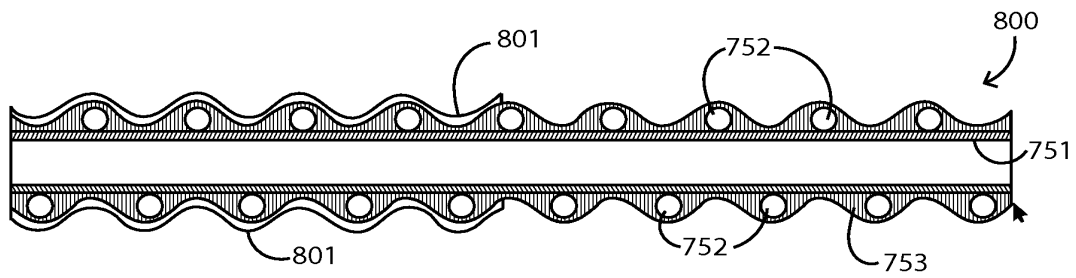


Fig.16

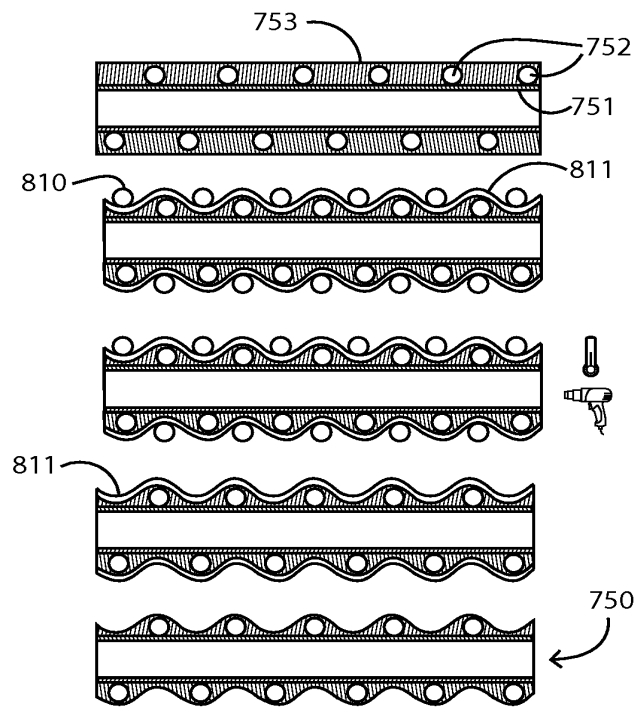


Fig.17

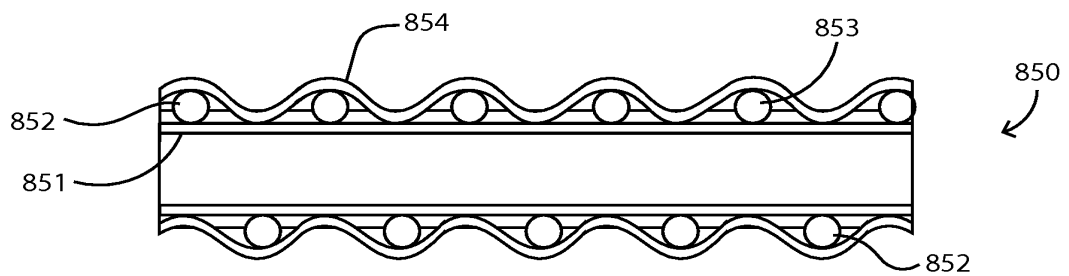


Fig.18

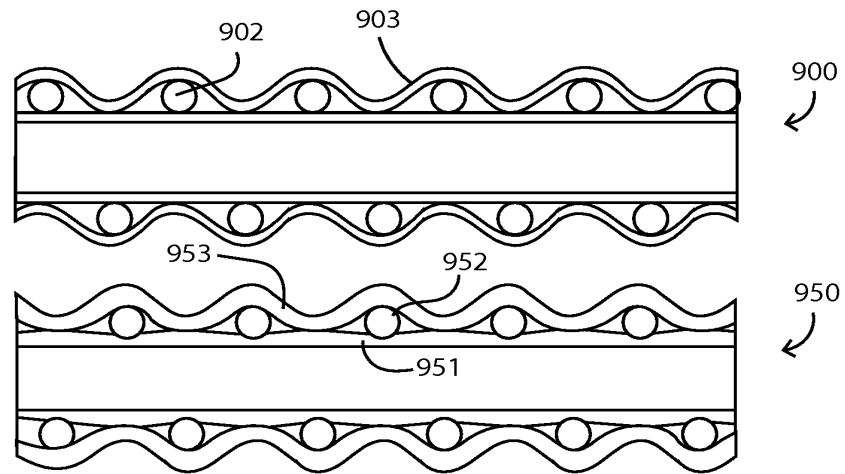


Fig.19

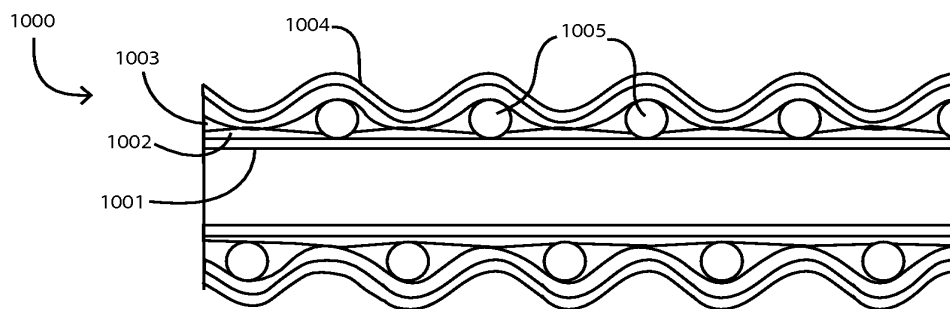


Fig.20

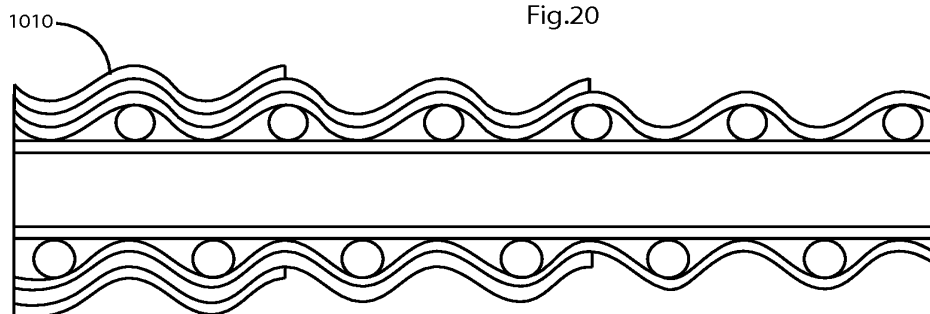
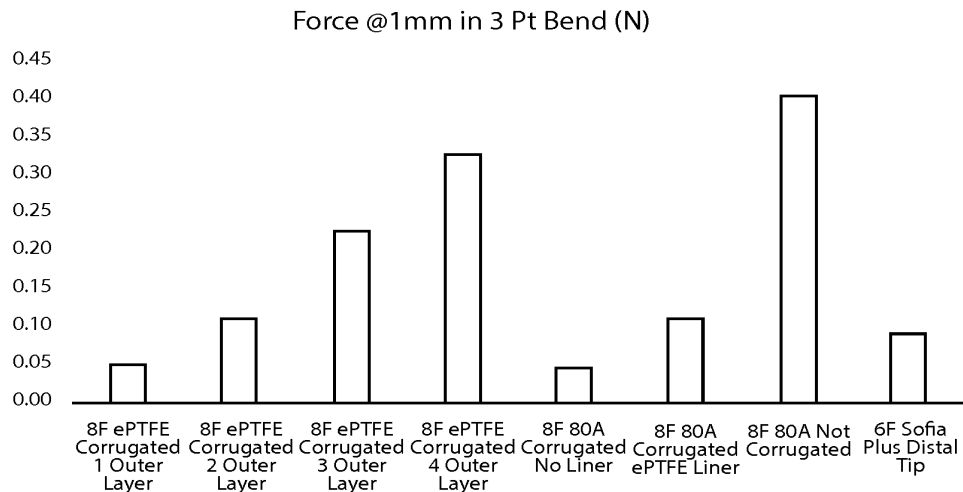
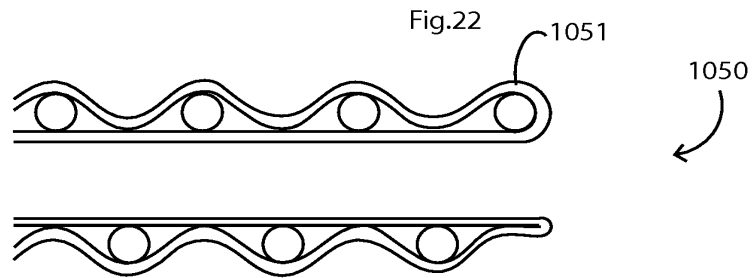
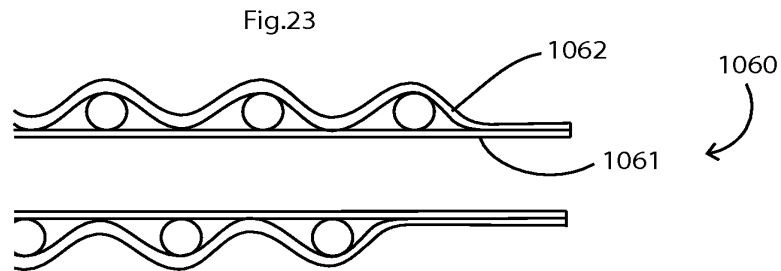
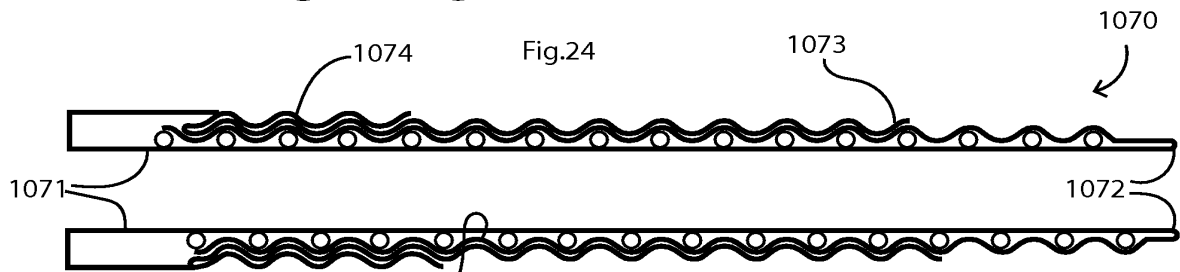
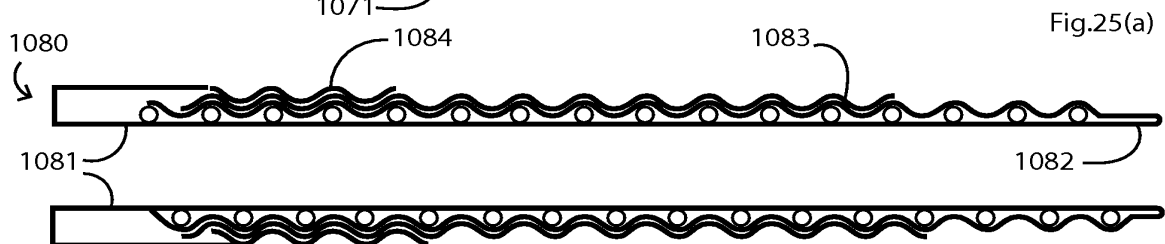


Fig.21



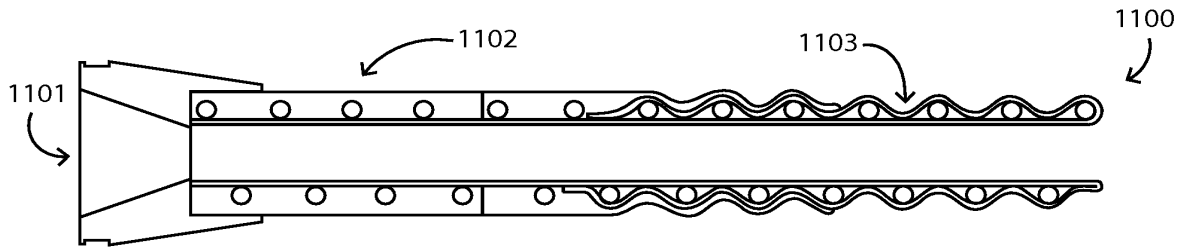


Fig.26

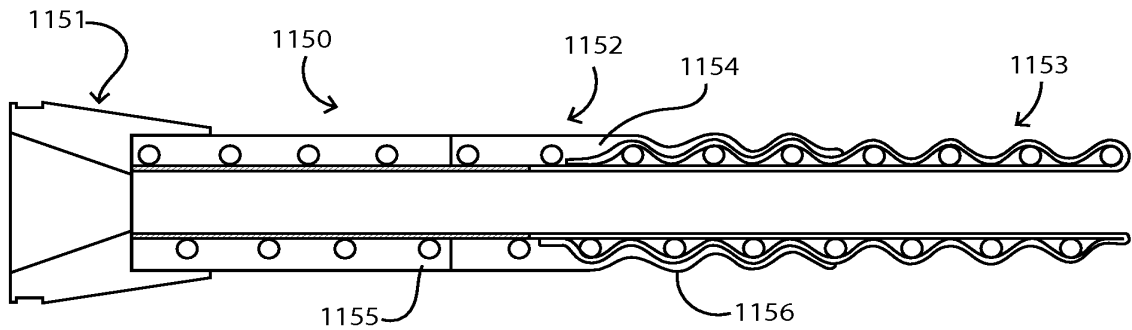


Fig.27

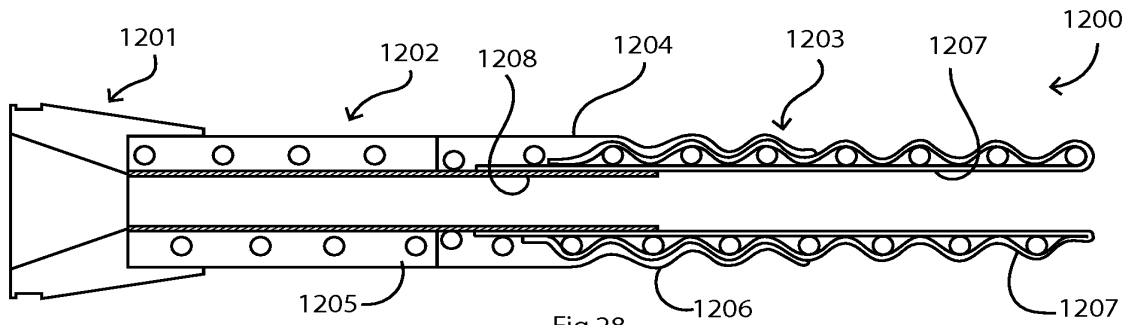


Fig.28

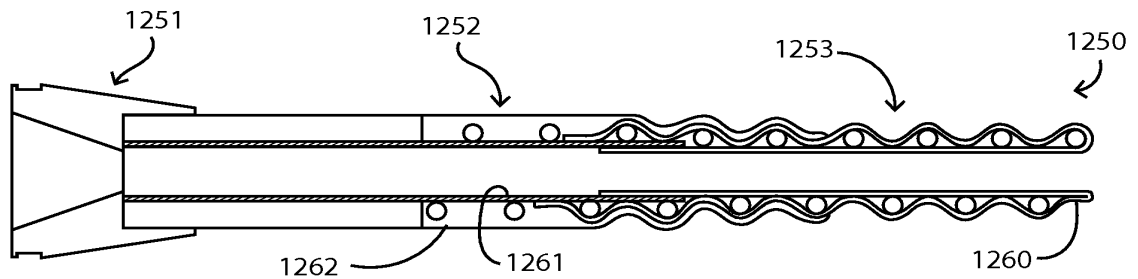


Fig.29

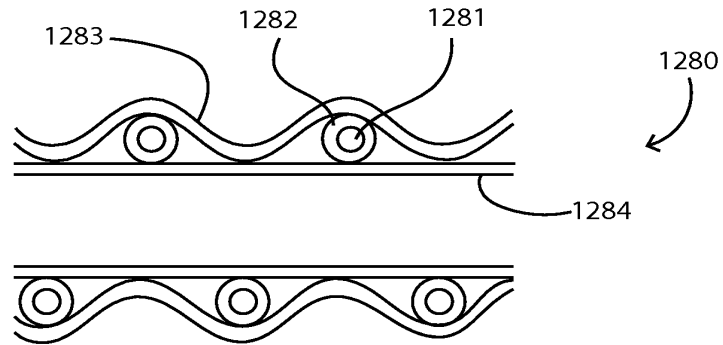


Fig.30

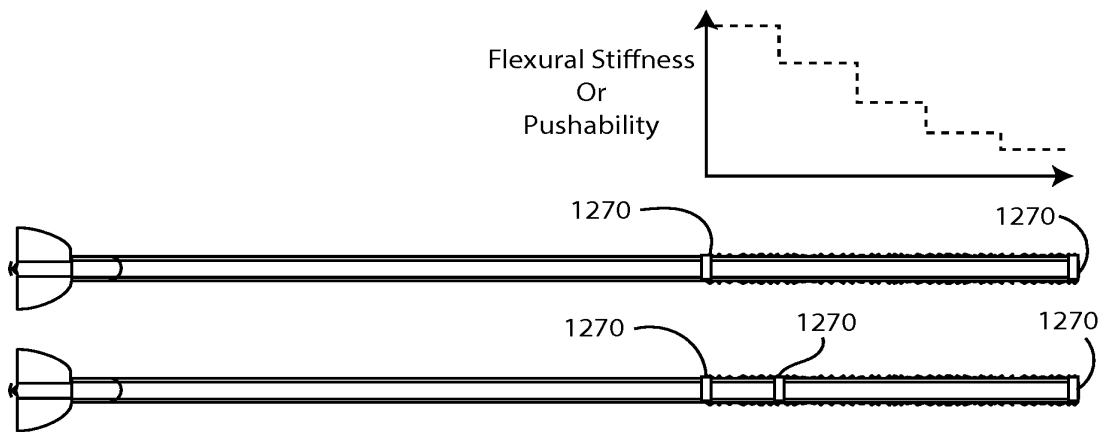


Fig.31

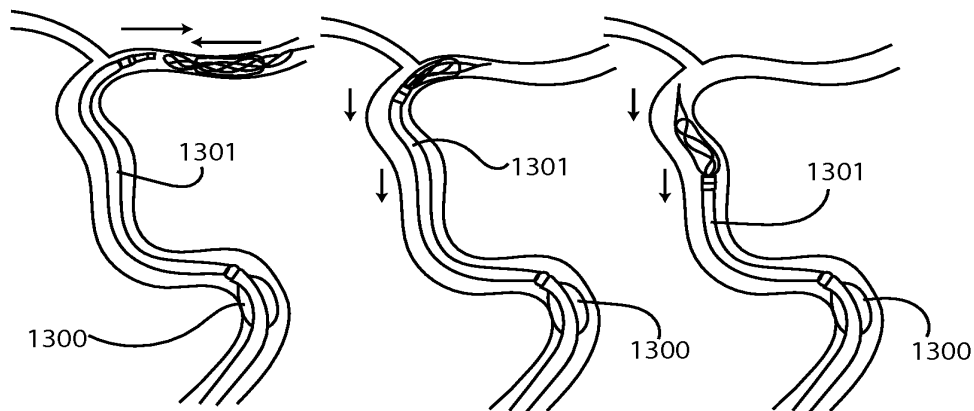
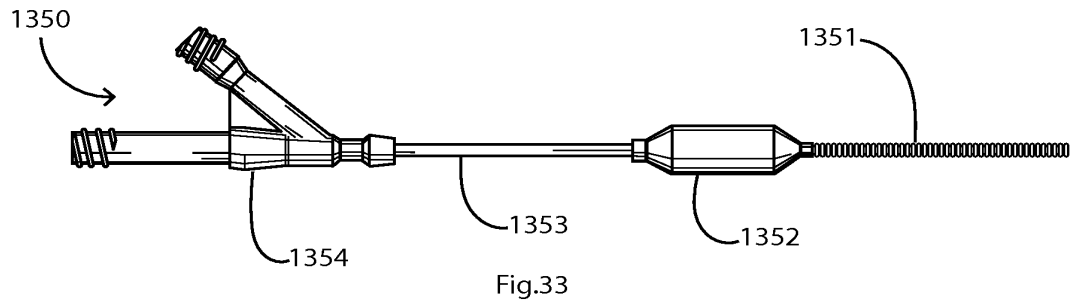
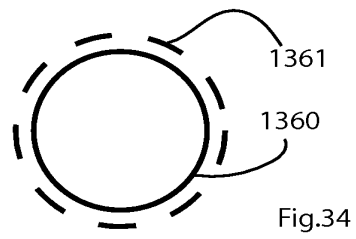
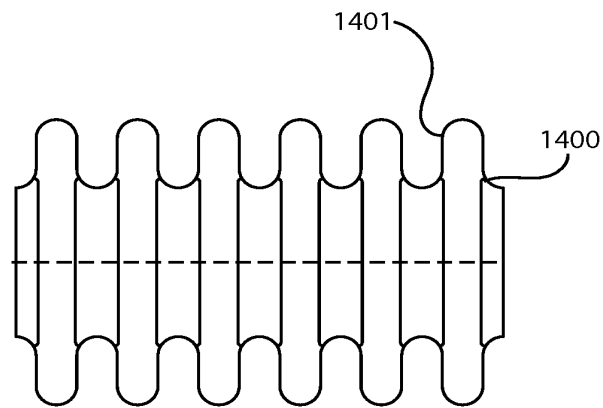
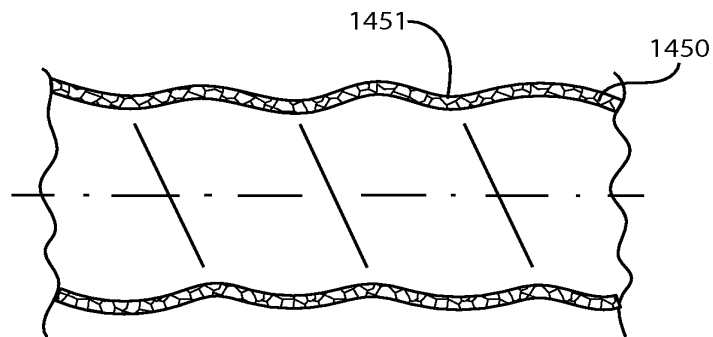


Fig.32 (PRIOR ART)



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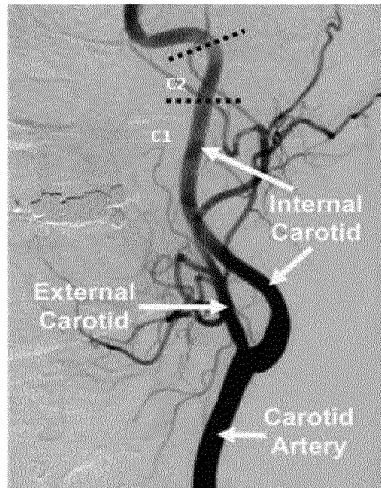
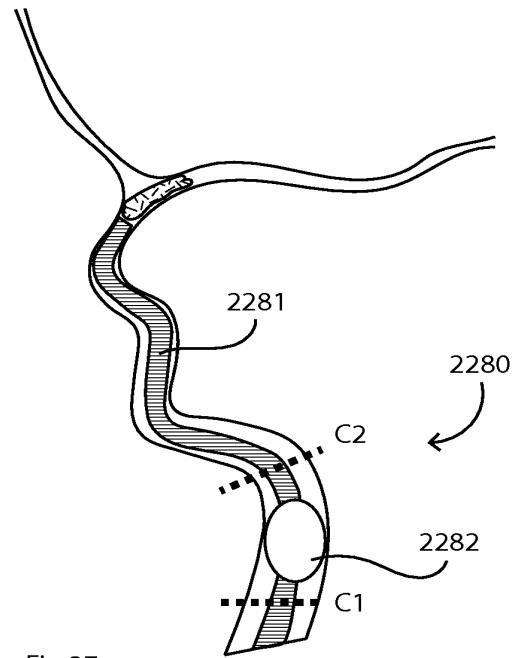


Fig.37

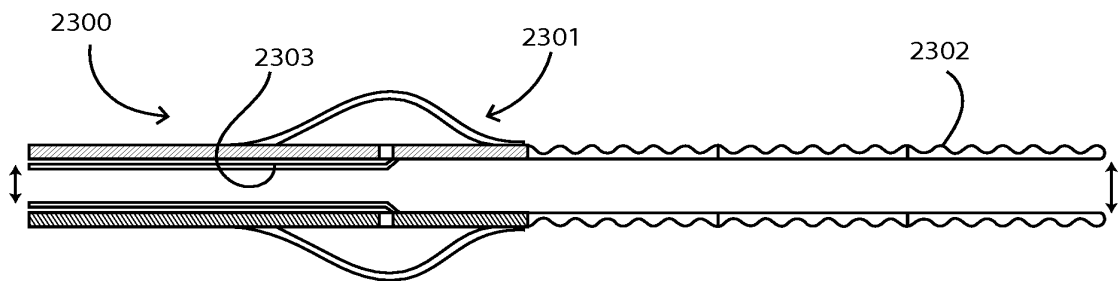


Fig.38

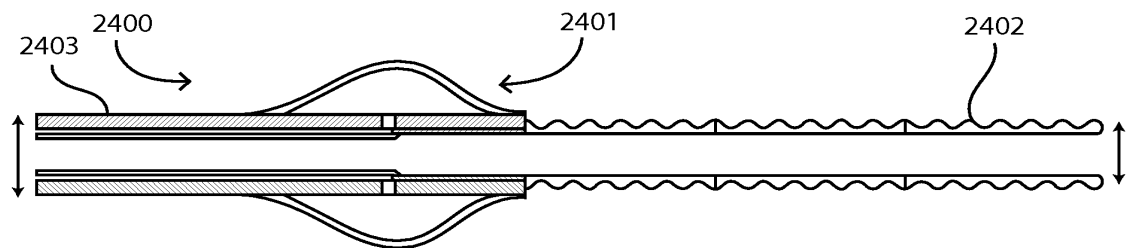


Fig.39

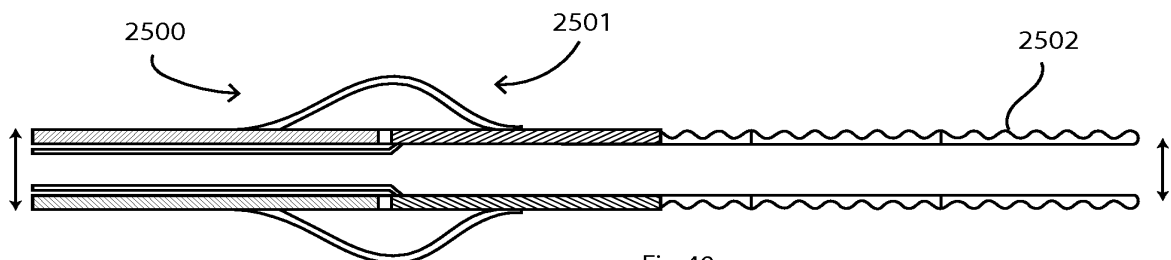


Fig.40

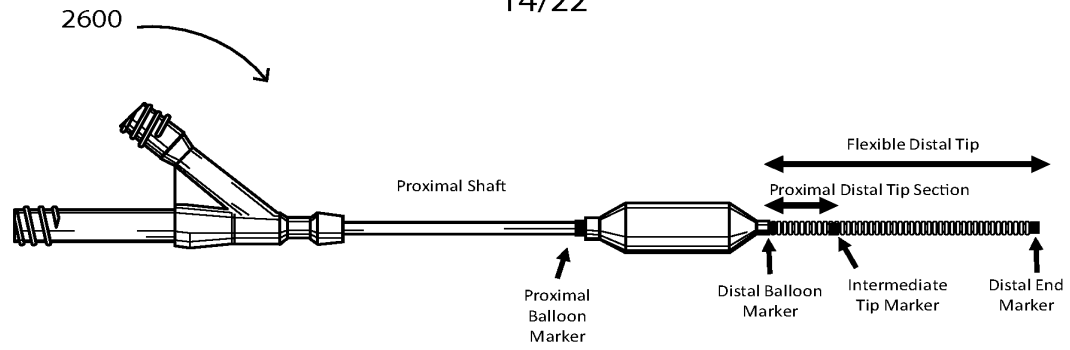


Fig.41

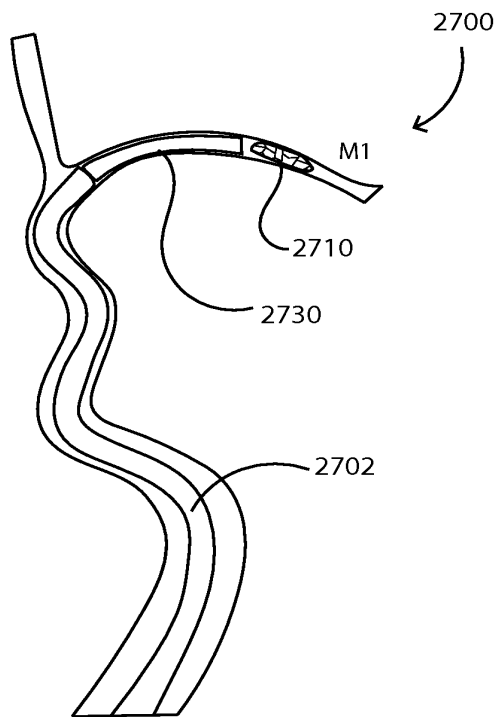


Fig.42

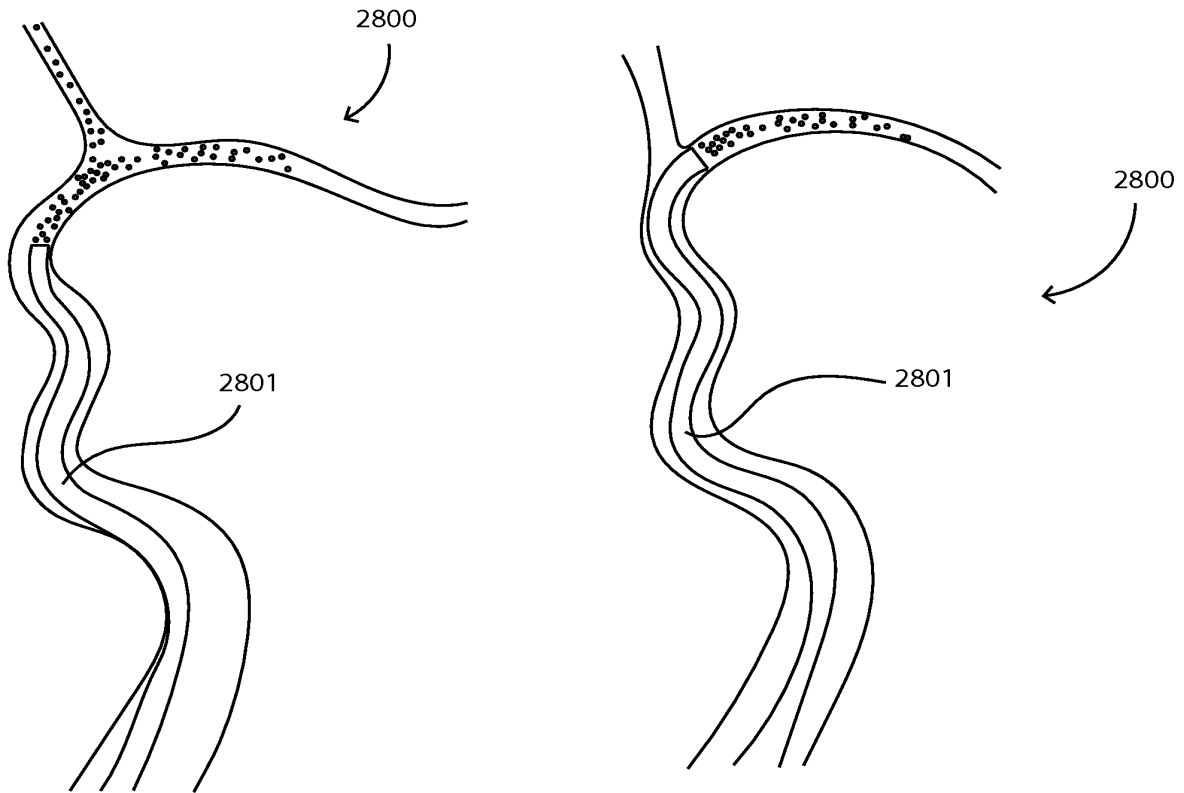


Fig.43

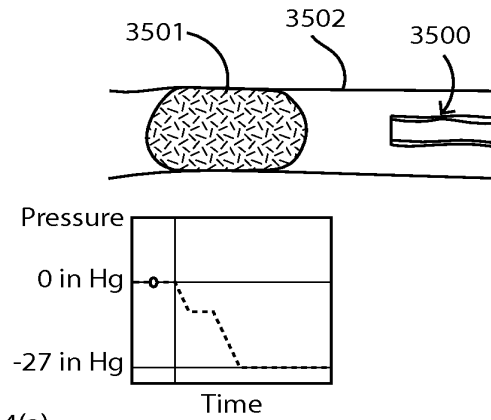


Fig. 44(a)

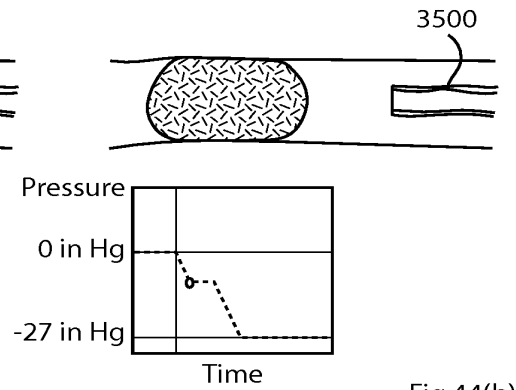


Fig. 44(b)

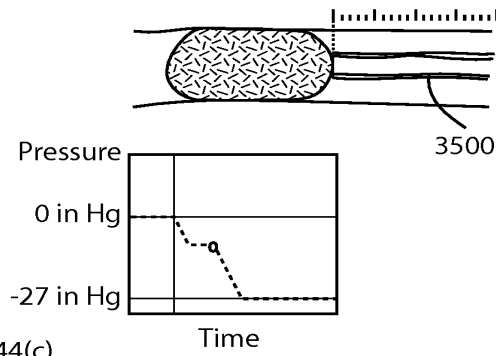


Fig. 44(c)

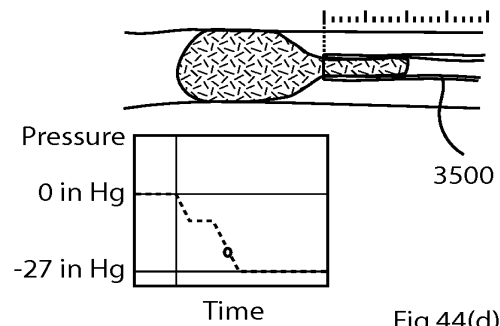


Fig. 44(d)

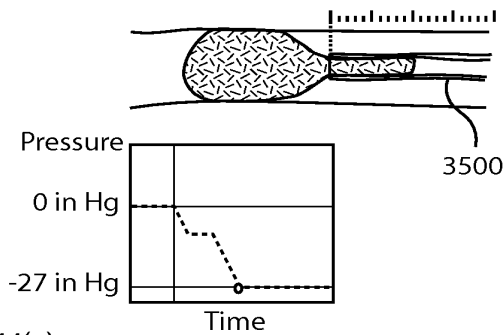


Fig. 44(e)

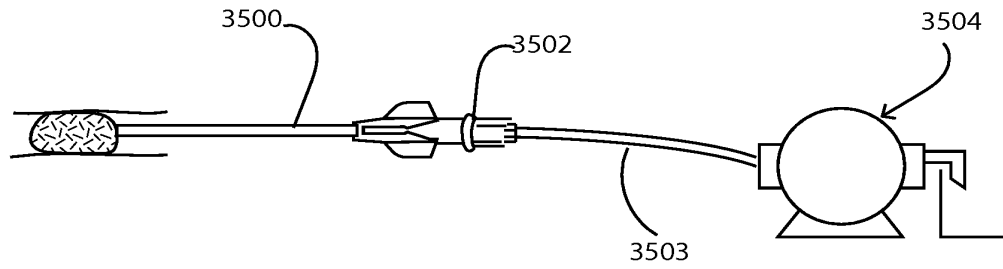


Fig.45

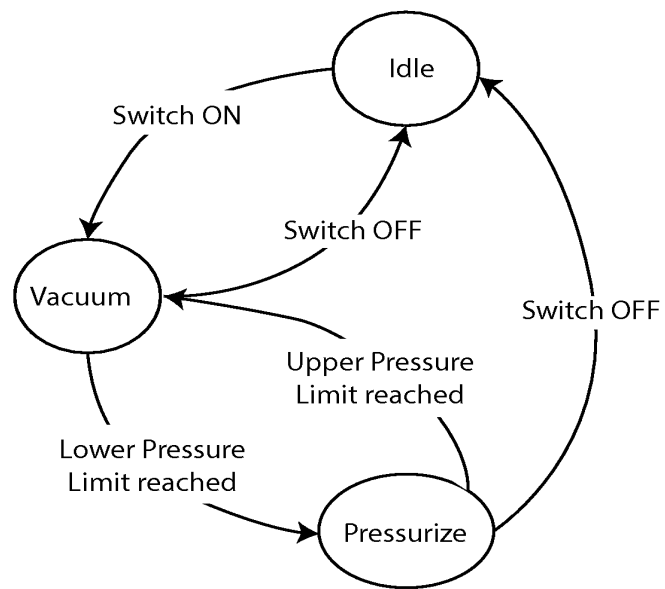


Fig.46

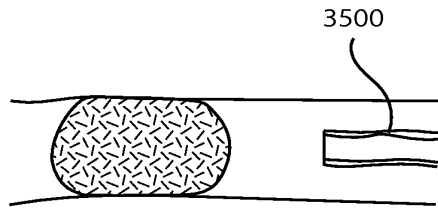
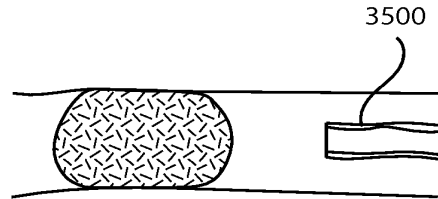
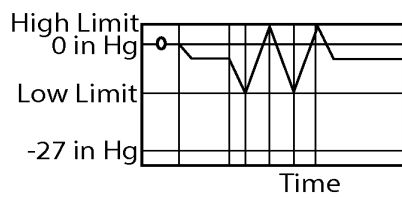


Fig.47(a)

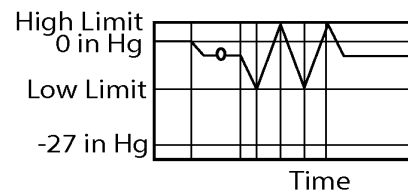


Fig.47(b)

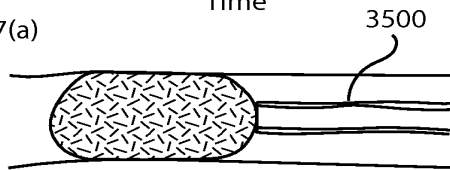
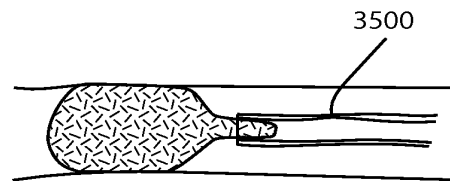
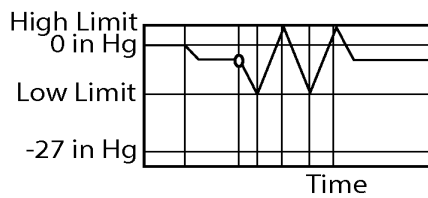


Fig.47(c)

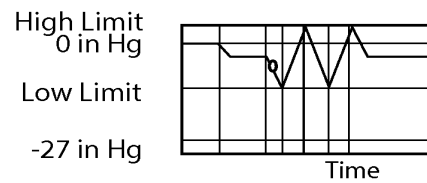


Fig.47(d)

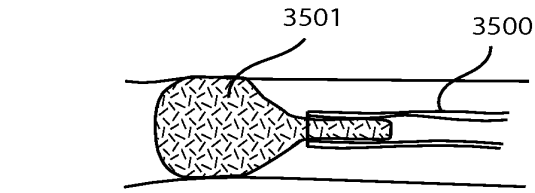
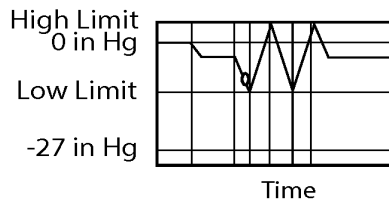


Fig.47(e)

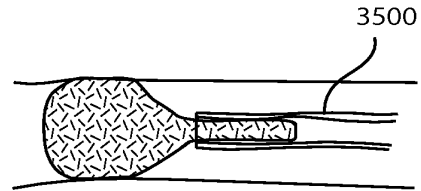
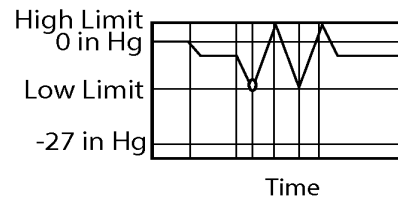


Fig.47(f)

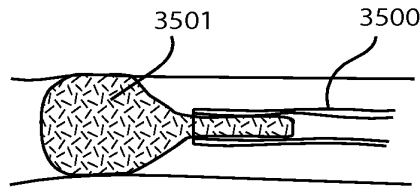
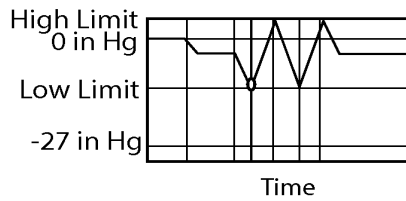


Fig.47(g)

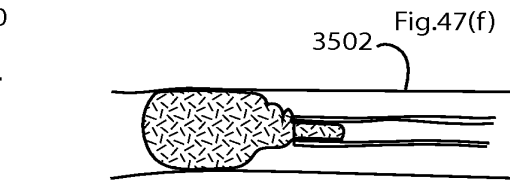
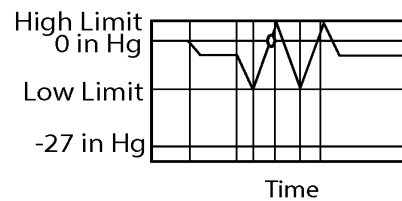


Fig.47(h)

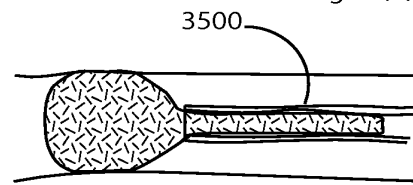
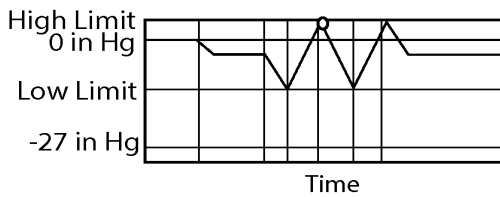


Fig.47(i)

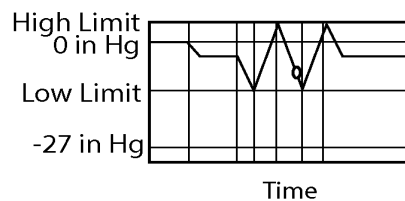


Fig.47(j)

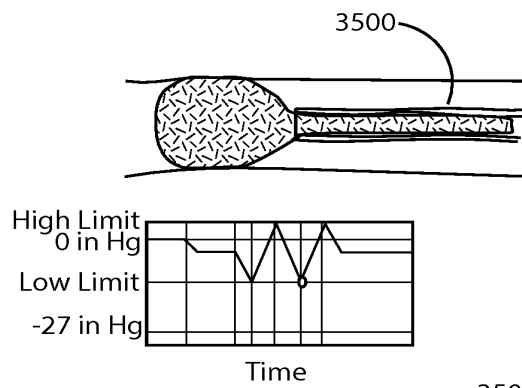


Fig.47(k)

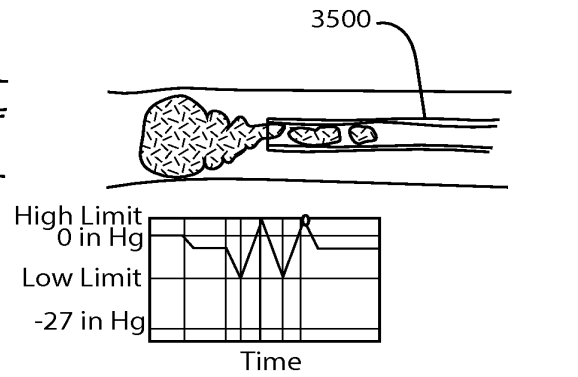


Fig.47(l)

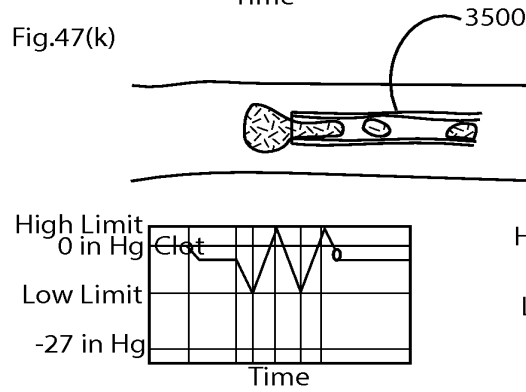


Fig.47(m)

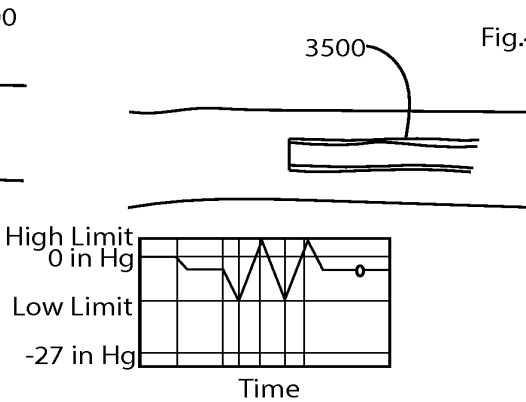


Fig.47(n)

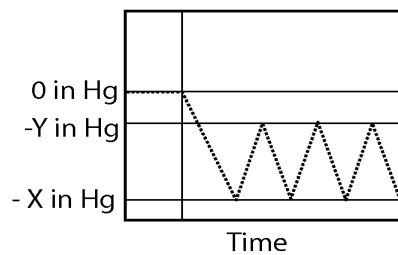


Fig.48(a)

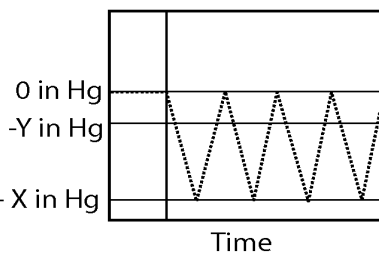


Fig.48(b)

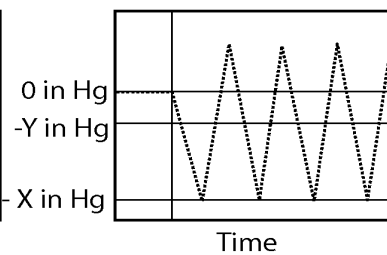


Fig.48(c)

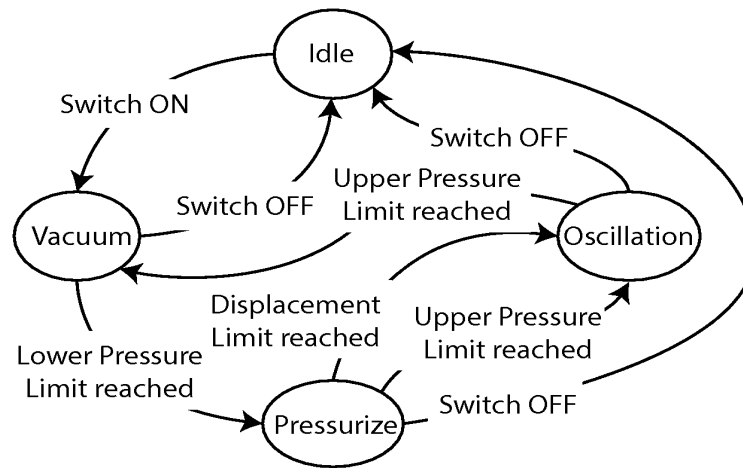


Fig.49

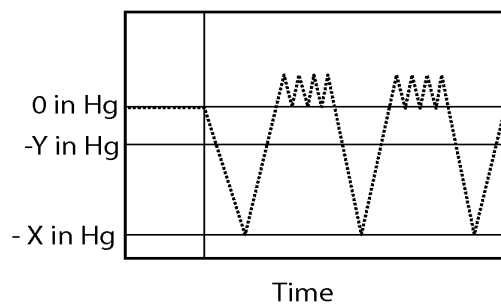


Fig.50(a)

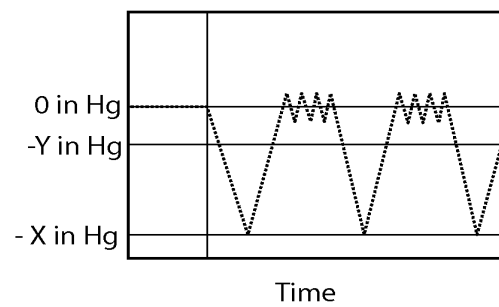


Fig.50(b)

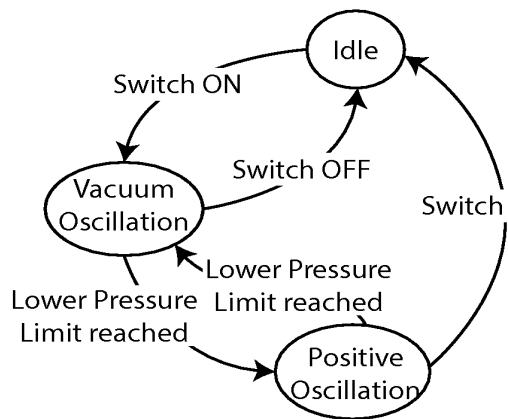


Fig.51(a)

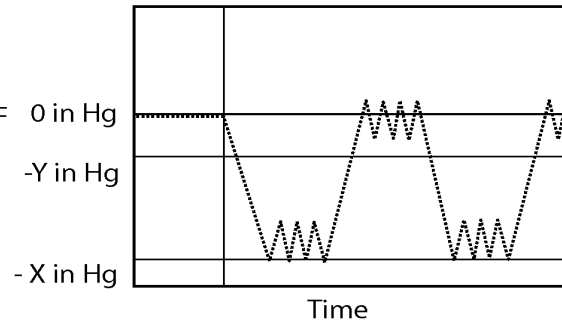


Fig.51(b)

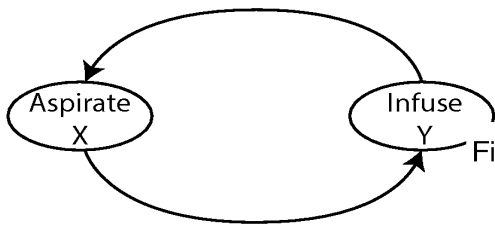


Fig.52(a)

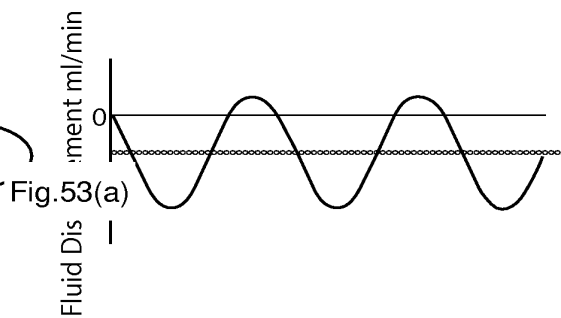


Fig.52(b)

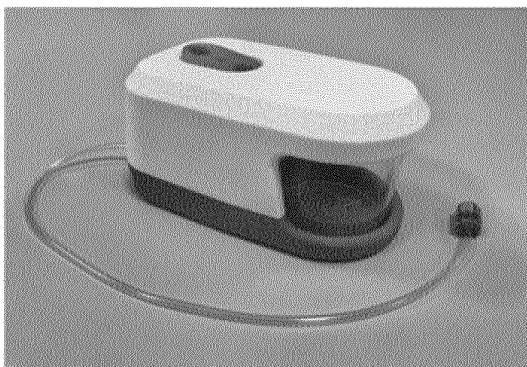


Fig.53(a)

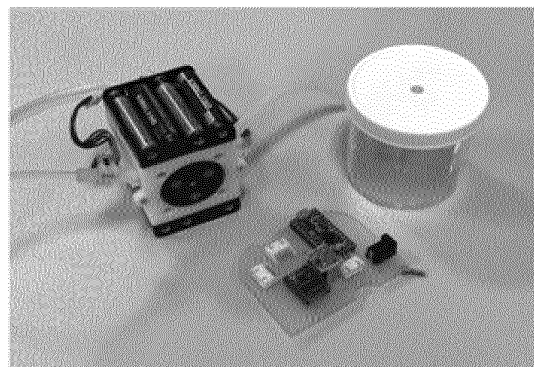


Fig.53(b)

INTERNATIONAL SEARCH REPORT

International application No

PCT/EP2018/085064

A. CLASSIFICATION OF SUBJECT MATTER

INV. A61M1/00 A61M25/00

ADD.

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

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

A61M

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

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

EPO-Internal , WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 93/15784 A1 (NAVARRE BIOMEDICAL LTD [US]) 19 August 1993 (1993-08-19)	1,13,36, 43-46, 49,53
A	the whole document	2,14-21, 23,26, 27,29, 32-35, 37,38, 42,47, 48,50, 54-64, 68, 74-76, 81-88

☐ 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

3 April 2019

Date of mailing of the international search report

11/04/2019

Name and mailing address of the ISA/

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
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Authorized officer

Amaro, Henrique

INTERNATIONAL SEARCH REPORT

International application No.
PCT/EP2018/085064

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.: 111, 112
because they relate to subject matter not required to be searched by this Authority, namely:
Rule 39.1(iv) PCT - Method for treatment of the human or animal body by surgery
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:

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fees, this Authority did not invite payment of additional fees.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ 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.:

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.

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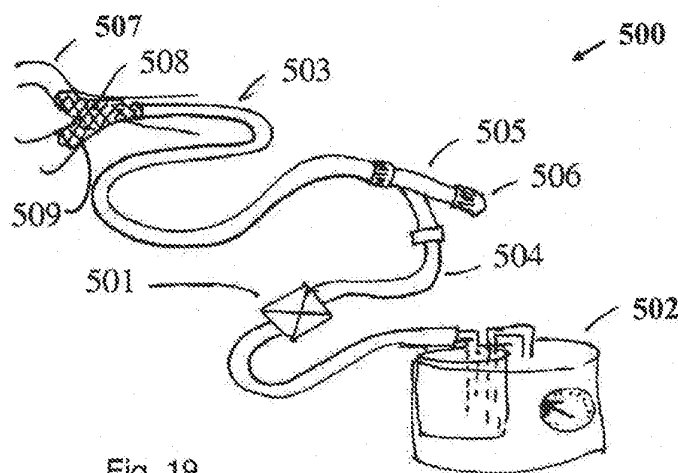


Fig. 19

(57) Abstract: A system for removing occlusive clot from a blood vessel comprises a catheter and an apparatus for generating a pulsatile vacuum force to pulse the pressure gradient at a distal end of the catheter. The pulse generator may be integral with or separate from the vacuum pump. The pulse generator may be applied to a flexible tubing between the vacuum pump and the proximal end of the catheter.

[Continued on next page]

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"A clot retrieval system for removing occlusive clot from a blood vessel"

Field of the Invention

5 This invention relates to devices intended for removing acute blockages from blood vessels. Acute obstructions may include clot, misplaced devices, migrated devices, large emboli and the like. Thromboembolism occurs when part or all of a thrombus breaks away from the blood vessel wall. This clot (now called an embolus) is then carried in the direction of blood flow. An ischemic stroke may result if the clot lodges in the cerebral vasculature. A pulmonary embolism
10 may result if the clot originates in the venous system or in the right side of the heart and lodges in a pulmonary artery or branch thereof. Clots may also develop and block vessels locally without being released in the form of an embolus - this mechanism is common in the formation of coronary blockages. The invention is particularly suited to removing clot from cerebral arteries in patients suffering acute ischemic stroke (AIS), from coronary native or graft vessels in
15 patients suffering from myocardial infarction (MI), and from pulmonary arteries in patients suffering from pulmonary embolism (PE) and from other peripheral arterial and venous vessels in which clot is causing an occlusion.

Background

20 Despite a wealth of information in the literature on the clotting cascade and on the biochemistry and etiology of thrombus in humans, remarkably little information is available on the physical and mechanical properties of this material. These properties are very pertinent to the interaction between thrombus and clot retrieval catheters and devices and the surrounding vasculature during mechanical thrombectomy of vessels occluded by thrombus material. Through extensive
25 experimentation and research into thrombus material the inventors have discovered aspects of the properties and behaviour of certain clot/thrombus types that help to explain why these clot types can be particularly challenging to retrieve. Some of these findings are described in our WO2012/120490A, the entire contents of which are herein incorporated by reference.

30 Clot is essentially a living polymer, comprising a matrix of intertwined and cross linked fibrin strands within which are situated red and white blood cells, platelets and numerous other proteins and components. The inventors have discovered that the mechanical properties of a clot are strongly influenced by the relative percentages of fibrin and red blood cells, and that clots with a high (and highly organised) fibrin content and low red blood cell content tend to be much firmer

clot
properties

and more cohesive than clots of a higher red cell content. Such clots have also been found to have a higher coefficient of friction, or in other words to be "stickier". These firm and sticky clots can be very challenging to remove from a vessel.

5 Clots with a low fibrin content and high red cell content have been found to be less cohesive and more friable and to have a lower coefficient of friction than the more organised fibrin rich clots previously described. These properties mean that such clots may be easier to dislodge from the site of occlusion, but may tend to fragment during the retrieval process, with the consequent risk of loss of clot fragments into distal or new vascular territories.

10 Furthermore, the inventors have discovered that the fibrin matrix of the clot can result in the clot material exhibiting viscoelastic behaviour in certain circumstances. A series of experiments were carried out in which a range of clots of varying fibrin content were tested. The clot samples were held in a receptacle and an indenter was placed on the surface of the clot and subject to a
15 fixed indenting force. The depth of penetration of the indenter into the clot was measured as a function of time for each clot type. Clots with a high fibrin content and low red blood cell content were found to exhibit the greatest viscoelastic effect, with the indenter effectively "creeping" into the clot over a period of several minutes, whereas with low fibrin content clots the indenter tended to almost fully penetrate the clots in a matter of seconds, greater levels of
20 organisation (and clot maturity) of the fibrin structure resulted in firmer clots which were penetrated to a much lesser extent by the indenter.

This behaviour combined with the higher frictional properties of fibrin rich clots tend to make these clot types particularly challenging to retrieve by mechanical thrombectomy. Conventional
25 stent-retrievers may find it difficult to penetrate and grip these firm clots, and the high level of friction they maintain with the vessel wall can result in a tendency for the clot to roll and compress.

Attempts to aspirate such clots into a catheter can also be very challenging as the clot must be
30 deformed in order to fit into the catheter lumen, and the energy required to deform such clots is not easily attained by aspiration. The high frictional coefficient of these clot types adds further to the challenge of aspirating them into the distal mouth of a catheter. Even maintaining a suction grip on such clots so that they can be retracted to the safety of a more proximal guide or sheath is very difficult, as these firm clots do not tend to deform and reshape easily and thus do

not readily conform to the shape of the catheter tip in order to effect a seal and consequent suction grip.

Statements of the Invention

5 This invention solves the challenge of aspirating fibrin rich clot material into a catheter by addressing the key challenges of 1) the friction between the clot and the catheter and 2) the energy/work required to deform these firm clots as they are aspirated into the catheter tip.

Conventional clot aspiration involves inserting a catheter (sometimes referred to as an
10 intermediate catheter or aspiration catheter or distal access catheter) into the patient's vasculature and advancing the catheter up to the occlusive clot. A syringe or vacuum pump is then attached to the proximal end of the catheter and a vacuum applied to attempt to suck the clot into the catheter tip and out through the catheter. The level of the vacuum applied can be controlled to a very limited extent by the force applied to the syringe or by the pump setting, and typically a
15 fairly constant pressure drop of 500mmHg to 760mmHg (or "full" vacuum) is applied. The difference in pressure between the blood vessel in which the clot is situated and the interior of the catheter creates a pressure gradient (which may exceed 760mmHg as the patient's blood pressure is higher than atmospheric pressure) which urges the clot into the catheter mouth.

20 The diameter of the clot however is greater than the diameter of the catheter therefore for a clot to be aspirated into a catheter the clot must deform and elongate to fit into the catheter tip. The energy to deform the clot to fit into the catheter is effectively an extrusion energy as the catheter tip acts as a form of extrusion die for the clot. This extrusion energy is related to the fibrin content of the clot with higher fibrin clots requiring increased extrusion energy to aspirate the
25 clot into the catheter. Current techniques to aspirate the clot involve applying a steady state vacuum to the tip of the catheter; however in many cases this does not provide sufficient energy to aspirate the clot fully into the catheter. Subsequent retrieval of the catheter either does not dislodge the clot or dislodges the partially retrieved clot and creates the risk of losing the partially exposed clot into a side branch or new vessel creating an ENT (Embolization in New
30 Territory).

This invention improves the ability of a catheter to aspirate a clot fully, including clots which have higher fibrin content. As stated above, vacuum is applied to the catheter tip to create a pressure differential between the catheter and the blood vessel with the aim of aspirating or

sucking the clot into the catheter and out of the vasculature. When the apparatus detailed in this invention is operating, the steady state vacuum normally applied at the tip of the catheter is modified to a pulsatile or wave configuration so that in one design configuration, the pressure differential between the catheter tip and the blood vessel plotted against time resembles a sine wave. The application of the aspiration force to the clot in a wave or pulsatile configuration applies an 'impact load' to the clot which can deform the clot and overcome the resistance or extrusion energy required to get the clot into the catheter more quickly and effectively than applying a continuous or steady aspiration force.

10 In addition, when clot occludes the distal tip of an aspiration catheter, part of the clot is inside the tip of the catheter. Testing has shown that compression and manipulation of thrombus increases the friction of the clot. Therefore compression of the clot at the tip of the catheter further increases the static friction between the clot and the inside surface of the catheter tip. The static friction between the clot and the catheter needs to be overcome to allow the clot to be aspirated 15 fully into the catheter. The application of a pulsatile force to the clot can cause the clot to vibrate or move slightly proximally and distally, so that the interaction between the clot and the internal surface of the catheter changes from static friction to a dynamic friction interaction. Dynamic friction of clot has been shown in our testing to be lower than static friction therefore the total force to remove the clot is reduced when using the apparatus detailed in this invention.

20 The fibrin matrix of a thrombus is porous and red blood cells can migrate and flow within the matrix depending on pressure differentials and fibrin density. Applying a pulsatile energy or vacuum at the catheter tip can promote this movement of clot elements, allowing the red blood cells to be aspirated out of the fibrin matrix. The thrombus is then easier to aspirate as the red 25 blood cell content of the clot decreases facilitating deformation of the fibrin matrix with reduced energy.

This invention is suitable for the aspiration of clots with varying fibrin content from 0% to 100%, and is particularly suited to the aspiration of clot or thrombus which has fibrin content 30 greater than 30%. The invention relates to the removal of a blood clot from the human vascular system. In particular it more specifically relates to the removal of a blood clot from the neurovasculature including the anterior and posterior circulation. Techniques and means of removing blood clots, or clotted blood particles in the form of emboli are already well known and established in use. When the presence of a clot is identified in the body it may be treated by

best medical treatment (BMT) in the form of medication or by surgical intervention. Surgical intervention can involve the use of mechanical means to dislodge and remove the clot. Blood clots may also be identified and referred to as emboli. Surgical intervention may be in the form of minimally invasive endovascular intervention where by the clot or embolism is accessed within the blood vessel by the distal end of a catheter that has been introduced within the arterial system at a remote location such as the Common Iliac artery. This is well known and relevant to the background of this invention.

Referring to an endovascular intervention described herein one of the means used to effect the removal of a clot through surgical endovascular intervention, is to use what is commonly referred to as 'aspiration' of the clot mass through a catheter. Aspiration is a technique whereby negative pressure or suction can be applied to the clot mass within the blood vessel through the distal end of a catheter, the catheter being connected at the proximal end to a vacuum source.

It is well known that there are clots which cannot be moved or removed even with the maximum intensity of vacuum or aspiration being applied to them. The present invention relates to but is not limited to this situation and to the removal of these types of arduous blood clots. This invention presents and describes a method of removing blood clots by applying a pulsatile energy comprising of a sequence of alternating forces through the distal tip of a catheter which is adjacent to or abutting the blood clot wherein this sequence of pulsatile forces applied to the clot and having the effect of deforming the clot in addition to aspirating the clot back through the catheter. The pulsatile force may also be described as being in the form of a sequence of pulses applied to the clot over a period of time, commonly referred to as frequency. Each pulse comprises of a sequential positive and negative volumetric displacement of fluid at the catheter distal tip. This cyclical positive and forward projecting pressure followed by negative pressure can be described mathematically in general but not limited to a sinusoidal function.

It is known that the aspiration function applies a negative force in the form of negative pressure of approximately 500 - 760 millimetres of mercury (mm Hg) at the tip of the catheter creating a flow from the distal to the proximal end of the catheter and recovering the content of this flow in a container which is part of the circuit and located close to the vacuum source. This pulsatile sequence of positive and negative pressures are applied through the catheter in conjunction with the aspirated negative pressure. The source of the pulsatile force is separate and independent of the source of the aspirated suction.

Waveforms which represent the sequence of pulsatile positive and negative pressures constitute inventive steps.

It is well known that there are clots which cannot be moved or removed by the level of aspiration being applied to them. The present invention relates to the removal of these types of clots. The invention describes in method of applying pulsatile force through a catheter at the distal tip to the clot which has the effect of aspirating the clot in one or more pieces and retrieving it into the catheter. The pulsatile force is in the form of a sequence of pulses applied to the clot over a period of time. Each pulse comprises of a sequential positive and negative volumetric displacement of fluid at the catheter distal tip or varying negative volumetric displacements.

This period cycle of varying negative pressure can be described mathematically in general but not limited to a sinusoidal function. The pulsatile sequence of pressures are applied in conjunction with the application of a steady state negative pressure / suction force. It has also been observed as a further inventive step that the blood clot can be recovered by applying the pulse without any aspiration.

With regard to the sinusoidal profile of the pressure emitted at the tip of the catheter then the pressure profile may vary about a pure sine wave in the following ways. A sine wave can be described for this purpose as having four components to it which are equal in frequency and amplitude but may be positive or negative. If the first part of the wave is an increasing pressure induced by the forward motion of a piston then the second part will be a negative pressure caused by a reverse motion of the piston. The piston is driven by a shaft or connecting rod that is rotated in a cycle along the length of the shaft and thus directing the piston in a forward and reverse motion. In terms of the sine wave describing this motion the first part of the curve indicating the increasing pressure is referred to as the rise time. The next part of the curve which represents a reverse motion of the piston and results in negative pressure at the catheter tip, this is referred to as the fall time or the decay time. The curve has one positive peak and one negative peak in each cycle. In a sequence of cycles constituting a sequence of pulses, the time from peak to peak is the same in a sine wave. The peak of a sine wave can be said to have no duration as the intensity or amplitude of the wave is changing continuously even as it transitions from positive to negative.

The present invention describes wave profiles applied at the catheter tip which can be at variance to a pure sine wave in the following manner. One is that the rise time may not be equal to the decay time. The rise time may be longer or shorter duration than the fall time duration. Secondly the peak of the wave may have a duration or a dwell time. The purpose of the dwell time is to allow fluid or blood some time to fill into the space in the piston chamber or time to pass through the orifice at the end of the chamber.

The nature of the pulse applied to dislodge and retrieve the blood clot can be defined by the following variables or control aspects:

10 Reciprocation

Frequency

Amplitude

Rise time

Dwell time

15 Decay / Fall time

While the application of the reciprocal motion of both positive and negative displacement in sequence is not well known, there are a number of methods available that are well known for reciprocal motion as described.

20 One is a purely mechanical cyclical drive system whereby the moving piston within the chamber is connected to crank shaft or the outer radius of a disk which is rotated so as to drive the piston to and fro. This to and fro distance is known as the stroke length. It is well known to use this method in positive displacement pumps but not positive and negative displacement in sequence.

25 Another well known method of generating reciprocal motion is by electromechanical means using electromagnetic induction whereby a magnetic field is induced in a coil of wire or alternately in two coils of wire for more control over different forces in each direction to create the forces necessary to move the piston to and fro in the chamber

30 The source of the power can be an alternating current and voltage or a direct current whereby the positive and negative cycles are achieved by switching mode control circuit.

As mentioned heretofore the cyclical motion which results in a symmetrical sinusoidal wave form of positive and negative pressure is the simplest. It may be desirable to alter the shape of the wave form so that the negative pressure is greater than the positive pressure or so that the rate of increase in pressure is greater of less than the rate of decline in pressure. It is recognised
5 herein that there may be an advantage in having no or less positive pressure than negative pressure so that vibration of the clot mass is reduced. It is recognised and presented as an inventive step that the introduction of dwell time on the peak and the trough of the wave form allows time for the fluid displacement to take place on both the positive and negative parts of each cycle. This is more relevant and important as the frequency of the cycles increases.

10

According to the invention there is provided a system for removing occlusive clot from a blood vessel comprising a vacuum source and collection chamber, a catheter to communicate the negative pressure to the location of the clot, and an apparatus to modify a steady state vacuum provided by a vacuum source to a series of pulses or a waveform configuration. In one iteration
15 this apparatus contains a mechanical drive system whereby a moving piston within a fluid chamber is connected to crank shaft or the outer radius of a disk which is rotated so as to drive the piston to and fro creating a positive and negative fluid displacement in sequence. This variable fluid displacement is combined with the steady state vacuum or negative displacement provided by the vacuum pump to produce a waveform pressure differential between the catheter
20 and the blood pressure at the tip of the catheter adjacent to the clot in the vasculature.

In one iteration the reciprocal motion to create the positive and negative fluid displacement is generated by electromechanical means using electromagnetic induction whereby a magnetic field is induced in a coil of wire or alternately in two coils of wire for more control over different
25 forces in each direction to create the forces necessary to move a piston to and fro in the fluid chamber.

In another iteration the fluid displacement is generated by moving the piston using other electromechanical means such as the piezoelectric effect.

30

In another iteration the fluid displacement is generated using other mechanical means such as a pneumatic drive.

In one configuration of the invention, the apparatus to create the pulsatile or waveform pressure differential is separate to the vacuum pump and chamber and is connected through tubing and connectors. In another iteration the apparatus of the invention and the vacuum pump are integrated in a single unit.

5

In one embodiment of the invention the piston to generate the pressure differential at the catheter tip is located within the catheter body which acts as the fluid chamber. The piston is moved proximally and distally in the catheter through a linear connection to a drive system located at the proximal end of the catheter. Alternatively the piston is moved in the catheter through
10 electronic means positioned within the catheter.

In one configuration of the invention, the apparatus to create the fluid displacement to produce a waveform pressure differential contains a single piston in a fluid chamber which is moved forward and back using a mechanical or electromechanical drive. In a different configuration of
15 the apparatus multiple fluid chambers with pistons are connected to facilitate complex waveforms. The displacement output of the apparatus can then be a summation of the displacements of each piston which can be programmed to operate independently.

In one iteration of the device the piston used to create the fluid displacement is similar to a
20 syringe with a moving seal between the piston and the fluid chamber. In another iteration other known hydraulic cylinder configurations are used to produce different waveform configurations.

In another iteration of the invention the tip of the catheter is vibrated by electromechanical means to reduce the friction between the catheter and the clot and help overcome the extrusion or
25 deformation energy required to aspirate the clot. The catheter tip vibration can be combined with a large aspiration lumen with a cross sectional area greater or equivalent to a 0.030" diameter lumen and in the preferred embodiment has a cross sectional area greater or equivalent to a 0.040" diameter lumen. The catheter with the vibrating tip may be used with a steady state aspiration vacuum or with the waveform pressure differential as described elsewhere in the
30 patent. The frequency of the tip vibration may range from 5 Hz to ultrasonic frequencies of greater than 20,000 Hz.

- uses guide + intermediate cath*
- Also according to the invention there is provided a method of removing occlusive clot from a blood vessel comprising the steps of:-
- providing a guide catheter or sheath and an intermediate catheter, the intermediate catheter having a distal mouth and being configured such that it is advancable within the lumen of the
- 5 guide catheter;
- inserting the guide catheter into a first vessel proximal of an occlusion;
- connecting the proximal end of the intermediate catheter to an aspiration source which consists of a vacuum pump, a collection chamber and the apparatus of the invention;
- advancing the intermediate catheter through the lumen of the guide catheter until the tip of the
- 10 intermediate catheter extends distal of the guide catheter into a vessel adjacent to the occlusion;
- applying steady state aspiration to the proximal end of the intermediate catheter;
- the intermediate catheter being configured to direct said aspiration through the distal lumen of the intermediate catheter to aspirate the clot into the mouth of said intermediate catheter.
- 15 If the clot is not aspirated switch on the apparatus of the invention to provide a waveform pressure differential between the catheter and the blood pressure surrounding the clot. The waveform pressure differential overcomes the extrusion energy of the clot and reduces friction between the clot and the catheter so that the clot can be aspirated through the intermediate catheter into the collection chamber and out of the vasculature.
- 20 In one embodiment of the invention, this waveform resembles a sine wave with a fixed frequency and amplitude, and equal rise and decay times.
- In another embodiment of the invention, the frequency or time between peaks of the waveform
- 25 may vary and increase or decrease with time. A repeating frequency pattern may also be utilised such as multiple high frequency pulses followed by a number of low frequency pulses.
- Similarly in another embodiment the amplitude of the waveform may vary with time and consist of increasing or decreasing amplitudes or a combination of different amplitude pulses.
- 30 In another embodiment the rise and decay times of the waveform may vary such that the decay time is shorter than the rise time or vice versa, or a combination of different rise and decay times may be beneficial in aspirating the clot, for example, a saw tooth waveform.

Another wave pattern utilised in an embodiment of the invention is a truncated or square wave pattern where a dwell time is incorporated into the wave cycle at the peak or trough of the wave or at both times. A dwell time may also be incorporated into a wave pattern at any point in the cycle, for example, producing a step wave pattern.

5

In another embodiment of the device the amplitude of the pressure differential is such that positive pressure may be applied to the clot for a fraction of the time of the wave cycle to increase the impact load applied to the clot.

10 In one embodiment of the invention the waveform is a combination of a number of the waveforms or features described elsewhere in this patent. In another embodiment, the invention may be programmable to apply specific pressure differential waveforms to the catheter tip which may be optimised for different clot types, for example, a pre-programmed optimized waveform may be applied for a fibrin rich clot which would be different to the waveform optimized for an erythrocyte rich clot.

Also provided are additional variants of this method, including:

A method as described above in which the waveform pressure differential is applied to the intermediate catheter as it approaches the occlusion for the first time.

20 An additional variant of this method is to apply the waveform pressure differential to the guide catheter or sheath if an intermediate catheter is not being used in the procedure. Alternatively the waveform pressure differential can be applied to both the intermediate catheter and the guide catheter at the same time.

25

The waveform or pulsatile pressure differential applied to the intermediate catheter described in this patent can also be used when the intermediate catheter is used in conjunction with a stentriever device. The waveform pressure differential reduces the friction between the clot and the catheter and helps to deform the clot. This gives additional benefits of reducing the shear forces acting on the clot as it is retrieved into the intermediate catheter by the stentriever device.

30

According to the invention there is provided a system for removing occlusive clot from a blood vessel comprising:-

a catheter; and

an apparatus for generating a pulsatile vacuum force to pulse the pressure gradient at a distal end of the catheter.

In one case the apparatus comprise a vacuum pump and a pulse generator.

5

In one embodiment the pulse generator is integral with the vacuum pump.

In another embodiment the pulse generator is separate from the vacuum pump.

10 The pulse generator in one case may be located between the vacuum pump and the proximal end of the catheter.

There may be a flexible tubing between the vacuum pump and the proximal end of the catheter.

15 In one embodiment the pulse generator is applied to the flexible tubing.

The pulse generator in one case comprises a reciprocating plunger.

The pulse generator in another case comprises a rotatable cam.

20

The cam may comprise an outer bearing to minimise drag on the tubing. The outer bearing may comprise a sliding outer layer.

In one case the flexible tubing is uniform cross section along the length thereof.

25

In one embodiment the flexible tubing is of variable cross section along the length thereof.

The system may comprise a controller for controlling the apparatus for generating a pulsatile vacuum source. The controller may be adapted or configured to vary the pressure over time in a waveform.

30

In one case the waveform has a fixed frequency and amplitude, and equal rise and decay times.

In another case the waveform has a varying frequency with time.

35

The waveform may have varying amplitude with time.

The waveform may have a different rise and decay time.

In one case the waveform rise and decay times change with time.

In some cases the waveform is a truncated or square waveform incorporating a dwell time at the
5 peak and trough of each wave.

The waveform may incorporate one or more dwell times within each wave producing a stepped wave configuration.

10 The invention also provides a method for removing occlusive clot from a blood vessel comprising the steps of:-

delivering a catheter to a location adjacent to an occlusive clot; and

applying a pulsatile vacuum to the clot using the catheter.

15 The method in some cases comprises the step of varying the pressure over time in a waveform.

The waveform may have a fixed frequency and amplitude, and equal rise and decay times.

The waveform may have a varying frequency with time.

20 The waveform may have varying amplitude with time.

The waveform may have a different rise and decay time.

25 The waveform rise and decay times may change with time.

The waveform may be a truncated or square waveform incorporating a dwell time at the peak and trough of each wave.

30 The waveform may incorporate one or more dwell times within each wave producing a stepped wave configuration.

In one embodiment the system comprises a canister which is configured to receive aspirated blood or material.

In one case the system comprises a vacuum pump which is connected to the canister. The vacuum may be drawn through the canister.

- 5 In one embodiment the system comprises a first vacuum pulse generator. In one case the system comprises a second vacuum pulse generator. The vacuum pulse generators may be configured to operate separately, at the same time, or at different times to vary the vacuum pulse generated.

In one case the first pulse generator comprises a valve having a housing and an element which is
10 rotatable and/or oscillatable in the housing.

In one case the second pulse generator is adapted to engage a flexible tube. The second vacuum pulse generator may comprise a rotatable cam.

- 15 In another case the first vacuum pulse generator comprises a pump. The system may further comprise non-return valves located on both sides of the pump.

In a further case the system comprises a canister configured to receive aspirated blood or material and the first pulse generator comprises an obturator which is movable through the
20 canister.

Brief Description of the Drawings

The invention will be more clearly understood from the following description of some
25 embodiments thereof, given by way of example only, with reference to the accompanying drawings, in which:

Fig. 1 is a view of a clot lodged in a representation of a similar cerebral vascular tubular network to the network in the brain for the purposes of describing the invention;

30

Fig. 2 illustrates by way of example only that the source of the aspiration or continuous negative suction and the source of the pulsatile pressure gradient are both combined to common effect through the catheter;

Fig. 3 shows the complete circuit interfacing with the circulation system in schematic form only;

Figs. 4A to 4C show by way of example only a means of generation cyclical motion which will generate the pressure differential waveform at the catheter distal tip;

Figs. 5A to 5E illustrate a number of possible wave form profiles representing positive and negative pressure pulses that are possible to generate with the reciprocation drive;

Fig. 6 is one example of a motorised reciprocal drive with variable speed;

Fig. 7 shows the distal tip of a catheter touching or abutting a blood clot that is lodged in a circuit representing cerebral vascular complexity;

Fig. 8 shows the distal tip of a catheter firmly engaged in a blood clot that is lodged in a circuit representing cerebral vascular complexity - this is as a result of aspiration or suction at a rate of -500 mm Hg;

Fig. 9 shows that the clot in Fig. 8 has been aspirated into the catheter following a small number of reciprocation pulses (3 to 5);

Figs. 10A - D are schematic illustrations of a clot being aspirated into a catheter inside a blood vessel;

Fig. 11 is a graph of pressure differential against time for a steady state vacuum;

Fig. 12 is a graph of pressure differential against time for a pulsatile pressure differential waveform generated by the invention;

Fig. 13 is a pressure differential waveform with negative and positive pressure differentials;

Fig. 14 is a pressure differential waveform with varying frequency;

Fig. 15 is a pressure differential waveform with different decay and rise times;

Fig. 16 is a pressure differential waveform with varying amplitude;

Fig. 17 is a pressure differential waveform with a truncated wave;

Fig. 18 shows a pressure differential waveform with a dwell time within the wave;

Fig. 19 is a diagram of a clot removal system of the invention;

Figs. 20A and 20B illustrate a piston type pulsatile vacuum generator;

Fig. 20C illustrates a cam type pulsatile vacuum generator;

Fig. 21 is a view of another pulsatile vacuum generator;

Figs. 22A and 22B illustrate another cam type pulsatile vacuum generator;

Fig. 23A illustrates a pulsatile aspiration system;

Figs. 23B and 23C illustrate an element of the pulsatile aspiration system of Fig. 23A;

Figs. 24A and 24B show pulsatile pressure waveforms;

Fig. 25 is a schematic of another pulsatile aspiration system of this invention;

Fig. 26 is a schematic of a portion of another pulsatile aspiration system of this invention;

Figs. 27A and 27B are views of a one way valve;

Fig. 28A illustrates a portion of a pulsatile aspiration system of this invention; and

Figs. 28B - 28D illustrate various states of an element of the pulsatile aspiration system of Fig. 28A.

Detailed description of the drawings

Specific embodiments of the present invention are now described in detail with reference to the
5 Figures, wherein identical reference numbers indicate identical or functionality similar elements.
The terms "distal" or "proximal" are used in the following description with respect to a position
or direction relative to the treating physician. "Distal" or "distally" are a position distant from or
in a direction away from the physician. "Proximal" or "proximally" or "proximate" are a
position near or in a direction toward the physician.
10 Accessing cerebral, coronary and pulmonary vessels involves the use of a number of
commercially available products and conventional procedural steps. Access products such as
guidewires, guide catheters, angiographic catheters and microcatheters are described elsewhere
and are regularly used in cath lab procedures. It is assumed in the descriptions below that these
15 products and methods are employed in conjunction with the device and methods of this invention
and do not need to be described in detail.

The following detailed description is merely exemplary in nature and is not intended to limit the
invention or the application and uses of the invention. Although the description of the invention
20 is in many cases in the context of treatment of intracranial arteries, the invention may also be
used in other body passageways as previously described.

Fig. 1; Reference numeral 1 illustrates an example only of a lumen network similar in
complexity to cerebral vasculature. Reference numeral 2 is an illustration representing a clot that
25 is lodged in the cerebral vasculature network. Reference numeral 3 shows where the blood
enters the network and reference numeral 4 shows where the blood exits the network.

Fig. 2 illustrates a schematic representation of the steady state vacuum pump combined into a
circuit with the pulse generation system. This circuit is then connected to the proximal end of a
30 catheter. A vacuum pump 11 for creating aspiration suction represented by the approved
standard drafting symbol. A cyclical reciprocation machine 12 is shown with a plunger 16 that
moves to and fro in a piston chamber. A fluid collection container 13 within the aspiration
circuit collects all the content aspirated from the body. Tubing 14 in the aspiration circuit is
joined to the catheter proximal end at the same point where the reciprocation connects to the

catheter proximal end. This is achieved using a Y junction connector. A connector 15 is provided for connection to the catheter proximal end. The catheter then passes through a haemostasis valve to enter the vascular system, usually at the common iliac artery (not shown here).

5 Fig. 3 is a full schematic of the entire system including the vascular and cerebral circulation systems. The apparatus of the invention is shown in schematic form 50 and contains a steady state vacuum pump 32 and a pulsatile flow generator 31. The output of these pumps is combined and connected to the proximal end of a catheter 34 at the connector 51. The catheter is
10 introduced into the vasculature at the haemostasis valve 40 and forwarded to the target location of the clot 41. When the catheter tip 35 approaches the clot 41, steady state vacuum from the pump 32 can be applied at the catheter tip. If the aspirate flow is blocked by the clot the pulsatile flow generator 31 can be engaged to produce a pressure differential waveform at the catheter tip to aspirate the clot 41.

15 Figs. 4 A to C are illustrations of a pulsatile flow generator that produces a pressure output which matches a sine wave configuration. A piston 65 is driven backwards and forwards by a rotating wheel 61 which contains a drive pin 63. This drive pin 63 engages in a slot of component 62, which is constrained so that it can only move in a linear direction. Therefore the rotational
20 movement of wheel 61 is converted into linear motion of piston 65 which travels in the direction 66 as shown, as the wheel rotates. The fluid pressure output at 68 matches a sine wave.

Fig. 5 illustrates a number of possible wave form profiles representing positive and negative pressure pulses that are possible to generate with the reciprocation drive which have varying
25 frequency.

Fig. 6 is one example of a motorised reciprocal drive 83 with variable speed. In this configuration the reciprocal drive shaft (not shown) is connected to the plunger of syringe 85. The drive is actuated using trigger 84 and moves the piston 81 backwards and forwards creating
30 a pulsatile pressure output at the tip of syringe 85.

Fig. 7 shows the distal tip of a catheter touching or abutting a blood clot that is lodged in a circuit representing cerebral vascular complexity. Fig. 8 shows the distal tip of the catheter firmly engaged in a blood clot that is still lodged in the circuit. In this example 500mm Hg vacuum was

applied to the catheter to aspirate the clot, however the application of this steady state aspiration energy was not sufficient to aspirate the clot. Fig. 9 shows that the clot in Fig. 8 has been fully aspirated into the catheter after a small number of reciprocation pulses (3 to 5) had been applied at the tip of the catheter.

Fig. 10A shows a schematic illustration of an occlusive clot 201 lodged in a blood vessel 205. Catheter 203 has been introduced to the vasculature and the tip 202 is approaching the clot. Fig. 10B illustrates the catheter 210 in contact with the clot 214. A portion of the clot 212 has been aspirated into the catheter tip 211 blocking the tip and sealing the end of the catheter 210. As the catheter is blocked the pressure in the catheter PA is different to the pressure in the blood vessel PB. The pressure differential acting across the clot is a function of $(PB - PA)$ and this urges the clot to deform and flow or extrude into the catheter. Applying a pulsatile pressure differential increases the energy applied to the clot and helps the clot to deform and flow. Fig. 10C illustrates that when a pulsatile pressure differential is applied to the clot 220 it can deform at the interface 223 where the clot enters the mouth of the catheter 221 to facilitate full aspiration. The friction between the clot 224 and the inner surface of the catheter 222 is also reduced by the application of the pulsatile pressure differential facilitating full aspiration of the clot. Fig. 10D shows the clot 232 approaching full aspiration into the catheter.

Figs. 11 to 18 are a series of graphs of the pressure differential against time for a range of waveforms. The pressure differential ΔP is the pressure acting across the clot as shown in Fig. 10B and is related to the difference between the blood pressure in the vessel and the pressure in the catheter tip when the tip is occluded by the clot.

Fig. 11 shows a graph of pressure differential against time for a steady state vacuum. In this graph, the pressure differential increases 300 after the vacuum pump is switched on until it reaches a plateau 301 when steady state conditions are achieved.

Fig. 12 shows a graph of pressure differential against time for a pulsatile pressure differential waveform generated by the invention. The graph 320 is similar to a sine wave with a fixed frequency (F) and amplitude (A).

Fig. 13 shows a pressure differential waveform 340 illustrating that during part of the wave cycle a positive pressure differential 341 is applied across the clot at the catheter tip.

Fig. 14 shows a pressure differential waveform with varying frequency where frequency F1 is different to F2 and is changing with time.

- 5 Fig. 15 shows a pressure differential waveform with different decay and rise times. In the example shown the decay time t1 is shorter than the rise time t2 producing a saw tooth waveform.

Fig. 16 shows a pressure differential waveform with varying amplitude. The absolute values of the amplitude can change with time as shown here where A1, A2, and A3 are all different. The
10 maximum and minimum values of the amplitude can also change with time.

Fig. 17 illustrates a pressure differential waveform with a truncated wave. This waveform allows for dwell times 400 and 401 at the point of minimum and maximum pressure differential.

- 15 Fig. 18 shows a pressure differential waveform where a dwell time has been introduced within the wave. Multiple dwell times can be introduced in the cycle such as 450 and 451, or a single dwell time as shown 452.

Fig. 19 is an illustration of another configuration 500 of the invention. In this schematic a pulse
20 generator (501) is a separate apparatus to a vacuum pump 502. This pulse generator 501 can produce a pressure differential waveform at the tip of the catheter 503 as described elsewhere in this patent but is non blood contacting. The pulse generator 501 creates the waveform by selective compression of connector tubing 504. This creates the benefit of not having to sterilise part of the apparatus prior to use, as the connector tubing 504 is disposable and single use only.

- 25 The method of use is the same as that described before with the vacuum pump 502 and pulse generator 501 connected to the proximal end of the catheter 503 at a connector 505 with a proximal valve / seal 506. The catheter 503 is introduced through the vasculature to the target location in a vessel 507 of the clot 508. In this case a stentriever type clot capture device 509 is also shown.

30 Fig. 20A shows internal details of a pulse generator 550 such as that illustrated in Fig. 19. In this configuration a reciprocating plunger 551 can compress the tubing 552 creating a pressure wave. The tubing 552 is elastic and recovers its shape as soon as the plunger moves up. The stroke of the plunger 560 shown in Fig. 20B can vary and different plunger widths or multiple plungers

can provide displacement variations. Fig. 20C shows a variation of this design where the plunger is replaced with a cam 562. Rotation of the cam provides a pulse generation capability.

Fig. 21 shows an advantageous design of the pulse generator which contains multiple cams in series. The cam 602 nearest the vacuum pump can rotate and seal the tubing 600 so that rotation of cams 604 and 605 can produce a positive pressure in the tubing. The tubing 600 is flexible and may be straight or have a stepped diameter as shown. The cams can be programmed so that some or all can work at any given time, each with a different frequency, or not be operated at all. Cams 603, 605 not mentioned anywhere else.

To reduce friction between the cam and the flexible tubing, each cam could have a sliding outer layer as shown in Figs. 22A and B. The cam 651 rotates on the eccentric axle 650 compressing the tubing 653. To reduce the friction the cam has a low friction sliding outer ring 652 which does not rotate relative to the tubing. Fig. 22B illustrates how the cam 670 position is rotated relative to Fig. 22A but the outer ring 672 has not rotated relative to the tubing wall 673.

Fig. 23a illustrates an apparatus 700 of this invention, comprising a vacuum pump 714 and a pulse generating system. Fig. 23b shows a more detailed view of the pulse generating components of the system. The vacuum pump 714 may comprise a diaphragm or vane or piston pump, or a peristaltic pump, or other means of generating a negative pressure differential. This vacuum pump is connected by tube 705 to a reception canister 707, which is configured to receive aspirated blood or material. A safety valve may be provided within the canister to prevent fluid or material entering tube 705 and damaging the pump. Tube 706 connects the canister to rotating valve 711. Tube 708 connects rotating valve 711 to a catheter (not shown) that is inserted within the patient, and does so either directly or via a further connecting tube or connector or rotating haemostasis valve or similar. Tube 708 is held in place by clips 709, which are configured so that the assembly of tube 708, rotating valve 711 and tube 707 can be easily assembled to or detached from the system (so that they may be disposable elements of the system). When clipped into place tube 708 sits between a rotatable cam 710 and a support plate 712. In use the system is capable of supplying a steady state vacuum by means of the vacuum pump 714 once switch 701 is moved to the "ON" position. The vacuum pump evacuates the canister 707 via tube 705, and thus a suction or aspiration force is transmitted through tubes 706 and 708 (once rotating valve 711 and cam 710 are in the open position).

Fig. 23b and Fig. 23c illustrate the operation of the pulse generating system. Rotating valve 711 comprises a housing 715 with inlet and outlet tube connectors 717 and 716, and an internal rotating element 713. When rotating element 713 covers the mouth of either connector 717 or 716 the valve is closed and tube 708 is no longer exposed to the vacuum within canister 707.

5 Thus by rotating or oscillating element 713 a vacuum pulse may be delivered through tube 708, and this may be beneficial for the retrieval of stubborn clot material as previously described. However the nature and condition of the material being aspirated may affect the waveform of the pulse generated in tube 708 and transmitted to the treatment catheter and thus to the patient. Fig. 24b illustrates a representative pulse generated by a vacuum pump with a simple on/off valve

10 such as rotating valve 711. The vertical axis 851 denotes pressure and the horizontal axis 850 denotes time. Prior to initiating any pulse a relatively steady state vacuum level 853 is provided in tube 708. Closure of valve 711 disconnects the tube from the vacuum source. In a case (case 1) where the tube 708 is connected to a catheter which is aspirating liquid blood or very soft clot the closure of valve 711 will cause the vacuum in the catheter to decay quickly, and angle 857

15 will be steep, allowing the vacuum to decay quickly from level 854 to 855. Once valve 711 is opened the vacuum is restored and the vacuum level in the catheter quickly returns to original level 853. In a case (case 2) where the tube 708 is connected to a catheter which is aspirating a resistant material such as fibrin rich thrombus the closure of valve 711 will cause the vacuum in the catheter to decay more slowly than in the previous case, and angle 857 will be more shallow,

20 so that the rate of decay of the vacuum is significantly reduced. A rate of change of vacuum level of greater than 100mmHg / second is necessary in order to create an effective pulse in the catheter. A rate of change of greater than 200mmHg / second is preferred, and a rate of change of greater than 400mmHg / second is more preferred, while a rate of change of greater than 600mmHg / second is most preferred.

25 The rotatable cam 710 and support plate 712 provide a means of increasing the rate of decay of the vacuum in tube 708 and any catheter to which it is connected, particularly in the scenario in which tube 708 is connected to a catheter which is aspirating a resistant material such as fibrin rich thrombus. This is achieved by creating a positive pulse of pressure to counteract the vacuum. This is achieved by rotation of the cam 710 to compress tube 708 between the cam and support plate 712, which in turn compresses the liquid or gas within tube 708 and thus rapidly

30 reduces the vacuum level within the tube. Fig. 23c illustrates this compression in action. The cam may be timed to compress the tube 708 at the same time as valve 711 closes, or fractionally later than closure of valve 711. The cam 710 may be timed to release the compression of tube

positive pulse from cam operation on tube

708 before, simultaneously or after the opening of valve 711. The impact of this system on the pulsatile waveform generated is illustrated in Fig. 24a.

NOT POSITIVE PRESSURE ABOVE
AMBIENT

The vertical axis 751 denotes pressure and the horizontal axis 750 denotes time. Prior to initiating any pulse a relatively steady state vacuum level 753 is provided in tube 708. Closure of valve 711 disconnects the tube from the vacuum source. In a case (case 3) where the tube 708 is connected to a catheter which is aspirating a resistant material such as fibrin rich thrombus the closure of valve 711 will cause the vacuum in the catheter to start to decay slowly at a first rate of decay illustrated by the line between points 754 and 755. Rotation of cam 710 to compress tube 708 causes the rate of decay of the vacuum to be significantly increased, illustrated by the line between points 755 and 756. A dwell period may be provided between points 756 and 757, after which cam 710 is rotated to remove the compression from tube 708 and valve 711 is opened, allowing the vacuum level in tube 708 to drop quickly from point 757 to point 758. Again a dwell period may be provided at vacuum level 753 before additional pulses are provided.

Fig. 25 is a schematic drawing of another pulsatile aspiration pump system 900 of this invention configured to provide pulses with a rapid rate of change of vacuum level. Catheter 901 is shown in the process of aspirating thrombus 907. This aspiration is caused by a pressure differential between the medium in which the thrombus is located outside the catheter and that of the internal lumen of the catheter. An aspiration force is provided to the catheter through tube 903, which is in turn connected to tube 908, which is itself connected to canister 904. Canister 904 is evacuated by pump 905. A second "pump" 902 is located between tubes 903 and 908 and consists in this embodiment of a piston pump, similar to a syringe. A pair of one way valves 906 and 909 are positioned either side of piston pump 902, so that when the piston moves downwards a small but limited positive pressure is applied to tube 903 and hence to catheter 901 before the valve 906 closes. This causes a rapid rate of change in the vacuum level within the catheter 901. Conversely when the piston moves upward the system will aspirate preferentially from the catheter rather than the canister, creating a rapid increase in the vacuum level within the catheter.

Fig. 26 is a schematic drawing of another pulsatile aspiration pump system 950 of this invention very similar to system 900. An aspiration force is provided through tube 953, which is in turn connected to tube 958, which is itself connected to canister 954. Canister 954 is evacuated by pump 955. A second "pump" 952 is located between tubes 953 and 958. Pump 952 consists in

- this embodiment of an oscillating diaphragm assembly 963, which is supported by compression spring 960 and actuated by the counteracting forces of this spring 960 and cam 961. Cam 961 may be operated by many means, including the gear assembly 962 illustrated herein. A pair of one way valves 956 and 959 are positioned either side of pump 952, so that when the diaphragm moves downwards a small but limited positive pressure is applied to tube 953 before the valve 956 closes. This causes a rapid rate of change in the vacuum level within the catheter 951. Conversely when the diaphragm moves upward the system will aspirate preferentially from the catheter rather than the canister, creating a rapid increase in the vacuum level within the catheter.
- 10 Figs. 27a and 27b are schematics of a simple one way valve 1000 of this invention. They are configured to open easily to allow flow in one direction, and close quickly and automatically once the direction of the pressure gradient (and hence the direction of flow) across the valve changes. Valve 1000 comprises a body section 1001 with a pair of tube connectors 1002 and 1003 at either end. The body 1001 has a generally square or rectangular section, so that flap 15 1004 can be hinged at an outer edge and move freely from an open to a closed position. A stop 1005 is provided so that the flap is prevented from reaching a fully open position where a change in flow direction would not cause it to close. A second stop 1006 prevents the flap from moving beyond the fully closed position once the pressure gradient is reversed.
- 20 Fig. 28a is a schematic of a portion of a pulsatile pump system 1050 of this invention. Canister 1051 is connected to a vacuum pump (not shown) by connecting tube 1052, and to a treatment catheter (not shown) by connecting tube 1053. In use a vacuum is generated within the canister by the vacuum pump and thus blood and thrombus are aspirated through a treatment catheter and through tube 1053 into the canister. A pulsatile waveform as described in relation to Fig. 24b 25 can be generated by oscillation back and forth of obturator 1055, which is guided through the canister by guide port 1056, and enters the mouth of tube 1053 on the other side of the canister. The obturator can be moved back and forth by a simple gear mechanism as shown or by any of the other means of reciprocation well known in the art. Figs. 28b-d show the obturator of Fig. 28a in various different positions, and also show a corrugated element 1056 which may be used 30 to ensure that movement of the obturator does not create leakage into the canister.
- Fig. 28b (and Fig. 28a) show the obturator in the open position where only the narrow guide portion 1057 is positioned within the mouth of tube 1053. In this position a steady state vacuum may be maintained with little or no restriction from the obturator. Fig. 28c shows the obturator

in the closed position where the tapered portion 1058 of the obturator is fully within the mouth of tube 1053. In this position tube 1053 is no longer subject to the vacuum within the canister and the vacuum level within the tube (and connected catheter) will start to decay. The rate of decay of this vacuum can be significantly accelerated by further advancement of the obturator to the position shown in Fig. 28d, which provides a positive displacement to the fluid (or gas) within tube 1053, having a similar effect to the piston and diaphragm movements described in systems 700, 900 and 950.

It will be apparent from the foregoing description that while particular embodiments of the present invention have been illustrated and described, various modifications can be made without departing from the spirit and scope of the invention. For example, while the embodiments described herein refer to particular features, the invention includes embodiments having different combinations of features. The invention also includes embodiments that do not include all of the specific features described.

The invention is not limited to the embodiments hereinbefore described which may be varied in construction and detail.

Claims

1. A system for removing occlusive clot from a blood vessel comprising:-
a catheter; and
5 an apparatus for generating a pulsatile vacuum force to pulse the pressure gradient at a distal end of the catheter.
2. A system as claimed in claim 1 wherein the apparatus comprise a vacuum pump and a pulse generator.
- 10 3. A system as claimed in claim 2 wherein the pulse generator is integral with the vacuum pump.
4. A system as claimed in claim 2 wherein the pulse generator is separate from the vacuum pump.
- 15 5. A system as claimed in claim 4 wherein the pulse generator is located between the vacuum pump and the proximal end of the catheter.
- 20 6. A system as claimed in claim 4 or 5 comprising a flexible tubing between the vacuum pump and the proximal end of the catheter.
7. A system as claimed in claim 6 wherein the pulse generator is applied to the flexible tubing.
- 25 8. A system as claimed in claim 7 wherein the pulse generator comprises a reciprocating plunger.
9. A system as claimed in claim 7 wherein the pulse generator comprises a rotatable cam.
- 30 10. A system as claimed in claim 9 wherein the cam comprises an outer bearing to minimise drag on the tubing.
11. A system as claimed in claim 10 wherein the outer bearing comprises a sliding outer layer.
- 35 12. A system as claimed in any of claims 7 to 11 wherein the flexible tubing is of uniform cross section along the length thereof.

13. A system as claimed in any of claims 7 to 11 wherein the flexible tubing is of variable cross section along the length thereof.
- 5 14. A system as claimed in any of claims 1 to 13 comprising a controller for controlling the apparatus for generating a pulsatile vacuum source.
15. A system as claimed in claim 14 wherein the controller is adapted to vary the pressure over time in a waveform.
- 10 16. A system as claimed in claim 15 wherein the waveform has a fixed frequency and amplitude, and equal rise and decay times.
17. A system as claimed in claim 15 wherein the waveform has a varying frequency with time.
- 15 18. A system as claimed in claim 15 wherein the waveform has varying amplitude with time.
19. A system as claimed in claim 15 wherein the waveform has different rise and decay times.
- 20 20. A system as claimed in claim 15 wherein the waveform rise and decay times change with time.
- 25 21. A system as claimed in claim 15 wherein the waveform is a truncated or square waveform incorporating a dwell time at the peak and trough of each wave.
22. A system as claimed in claim 15 wherein the waveform incorporates one or more dwell times within each wave producing a stepped wave configuration.
- 30 23. A method for removing occlusive clot from a blood vessel comprising the steps of:
delivering a catheter to a location adjacent to an occlusive clot; and
applying a pulsatile vacuum to the clot using the catheter.
- 35 24. A method as claimed in claim 23 comprising the step of varying the pressure over time in a waveform.

25. A method as claimed in claim 24 wherein the waveform has a fixed frequency and amplitude, and equal rise and decay times.
26. A method as claimed in claim 24 wherein the waveform has a varying frequency with
5 time.
27. A method as claimed in claim 24 wherein the waveform has varying amplitude with time.
28. A method as claimed in claim 24 wherein the waveform has a different rise and decay
10 time.
29. A method as claimed in claim 24 wherein the waveform rise and decay times change with time.
- 15 30. A method as claimed in claim 24 wherein the waveform is a truncated or square waveform incorporating a dwell time at the peak and trough of each wave.
31. A method as claimed in claim 24 wherein the waveform incorporates one or more dwell times within each wave producing a stepped wave configuration.
- 20 32. A system for removing occlusive clot from a blood vessel comprising:-
a catheter for applying a vacuum to an occlusive clot; and
an apparatus for generating an additional energy to be applied to the clot.
- 25 33. A system as claimed in claim 32 wherein the apparatus is adapted to apply a variable pressure to the clot at the distal tip of the catheter.
34. A system as claimed in claim 32 or 33 wherein the variable pressure applied by the apparatus is adapted to produce a variable pressure differential between the catheter and
30 the blood pressure around the clot.
35. A system as claimed in claim 34 wherein the variable pressure differential is adapted to provide additional energy to the clot to overcome the extrusion energy required to deform and aspirate the clot.

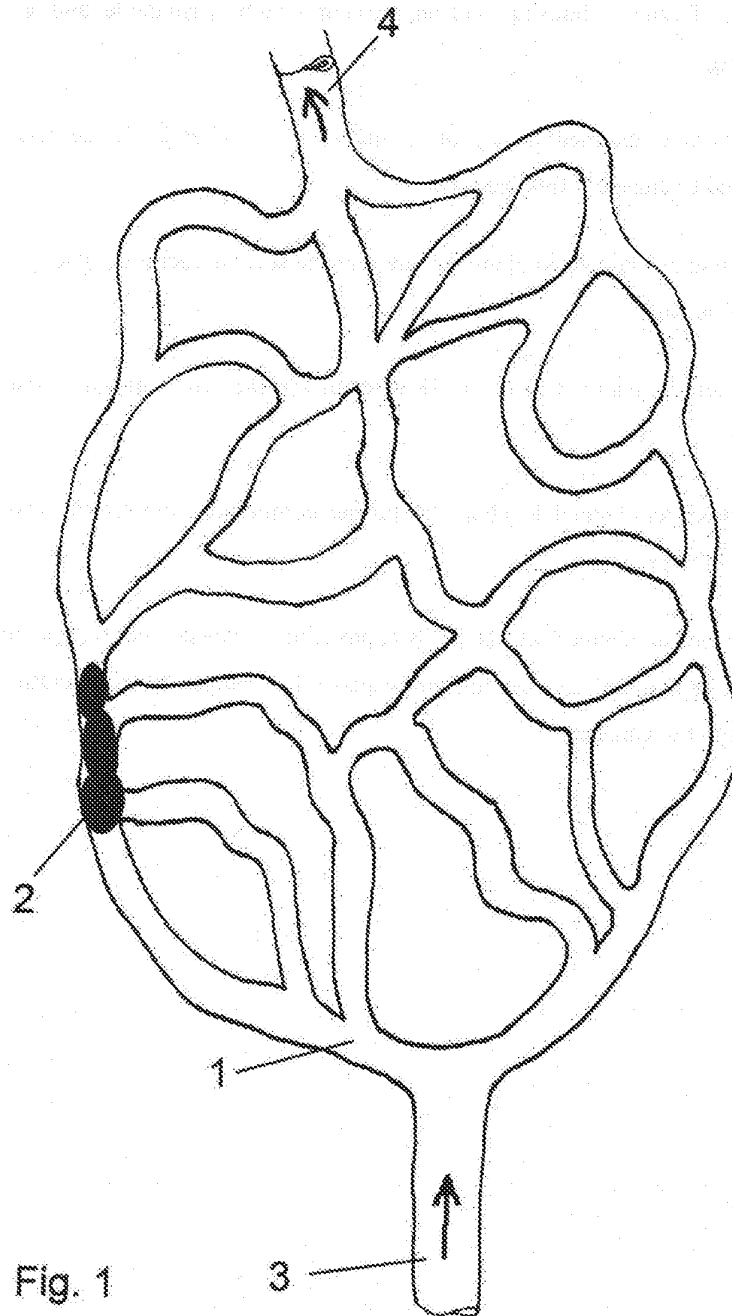
36. A system as claimed in claim 34 wherein applying a variable pressure differential to the clot is adapted to change the friction between the clot and the catheter from static to dynamic friction reducing the total friction and facilitating aspiration into the catheter.
- 5 37. A system as claimed in claim 34 wherein applying a variable pressure differential to the clot is adapted to increase the porosity of the clot reducing the deformation force required to aspirate the clot.
- 10 38. A system as claimed in claim 34 wherein a plot of pressure differential against time produces a waveform.
39. A system as claimed in claim 38 wherein the pressure differential waveform is similar to a sine wave with fixed frequency and amplitude, and equal rise and decay times.
- 15 40. A system as claimed in claim 38 wherein the pressure differential waveform has a varying frequency with time.
41. A system as claimed in claim 38 wherein the pressure differential waveform has varying amplitude with time.
- 20 42. A system as claimed in claim 38 wherein the pressure differential waveform has different rise and decay times.
- 25 43. A system as claimed in claim 38 wherein the pressure differential waveform rise and decay times change with time.
44. A system as claimed in claim 38 wherein the pressure differential waveform is a truncated or square waveform incorporating a dwell time at the peak and trough of each wave.
- 30 45. A system as claimed in claim 38 wherein the pressure differential waveform incorporates one or more dwell times within each wave producing a stepped wave configuration.

46. A system as claimed in claim 34 and 38 wherein the pressure in the catheter tip is always less than the surrounding blood pressure.
47. A system as claimed in claim 34 and 38 wherein the pressure in the catheter tip is greater than the surrounding blood pressure for a fraction of the waveform.
48. A system as claimed in claim 38 wherein the pressure differential waveform is a combination of some or all the waveforms detailed in claims 39 to 45.
49. A system as claimed in claim 48 wherein the pressure differential waveform is pre-programmed in the apparatus
50. A system as claimed in claim 49 wherein the pre-programmed pressure differential waveform is optimized for a particular clot type.
51. A system as claimed in claim 38 wherein the pressure differential waveform is produced in the apparatus by moving one or more pistons in a fluid chamber similar to a syringe.
52. A system as claimed in claim 51 where the piston is driven by a rotating mechanical drive system
53. A system as claimed in claim 51 where the piston is driven by a electromechanical means such as a linear drive system
54. A system as claimed in claim 51 where the piston is driven by piezoelectric means.
55. A system as claimed in claim 51 where the piston is driven by a pneumatic cylinder.
56. A system as claimed in any of claims 32 to 55 wherein the apparatus for generating an additional energy is separate from the catheter.
57. A system as claimed in any of claims 32 to 56 wherein the apparatus for generating an additional energy is integral with the catheter.

58. A system as claimed in claim 57 wherein the catheter contains a piston.
59. A system as claimed in claim 58 wherein the piston is actuated by a drive system external to the catheter.
- 5 60. A system as claimed in any of claims 32 to 59 wherein the additional energy applied to the clot comprises a vibration force.
61. A system as claimed in claim 60 wherein the catheter incorporates a vibrating tip.
- 10 62. A system as claimed in claim 60 wherein the frequency of the vibrating tip is variable from 5 Hz to greater than 20,000 Hz.
63. A system as claimed in claim 61 wherein the vibrating tip contains one or more aspiration lumens with a total cross sectional area greater than 0.78mm².
- 15 64. A system as claimed in claim 34 wherein the apparatus comprises a steady state vacuum generator and a pulsatile flow generator.
- 20 65. A method for removing an occlusive clot from a blood vessel comprising the steps of :
delivering a catheter to a location adjacent to an occlusive clot;
applying a vacuum to the clot using the catheter; and
applying an additional energy to the clot.
- 25 66. A method as claimed in claim 65 wherein the additional energy is applied to the clot via the catheter.
67. A method as claimed in claim 66 wherein the additional energy is applied to the clot via the catheter as the catheter approaches the clot.
- 30 68. A method as claimed in claim 66 wherein the additional energy is applied to the clot via the catheter only after the catheter fails to aspirate the clot with steady state vacuum.

69. A method as claimed in claim 65 wherein the additional energy is applied to a guide catheter or sheath positioned proximal of the clot in the vasculature.
70. A method as claimed in claim 65 wherein the additional energy is applied to a guide catheter or sheath and an intermediate catheter simultaneously.
71. A method as claimed in claim 65 wherein the additional energy is applied to the clot via the catheter in conjunction with the use of a stentriever device.
72. A method as claimed in claim 65 wherein the additional energy is applied to the clot through the catheter.
73. A method as claimed in any of claims 65 to 72 comprising:
- a. delivering the auxiliary apparatus to a location adjacent to the clot; and
 - b. applying the additional energy directly to the clot.
74. A method as claimed in claim 73 comprising delivering the catheter and the auxiliary apparatus simultaneously.
75. A system as claimed in any of claims 1 to 22 or 32 to 64 comprising a canister which is configured to receive aspirated blood or material.
76. A system as claimed in claim 75 wherein the system comprises a vacuum pump which is connected to the canister.
77. A system as claimed in claim 76 wherein the vacuum is drawn through the canister.
78. A system as claimed in any of claims 1 to 22, 32 to 64, or 75 to 77 comprising a first vacuum pulse generator.
79. A system as claimed in claim 78 comprising a second vacuum pulse generator.
80. A system as claimed in claim 79 wherein the vacuum pulse generators are configured to operate separately, at the same time, or at different times to vary the vacuum pulse generated.

81. A system as claimed in any of claims 78 to 80 wherein the first pulse generator comprises a valve having a housing and an element which is rotatable and/or oscillatable in the housing.
- 5 82. A system as claimed in any of claims 78 to 81 wherein the second pulse generator is adapted to engage a flexible tube.
83. A system as claimed in claim 82 wherein the second vacuum pulse generator comprises a rotatable cam.
- 10 84. A system as claimed in claim 78 wherein the first vacuum pulse generator comprises a pump.
- 15 85. A system as claimed in claim 84 further comprising non-return valves located on both sides of the pump.
86. A system as claimed in claim 78 comprising a canister configured to receive aspirated blood or material and the first pulse generator comprises an obturator which is movable
- 20 through the canister.
- 25
- 30



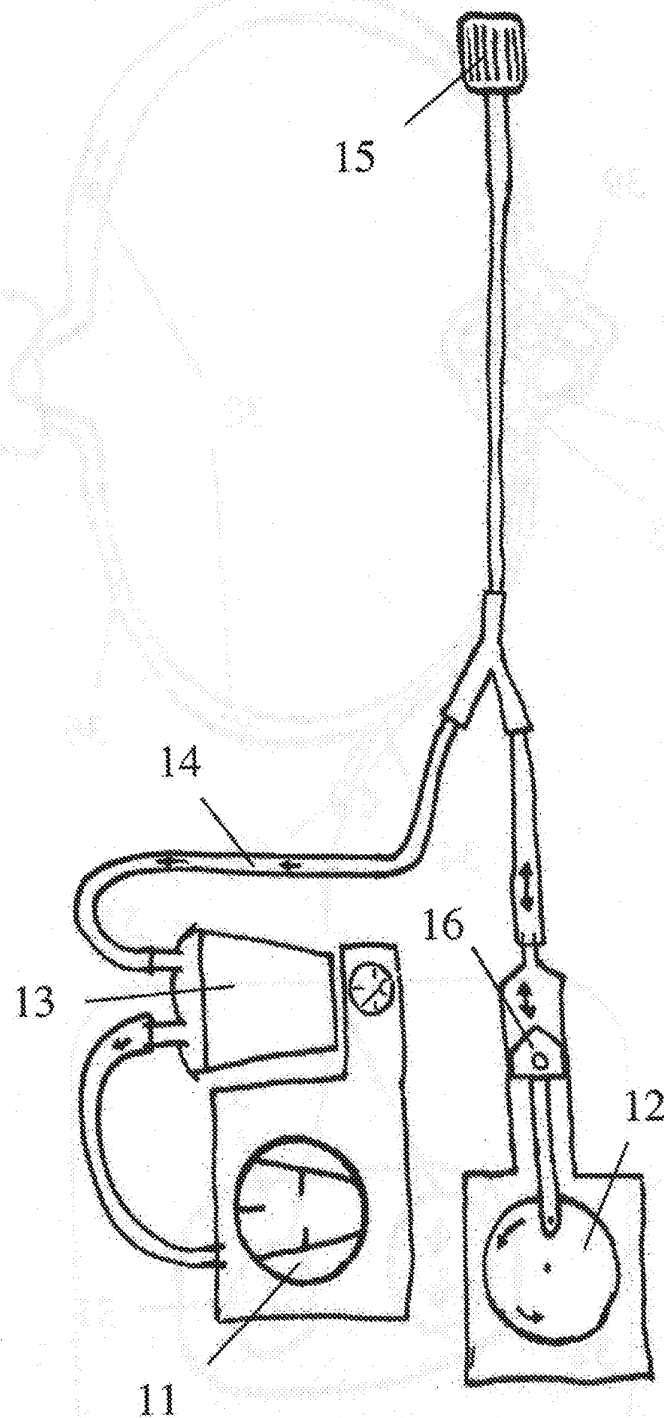
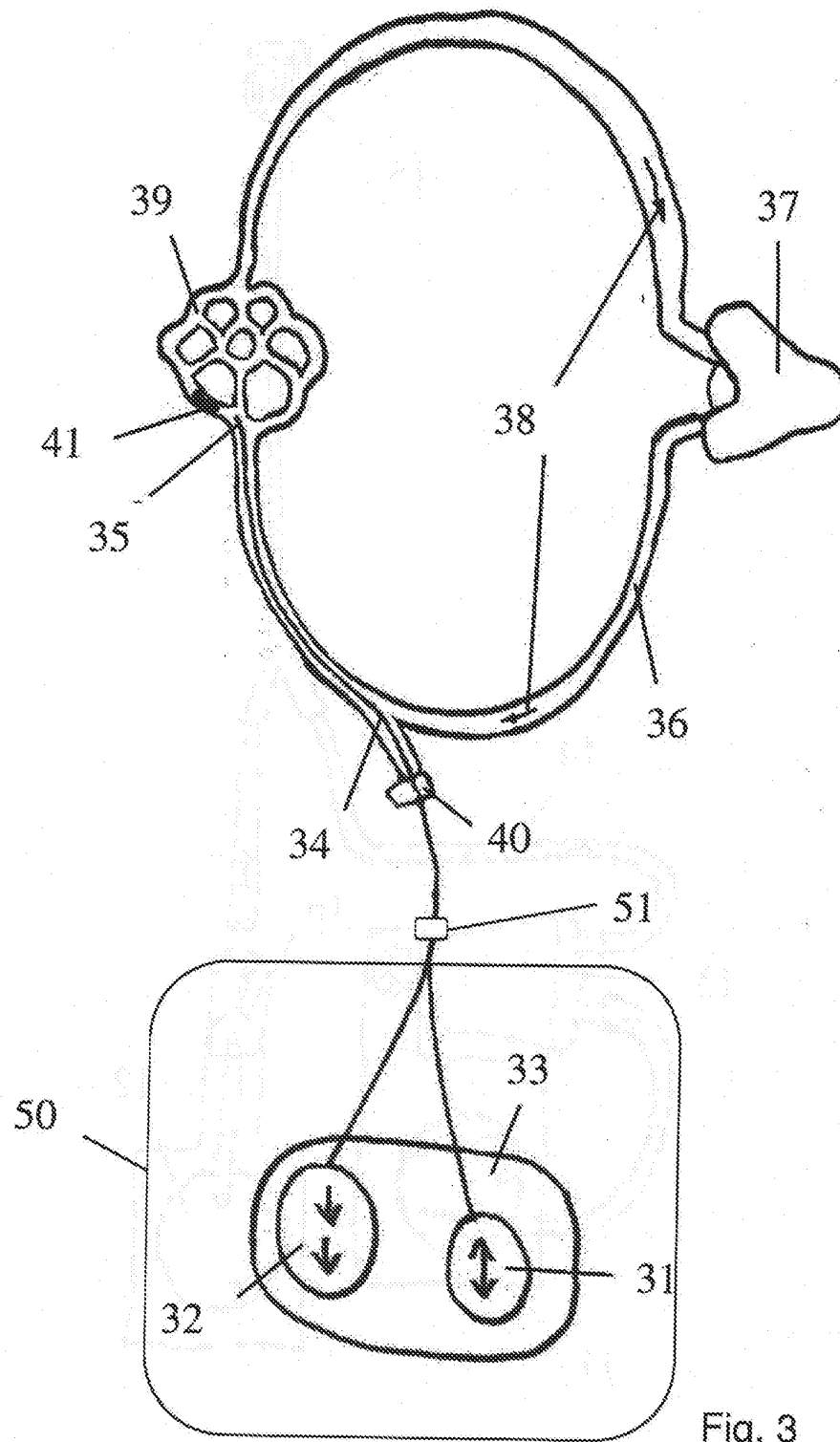


Fig. 2



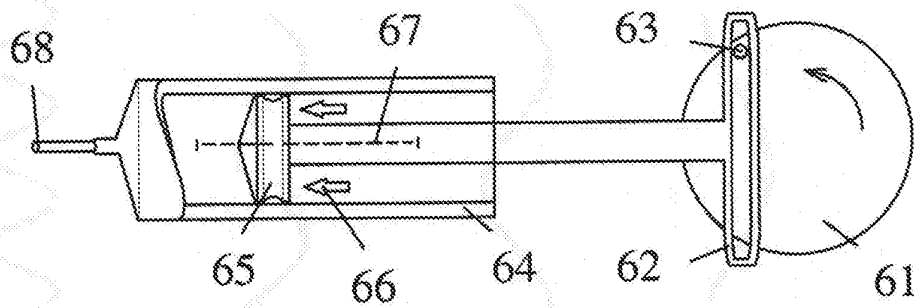


Fig. 4A

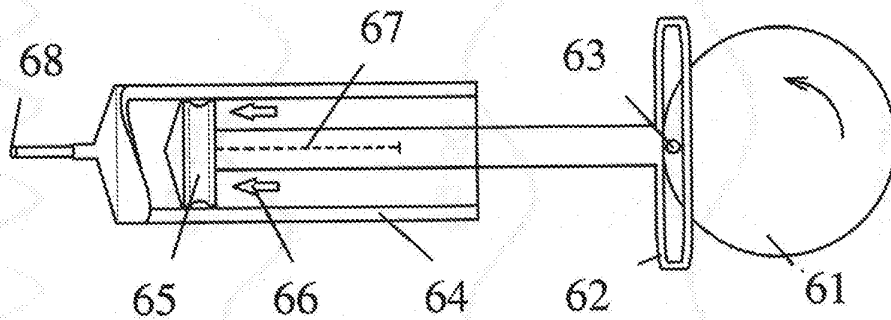


Fig. 4B

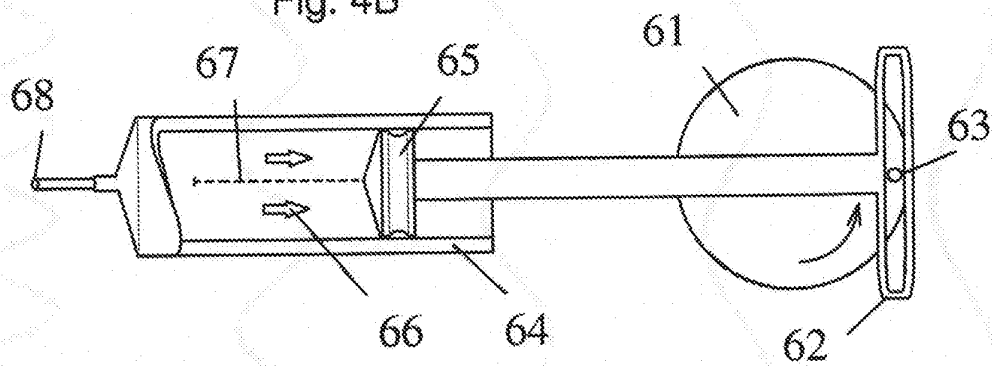
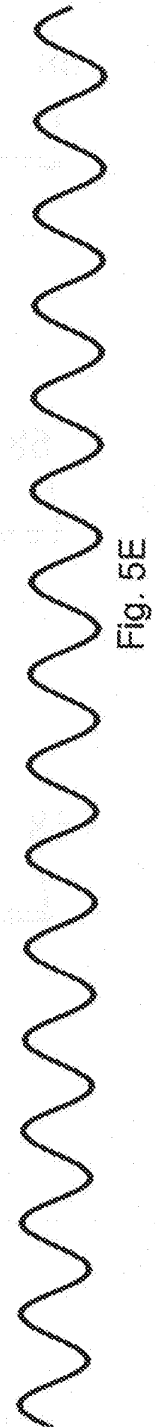


Fig. 4C



SUBSTITUTE SHEET (RULE 26)

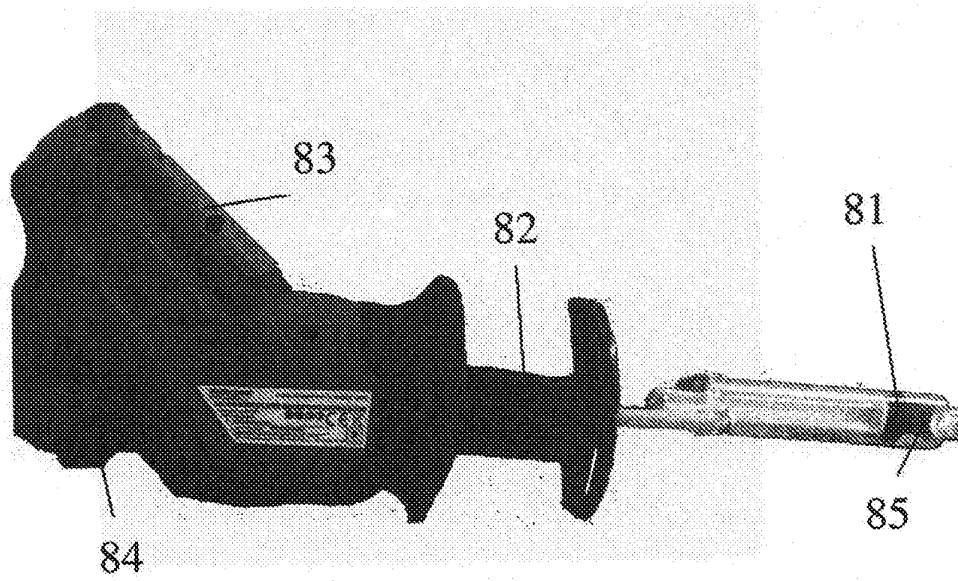


Fig. 6

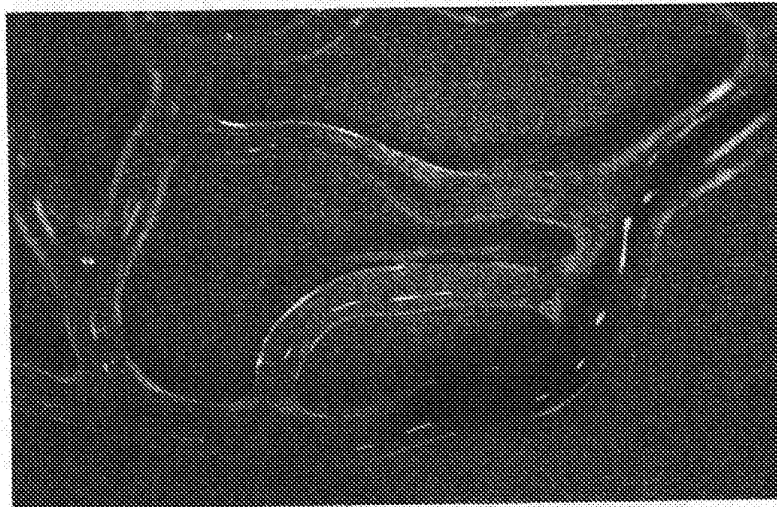


Fig. 7

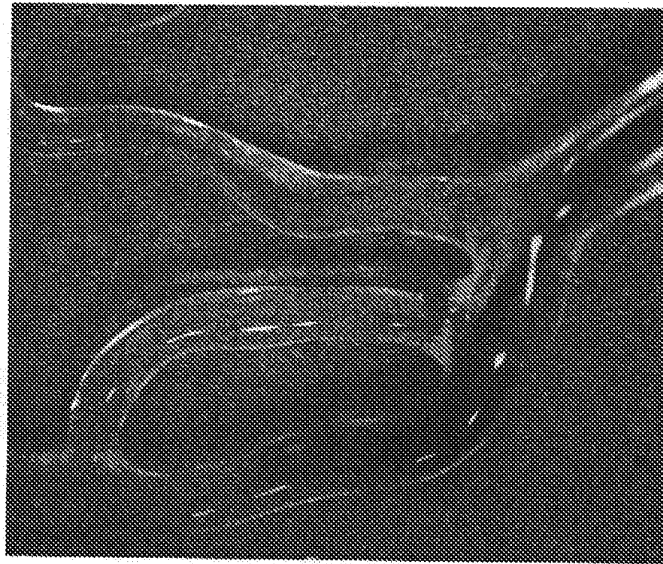


Fig. 8

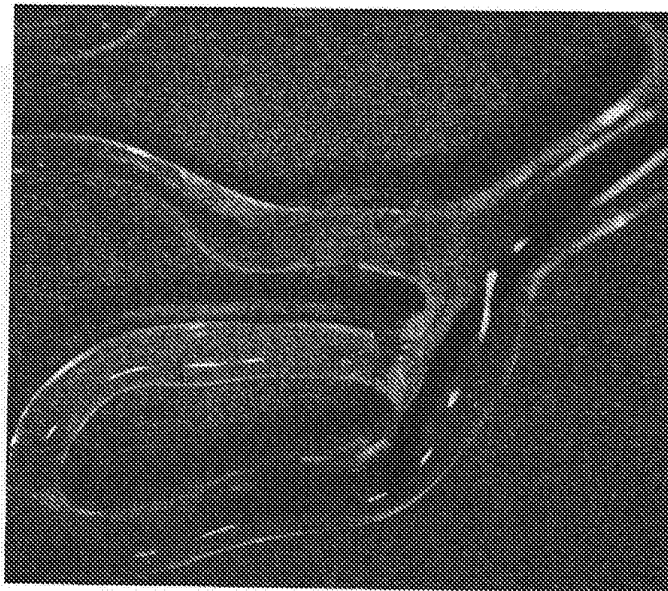


Fig. 9

Fig. 10A

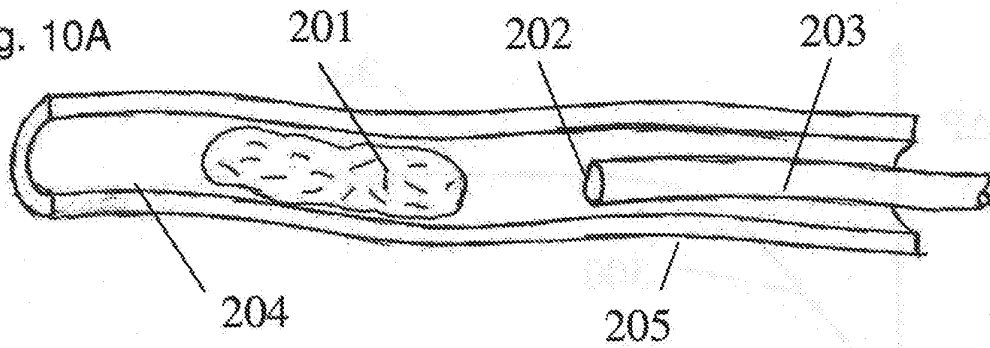


Fig. 10B

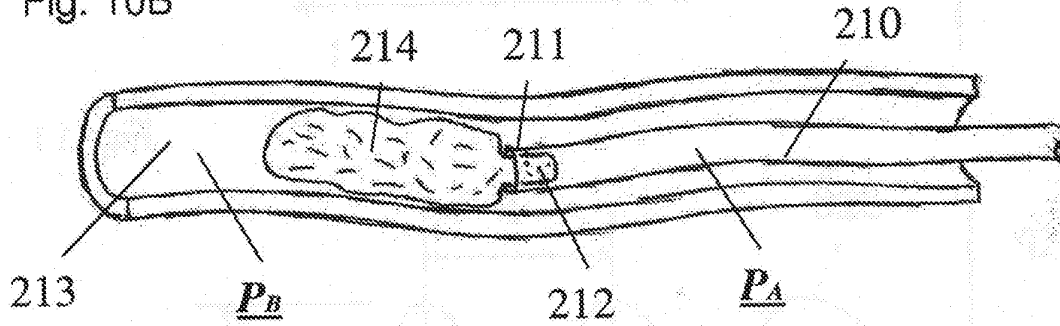


Fig. 10C

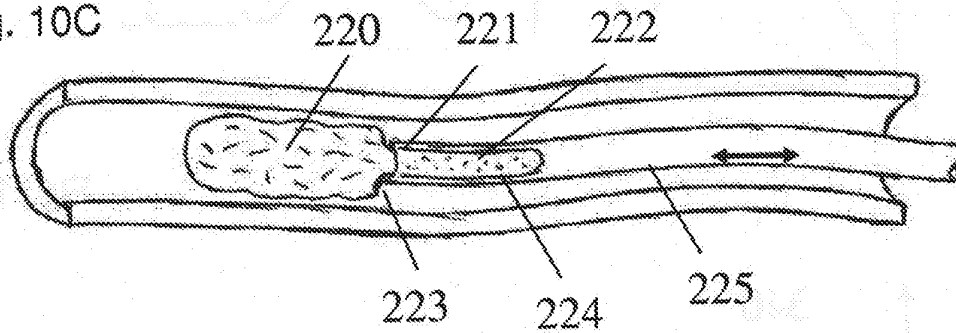
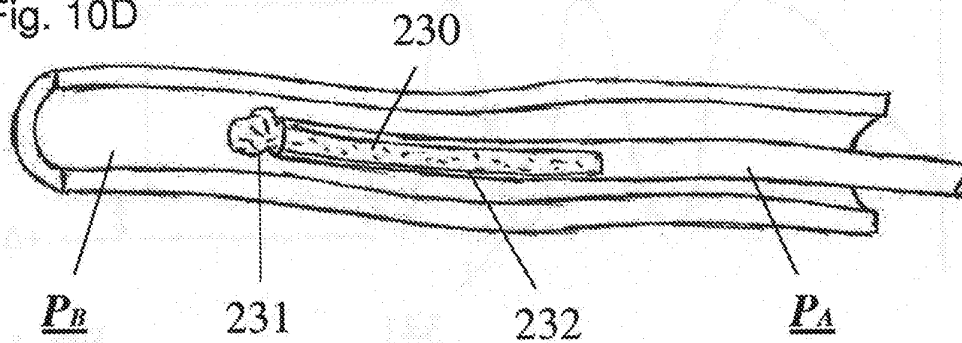


Fig. 10D



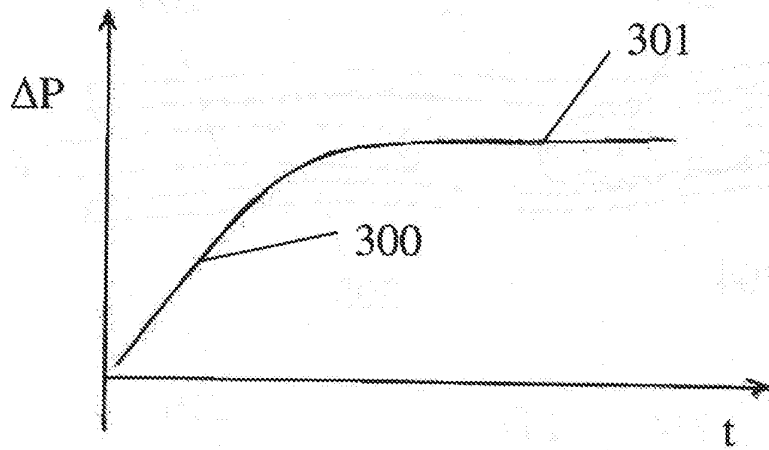


Fig. 11

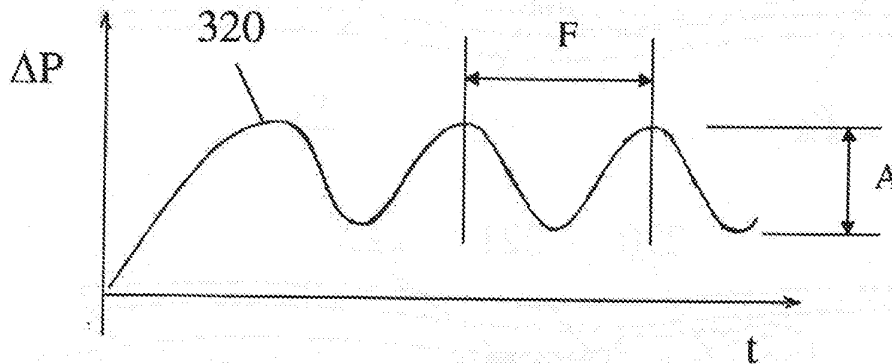


Fig. 12

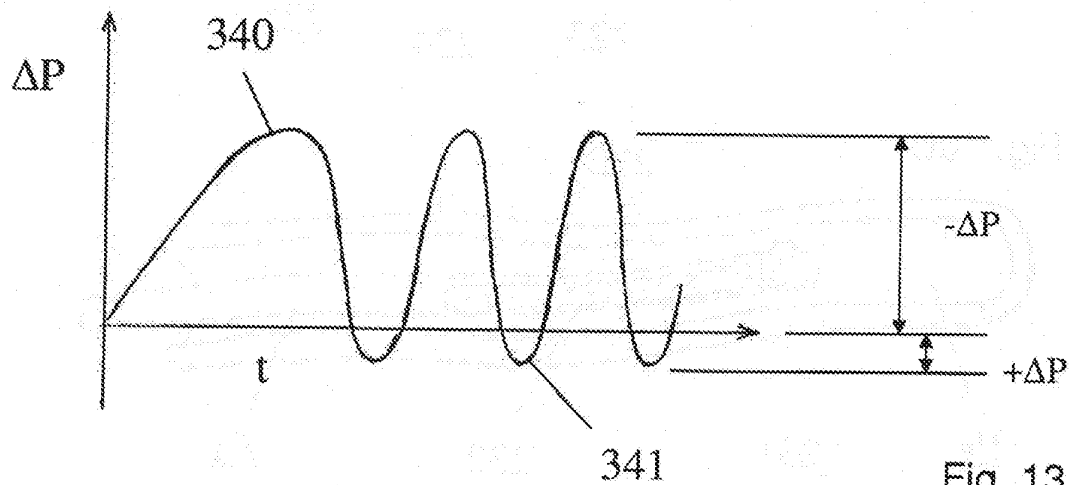


Fig. 13

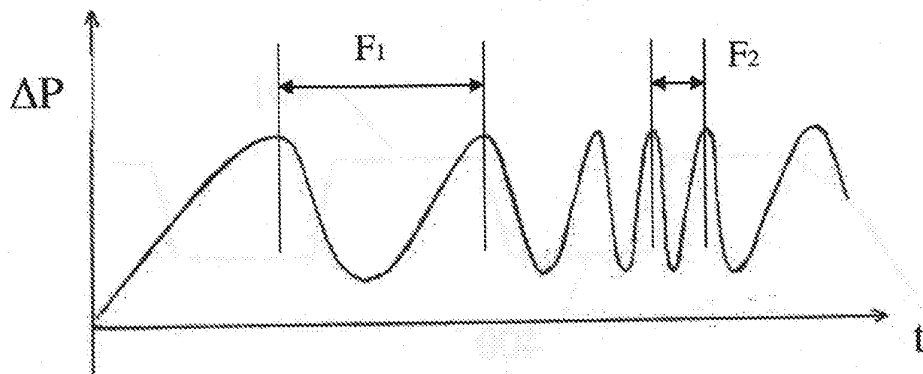


Fig. 14

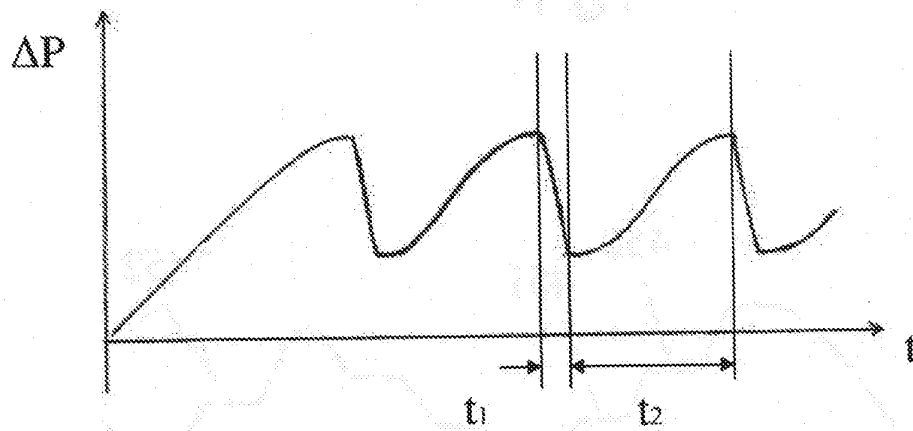


Fig. 15

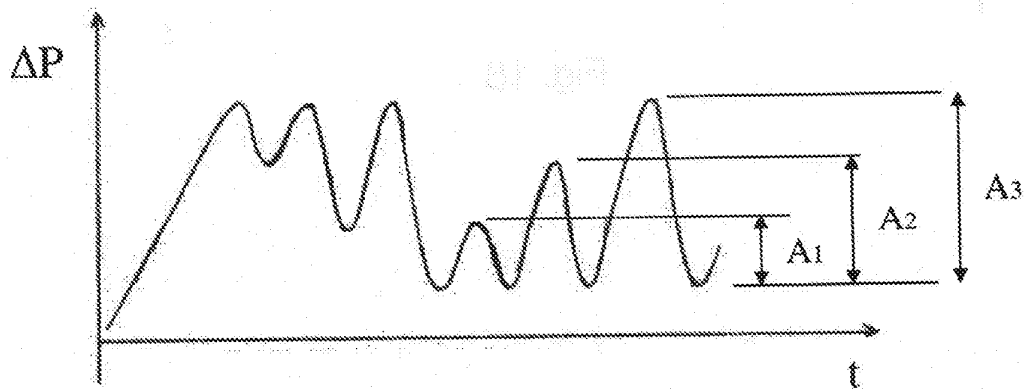


Fig. 16

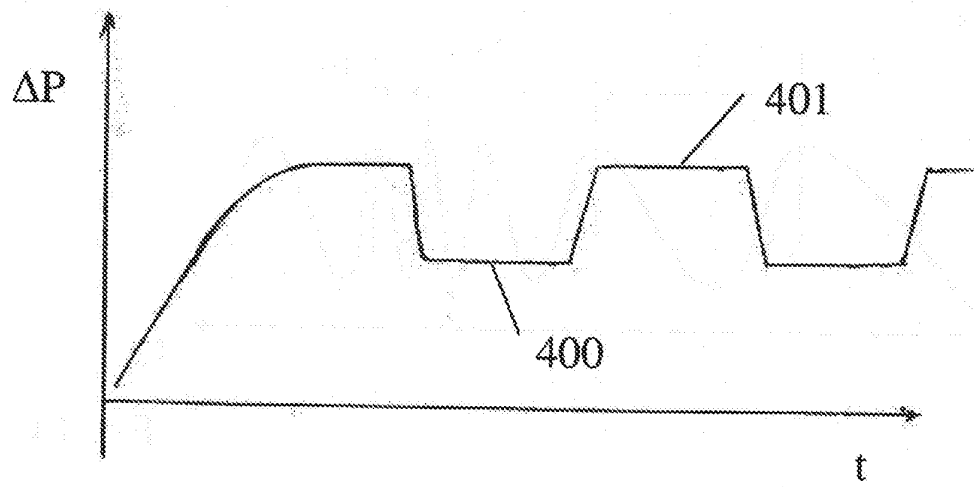


Fig. 17

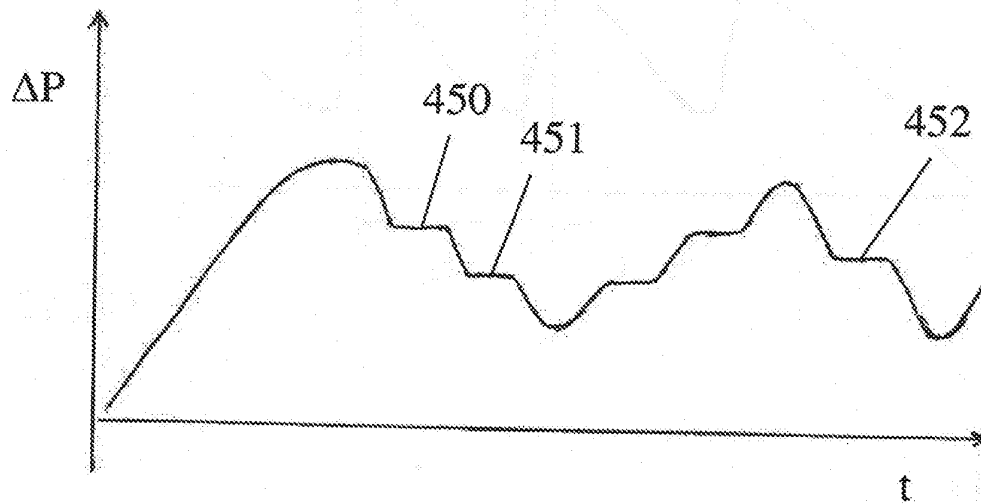


Fig. 18

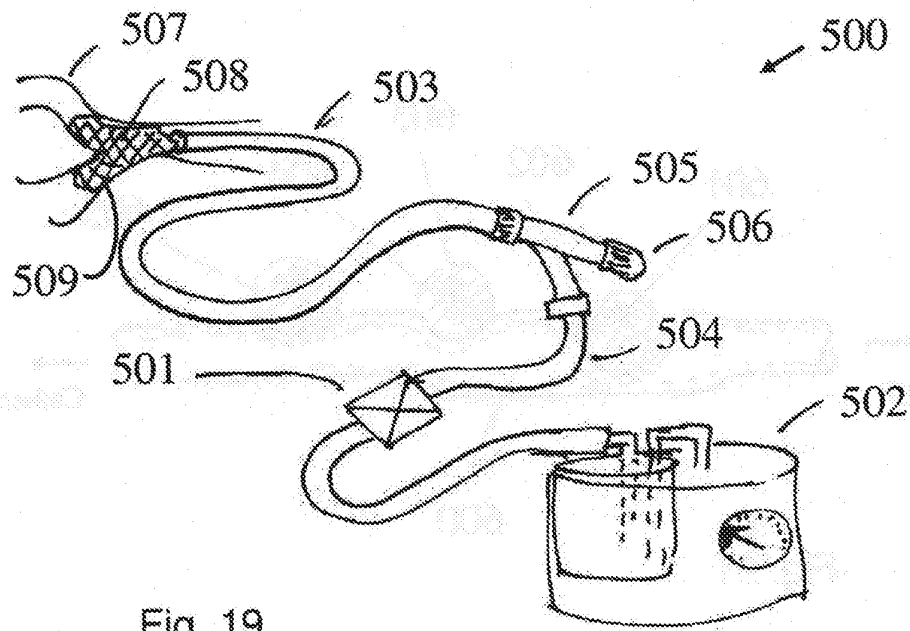


Fig. 19

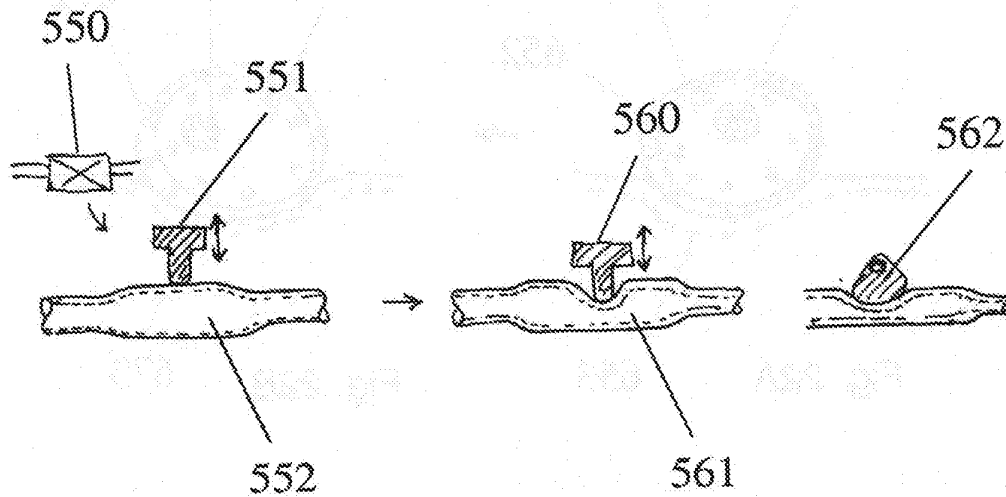


Fig. 20A

Fig. 20B

Fig. 20C

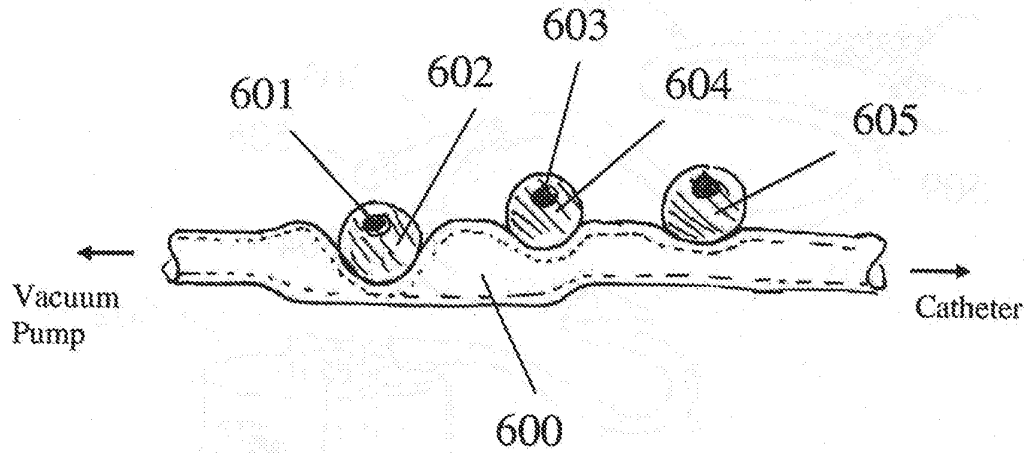


Fig. 21

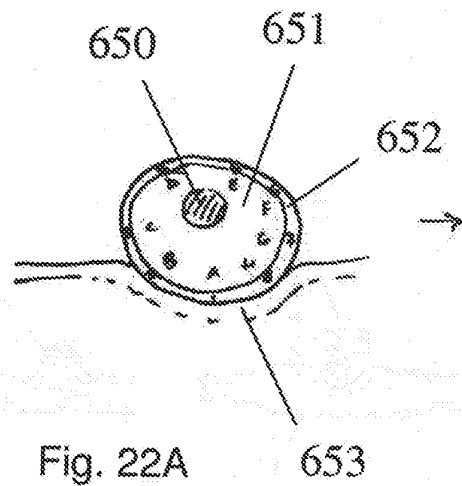


Fig. 22A

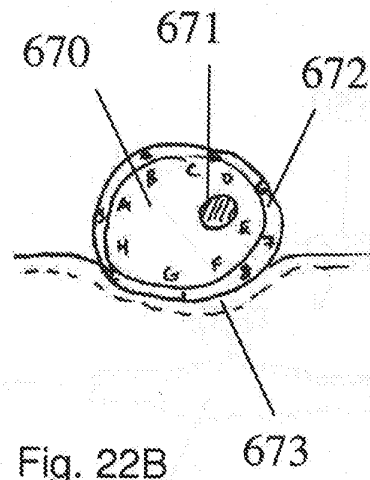


Fig. 22B

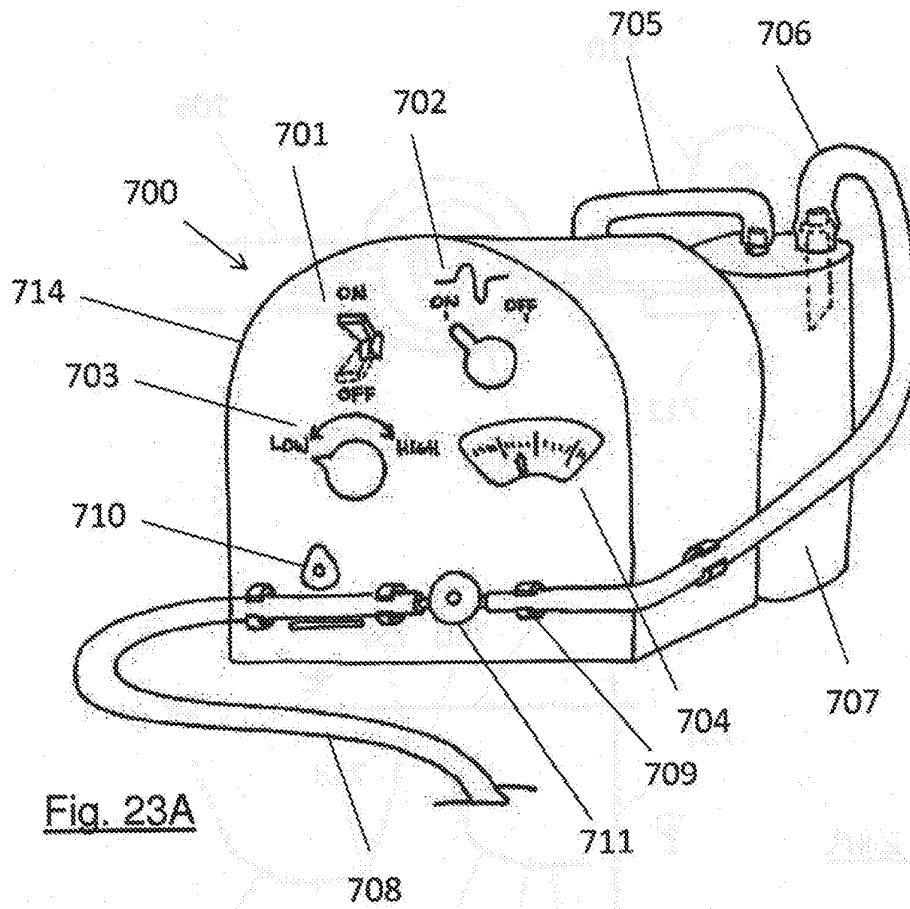


Fig. 23A

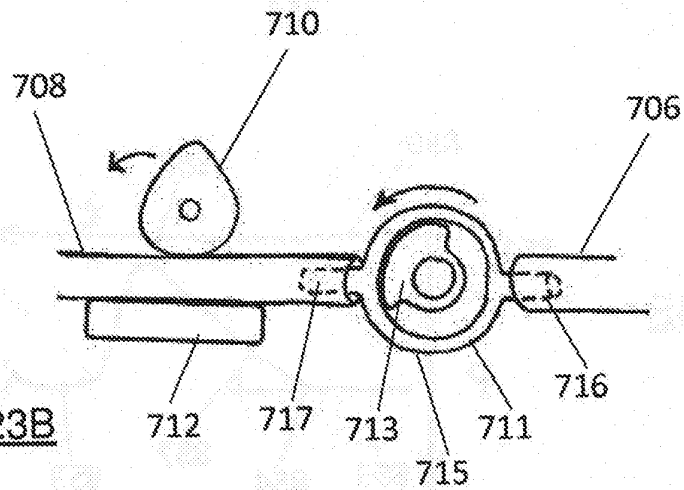
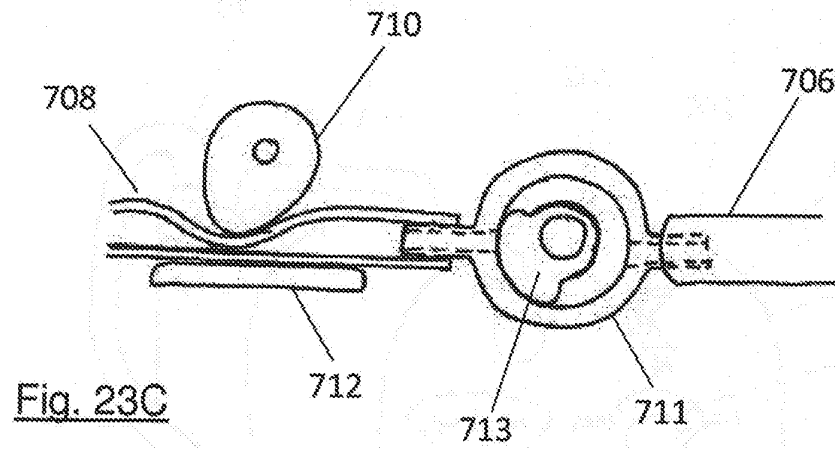
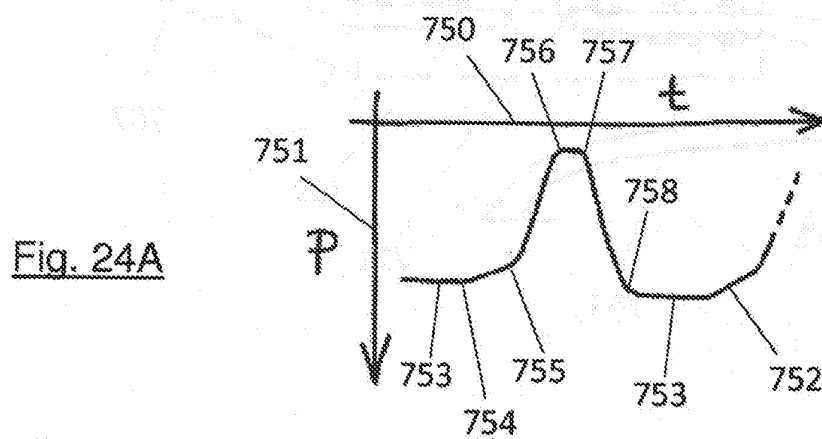
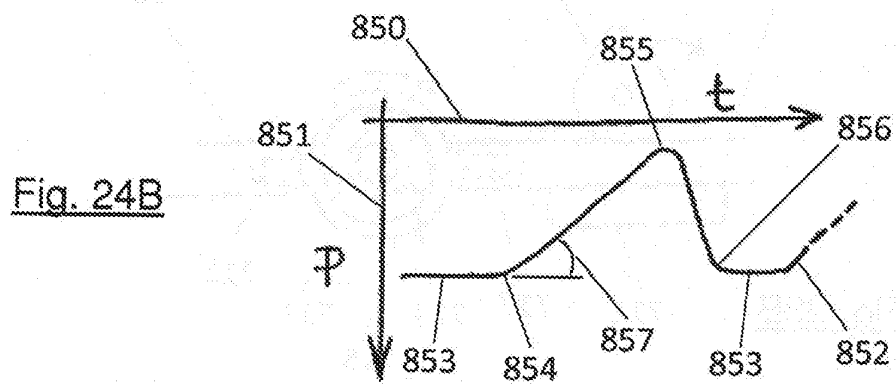


Fig. 23B



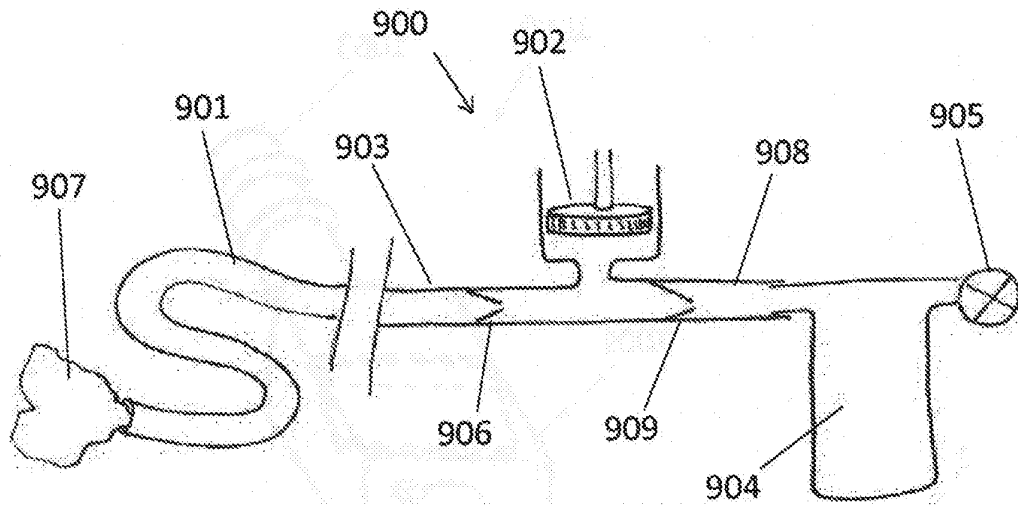


Fig. 25

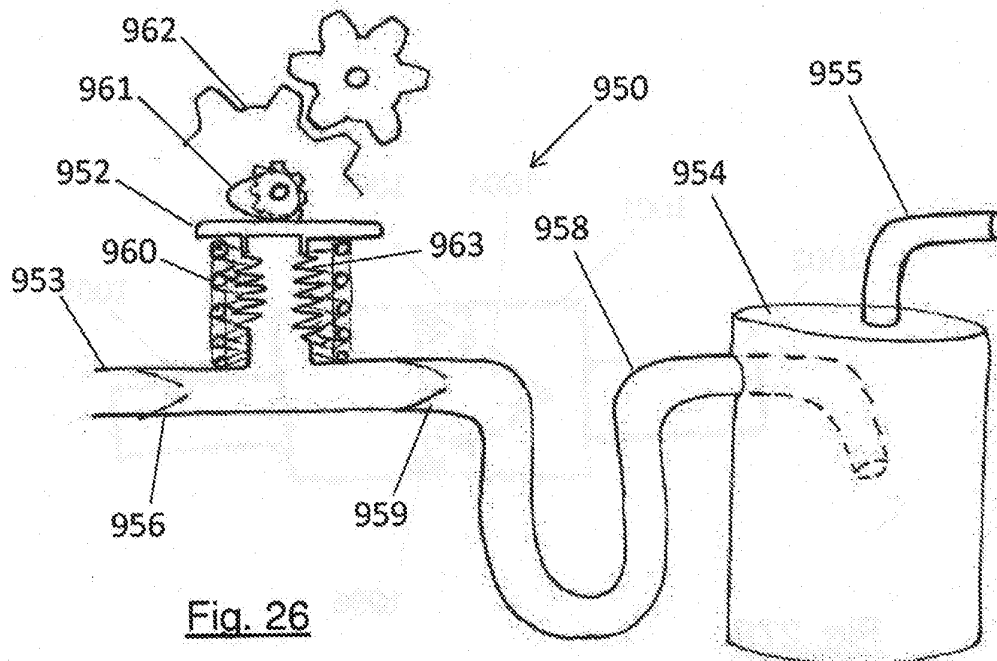
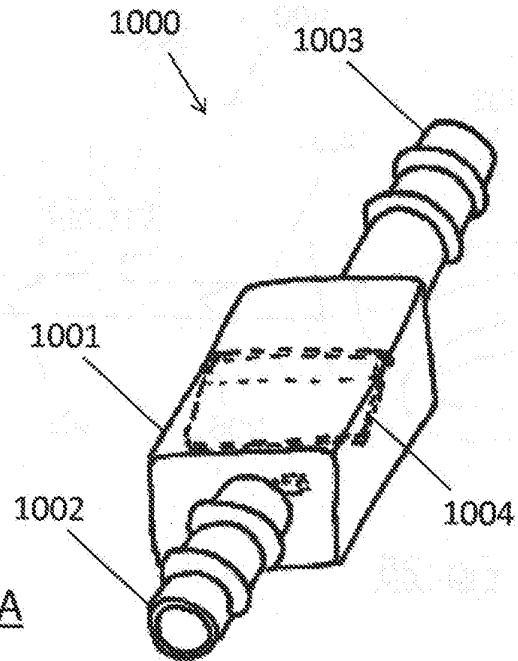
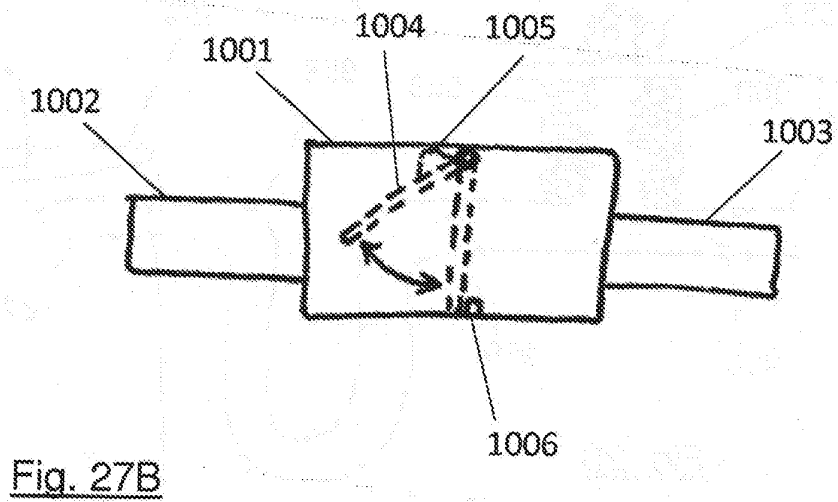


Fig. 26



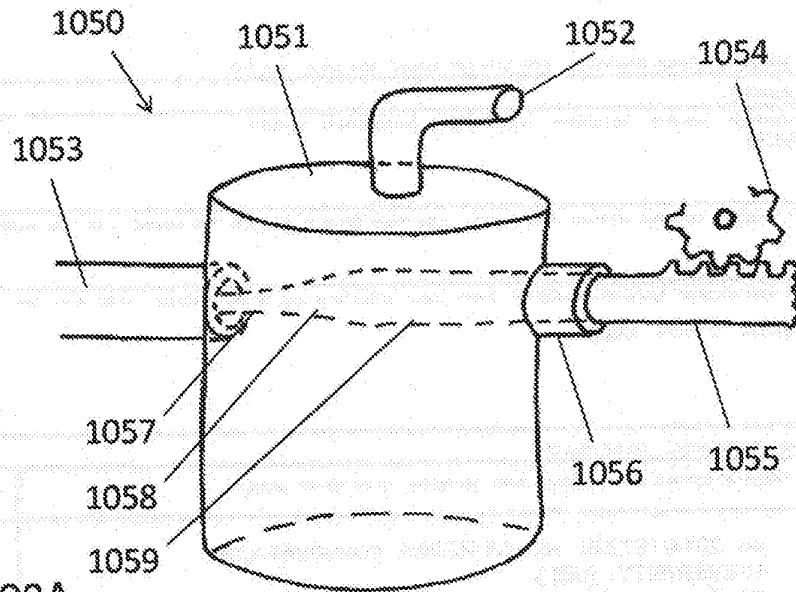


Fig. 28A

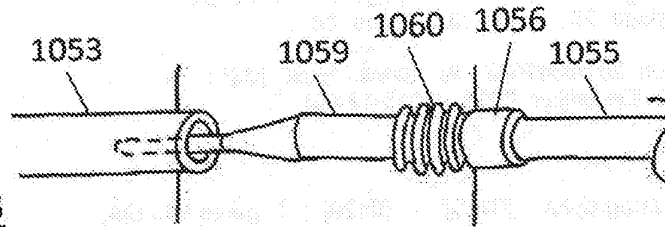


Fig. 28B

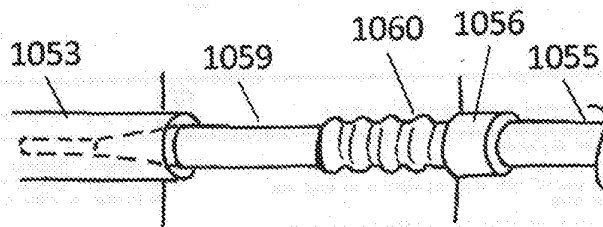


Fig. 28C

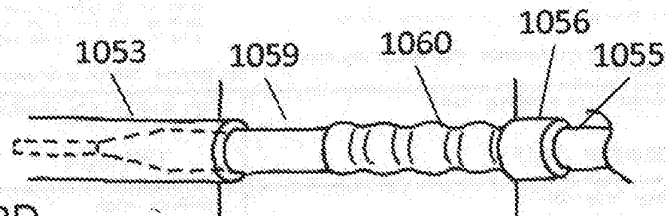


Fig. 28D

INTERNATIONAL SEARCH REPORT

International application No

PCT/EP2017/068759

<p>A. CLASSIFICATION OF SUBJECT MATTER</p> <p>INV. A61B17/22 A61M1/00</p> <p>ADD.</p>		
<p>According to International Patent Classification (IPC) or to both national classification and IPC</p>		
<p>B. FIELDS SEARCHED</p> <p>Minimum documentation searched (classification system followed by classification symbols)</p> <p>A61B A61M</p>		
<p>Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched</p>		
<p>Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)</p> <p>EPO-internal , WPI Data</p>		
<p>C. DOCUMENTS CONSIDERED TO BE RELEVANT</p>		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>WO 2014/151209 AI (VIRGINIA COMMONWEALTH UNIVERSITY [US])</p> <p>25 September 2014 (2014-09-25)</p> <p>page 2, line 24 - page 4, line 12; figures 2A-3C, 6-10, 11B, 11C</p> <p>page 7, line 13 - page 13, line 12</p> <p>page 13, line 19 - page 21, line 22</p> <p>page 25, line 23 - line 24</p> <p>-----</p>	<p>1-5 ,</p> <p>14-22 ,</p> <p>32-59 , 64</p>
X	<p>US 2015/342682 AI (BOWE WADE [US])</p> <p>3 December 2015 (2015-12-03)</p> <p>-----</p> <p>paragraphs [0110] - [0120] ; figures 4, 12A, 12B</p> <p>-----</p> <p>-/-</p>	<p>1, 2, 4, 5 ,</p> <p>14-19 ,</p> <p>32-42 ,</p> <p>56, 64,</p> <p>75-77</p>
<p>☒ Further documents are listed in the continuation of Box C. ☒ See patent family annex.</p>		
<p>* Special categories of cited documents:</p> <p>"A" document defining the general state of the art which is not considered to be of particular relevance</p> <p>"E" earlier application or patent but published on or after the international filing date</p> <p>"L" document which may throw doubts on priority claim(s) which is cited to establish the publication date of another claim or other special reason (as specified)</p> <p>"O" document referring to an oral disclosure, use, exhibition, or other means</p> <p>"P" document published prior to the international filing date but later than the priority date claimed</p> <p>"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</p> <p>"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</p> <p>"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</p> <p>"S" document: member of the same patent family</p>		
<p>Date of the actual completion of the international search</p> <p>12 September 2017</p>		<p>Date of mailing of the international search report</p> <p>17/11/2017</p>
<p>Name and mailing address of the ISA/</p> <p>European Patent Office, P.B. 5518 Patendean 2</p> <p>NL - 2280 HV Rijswijk</p> <p>Tel. (+31-70) 340-2040,</p> <p>Fax: (+31-70) 340-3016</p>		<p>Authorized officer</p> <p>Friedrich, Franz</p>

Form PCT/ISA/210 (second sheet) (April 2005)

INTERNATIONAL SEARCH REPORT

International application No
PCT/EP2017/068759

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2016/165265 A1 (NITA HENRY [US]) 16 June 2016 (2015-06-16) paragraphs [0055], [0124] ~ [0138]; figures 8-10 -----	1,2,4, 14,15, 32-38,64
E	WO 2017/147493 A1 (INCEPT LLC [US]) 31 August 2017 (2017-08-31) page 24, paragraph 3 ~ page 26, paragraph 1; figures 13-15 page 30, paragraph 3 ~ page 32, paragraph 4 -----	1,2,4,5, 14-17, 21,22, 32-38, 40,44, 45,49, 55,64, 75-77

INTERNATIONAL SEARCH REPORT

International application No.
PCT/EP2017/068759

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.: 23-31, 65-74
because they relate to subject matter not required to be searched by this Authority, namely:
see FURTHER INFORMATION sheet PCT/ISA/210
2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

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

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

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of additional fees.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ 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.:
1-5, 14-22, 32-59, 64, 75-77

Remark on Protest

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

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

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

1. claims: 1-5, 14-22, 32-59, 64, 75-77

Surgical systems for removing clots using pulsatile vacuum flows

2. claims: 6-13

Peristaltic pumps for generating pulsatile flows

3. claims: 60-63

Clot removal through combined suction/ultrasonic vibration

4. claims: 78-86

Surgical systems for removing clots using pulsatile vacuum flows with two vacuum pulse generators

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box II.

Claims Nos.: 23-31, 65-74

Pursuant to Article 17(2)(a)(i) and Rule 39.1(iv) PCT, the subject-matter of claims 23-31 and 65-74 has not been searched, since it is directed to a method for treatment of the human body by surgery. Independent claims 23 and 65 relate to a "method for removing occlusive clot from a blood vessel". Thus, no examination is carried out for claims 23-31 and 65-74 (Article 34(4)(a)(i) and Rule 67.1(iv) PCT).

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/EP2017/068759

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 2014151209	A1	25-09-2014	NONE
US 2015342682	A1	03-12-2015	NONE
US 2016166265	A1	16-06-2016	NONE
WO 2017147493	A1	31-08-2017	US 2017238950 A1 24-08-2017
			US 2017238951 A1 24-08-2017
			US 2017238953 A1 24-08-2017
			US 2017239440 A1 24-08-2017
			US 2017239441 A1 24-08-2017
			US 2017239447 A1 24-08-2017
			US 2017252536 A1 07-09-2017
			WO 2017147493 A1 31-08-2017

Form PCT/ISA/210 (patent family annex) (April 2006)

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100	1130	1130	1130	1130	1130



(51) International Patent Classification:

A61B 17/00 (2006.01) A61M 25/01 (2006.01)
A61M 25/00 (2006.01) A61M 29/00 (2006.01)

(21) International Application Number:

PCT/US2017/019453

(22) International Filing Date:

24 February 2017 (24.02.2017)

(25) Filing Language:

English

(26) Publication Language:

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(30) Priority Data:

62/299,418 24 February 2016 (24.02.2016) US
62/443,595 6 January 2017 (06.01.2017) US

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(81) Designated States (unless otherwise indicated, for every

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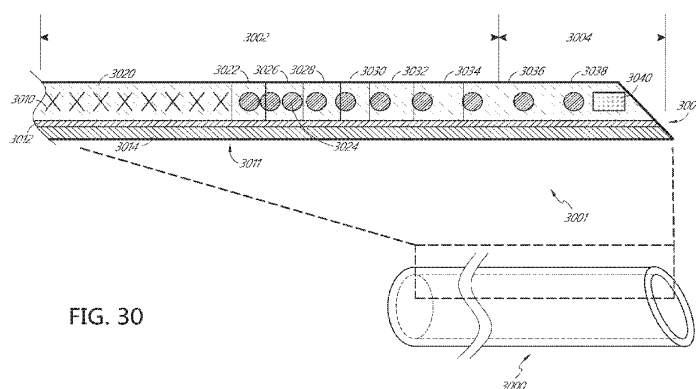


FIG. 30

(57) Abstract: A catheter is provided, such as for distal neurovascular access or aspiration. The catheter includes an elongate flexible body, having a proximal end, a distal end and a side wall defining a central lumen. A distal zone of the side wall includes a tubular inner liner, a tie layer separated from the lumen by the inner liner, a helical coil surrounding the tie layer, adjacent windings of the coil spaced progressively further apart in the distal direction. An outer jacket surrounds the helical coil. The outer jacket is formed from a plurality of tubular segments positioned end to end, coaxially about the coil. The flexural load profile of the catheter as a function of catheter length is configured to provide enhanced distal flexibility while maintaining high backup support.

ENHANCED FLEXIBILITY NEUROVASCULAR CATHETER

Cross-reference to Related Applications

This application claims the benefit of U.S. Provisional Application No. 62/299,418, filed February 24, 2016, and U.S. Provisional Application No. 62/443,595, filed January 6, 2017, the entirety of these applications are hereby incorporated by reference herein.

BACKGROUND OF THE INVENTION

Stroke is the third most common cause of death in the United States and the most disabling neurologic disorder. Approximately 700,000 patients suffer from stroke annually. Stroke is a syndrome characterized by the acute onset of a neurological deficit that persists for at least 24 hours, reflecting focal involvement of the central nervous system, and is the result of a disturbance of the cerebral circulation. Its incidence increases with age. Risk factors for stroke include systolic or diastolic hypertension, hypercholesterolemia, cigarette smoking, heavy alcohol consumption, and oral contraceptive use.

Hemorrhagic stroke accounts for 20% of the annual stroke population. Hemorrhagic stroke often occurs due to rupture of an aneurysm or arteriovenous malformation bleeding into the brain tissue, resulting in cerebral infarction. The remaining 80% of the stroke population are ischemic strokes and are caused by occluded vessels that deprive the brain of oxygen-carrying blood. Ischemic strokes are often caused by emboli or pieces of thrombotic tissue that have dislodged from other body sites or from the cerebral vessels themselves to occlude in the narrow cerebral arteries more distally. When a patient presents with neurological symptoms and signs which resolve completely within 1 hour, the term transient ischemic attack (TIA) is used. Etiologically, TIA and stroke share the same pathophysiologic mechanisms and thus represent a continuum based on persistence of symptoms and extent of ischemic insult.

Emboli occasionally form around the valves of the heart or in the left atrial appendage during periods of irregular heart rhythm and then are dislodged and follow the blood flow into the distal regions of the body. Those emboli can pass to the brain and cause an embolic stroke. As will be discussed below, many such occlusions occur in the middle cerebral artery (MCA), although such is not the only site where emboli come to rest.

When a patient presents with neurological deficit, a diagnostic hypothesis for the cause of stroke can be generated based on the patient's history, a review of stroke risk factors, and a neurologic examination. If an ischemic event is suspected, a clinician can tentatively assess whether the patient has a cardiogenic source of emboli, large artery extracranial or intracranial disease, small artery intraparenchymal disease, or a hematologic or other systemic disorder. A head CT scan is often performed to determine whether the patient has suffered an ischemic or hemorrhagic insult. Blood would be present on the CT scan in subarachnoid hemorrhage, intraparenchymal hematoma, or intraventricular hemorrhage.

Traditionally, emergent management of acute ischemic stroke consisted mainly of general supportive care, e.g. hydration, monitoring neurological status, blood pressure control, and/or anti-platelet or anti-coagulation therapy. In 1996, the Food and Drug Administration approved the use of Genentech Inc.'s thrombolytic drug, tissue plasminogen activator (t-PA) or Activase®, for treating acute stroke. A randomized, double-blind trial, the National Institute of Neurological Disorders and t-PA Stroke Study, revealed a statistically significant improvement in stroke scale scores at 24 hours in the group of patients receiving intravenous t-PA within 3 hours of the onset of an ischemic stroke. Since the approval of t-PA, an emergency room physician could, for the first time, offer a stroke patient an effective treatment besides supportive care.

However, treatment with systemic t-PA is associated with increased risk of intracerebral hemorrhage and other hemorrhagic complications. Patients treated with t-PA were more likely to sustain a symptomatic intracerebral hemorrhage during the first 36 hours of treatment. The frequency of symptomatic hemorrhage increases when t-PA is administered beyond 3 hours from the onset of a stroke. Besides the time constraint in using t-PA in acute ischemic stroke, other contraindications include the following: if the patient has had a previous stroke or serious head trauma in the preceding 3 months, if the patient has a systolic blood pressure above 185 mm Hg or diastolic blood pressure above 110 mmHg, if the patient requires aggressive treatment to reduce the blood pressure to the specified limits, if the patient is taking anticoagulants or has a propensity to hemorrhage, and/or if the patient has had a recent invasive surgical procedure. Therefore, only a small percentage of selected stroke patients are qualified to receive t-PA.

Obstructive emboli have also been mechanically removed from various sites in the vasculature for years. Mechanical therapies have involved capturing and removing the clot, dissolving the clot, disrupting and suctioning the clot, and/or creating a flow channel through the clot. One of the first mechanical devices developed for stroke treatment is the MERCI Retriever System (Concentric Medical, Redwood City, Calif.). A balloon-tipped guide catheter is used to access the internal carotid artery (ICA) from the femoral artery. A microcatheter is placed through the guide catheter and used to deliver the coil-tipped retriever across the clot and is then pulled back to deploy the retriever around the clot. The microcatheter and retriever are then pulled back, with the goal of pulling the clot, into the balloon guide catheter while the balloon is inflated and a syringe is connected to the balloon guide catheter to aspirate the guide catheter during clot retrieval. This device has had initially positive results as compared to thrombolytic therapy alone.

Other thrombectomy devices utilize expandable cages, baskets, or snares to capture and retrieve clot. Temporary stents, sometimes referred to as stentriever or revascularization devices, are utilized to remove or retrieve clot as well as restore flow to the vessel. A series of devices using active laser or ultrasound energy to break up the clot have also been utilized. Other active energy devices have been used in conjunction with intra-arterial thrombolytic infusion to accelerate the dissolution of the thrombus. Many of these devices are used in conjunction with aspiration to aid in the removal of the clot and reduce the risk of emboli. Suctioning of the clot has also been used with single-lumen catheters and syringes or aspiration pumps, with or without adjunct disruption of the clot. Devices which apply powered fluid vortices in combination with suction have been utilized to improve the efficacy of this method of thrombectomy. Finally, balloons or stents have been used to create a patent lumen through the clot when clot removal or dissolution was not possible.

Notwithstanding the foregoing, there remains a need for new devices and methods for treating vasculature occlusions in the body, including acute ischemic stroke and occlusive cerebrovascular disease.

SUMMARY OF THE INVENTION

There is provided in according with one aspect, a telescoping catheter, comprising: an elongate, flexible tubular body, comprising a proximal section having at least one lumen and

a distal section axially movably positioned within the lumen; and a control for advancing the distal section from a first, proximally retracted position within the proximal section to a second, extended position, extending distally beyond the proximal section; and an active tip on the distal end of the distal section, comprising a distal opening that is movable between a smaller and a larger configuration.

In one aspect of present disclosure, the control comprises a pull wire extending through the proximal section. In another aspect of present disclosure, the distal section is distally advanceable to extend beyond the proximal section for a distance of at least about 10 cm. In yet another aspect of present disclosure, the distal section is distally advanceable to extend beyond the proximal section for a distance of at least about 25 cm.

In one aspect of present disclosure, the distal opening is movable in response to movement of a control wire. In another aspect of present disclosure, the distal opening is movable between a smaller and a larger configuration in response to application of vacuum to the lumen. In yet another aspect of present disclosure, the size of the distal opening is changed by lateral movement of a side wall on the distal section. In yet another aspect of present disclosure, the distal opening comprises at least one movable jaw. In another aspect of present disclosure, the distal end of the distal section comprises a duck bill valve configuration.

In one aspect of present disclosure, the telescoping catheter may further comprise a controller for applying intermittent vacuum to the lumen. The controller may be configured to apply pulses of vacuum to the lumen spaced apart by spaces of neutral pressure. The controller may be configured to alternate between applying pulses of higher negative pressure and lower negative pressure. The distal tip of the catheter may axially reciprocate in response to application of pulses of vacuum to the lumen.

In accordance with one aspect, there is provided a system for aspirating a vascular occlusion from a remote site, comprising: an elongate, flexible tubular body, comprising at least one central lumen extending along its longitudinal length; an agitator extendable through the central lumen of the tubular body to position a distal end of the agitator near a distal end of the tubular body; a driver connectable to a proximal end of the agitator and

configured to actuate the agitator; and a vacuum port near the proximal end of the tubular body and in fluid communication with the central lumen of the tubular body.

In one aspect of present disclosure, the agitator comprises an elongate tube. The agitator may comprise a wire extending through the elongate tube and having at least one bend near its distal end. In another aspect of present disclosure, the agitator comprises a proximal end, a distal end, and a loop at the distal end. In yet another aspect of present disclosure, the driver is configured to rotate the agitator cyclically in alternating directions.

In one aspect of present disclosure, the agitator comprises: at least one lumen along its longitudinal length, an influent port near its proximal end configured to allow fluid communication between the lumen of the agitator and a source of media, and at least one effluent port configured to allow fluid communication between the lumen of the agitator and the central lumen of the tubular body. The system for aspirating a vascular occlusion may further comprise a control, for expressing media from the effluent port of the agitator into the central lumen of the tubular body. The distal portion of the tubular body may be configured to vibrate in a transverse direction in response to the injection of media.

In one aspect of present disclosure, the system for aspirating a vascular occlusion further comprises a controller for applying a pulsatile vacuum cycle to the central lumen. In another aspect of present disclosure, the system for aspirating a vascular occlusion further comprises a rotating hemostasis valve coupled to the proximal end of the tubular body, the rotating hemostasis valve comprising: at least one main lumen along its longitudinal length, through which the proximal portion of the agitator is configured to pass, and an aspiration lumen bifurcating from the main lumen and provided with a vacuum port. In yet another aspect of present disclosure, the system further comprises a proximal drive assembly coupled to the proximal end of the tubular body, the proximal drive assembly comprising: at least one main lumen along its longitudinal length for receiving the agitator; a media injection port, into which media is injected, in fluid communication with the central lumen of the tubular body, and a proximal drive connection at the proximal end, which operably connects between the agitator and the driver.

In accordance with one aspect, there is provided an enhanced flexibility neurovascular catheter, comprising: an elongate flexible body, having a proximal end, a distal end and a

side wall defining a central lumen, a distal zone of the side wall comprising: a tubular inner liner; a soft tie layer separated from the lumen by the inner liner; a helical coil surrounding the tie layer, adjacent windings of the coil spaced progressively further apart in the distal direction; and an outer jacket surrounding the helical coil, the outer jacket formed from a plurality of tubular segments positioned coaxially about the coil; wherein a proximal one of the tubular segments has a durometer of at least about 60D and a distal one of the tubular segments has a durometer of no more than about 35D. In one aspect of present disclosure, the tubular liner is formed by dip coating a removable mandrel. In another aspect of present disclosure, the tubular liner comprises PTFE.

In yet another aspect of present disclosure, the tie layer comprises polyurethane. The tie layer may have a wall thickness of no more than about 0.005 inches and may extend along at least the most distal 20 cm of the flexible body. In one aspect of present disclosure, the coil comprises a shape memory material. The coil may comprise Nitinol, and the Nitinol may comprise an Austenite state at body temperature.

In one aspect of present disclosure, the outer jacket is formed from at least five discrete tubular segments. The outer jacket may be formed from at least nine discrete tubular segments. The difference in durometer between a proximal one of the tubular segments and a distal one of the tubular segments may be at least about 20D. The difference in durometer between a proximal one of the tubular segments and a distal one of the tubular segments may be at least about 30D.

In another aspect of present disclosure, the enhanced flexibility neurovascular catheter, further comprises a tension support for increasing the tension resistance in the distal zone. The tension support may comprise a filament and may comprise an axially extending filament. The axially extending filament may be carried between the inner liner and the helical coil. The axially extending filament may increase the tensile strength to at least about 5 pounds.

In accordance with one aspect, there is provided an enhanced flexibility neurovascular catheter, comprising: an elongate flexible body, having a proximal end, a distal end and a side wall defining a central lumen, a distal zone of the side wall comprising: an outer jacket surrounding a helical coil, the outer jacket formed from a plurality of tubular segments

positioned coaxially about the coil; wherein a proximal one of the tubular segments has a durometer of at least about 60D and a distal one of the tubular segments has a durometer of no more than about 35D; and an axially extending filament within the side wall, extending at least about the most distal 10 cm of the length of the catheter. The filament may extend at least about the most distal 15 cm of the length of the catheter. The filament may extend at least about the most distal 20 cm of the length of the catheter. The filament may comprise multiple fibers and may extend axially in between the coil and the inner liner.

In one aspect of present disclosure, the side wall further comprises: a tubular inner liner; a soft tie layer separated from the lumen by the inner liner; wherein the helical coil surrounds the tie layer, and adjacent windings of the coil are spaced progressively further apart in the distal direction. The tubular liner may be formed by dip coating a removable mandrel and may comprise PTFE. The tie layer may comprise polyurethane and may have a wall thickness of no more than about 0.005 inches. The tie layer may extend along at least the most distal 20 cm of the flexible body. The coil may comprise a shape memory material and may comprise Nitinol. The Nitinol may comprise an Austenite state at body temperature.

In one aspect of present disclosure, the outer jacket may be formed from at least five discrete tubular segments. In another aspect of present disclosure, the outer jacket may be formed from at least nine discrete tubular segments. The difference in durometer between a proximal one of the tubular segments and a distal one of the tubular segments may be at least about 20D. The difference in durometer between a proximal one of the tubular segments and a distal one of the tubular segments may be at least about 30D. In another aspect of present disclosure, the catheter can withstand at least about 3.5 pounds tension before failure. In yet another aspect, the catheter can withstand at least about 5 pounds tension before failure.

In accordance with one aspect, there is provided a method of making a high flexibility distal zone on a neurovascular catheter, comprising the steps of: dip coating a removable mandrel to form a tubular inner layer on the mandrel; coating the tubular inner layer with a soft tie layer; applying a helical coil to the outside of the tie layer; positioning a plurality of tubular segments on the helical coil; the plurality of segments having durometers that decrease in a distal direction; heating the tubular segments to form the high flexibility distal zone on the neurovascular catheter; and removing the mandrel. In one aspect of present

disclosure, removing the mandrel step includes axially elongating the mandrel. In another aspect of present disclosure, the method of making a high flexibility distal zone on a neurovascular catheter comprises positioning at least seven segments on the helical coil. In yet another aspect of present disclosure, the method of making a high flexibility distal zone on a neurovascular catheter comprises positioning at least nine segments on the helical coil.

In one aspect of present disclosure, the difference in durometer between a proximal one of the tubular segments and a distal one of the tubular segments is at least about 20D. The difference in durometer between a proximal one of the tubular segments and a distal one of the tubular segments may be at least about 30D. The tubular inner layer may comprise PTFE. In another aspect of present disclosure, the tie layer comprises polyurethane. The tie layer may have a wall thickness of no more than about 0.005 inches. The tie layer may extend along at least the most distal 20 cm of the flexible body.

In one aspect of present disclosure, the coil comprises a shape memory material. The coil may comprise Nitinol. The Nitinol may comprise an Austenite state at body temperature. In another aspect of present disclosure, the method of making a high flexibility distal zone on a neurovascular catheter further comprises the step of positioning at least one tensile strength enhancing filament in between the coil and the tie layer prior to heat shrinking the tubular segments. The filament may extend along at least about the most distal 15 cm of the length of the catheter. The filament may extend along at least about the most distal 20 cm of the length of the catheter. The filament may comprise multiple fibers. In yet another aspect of present disclosure, the method of making a high flexibility distal zone on a neurovascular catheter further comprises the step of positioning at least one tensile strength enhancing filament over the tie layer before the applying a helical coil step.

In accordance with one aspect, there is provided a neurovascular catheter, comprising: an elongate flexible tubular body, having a proximal end, a distal end and a side wall defining a central lumen, a distal zone of the tubular body comprising: a tubular inner liner; a tie layer separated from the lumen by the inner liner; a helical coil surrounding the tie layer, adjacent windings of the coil spaced progressively further apart in the distal direction; an outer jacket surrounding the helical coil, and an opening at the distal end which is enlargeable from a first inside diameter for transluminal navigation to a second, larger inside diameter to facilitate

aspiration of thrombus into the lumen. In one aspect of present disclosure, the distal opening is enlargeable in response to exposure to blood. In another aspect of present disclosure, the distal opening is enlargeable in response to exposure to body temperature. In yet another aspect of present disclosure, the distal opening is enlargeable in response to removal of a constraint. The constraint may comprise a polymer having a structural integrity that decreases in the intravascular environment.

In one aspect of present disclosure, the catheter body adjacent the distal opening comprises a radially outwardly biased embedded support. The catheter body adjacent the distal opening may comprise an embedded Nitinol frame. The support may comprise a wire mesh. The support may comprise a stent. In another aspect of present disclosure, the catheter body adjacent the distal opening comprises a hydrophilic blend. In yet another aspect of present disclosure, the tubular liner is formed by dip coating a removable mandrel. The tubular liner may comprise PTFE.

In one aspect of present disclosure, the tie layer comprises polyurethane. The tie layer may have a wall thickness of no more than about 0.005 inches. The tie layer may extend along at least the most distal 20 cm of the flexible body. In another aspect of present disclosure, the coil comprises a shape memory material. The coil may comprise Nitinol. The Nitinol may comprise an Austenite state at body temperature. In one aspect of present disclosure, the outer jacket is formed from at least five discrete tubular segments. The outer jacket may be formed from at least nine discrete tubular segments. The difference in durometer between a proximal one of the tubular segments and a distal one of the tubular segments may be at least about 20D. The difference in durometer between a proximal one of the tubular segments and a distal one of the tubular segments may be at least about 30D.

In accordance with one aspect, there is provided a neurovascular catheter extension segment, comprising: an elongate flexible control wire, having a proximal end and a distal end; a tubular extension segment having a side wall defining a central lumen carried by the distal end of the control wire, the side wall comprising: a tubular inner liner; a tie layer separated from the lumen by the inner liner; a helical coil surrounding the tie layer; and an outer jacket surrounding the helical coil. In one aspect of present disclosure, the outer jacket is formed from a plurality of tubular segments positioned coaxially about the coil. A

proximal one of the tubular segments may have a durometer of at least about 60D, and a distal one of the tubular segments may have a durometer of no more than about 35D.

In another aspect of present disclosure, the tubular liner is formed by dip coating a removable mandrel. The tubular liner may comprise PTFE. In yet another aspect of present disclosure, the tie layer comprises polyurethane. The tie layer may have a wall thickness of no more than about 0.005 inches. The tie layer may extend along at least the most distal 20 cm of the tubular extension segment. In one aspect of present disclosure, the coil comprises a shape memory material. The coil may comprise Nitinol. The Nitinol may comprise an Austenite state at body temperature.

In one aspect of present disclosure, the outer jacket is formed from at least five discrete tubular segments. The outer jacket may be formed from at least nine discrete tubular segments. The difference in durometer between a proximal one of the tubular segments and a distal one of the tubular segments may be at least about 20D. The difference in durometer between a proximal one of the tubular segments and a distal one of the tubular segments may be at least about 30D. In another aspect of present disclosure, the control wire comprises a central lumen. The control wire central lumen may be in communication with the central lumen of the tubular extension segment. In yet another aspect of present disclosure, the inside diameter of the neurovascular catheter extension segment is at least 2X the inside diameter of the control wire central lumen. The inside diameter of the neurovascular catheter extension segment may be at least 3X the inside diameter of the control wire central lumen.

In accordance with another aspect, there is provided a neurovascular catheter extension segment system, comprising the neurovascular catheter extension segment described above and an agitator configured to extend through the control wire central lumen and into the central lumen of the tubular extension segment.

Any feature, structure, or step disclosed herein can be replaced with or combined with any other feature, structure, or step disclosed herein, or omitted. Further, for purposes of summarizing the disclosure, certain aspects, advantages, and features of the embodiments have been described herein. It is to be understood that not necessarily any or all such advantages are achieved in accordance with any particular embodiment disclosed herein. No individual aspects of this disclosure are essential or indispensable. Further features and

advantages of the embodiments will become apparent to those of skill in the art in view of the Detailed Description which follows when considered together with the attached drawings and claims.

BRIEF DESCRIPTION OF THE DRAWINGS

FIG. 1 is a side elevational schematic view of an intracranial aspiration catheter in accordance with the present invention, with a distal segment in a proximally retracted configuration.

FIG. 2 is a side elevational view as in FIG. 1, with the distal segment in a distally extended configuration.

FIGS. 3A–3B are cross-sectional elevational views of a distal end of catheter 10, with the distal section 34 fully extended.

FIGS. 4A–4C schematically illustrate different cutting tip configurations.

FIGS. 4D–4E and 4J–4K schematically illustrate a distal dynamic funnel tip configuration.

FIGS. 4F–4G illustrate a dynamic flared tip having a first restraint system.

FIGS. 4H–4I illustrate a dynamic flared tip having an alternative restraint system.

FIG. 5 depicts cerebral arterial vasculature including the Circle of Willis, and an access catheter positioned at an occlusion in the left carotid siphon artery.

FIGS. 6 through 9 show a sequence of steps involved in positioning of the catheter and aspirating obstructive material from the middle cerebral artery.

FIG. 10 illustrates removal of the catheter following aspiration of obstructive material.

FIGS. 11A–11F depict a sequence of steps to access a neurovascular occlusion for aspiration.

FIGS. 12A–12F depict an alternative sequence of steps in accordance with an aspect of the present invention involved in accessing a neurovascular occlusion for aspiration.

FIG. 13 illustrates an aspiration system configured to apply pulsatile negative pressure through the aspiration catheter.

FIG. 14 illustrates an alternative aspiration system configured to apply pulsatile negative pressure through the aspiration catheter.

FIG. 15 illustrates a further alternative aspiration system configured to apply mechanical vibration through the aspiration catheter.

FIGS. 16 and 17 illustrate a further alternative aspiration system configured to apply mechanical vibration through the aspiration catheter.

FIG. 18 illustrates a further alternative aspiration system having an agitator configured to apply mechanical vibration at a vibration zone on the aspiration catheter.

FIG. 19 depicts a simplified agitator such as a hypo tube supported wire placed in a catheter to create a vibration zone.

FIGS. 20A–20C depict agitators with various distal tip configurations.

FIGS. 20D–20E depict an agitator positioned within a swellable polymer distal funnel tip.

FIGS. 21A–21B illustrate a moving or wiggling distal tip of a catheter in response to activating the agitator.

FIGS. 22A–22B illustrate media injection from a moving or wiggling distal tip of an agitator.

FIGS. 23A–23B illustrate media injection from a distal tip of an agitator to assist aspiration.

FIG. 24 depicts a proximal aspiration port carried by a catheter.

FIGS. 25A–25C depict a pulsed aspiration cycle according to an embodiment.

FIG. 26 depicts a perspective view of a rotating hemostasis valve and a proximal drive assembly.

FIG. 27A illustrates a longitudinal cross-sectional elevational view taken along the line 27A-27A in FIG. 26.

FIG. 27B illustrates an enlarged longitudinal cross-sectional elevational view of the proximal drive assembly 2602 from FIG. 27A.

FIG. 28 depicts a cross-sectional perspective view of the proximal portion of FIG. 26.

FIG. 29 depicts a perspective view of an agitator driver, a proximal drive assembly, and a rotating hemostasis valve.

FIG. 30 illustrates a cross-sectional elevational view of a catheter wall according to an embodiment.

FIG. 31A illustrates a cross-sectional elevational view of a catheter wall according to another embodiment, showing one or more axially extending filaments.

FIG. 31B describes a side elevational view of the catheter of FIG. 31A

FIG. 31C illustrates a cross-sectional view taken along the line C-C of FIG. 31B, showing one or more axially extending filaments.

FIG. 32A depicts a side elevational view of a catheter according to one embodiment.

FIG. 32B describes a cross-sectional elevational view taken along the line A-A of FIG. 32A.

FIG. 32C illustrates a cross-sectional view taken along the line B-B of FIG. 32A.

FIG. 33A depicts a side elevational view of a catheter according to another embodiment.

FIG. 33B describes a cross-sectional elevational view taken along the line A-A of FIG. 33A, showing one or more axially extending filaments.

FIG. 33C illustrates a cross-sectional view taken along the line B-B of FIG. 33A, showing one or more axially extending filaments.

FIG. 34A illustrates a side elevational view of a progressively enhanced flexibility catheter according to an embodiment.

FIG. 34B is a proximal end view of the enhanced flexibility catheter of FIG. 34A.

FIG. 35 illustrates back-up support of the catheter in accordance with the present invention.

FIG. 36 depicts a graph of modulus or durometer of the catheter along the length of the catheter, from the proximal end to the distal end.

FIG. 37 depicts a graph of flexure test profiles of catheters in accordance with the present invention compared with conventional catheters.

FIG. 38 is a side elevational schematic view of a transformable catheter in accordance with the present invention.

FIG. 39 is a cross-sectional view taken along the lines 18-18 of FIG. 38, showing heating elements within the catheter sidewall.

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENT

Referring to FIG. 1, there is disclosed a catheter 10 in accordance with one aspect of the present invention. Although primarily described in the context of an axially extendable distal segment aspiration catheter with a single central lumen, catheters of the present invention can readily be modified to incorporate additional structures, such as permanent or removable column strength enhancing mandrels, two or more lumen such as to permit drug, contrast or irrigant infusion or to supply inflation media to an inflatable balloon carried by the catheter, or combinations of these features, as will be readily apparent to one of skill in the art in view of the disclosure herein. In addition, the present invention will be described primarily in the context of removing obstructive material from remote vasculature in the brain, but has applicability as an access catheter for delivery and removal of any of a variety of diagnostics or therapeutic devices with or without aspiration.

The catheters disclosed herein may readily be adapted for use throughout the body wherever it may be desirable to distally advance a low profile distal catheter segment from a larger diameter proximal segment. For example, axially extendable catheter shafts in accordance with the present invention may be dimensioned for use throughout the coronary and peripheral vasculature, the gastrointestinal tract, the urethra, ureters, Fallopian tubes and other lumens and potential lumens, as well. The telescoping structure of the present invention may also be used to provide minimally invasive percutaneous tissue access, such as for diagnostic or therapeutic access to a solid tissue target (e.g., breast or liver or brain biopsy or tissue excision), delivery of laparoscopic tools or access to bones such as the spine for delivery of screws, bone cement or other tools or implants.

The catheter 10 generally comprises an elongate tubular body 16 extending between a proximal end 12 and a distal functional end 14. The length of the tubular body 16 depends upon the desired application. For example, lengths in the area of from about 120 cm to about 140 cm or more are typical for use in femoral access percutaneous transluminal coronary applications. Intracranial or other applications may call for a different catheter shaft length depending upon the vascular access site, as will be understood in the art.

In the illustrated embodiment, the tubular body 16 is divided into at least a fixed proximal section 33 and an axially extendable and retractable distal section 34 separated at a transition 32.

Referring to FIG. 3A and 3B, there is illustrated a cross-sectional view of the distal segment 34 shown extended distally from the proximal segment 33 in accordance with the present invention. Distal segment 34 extends between a proximal end 36 and a distal end 38 and defines at least one elongate central lumen 40 extending axially therethrough. Distal end 38 may be provided with one or more movable side walls or jaws 39, which move laterally in the direction of an opposing side wall or jaw 41 under the influence of aspiration, to enable the distal end 38 to bite or break thrombus or other material into smaller particles, to facilitate aspiration through lumen 40. Both walls 39 and 41 may be movable towards and away from each other to break up thrombus as is discussed further below. For certain applications, the proximal section 33 may also or alternatively be provided with one or two opposing jaws, also responsive to vacuum or mechanical actuation to break up thrombus.

The inner diameter of the distal section 34 may be between about 0.030 inches and about 0.112 inches, between about 0.040 inches and about 0.102 inches, between about 0.045 inches and about 0.097 inches, between about 0.050 inches and about 0.092 inches, between about 0.055 inches and about 0.087 inches, between about 0.060 inches and about 0.082 inches, between about 0.062 inches and about 0.080 inches, between about 0.064 inches and about 0.078 inches, between about 0.066 inches and about 0.076 inches, between about 0.068 inches and about 0.074 inches, or between about 0.070 inches and about 0.072 inches.

The inner diameter and the outer diameter of the distal section 34 may be constant or substantially constant along its longitudinal length. Alternatively, the distal section 34 may be tapered near its distal end. The distal section 34 may be tapered at less than or equal to about 5cm, about 10cm, about 15cm, about 20cm, about 23cm, about 25cm, about 30cm, about 31cm, about 35cm, about 40cm, about 45cm, about 50cm, about 60cm, or about 70cm from its distal end.

The inner diameter of the distal section 34 may be tapered or decreased near the distal end by less than or equal to about 95%, about 90%, about 85%, about 80%, about 75%, about 70%, about 65%, about 60%, about 55%, about 50%, about 45%, about 40%, about 35%,

about 30%, about 25%, about 20%, about 10%, or about 5%. The inner diameter of the distal section 34 may be tapered or decreased near the distal end by greater than or equal to about 95%, about 90%, about 85%, about 80%, about 75%, about 70%, about 65%, about 60%, about 55%, about 50%, about 45%, about 40%, about 35%, about 30%, about 25%, about 20%, about 10%, or about 5%. The tapered inner diameter of the distal section 34 may be by less than or equal to about 0.11 inches, about 0.1 inches, about 0.090 inches, about 0.080 inches, about 0.070 inches, about 0.065 inches, about 0.060 inches, about 0.055 inches, about 0.050 inches, about 0.045 inches, about 0.040 inches, about 0.035 inches, about 0.030 inches, about 0.025 inches, about 0.020 inches, about 0.015 inches, or about 0.010 inches.

The length of the distal section 34 may be between about 13cm and about 53cm, between about 18cm and about 48cm, between about 23cm and about 43cm, or between about 28cm and about 38cm. The length of the distal section 34 may be less than or equal to about 20cm, about 25cm, about 30cm, about 33cm, about 35cm, about 40cm, about 41cm, about 45cm, about 50cm, about 55cm, about 60cm, about 70cm, or about 80cm. The length of the distal section 34 may depend on the degree of tapering of the internal diameter of the distal section 34.

The proximal end 36 of distal section 34 is provided with a proximally extending pull wire 42. Pull wire 42 extends proximally throughout the length of the tubular body 16, to control 24 which may be carried by manifold 18. Axial movement of control 24 produces a corresponding axial movement of distal section 34 with respect to proximal section 33 as has been discussed. Alternatively, the proximal end of pull wire 42 may exit through a port on manifold 18, such that it may be manually grasped and pulled or pushed by the clinician to extend or retract the distal section 34. The length of the pull wire 42 may be between about 700mm and about 1556mm, between about 800mm and about 1456mm, between about 850mm and about 1406mm, between about 900mm and about 1356mm, between about 950mm and about 1306mm, between about 1000mm and about 1256mm, between about 1020mm and about 1236mm, between about 1040mm and about 1216mm, between about 1060mm and about 1196mm, between about 1080mm and about 1176mm, between about 1100mm and about 1156mm, between about 1110mm and about 1146mm, or between about 1120mm and about 1136mm.

Upon distal advance of pull wire 42 to its limit of travel, an overlap 44 remains between the proximal end 36 of distal section 34 and the proximal section 33. This overlap 44 is configured to provide a seal to enable efficient transmission of vacuum from proximal section 33 to distal section 34. Overlap 44 may be provided with any of a variety of additional features to facilitate a seal, such as a gasket, coating or tightly toleranced sliding fit. Preferably the clearance between the OD of the distal section 34 and ID of the proximal section 33, at least in the vicinity of transition 32, will be no more than about 0.005 inches and preferably no more than about 0.003 inches to provide an effective seal in a blood environment.

Following positioning of the distal end of proximal section 33 within the vasculature, such as within the cervical carotid artery, the control 24 is manipulated to distally advance distal section 34 deeper into the vasculature. For this purpose, the pull wire 42 will be provided with sufficient column strength to enable distal advance of the distal tip 38 as will be discussed below.

The pull wire 42 and distal section 34 may be integrated into a catheter as illustrated in Figures 1 and 2. Alternatively, distal section 34 and pull wire 42 may be configured as a stand-alone catheter extension device as is discussed in greater detail below. The catheter extension device may be introduced into the proximal end of proximal section 33 after placement of proximal section 33 and advanced distally there through as illustrated in Figure 3 A, to telescopically extend the reach of the aspiration system.

Referring to FIG. 3B, the pull wire 42 may comprise a tubular wall having an axially extending central lumen 45. The central lumen 45 permits introduction of media such as lubricants, drugs, contrast agents or others into the distal section 34. In addition, the central lumen 45 extending through pull wire 42 permits introduction of an agitator as is discussed in greater detail below.

Referring to FIGS. 4A through 4C, the distal tip 38 may be provided any of a variety of structures which produce an active movement such as a biting action in response to the application of an activation force such as a vacuum in lumen 40. Alternatively, an axially movable control wire may be connected with respect to a side wall of the distal tip 38, to enable cutting action under positive mechanical force. FIG. 4A illustrates a distal tip 38 in an

open configuration, while FIG. 4B illustrates distal tip 38 with opposing side walls 39 and 41 drawn together by the negative pressure in aspiration lumen 40. This may be accomplished by providing a tapered thickness in side walls 39 and 41, or a groove or living hinge which facilitates lateral movement of at least one of side wall 39 or 41.

Alternatively, referring to FIG. 4C, a pivot point or hinge 43 may be provided to enable lateral movement of side wall 39 to operate as a jaw. Two opposing side walls may be moveable medially and laterally with bilateral symmetry like a duck bill valve. Three or more jaws may be provided, such as three triangular jaws separated at about 120° spacing which under an aspiration pulse close to form a pyramid closed tip.

In some implementations of the present invention, the distal tip 14 is preferably provided with the capability to dilate beyond the nominal diameter of distal section 34. This provides a conical funnel like tip with an enlarged distal opening, to facilitate introduction of thrombotic material into the lumen 40. See FIGS. 4D-4K. The diameter at the distal opening of the fully opened funnel exceeds the diameter of a cylindrical extension of the adjacent tubular body by at least about 10%, preferably at least about 25% or 45% or more. This may be accomplished by providing the distal end 14 with an expandable material, or a plurality of laterally movable jaws or petals such as at least about three or five or six or more petals that are advanceable radially inwardly into a coaptive orientation, and radially outwardly to provide a flared inside diameter of aspiration lumen 40 which increases in the distal direction.

The flexible petals may be retained in a radially inwardly inclined configuration such as by application of negative pressure via lumen 40 during transluminal navigation of the distal section 34. Upon removal of the negative pressure, the panels may incline radially outwardly in response to a preset bias. Application of pulsatile vacuum may thereafter cause the panels to close radially inwardly to perform the biting function described previously.

The distal funnel opening may be actuated in a variety of other ways as will be apparent to those of skill in the art, such as by providing a pull wire or axially slideable outer or inner sleeve to open and close the funnel in response to mechanical movement of the wire or sleeve. Alternatively the funnel opening may be controlled by rotation of a control wire or

tubular sleeve relative to the distal section 34, to activate an iris or spiral mechanism such as a helical ribbon or wire carried by the distal tip.

The normal state of the distal funnel may be a cylindrical configuration, and a mechanical, thermal or electrical actuator may be utilized to enlarge the distal funnel opening. Alternatively, the normal state of the funnel may be conical, and a mechanical, thermal or electrical actuator may be utilized to reduce the diameter such as for transluminal navigation. The petals or other wall of the funnel or elements disposed within the wall of the funnel may comprise a shape memory material such as a shape memory polymer or metal alloy such as nitinol, which may be laser cut from tube stock or woven into a fine mesh. The geometry of the funnel may be transformed by application of heat, such as body heat, or heat from a heat source carried by the catheter such as an electrical resistance wire within the wall or adjacent the catheter tip. Heat may alternatively be applied from a heat source introduced by way of central lumen 40, such as a heated fluid, or a removable heater such as an elongate flexible body carrying a resistance coil. Transformation of the funnel from one configuration to the other may alternatively be accomplished by reducing the temperature of the funnel below body temperature such as by introducing a cooled fluid into thermal communication with the funnel tip or providing the catheter or a removable cooling catheter with a Joule – Thomson expansion chamber located near the distal end.

In an alternate configuration, the sidewall of the funnel is provided with an inflatable balloon in the form of a ring or hoop, in communication with an inflation lumen extending throughout the length of the catheter. Introduction of inflation media inflates the annular balloon, transforming the configuration of the funnel tip from a reduced diameter to an enlarged diameter.

In an alternate configuration, the distal tip is biased into the funnel configuration, and restrained into a cylindrical configuration such as for transluminal navigation. When the funnel tip is desired to be enlarged, the restraint can be removed. The restraint may comprise an outer tubular covering membrane or loop configured to be removed by pulling a pull wire in a proximal direction. Alternatively, the restraint may be a bioabsorbable material, which dissolves following a preset amount of time that exceeds the anticipated time from vascular access to reach the final intravascular position.

Referring to FIGS. 4J– 4K, the distal flared tip may comprise embedded elastic elements (e.g., a coil, struts or cage) such as spring steel, Nitinol or others known in the art that bias the tip into the flared configuration. The elastic elements such as in the form of a Nitinol cage may alternatively reside on the ID of the catheter. The polymer tip restrains the elastic elements to provide a cylindrical exterior configuration for transluminal navigation as seen in FIG. 4J. Softening the polymer (e.g., a hydrophilic blend) such as by body heat or moisture allows the elastic elements to transform the tip into the funnel configuration as seen in FIG. 4K. Alternatively, a conical NiTi cage at the tip is coated with a double hydrophilic non-cross linked glue. As the catheter advances the glue dissolves and gradually flares the tip into a funnel. The polymer tip may be formed without embedded elastic components and instead comprise a coextrusion with multiple layers, varying thickness in multiple layers, blending hydrophilic components at different ratios to control flaring. Multiple axially extending pull wires may be embedded through extruded lumen extending axially throughout the catheter wall. The wires are pushed or pulled to open/close the catheter distal end to flare or collapse. Funnel-shaped, underexpanded NiTi stent can be deployed at the tip area straddling between high and low durometer regions but greater length into high durometer region. Once ready to engage a clot, the stent can be pushed distally further into the low durometer tip. After complete clot retrieval the stent is pulled back into high durometer region, collapsing the funnel. This is an example of an active on-demand funneling tip.

Referring to FIG. 4F, there is illustrated a cross-sectional view of a distal end of a tubular catheter body such as distal section 34. The tubular body is provided with a distal tip 38 in the form of a self expandable (e.g., NiTiNol) mesh 50, constrained by an outer tubular restraint 52. Restraint 52 may comprise a proximately retractable tubular body extending proximally to a control on the proximal manifold; a peel away sheath carried by an elongate proximally retractable pull wire, or other mechanism disclosed elsewhere herein. As shown in FIG 4G, proximal retraction of tubular restraint 52 with respect to tubular body 34, or distal advance of tubular body 34 with respect to restraint 52 exposes and releases the mesh 50 to self expand to a funnel shape to facilitate capture and removal of intravascular debris.

Referring to FIGS. 4H and 4I, the self expandable conical mesh 50 is restrained by interweaving an internal restraint wire 54. Restraint wire 54 may be a procedure guide wire,

or a dedicated restraint wire. Proximal retraction of the restraint wire 54 releases the mesh 50, to self expanded to a final, funnel configuration. Release of the mesh 50 may be accomplished in a variety of alternative ways, such as bio absorbable materials, and electrolytic detachment.

The proximal end 12 of catheter 10 is additionally provided with a manifold 18 having one or more access ports as is known in the art. Generally, manifold 18 is provided with a proximal port such as a guidewire port 20 in an over-the-wire construction, and at least one side port such as aspiration port 22. Alternatively, the aspiration port 22 may be omitted if the procedure involves removal of the guidewire proximally from the guidewire port 20 following placement of the aspiration catheter, and aspiration through the guidewire port. Additional access ports and lumen may be provided as needed, depending upon the functional capabilities of the catheter. Manifold 18 may be injection molded from any of a variety of medical grade plastics, or formed in accordance with other techniques known in the art.

Manifold 18 may additionally be provided with a control 24, for controlling the axial position of the distal segment 34 of the catheter. Control 24 may take any of a variety of forms depending upon the mechanical structure and desired axial range of travel of the distal segment 34. In the illustrated embodiment, control 24 comprises a slider switch which is mechanically axially movably linked to the distal segment such that proximal retraction of the slider switch 24 produces a proximal movement of the distal segment 34. This retracts the distal segment 34 into the proximal section 33 as illustrated in FIG. 1. Distal axial advancement of the slider switch 24 produces a distal axial advance of the distal segment 34, as illustrated in FIGS. 2 and 3.

Any of a variety of controls may be utilized, including switches, buttons, levers, rotatable knobs, pull/push wires, and others which will be apparent to those of skill in the art in view of the disclosure herein. The control will generally be linked to the distal segment by a control wire 42.

Alternatively, the proximal section 33 and distal section 34 maybe provided as separate devices, in which construction the proximal control may be omitted. The distal end of proximal section 33 may be provided with one or more jaws as has been discussed

previously herein, for morcellating or otherwise breaking thrombus or other obstruction into pieces or otherwise facilitating aspiration. The proximal section 33 may additionally be mechanically coupled to or adapted for coupling to a source of vibrational or rotational movement, such as to provide the intermittent or pulsatile movement discussed elsewhere herein to facilitate navigation into the vasculature.

Using axial reciprocation, and/or rotation, and/or biting action of the distal jaws, the clinician may be able to reach the obstruction using proximal section 33. See, for example, FIG. 5 in which proximal section 33 is able to reach an obstruction in the left carotid siphon. If, however, the proximal section 33 is not able to advance sufficiently close to the obstruction, a separate telescoping distal section 34 may be introduced into the proximal section 33 and advanced therethrough and beyond, as illustrated in FIGS. 2 and 6-10, to reach the obstruction.

The cerebral circulation is regulated in such a way that a constant total cerebral blood flow (CBF) is generally maintained under varying conditions. For example, a reduction in flow to one part of the brain, such as in acute ischemic stroke, may be compensated by an increase in flow to another part, so that CBF to any one region of the brain remains unchanged. More importantly, when one part of the brain becomes ischemic due to a vascular occlusion, the brain compensates by increasing blood flow to the ischemic area through its collateral circulation.

FIG. 5 depicts cerebral arterial vasculature including the Circle of Willis. Aorta 100 gives rise to right brachiocephalic artery 82, left common carotid artery (CCA) 80, and left subclavian artery 84. The brachiocephalic artery 82 further branches into right common carotid artery 85 and right subclavian artery 83. The left CCA gives rise to left internal carotid artery (ICA) 90 which becomes left middle cerebral artery (MCA) 97 and left anterior cerebral artery (ACA) 99. Anteriorly, the Circle of Willis is formed by the internal carotid arteries, the anterior cerebral arteries, and anterior communicating artery 91 which connects the two ACAs. The right and left ICA also send right posterior communicating artery 72 and left posterior communicating artery 95 to connect, respectively, with right posterior cerebral artery (PCA) 74 and left PCA 94. The two posterior communicating arteries and PCAs, and

the origin of the posterior cerebral artery from basilar artery 92 complete the circle posteriorly.

When an occlusion occurs acutely, for example, in left carotid siphon 70, as depicted in FIG. 5, blood flow in the right cerebral arteries, left external carotid artery 78, right vertebral artery 76 and left vertebral artery 77 increases, resulting in directional change of flow through the Circle of Willis to compensate for the sudden decrease of blood flow in the left carotid siphon. Specifically, blood flow reverses in right posterior communicating artery 72, right PCA 74, left posterior communicating artery 95. Anterior communicating artery 91 opens, reversing flow in left ACA 99, and flow increases in the left external carotid artery, reversing flow along left ophthalmic artery 75, all of which contribute to flow in left ICA 90 distal the occlusion to provide perfusion to the ischemic area distal to the occlusion.

As illustrated in FIG. 5, the proximal segment of catheter 10 is transluminally navigated along or over the guidewire, to the proximal side of the occlusion. Transluminal navigation may be accomplished with the distal section 34 of the catheter in the first, proximally retracted configuration. This enables distal advance of the proximal section 33 until further progress is inhibited by small and/or tortuous vasculature. Alternatively, the distal section 34 is a separate device, and is not inserted into the proximal section 33 until it is determined that the proximal section 33 cannot safely reach the occlusion. In the example illustrated in FIG. 5, the occlusion may be safely reached by the proximal section 33, without the need to insert or distally extend a distal section 34.

The distal end of the proximal section 33 of aspiration catheter 10 is inserted typically through an incision on a peripheral artery over a guidewire and advanced as far as deemed safe into a more distal carotid or intracranial artery, such as the cervical carotid, terminal ICA, carotid siphon, MCA, or ACA. The occlusion site can be localized with cerebral angiogram or IVUS. In emergency situations, the catheter can be inserted directly into the symptomatic carotid artery after localization of the occlusion with the assistance of IVUS or standard carotid doppler and TCD.

If it does not appear that sufficient distal navigation of the proximal section 33 to reach the occlusion can be safely accomplished, the distal section 34 is inserted into the

proximal port 20 and/or distally extended beyond proximal section 33 until distal tip 38 is positioned in the vicinity of the proximal edge of the obstruction.

Referring to FIG. 6, an obstruction 70 is lodged in the middle cerebral artery 97. Proximal section 33 is positioned in the ICA and not able to navigate beyond a certain point such as at the branch 96 to the MCA artery 97. The proximal section 33 may be provided with a distal section 34 carried there in. Alternatively, a separate distal section 34 may be introduced into the proximal end of proximal section 33 once the determination has been made that the obstruction 70 cannot be reached directly by proximal section 33 alone. As seen in FIGS. 7 and 8, the distal section 34 may thereafter be transluminally navigated through the distal tortuous vasculature between proximal section 33 and the obstruction 70.

Referring to FIG. 9, the obstruction 70 may thereafter be drawn into distal section 34 upon application of constant or pulsatile negative pressure with or without the use of jaws or other activation on the distal end of distal section 34 as discussed elsewhere herein. Once the obstruction 70 has either been drawn into distal section 34, or drawn sufficiently into distal section 34 that it may be proximally withdrawn from the body, proximal section 33 and distal section 34 are thereafter proximally withdrawn.

Aspiration may be applied via lumen 40, either in a constant mode, or in a pulsatile mode. Preferably, pulsatile application of vacuum will cause the distal tip 38 to open and close like a jaw, which facilitates reshaping the thrombus or biting or nibbling the thrombus material into strands or pieces to facilitate proximal withdrawal under negative pressure through lumen 40. Application of aspiration may be accompanied by distal advance of the distal tip 38 into the thrombotic material.

Pulsatile application of a vacuum may oscillate between positive vacuum and zero vacuum, or between a first lower negative pressure and a second higher negative pressure. Alternatively, a slight positive pressure may be alternated with a negative pressure, with the application of negative pressure dominating to provide a net aspiration through the lumen 40. Pulse cycling is discussed in greater detail in connection with FIG. 25.

The proximal manifold and/or a proximal control unit (not illustrated) connected to the manifold may enable the clinician to adjust any of a variety of pulse parameters including

pulse rate, pulse duration, timing between pulses as well as the intensity of the pulsatile vacuum.

The distal section may thereafter be proximally retracted into proximal section 33 and the catheter proximally retracted from the patient. Alternatively, proximal retraction of the catheter 10 may be accomplished with the distal section 34 in the distally extended position. A vasodilator, e.g., nifedipine or nitroprusside, may be injected through a second lumen to inhibit vascular spasm induced as a result of instrumentation.

Pressure may be monitored by a manometer carried by the catheter or a wire positioned in a lumen of the catheter. A pressure control and display may be included in the proximal control unit or proximal end of the catheter, allowing suction within the vessel to be regulated.

Focal hypothermia, which has been shown to be neuroprotective, can be administered by perfusing hypothermic oxygenated blood or fluid. Moderate hypothermia, at approximately 32 to 34°C, can be introduced during the fluid infusion. Perfusion through a port on manifold 18 can be achieved by withdrawing venous blood from a peripheral vein and processing through a pump oxygenator, or by withdrawing oxygenated blood from a peripheral artery, such as a femoral artery, and pumping it back into the carotid artery.

If continuous and/or intermittent suction fails to dislodge the occlusion, a thrombolytic agent, e.g., t-PA, can be infused through central lumen 40 or a second lumen to lyse any thrombotic material with greater local efficacy and fewer systemic complications. Administration of thrombolytic agent, however, may not be recommended for devices which are inserted directly into the carotid artery due to increased risk of hemorrhage.

The intensity of intermittent or pulsatile vacuum applied to lumen 40 may be adjusted to cause the distal tip 38 of the catheter 10 to experience an axial reciprocation or water hammer effect, which can further facilitate both transluminal navigation as well as dislodging or breaking up the obstruction. Water hammer, or more generally fluid hammer, is a pressure surge or wave caused when a fluid in motion is forced to stop or change direction suddenly, creating a momentum change. A water hammer commonly occurs when a valve closes suddenly at the end of a pipeline system, and a pressure wave propagates in the pipe. A pressure surge or wave is generated inside the lumen 40 of the aspiration catheter 10

when a solenoid or valve closes and stops the fluid flow suddenly, or other pulse generator is activated. As the pressure wave propagates in the catheter 10, it causes the catheter 10 to axially vibrate. Since vibration can reduce surface friction between the outer diameter of the catheter 10 and the inner diameter of the vessel wall, it enables catheter to track through tortuous anatomies as well as assist capturing thrombus.

Referring to FIGS. 11A-11F, the cerebral circulation 1100 is simplified for the ease of demonstrating procedural steps. A thrombotic occlusion 1102 is in the right middle cerebral artery (RMCA) 1104. The RMCA 1104 branches from the right internal carotid artery (RICA) 1106. The RICA 1106 branches from the right common carotid artery (RCCA) (not shown). The RICA 1106 comprises cerebral 1108 (most distal from the aorta 100), cavernous 1110, and petrous 1112 (most proximal from the aorta 100) segments. The RCCA branches from the brachiocephalic artery. The brachiocephalic artery branches from the arch 1114 of the aorta 100.

The procedural steps for aspirating a thrombotic occlusion are described as follows. Referring to FIG. 11A, an introducer sheath 1120 is introduced at the femoral artery 1118. The outer diameter of the introducer sheath 1120 may be equal to or less than about 12F, 11F, 10F, 9F, 8F, 7F, or 6F. Then, a guide sheath 1122 is inserted through the introducer sheath 1120. The outer diameter of the guide sheath 1122 may be equal to or less than about 9F, 8F, 7F, 6F, 5F, 4F, or 3F, and the inner diameter of the introducer sheath 1120 may be greater than the outer diameter of the guide sheath 1122.

Referring to FIG. 11B, an insert catheter 1124 is inserted through the guide sheath 1122. The outer diameter of the insert catheter 1124 may be equal to or less than about 9F, 8F, 7F, 6F, 5F, 4F, or 3F, and the inner diameter of the guide sheath 1122 may be greater than the outer diameter of the insert catheter 1124. In some cases, a first guidewire 1126 may be introduced through the insert catheter 1124 (not shown in FIG. 11B). Then, the guide sheath 1122, the insert catheter 1124, and optionally the first guidewire 1126 are tracked up to the aortic arch 1114. The insert catheter 1124 is used to engage the origin of a vessel. In FIG. 11B, the insert catheter 1124 engages the origin 1116 of the brachiocephalic artery 82. An angiographic run is performed by injecting contrast media through the insert catheter 1124.

In the cases where the first guidewire 1126 is used before the angiographic run, the first guidewire 1126 is removed prior to injecting the contrast media.

Referring to FIG. 11C, the first guidewire 1126 is inserted through the lumen of the insert catheter 1124. Then, the first guidewire 1126, the insert catheter 1124, and the guide sheath 1122 are advanced together to the ICA 1106. Referring to FIG. 11D, due to the stiffness of a typical guide sheath 1122 currently available in the market (e.g., Neuron MAX System produced by Penumbra Inc.), the most distal vessel that the guide sheath 1122 could navigate to is the petrous segment 1112 of the ICA 1106. Once the first guidewire 1126, the insert catheter 1124, and the guide sheath 1122 are advanced to the ICA 1106, both the first guidewire 1126 and the insert catheter 1124 are removed.

Referring to FIG. 11E, a second guidewire 1132 loaded inside the central lumen of a reperfusion catheter 1130 (e.g., 3Max), which is loaded inside the central lumen of an aspiration catheter 1128 (e.g., ACE 68), are introduced through the guide sheath 1122. The diameter of the second guidewire 1132 may be equal to or less than about 0.03", about 0.025", about 0.02", about 0.016", about 0.014", about 0.01", or about 0.005". The inner diameter of the reperfusion catheter 1130 may be greater than the outer diameter of the second guidewire 1132. The inner diameter of the aspiration catheter 1128 may be greater than the outer diameter of the reperfusion catheter 1130. The inner diameter of the guide sheath 1122 may be greater than the outer diameter of the aspiration catheter 1128. Then, the second guidewire 1132 is advanced distally and positioned at the proximal end of the clot 1102 in the MCA 1104.

Referring to FIG. 11F, the aspiration catheter 1128 is tracked over the reperfusion catheter 1130 and the second guidewire 1132 to the proximal end of the clot 1102 in the MCA 1104. Both the second guidewire 1132 and the reperfusion catheter 1130 are removed. A vacuum pressure is then applied at the proximal end of the aspiration catheter 1128 to aspirate the clot 1102 through the central lumen of the aspiration catheter 1128.

A preferable, simplified method for aspirating a thrombotic occlusion in accordance with the present invention is described in connection with FIGS. 12A—12F. The alternative steps for aspirating a thrombotic occlusion make use of a transitional guidewire and a transitional guide sheath. The transitional guidewire has a soft and trackable distal segment

with a smaller diameter so that the transitional guidewire may be advanced deeper than the guidewire 1126 described in FIG. 11C. In addition, the transitional guide sheath has a soft and trackable distal segment such that the transitional guide sheath may be advanced deeper than the guide sheath 1122 described in FIG. 11D. Using a transitional guidewire and a transitional guide sheath that can be advanced to an area near the clot eliminates the need to use a second guidewire or a reperfusion catheter to reach the clot.

Referring to FIG. 12A, an introducer sheath 1220 is introduced at the femoral artery 1218. The outer diameter of the introducer sheath 1220 may be equal to or less than about 12F, 11F, 10F, 9F, 8F, 7F, or 6F. Then, a transitional guide sheath 1222 such as the combination access and aspiration catheter discussed in greater detail below is inserted through the introducer sheath 1220 at the femoral artery 1218. The outer diameter of the guide sheath 1222 may be equal to or less than about 9F, 8F, 7F, 6F, 5F, 4F, or 3F. Referring to FIG. 12B, an insert catheter 1224 is inserted through the transitional guide sheath 1222. The outer diameter of the insert catheter 1224 may be less than about 9F, 8F, 7F, 6F, 5F, 4F, or 3F, and the inner diameter of the transitional guide sheath 1222 may be greater than the outer diameter of the insert catheter 1224. In some cases, a first guidewire may be introduced through the insert catheter 1224 (not shown in FIG. 12B). The diameter of the proximal section of the first guidewire may be equal to or less than about 0.079", about 0.066", about 0.053", about 0.038", about 0.035", about 0.030", or about 0.013".

The transitional guide sheath 1222, the insert catheter 1224, and optionally the first guidewire are tracked up to the aortic arch 1214. See FIG. 12B. The insert catheter 1224 may be used to select the origin of a vessel. In FIG. 12B, the insert catheter 1224 engages the origin 1216 of the brachiocephalic artery 82. An angiographic run may be performed by injecting contrast media through the insert catheter 1224. In the cases where the first guidewire is used before the angiographic run, the first guidewire is preferably removed prior to injecting the contrast media.

Referring to FIG. 12C, the transitional guidewire 1226 is inserted through the lumen of the insert catheter 1224 or guide sheath 1222. The diameter of at least a portion of the transitional guidewire 1226 (e.g., proximal diameter) is substantially similar to that of the first guidewire 1126. The diameter of at least a portion of the transitional guidewire 1226

(e.g., distal diameter) may be smaller than that of the first guidewire 1126 and may have a diameter along a proximal segment of at least about 0.030" and in one implementation about 0.038". A transition begins within the range of from about 15 cm – 30 cm from the distal end, and typically no more than about 20 cm or 25 cm from the distal end, distally of which the diameter tapers down to no more than about 0.018" and in one implementation about 0.016". Referring to FIG. 12D, if utilized, the insert catheter 1224 may be removed because it is too stiff to be advanced to the MCA 1204. In certain implementations of the invention, the transitional guidewire 1226 provides sufficient back up support that the combination access and aspiration catheter 1224 may be advanced directly over the transitional guidewire without any intervening devices. Then, the transitional guidewire 1226 is advanced to the MCA 1204. The transitional guidewire 1226 has a distal segment that has a smaller diameter than that of the first guidewire 1126 described in FIG. 11C. The distal segment of the transitional guidewire 1226 comprises a soft and atraumatic tip and can be tracked to the remote neurovasculature such as the MCA 1204, which is distal to the petrous segment 1212 of the ICA 1206.

Referring to FIG. 12E, the transitional guide sheath 1222 is advanced to or beyond the cavernous segment 1210 or the cerebral 1208 segment of the ICA 1206. Unlike the guide sheath 1122 described in FIG. 11D, the transitional guide sheath 1222 may be advanced to the cavernous segment 1210 or the cerebral 1208 segment of the ICA 1206 beyond the petrous segment 1212 because the transitional guide sheath 1222 has a soft yet trackable distal segment described in further detail below, for example in connection with Figure 30. The larger proximal diameter and stiffer body of the transitional guidewire 1226 may provide better support for the transitional guide sheath 1222 to track through the vasculature.

Referring to FIG. 12F, after the transitional guide sheath 1222 is advanced to the cerebral segment 1208 of the ICA 1206, the transitional guidewire 1226 is removed. Then, a vacuum pressure is applied at the proximal end of the transitional guide sheath 1222 to aspirate the clot 1202 through the central lumen of the transitional guide sheath 1222. The inner diameter of the transitional guide sheath 1222 may be equal to about or greater than about 0.100", about 0.088", about 0.080", about 0.070", or about 0.060". The inner diameter of the transitional guide sheath 1222 is larger than the aspiration catheter 1128 described in

FIG. 11E, which translates to more effective aspiration. The cross-sectional area of the central lumen of the transitional guide sheath 1222 may be almost twice as large as that of the largest aspiration catheter 1128 currently available.

If the guide sheath 1222 is not able to track deep enough into the distal vasculature to reach the clot or other desired target site, a telescopic extension segment as discussed elsewhere herein may be introduced into the proximal end of sheath 1222 and advanced distally to extend beyond the distal end of the sheath 1222 and thereby extend the reach of the aspiration system. In one implementation of the invention, the extension segment has an ID of about 0.070".

If thrombotic material is not able to be drawn into the sheath 1222 or extension segment under constant vacuum, pulsatile vacuum may be applied as discussed below. If pulsatile vacuum does not satisfactorily capture the clot, an agitator may be advanced through the sheath 1222 and extension segment to facilitate drawing the clot into the central lumen. Additional details of the agitator and its use are disclosed below.

A pulsatile vacuum pressure aspirator may be used in order to improve effectiveness of aspiration for vascular thrombectomy and to improve catheter trackability through tortuous vasculatures. FIG. 13 shows an embodiment of a pulsatile vacuum pressure aspirator 300 that applies intermittent or pulsatile vacuum to lumen 40. In the illustrated embodiment, the pulsatile vacuum pressure aspirator 300 is in fluid connection with the proximal end 12 of the catheter 10 and comprises vacuum generator 302, vacuum chamber 310, collection canister 312, solenoid valve 314, frequency modulator 316, valve controller 318, and remote controller 320.

Vacuum generator 302 comprises a vacuum pump 304, a vacuum gauge 306, and a pressure adjustment control 308. The vacuum pump 304 generates vacuum. The vacuum gauge 306 is in fluid connection with the vacuum pump 304 and indicates the vacuum pressure generated by the pump 304. The pressure adjustment control 308 allows the user to set to a specific vacuum pressure. Any of a variety of controls may be utilized, including switches, buttons, levers, rotatable knobs, and others which will be apparent to those of skill in the art in view of the disclosure herein.

Vacuum chamber 310 is in fluid connection with the vacuum generator 302 and acts as a pressure reservoir and/or damper. Collection canister 312 is in fluid connection with the vacuum chamber 310 and collects debris. The collection canister 312 may be a removable vial that collects debris or tissues, which may be used for pathologic diagnosis. Vacuum chamber 310 and collection canister 312 may be separate components that are in fluid connection with each other or a merged component. In the illustrated embodiment, the vacuum chamber 310 and the collection canister 312 is a merged component and is in fluid connection with the vacuum generator 302.

Solenoid valve 314 is located in the fluid connection path between a luer or other connector configured to releasably connect to an access port of the catheter 10 and the vacuum chamber 310 / collection canister 312. The solenoid valve 314 controls the fluid flow from the catheter 10 to the vacuum chamber 310 / collection canister 312.

Pulsatile vacuum pressure aspirator 300 may comprise frequency modulator 316 for control of the solenoid valve 314. The frequency modulator 316 generates different electrical wave frequencies and forms, which are translated into the movement of the solenoid valve 314 by the valve controller 318. The wave forms generated from the frequency modulator 316 comprise sinusoidal, square, and sawtooth waves. The wave forms generated from the frequency modulator 316 typically have frequencies less than about 500 Hz, in some modes of operation less than about 20 Hz or less than about 5 Hz. The wave forms have duty cycles ranging from 0%, in which the solenoid valve 314 is fully shut, to 100%, in which the solenoid valve 314 is fully open.

Valve controller 318 modulates the solenoid valve 314 on and off. The valve controller 318 may be electrically or mechanically connected to the solenoid valve 314. Any of a variety of controls may be utilized, including electrical controllers, switches, buttons, levers, rotatable knobs, and others which will be apparent to those of skill in the art in view of the disclosure herein. The valve controller 318 may be mechanically controlled by users or may be electrically controlled by the frequency modulator 316. The frequency modulator 316 and the valve controller 318 may be separate components that are electrically or mechanically connected or a merged component.

Remote control 320 enables physicians to control the frequency modulator 316 and/or the valve controller 318 for various purposes, such as turning the valve on/off, selecting different wave frequencies, and selecting different wave forms, while manipulating the catheter 10 at the patient side. Remote control 320 may be in wired or wireless communication with aspirator 300.

By tuning frequency, duty cycle, and wave form, one skilled in the art may match or approximate the resonating frequency to the natural frequency of the catheter. This may further enhance the efficacy of aspiration. The natural frequency of the catheter is typically less than about 260 Hz.

In another embodiment, shown in FIG. 14, the solenoid valve 414 is positioned in and fluidly connects between the air/fluid reservoir 422 at the atmospheric pressure and the aspiration line 424 connecting the catheter 10 to the vacuum chamber 410 / collection canister 412. Unlike the first embodiment in FIG. 13, this system modulates pressure in the catheter 10 by allowing pressure to vary from vacuum to atmospheric pressure. When the solenoid valve 414 is open to the air/fluid reservoir 422 at the atmospheric pressure, the vacuum pressure in the aspiration line 424 decreases to the atmospheric pressure. When the solenoid valve 414 is closed, it increases the vacuum pressure in the aspiration line 424.

In yet another embodiment, shown in FIG. 15, an electro-magnetic actuated diaphragm 522 is attached to the aspiration line 524 connecting the catheter 10 to the vacuum chamber 510 / collection canister 512. The electromagnetic actuated diaphragm 522, which is similar to that of a speaker driver, generates acoustic pressure waves in the catheter 10. The diaphragm 522 typically has a structure similar to a speaker driver and comprises frame 526, cone 528, dust cap 530, surround 532, spider or damper 534, voice coil 536 and magnet 538. Strength of the acoustic pressure waves may be modulated by the strength of the magnet 538. The frequency modulator 516 connected to the remote control 520 is electrically connected to the diaphragm 522 and generates different electrical wave frequencies and forms, which are translated by the diaphragm 522 into acoustic pressure waves in the aspiration line 524 and the catheter 10.

Tortuous vasculature is a common reason for failure to treat vasculature occlusions in the body due to inability to track the catheter to the location of the disease. Navigating

catheters through tortuous anatomy such as neurovasculature can be a challenge. The catheter has to be very soft as not to damage the vessel wall. At the same time, it also has to be able to negotiate multiple tight turns without kinking. In addition, it has to have sufficient column strength to transmit force axially for advancing through the vasculature. All these performance characteristics are competing design requirements. It is difficult to optimize one performance characteristic without sacrificing the others.

Reducing friction between the inner diameter of the vessel and the outer diameter of the catheter can minimize axial force required to advance catheter through tortuous vasculature. Therefore, the column strength of the catheter may be traded off for optimizing other performance requirements of the catheter. An example of a method to reduce friction between the inner diameter of the blood vessel and the outer diameter of the catheter is to apply a thin layer of coating, usually hydrophilic in nature, to the outer diameter of the catheter to reduce its surface friction coefficient while in vivo.

In addition or as an alternative to the water hammer construction discussed above, axial mechanical vibration or shock waves may be propagated to or generated at the distal end of the catheter using a variety of vibration generators, such as spark gap generators, piezoelectric pulse generators, electric solenoids, rotational shaft (wire) having one or more bends or carrying an eccentric weight, or any of a variety of other impulse generating sources well understood for example in the lithotripsy arts. Mechanical shock wave or pulse generators may be built into the proximal manifold 18, and or mechanically coupled to the manifold or proximal catheter shaft as desired. Preferably, controls are provided on the manifold or on a proximal control coupled to the manifold, to enable the clinician to vary the intensity and time parameters of the mechanical pulses. Shock waves may be propagated along the proximal section 33 to assist in transluminal advance, and/or distal section 34 by way of pull wire 42, depending upon the desired clinical performance.

In an embodiment shown in FIGS. 16 and 17, the distal end 608 of a vibrating device 600 is placed in fluid connection with the proximal end 12 of the catheter 10 (not illustrated) and generates transverse and/or longitudinal vibration in the catheter 10. By inducing transverse vibration in the catheter 10, it reduces effective contact surface area between the vessel and the catheter 10, which in turn reduces surface friction force between the inner

diameter of the vessel and the outer diameter of the catheter. In addition, by inducing longitudinal vibration in the catheter 10, the vibrating device 600 breaks static friction between the inner diameter of the vessel and the outer diameter of the catheter 10, which reduces overall surface friction. By reducing the friction between the inner diameter of the vessel and the outer diameter of the catheter 10, the vibrating device 600 improves catheter trackability through tortuous vasculatures.

In the illustrated embodiment, the proximal end 602 of the vibrating device 600 may be connected to a vacuum pressure source such as a vacuum generator. The proximal connector 604 is attached to the housing 606. In at least one embodiment, the proximal connector 604 may be a luer connector. The distal end 608 of the vibrating device 600 is connected to the catheter 10. The distal connector 610 is held in place by a flexible seal 612 that is attached to the housing 606. In at least one embodiment, the distal connector 610 may be a luer connector. The flexible seal 612 allows the distal connector 610 to move longitudinally as well as transversely. The flexible tubing links the proximal connector 604 and the distal connector 610, creating an aspiration channel 614 for the fluid to travel through.

The vibrating device has a controller 616 to turn on/off the vibrating action as well as to vary its frequency. In this embodiment, the controller 616 is drawn as a sliding switch. Any of a variety of controls may be utilized, including electrical controllers, switches, buttons, levers, rotatable knobs, and others which will be apparent to those of skill in the art in view of the disclosure herein.

A vibration generator such as a motor 618 has an eccentrically mounted inertial weight on its shaft generating vibration. Any of a variety of motors may be used, including an electric motor, an electro-magnetic actuator, and a piezoelectric transducer. The frequency of the vibration is related to the RPM of the motor 618. A driving circuit 620 is connected to the motor 618 and the controller 616 and drives the motor 618 at different RPMs based on the manipulation of the controller 616. In the illustrated embodiment, the circuit 620 drives the motor 618 at different RPMs based on the position of the sliding switch. A battery 622 is connected to and powers the driving circuit 620 and the motor 618.

The motor 618 may be mounted perpendicularly to the length of the aspiration channel 614 to create longitudinal vibration. Also, a mechanical cam may be attached to the

motor 618 to create larger magnitude longitudinal reciprocating motion. The frequency range generated by the electric motor is typically less than about 85 Hz. To achieve sonic frequencies in the range from about 85 Hz to about 260 Hz, one might replace the electric motor with an electro-magnetic actuator. To achieve ultrasonic frequencies in the range of about 20 Hz to about 1.6MHz, one might employ a piezoelectric transducer.

In yet another embodiment, shown in FIG. 18, an agitator such as stylet 702 is permanently or removably inserted into a lumen 40 of the catheter 10 and rotated to generate vibration in the catheter 10 and thus improve catheter trackability through tortuous vasculatures. The stylet 702, whose outer diameter is within the range of from about 0.005 inches (about 0.127mm) to about 0.035 inches (about 0.889mm), may have at least one bend or at least one weight. The peak to peak transverse distance between the bends will be less than the inner diameter of the catheter 10 when positioned within the catheter. The bends or weights of the stylet 702 may be positioned at different locations along the entire length of the catheter 10 or contained within a vibration zone within the distal most 50% or 30% or 10% of the length of the catheter depending upon desired performance, with the purpose to create the most desirable vibration when tracking the catheter 10 through the distal vasculature.

Alternatively, the stylet 702 may have an asymmetric weight such as a bead at a distal vibration zone or at its distal end. The stylet 702 may comprise a monofilament or braided or woven filaments or wires.

In another alternative, the stylet 702 may have a heater (e.g., an electric coil) at its distal end that facilitates the dissolution of the thrombus or changes the size of the thrombus that is aspirated into the catheter.

The proximal end of the stylet is attached to a motor driver 704 capable of generating rotational and or axially reciprocating motion at various frequencies to form a motor driver-stylet assembly 700. The assembly 700 has a controller 706 to turn on/off the rotating action as well as to vary its frequency. In this embodiment, the controller 706 is drawn as an on/off button. Any of a variety of controls may be utilized, including electrical controllers, switches, buttons, levers, rotatable knobs, and others which will be apparent to those of skill in the art

in view of the disclosure herein. The proximal luer 708 or other connector of the catheter 10 reversibly attaches the catheter 10 to the motor driver 804.

Once the catheter 10 has reached its intended location, the entire motor driver-stylet assembly 700 may be detached and removed from the catheter 10 leaving a central aspiration lumen.

In patients with vertebral artery occlusions, treatment with angioplasty can result in complications due to embolization of the occlusive lesion downstream to the basilar artery. Emboli small enough to pass through the vertebral arteries into the larger basilar artery are usually arrested at the top of the basilar artery, where it bifurcates into the posterior cerebral arteries. The resulting reduction in blood flow to the ascending reticular formation of the midbrain and thalamus produces immediate loss of consciousness. The devices described herein can be used to remove thromboembolic material from the vertebral artery or more distally such as in M1, M2, or M3 arteries.

Agitators for providing vibratory assistance for navigation and/or assisting in the capture and aspiration of debris are described further in connection with FIGS. 19-24. Referring to FIG. 19, an agitator 1900 may comprise an elongate, flexible body such as a wire or hypo tube having a proximal, control end and a distal, active zone or end. The hypo tube agitator has an inside lumen extending longitudinally that allows infusion of media. Referring to FIG. 19, an agitator 1900 comprises a wire or hypo tube 1904, introduced into the proximal end of a catheter 1902 and advanced to the distal end 1907 of the catheter 1902. The distal tip 1905 of the agitator 1900 may be placed at, beyond, or inside the distal end of the catheter 1902. The agitator 1900 can be either preloaded into the catheter 1902 and inserted into the patient's body together with the catheter 1902 or added after the catheter 1902 has been placed. When loaded inside the catheter 1902, the agitator 1900 may extend substantially longitudinally along the length of the catheter 1902. The agitator 1900 may further comprise a controller at the proximal end to axially adjust the distal tip position. The controller of the agitator 1900 may be used to axially adjust the position of the distal tip 1905 when the agitator 1900 is introduced into a variable length catheter such as that discussed in connection with FIG. 3.

In one implementation of the invention, the agitator and drive system are configured as a stand-alone device. Once the distal section 34 (Figure 3B) has been positioned within a few (e.g., no more than about 3 or 2) centimeters of the obstruction, the distal end of agitator 1900 may be introduced into the proximal end of central lumen 45 of pull wire 42. Agitator 1900 may thereafter be distally advanced so that a distal segment of agitator 1900 extends beyond the distal end of pull wire 42, and into the distal section 34. The portion of the agitator 1900 contained within lumen 45 of pull wire 42 is restrained from any significant lateral motion. However, the distal portion of agitator 1900 which extends beyond the distal end of pull wire 42 is relatively laterally unconstrained and is able to agitate thrombus to facilitate drawing the thrombus into and through the distal section 34. Once the thrombus has been drawn proximally under vacuum and with activation of the agitator as needed, to reach the step up in ID at the proximal end of distal section 34, the risk of clogging is greatly reduced.

The agitator 1900 may be rotated manually or via a motor 1906 driven from the catheter 1902's proximal end to rotate or translate the distal end of the agitator 1900. The driver 1906 may be connected to the proximal end of the agitator 1900 either permanently or removably. The driver 1906 may be a manual driver that is manually controlled such as a guidewire torquer. The driver 1906 may be a motorized driver. The motorized driver may be manually controlled with respect to one or more factors such as rotational direction (CCW/CW), speed, duration, etc. The motorized driver may be automatically controlled with respect to one or more factors such as direction (CCW/CW), speed, duration, etc. In one mode, the rotational direction of the agitator is periodically reversed.

The automatically controlled driver may comprise an actuator, and actuating the actuator may execute a pre-programmed series of steps. The actuator may be a button, a dial, a knob, a switch, a lever, a valve, a slide, a keypad, or any combinations thereof. The driver 1906 may also be under synchronized control, in which the driver 1906 drives the agitator 1900 in synchronization with aspiration and media injection. The agitator 1900 may be configured to promote motion at the distal end to help engage and move the clot.

Media may be infused into/around the clot area to help liberate the clot from the vasculature.

The agitator 1900 comprises a distal end 1912, a proximal end 1914 and a distal tip 1905. The proximal end 1914 of the agitator 1900 has a cross-section and/or wall thickness that is large enough to transmit the torque required to rotate the distal end 1912 of the agitator 1900 when placed in the catheter 1902, within the curved vasculature. The outer diameter of the agitator 1900 may be from about 0.25 mm to about 0.65 mm, from about 0.3 mm to about 0.6 mm, from about 0.35 mm to about 0.55 mm, from about 0.4 mm to about 0.5 mm, from about 0.42 mm to about 0.48 mm, or from about 0.44 mm to about 0.46 mm. In case of the hypo tube 1904, the wall thickness of the hypo tube 1904 may be from about 0.01 mm to about 0.29 mm, from about 0.05 mm to about 0.25 mm, from about 0.1 mm to about 0.2 mm, from about 0.12 mm to about 0.18 mm, from about 0.13 mm to about 0.17 mm, or from about 0.14 mm to about 0.16 mm.

The agitator 1900 may additionally be provided with a guide tube 1910, such as a hypo tube, to allow the agitator to spin, or axially or rotationally reciprocate, while constraining a proximal drive segment of the agitator 1900 against lateral motion. A distal end 1911 of guide tube 1910 may be positioned within about 25 cm or within about 20 cm or 15 cm or less of the distal end of the agitator 1900, depending upon desired performance. The distal section of the agitator 1900, extending beyond distal end 1911 of guide tube 1910, is laterally unconstrained within the ID of distal segment 34 and available to agitate and facilitate aspiration of material into and through the central lumen.

The diameter of the agitator 1900 may be constant along its longitudinal length. The diameter of the agitator 1900 may increase or decrease along its longitudinal length to coincide with features of the catheter 1902. In one implementation, the diameter of the agitator 1900 decreases in the distal direction along its longitudinal length by at least one step or tapered zone to provide increasing flexibility.

The distal end 1912 of the agitator 1900 may be straight. Alternatively, the distal end 1912 of the agitator 1900 may be curved or formed into different shapes to interact with the clot. FIG. 19 illustrates a bend 1917 spaced apart from the distal tip 1905 by a motion segment 1909 having a length of from about 1 mm to about 15 mm. FIGS. 20A-20C depict more complex exemplary shapes of the motion segment 1909 of the agitator 1900. FIGS. 20D-20E depict an agitator positioned within a swellable polymer distal funnel tip.

The agitator 1900 may be comprise a single, uniform material or multiple materials. The materials of the agitator 1900 may be processed (e.g., heat treatment/annealing) to give varying properties for the local performance requirements. The agitator 1900 may be structured to provide flexibility while exhibiting high torque transmission. The agitator 1900 may made of Nitinol, 304 Stainless Steel, 316 LVM Stainless Steel, PTFE, Parylene, or any combinations thereof. At least a portion of the surface of the agitator 1900 may be coated. The entire length of the agitator 1900 may be coated. The coating on the agitator 1900 may provide lubrication between the ID wall of the catheter 1902 and the agitator 1900. In a case that an intermediate hypotube is placed between the wall of the catheter 1902 and the agitator 1900, e.g., constraining tube 1910 or tubular pull wire 42, the coating on the agitator 1900 may provide lubrication between the intermediate hypotube and the proximal drive portion of the agitator 1900. The coating materials of the wire or hypo tube 1904 include PTFE, Parylene, Teflon, or any combinations thereof.

Any of the ID or OD of any of the catheter shafts or other catheter components disclosed herein may be provided with a lubricious coating or may be made from a lubricious material. For example, a hydrophilic polymer such as Polyacrylamide, PEO, thermoplastic starch, PVP, copolymers of hydrophilic polymer can be extruded with hydrophobic polymers such as PEO soft segmented polyurethane blended with Tecoflex. The lubricious coating or the lubricious material may include surface modifying additive (SMA) during melt processing. The lubricious coating or the lubricious material contributes to at least ease of navigation, lower ID skin friction, or better clot removal. In some embodiments, post processing wire ebeam, Gamma, UV, etc. additionally may be desirable to expose to moisture, temperature, etc. Catheters may be made from PEO impregnated polyurethanes such as Hydrothane, Tecophilic polyurethane for both OD and ID lubricity and inherent thromboresistant property without requiring a secondary coating process.

Referring to FIG. 20A, the distal end 2012 of the agitator 1900 may comprise a coil 2020 to grip a caked clot and wiggle the distal end 2010 of the catheter 2002 and the clot during rotation 2006. The coil 2020 may be a tight, offset coil, and may comprise at least one and optionally two or three or more complete revolutions.

Referring to FIG. 20B, the distal end 2012 of the agitator 1900 may comprise a hook 2022 to grip and emulsify a clot. The hook 2022 may be concave proximally, or may extend transversely to the axis of the agitator body, extending in a circumferential orientation. Referring to FIG. 20C, the distal end 2012 of the agitator 1900 may comprise a loose coil or spring 2024. The loose coil or spring 2024 may expand (lengthen) and contract (shorten) with a change in direction of rotation.

Referring to FIGS. 20D–20E, the distal end 2012 of the agitator 2000 may comprise a coil 2026 to grip a corked clot and wiggle the distal end 2010 of the catheter 2002 and the clot during rotation. In addition, the distal end 2010 of the catheter 2002 may include a polymer sidewall that reforms by hydration. The coil 2026 maintains a guide wire lumen during placement of the catheter. The polymer enables the distal end 2010 of the catheter 2002 to expand to a funnel shape after absorption of serum from blood. See FIG. 20E.

Referring to FIGS. 21A–21B, the distal tip 2110 of the catheter 2102 may move or wiggle by interacting with the agitator 1900. When the distal end of the agitator 1900 rotates (e.g., via a driver 2106), the motion segment 1909 and distal tip 1905 of the agitator interact with the side wall of the catheter 2102 which wiggles as shown by broken lines 2112. The length of the motion segment, stiffness of the agitator 1900 and rotational velocity determines the interaction with the wall of the catheter 2102 and the amount of wiggle transmitted to the catheter 2101 with rotation of the agitator 1900.

Alternatively, the distal tip 2110 of the catheter 2102 may move or wiggle by pulsed media jets existing one or more holes near the distal end of the hypo tube 2124. The hypo tube 2124 has an inside lumen extending along the longitudinal length of the hypo tube 2124. One or more side holes 2128 may be placed near the distal end of the hypo tube 2124 and allow fluid communication between the lumen of the hypo tube 2124 and the outside of the hypo tube 2124 (i.e., the lumen of the catheter 2102). Media (e.g. saline) may be introduced under pressure into the proximal end of the hypo tube 2124, through the lumen of the hypo tube 2124, and then through the one or more holes of the hypo tube 2124. When media is injected into the hypo tube 2124 in a pulsed manner, pulsed media jets eject from the holes of the hypo tube 2124 and transmit forces on the wall of the catheter 2102, resulting in a wiggle

motion of the catheter 2102. The hypo tube 2124 may additionally rotate (e.g., via a driver 2106) to facilitate a wiggle motion of the catheter 2102.

Referring to FIGS. 22A–22B, the hypo tube 2204 may have one or more holes 2210 and is bent near its distal portion to provide a motion segment 1909. Media (e.g. saline, a drug, a lubricant such as polyethylene glycol) is injected from the proximal end 2200, through the inside lumen, and out of the holes 2210 of the hypo tube 2204 (direction of media ejection shown as 2208). Vacuum is applied to the central lumen at the proximal end 2200 of the catheter 2202 such that media ejecting from the holes 2210 of the hypo tube 2204 is drawn proximally along the central lumen of the catheter 2202 toward its proximal end 2200.

As the hypo tube 2204 rotates, the hypo tube 2204 ejects media and simultaneously makes the distal tip of the catheter 2202 wriggle. When the distal tip of the catheter 2202 wriggles by the rotation of the hypo tube 2204, the wriggle of the catheter 2202 may push the clot 2214 from side to side, and the hypo tube 2204 simultaneously ejects media at the interface between the clot 2214 and the catheter 2202, providing a lubricious avenue for the clot 2214 to release and flow into the catheter 2202.

With or without injection of media, rotation of the motion segment 1909 helps to break up or reshape the thrombus and facilitate entry into the aspiration lumen. In certain situations, the clot can be aspirated completely within the central lumen. In other situations, the clot may only be able to be partially drawn into the central lumen, such as illustrated in FIG. 22B. In this situation, rotation of the agitator may be stopped with application of vacuum remaining on to retain the clot on the distal end of the catheter. The catheter may then be proximally withdrawn, pulling the clot along with it, into the access sheath and out of the proximal vascular access point.

Referring to FIGS. 23A–23B, the hypo tube 2304 may have one or more holes along its surface more proximal from the distal end to facilitate the movement or flow of the clot 2314 inside the catheter 2302 toward its proximal end 2300. Vacuum 2316 is applied at the proximal end 2300 of the catheter 2302 to move the removed clot 2314 from the distal end to the proximal end 2300 of the catheter 2302. As shown in FIG. 23A, the holes may provide a thin film 2312 around the inside of the wall of the catheter 2302 to facilitate the flow of media and/or the clot 2314 and minimize any clogging of the clot 2314. As shown in FIG.

23B, the hypo tube 2304 may have one or more holes to provide media jets ejecting radially from the hypo tube 2304 to grab, pull, and/or emulsify the clot 2314 as the clot 2314 passes by the one or more holes on the surface of the hypo tube 2304.

Referring to FIG. 24, a vacuum port 2416 may be provided near the proximal end 2400 of the catheter 2402 such as on the manifold for releasable connection to a vacuum source to aspirate the clot from the vasculature. This allows the vacuum port 2416 to be distinct from the proximal port 2417 for receiving the agitator 1900. This can minimize the risk that the movement or control of the wire or hypo tube 2404 at its proximal end may be adversely affected by vacuum, aspirated clot, and/or media. The vacuum port may be connected to the catheter 2400 via a rotating hemostasis valve, discussed below.

Referring to FIGS. 25A–25C, experiments showed that an interrupted vacuum can help aspirating a corked clot stuck at the distal end 2512 of the catheter 2510 by loosening the clot and reshaping it to fit into the catheter 2510 after each vacuum and release cycle. Merely stopping the vacuum is not sufficient to loosen the clot. Completely releasing (venting to atmospheric pressure) the vacuum and allowing the clot to relax before reapplying a vacuum is found to aspirate the corked clot most efficiently. The period of each vacuum and release cycle may be equal to or greater than about 0.1, 0.5, 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 seconds.

FIGS. 25A–25C show a logical progression of the vacuum and release cycle as applied to the catheter 2510. A release line 2518 and a vacuum line 2520 are connected to or near the proximal end of the catheter 2510. The release line 2518 is in communication with atmospheric pressure on its proximal end and has a release valve 2514 configured to open or close the fluid communication between the catheter 2510 and the vacuum. The vacuum line 2520 is connected to vacuum on its proximal end and has a vacuum valve 2516 configured to open or close the fluid communication between the catheter 2510 and the vacuum.

In the first step as shown in FIG. 25A, the release valve 2514 is closed, and the vacuum valve 2516 is open such that the vacuum is applied to the catheter 2510 to aspirate the clot. Then, as shown in FIG. 25B, the release valve 2514 is opened while the vacuum valve 2516 stays open. Because the release line 2518 and the vacuum line 2520 are in fluid communication, either directly or via at least a portion of the catheter 2510, the vacuum is applied mainly through the release line 2518, dropping vacuum applied to the catheter.

Finally, as shown in FIG. 25C, the vacuum valve 2516 is shut off, allowing the vacuum to be completely released and the clot to relax. Then, another cycle from FIG. 25A to FIG. 25C begins by closing the release valve 2514 and opening the vacuum valve 2516.

Referring to FIG. 26, there is illustrated a proximal drive assembly and/or the rotating hemostasis valve to provide the interface for driving the agitator 1900, providing the port for injecting media, and the aspiration port. Referring to FIGS. 26, 27A, 27B, and 28, the proximal drive assembly 2602 and the rotating hemostasis valve 2620 may be releasably or permanently coupled to the proximal end of the agitator 1900. The proximal portion of the agitator 1900 passes proximally through a lumen of the rotating hemostasis valve 2620 and then that of the proximal drive assembly 2602. The proximal end of the agitator 1900 may terminate inside the lumen of the proximal drive assembly 2602. The distal portion of the proximal drive assembly 2602 is inserted into the proximal end of the rotating hemostasis valve 2620. In another embodiment, the proximal drive assembly 2602 may be integrated into the rotating hemostasis valve 2620.

The rotating hemostasis valve (RHV) 2620 comprises a distal connector 2630 at its distal end, which is configured to couple the rotating hemostasis valve to the proximal end of the catheter (not shown). The distal connector 2630 may be a luer connector. The rotating hemostasis valve 2620 comprises a central lumen along its longitudinal length, through which a proximal section of agitator 1900 passes. The rotating hemostasis valve 2620 further comprises an aspiration port 2622, which bifurcates from the central lumen of the rotating hemostasis valve 2620 and provides the aspiration flow path. The rotating hemostasis valve 2620 comprises a RHV seal 2626 and a proximal rotating collar 2628 at its proximal end. The proximal rotating collar 2628 controls the opening and closing of the RHV seal 2626. The user (e.g., physician) can either open or close the RHV seal 2626 by rotating the proximal rotating collar 2628. The RHV seal 2626, when closed, does not allow fluid communication between the inside lumen distal of the RHV seal 262 and the inside lumen proximal of the RHV seal 262. At the same time, the RHV seal 262 does not hamper the longitudinal movement of the distal portion of the proximal drive assembly 2602 inside the rotating hemostasis valve 2629.

Experiments showed that as the wire or hypo tube 1900 is rotated back and forth (i.e., oscillating), the distal end of the agitator 1900 changes its position relative to the catheter. The distal end of the agitator 1900 was shown to foreshorten/lengthen as the wire or hypo tube 2624 wound/unwound within the catheter due to the rotation of the agitator 1900 or the increase/decrease in media injection pressure. The proximal rotating collar 2628 and the RHV seal 2626 permit the user (e.g., physician) to account for this variance in length and advance/withdraw the agitator 1900 relative to the catheter and fix it in place by simply moving the proximal drive assembly 2602 in/out of the rotating hemostasis valve 2629. If the agitator 1900 is preloaded into the catheter, the distance may be initially set at a nominal position. In another embodiment, the proximal rotating collar 2628 of the rotating hemostasis valve 2620 may be part of the proximal drive assembly 2602.

The proximal drive assembly 2602 comprises a proximal drive connector 2604, to which the driver is connected, and a media injection port 2610, into which media is injected. The proximal drive assembly also comprises a bearing 2606, which allows free rotation of the proximal drive connector 2604 with respect to the proximal drive assembly 2602. The proximal drive connection 2604 may be coupled to the proximal end of the agitator 1900 such that the rotation of the proximal drive connector 2604 is translated to the rotation of the wire or hypo tube 1900. The proximal drive assembly further comprises a drive tube seal 2608, which prevents fluid communication between the inside lumen (of the proximal drive assembly 2602) distal of the drive tube seal 2608 and the inside lumen proximal of the drive tube seal 2608.

Referring to FIG. 29, the driver 2950 is removably connected to the proximal end of the proximal drive assembly 2902 via the proximal drive connection 2604. The driver 2950 is configured to drive the agitator 1900. The driver 2950 is a motorized driver that is automatically controlled with respect to one or more factors such as direction (CCW/CW), speed, duration, etc. The driver 2950 comprises a control 2954 such as a button, which executes a pre-programmed series of steps when pushed. The driver 2954 may be under synchronized control, in which the driver 2954 drives the agitator 1900 in synchronization with aspiration and media injection, when the back of the driver 2950 is plugged into the synchronization port 2952.

The system for retrieving clots comprises the aspiration catheter; the agitator 1900 longitudinally extendable inside the lumen of the aspiration catheter; and the driver connectable to the proximal end of the agitator 1900 (e.g., via the rotating hemostasis valve or the proximal drive assembly) with or without a synchronization port. The system may allow impulse aspiration and/or impulse injection of media. The media may comprise water, saline solution, or media with an effective amount of drug (e.g., drug therapy such as heparin, plavix, tPA). The components may be manipulated individually or in a synchronized manner using predetermined operating parameters (e.g., for synchronized aspiration, injection, and rotation).

The method of retrieving a clot may comprise providing the aspiration catheter, the agitator longitudinally extending or positionable inside the lumen of the aspiration catheter; and the driver coupled to the proximal end of the agitator; placing the catheter adjacent to the clot; attempting to aspirate clot; if not successful, advancing an agitator distally through the catheter; activating the driver to rotate the agitator and loosen the clot; optionally injecting media through the agitator to lubricate the clot and/or create a media jet from the distal end of the agitator, configured to help aspirate the clot; transporting the clot proximally inside the lumen of the catheter by applying the vacuum at the proximal end of the catheter; and optionally pulsing the vacuum. As pieces of the clot separate, transport may be assisted by the rotating agitator and/or injection media.

In order to detach a more stubborn clot, aspiration, media injection, and/or rotation of the wire or hypo tube may be timed. Building up a surplus of media around the clot will form a plug. When aspiration is activated and/or pulsed, the vacuum can draw the “plug” proximally inside the lumen of the wire or hypo tube like a syringe plunger. A higher local vacuum around the clot is maintained, and more momentum is added to the “plug” as more media is added. Timing the rotation of the wire or hypo tube with aspiration and media injection may help wiggle or fatigue the clot and detach it out of the vasculature.

Any of the catheter shaft or sections of the catheter shaft or telescoping extensions in accordance with the present invention may comprise a multi-layer construct having a high degree of flexibility and sufficient push ability to reach deep into the cerebral vasculature,

such as at least as deep as the petrous, cavernous, or cerebral segment of the internal carotid artery (ICA).

In one example, referring to FIG. 30, the catheter 3000 may have an effective length from the manifold to distal tip from about 70cm to about 150cm, from about 80cm to about 140cm, from about 90cm to about 130cm, from about 100cm to about 120cm, or from about 105cm to about 115cm. The outer diameter of the catheter 3000 may be from about 0.07 inches to about 0.15 inches, from about 0.08 inches to about 0.14 inches, from about 0.09 inches to about 0.13 inches, from about 0.1 inches to about 0.12 inches, or from about 0.105 inches to about 0.115 inches, and may be lower in a distal segment than in a proximal segment. The inner diameter 3108 of the catheter 3000 in a single central lumen embodiment may be greater than or equal to about 0.11 inches, greater than or equal to about 0.1 inches, greater than or equal to about 0.09 inches, greater than or equal to about 0.088 inches, greater than or equal to about 0.08 inches, greater than or equal to about 0.07 inches, greater than or equal to about 0.06 inches, or greater than or equal to about 0.05 inches. The inner diameter 3108 of the catheter 3000 in a single central lumen embodiment may be less than or equal to about 0.11 inches, less than or equal to about 0.1 inches, less than or equal to about 0.09 inches, less than or equal to about 0.088 inches, less than or equal to about 0.08 inches, less than or equal to about 0.07 inches, less than or equal to about 0.06 inches, or less than or equal to about 0.05 inches. Referring to FIG. 30, an inner liner 3014 may be formed by dip coating a mandrel (not shown) to provide a thin walled tubular inside layer of the catheter body 3000. The dip coating may be produced by coating a wire such as a silver coated copper wire in PTFE. The mandrel may thereafter be axially elongated to reduce diameter, and removed to leave the tubular inner liner. The outside surface of the tubular inner liner 3014 may thereafter be coated with a soft tie layer 3012 such as polyurethane (e.g., TecoflexTM), to produce a layer having a thickness of no more than about 0.005 inches, and in some implementations approximately 0.001 inches. The tie layer 3012 will generally extend along at least about the most distal 10 cm or 20 cm of the catheter shaft 3000 generally less than about 50 cm and may in one implementation extend approximately the distal 30 cm of the catheter shaft 3000, 3100.

A braid such as a 75 ppi stainless steel braid 3010 may thereafter be wrapped around the inner liner 3014 through a proximal zone up to a distal transition 3011. From the distal transition 3011 to the distal end of the catheter 3000, a coil 3024 comprising a shape memory material such as a Nitinol alloy may thereafter be wrapped around the inner liner 3014. In one implementation, the Nitinol coil has a transition temperature below body temperature so that the Nitinol reside in the austenite (springy) state at body temperature. Adjacent loops or filars of the coil may be closely tightly wound in a proximal zone with a distal section having looser spacing between adjacent loops. In an embodiment having a coil section 3024 with an axial length of between about 20% and 30% of the overall catheter length, (e.g., 28 cm coil length in a 110 cm catheter shaft 3000), at least the distal 1 or 2 or 3 or 4 cm of the coil will have a spacing that is at least about 130%, and in some implementations at least about 150% or more than the spacing in the proximal coil section. In a 110 cm catheter shaft 3000 having a Nitinol coil the spacing in the proximal coil may be about 0.004 inches and in the distal section may be at least about 0.006 inches or 0.007 inches or more.

The distal end of the coil 3024 is spaced proximally from the distal end of the inner liner 3014 to provide room for an annular radiopaque marker 3040. In one embodiment, the distal end of the catheter 3000 is provided with a beveled distal surface 3006 residing on a plane having an angle of at least about 10° or 20° and in one embodiment about 30° with respect to a longitudinal axis of the catheter 3000. The radiopaque marker 3040 may reside in a plane that is transverse to the longitudinal axis. Alternatively, at least the distally facing edge of the annular radiopaque marker 3040 may be an ellipse, residing on a plane which is inclined with respect to the longitudinal axis to complement the bevel angle of the distal surface 3006.

After applying the proximal braid 3010, the distal coil 3024 and the RO marker 3040 an outer Jacket 3020 maybe applied such as a shrink wrap tube to enclose the catheter body 3000. The outer shrink-wrapped sleeve 3020 may comprise any of a variety of materials, such as polyethylene, polyurethane, PEBAX, nylon or others known in the art. Sufficient heat is applied to cause the polymer to flow into and embed the proximal braid and distal coil.

In one implementation, the outer shrink wrap jacket 3020 is formed by sequentially advancing a plurality of short tubular segments 3022, 3026, 3028, 3030, 3032, 3034, 3036,

3038 concentrically over the catheter shaft subassembly, and applying heat to shrink the sections on to the catheter 3000 and provide a smooth continuous outer tubular body. The foregoing construction may extend a long at least the most distal 10 cm, and preferably at least about the most distal 20 or 25 cm of the catheter body 3000.

The durometer of the outer wall segments may decrease in a distal direction. For example, proximal segments such as 3022 and 3026, may have a durometer of at least about 60 or 70D, with gradual decrease in durometer of successive segments in a distal direction to a durometer of no more than about 35D or 25D or lower. A 25 cm section may have at least about 3 or 5 or 7 or more segments and the catheter 3000 overall may have at least about 6 or 8 or 10 or more distinct flexibility zones. The distal 1 or 2 or 4 or more segments 3036, 3038, may have a smaller OD following shrinking than the more proximal segments 3022-3034 to produce a step down in OD for the finished catheter body 3000. The length of the lower OD section 3004 may be within the range of from about 3 cm to about 15 cm and in some embodiments is within the range of from about 5 cm to about 10 cm such as about 7 or 8 cm, and may be accomplished by providing the distal segments 3036, 3038 with a lower wall thickness.

Referring to FIGS. 31A-31C, the catheter may further comprise a tension support for increasing the tension resistance in the distal zone. The tension support may comprise a filament and, more specifically, may comprise one or more axially extending filaments 3042. The one or more axially extending filaments 3042 may be axially placed inside the catheter wall near the distal end of the catheter. The one or more axially extending filaments 3042 serve as a tension support and resist elongation of the catheter wall under tension (e.g., when the catheter is being proximally retracted through tortuous vasculature). At least one of the one or more axially extending filaments 3042 may proximally extend along the length of the catheter wall from near the distal end of the catheter to less than about 5cm from the distal end of the catheter, less than about 10cm from the distal end of the catheter, less than about 15cm from the distal end of the catheter, less than about 20cm from the distal end of the catheter, less than about 25cm from the distal end of the catheter, less than about 30cm from the distal end of the catheter, less than about 35cm from the distal end of the catheter, less than about 40cm from the distal end of the catheter, or less than about 50cm from the distal

end of the catheter. The one or more axially extending filaments 3042 may have a length greater than or equal to about 50cm, greater than or equal to about 40cm, greater than or equal to about 35cm, greater than or equal to about 30cm, greater than or equal to about 25cm, greater than or equal to about 20cm, greater than or equal to about 15cm, greater than or equal to about 10cm, or greater than or equal to about 5cm. At least one of the one or more axially extending filaments 3042 may have a length less than or equal to about 50cm, less than or equal to about 40cm, less than or equal to about 35cm, less than or equal to about 30cm, less than or equal to about 25cm, less than or equal to about 20cm, less than or equal to about 15cm, less than or equal to about 10cm, or less than or equal to about 5cm. At least one of the one or more axially extending filaments 3042 may extend at least about the most distal 50 cm of the length of the catheter, at least about the most distal 40 cm of the length of the catheter, at least about the most distal 35 cm of the length of the catheter, at least about the most distal 30 cm of the length of the catheter, at least about the most distal 25 cm of the length of the catheter, at least about the most distal 20 cm of the length of the catheter, at least about the most distal 15 cm of the length of the catheter, at least about the most distal 10 cm of the length of the catheter, or at least about the most distal 5 cm of the length of the catheter.

The one or more axially extending filaments 3042 may be placed near or radially outside the tie layer 3012 or the inner liner 3014. The one or more axially extending filaments 3042 may be placed near or radially inside the braid 3010 and/or the coil 3024. The one or more axially extending filaments 3042 may be carried between the inner liner 3014 and the helical coil 3024.

When more than one axially extending filaments 3042 are placed in the catheter wall, the axially extending filaments 3042 may be placed in a radially symmetrical manner. For example, the angle between the two axially extending filaments 3042 with respect to the radial center of the catheter may be about 180 degree. Alternatively, depending on desired clinical performances (e.g., flexibility, trackability), the axially extending filaments 3042 may be placed in a radially asymmetrical manner. The angle between any two axially extending filaments 3042 with respect to the radial center of the catheter may be less than about 180 degree, less than or equal to about 165 degree, less than or equal to about 150 degree, less

than or equal to about 135 degree, less than or equal to about 120 degree, less than or equal to about 105 degree, less than or equal to about 90 degree, less than or equal to about 75 degree, less than or equal to about 60 degree, less than or equal to about 45 degree, less than or equal to about 30 degree, less than or equal to about 15 degree, less than or equal to about 10 degree, or less than or equal to about 5 degree.

The one or more axially extending filaments 3042 may be made of materials such as Kevlar, Polyester, Meta-Para-Aramid, or any combinations thereof. At least one of the one or more axially extending filaments 3042 may comprise a single fiber or a multi-fiber bundle, and the fiber or bundle may have a round or rectangular cross section. The terms fiber or filament do not convey composition, and they may comprise any of a variety of high tensile strength polymers, metals or alloys depending upon design considerations such as the desired tensile failure limit and wall thickness. The cross-sectional dimension of the one or more axially extending filaments 3042, as measured in the radial direction, may be no more than about 1%, 2%, 3%, 4%, 5%, 6%, 7%, 8%, 9%, 10%, 11%, 12%, 13%, 14%, 15%, 20%, 25%, or 30% of that of the catheter 3000. The cross-sectional dimension of the one or more axially extending filaments 3042, as measured in the radial direction, may be no more than about 0.001 inches, about 0.002 inches, about 0.003 inches, about 0.004 inches, about 0.005 inches, about 0.006 inches, about 0.007 inches, about 0.008 inches, about 0.009 inches, about 0.010 inches, about 0.015 inches, about 0.020 inches, about 0.025 inches, or about 0.030 inches.

The one or more axially extending filaments 3042 may increase the tensile strength of the distal zone of the catheter to at least about 1 pound, at least about 2 pounds, at least about 3 pounds, at least about 4 pounds, at least about 5 pounds, at least about 6 pounds, at least about 7 pounds, at least about 8 pounds, or at least about 10 pounds or more.

Referring to FIGS. 32A-32C, depending on whether the catheter 3000 is able to navigate sufficiently distally to reach the target site, an intraluminal catheter 3200 such as a telescopic extension segment having a proximally extending control wire as has been described elsewhere herein (e.g., distal segment 34 in FIGS. 3A and 3B) may be inserted through the catheter 3000 from the proximal end of the catheter 3000. The intraluminal catheter 3200 is inserted such that the distal end of the intraluminal catheter 3200 reaches further distally beyond the distal end of the catheter 3000. The outer diameter of the

intraluminal catheter 3200 is smaller than the inner diameter of the catheter 3000. This way, the intraluminal catheter 3200 can slide inside the lumen of the catheter 3000.

The intraluminal catheter 3200 incorporates characteristics of the side wall construction of the catheter 3000 described herein. The axial length of the tubular extension segment may be less than about 50 % and typically less than about 25% of the length of the catheter 3000. The axial length of the tubular extension segment will generally be at least about 10 cm or 15 cm or 20 cm or 25 cm or more but generally no more than about 70 cm or 50 cm or 30 cm.

Referring to FIGS. 33A-33C, the intraluminal catheter 3200 may have one or more axially extending filaments 3242. The one or more axially extending filaments 3242 incorporate characteristics of the one or more axially extending filaments 3042 of the catheter 3000, except the cross-sectional dimension as measured in the radial direction of the one or more axially extending filaments 3242 of the intraluminal catheter 3200 may be less than the corresponding dimension of the filament 3042 in the catheter 3000.

Referring to FIGS. 34A-34B, there is illustrated one example of an outer jacket segment stacking pattern for a progressive flexibility catheter of the type discussed in connection with FIG. 30. A distal segment 3038 may have a length within the range of about 1 – 3 cm, and a durometer of less than about 35D or 30D. An adjacent proximal segment 3036 may have a length within the range of about 4 – 6 cm, and a durometer of less than about 35D or 30D. An adjacent proximal segment 3034 may have a length within the range of about 4 – 6 cm, and a durometer of about 35D or less. An adjacent proximal segment 3032 may have a length within the range of about 1 – 3 cm, and a durometer within the range of from about 35D to about 45D (e.g., 40D). An adjacent proximal segment 3030 may have a length within the range of about 1 – 3 cm, and a durometer within the range of from about 50D to about 60D (e.g., about 55D). An adjacent proximal segment 3028 may have a length within the range of about 1 – 3 cm, and a durometer within the range of from about 35D to about 50D to about 60D (e.g., about 55D). An adjacent proximal segment 3026 may have a length within the range of about 1 – 3 cm, and a durometer of at least about 60D and typically less than about 75D. More proximal segments may have a durometer of at least about 65D or 70D. The distal most two or three segments may comprise a material such as Tecothane, and

more proximal segments may comprise PEBAX or other catheter jacket materials known in the art. At least three or five or seven or nine or more discrete segments may be utilized, having a change in durometer between highest and lowest along the length of the catheter shaft of at least about 10D, preferably at least about 20D and in some implementations at least about 30D or 40D or more.

Performance metrics of a catheter include back-up support, trackability, pushability, and kink resistance. Back-up support means ability of the catheter to remain in position within anatomy and provide a stable platform through which endoluminal devices may advance. Referring to FIG. 35, when the devices are pushed through the catheter 3202, if there is not enough back-up support in the catheter 3202, the distal portion 3204 of the catheter 3202 may prolapse, pull out, or back out of a vessel 3206 that branches out of a main blood vessel (e.g., brachiocephalic artery 82, common carotid artery 80, or subclavian artery 84). Back-up support for the catheter 3202 may be improved by providing a proximal region with high durometer or modulus and a distal region with low durometer or modulus. Durometer or modulus of the proximal region of the catheter 3202 may be improved by braid reinforcement. The region of the catheter at which durometer or modulus is strengthened may be placed near branching points at which the aortic arch 1114, 1214 branches into brachiocephalic artery 82, common carotid artery 80, or subclavian artery 84 or near other anatomical structures (i.e., branching points) at which a main vessel branches into one or more smaller vessels, providing an opportunity for a catheter with poor back-up support to prolapse. For example, the region of the catheter at which durometer or modulus is strengthened may be placed within about 0.5cm, about 1cm, about 2cm, about 3cm, about 4cm, about 5cm, or about 6cm from a branching point at which a main vessel branches into one or more smaller vessels.

Trackability means ability of the catheter to track further distally than other catheters (e.g., to M1). For example, a catheter that can reach a cerebral segment of the internal carotid artery (ICA) has better trackability than a catheter that can reach a cavernous or petrous segment of the ICA. Trackability of the catheter may be improved by using a catheter wall with low durometer or modulus or by adding a coating (e.g., a hydrophilic coating) on at least a portion of the catheter wall. In one embodiment, the hydrophilic coating may be placed

along the distal most region of the catheter. The hydrophilic coating on the catheter may extend to about 1cm, about 5cm, about 10cm, about 15cm, or about 20cm from the distal end of the catheter. The region with lower durometer or modulus may locate at the distal most region of the catheter. The region with lower durometer or modulus may extend to about 1cm, about 5cm, about 10cm, about 15cm, or about 20cm from the distal end of the catheter.

Pushability means rigidity of the catheter sufficient to push through anatomy without “buckling”. Pushability of the catheter may be improved by increasing its durometer or modulus. Pushability of the catheter may also be improved by providing a proximal region with high durometer or modulus and a distal region with low durometer or modulus. A transition region of the catheter in which durometer or modulus changes along its longitudinal length (e.g., decreasing durometer or modulus from the proximal end to the distal end) may begin at about 50%, 60%, 70%, 75%, 80%, or more of the length of the catheter from its proximal end.

Kink resistance means resistance of the catheter to kinking. In addition, if the catheter does kink, kink resistance of the catheter helps it return to its original shape. Kink resistance is important in the distal segment of the catheter, which is more prone to kinking than the proximal segment. Kink resistance of the catheter may be improved by adding one or more NiTi coils (or a coil at least portion of which is Nitinol) to the catheter wall.

FIG. 36 describes a graph of durometer or modulus of a catheter in accordance with the present invention along the length of the catheter, from the proximal end ($x = 0$) to the distal end ($x = 1$). The catheter according to an embodiment may have a decreasing durometer or modulus (E) approaching its distal end. The proximal end of the catheter has higher durometer or modulus than that of the distal end of the catheter. High durometer or modulus near the proximal end provides superior back-up support of the catheter. Durometer or modulus of the catheter is substantially constant along its length near the proximal end 3302 of the catheter. Then, durometer or modulus of the catheter decreases near the distal end 3304 of the catheter. Durometer or modulus of the catheter may begin to decrease (i.e., transition region) at about 50%, 70%, 75%, 80%, or 90% of the length of the catheter from its proximal end. The catheter may have successively decreasing durometer or modulus near its distal end by using materials with less durometer or modulus or having a thinner catheter wall

near the distal end. Decreased durometer or modulus near the distal end provides superior trackability of the catheter.

FIG. 37 describes flexibility test profiles of catheters in accordance with the present invention compared with conventional catheters. Flexibility of a catheter was measured by the three point flexural test with a span of one inch and a displacement of 2mm. In other words, FIG. 37 describes a force (i.e., flexural load) necessary to vertically displace an one-inch-long catheter segment by 2 mm with respect to distance from strain relief (i.e., proximal end of the catheter) to the point of force application. All catheters tested in FIG 37 show modulus or flexibility profiles similar to one shown in FIG. 36. Modulus of the catheters stays substantially constant along its length near the proximal end and then gradually decreases near the distal end.

Catheters according to the present invention have a flexural load that is substantially constant along the longitudinal length near the proximal end and a rapidly decreasing flexural load near the distal end. In a catheter having a length of about 125 cm, the catheters may have a flexural load greater than or equal to about 1.0 lbF, about 1.5 lbF, about 2.0 lbF, about 2.5 lbF, about 3.0 lbF, or about 3.5 lbF at about 85 cm from the proximal end. The catheters may have a flexural load less than or equal to about 2.5 lbF, about 2.0 lbF, about 1.5 lbF, about 1.0 lbF, or about 0.5 lbF at about 95 cm from the proximal end. The catheters may have a flexural load less than or equal to about 1.5 lbF, about 1.0 lbF, about 0.75 lbF, about 0.5 lbF, about 0.25 lbF, or about 0.1 lbF at about 105 cm from the proximal end. The catheters may have a flexural load less than or equal to about 1.0 lbF, about 0.75 lbF, about 0.5 lbF, about 0.4 lbF, about 0.3 lbF, about 0.2 lbF, or about 0.1 lbF at about 115 cm from the proximal end. For catheters having different lengths, the foregoing dimensions can be scaled from the distal end of the catheter as a percentage of catheter length.

In certain implementations constructed in accordance with FIG. 30, the flexural load is less than about 3.0 or 3.25 lbF at 65 cm from the proximal end and greater than about 2.25 or 2.5 lbF on average from 65 cm to 85 cm from the proximal end. Flexural load drops to no more than about 1.0 and preferably no more than about 0.5 lbF at about 95 cm from the proximal end. This provides enhanced backup support in the aorta while maintaining enhanced trackability into the distal vasculature.

In other embodiments, the catheters may have a flexural load greater than or equal to about 1.0 lbF, about 1.5 lbF, about 2.0 lbF, about 2.5 lbF, about 3.0 lbF, or about 3.5 lbF at about 60 cm from the proximal end. The catheters may have a flexural load less than or equal to about 2.0 lbF, about 1.5 lbF, about 1.0 lbF, or about 0.5 lbF at about 70 cm from the proximal end. The catheters may have a flexural load less than or equal to about 1.0 lbF, about 0.75 lbF, about 0.5 lbF, about 0.4 lbF, about 0.3 lbF, about 0.2 lbF, or about 0.1 lbF at about 80 cm from the proximal end. The catheters may have a flexural load less than or equal to about 1.0 lbF, about 0.75 lbF, about 0.5 lbF, about 0.4 lbF, about 0.3 lbF, about 0.2 lbF, or about 0.1 lbF at about 90 cm from the proximal end.

The catheters may have a transition region, in which its flexural load changes by greater than or equal to about 1.0 lbF, about 1.5 lbF, about 2.0 lbF, about 2.5 lbF, about 3.0 lbF, or about 3.5 lbF. The longitudinal length of the transition region may be less than or equal to about 20cm, about 15cm, about 10cm, about 5 cm, about 3cm, or about 1cm.

Compared to Neuron Max (Penumbra, Inc.) 3402, catheters according to the present invention (e.g., 3404, 3406, 3408, 3410) have comparable modulus near its proximal end. This way, the catheters according to the present invention provide back-up support comparable to that of Neuron Max. In addition, the catheters have modulus that falls more rapidly near the transition region (between the proximal end and the distal end) than that of Neuron Max.

Compared to Ace 68 catheter (Penumbra) 3412, Ace 64 catheter (Penumbra) 3414, Benchmark 71 catheter (Penumbra) 3416, and Sofia Plus (MicroVention) 3418, the catheters according to the present inventions have greater modulus near its proximal end and comparable modulus near its distal end. This way, the catheters according to the present invention provide superior back-up support with comparable trackability compared to conventional catheters. The catheters according to the present invention may achieve this modulus profile even when their inner diameters (and thus lumen volumes) are greater than or equal to those of Ace 68, Ace 64, Benchmark 71, and Sofia Plus, which range from 0.064 inch to 0.071 inch.

Referring to FIG. 38, there is illustrated a transformable access sheath 200. The access sheath 200 comprises an elongate flexible tubular body 202 extending between a proximal

end 204 and a distal end 206. A proximal access port 208 is in communication with a distal port 210 on the distal end 206 by way of a central lumen 212. See FIG. 39.

At least one transition zone 214 is provided on the tubular body 202. Transition zone 214 is controllably transformable between a relatively stiff configuration and a relatively flexible configuration. The access sheath 200 may be distally advanced through tortuous anatomy with at least one transition zone 214 in a relatively stiff configuration as desired such as to provide column strength or to facilitate the introduction of instruments therethrough. The transition zone 214 may be controllably transformed to a relatively flexible configuration as desired, such as to navigate tight bends in the vasculature.

In the illustrated embodiment, three transition zones 214 are shown. However, one or two or three or four or more transition zones may be utilized, depending upon the desired clinical performance. The transition zone 214 may be from about 1 cm to about 20 or 30 cm or more in length. In certain embodiments, the transition zones will be within the range of from about 2 cm to about 10 cm in length. The length and location of the transition zones may depend upon the target anatomy for the access catheter, and can be located accordingly.

Referring to FIG. 39, there is illustrated a cross-sectional view taken along the lines 18-18 of FIG. 38, through a transition zone 214. The tubular body 202 comprises a sidewall 216 having at least one heating element 218 carried by or embedded within the sidewall 216. In the illustrated embodiment, the heater 218 may be an electrically conductive filament, such as a filar on an electrically conductive helical coil or braid. The electrically conductive filament may be placed within or laminated within an inner layer and an outer layer of the sidewall 216. In at least one embodiment, an inner layer of the sidewall 216 may comprise polytetrafluoroethylene (PTFE) for lubricity. In at least one embodiment, an outer layer of the sidewall 216 may comprise biocompatible material preferably with a glass transition temperature from about 40 °C to about 80 °C.

Alternatively, an electrically conductive polymer may be utilized to form the sidewall 216. Electrically conductive coatings may alternatively be printed, laminated, embedded or otherwise applied to the outside, the inside, or laminated within an inner layer and an outer layer of the sidewall 216. In at least one embodiment, the resistance of the heater 218 may be calibrated to a specific heating temperature, such as 40 – 80°C, for a predetermined voltage

level of the power source. This may eliminate the need for a thermocouple and prevent potential overheating.

One or more electrical conductors may extend between the transition zone 214 and a proximal activation port 215, adapted for coupling to a source of electricity from an external controller. In a mono polar construction, a single conductor for each transition zone 214 may extend proximally to the activation port 215. A second conductor may lead to or comprise an electrically conductive surface on the tubular body 202, for conducting electricity through the body of the patient to an external electrode as is understood in the art. Alternatively, in a bipolar embodiment, each transition zone 214 may be provided with at least two electrical conductors extending proximally to the activation port 215.

At least the transition zone comprises a biocompatible material that is relatively firm at body temperature (e.g., 37°C) but transitions to a relatively soft, flexible material upon application of heat. Typical suitable materials have a relatively low melting point so as to be softenable at temperatures not so high as to damage living vessels. In any event the material will have a softening point or a glass transition temperature above body temperature, with a melting point significantly above body temperature and above the temperature reached by activating the heating element 218. In one embodiment, the biocompatible material preferably has a glass transition temperature from about 40°C to about 80°C. Suitable materials may include polymers with a polymer chain orientation that causes the polymer to break when heated.

Examples of suitable biostable materials are polymers, typically thermoplastic polymers such as polyolefins and polyurethanes and most other biocompatible polymers. Typical suitable bioabsorbable materials include polyglycolide (PGA), poly(L-lactide) (PLLA), poly(epsilon-caprolactone) (PCL), and blends or combinations thereof. Polyglycolide for example has a glass transition temperature between 35-40°C, such having a considerably higher melting point.

Typical operating (softening) temperatures in this regard are on the order of between about 40 and 80°C, often between about 40°C and 60°C to cause a softening transition of the transition zone 214, and allow a transition back to a firm state upon removal of power and reversion of the transition zone 214 back to body temperature. A temperature higher than

about 80°C may be acceptable for a short period of time, depending upon the total energy delivered. Any temperature to which the heater 218 is elevated is limited by what the body of the patient can handle without causing damage to the vessel wall or causing thrombus to form. For this reason, it may be desirable to remain within the lower end of the temperature ranges illustrated above if the eligible polymers exhibit suitable flexibility at the softening point temperature and suitable firmness at the lower body temperature.

Upon being heated, the biocompatible energy-activated transition zone 214 softens so that it may be navigated through a tight bend for example. The material is to be softened enough by the energy application so that it increases in flexibility, but retains the structural integrity necessary for navigation and retains its shape so that upon interruption of the heat source it will harden back to its original configuration. To maintain the integrity of the tubular body, side wall 216 may be provided with flexible reinforcing structures such as a helically wrapped wire, ribbon or polymeric strand such as polyimide, or other braid or weave as is understood in the neurovascular catheter arts. A resistance coil or other resistance filaments may also provide the mechanical reinforcing function while the transition zone is in the softened state.

Heating may alternatively be provided by positioning a heat source such as a resistance heat element carried by a heater catheter within the central lumen 212. Once the catheter has reached its final position in the vasculature, the heater catheter may be proximally withdrawn from the central lumen 212, which is now available for aspiration or to receive a distal section 34 therethrough. In either heater configuration, a power source may be provided within or electrically coupled to a proximal manifold on the aspiration catheter or heater catheter.

Access for the catheter of the present invention can be achieved using conventional techniques through an incision on a peripheral artery, such as right femoral artery, left femoral artery, right radial artery, left radial artery, right brachial artery, left brachial artery, right axillary artery, left axillary artery, right subclavian artery, or left subclavian artery. An incision can also be made on right carotid artery or left carotid artery in emergency situations.

Avoiding a tight fit between the guidewire 40 and inside diameter of guidewire lumen 28 enhances the slidability of the catheter over the guidewire. In ultra small diameter catheter

designs, it may be desirable to coat the outside surface of the guidewire 40 and/or the inside surface of the wall defining lumen 38 with a lubricous coating to minimize friction as the catheter 10 is axially moved with respect to the guidewire 40. A variety of coatings may be utilized, such as Paralene, Teflon, silicone, polyimide-polytetrafluoroethylene composite materials or others known in the art and suitable depending upon the material of the guidewire or inner tubular wall 38.

Aspiration catheters of the present invention which are adapted for intracranial applications generally have a total length in the range of from 60 cm to 250 cm, usually from about 135 cm to about 175 cm. The length of the proximal segment 33 will typically be from 20 cm to 220 cm, more typically from 100 cm to about 120 cm. The length of the distal segment 34 will typically be in the range from 10 cm to about 60 cm, usually from about 25 cm to about 40 cm.

The catheters of the present invention may be composed of any of a variety of biologically compatible polymeric resins having suitable characteristics when formed into the tubular catheter body segments. Exemplary materials include polyvinyl chloride, polyethers, polyamides, polyethylenes, polyurethanes, copolymers thereof, and the like. In one embodiment, both the proximal body segment 33 and distal body segment 34 will comprise a polyvinyl chloride (PVC), with the proximal body segment being formed from a relatively rigid PVC and the distal body segment being formed from a relatively flexible, supple PVC. Optionally, the proximal body segment may be reinforced with a metal or polymeric braid or other conventional reinforcing layer.

The proximal body segment will exhibit sufficient column strength to permit axial positioning of the catheter through a guide catheter with at least a portion of the proximal body segment 33 extending beyond the guide catheter and into the patient's vasculature. The proximal body segment may have a shore hardness in the range from 50 D to 100 D, often being about 70 D to 80 D. Usually, the proximal shaft will have a flexural modulus from 20,000 psi to 1,000,000 psi, preferably from 100,000 psi to 600,000 psi. The distal body segment 34 will be sufficiently flexible and supple so that it may navigate the patient's more narrow distal vasculature. In highly flexible embodiments, the shore hardness of the distal

body segment 34 may be in the range of from about 20 A to about 100 A, and the flexural modulus for the distal segment 34 may be from about 50 psi to about 15,000 psi.

The catheter body may further comprise other components, such as radiopaque fillers; colorants; reinforcing materials; reinforcement layers, such as braids or helical reinforcement elements; or the like. In particular, the proximal body segment may be reinforced in order to enhance its column strength and torqueability (torque transmission) while preferably limiting its wall thickness and outside diameter.

Usually, radiopaque markers will be provided at least at the distal end 14 and the transition region 32 at the distal end of proximal segment 33. One radiopaque marker comprises a metal band which is fully recessed within or carried on the outside of the distal end of the proximal body segment 33. Suitable marker bands can be produced from a variety of materials, including platinum, gold, and tungsten/rhenium alloy. Preferably, the radiopaque marker band will be recessed in an annular channel to produce a smooth exterior surface.

The proximal section 33 of tubular body 16 may be produced in accordance with any of a variety of known techniques for manufacturing interventional catheter bodies, such as by extrusion of appropriate biocompatible polymeric materials. Alternatively, at least a proximal portion or all of the length of tubular body 16 may comprise a polymeric or metal spring coil, solid walled hypodermic needle tubing, or braided reinforced wall, as is known in the microcatheter arts.

In a catheter intended for neurovascular applications, the proximal section 33 of body 16 will typically have an outside diameter within the range of from about 0.117 inches to about 0.078 inches. In one implementation, proximal section 33 has an OD of about 0.104 inches and an ID of about 0.088 inches. The distal section 34 has an OD of about 0.085 inches and an ID of about 0.070 inches.

Diameters outside of the preferred ranges may also be used, provided that the functional consequences of the diameter are acceptable for the intended purpose of the catheter. For example, the lower limit of the diameter for any portion of tubular body 16 in a given application will be a function of the number of fluid or other functional lumen

contained in the catheter, together with the acceptable minimum aspiration flow rate and collapse resistance.

Tubular body 16 must have sufficient structural integrity (e.g., column strength or "pushability") to permit the catheter to be advanced to distal locations without buckling or undesirable bending of the tubular body. The ability of the body 16 to transmit torque may also be desirable, such as to avoid kinking upon rotation, to assist in steering. The tubular body 16, and particularly the distal section 34, may be provided with any of a variety of torque and/or column strength enhancing structures. For example, axially extending stiffening wires, spiral wrapped support layers, braided or woven reinforcement filaments may be built into or layered on the tubular body 16. See, for example, U.S. Pat. No. 5,891,114 to Chien, et al., the disclosure of which is incorporated in its entirety herein by reference.

In many applications, the proximal section 33 will not be required to traverse particularly low profile or tortuous arteries. For example, the proximal section 33 will be mostly or entirely within the relatively large diameter guide catheter. The transition 32 can be located on the catheter shaft 16 to correspond approximately with or beyond the distal end of the guide catheter.

For certain applications, such as intracranial catheterizations, the distal section 34 is preferably at least about 5 cm or 10 cm long and small enough in diameter to pass through vessels as low as 3 mm or 2 mm or lower. The distal section may have a length of at least about 20 cm or 30 cm or 40 cm or more, depending upon the intended target vessel or treatment site.

The distal section, whether carried within the proximal section as an integrated device, or is a separate device to be inserted into the proximal section during a procedure, is substantially shorter than the proximal section. When the distal end of the distal section and the distal end of the proximal section are axially aligned, the proximal end of the distal section is spaced distally apart from the proximal end of the proximal section. The control element such as a control wire or tube spans the distance between the proximal end of the distal section and the proximal manifold or proximal control.

In the foregoing configuration, the proximal end of the distal section will generally be spaced apart distally from the proximal end of the proximal section by at least about 25%, and in some embodiments at least about 50% or 70% or more of the length of the proximal section.

Although the present invention has been described in terms of certain preferred embodiments, it may be incorporated into other embodiments by persons of skill in the art in view of the disclosure herein. The scope of the invention is therefore not intended to be limited by the specific embodiments disclosed herein, but is intended to be defined by the full scope of the following claims.

WHAT IS CLAIMED IS:

1. An enhanced flexibility neurovascular catheter, comprising:
an elongate flexible body, having a proximal end, a distal end and a side wall defining a central lumen, a distal zone of the side wall comprising:
a tubular inner liner;
a tie layer separated from the lumen by the inner liner;
a helical coil surrounding the tie layer, adjacent windings of the coil spaced progressively further apart in the distal direction; and
an outer jacket surrounding the helical coil, the outer jacket formed from a plurality of tubular segments positioned coaxially about the coil; wherein
a proximal one of the tubular segments has a durometer of at least about 60D and a distal one of the tubular segments has a durometer of no more than about 35D.
2. An enhanced flexibility neurovascular catheter as in Claim 1, wherein the tubular liner is formed by dip coating a removable mandrel.
3. An enhanced flexibility neurovascular catheter as in Claim 1, wherein the tubular liner comprises PTFE.
4. An enhanced flexibility neurovascular catheter as in Claim 1, wherein the tie layer comprises polyurethane.
5. An enhanced flexibility neurovascular catheter as in Claim 4, wherein the tie layer has a wall thickness of no more than about 0.005 inches.
6. An enhanced flexibility neurovascular catheter as in Claim 4, wherein the tie layer extends along at least the most distal 20 cm of the flexible body.
7. An enhanced flexibility neurovascular catheter as in Claim 1, wherein the coil comprises a shape memory material.
8. An enhanced flexibility neurovascular catheter as in Claim 7, wherein the coil comprises Nitinol.

9. An enhanced flexibility neurovascular catheter as in Claim 8, wherein the Nitinol comprises an Austenite state at body temperature.

10. An enhanced flexibility neurovascular catheter as in Claim 1, wherein the outer jacket is formed from at least five discrete tubular segments.

11. An enhanced flexibility neurovascular catheter as in Claim 1, wherein the outer jacket is formed from at least nine discrete tubular segments.

12. An enhanced flexibility neurovascular catheter as in Claim 11, wherein the difference in durometer between a proximal one of the tubular segments and a distal one of the tubular segments is at least about 20D.

13. An enhanced flexibility neurovascular catheter as in Claim 11, wherein the difference in durometer between a proximal one of the tubular segments and a distal one of the tubular segments is at least about 30D.

14. An enhanced flexibility neurovascular catheter as in Claim 1, further comprising a tension support for increasing the tension resistance in the distal zone.

15. An enhanced flexibility neurovascular catheter as in Claim 14, wherein the tension support comprises a filament.

16. An enhanced flexibility neurovascular catheter as in Claim 15, wherein the tension support comprises an axially extending filament.

17. An enhanced flexibility neurovascular catheter as in Claim 16, wherein the axially extending filament is carried between the inner liner and the helical coil.

18. An enhanced flexibility neurovascular catheter as in Claim 16, wherein the axially extending filament increases the tensile strength to at least about 5 pounds.

19. A telescoping catheter, comprising:

an elongate, flexible tubular body, comprising a proximal section having at least one lumen and a distal section axially movably positioned within the lumen; and
a control for advancing the distal section from a first, proximally retracted position within the proximal section to a second, extended position, extending distally beyond the proximal section; and

an active tip on the distal end of the distal section, comprising a distal opening that is movable between a smaller and a larger configuration.

20. A telescoping catheter as in Claim 19, wherein the control comprises a pull wire extending through the proximal section.

21. A telescoping catheter as in Claim 19, wherein the distal section is distally advanceable to extend beyond the proximal section for a distance of at least about 10 cm.

22. A telescoping catheter as in Claim 19, wherein the distal section is distally advanceable to extend beyond the proximal section for a distance of at least about 25 cm.

23. A telescoping catheter as in Claim 19, wherein the distal opening is movable in response to movement of a control wire.

24. A telescoping catheter as in Claim 19, wherein the distal opening is movable between a smaller and a larger configuration in response to application of vacuum to the lumen.

25. A telescoping catheter as in Claim 19, wherein the size of the distal opening is changed by lateral movement of a side wall on the distal section.

26. A telescoping catheter as in Claim 19, wherein the distal opening comprises at least one movable jaw.

27. A telescoping catheter as in Claim 19, wherein the distal end of the distal section comprises a duck bill valve configuration.

28. A telescoping catheter as in Claim 19, further comprising a controller for applying intermittent vacuum to the lumen.

29. A telescoping catheter as in Claim 28, wherein the controller is configured to apply pulses of vacuum to the lumen spaced apart by spaces of neutral pressure.

30. A telescoping catheter as in Claim 28, wherein the controller is configured to alternate between applying pulses of higher negative pressure and lower negative pressure.

31. A telescoping catheter as in Claim 28, wherein the distal tip of the catheter axially reciprocates in response to application of pulses of vacuum to the lumen.

32. A system for aspirating a vascular occlusion from a remote site, comprising:
an elongate, flexible tubular body, comprising at least one central lumen extending along its longitudinal length;

an agitator extendable through the central lumen of the tubular body to position a distal end of the agitator near a distal end of the tubular body;

a driver connectable to a proximal end of the agitator and configured to actuate the agitator; and

a vacuum port near the proximal end of the tubular body and in fluid communication with the central lumen of the tubular body.

33. A system as in Claim 32, wherein the agitator comprises an elongate tube.

34. A system as in Claim 33, wherein the agitator comprises a wire extending through the elongate tube and having at least one bend near its distal end.

35. A system as in Claim 32, wherein the agitator comprises a proximal end, a distal end, and a loop at the distal end.

36. A system as in Claim 32, wherein the driver is configured to rotate the agitator cyclically in alternating directions.

37. A system as in Claim 32, wherein the agitator comprises:

at least one lumen along its longitudinal length,

an influent port near its proximal end configured to allow fluid communication between the lumen of the agitator and a source of media, and

at least one effluent port configured to allow fluid communication between the lumen of the agitator and the central lumen of the tubular body.

38. A system as in Claim 37, further comprising a control, for expressing media from the effluent port into the central lumen of the tubular body.

39. A system as in Claim 37, wherein the distal portion of the tubular body is configured to vibrate in a transverse direction in response to the injection of media.

40. A system as in Claim 32, further comprising a controller for applying a pulsatile vacuum cycle to the central lumen.

41. A system as in Claim 32, further comprising a rotating hemostasis valve coupled to the proximal end of the tubular body, the rotating hemostasis valve comprising:

at least one main lumen along its longitudinal length, through which the proximal portion of the agitator is configured to pass, and

an aspiration lumen bifurcating from the main lumen and provided with a vacuum port.

42. A system as in Claim 32, further comprising a proximal drive assembly coupled to the proximal end of the tubular body, the proximal drive assembly comprising:

- at least one main lumen along its longitudinal length for receiving the agitator;
- a media injection port, into which media is injected, in fluid communication with the central lumen of the tubular body, and
- a proximal drive connection at the proximal end, which operably connects between the agitator and the driver.

43. An enhanced flexibility neurovascular catheter, comprising:

an elongate flexible body, having a proximal end, a distal end and a side wall defining a central lumen, a distal zone of the side wall comprising:

an outer jacket surrounding a helical coil, the outer jacket formed from a plurality of tubular segments positioned coaxially about the coil; wherein

a proximal one of the tubular segments has a durometer of at least about 60D and a distal one of the tubular segments has a durometer of no more than about 35D; and

an axially extending filament within the side wall, extending at least about the most distal 10 cm of the length of the catheter.

44. An enhanced flexibility neurovascular catheter as in Claim 43, wherein the filament extends at least about the most distal 15 cm of the length of the catheter.

45. An enhanced flexibility neurovascular catheter as in Claim 43, wherein the filament extends at least about the most distal 20 cm of the length of the catheter.

46. An enhanced flexibility neurovascular catheter as in Claim 44, wherein the filament comprises multiple fibers.

47. An enhanced flexibility neurovascular catheter as in Claim 44, wherein the filament extends axially in between the coil and the inner liner.

48. An enhanced flexibility neurovascular catheter as in Claim 44, wherein the side wall further comprises:

- a tubular inner liner;
- a soft tie layer separated from the lumen by the inner liner;

wherein the helical coil surrounds the tie layer, and adjacent windings of the coil are spaced progressively further apart in the distal direction.

49. An enhanced flexibility neurovascular catheter as in Claim 48, wherein the tubular liner is formed by dip coating a removable mandrel.

50. An enhanced flexibility neurovascular catheter as in Claim 48, wherein the tubular liner comprises PTFE.

51. An enhanced flexibility neurovascular catheter as in Claim 48, wherein the tie layer comprises polyurethane.

52. An enhanced flexibility neurovascular catheter as in Claim 51, wherein the tie layer has a wall thickness of no more than about 0.005 inches.

53. An enhanced flexibility neurovascular catheter as in Claim 51, wherein the tie layer extends along at least the most distal 20 cm of the flexible body.

54. An enhanced flexibility neurovascular catheter as in Claim 48, wherein the coil comprises a shape memory material.

55. An enhanced flexibility neurovascular catheter as in Claim 54, wherein the coil comprises Nitinol.

56. An enhanced flexibility neurovascular catheter as in Claim 55, wherein the Nitinol comprises an Austenite state at body temperature.

57. An enhanced flexibility neurovascular catheter as in Claim 48, wherein the outer jacket is formed from at least five discrete tubular segments.

58. An enhanced flexibility neurovascular catheter as in Claim 48, wherein the outer jacket is formed from at least nine discrete tubular segments.

59. An enhanced flexibility neurovascular catheter as in Claim 58, wherein the difference in durometer between a proximal one of the tubular segments and a distal one of the tubular segments is at least about 20D.

60. An enhanced flexibility neurovascular catheter as in Claim 58, wherein the difference in durometer between a proximal one of the tubular segments and a distal one of the tubular segments is at least about 30D.

61. An enhanced flexibility neurovascular catheter as in Claim 43, wherein the catheter can withstand at least about 3.5 pounds tension before failure.

62. An enhanced flexibility neurovascular catheter as in Claim 43, wherein the catheter can withstand at least about 5 pounds tension before failure.

63. An enhanced flexibility neurovascular catheter as in Claim 43, wherein the catheter can withstand at least about 7 pounds tension before failure.

64. A method of making a high flexibility distal zone on a neurovascular catheter, comprising the steps of:

dip coating a removable mandrel to form a tubular inner layer on the mandrel;
coating the tubular inner layer with a soft tie layer;
applying a helical coil to the outside of the tie layer;
positioning a plurality of tubular segments on the helical coil; the plurality of segments having durometers that decrease in a distal direction;
heating the tubular segments to form the high flexibility distal zone on the neurovascular catheter; and
removing the mandrel.

65. A method as in Claim 64, wherein removing the mandrel step includes axially elongating the mandrel.

66. A method as in Claim 64, comprising positioning at least seven segments on the helical coil.

67. A method as in Claim 64, comprising positioning at least nine segments on the helical coil.

68. A method as in Claim 67, wherein the difference in durometer between a proximal one of the tubular segments and a distal one of the tubular segments is at least about 20D.

69. A method as in Claim 68, wherein the difference is at least about 30D.

70. A method as in Claim 64, wherein the tubular inner layer comprises PTFE.

71. A method as in Claim 64, wherein the tie layer comprises polyurethane.

72. A method as in Claim 71, wherein the tie layer has a wall thickness of no more than about 0.005 inches.

73. A method as in Claim 71, wherein the tie layer extends along at least the most distal 20 cm of the flexible body.

74. A method as in Claim 64, wherein the coil comprises a shape memory material.

75. A method as in Claim 74, wherein the coil comprises Nitinol.

76. A method as in Claim 75, wherein the Nitinol comprises an Austenite state at body temperature.

77. A method as in Claim 64, further comprising the step of positioning at least one tensile strength enhancing filament in between the coil and the tie layer prior to heat shrinking the tubular segments.

78. A method as in Claim 77, wherein the filament extends along at least about the most distal 15 cm of the length of the catheter.

79. A method as in Claim 77, wherein the filament extends along at least about the most distal 20 cm of the length of the catheter.

80. A method as in Claim 77, wherein the filament comprises multiple fibers

81. A method as in Claim 64, further comprising the step of positioning at least one tensile strength enhancing filament over the tie layer before the applying a helical coil step.

82. A neurovascular catheter, comprising:

an elongate flexible tubular body, having a proximal end, a distal end and a side wall defining a central lumen, a distal zone of the tubular body comprising:

a tubular inner liner;

a tie layer separated from the lumen by the inner liner;

a helical coil surrounding the tie layer, adjacent windings of the coil spaced progressively further apart in the distal direction;

an outer jacket surrounding the helical coil, and

an opening at the distal end which is enlargeable from a first inside diameter for transluminal navigation to a second, larger inside diameter to facilitate aspiration of thrombus into the lumen.

83. A neurovascular catheter as in Claim 82, wherein the distal opening is enlargeable in response to exposure to blood.

84. A neurovascular catheter as in Claim 82, wherein the distal opening is enlargeable in response to exposure to body temperature.

85. A neurovascular catheter as in Claim 82, wherein the distal opening is enlargeable in response to removal of a constraint.

86. A neurovascular catheter as in Claim 85, wherein the constraint comprises a polymer having a structural integrity that decreases in the intravascular environment.

87. A neurovascular catheter as in Claim 82, wherein the catheter body adjacent the distal opening comprises a radially outwardly biased embedded support.

88. A neurovascular catheter as in Claim 87, wherein the catheter body adjacent the distal opening comprises an embedded Nitinol frame.

89. A neurovascular catheter as in Claim 82, wherein the catheter body adjacent the distal opening comprises a hydrophilic blend.

90. A neurovascular catheter as in Claim 82, wherein the tubular liner is formed by dip coating a removable mandrel.

91. A neurovascular catheter as in Claim 82, wherein the tubular liner comprises PTFE.

92. A neurovascular catheter as in Claim 82, wherein the tie layer comprises polyurethane.

93. A neurovascular catheter as in Claim 92, wherein the tie layer has a wall thickness of no more than about 0.005 inches.

94. A neurovascular catheter as in Claim 92, wherein the tie layer extends along at least the most distal 20 cm of the flexible body.

95. A neurovascular catheter as in Claim 82, wherein the coil comprises a shape memory material.

96. A neurovascular catheter as in Claim 95, wherein the coil comprises Nitinol.

97. A neurovascular catheter as in Claim 96, wherein the Nitinol comprises an Austenite state at body temperature.

98. A neurovascular catheter as in Claim 82, wherein the outer jacket is formed from at least five discrete tubular segments.

99. A neurovascular catheter as in Claim 82, wherein the outer jacket is formed from at least nine discrete tubular segments.

100. A neurovascular catheter as in Claim 98, wherein the difference in durometer between a proximal one of the tubular segments and a distal one of the tubular segments is at least about 20D.

101. A neurovascular catheter as in Claim 98, wherein the difference in durometer between a proximal one of the tubular segments and a distal one of the tubular segments is at least about 30D.

102. A neurovascular catheter as in Claim 87, wherein the support comprises a wire mesh.

103. A neurovascular catheter as in Claim 87, wherein the support comprises a stent.

104. A neurovascular catheter extension segment, comprising:
an elongate flexible control wire, having a proximal end and a distal end;
a tubular extension segment having a side wall defining a central lumen carried by the distal end of the control wire, the side wall comprising:
a tubular inner liner;
a tie layer separated from the lumen by the inner liner;
a helical coil surrounding the tie layer; and
an outer jacket surrounding the helical coil.

105. A neurovascular catheter extension segment as in Claim 104, wherein the outer jacket is formed from a plurality of tubular segments positioned coaxially about the coil.

106. A neurovascular catheter extension segment as in Claim 105, wherein a proximal one of the tubular segments has a durometer of at least about 60D and a distal one of the tubular segments has a durometer of no more than about 35D.

107. A neurovascular catheter extension segment as in Claim 104, wherein the tubular liner is formed by dip coating a removable mandrel.

108. A neurovascular catheter extension segment as in Claim 104, wherein the tubular liner comprises PTFE.

109. A neurovascular catheter extension segment as in Claim 104, wherein the tie layer comprises polyurethane.

110. A neurovascular catheter extension segment as in Claim 109, wherein the tie layer has a wall thickness of no more than about 0.005 inches.

111. A neurovascular catheter extension segment as in Claim 109, wherein the tie layer extends along at least the most distal 20 cm of the tubular extension segment.

112. A neurovascular catheter extension segment as in Claim 104, wherein the coil comprises a shape memory material.

113. A neurovascular catheter extension segment as in Claim 112, wherein the coil comprises Nitinol.

114. A neurovascular catheter extension segment as in Claim 113, wherein the Nitinol comprises an Austenite state at body temperature.

115. A neurovascular catheter extension segment as in Claim 105, wherein the outer jacket is formed from at least five discrete tubular segments.

116. A neurovascular catheter extension segment as in Claim 115, wherein the outer jacket is formed from at least nine discrete tubular segments.

117. A neurovascular catheter extension segment as in Claim 116, wherein the difference in durometer between a proximal one of the tubular segments and a distal one of the tubular segments is at least about 20D.

118. A neurovascular catheter extension segment as in Claim 117, wherein the difference is at least about 30D.

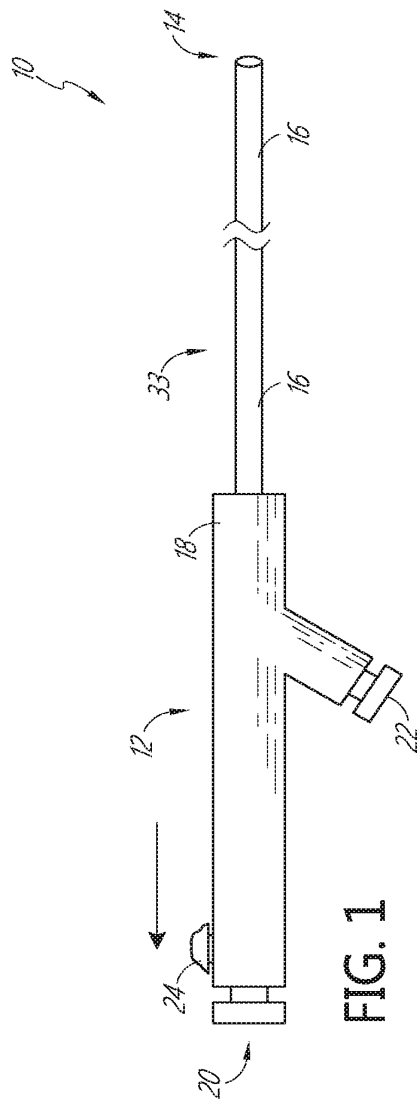
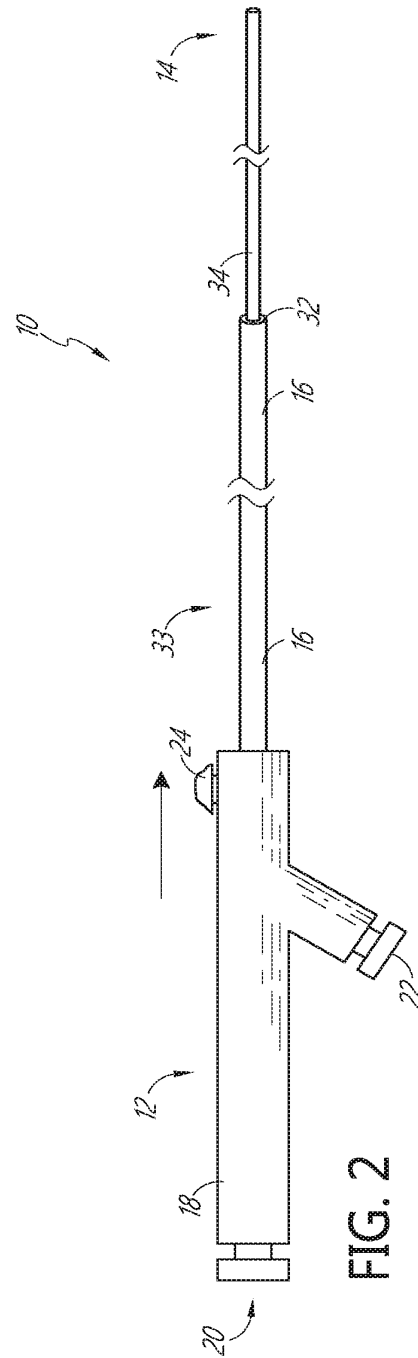
119. A neurovascular catheter extension segment as in Claim 104, wherein the control wire comprises a central lumen.

120. A neurovascular catheter extension segment as in Claim 119, wherein the control wire central lumen is in communication with the central lumen of the tubular extension segment.

121. A neurovascular catheter extension segment system, comprising a neurovascular catheter extension segment as in Claim 119, and an agitator configured to extend through the control wire central lumen and into the central lumen of the tubular extension segment.

122. A neurovascular catheter extension segment as in Claim 119, wherein the inside diameter of the neurovascular catheter extension segment is at least 2X the inside diameter of the control wire central lumen.

123. A neurovascular catheter extension segment as in Claim 122, wherein the inside diameter of the neurovascular catheter extension segment is at least 3X the inside diameter of the control wire central lumen.



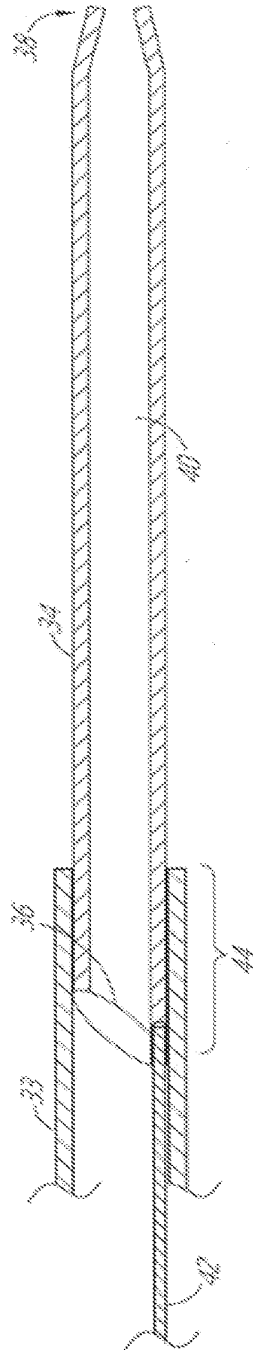


FIG. 3A

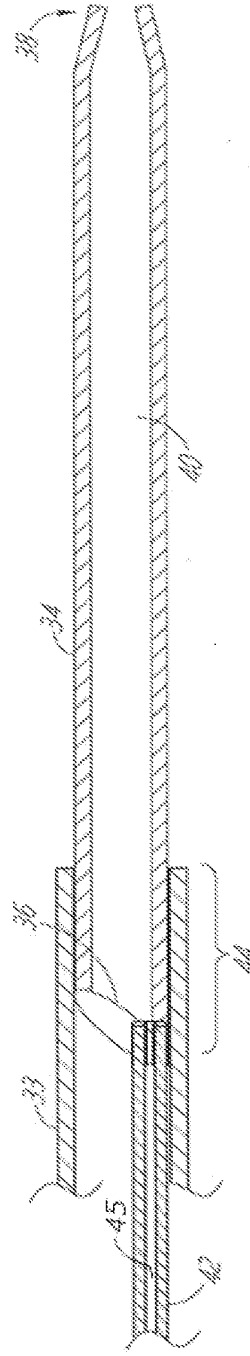


FIG. 3B

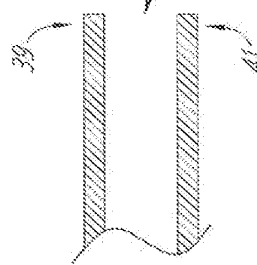


FIG. 4A

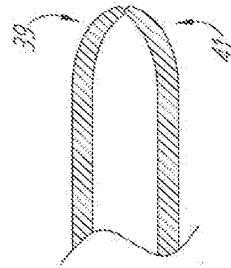


FIG. 4B

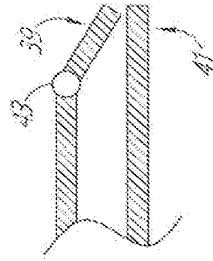


FIG. 4C

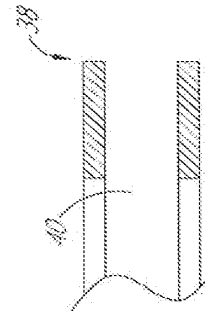


FIG. 4D

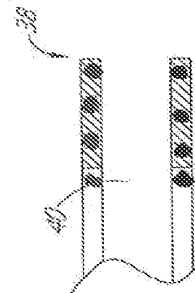


FIG. 4J

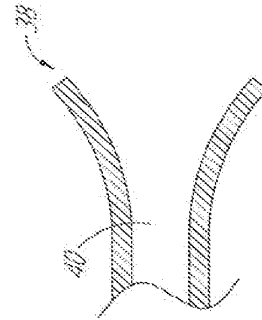


FIG. 4E

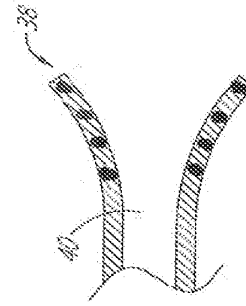


FIG. 4K



FIG. 4F

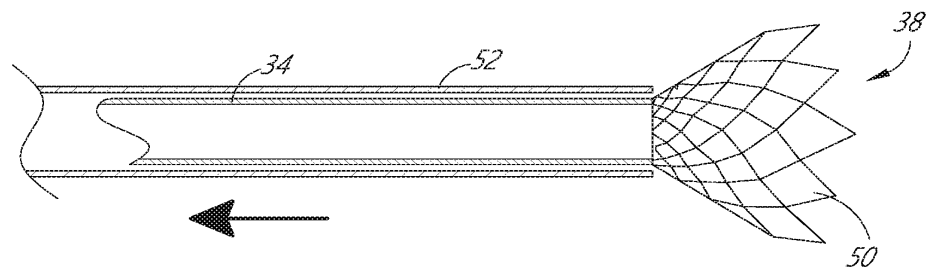


FIG. 4G

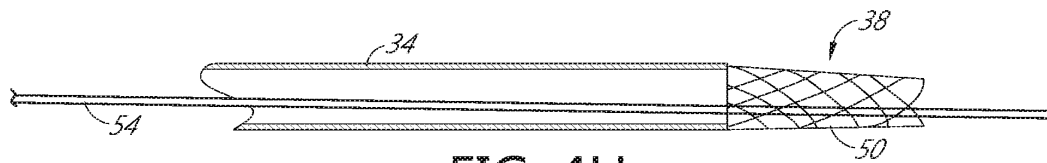


FIG. 4H

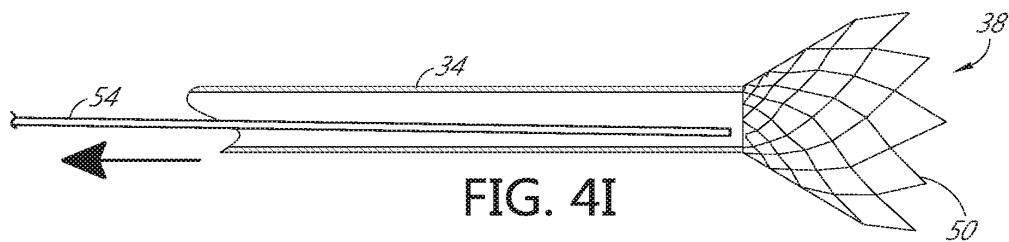
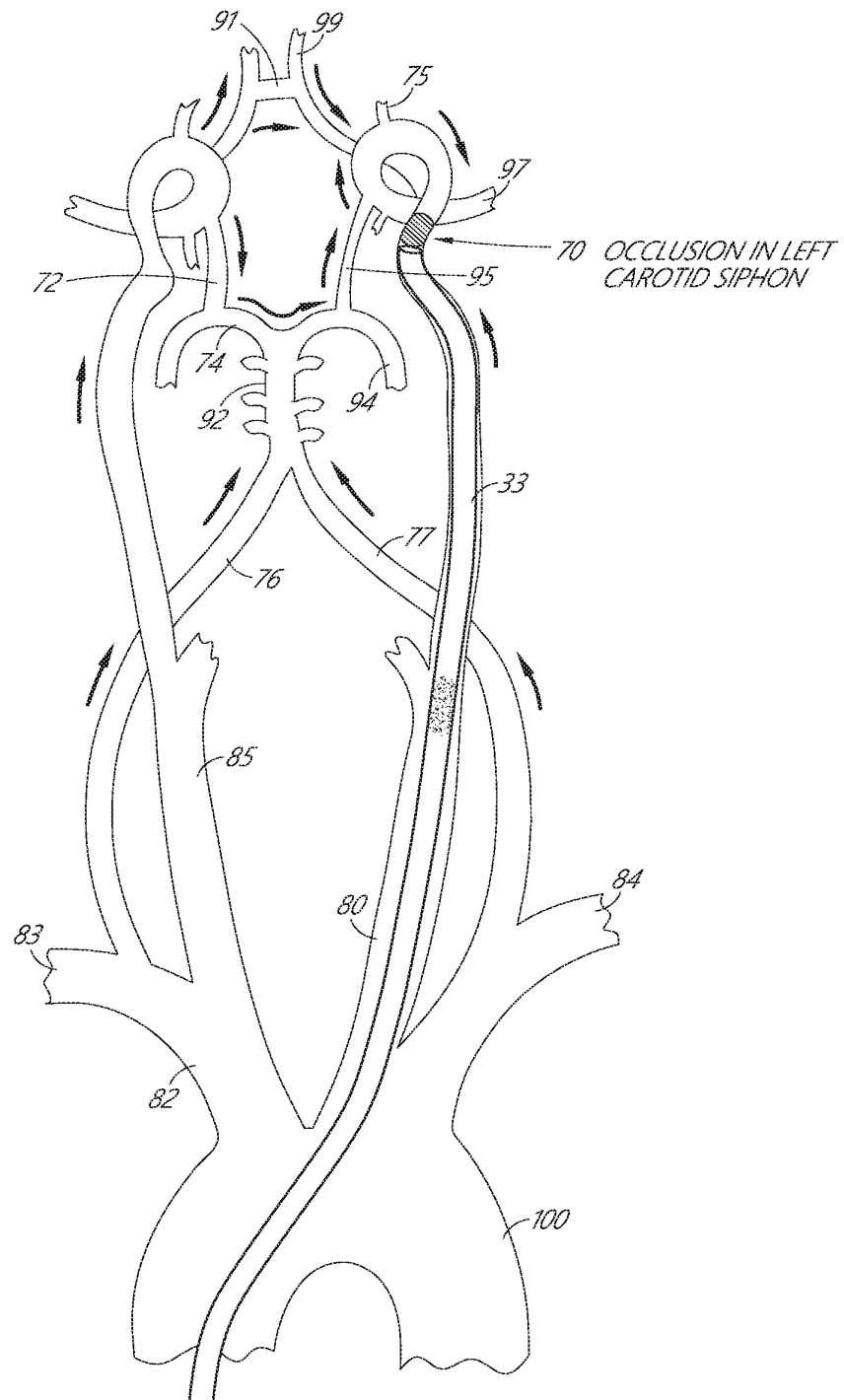


FIG. 4I

FIG. 5



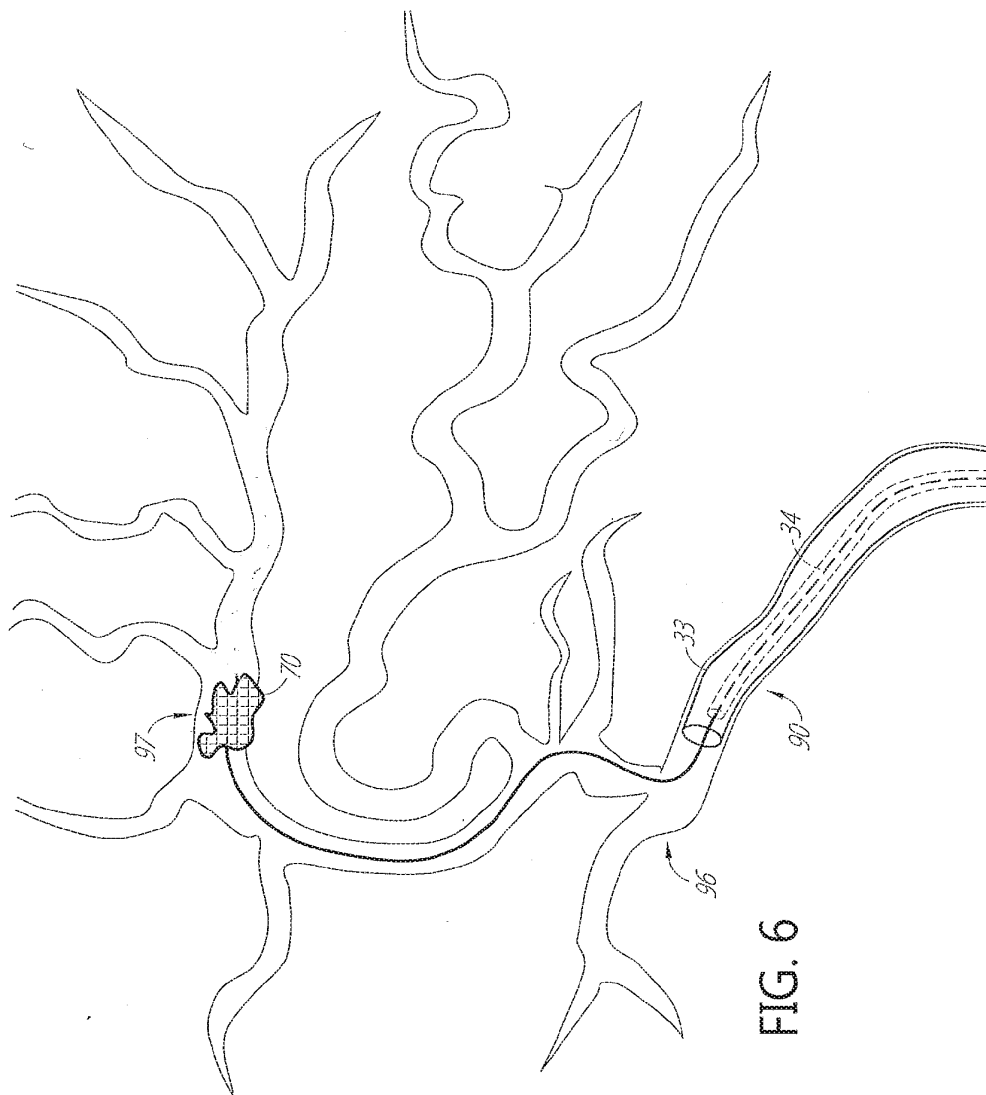
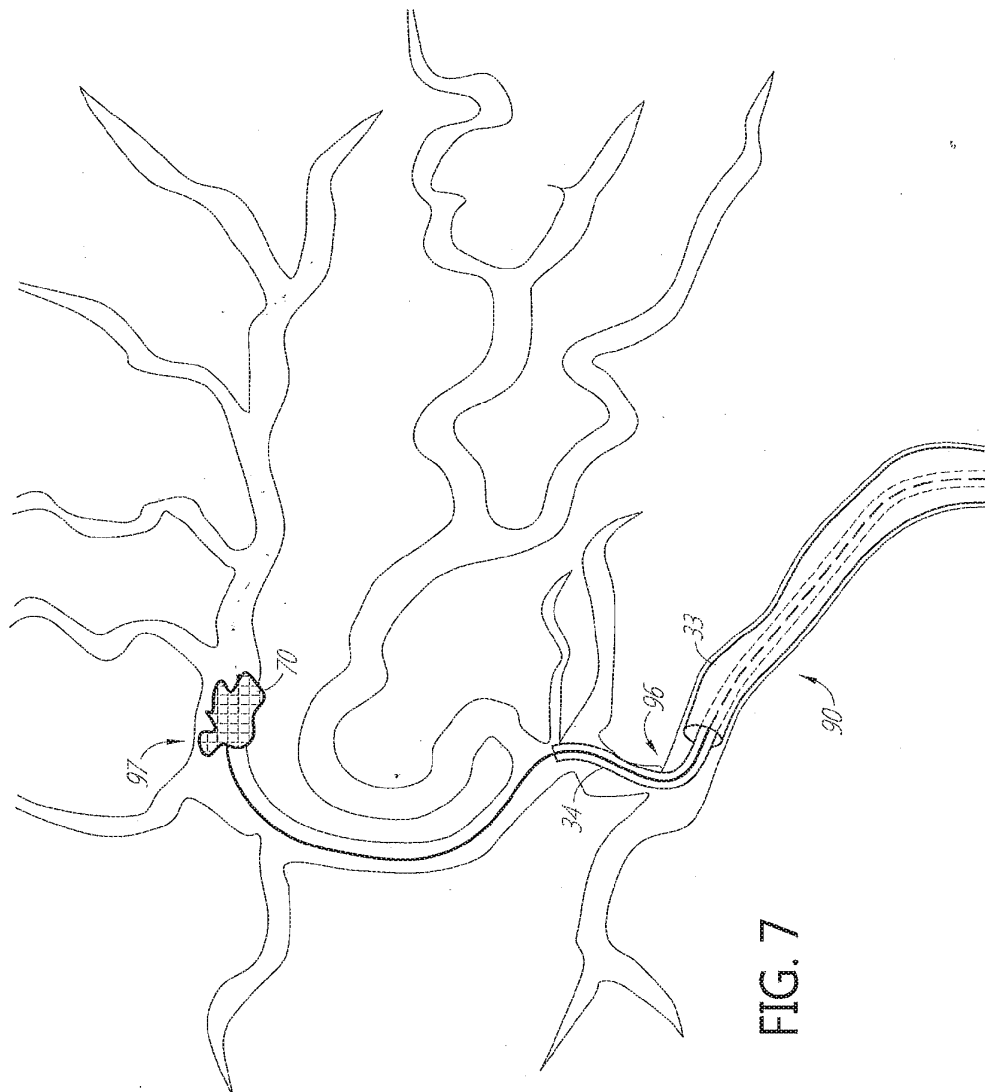
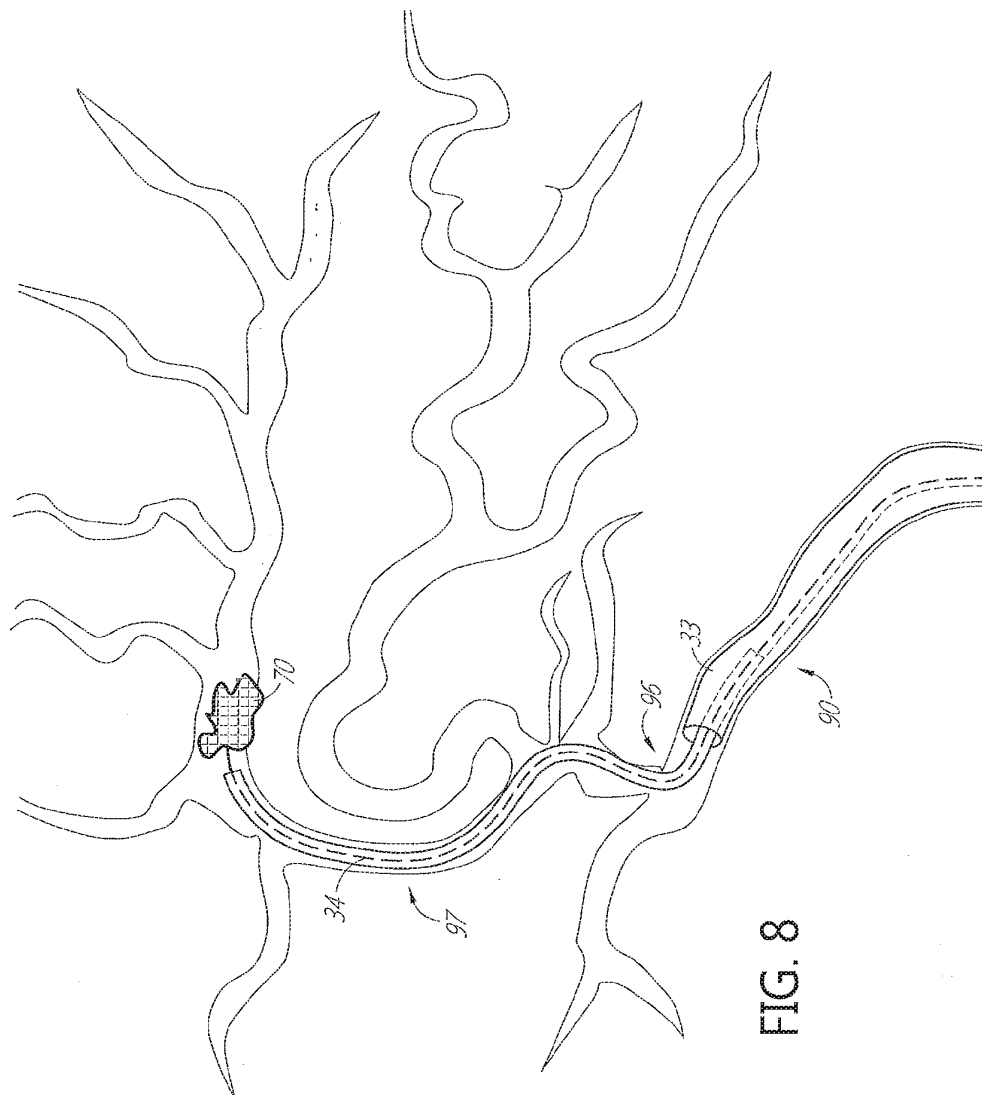


FIG. 6





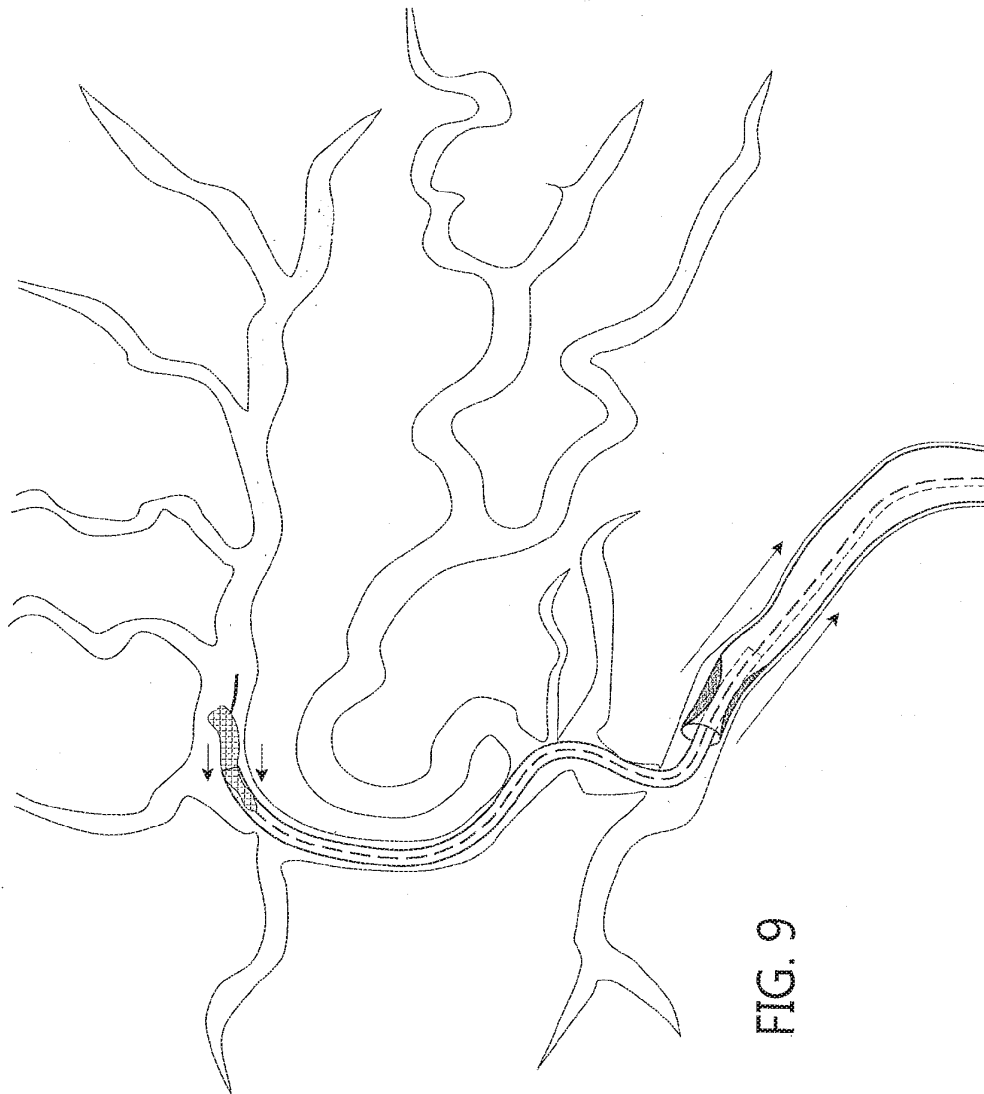
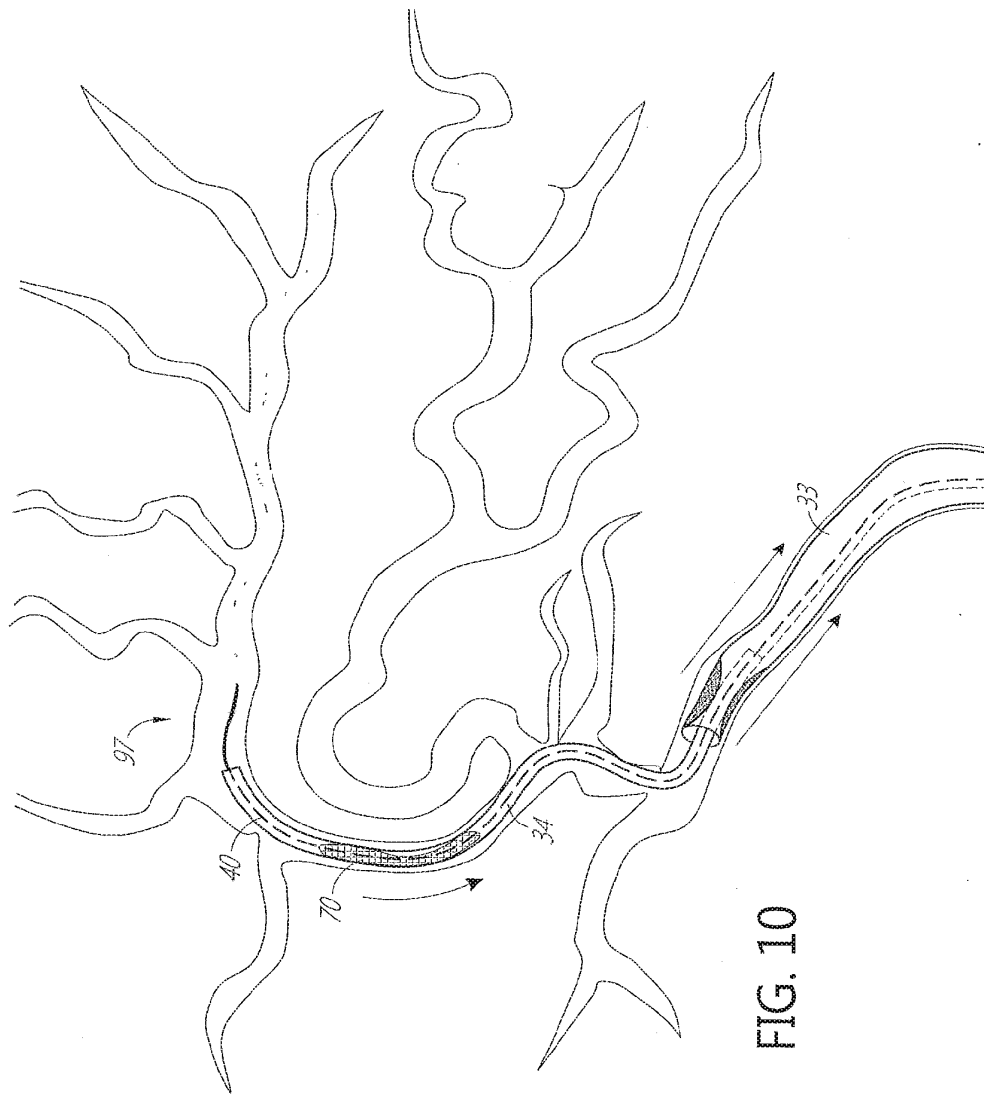
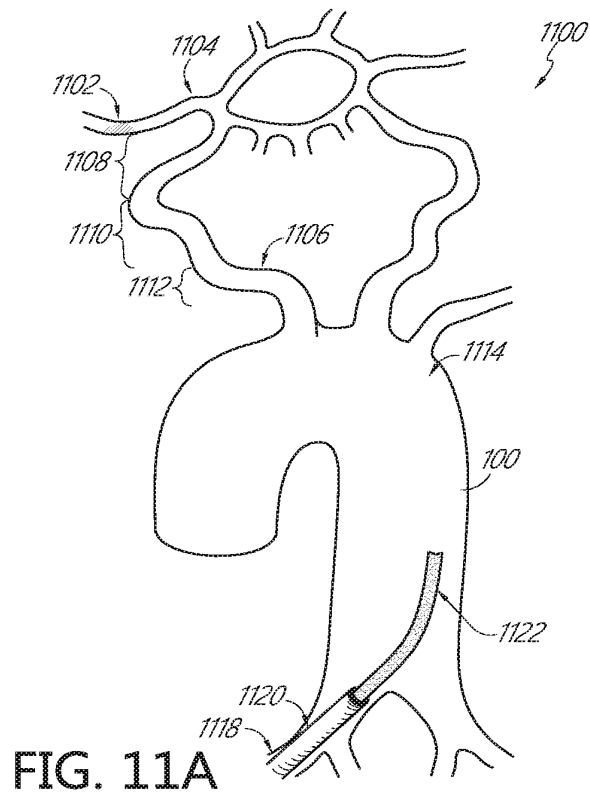
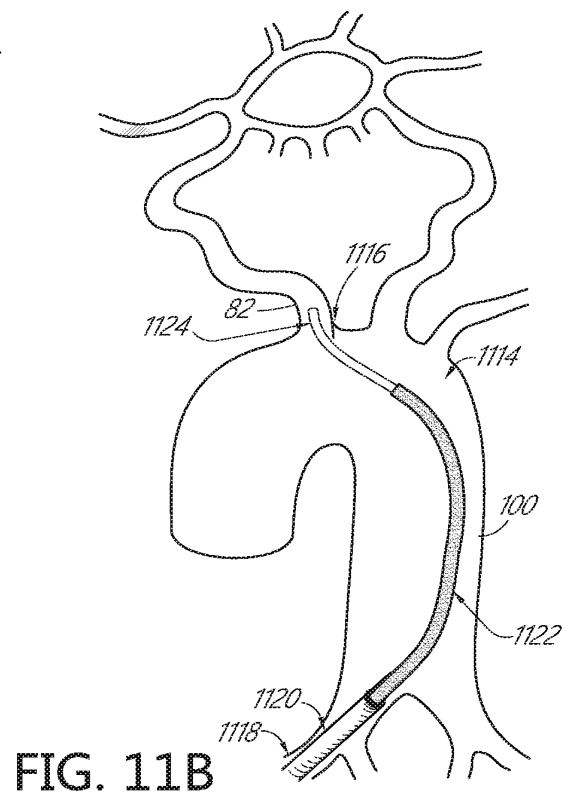
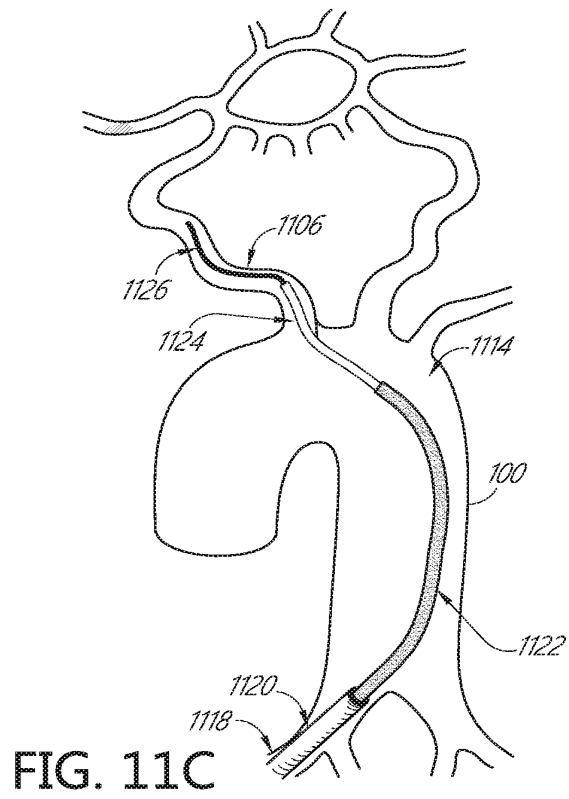
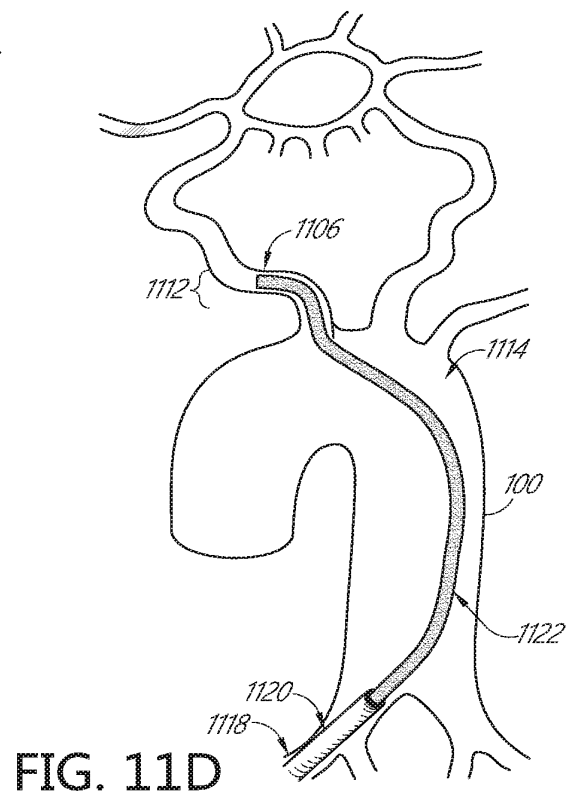


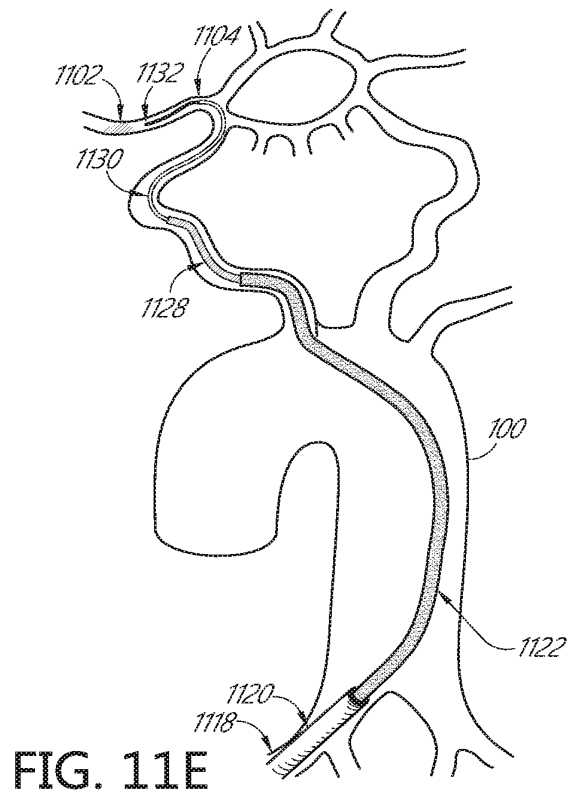
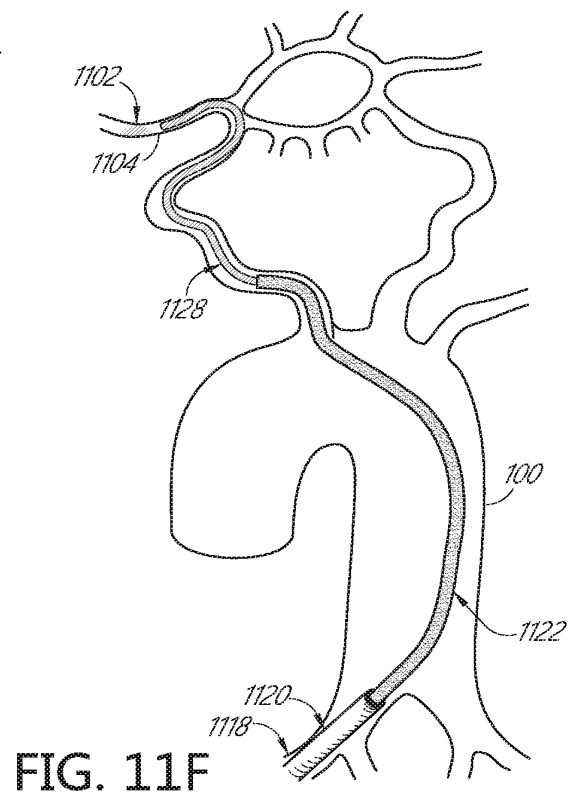
FIG. 9

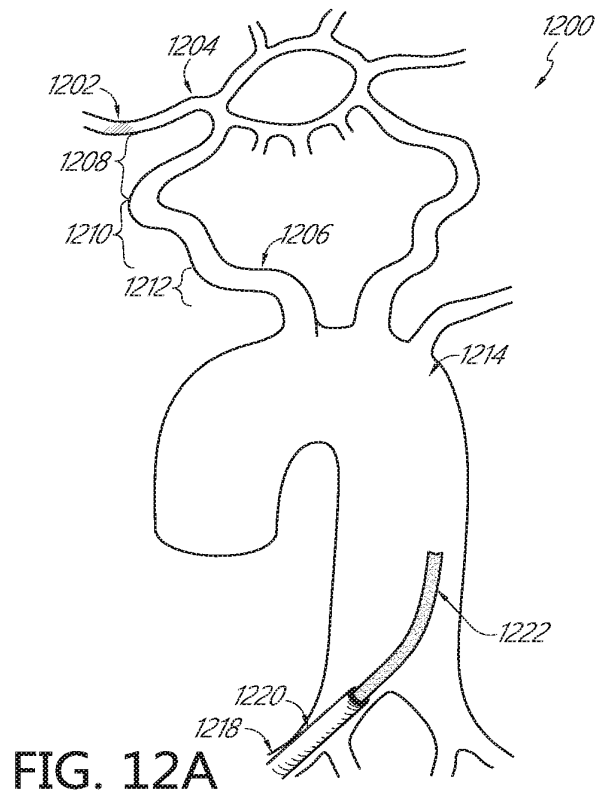
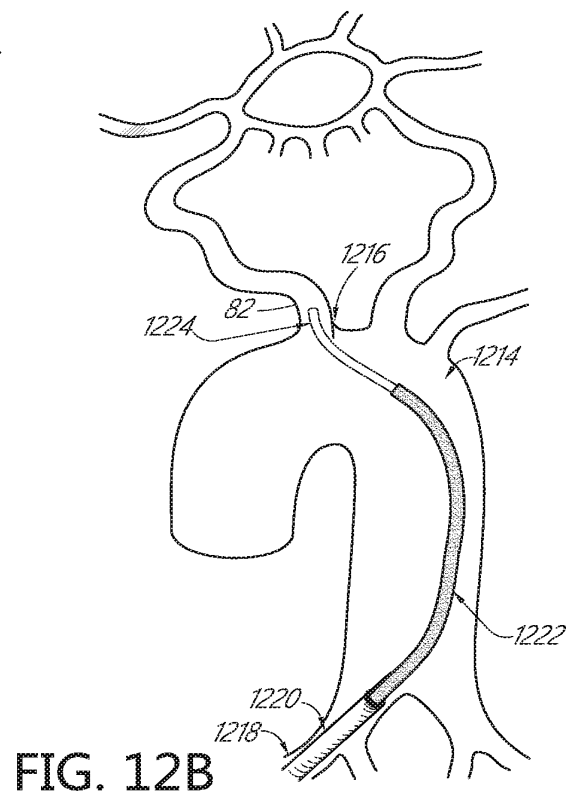
10/41

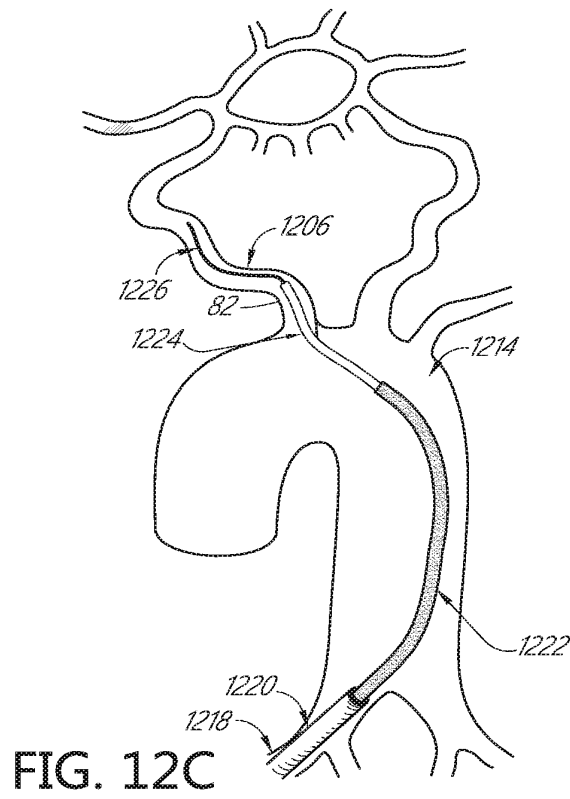
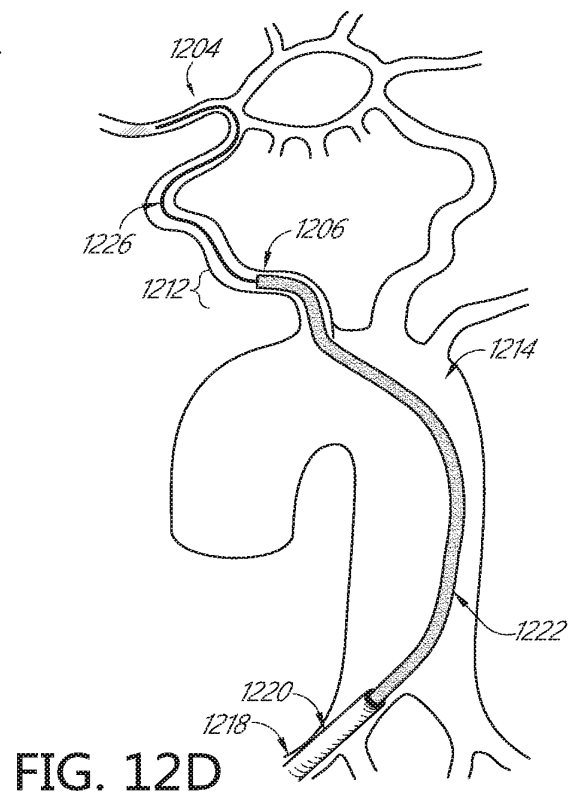


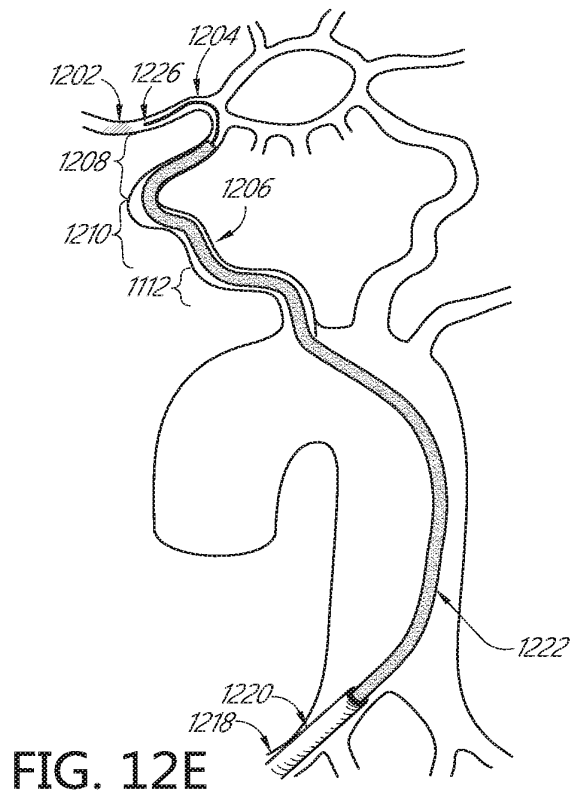
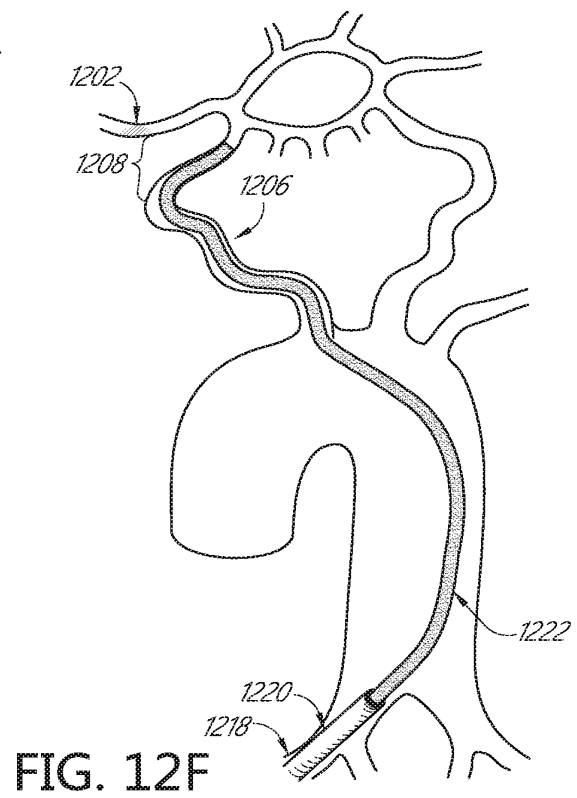












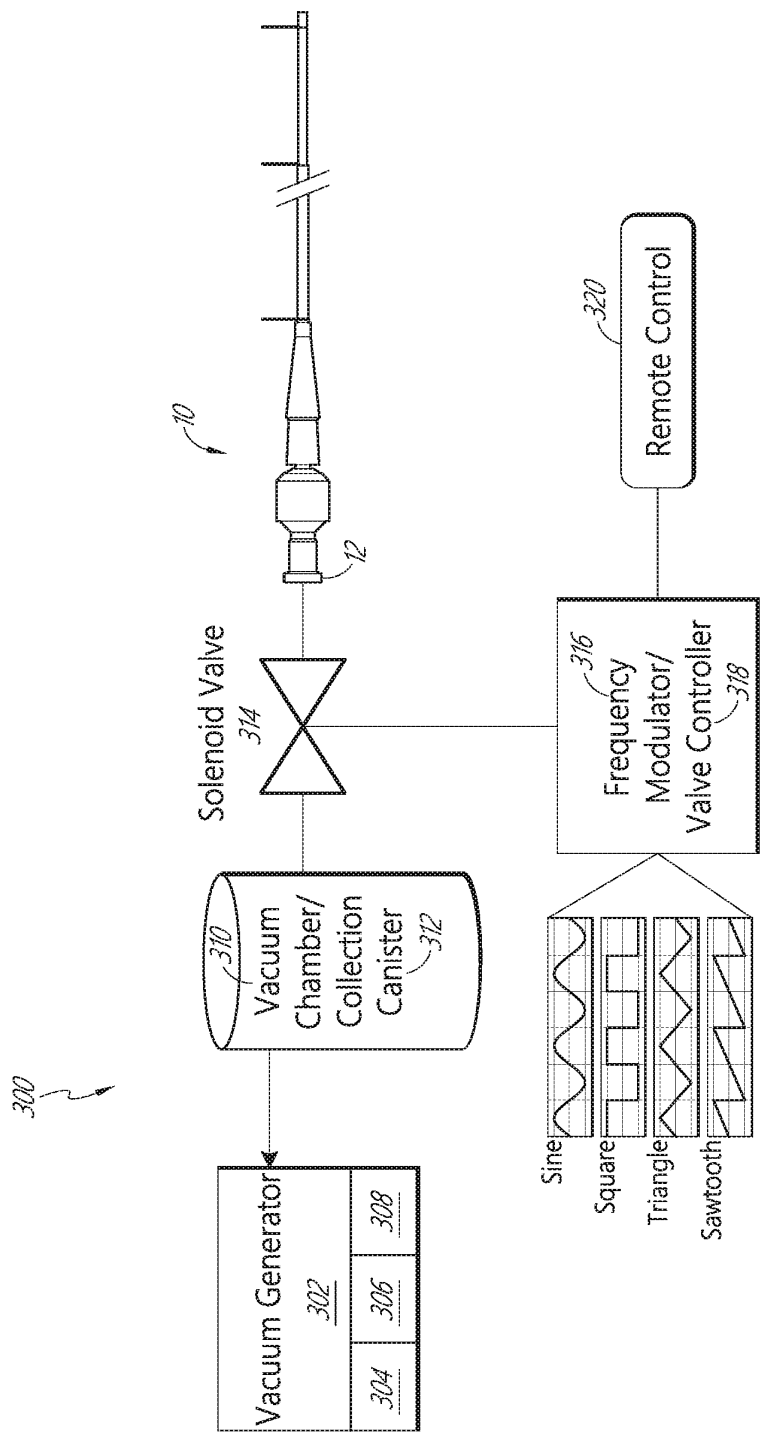


FIG. 13

FIG. 14

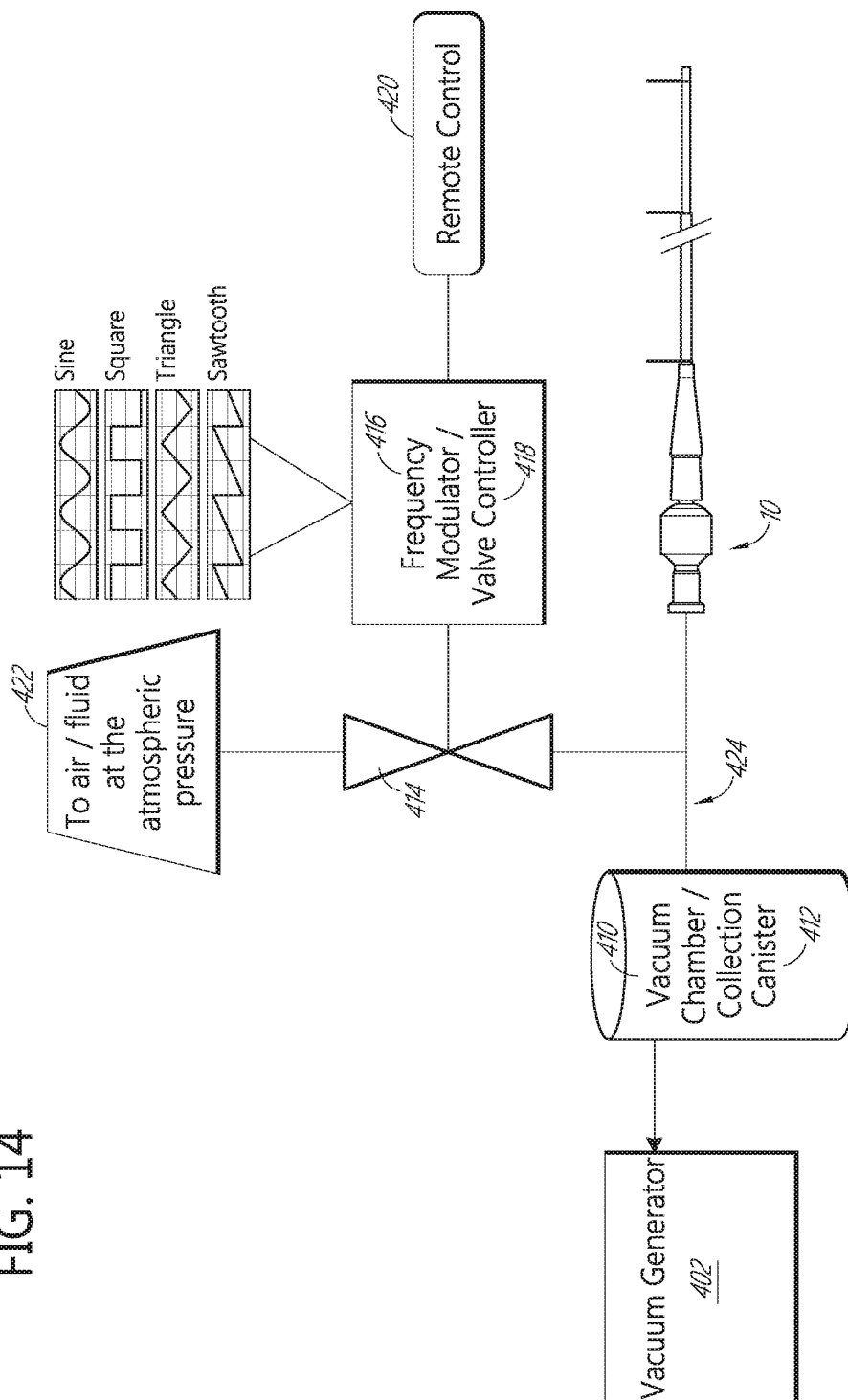
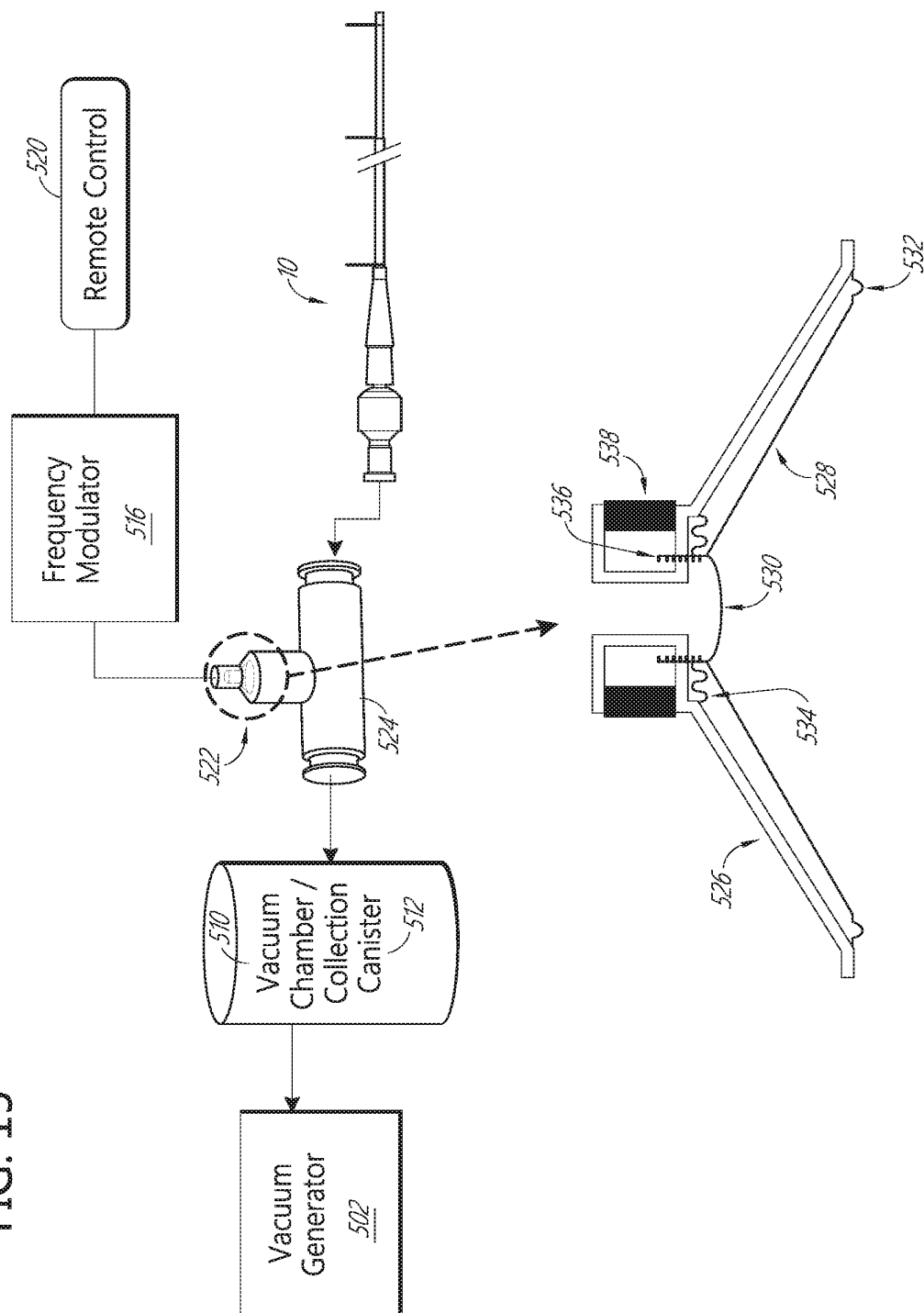


FIG. 15



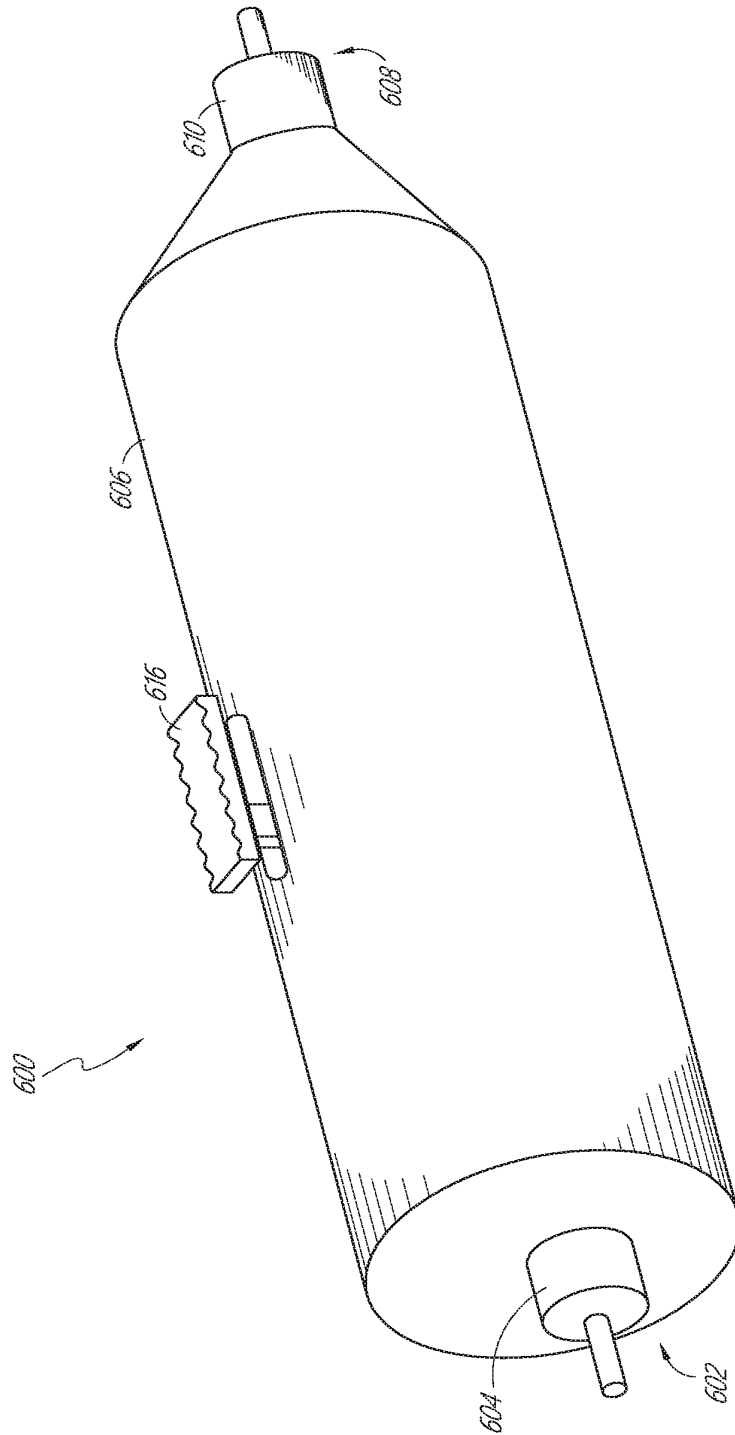


FIG. 16

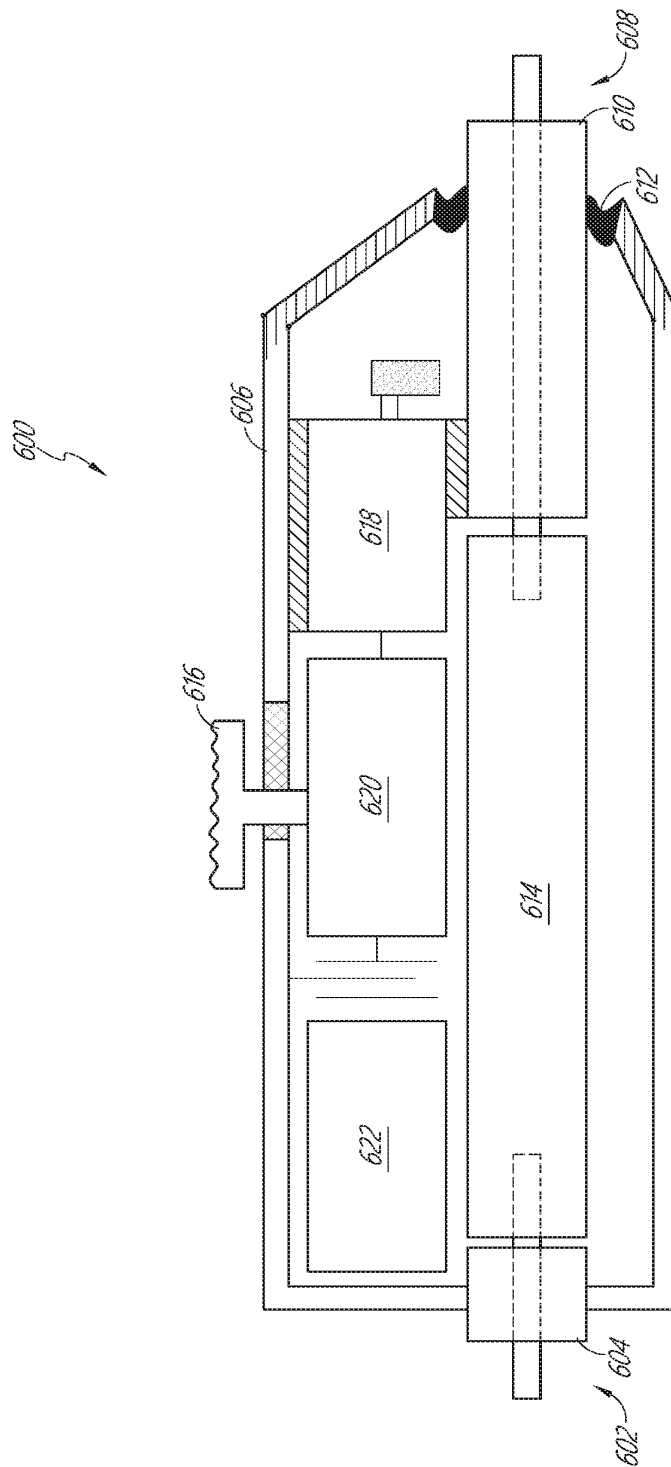


FIG. 17

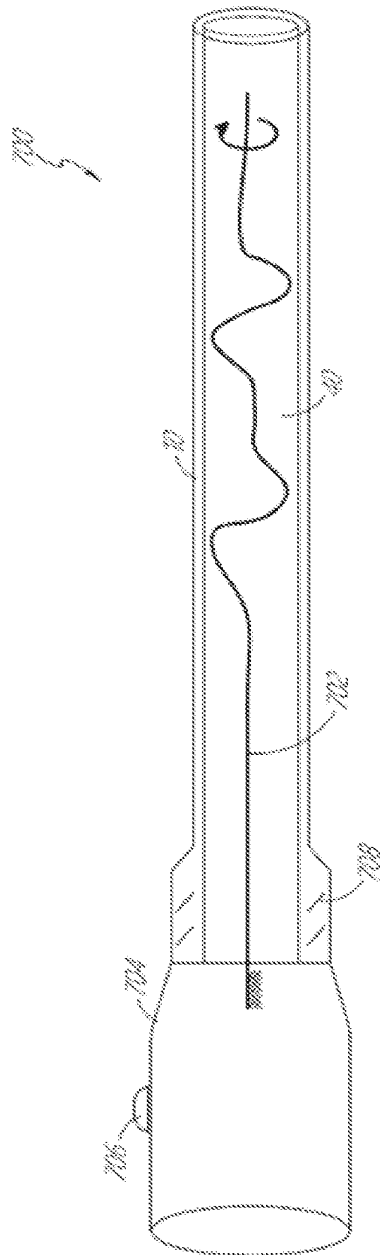


FIG. 18

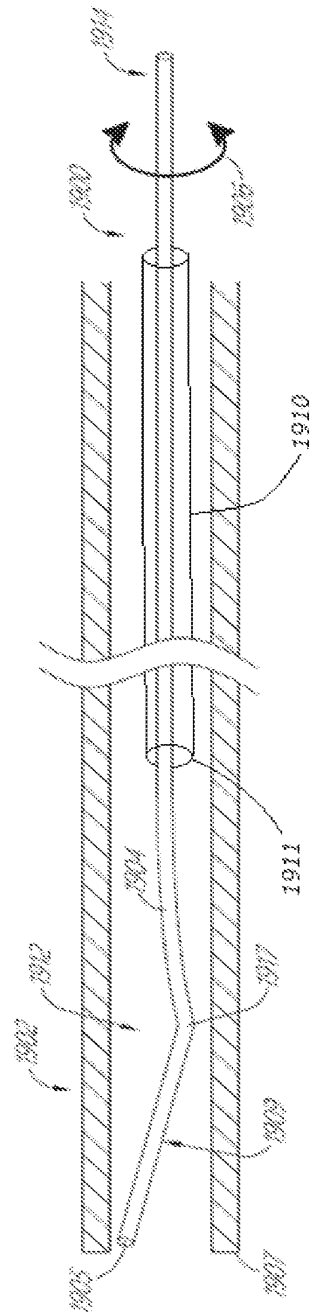
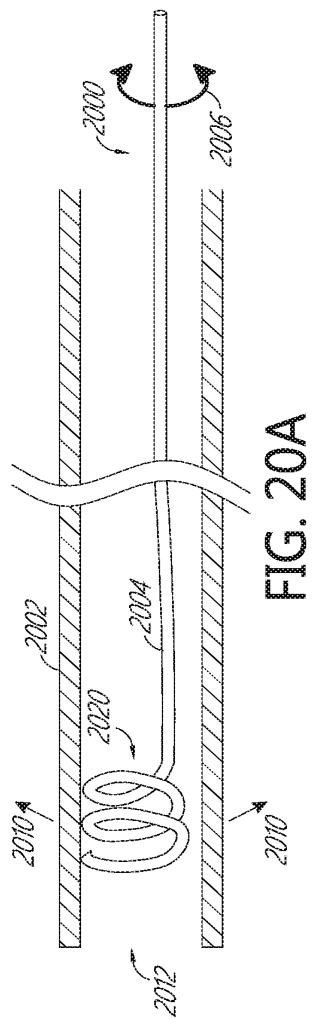
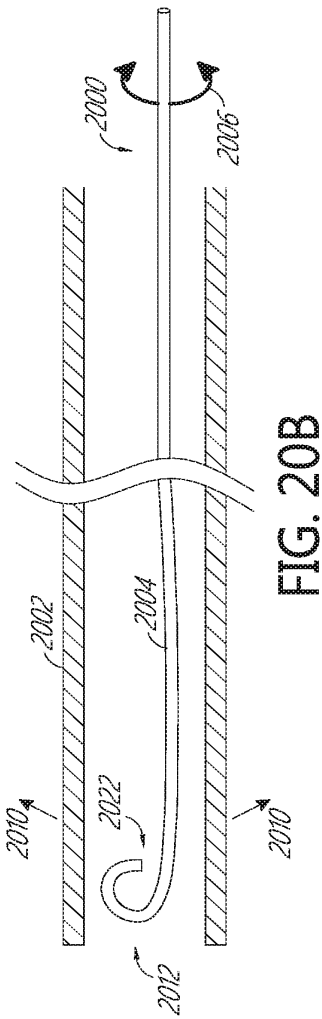
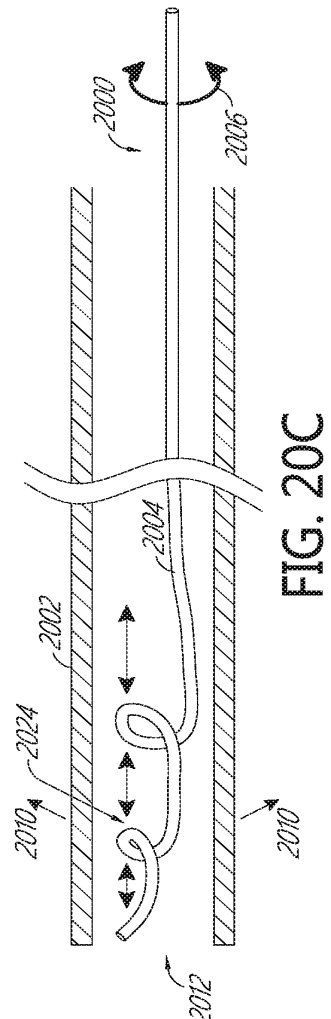


FIG. 19



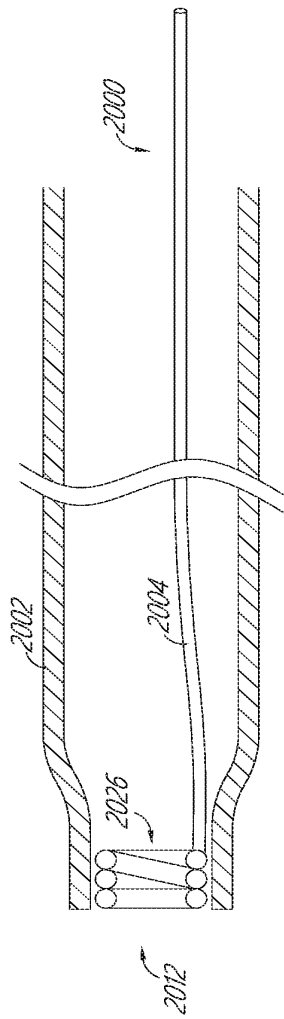


FIG. 20D

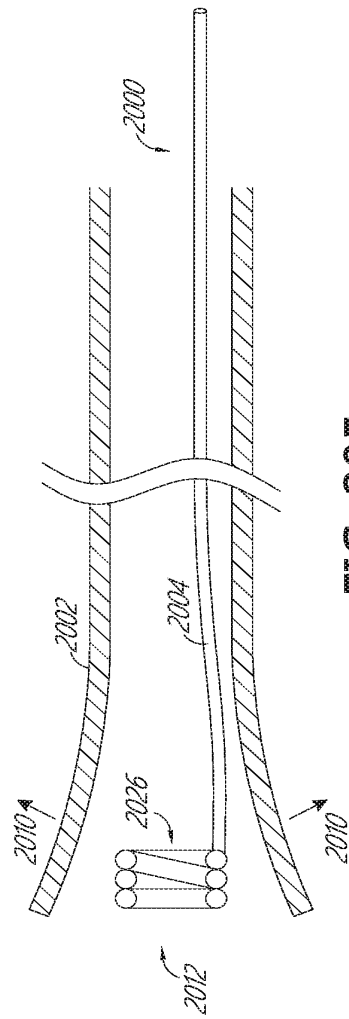


FIG. 20E

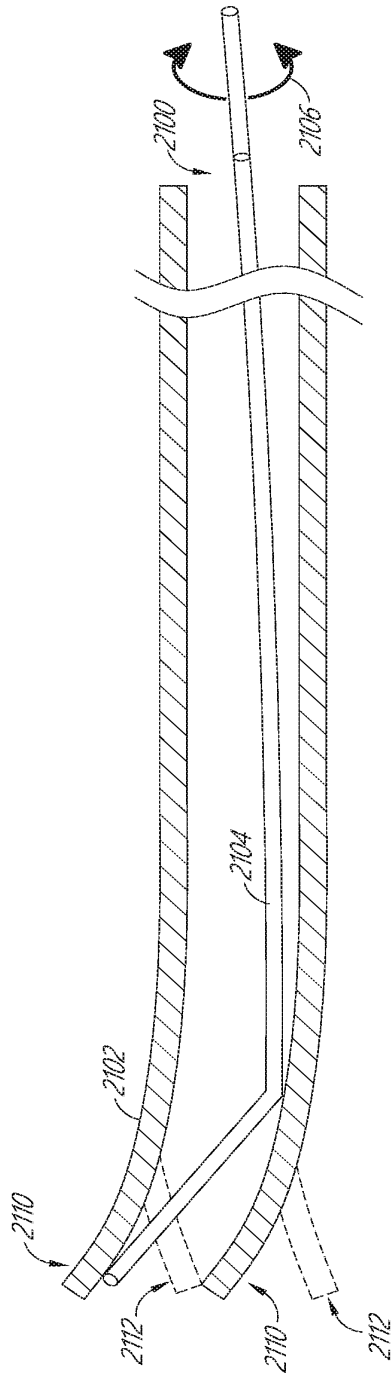


FIG. 21A

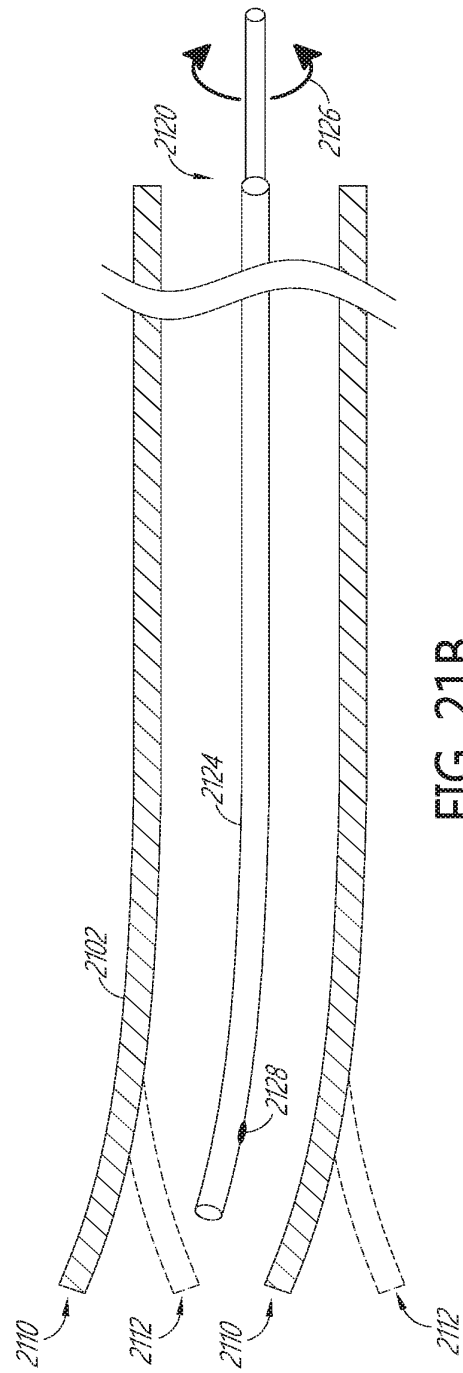


FIG. 21B

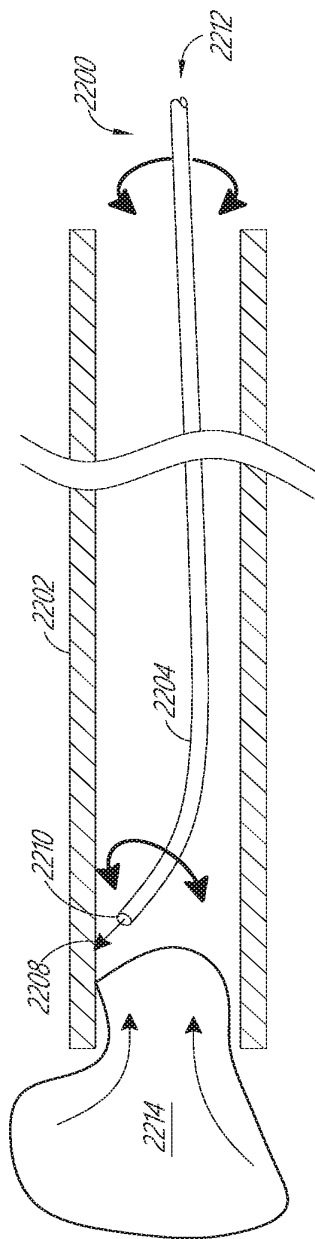


FIG. 22A

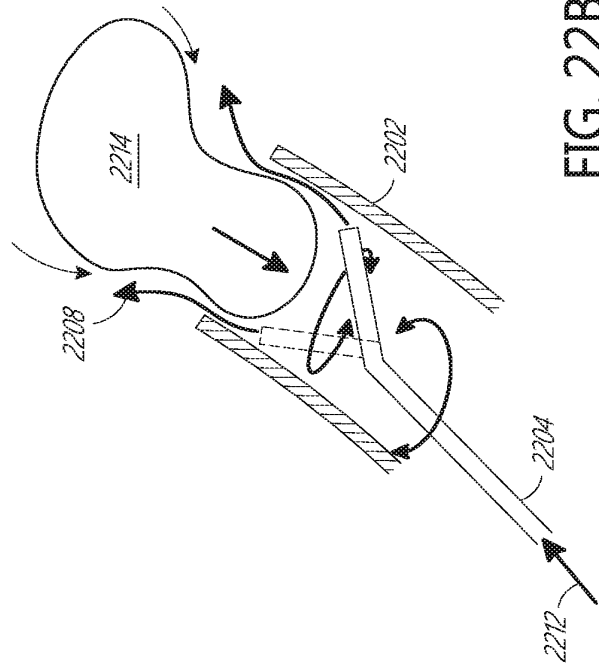


FIG. 22B

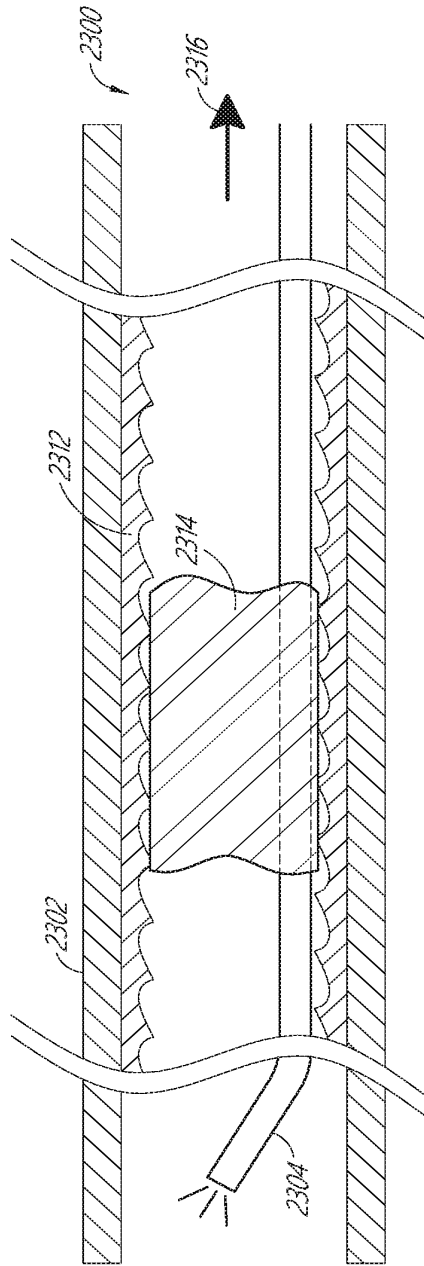


FIG. 23A

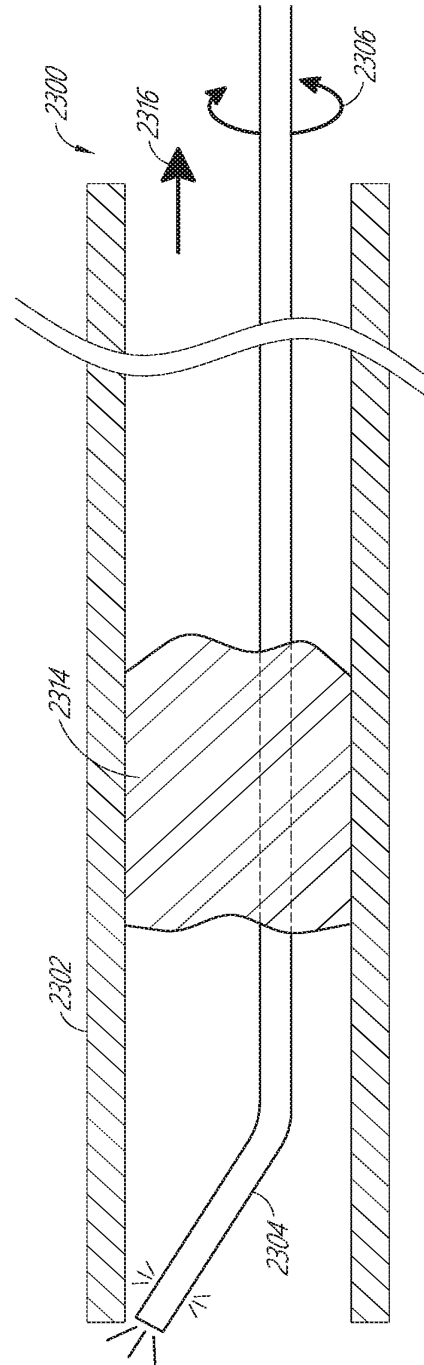


FIG. 23B

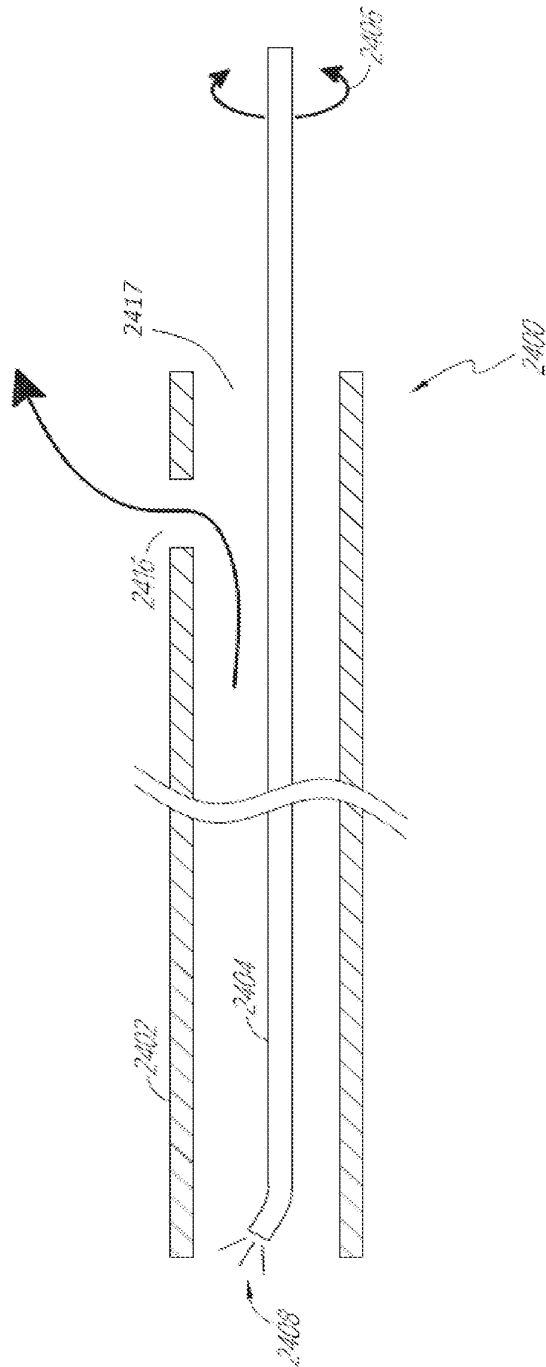


FIG. 24

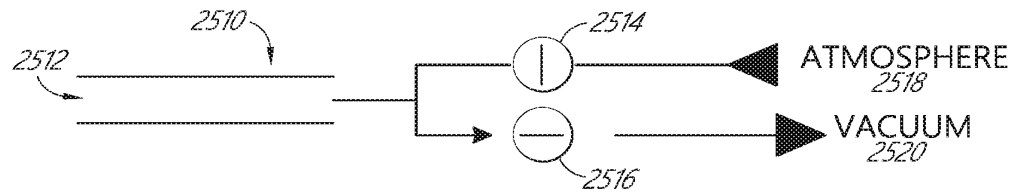


FIG. 25A

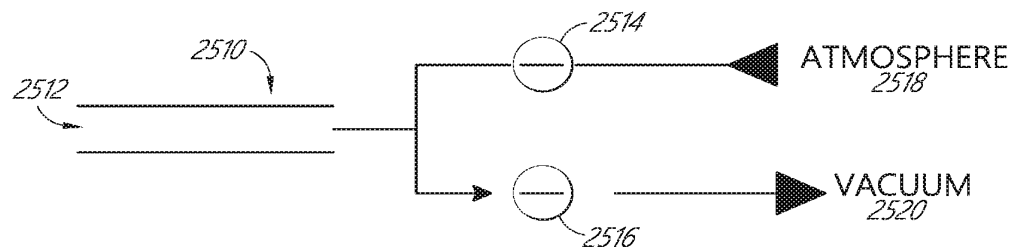


FIG. 25B

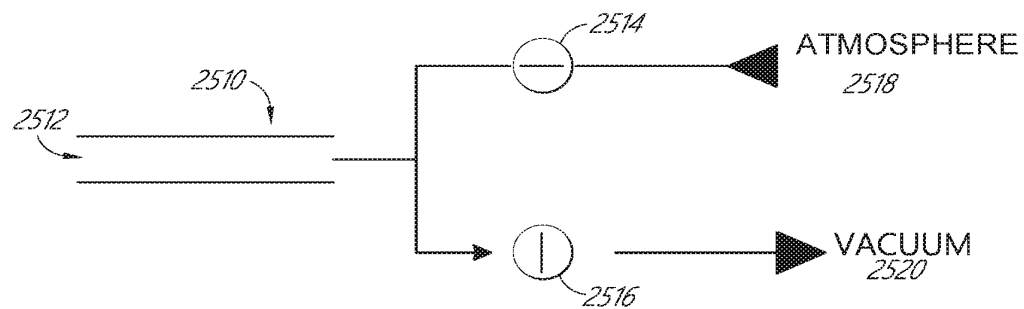


FIG. 25C

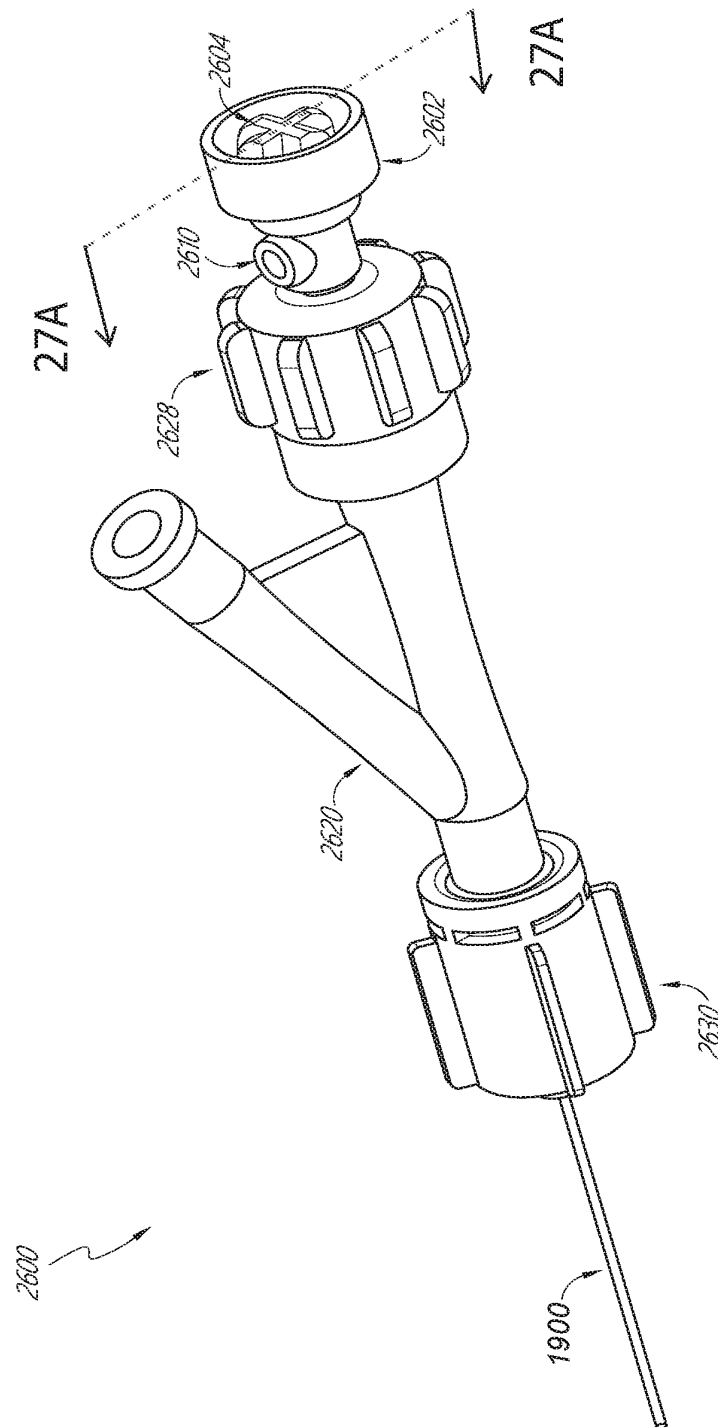


FIG. 26

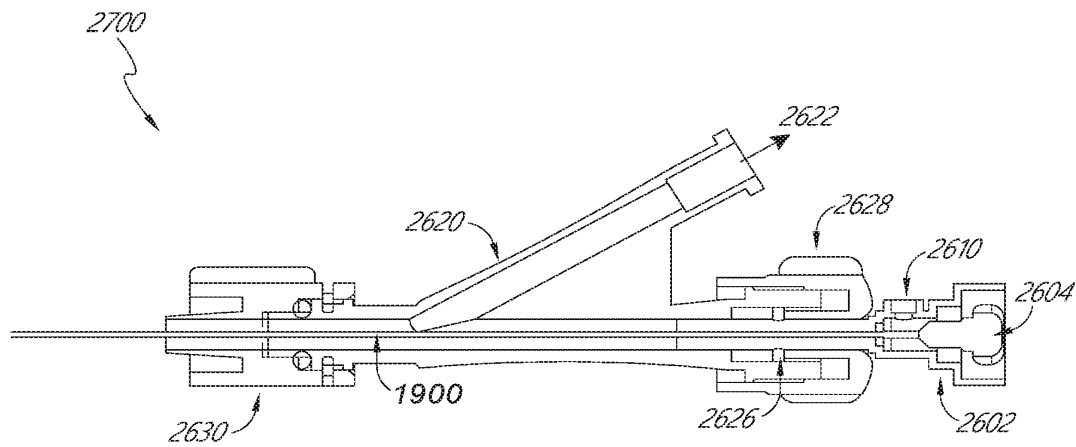


FIG. 27A

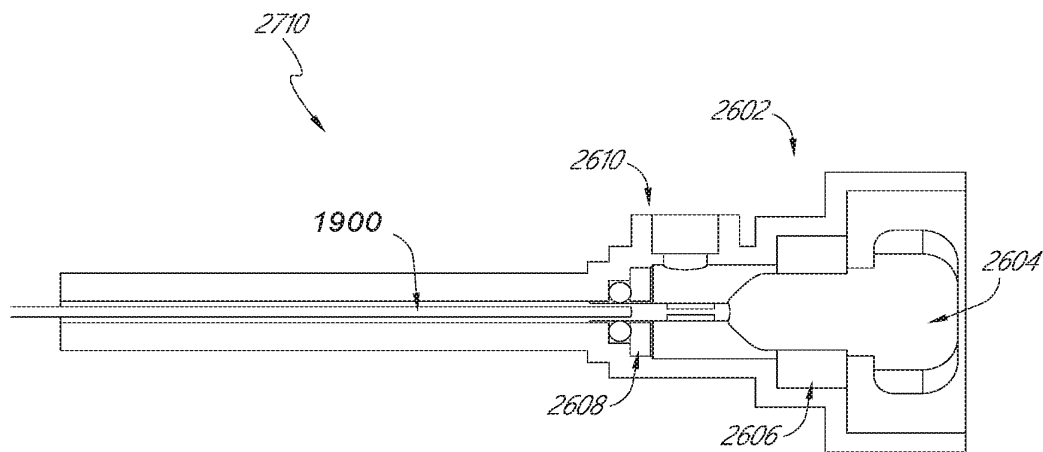


FIG. 27B

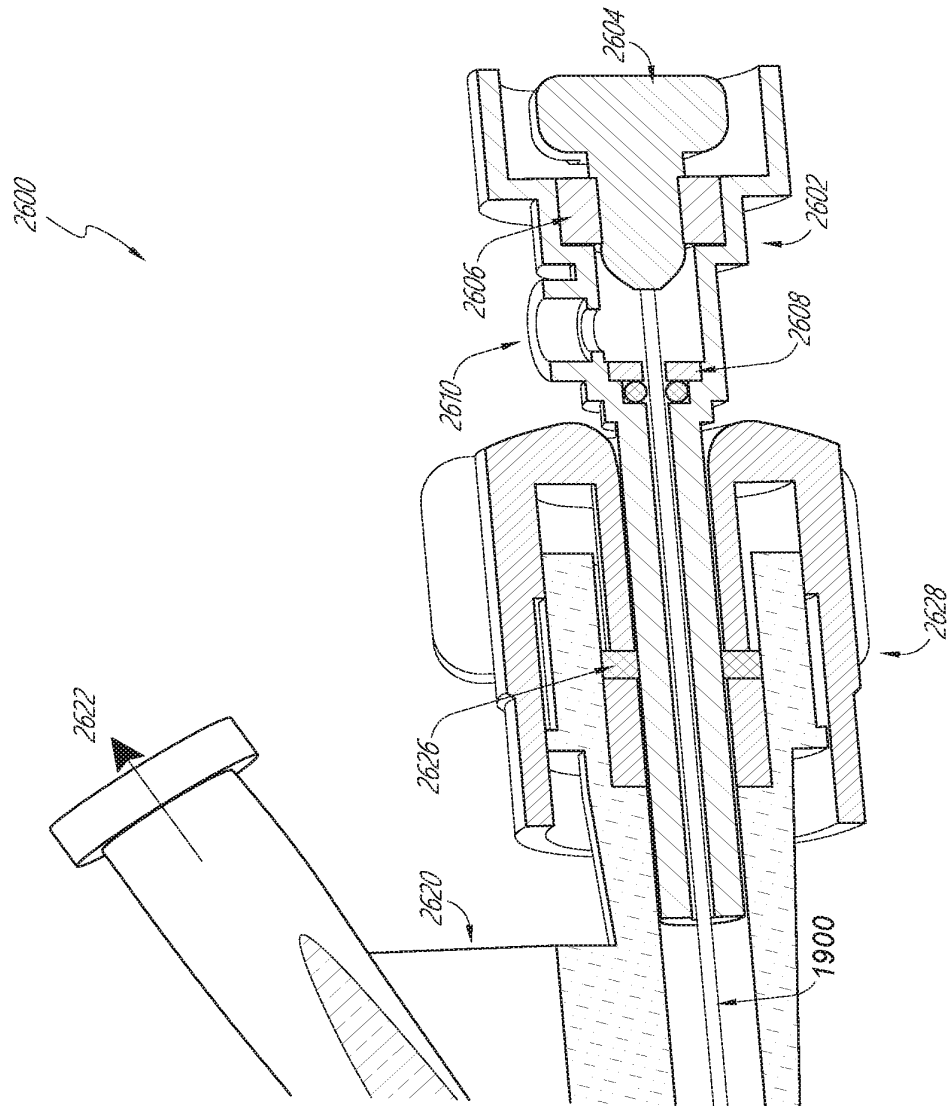


FIG. 28

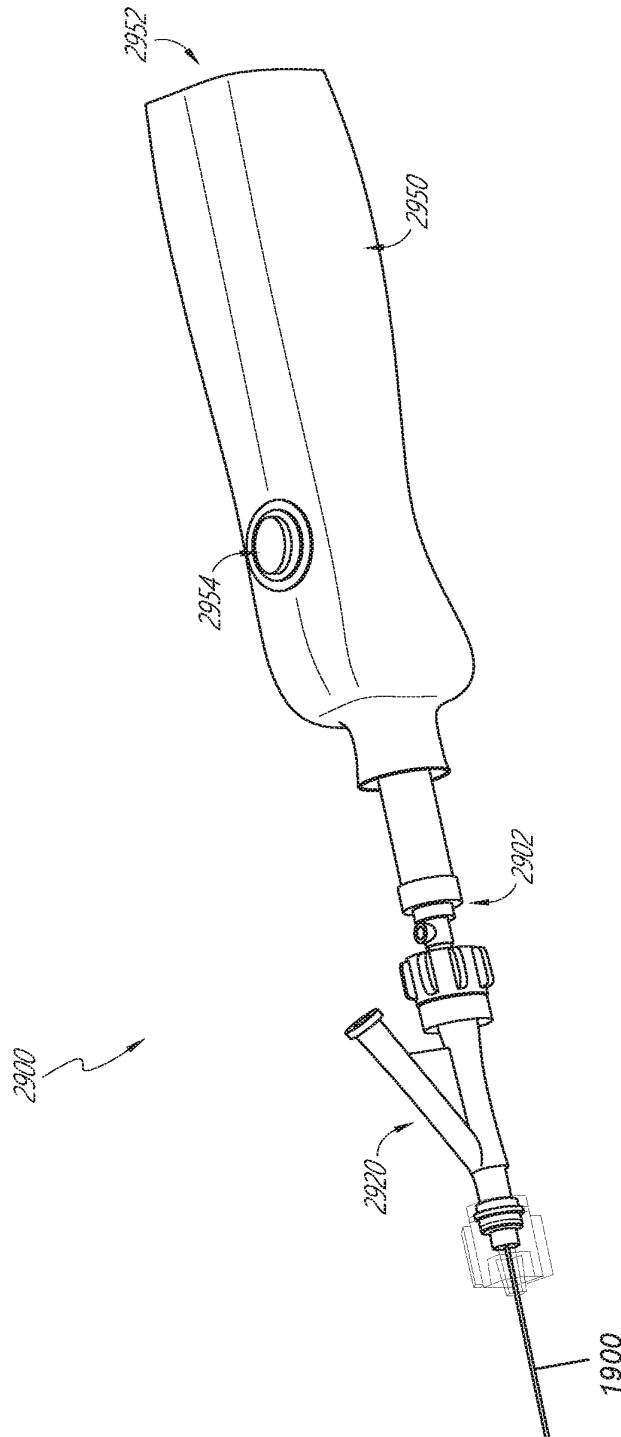


FIG. 29

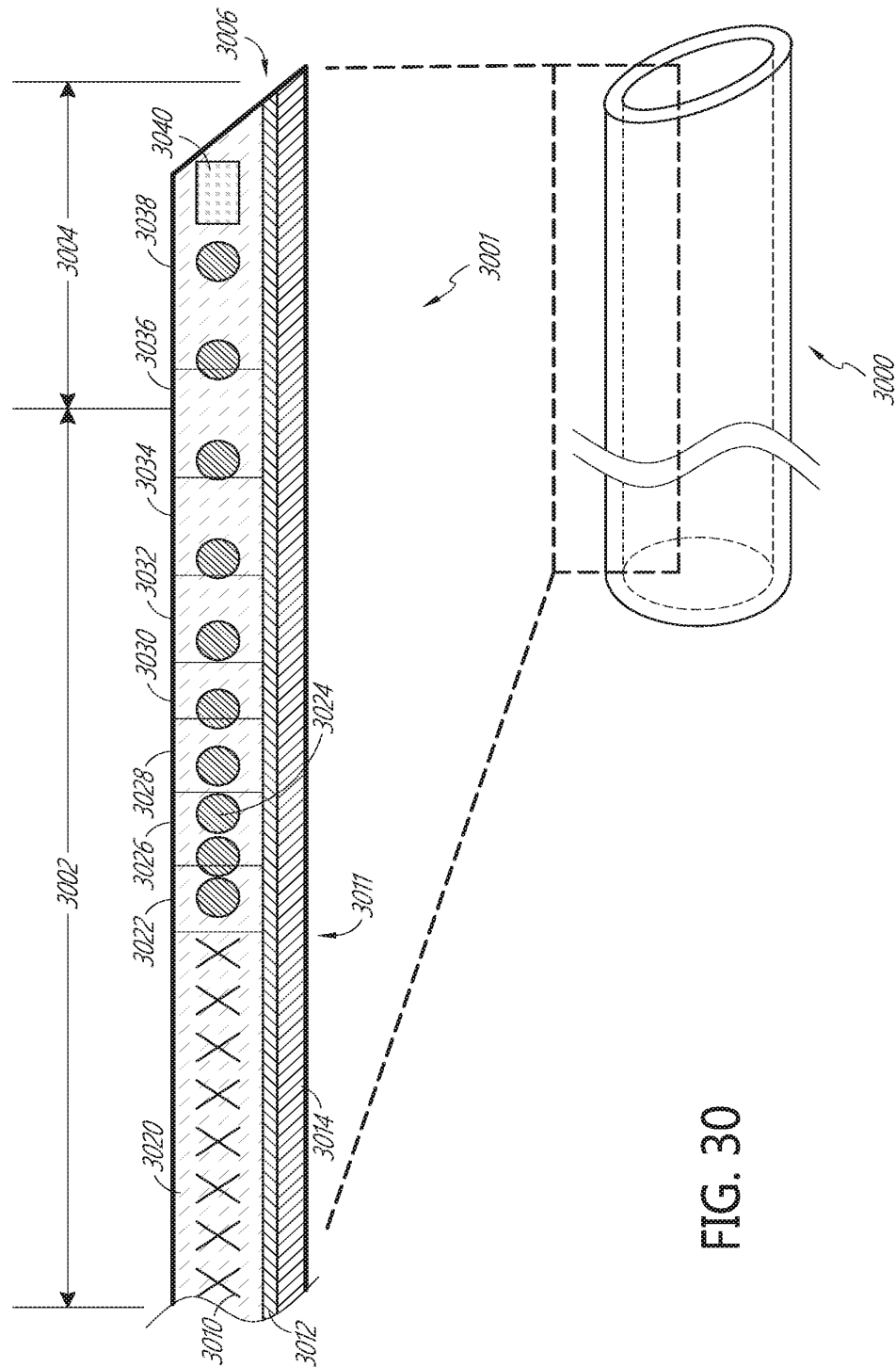


FIG. 30

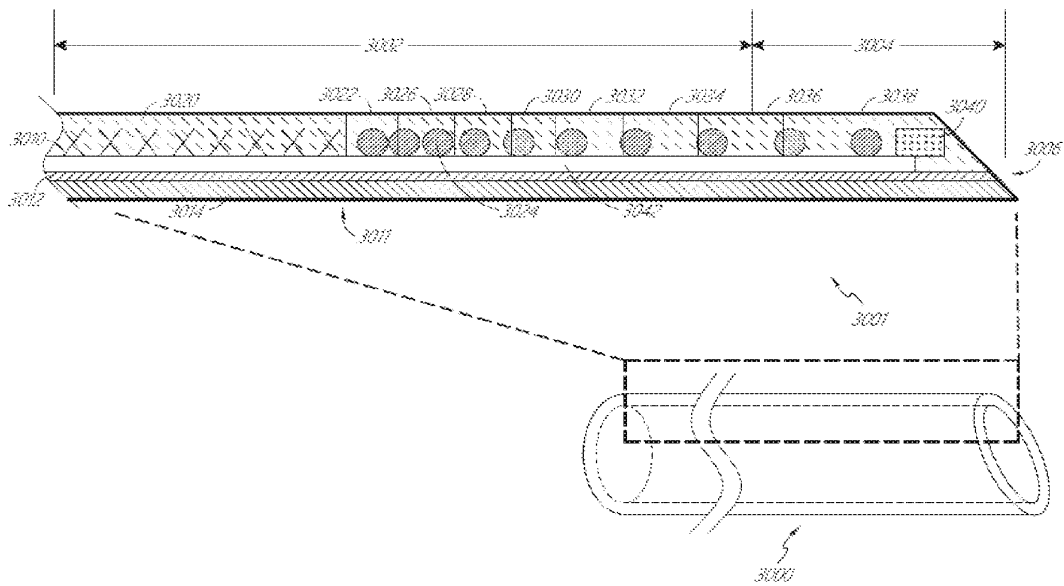


FIG. 31A

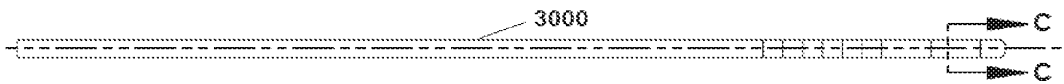


FIG. 31B

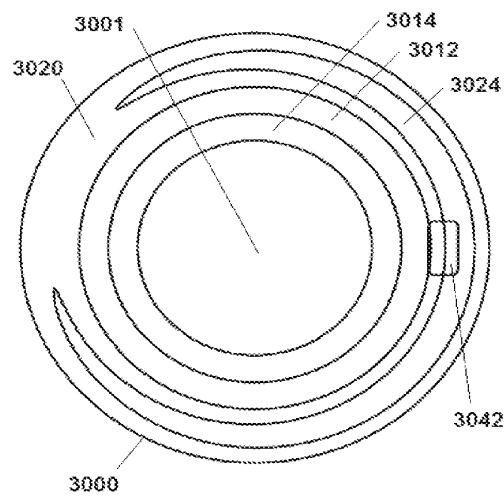


FIG. 31C

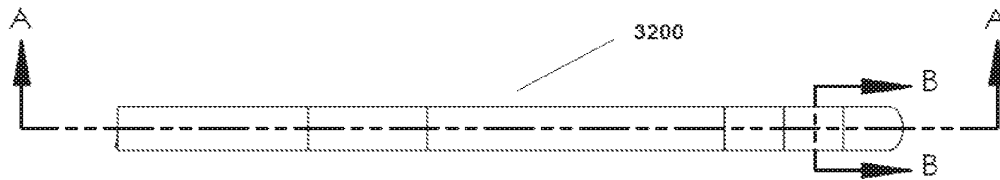


FIG. 32A

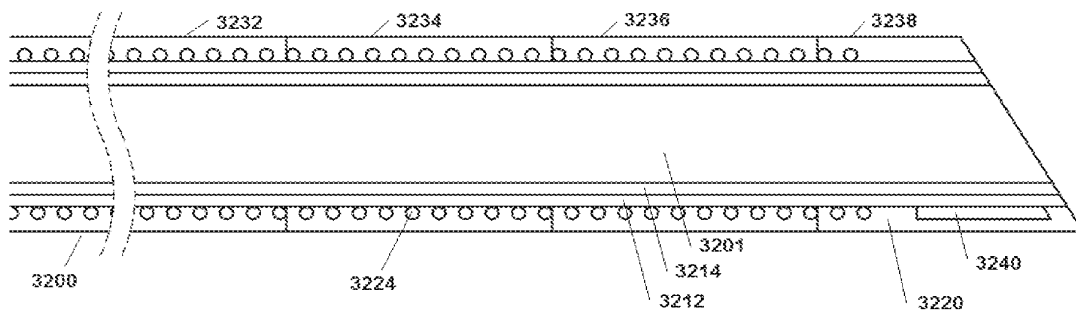


FIG. 32B

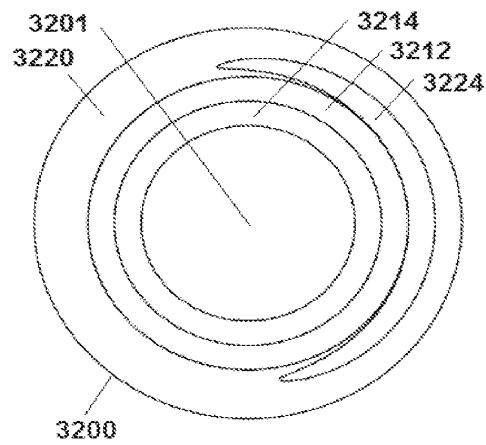


FIG. 32C

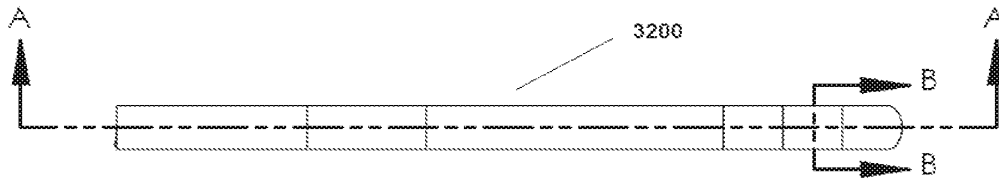


FIG. 33A

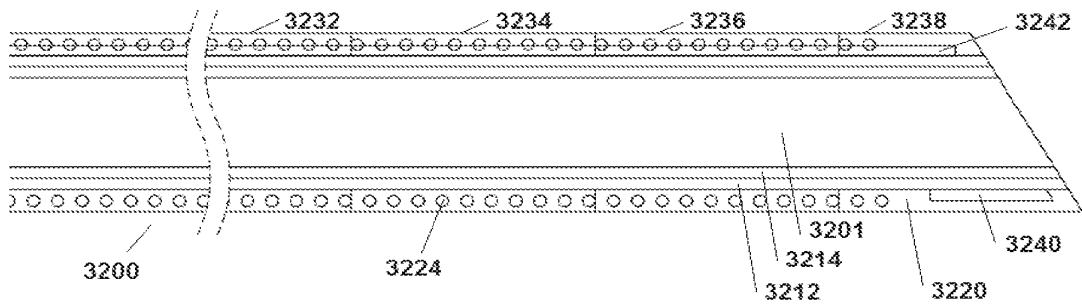


FIG. 33B

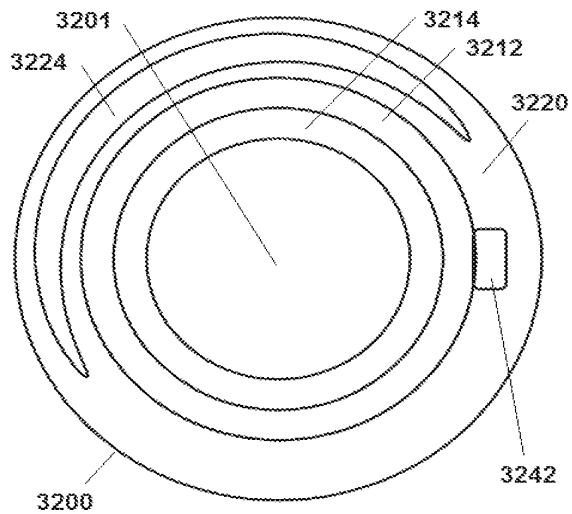
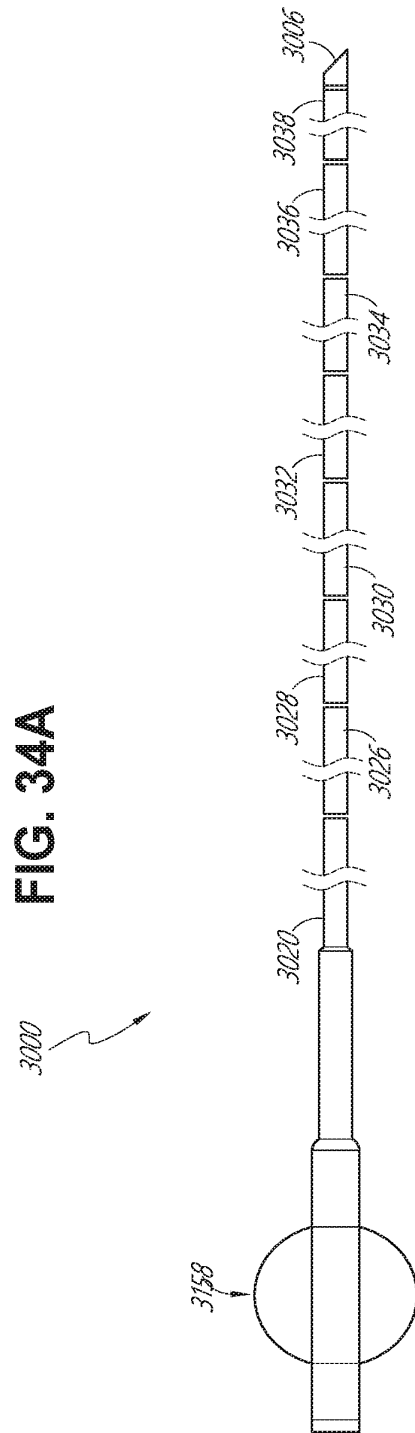
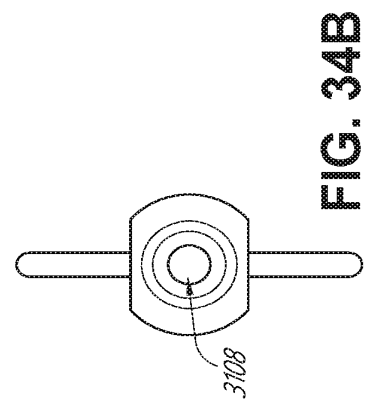


FIG. 33C



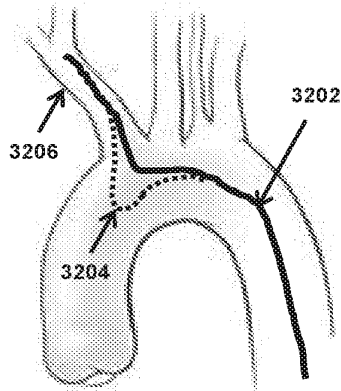


FIG. 35

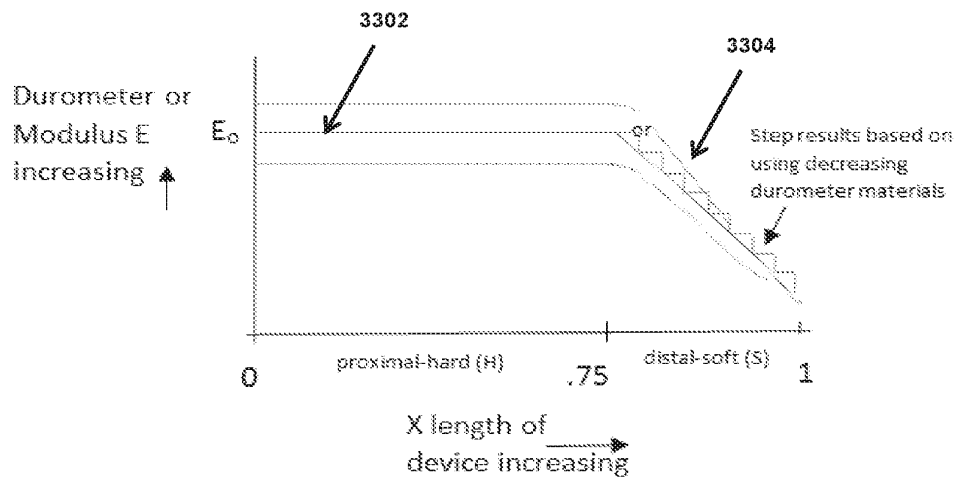
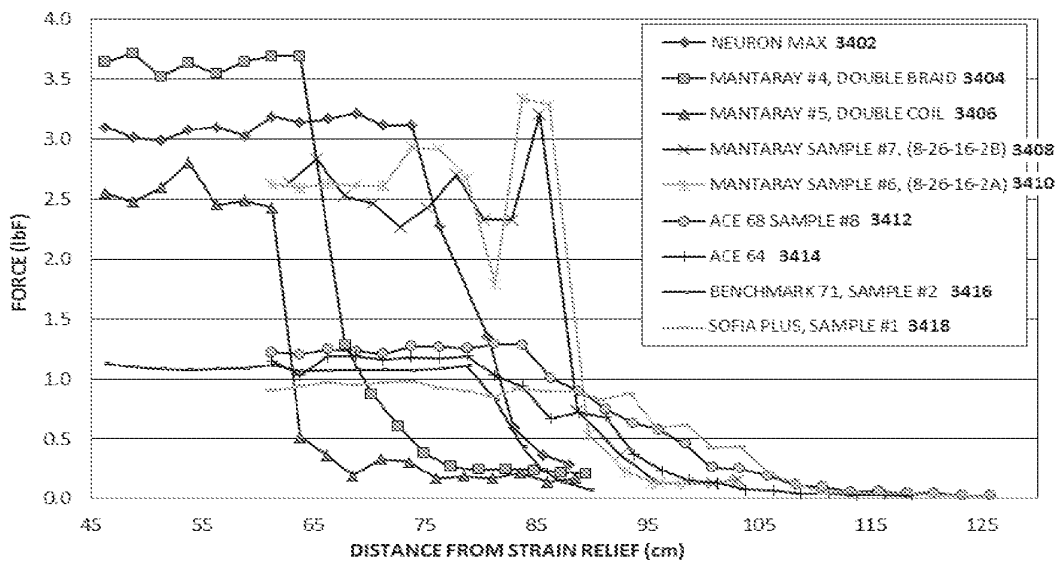


FIG. 36



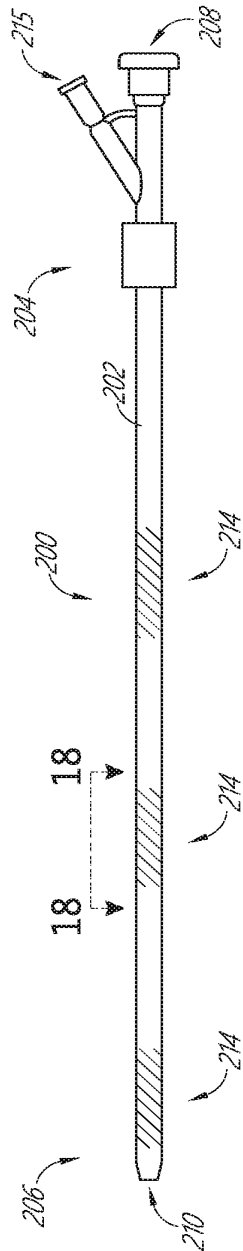


FIG. 38

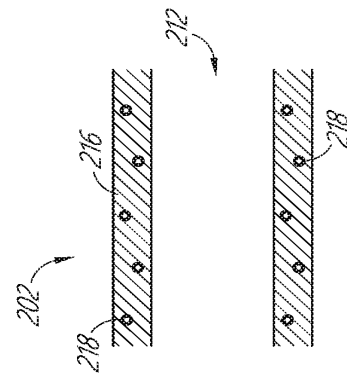


FIG. 39

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US2017/019453

A. CLASSIFICATION OF SUBJECT MATTER IPC(8) - A61B 17/00; A61M 25/00; A61M 25/01; A61M 29/00 (2017.01) CPC - A61M 25/0053; A61M 25/0012; A61M 25/0045; A61M 25/005; A61M 25/0051; A61M 25/0054; A61M 25/0662; A61M 25/09; A61M 25/104 (2017.02)		
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) See Search History document		
Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched USPC - 604/525; 604/264; 604/523; 604/524; 604/526; 604/527 (keyword delimited)		
Electronic data base consulted during the international search (name of data base and, where practicable, search terms used) See Search History document		
C. DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2013/0046285 A1 (GRIFFIN et al) 21 February 2013 (21.02.2013) entire document	1, 3-13
A	US 2004/0153049 A1 (HEWITT et al) 05 August 2004 (05.08.2004) entire document	1-18, 64-81
A	US 2007/0016132 A1 (OEPEN et al) 18 January 2007 (18.01.2007) entire document	1-18, 64-81
A	US 2010/0049168 A1 (PARKER et al) 25 February 2010 (25.02.2010) entire document	1-18, 64-81
☐ 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 17 May 2017		Date of mailing of the international search report 09 JUN 2017
Name and mailing address of the ISA/US Mail Stop PCT, Attn: ISA/US, Commissioner for Patents P.O. Box 1450, Alexandria, VA 22313-1450 Facsimile No. 571-273-8300		Authorized officer Blaine R. Copenheaver PCT Helpdesk: 571-272-4300 PCT OSP: 571-272-7774

Form PCT/ISA/210 (second sheet) (January 2015)

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US2017/019453

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.:
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

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

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

See extra sheet(s).

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying additional fees, this Authority did not invite payment of additional fees.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ 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.:
1-18, 64-81

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.

Form PCT/ISA/210 (continuation of first sheet (2)) (January 2015)

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US2017/019453

Continued from Box No. III Observations where unity of invention is lacking

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees need to be paid.

Group I, claims 1-18, 64-81 are drawn to a flexible catheter with variably flexible tubular segments.

Group II, claims 19-31, 82-103 are drawn to a catheter with an expanding distal opening.

Group III, claims 32-42 are drawn to a catheter having an agitator, driver and vacuum port.

Group IV, claims 43-63, 104-123 are drawn to a neurovascular catheter with a control filament.

The inventions listed in Groups I, II, III, and IV do not relate to a single general inventive concept under PCT Rule 13.1, because under PCT Rule 13.2 they lack the same or corresponding special technical features for the following reasons:

The special technical features of Group I, dip coating a removable mandrel to form a tubular inner layer on the mandrel; coating the tubular inner layer with a soft tie layer; applying a helical coil to the outside of the tie layer; positioning a plurality of tubular segments on the helical coil; the plurality of segments having durometers that decrease in a distal direction; heating the tubular segments to form the high flexibility distal zone on the neurovascular catheter; and removing the mandrel, are not present in Groups II, III, or IV; the special technical features of Group II, a control for advancing the distal section from a first, proximally retracted position within the proximal section to a second, extended position, extending distally beyond the proximal section; and an active tip on the distal end of the distal section, comprising a distal opening that is movable between a smaller and a larger configuration, an opening at the distal end which is enlargeable from a first inside diameter for transluminal navigation to a second, larger inside diameter to facilitate aspiration of thrombus into the lumen, are not present in Groups I, III, and IV; the special technical features of Group III, an agitator extendable through the central lumen of the tubular body to position a distal end of the agitator near a distal end of the tubular body; a driver connectable to a proximal end of the agitator and configured to actuate the agitator; and a vacuum port near the proximal end of the tubular body and in fluid communication with the central lumen of the tubular body, are not present in Groups I, II, or IV; and the special technical features of Group IV, an axially extending filament within the side wall, extending at least about the most distal 10 cm of the length of the catheter, an elongate flexible control wire, having a proximal end and a distal end; a tubular extension segment having a side wall defining a central lumen carried by the distal end of the control wire, are not present in Groups I, II, or III.

Groups I, II, III, and IV share the technical features of a medical system comprising an elongate, flexible tubular body, comprising at least one central lumen extending along its longitudinal length. However, these shared technical features do not represent a contribution over the prior art. Specifically, US 2002/0139785 A1 to Peacock, III et al. teaches of a medical system (Abstract) comprising an elongate, flexible tubular body (Fig. 1, catheter 10 is a flexible tubular body, para. [0010]), comprising at least one central lumen extending along its longitudinal length (Fig. 1, inner lumen 14 extends along the catheter 10, para. [0023]).

Groups I and II share the technical features of a medical system comprising an elongate flexible tubular body, having a proximal end, a distal end and a side wall defining a central lumen, a distal zone of the tubular body comprising: a tubular inner liner; a tie layer separated from the lumen by the inner liner; a helical coil surrounding the tie layer; an outer jacket surrounding the helical coil. However, these shared technical features do not represent a contribution over the prior art. Specifically, US 2002/0139785 A1 to Peacock, III et al. teaches of a medical system (Abstract) comprising an elongate flexible tubular body (Fig. 1, catheter 10 is a flexible tubular body, para. [0010]), having a proximal end, a distal end and a side wall defining a central lumen (Fig. 1, inner lumen 14 extends along the catheter 10, para. [0023]), a distal zone of the tubular body comprising: a tubular inner liner (Fig. 1, inner lining 13, para. [0023]); a tie layer separated from the lumen by the inner liner (Fig. 1, adhesive 18 is separate from lumen 14 by lining 13, para. [0023]); a helical coil surrounding the tie layer (Fig. 1, coil 15 includes spaces 16, wherein the adhesive 18 is within the spaces 16, the coil thereby surrounds the adhesive layer 18, para. [0023]); an outer jacket surrounding the helical coil (Fig. 1, outer jacket 17 surrounding the coil 15, para. [0023]).

Groups I and IV share the technical features of a medical system comprising a tubular extension segment having a side wall defining a central lumen carried by the distal end of the control wire, the side wall comprising: a tubular inner liner; a tie layer separated from the lumen by the inner liner; a helical coil surrounding the tie layer; and an outer jacket surrounding the helical coil. However, these shared technical features do not represent a contribution over the prior art. Specifically, US 2002/0139785 A1 to Peacock, III et al. teaches of a medical system (Abstract) comprising an elongate flexible tubular body (Fig. 1, catheter 10 is a flexible tubular body, para. [0010]), having a proximal end, a distal end and a side wall defining a central lumen (Fig. 1, inner lumen 14 extends along the catheter 10, para. [0023]), a distal zone of the tubular body comprising: a tubular inner liner (Fig. 1, inner lining 13, para. [0023]); a tie layer separated from the lumen by the inner liner (Fig. 1, adhesive 18 is separate from lumen 14 by lining 13, para. [0023]); a helical coil surrounding the tie layer (Fig. 1, coil 15 includes spaces 16, wherein the adhesive 18 is within the spaces 16, the coil thereby surrounds the adhesive layer 18, para. [0023]); an outer jacket surrounding the helical coil (Fig. 1, outer jacket 17 surrounding the coil 15, para. [0023]).

Groups II and III share the technical features of a medical system comprising an elongate, flexible tubular body, comprising a proximal section having at least one lumen, the lumen configured to facilitate aspiration of thrombus into the lumen. However, these shared technical features do not represent a contribution over the prior art. Specifically, US 2007/0106211 A1 to Provost-Timé et al. teaches of a medical system (Abstract) comprising an elongate, flexible tubular body (Fig. 1, catheter 10 is a flexible tubular body, para. [0027] & [0015]), comprising a proximal section having at least one lumen (Fig. 1, aspiration lumen 12, para. [0027]), the lumen configured to facilitate aspiration of thrombus into the lumen (Fig. 1, wherein the aspiration lumen 12 is configured to aspirate a thrombus therethrough, para. [0027] & [0015]).

Since none of the special technical features of the Group I, II, III, and IV inventions are found in more than one of the inventions, unity is lacking.

Electronic Acknowledgement Receipt	
EFS ID:	38101943
Application Number:	16681564
International Application Number:	
Confirmation Number:	6608
Title of Invention:	ASPIRATION THROMBECTOMY SYSTEM AND METHODS FOR THROMBUS REMOVAL WITH ASPIRATION CATHETER
First Named Inventor/Applicant Name:	Derek Dee Deville
Customer Number:	27316
Filer:	Gregory L. Mayback/Chris Mendez
Filer Authorized By:	Gregory L. Mayback
Attorney Docket Number:	Syn2.0/ROAR CON
Receipt Date:	20-DEC-2019
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Time Stamp:	12:44:37
Application Type:	Utility under 35 USC 111(a)

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File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Information Disclosure Statement (IDS) Form (SB08)	2019-12-20_IDS_1.pdf	1040313	no	26
			d99211c6f5719c02b8bd436ecd435cdcd01272a		

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Warnings:					
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4	Foreign Reference	WO2013184595A1_Penmbra_Inc.pdf	2222159 89cd2613fa1e7460456ed0805f5afcea015e62d9	no	42
Warnings:					
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5	Foreign Reference	WO002014151209A1_Virginia_Commonwealth.pdf	2016499 bece01f7ffb3235ff7d364c174c042ca385d2fd8	no	51
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6	Foreign Reference	WO2019115809A1_Perfuze_Limited.pdf	1505507 fd3c73d46f0a13cc09fce95253f8ffe39f7db664	no	87
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	Filing Date	2019-11-12
	First Named Inventor	Derek Dee Deville
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	Attorney Docket Number	Syn2.0/ROAR CON

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CERTIFICATION STATEMENT

Please see 37 CFR 1.97 and 1.98 to make the appropriate selection(s):

That each item of information contained in the information disclosure statement was first cited in any communication from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e)(1).

OR

☐ That no item of information contained in the information disclosure statement was cited in a communication from a foreign patent office in a counterpart foreign application, and, to the knowledge of the person signing the certification after making reasonable inquiry, no item of information contained in the information disclosure statement was known to any individual designated in 37 CFR 1.56(c) more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e)(2).

See attached certification statement.

The fee set forth in 37 CFR 1.17 (p) has been submitted herewith.

☒ A certification statement is not submitted herewith.

SIGNATURE

A signature of the applicant or representative is required in accordance with CFR 1.33, 10.18. Please see CFR 1.4(d) for the form of the signature.

Signature	/Gregory L. Mayback/	Date (YYYY-MM-DD)	2019-12-20
Name/Print	Gregory L. Mayback	Registration Number	40719

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 1 hour to complete, including gathering, preparing and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. **DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

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PATENT COOPERATION TREATY

From the INTERNATIONAL SEARCHING AUTHORITY

To: GREGORY L. MAYBACK
 DICKINSON WRIGHT, PLLC
 350 E. LAS OLAS BLVD, SUITE 1750
 FORT LAUDERDALE, FL 33301

PCT

NOTIFICATION OF TRANSMITTAL OF
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 THE WRITTEN OPINION OF THE INTERNATIONAL
 SEARCHING AUTHORITY, OR THE DECLARATION

(PCT Rule 44.1)

Date of mailing
 (day/month/year) **07 OCT 2019**

Applicant's or agent's file reference
SYN 2.0/ROAR

FOR FURTHER ACTION See paragraphs 1 and 4 below

International application No.
PCT/US 19/42546

International filing date
 (day/month/year) **19 July 2019 (19.07.2019)**

Applicant **SYNTHEON 2.0, LLC**

1. ☒ The applicant is hereby notified that the international search report and the written opinion of the International Searching Authority have been established and are transmitted herewith.

Filing of amendments and statement under Article 19:

The applicant is entitled, if he so wishes, to amend the claims of the international application (see Rule 46):

When? The time limit for filing such amendments is normally two months from the date of transmittal of the international search report.

How? Directly to the International Bureau of WIPO preferably through ePCT or on paper to, 34 chemin des Colombettes
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For more detailed instructions, see *PCT Applicant's Guide*, International Phase, paragraphs 9.004 – 9.011.

2. ☐ The applicant is hereby notified that no international search report will be established and that the declaration under Article 17(2)(a) to that effect and the written opinion of the International Searching Authority are transmitted herewith.
3. ☐ **With regard to any protest against payment of (an) additional fee(s) under Rule 40.2, the applicant is notified that:**
- ☐ the protest together with the decision thereon has been transmitted to the International Bureau together with any request to forward the texts of both the protest and the decision thereon to the designated Offices.
 - ☐ no decision has been made yet on the protest; the applicant will be notified as soon as a decision is made.

4. Reminders

The applicant may submit comments on an informal basis on the written opinion of the International Searching Authority to the International Bureau. These comments will be made available to the public after international publication. The International Bureau will send a copy of such comments to all designated Offices unless an international preliminary examination report has been or is to be established.

Shortly after the expiration of **18 months from the priority date, the international application will be published** by the International Bureau. If the applicant wishes to avoid or postpone publication, a notice of withdrawal of the international application, or of the priority claim, must reach the International Bureau before the completion of the technical preparations for international publication (Rules 90*bis*.1 and 90*bis*.3).

Within **19 months** from the priority date, but only in respect of some designated Offices, a demand for international preliminary examination must be filed if the applicant wishes to postpone the entry into the national phase **until 30 months** from the priority date (in some Offices even later); otherwise, the applicant must, **within 20 months** from the priority date, perform the prescribed acts for entry into the national phase before those designated Offices. In respect of other designated Offices, the time limit of **30 months** (or later) will apply even if no demand is filed within 19 months. For details about the applicable time limits, Office by Office, see www.wipo.int/pct/en/texts/time_limits.html and the *PCT Applicant's Guide*, National Chapters.

Within **22 months from the priority date, the applicant may request that a supplementary international search be carried out** by a different International Searching Authority that offers this service (Rule 45*bis*.1). The procedure for requesting supplementary international search is described in the *PCT Applicant's Guide*, International Phase, paragraphs 8.006-8.032.

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PATENT COOPERATION TREATY

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INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference SYN 2.0/ROAR	FOR FURTHER ACTION see Form PCT/ISA/220 as well as, where applicable, item 5 below.	
International application No. PCT/US 19/42546	International filing date (<i>day/month/year</i>) 19 July 2019 (19.07.2019)	(Earliest) Priority Date (<i>day/month/year</i>) 20 July 2018 (20.07.2018)
Applicant SYNTHEON 2.0, LLC		

This international search report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This international search report consists of a total of 2 sheets.

☐ It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the report

a. With regard to the **language**, the international search was carried out on the basis of:

- ☒ the international application in the language in which it was filed.
☐ a translation of the international application into _____ which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1(b)).

b. ☐ This international search report has been established taking into account the **rectification of an obvious mistake** authorized by or notified to this Authority under Rule 91 (Rule 43.6bis(a)).

c. ☐ With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, see Box No. I.

2. ☐ **Certain claims were found unsearchable** (see Box No. II).

3. ☐ **Unity of invention is lacking** (see Box No. III).

4. With regard to the **title**,

- ☒ the text is approved as submitted by the applicant.
☐ the text has been established by this Authority to read as follows:

5. With regard to the **abstract**,

- ☒ the text is approved as submitted by the applicant.
☐ the text has been established, according to Rule 38.2, by this Authority as it appears in Box No. IV. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. With regard to the **drawings**,

- a. the figure of the drawings to be published with the abstract is Figure No. 48
☒ as suggested by the applicant.
☐ as selected by this Authority, because the applicant failed to suggest a figure.
☐ as selected by this Authority, because this figure better characterizes the invention.
- b. ☐ none of the figures is to be published with the abstract.

Form PCT/ISA/210 (first sheet) (January 2015)

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 19/42546

A. CLASSIFICATION OF SUBJECT MATTER
IPC(8) - A61M 1/00, A61M 25/00 (2019.01)
CPC - A61B 17/22, A61M 2210/12, A61B 2017/22079, A61M 5/007, A61B 17/12163, A61M 1/0023

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)

See Search History Document

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

See Search History Document

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

See Search History Document

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2016/0220741 A1 (Route 92 Medical, Inc.) 04 August 2016 (04.08.2016) entire document, especially abstract, Figs. 2B, 11, paras [0046], [0113]-[0114].	20
---		---
A		1-19
A	US 2017/0181760 A1 (Incuvate, LLC) 29 June 2017 (29.06.2017) entire document.	1-20
A	WO 2018/019829 A1 (Neuravi Limited) 01 February 2018 (01.02.2018) entire document.	1-20

☐ 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

05 September 2019

Date of mailing of the international search report

07 OCT 2019

Name and mailing address of the ISA/US

Mail Stop PCT, Attn: ISA/US, Commissioner for Patents
P.O. Box 1450, Alexandria, Virginia 22313-1450
Facsimile No. 571-273-8300

Authorized officer:

Lee W. Young

PCT Helpdesk: 571-272-4300
PCT OSP: 571-272-7774

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To: GREGORY L. MAYBACK
DICKINSON WRIGHT, PLLC
350 E. LAS OLAS BLVD, SUITE 1750
FORT LAUDERDALE, FL 33301

PCT

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43bis.1)

Date of mailing
(day/month/year)

07 OCT 2019

Applicant's or agent's file reference
SYN 2.0/ROAR

FOR FURTHER ACTION

See paragraph 2 below

International application No.

PCT/US 19/42546

International filing date (day/month/year)

19 July 2019 (19.07.2019)

Priority date (day/month/year)

20 July 2018 (20.07.2018)

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

IPC(8) - A61M 1/00, A61M 25/00 (2019.01)

CPC - A61B 17/22, A61M 22/10/12, A61B 2017/22079, A61M 5/007, A61B 17/12163, A61M 1/0023

Applicant SYNTHEON 2.0, LLC

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step and industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

Name and mailing address of the ISA/US
Mail Stop PCT, Attn: ISA/US
Commissioner for Patents
P.O. Box 1450, Alexandria, Virginia 22313-1450
Facsimile No. 571-273-8300

Date of completion of this opinion

05 September 2019

Authorized officer

Lee W. Young

PCT Helpdesk: 571-272-4300
PCT OSP: 571-272-7774

Form PCT/ISA/237 (cover sheet) (January 2015)

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.

PCT/US 19/42546

Box No. 1 Basis of this opinion

1. With regard to the **language**, this opinion has been established on the basis of:
 - ☒ the international application in the language in which it was filed.
 - ☐ a translation of the international application into _____ which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1(b)).
2. ☐ This opinion has been established taking into account the **rectification of an obvious mistake** authorized by or notified to this Authority under Rule 91 (Rule 43*bis*.1(a)).
3. ☐ With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, this opinion has been established on the basis of a sequence listing:
 - a. ☐ forming part of the international application as filed:
 - ☐ in the form of an Annex C/ST.25 text file.
 - ☐ on paper or in the form of an image file.
 - b. ☐ furnished together with the international application under PCT Rule 13*ter*.1(a) for the purposes of international search only in the form of an Annex C/ST.25 text file.
 - c. ☐ furnished subsequent to the international filing date for the purposes of international search only:
 - ☐ in the form of an Annex C/ST.25 text file (Rule 13*ter*.1(a)).
 - ☐ on paper or in the form of an image file (Rule 13*ter*.1(b) and Administrative Instructions, Section 713).
4. ☐ In addition, in the case that more than one version or copy of a sequence listing has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that forming part of the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
5. Additional comments:

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.

PCT/US 19/42546

Box No. V	Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement			
1.	Statement			
	Novelty (N)	Claims	1-19	YES
		Claims	20	NO
	Inventive step (IS)	Claims	1-19	YES
		Claims	20	NO
	Industrial applicability (IA)	Claims	1-20	YES
		Claims	None	NO
<p>2. Citations and explanations:</p> <p>Claim 20 lacks novelty under PCT Article 33(2) as being anticipated by US 2016/0220741 A1 to Route 92 Medical, Inc. (hereinafter "Route 92")</p> <p>Regarding claim 20, Route 92 teaches a clot removal system, comprising: a catheter (222, Fig. 11) having a distal end and defining a lumen (223, Fig. 2B) filled with a liquid column (when the flush fluid is present in the catheter lumen, it creates a liquid column) having a proximal portion and a distal portion ("an inner lumen 223 extending between a proximal end and a distal end region of the sheath body 222.", para [0046]); a vacuum source (600, Fig. 11); a vent liquid source (288, Fig. 11); and a vacuum and vent control system configured to cyclically fluidically connect ("In yet another aspiration source implementation, the aspiration source 600 provides a cyclic level of aspiration force, for example, an aspiration force that cycles between a high level of vacuum to a lower level of vacuum at a set frequency, or from a high level of vacuum to no vacuum, or from a high level of vacuum to a pressure source.", para [0114]) to the proximal portion at least one of: vacuum from the vacuum source ("In another example, as shown in FIG. 11, the aspiration source 600 further includes a flow sensor 275 that senses flow in the aspiration line 230, coupled to a controller that controls the level of aspiration.", para [0113]); vent liquid from the vent liquid source; and neither the vacuum nor the vent liquid, and thereby change a level of vacuum ("coupled to a controller that controls the level of aspiration.", para [0113]) at the distal end and substantially prevent forward flow (when changed to high vacuum, forward flow will be prevented by increasing the aspiration).</p> <p>Claims 1-19 meet the criteria of PCT Article 33(2) - 33(3) because, as will be shown, the prior art does not teach, nor does it fairly suggest, the claimed limitations.</p> <p>The prior art is exemplified by (1) Route 92. (1) Route 92 teaches an aspiration thrombectomy system comprising a catheter, a vacuum source, a liquid source, and a controller (Abstract, para [0113]-[0114]).</p> <p>Regarding claim 1, Route 92 teaches a clot removal system, comprising: a catheter (222, Fig. 11) having a distal end and defining a lumen (223, Fig. 2B) filled with a liquid column (when the flush fluid is present in the catheter lumen, it creates a liquid column) having a proximal portion and a distal portion ("an inner lumen 223 extending between a proximal end and a distal end region of the sheath body 222.", para [0046]);</p> <p>but the prior art does not teach nor fairly suggest a controllable vacuum valve; a vacuum source fluidically connected to the vacuum valve; a controllable vent valve having a vent liquid input; a vent fluid source containing a vent liquid and fluidically connected to the vent valve to retain the vent liquid at the vent fluid input; a manifold connected to the catheter, to the vacuum valve, and to the vent valve, the manifold fluidically connecting the proximal portion of the liquid column in the lumen: to the vacuum source through the vacuum valve; and to the vent fluid source through the vent valve; a controller connected to the vacuum valve and the vent valve and configured to selectively open and close the vacuum valve and the vent valve such that: responsive to opening the vacuum valve, the vacuum source is fluidically connected to the liquid column in the lumen; and responsive to opening the vent valve, the vent fluid source is fluidically connected to the liquid column in the lumen, the controller configured to cyclically open and close the vacuum valve and the vent valve to: change a level of vacuum at the distal end; and prevent forward flow of the distal portion out from the distal end during each cycle.</p> <p>Regarding claims 2-17, the prior art does not teach nor fairly suggest the clot removal system as claimed since they are dependent upon claim 1.</p> <p>-*-Continued in Supplemental Box.-*-</p>				

Form PCT/ISA/237 (Box No. V) (January 2015)

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.

PCT/US 19/42546

Supplemental Box

In case the space in any of the preceding boxes is not sufficient.

Continuation of:

-Box V.2 - Citations and Explanations-

Regarding claim 18, Route 92 teaches a clot removal system, comprising:

a catheter (222, Fig. 11) having a distal end and defining a lumen (223, Fig. 2B) filled with a liquid column (when the flush fluid is present in the catheter lumen, it creates a liquid column) having a proximal portion and a distal portion ("an inner lumen 223 extending between a proximal end and a distal end region of the sheath body 222.", para [0046]);

but the prior art does not teach nor fairly suggest a controllable vacuum valve;

a vacuum source fluidically connected to the vacuum valve;

a controllable vent valve having a vent liquid input;

a vent fluid source containing a vent liquid and fluidically connected to the vent valve to retain the vent liquid at the vent fluid input;

a manifold connected to the catheter, to the vacuum valve, and to the vent valve, the manifold fluidically connecting the proximal portion of the liquid column in the lumen:

to the vacuum source through the vacuum valve; and

to the vent fluid source through the vent valve;

a controller connected to the vacuum valve and the vent valve and configured to selectively open and close the vacuum valve and the vent valve such that:

responsive to opening the vacuum valve, the vacuum source is fluidically connected to the liquid column in the lumen; and

responsive to opening the vent valve, the vent fluid source is fluidically connected to the liquid column in the lumen,

the controller configured to cyclically open and close the vacuum valve and the vent valve in a repeated cycle comprising a double-closed state in which the vacuum valve is closed and the vent valve is closed to:

change a level of vacuum at the distal end; and

prevent forward flow of the distal portion out from the distal end during each cycle, and a time of the double-closed state is no greater than approximately 30 ms.

Regarding claim 19, Route 92 teaches a clot removal system, comprising:

a catheter (222, Fig. 11) having a distal end and defining a lumen (223, Fig. 2B) filled with a liquid column (when the flush fluid is present in the catheter lumen, it creates a liquid column) having a proximal portion and a distal portion ("an inner lumen 223 extending between a proximal end and a distal end region of the sheath body 222.", para [0046]);

a vacuum source (600, Fig. 11);

a vent liquid source (288, Fig. 11); and

but the prior art does not teach nor fairly suggest a vacuum and vent control system configured to cyclically connect or disconnect the vacuum source and the vent liquid source to:

change a level of vacuum at the distal end; and

substantially prevent forward flow

Claims 1-20 have industrial applicability as defined by PCT Article 33(4) because the subject matter can be made or used by industry.

Electronic Acknowledgement Receipt	
EFS ID:	38104959
Application Number:	16681564
International Application Number:	
Confirmation Number:	6608
Title of Invention:	ASPIRATION THROMBECTOMY SYSTEM AND METHODS FOR THROMBUS REMOVAL WITH ASPIRATION CATHETER
First Named Inventor/Applicant Name:	Derek Dee Deville
Customer Number:	27316
Filer:	Gregory L. Mayback/Chris Mendez
Filer Authorized By:	Gregory L. Mayback
Attorney Docket Number:	Syn2.0/ROAR CON
Receipt Date:	20-DEC-2019
Filing Date:	12-NOV-2019
Time Stamp:	14:33:39
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	no
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File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Information Disclosure Statement (IDS) Form (SB08)	2019-12-20_IDS_2.pdf	1039998	no	8
			00be4efb32251ffe76411b7c4819593d4480b34f		

Warnings:

Information:					
A U.S. Patent Number Citation or a U.S. Publication Number Citation is required in the Information Disclosure Statement (IDS) form for autoloading of data into USPTO systems. You may remove the form to add the required data in order to correct the Informational Message if you are citing U.S. References. If you chose not to include U.S. References, the image of the form will be processed and be made available within the Image File Wrapper (IFW) system. However, no data will be extracted from this form. Any additional data such as Foreign Patent Documents or Non Patent Literature will be manually reviewed and keyed into USPTO systems.					
2	Non Patent Literature	International_Search_Report- WO_PCT- US2019-42546_dated_OCTOBE R_7_2019.pdf	360960 8fb5b8921084f7e832e3a80dea18f0f64e62e86	no	7
Warnings:					
Information:					
3	Non Patent Literature	Penumbra_Pivotal_Trial_2009. pdf	120424 e4234007ffbec15e6482e1bd2ae67a773c88436c	no	8
Warnings:					
Information:					
4	Non Patent Literature	Alawieh_adapt_500.pdf	834892 5aacffa463076105c32de126ca578cd08145b55d	no	10
Warnings:					
Information:					
5	Non Patent Literature	Arslanian_2019_Complete_clot _full.pdf	978357 e3883fbfb6dd7377c144c06153039d5c3172c276	no	6
Warnings:					
Information:					
6	Non Patent Literature	Arslanian_Bigger_Better.pdf	77876 7524361e791e43107316edf20f397413c16b6949	no	2
Warnings:					
Information:					
7	Non Patent Literature	Bhaskar_Reperfusion_therapy_ 12883_2017_Article_1007.pdf	1515692 eb2f55c0074f90f46e8967610e70c52716a61e02	no	26
Warnings:					
Information:					

8	Non Patent Literature	Brinjikji_2017_Correlation_of_imaging.pdf	525179	no	6
			01e4a4f00d7a58a026361cb7816c70e53307ab28		
Warnings:					
Information:					
9	Non Patent Literature	Brouwer_2018_Clot_Pathophysiology.pdf	3901707	no	13
			5c4c04541215a9c2d0a513993a72e24c41a4f2fb		
Warnings:					
Information:					
10	Non Patent Literature	Chueh_2012_Feb_Abstract_3750_Embolus_Adhesion.pdf	71301	no	1
			8408e6ab57e17010001ef63f9add1394c446532a		
Warnings:					
The page size in the PDF is too large. The pages should be 8.5 x 11 or A4. If this PDF is submitted, the pages will be resized upon entry into the Image File Wrapper and may affect subsequent processing					
Information:					
11	Non Patent Literature	Chueh_2012_Nov_Effectiveness_of_Mechanical_Endovascular.pdf	1852881	no	6
			b922f429840da38ea8fc446543b052b4fb38680a		
Warnings:					
Information:					
12	Non Patent Literature	Chueh_2011_Aug_Mechanical_Characterization.pdf	3376882	no	8
			a77d6a6bb76a27b7afeac38608bf5904eab66d74		
Warnings:					
Information:					
13	Non Patent Literature	Cline_2013_Pathological_Analysis.pdf	278455	no	2
			4aff18b6a538739f97f418d0608d86757c24ba45		
Warnings:					
Information:					
14	Non Patent Literature	DeMeyer_2017_Analyses_of_thrombi.pdf	3017791	no	9
			75bfb0bc5445e735768dce014cd50c26ba6a53e3		
Warnings:					
Information:					

15	Non Patent Literature	Delgado_Almandoz_2018_Larger_ACE_68_aspiration.pdf	376063	no	6
			951ef3e00be492b76e9a70c6d966ba2b8f587273		
Warnings:					
Information:					
16	Non Patent Literature	Duffy_2017_Novel_methodology.pdf	1091640	no	7
			0dfc8864e9570b8a7bd388731a80919d0519bd53		
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Information:					
17	Non Patent Literature	Duffy_2019_Per-Pass_Analysis.pdf	1055427	no	8
			5d40bb69b5de3e229faa09af3e627832afacdd7a		
Warnings:					
Information:					
18	Non Patent Literature	Almekhlafi_Calcification_of_Thrombi-Almekhlafi_etal_2008-.pdf	2421960	no	6
			6dbde8c3c70df956b2404abe1e37544db46e4b9e		
Warnings:					
Information:					
19	Non Patent Literature	Fitzgerald_2017_Machine-learned_Characterization-.pdf	926163	no	1
			103c992a62ab3e4cba28a0091ba520125fa86a2b		
Warnings:					
Information:					
20	Non Patent Literature	Health_Mechanical-Thrombectomy-technical-report_2017_pg_1-100.pdf	19161701	no	100
			281eaa556549002f95703798717a58ecc885bd9c		
Warnings:					
Information:					
21	Non Patent Literature	Health_Mechanical-Thrombectomy-technical-report_2017-pg_101-197.pdf	16645071	no	97
			6f6a5b51bac06c3320d264d1be7d12857a1c0b6e		
Warnings:					
Information:					

22	Non Patent Literature	Ganesh_2018_Thrombectomy_for_Acute_Ischemic_Stroke.pdf	837641	no	13
			cc4dce4c771a530f04580bc2737a6c339cf5251b		
Warnings:					
Information:					
23	Non Patent Literature	Gory_2018_A_direct_aspiration.pdf	512451	no	9
			3d50b8205a72b0b14f583c18c6f6df0fb79fa0bc		
Warnings:					
Information:					
24	Non Patent Literature	Gralla_2006_June_A_Dedicated_animal_model.pdf	213034	no	5
			c13050d6d687ceb4e1df0b0b2e38604391bc256b		
Warnings:					
Information:					
25	Non Patent Literature	Gratz_2015_Whole_Brain_Susceptibility-Weighted_Thrombus.pdf	790242	no	6
			4ff6be36008350341956d69f7144065bb5a9587e		
Warnings:					
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26	Non Patent Literature	Heit_2018_Sofia_intermediate_catheter.pdf	1285954	no	6
			f4e9fb1f1c7dd4d24062106afddac710834cb894		
Warnings:					
Information:					
27	Non Patent Literature	Hesse_2018_Comparing_differential_thrombectomy.pdf	223223	no	5
			c8d058b9e0b8814052649352f7d8534534cdcf9		
Warnings:					
Information:					
28	Non Patent Literature	Hu_2015_Force_and_aspiration.pdf	170468	no	4
			cfce0b829a5a76c5197d84b33a8bd9546a4b28f8		
Warnings:					
Information:					

29	Non Patent Literature	Kaesmacher_2007_Risk_of_Thrombus_Fragmentation.pdf	2874556	no	8
			99922f5aeba9bce65dce44ab2efe2b14ec7f5a95		
Warnings:					
Information:					
30	Non Patent Literature	Kallmes_2018_Nov_The_Truth_and_Fiction.pdf	146197	no	2
			73d4bf8cac2f4da5a714bae9e62ca5d39add5d4a		
Warnings:					
Information:					
31	Non Patent Literature	Kallmes_2018_April_To_be_or_not2b.pdf	176232	no	2
			c5393a9849bb66427984e9c1dcf93f43a488632		
Warnings:					
Information:					
32	Non Patent Literature	Kurzawski_Left_Atrial.pdf	8264282	no	8
			44191c48b41a31eb11a5b0adfadd30fb432ef164		
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Information:					
33	Non Patent Literature	Legrand_2013_July_Clot_Burden_Score.pdf	919881	no	7
			816619e6696842a4deb5b54e4b412a2b6214eeef		
Warnings:					
Information:					
34	Non Patent Literature	Liebeskind_2003_Sept_Collateral_Circulation.pdf	181051	no	6
			8174eb5c78a1f0e42c095bb1cc26255fb2a4a093		
Warnings:					
Information:					
35	Non Patent Literature	Liebeskind_2011_May_CT_MRI_Early_Vessel.pdf	987113	no	7
			3748ac2072e4866d0d6a23652f6214ba7a76ccce		
Warnings:					
Information:					

36	Non Patent Literature	Frie_2014_Feb_ADAPT_FAST_study-.pdf	2888720	no	7
			1c6099af16353b667d5f1419cd0f40b7f97d62b7		
Warnings:					
Information:					
37	Non Patent Literature	Froehler_2017_May_Comparison_of_Vacuum_Pressures-.pdf	1801773	no	8
			885b0f94afc80a20411e585b92e0bb0ad256553a		
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38	Non Patent Literature	Gounis_2017_From_Bench_to_Brain-.pdf	8489800	no	34
			7aa79db87ab7366b00b2e544a56a213902705817		
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39	Non Patent Literature	Kallmes_2018_April_Stroke_Thromboembolism_Registry-.pdf	2544198	no	5
			e81b744f0c4f16d7f2d8daacd486fe2111efceac		
Warnings:					
Information:					
40	Non Patent Literature	Kan_2010_Oct_A_Novel_Method.pdf	1989103	no	3
			889adb5122407617469adcb251427e2ceded44cf3		
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41	Non Patent Literature	Long_2018_Novel_aspiration_catheter.pdf	704243	no	6
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42	Non Patent Literature	Merritt_2018_Quantifying_the_Mechanical.pdf	2264385	no	6
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Warnings:					
Information:					

43	Non Patent Literature	Moore_2006_Feb_3D_Models_of_Blood_Flow.pdf	1120193	no	11
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Warnings:					
Information:					
44	Non Patent Literature	Niesten_2014_Feb_Histopathologic_Comp.PDF	280852	no	7
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Warnings:					
Information:					
45	Non Patent Literature	Nikoubashman_2017_Dec_Necessary_Cath.pdf	533086	no	5
			a1c576cc214b9476b821edcc2e2cd7bbb1ad3df6		
Warnings:					
Information:					
46	Non Patent Literature	Nogueira_2012_TheTrevo_devilce.pdf	1263271	no	6
			662709ecc77f656b265d2aab0cc7f77c5e66dff3		
Warnings:					
Information:					
47	Non Patent Literature	Petty_2000_Ischemic_Stroke_Subtypes.pdf	110949	no	7
			0cb6437851b76a88a63194cb9f27d10970417009		
Warnings:					
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48	Non Patent Literature	Price_Bleeding_Outcomes.pdf	6679790	no	8
			0ae4a439c5d5d506a71f1e5de845ee927e042989		
Warnings:					
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49	Non Patent Literature	Puetz_2008_Nov_Intracranial_thrombus_extnt.pdf	220821	no	7
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50	Non Patent Literature	Rizvi_2018_redefining_success.pdf	1655793	no	5
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51	Non Patent Literature	Marder_2006_Analysis_of_Thrombi_Retrieved.pdf	628800	no	8
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52	Non Patent Literature	Preut_2018_Novel_Methodology_for_Emboli_Analog-.pdf	12389020	no	73
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INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)	Application Number	16681564
	Filing Date	2019-11-12
	First Named Inventor	Derek Dee Deville
	Art Unit	
	Examiner Name	
	Attorney Docket Number	Syn2.0/ROAR CON

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	Filing Date	2019-11-12
	First Named Inventor	Derek Dee Deville
	Art Unit	
	Examiner Name	
	Attorney Docket Number	Syn2.0/ROAR CON

1	ROBBIE, et al., "Thrombi Formed in a Chandler Loop Mimic Human Arterial Thrombi in Structure and PAI-1 Content and Distribution, F.K. Schattauer Verlagsgesellschaft mbH (Struttgar) 77 (3) 510-5 (1997)
2	ROMERO, et al., "Analysis and simulation of the adhesion forces between clot and the artery wall for a novel thrombectomy device applied to the Middle Cerebral Artery, ETSI Engineering, Universidad Politecnica de Madrid Spain pp1-6
3	SALEH, et al., "Safety and efficacy of the Aperio thrombectomy device when compared to the Solitaire AB/FR and the Revive devices in a pulsatile flow system, Am J Cardiovasc Dis 2012;2(4):301-308
4	SAMANIEGO, et al., "Mechanical Thrombectomy: Emerging Technologies and Techniques, Journal of Stroke and Cerebrovascular Diseases, Vol., No., (), 2018: pp1-17
5	SCHUHMANN, et al., "Immunohistochemical Analysis of Cerebral Thrombi Retrieved by Mechanical Thrombectomy from Patients with Acute Ischemic Stroke, Int. J. Mol. Sci. 2016, 17,298: doi:10.3390/ijms17030298
6	SILLANPAA, et al., "the clot burden score, the Boston Acute Stroke Imaging Scale, the cerebral blood volume ASPECTS, and two novel imaging parameters in the prediction of clinical outcome of ischemic stroke patients receiving intravenous thrombolytic therapy", Neuroradiology (2012) 54:663-672; DOI 10.1007/s00234-011-0954-z
7	SIMON, et al., "Exploring the efficacy of cyclic vs static aspiration in a cerebral thrombectomy model: an initial proof of concept study, J NeuroIntervent Surg 2014;6:677-683. doi:10.1136/neurintsurg-2013-010941
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9	SORIMACHI, et al., "Blood pressure measurement in the artery proximal and distal to an intra-arterial embolus during thrombolytic therapy, J NeuroIntervent Surg 2011;3:43-46. doi:10.1136/jmis.2010.003061
10	SPIOTTA, et al., "Hounsfield unit value and clot length in the acutely occluded vessel and time required to achieve thrombectomy, complications and outcome, J NeuroIntervent Surg 2014;6:423-427. Doi:10.1136/neurintsurg-203-010765
11	TAN, et al., "CT Angiography Clot Burden Score and Collateral Score: Correlation and Clinical and Radiologic Outcomes in Acute Middle Cerebral Artery infarct, AJNR Am J Neuroradiol 30:525-31/ Mar 2009/ www.ajnr.org; DOI 10.3174/ajnr.A1408

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)	Application Number		16681564
	Filing Date		2019-11-12
	First Named Inventor	Derek Dee Deville	
	Art Unit		
	Examiner Name		
	Attorney Docket Number		Syn2.0/ROAR CON

12	TURK, et al., "Initial clinical experience with the ADAPT technique: A direct aspiration first pass technique for stroke thrombectomy, J NeuroIntervent Surg 2013;0:1-7. doi:10.1136/neurintsurg-2013-010713
13	YUKI, et al., "The Impact of Thromboemboli Histology on the Performance of a mechanical thrombectomy Device, AJNR Am J Neuroradiol 33:643-48/april 2012/ www.ajnr.org
14	ZAIDAT, et al., "First Pass Effect: A New Measure for Stroke Thrombectomy Devices, Stroke. 2018;49:660-666; originally published on line February 19, 2018;; DOI: 10.1161/STROKEAHA.117.020315
15	ZARRINKOOB, et al., "Blood flow distribution in cerebral arteries, Journal of Cerebral Blood Flow & Metabolism (2015) 35,648-654

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EXAMINER SIGNATURE

Examiner Signature		Date Considered	
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*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through a citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

¹ See Kind Codes of USPTO Patent Documents at www.USPTO.GOV or MPEP 901.04. ² Enter office that issued the document, by the two-letter code (WIPO Standard ST.3). ³ For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. ⁴ Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. ⁵ Applicant is to place a check mark here if English language translation is attached.

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	Filing Date	2019-11-12
	First Named Inventor	Derek Dee Deville
	Art Unit	
	Examiner Name	
	Attorney Docket Number	Syn2.0/ROAR CON

CERTIFICATION STATEMENT

Please see 37 CFR 1.97 and 1.98 to make the appropriate selection(s):

That each item of information contained in the information disclosure statement was first cited in any communication from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e)(1).

OR

☐ That no item of information contained in the information disclosure statement was cited in a communication from a foreign patent office in a counterpart foreign application, and, to the knowledge of the person signing the certification after making reasonable inquiry, no item of information contained in the information disclosure statement was known to any individual designated in 37 CFR 1.56(c) more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e)(2).

See attached certification statement.

The fee set forth in 37 CFR 1.17 (p) has been submitted herewith.

☒ A certification statement is not submitted herewith.

SIGNATURE

A signature of the applicant or representative is required in accordance with CFR 1.33, 10.18. Please see CFR 1.4(d) for the form of the signature.

Signature	/Gregory L. Mayback/	Date (YYYY-MM-DD)	2019-12-20
Name/Print	Gregory L. Mayback	Registration Number	40719

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 1 hour to complete, including gathering, preparing and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. **DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

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The Privacy Act of 1974 (P.L. 93-579) requires that you be given certain information in connection with your submission of the attached form related to a patent application or patent. Accordingly, pursuant to the requirements of the Act, please be advised that: (1) the general authority for the collection of this information is 35 U.S.C. 2(b)(2); (2) furnishing of the information solicited is voluntary; and (3) the principal purpose for which the information is used by the U.S. Patent and Trademark Office is to process and/or examine your submission related to a patent application or patent. If you do not furnish the requested information, the U.S. Patent and Trademark Office may not be able to process and/or examine your submission, which may result in termination of proceedings or abandonment of the application or expiration of the patent.

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6. A record in this system of records may be disclosed, as a routine use, to another federal agency for purposes of National Security review (35 U.S.C. 181) and for review pursuant to the Atomic Energy Act (42 U.S.C. 218(c)).
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EFS ID:	38107427
Application Number:	16681564
International Application Number:	
Confirmation Number:	6608
Title of Invention:	ASPIRATION THROMBECTOMY SYSTEM AND METHODS FOR THROMBUS REMOVAL WITH ASPIRATION CATHETER
First Named Inventor/Applicant Name:	Derek Dee Deville
Customer Number:	27316
Filer:	Gregory L. Mayback/Chris Mendez
Filer Authorized By:	Gregory L. Mayback
Attorney Docket Number:	Syn2.0/ROAR CON
Receipt Date:	20-DEC-2019
Filing Date:	12-NOV-2019
Time Stamp:	15:47:55
Application Type:	Utility under 35 USC 111(a)

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Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Information Disclosure Statement (IDS) Form (SB08)	2019-12-20_IDS_3.pdf	1036810	no	5
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Warnings:					
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5	Non Patent Literature	Schuhmann_2016_Immunohistochemical_analysis.pdf	3328870 a3e75a287f141633b282a4e17688671f18b9d239	no	11
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12	Non Patent Literature	Turk_2013_Initial_clinical.pdf	643951	no	8
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13	Non Patent Literature	Yuki_2012_April_The_Impact_of_Thrombi.pdf	2257567	no	6
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15	Non Patent Literature	ROBBIE_ETAL_THROMBI_FORM ED.pdf	4155921	no	6
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16	Non Patent Literature	Zaidat_et al_2018_FirstPassEffec- t-.pdf	5076145	no	9
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APPLICATION NUMBER	FILING OR 371(C) DATE	FIRST NAMED APPLICANT	ATTY. DOCKET NO./TITLE
16/681,564	11/12/2019	Derek Dee Deville	Syn2.0/ROAR CON

CONFIRMATION NO. 6608

FORMALITIES LETTER



27316
Mayback & Hoffman, P.A.
350 East Las Olas Blvd
Suite 1750
Fort Lauderdale, FL 33301

Date Mailed: 12/17/2019

NOTICE TO FILE MISSING PARTS OF NONPROVISIONAL APPLICATION

FILED UNDER 37 CFR 1.53(b)

Filing Date Granted

Items Required To Avoid Abandonment:

An application number and filing date have been accorded to this application. The item(s) indicated below, however, are missing.

Applicant is given **TWO MONTHS** from the date of this Notice within which to file all required items below to avoid abandonment. Extensions of time may be obtained by filing a petition accompanied by the extension fee under the provisions of 37 CFR 1.136(a).

- Surcharge as set forth in 37 CFR 1.16(f) must be submitted.
The surcharge is due for any one of:
 - late submission of the basic filing fee, search fee, or examination fee,
 - late submission of inventor's oath or declaration,
 - filing an application that does not contain at least one claim on filing, or
 - submission of an application filed by reference to a previously filed application.

SUMMARY OF FEES DUE:

The fee(s) required within **TWO MONTHS** from the date of this Notice to avoid abandonment is/are itemized below. Small entity discount is in effect. If applicant is qualified for micro entity status, an acceptable Certification of Micro Entity Status must be submitted to establish micro entity status. (See 37 CFR 1.29 and forms PTO/SB/15A and 15B.)

- \$ **80** surcharge.
- \$(**0**) previous unapplied payment amount.
- \$ **80** TOTAL FEE BALANCE DUE.

Items Required To Avoid Processing Delays:

Applicant is notified that the above-identified application contains the deficiencies noted below. No period for reply is set forth in this notice for correction of these deficiencies. However, if a deficiency relates to the inventor's oath or declaration, the applicant must file an oath or declaration in compliance with 37 CFR 1.63, or a substitute statement in compliance with 37 CFR 1.64, executed by or with respect to each actual inventor no later than the expiration of the time period set in the "Notice of Allowability" to avoid abandonment. See 37 CFR 1.53(f).

- A properly executed inventor's oath or declaration has not been received for the following inventor(s) as named on the application data sheet:

William T. Bales JR.

An inventor's oath or declaration in compliance with 37 CFR 1.63 or 1.64 executed by or with respect to each inventor must be submitted no later than the date on which the issue fee is paid in response to a notice requiring such fee. See 37 CFR 1.53(f).

If the name of the inventor provided on the ADS is not correct, applicant must submit a request to correct the inventor name according to 37 CFR 1.48(f), accompanied by the appropriate fee under 37 CFR 1.17(i) and a corrected ADS in compliance with 37 CFR 1.76(c), i.e., identifying the information that is being changed with underlining for insertions, and strike-through or brackets for text removed.

Replies must be received in the USPTO within the set time period or must include a proper Certificate of Mailing or Transmission under 37 CFR 1.8 with a mailing or transmission date within the set time period. For more information and a suggested format, see Form PTO/SB/92 and MPEP 512.

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APPLICATION NUMBER	FILING or 371(c) DATE	GRP ART UNIT	FIL FEE REC'D	ATTY. DOCKET NO	TOT CLAIMS	IND CLAIMS
16/681,564	11/12/2019	3783	835	Syn2.0/ROAR CON	21	2

CONFIRMATION NO. 6608

FILING RECEIPT



0000000113374965

27316

Mayback & Hoffman, P.A.
350 East Las Olas Blvd
Suite 1750
Fort Lauderdale, FL 33301

Date Mailed: 12/17/2019

Receipt is acknowledged of this non-provisional utility patent application. The application will be taken up for examination in due course. Applicant will be notified as to the results of the examination. Any correspondence concerning the application must include the following identification information: the U.S. APPLICATION NUMBER, FILING DATE, NAME OF FIRST INVENTOR, and TITLE OF INVENTION. Fees transmitted by check or draft are subject to collection.

Please verify the accuracy of the data presented on this receipt. If an error is noted on this Filing Receipt, please submit a written request for a corrected Filing Receipt, including a properly marked-up ADS showing the changes with strike-through for deletions and underlining for additions. If you received a "Notice to File Missing Parts" or other Notice requiring a response for this application, please submit any request for correction to this Filing Receipt with your reply to the Notice. When the USPTO processes the reply to the Notice, the USPTO will generate another Filing Receipt incorporating the requested corrections provided that the request is grantable.

Inventor(s)

Derek Dee Deville, Coral Gables, FL;
Matthew A. Palmer, Miami, FL;
William T. Bales JR., Miami, FL;
M. Sean McBrayer, Coral Gables, FL;
Eric Petersen, Homestead, FL;
Richard Cartledge, Boca Raton, FL;
Thomas O. Bales, Miami, FL;
Carlos Rivera, Cooper City, FL;

Applicant(s)

Syntheon 2.0, LLC, Miami, FL;

Assignment For Published Patent Application

Syntheon 2.0, LLC, Miami, FL

Power of Attorney: The patent practitioners associated with Customer Number 27316

Domestic Priority data as claimed by applicant

This application is a CON of 16/516,232 07/18/2019
which claims benefit of 62/701,086 07/20/2018
and claims benefit of 62/750,011 10/24/2018
This application 16/681,564
is a CON of PCT/US2019/042546 07/19/2019
which is a CON of 16/516,232 07/18/2019
which claims benefit of 62/701,086 07/20/2018

page 1 of 4

and claims benefit of 62/750,011 10/24/2018

Foreign Applications for which priority is claimed (You may be eligible to benefit from the **Patent Prosecution Highway** program at the USPTO. Please see <http://www.uspto.gov> for more information.) - None.

Foreign application information must be provided in an Application Data Sheet in order to constitute a claim to foreign priority. See 37 CFR 1.55 and 1.76.

Permission to Access Application via Priority Document Exchange: Yes

Permission to Access Search Results: Yes

Applicant may provide or rescind an authorization for access using Form PTO/SB/39 or Form PTO/SB/69 as appropriate.

If Required, Foreign Filing License Granted: 12/16/2019

The country code and number of your priority application, to be used for filing abroad under the Paris Convention, is **US 16/681,564**

Projected Publication Date: 03/26/2020

Non-Publication Request: No

Early Publication Request: No

**** SMALL ENTITY ****

Title

ASPIRATION THROMBECTOMY SYSTEM AND METHODS FOR THROMBUS REMOVAL WITH
ASPIRATION CATHETER

Preliminary Class

604

Statement under 37 CFR 1.55 or 1.78 for AIA (First Inventor to File) Transition Applications: No

PROTECTING YOUR INVENTION OUTSIDE THE UNITED STATES

Since the rights granted by a U.S. patent extend only throughout the territory of the United States and have no effect in a foreign country, an inventor who wishes patent protection in another country must apply for a patent in a specific country or in regional patent offices. Applicants may wish to consider the filing of an international application under the Patent Cooperation Treaty (PCT). An international (PCT) application generally has the same effect as a regular national patent application in each PCT-member country. The PCT process **simplifies** the filing of patent applications on the same invention in member countries, but **does not result** in a grant of "an international patent" and does not eliminate the need of applicants to file additional documents and fees in countries where patent protection is desired.

Almost every country has its own patent law, and a person desiring a patent in a particular country must make an application for patent in that country in accordance with its particular laws. Since the laws of many countries differ in various respects from the patent law of the United States, applicants are advised to seek guidance from specific foreign countries to ensure that patent rights are not lost prematurely.

Applicants also are advised that in the case of inventions made in the United States, the Director of the USPTO must issue a license before applicants can apply for a patent in a foreign country. The filing of a U.S. patent application

page 2 of 4

serves as a request for a foreign filing license. The application's filing receipt contains further information and guidance as to the status of applicant's license for foreign filing.

Applicants may wish to consult the USPTO booklet, "General Information Concerning Patents" (specifically, the section entitled "Treaties and Foreign Patents") for more information on timeframes and deadlines for filing foreign patent applications. The guide is available either by contacting the USPTO Contact Center at 800-786-9199, or it can be viewed on the USPTO website at <http://www.uspto.gov/web/offices/pac/doc/general/index.html>.

For information on preventing theft of your intellectual property (patents, trademarks and copyrights), you may wish to consult the U.S. Government website, <http://www.stopfakes.gov>. Part of a Department of Commerce initiative, this website includes self-help "toolkits" giving innovators guidance on how to protect intellectual property in specific countries such as China, Korea and Mexico. For questions regarding patent enforcement issues, applicants may call the U.S. Government hotline at 1-866-999-HALT (1-866-999-4258).

LICENSE FOR FOREIGN FILING UNDER

Title 35, United States Code, Section 184

Title 37, Code of Federal Regulations, 5.11 & 5.15

GRANTED

The applicant has been granted a license under 35 U.S.C. 184, if the phrase "IF REQUIRED, FOREIGN FILING LICENSE GRANTED" followed by a date appears on this form. Such licenses are issued in all applications where the conditions for issuance of a license have been met, regardless of whether or not a license may be required as set forth in 37 CFR 5.15. The scope and limitations of this license are set forth in 37 CFR 5.15(a) unless an earlier license has been issued under 37 CFR 5.15(b). The license is subject to revocation upon written notification. The date indicated is the effective date of the license, unless an earlier license of similar scope has been granted under 37 CFR 5.13 or 5.14.

This license is to be retained by the licensee and may be used at any time on or after the effective date thereof unless it is revoked. This license is automatically transferred to any related applications(s) filed under 37 CFR 1.53(d). This license is not retroactive.

The grant of a license does not in any way lessen the responsibility of a licensee for the security of the subject matter as imposed by any Government contract or the provisions of existing laws relating to espionage and the national security or the export of technical data. Licensees should apprise themselves of current regulations especially with respect to certain countries, of other agencies, particularly the Office of Defense Trade Controls, Department of State (with respect to Arms, Munitions and Implements of War (22 CFR 121-128)); the Bureau of Industry and Security, Department of Commerce (15 CFR parts 730-774); the Office of Foreign Assets Control, Department of Treasury (31 CFR Parts 500+) and the Department of Energy.

NOT GRANTED

No license under 35 U.S.C. 184 has been granted at this time, if the phrase "IF REQUIRED, FOREIGN FILING LICENSE GRANTED" DOES NOT appear on this form. Applicant may still petition for a license under 37 CFR 5.12, if a license is desired before the expiration of 6 months from the filing date of the application. If 6 months has lapsed from the filing date of this application and the licensee has not received any indication of a secrecy order under 35 U.S.C. 181, the licensee may foreign file the application pursuant to 37 CFR 5.15(b).

SelectUSA

The United States represents the largest, most dynamic marketplace in the world and is an unparalleled location for business investment, innovation, and commercialization of new technologies. The U.S. offers tremendous resources and advantages for those who invest and manufacture goods here. Through SelectUSA, our nation works to promote and facilitate business investment. SelectUSA provides information assistance to the international investor community; serves as an ombudsman for existing and potential investors; advocates on behalf of U.S. cities, states, and regions competing for global investment; and counsels U.S. economic development organizations on investment attraction best practices. To learn more about why the United States is the best country in the world to develop technology, manufacture products, deliver services, and grow your business, visit <http://www.SelectUSA.gov> or call +1-202-482-6800.

PATENT APPLICATION FEE DETERMINATION RECORD Substitute for Form PTO-875						Application or Docket Number 16/681,564				
APPLICATION AS FILED - PART I										
(Column 1)		(Column 2)		SMALL ENTITY		OTHER THAN SMALL ENTITY				
FOR	NUMBER FILED	NUMBER EXTRA	RATE(\$)	FEE(\$)		RATE(\$)	FEE(\$)			
BASIC FEE (37 CFR 1.16(a), (b), or (c))	N/A	N/A	N/A	75		N/A				
SEARCH FEE (37 CFR 1.16(k), (j), or (m))	N/A	N/A	N/A	330		N/A				
EXAMINATION FEE (37 CFR 1.16(o), (p), or (q))	N/A	N/A	N/A	380		N/A				
TOTAL CLAIMS (37 CFR 1.16(i))	21	minus 20 = *	1	x 50 = 50	OR					
INDEPENDENT CLAIMS (37 CFR 1.16(h))	2	minus 3 = *		x 230 = 0.00						
APPLICATION SIZE FEE (37 CFR 1.16(s))	If the specification and drawings exceed 100 sheets of paper, the application size fee due is \$310 (\$155 for small entity) for each additional 50 sheets or fraction thereof. See 35 U.S.C. 41(a)(1)(G) and 37 CFR 1.16(s).			0.00						
MULTIPLE DEPENDENT CLAIM PRESENT (37 CFR 1.16(j))				0.00						
* If the difference in column 1 is less than zero, enter "0" in column 2.				TOTAL		TOTAL				
				835						
APPLICATION AS AMENDED - PART II										
(Column 1)		(Column 2)		(Column 3)		SMALL ENTITY		OTHER THAN SMALL ENTITY		
AMENDMENT A		CLAIMS REMAINING AFTER AMENDMENT		HIGHEST NUMBER PREVIOUSLY PAID FOR	PRESENT EXTRA	RATE(\$)	ADDITIONAL FEE(\$)		RATE(\$)	ADDITIONAL FEE(\$)
	Total (37 CFR 1.16(i))	*	Minus	**	=	x	=	OR	x	=
	Independent (37 CFR 1.16(h))	*	Minus	***	=	x	=	OR	x	=
	Application Size Fee (37 CFR 1.16(s))							OR		
	FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))							OR		
						TOTAL ADD'L FEE		OR	TOTAL ADD'L FEE	
AMENDMENT B		CLAIMS REMAINING AFTER AMENDMENT		HIGHEST NUMBER PREVIOUSLY PAID FOR	PRESENT EXTRA	RATE(\$)	ADDITIONAL FEE(\$)		RATE(\$)	ADDITIONAL FEE(\$)
	Total (37 CFR 1.16(i))	*	Minus	**	=	x	=	OR	x	=
	Independent (37 CFR 1.16(h))	*	Minus	***	=	x	=	OR	x	=
	Application Size Fee (37 CFR 1.16(s))							OR		
	FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))							OR		
						TOTAL ADD'L FEE		OR	TOTAL ADD'L FEE	
<p style="font-size: x-small;">* If the entry in column 1 is less than the entry in column 2, write "0" in column 3.</p> <p style="font-size: x-small;">** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 20, enter "20".</p> <p style="font-size: x-small;">*** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 3, enter "3".</p> <p style="font-size: x-small;">The "Highest Number Previously Paid For" (Total or Independent) is the highest found in the appropriate box in column 1.</p>										

POWER OF ATTORNEY TO PROSECUTE APPLICATIONS BEFORE THE USPTO

I hereby revoke all previous powers of attorney given in the application identified in the attached statement under 37 CFR 3.73(c).

I hereby appoint:

☒ Practitioners associated with Customer Number: 27316

OR

☐ Practitioner(s) named below (if more than ten patent practitioners are to be named, then a customer number must be used):

Name	Registration Number

Name	Registration Number

As attorney(s) or agent(s) to represent the undersigned before the United States Patent and Trademark Office (USPTO) in connection with any and all patent applications assigned only to the undersigned according to the USPTO assignment records or assignment documents attached to this form in accordance with 37 CFR 3.73(c).

Please change the correspondence address for the application identified in the attached statement under 37 CFR 3.73(c) to:

☒ The address associated with Customer Number: 27316

OR

☐	Firm or individual name		
	Address		
	City	State	Zip
	Country		
	Telephone	Email	

Assignee name and address: Syntheon 2.0, LLC
13755 S.W. 119th Avenue
Miami, FL 33186 US

A copy of this form, together with a statement under 37 CFR 3.73(c) (Form PTO/AIA/96 or equivalent) is required to be filed in each application in which this form is used. The statement under 37 CFR 3.73(c) may be completed by one of the practitioners appointed in this form, and must identify the application in which this Power of Attorney is to be filed.

SIGNATURE of Assignee of Record

The individual whose signature and title is supplied below is authorized to act on behalf of the assignee.

Signature 	Date 11/7/19
Name M. Sean McBrayer	Telephone
Title Managing Member	

This collection of information is required by 37 CFR 1.31, 1.32, and 1.33. The information is required to obtain or retain a benefit by the public, which is to update (and by the USPTO to process) the file of a patent or reexamination proceeding. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.11 and 1.14. This collection is estimated to take 18 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

If you need assistance in completing the form, call 1-800-PTO-9199 and select option 2.

STATEMENT UNDER 37 CFR 3.73(c)

Applicant/Patent Owner: Syntheon 2.0, LLC
Application No./Patent No.: 16/681,564 Filed/Issue Date: November 12/2019
Titled: ASPIRATION THROMBECTOMY SYSTEM AND METHODS FOR THROMBUS REMOVAL WITH ASPIRATION CATHETER
Syntheon 2.0., LLC, a Limited Liability Company
(Name of Assignee) (Type of Assignee, e.g., corporation, partnership, university, government agency, etc.)

states that, for the patent application/patent identified above, it is (choose **one** of options 1, 2, 3 or 4 below):

1. ☒ The assignee of the entire right, title, and interest.
2. ☐ An assignee of less than the entire right, title, and interest (check applicable box):
- ☐ The extent (by percentage) of its ownership interest is ____%. Additional Statement(s) by the owners holding the balance of the interest must be submitted to account for 100% of the ownership interest.
- ☐ There are unspecified percentages of ownership. The other parties, including inventors, who together own the entire right, title and interest are:

Additional Statement(s) by the owner(s) holding the balance of the interest must be submitted to account for the entire right, title, and interest.

3. ☐ The assignee of an undivided interest in the entirety (a complete assignment from one of the joint inventors was made). The other parties, including inventors, who together own the entire right, title, and interest are:

Additional Statement(s) by the owner(s) holding the balance of the interest must be submitted to account for the entire right, title, and interest.

4. ☐ The recipient, via a court proceeding or the like (e.g., bankruptcy, probate), of an undivided interest in the entirety (a complete transfer of ownership interest was made). The certified document(s) showing the transfer is attached.

The interest identified in option 1, 2 or 3 above (not option 4) is evidenced by either (choose **one** of options A or B below):

- A. ☒ An assignment from the inventor(s) of the patent application/patent identified above. The assignment was recorded in the United States Patent and Trademark Office at Reel 051072, Frame 0981, or for which a copy thereof is attached.

- B. ☐ A chain of title from the inventor(s), of the patent application/patent identified above, to the current assignee as follows:

1. From: _____ To: _____

The document was recorded in the United States Patent and Trademark Office at
Reel _____, Frame _____, or for which a copy thereof is attached.

2. From: _____ To: _____

The document was recorded in the United States Patent and Trademark Office at
Reel _____, Frame _____, or for which a copy thereof is attached.

[Page 1 of 2]

This collection of information is required by 37 CFR 3.73(b). The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.11 and 1.14. This collection is estimated to take 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

If you need assistance in completing the form, call 1-800-PTO-9199 and select option 2.

STATEMENT UNDER 37 CFR 3.73(c)

3. From: _____ To: _____

The document was recorded in the United States Patent and Trademark Office at
Reel _____, Frame _____, or for which a copy thereof is attached.

4. From: _____ To: _____

The document was recorded in the United States Patent and Trademark Office at
Reel _____, Frame _____, or for which a copy thereof is attached.

5. From: _____ To: _____

The document was recorded in the United States Patent and Trademark Office at
Reel _____, Frame _____, or for which a copy thereof is attached.

6. From: _____ To: _____

The document was recorded in the United States Patent and Trademark Office at
Reel _____, Frame _____, or for which a copy thereof is attached.

☐ Additional documents in the chain of title are listed on a supplemental sheet(s).

☒ As required by 37 CFR 3.73(c)(1)(i), the documentary evidence of the chain of title from the original owner to the assignee was, or concurrently is being, submitted for recordation pursuant to 37 CFR 3.11.

[NOTE: A separate copy (i.e., a true copy of the original assignment document(s)) must be submitted to Assignment Division in accordance with 37 CFR Part 3, to record the assignment in the records of the USPTO. See MPEP 302.08]

The undersigned (whose title is supplied below) is authorized to act on behalf of the assignee.

/gregory l. mayback/

Signature

Gregory L. Mayback

Printed or Typed Name

2019-11-22

Date

40719

Title or Registration Number

Privacy Act Statement

The **Privacy Act of 1974 (P.L. 93-579)** requires that you be given certain information in connection with your submission of the attached form related to a patent application or patent. Accordingly, pursuant to the requirements of the Act, please be advised that: (1) the general authority for the collection of this information is 35 U.S.C. 2(b)(2); (2) furnishing of the information solicited is voluntary; and (3) the principal purpose for which the information is used by the U.S. Patent and Trademark Office is to process and/or examine your submission related to a patent application or patent. If you do not furnish the requested information, the U.S. Patent and Trademark Office may not be able to process and/or examine your submission, which may result in termination of proceedings or abandonment of the application or expiration of the patent.

The information provided by you in this form will be subject to the following routine uses:

1. The information on this form will be treated confidentially to the extent allowed under the Freedom of Information Act (5 U.S.C. 552) and the Privacy Act (5 U.S.C. 552a). Records from this system of records may be disclosed to the Department of Justice to determine whether disclosure of these records is required by the Freedom of Information Act.
2. A record from this system of records may be disclosed, as a routine use, in the course of presenting evidence to a court, magistrate, or administrative tribunal, including disclosures to opposing counsel in the course of settlement negotiations.
3. A record in this system of records may be disclosed, as a routine use, to a Member of Congress submitting a request involving an individual, to whom the record pertains, when the individual has requested assistance from the Member with respect to the subject matter of the record.
4. A record in this system of records may be disclosed, as a routine use, to a contractor of the Agency having need for the information in order to perform a contract. Recipients of information shall be required to comply with the requirements of the Privacy Act of 1974, as amended, pursuant to 5 U.S.C. 552a(m).
5. A record related to an International Application filed under the Patent Cooperation Treaty in this system of records may be disclosed, as a routine use, to the International Bureau of the World Intellectual Property Organization, pursuant to the Patent Cooperation Treaty.
6. A record in this system of records may be disclosed, as a routine use, to another federal agency for purposes of National Security review (35 U.S.C. 181) and for review pursuant to the Atomic Energy Act (42 U.S.C. 218(c)).
7. A record from this system of records may be disclosed, as a routine use, to the Administrator, General Services, or his/her designee, during an inspection of records conducted by GSA as part of that agency's responsibility to recommend improvements in records management practices and programs, under authority of 44 U.S.C. 2904 and 2906. Such disclosure shall be made in accordance with the GSA regulations governing inspection of records for this purpose, and any other relevant (*i.e.*, GSA or Commerce) directive. Such disclosure shall not be used to make determinations about individuals.
8. A record from this system of records may be disclosed, as a routine use, to the public after either publication of the application pursuant to 35 U.S.C. 122(b) or issuance of a patent pursuant to 35 U.S.C. 151. Further, a record may be disclosed, subject to the limitations of 37 CFR 1.14, as a routine use, to the public if the record was filed in an application which became abandoned or in which the proceedings were terminated and which application is referenced by either a published application, an application open to public inspection or an issued patent.
9. A record from this system of records may be disclosed, as a routine use, to a Federal, State, or local law enforcement agency, if the USPTO becomes aware of a violation or potential violation of law or regulation.

Electronic Acknowledgement Receipt	
EFS ID:	37830539
Application Number:	16681564
International Application Number:	
Confirmation Number:	6608
Title of Invention:	ASPIRATION THROMBECTOMY SYSTEM AND METHODS FOR THROMBUS REMOVAL WITH ASPIRATION CATHETER
First Named Inventor/Applicant Name:	Derek Dee Deville
Customer Number:	27316
Filer:	Gregory L. Mayback/Chris Mendez
Filer Authorized By:	Gregory L. Mayback
Attorney Docket Number:	Syn2.0/ROAR CON
Receipt Date:	22-NOV-2019
Filing Date:	
Time Stamp:	12:03:07
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	no				
File Listing:					
Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Power of Attorney	2019-11-22_Syn_ROAR_Executed_POA_Sean_86082-13.pdf	598193 ce8fcba02620d7f1e8f17334d158110e4ff24990	no	1
Warnings:					

Information:					
2	Assignee showing of ownership per 37 CFR 3.73	2019-11-22_Syn_Roar_Con_Sta tement373_86082-13.pdf	117987	no	3
			95731a7392856a59995617194041b10c7e3029aa		
Warnings:					
Information:					
Total Files Size (in bytes):			716180		
<p>This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.</p> <p><u>New Applications Under 35 U.S.C. 111</u> If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.</p> <p><u>National Stage of an International Application under 35 U.S.C. 371</u> If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.</p> <p><u>New International Application Filed with the USPTO as a Receiving Office</u> If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.</p>					

SCORE Placeholder Sheet for IFW Content

Application Number: 16681564

Document Date: 11/12/2019

The presence of this form in the IFW record indicates that the following document type was received in electronic format on the date identified above. This content is stored in the SCORE database.

Since this was an electronic submission, there is no physical artifact folder, no artifact folder is recorded in PALM, and no paper documents or physical media exist. The TIFF images in the IFW record were created from the original documents that are stored in SCORE.

- Drawing

At the time of document entry (noted above):

- USPTO employees may access SCORE content via DAV or via the SCORE web page.
- External customers may access SCORE content via PAIR using the Supplemental Content tab.

**CERTIFICATION AND REQUEST FOR PRIORITIZED EXAMINATION
UNDER 37 CFR 1.102(e) (Page 1 of 1)**

First Named Inventor:	Derek Dee Deville	Nonprovisional Application Number (if known):	
Title of Invention:	ASPIRATION THROMBECTOMY SYSTEM AND METHODS FOR THROMBUS REMOVAL WITH ASPIRATION CATHETER		

APPLICANT HEREBY CERTIFIES THE FOLLOWING AND REQUESTS PRIORITIZED EXAMINATION FOR THE ABOVE-IDENTIFIED APPLICATION.

1. The processing fee set forth in 37 CFR 1.17(i)(1) and the prioritized examination fee set forth in 37 CFR 1.17(c) have been filed with the request. The publication fee requirement is met because that fee, set forth in 37 CFR 1.18(d), is currently \$0. The basic filing fee, search fee, and examination fee are filed with the request or have been already been paid. I understand that any required excess claims fees or application size fee must be paid for the application.
2. I understand that the application may not contain, or be amended to contain, more than four independent claims, more than thirty total claims, or any multiple dependent claims, and that any request for an extension of time will cause an outstanding Track I request to be dismissed.
3. The applicable box is checked below:
 - I. ☒ **Original Application (Track One) - Prioritized Examination under § 1.102(e)(1)**
 - i. (a) The application is an original nonprovisional utility application filed under 35 U.S.C. 111(a). This certification and request is being filed with the utility application via EFS-Web.
---OR---
 - (b) The application is an original nonprovisional plant application filed under 35 U.S.C. 111(a). This certification and request is being filed with the plant application in paper.
 - ii. An executed inventor's oath or declaration under 37 CFR 1.63 or 37 CFR 1.64 for each inventor, or the application data sheet meeting the conditions specified in 37 CFR 1.53(f)(3)(i) is filed with the application.
 - II. ☐ **Request for Continued Examination - Prioritized Examination under § 1.102(e)(2)**
 - i. A request for continued examination has been filed with, or prior to, this form.
 - ii. If the application is a utility application, this certification and request is being filed via EFS-Web.
 - iii. The application is an original nonprovisional utility application filed under 35 U.S.C. 111(a), or is a national stage entry under 35 U.S.C. 371.
 - iv. This certification and request is being filed prior to the mailing of a first Office action responsive to the request for continued examination.
 - v. No prior request for continued examination has been granted prioritized examination status under 37 CFR 1.102(e)(2).

Signature /Gregory L. Mayback/	Date 2019-11-12
Name (Print/Typed) Gregory L. Mayback	Practitioner Registration Number 40719
Note: This form must be signed in accordance with 37 CFR 1.33. See 37 CFR 1.4(d) for signature requirements and certifications. Submit multiple forms if more than one signature is required.*	
☐ *Total of _____ forms are submitted.	

Privacy Act Statement

The **Privacy Act of 1974 (P.L. 93-579)** requires that you be given certain information in connection with your submission of the attached form related to a patent application or patent. Accordingly, pursuant to the requirements of the Act, please be advised that: (1) the general authority for the collection of this information is 35 U.S.C. 2(b)(2); (2) furnishing of the information solicited is voluntary; and (3) the principal purpose for which the information is used by the U.S. Patent and Trademark Office is to process and/or examine your submission related to a patent application or patent. If you do not furnish the requested information, the U.S. Patent and Trademark Office may not be able to process and/or examine your submission, which may result in termination of proceedings or abandonment of the application or expiration of the patent.

The information provided by you in this form will be subject to the following routine uses:

1. The information on this form will be treated confidentially to the extent allowed under the Freedom of Information Act (5 U.S.C. 552) and the Privacy Act (5 U.S.C. 552a). Records from this system of records may be disclosed to the Department of Justice to determine whether disclosure of these records is required by the Freedom of Information Act.
2. A record in this system of records may be disclosed, as a routine use, in the course of presenting evidence to a court, magistrate, or administrative tribunal, including disclosures to opposing counsel in the course of settlement negotiations.
3. A record in this system of records may be disclosed, as a routine use, to a Member of Congress submitting a request involving an individual, to whom the record pertains, when the individual has requested assistance from the Member with respect to the subject matter of the record.
4. A record in this system of records may be disclosed, as a routine use, to a contractor of the Agency having need for the information in order to perform a contract. Recipients of information shall be required to comply with the requirements of the Privacy Act of 1974, as amended, pursuant to 5 U.S.C. 552a(m).
5. A record related to an International Application filed under the Patent Cooperation Treaty in this system of records may be disclosed, as a routine use, to the International Bureau of the World Intellectual Property Organization, pursuant to the Patent Cooperation Treaty.
6. A record in this system of records may be disclosed, as a routine use, to another federal agency for purposes of National Security review (35 U.S.C. 181) and for review pursuant to the Atomic Energy Act (42 U.S.C. 218(c)).
7. A record from this system of records may be disclosed, as a routine use, to the Administrator, General Services, or his/her designee, during an inspection of records conducted by GSA as part of that agency's responsibility to recommend improvements in records management practices and programs, under authority of 44 U.S.C. 2904 and 2906. Such disclosure shall be made in accordance with the GSA regulations governing inspection of records for this purpose, and any other relevant (*i.e.*, GSA or Commerce) directive. Such disclosure shall not be used to make determinations about individuals.
8. A record from this system of records may be disclosed, as a routine use, to the public after either publication of the application pursuant to 35 U.S.C. 122(b) or issuance of a patent pursuant to 35 U.S.C. 151. Further, a record may be disclosed, subject to the limitations of 37 CFR 1.14, as a routine use, to the public if the record was filed in an application which became abandoned or in which the proceedings were terminated and which application is referenced by either a published application, an application open to public inspection or an issued patent.
9. A record from this system of records may be disclosed, as a routine use, to a Federal, State, or local law enforcement agency, if the USPTO becomes aware of a violation or potential violation of law or regulation.

Under the Paperwork Reduction Act of 1995 no persons are required to respond to a collection of information unless it displays a valid OMB control number.

UTILITY PATENT APPLICATION TRANSMITTAL <i>(Only for new nonprovisional applications under 37 CFR 1.53(b))</i>	<table border="1" style="width: 100%; border-collapse: collapse;"> <tr> <td style="width: 50%;"><i>Attorney Docket No.</i></td> <td>Syn 2.0/Roar/Con</td> </tr> <tr> <td><i>First Named Inventor</i></td> <td>Derek Dee Deville</td> </tr> <tr> <td><i>Title</i></td> <td>Aspiration Thrombectomy System and Methods for Thrombus Removal with Aspiration</td> </tr> <tr> <td><i>Priority Mail Express® Label No.</i></td> <td>N/A</td> </tr> </table>	<i>Attorney Docket No.</i>	Syn 2.0/Roar/Con	<i>First Named Inventor</i>	Derek Dee Deville	<i>Title</i>	Aspiration Thrombectomy System and Methods for Thrombus Removal with Aspiration	<i>Priority Mail Express® Label No.</i>	N/A
<i>Attorney Docket No.</i>	Syn 2.0/Roar/Con								
<i>First Named Inventor</i>	Derek Dee Deville								
<i>Title</i>	Aspiration Thrombectomy System and Methods for Thrombus Removal with Aspiration								
<i>Priority Mail Express® Label No.</i>	N/A								

APPLICATION ELEMENTS <i>See MPEP chapter 600 concerning utility patent application contents.</i>	ADDRESS TO: Commissioner for Patents P.O. Box 1450 Alexandria, VA 22313-1450
<ol style="list-style-type: none"> 1. ☐ Fee Transmittal Form (PTO/SB/17 or equivalent) 2. ☒ Applicant asserts small entity status. See 37 CFR 1.27 3. ☐ Applicant certifies micro entity status. See 37 CFR 1.29. Applicant must attach form PTO/SB/15A or B or equivalent. 4. ☒ Specification [Total Pages <u>84</u>] Both the claims and abstract must start on a new page. (See MPEP § 608.01(a) for information on the preferred arrangement) 5. ☒ Drawing(s) (35 U.S.C. 113) [Total Sheets <u>29</u>] 6. ☒ Inventor's Oath or Declaration [Total Pages <u>8</u>] (including substitute statements under 37 CFR 1.64 and assignments serving as an oath or declaration under 37 CFR 1.63(e)) <ol style="list-style-type: none"> a. ☒ Newly executed (original or copy) b. ☐ A copy from a prior application (37 CFR 1.63(d)) 7. ☒ Application Data Sheet * See note below. See 37 CFR 1.76 (PTO/AIA/14 or equivalent) 8. ☐ CD-ROM or CD-R in duplicate, large table, or Computer Program (Appendix) ☐ Landscape Table on CD 9. Nucleotide and/or Amino Acid Sequence Submission (if applicable, items a. – c. are required) <ol style="list-style-type: none"> a. ☐ Computer Readable Form (CRF) b. ☐ Specification Sequence Listing on: <ol style="list-style-type: none"> i. ☐ CD-ROM or CD-R (2 copies); or ii. ☐ Paper c. ☐ Statements verifying identity of above copies 	ACCOMPANYING APPLICATION PAPERS <ol style="list-style-type: none"> 10. ☐ Assignment Papers (cover sheet & document(s)) Name of Assignee _____ 11. ☐ 37 CFR 3.73(c) Statement ☐ Power of Attorney (when there is an assignee) 12. ☐ English Translation Document (if applicable) 13. ☐ Information Disclosure Statement (PTO/SB/08 or PTO-1449) ☐ Copies of citations attached 14. ☐ Preliminary Amendment 15. ☐ Return Receipt Postcard (MPEP § 503) (Should be specifically itemized) 16. ☐ Certified Copy of Priority Document(s) (if foreign priority is claimed) 17. ☐ Nonpublication Request Under 35 U.S.C. 122(b)(2)(B)(i). Applicant must attach form PTO/SB/35 or equivalent. 18. ☒ Other: Request for Prioritized Examination _____ _____ _____

***Note:** (1) Benefit claims under 37 CFR 1.78 and foreign priority claims under 1.55 **must** be included in an Application Data Sheet (ADS).
(2) For applications filed under 35 U.S.C. 111, the application must contain an ADS specifying the applicant if the applicant is an assignee, person to whom the inventor is under an obligation to assign, or person who otherwise shows sufficient proprietary interest in the matter. See 37 CFR 1.46(b).

19. CORRESPONDENCE ADDRESS					
☒ The address associated with Customer Number: <u>27316</u> OR ☐ Correspondence address below					
Name					
Address					
City	State		Zip Code		
Country	Telephone		Email		
Signature	/Gregory L. Mayback/		Date	2019-11-12	
Name (Print/Type)	Gregory L. Mayback		Registration No. (Attorney/Agent)	40719	

This collection of information is required by 37 CFR 1.53(b). The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.11 and 1.14. This collection is estimated to take 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

If you need assistance in completing the form, call 1-800-PTO-9199 and select option 2.

Privacy Act Statement

The **Privacy Act of 1974 (P.L. 93-579)** requires that you be given certain information in connection with your submission of the attached form related to a patent application or patent. Accordingly, pursuant to the requirements of the Act, please be advised that: (1) the general authority for the collection of this information is 35 U.S.C. 2(b)(2); (2) furnishing of the information solicited is voluntary; and (3) the principal purpose for which the information is used by the U.S. Patent and Trademark Office is to process and/or examine your submission related to a patent application or patent. If you do not furnish the requested information, the U.S. Patent and Trademark Office may not be able to process and/or examine your submission, which may result in termination of proceedings or abandonment of the application or expiration of the patent.

The information provided by you in this form will be subject to the following routine uses:

1. The information on this form will be treated confidentially to the extent allowed under the Freedom of Information Act (5 U.S.C. 552) and the Privacy Act (5 U.S.C. 552a). Records from this system of records may be disclosed to the Department of Justice to determine whether disclosure of these records is required by the Freedom of Information Act.
2. A record from this system of records may be disclosed, as a routine use, in the course of presenting evidence to a court, magistrate, or administrative tribunal, including disclosures to opposing counsel in the course of settlement negotiations.
3. A record in this system of records may be disclosed, as a routine use, to a Member of Congress submitting a request involving an individual, to whom the record pertains, when the individual has requested assistance from the Member with respect to the subject matter of the record.
4. A record in this system of records may be disclosed, as a routine use, to a contractor of the Agency having need for the information in order to perform a contract. Recipients of information shall be required to comply with the requirements of the Privacy Act of 1974, as amended, pursuant to 5 U.S.C. 552a(m).
5. A record related to an International Application filed under the Patent Cooperation Treaty in this system of records may be disclosed, as a routine use, to the International Bureau of the World Intellectual Property Organization, pursuant to the Patent Cooperation Treaty.
6. A record in this system of records may be disclosed, as a routine use, to another federal agency for purposes of National Security review (35 U.S.C. 181) and for review pursuant to the Atomic Energy Act (42 U.S.C. 218(c)).
7. A record from this system of records may be disclosed, as a routine use, to the Administrator, General Services, or his/her designee, during an inspection of records conducted by GSA as part of that agency's responsibility to recommend improvements in records management practices and programs, under authority of 44 U.S.C. 2904 and 2906. Such disclosure shall be made in accordance with the GSA regulations governing inspection of records for this purpose, and any other relevant (*i.e.*, GSA or Commerce) directive. Such disclosure shall not be used to make determinations about individuals.
8. A record from this system of records may be disclosed, as a routine use, to the public after either publication of the application pursuant to 35 U.S.C. 122(b) or issuance of a patent pursuant to 35 U.S.C. 151. Further, a record may be disclosed, subject to the limitations of 37 CFR 1.14, as a routine use, to the public if the record was filed in an application which became abandoned or in which the proceedings were terminated and which application is referenced by either a published application, an application open to public inspection or an issued patent.
9. A record from this system of records may be disclosed, as a routine use, to a Federal, State, or local law enforcement agency, if the USPTO becomes aware of a violation or potential violation of law or regulation.

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Application Data Sheet 37 CFR 1.76		Attorney Docket Number	Syn2.0/ROAR CON
		Application Number	
Title of Invention	ASPIRATION THROMBECTOMY SYSTEM AND METHODS FOR THROMBUS REMOVAL WITH ASPIRATION CATHETER		
<p>The application data sheet is part of the provisional or nonprovisional application for which it is being submitted. The following form contains the bibliographic data arranged in a format specified by the United States Patent and Trademark Office as outlined in 37 CFR 1.76.</p> <p>This document may be completed electronically and submitted to the Office in electronic format using the Electronic Filing System (EFS) or the document may be printed and included in a paper filed application.</p>			

Secrecy Order 37 CFR 5.2:

☐ Portions or all of the application associated with this Application Data Sheet may fall under a Secrecy Order pursuant to 37 CFR 5.2 (Paper filers only. Applications that fall under Secrecy Order may not be filed electronically.)

Inventor Information:

Inventor	1				Remove	
Legal Name						
Prefix	Given Name	Middle Name	Family Name	Suffix		
	Derek	Dee	Deville			
Residence Information (Select One) ☒ US Residency ☐ Non US Residency ☐ Active US Military Service						
City	Coral Gables	State/Province	FL	Country of Residence	US	
Mailing Address of Inventor:						
Address 1	5500 Oak Lane					
Address 2						
City	Coral Gables	State/Province	FL			
Postal Code	33156	Country	US			
Inventor	2				Remove	
Legal Name						
Prefix	Given Name	Middle Name	Family Name	Suffix		
	Matthew	A.	Palmer			
Residence Information (Select One) ☒ US Residency ☐ Non US Residency ☐ Active US Military Service						
City	Miami	State/Province	FL	Country of Residence	US	
Mailing Address of Inventor:						
Address 1	12790 SW 64 Court					
Address 2						
City	Miami	State/Province	FL			
Postal Code	33156	Country	US			
Inventor	3				Remove	
Legal Name						
Prefix	Given Name	Middle Name	Family Name	Suffix		
	William	T.	Bales	Jr.		
Residence Information (Select One) ☒ US Residency ☐ Non US Residency ☐ Active US Military Service						

Application Data Sheet 37 CFR 1.76		Attorney Docket Number		Syn2.0/ROAR CON	
		Application Number			
Title of Invention		ASPIRATION THROMBECTOMY SYSTEM AND METHODS FOR THROMBUS REMOVAL WITH ASPIRATION CATHETER			

City	Miami	State/Province	FL	Country of Residence ⁱ	US
------	-------	----------------	----	-----------------------------------	----

Mailing Address of Inventor:

Address 1	7630 S.W. 54 Avenue				
Address 2					
City	Miami	State/Province	FL		
Postal Code	33143	Country ⁱ	US		
Inventor	4				Remove
Legal Name					
Prefix	Given Name	Middle Name	Family Name	Suffix	
	M.	Sean	McBrayer		
Residence Information (Select One) ☒ US Residency ☐ Non US Residency ☐ Active US Military Service					
City	Coral Gables	State/Province	FL	Country of Residence ⁱ	US

Mailing Address of Inventor:

Address 1	6940 Sunrise Drive				
Address 2					
City	Coral Gables	State/Province	FL		
Postal Code	33133	Country ⁱ	US		
Inventor	5				Remove
Legal Name					
Prefix	Given Name	Middle Name	Family Name	Suffix	
	Eric		Petersen		
Residence Information (Select One) ☒ US Residency ☐ Non US Residency ☐ Active US Military Service					
City	Homestead	State/Province	FL	Country of Residence ⁱ	US

Mailing Address of Inventor:

Address 1	27025 SW 197 Avenue				
Address 2					
City	Homestead	State/Province	FL		
Postal Code	33031	Country ⁱ	US		
Inventor	6				Remove
Legal Name					
Prefix	Given Name	Middle Name	Family Name	Suffix	
	Richard		Cartledge		
Residence Information (Select One) ☒ US Residency ☐ Non US Residency ☐ Active US Military Service					
City	Boca Raton	State/Province	FL	Country of Residence ⁱ	US

Application Data Sheet 37 CFR 1.76		Attorney Docket Number	Syn2.0/ROAR CON
		Application Number	
Title of Invention	ASPIRATION THROMBECTOMY SYSTEM AND METHODS FOR THROMBUS REMOVAL WITH ASPIRATION CATHETER		

Mailing Address of Inventor:				
Address 1		2268 Acorn Palm Road		
Address 2				
City	Boca Raton	State/Province	FL	
Postal Code	33432	Country i	US	
Inventor	7			<input type="button" value="Remove"/>
Legal Name				
Prefix	Given Name	Middle Name	Family Name	Suffix
	Thomas	O.	Bales	
Residence Information (Select One) ☒ US Residency ☐ Non US Residency ☐ Active US Military Service				
City	Miami	State/Province	FL	Country of Residence i US

Mailing Address of Inventor:				
Address 1		4745 SW 80th Street		
Address 2				
City	Miami	State/Province	FL	
Postal Code	33145	Country i	US	
Inventor	8			<input type="button" value="Remove"/>
Legal Name				
Prefix	Given Name	Middle Name	Family Name	Suffix
	Carlos		Rivera	
Residence Information (Select One) ☒ US Residency ☐ Non US Residency ☐ Active US Military Service				
City	Cooper City	State/Province	FL	Country of Residence i US

Mailing Address of Inventor:				
Address 1		5817 SW120th Avenue		
Address 2				
City	Cooper City	State/Province	FL	
Postal Code	33330	Country i	US	
All Inventors Must Be Listed - Additional Inventor Information blocks may be generated within this form by selecting the Add button. <input type="button" value="Add"/>				

Correspondence Information:

Enter either Customer Number or complete the Correspondence Information section below. For further information see 37 CFR 1.33(a).	
☐ An Address is being provided for the correspondence information of this application.	
Customer Number	27316

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Application Data Sheet 37 CFR 1.76		Attorney Docket Number	Syn2.0/ROAR CON
		Application Number	
Title of Invention	ASPIRATION THROMBECTOMY SYSTEM AND METHODS FOR THROMBUS REMOVAL WITH ASPIRATION CATHETER		
Email Address	mhpatents@dickinsonwright.com		<input type="button" value="Add Email"/> <input type="button" value="Remove Email"/>

Application Information:

Title of the Invention	ASPIRATION THROMBECTOMY SYSTEM AND METHODS FOR THROMBUS REMOVAL WITH ASPIRATION CATHETER		
Attorney Docket Number	Syn2.0/ROAR CON	Small Entity Status Claimed	☒
Application Type	Nonprovisional		
Subject Matter	Utility		
Total Number of Drawing Sheets (if any)	29	Suggested Figure for Publication (if any)	48

Filing By Reference:

Only complete this section when filing an application by reference under 35 U.S.C. 111(c) and 37 CFR 1.57(a). Do not complete this section if application papers including a specification and any drawings are being filed. Any domestic benefit or foreign priority information must be provided in the appropriate section(s) below (i.e., "Domestic Benefit/National Stage Information" and "Foreign Priority Information").

For the purposes of a filing date under 37 CFR 1.53(b), the description and any drawings of the present application are replaced by this reference to the previously filed application, subject to conditions and requirements of 37 CFR 1.57(a).

Application number of the previously filed application	Filing date (YYYY-MM-DD)	Intellectual Property Authority or Country

Publication Information:

☐ Request Early Publication (Fee required at time of Request 37 CFR 1.219)
☐ Request Not to Publish. I hereby request that the attached application not be published under 35 U.S.C. 122(b) and certify that the invention disclosed in the attached application has not and will not be the subject of an application filed in another country, or under a multilateral international agreement, that requires publication at eighteen months after filing.

Representative Information:

Representative information should be provided for all practitioners having a power of attorney in the application. Providing this information in the Application Data Sheet does not constitute a power of attorney in the application (see 37 CFR 1.32). Either enter Customer Number or complete the Representative Name section below. If both sections are completed the customer Number will be used for the Representative Information during processing.			
Please Select One:	☒ Customer Number	US Patent Practitioner	☐ Limited Recognition (37 CFR 11.9)
Customer Number	27316		

Application Data Sheet 37 CFR 1.76		Attorney Docket Number	Syn2.0/ROAR CON
		Application Number	
Title of Invention	ASPIRATION THROMBECTOMY SYSTEM AND METHODS FOR THROMBUS REMOVAL WITH ASPIRATION CATHETER		

Domestic Benefit/National Stage Information:

This section allows for the applicant to either claim benefit under 35 U.S.C. 119(e), 120, 121, 365(c), or 386(c) or indicate National Stage entry from a PCT application. Providing benefit claim information in the Application Data Sheet constitutes the specific reference required by 35 U.S.C. 119(e) or 120, and 37 CFR 1.78.

When referring to the current application, please leave the "Application Number" field blank.

Prior Application Status	Pending		Remove
Application Number	Continuity Type	Prior Application Number	Filing or 371(c) Date (YYYY-MM-DD)
	Continuation of	16516232	2019-07-18
Prior Application Status	Expired		Remove
Application Number	Continuity Type	Prior Application Number	Filing or 371(c) Date (YYYY-MM-DD)
16516232	Claims benefit of provisional	62701086	2018-07-20
Prior Application Status	Expired		Remove
Application Number	Continuity Type	Prior Application Number	Filing or 371(c) Date (YYYY-MM-DD)
16516232	Claims benefit of provisional	62750011	2018-10-24
Prior Application Status			Remove
Application Number	Continuity Type	Prior Application Number	Filing or 371(c) Date (YYYY-MM-DD)
	Continuation of	PCT/US2019/042546	2019-07-19
Prior Application Status	Pending		Remove
Application Number	Continuity Type	Prior Application Number	Filing or 371(c) Date (YYYY-MM-DD)
PCT/US2019/042546	Continuation of	16516232	2019-07-18
Prior Application Status	Expired		Remove
Application Number	Continuity Type	Prior Application Number	Filing or 371(c) Date (YYYY-MM-DD)
16516232	Claims benefit of provisional	62701086	2018-07-20
Prior Application Status	Expired		Remove
Application Number	Continuity Type	Prior Application Number	Filing or 371(c) Date (YYYY-MM-DD)
16516232	Claims benefit of provisional	62750011	2018-10-24
Additional Domestic Benefit/National Stage Data may be generated within this form by selecting the Add button. Add			

Application Data Sheet 37 CFR 1.76		Attorney Docket Number	Syn2.0/ROAR CON
		Application Number	
Title of Invention	ASPIRATION THROMBECTOMY SYSTEM AND METHODS FOR THROMBUS REMOVAL WITH ASPIRATION CATHETER		

Foreign Priority Information:

This section allows for the applicant to claim priority to a foreign application. Providing this information in the application data sheet constitutes the claim for priority as required by 35 U.S.C. 119(b) and 37 CFR 1.55. When priority is claimed to a foreign application that is eligible for retrieval under the priority document exchange program (PDX)ⁱ the information will be used by the Office to automatically attempt retrieval pursuant to 37 CFR 1.55(i)(1) and (2). Under the PDX program, applicant bears the ultimate responsibility for ensuring that a copy of the foreign application is received by the Office from the participating foreign intellectual property office, or a certified copy of the foreign priority application is filed, within the time period specified in 37 CFR 1.55(g)(1).

Application Number	Country ⁱ	Filing Date (YYYY-MM-DD)	Access Code ⁱ (if applicable)	Remove

Additional Foreign Priority Data may be generated within this form by selecting the **Add** button.

Statement under 37 CFR 1.55 or 1.78 for AIA (First Inventor to File) Transition Applications

☐ This application (1) claims priority to or the benefit of an application filed before March 16, 2013 and (2) also contains, or contained at any time, a claim to a claimed invention that has an effective filing date on or after March 16, 2013.

NOTE: By providing this statement under 37 CFR 1.55 or 1.78, this application, with a filing date on or after March 16, 2013, will be examined under the first inventor to file provisions of the AIA.

Application Data Sheet 37 CFR 1.76		Attorney Docket Number	Syn2.0/ROAR CON
		Application Number	
Title of Invention	ASPIRATION THROMBECTOMY SYSTEM AND METHODS FOR THROMBUS REMOVAL WITH ASPIRATION CATHETER		

Authorization or Opt-Out of Authorization to Permit Access:

When this Application Data Sheet is properly signed and filed with the application, applicant has provided written authority to permit a participating foreign intellectual property (IP) office access to the instant application-as-filed (see paragraph A in subsection 1 below) and the European Patent Office (EPO) access to any search results from the instant application (see paragraph B in subsection 1 below).

Should applicant choose not to provide an authorization identified in subsection 1 below, applicant **must opt-out** of the authorization by checking the corresponding box A or B or both in subsection 2 below.

NOTE: This section of the Application Data Sheet is **ONLY** reviewed and processed with the **INITIAL** filing of an application. After the initial filing of an application, an Application Data Sheet cannot be used to provide or rescind authorization for access by a foreign IP office(s). Instead, Form PTO/SB/39 or PTO/SB/69 must be used as appropriate.

1. Authorization to Permit Access by a Foreign Intellectual Property Office(s)

A. Priority Document Exchange (PDX) - Unless box A in subsection 2 (opt-out of authorization) is checked, the undersigned hereby **grants the USPTO authority** to provide the European Patent Office (EPO), the Japan Patent Office (JPO), the Korean Intellectual Property Office (KIPO), the State Intellectual Property Office of the People's Republic of China (SIPO), the World Intellectual Property Organization (WIPO), and any other foreign intellectual property office participating with the USPTO in a bilateral or multilateral priority document exchange agreement in which a foreign application claiming priority to the instant patent application is filed, access to: (1) the instant patent application-as-filed and its related bibliographic data, (2) any foreign or domestic application to which priority or benefit is claimed by the instant application and its related bibliographic data, and (3) the date of filing of this Authorization. See 37 CFR 1.14(h)(1).

B. Search Results from U.S. Application to EPO - Unless box B in subsection 2 (opt-out of authorization) is checked, the undersigned hereby **grants the USPTO authority** to provide the EPO access to the bibliographic data and search results from the instant patent application when a European patent application claiming priority to the instant patent application is filed. See 37 CFR 1.14(h)(2).

The applicant is reminded that the EPO's Rule 141(1) EPC (European Patent Convention) requires applicants to submit a copy of search results from the instant application without delay in a European patent application that claims priority to the instant application.

2. Opt-Out of Authorizations to Permit Access by a Foreign Intellectual Property Office(s)

☐ A. Applicant **DOES NOT** authorize the USPTO to permit a participating foreign IP office access to the instant application-as-filed. If this box is checked, the USPTO will not be providing a participating foreign IP office with any documents and information identified in subsection 1A above.

☐ B. Applicant **DOES NOT** authorize the USPTO to transmit to the EPO any search results from the instant patent application. If this box is checked, the USPTO will not be providing the EPO with search results from the instant application.

NOTE: Once the application has published or is otherwise publicly available, the USPTO may provide access to the application in accordance with 37 CFR 1.14.

Application Data Sheet 37 CFR 1.76		Attorney Docket Number	Syn2.0/ROAR CON
		Application Number	
Title of Invention	ASPIRATION THROMBECTOMY SYSTEM AND METHODS FOR THROMBUS REMOVAL WITH ASPIRATION CATHETER		

Applicant Information:

Providing assignment information in this section does not substitute for compliance with any requirement of part 3 of Title 37 of CFR to have an assignment recorded by the Office.			
Applicant	1		<input type="button" value="Remove"/>
<p>If the applicant is the inventor (or the remaining joint inventor or inventors under 37 CFR 1.45), this section should not be completed. The information to be provided in this section is the name and address of the legal representative who is the applicant under 37 CFR 1.43; or the name and address of the assignee, person to whom the inventor is under an obligation to assign the invention, or person who otherwise shows sufficient proprietary interest in the matter who is the applicant under 37 CFR 1.46. If the applicant is an applicant under 37 CFR 1.46 (assignee, person to whom the inventor is obligated to assign, or person who otherwise shows sufficient proprietary interest) together with one or more joint inventors, then the joint inventor or inventors who are also the applicant should be identified in this section.</p>			
		<input type="button" value="Clear"/>	
☒ Assignee	Legal Representative under 35 U.S.C. 117		Joint Inventor
Person to whom the inventor is obligated to assign.		Person who shows sufficient proprietary interest	
If applicant is the legal representative, indicate the authority to file the patent application, the inventor is:			
<div style="border: 1px solid black; height: 20px; width: 100%;"></div>			
Name of the Deceased or Legally Incapacitated Inventor: <div style="border: 1px solid black; height: 20px; width: 100%;"></div>			
If the Applicant is an Organization check here. ☒			
Organization Name	Syntheon 2.0, LLC		
Mailing Address Information For Applicant:			
Address 1	13755 S.W. 119 Avenue		
Address 2			
City	Miami	State/Province	FL
Country	US	Postal Code	33186
Phone Number	954-991-5420	Fax Number	844-670-6009
Email Address	mhpatents@dickinsonwright.com		
Additional Applicant Data may be generated within this form by selecting the Add button.			<input type="button" value="Add"/>

Assignee Information including Non-Applicant Assignee Information:

Providing assignment information in this section does not substitute for compliance with any requirement of part 3 of Title 37 of CFR to have an assignment recorded by the Office.

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Application Data Sheet 37 CFR 1.76		Attorney Docket Number	Syn2.0/ROAR CON
		Application Number	
Title of Invention	ASPIRATION THROMBECTOMY SYSTEM AND METHODS FOR THROMBUS REMOVAL WITH ASPIRATION CATHETER		

Assignee 1			
Complete this section if assignee information, including non-applicant assignee information, is desired to be included on the patent application publication. An assignee-applicant identified in the "Applicant Information" section will appear on the patent application publication as an applicant. For an assignee-applicant, complete this section only if identification as an assignee is also desired on the patent application publication.			
Remove			
If the Assignee or Non-Applicant Assignee is an Organization check here. ☒			
Organization Name	Syntheon 2.0, LLC		
Mailing Address Information For Assignee including Non-Applicant Assignee:			
Address 1	13755 SW 119 Avenue		
Address 2			
City	Miami	State/Province	FL
Country i	US	Postal Code	33186
Phone Number	954-991-5420	Fax Number	844-670-6009
Email Address	mhpatents@dickinsonwright.com		
Additional Assignee or Non-Applicant Assignee Data may be generated within this form by selecting the Add button. Add			

Signature:[Remove](#)

NOTE: This Application Data Sheet must be signed in accordance with 37 CFR 1.33(b). However, if this Application Data Sheet is submitted with the INITIAL filing of the application and either box A or B is not checked in subsection 2 of the "Authorization or Opt-Out of Authorization to Permit Access" section, then this form must also be signed in accordance with 37 CFR 1.14(c).

This Application Data Sheet **must** be signed by a patent practitioner if one or more of the applicants is a **juristic entity** (e.g., corporation or association). If the applicant is two or more joint inventors, this form must be signed by a patent practitioner, **all** joint inventors who are the applicant, or one or more joint inventor-applicants who have been given power of attorney (e.g., see USPTO Form PTO/AIA/81) on behalf of **all** joint inventor-applicants.

See 37 CFR 1.4(d) for the manner of making signatures and certifications.

Signature	/gregory I. mayback/		Date (YYYY-MM-DD)	2019-11-12
First Name	Gregory L.	Last Name	Mayback	Registration Number
				40719
Additional Signature may be generated within this form by selecting the Add button. Add				

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Application Data Sheet 37 CFR 1.76		Attorney Docket Number	Syn2.0/ROAR CON
		Application Number	
Title of Invention	ASPIRATION THROMBECTOMY SYSTEM AND METHODS FOR THROMBUS REMOVAL WITH ASPIRATION CATHETER		

This collection of information is required by 37 CFR 1.76. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 23 minutes to complete, including gathering, preparing, and submitting the completed application data sheet form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

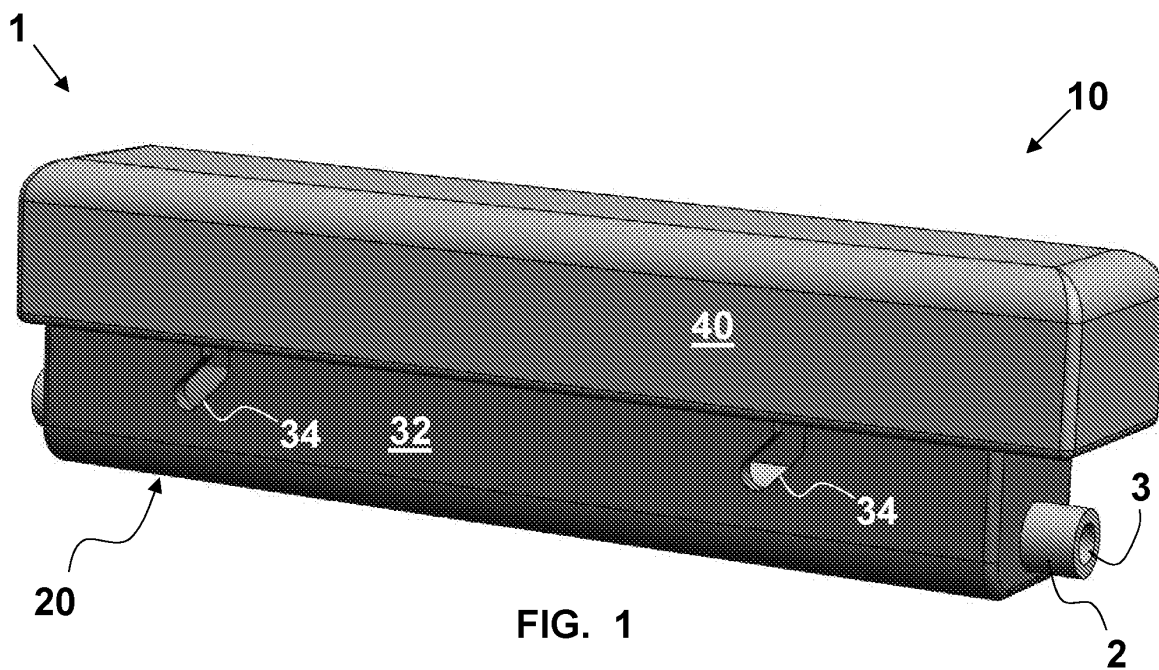
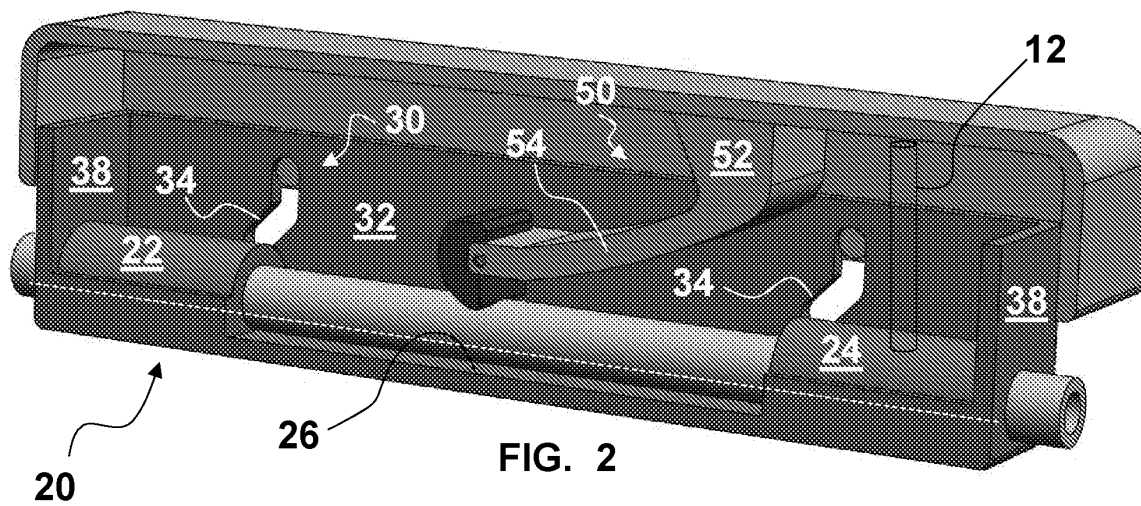
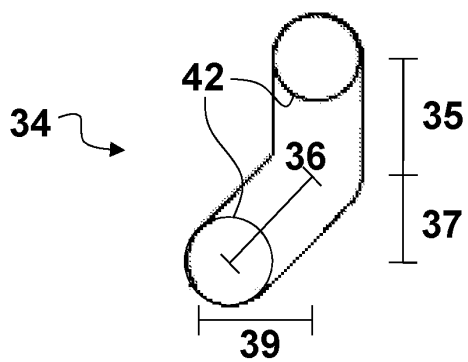
Privacy Act Statement

The Privacy Act of 1974 (P.L. 93-579) requires that you be given certain information in connection with your submission of the attached form related to a patent application or patent. Accordingly, pursuant to the requirements of the Act, please be advised that: (1) the general authority for the collection of this information is 35 U.S.C. 2(b)(2); (2) furnishing of the information solicited is voluntary; and (3) the principal purpose for which the information is used by the U.S. Patent and Trademark Office is to process and/or examine your submission related to a patent application or patent. If you do not furnish the requested information, the U.S. Patent and Trademark Office may not be able to process and/or examine your submission, which may result in termination of proceedings or abandonment of the application or expiration of the patent.

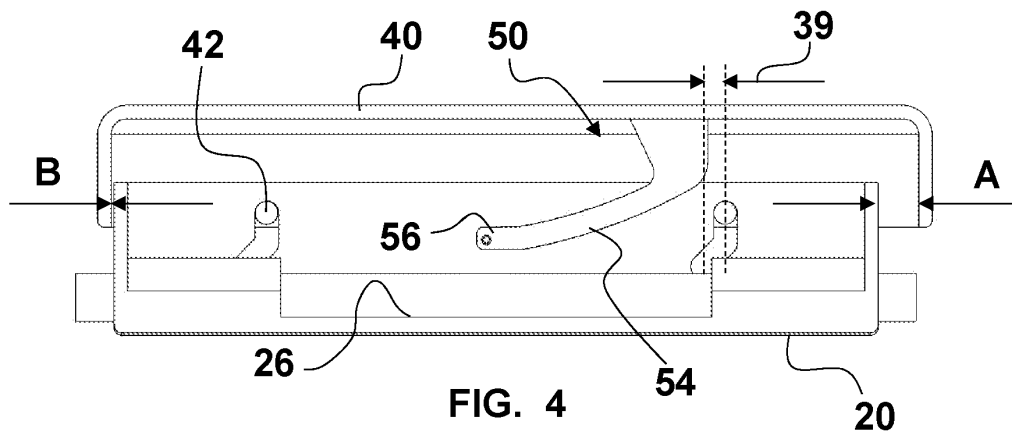
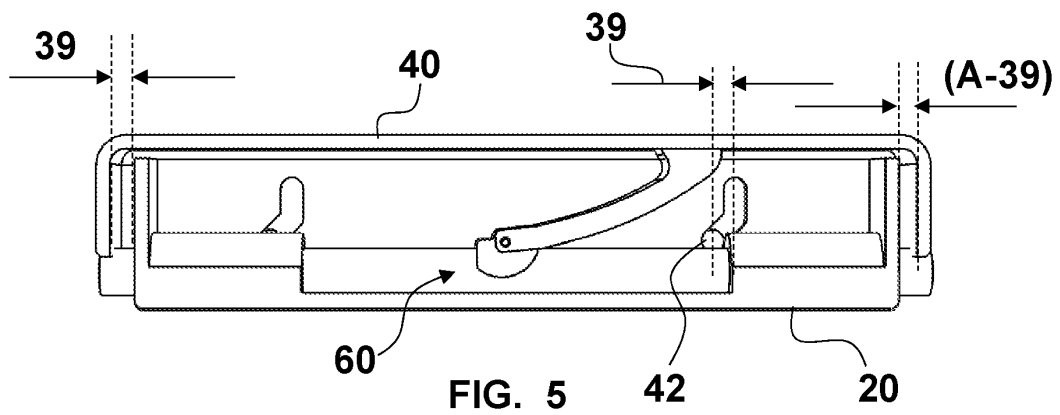
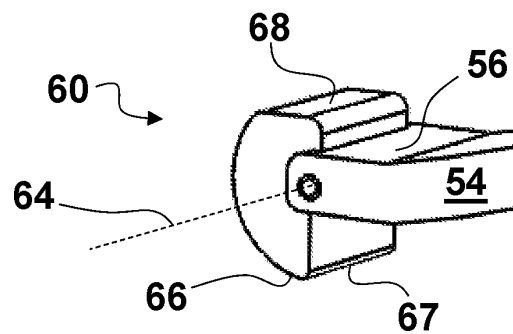
The information provided by you in this form will be subject to the following routine uses:

1. The information on this form will be treated confidentially to the extent allowed under the Freedom of Information Act (5 U.S.C. 552) and the Privacy Act (5 U.S.C. 552a). Records from this system of records may be disclosed to the Department of Justice to determine whether the Freedom of Information Act requires disclosure of these records.
2. A record from this system of records may be disclosed, as a routine use, in the course of presenting evidence to a court, magistrate, or administrative tribunal, including disclosures to opposing counsel in the course of settlement negotiations.
3. A record in this system of records may be disclosed, as a routine use, to a Member of Congress submitting a request involving an individual, to whom the record pertains, when the individual has requested assistance from the Member with respect to the subject matter of the record.
4. A record in this system of records may be disclosed, as a routine use, to a contractor of the Agency having need for the information in order to perform a contract. Recipients of information shall be required to comply with the requirements of the Privacy Act of 1974, as amended, pursuant to 5 U.S.C. 552a(m).
5. A record related to an International Application filed under the Patent Cooperation Treaty in this system of records may be disclosed, as a routine use, to the International Bureau of the World Intellectual Property Organization, pursuant to the Patent Cooperation Treaty.
6. A record in this system of records may be disclosed, as a routine use, to another federal agency for purposes of National Security review (35 U.S.C. 181) and for review pursuant to the Atomic Energy Act (42 U.S.C. 218(c)).
7. A record from this system of records may be disclosed, as a routine use, to the Administrator, General Services, or his/her designee, during an inspection of records conducted by GSA as part of that agency's responsibility to recommend improvements in records management practices and programs, under authority of 44 U.S.C. 2904 and 2906. Such disclosure shall be made in accordance with the GSA regulations governing inspection of records for this purpose, and any other relevant (i.e., GSA or Commerce) directive. Such disclosure shall not be used to make determinations about individuals.
8. A record from this system of records may be disclosed, as a routine use, to the public after either publication of the application pursuant to 35 U.S.C. 122(b) or issuance of a patent pursuant to 35 U.S.C. 151. Further, a record may be disclosed, subject to the limitations of 37 CFR 1.14, as a routine use, to the public if the record was filed in an application which became abandoned or in which the proceedings were terminated and which application is referenced by either a published application, an application open to public inspections or an issued patent.
9. A record from this system of records may be disclosed, as a routine use, to a Federal, State, or local law enforcement agency, if the USPTO becomes aware of a violation or potential violation of law or regulation.

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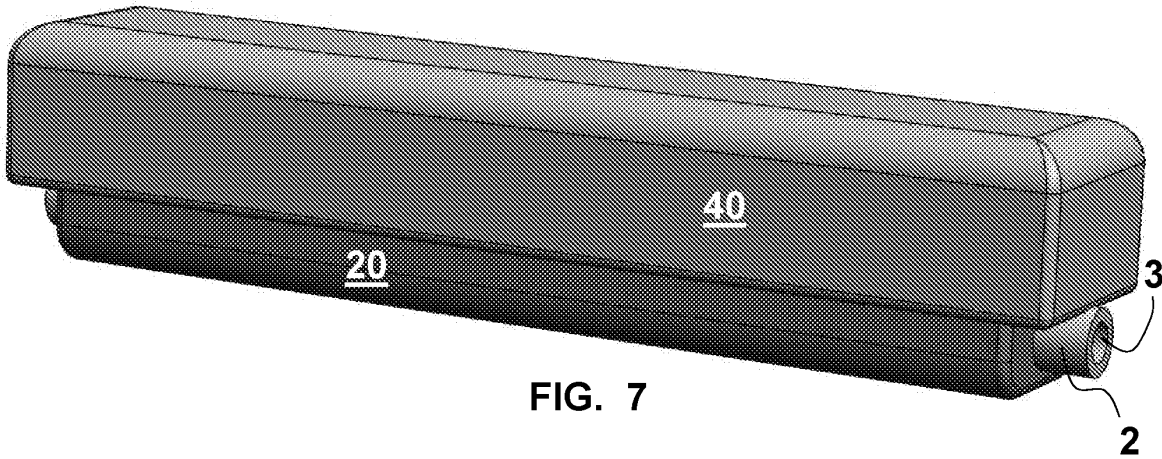
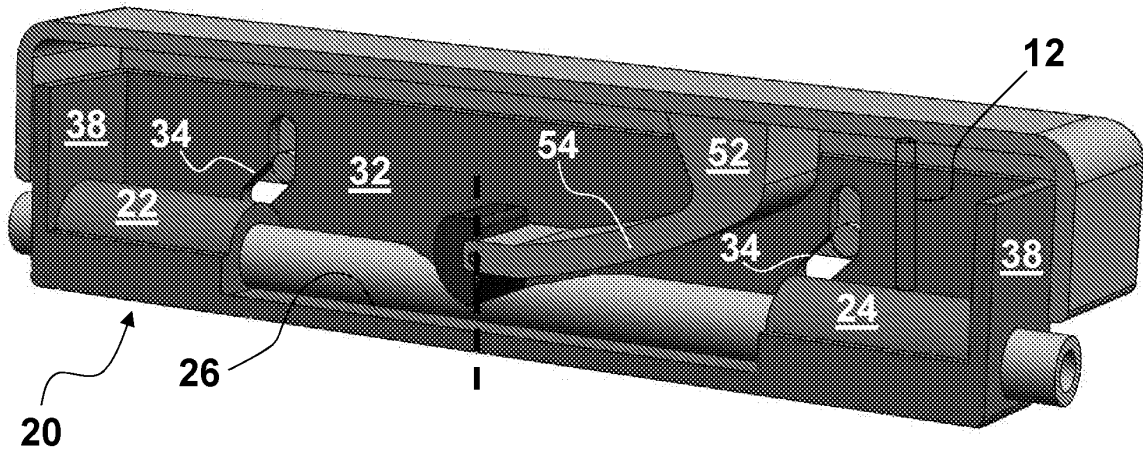
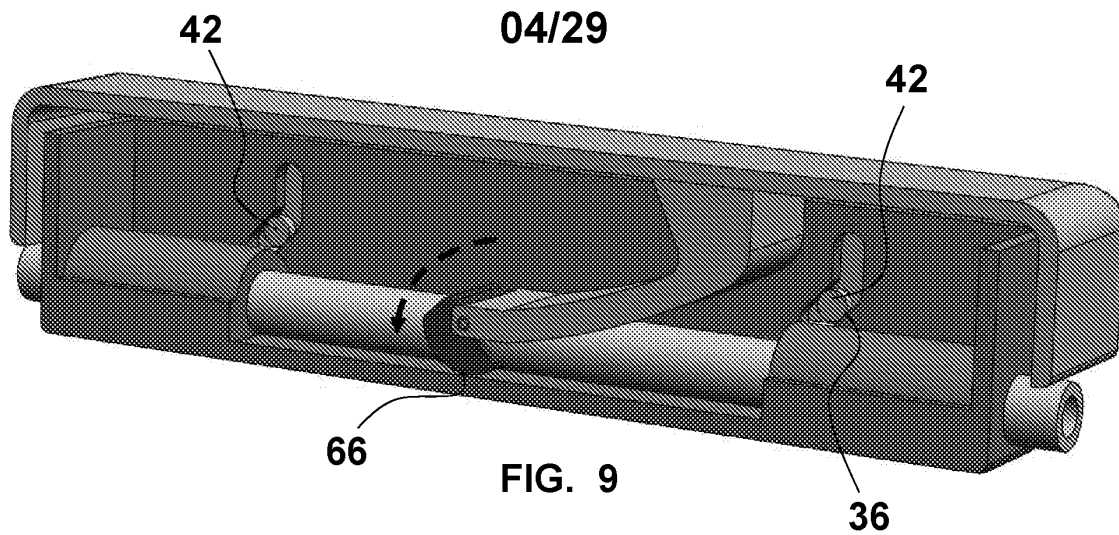
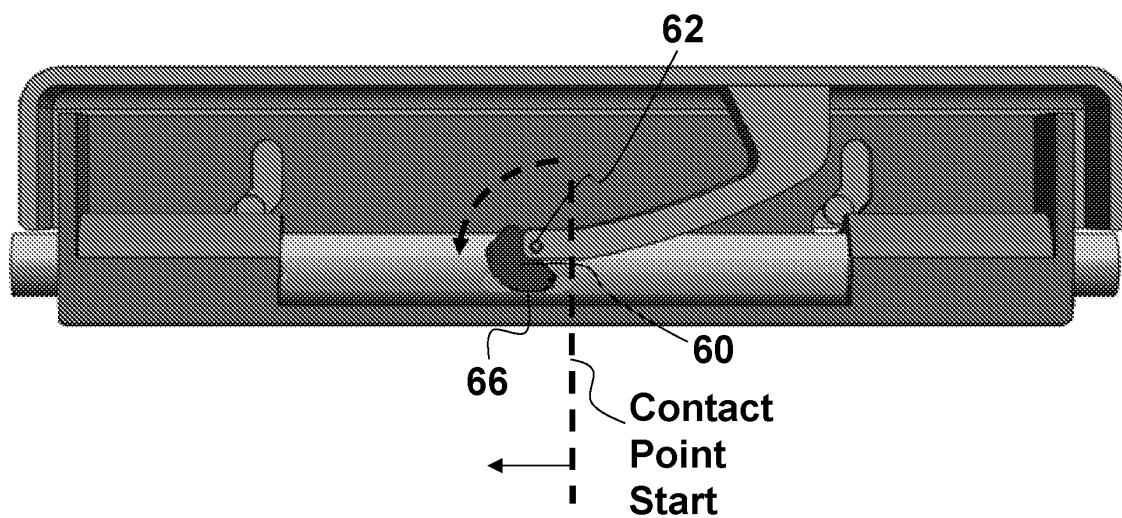
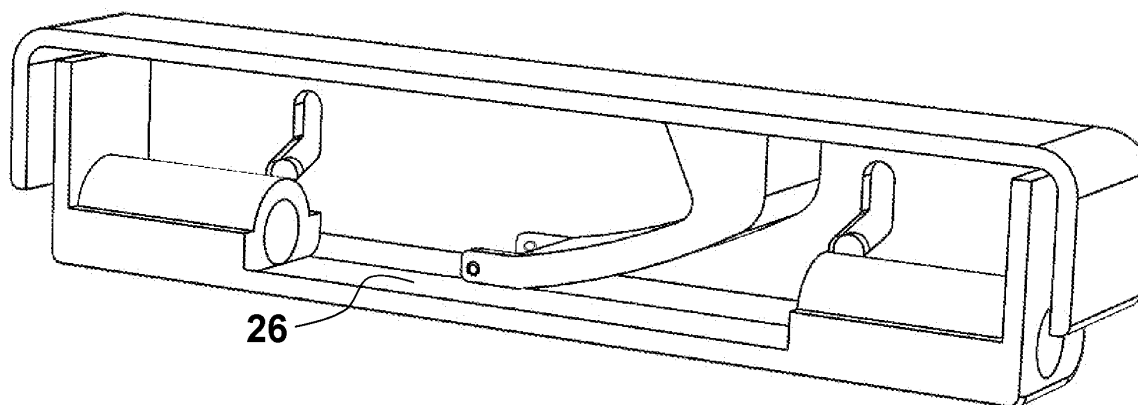
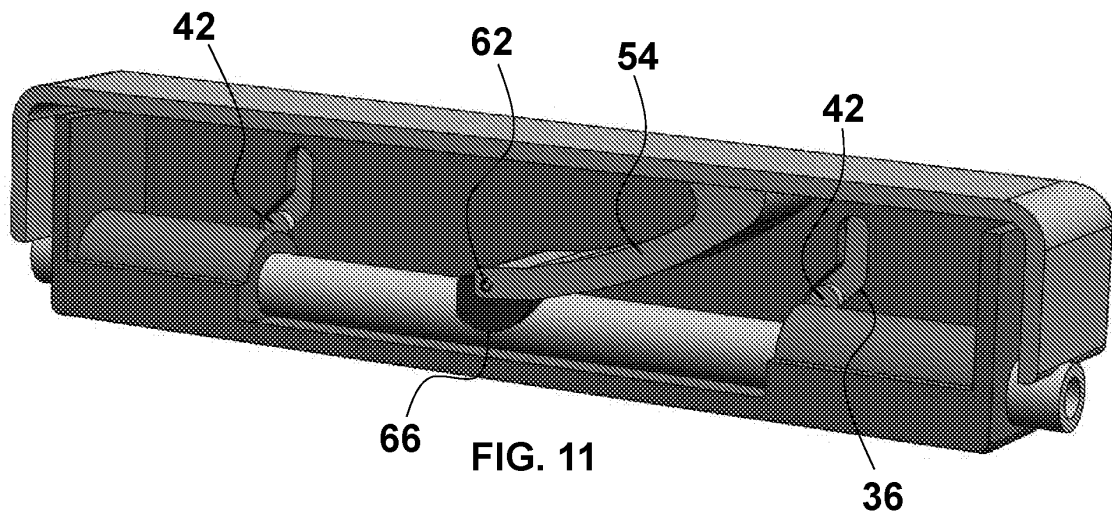
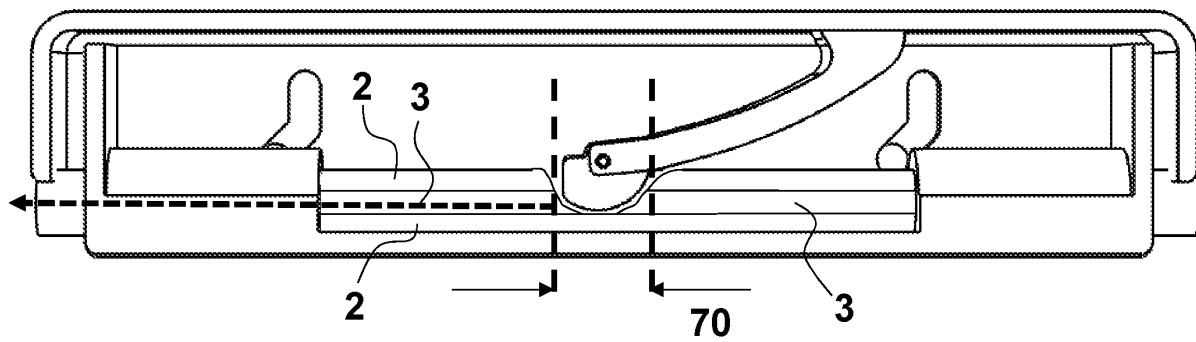
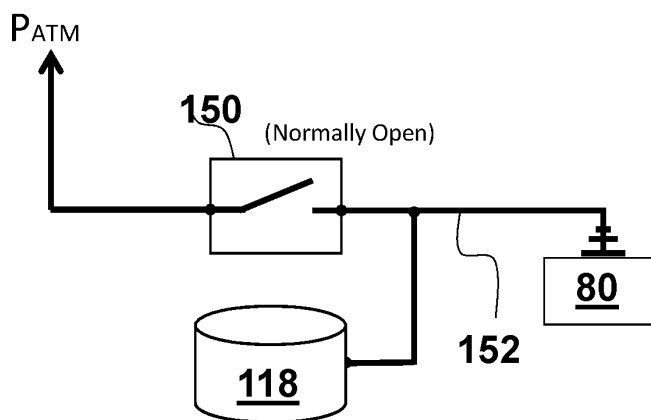
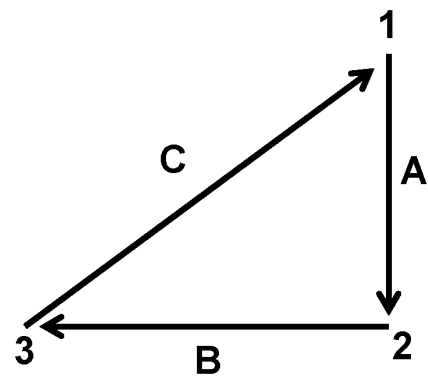


FIG. 8

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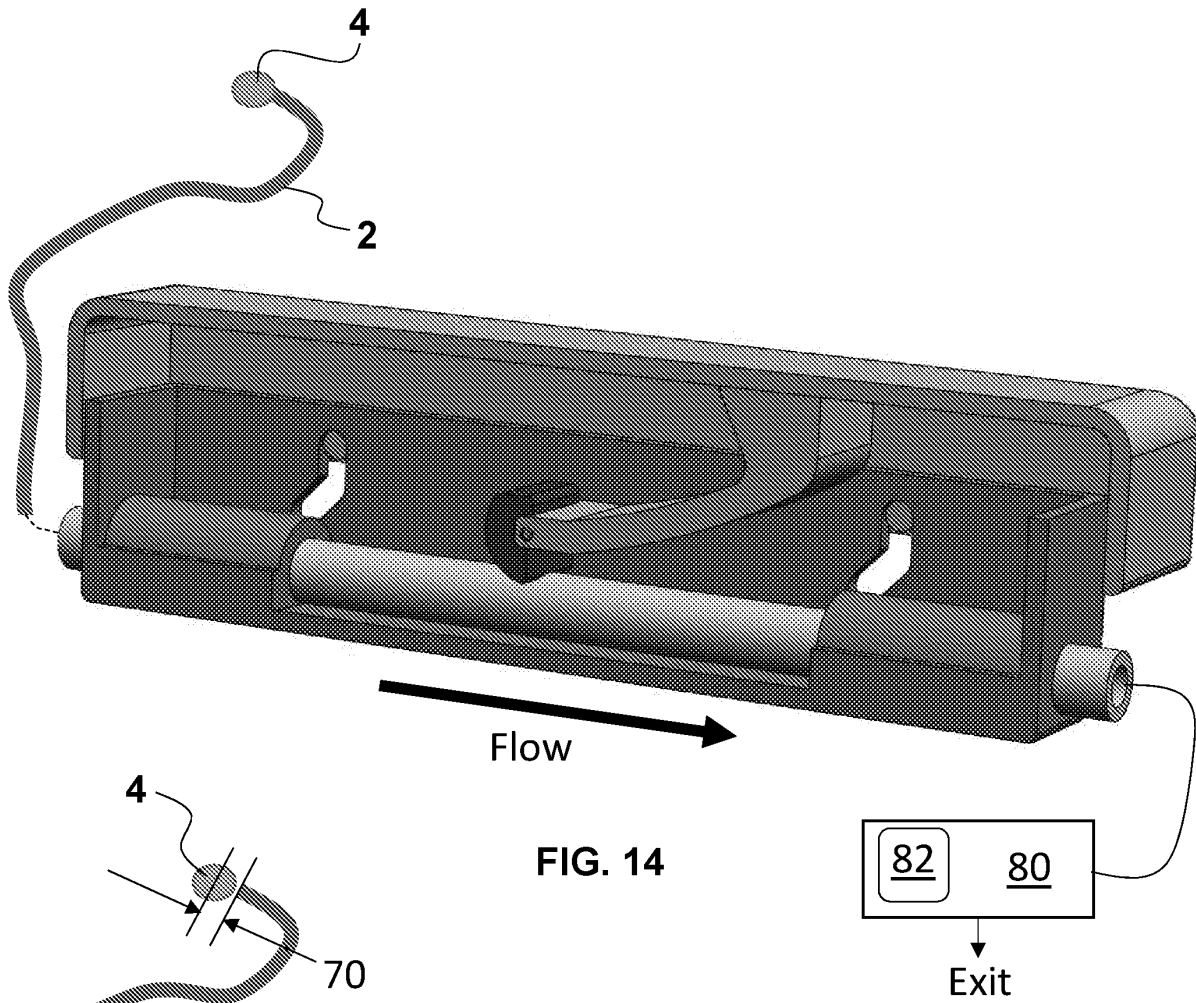
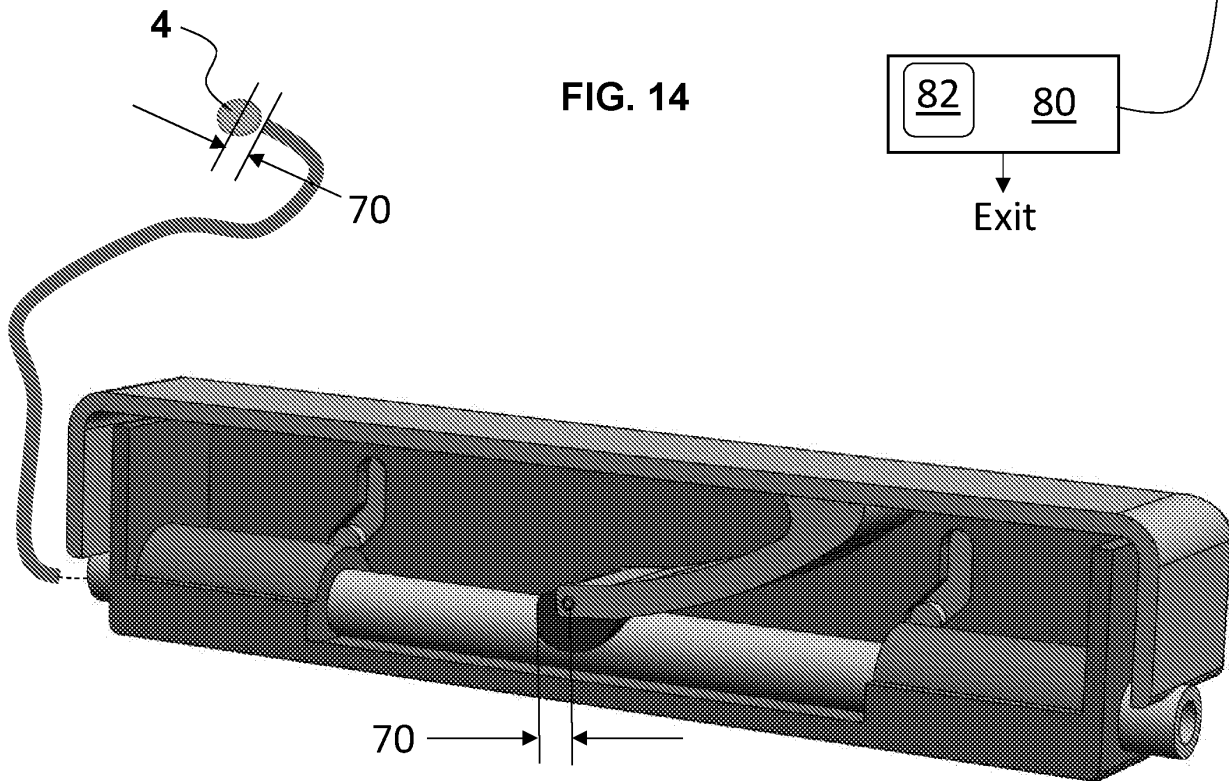
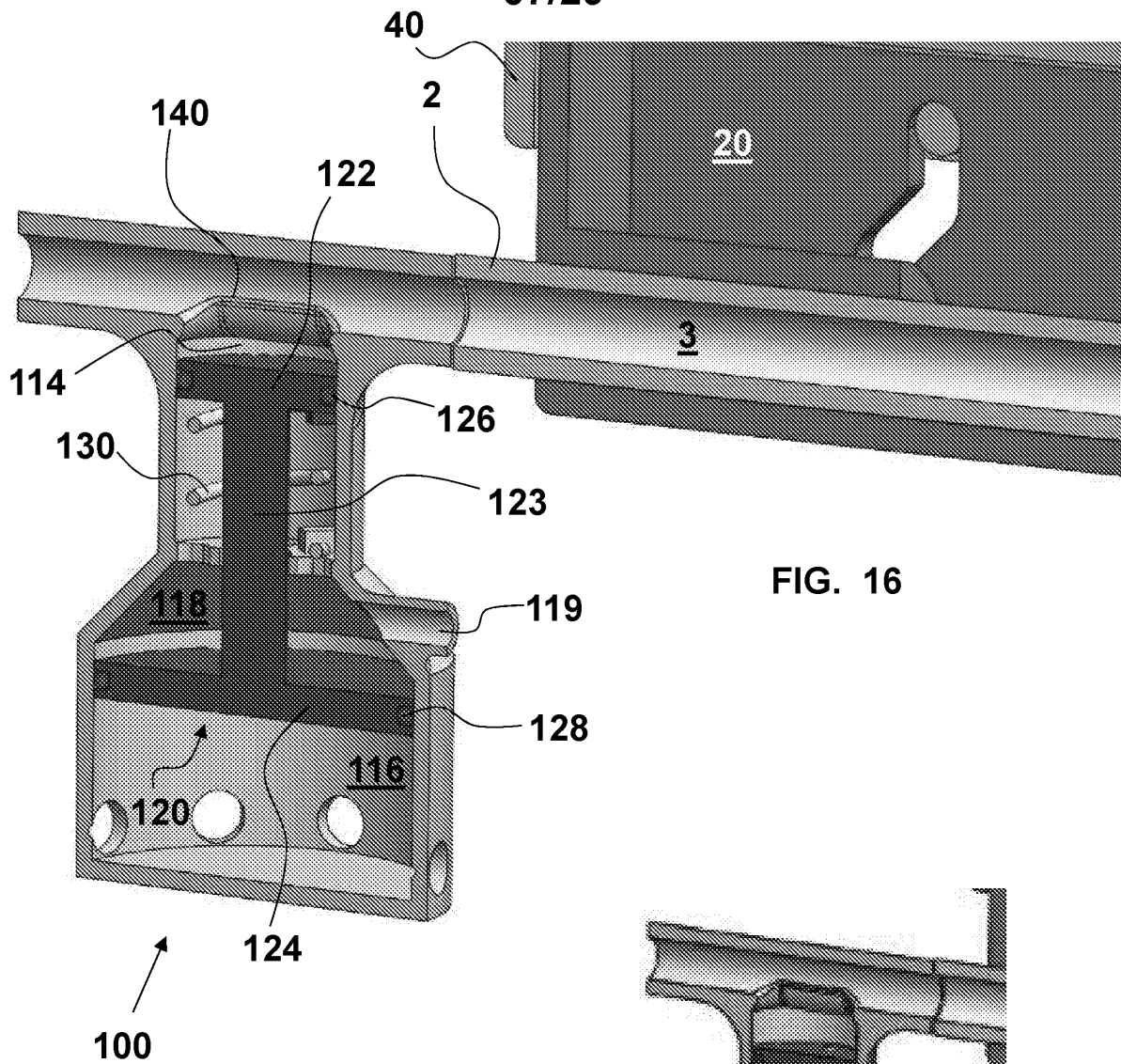
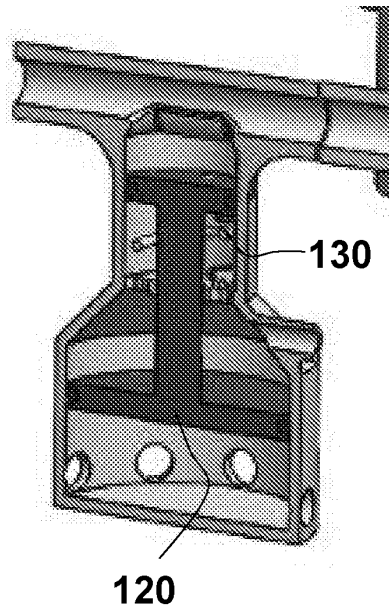
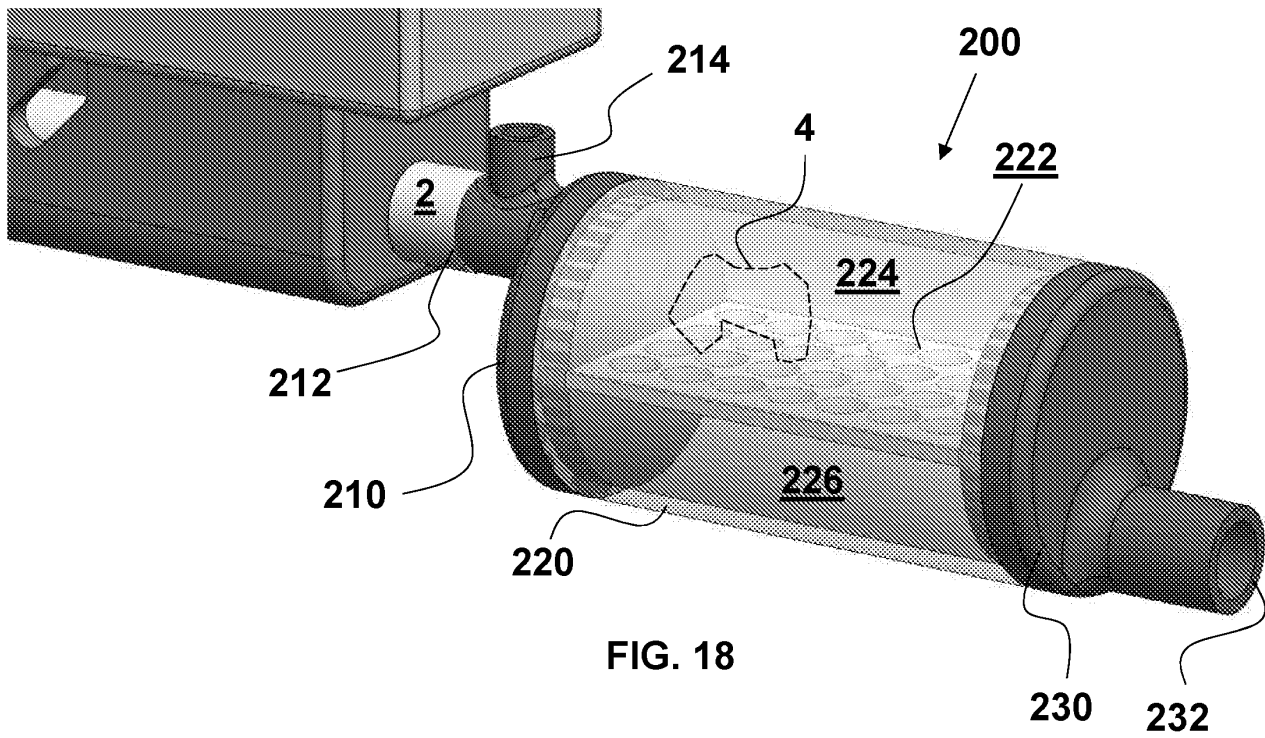
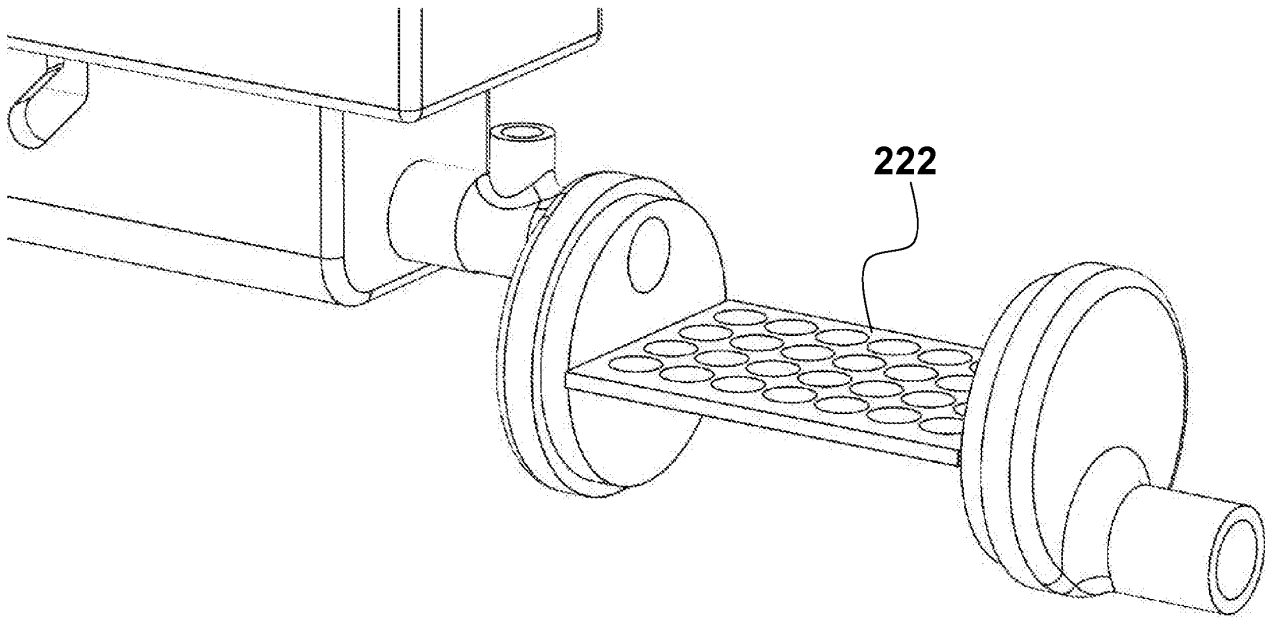


FIG. 15

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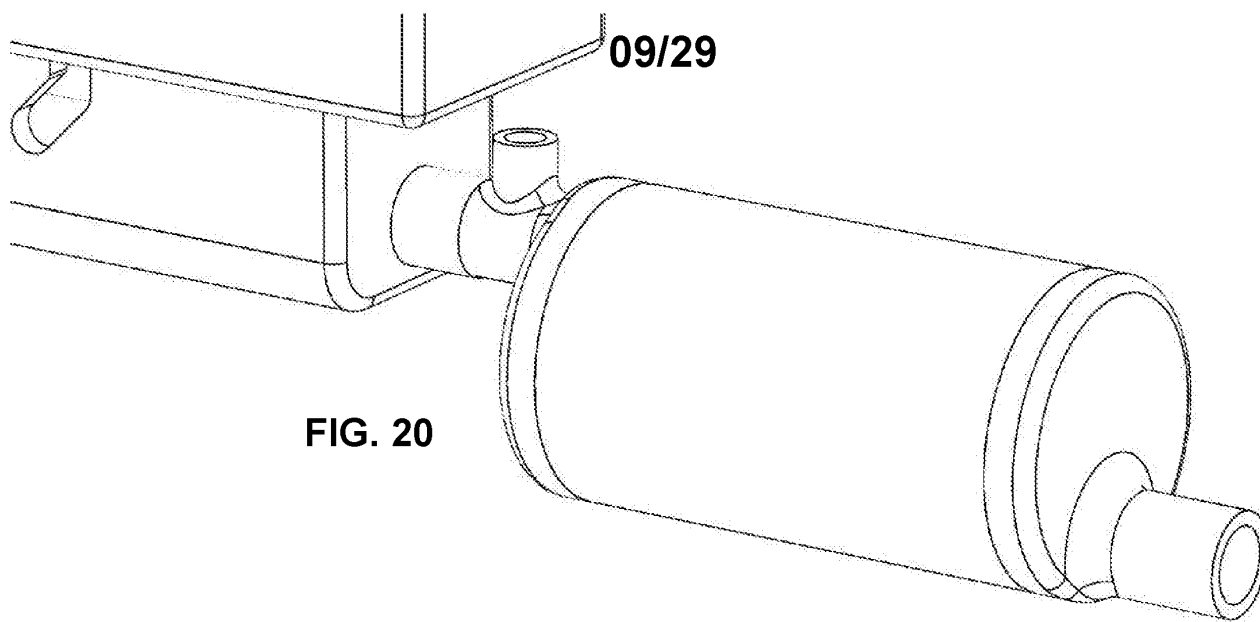


FIG. 20

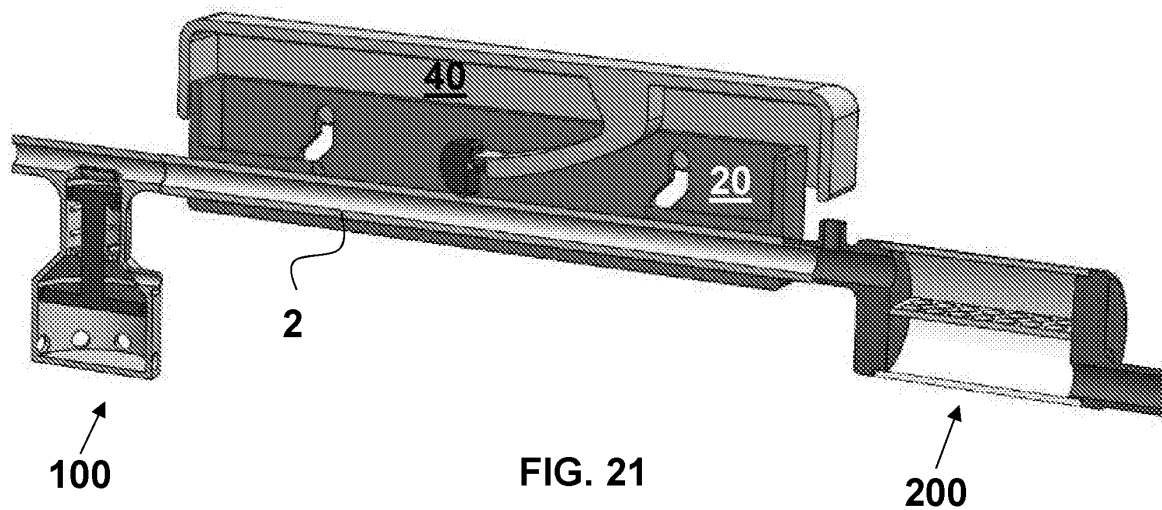


FIG. 21

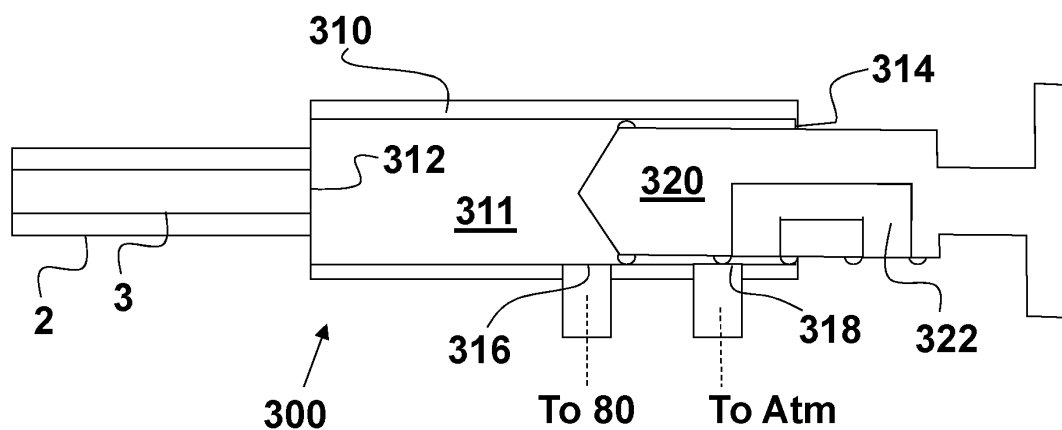
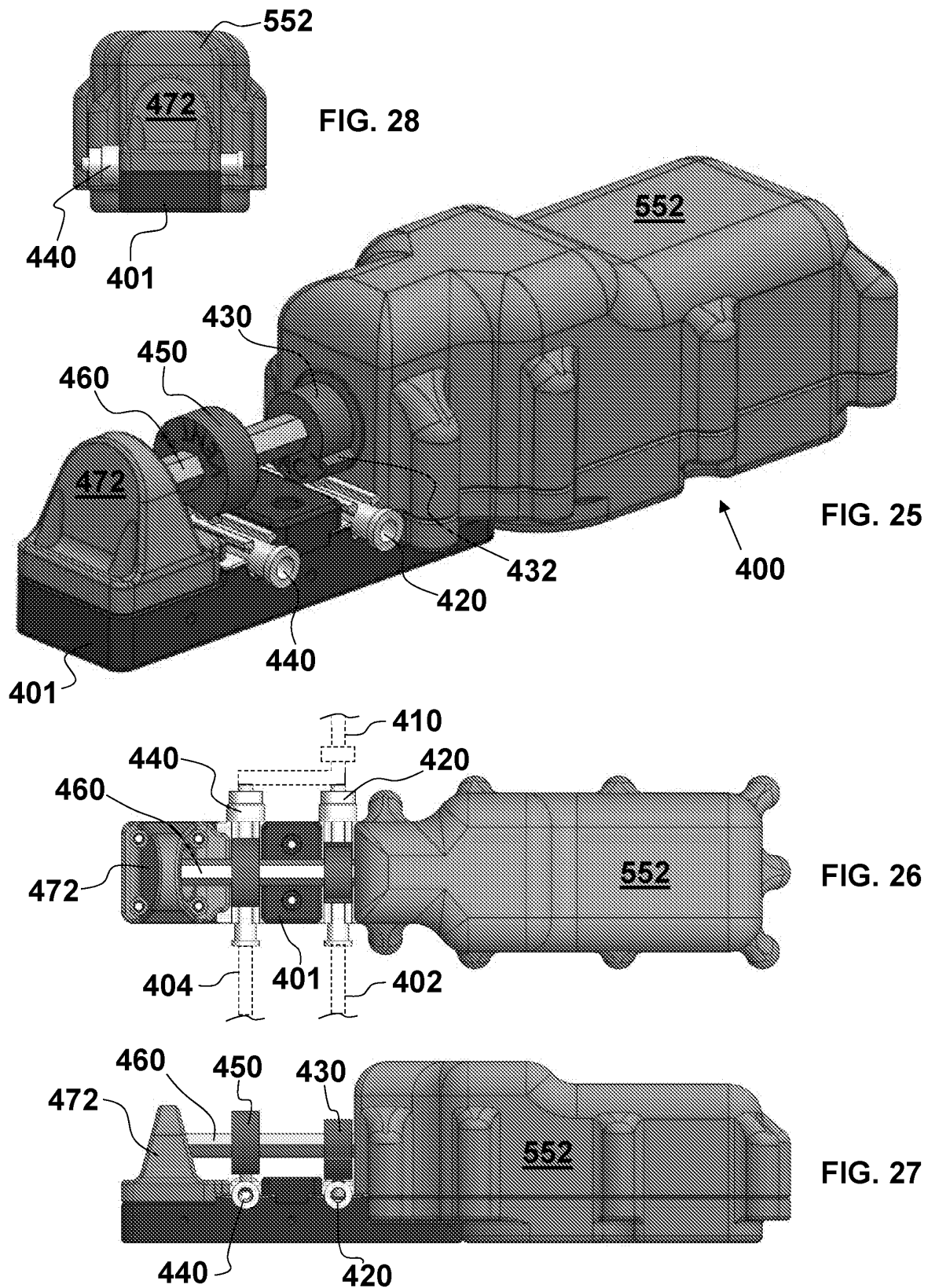


FIG. 22



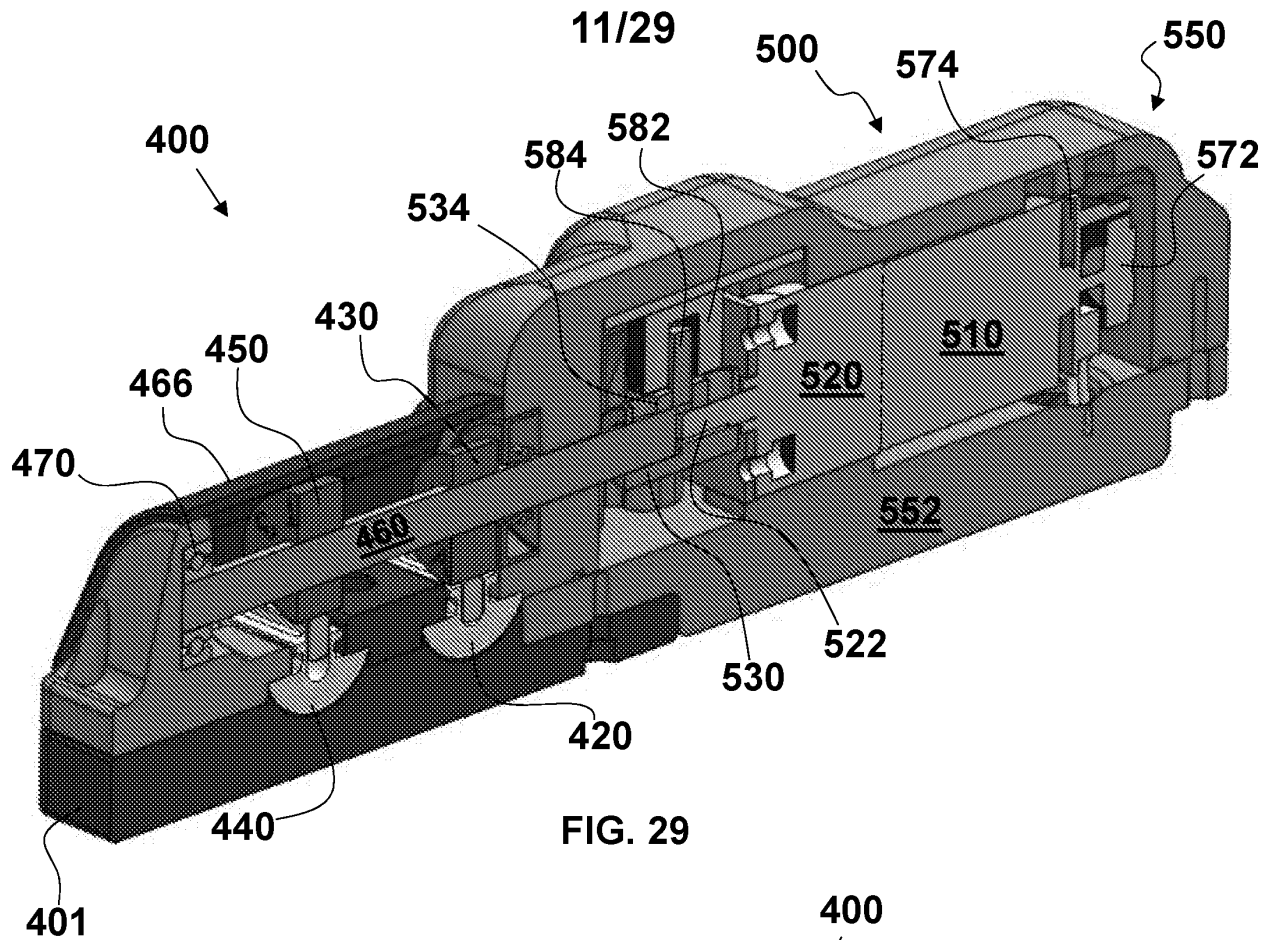


FIG. 29

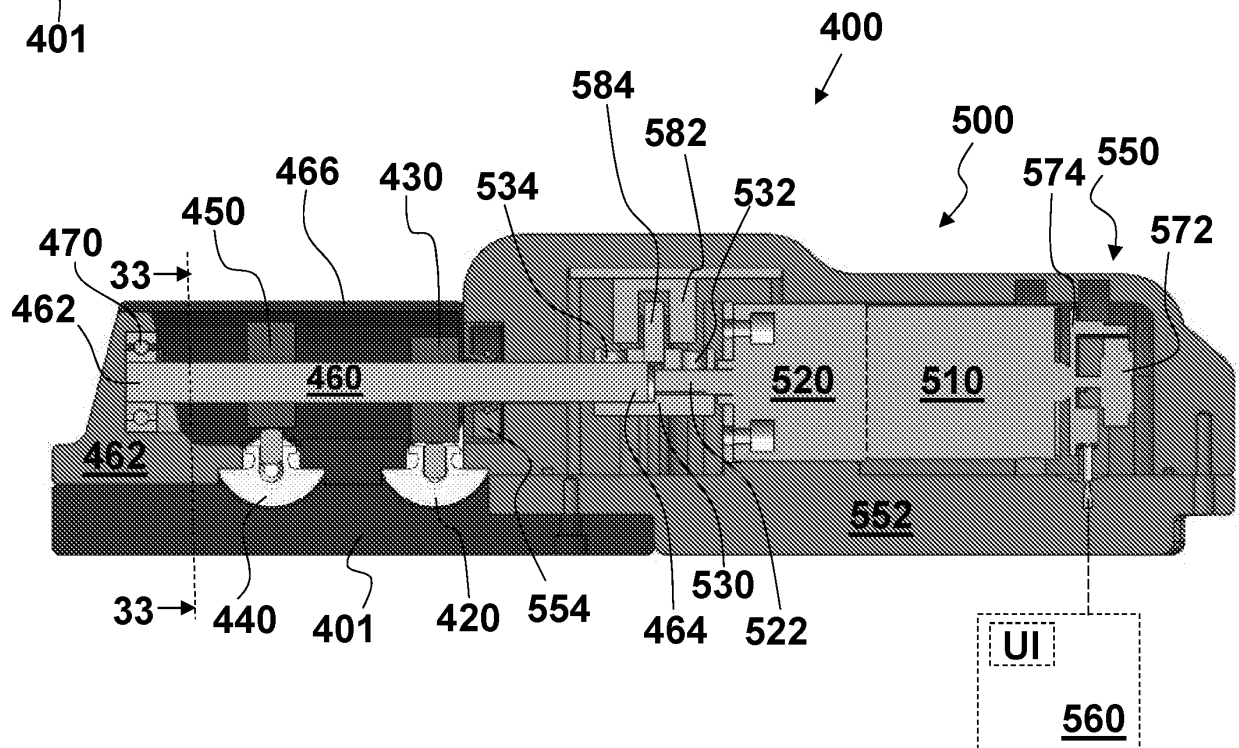
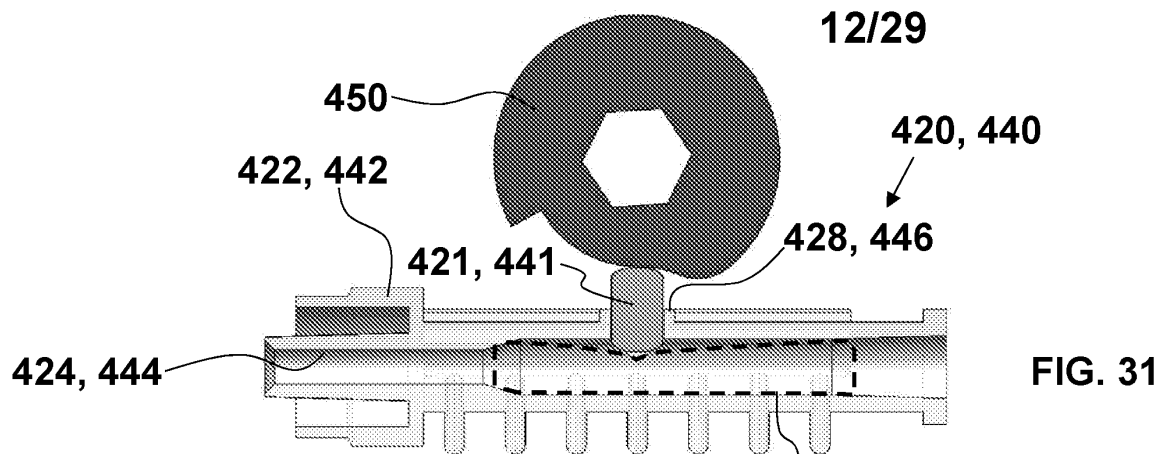
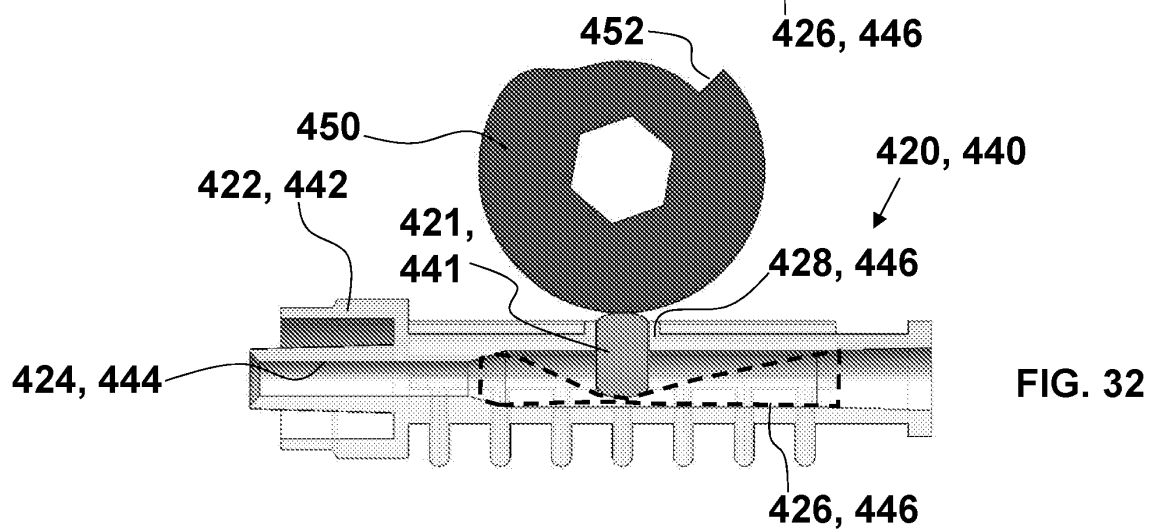
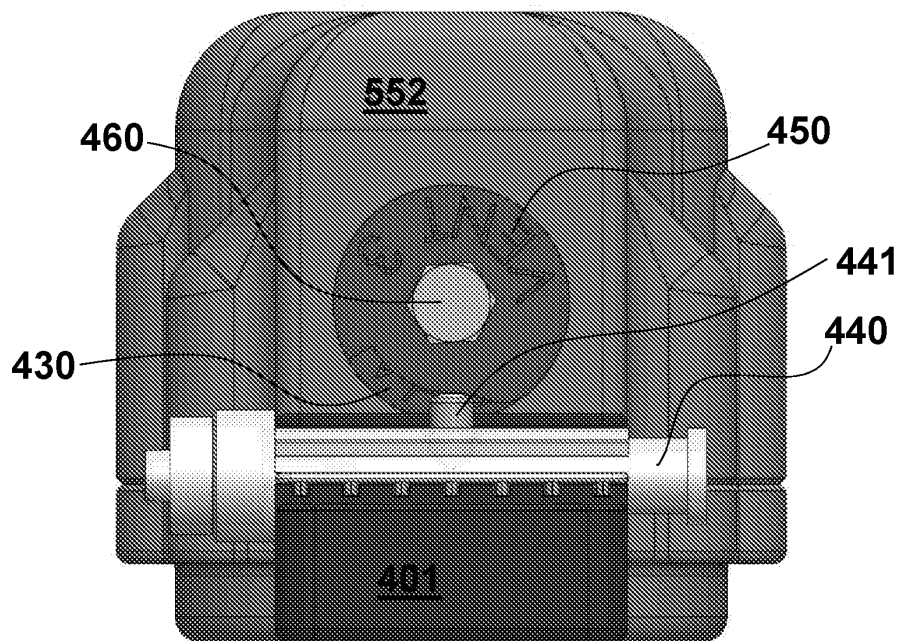
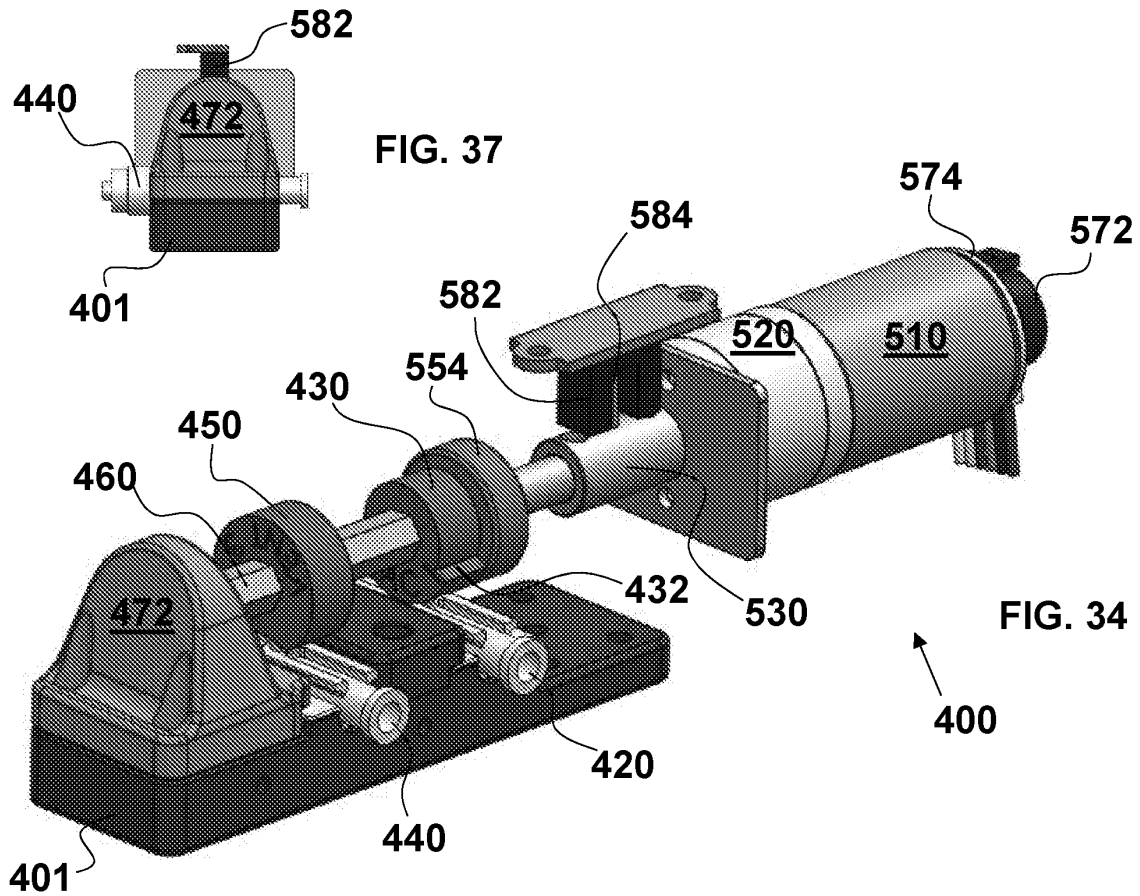
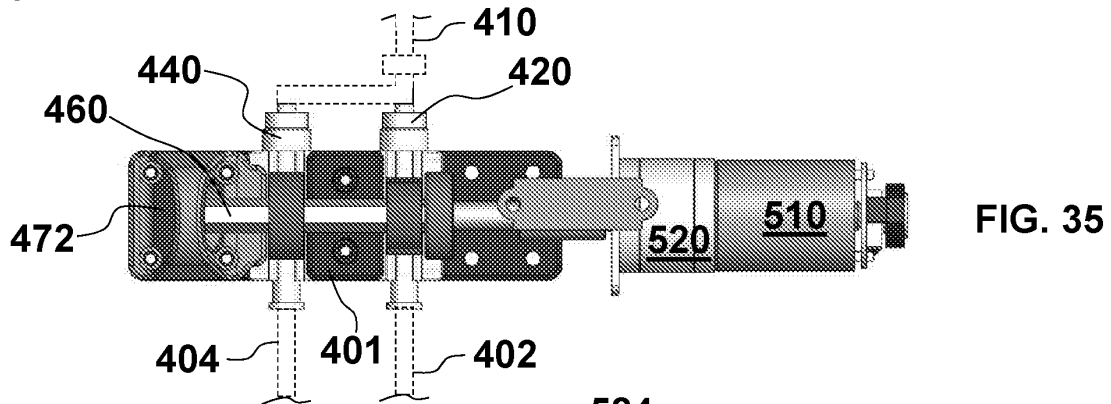
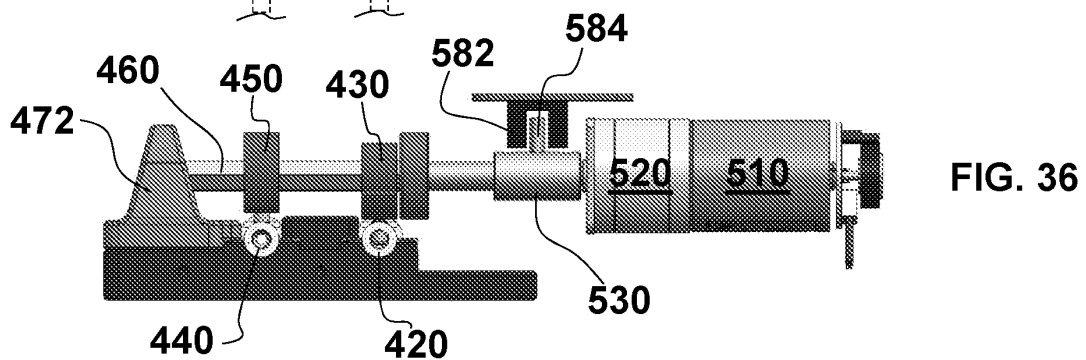
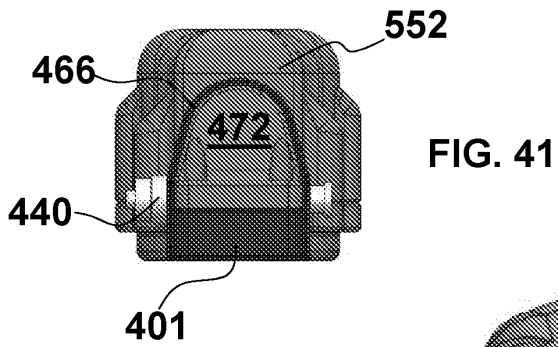
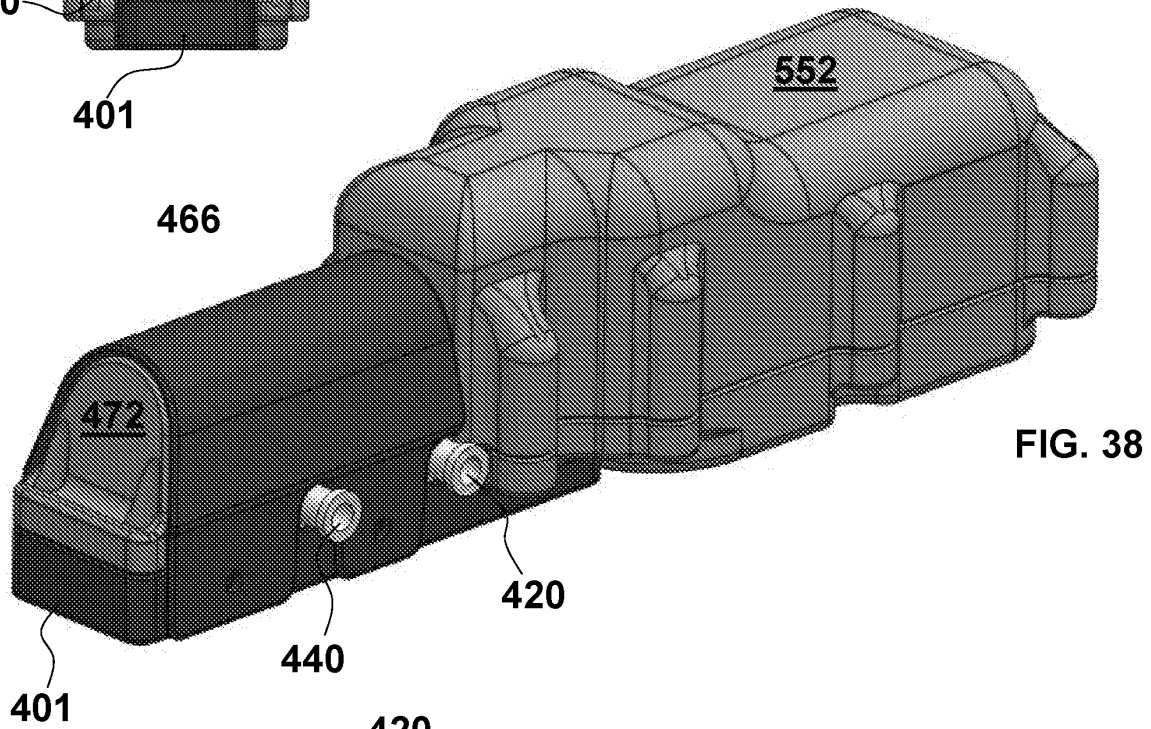
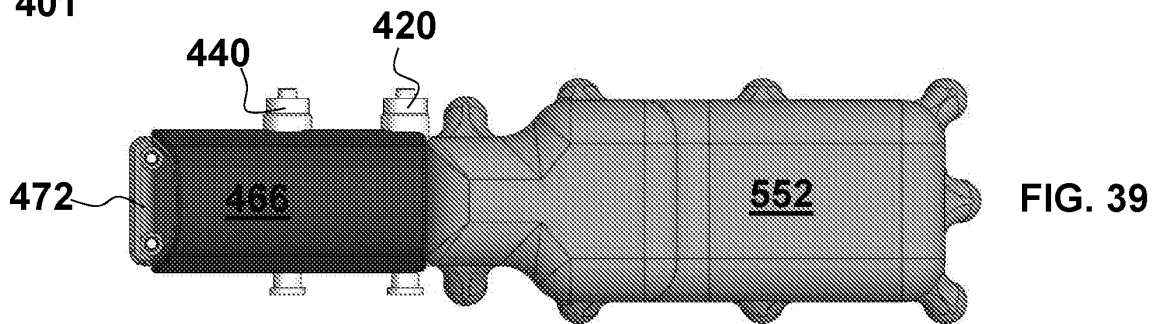
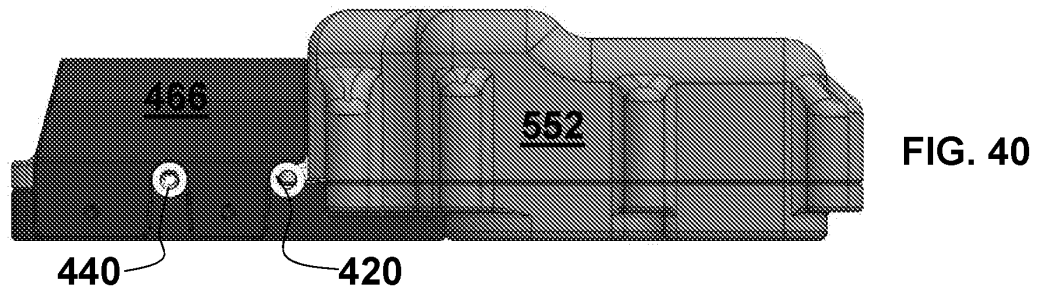


FIG. 30







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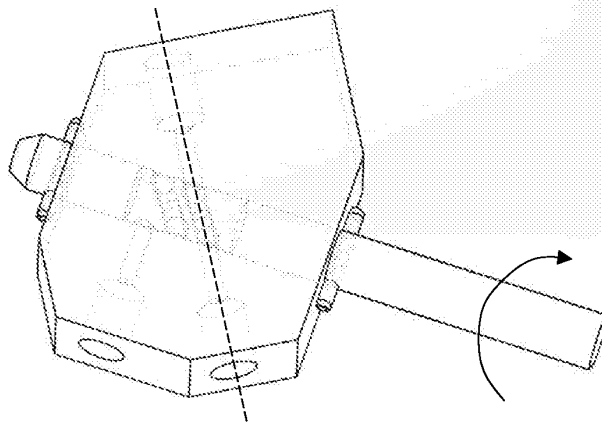


FIG. 42

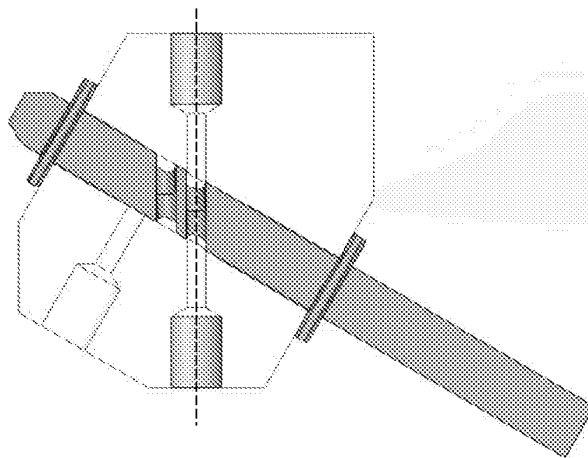


FIG. 43

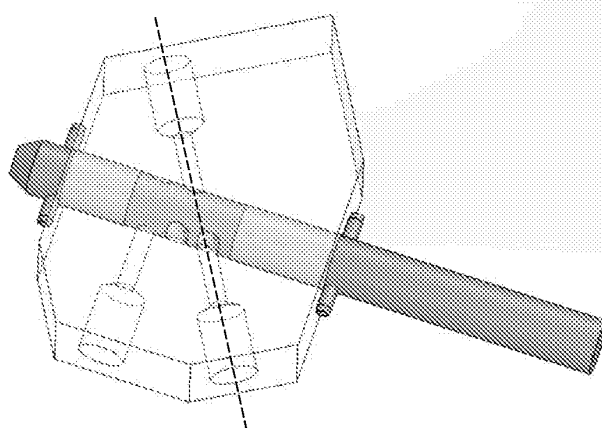


FIG. 44

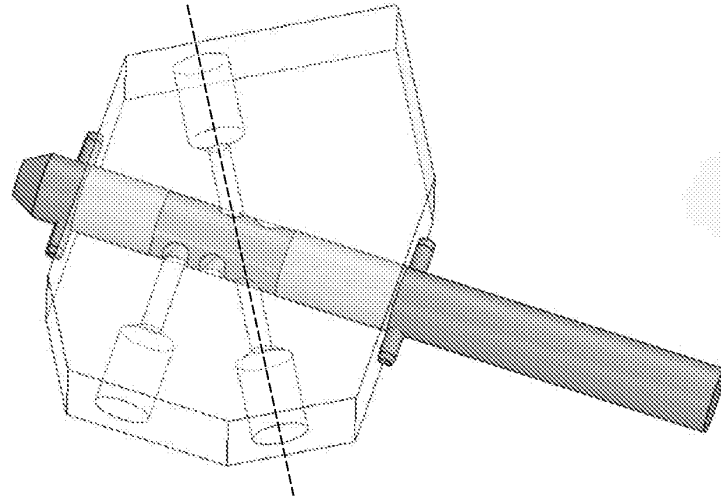


FIG. 45

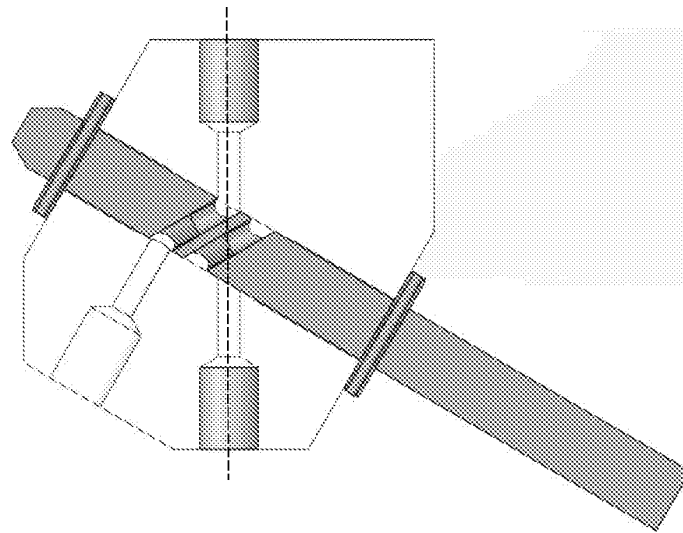


FIG. 46

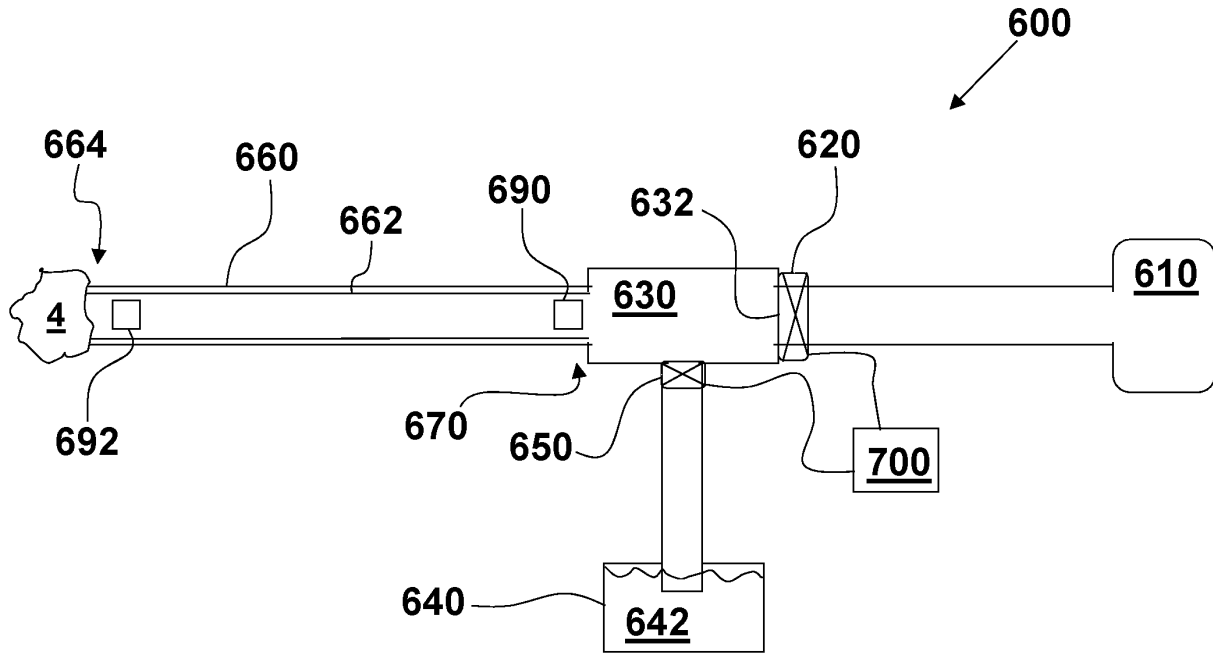


FIG. 47

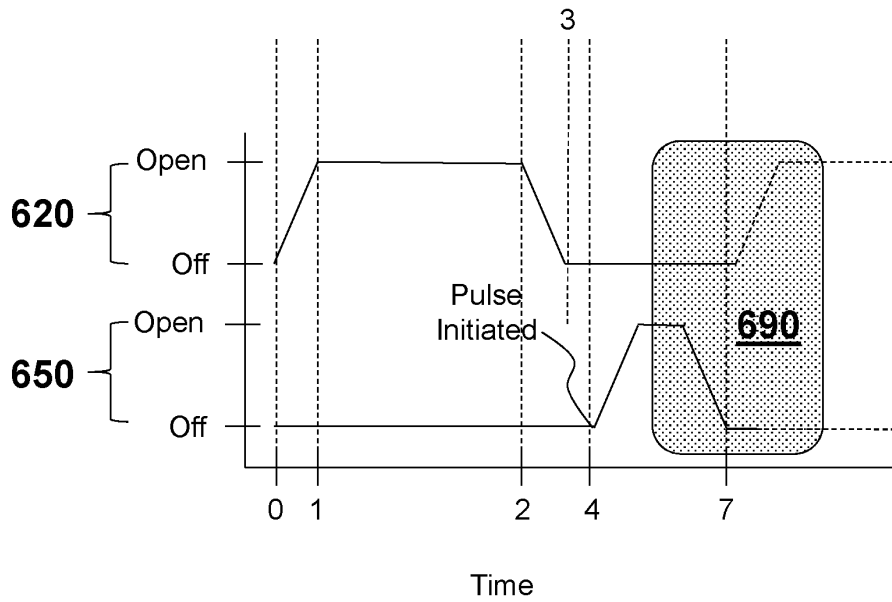
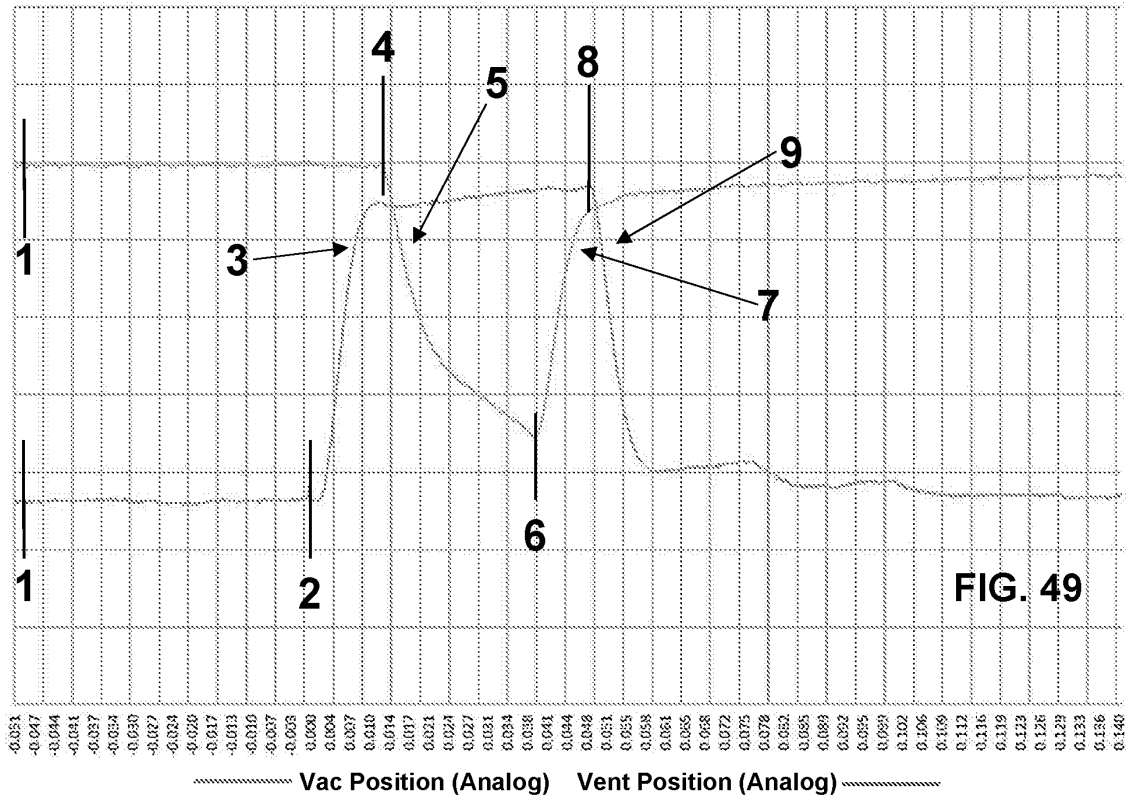
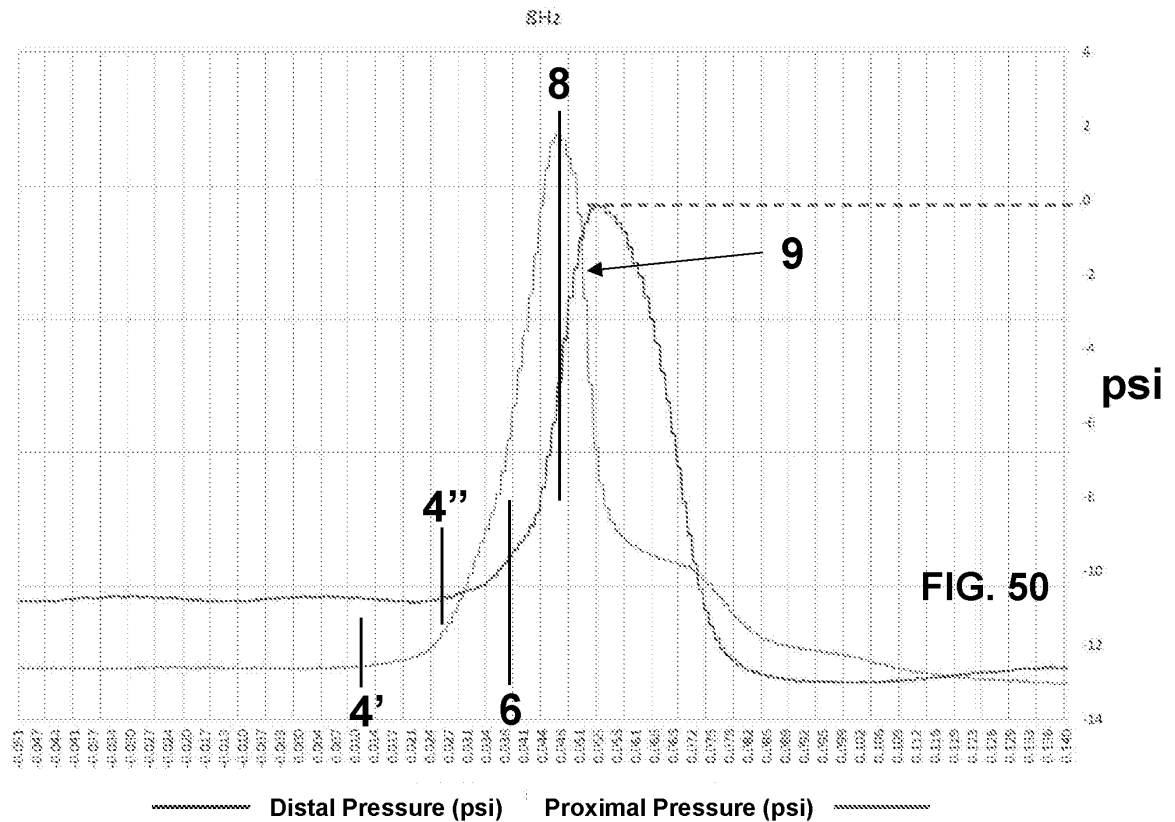


FIG. 48

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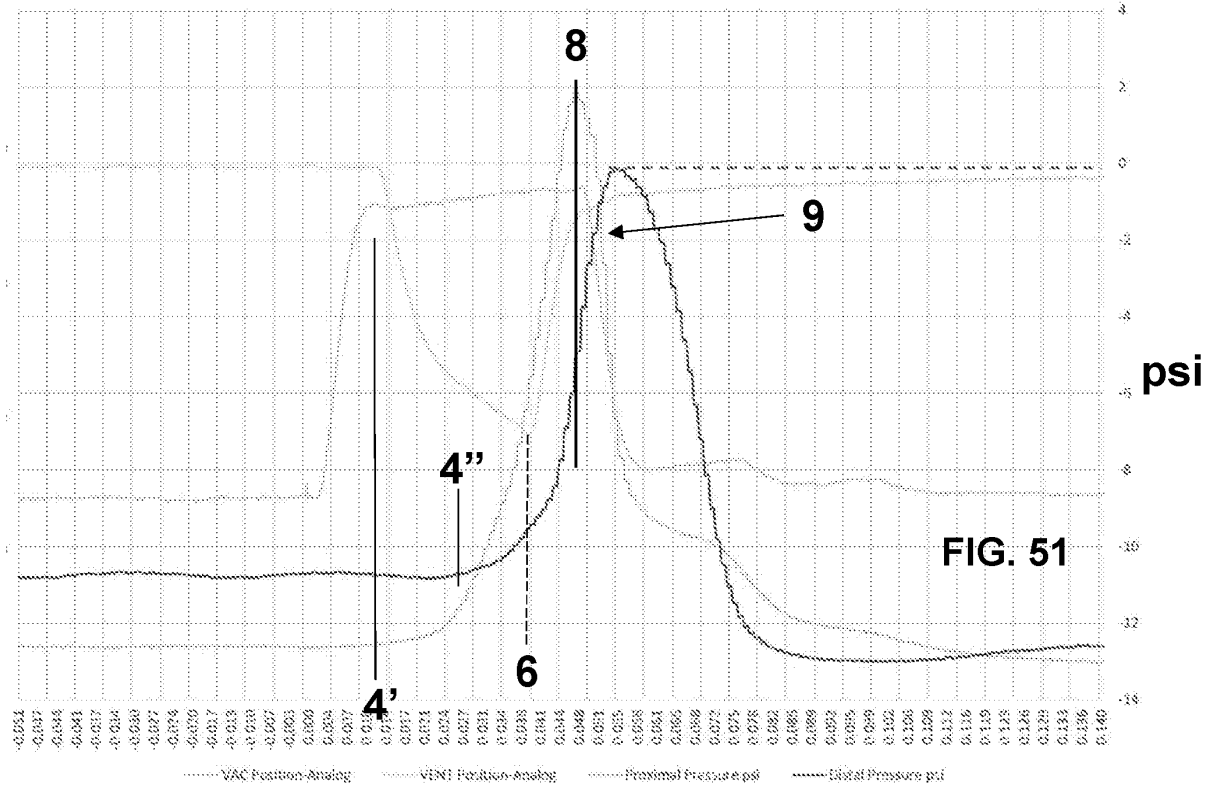
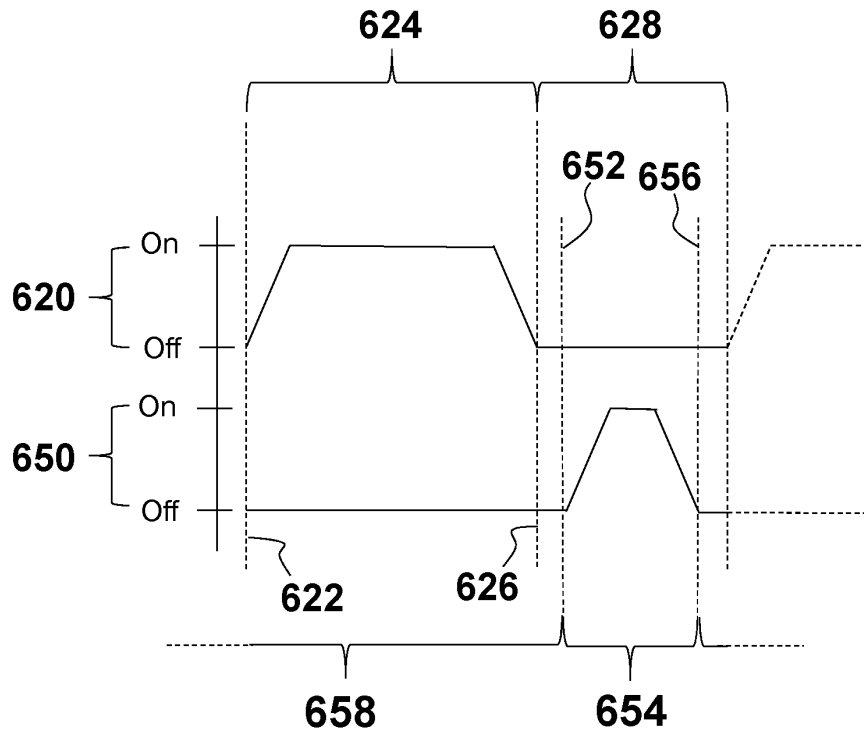


FIG. 52

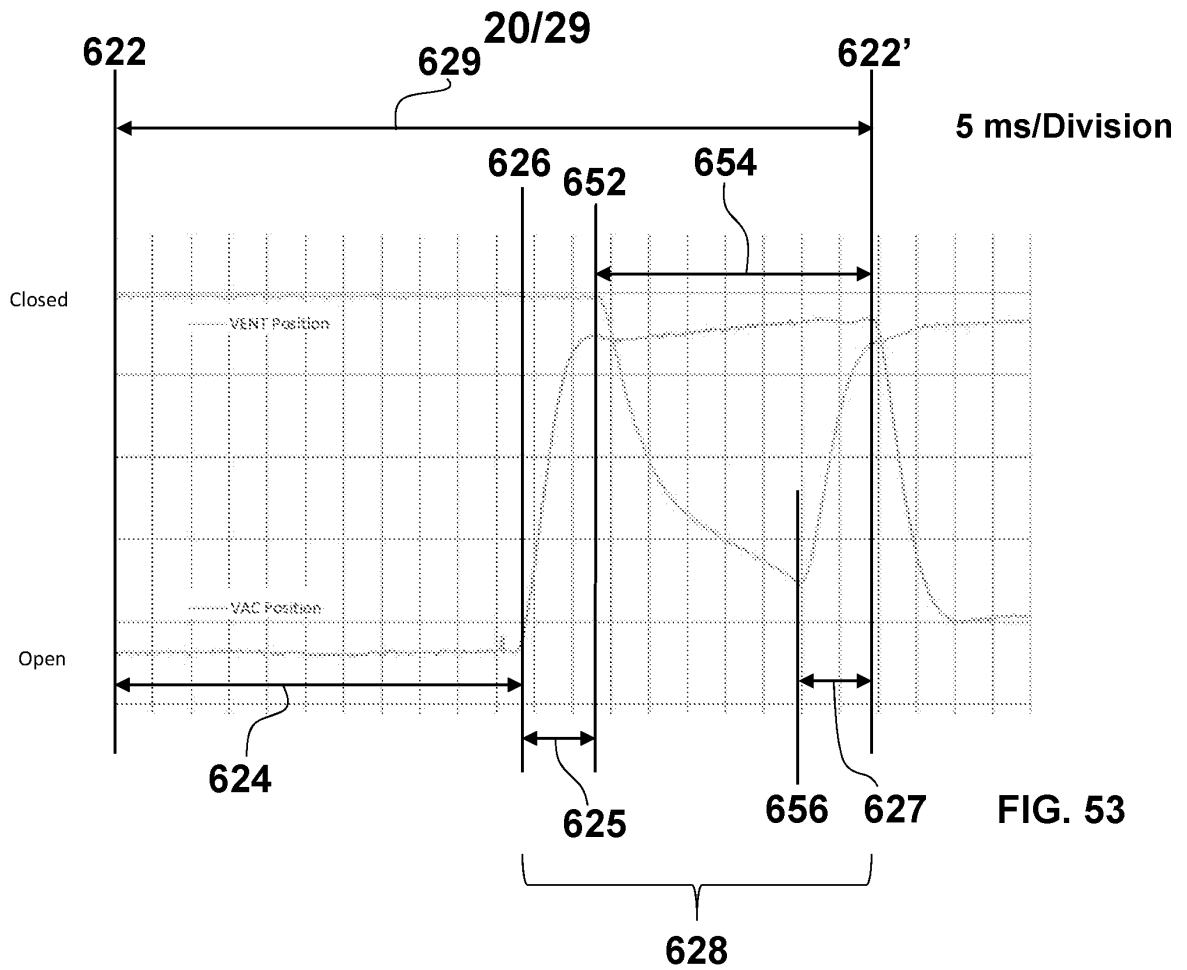
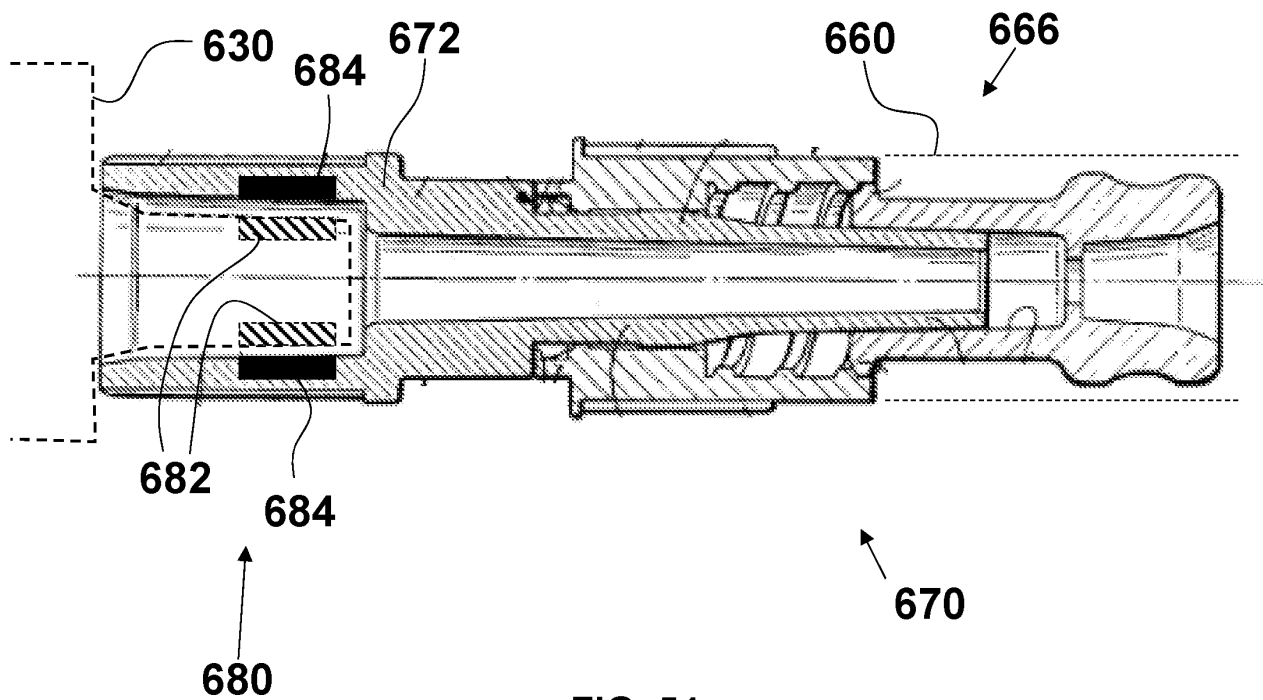


FIG. 54

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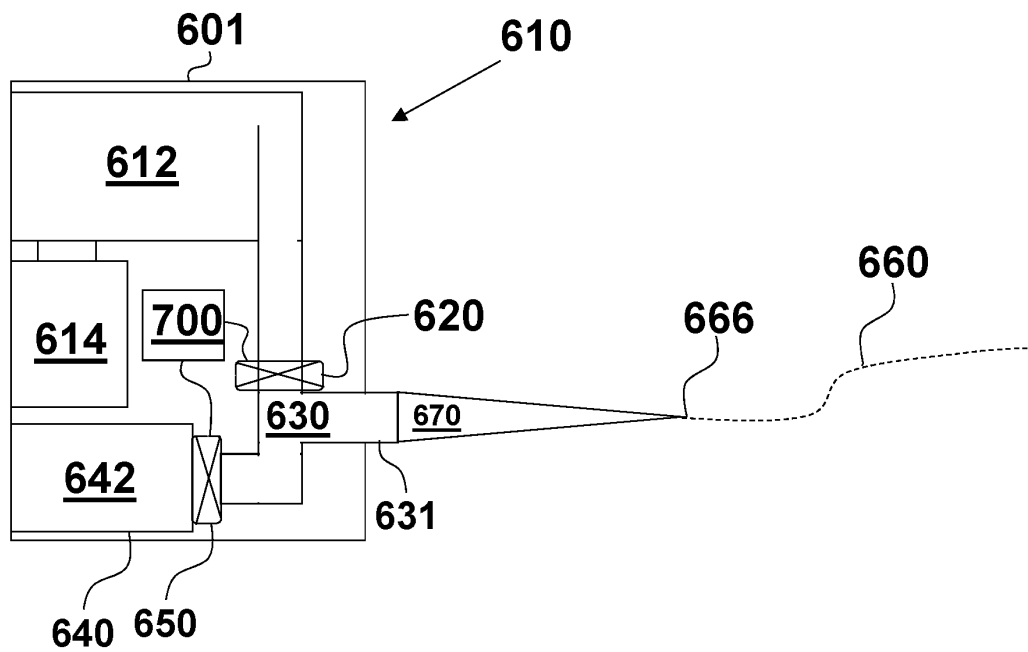


FIG. 55

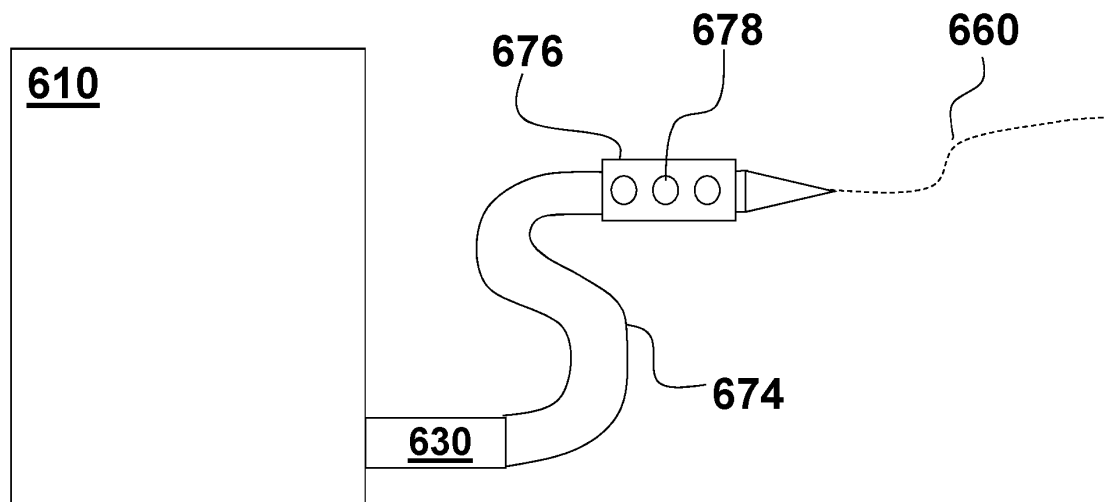


FIG. 56

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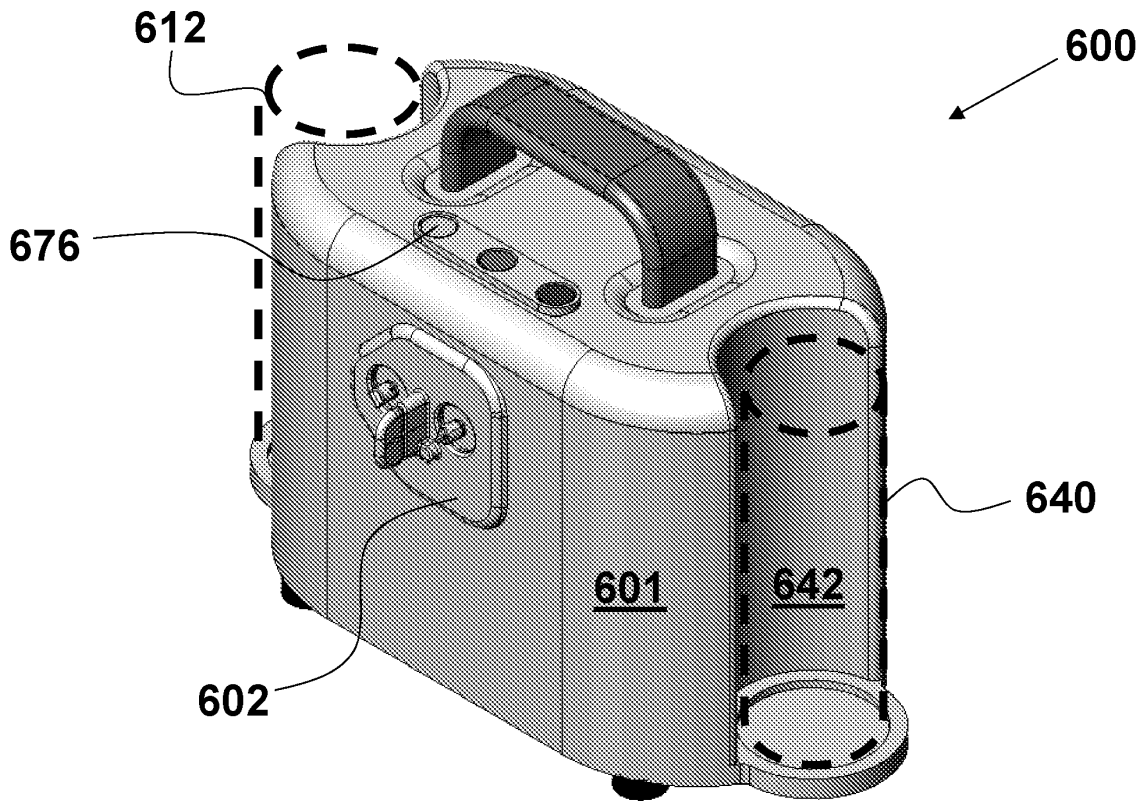


FIG. 57

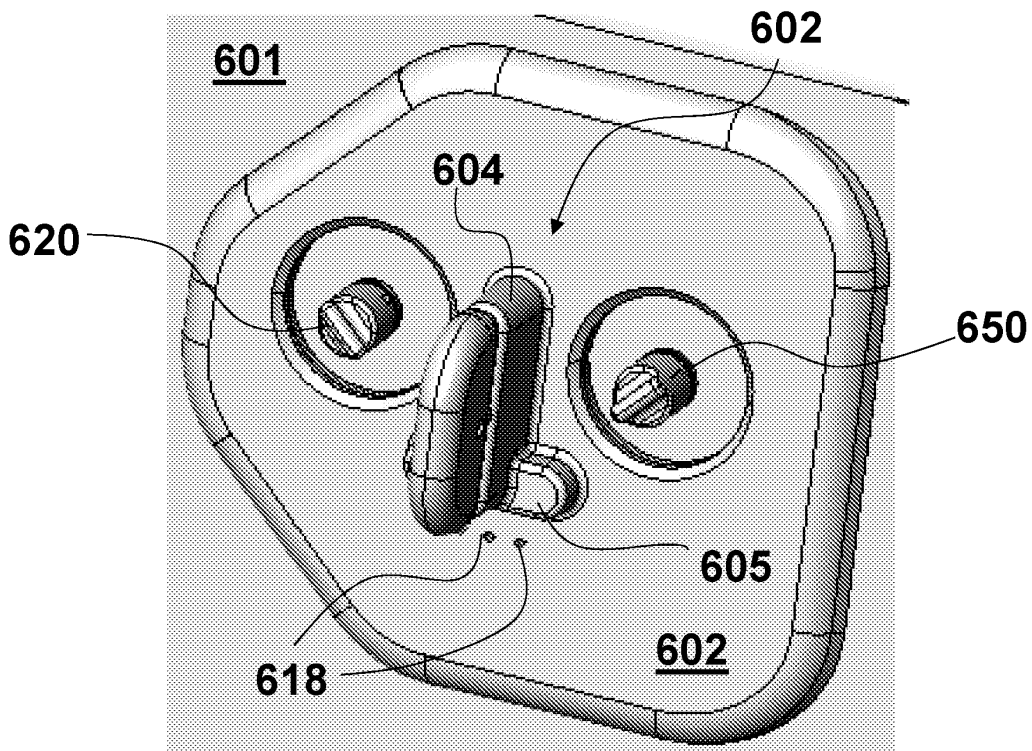


FIG. 58

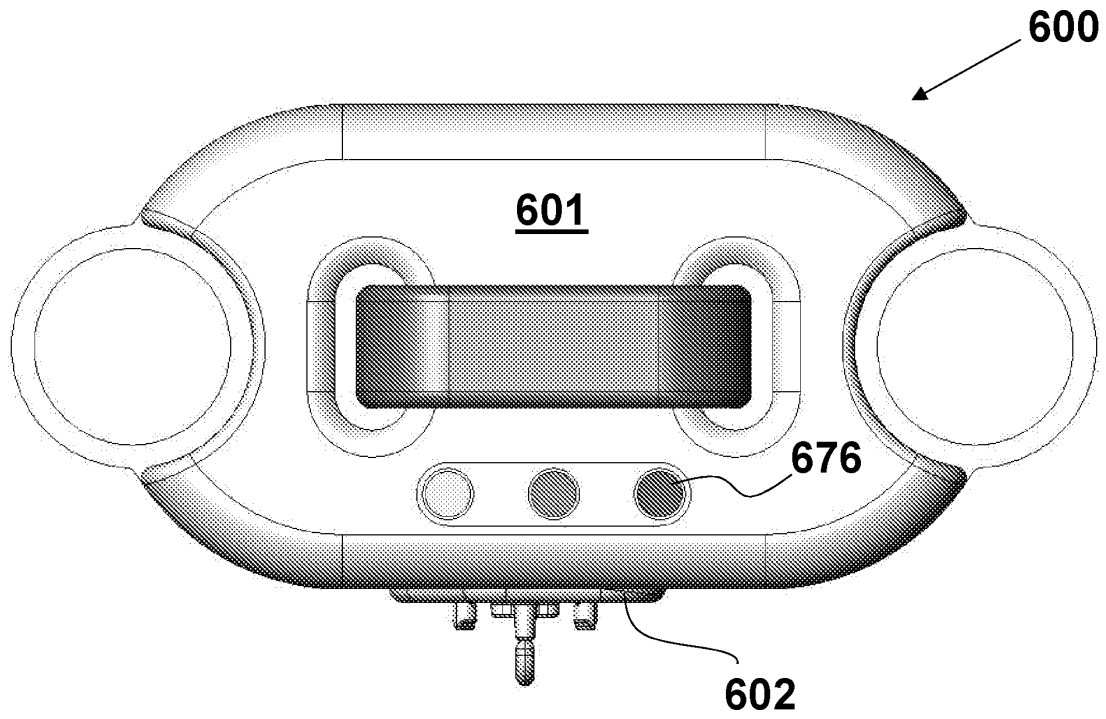


FIG. 59

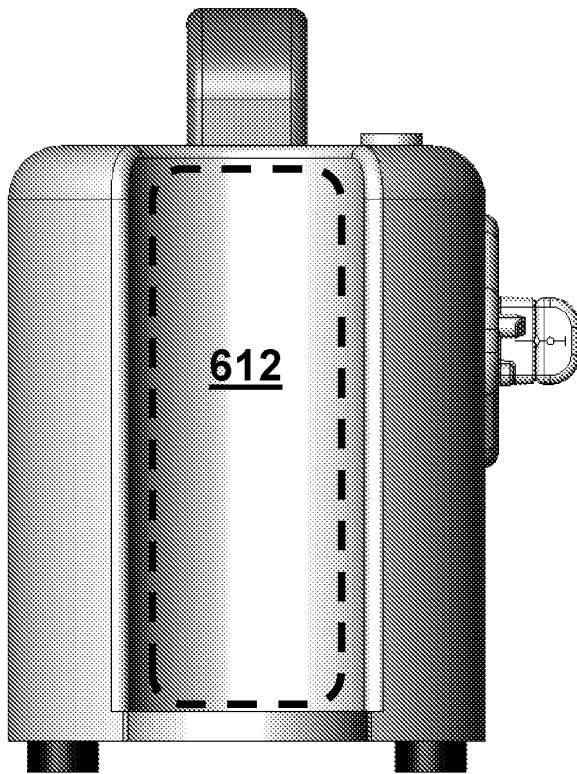


FIG. 60

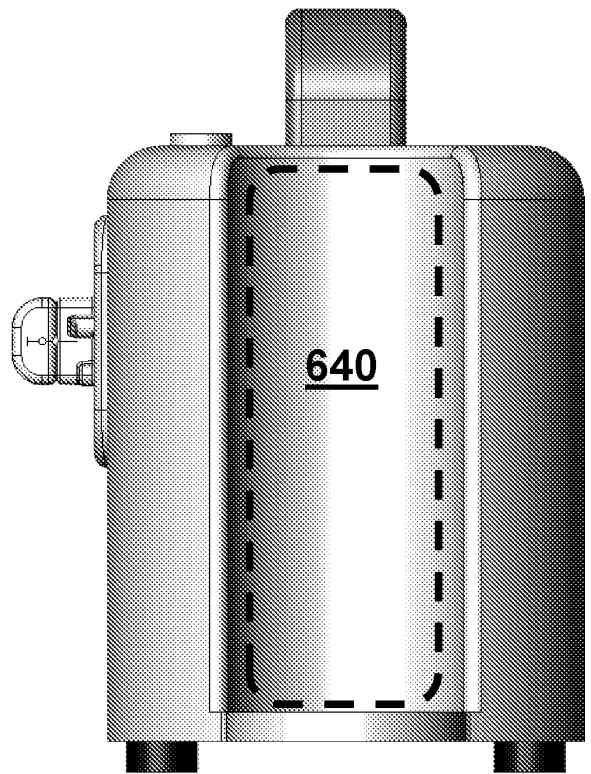


FIG. 61

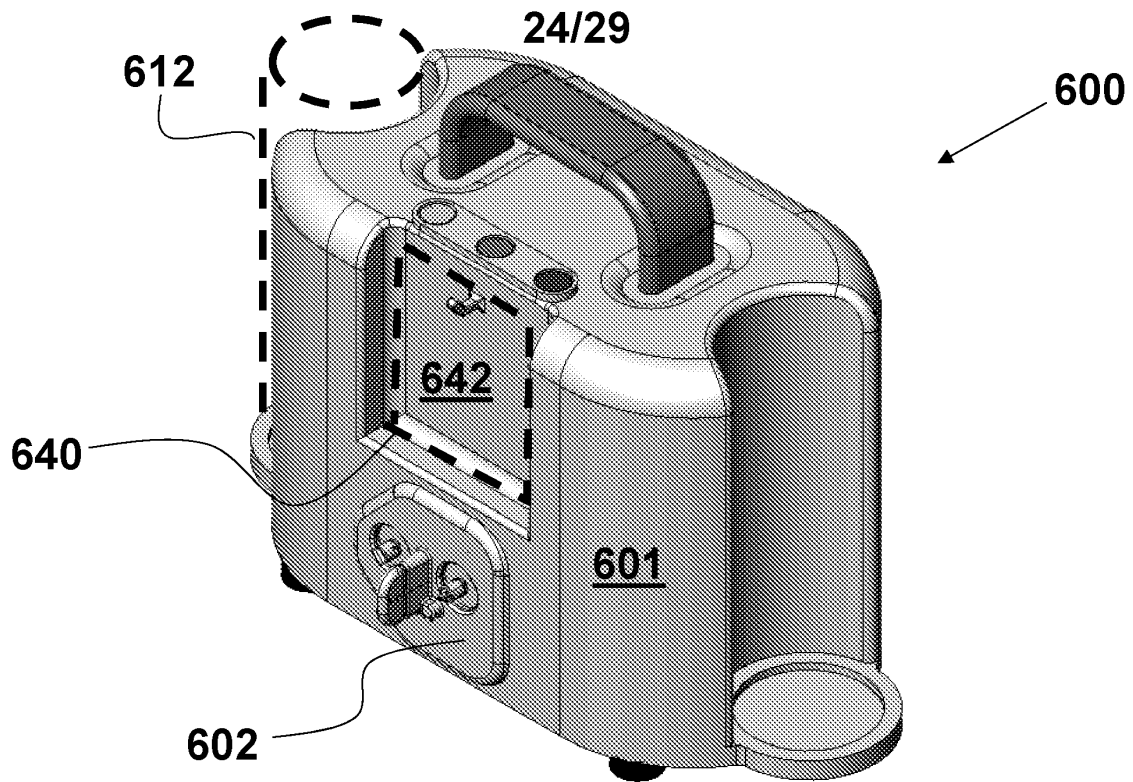


FIG. 62

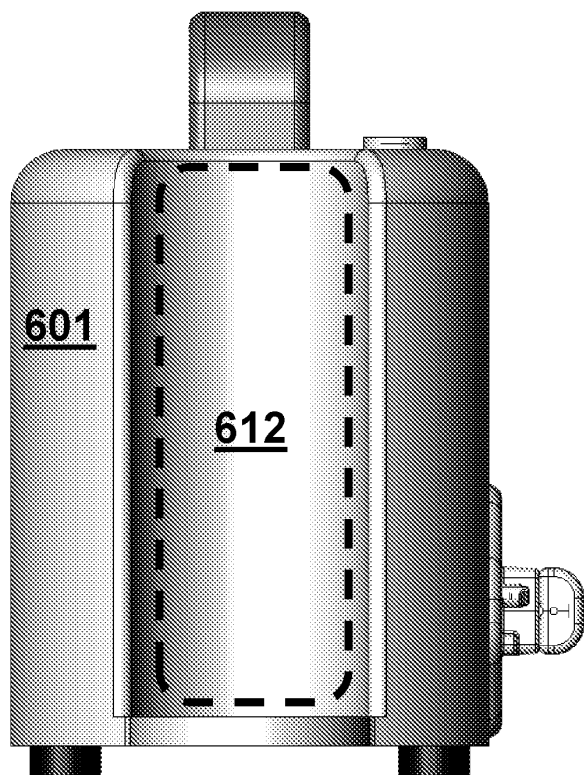


FIG. 63

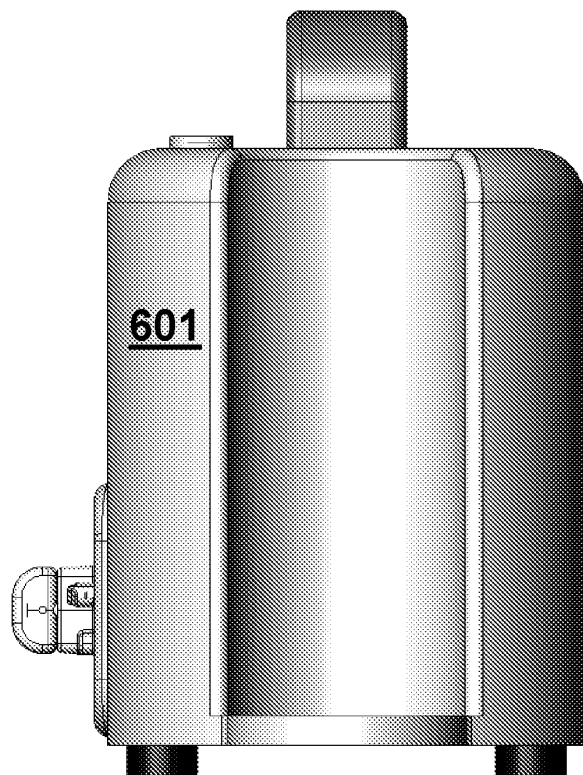


FIG. 64

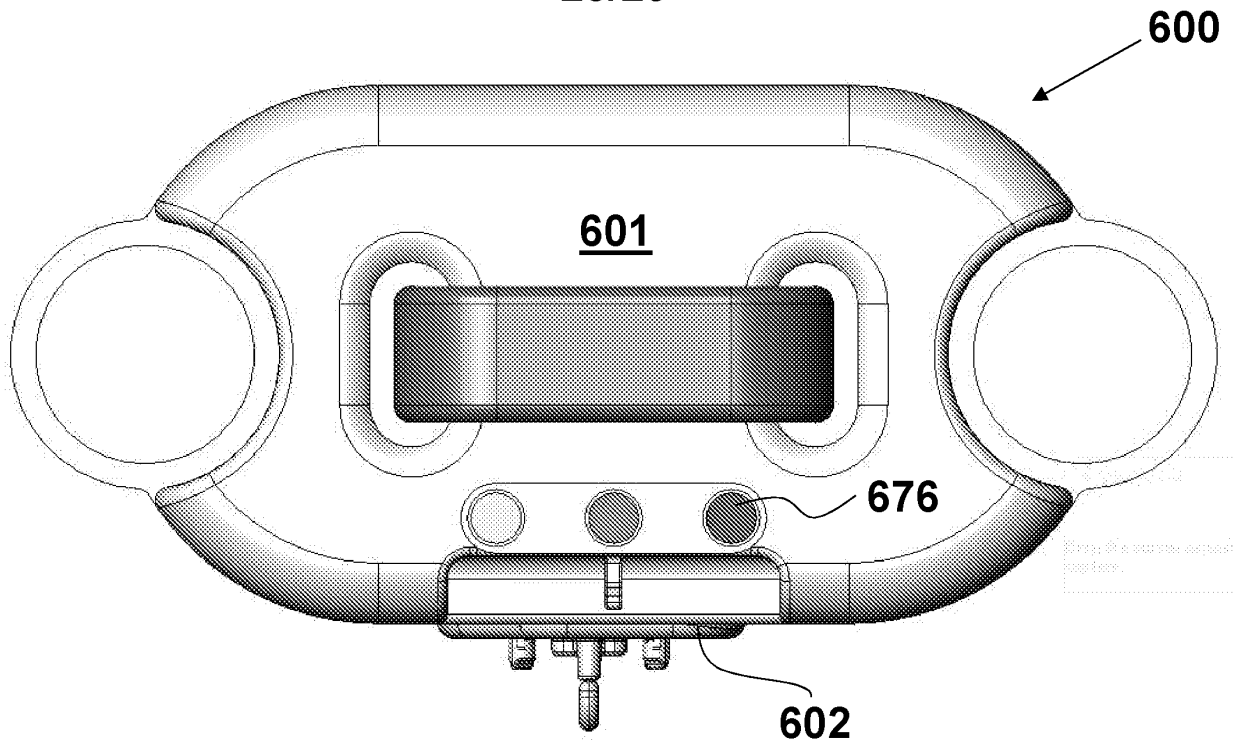


FIG. 65

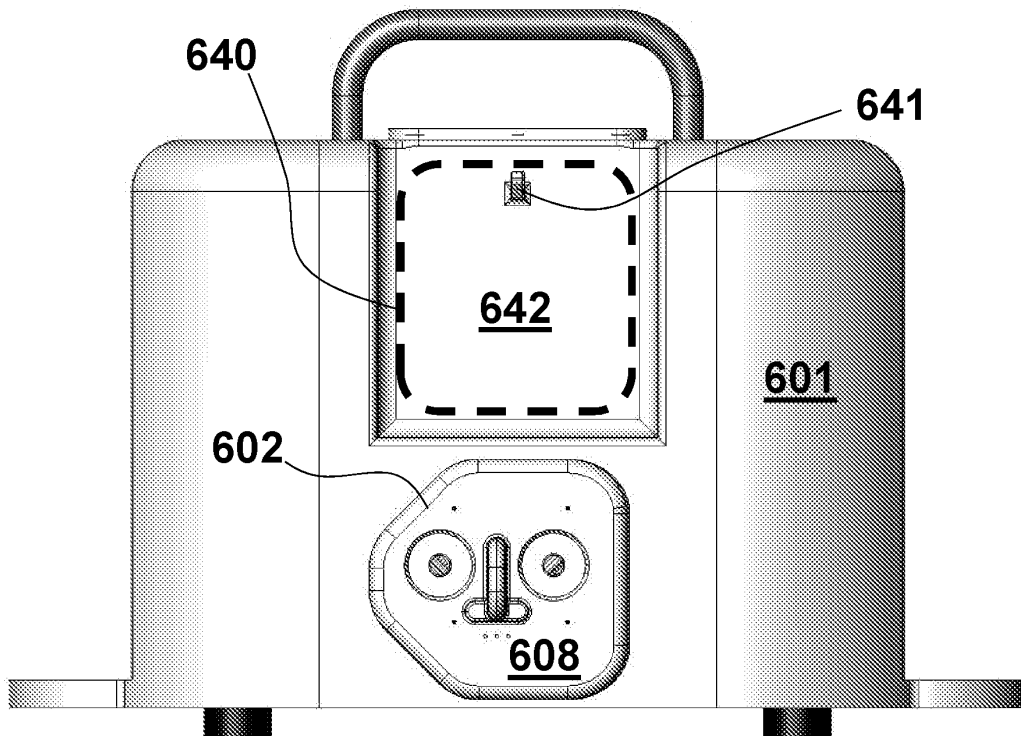


FIG. 66

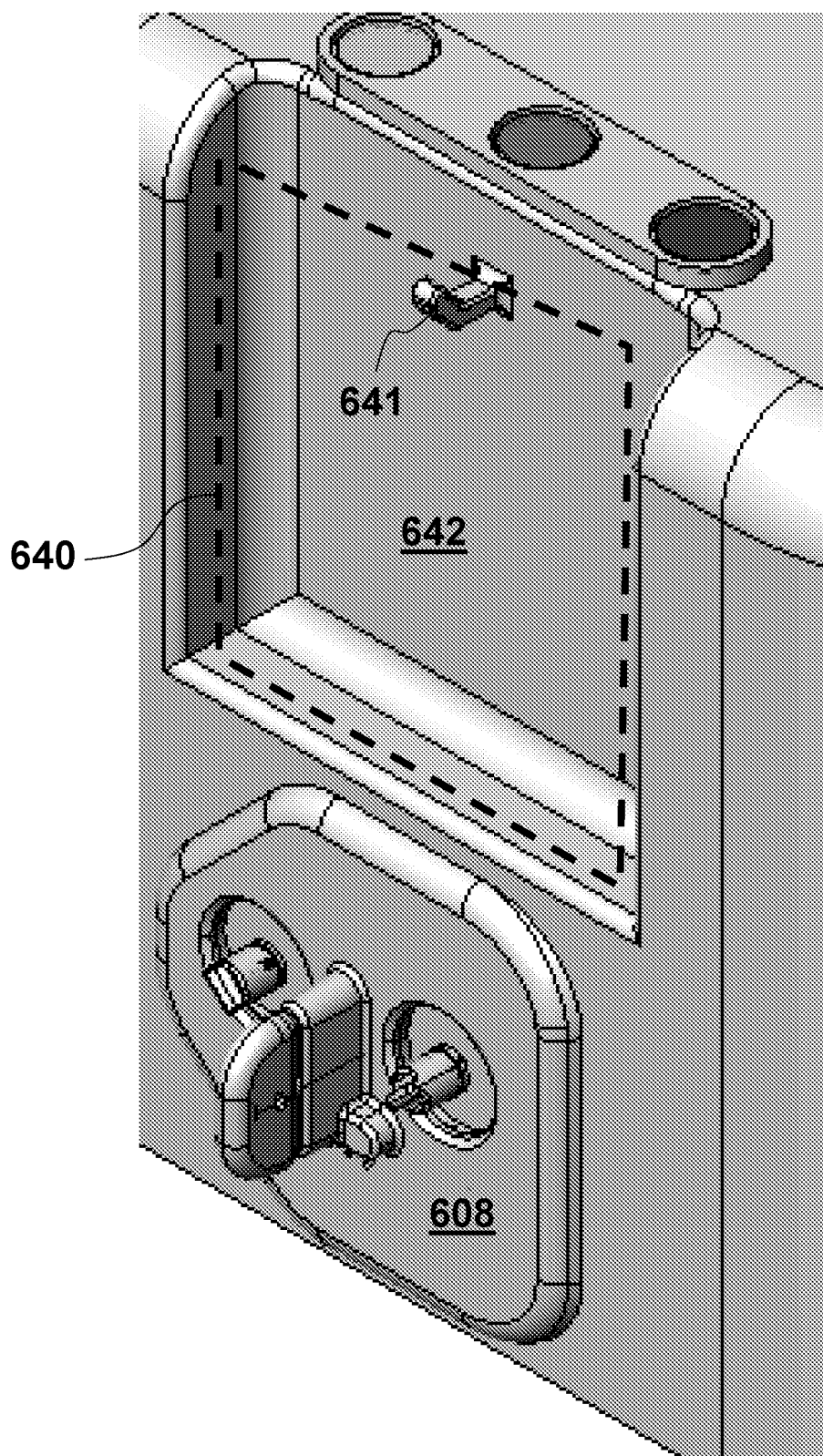
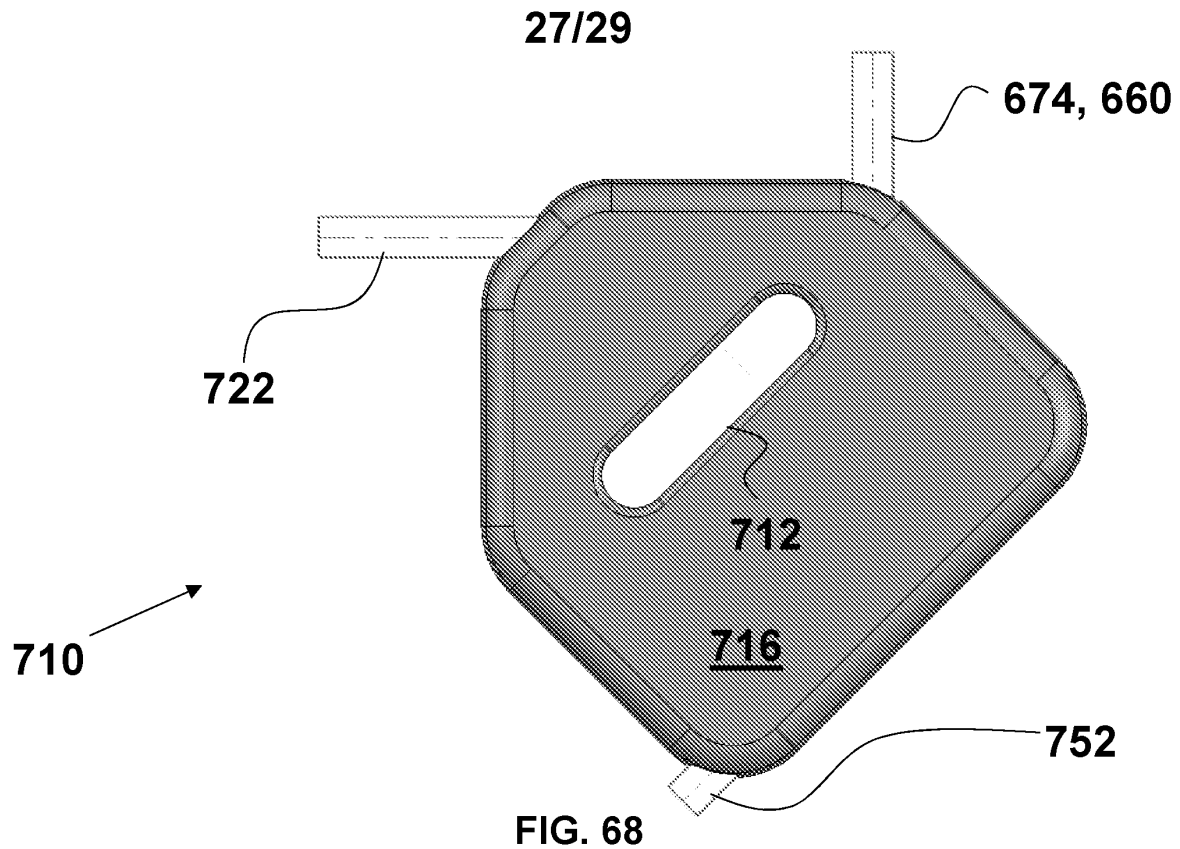
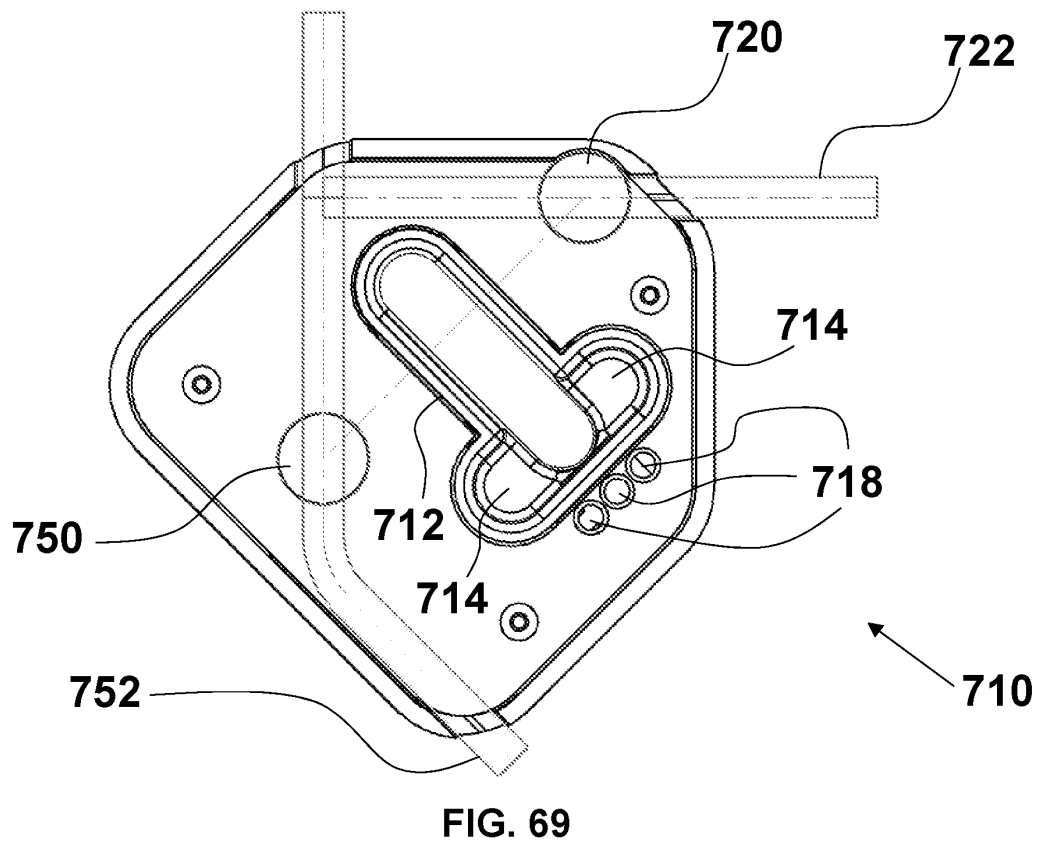


FIG. 67



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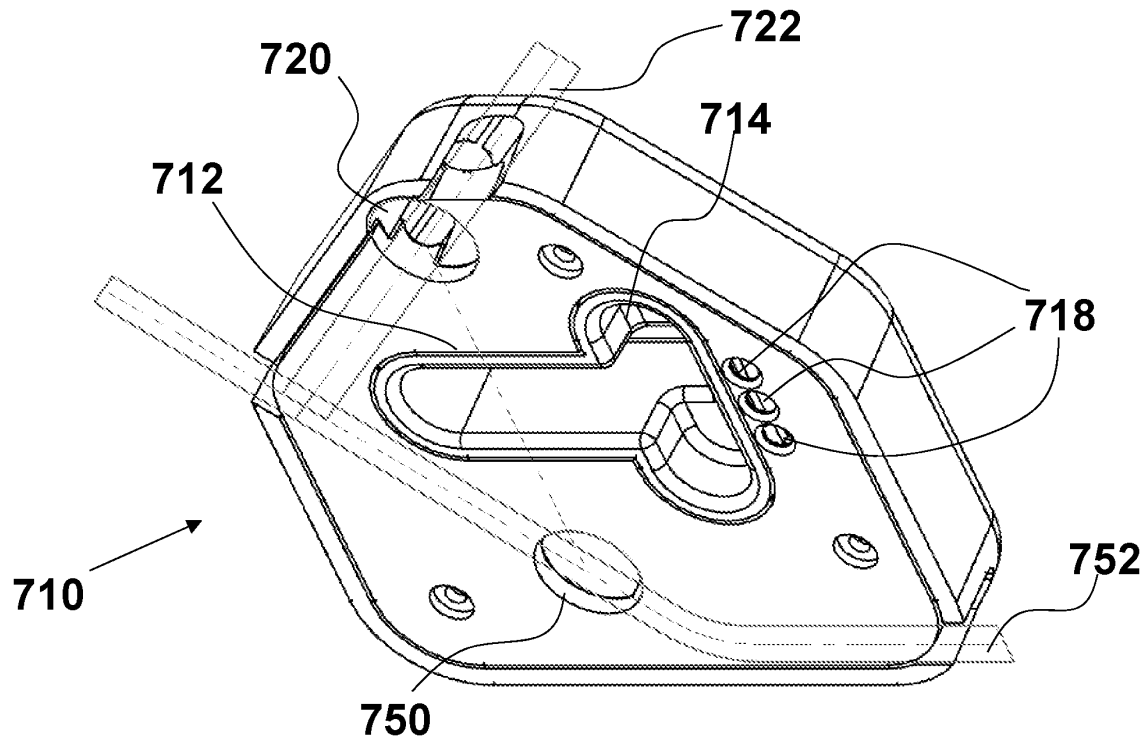


FIG. 70

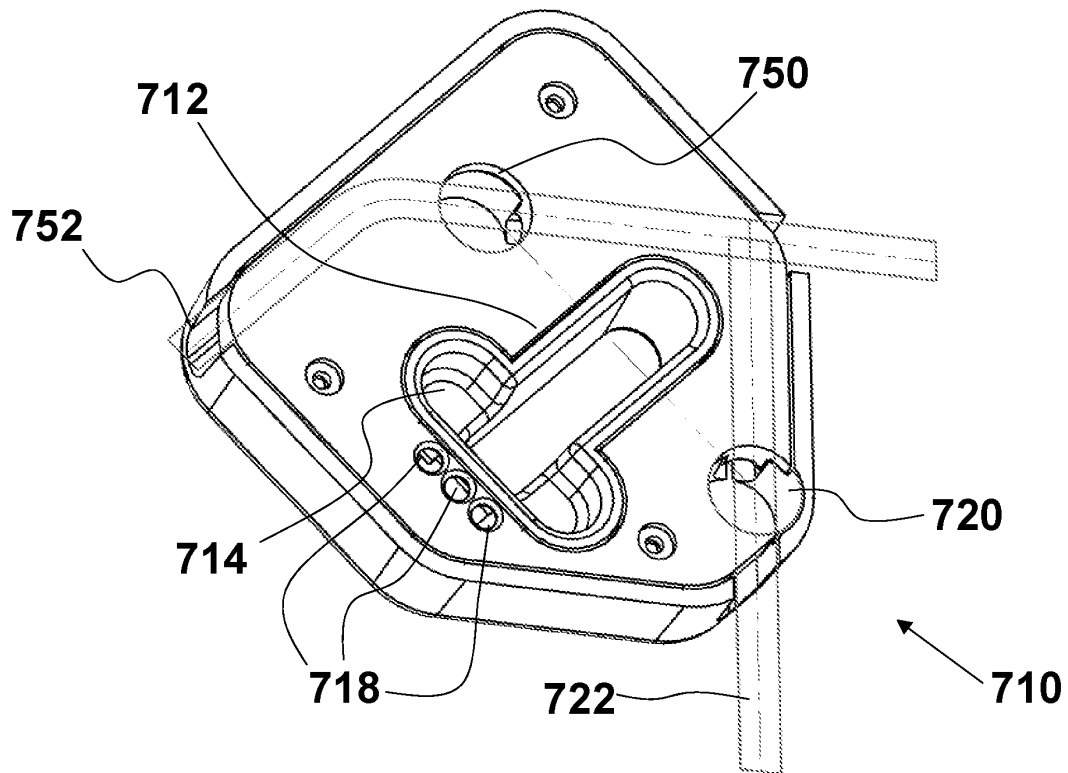
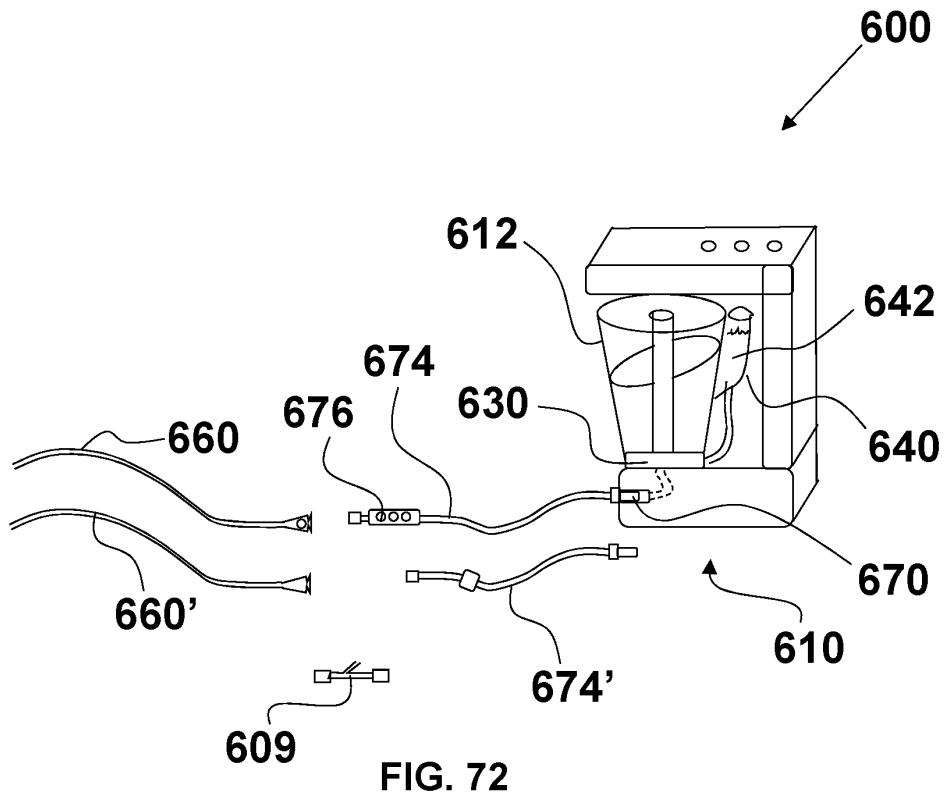


FIG. 71



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**DECLARATION (37 CFR 1.63) FOR UTILITY OR DESIGN APPLICATION USING AN
APPLICATION DATA SHEET (37 CFR 1.76)**

Title of Invention	ASPIRATION THROMBECTOMY SYSTEM AND METHODS FOR THROMBOSIS REMOVAL WITH ASPIRATION CATHETER
-------------------------------	---

As the below named inventor, I hereby declare that:

This declaration is directed to: ☒ The attached application, or
☐ United States application or PCT international application number _____
filed on _____.

The above-identified application was made or authorized to be made by me.

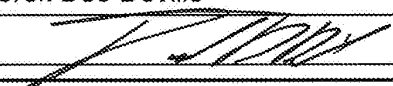
I believe that I am the original inventor or an original joint inventor of a claimed invention in the application.

I hereby acknowledge that any willful false statement made in this declaration is punishable under 18 U.S.C. 1001 by fine or imprisonment of not more than five (5) years, or both.

WARNING:

Petitioner/applicant is cautioned to avoid submitting personal information in documents filed in a patent application that may contribute to identity theft. Personal information such as social security numbers, bank account numbers, or credit card numbers (other than a check or credit card authorization form PTO-2038 submitted for payment purposes) is never required by the USPTO to support a petition or an application. If this type of personal information is included in documents submitted to the USPTO, petitioners/applicants should consider redacting such personal information from the documents before submitting them to the USPTO. Petitioner/applicant is advised that the record of a patent application is available to the public after publication of the application (unless a non-publication request in compliance with 37 CFR 1.213(a) is made in the application) or issuance of a patent. Furthermore, the record from an abandoned application may also be available to the public if the application is referenced in a published application or an issued patent (see 37 CFR 1.14). Checks and credit card authorization forms PTO-2038 submitted for payment purposes are not retained in the application file and therefore are not publicly available.

LEGAL NAME OF INVENTOR

Inventor: Derek Dee Deville Date (Optional): 11/7/19
Signature: 

Note: An application data sheet (PTO/SB/14 or equivalent), including naming the entire inventive entity, must accompany this form or must have been previously filed. Use an additional PTO/AIA/01 form for each additional inventor.

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**DECLARATION (37 CFR 1.63) FOR UTILITY OR DESIGN APPLICATION USING AN
APPLICATION DATA SHEET (37 CFR 1.76)**

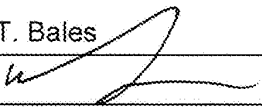
Title of Invention	ASPIRATION THROMBECTOMY SYSTEM AND METHODS FOR THROMBOSIS REMOVAL WITH ASPIRATION CATHETER
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<p>LEGAL NAME OF INVENTOR</p> <p>Inventor: <u>Matthew A. Palmer</u> Date (Optional): <u>11/12/19</u></p> <p>Signature: </p>	
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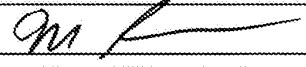
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LEGAL NAME OF INVENTOR

Inventor: M. Sean McBrayer Date (Optional): 11/7/19

Signature: 

Note: An application data sheet (PTO/SB/14 or equivalent), including naming the entire inventive entity, must accompany this form or must have been previously filed. Use an additional PTO/AIA/01 form for each additional inventor.

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LEGAL NAME OF INVENTOR

Inventor: Richard Cartledge Date (Optional) : _____Signature:  _____

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Privacy Act Statement

The **Privacy Act of 1974 (P.L. 93-579)** requires that you be given certain information in connection with your submission of the attached form related to a patent application or patent. Accordingly, pursuant to the requirements of the Act, please be advised that: (1) the general authority for the collection of this information is 35 U.S.C. 2(b)(2); (2) furnishing of the information solicited is voluntary; and (3) the principal purpose for which the information is used by the U.S. Patent and Trademark Office is to process and/or examine your submission related to a patent application or patent. If you do not furnish the requested information, the U.S. Patent and Trademark Office may not be able to process and/or examine your submission, which may result in termination of proceedings or abandonment of the application or expiration of the patent.

The information provided by you in this form will be subject to the following routine uses:

1. The information on this form will be treated confidentially to the extent allowed under the Freedom of Information Act (5 U.S.C. 552) and the Privacy Act (5 U.S.C. 552a). Records from this system of records may be disclosed to the Department of Justice to determine whether disclosure of these records is required by the Freedom of Information Act.
2. A record from this system of records may be disclosed, as a routine use, in the course of presenting evidence to a court, magistrate, or administrative tribunal, including disclosures to opposing counsel in the course of settlement negotiations.
3. A record in this system of records may be disclosed, as a routine use, to a Member of Congress submitting a request involving an individual, to whom the record pertains, when the individual has requested assistance from the Member with respect to the subject matter of the record.
4. A record in this system of records may be disclosed, as a routine use, to a contractor of the Agency having need for the information in order to perform a contract. Recipients of information shall be required to comply with the requirements of the Privacy Act of 1974, as amended, pursuant to 5 U.S.C. 552a(m).
5. A record related to an International Application filed under the Patent Cooperation Treaty in this system of records may be disclosed, as a routine use, to the International Bureau of the World Intellectual Property Organization, pursuant to the Patent Cooperation Treaty.
6. A record in this system of records may be disclosed, as a routine use, to another federal agency for purposes of National Security review (35 U.S.C. 181) and for review pursuant to the Atomic Energy Act (42 U.S.C. 218(c)).
7. A record from this system of records may be disclosed, as a routine use, to the Administrator, General Services, or his/her designee, during an inspection of records conducted by GSA as part of that agency's responsibility to recommend improvements in records management practices and programs, under authority of 44 U.S.C. 2904 and 2906. Such disclosure shall be made in accordance with the GSA regulations governing inspection of records for this purpose, and any other relevant (*i.e.*, GSA or Commerce) directive. Such disclosure shall not be used to make determinations about individuals.
8. A record from this system of records may be disclosed, as a routine use, to the public after either publication of the application pursuant to 35 U.S.C. 122(b) or issuance of a patent pursuant to 35 U.S.C. 151. Further, a record may be disclosed, subject to the limitations of 37 CFR 1.14, as a routine use, to the public if the record was filed in an application which became abandoned or in which the proceedings were terminated and which application is referenced by either a published application, an application open to public inspection or an issued patent.
9. A record from this system of records may be disclosed, as a routine use, to a Federal, State, or local law enforcement agency, if the USPTO becomes aware of a violation or potential violation of law or regulation.

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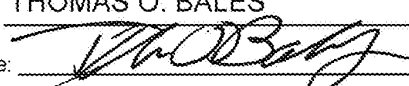
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LEGAL NAME OF INVENTOR

Inventor: THOMAS O. BALES Date (Optional): 11/11/19
Signature: 

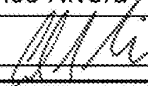
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APPLICATION
FOR
UNITED STATES LETTERS PATENT

TITLE OF INVENTION

ASPIRATION THROMBECTOMY SYSTEM AND METHODS FOR
THROMBUS REMOVAL WITH ASPIRATION CATHETER

Inventors:

DEREK DEE DEVILLE
MATTHEW A. PALMER
WILLIAM T. BALES
M. SEAN McBRAYER
ERIC PETERSEN
RICHARD CARTLEDGE
THOMAS O. BALES
CARLOS RIVERA

Dickinson Wright PLLC
350 East Las Olas Blvd, Suite 1750
Fort Lauderdale, Florida 33301
Tel: (954) 991-5420
Fax: (844) 670-6009

Attorney Docket No.: Syn2.0/ROAR Continuation

CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] This application is:

- a continuation of U.S. Patent Application Serial No. 16/516,232, filed on July 18, 2019 (which application claims priority to U.S. Provisional Application Serial Nos. 62/701,086, filed July 20, 2018, and 62/750,011, filed October 24, 2018); and
- a continuing application, under 35 U.S.C. § 120, of copending international application No. PCT/US2019/042546, filed July 19, 2019, which designated the United States, which international application claims the priority, under 35 U.S.C. § 119, of U.S. Patent Application Serial No. 16/516,232, filed on July 18, 2019 (which application claims priority to U.S. Provisional Application Serial Nos. 62/701,086, filed July 20, 2018, and 62/750,011, filed October 24, 2018),

the entire disclosures of which are hereby incorporated herein by reference in their entireties.

STATEMENT REGARDING FEDERALLY SPONSORED RESEARCH OR DEVELOPMENT

[0002] Not Applicable

FIELD OF THE INVENTION

[0003] The present systems, apparatuses, and methods lie in the field of thrombus removal. The present disclosure relates to an aspiration thrombectomy system and methods for thrombus removal with aspiration catheter.

BACKGROUND OF THE INVENTION

[0004] Ischemic strokes are usually caused by a blood clot that blocks or plugs a blood vessel in the brain. This blockage prevents blood from flowing to the brain. Within minutes, brain cells begin to die, which, if not treated rapidly, causes brain damage or death. The costs associated with removing a clot are significant. Most treatments involve thrombectomy: the removal of the clot by aspiration, mechanical retrieval, or some combination thereof.

[0005] Removal by aspiration is effected by placing a source of vacuum, e.g., an aspiration or vacuum catheter, upstream of the clot and drawing the clot into or against the distal end of the catheter. Conceptually, aspiration is effective but some significant problems occur in practice.

The basic configuration for an aspiration catheter includes a length of hollow catheter having a proximal end fluidically connected to a vacuum or suction pump. In this configuration, operation of the suction pump causes fluid and particulates at the distal end of the catheter to enter the distal opening of the hollow lumen and travel to the proximal end of the lumen near or into the suction pump. Conventional aspiration catheters are threaded through a balloon guide catheter. In one exemplary procedure, the balloon of the guide catheter is guided into the internal carotid artery of the brain. The balloon is inflated to occlude the vessel. The aspiration catheter is threaded through the balloon guide catheter and out the distal end of the guide catheter past the balloon. The distal end of the aspiration catheter is advanced to the clot that is occluding the brain vessel. Suction connected to the aspiration catheter is turned on to cause flow reversal. Ideally, this system aspirates the clot entirely out of the neurovasculature and to the proximal end of the aspiration catheter so that extraction and re-establishment of blood flow could be confirmed. In practice, however, this rarely occurs.

[0006] Thrombi are frequently of a larger diameter than the catheter being used to aspirate them. For aspiration to be successful, the thrombus must deform to conform to the inner diameter of the aspiration catheter. During conventional aspirations, it is common for applied vacuum to partially draw a thrombus into the distal opening of the aspiration catheter's lumen, thereby deforming some of the thrombus to the catheter's inner diameter. At this point, the thrombus becomes lodged completely within, partially within, or at the distal opening of the aspiration catheter, a condition that can be referred to as corked or corking. In effect, the distal end becomes a suction cup grasper for the clot. When this situation occurs, a surgeon's only option is to use the aspiration catheter as a fishing line to pull the clot back through the balloon guide and out of body. The other option is not viable, that is, reversing the suction to pressurize the clot and eject it forcibly and uncontrollably out of the distal opening of the aspiration catheter. Such action is dangerous to the patient for many reasons, the primary one being that forcibly and uncontrollably ejecting the clot may cause the clot to move further distally within the vessel in which it was originally lodged. That distal movement would not only cause the clot to be further within the vessel -- i.e., in an even smaller diameter of the vessel than when it was originally lodged -- but it could permanently lodge the clot into that vessel, making it impossible to remove, or it could burst the vessel. Those of skill in the art know that these situations are to be avoided because of the serious potential risks to the patient.

[0007] Even when the surgeon uses the aspiration catheter to fish out the clot, there is no assurance that the entirety of the clot will be removed. Pieces of the clot can break off during movement, when that occurs, the pieces re-embolize within the same vessel or within different vessels that might be even more difficult to remove.

[0008] When all or most of the clot is drawn out from the patient, it is difficult to confirm that the entire thrombus was removed. A significant disadvantage of current thrombus removal devices is the inability of a surgeon to ascertain thrombus capture/removal without the full withdrawal of a given therapeutic device from a patient's anatomy. Even systems capable of fully aspirating a given thrombus are problematic, because the reservoirs into which aspirated contents are deposited are located outside of the sterile field in an operating room setting. This location, outside the sterile field, makes it difficult or impossible for physicians operating aspiration catheters to easily visualize and appraise aspirated thrombus material.

[0009] To confirm thrombus removal can require the surgeon to attempt aspiration again. The aspiration and balloon guide catheters have to be cleaned out, access to distal anatomy has to be re-established, and, when the aspiration catheter finally is located back at the embolism site, the same issues may be present again with whatever embolus material remains. A disadvantage of these procedures is the significant increase in procedure time, which not only significantly increases the cost (as each minute in an operating room is expensive), it also increases the surgeon's stress, which decreases the success rate of the operation.

[0010] First-pass recanalization rate is a metric used to determine the efficacy of thrombectomy systems. Most current systems offer rates of between 30% and 60%. A system that increases the first-pass recanalization rate is valuable and desirable.

[0011] Even with an attempt to maintain vacuum pressure utilizing manual periodic cycling, prior art systems are not capable of avoiding positive pressures at the distal end of the catheter. Prior art systems are not able to react quickly enough to keep the distal end of the catheter from experiencing a positive pressure. When positive pressure exists at the distal end of the lumen, liquid from inside the lumen exits out from the distal end of the catheter in a distal direction. This is referred to as forward flow. The prior art do not have a fast enough reaction time to quell forward flow. Forward flow, therefore, can and does remove thrombi off of the distal end and risk sending thrombi further distally in the vasculature. Such systems cannot guarantee removing all forward flow eliminating positive pressure at the distal end of the catheter.

[0012] Thus, a need exists to overcome the problems with the prior art systems, designs, and processes as discussed above.

SUMMARY OF THE INVENTION

[0013] The systems, apparatuses, and methods described provide an aspiration thrombectomy system and methods for thrombus removal with an aspiration thrombectomy system that overcome the hereinafore-mentioned disadvantages of the heretofore-known devices and methods of this general type and that provide such features with increased first-pass recanalization rate by completely pulling the embolus out and, thereby, reducing the instance of aspiration catheter obstruction/clogging by the embolus.

[0014] The systems, apparatuses, and methods provide an aspiration thrombectomy system that completely vacuums up the clot so that clots are no longer dragged out of vasculature while half hanging out of a catheter tip. The aspiration thrombectomy system moves the vacuumed clot all the way to the proximal end of the vacuum channel and allows the surgeon to confirm recanalization of the vessel in which the clot formerly resided (for example, by injecting contrast through the catheter that remains in place after clot removal) and provides structure to indicate to the surgeon that the thrombus has been removed and that flow has been restored.

[0015] The systems, apparatuses, and methods provide an aspiration thrombectomy system that can be coupled with conventional aspiration catheters to significantly increase the efficacy of such catheter and pump systems. Vacuum level is indicated herein in two different ways:

- 1) as the absolute level of pressure, where a "high vacuum" approaches zero absolute pressure. This is the "absolute pressure" way of measuring vacuum. A perfect vacuum would be zero, and atmospheric pressure would be indicated by measuring the height of a column of mercury that can be supported by a standard atmosphere (760 mm Hg). Hence, lower values indicate an increased level of vacuum relative to the ambient atmospheric pressure.
- 2) The pressure relative to atmospheric pressure may be indicated. This way of measuring pressure relative to a standard atmospheric pressure is known as "gage pressure." The most common way of measuring pressure in the vacuum realm (below atmospheric pressure) is by using a gage calibrated so that one atmosphere reads zero (standard atmospheric pressure), and the highest possible level of vacuum would be indicated as "29.92 inches of

mercury” Common mechanical vacuum gauges work this way, so this usage has become common.

Herein, the “gage pressure” is used as method of indicating vacuum level; i.e., “zero inches of mercury” means atmospheric pressure, no suction at all. A high number (e.g., 25” Hg) means a high level of vacuum suction. (The highest possible level of vacuum measured this way would be 29.92” Hg.) “Vacuum” as used herein is a condition below normal atmospheric pressure. In the instant application, the units of pressure for vacuum is pounds per square inch (“PSI”), psi), inches of mercury, or mmHg. Depending on the context of use of the word vacuum, a “high” vacuum is referred to herein as a low pressure that is lower than atmospheric pressure. Vacuum also refers to a negative pressure(s) and a pressure above atmospheric pressure is referred to as a positive pressure. In some instances, however, use of the word “high” with respect to pressure can mean a greater negative or can mean a greater positive based on the context. Likewise, use of the words “low” or “lower” with respect to pressure can mean a lesser negative or can mean a lesser positive based on the context

[0016] Thrombi are frequently of a larger diameter than the catheter being used to aspirate them. In order for aspiration to be successful, the thrombus must deform to conform to the inner diameter of the aspiration catheter. During conventional aspirations, it is common for applied vacuum to partially draw a thrombus into the distal opening of the aspiration catheter’s lumen. At this point, the thrombus becomes stuck with some of the thrombus resting within the catheter’s inner diameter and some of the thrombus protruding from the distal end.

[0017] The systems, apparatuses, and methods provide an aspiration thrombectomy system with an unclogging structure and technique that temporarily halts vacuum at the distal end of the aspiration catheter, pushes the thrombus distally out of the lumen, and then re-applies vacuum — an occlusion-vacuum-pressure sequence of operation. Upon re-application of the vacuum, the thrombus accelerates back into the catheter and deforms to a diameter allowing it to be completely aspirated. Each halting of the vacuum, thrombus pushing, and reapplication of the vacuum is controlled by the surgeon.

[0018] The systems and methods operate an aspiration/suction catheter with a mechanism to stop the vacuum and then press the distal fluid column in reverse, i.e., a positive displacement without a check valve, referred to herein as a column shift. All functions can be controlled with a single handle, including vacuum shut off and column shift while limiting the amount and the force for

the column shift. When the controller is actuated, a positive amount of exit flow is created without possibility of overshooting. The exiting movement of fluid is limited to a specific volume and/or pressure and is automatically and precisely controlled. It is the user who controls when the column shift occurs and when it returns. A trap is disposed at an exit to catch and display the thrombus. A vent can be opened to atmosphere to clear fluid in the trap and show what thrombus remains.

[0019] With the foregoing and other objects in view, there is provided, a vacuum catheter for removing an object from within a human vessel comprising a vacuum tube defining an interior vacuum channel comprising a proximal opening for receiving application of vacuum and a distal capture opening fluidically connected to the proximal opening, the distal capture opening configured to receive therein the object responsive to application of the vacuum, and comprising an intermediate section between the proximal opening and the distal capture opening, and a vacuum interruption controller comprising a body through which a portion of the intermediate section passes and an extrusion compressor movably disposed with respect to the body towards and away from the portion of the intermediate section such that, in a rest state, the extrusion compressor does not occlude the vacuum channel and, in an actuated state, the extrusion compressor first occludes the vacuum channel and then moves fluid disposed between the portion of the intermediate section and the distal capture opening a given distance distally towards the distal capture opening.

[0020] In accordance with another feature, there is provided a vacuum pump selectively applying vacuum to the proximal opening.

[0021] In accordance with a further feature, the vacuum tube has a proximal portion and which further comprises a catheter body surrounding the vacuum tube and configured to steer at least the proximal portion of the vacuum tube.

[0022] In accordance with an added feature, the vacuum tube has a proximal portion sized to fit within the Circle of Willis in a brain and the object is a blood clot adjacent the Circle of Willis.

[0023] With the foregoing and other objects in view, there is provided, a clot removal system comprising a catheter having a distal end and defining a lumen filled with a liquid column having a proximal portion and a distal portion, a controllable vacuum valve, a vacuum source fluidically connected to the vacuum valve, a controllable vent valve having a vent liquid input, a vent fluid source containing a vent liquid and fluidically connected to the vent valve to retain the vent liquid at the vent fluid input, a manifold connected to the catheter, to the vacuum valve, and to the vent

valve, the manifold fluidically connecting the proximal portion of the liquid column in the lumen to the vacuum source through the vacuum valve and to the vent fluid source through the vent valve, a controller connected to the vacuum valve and the vent valve and configured to selectively open and close the vacuum valve and the vent valve such that, responsive to opening the vacuum valve, the vacuum source is fluidically connected to the liquid column in the lumen and, responsive to opening the vent valve, the vent fluid source is fluidically connected to the liquid column in the lumen, the controller configured to cyclically open and close the vacuum valve and the vent valve to change a level of vacuum at the distal end and prevent forward flow of the distal portion out from the distal end during each cycle.

[0024] With the objects in view, there is also provided a clot removal system comprising a catheter having a distal end and defining a lumen filled with a liquid column having a proximal portion and a distal portion, a controllable vacuum valve, a vacuum source fluidically connected to the vacuum valve, a controllable vent valve having a vent liquid input, a vent fluid source containing a vent liquid and fluidically connected to the vent valve to retain the vent liquid at the vent fluid input, a manifold connected to the catheter, to the vacuum valve, and to the vent valve, the manifold fluidically connecting the proximal portion of the liquid column in the lumen to the vacuum source through the vacuum valve and to the vent fluid source through the vent valve, a controller connected to the vacuum valve and the vent valve and configured to selectively open and close the vacuum valve and the vent valve such that responsive to opening the vacuum valve, the vacuum source is fluidically connected to the liquid column in the lumen and responsive to opening the vent valve, the vent fluid source is fluidically connected to the liquid column in the lumen. the controller configured to cyclically open and close the vacuum valve and the vent valve in a repeated cycle comprising a double-closed state in which the vacuum valve is closed and the vent valve is closed to change a level of vacuum at the distal end and prevent forward flow of the distal portion out from the distal end during each cycle, and a time of the double-closed state is no greater than approximately 30 ms.

[0025] With the objects in view, there is also provided a clot removal system comprising a catheter having a distal end and defining a lumen filled with a liquid column having a proximal portion and a distal portion, a vacuum source, a vent liquid source, and a vacuum and vent control system configured to cyclically connect or disconnect the vacuum source and the vent liquid source to change a level of vacuum at the distal end and substantially prevent forward flow.

[0026] With the objects in view, there is also provided a clot removal system comprising a catheter having a distal end and defining a lumen filled with a liquid column having a proximal portion and a distal portion, a vacuum source, a vent liquid source, and a vacuum and vent control system configured to cyclically fluidically connect to the proximal portion at least one of vacuum from the vacuum source, vent liquid from the vent liquid source, and neither the vacuum nor the vent liquid, and thereby change a level of vacuum at the distal end and substantially prevent forward flow.

[0027] In accordance with another feature, the controller is configured to cyclically open and close the vacuum valve and the vent valve in a repeated cycle comprising a double-closed state in which the vacuum valve is closed and the vent valve is closed.

[0028] In accordance with a further feature, a time of the double-closed state is no greater than 30 ms.

[0029] In accordance with an added feature, the controller is configured to cyclically open and close the vacuum valve and the vent valve in a repeated cycle comprising a vent-only state in which the vacuum valve is closed and the vent valve is open.

[0030] In accordance with an additional feature, a time of the vent-only state is no greater than 50 ms.

[0031] In accordance with yet another feature, the controller is configured to selectively open and close the vacuum valve and the vent valve cycle in a repeated cycle comprising a vacuum-only state in which the vacuum valve is open and the vent valve is closed, a first double-closed state in which the vacuum valve is closed and the vent valve is closed, a vent-only state in which the vacuum valve is closed and the vent valve is open, and a second double-closed state in which the vacuum valve is closed and the vent valve is closed.

[0032] In accordance with yet a further feature, a time between an opening of the vent valve and a closing of the vent valve is between approximately 10 ms and approximately 50 ms.

[0033] In accordance with yet an added feature, a period of the cycle is between approximately 6 Hz and approximately 16 Hz.

[0034] In accordance with yet an additional feature, a period of the cycle is between approximately 8 Hz and 12 Hz.

[0035] In accordance with again another feature, the change in the level of vacuum at the distal end is greater than approximately 15 inHg in no greater than approximately 50 ms.

[0036] In accordance with again another feature, the change in the level of vacuum at the distal end is greater than approximately 20 inHg and no greater than approximately 30 ms; and

[0037] In accordance with again another feature, the change in the level of vacuum at the distal end is greater than approximately 25 inHg and no greater than approximately 20 ms.

[0038] In accordance with again an added feature, the lumen has an internal diameter of between approximately 0.038" and approximately 0.106" and the controller is configured to cyclically open and close the vacuum valve and the vent valve at a frequency of between 2 and 16 Hz.

[0039] In accordance with again an additional feature, the lumen has an internal diameter of between approximately 0.068" and approximately 0.088" and the controller is configured to cyclically open and close the vacuum valve and the vent valve at a frequency of between 2 and 16 Hz.

[0040] In accordance with still another feature, the controller is configured to cyclically open and close the vacuum valve and the vent valve in a repeated cycle and prevent forward flow of the distal portion out from the distal end during each cycle by regulating timing of the vent valve.

[0041] In accordance with still a further feature, the controller is configured to cyclically open and close the vacuum valve and the vent valve to retain a level of pressure at the distal end at less than physiological pressure.

[0042] In accordance with a concomitant feature, there is provided a shaft and the vacuum valve and the vent valve are mounted together on the shaft.

[0043] Operation of a ROAR process as described hereinbelow successfully removes thrombi for two reasons. First, the ROAR effect overcomes the static friction of a clot that is fixed or "stuck" on the catheter tip while under constant suction. The ROAR process provides an oscillating/alternating displacement that causes the clot to "shuttle" back and forth to overcome static frictional force. Second, there is a morcellation of the clot that overcomes different clot morphologies as well as overriding volume and diameter constraints of the small, fixed luminal volume dictated by the micro-anatomic environment.

[0044] The systems and methods described and shown herein react quickly enough to keep pressure at the distal end from going positive. By cycling the vacuum and vent valves at a sufficiently fast rate, a pressure measurement at a rate of one thousand samples per second at the distal end of the catheter lumen proves that the distal end of the ROAR catheter does not experience positive pressure and substantially quells forward flow. The timing between operating the vacuum

and vent valves can be adjusted so that physical mechanisms that would cause distal end positive pressure can be avoided in both the open flow condition and in the corked condition.

[0045] In accordance with an exemplary embodiment, the distal portion of the liquid column exiting the distal end is limited to no more than approximately 2 microliters.

[0046] In accordance with an exemplary embodiment, a clot removal system comprises a catheter having a distal end and defining a lumen filled with a liquid column having a proximal portion and a distal portion, a vacuum source, a vent fluid source containing a vent liquid, and a vacuum and vent control system configured to cyclically fluidically connect to and disconnect from the proximal portion at least one of vacuum from the vacuum source and vent fluid from the vent fluid source, and thereby change a level of vacuum at the distal end and substantially prevent the distal portion of the liquid column from exiting the distal end.

[0047] In accordance with an exemplary embodiment, a clot removal system comprises a catheter having a distal end and defining a lumen filled with a liquid column having a proximal portion and a vacuum and vent control system configured to cyclically connect to and disconnect from the proximal portion vacuum and vent fluid to create therein a forward flow pressure pulse and thereby reverse flow in the liquid column and substantially prevent the forward flow pressure pulse from reaching the distal end.

[0048] In accordance with an exemplary embodiment, a clot removal system comprises a catheter having a distal end and defining a lumen filled with a liquid column having a proximal portion and a vacuum and vent control system configured to cyclically connect to and disconnect from the proximal portion vacuum and vent fluid to create therein a forward flow pressure pulse and, before the forward flow pressure pulse reaches the distal end, reverse flow in the liquid column and thereby substantially prevent the forward flow pressure pulse from reaching the distal end.

[0049] In accordance with an exemplary embodiment, a clot removal system comprises a catheter having a distal end and defining a lumen filled with a liquid column having a proximal portion and a vacuum and vent control system configured to cyclically connect to and disconnect from the proximal portion vacuum and vent fluid and thereby allow the liquid column to move and stop to create therein a forward flow pressure pulse and, before the forward flow pressure pulse reaches the distal end, alternate control to reverse flow in the liquid column and thereby control

the forward flow pressure pulse by substantially preventing the forward flow pressure pulse from reaching the distal end.

[0050] In accordance with an exemplary embodiment, the controller is configured to change the level of vacuum at the distal end in a cycle while simultaneously preventing distal movement of the distal portion of the liquid column.

[0051] In accordance with an exemplary embodiment, the controller is configured to selectively open and close the vacuum valve and the vent valve cycle in a repeated cycle comprising a first state in which the vacuum valve is open and the vent valve is closed, a second state in which the vacuum valve is closed and the vent valve is closed, a third state in which the vacuum valve is closed and the vent valve is open, and a fourth state in which the vacuum valve is closed and the vent valve is closed.

[0052] In accordance with an exemplary embodiment, a clot removal system comprises a catheter defining a lumen filled with a liquid column from a proximal portion to a distal end and a water hammer controller configured to alternatively connect vacuum and/or fluid at atmospheric or body or lower pressure to the lumen, thereby allowing the liquid column to move and stop to create therein a water hammer and, before the water hammer reaches the distal end, alternate control to reverse flow and thereby control the water hammer by substantially preventing the water hammer from reaching the distal end.

[0053] In accordance with an exemplary embodiment, a clot removal system comprises a catheter with a lumen, a vacuum source, a controllable vacuum valve, a vent fluid source, a controllable vent valve, a manifold connected to the catheter, to the vacuum valve, and to the vent valve, and a controller controlling the vacuum valve and the vent valve.

[0054] In accordance with an exemplary embodiment, the controller is configured to modulate the vacuum valve and the vent valve in a cycle that, responsive to vacuum being applied to the catheter, the compliance of the catheter causes a reduction in volume such that, when the vacuum is closed and the vent is open, the compliance acts as a spring and the lumen ingests vent fluid in a distal direction and, before a momentum induced by the ingested fluid reaches the distal end of the catheter, the controller modulates the valves to reverse a direction and quell movement of the fluid of the fluid and prevent the fluid from exiting the distal end of the catheter.

[0055] In accordance with an exemplary embodiment, a clot removal system comprises a catheter having a lumen, a substantially incompressible connection tube having interior lumen with

a proximal end and a distal end fluidically connected to the lumen, a vacuum source, and a vacuum/vent manifold comprising a manifold chamber having an output fluidically connected to the proximal end, a vacuum line fluidically connected to the manifold and to the vacuum source to present vacuum from the source to the manifold chamber, and a vent line fluidically connected to the manifold and to a fluid bath at atmospheric pressure.

[0056] In accordance with an exemplary embodiment, the clot removal system comprises a fixed cycle with plurality of pinch valves and plurality of cams mechanically coupled to the valves so that orientations of the cams cannot be changed.

[0057] In accordance with an exemplary embodiment, the time within which the forward flow pulse is quelled is no greater than approximately 20 ms.

[0058] In accordance with an exemplary embodiment, a clot removal system comprises a pulsatile vacuum controller configured to alternatively connect vacuum and/or fluid at atmospheric/body/slightly lower than body/slightly higher than body pressure to the lumen and thereby allow the liquid column to move and stop to create therein a forward flow pressure pulse and (before the forward flow pressure pulse reaches the distal end, alternating control to reverse flow and thereby) control the forward flow pressure pulse by substantially preventing the forward flow pressure pulse from reaching the distal end.

[0059] With the foregoing and other objects in view, there is provided, a clot removal system comprising a catheter having a proximal end and a distal end and defining a lumen configured to be filled with a liquid column having a proximal portion, a vacuum pump configured to supply vacuum, a vent container holding a vent liquid, a vent valve configured to fluidically communicate with the vent liquid in the vent container and with the proximal portion of the liquid column at the proximal end of the catheter, a vacuum valve configured to fluidically communicate with the vacuum from the vacuum pump and with the proximal portion of the liquid column at the proximal end of the catheter, and a controller configured to carry out a pre-determined pattern of opening and closing the vent and vacuum valves to change a level of vacuum at the distal end and, while changing the level of vacuum at the distal end, to substantially prevent forward flow of the liquid at a distal end of the liquid column.

[0060] With the objects in view, there is also provided a clot removal system comprising a catheter having a proximal end and a distal end and defining a lumen configured to be filled with a liquid column having a proximal portion, a vacuum pump configured to supply vacuum, a vent

liquid container holding a vent liquid, a vent valve configured to fluidically communicate with the vent liquid in the liquid container and with the proximal portion of the liquid column at the proximal end of the catheter, a vacuum valve configured to fluidically communicate with the vacuum from the vacuum pump, and with the proximal portion of the liquid column at the proximal end of the catheter, and a controller configured to carry out a pre-determined cycle of opening and closing the vent and vacuum valves to change a level of vacuum at the distal end and, during each cycle, to substantially prevent forward flow of liquid at the distal end of the liquid column.

[0061] In accordance with another feature, the liquid at the distal end of the liquid column is one or more of albumin, d5W water, normal saline, half-normal saline, lactated Ringer's solution, and blood, and mixtures thereof.

[0062] In accordance with a further feature, there is provided a manifold comprising the vent valve, the vacuum valve, and an output and an extension line fluidically connecting the proximal end of the catheter to the output of the manifold.

[0063] In accordance with an added feature, a portion of the pre-determined pattern includes a time period where both the vent and vacuum valves are closed.

[0064] In accordance with an additional feature, the controller is configured to open and close the vent and vacuum valves in a repeated cycle comprising a double-closed state in which both the vent and vacuum valves are closed.

[0065] In accordance with yet another feature, a time of the double-closed state is no greater than 30 ms.

[0066] In accordance with yet a further feature, the controller is configured to open and close the vent and vacuum valves in a repeated cycle comprising a vent-only state in which the vacuum valve is closed and the vent valve is open, and a time of the vent-only state is no greater than 50 ms.

[0067] In accordance with yet an added feature, the controller is configured to repeatedly and periodically carry out the pre-determined pattern.

[0068] In accordance with yet an additional feature, the controller is configured to selectively open and close the vent and vacuum valves in a repeated cycle comprising a vacuum-only state in which the vacuum valve is open and the vent valve is closed, a first double-closed state in which the vacuum valve is closed and the vent valve is closed, a vent-only state in which the vacuum

valve is closed and the vent valve is open, and a second double-closed state in which the vacuum valve is closed and the vent valve is closed.

[0069] In accordance with again another feature, the controller is configured to selectively open and close the vent and vacuum valves in a repeated cycle comprising a vacuum-only state in which the vacuum valve is open and the vent valve is closed, followed by a first double-closed state in which the vacuum valve is closed and the vent valve is closed and a time of the first double-closed state is no greater than 30 ms, followed by a vent-only state in which the vacuum valve is closed and the vent valve is open, followed by a second double-closed state in which the vacuum valve is closed and the vent valve is closed.

[0070] In accordance with again a further feature, a time between an opening of the vent valve and a closing of the vent valve is between approximately 10 ms and approximately 50 ms.

[0071] In accordance with again an added feature, a frequency of the cycle is between approximately 6 Hz and approximately 16 Hz.

[0072] In accordance with still another feature, a frequency of the cycle is between approximately 8 Hz and 12 Hz.

[0073] In accordance with still a further feature, the change in the level of vacuum at the distal end is one of greater than approximately 15 inHg and occurs in no greater than approximately 50 ms, greater than approximately 20 inHg and occurs in no greater than approximately 30 ms, and greater than approximately 25 inHg and occurs in no greater than approximately 20 ms.

[0074] In accordance with still an added feature, the lumen has a diameter of between approximately 0.038" and approximately 0.106" and the controller is configured to repeatedly and periodically carry out the pre-determined pattern of opening and closing the vent and vacuum valves at a frequency of between 2 and 16 Hz.

[0075] In accordance with still an additional feature, the lumen has an internal diameter of between approximately 0.068" and approximately 0.088" and the controller is configured to repeatedly and periodically carry out the pre-determined pattern of opening and closing the vent and vacuum valves at a frequency of between 6 and 12 Hz.

[0076] In accordance with another feature, the controller is configured to open and close the vent and vacuum valves in a repeated cycle of the pre-determined pattern and prevent forward flow of the distal portion out from the distal end during each cycle by regulating timing of the vent valve.

[0077] In accordance with a further feature, the controller is configured to open and close the vacuum valve and the vent valve in a repeated cycle of the pre-determined pattern to retain a level of pressure at the distal end at less than physiological pressure.

[0078] In accordance with an added feature, the controller is one of a mechanical valve controller and an electronic valve controller.

[0079] In accordance with a concomitant feature, there is provided a shaft and the vent and vacuum valves are cam-driven valves with respective cams mounted together on the shaft.

[0080] Although the systems, apparatuses, and methods are illustrated and described herein as embodied in an aspiration thrombectomy system and methods for thrombus removal with aspiration catheter, it is, nevertheless, not intended to be limited to the details shown because various modifications and structural changes may be made therein without departing from the spirit of the invention and within the scope and range of equivalents of the claims. Additionally, well-known elements of exemplary embodiments will not be described in detail or will be omitted so as not to obscure the relevant details of the systems, apparatuses, and methods.

[0081] Additional advantages and other features characteristic of the systems, apparatuses, and methods will be set forth in the detailed description that follows and may be apparent from the detailed description or may be learned by practice of exemplary embodiments. Still other advantages of the systems, apparatuses, and methods may be realized by any of the instrumentalities, methods, or combinations particularly pointed out in the claims.

[0082] Other features that are considered as characteristic for the systems, apparatuses, and methods are set forth in the appended claims. As required, detailed embodiments of the systems, apparatuses, and methods are disclosed herein; however, it is to be understood that the disclosed embodiments are merely exemplary of the systems, apparatuses, and methods, which can be embodied in various forms. Therefore, specific structural and functional details disclosed herein are not to be interpreted as limiting, but merely as a basis for the claims and as a representative basis for teaching one of ordinary skill in the art to variously employ the systems, apparatuses, and methods in virtually any appropriately detailed structure. Further, the terms and phrases used herein are not intended to be limiting; but rather, to provide an understandable description of the systems, apparatuses, and methods. While the specification concludes with claims defining the systems, apparatuses, and methods of the invention that are regarded as novel, it is believed that the systems, apparatuses, and methods will be better understood from a consideration of the

following description in conjunction with the drawing figures, in which like reference numerals are carried forward.

BRIEF DESCRIPTION OF THE DRAWINGS

[0083] The accompanying figures, where like reference numerals refer to identical or functionally similar elements throughout the separate views, which are not true to scale, and which, together with the detailed description below, are incorporated in and form part of the specification, serve to illustrate further various embodiments and to explain various principles and advantages all in accordance with the systems, apparatuses, and methods. Advantages of embodiments of the systems, apparatuses, and methods will be apparent from the following detailed description of the exemplary embodiments thereof, which description should be considered in conjunction with the accompanying drawings in which:

[0084] FIG. 1 is a fragmentary, perspective view of an exemplary embodiment of a controller for a thrombectomy aspiration catheter in an unactuated state;

[0085] FIG. 2 is a fragmentary, perspective, longitudinal cross-sectional view of the controller of FIG. 1;

[0086] FIG. 3 is an enlarged, diagrammatic, side elevational view of a compression cam assembly of the controller of FIG. 1;

[0087] FIG. 4 is a fragmentary, longitudinal cross-sectional view of the controller of FIG. 1 with a compression roller removed;

[0088] FIG. 5 is a fragmentary, longitudinal cross-sectional view of the controller of FIG. 1 in an actuated state;

[0089] FIG. 6 is a fragmentary, enlarged, perspective view of a portion of an extrusion compressor of the controller of FIG. 1;

[0090] FIG. 7 is a fragmentary, perspective view of the controller of FIG. 1 in the actuated state;

[0091] FIG. 8 is a fragmentary, perspective and partially longitudinal cross-sectional view of the controller of FIG. 7;

[0092] FIG. 9 is a fragmentary, perspective and longitudinal cross-sectional view of the controller of FIG. 1 in an intermediate actuated state with the compression roller occluding the aspiration catheter and partially rolled to cause fluid column shift;

[0093] FIG. 10 is a fragmentary, longitudinal cross-sectional view of the controller of FIG.

[0094] FIG. 11 is a fragmentary, perspective and longitudinal cross-sectional view of the controller of FIG. 1 in the actuated state with the compression roller occluding the aspiration catheter and fully rolled to cause fluid column shift;

[0095] FIG. 12 is a fragmentary, longitudinal cross-sectional view of the controller of FIG. 11;

[0096] FIG. 13 is a longitudinal cross-sectional view of the controller of FIG. 9 with the compression roller and the aspiration catheter removed;

[0097] FIG. 14 is a fragmentary, perspective and longitudinal cross-sectional view of the controller of FIG. 1 in the unactuated state and diagrammatically connected to a distal portion of the aspiration catheter with a thrombus lodged in a distal opening of a vacuum channel;

[0098] FIG. 15 is a fragmentary, perspective and longitudinal cross-sectional view of the controller of FIG. 12 in the actuated state with the column shift that distally dislodges the thrombus from the distal opening of the vacuum channel;

[0099] FIG. 16 is a fragmentary, enlarged, perspective and longitudinal cross-sectional view of a distal portion of the controller of FIG. 1 and an exemplary embodiment of a vacuum booster disposed between the controller and a distal extent of the aspiration catheter with the vacuum booster in an energized state;

[00100] FIG. 17 is a fragmentary, enlarged, perspective and longitudinal cross-sectional view of the controller and the vacuum booster of FIG. 16 with the vacuum booster in a relaxed state;

[00101] FIG. 18 is a fragmentary, enlarged, perspective and partially transparent view of a proximal portion of the controller of FIG. 1 and an exemplary embodiment of a thrombus trap;

[00102] FIG. 19 is a fragmentary, enlarged, perspective view of the controller and thrombus trap of FIG. 18 with the intermediate shell of the thrombus trap removed;

[00103] FIG. 20 is a fragmentary, enlarged, perspective view of the controller and thrombus trap of FIG. 18;

[00104] FIG. 21 is a fragmentary, perspective and longitudinal cross-sectional view of the controller of FIG. 16, and the thrombus trap of FIG. 18;

[00105] FIG. 22 is a fragmentary, longitudinal cross-sectional view of an exemplary embodiment of a volume changing controller;

[00106] FIG. 23 is a vacuum circuit diagram of an exemplary embodiment of a vacuum booster and vacuum booster control device;

[00107] FIG. 24 is a cycle flow diagram of the operation of exemplary embodiments of the controller with the vacuum booster and the thrombus trap;

[00108] FIG. 25 is a perspective view of an automatic aspiration thrombectomy system to be connected distally to an aspiration catheter and proximally to vacuum and vent lines and with a cam housing removed;

[00109] FIG. 26 is a fragmentary, top plan view of the aspiration thrombectomy system of FIG. 25 with diagrammatic illustration of the aspiration catheter and the vacuum and vent lines;

[00110] FIG. 27 is an elevational view of a proximal side of the aspiration thrombectomy system of FIG. 25;

[00111] FIG. 28 is an elevational view of a bearing side of the aspiration thrombectomy system of FIG. 25;

[00112] FIG. 29 is a perspective and longitudinally cross-sectional view of the aspiration thrombectomy system of FIG. 25 with a vacuum valve in a closed state, a vent valve in an open state, and a flag of a positional reset assembly in a zero reset state;

[00113] FIG. 30 is a longitudinally cross-sectional view of the aspiration thrombectomy system of FIG. 29;

[00114] FIG. 31 is an enlarged cross-sectional view of a valve and cam set of the aspiration thrombectomy system of FIG. 25 with the cam in a rotational position to set an intermediate closing of the valve;

[00115] FIG. 32 is an enlarged cross-sectional view of the valve and cam set of FIG. 31 with the cam in a rotational position to close the valve;

[00116] FIG. 33 is a cross-sectional view of the aspiration thrombectomy system of FIG. 25 along section line 33-33 in FIG. 30 with the cam housing removed;

[00117] FIG. 34 is a perspective view of the aspiration thrombectomy system of FIG. 25 with the motor assembly housing removed;

[00118] FIG. 35 is a top plan view of the aspiration thrombectomy system of FIG. 26 with the motor assembly housing removed;

[00119] FIG. 36 is an elevational view of the aspiration thrombectomy system of FIG. 27 with the motor assembly housing removed;

[00120] FIG. 37 is an elevational view of the bearing side of the aspiration thrombectomy system of FIG. 28 with the motor assembly housing removed;

[00121] FIG. 38 is a perspective view of the aspiration thrombectomy system of FIG. 25 with the cam housing;

[00122] FIG. 39 is a top plan view of the aspiration thrombectomy system of FIG. 26 with the cam housing;

[00123] FIG. 40 is an elevational view of the aspiration thrombectomy system of FIG. 27 with the cam housing;

[00124] FIG. 41 is an elevational view of the bearing side of the aspiration thrombectomy system of FIG. 28 with the cam housing;

[00125] FIG. 42 is a fragmentary, partially hidden, perspective view of an exemplary embodiment of a rotational pintle valve to be employed with the aspiration thrombectomy system in a first valve state;

[00126] FIG. 43 is a fragmentary, cross-sectional view of the valve of FIG. 42;

[00127] FIG. 44 is a fragmentary, partially hidden, perspective view of the valve of FIG. 42;

[00128] FIG. 45 is a fragmentary, partially hidden, perspective view of the valve of FIG. 42 in a second valve state;

[00129] FIG. 46 is a fragmentary, cross-sectional view of the valve of FIG. 45;

[00130] FIG. 47 is a diagrammatic, cross-sectional view of an exemplary embodiment of an aspiration thrombectomy system;

[00131] FIG. 48 is a graph of an exemplary embodiment of a waveform for operating the system of FIG. 47 with a ROAR process to quell pressure pulses;

[00132] FIG. 49 is a graph illustrating an exemplary embodiment of one cycle of a waveform operation of a vacuum valve and a vent valve of the system of FIG. 47;

[00133] FIG. 50 is a graph illustrating pressure curves at a proximal portion and a distal portion of a lumen of a catheter of the system of FIG. 47 operating with the waveform of FIG. 49;

[00134] FIG. 51 is a graph illustrating the waveforms of FIG. 49 and 50 combined together in time;

[00135] FIG. 52 is a graph of an exemplary embodiment of a waveform for operating the system of FIG. 47 with a ROAR process to quell pressure pulses;

[00136] FIG. 53 is a graph illustrating positions of the vacuum and vent valves of the system of FIG. 47 for tuning the valves to create a ROAR effect;

- [00137] FIG. 54 is a fragmentary, longitudinal cross-sectional view of a proximal manifold connector assembly for the system of FIG. 47;
- [00138] FIG. 55 is a block diagram of an exemplary embodiment of a self-contained, aspiration thrombectomy system;
- [00139] FIG. 56 is a block diagram of the system of FIG. 55 with an exemplary embodiment of a proximal manifold connector assembly having remote controls;
- [00140] FIG. 57 is a perspective view of an exemplary embodiment of a self-contained, aspiration thrombectomy system with a collection canister and a vent liquid reservoir indicated diagrammatically;
- [00141] FIG. 58 is a fragmentary, perspective view of a cassette connection assembly of the system of FIG. 57;
- [00142] FIG. 59 is a top plan view of the system of FIG. 57;
- [00143] FIG. 60 is a left side elevational view of the system of FIG. 57;
- [00144] FIG. 61 is a right side elevational view of the system of FIG. 57;
- [00145] FIG. 62 is a perspective view of an exemplary embodiment of a self-contained, aspiration thrombectomy system with a collection canister and a hanging vent liquid reservoir indicated diagrammatically;
- [00146] FIG. 63 is a left side elevational view of the system of FIG. 62;
- [00147] FIG. 64 is a right side elevational view of the system of FIG. 62;
- [00148] FIG. 65 is a top plan view of the system of FIG. 62;
- [00149] FIG. 66 is a front elevational view of the system of FIG. 57;
- [00150] FIG. 67 is a fragmentary, front perspective view of cassette connection assembly and the hanging vent liquid reservoir of the system of FIG. 57;
- [00151] FIG. 68 is a top plan view of an exemplary embodiment of a valve cassette for the systems of FIGS. 57 to 67 with hidden line views of fluid lumens;
- [00152] FIG. 69 is a bottom plan view of the valve cassette of FIG. 69;
- [00153] FIG. 70 is a bottom perspective view of the valve cassette of FIG. 69;
- [00154] FIG. 71 is a bottom perspective view of the valve cassette of FIG. 69; and
- [00155] FIG. 72 is a diagrammatic illustrated of an exemplary embodiment of a self-contained, aspiration thrombectomy system.

DETAILED DESCRIPTION OF THE EMBODIMENTS

[00156] As required, detailed embodiments of the systems, apparatuses, and methods are disclosed herein; however, it is to be understood that the disclosed embodiments are merely exemplary of the systems, apparatuses, and methods, which can be embodied in various forms. Therefore, specific structural and functional details disclosed herein are not to be interpreted as limiting, but merely as a basis for the claims and as a representative basis for teaching one skilled in the art to variously employ the systems, apparatuses, and methods in virtually any appropriately detailed structure. Further, the terms and phrases used herein are not intended to be limiting; but rather, to provide an understandable description of the systems, apparatuses, and methods. While the specification concludes with claims defining the features of the systems, apparatuses, and methods that are regarded as novel, it is believed that the systems, apparatuses, and methods will be better understood from a consideration of the following description in conjunction with the drawing figures, in which like reference numerals are carried forward.

[00157] In the following detailed description, reference is made to the accompanying drawings which form a part hereof, and in which are shown by way of illustration embodiments that may be practiced. It is to be understood that other embodiments may be utilized and structural or logical changes may be made without departing from the scope. Therefore, the following detailed description is not to be taken in a limiting sense, and the scope of embodiments is defined by the appended claims and their equivalents.

[00158] Alternate embodiments may be devised without departing from the spirit or the scope of the invention. Additionally, well-known elements of exemplary embodiments of the systems, apparatuses, and methods will not be described in detail or will be omitted so as not to obscure the relevant details of the systems, apparatuses, and methods.

[00159] Before the systems, apparatuses, and methods are disclosed and described, it is to be understood that the terminology used herein is for the purpose of describing particular embodiments only and is not intended to be limiting. The terms “comprises,” “comprising,” or any other variation thereof are intended to cover a non-exclusive inclusion, such that a process, method, article, or apparatus that comprises a list of elements does not include only those elements but may include other elements not expressly listed or inherent to such process, method, article, or apparatus. An element preceded by “comprises ... a” does not, without more constraints, preclude the existence of additional identical elements in the process, method, article, or apparatus

that comprises the element. The terms “including” and/or “having,” as used herein, are defined as comprising (i.e., open language). The terms “a” or “an,” as used herein, are defined as one or more than one. The term “plurality,” as used herein, is defined as two or more than two. The term “another,” as used herein, is defined as at least a second or more. The description may use the terms “embodiment” or “embodiments,” which may each refer to one or more of the same or different embodiments.

[00160] The terms “coupled” and “connected,” along with their derivatives, may be used. It should be understood that these terms are not intended as synonyms for each other. Rather, in particular embodiments, “connected” may be used to indicate that two or more elements are in direct physical or electrical contact with each other. “Coupled” may mean that two or more elements are in direct physical or electrical contact (e.g., directly coupled). However, “coupled” may also mean that two or more elements are not in direct contact with each other, but yet still cooperate or interact with each other (e.g., indirectly coupled).

[00161] For the purposes of the description, a phrase in the form “A/B” or in the form “A and/or B” or in the form “at least one of A and B” means (A), (B), or (A and B), where A and B are variables indicating a particular object or attribute. When used, this phrase is intended to and is hereby defined as a choice of A or B or both A and B, which is similar to the phrase “and/or”. Where more than two variables are present in such a phrase, this phrase is hereby defined as including only one of the variables, any one of the variables, any combination of any of the variables, and all of the variables, for example, a phrase in the form “at least one of A, B, and C” means (A), (B), (C), (A and B), (A and C), (B and C), or (A, B and C).

[00162] Relational terms such as first and second, top and bottom, and the like may be used solely to distinguish one entity or action from another entity or action without necessarily requiring or implying any actual such relationship or order between such entities or actions. The description may use perspective-based descriptions such as up/down, back/front, top/bottom, and proximal/distal. Such descriptions are merely used to facilitate the discussion and are not intended to restrict the application of disclosed embodiments. Various operations may be described as multiple discrete operations in turn, in a manner that may be helpful in understanding embodiments; however, the order of description should not be construed to imply that these operations are order dependent.

[00163] As used herein, the term "about" or "approximately" applies to all numeric values, whether or not explicitly indicated. These terms generally refer to a range of numbers that one of skill in the art would consider equivalent to the recited values (i.e., having the same function or result). In many instances these terms may include numbers that are rounded to the nearest significant figure. As used herein, the terms "substantial" and "substantially" means, when comparing various parts to one another, that the parts being compared are equal to or are so close enough in dimension that one skill in the art would consider the same. Substantial and substantially, as used herein, are not limited to a single dimension and specifically include a range of values for those parts being compared. The range of values, both above and below (e.g., "+/-" or greater/lesser or larger/smaller), includes a variance that one skilled in the art would know to be a reasonable tolerance for the parts mentioned.

[00164] It will be appreciated that embodiments of the systems, apparatuses, and methods described herein may be comprised of one or more conventional processors and unique stored program instructions that control the one or more processors to implement, in conjunction with certain non-processor circuits and other elements, some, most, or all of the functions of the systems, apparatuses, and methods described herein. The non-processor circuits may include, but are not limited to, signal drivers, clock circuits, power source circuits, and user input and output elements. Alternatively, some or all functions could be implemented by a state machine that has no stored program instructions, or in one or more application specific integrated circuits (ASICs) or field-programmable gate arrays (FPGA), in which each function or some combinations of certain of the functions are implemented as custom logic. Of course, a combination of these approaches could also be used. Thus, methods and means for these functions have been described herein.

[00165] The terms "program," "software," "software application," and the like as used herein, are defined as a sequence of instructions designed for execution on a computer system or programmable device. A "program," "software," "application," "computer program," or "software application" may include a subroutine, a function, a procedure, an object method, an object implementation, an executable application, an applet, a servlet, a source code, an object code, any computer language logic, a shared library/dynamic load library and/or other sequence of instructions designed for execution on a computer system.

[00166] Herein various embodiments of the systems, apparatuses, and methods are described. In many of the different embodiments, features are similar. Therefore, to avoid redundancy, repetitive description of these similar features may not be made in some circumstances. It shall be understood, however, that description of a first-appearing feature applies to the later described similar feature and each respective description, therefore, is to be incorporated therein without such repetition.

[00167] Described now are exemplary embodiments. Referring now to the figures of the drawings in detail and first, particularly to FIGS. 1 to 13, there is shown a first exemplary embodiment of a one-handed controller 10 for an aspiration thrombectomy system 1 utilizing a vacuum tube 2. The controller 10 comprises a first handle part 20 and a second handle part 40. The first handle part 20 is connected to and holds the vacuum tube 2 and, therefore, is also referred to as a handle base. The second handle part 40 moves with respect to the first handle part 20 and, therefore, the second handle part 40 is also referred to as a compressor-actuator 40.

[00168] In an exemplary embodiment, the first handle part 20 has a distal tube anchor 22 and a proximal tube anchor 24. In this embodiment, the distal and proximal tube anchors 22, 24 are in the form of hollow tubes through which the vacuum tube 2 traverses. The distal and proximal tube anchors 22, 24 hold the vacuum tube 2 therein substantially without compressing the vacuum tube 2 (and thereby does not reduce or close the inner vacuum channel 3). The vacuum tube 2 can be of many materials, including latex, silicone, Pebax®, polyurethane, polyvinyl chloride, or other synthetic rubber. Exemplary sizes for the vacuum tube 2 have an inner diameter (I.D.) of approximately 0.055 to 0.095 inches. One exemplary embodiment for retaining the vacuum tube 2 is an adhesive that bonds the material of the vacuum tube 2 to the interior lumens of the tubular tube anchors 22, 24. In this exemplary embodiment, the vacuum tube 2 is fixed to the first handle part 20. In an alternative embodiment, the first handle part 20 is a clamshell having two first handle part halves (not illustrated) that open to receive the cylindrical vacuum tube 2 and, when closed thereupon, the tube anchors 22, 24 tightly grip the vacuum tube 2 therein substantially without closing or occluding the vacuum channel 3 of the vacuum tube 2. In one exemplary clamshell embodiment, the first handle part 20 is split horizontally at the dashed line in FIG. 2 with a hinge, allowing a portion of the vacuum tube 2 to be inserted into and removed from the distal and proximal tube anchors 22, 24. A lock secures the vacuum tube 2 therein until the user

desires removal. The hinge is useful to allow the surgeon to reposition the controller 10 along the vacuum tube 2.

[00169] The exemplary embodiment of the distal and proximal tube anchors 22, 24 are separated from one another over a distance. Between the distal and proximal tube anchors 22, 24 of the first handle part 20 is a compression floor 26. When installed within the first handle part 20, the vacuum tube 2 lays against the compression floor 26 between the distal and proximal tube anchors 22, 24 substantially without closing or occluding the vacuum channel 3. FIG. 13 illustrates the compression floor 26 of first handle part 20 with the vacuum tube 2 removed.

[00170] The first handle part 20 has a hollow interior that defines a set of parallel lateral walls 32 on either side of the vacuum tube 2. The first handle part 20 comprises a compression cam assembly 30 that permits the second handle part 40 to move in two directions with respect to the first handle part 20. More specifically, in the exemplary embodiment, the compression cam assembly 30 comprises a set of slots 34 formed in the lateral walls 32 of the first handle part 20. As shown in the enlarged view of FIG. 3, these slots 34 have a vertical extent 35 and an angled extent 36. The vertical extent 35 has a vertical length and the angled extent 36 has a vector length that is comprised of a second vertical extent 37 and a horizontal extent 39. Accordingly, as explained below, the slots 34 provide a cam surface for movement of the second handle part 40 in the same shape as the slot 34.

[00171] In the exemplary embodiment, to contact the first and second handle parts 20, 40 together, the second handle part 40 has a hollow interior into which the first handle part 20 is inserted and projects. (In an alternative embodiment, the first handle part 20 has a hollow interior into which the second handle part 40 is inserted and projects.) A width between interior facing lateral surfaces of the hollow compartment of the second handle part 40 is approximately equal to the width of the exterior surfaces of the lateral walls 32 such that the second handle part 40 can move up and down on the first handle part 20 tightly but smoothly with little or substantially no friction. In comparison, the length between interior facing longitudinal surfaces of the hollow compartment of the second handle part 40 is greater than the length of the exterior surfaces of the longitudinal walls 38. The difference in length is sufficiently long enough to allow the second handle part 40 to move along the horizontal extent 39 longitudinally parallel with the vacuum tube 2 throughout the horizontal extent 39.

[00172] Movement of the compressor-actuator 40 with respect to the handle base 20 follows the slots 34 by providing the compressor-actuator 40 with bosses 42 protruding from the interior facing surfaces of the lateral walls 42 of the hollow compartment of the compressor-actuator 40; one circular boss 42 is associated with each of the slots 34. In this way, movement of the compressor-actuator 40 is guided by and restricted by the shape of the slots 34. In an unactuated state of the controller 10, shown in FIGS. 1, 2, and 4, the bosses 42 reside at the end of the vertical extent 35, which in the exemplary embodiment is at the uppermost end of the slot 34. (It is noted that the embodiment shown in FIGS. 1 to 13 provide four slots 34 and four bosses 42. This number is merely exemplary. The cam surface of the slots 34, the extents 35, 36 of the slots 34, and the cam follower of the bosses 42 can take any form or shape that causes the controller to operate as described herein.) As seen most clearly in FIG. 4, a distance A between an interior of the proximal longitudinal wall 38 of the compressor-actuator 40 and an exterior of the proximal wall of the first handle part 20 is longer than the horizontal extent 39 (i.e., $|A| > |39|$). When the compressor-actuator 40 is fully actuated as shown in FIG. 5, the bosses 42 travel to the opposite (lowermost) end of the slot 34. The compressor-actuator 40, therefore, has traveled a vertical distance equal to the vertical movement of the bosses 42 within the vertical and angled extents 35, 36 and has traveled a horizontal distance equal to the horizontal extent 39. The exemplary embodiments of the first and second handle parts 20, 40 have the interior surface of the distal longitudinal wall of the compressor-actuator 40 touching the exterior surface of the distal longitudinal wall of the handle base 20, this touch being indicated with arrows B in FIG. 4 (i.e., $|B| = 0$). When the compressor-actuator 40 is fully actuated, therefore, these two distal longitudinal walls separate to a distance equal to the horizontal extent 39. Likewise, the distance between an exterior surface of the proximal longitudinal wall of the handle base 20 and an interior surface of the proximal longitudinal wall of the compressor-actuator 40 shortens from A by a length equal to the horizontal extent 39 (i.e., $(A-|39|)$), which is illustrated in FIG. 5. Alternately, a four-bar linkage could be provided to join 20 and 40 to create the same motion as the cam slots and bosses.

[00173] What becomes apparent from movement of the compressor-actuator 40 following the slots 34 is how an extrusion compressor 50 connected to the compressor-actuator 40 operates during this movement. The exemplary embodiment of the extrusion compressor 50 in FIGS. 1, 2 and 4 to 13 has the extrusion compressor 50 project from an interior surface of a ceiling of the hollow compartment of the compressor-actuator 40 downwards towards the handle base 20. In

particular, the extrusion compressor 50 projects downwards towards the compression floor 26 of the handle base 20. The extrusion compressor 50 has a base 52 attached to the second handle part 40. A flex arm 54 projects from the base 52 and extends towards the compression floor 26. In the exemplary embodiment, the flex arm 54 is thinner than the base 52. A material from which the base 52 and flex arm 54 are made is not substantially rigid and, therefore, responsive to moving downwards to have a portion of the extrusion compressor 50 touch the compression floor 26 before the entire vertical movement of the compressor-actuator 40 is complete, the flex arm 54 flexes. Example materials for the base 52 and flex arm 54 include ABS, polycarbonate and Nylon®, polypropylene, polyurethane, or other thermoplastic or thermoplastic elastomer and/or fiber filled ABS, polycarbonate and Nylon®. At a distal end of the flex arm 54 is a gear flange 56 shaped to hold thereat a compression roller 60. The gear flange 56 has axle ports in which an axle 62 of the compression roller 60 resides. When installed between the interior sides of the gear flange 56, the compression roller 60 becomes fixed to the gear flange 56 in all directions except for rotational movement of the compression roller 60 about a rotation axis 64 of the roller 60; in other words, the roller 60 is allowed to rotate about the axis 64.

[00174] It is noted that the extrusion compressor 50 shown is an exemplary embodiment. Different mechanical structures performing the same function can be used. For example, the base 52 and flex arm 54 can be replaced with a single beam that is hinged to the ceiling of the interior hollow of the compressor-actuator 40 and biased with a bias device (e.g., a spring) towards the compression floor 26 such that the point of the compression roller 60 touches the vacuum tube 2 as shown in FIG. 2 enough to grip the vacuum tube 2 but substantially not reduce the cross-sectional area of the vacuum channel 3.

[00175] Rotation of the roller 60 is dependent upon how the roller 60 moves towards the vacuum tube 2 and along the vacuum tube 2. In this regard, the compression roller 60 has an exterior contact surface 66 that contacts the vacuum tube 2 in various ways when the compressor-actuator 40 is moved towards the handle base 20. As shown in FIG. 6, a longitudinal cross-section of the exterior surface 66 is approximately in the shape of a nautilus (alternatively, the shape can be cylindrical). The exterior surface 66 has a contact point 67, which is in contact with the exterior surface of the vacuum tube 2 in the unactuated state of the compressor-actuator 40 as shown in FIG. 2 (the vacuum channel 3 is unoccluded with a substantially patent and open cross-section). As the compressor-actuator 40 is actuated, the compressor-actuator 40 travels along the vertical

extent 35. This moves the contact point 67 towards the compression floor 26. When the compressor-actuator 40 has travelled along the entirety of the vertical extent 35, as shown in FIGS. 7 and 8, the contact point 67 has moved against the vacuum tube 2 to occlude the vacuum channel 3 completely. At the stage where the bosses 42 are at this transition point from the vertical extent 35 to the angled extent 36, the contact point 67 is as far towards the compression floor 26 as it can move in that direction – because the thickness of the vacuum tube 2 prevents further movement of the contact point 67 towards the compression floor 26.

[00176] In a procedure where the vacuum tube 2 is used in a thrombectomy, the vacuum channel 3 will be filled with a fluid, i.e., blood. When the vacuum channel 3 is completely occluded, the blood that fills up the vacuum channel 3 from the contact point 67 of the compression roller 60 distally to the distal end of the vacuum channel 3 defines a column of fluid, which fluid is not compressible. The controller 10 is configured to apply the extrusion compressor 50 and the compression roller 60 to move this column of fluid a shift distance 70 in the distal direction. An exemplary volume of the shift distance is approximately 0.001 ml to approximately 1.0 ml, in particular, approximately 0.1 ml to approximately 0.5 ml. An exemplary length of the shift distance 70 is approximately 0.5 mm to approximately 30 mm, in particular, approximately 0.5 mm to approximately 15 mm. To effect such a movement, the compressor-actuator 40 is moved further in the direction towards the handle base 20, which means that the bosses 42 travel along and through to the end of the angled extent 36. Because the contact point 67 is already as far towards the compression floor 26 as it can move in that direction (i.e., when the bosses 42 are at the transition point from the vertical extent 35 to the angled extent 36), the extrusion compressor 50 has no other way to move than to flex the flex arm 54 and/or to roll the compression roller 60. The contact surface 66 of the compression roller 60 is shaped to roll (counterclockwise in the views of FIGS. 2 and 8 to 12) against an upper surface of the vacuum tube 2. FIGS. 9 and 10 illustrate the rolling start of the compression roller 60 at a point where the bosses 42 are approximately halfway to the distal end of the slot 34 within the angled extent 36. (It is noted that limitation of the computer software that generates FIG. 9 to 12 do not allow for displaying a realistic view of how the vacuum tube 2 compresses as the compression roller 60 rotates. These figures, therefore, illustrate an approximation of the compression roller 60 rolling on and over the shift distance 70 of the vacuum tube 2.) The contact point 67 of the compression roller 60 is offset from the rotation axis 64 towards the contact surface 66. This forms an over center, or toggle, such that the initial

rolling motion of the compression roller must first force the contact point 67 over the center of the rotation axis 64. In such a configuration, not only does the compression roller 60 roll once the bosses 42 of the compression-actuator 40 start traveling in the angled extent 37, but there is also a tactile feedback transmitted to the compression-actuator 40 once the axle 62 moves slightly forward. This feedback, when felt by the user, indicates to the user that the contact surface 66 of the compression roller 60 has rolled onto a portion of the vacuum tube 2 and, as it moves along the vacuum tube 2, squeezes that portion to translate the fluid column in the distal direction of the vacuum tube 2. With complete movement of the compression-actuator 40 towards the handle base 20 as shown in FIGS. 11 and 12, the compression roller 60 has completed its defined rotation over the vacuum tube 2 and, in doing so, has squeezed a segment of the vacuum channel 3 from proximal to distal over the length to shift the fluid column distally to a length equal to the shift distance 70.

[00177] To return the controller 10 to the initial, unactuated state shown in FIGS. 1 and 2, for example, a bias device 12 is interposed between any surface of the interior hollow of the compression-actuator 40 and any surface of interior hollow of the handle base 20. In the exemplary embodiment shown in FIGS. 2 and 8, the bias device 12 is disposed between the surface of the ceiling within the interior hollow of the compression-actuator 40 and an upper surface of the proximal tube anchor 24. This configuration for the bias device 12 is merely exemplary and any return spring or similar mechanical device can be placed and used. When the user releases pressure on the compression-actuator 40, the flex arm 54 and/or the bias device 12 causes the compression-actuator 40 to return to the initial, unactuated state. This action rolls the compression roller 60 in the opposite direction (i.e., the progression from FIG. 11 to FIG. 9 to FIG. 8). As the distal end of the vacuum channel 3 experiences positive pressure from the patient and also from the increase in volume as the crushed tube rebounds, the fluid column retreats proximally back into the vacuum channel 3 and, when the compression roller 60 releases from the vacuum tube 2 to cease occluding the vacuum channel 3, vacuum being placed in the vacuum channel 3 from a vacuum pump 80 proximal to the controller 10 automatically reestablishes and draws the fluid column through the segment of the vacuum tube 2 within the controller 10.

[00178] As set forth herein, the vacuum tube 2 is sized to lay against the compression floor 26 on one side and to have the point of the compression roller 60 touch the outer surface of the vacuum tube 2 just slightly enough to grip the vacuum tube 2 but substantially not reduce the cross-

sectional area of vacuum channel 3. In an embodiment where the vacuum tube 2 is not fixed within the handle base 20, the compression roller 60 is provided with a non-illustrated bias device that biases the compression roller 60 rotationally into a position shown in FIG. 2. This bias compensates in a situation where the vacuum tube 2 is not touching the compression roller in the unactuated position of the compressor-actuator 40.

[00179] With a configuration as described, the controller 10 is to be used with a vacuum tube 2 that is or is part of a thrombectomy aspiration catheter. Such use is described with regard to FIGS. 14 and 15, in which the vacuum lumen 3 is shown as being an aspiration controller that, distal to the controller 10, is threaded through vasculature and up to a thrombus 4, which in the form of a blood clot, that has clogged within or at the distal opening of the vacuum channel 3. On the proximal side of the controller 10, the vacuum channel 3 is fluidically connected to the vacuum pump 80. As indicated above, thrombi typically are trapped at the end of an aspiration catheter and removing the entire catheter from the patient when that occurs is not desirable. The inventors have discovered that removal of the catheter can be prevented using the controller 10. More particular, when the distal end of the vacuum tube 2 is clogged by a thrombus, the controller 10 is actuated to occlude all flow through the vacuum channel 3. This occurs by the first movement of the compressor-actuator 40 towards the handle base 20. The controller 10 is actuated to cause the fluid column to shift distally to the shift distance 70. This imparts a controlled reversal of flow to the fluid column within the vacuum channel 3 that slightly translates the thrombus to a prescribed shift distance 70 distally relative to the distal opening of the vacuum channel 3. During a third and final phase, the user releases actuation of the controller 10 to reset the fluid column within the vacuum channel 3 and, once again, allows the fluid to flow freely. The inventors have discovered that such movement causes either a repositioning of the thrombus or a deformation of the thrombus or both and that this movement allows the thrombus to pass entirely into and through the vacuum channel 3 where such passage was not possible before.

[00180] Operation of the controller 10 is explained with regard to the system cycle diagram of FIG. 24.

- **State 1:** Normal aspiration is occurring. The vacuum channel 3 is not occluded. The controller 100 is in a rest state where the vacuum pump 80 is connected to the vacuum channel 3.

- **Transition A – Occlusion:** Thrombus 4 occludes distal end of vacuum channel 3. Unclogging controller 10 actuates to occlude vacuum channel 3 and stop vacuum flow distal of the controller 10.
- **State 2:** Flow through the vacuum channel 3 has stopped.
- **Transition B – Unclogging:** Controller 10 continues actuation to cause reverse flow in vacuum channel 3 for a metered volumetric column shift.
- **State 3:** Flow reversal stops.
- **Transition C – Return Column Shift:** Controller 10 is reversed to return column and accelerate thrombus 4 into catheter tip by reconnecting the vacuum pump 80 to the vacuum channel 3.
- **Return to State 1 and Repeat:** Normal aspiration occurs.

[00181] The inventors further discovered that greater accelerations of the thrombus into the catheter provide proportionally quicker aspirations. A magnitude of the thrombus' impact velocity, and therefore its kinetic energy, when it impacts the aspiration catheter's distal tip, affects the amount of the thrombus that is deformed to fit within the diameter of the vacuum channel 3. When a catheter is extended to a thrombus that is lodged in a vessel, e.g., a vessel within the brain, the controller 10 is not needed until the thrombus 4 is stuck at the distal opening of the vacuum channel 3. Thus, the thrombus does not have any distance to move in order to accelerate towards the opening of the vacuum channel 3. Imparting the shift distance to the thrombus as described maximizes the kinetic energy of the thrombus at the point when it impacts the catheter's tip. The thrombus' acceleration (and therefore its kinetic energy) are generated by a pressure differential between intracranial pressure and the effective aspiration pressure at the catheter's tip. For the thrombus to accelerate, both it and the fluid column within the catheter system must attain a velocity. After catheters are occluded, the fluid velocity within the catheter is substantially zero. In conventional catheter architecture, the pressure that attempts to accelerate this fluid column is provided solely by an external vacuum pump. Significantly, however, this pressure is reduced by head losses in the tubing connecting the vacuum pump to the catheter's proximal end. Accordingly, conventional catheters must be fished out of the vasculature entirely because the thrombus is corked within the distal opening of the vacuum channel.

[00182] This disadvantage is removed by the controller 10. After the distal opening of the vacuum channel 3 is occluded by the thrombus, the fluid velocity within the catheter is

substantially zero. The controller 10 is used to unclog the vacuum channel 3 and displace the thrombus 4 distally out from the distal opening. Then, the controller 10 re-applies vacuum. Upon re-application of vacuum, the fluid column accelerates and the thrombus 4 accelerates back into the vacuum channel 3. With such acceleration, the thrombus is deformed to a diameter allowing it to be aspirated. With one or just a few applications to displace the thrombus by the shift distance 70 with the controller 10, the vacuum channel 3 becomes unclogged and the thrombus 4 accelerates sufficiently to be completely aspirated through and out of the vacuum tube 2. With the controller 10, the head losses in the tubing are minimized, thereby allowing the thrombus to accelerate to a much greater extent than in conventional product architectures.

[00183] Realizing that acceleration of the thrombus proximally is a desirable trait, it becomes possible to enhance acceleration in the proximal direction when deactuation of the controller 10 occurs to re-establish vacuum. To maximize the acceleration of the thrombus and the fluid column within the vacuum channel 3 for the purpose of maximizing the thrombus' kinetic energy upon its impact with the distal tip of the vacuum tube 2, a vacuum booster 100, illustrated in FIG. 16, is fluidically connected to the vacuum channel 3 of the vacuum tube 2. In general, the vacuum booster 100 applies suction to the fluid column in a region of the aspiration catheter's proximal end to maximize acceleration of the catheter's fluid column at a user-selected time. This exemplary embodiment of the vacuum booster 100 comprises a booster body 110 defining a plunger bore 112, a plunger 120 housed within the bore 112, and a bias device 130. The plunger bore 112 is shaped to define a vacuum chamber 114 and an ambient chamber 116. In the exemplary embodiment, the vacuum chamber 114 is cylindrical and has a first inner diameter and the ambient chamber 116 is cylindrical and has a second inner diameter larger than the first inner diameter. The vacuum chamber 114 has a volume that is smaller than a volume of the ambient chamber 116.

[00184] The plunger 120 has a vacuum piston 122 and an ambient piston 124, which is connected to the vacuum piston 122 through a rod 123. In the exemplary embodiment, the vacuum piston 122 has a diameter substantially equal to the first inner diameter of the vacuum chamber 114 and is able to move within the vacuum chamber 114. The ambient piston 124 has a diameter substantially equal to the second inner diameter of the ambient chamber 116 and is able to move within the ambient chamber 116. Between the vacuum piston 122 and the ambient piston 124 is a pressure chamber 118 in which is located the rod 123 connecting the two pistons 122, 124 together, for example, in the shape of an asymmetric dumbbell. To seal the pressure chamber 118 off from

both the vacuum chamber 114 and the ambient chamber 116, a vacuum seal 126 is disposed between the vacuum piston 112 and the wall of the vacuum chamber 114 and an ambient seal 128 is disposed between the ambient piston 124 and the wall of the ambient chamber 116. The booster body 110 defines the pressure chamber 118 and a pressure port 119 that fluidically connects the pressure chamber 118 to a boost control valve or switch 150. This connection is illustrated diagrammatically in FIG. 23.

[00185] The vacuum chamber 114 operatively communicates with the vacuum channel 3 at a connection 140. The plunger 120 and the bias device 130 are disposed such that, when the bias device 130 is in a relaxed state, the vacuum piston 122 is at a given distance from the connection 140 to the vacuum channel 3; this relaxed state is illustrated in FIG. 17. In the relaxed state, the spring is at a steady state – there is no potential energy stored in the spring. With regard to pressure, in the relaxed state, both the pressure chamber 118 and the ambient chamber 116 are at ambient pressure, i.e., they are substantially equal. When the plunger 120 is moved towards the vacuum channel 3 into an energized state (which is shown in FIG. 16), the bias device 130 (e.g., in the form of a spring that is stretched) thereby stores strain energy that is directed to move the plunger 120 away from the connection 140. Such movement, when it occurs, creates suction within the vacuum chamber 114 and the vacuum channel 3 that communicates with the vacuum chamber 114.

[00186] To actuate the embodiment of the pneumatically actuated vacuum booster 100, the pressure chamber 118 is connected to the vacuum pump 80 (the vacuum source) through a relatively high impedance conduit 152. The pressure chamber 118 is also connected to the boost control valve 150, which is connected to ambient pressure but is normally open to prevent flow from the pressure chamber 118 to the environment (P_{atm}). When the vacuum booster 100 is in a cocked state (FIG. 16), the boost control valve 150 is open (as shown) and, as such, the vacuum pump 80 is able to significantly lower pressure within the pressure chamber 118. When the boost control valve 150 is actuated (i.e., connecting the pressure chamber 118 to the ambient environment), pressure equalization occurs between the pressure chamber 118 and the ambient chamber 116. An impedance of a connection between the pressure chamber 118 and the boost control valve 150 is designed to be substantially less than the impedance between the pressure chamber 118 and the vacuum pump 80 such that, upon actuation of the boost control valve 150 (i.e., closure), rapid pressure equalization is possible.

[00187] Operation of the vacuum booster 100 is explained with regard to the system cycle diagram of FIG. 24.

- **State 1:** Normal aspiration is occurring. The vacuum channel 3 is not occluded. The controller 100 is in a rest state where the vacuum pump 80 is connected to the vacuum channel 3. The vacuum booster 100 is in the cocked state. The thrombus trap 200 is operating without bleed purge.
- **Transition A – Occlusion:** Thrombus 4 occludes distal end of vacuum channel 3. Unclogging controller 10 actuates to occlude vacuum channel 3 and stop vacuum flow distal of the controller 10.
- **State 2:** Flow through the vacuum channel 3 has stopped.
- **Transition B – Unclogging:** Controller 10 continues actuation to cause reverse flow in vacuum channel 3 for a metered volumetric column shift.
- **State 3:** Flow reversal stops.
- **Transition C – Vacuum Boost:** Vacuum booster 100 actuated to re-initiate flow in nominal direction and accelerate thrombus 4 into catheter tip. Shortly before, at the same time, or shortly thereafter, controller 10 opens vacuum channel 3 to reinitiate vacuum of pump 80 for fluid flow and aspiration of thrombus 4 into thrombus trap 200. Simultaneously or thereafter, controlled purging or automatic purging of thrombus trap 200 occurs allowing inspection of thrombus 4.
- **Return to State 1 and Repeat:** Vacuum booster 100 and self-purging trap 200 are de-actuated. Normal aspiration occurs.

[00188] During the occlusion and column shift phases in the operation of the controller 10, the plunger 120 is held in the energized state, with the plunger 120 raised to place the vacuum piston 122 closer to the connection 140. During or immediately upon the end of the reversal phase, the plunger 120 is released, generating suction within the locally communicating lumen of the vacuum channel 3 and thereby accelerating the fluid column proximally in the vacuum direction. What fluid is begin drawn into or towards the vacuum chamber has an effect on the efficiency of the vacuum booster 100. More specifically, if the fluid arrives only from downstream of the vacuum booster 100 when actuated, then the fluid column will not accelerate proximally as desired. When the controller 10 occludes the vacuum channel 3, fluid into and towards the vacuum chamber 114 will arrive substantially from upstream of the vacuum channel 3, thereby accelerating the fluid

column in the desired direction. In an intermediate stage where fluid arrives from both upstream and downstream, the downstream portion can be limited, for example, by placing a non-illustrated check valve between the thrombus trap 200 and the connection 140, in particular, between the connection 140 and the controller 10. The check valve can be external or can use the occlusive function of unclogging handle.

[00189] The following description summarizes the forces in a pneumatic embodiment of the vacuum booster 100. In an un-cocked state of the plunger 120, the pressure chamber 118 and the ambient chamber 116 are at ambient pressure and the bias device 130 is in substantially in the relaxed state, storing little or no strain energy. In a cocked state of the plunger 120, the pressure chamber 118 is caused by the boost control valve 118 to be at a significantly lower pressure than the ambient chamber 116. The geometries of the chambers 114, 116, 118 and the pistons 122, 124, and the characteristics of the bias device 130 are selected such that, in this configuration, a force created by the pressure difference across the ambient (larger) piston is significantly greater than the force required to expand the spring. As such, when the given pressures are held, the piston and spring system translates upwards into a "cocked" position. When the vacuum booster 100 is actuated, the pressure chamber 118 is allowed to rapidly equalize to ambient pressure. With no net force input from the ambient piston 124 (the larger of the two pistons), any motion of the piston and spring system are now caused by the actions of the bias device 130 and the pressure differential across the smaller, vacuum piston 122. The geometries of the chambers 114, 116, 118 and the pistons 122, 124, and the characteristics of the bias device 130 are selected such that the bias device's restoring force in the cocked configuration is much higher than an opposing force caused by the pressure difference across the smaller vacuum piston 122, which is disposed between ambient pressure and a pressure within the vacuum channel 3. As such, when the vacuum booster 100 is actuated and the pressure chamber 118 is allowed to equalize to ambient pressure, the piston and spring system energetically drives "downwards", generating a negative displacement and a dramatic pressure decrease within the vacuum chamber 114 and thereby the vacuum channel 3 of the aspiration device.

[00190] As indicated herein, current thrombus removal devices are not able to inform the surgeon that the thrombus has been removed without full withdrawal of the device from a patient's anatomy. Surgeons do not have an ability to view the reservoirs into which aspirated contents are deposited, not only because the reservoirs are located outside of the sterile field in an operating

room setting, but also because the removed thrombus is present within a significant quantity of blood contained in the reservoir.

[00191] To overcome an inability to visualize the thrombus actually retrieved, a visualization-aiding thrombus trap 200 is provided and shown in FIGS. 18 to 21. The thrombus trap 200 is placed in-line with the aspiration system, in particular, the vacuum channel 3. In the exemplary embodiment, the thrombus trap 200 is within the catheter operator's immediate vicinity between the aspiration catheter and the vacuum source, in particular, between the controller 10 and the vacuum pump 80, so that the surgeon can see the thrombus trap 200 during use of the controller 10. In use, all aspirated material flows through the thrombus trap 200.

[00192] The thrombus trap 200 comprises a container having an inflow section 210 having an input orifice 212 fluidically connected to the vacuum channel 3, a transparent intermediate trap section 220 in which the thrombus is trapped, and an outflow section 230 fluidically connected to the vacuum pump 80. In operation, aspirated material and fluid travel from the vacuum channel 3 past the controller 10 through the inflow section 210 and into the trap section 220. The trap section 220 contains a trap filter 222 that is, in an exemplary embodiment, a screen or a filter through which all aspirated flow must pass. The filter 222 is configured to stop and capture thrombus material therein but allow the passage of air and fluid with minimal impedance therethrough and, thereby out of the outflow section 230 to the vacuum pump 80 and any associated vacuum pump reservoir 82. In the exemplary embodiment of FIGS. 18 to 22, the filter 222 is in the form of a grating or screen having orifices sufficiently large enough for fluid and air to pass therethrough but sufficiently small enough to substantially prevent the thrombus from passing across the filter 222 from an inflow or trap chamber 224 of the trap section 220 to an outflow chamber 226 of the trap section 220. As used herein, the term "filter" includes any structure that is able to separate fluid from particulate matter by allowing the fluid to pass through the structure while preventing the particular matter from passing through. Other exemplary embodiments of the filter 222 include perforated polymer, textile, or sintered semi-permeable polymer. The outflow section 230 has an output orifice 232 that fluidically connects the outflow chamber 226 to the vacuum pump 80 for directly receiving the vacuum generated.

[00193] The container of the thrombus trap 200 is sealed when closed and in use during a surgical procedure. In an exemplary embodiment, the thrombus trap 200 can be taken apart and opened

for removal of the thrombus out of the trap chamber 224 and inspection by the surgeon or pathologist, as well as for sterilization when the thrombus trap 200 is reusable.

[00194] It is noted that when a thrombus 4 is captured in the trap chamber 224, whether or not vacuum is still being applied, the trap chamber 224 is also filled with blood. Thus, the thrombus 4 cannot be visualized even if the entirety of the thrombus trap 200 is transparent for viewing inside by a user. To assist with visualization of the thrombus 4 contained within the trap chamber 224, the thrombus trap 200 is configured to temporarily purge itself of fluids that visually impede inspection of captured thrombus material. In an exemplary embodiment, therefore, the inflow section 212 is formed with an intake bleed valve 214 fluidically connected to the vacuum channel 3 and to the trap chamber 224. The bleed valve 214 is configured to operate in a closed mode, in which any flow of air and/or fluid through the bleed valve 214 and into the trap chamber 224 (or vacuum channel 3) is fully restricted, and a bleed mode, in which the bleed valve 214 intakes a fluid, in particular, ambient air. (Alternatively, if desired, in the bleed mode, the bleed valve 214 can intake a clear liquid such as saline.) During the closed mode operation, the exit of the bleed valve 214 is closed and aspirated materials are unhindered to flow through the thrombus trap 200 from the input orifice 212 and out the output orifice 232 away towards the vacuum source, leaving aspirated thrombus and other solid matter in the trap chamber 224. Accordingly, when the surgeon has captured a thrombus 4 in the trap chamber 224 during a thrombectomy procedure, the surgeon can immediately visualize that thrombus 4 by setting the bleed valve 214 into the bleed mode, which, due to a relatively larger size of the bleed valve's 214 input opening and to a decreased resistance to the vacuum by opening to ambient air, causes the vacuum pump to draw ambient air rapidly into the trap chamber 224 and thereby evacuate all fluid from the trap chamber 224. During inspection, the bleed valve 214 can be configured to occlude the fluidic connection between the trap chamber 224 and the vacuum channel 3. Actuation of the bleed valve 214 can be separate from the controller 10 or mechanically connected to the controller 10 so that, when the controller 10 is in an unactuated state where aspiration is occurring, a bleed switch on the controller can activate the bleed valve 214. The rapid inflow of air into the trap chamber 224 is directed by the descending pressure gradient between the outside environment and the relatively low pressure existing within the volume existing between the trap chamber 224 and the vacuum pump 80. As such, while the bleed 214 valve is open, airflow displaces fluids from the volume of the thrombus trap 200, leaving the volume mostly full of transparent air, instead of opaque blood. This

temporary transparency allows for easier inspection of the material caught by the filter 222. The surgeon then can view the thrombus 4 unobstructed within the trap chamber 224. During this examination, the control of the bleed valve 214 (which can be a mechanical or a processor-based controller) can cause the vacuum pump 80 to reduce vacuum or to shut off completely, at least until the surgeon is ready to continue the thrombectomy procedure if continuation is desired. When the bleed valve 214 is set back to the closed mode and re-connection of the trap chamber 224 to the vacuum channel 3 occurs, normal aspiration resumes. Alternatively the bleed valve can be connected to a fluid flush line such as a saline drip bag.

[00195] Inspection of the thrombus 4 may be enhanced by providing the thrombus trap 200 with optical filters optimized for visual contrast, transparent trap enclosures as described, built-in magnification or visualization systems, lighting, and/or sensor-based thrombus-detection methods.

[00196] In the exemplary configuration, the vacuum booster 100 is disposed upstream of the thrombus trap 200 and is on a side of controller 10 opposite the thrombus trap 200 as shown in FIG. 21. Accordingly, to maintain efficacy of the thrombus trap 200 as a terminus for all aspirated thrombi 4, vacuum booster configurations that might entrap or significantly damage or macerate the thrombus are less desirable. One exemplary embodiment of a gentler vacuum booster 200, instead of the piston design of FIGS. 16 and 17, couples a section of the tubing of the vacuum tube 2 having a deformable interior volume with a mechanical actuation mechanism. This mechanism is able to collapse and expand the interior cross-section of a length of the vacuum channel 3 to provide an increase or a decrease in pressure along that length. Another mechanical embodiment for the vacuum booster having no pneumatic actuation takes energy for vacuum boost from energy imparted by actuation of the controller 10 or from a separate energy input. For example, as user depresses a lever in the controller 10 that occludes flow and temporarily causes the column shift, the lever's motion also cocks and releases a spring-loaded piston that creates the vacuum boost. Another exemplary embodiment of the vacuum booster places a screen between the vacuum chamber 114 of the vacuum booster 100 and the vacuum channel 3 of the aspiration system. This screen allows fluid communication between the two interior volumes but occludes particulate matter from entering the piston bore defined by the vacuum chamber 114. A further exemplary embodiment that guards against clogging/accidental maceration of the thrombus alters the piston configuration of FIGS. 16 and 17 by having the connection 140 be a flexible diaphragm mechanically disposed between the surface of the vacuum piston 122 and the opening into the

vacuum channel 3. The diaphragm can be contained in and cross the actual opening of the vacuum channel 3, for example. Such a membrane transmits volumetric displacement while excluding all flow. The membrane can be separate from the vacuum piston 122, fluidically coupled thereto, or attached. In each of these configurations, the volume through which the fluid column flows is unhindered to prevent entrapping or damaging the thrombus 4 when traveling thereby, whether the vacuum booster 100 is in an energized state or a resting state.

[00197] Both the vacuum booster and the blood-purging clot trap rely on the timely and controlled application of either vacuum or ambient pressures to specific parts of the device, namely the bleed valve 214 of the thrombus trap 200 or the plunger 120 of the vacuum booster 100. The self-unclogging thrombectomy aspiration catheter described and shown herein can be provided with additional features actuated by the same user input as the self-unclogging function, e.g., at or by the controller 10, but which serve to either open or occlude additional conduits for vacuum or atmospheric pressure air that control device features such as the self-purging thrombus trap 200 and/or the vacuum booster 100.

[00198] The vacuum channel 3 of the vacuum tube 2 (and any other tubing within the catheter) can be coated with a hydrophobic coating, such as carnauba wax, for example, to decrease head loss during aspiration.

[00199] With an appropriate pressure sensor (for example, a piezoelectric diaphragm transducer, an electromagnetic diaphragm transducer, a strain-gage diaphragm transducer, or a MEMS pressure integrated circuit transducer), the controller 10 can determine when the vacuum channel 3 is clogged by a thrombus and automatically perform the unclogging procedures described herein. In an exemplary embodiment, a computer connected to the sensor can detect a pressure drop and lack of flow associated with a thrombus clog in or at the vacuum channel 3. When the clog is detected, the sensor triggers the sequence that halts application of vacuum in the vacuum channel 3 and carries out the column shift sequence. With respect to visualization of the thrombus 4 in the device, another exemplary embodiment of a sensor includes an optical sensor that detects the presence of the thrombus in either or both of the distal opening of the vacuum channel 3 and the thrombus trap 200. In the latter configuration, the optical sensor associated with the trap section 220 detects when the thrombus 4 is present and cause purging of fluid by opening the bleed valve 214.

[00200] As set forth herein, the vacuum tube 2 can be made from various materials. Some materials for the vacuum tube 2 have a relatively lower compression strength, such as latex, silicone, and other synthetic rubbers. Other materials for the vacuum tube 2 have a relatively higher compression strength, such as Pebax®, polyurethane, and polyvinyl chloride. Because the vacuum tube 2 within the controller 10 is subject to expansion when positively pressured in the vacuum channel 3 and is subject to contraction when negative pressured, this flexible attribute of the material from which the vacuum tube 2 is made could possibly contribute to a less effective column shift. In order to reduce these effects of pressure (both positive and negative) on the vacuum tube 2, the vacuum tube 2 can be reinforced with a braid or coil or other mechanical structure to support the portion of the vacuum tube 2 within the controller 10 against pressure changes. Where the vacuum tube 2 is made from a material with a relatively lower compression strength, the section of the vacuum tube 2 that resides within the controller 10 is made as short as possible to minimize the expansion/contraction effects.

[00201] An alternative embodiment to the controller 10 of FIG. 1, which indirectly operates on the vacuum channel 3 through the compression roller 60, is shown in FIG. 22. In the exemplary embodiment of FIG. 22, the extrusion compressor is replaced with a volume changing controller 300 that is directly fluidically connected to the vacuum channel 3 of the vacuum tube 3. The volume changing controller 300 has a barrel body 310 with an interior 311 defining an input orifice 312 fluidically connected to the vacuum channel 3. The barrel body 310 also defines a plunger orifice 314, a pump orifice 316, and a purge orifice 318. A plunger 320 sealably connects to the interior 311 of the barrel body 310 movably towards and away from the input orifice 314. When in the position shown in FIG. 22, vacuum applied by the vacuum pump 80 is connected to the distal opening of the vacuum channel 3 for aspiration of material. When a thrombus becomes clogged at the distal opening, the surgeon presses the plunger 320 inwards. In a first portion of the inwards motion, a surface of the plunger 320 seals off the pump orifice 316 to stop the application of vacuum to the vacuum channel 3. In a second portion of the inwards motion, the plunger 320 moves all fluid contained within the interior 311 and the vacuum channel 3 distally to cause the column shift. Reversal of the plunger reverses the column shift and reapplies vacuum to the vacuum channel 3.

[00202] The plunger 320 can also be used to control purging of the thrombus trap 200. The plunger is provided with a purge conduit 322. When the plunger 320 is placed in a purge position,

the plunger 320 closes off the vacuum channel 3 from the vacuum pump 80 and fluidically connects the pump orifice 316 to the purge orifice 318 through the purge conduit 322. In this position, a fluid connected to the purge orifice, e.g., ambient air, is drawn through the purge conduit 322, through the purge orifice 318, and into the thrombus trap 200.

[00203] Operation of the volume changing controller 300 is explained with regard to the system cycle diagram of FIG. 24.

- **State 1:** Normal aspiration is occurring. The vacuum channel 3 is not occluded. The volume changing controller 300 is in a rest state where the vacuum pump 80 is connected to the vacuum channel 3.
- **Transition A – Occlusion:** Thrombus 4 occludes distal end of vacuum channel 3. Controller 300 actuates (plunges) to occlude vacuum channel 3 and stop vacuum flow distal of the controller 300.
- **State 2:** Flow through the vacuum channel 3 has stopped.
- **Transition B – Unclogging:** Controller 300 continues to plunge to cause reverse flow in vacuum channel 3 for a metered volumetric column shift.
- **State 3:** Flow reversal stops.
- **Transition C – Return Column Shift:** Controller 300 is reversed to return column and accelerate thrombus 4 into catheter tip by reconnecting the vacuum pump 80 to the vacuum channel 3.
- **Return to State 1 and Repeat:** Normal aspiration occurs.

[00204] FIGS. 25 to 41 illustrate an exemplary embodiment of an aspiration thrombectomy system 400 operating with an automatic, rapid, and repeated onset of pressure change. An aspiration catheter 410 is diagrammatically indicated in FIG. 26 leading from distal orifices of a pair of valves 420, 440, which in this exemplary embodiment are pinch valves 420, 440. One of these valves is a pinch valve 420 to control vacuum flow and is connected between the aspiration catheter 410 and the aspiration pump (e.g., vacuum pump 80). The other of these valves is a pinch valve 440 to control vent flow and is connected to a supply of vent liquid. In an exemplary embodiment, the vent liquid can be any of albumin, d5W water, normal saline, half-normal saline, and lactated Ringer's solution, to name a few. The vent liquid can also be any other biocompatible fluid such as contrast media or tissue plasminogen activator (tPa). With such fluids, the catheter 410 can perform different functions. For example, switching the vent liquid to contrast media after

it is believed that a clot has been successfully removed allows the surgeon to inject that media into the vessel to confirm removal of the clot. This is significant because the catheter 410 changes from the aspiration function to the contrast injection function without any significant movement within the vasculature. With standard aspiration catheters where a clot becomes lodged in the distal end, the entire catheter needs to be removed from the patient and, if contrast needs to be injected at the site, the catheter needs to be reintroduced through the vasculature just to perform this visualization. The vent liquid can be at atmospheric pressure or at a higher or lower than atmospheric pressure.

[00205] In an exemplary configuration, these valves 420, 440 are mounted to a base 401. Operatively associated with the pinch valves 420, 440 are respective cams, a vacuum cam 430 and a vent cam 450. These cams 430, 450 are connected to a cam shaft 460. A first shaft end 462 of the cam shaft 460 is fixedly connected to a shaft bearing 470 in a freely rotatable manner. The shaft bearing 470 has a bearing body 472 mounted to the base 401. A second shaft end 464 of the cam shaft 460 is connected to a shaft drive assembly 500. The shaft drive assembly 500 comprises a motor 510, a transmission or gear box 520, a shaft coupler 530, and a motor controller assembly 550.

[00206] The transmission 520 has an output shaft 522. To connect the transmission 520 to the cam shaft 460, a first coupler end 532 of the shaft coupler 530 is connected to the output shaft 522 and a second coupler end 534 of the shaft coupler 530 is connected to the second shaft end 464. In this manner, rotation of the motor 510 corresponds to a rotation (at the same or different speed based upon the gearing of the transmission 520) of the cam shaft 460 with a corresponding rotation of the vacuum and vent cams 430, 450.

[00207] Control of the motor 510 originates from the motor controller assembly 550, which comprises a controller 560, a positional encoder 570 and a positional reset assembly 580. In an exemplary embodiment, the controller 560 is a microcontroller that has a user interface (UI) comprising user inputs that include, for example, control buttons to operate the aspiration thrombectomy system 400 in various states, examples of which are described in further detail below. The controller 560 with the UI is illustrated diagrammatically in FIG. 30. To isolate parts from fluid, in the exemplary embodiment, the motor 510, the transmission 520, the shaft coupler 530, and the motor controller assembly 550, 560, 570, 580 are contained in a motor assembly housing 552. The connection of the motor assembly housing 552 to the cam shaft 460 is sealed

fluidically with a shaft seal 554. Similarly, the cams 430, 450, the cam shaft 460, and the shaft bearing 470 are covered with a cam housing 466. The controller 560 is indicated in FIG. 30 as separate from the motor assembly housing 552 (either wired or wireless) but it can also be integrated into or attached to the motor assembly housing 552. In a wireless configuration, the controller 560 can be an app on a computer or smartphone, for example, with all of the UI being available through a touchscreen.

[00208] The vacuum and vent cams 430, 450 are fixed rotationally to the cam shaft 460. These cams 430, 450 have various cam profiles to operate the valves 420, 440. It is desirable to know the exact rotational position of the cams 430, 450 and, therefore, cam shaft 460, so that the controller 560 can set the valves 420, 440 in whatever state that is desired. Because the motor 510 rotates freely and can end its rotation at any rotational position, it is desirable to know the exact rotational position of the cam shaft 560 at all given times. Accordingly, the motor controller assembly 550 includes the positional encoder 570 associated with the motor 510. With this association, the controller is provided with information on the exact rotational state of the cam shaft 460 and, therefore, the cams 430, 450. The positional encoder 570 comprises an encoder disk 572 and an encoder circuit 574. The encoder 570 is able to detect and report out to the controller 560 the current relative rotational position of the motor 510 at any point in time.

[00209] Those of skill in the art know that the motor 510 and/or the positional encoder 570 can drift in use. To account for and correct any drift, the motor controller assembly 550 comprises the positional reset assembly 580. This positional reset assembly 580 assigns a single rotational position of the cam shaft 460 as a reset point and every time that position crosses a zero-line the positional encoder resets the position of the motor 510 to zero, which in turn allows the system to know the absolute position of the cam shaft 460. In an exemplary embodiment, the positional reset assembly 580 comprises a photodiode 582 and a flag or interrupter 584. As shown in FIG. 30, the flag 584 is fixed to the shaft coupler 530. The photodiode 582 is placed at the path of the flag 584 so that the flag 584 interrupts the photodiode 582 once for each rotation of the cam shaft 460. This exemplary embodiment allows for immediate correction of any skipped steps of the encoder 570.

[00210] The exemplary embodiment of the pinch valves 420, 440 is explained with regard to FIGS. 31 to 33 using the vent pinch valve 440. Each valve 420, 440 comprises a valve body 422, 442 defining a vacuum or vent lumen 424, 444. An elastomeric tube 426, 446 is secured within the lumen 424, 444 at each end of the tube 426, 446. Exemplary embodiments for this connection

include but are not limited to fusing, compression sealing, and fixation with an adhesive. Accordingly, the tube 426, 446 spans an extent of the lumen 424, 444 with an intermediate portion of the tube 426, 446 unattached to the lumen 424, 444. A lumen of the tube 426, 446 fluidically connects a distal end of the lumen 424, 444 (to the left of FIGS. 31 and 32) to the proximal end of the lumen 424, 444 (to the right of FIGS. 31 and 32). The intermediate section of the valve body 422, 442 defines a follower connection in which is movably secured a cam follower 421. A first end of the cam follower 421 is biased against the outer surface of the cam 430, 450 with a non-illustrated bias device or is simply trapped in place. The opposing second end of the cam follower 421 rests against the intermediate portion of the tube 426, 446. Accordingly, when moved by the cam 430, 450 towards the tube 426, 446, as shown in FIG. 32, the cam follower 421 fluidically seals off the lumen of the tube 426, 446 and, when allowed to return away from the tube 426, 446, as shown in FIG. 31, the cam follower 421 opens the lumen of the tube 426, 446. In the exemplary embodiment, the cam follower 421 is pill-shaped but it can be formed in any shape to provide the function of closing off the tube 426, 446.

[00211] Both a vacuum line 402 and a vent line 404 are connected through the selectively openable valves 420, 440 to a proximal end of the aspiration catheter 410. In operation, the vacuum cam 430 and the vent cam 450 push down on the respective cam followers 421, which pinch down the short sections of tubing 426, 446, each respectively fluidically connected to the vacuum line 402 and the vent line 404. When the vacuum line 402 is open and the vent line 404 is closed, vacuum is drawn on the aspiration catheter 410. When the distal end of the catheter 410 is clogged with a clot, the closure raises a vacuum level within the catheter 410 to full (the greatest current vacuum generated by the vacuum pump). This closure creates a delta in pressure between the internal lumen of the catheter 410 and the environment external to the catheter 410, which change squeezes down the body of the catheter 410 both radially and longitudinally (e.g., the diameter and length become incrementally smaller). This change also draws out a small volume of liquid from within the lumen of the catheter 410. In an exemplary embodiment, the volume is approximately 0.2 ml. The end effect is the creation of a spring-like force within the catheter 410 that wants to expand the catheter 410 back to its steady state, but when the vacuum line 402 is closed off, that cannot happen. Thus, the vacuum is stored as potential energy until the vent line 404 is opened (as can be seen in FIG. 26, for example, the vacuum and vent lines 402, 404 are connected together distal of the valves 420, 440). When the vent line 404 is opened, there is an

in-rush of fluid because of the pressure delta. This rush of fluid balances the radial force of the catheter 410 and draws in fluid to create a distally directed momentum in the column of fluid residing in the catheter 410 distal of the valves 420, 440. The momentum causes a small amount of fluid to move through a distal portion of the catheter 410 and create a small distal movement of the clot that is stuck in the distal opening at the end of the catheter 410. Once the clot is no longer stuck at the distal opening, it is able to be moved proximally into and through the catheter 410 with subsequent vacuum imparted to the catheter 410. Repeated selective actuation of vacuum and venting macerates the clot at the distal opening, thereby reforming it into a state where it can be completely drawn into the lumen of the catheter 410 and out of the vasculature. The flow of fluid forward in this exemplary embodiment is intentional, which is in contrast to other exemplary embodiments herein where substantially no forward flow occurs.

[00212] The system 400 can be operated in various modes to remove clots in the vasculature. Rotation of the cams are measured in degrees, a full rotation being 360° of movement. In a first exemplary embodiment, the vacuum cam 430 is configured to establish vacuum in the catheter 410 through approximately 220° of rotation. The vent cam 450 is configured to have venting on through approximately 80° of rotation. The configuration of the cams 430, 450 stop both venting and vacuum between each respective application of vacuum and venting, for example, with a 30° rotation. This configuration, therefore results in operation states according to Table 1 below.

State	Vacuum	Venting	Cam Angle
Off	0	0	0 to +30
Vac	1	0	+30 to +250
Off	0	0	+250 to +280
Vent	0	1	+280 to 0

Table 1

As soon as the vent is opened, there is an in-rush of fluid to balance out the vacuum pressure, then the vent line 404 is closed and the vacuum line 402 is opened, suddenly causing a rapid decrease in pressure that serves to forcefully pull the clot to the catheter. It is desirable, therefore, to close both vacuum and vent lines before resuming vacuum.

[00213] In another exemplary embodiment, the vacuum cam 430 is configured to establish vacuum in the catheter 410 through approximately 220° of rotation. The vent cam 450 is configured to have venting on through approximately 80° of rotation. Thus, there is created, in a desirable second exemplary configuration, a pause between vacuum draw in the catheter and venting of the catheter and another pause between venting of the catheter and resuming vacuum

draw in the catheter. In this exemplary configuration, the pause can be through approx. 30° of rotation. To create a purge state, where vacuum and venting occur simultaneously, the vent cam 450 has a small inwards depression in a position of the vent cam 450 that occurs during a long vacuum-on stage (e.g., between +30° to +250°). The extent of the venting is configured to not provide a significant change in pressure or change in the vacuum energy but, instead, is configured to create a single rotation position of the cams 430, 450 where the motor control assembly 550 can stop rotation of the cam shaft 460 in that orientation where both the vacuum line 402 and the vent line 404 are connected to the catheter 410, which allows the user to purge out any air that might be present in the system (e.g., in the vacuum line 402, the vent line 404, and/or the catheter 410). The extent of the depression can be such that it only partially opens the vent to reduce the amount of vent liquid that is drawn in during this purge state. This purging can be a known position of the cam rotation and is placed in that position to ensure that all lines in the system 400 are cleared of air. Such a configuration results in operation states according to Table 2 below.

State	Vacuum	Venting	Cam Angle
Off	0	0	0 to +30
Vac	1	0	+30 to +120
Purge	1	1	+120 to +140
Vac	1	0	+140 to +250
Off	0	0	+250 to +280
Vent	0	1	+280 to 0

Table 2

[00214] A third alternative configuration for operation of the system 400 can include a full-time vacuum with a pulsed venting including the operating states according to Table 3 below.

State	Vacuum	Venting	Cam Angle
Vac	1	0	0 to +120
Purge	1	1	+120 to +150
Vac	1	0	+150 to 0

Table 3

An opposite configuration to the states of Table 3 can including a full-time venting with a vacuum overlap.

[00215] A fourth alternative configuration for operation of the system 400 can include a vacuum during venting, which configuration includes the operating states according to Table 4 below.

State	Vacuum	Venting	Cam Angle
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Purge	1	1	0 to +30
Vac	1	0	+30 to +250
Off	0	0	+250 to +280
Vent	0	1	+280 to 0

Table 4

An opposite configuration to the states of Table 3 can include a full-time venting with a vacuum overlap.

[00216] A fifth alternative configuration for operation of the system 400 can include a venting during vacuum, which configuration includes the operating states according to Table 5 below.

State	Vacuum	Venting	Cam Angle
Off	0	0	0 to +30
Vac	1	0	+30 to +250
Purge	1	1	+250 to +280
Vent	0	1	+280 to 0

Table 5

[00217] In further alternative configurations, there can be a variation overlapping of venting and vacuum, which would delete one or more of the OFF states in any of the state tables above.

[00218] The cam-driven valves 420, 440 allow the positional encoder driven motor to create positions for vacuum, venting, off, and purge. The motor controller assembly 550 allows the cams 420, 440 to be controlled by any frequency, e.g., they can be set to move through the various states at any given speed, for example, at 4 Hz. The frequency at which the motor runs may be more appropriate to run at lower frequencies such as 0.5 Hz, 1 Hz, or 2 Hz. Alternatively, it may be more effective to run at higher frequencies such as 8 Hz, 12 Hz, or 16 Hz. The motor control assembly 550 can also dynamically change the rate of cam shaft 460 rotation to sweep the frequency of rotation. In exemplary embodiments, the step in speed is in a range from 1 Hz to approximately 4 Hz, the change in increment is between approximately 0.25 seconds to approximately 5 seconds, and the range of rotation is between approximately 2 Hz to approximately 12 Hz. One example for the step, increment, and range is 2 Hz and 1 second increments in the following progression 2 Hz/4/6/8/10/12/10/8/6/4/2/... Another example is 4 Hz with 0.5 sec increments in the following progression 4 Hz/8/12/8/4/... In exemplary embodiments, the system uses the higher frequencies in the 8 Hz to 12 Hz range, which has been observed to have less movement of the proximal end of a clot stuck at the distal end of the catheter 410. Alternatively, further increments can be used to sweep the frequency through complex forms, such as sine, sawtooth, stepped, and pulsing variations.

[00219] In an exemplary alternative to the pinch valves 420, 440, the valves can be solenoid-driven pinch valves or voice coil actuators. In another exemplary alternative, a rotational pintle valve can be used, as shown in FIGS. 42 to 46. The first valve state shown in FIGS. 42 to 44 can, for example, be a vacuum-on/vent-off state and the second valve state shown in FIGS. 45 and 46 can be a vacuum-off/vent-on state.

[00220] It has been determined that the most rapid onset of vacuum and venting is desirable. To create this rapid onset, the cams 430, 450 start vacuum and venting, respectively, with a cliff 452 in the shape of the cam 430, 450. Sudden creation of vacuum creates a rapid decrease of pressure inside the catheter 410, which draws the clot aggressively against the distal end of the catheter 410. Venting, as described above, creates a distal momentum that unsticks the clot and repetition of the vacuum and venting causes mechanical maceration of the clot at the distal opening until the clot completely enters the lumen of the catheter 410 and is removed from the vasculature. Therefore, the instant system 400 can be described as a Rapid Onset Aspiration Repeater or ROAR.

[00221] The control carried out by the motor controller assembly 550 has a selection of user-actuated buttons. In an exemplary embodiment, one button causes both vacuum and venting to be shut off, i.e., off operation. One button causes vacuum to occur in a continuous manner, i.e., manual control. One button causes venting to occur in a continuous manner, i.e., manual control. One button causes the cam shaft 460 to rotate the cams 430, 450 to the position in which the vacuum and vent lines 402, 404 can be purged, i.e., the purge function. One button causes the system to run or pulse repeatedly according to a desired set of states (e.g., according to any of Tables 1 to 5) along with a selection of any number of sets for step, increment, and range. As such, if the surgeon desires to use the system 400 as a simple thrombectomy device, the surgeon can just use the vacuum button. In this condition, the encoder 570 assists to have the cam shaft 460 to rotate to a position in which vacuum is open. The vacuum pump runs with a fully open vacuum until the surgeon releases the button. If the surgeon wants to purge or inject contrast, for example, then the surgeon can use the vent button to have the encoder 570 assist to rotate the cam shaft 460 to a position in which the vent is open. Likewise, the off button rotates the cam shaft 460 to a position where the cams 430, 450 close both the vacuum and vent lines 402, 404. The purge button causes rotation of the cam shaft 460 to a position where the cams 430, 450 allow simultaneous vacuum and venting.

[00222] In an exemplary embodiment of the run or ROAR mode, rotation of the cam shaft 460 is between approximately 0.5 Hz and approximately 25 Hz, further, approximately 6 Hz and approximately 16 Hz, in particular, between approximately 8 Hz and approximately 12 Hz. In this exemplary ROAR cycle, the cam shaft 460 is rotated for between approximately 10 seconds and approximately 30 seconds and, during that time, the motor controller assembly 550 causes the motor 410 to sweep through frequencies between approximately 2 Hz and approximately 12 Hz.

[00223] As set forth above, the elastomeric tube 426, 446 is attached to distal and proximal locations of the valve lumen 424, 444. Compliance in the system 400 distal of the vacuum valve (described above as including reduction of the diameter and/or length of the catheter 410 as well as compliance of the tube 426, 446) when vacuum is applied to the catheter 410 and a clot is stuck at the distal end determines how much fluid is drawn out when the system 400 is under full vacuum and, conversely, how much fluid rushes back into the system 400 when that state is released. In other words, with a greater amount of compliance distal of the valves 420, 440, momentum imparted to the stuck clot by the column of fluid increases. It is desirable to have a minimal amount of momentum transfer from the fluid column to the stuck clot to unstick the clot sufficiently so that the next vacuum cycle macerates the clot against the distal end of the catheter 410 and causes it to enter the lumen of the catheter 410 and be removed from the vessel. To minimize this compliance (which is fixed for a given catheter 410), this tube 426, 446 is made as short as possible to still allow valve operation by the cam follower. Compliance as used herein refers to mechanical compliance of the catheter 410 and the tube 426, 446; it does not refer to any air that might be in the system 400, which air is purged before use as set forth herein. This desire for a reduction in compliance is one reason the valving system is connected directly to the proximal end of the catheter 410. This close connection minimizes overall compliance. In an exemplary embodiment, the valving system can be located away from the catheter 410 and, in such a case, substantially non-compliant tubing is desired. This configuration may experience lower performance due to the excess compliance.

[00224] To determine the status of a clot at the distal end of the catheter 410, the system 400 is put in the ROAR mode. If there are no sensors associated with the system 400, a surgeon cannot distinguish the situation when a clot is corked during ROAR or not. The surgeon has to turn off ROAR and visualize whether the catheter is corked (in which nothing is being drawn in by the catheter 410) or is not corked (in which blood is being drawn into the catheter 410). With the

different situations of aborting pulse based on flow and pulsing until not corked, it is hard to know when a clot is corked.

[00225] The vent line 404 is connected to a vent liquid reservoir (not illustrated), which can contain for example, any of albumin, d5 water, normal saline, half-normal saline, and lactated ringers. When a fluid is used to vent the system 400, as described above, all air can be purged out of the system 400. Additionally, knowing that a given amount of vent liquid is used at various stages of clot removal can allow the user to correlate removal of a clot into the catheter after being stuck at the distal end to a rate of vent liquid use. In other words, the amount of vent liquid is different when the clot corked from when it is not corked. Thus, a user or a sensor can look at or measure vent liquid use to determine to turn off the system. If the catheter 410 is aspirating without obstruction (uncorked), then a significant flow of blood will exit the system 400. If the catheter 410 is aspirating while corked, then no blood will appear at the vacuum exit. During a ROAR operation and the catheter 410 is uncorked, the user/sensor will detect some blood at the vacuum exit. Finally, during the ROAR operation when the catheter 410 is corked, the vacuum exit will receive some fluid that is a combination of both blood and vent liquid and, in this state, the flow rate of the vent liquid can indicate if the catheter is corked or uncorked.

[00226] If a surgeon visualizes free flow during vacuum and see a captured clot (for example, in the thrombus trap 200), then the surgeon has the ability to perform a contrast injection with the catheter 410 to confirm revascularization without moving or removing the aspiration catheter 410. This is in contrast to current state-of-the-art aspiration catheters where the catheter removes the clot by holding the clot corked on the end and the surgeon retracts the entire catheter to drag out the corked clot. The increased ability of a smaller diameter catheter to be able to fully ingest or secure a better grip on the clot by drawing a greater amount of it into the catheter is a significant benefit. Many clots are deep enough into the anatomy that it is difficult to get large catheters to the site of the clot. If a smaller diameter catheter can have increased effectiveness through ROAR than a greater number of clots can be accessed and retrieved.

[00227] It is noted that one desirable goal to achieve with the system 400 is to fully ingest a clot and bring it back a standard aspiration canister (in a typical thrombectomy end reservoir) or into the thrombus trap 200. When using a standard aspiration canister and the thrombus trap 200, the system 400 can use the vent liquid to flush the thrombus trap 200 through the intake bleed valve 214 instead of using air. This allows retention of vacuum pressure in the aspiration canister.

[00228] Turning now to embodiments that create maceration but without the forward flow, FIG. 47 illustrates diagrammatically an exemplary embodiment of an aspiration thrombectomy system 600 that operates in a ROAR mode. The system 600 comprises a vacuum source 610 fluidically connected to an input of a controllable vacuum valve 620. (Parts of the vacuum source 610, such as the collection canister, are not illustrated in FIG. 47 for reasons of clarity but are detailed below.) The vacuum valve 620 is fluidically connected to a vacuum input 632 of a manifold 630. The connection can be direct or through a conduit, such as silicone tubing. A vent fluid source or reservoir 640 containing a vent liquid 642 is fluidically connected to a controllable vent valve 650. The vent liquid 642 can be, for example, any of albumin, d5 water, normal saline, half-normal saline, and lactated ringers, to name a few. As used herein, "controllable" means that the device is able to be selected between various states, the selection including analog and/or digital switching. One exemplary embodiment is a digital switching between an open position and a closed with a single command (e.g., a change of bit I/O). The entire working channel of the aspiration thrombectomy system 600 is to be free from air or other gaseous bubbles during use.

[00229] The vent fluid source 640 has a sufficient amount of vent liquid in the reservoir that will not end during a given surgical procedure and this prevents any possibility of air entering the system. If the vent fluid source 640 is flexible, such as with fluid supplied by a parenteral fluid containment bag or an intravenous therapy bag, the gas-free container will shrink as the vent liquid 642 is used. If the vent fluid source 640 is inflexible and has an air or gas pocket, as in a replaceable/removable and sterilizable container, the conduit that transfers the vent liquid 642 from the vent fluid source 640 to the vent valve 650 is at a level within the reservoir to keep the input of that conduit submerged within the vent liquid 642 throughout a given procedure.

[00230] A ROAR catheter 660 defines a working lumen 662 fluidically connecting a distal end 664 thereof to a proximal manifold connector assembly 670 at a proximal end of the ROAR catheter 660, which assembly 670 is described in greater detail below. The ROAR catheter 660 is configured to operate in relatively small vessels. Thus, in an exemplary embodiment, the lumen has an internal diameter of between approximately 0.038" and approximately 0.106" and, in particular, an internal diameter of between approximately 0.068" and approximately 0.088". The proximal manifold connector assembly 670 fluidically connects the lumen 662 to the interior of the manifold 630 and, thereby, the manifold 630 fluidically connects the lumen 662 to the vacuum source 610 through the vacuum valve 620 and to the vent fluid source 640 through the vent valve

650. In use within a vessel, the lumen 662 is filled with a liquid column having a proximal portion and a distal portion. Depending on the context used with respect to the catheter 660, the proximal and distal portions of the liquid column can be a given amount (e.g., less than 20 microliters or less than 5 microliters), can be a given length (e.g., a few mm or cm) or it can be an instance of the column that is approximated by using statistical flow analyses. For example, when discussing whether a distal portion of the fluid column exits the distal end of the lumen 662, that distal portion is a measurable distance at the distal end of the liquid column equal to an instance of liquid present at the plane of the lumen distal exit. In the realm of statistical analysis in this example, the distal portion is a last distal finite element in a finite element analysis (FEA) of the liquid column. Here, the system 600 is used to substantially prevent forward flow. The term "forward flow" is used herein to define an amount of liquid in the lumen 662 that exits the distal end 664 in a distal direction. Forward flow is defined as greater than 6 microliters of fluid (approximately 1 mm of catheter length of ID 0.071" $\approx$ 5.7 μ L). Less forward flow is also included in this definition. For example, the amount of forward flow can be restricted to no greater than 2 microliters or, in a particularly beneficial embodiment, forward flow is approximately zero microliters. In each case, no forward flow means that substantially no liquid exits the distal end 664 in the distal direction.

[00231] Operation of the aspiration thrombectomy system 600 occurs through a controller 700, which can be an analog controller or a digital controller. Examples of the analog controller are shown in FIGS. 25 to 46. An example of a digital controller is described in further detail below. One exemplary configuration for a digital controller is a microcontroller manufactured by Microchip Technology, Inc. The controller 700 is operatively connected to each of the vacuum valve 620 and the vent valve 650 (and to a vacuum motor as described below). The controller 700 selectively opens and closes the vacuum and vent valves 620, 650 such that, when the vacuum valve 620 is opened, the vacuum source 610 is fluidically connected to the liquid column in the lumen 662 and, when the vent valve 650 is opened, vent liquid 642 is fluidically connected to the liquid column in the lumen 662. The timing of these valves is significant so that the controller 700 can change a level of vacuum at the distal end 664 and prevent the distal portion of the liquid column in the lumen 662 from exiting the distal end 664 -- substantially no forward flow. There are two significant actions that contribute to forward flow when operating the valves 620, 650: compliance of the catheter system and the water hammer effect. Each will be discussed in turn. Exemplary configurations of the vacuum and vent valves is shown in FIGS. 25 to 36 in FIGS. 42

to 46. Configurations for the valves include spool valves, pinch valves, rotary valves, and rotary valve having a pintel design.

[00232] To explain timing of the valves to eliminate forward flow, reference is first made to the system depicted in the diagram of FIG. 47. It is noted that the ROAR catheter 660 is a flexible body and, therefore, it has compliance both in the radial direction and in the longitudinal direction. When the distal end 664 is corked with a thrombus (as shown in FIG. 47), vacuum is being applied to the lumen 662. Compliance of the catheter 660, therefore, causes reduction in the diameter of the catheter and reduction in the length of the catheter. When the catheter 660 corks, no flow occurs in the lumen. By having pressure lower than atmosphere within the lumen 662, the catheter 660 shrinks and reduces (shortens radially and longitudinally). This shrinkage acts like a spring squeezing down on the lumen in the catheter – in other words, it is a storage of potential energy. If the vacuum source is then cut off (e.g., the vacuum valve 620 is closed) and the vent valve 650 is opened to the vent fluid source 640, then the catheter 660 elongates and acts as a piston pulling against the vent liquid 642. Further, the vent liquid 642 is at a higher pressure (e.g., atmospheric pressure or slightly elevated by having a higher physical position than the patient) than the fluid in the lumen 662. Consequently, an amount of the vent liquid 642 enters through the vent valve 640 into the manifold 630 and then into the lumen 662 through the proximal manifold connector assembly 670. As the vent liquid 642 flows in and the catheter 660 expands to its normal or free steady state, momentum is created in the fluid column directed towards the distal end 664, referred to herein as a pressure pulse or pressure wave. In other words, a “pressure pulse” or “pressure wave” is momentum within a column of fluid that can act to move a distal portion of the fluid column in the catheter lumen distally out from a distal end of the catheter. This term relates to a given cycle of the vacuum and vent valves 620, 650 and is not limited to a single pressure transmission with that cycle. A pressure pulse, therefore, can include multiple pressure differentials with a given cycle of the vacuum and vent valves 620, 650. Thus, by adjusting a timing of the vacuum and vent valves to match a compliance and length of a particular catheter system (which can include the catheter and also the manifold and valves and other lumens in line with the catheter), a ROAR effect can be achieved for that catheter. In particular, one way to achieve the ROAR effect and prevent forward flow of the distal portion out from the distal end during each cycle is by regulating a timing of the vent valve 650.

[00233] Prior art aspiration thrombectomy systems periodically open and close a vacuum valve. Fluid rushes into the distal end of the catheter while the vacuum valve is open and vacuum is being applied to the fluid column. When the vacuum valve is closed, liquid rushing proximally through the lumen stops by hitting the closed vacuum valve. This causes pressure to build at the vacuum valve and create a bounce-back wave that carries momentum distally towards the distal end and ejects an amount of fluid distally from the distal end of the catheter. This action is referred to as a water hammer effect. The prior art repetitively opens and closes that vacuum valve. Thus, an amount of liquid ejects in a periodic manner out of the distal opening in those devices. This forward flow phenomena is undesirable in the area of thrombus removal because, when liquid is allowed to eject from the distal end and the physician is causing the distal end to approach the thrombus, the liquid could or will move the thrombus further distally, or it could break the thrombus up to allow arterial pressure to push the broken pieces further downstream, e.g., into smaller brain arterial vessels. It would be, therefore, desirable to entirely prevent any distally directed pressure pulse reaching the distal end of the aspiration catheter in a thrombus aspiration removal system. As described herein, the system 600 has a response to the water hammer effect that is tuned to achieve a maximum water hammer effect without causing forward flow, which response achieves the most effective engagement and disruption of the thrombus.

[00234] Proximal and distal pressure measurement devices 690, 692 are illustrated diagrammatically in FIG. 47. In this exemplary embodiment, the proximal pressure measurement device 690 is adjacent or within the proximal manifold connector assembly 670 and/or within the proximal portion of the fluid column, and the distal pressure measurement device 692 is adjacent or within the distal end 664 or within the distal portion of the fluid column. An exemplary embodiment for measurement devices 690, 692 include a pressure transducer manufactured by TransducersDirect.com.

[00235] Measurement in the fluid column of the catheter 660 at or adjacent the manifold 630 and adjacent the distal end 664 reveals a time delay in travel of the pressure pulse — the pressure rises at the manifold 630 first and then pressure rises at the distal end 664 later. By knowing the time delay and the distance between the sensors, the speed of the wave can be calculated. By knowing the distance from the most distal sensor to the tip of the catheter 660, the time it will take for the wave to travel to the distal tip can be calculated. This information can be used by the controller to time the valves properly to stop the pressure pulse. If the pressure pulse is allowed to travel all the

way to the distal end 664, then a distal portion of the fluid column in the lumen 662 will exit the distal end 664, e.g., forward flow. If, during this time, the distal end 664 is corked with a thrombus 4, that pressure pulse could or will eject the thrombus 4 distally. Alternatively, if the distal end 664 is approaching a thrombus 4, any pressure pulse exiting the distal end 664 could or will move the thrombus 4 further distally. Movement of the thrombus 4 in a distal direction before or after it has been captured and corked at the distal end 664 of the catheter 660 is to be avoided. Therefore, the pressure pulse needs to be reversed or stopped before that pressure pulse reaches a point where it could move the thrombus 4 either further downstream or off of the distal end 664 in the distal direction. Such reversal is referred to herein as “quelling” the pressure pulse.

[00236] Operation of the aspiration thrombectomy system 600 with the ROAR effect does not produce the same results as prior art catheters. When operated with the distal end 664 unobstructed, the vacuum valve 620 and the vent valve 650 are periodically opened and closed. Fluid rushes into the distal end 664 of the catheter 660 and into the canister of the vacuum source 610 while the vacuum valve 620 is open and vacuum is being applied to the fluid column. When the vacuum valve 620 is closed, the sudden stop of flow creates the pressure wave generated as described above due to the water hammer effect from the closing of the vacuum valve 620. The controller 700 is timed to control the vacuum and vent valves 620, 650 to create the ROAR effect even when the distal end 664 is open to vasculature and, therefore, any distally directed pressure pulse in the aspiration thrombectomy system 600 is quelled so that substantially no forward flow occurs during a thrombus retrieval procedure. Through experimentation, net flow of liquid at the distal end 664 remains positive in the proximal direction – in other words, while operating with the ROAR effect in the corked or un-corked state, liquid either moves through the distal end 664 towards the vacuum source (when un-corked) or does not flow at all (when corked). In both circumstances, substantially no liquid exits the distal tip 610.

[00237] To accomplish the ROAR effect, the change in the level of vacuum at the distal end is at least approximately 15 inHg, further, at least approximately 20 inHg, and, in particular, at least approximately 25 inHg. A time for the change in the level of vacuum from low to high or from high to low at the distal end is no greater than approximately 50 ms, further, no greater than approximately 30 ms, and, in particular, no greater than approximately 20 ms. This change can be referred to as a maximum pressure delta. Various combinations of these variables include a change in the level of vacuum of approximately 15 inHg and a time for that of no greater than 50 ms, or

the change in the level of vacuum of approximately 20 inHg and a time for that change of no greater than 30 ms, or the change in the level of vacuum of approximately 25 inHg and a time for that change of no greater than 20 ms.

[00238] The ROAR catheter 660 is operated to quell all pressure pulses in an exemplary embodiment according to the graph of FIG. 48. The state of the vacuum valve 620 is shown in the waveform at the top of the graph and the state of the vent valve 650 is shown in the waveform at the bottom of the graph. The repetitive cycle starts at time 0 with the valve starting to open in this exemplary embodiment. At time 1, the vacuum valve 620 is fully open and the vent valve 650 is closed. Vacuum continues until time 2, when the vacuum valve 620 starts to close. Closing of the vacuum valve 620 is not instantaneous and, therefore, the vacuum valve waveform decreases at a sharp angle and is fully closed at time 3. After the vacuum valve 620 is closed, at time 4, the vent valve 650 starts to open. This closing of the vacuum valve 620 initiates a water hammer and the closing of the vacuum valve 620 and subsequent opening of the vent valve 650 causes vent liquid 642 to enter the manifold 630 (and possibly the proximal end of the lumen 662). The potential energy stored in the compliant catheter 660 is also allowed to release due to the change in pressure from the negative pressure generated by the vacuum source 610 to the relatively larger pressure (e.g., arterial) existing in the vent fluid source 640. This combination of events initiates a pressure pulse at time 2 that travels distally through the lumen 662 towards the distal end. If there was no further change in the valves 620, 650, then liquid in the column will eject out from the distal end 664, i.e., forward flow. However, as shown in FIG. 48, after a relatively short vent-open time compared to the vacuum-on time, the vent valve 650 is closed (at time 7) and, shortly thereafter, the vacuum valve 620 is opened. This means that, while the pressure wave is travelling distally along the length of the lumen 662 of the catheter 660, when the vent valve 650 is closed to turn the vent liquid 642 off and the vacuum valve 620 is opened to turn vacuum back on (time 0 of the repeating waveform), switching of these valves 620, 650 causes vent liquid 642 to cease entering the manifold 630 and to move the fluid in the manifold 630 and in the lumen 662 proximally into the collection canister 612 of the vacuum source 610 (see, e.g., FIG. 55). Thus, a reverse momentum is imparted within the fluid column. This reverse momentum is sufficiently large enough to prevent the pressure pulse from ever reaching a point where the distal portion of fluid in the lumen 662 exits the distal end 664 — thereby quelling the pressure pulse and preventing forward flow. The ROAR effect, therefore, retains a level of pressure at the distal end at less than

or equal to physiological pressure. The area 690 of the two waveforms shown in FIG. 48 includes a time at which the pressure pulse has been quelled. The waveforms repeat in a periodic manner to continue the distal-then-proximal momentum pulse without ever allowing the distal portion to exit the distal end 664 of the catheter 660. The rapid change in pressure at the catheter tip from near full vacuum to nearly zero vacuum pressure is the ROAR effect. Under the ROAR effect, pressure at the distal end 664 can rise to just short of being arterial pressure and reversal of that rise is, then, started due to the reestablishment of vacuum. This allows the aspiration thrombectomy system 600 to approach a thrombus 4 without imparting distal movement to the thrombus 4 and to retain the corked thrombus 4 at the distal end 664 without any distal movement of the thrombus 4 caused by a change in pressure within the fluid column.

[00239] Another exemplary embodiment for creating the ROAR effect with the catheter 660 utilizing the vacuum valve 620 and the vent valve 650 is shown in the waveforms of FIG. 49, which are repeated at an exemplary rate of between approximately 1 Hz and approximately 250 Hz, further, between approximately 2 Hz and approximately 20 Hz, still further, between approximately 4 Hz and approximately 12 Hz, in particular, between approximately 6 Hz and approximately 8 Hz. At time 1, the vacuum valve 620 is in the open/on position and the vent valve 650 is in the closed/off position. At approximately time 2, the vacuum valve 620 starts transitioning to the closed/off position. At approximately time 3, the vacuum valve 620 is closed/off. At time 4, the vent valve 650 starts to open and at approximately time 5, the vent valve 650 is fully open. The vent valve 650 remains open while the vacuum valve 620 is closed until time 6, at which the vent valve 650 starts to close. The vent valve 650 is closed at approximately time 7. The vacuum valve 620 starts to open at time 8 and is partially open at approximately time 9. The vacuum valve 620 is full open when near the bottom extent of the curve in the graph. This process is repeated periodically, which in this example is at 10 Hz.

[00240] In what is referred to herein as static aspiration, the distal end 664 of the catheter 660 is pushed against a thrombus 4 while suction is applied to the catheter 660. The lower pressure in the catheter 660 creates a force on the clot 4 equal to a pressure differential across the clot 4 multiplied by the area of the inner diameter of the catheter 660. It is this force that "sticks" the clot 4 to the distal end 664 of the catheter 660 in an attempt to retrieve the clot 4 entirely.

[00241] In the ROAR cycle, suction is applied to the clot by rapidly opening a valve, causing a rapid rise in vacuum pressure. The source of suction is then turned off and a vent fluid source is

rapidly opened. This relieves the vacuum present in the catheter 660, which again rapidly changes the pressure applied to the clot. The vent valve 650 is then rapidly closed and the vacuum valve 620 is rapidly opened. This cycle is repeated multiple times per second. For example, the period for repetition is between approximately 2 Hz and approximately 16 Hz, in particular, between approximately 8 Hz and approximately 12 Hz. The rapid drop of pressure across the clot 4 when the vacuum valve 620 is opened causes the clot 4 to accelerate into the lumen 662 of the catheter 660. The release of vacuum pressure when the vent valve 650 is opened causes the clot 4 to rebound back from the catheter 660. When the vacuum is applied again, the clot 4 once again accelerates towards the catheter 660. These accelerations and rebounds cause the distributed mass of the clot 4 to oscillate. The large internal accelerations of the distributed mass from the oscillation creates internal forces in the clot 4 that are high enough to exceed the tensile strength of the clot 4 and cause it to fail. The torn pieces of clot 4 are then aspirated all the way through the catheter 660 and into the vacuum collection canister 612. To maximize forces in the clot, the pressure differential across the clot and the rate at which this differential pressure is applied is maximized. The higher the rate at which this force is applied to the clot, the higher the internal acceleration of the distributed mass of the clot, and thus the higher the internal forces within the clot, and thus the higher the likelihood of the clot to tear. The times for the pressure change in both the up and down directions are about 20 ms either way. At 8 Hz, for example, each cycle is 125 ms and at 12 Hz each cycle is 83ms. The greater the frequency of the cycle, the greater the number of these impacts that the catheter can have to interact with the clot. Using higher frequencies is, therefore, better, but only up to a point where there is not enough time to cause an effective enough pressure delta within each cycle.

[00242] During operation of the catheter 660 with the ROAR effect, measurement of the pressure pulse can be undertaken with the proximal and distal pressure measurement devices 690, 692. The graph of FIG. 50 illustrates pressure sensed by these devices 690, 692 during the exemplary 10 Hz pulse present in FIG. 49 (FIG. 51 illustrates the graphs of FIGS. 49 and 50 superimposed on one another). The pressure sensed by the proximal pressure measurement device 690 starts at the lower pressure value (approximately at -13 psi) and the pressure sensed by the distal pressure measurement device 692 starts at a higher pressure value (approximately at -11 psi). This represents a partially coked system where an incomplete seal of the thrombus simulant to the catheter allows some flow by creating a slightly lower pressure at the distal measurement. At time

4, vacuum is off and the vent valve 650 starts to open. Accordingly, vacuum in the lumen 662 starts to be relieved. This means that pressure at the proximal pressure measurement device 690 starts to increase, which is evidenced by the upwards curve starting at approximately 4'. A short while later, as the change in pressure propagates distally down the catheter 660, pressure at the distal pressure measurement device 692 starts to increase, which is evidenced by the upwards curve starting at approximately 4''. At time 6, the vent valve 650 starts to close and, therefore, no more vent liquid 642 is entering the manifold 630 to add to or augment the fluid column in the lumen 662. Pressure at the proximal pressure measurement device 690, nonetheless, continues to rise as the vacuum (negative pressure) is entirely removed or is compensated by the pressure of the vent liquid 642. Pressure at the proximal pressure measurement device 690 peaks and, as shown in FIG. 50, the pressure at the peak is at a positive pressure of approximately 2 psi – this occurs even though the aspiration thrombectomy system 600 does not actively apply any positive pressure to the fluid or the lumen 662. Rather, this level of pressure being > 0.0 psi is due to the momentum of the fluid traveling within the lumen 662. Thus, a positive pressure within the lumen 662 is acceptable but it needs to be suppressed before arriving at distal end. At time 8, the vent valve 650 has already closed and the vacuum valve 620 starts to open at approximately the time of peak pressure at the proximal pressure measurement device 690. Opening of the vacuum valve 620 drops pressure within the lumen 662 and stops pressure at the proximal pressure measurement device 690 from going any higher (if not stopped at this level, then it is possible that pressure at the distal pressure measurement device 692 would be > 0.0 psi, which means distal forward flow will occur out from the distal end). Quelling of the pressure pulse is proven by review of the pressure track of the distal pressure measurement device 692. As can be seen in the graph of FIG. 50, the pressure increase at the distal pressure measurement device 692 follows the pressure increase at the proximal pressure measurement device 690. At time 8, pressure recorded at the distal pressure measurement device 692 is still negative (approximately at -5 psi), but is rising. With continued operation of vacuum to and past time 9 (when the vacuum valve 620 is fully open), the peak pressure measured at the distal end 664 by the distal pressure measurement device 692 is less than 0.0 psi (horizontal dashed line), which means that the pressure pulse is quelled and that liquid from the distal portion does not exit the distal end 664, in other words, substantially no forward flow. The ROAR effect allows the clot simulant to remain sealed to the catheter and the system 600 is able to achieve the full vacuum of -13 psi at both measurements. Because the distal

pressure is relieved almost to zero but then shortly arrives at the full -13 psi vacuum, the pressure delta illustrated is approximately 13 psi.

[00243] As described herein, it is possible to force flow from the distal end 664 of the catheter 660 while cycling between vacuum and vent. The rapid switching between vacuum and vent creates forward flow pressure pulses in the fluid column that, if not managed, will force the fluid column out of the distal end 664 of the catheter 660. The waves move through the fluid column at a very high speed through the medium. The speed is primarily a function of the density of the fluid, the compliance of the system (the bulk modulus), and the length of the fluid column. To prevent these waves from forcing the fluid column out of the catheter, the system is considered as a whole and the parameters of the valve switching cycle are set such that the forces that cause the fluid column to flow are controlled. To ensure that the fluid column does not exit the distal end 664 of the catheter 660, it is important that the catheter 660, any extension tube that connects to the catheter 660, the controller 700, and the valving sequence be tuned as a system.

[00244] The goal of the tuning process is at least two-fold: prevent the pressure waves generated during ROAR operation from causing forward flow and optimize the ROAR effect. The length of the fluid column is critical to the tuning of the system. The pressure wave moves rapidly within the fluid column. The time for the wave to reach the distal tip of the catheter is a function of this speed and the length of the fluid column. The speed is a function of the density of the fluid in the column and the bulk modulus of the catheter and extension. The bulk modulus refers to the compliance of the system: both the radial and the longitudinal flexibility of the catheter and the extension tube. The density of the fluid column is not as significant a variable as the bulk modulus unless it changes greatly, such as is the case if the fluid column has gaseous (air) bubbles in it. It is thus, important, to have all air purged from the system prior to implementing ROAR operation. For a given catheter and extension tube configuration, the bulk modulus and the length of the system is fixed. Compliance can be added to the system to change the speed and thus tune the timing of the pressure wave. A flexible length of tubing could be added in-line with the relatively stiff catheter and extension, for example. This flexible length of tubing expands as the pressure pulses occur during ROAR operation. This decreases the bulk modulus of the system and reduces the speed, thus slowing down the pressure wave and increasing its transit time to the distal tip of the catheter. Compliance can be added in other ways as well, such as by including a piston backed by a spring in a bore that communicates with the catheter lumen such that the pressure wave

displaces the piston, which increases compliance of the system. By manipulating the compliance and the valve timing, the system can be tuned for many different combinations of catheters and extension lines. Careful tuning results in achieving a resonant condition. If the suction and release pulses in the catheter are tuned to match a natural frequency of the clot, enhanced ROAR effect can be achieved.

[00245] Tuning can happen statically or dynamically. A statically tuned system is tuned so that the catheter 660 (and any extension tube that connects to the catheter 660) is mated to the controller 700 with a fixed valving sequence (such as the exemplary configuration shown in FIGS. 29 and 30). The controller 700 senses the presence of the catheter 660 when it is attached and verifies that it is the correct one for the tuned sequence of that controller 700. If the correct catheter is not sensed, the tuned sequence does not initiate. A dynamically tuned system is, in comparison, tuned during operation. Prior to operation, a valve sequence is initiated that creates a series of pressure pulses in the catheter 660. Sensors, such as strain gauges, on the catheter 660 and/or an extension tube detect these pulses and are used to adjust parameters of the controller 700 for operation to create the ROAR effect. The catheter 660 contains and transmits critical data, such as its length, to the controller 700. Using this tuning, any catheter, within limits, could be used without causing the fluid column to flow from the distal end 664 during ROAR operation. Alternatively, the catheter 660 and the extension can be tuned at the manufacturer and the specifics of the valve timing can be transmitted to the controller 700 by the catheter 660.

[00246] In an exemplary embodiment, the valve sequence is as follows:

- the vacuum valve 620 is closed;
- a time later the vent valve 650 is opened;
- a time later the vent valve 650 is closed;
- a time later the vacuum valve 620 is opened; and
- a time later the sequence is repeated.

When the vent valve 650 is opened, a bit of vent liquid 642 enters the system and creates a pressure pulse. If the vent valve 650 is not closed, and the vacuum valve 620 is not opened before the pulse reaches the distal end 664 of the catheter 660, the fluid column will exit the distal end 664 of the catheter 660 as forward flow. To prevent the fluid column from exiting the catheter 660, it is this time -- the time that it takes for the pressure pulse to traverse the catheter -- for which the system must be tuned. Additionally, the pressure pulse from closing the vacuum valve 620 in a flow

condition will cause a pressure increase that must be quelled by opening the vent valve 650 before it causes forward flow.

[00247] Tuning is accomplished by selecting appropriate times for the vacuum cycle and the vent cycle. In this regard, the vacuum cycle includes Vacon time 622, Vacon duration 624, Vacoff time 626, and Vacoff duration 628 and the vent cycle includes Vnton time 652, Vnton duration 654, Vntoff time 656, and Vntoff duration 658. Accordingly, tuning is explained with reference to FIG. 52. A cycle time is the duration of the repetition of the entire cycle. At 8 Hz, the cycle time is 125 ms and at 12 Hz, the cycle time is 83.33 ms. The cycle time is determined by adding the Vacon duration 624, the Vnton duration 654 and the first and second times in the cycle that both the vacuum and vent valves 620, 650 are off, referred to as the "double-off" or "double-closed" times or states. The cycle time is optimized by the dynamics or the resonance of a particular catheter 660. The Vacon duration 624 must be long enough for the system to pump down to full vacuum and the longer the vacuum is on during a particular cycle, the better the aspiration of the thrombus 4. In this embodiment, opening only the vacuum valve is referred to as the "vacuum-only" state. The first double-off time, which is the time after the vacuum is turned off (vacuum valve 620 closed) up until the time that venting begins (vent valve 650 opens), has an effect on the extent to which forward flow occurs. As this is a short time, such forward flow is referred to as flow burping. Through experimentation, an exemplary embodiment of an 0.071" inner diameter catheter 660 experiences flow burping when the first double-off time is greater than approximately 30 ms; the longer the double-off time, the greater flow burping. During ROAR operation, the first double-off time is about 10 ms; therefore, this is significantly less than the flow burping threshold, which means that substantially all forward flow is quelled. The Vnton duration 654 is determined by a maximum time that occurs before a coked clot 4 is dropped from forward flow. A ratio between the Vnton duration 654 and the second double-off time is a compromise for the longest Vnton time 654 and a minimum of the first double-off time. In this embodiment, opening only the vent valve is referred to as the "vent-only" state. Finally, with respect to the second double-off time, the vent valve 650 is off (fully closed) before the vacuum valve 620 is opened and vacuum recommences.

[00248] The calculation is explained further with regard to the valve position graphs in FIG. 53. Starting from the left of the graph at Vacon time 622, the vent valve 650 is closed and the vacuum valve 620 is open. The Vacon duration 624 is long enough for the system 600 to pump down to

full vacuum (between approximately 10 ms and approximately 50 ms, in particular, approximately 30 ms). The longer the Vacon duration 624, the better the catheter 660 performs because of increased flow rate in the proximal direction. There is a compromise based on achieving a higher frequency for more hits/sec on the clot 4. In an exemplary embodiment, the Vacon duration 624, calculated from the Vacon time 622 to the Vacoff time 626, is between approximately 40% and approximately 60% of the cycle time 629. As set forth above, the cycle time 629 is a minimum determined by summation of Vacon duration 624 plus the first and second double-off times 625, 627 plus the Vnton duration 654. The Vnton duration 654 is short enough to fill the lumen with vent liquid without causing forward flow (between approximately 10 ms and approximately 50 ms, in particular, approximately 30 ms). The first double-off time 625 is set based upon when open flow burping occurs. The maximum value for the first double-off time 625 applies to either of the periods from the Vacoff time 626 to the Vnton time 652 or the Vacoff time 626 to the Vacon time 622' whichever is shorter. Each of these values are optimized by the dynamics/resonance/compliance/length of the particular catheter 660 and extension set.

[00249] From this, some observations can be made. When the vent is opened, a pressure pulse is generated. It is important to stop the pressure pulse before it reaches the distal end. If the pressure pulse is not stopped before it reaches the distal end, the catheter 660 will experience forward flow. The way to stop the pressure pulse is to either close the vent and/or turn the vacuum back on if the vacuum was off prior to venting. If the vacuum remains on, then there is a need to turn the vent off. Or, if the vacuum does not remain on, the vent is turned off and the vacuum is turned back on before the pressure pulse makes it to the distal end 664. In other words, the vent needs to be closed before the pressure pulse makes it to the distal end 664 and the vacuum has to be turned on. So, the condition of merely opening the vacuum valve 620 when the vent valve 650 is opened may not be enough to quell the pressure pulse because of the low resistance between the vent and the vacuum; the vent will overwhelm the vacuum so the vacuum cannot have an effect over the length of the catheter. The time that it takes for the pressure pulse to propagate to the tip of the catheter 660 and then cause forward flow is used to define the time that the vent valve 650 is left open. The time that the vent is left open is selected to be shorter than the time it takes for the pressure pulse to propagate to the distal end 664.

[00250] In an exemplary embodiment illustrated diagrammatically in FIG. 55, all portions of the aspiration thrombectomy system 600 except for the ROAR catheter 660 are incorporated into the

body 601 of the vacuum source 610. In particular, the vacuum source 610 comprises the body 601, a collection canister 612, and a vacuum motor 614. The vacuum motor 614 is fluidically connected to an outlet of the collection canister 612 and the input of the collection canister 612 is fluidically connected to a vacuum side of the manifold 630. Accordingly, vacuum generated by the vacuum motor 614 imparts vacuum within the collection canister 612 to draw fluid into the collection canister 612 from the manifold 630 but not into the vacuum motor 614. The vacuum valve 620 present at the manifold 630 prevents input fluid received at the manifold 630 from entering the collection canister 612 and closes off the manifold 630 from vacuum generated by the vacuum motor 614. The vent fluid reservoir 640 containing the vent liquid 642 is fluidically connected to a vent side of the manifold 630. The vent valve 650 present at the manifold 630 closes off the manifold 630 from the vent liquid 642 and prevents liquid within the manifold 630 from entering the vent fluid reservoir 640 (as pressure in the manifold 630 is typically lower than pressure within the reservoir 640, liquid from the manifold 630 will not typically enter the reservoir 640). In summary, a catheter input port 631 of the manifold 630 is fluidically connected to the collection canister 612 through the vacuum valve 620 and is fluidically connected to the vent liquid 642 in the reservoir 640 through the vent valve 650. The catheter input port 631 is fluidically connected to the downstream end of the proximal manifold connector assembly 670. The upstream end of the proximal manifold connector assembly 670 is fluidically connected to the proximal end of the catheter 660.

[00251] Direct connection of the catheter 660 to the aspiration thrombectomy system 600 is explained with regard to FIGS. 54 and 55. The proximal manifold connector assembly 670 connects the proximal end 666 of the ROAR catheter 660 to the manifold 630. In an exemplary embodiment shown in FIG. 54, the proximal manifold connector assembly 670 comprises a male luer lock fitting 672 connected to the manifold 630 (shown in dashed lines), either removably or integrally. The assembly 670 includes a ROAR identification (ID) sub-assembly 680. The exemplary embodiment of the ID sub-assembly 680 shown in FIG. 54 comprises an inductive sensing device or sensor 682 connected to the manifold 630. The inductive sensor 682 detects the presence of an inductive sensed part 684 that is present in or integral with the proximal manifold connector assembly 670. In an exemplary embodiment where the manifold 630 can be used with various different ROAR catheters 660, each of the types of ROAR catheters has a unique inductive sensed part 684 and the inductive sensor 682 of the manifold 630 is able to determine which type

of ROAR catheter 660 is attached. Accordingly, with an appropriate communication of the ROAR catheter 660 type to the controller 700, the controller 700 is able to operate the ROAR catheter 660 according to its own unique configuration to produce the ROAR effect for every one of the different ROAR catheters 660 that are used. When the sensor 682 does not detect a sensed part 684 and the aspiration thrombectomy system 600 is, nonetheless, operated, the controller 700 will automatically prevent ROAR operation of aspiration thrombectomy system 600 and that connected catheter will only be operated as a standard vacuum catheter.

[00252] Indirect connection of the catheter 660 to the aspiration thrombectomy system 600 is explained with regard to FIGS. 56. The proximal manifold connector assembly 670 can simply be a fitting 672 as shown in FIG. 54 or it can be or include a separate extension line 674 between the catheter input port 631 and whatever catheter 660 (standard or ROAR) that is to be used along with the aspiration thrombectomy system 600. In an exemplary embodiment of the extension line 674, not only does the extension line 674 comprise a lumen extension for aspiration through the catheter 600, the extension line 674 also comprises system controls for operating the aspiration thrombectomy system 600. These controls include, for example, turning on and off the vacuum motor 614 and turning on the ROAR operation (e.g., one button for each of these or an on/off switch for vacuum and a push-to-start button for ROAR). As shown in the diagram of FIG. 56, the extension line 674 has a distal end that is able to connect to both standard catheters and ROAR catheters 600 -- as both can be used with the aspiration thrombectomy system 600. When the standard catheter is connected to the extension line 674, the aspiration thrombectomy system 660 only acts as a standard vacuum pump and ROAR is disabled. When a ROAR catheter 660 is connected to the extension line 674, identification sub-assemblies in the ROAR catheter 660 and the extension line 674 inform the system 600 which ROAR catheter 660 and which extension line 674 are connected.

[00253] In the exemplary embodiments with digital control of the vacuum and vent valves 620, 650, a processor and memory in the controller 700 stores the identification data and, upon identification of a particular ROAR catheter (e.g., different lengths, different outer diameters, different materials), the controller 700 loads the valve sequence and operates the vacuum and vent valves 620, 650 according to the characteristics of the particular catheter connected to the vacuum source 610. In one exemplary embodiment, the identification data can be preprogrammed at the manufacturer for all ROAR catheters 660 that currently exist. Thus, with direct connection of the

ROAR catheter 660 to the system 600, the controller 700 can operate without receiving any information other than the identity of the catheter 660. If a ROAR extension line 674 is used between the ROAR catheter 660 and the controller 700 (in other words, an extension line that is ROAR compatible and is able to inform the system 600 of its augmentary characteristics to those of the ROAR catheter 660 to which it is connected), the controller 700 can operate without receiving any information other than the identity of the catheter 660 and the identity of the intermediate extension line 674 because connection with the ROAR extension line 674 allows the system 600 to detect which particular one of the different ROAR catheters 660 has been connected to the distal end of the ROAR extension line 674 and then to operate ROAR in a predefined manner appropriate for that particular ROAR catheter 660 with the ROAR extension line 674. In the case of RFID or near field communication (NFC), the chip embedded in the ROAR catheter 660 is programmed with the specific valve timings required by that catheter 660. The controller 700 reads these values and functions properly for that catheter 660. This ensures future compatibility with new generation catheters that require different tuning, which tuning would not be known at the time the controller 700 is programmed at the manufacturer. If the catheter to be used is not a ROAR catheter 660, then ROAR should not be used with that catheter because of the high probability of forward flow at the distal end. Accordingly, the system 600 automatically prevents use of the ROAR effect when a non-ROAR catheter is connected to the distal end of the ROAR extension line 674 or is connected directly to the system 600 or is connected to the distal end of a non-ROAR extension line 674.

[00254] The identification sub-assemblies include various measures present at least at the proximal end of the ROAR catheter 660 (e.g., the inductive sensing system 682, 684 or a I-wire detection system, such as a DALLAS Semiconductor encryption chip, RFID, Bluetooth low energy (BLE), metallic touch pads, a simple passive design based upon resistors (in series for catheter and extension, to name a few). In the sub-assemblies, there can be two or more electrical contacts. For example, there can be three contacts including power, ground, and a signal using a Hall sensor. In a two-contact configuration, there can be a 2-wire configuration using resistors and mechanical switches. Resistance can be measured between two contacts and, depending on the resistance, a state of the switch can be detected. Power and signal can be combined on one line (plus an additional ground line) to create a "one-wire" connection, for example, using a DALLAS chip mentioned above. An identification sub-assembly also can be present at the distal connection (e.g.,

a Luer fitting) of the extension line 674 (to contact with the identification sub-assembly at the proximal end of the ROAR catheter 660) and extend back through the extension line 674 to a communication connection with the vacuum source 610, e.g., the proximal manifold connector assembly 670. Therefore, the aspiration thrombectomy system 600 has an ability to sense/detect when a ROAR catheter 660 is connected as differentiated from a standard catheter (i.e., not ROAR). Connection of the ROAR catheter 660 enables use of the ROAR function; connection of a non-ROAR catheter (or, e.g., to a side port of a rotating hemostasis valve (RHV)) disables use of the ROAR function and only normal aspiration is available. Where the identification sub-assembly includes electrical contacts in the ROAR catheter 660, the conductive connection to the vacuum motor 614 can utilize one or more coils of the ROAR catheter 660 as one of these conductors. Alternatively, two or more conductors can be wrapped within the ROAR catheter 660. Alternatively, or additionally, conductors can be bonded on the outside of the ROAR catheter 660. [00255] In addition to the exemplary embodiments where the system 600 already stores the operating parameters for performing aspiration and automatically uses those parameters when the ROAR catheter 660 and/or the extension line 674 is connected or where the ROAR catheter 660 or the extension line 674 provides the operating parameters for performing aspiration, the user can be provided with selectable programs in the controller. These selectable programs can be, in one exemplary embodiment, programmed where the controller 700 is manufactured. The user has an instruction manual associating the particular ROAR catheter 660 and/or the extension line 674 being used with a code that loads in the operating parameters, such as pressures, delays, timing. Instead of an instruction manual, these operating parameters can be manually entered by the user instead of through the selectable program(s), for example, by reading the information the instructions for use (IFU) or the packaging of the system 600, or ROAR catheter 660, or extension line 674. In addition, if the user has a desired method of operation (for example, to increase a particular timing), the user can enter the parameter(s) directly through a user interface on the system 600. In other exemplary embodiments, a code supplier (e.g., a QR code, a barcode, or an RFID chip) could be on the packaging of one or more of the components and the user presents that code supplier to the controller for reading. In this regard, the system 600 comprises a bar-code reader and/or a QR code reader and/or an RFID communication device. With a display on the system 600, in another exemplary embodiment, the screen presents parameters to the user and those parameters could be fixed or alterable by the user. In other words, the user could accept or

alter the parameters shown. In a particularly inexpensive embodiment, the parameters can be "stored" on a punch card that is supplied with the ROAR catheter 660 or the extension line 674 and the system 600 has a punch card reader. In this embodiment, the user inserts the inexpensive card (e.g., provided with a covering that protects it from liquids present in the operating room) into the card reader and the controller 700 utilizes the parameters on the card or utilizes a code on the card, which code is associated with a set of stored parameters.

[00256] All of these embodiments could present the operator with a choice of alternative programs or parameters, or the system 600 could list the parameters that are about to be utilized separately on a display screen and then allow the operator to select those parameters or alter the provided parameters. Similarly, operators are able to store parameters/programs into empty memories within the controller 700. The stored information provided by the catheter, the extension line, the card, the code, etc., could be either ROAR parameters or, alternatively, the information can be characteristics of the catheter and the extension line so that the controller 700 could make compensations to provide a predefined ROAR waveform at catheter tip. In other words, rather than offer up stored ROAR programs, the catheter and the extension line could simply give information to the controller 700 so that the timing and pressures could be modified for each catheter/extension line combination to achieve the predefined ROAR pressure/time profile. By storing either compensation parameters or actual time/pressure parameters, the controller 700 is able to allow future catheters and extensions not yet available. Further, chips, resistors, RFIDs, or BLE could be used to prevent use of the system 600 with catheters not provided by the manufacturer of the system 600, and/or to present a warning or alarm condition to the operator so that they know that the catheter and/or extension is not supported by the system 600.

[00257] One exemplary embodiment of the proximal manifold connector assembly 670 comprises the extension line 674 having a system control board 676 with remote controls 678 illustrated in FIG. 56. An exemplary embodiment of the remote control 678 is a mechanical slide switch that turns vacuum on or off based upon a longitudinal position. This can be a two position switch with a button for ROAR operation. Alternatively, a three-position switch can be provided. In a forward position, the vacuum is off, in a middle or intermediate position the vacuum is on, and in a rear position ROAR operation takes place. When the remote switch is connected, any control buttons on pump are disengaged but the pump can have an "emergency off" switch on the pump that allows the user to turn off the pump if desired regardless of the operation of the remote controls. LEDs

can be provided on the remote controls 678 and/or on the body 601. These LEDs can, for example, be: Red = off, Green = Vacuum on, Blinking Green = ROAR, Blinking Red = Error, Blue = vent/purge. In an exemplary embodiment, a mechanical redundant pinch valve is present against catheter that, when actuated, pinches closed the lumen of the catheter. In the exemplary embodiment, the distal end of the proximal manifold connector assembly 670 that connected to the ROAR catheter 660 comprises a luer lock part that connects to another luer lock part on the ROAR catheter 660. In various exemplary embodiments, the switch is passive (e.g., a simple mechanical switch) or it is an active switch (e.g., capacitive, pressure, magnetic). In such a case, the switch is powered by wires through the extension line 674. In an alternative embodiment, the switch is a separate module that attaches to the extension line 674 and is, for example, battery-powered.

[00258] A first benefit of the aspiration thrombectomy system 600 is that, with such a configuration, the same vacuum source 610 can be used with all catheters that previously could be connected to any surgical aspiration devices/vacuum pumps. A second advantage relates to security for enacting the ROAR effect. In such a configuration, users are persuaded to connect the proximal end of the ROAR catheter 660 to the distal end of the proprietary extension line 674. This is beneficial for various reasons. First, ROAR will not work unless the two unique ROAR parts are directly connected and a positive ROAR ID is established. Second, if a standard rotating hemostasis valve is connected between the ROAR catheter 660 and the extension line 674 (for whatever reason that the surgeon/nurse may have), then identification will be negative and ROAR will be disabled. There is a risk that fluid contained within lumens of such rotating hemostasis valves will enter into the ROAR catheter's fluid column and, thereby, introduce air bubbles, which need to be purged entirely from the system for use. An RHV 609 increases the probability of air remaining in the lumens or entering the fluid system. See FIG. 72. Thus, a particularly desirable configuration for the ROAR catheter 660 is a direct connection between the proximal end of the ROAR catheter 660 and a distal end of the proprietary extension line 674. There is also an issue of safety to ensure that the ROAR effect is utilized only with ROAR catheters 660. As described above, each ROAR catheter 660 has a particular set of characteristics related to compliance and, therefore, operation of the vacuum and vent valves 620, 650 is set for that characteristic set. The system 600 is set to react with a particular ROAR configuration based upon the physical

characteristics of the ROAR catheter 600 connected, such as length and lumen size. Therefore, the system 600 is tuned/programmed to store a given ROAR setting for each ROAR catheter 660. [00259] However, it is possible that new ROAR catheters 660 and new ROAR extension lines 674 are created after the system 600 or the controller 700 are put into the field. Providing the identity of the ROAR catheter 660 or the ROAR extension line 674 would, therefore, not be sufficient to permit operation of those components properly. Thus, in an additional or alternative embodiment, each of the ROAR catheters 660 and the ROAR extension lines 674 are provided with a memory device (e.g., a DS28E07 EEPROM memory chip) that, when connected to the system 600, provides the controller 700 with the variables necessary for that ROAR catheter 660 and/or that ROAR extension line 674 to operate with the ROAR effect. Example variables that are stored in the memory of each of the ROAR catheters 660 and the ROAR extension lines 674 include, but are not limited to, the frequency of the waveform cycle, a time in the cycle at which the vacuum turns on (Vac on time 622), a duration of the vacuum (Vac on duration 624), a time in the cycle at which the vacuum turns off (Vac off time 626), a duration that the vacuum is off (Vac off duration 628), a time in the cycle at which the vent turns on (Vent on time 652), a duration of the vent (Vent on duration 654), a time in the cycle at which the vent turns off (Vent off time 656), and/or a duration that the vent is off (Vent off duration 658). By being able to provide such information to the controller 700, the system 600 can utilize any future ROAR catheter 660 and/or ROAR extension line 674 that might be created for use with the system 600.

[00260] An exemplary embodiment of a self-contained aspiration thrombectomy system 600 is shown in FIGS. 57 to 71. The system 600 has an exterior body 601 containing therein a vacuum motor 614, the controller 700, and controls for the vacuum and vent valves 620, 650 (exemplary embodiments of the controls for the valves are shown in FIG. 29 and FIGS. 42 to 46). The vacuum motor 614 is fluidically connected to a collection canister 612 (shown diagrammatically with dashed lines). The body 601 houses a set of system controls 676 (in an alternative embodiment, the controls 676 can be located on/also located on the extension line 674). In this exemplary embodiment, there are three buttons: off, purge, and ROAR/Vac. (The purge function will be described in further detail below.) On a side opposite the collection canister 612 is a vent fluid reservoir 640 (shown diagrammatically with dashed lines) containing therein vent liquid 642. As mentioned above, the fluid path of the catheter 660 is to be free from bubbles/air at all times during a surgical procedure.

[00261] The body 601 has cassette connection assembly 602 on a front face thereof. The cassette connection assembly 602 protrudes from the front face and has an exterior shape substantially the same as a cassette 710 that will be attached thereto. The vacuum and vent valves 620, 650 protrude from the front face 608 of the cassette connection assembly 602 and, in an exemplary embodiment, are centered within respective depressions of the cassette connection assembly 602. In this embodiment, the vacuum and vent valves 620, 650 are pistons that have at a distal-most end thereof a pinching structure. In this exemplary embodiment, the pinching structure is substantially in the shape of a standard slot screwdriver. As the vacuum and vent pistons extend out from the depression a given distance (e.g., 8 mm), the slot presses against tubing (in the cassette 710) to close off the lumen within the respective vacuum or vent hose. Closing off the hose acts as a shut-off of the respective valve and releasing away from the hose acts to open the vacuum or vent, respectively. Thus, if the hoses for each of the vacuum and vent lines are placed directly in front of the pistons, the valves 620, 650 will control vacuum and vent according to the ROAR process described herein. (As described below, the cassette 710 positions those hoses in this manner.) In between the valves 620, 650 is a boss 604 protruding from the front face 608 of the cassette connection assembly 602. The boss 604 has an exterior surface with a given shape, e.g., a raceway, and orientation wings 605. At the end of the boss 604 is a rotating lock 606 in the shape of half circle or half oval. The rotating lock 606 has a central pivot to allow it to rotate 90 degrees from the position shown in FIGS. 57 to 67. In the rotated orientation, therefore, the rotating lock 606 defines lower surfaces (opposite the front face 608 of the cassette connection assembly 602) that are perpendicular to the protruding extent of the boss 604. These lower surfaces are set at a distance to define a gap between the lower surface of the rotating lock 606 and the front face 608 of the cassette connection assembly 602. Also present on the front face 608 of the cassette connection assembly 602 is/are conductive connectors 618. The conductive connectors 618 are used to detect when a cassette 710 is present and locked on the cassette connection assembly 602. Detection of the cassette 710 can be made by mechanical measures (such as a pogo pin) or a combination of mechanical and optical and electrical measures.

[00262] A cassette 710 is removably connected to the cassette connection assembly 602 and an exemplary embodiment of this cassette 710 is illustrated in FIGS. 68 to 71. As shown in FIG. 68, the cassette 710 has an interior orifice 712 with a shape corresponding to the given shape of the boss 604. The boss 604 and interior orifice are matched in shape so that the cassette 710 can fit

onto the boss 604 and slide down thereon until the rear face of the cassette 710 aligns with and/or touches the front face 608 of the cassette connection assembly 602. The rear face of the cassette 710 is depicted in FIG. 69. In the view of FIG. 69, pockets 714 corresponding in shape to the orientation wings 605 are present in the interior surface of the cassette 710 at the interior orifice 712. In this regard, when the cassette 710 is slid down the boss 604, there is only one orientation in which the cassette 710 can approach the front face 608 in a lower-most position e.g., as in a key within a keyhole. This placement insures that the distal end effectors of the vacuum and vent valves 620, 650 are always aligned with vacuum valve area 720 and the vent valve area 750 within the cassette 710.

[00263] When the "T" shape of the boss 604 and wings 605 are matched with the interior T-shape of the orifice 712, three connections are made possible. First, as set forth above, the distal end effectors of the vacuum and vent valves 620, 650 are aligned with vacuum and vent valve areas 720, 750 within the cassette 710. Second, conductive connectors 718 on a rear face of the cassette 710 are aligned with and make contact with respective conductive connectors 618 adjacent the boss 604. These connectors 718, 618 can be, for example, respective pads and pogo pins to insure positive electrical connection when the rotating lock 606 is used to lock the cassette 610 onto the body 611. With appropriate electrical connections, these connectors 718, 618 can inform the controller 700 that the cassette 710 is installed and ready for use and which kind of cassette 710 is installed if it is associated with a particular ROAR catheter 660 and needs identification. Finally, the rotating lock 606 is located above the front face 608 of the cassette connection assembly 602 and the bottom surfaces of the rotating lock 606 are above the outer front face 716 of the cassette 710. A protrusion distance of the boss 604 is configured to place bottom surfaces of the rotating lock 606 (those surfaces facing the front face 608) at a distance approximately equal to the thickness of the cassette 710 such that, with rotation of the lock 606, the bottom surfaces of the lock 606 engage the outer front face 716 of the cassette 710, thereby pressing the cassette 710 firmly in place against the front face 608 to touch the connectors 718, 618 together and locking the cassette 710 to the body 601. The quarter-turn rotating lock 606 secures the cassette 710 on the body 601 and also provides a cam force that holds the cassette 710 thereon, in particular, while the valves 620, 650 actuate against vacuum and vent tubing present within the cassette 710. In an exemplary embodiment, a non-illustrated switch is integrated in the rotating lock 606, the switch

detecting the quarter-turn and, with the electrical connectors 718, 618, verifying that the system 600 is armed and ready for use.

[00264] In a particularly efficient configuration, the cassette 710 can be removable, replaceable, and disposable as an entire set including the junction box shown in FIGS. 68 to 71 and a tubing set. The cassette 710 has as set of relatively short whips of tubing including a first tubing whip 722 fluidically connected to the collection canister 612 of the vacuum source 610 and a second tubing whip 752 fluidically connected to an intake of the vent valve 650, and an extension whip that can be the extension line 674 or it can be a short tubing to be connected directly to the catheter 660. Once connected, this efficient configuration allows the system of lumens to be automatically cleared of air/bubbles. By locating the vent liquid above all of the lumens (such as with the bag 640 in FIG. 67), the catheter 660, and the collection canister, opening the output of the vent fluid reservoir 640 will fill all interior lumens and clear the system of any air/bubbles before use. If desired, a cam lock can be mechanically connected to the vacuum motor 614 (either temporarily or fixed) and the motor 614 can be operated to actively draw all air into the collection canister and thereby purge the system 600. As an alternative to the front-loaded configuration of the cassette 710, the cassette 710 can be connected or molded as a part of a bottom of the disposable collection canister 612. In this configuration, two disposable parts can be provided together in a sterile packaging and disposed of in one piece. With a vent fluid reservoir that is either a hard container (FIGS. 57 to 61) or a bag (FIGS. 62 to 67), the vent liquid 642 can be part of the cassette 700 with all lumens pre-filled with saline and part of a single disposable package. The vent fluid reservoir 640 and the collection canister 612 can either or both be part of a disposable cassette 700 system. All of the disposable parts used in a catheter procedure can be integrated together in one disposable package.

[00265] As explained previously, it is important for the system to be purged of air to achieve the ROAR effect. Purging can be achieved in several ways. The two main methods used to purge the system are forced purge and dribble purge. The forced purge method involves submerging the tip of the extension line 674 into sterile fluid such as saline and while submerged activating the "purge" function. The controller 700 will then alternatively open one or both of the control valves for a predetermined time and sequence to pull the sterile fluid through the extension line 674 and valves and displace all the air that may have been in the system. Once this purge process is complete, both valves will close and the extension line 674 with a full fluid column can be

connected to the catheter which has also be de-aired and ROAR applied. In comparison, the dribble method relies on a small positive pressure (created by gravity, squeezing the fluid bag, pressurizing the vent fluid tank, or a peristaltic pump or any similar measures) to allow the vent fluid to dribble through the lumens and, thus, flood them. In an exemplary case of the dribble purge system, the vent fluid source 640 is higher than the exit of the extension line 674 and the vent liquid path does not contain any air traps.

[00266] For the dribble method, the purge cycle is initiated by pressing the purge button and, in an exemplary embodiment, is performed by the controller 700. With the vacuum valve 620 closed, the vacuum source 610 is turned on and the vacuum vessel is pumped down to a desired vacuum level. The vent valve 650 is opened and vent liquid 642 is allowed to flood the vent line and the extension line 674. To ensure that all air is removed from the manifold 630, the vacuum valve 620 is opened momentarily while the vent valve 650 is also open. This allows the vent liquid 642 to be drawn from the vent fluid source 640 and from the extension line 674, and through the vacuum manifold passageways thus purging them of air. The vent valve 650 is left open for a period of time after the vacuum valve 620 closes to ensure that the quantity of fluid that the vacuum cycle removed from the extension line 674 is replenished. This cycle of vent liquid flow and momentary vacuum can be repeated several times to ensure complete purging. The purge pump can be a peristaltic pump, a pressurized cuff around a flexible vent liquid container (such as an IV bag), and/or a vent fluid canister pressurized by using the exhaust from the vacuum source 610.

[00267] The presence of bubbles in the fluid system adversely affects the water-hammer effect. Accordingly, the system 600 facilitates or automatically purges air from the fluid lumens. In an exemplary embodiment, bubble sensors (either optical, ultrasonic, or fluid-pressure-profile based) are incorporated into the system 600 to facilitate this purging or to automatically engage a purging function (e.g., under operator control to prevent purging when the catheter 660 is present in the bloodstream). There are various measures for bubble detection. For example, an optical sensor could be placed in the cassette 710 to sense the presence of bubbles. With a sensor coupled to the vacuum source 610, a slow rise in pressure can be sensed to prevent using the incorrect catheter or extension. The specific compliance of a catheter 660 or an extension line 674 is among the parameters used to program or compensate the system 600. A user-feedback indication informs the user when the system has been sufficiently purged. In an exemplary embodiment, the compliance of the catheter 660 and the extension line 674 are controlled to be below some optimum

range. Also, pressure-rise information is used to modify the ROAR settings, for example, to detect corking and provide an optimum pressure profile for that condition.

[00268] The exemplary configurations of the aspiration thrombectomy system 600 described and shown provide various significant benefits. Before describing these additional benefits, reference is made to FIG. 72, which illustrates one exemplary embodiment of the aspiration thrombectomy system 600 with extension lines 674, and catheters 660. The aspiration thrombectomy system 600 comprises the vacuum source 610 with the collection canister 612, the vent liquid reservoir 640 with the vent liquid 642, the manifold 630, and the proximal manifold connector assembly 670. Removably connected to the proximal manifold connector assembly 670 is a ROAR extension line 674. Next to the ROAR extension line 674 is an off-the-shelf extension line 674' usable both with the system 600 by connecting through the proximal manifold connector assembly 670 and with conventional surgical vacuum sources. The ROAR extension line 674 comprises the system controls 676, which are also shown on a top surface of a frame of the system 600. Also shown is a ROAR catheter 660 and an off-the-shelf aspiration catheter 660'. With proximal Luer connectors, both catheters 660, 660' can be used with either extension line 674, 674'.

[00269] There are several topologies for the disposable, reusable, and limited-reuse components of the aspiration thrombectomy system 600 as described and shown herein. The vacuum source 610 can be a limited-reuse component that plugs into a reusable electronics/power-supply system, such as the frame in FIG. 72. The valve-element cassette 710 includes pinch-tubes and, therefore, it is a single-use only component. Alternatively, the valving components can be reusable, for example, where the valve actuator is separate, either in a separate semi-reusable module, or part of the pump/control system. The different kinds of valves (e.g., rotary, trumpet) that have different ways to separate the disposable/reusable portions of the system 600. The valve actuators can be part of a reusable portion or part of a limited-reuse portion (e.g., along with a pump module). Alternatively, the valve-actuators can be a second limited-reuse module. The cassette 710 with the valve elements can include a diaphragm or piston that is actuated by a mechanical actuator in the reusable part of the system 600. With such modularity, the architecture of the system 600 becomes adaptable to use with any vacuum source, even a household vacuum system (which could include a vacuum pressure regulator to ensure uniformity of the system 600. The power source for the system 600 may be a rechargeable battery or a replaceable module attached to the system 600, in which case the latter does not require sterility. Alternatively, the power source is a primary

battery included as part of the disposable components, which could include disposable pumping elements.

[00270] The various configurations permit multiple product topologies specifically targeted at different use cases. For example, one topology is a minimum-recurring-cost system with only the tubing set being disposable. Alternatively, another topology is a system requiring minimum capital cost and incorporating modules whose costs are easily amortized for each surgical case.

[00271] Various additional safety measures can be added to the system 600. For example, a liquid level detector can be provided at or with the vent fluid reservoir 640 to confirm that vent liquid 642 is within the tank or pouch, to indicate a warning to the user when the level of vent liquid is low, and to prevent operation of the system 600 if the vent liquid about to run out or is empty. In the configurations with the cassette 710, the system 600 will not start unless the cassette 710 is in place and is correctly installed. The system 600 can have a purging function that is used to fill the various lumens of the catheter 660, the extension line 674, and any tubing connecting the vent fluid reservoir 640 and the collection canister 612 before use. It is noted that the system 600 should not be operated if air is present anywhere in the lumens. Thus, the controller 700 can operate the system to draw in vent liquid 642 and fill the various lumens in a pre-use setup phase. This could include having the vacuum motor 614 operate in reverse to apply positive pressure for purging the various lumens. Alternatively, the controller 700 could actuate a peristaltic pump to purge vent fluid through the lumens. The controller 700 can be programmed, during operation of the system 600, to detect peaks of use during ROAR. If these peaks are not sharp, then a conclusion that air is present in the system can be determined. Bubble detectors (i.e., ultrasonic) can be added to the system such that they straddle the tubing in the cassette and provide feedback to the controller to ensure that the tubing has been properly purged. With such a conclusion, the controller 700 can be programmed to cease operation and start an auto-purge routine to flush the various lumens with an external liquid source or from the vent fluid reservoir 640.

[00272] It is noted that various individual features of the inventive processes and systems may be described only in one exemplary embodiment herein. The particular choice for description herein with regard to a single exemplary embodiment is not to be taken as a limitation that the particular feature is only applicable to the embodiment in which it is described. All features described herein are equally applicable to, additive, or interchangeable with any or all of the other exemplary embodiments described herein and in any combination or grouping or arrangement. In particular,

use of a single reference numeral herein to illustrate, define, or describe a particular feature does not mean that the feature cannot be associated or equated to another feature in another drawing figure or description. Further, where two or more reference numerals are used in the figures or in the drawings, this should not be construed as being limited to only those embodiments or features, they are equally applicable to similar features or not a reference numeral is used or another reference numeral is omitted.

[00273] The foregoing description and accompanying drawings illustrate the principles, exemplary embodiments, and modes of operation of the systems, apparatuses, and methods. However, the systems, apparatuses, and methods should not be construed as being limited to the particular embodiments discussed above. Additional variations of the embodiments discussed above will be appreciated by those skilled in the art and the above-described embodiments should be regarded as illustrative rather than restrictive. Accordingly, it should be appreciated that variations to those embodiments can be made by those skilled in the art without departing from the scope of the systems, apparatuses, and methods as defined by the following claims.

CLAIMS

What is claimed is:

1. A clot removal system, comprising:

a catheter having a proximal end and a distal end and defining a lumen configured to be filled with a liquid column having a proximal portion;

a vacuum pump configured to supply vacuum;

a vent container holding a vent liquid;

a vent valve configured to fluidically communicate:

with the vent liquid in the vent container; and

with the proximal portion of the liquid column at the proximal end of the catheter;

a vacuum valve configured to fluidically communicate:

with the vacuum from the vacuum pump; and

with the proximal portion of the liquid column at the proximal end of the catheter; and

a controller configured to carry out a pre-determined pattern of opening and closing the vent and vacuum valves to change a level of vacuum at the distal end and, while changing the level of vacuum at the distal end, to substantially prevent forward flow of liquid at a distal end of the liquid column.

2. The system according to claim 1, wherein the liquid at the distal end of the liquid column is one or more of albumin, d5W water, normal saline, half-normal saline, lactated Ringer's solution, and blood, and mixtures thereof.

3. The system according to claim 1, further comprising:

a manifold comprising the vent valve, the vacuum valve, and an output; and

an extension line fluidically connecting the proximal end of the catheter to the output of the manifold.

4. The system according to claim 1, wherein a portion of the pre-determined pattern includes a time period where both the vent and vacuum valves are closed.

5. The system according to claim 4, wherein the controller is configured to open and close the vent and vacuum valves in a repeated cycle comprising a double-closed state in which both the vent and vacuum valves are closed.

6. The system according to claim 5, wherein a time of the double-closed state is no greater than 30 ms.

7. The system according to claim 1, wherein the controller is configured to open and close the vent and vacuum valves in a repeated cycle comprising a vent-only state in which the vacuum valve is closed and the vent valve is open, and a time of the vent-only state is no greater than 50 ms.

8. The system according to claim 1, wherein the controller is configured to repeatedly and periodically carry out the pre-determined pattern.

9. The system according to claim 1, wherein the controller is configured to selectively open and close the vent and vacuum valves in a repeated cycle comprising:

a vacuum-only state in which the vacuum valve is open and the vent valve is closed;

a first double-closed state in which the vacuum valve is closed and the vent valve is closed;

a vent-only state in which the vacuum valve is closed and the vent valve is open; and

a second double-closed state in which the vacuum valve is closed and the vent valve is closed.

10. The system according to claim 1, wherein the controller is configured to selectively open and close the vent and vacuum valves in a repeated cycle comprising a vacuum-only state in which the vacuum valve is open and the vent valve is closed, followed by a first double-closed state in which the vacuum valve is closed and the vent valve is closed and a time of the first double-closed state is no greater than 30 ms, followed by a vent-only state in which the vacuum valve is closed and the vent valve is open, followed by a second double-closed state in which the vacuum valve is closed and the vent valve is closed.

11. The system according to claim 9, wherein a time between an opening of the vent valve and a closing of the vent valve is between approximately 10 ms and approximately 50 ms.

12. The system according to claim 9, wherein a frequency of the cycle is between approximately 6 Hz and approximately 16 Hz.

13. The system according to claim 9, wherein a frequency of the cycle is between approximately 8 Hz and 12 Hz.

14. The system according to claim 1, wherein the change in the level of vacuum at the distal end is one of:

greater than approximately 15 inHg and occurs in no greater than approximately 50 ms;

greater than approximately 20 inHg and occurs in no greater than approximately 30 ms; and

greater than approximately 25 inHg and occurs in no greater than approximately 20 ms.

15. The system according to claim 1, wherein:

the lumen has a diameter of between approximately 0.038" and approximately 0.106"; and

the controller is configured to repeatedly and periodically carry out the pre-determined pattern of opening and closing the vent and vacuum valves at a frequency of between 2 and 16 Hz.

16. The system according to claim 1, wherein:

the lumen has an internal diameter of between approximately 0.068" and approximately 0.088";
and

the controller is configured to repeatedly and periodically carry out the pre-determined pattern of opening and closing the vent and vacuum valves at a frequency of between 6 and 12 Hz.

17. The system according to claim 1, wherein the controller is configured to open and close the vent and vacuum valves in a repeated cycle of the pre-determined pattern and prevent forward flow of the liquid column out from the distal end during each cycle by regulating timing of the vent valve.

18. The system according to claim 1, wherein the controller is configured to open and close the vacuum valve and the vent valve in a repeated cycle of the pre-determined pattern to retain a level of pressure at the distal end at less than physiological pressure.

19. The system according to claim 1, wherein the controller is one of a mechanical valve controller and an electronic valve controller.

20. The system according to claim 1, which further comprises a shaft and the vent and vacuum valves are cam-driven valves with respective cams mounted together on the shaft.

21. A clot removal system, comprising:

a catheter having a proximal end and a distal end and defining a lumen configured to be filled with a liquid column having a proximal portion;

a vacuum pump configured to supply vacuum;

a vent liquid container holding a vent liquid;

a vent valve configured to fluidically communicate:

with the vent liquid in the liquid container; and

with the proximal portion of the liquid column at the proximal end of the catheter;

a vacuum valve configured to fluidically communicate:

with the vacuum from the vacuum pump; and

with the proximal portion of the liquid column at the proximal end of the catheter; and

a controller configured to carry out a pre-determined cycle of opening and closing the vent and vacuum valves to change a level of vacuum at the distal end and, during each cycle, to substantially prevent forward flow of liquid at the distal end of the liquid column.

ASPIRATION THROMBECTOMY SYSTEM AND METHODS FOR THROMBUS REMOVAL WITH
ASPIRATION CATHETER

Abstract of the Disclosure

A clot removal system includes a catheter having proximal and distal ends and defining a lumen configured to be filled with a liquid column having a proximal portion, a vacuum pump supplying vacuum, a vent container holding vent liquid, a vent valve configured to fluidically communicate with the vent liquid and with the proximal portion of the liquid column at the proximal end of the catheter, a vacuum valve configured to fluidically communicate with the vacuum and with the proximal portion of the liquid column at the proximal end of the catheter, and a controller configured to carry out a pre-determined pattern of opening and closing the vent and vacuum valves to change a level of vacuum at the distal end and, while changing the level of vacuum at the distal end, to substantially prevent forward flow of the liquid at a distal end of the liquid column.

Electronic Patent Application Fee Transmittal				
Application Number:				
Filing Date:				
Title of Invention:		ASPIRATION THROMBECTOMY SYSTEM AND METHODS FOR THROMBUS REMOVAL WITH ASPIRATION CATHETER		
First Named Inventor/Applicant Name:		DEREK DEE DEVILLE		
Filer:		Gregory L. Mayback/Chris Mendez		
Attorney Docket Number:		Syn2.0/ROAR CON		
Filed as Small Entity				
Filing Fees for Track I Prioritized Examination - Nonprovisional Application under 35 USC 111(a)				
Description	Fee Code	Quantity	Amount	Sub-Total in USD(\$)
Basic Filing:				
UTILITY FILING FEE (ELECTRONIC FILING)	4011	1	75	75
UTILITY SEARCH FEE	2111	1	330	330
UTILITY EXAMINATION FEE	2311	1	380	380
REQUEST FOR PRIORITIZED EXAMINATION	2817	1	2000	2000
Pages:				
Claims:				
CLAIMS IN EXCESS OF 20	2202	1	50	50
Miscellaneous-Filing:				

Description	Fee Code	Quantity	Amount	Sub-Total in USD(\$)
PROCESSING FEE, EXCEPT PROV. APPLS.	2830	1	70	70
Petition:				
Patent-Appeals-and-Interference:				
Post-Allowance-and-Post-Issuance:				
Extension-of-Time:				
Miscellaneous:				
Total in USD (\$)				2905

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Title of Invention:	ASPIRATION THROMBECTOMY SYSTEM AND METHODS FOR THROMBUS REMOVAL WITH ASPIRATION CATHETER
First Named Inventor/Applicant Name:	DEREK DEE DEVILLE
Customer Number:	27316
Filer:	Gregory L. Mayback/Chris Mendez
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The Director of the USPTO is hereby authorized to charge indicated fees and credit any overpayment as follows:	

File Listing:					
Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	TrackOne Request	2019-11-12_Syn_ROAR_Con_Request_Expedited_Examination_86082-13.pdf	113952	no	2
			432def480e685320f5d1e5b7ddd43c8879da8a14		
Warnings:					
Information:					
2	Transmittal of New Application	2019-11-12_Syn_ROAR_Utility_Transmittal_86082-13.pdf	280598	no	2
			060a3ddb3c3512e0435b55c578ed7ef78292beb15		
Warnings:					
Information:					
3	Application Data Sheet	2019-11-12_SYN_ROAR_Con_A DS_86082-13f.pdf	1257038	no	11
			579a42fd2a69e89e1c7765d29b69dd8d8fbc9eb0		
Warnings:					
Information:					
4	Drawings-other than black and white line drawings	2019-11-12_Syn_Roar_CON_Drawings_86082-13.pdf	4431374	no	29
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Warnings:					
Information:					
5	Oath or Declaration filed	2019-11-12_Syn_ROAR_Con_Executed_Dec_Derek_Deville_86082-13.pdf	654980	no	1
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Warnings:					
Information:					
6	Oath or Declaration filed	2019-11-12_Syn_ROAR_Con_Executed_Dec_Matthew_Palmer_86082-13.pdf	675656	no	1
			d430e6c38de96bd4d43fe5b2be4498fb586b18a7		
Warnings:					
Information:					

7	Oath or Declaration filed	2019-11-12_Syn_ROAR_Con_Executed_Dec_William_Bales_86082-13.pdf	646971	no	1
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Warnings:					
Information:					
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Warnings:					
Information:					
9	Oath or Declaration filed	2019-11-12_Syn_ROAR_Con_Executed_Dec_Eric_Petersen_86082-13.pdf	647757	no	1
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Warnings:					
Information:					
11	Oath or Declaration filed	2019-11-12_Syn_ROAR_Con_Executed_Dec_Thomas_Bales_86082-13.pdf	645272	no	1
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Warnings:					
Information:					
12	Oath or Declaration filed	2019-11-12_Syn_ROAR_Con_Executed_Dec_Carlos_Rivera_86082-13.pdf	644794	no	1
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Warnings:					
Information:					
13		2019-11-12_ROAR_Con_Spec_f.pdf	2400286	yes	84
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	Multipart Description/PDF files in .zip description				
	Document Description		Start	End	

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	Claims		79	83
	Abstract		84	84
Warnings:				
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Information:				
14	Fee Worksheet (SB06)	fee-info.pdf	40464	no
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Warnings:				
Information:				
Total Files Size (in bytes):			13328460	
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