

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 guide catheter;
- 5 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.

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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.

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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.

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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.

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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.

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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.

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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.

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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.

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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;

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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.

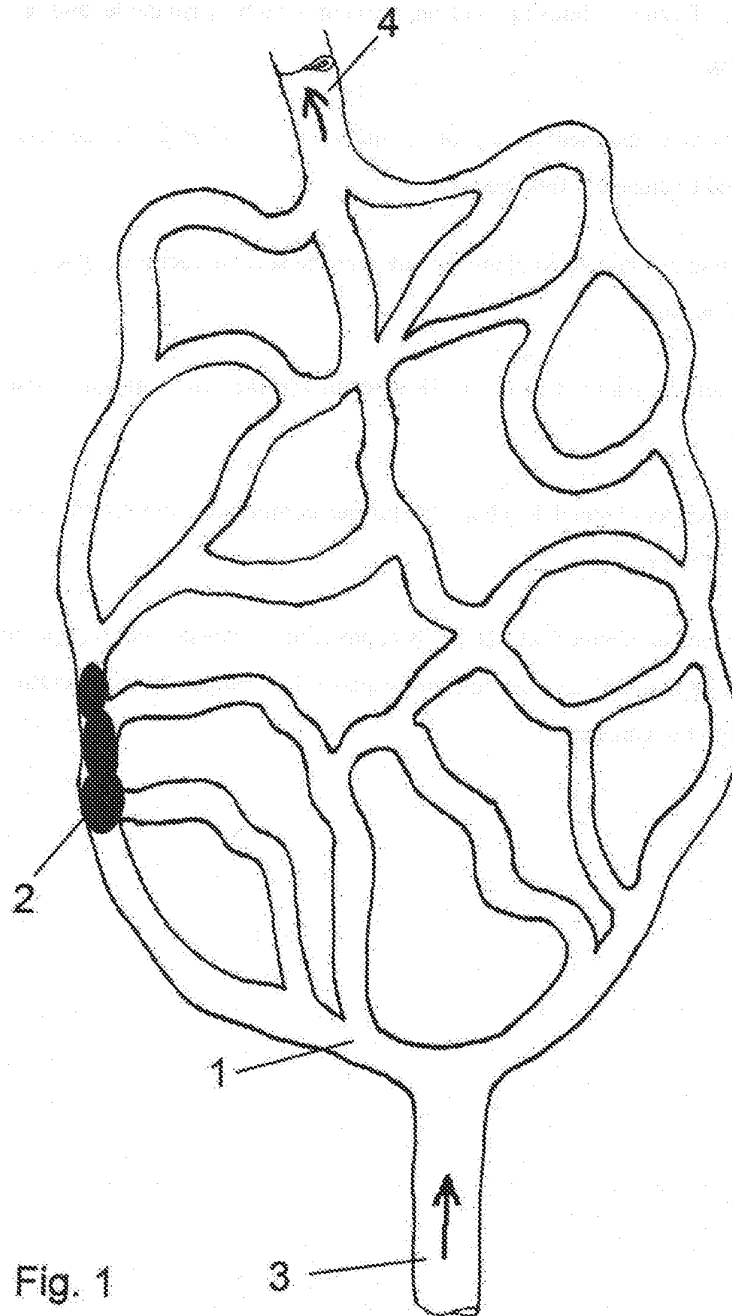
36. A system as claimed in claim 34 wherein applying a variable pressure differential to the clot is adapted to change the friction between the clot and the catheter from static to dynamic friction reducing the total friction and facilitating aspiration into the catheter.
- 5 37. A system as claimed 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.
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



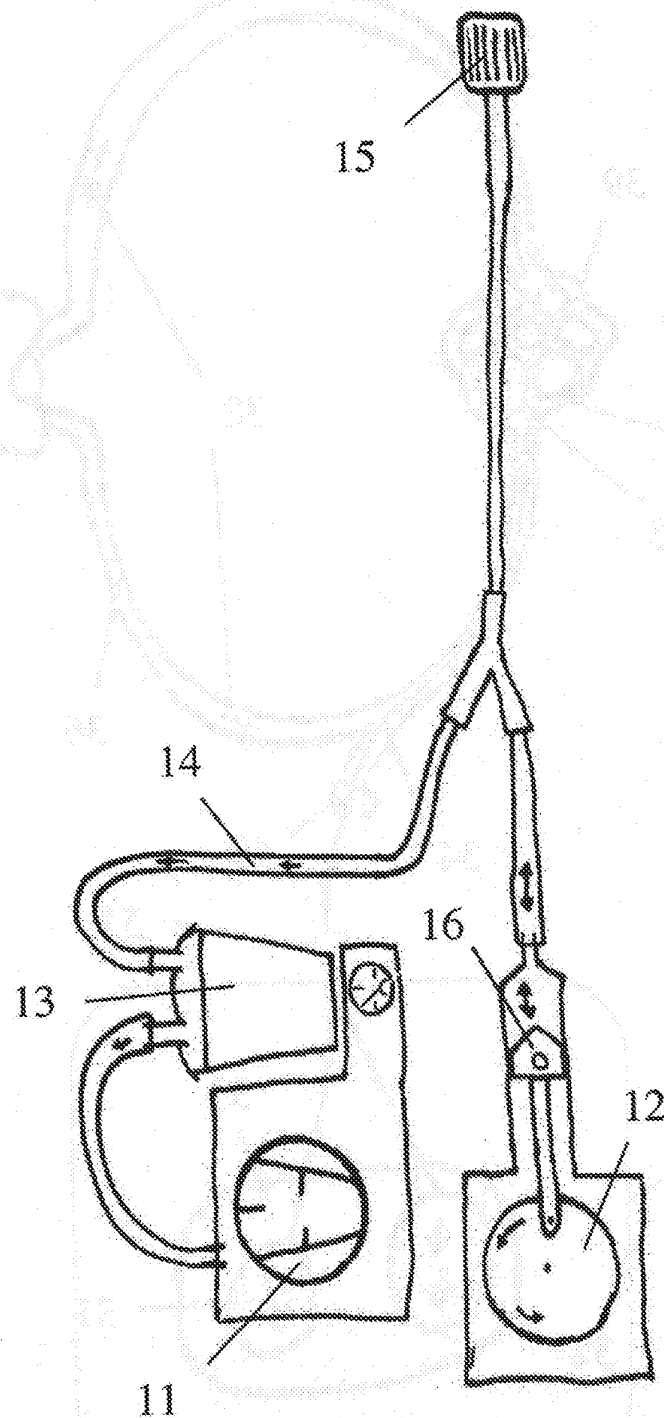
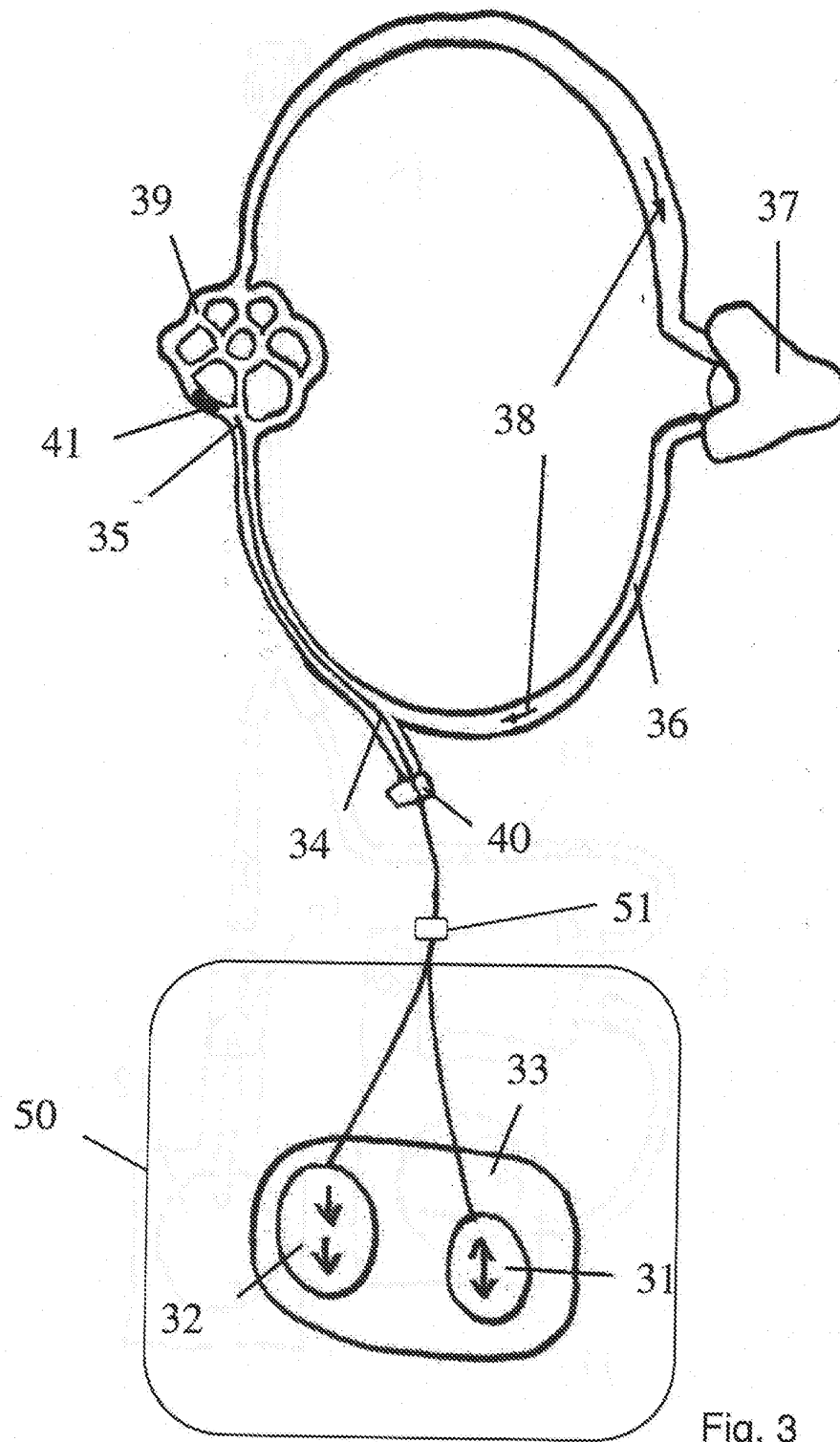


Fig. 2



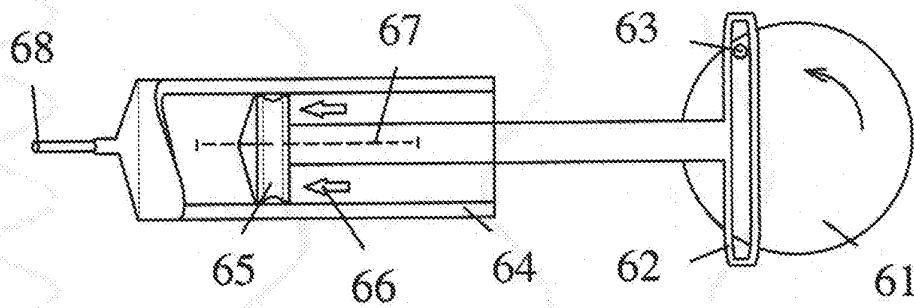


Fig. 4A

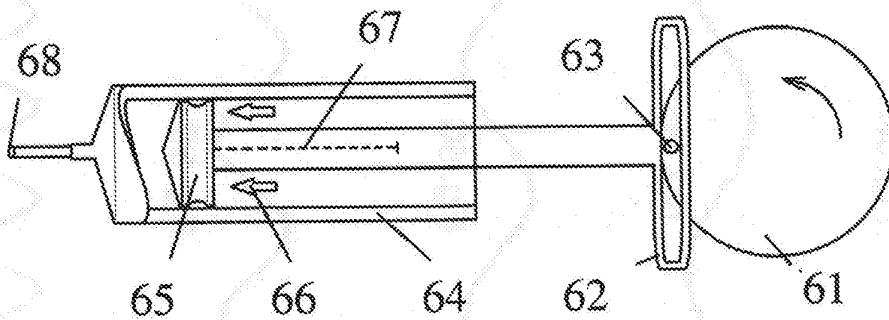


Fig. 4B

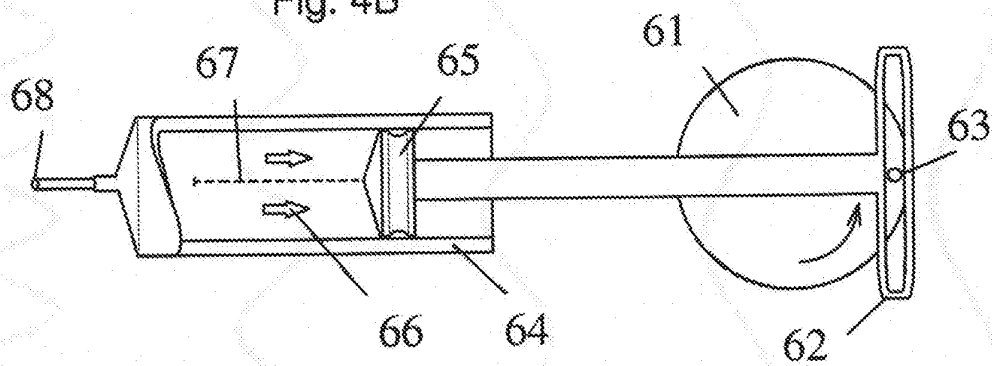
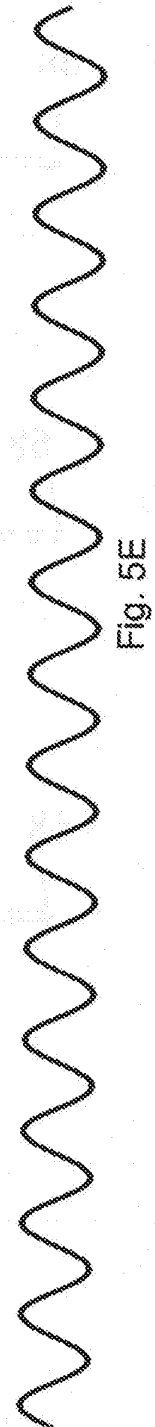


Fig. 4C



SUBSTITUTE SHEET (RULE 26)

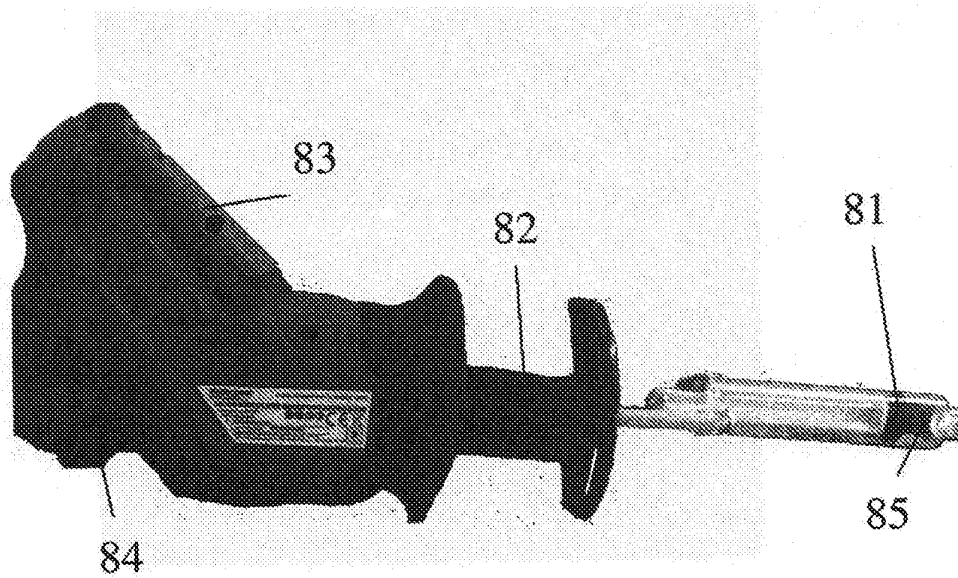


Fig. 6

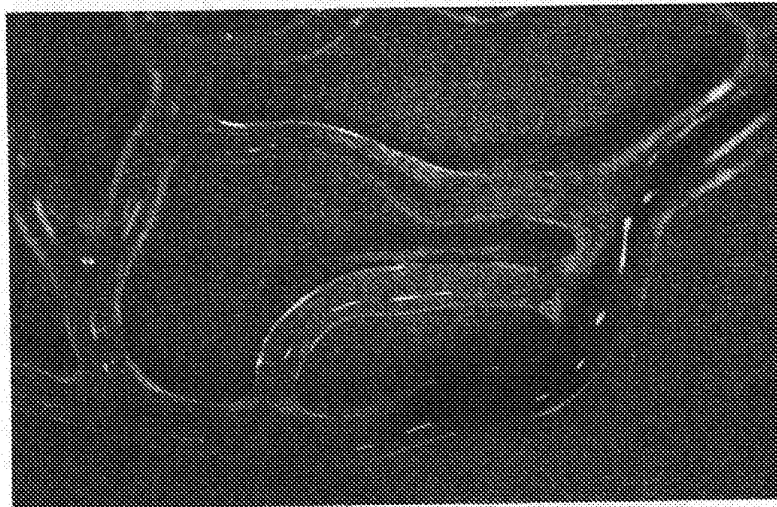


Fig. 7

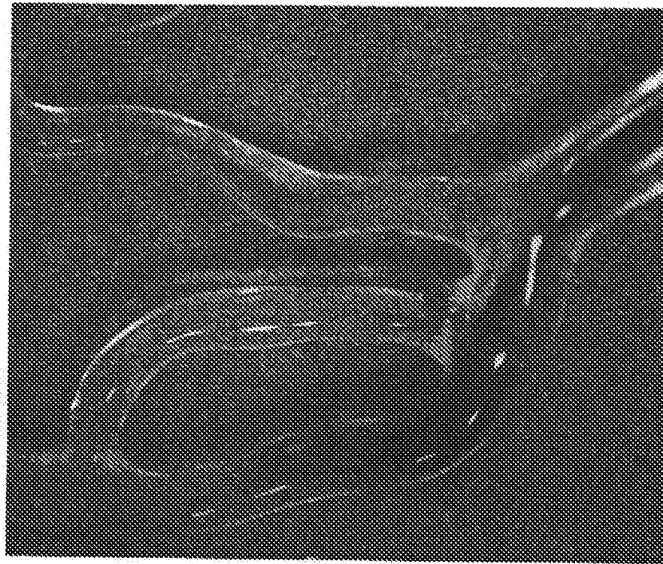


Fig. 8

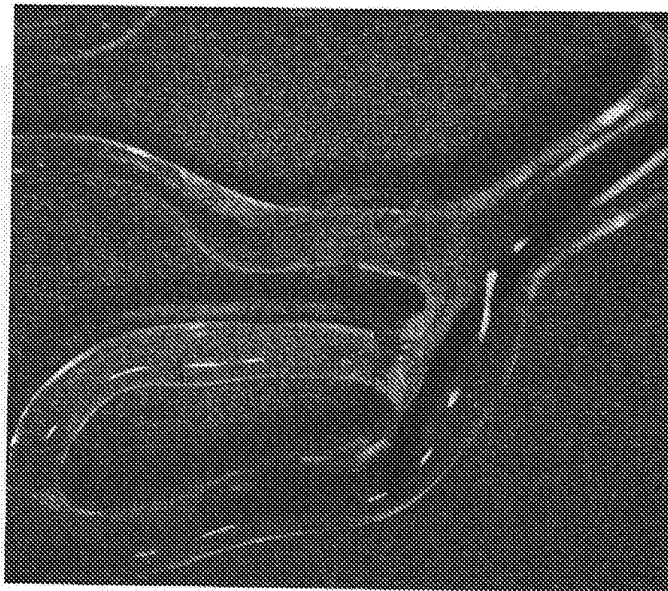


Fig. 9

Fig. 10A

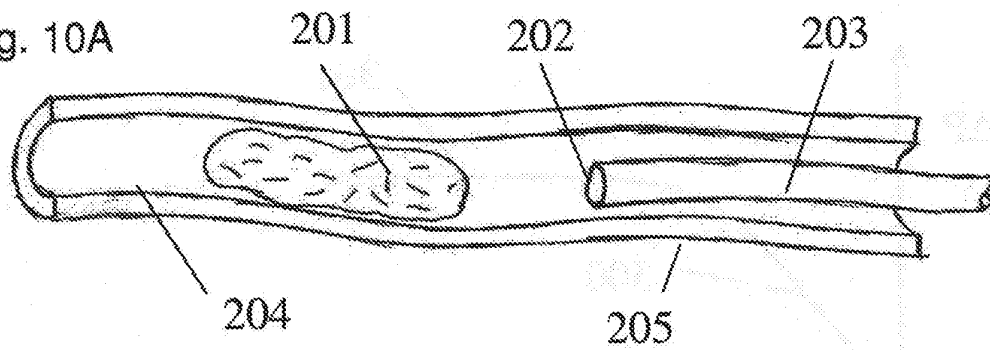


Fig. 10B

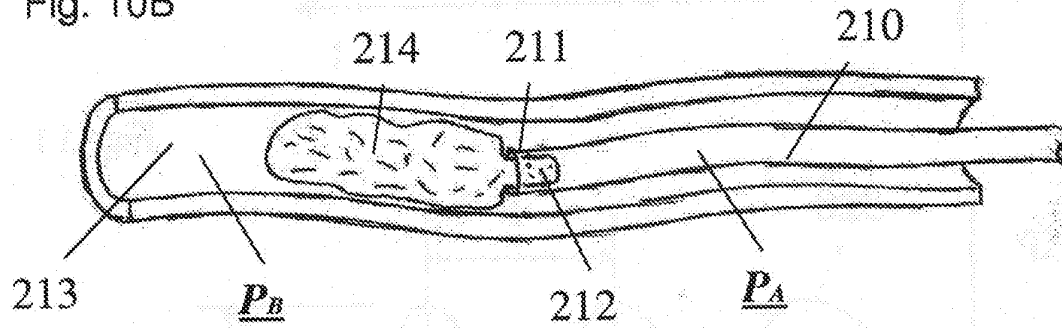


Fig. 10C

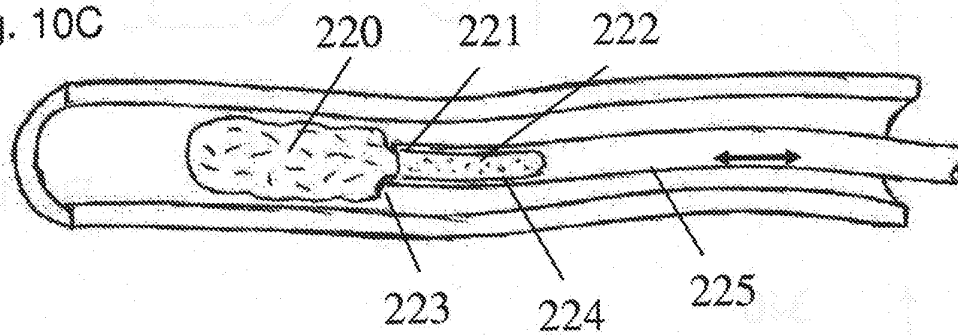
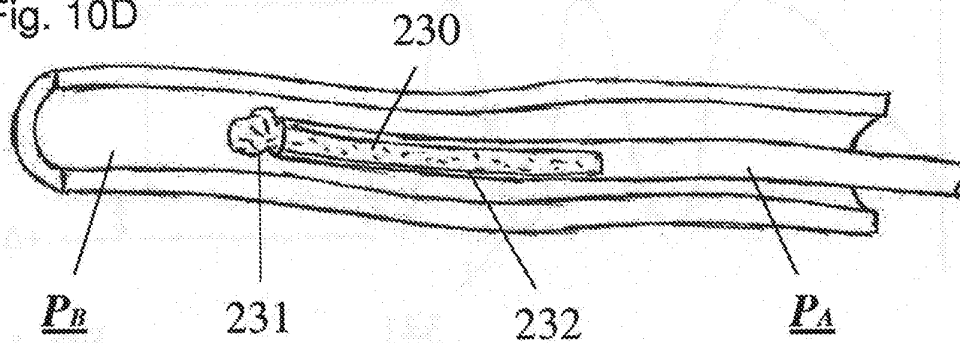


Fig. 10D



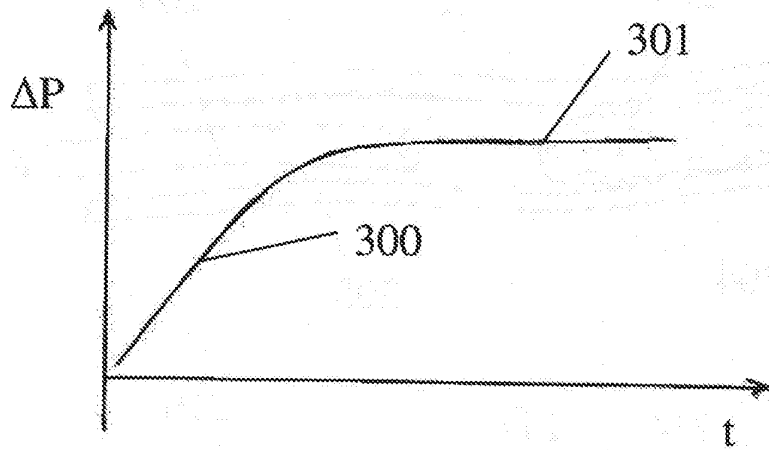


Fig. 11

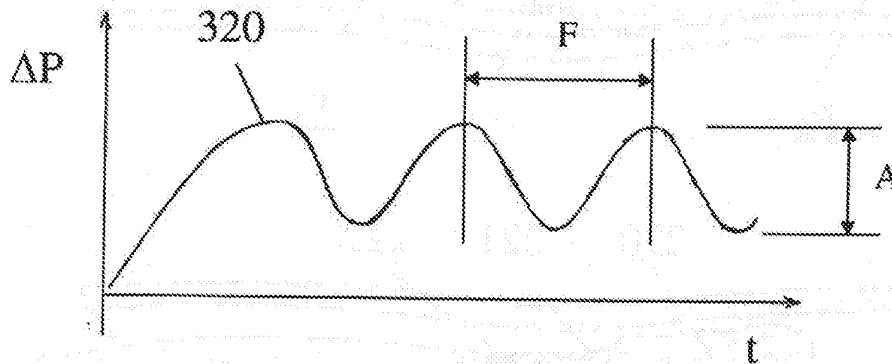


Fig. 12

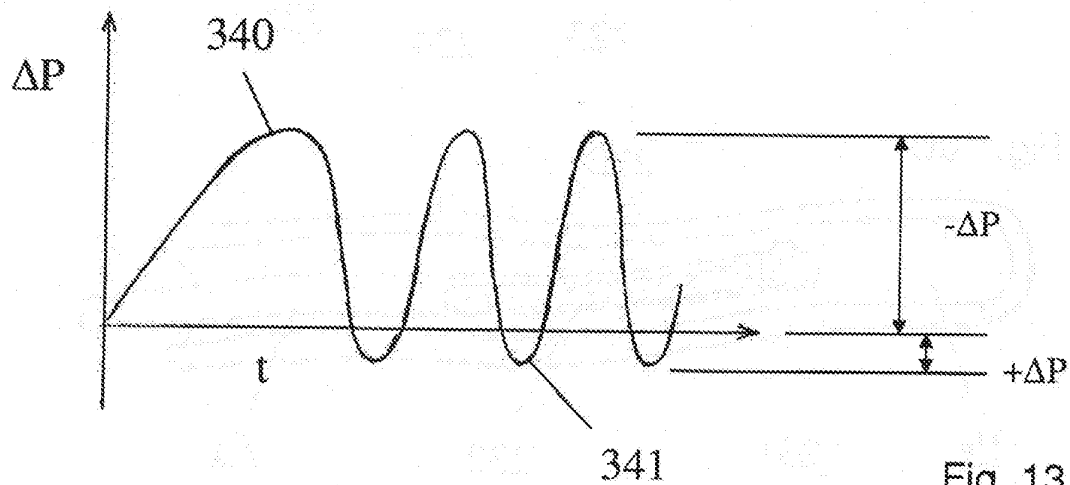


Fig. 13

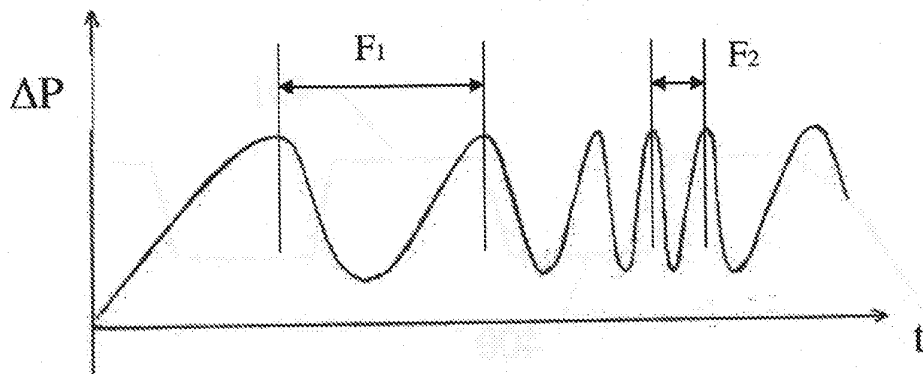


Fig. 14

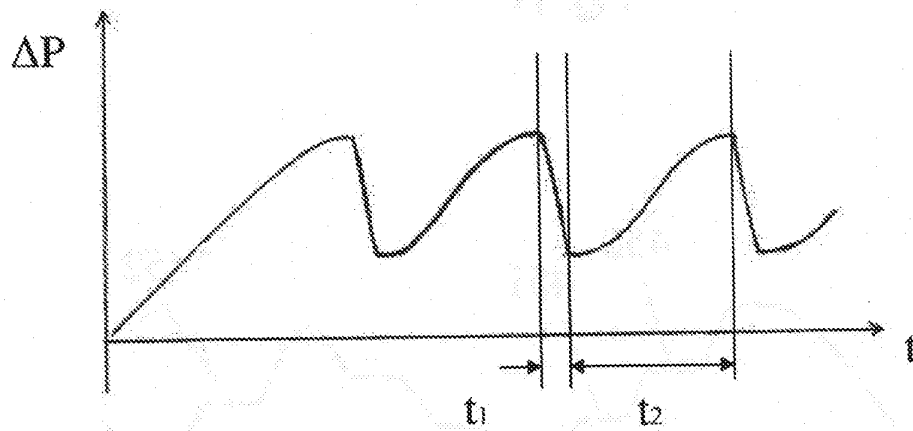


Fig. 15

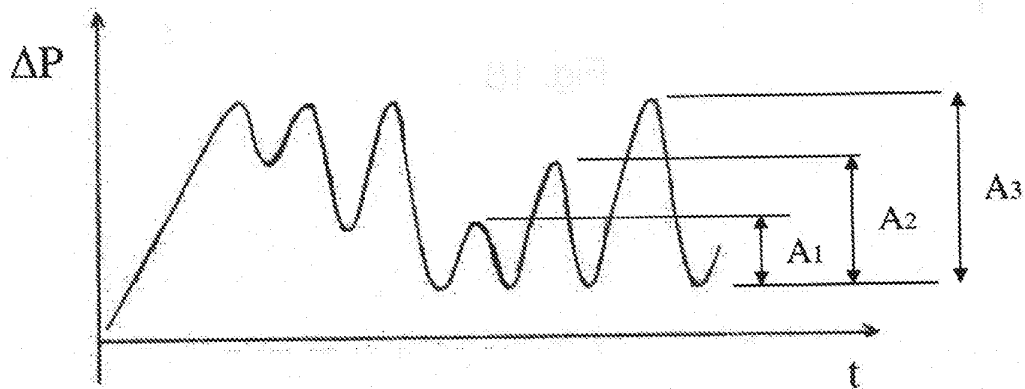


Fig. 16

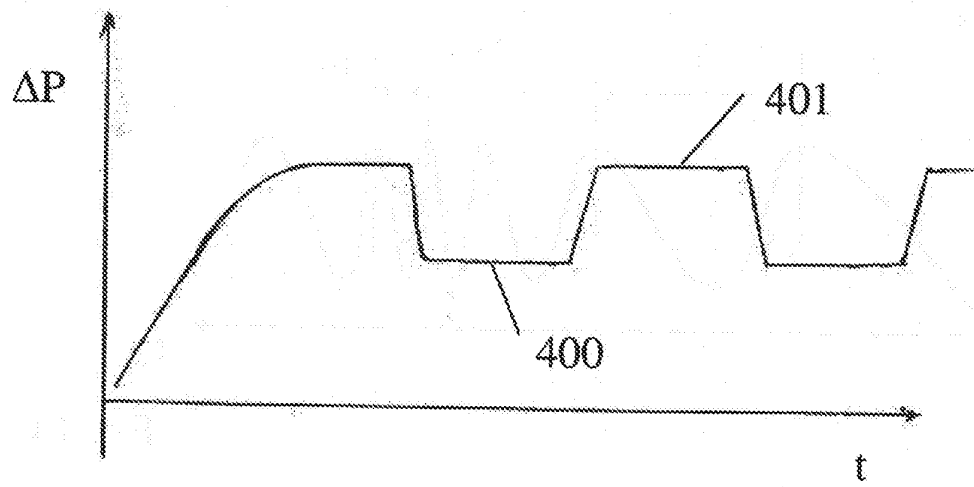


Fig. 17

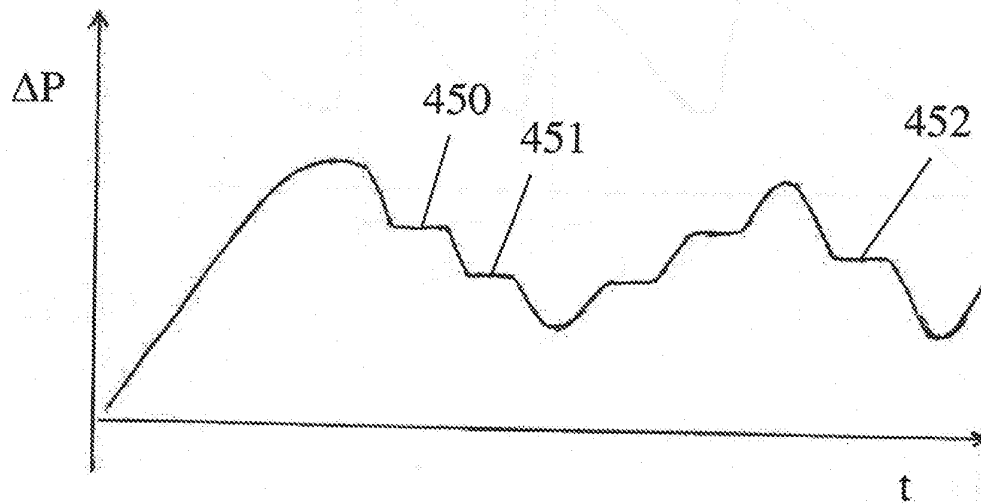
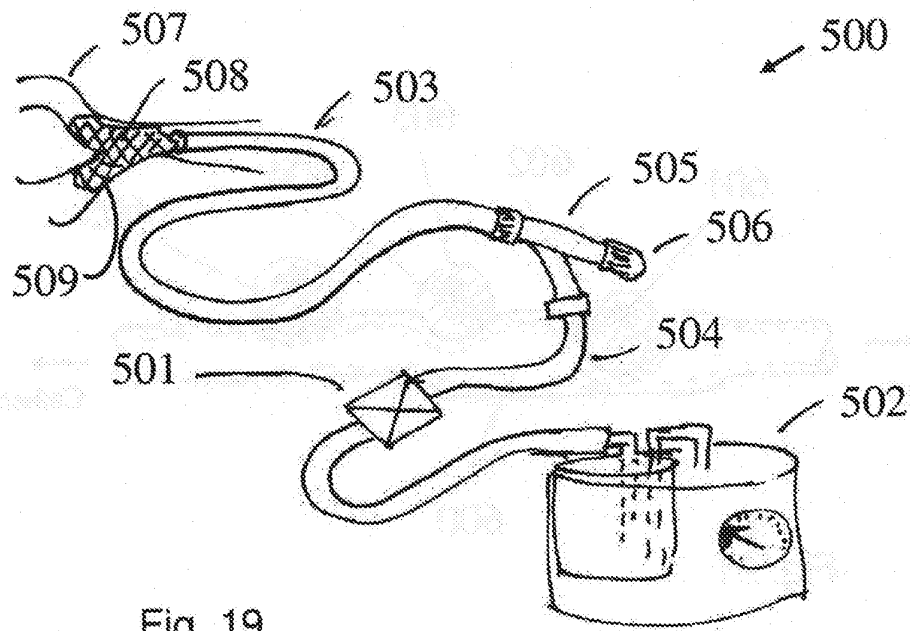
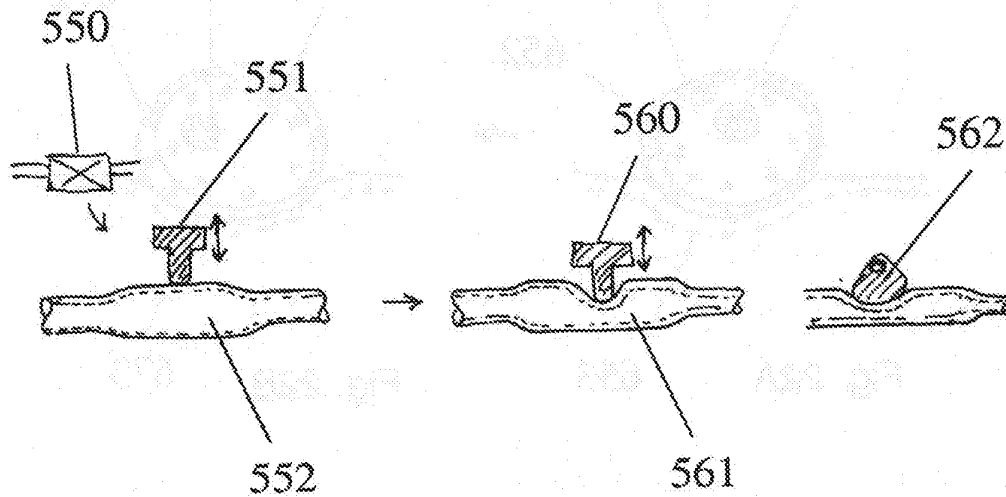


Fig. 18



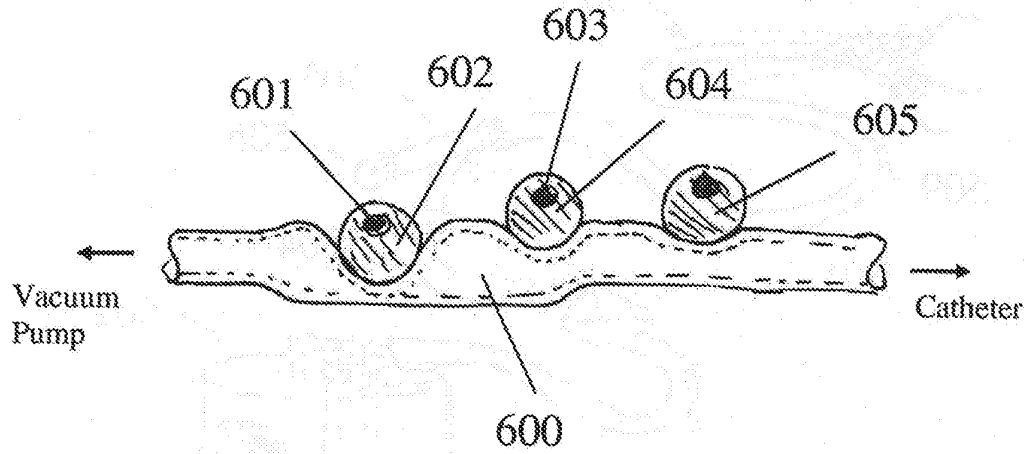


Fig. 21

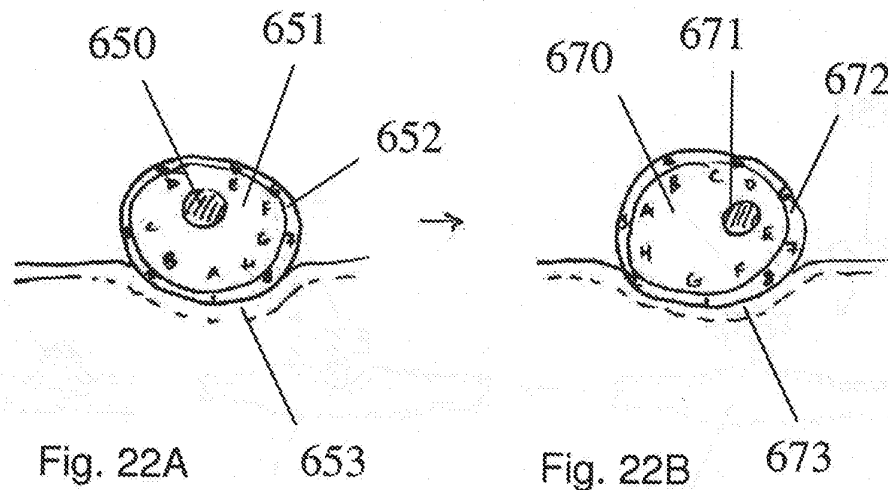
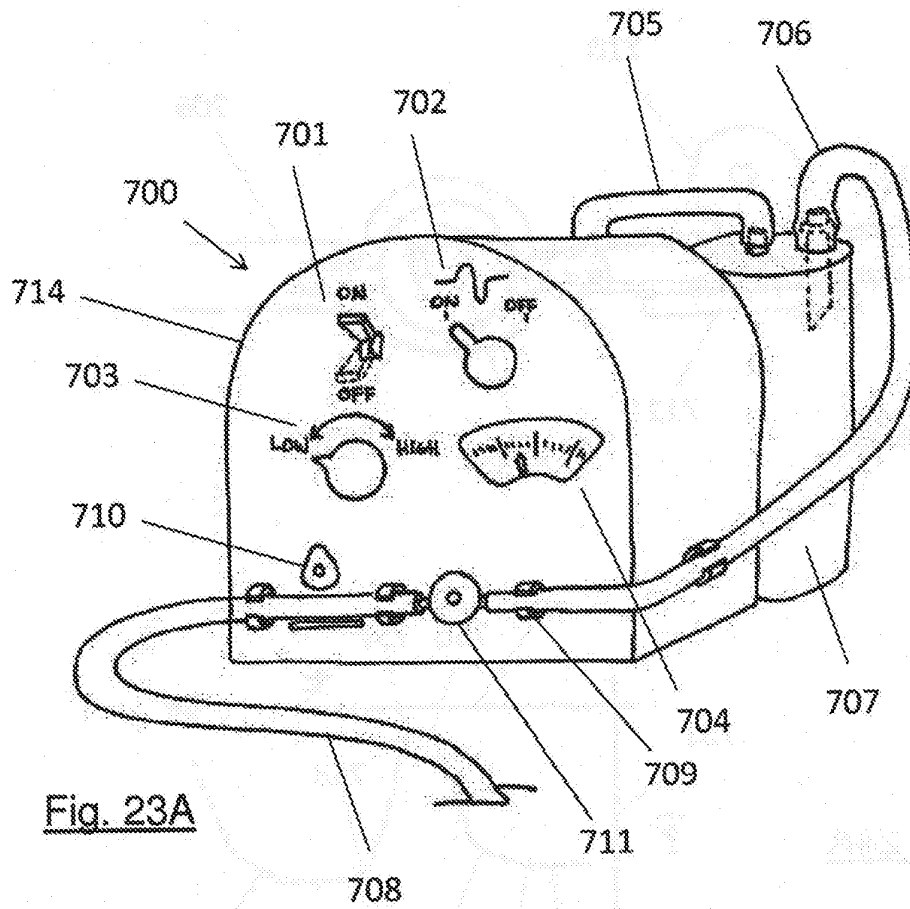
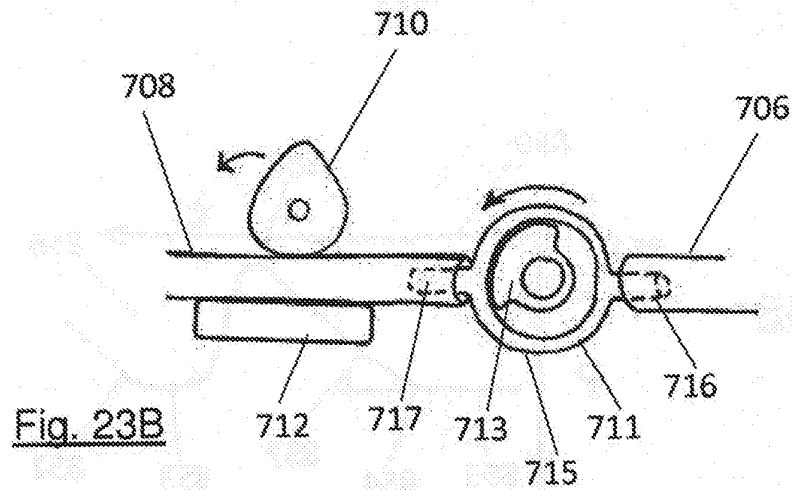
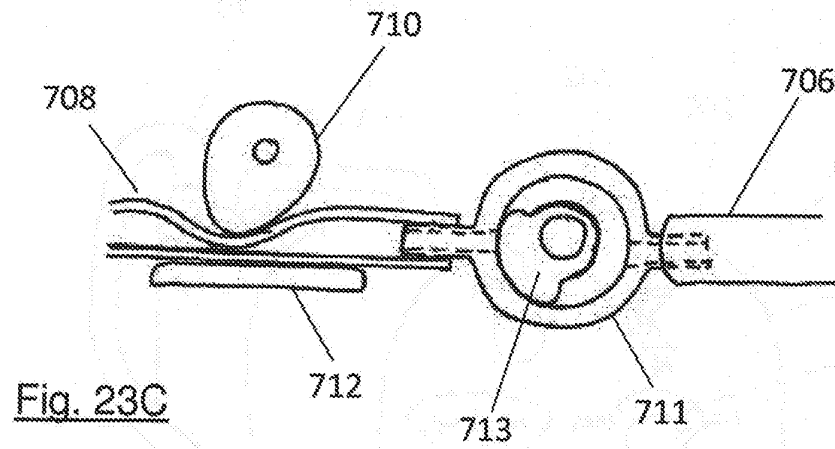
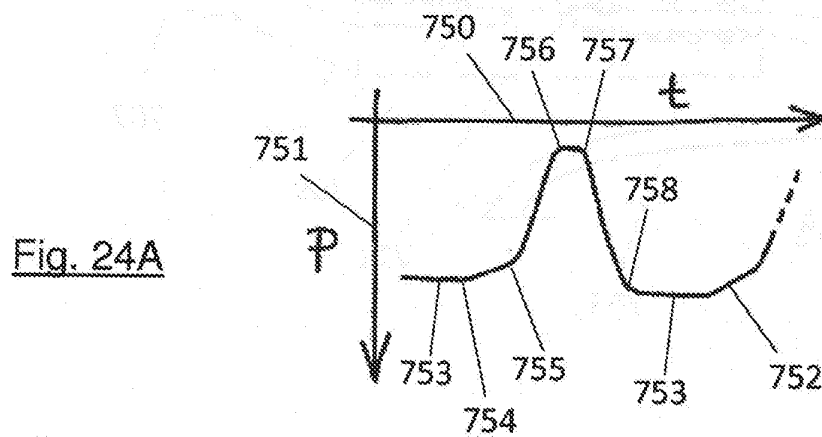
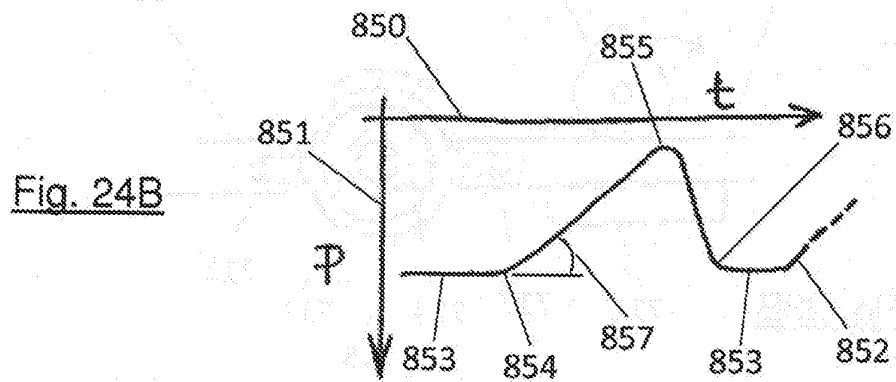


Fig. 22A

Fig. 22B





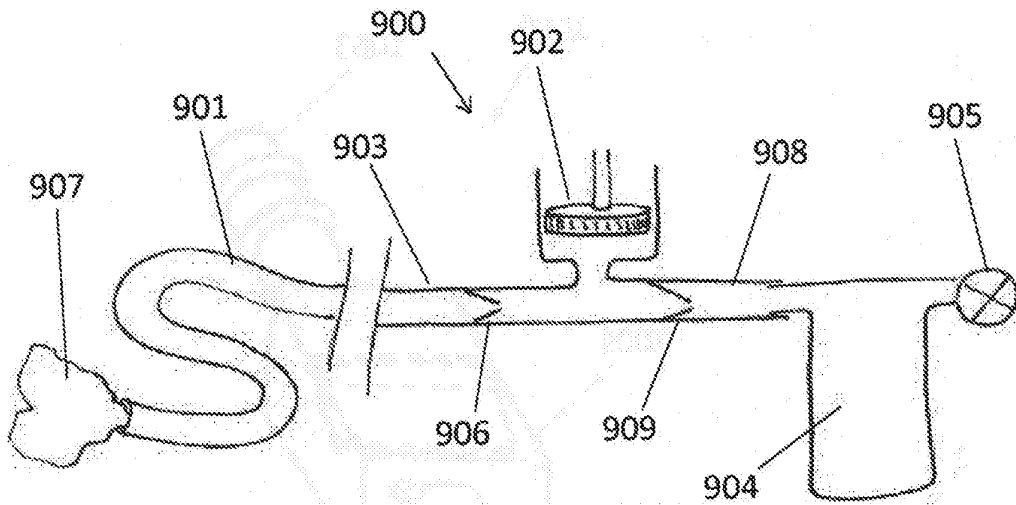


Fig. 25

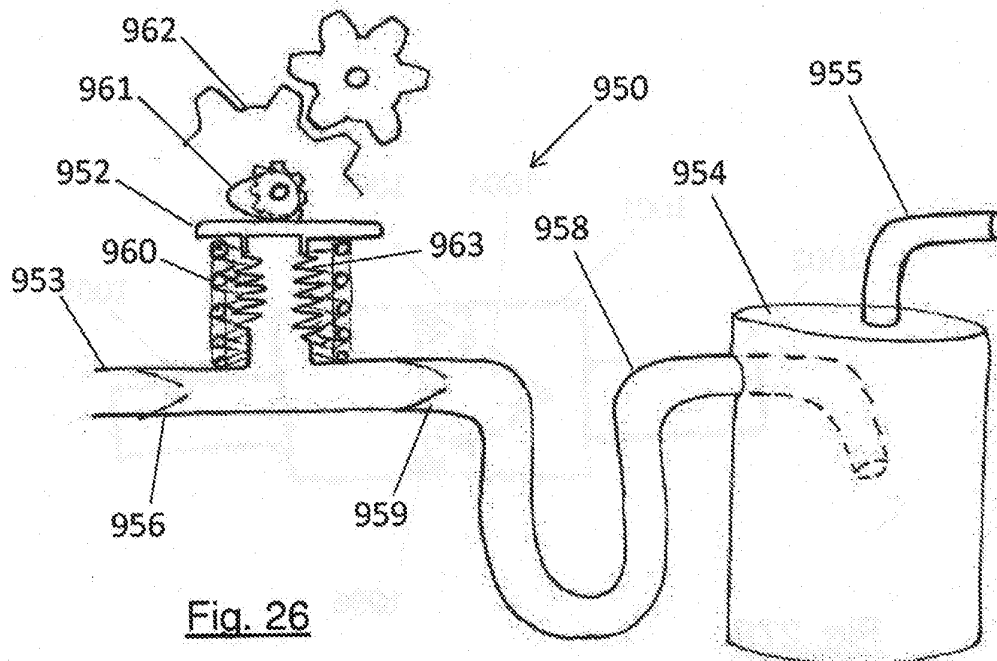
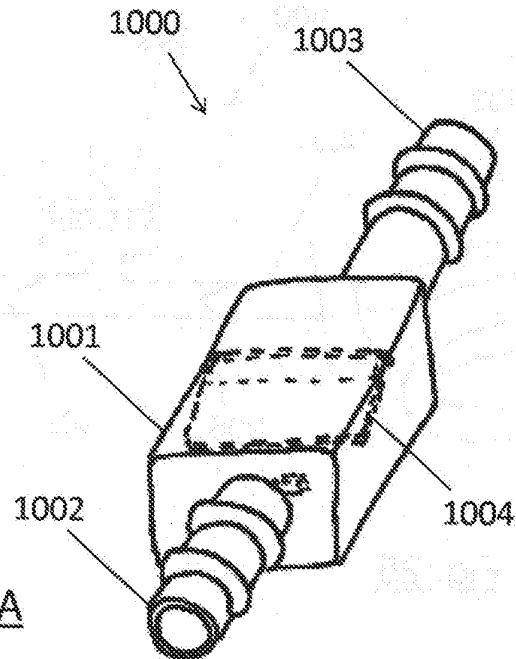
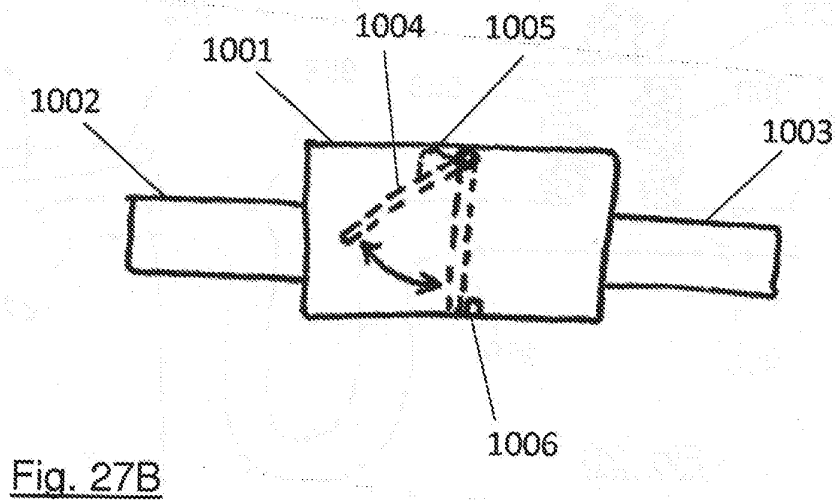


Fig. 26



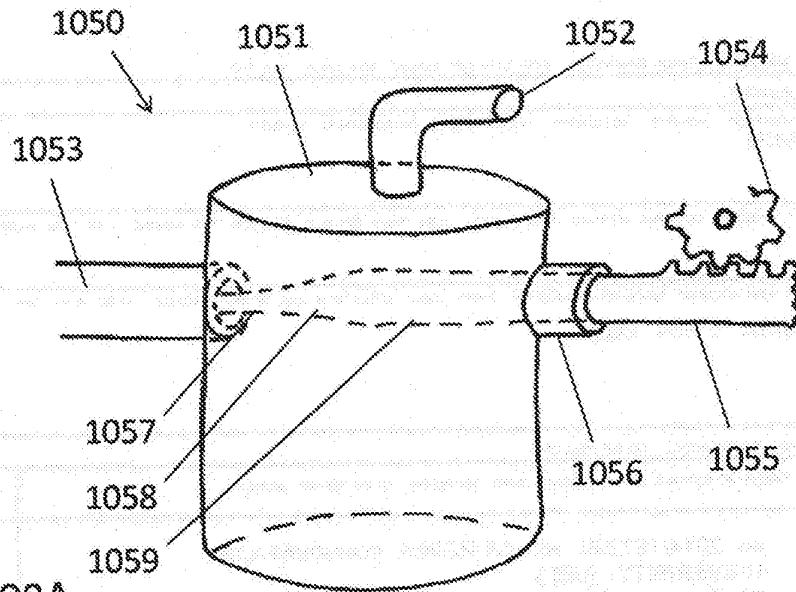


Fig. 28A

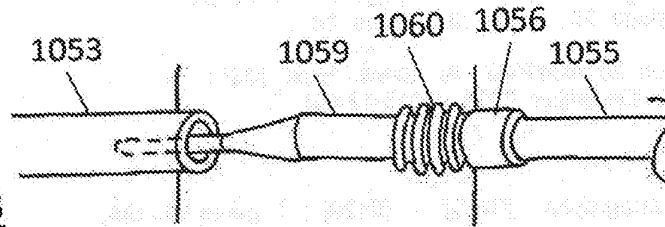


Fig. 28B

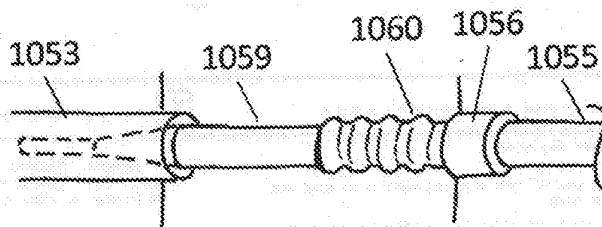


Fig. 28C

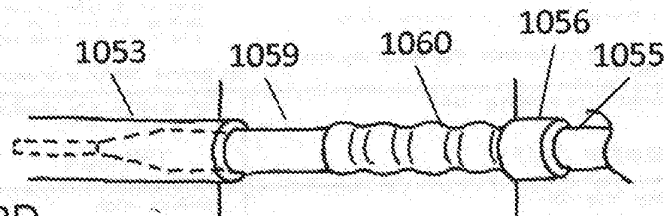


Fig. 28D

INTERNATIONAL SEARCH REPORT

International application No.

PCT/EP2017/068759

A. CLASSIFICATION OF SUBJECT MATTER INV. A61B17/22 A61M1/00 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) A61B 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 2014/151209 AI (VIRGINIA COMMONWEALTH UNIVERSITY [US]) 25 September 2014 (2014-09-25) page 2, line 24 - page 4, line 12; figures 2A-3C, 6-10, 11B, 11C page 7, line 13 - page 13, line 12 page 13, line 19 - page 21, line 22 page 25, line 23 - line 24 -----	1-5, 14-22, 32-59, 64
X	US 2015/342682 AI (BOWE WADE [US]) 3 December 2015 (2015-12-03) paragraphs [0110] - [0120]; figures 4, 12A, 12B ----- -/-	1, 2, 4, 5, 14-19, 32-42, 56, 64, 75-77
☒ 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) which is cited to establish the publication date of another claim 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 "S" document: member of the same patent family		
Date of the actual completion of the international search 12 September 2017		Date of mailing of the international search report 17/11/2017
Name and mailing address of the ISA/ European Patent Office, P.O. Box 5518 Patentkanal 2 NL-2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016		Authorized officer Friedrich, Franz

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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International Bureau

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20 June 2019 (20.06.2019)



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WO 2019/115809 A1

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English

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62/599,573 15 December 2017 (15. 12.2017) US
62/616,188 11 January 2018 (11.01.2018) US

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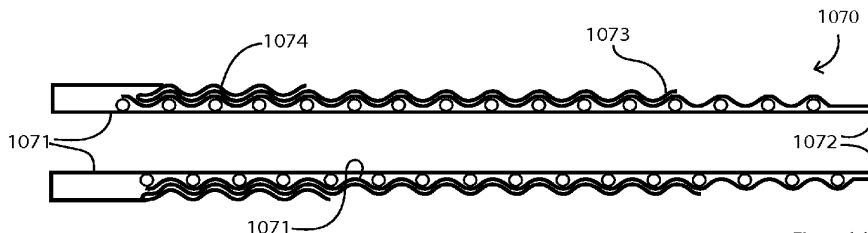


Fig.25(a)

(57) Abstract: A catheter has a jacket (10, 11, 5) defining a lumen and a helical support (6). The catheter has a proximal portion (4) and a distal portion (3), the distal portion having for at least some of its length a corrugated outer surface. A transition portion has a flexural stiffness which is less than that of the distal portion and more than that of the proximal portion. The transition portion provides an optimum transition in flexural stiffness by way of features of the jacket including geometry of jacket corrugations (15), or overlapping tubular layers (1073, 1074). The distal end of the distal portion may have an extension of liner material folded over (1072, 1082) to provide a particularly soft tip. In other examples the liner is terminated (763) before the distal tip. The catheter is particularly suited to an aspiration device (1350) with a flow restrictor (1353) and the distal portion distal of the flow restrictor. An aspiration system (3500) may employ the catheter with a pump which dynamically applies negative or positive pressure to optimally aspirate a clot.

WO 2019/115809 A1

“Improved Catheters and Devices and Systems Incorporating such Catheters”

INTRODUCTION

5 Field of the Invention

The present disclosure relates to catheters and to devices and systems incorporating such catheters, and to their methods of use. An example is a flexible catheter for endovascular procedures.

10 Prior Art Discussion

Most endovascular procedures require the use of flexible catheters, for example, to deliver contrast injection, to deliver implantable devices, perform vascular procedures, or to aspirate. Due to the tortuous nature of the vasculature, it is important for catheters to be flexible enough to travel through vessels without excessive force. However, there is generally a trade-off between
15 the features of catheter diameter, trackability, flexibility, and kink resistance. An increase in catheter diameter tends to increase its stiffness, which lowers its trackability and may dangerously increase vascular sheer forces. An increase in flexibility tends to increase the tendency of the catheter to kink as it is pushed through the vasculature, which limits the catheter to vessels with gentle curves. In general, a decrease in wall thickness increases flexibility and
20 allows access to more tortuous vessels, there being a trade-off between flexural stiffness and kink resistance.

The invention is directed towards providing a catheter with improved properties for desired flexural stiffness and flexibility, to thereby allow use in difficult locations such as where there
25 are significant curves and small dimensions in the patient vessels.

SUMMARY OF THE INVENTION

A catheter has a jacket defining a lumen and a helical support. The catheter has a proximal portion and a distal portion the distal portion having for at least some of its length a corrugated
30 outer surface. A transition portion has a flexural stiffness which is less than that of the distal portion and more than that of the proximal portion. The transition portion provides an optimum transition in flexural stiffness by way of features of the jacket including geometry of jacket corrugations, or overlapping tubular layers. The distal end of the distal portion may in some examples have an extension of liner material folded over to provide a particularly soft tip. In

other examples the liner is terminated before the distal tip. The catheter is particularly suited to an aspiration device with a flow restrictor and the distal portion distal of the flow restrictor. An aspiration system may employ the catheter with a pump which dynamically applies negative or positive pressure to optimally aspirate a clot.

5

In one aspect we describe a catheter comprising a jacket defining a lumen and comprising a helical support in jacket material along at least some of its length, the catheter comprising at least a proximal portion and a distal portion, said distal portion having for at least some of its length a corrugated outer surface. The catheter preferably comprises a transition portion between said proximal portion and said distal portion, said transition portion having a flexural stiffness which is less than that of the distal portion and more than that of the proximal portion. The transition portion preferably has a corrugated outer surface in which at least some corrugations of the corrugated outer surface have a smaller depth and/or width than corrugations of the surface of the distal portion.

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15

Other aspects of the catheter are set out in the attached claims 4 to 88.

We also describe a method of manufacturing a catheter of any embodiment, wherein the jacket is formed in at least some regions by positioning a membrane over a helical structure, applying heat so that the membrane reflows such that it forms around the helical structure, winding a tensioned cinch wire around the outside of the membrane such that it forces membrane material into grooves between each loop of the helical structure, heat setting the membrane to fix the corrugations in place, and unwinding the tensioned cinch wire leaving the corrugations behind.

20
25 The jacket may include fluoropolymers and said fluoropolymers may be bonded with each other and/or with other polymers at bonding interfaces. Chemical treatment may be applied at said interfaces using an etching solution. The etched fluoropolymer may be coated with a thin layer of urethane such as Chornoflex, and on the application of heat, this layer flows and acts to tie the fluoropolymer to a second etched fluoropolymer layer or to a different polymer layer.

30

In one aspect, the method comprises providing the helical support within a polymer jacket which is bonded to a liner to form a base assembly, placing an outer liner which will not bond to the polymer jacket over the jacketed coil, winding the cinch wire in a helix onto the outside of the outer liner under tension thereby imparting a corrugate geometry, heating to reflow or anneal the

material to set said material into the corrugate geometry, cooling the assembly, removing the cinch wire, and peeling off the outer liner.

We also describe an aspiration device comprising a catheter of any embodiment described herein and a flow restrictor, in which the distal portion is distal of the flow restrictor. The catheter may comprise a transition portion between said proximal portion and said distal portion, said transition portion having a flexural stiffness which is less than that of the distal portion and more than that of the proximal portion, and at least part of said transition portion extends distally of the flow restrictor.

The flow restrictor may comprise a balloon and the balloon is arranged to inflate to block blood flow before aspiration of a clot into the catheter distal portion. Alternatively it may be used to block blood flow before precise delivery of an embolic agent to region of the vasculature, tumour, or organ.

Length of the distal portion is in one case suited to reach specific anatomical locations, such as the distal internal carotid artery, terminus of the internal carotid artery, proximal MI, distal MI, proximal M2, distal M2, basilar, or vertebral vessels, wherein the flow restrictor remains in or proximal of the C1 segment of the ICA.

Various aspects of the aspiration device are set out in appended claims 94 to 110.

We also describe a method of use of an aspiration device of any embodiment, the method comprising steps of deploying the aspiration device in a patient's blood vessel, navigating the distal portion to a clot in the vessel, causing the flow restrictor to block blood flow, applying a vacuum to the catheter so that the clot is aspirated into the distal portion.

In one example, the method comprises:

- performing an angiogram to determine location of an occlusion, and distance between petrous or cavernous carotid and the occlusion,
- choosing a catheter with a distal portion length suitable to reach a clot causing the occlusion, while ensuring that the flow restrictor does not land beyond the cervical carotid,
- navigating the distal portion of the catheter to the clot,

activating the flow restrictor such that flow arrest is enabled, and alternative flow pathways which could reduce the effectiveness of the aspiration are minimised, applying a vacuum to the lumen of the catheter to aspirate the clot, if the clot is retrieved, performing another angiogram through the balloon guide catheter or a diagnostic catheter, and removing the catheter.

We also describe an aspiration system comprising a catheter of any embodiment, a pump linked with the catheter proximal portion, and a controller arranged to vary aspiration pressure during aspiration of a clot. The system may comprise a lumen pressure sensor and the controller is configured to vary aspiration pressure according to sensed pressure within the catheter lumen. The system may comprise a lumen fluid flow sensor, and the controller is configured to vary aspiration pressure according to sensed fluid displacement in the lumen.

The controller may be configured to improve the efficiency of aspiration by preventing clogging of the catheter, and/or to promote maceration and deformation of a clot to enable it to travel through the lumen.

Various aspects of the aspiration system are set out in the appended claims 113 to 135.

We also describe methods of use of an aspiration system of any embodiment, in which the controller varies aspiration pressure during aspiration of a clot. There may be a lumen pressure sensor and the controller varies aspiration pressure according to sensed pressure within the catheter lumen. There may be a lumen fluid flow sensor, and the controller varies aspiration pressure according to sensed fluid displacement in the lumen. Preferably, the controller improves efficiency of aspiration by preventing clogging of the catheter, and/or promotes maceration and deformation of a clot to enable it to travel through the lumen. Also, the controller may provide a vacuum or a positive pressure based on measured pressure, and change direction hence altering the pressure and fluid displacement.

The controller may have defined upper and lower limits of pressure or displacement to decide whether to apply a vacuum or pressurize, and/or it may cause the catheter to cyclically ingest and if required expel, at least some of a clot, whereby there is deformation of the clot to improve efficiency of aspiration and prevent clogging of the catheter. The controller may begin to draw some vacuum so that a negative pressure is measured and in the absence of an occlusion or

partial occlusion of the catheter tip, this will be a nominal reading, representing free-flow of fluid through the catheter, and once the catheter is advanced and engaged with the clot, an increase in the vacuum is observed.

- 5 The controller may increase a vacuum to ingest more of a clot and reverse at a low limit of pressure defined such that during vacuum, a portion of the clot has been aspirated but not so much that the clot has become irreversibly clogged and the lower limit of vacuum can be set above a full vacuum pressure to prevent ingestion of too large a clot that could clog the catheter.
- 10 Other aspects of the method of operation of the aspiration system are set out in the attached claims 113 to 135. For example, the controller may set the low limit between -100 mm-Hg and -200 mm-Hg, preferably between -200 mm-Hg and -300 mm-Hg, more preferably between -400 mm-Hg and -500 mm-Hg, and more preferably between -600 mm-Hg and -700 mm-Hg; and it may cause direction of fluid displacement of the pump to be reversed thereby increasing
- 15 the pressure measured, and unloading a clot.

DETAILED DESCRIPTION OF THE INVENTION

Brief Description of the Drawings

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

Fig. 1 is a schematic cross-sectional view of a distal end of a catheter;

25

Fig. 2 is a cross-sectional view of a catheter wall portion having varying depths of corrugation;

Fig. 3 illustrates an outer surface of the catheter shown in Fig. 1;

30

Fig. 4 is a cross-sectional view of the full catheter shown in Fig. 1;

Fig. 5 is a schematic cross-sectional view of a catheter wall portion having an outer tubular layer bonded with an inner tubular layer;

35

Fig. 6 is a schematic cross-sectional view of a transition between a distal wall portion and a proximal wall portion;

Fig. 7 is a schematic cross-sectional view of another transition between a distal wall portion and a proximal wall portion;

Fig. 8 shows force measured at a 1mm displacement in a 3-point bend test of a conventional catheter design (0.80A urethane jacket over a 0.005in NiTi coil over on a 0.001in PTFE Liner), and highly flexible corrugated ePTFE design;

Fig. 9 shows behaviour of a conventional catheter under compression when pushed against restriction, and Fig. 10 shows behaviour of a corrugated catheter under compression when pushed against a restriction;

Fig. 11 shows in a catheter use of progressively more flexible (or less “pushable”) sections of catheter wall within the distal tip, distally of a proximal portion;

Fig. 12 is a section through an outer wall having a corrugated surface, with an inner liner;

Figs. 13 shows a section through a catheter in which the inner liner terminates before the of the catheter

Fig. 14 shows a cross section of the catheter where the helical support is not exposed to the inner lumen of the catheter.

Fig. 15 show further constructional details of catheter walls to achieve desired flexibility at the proximal and distal portions;

Fig. 16 shows an outer tubular layer added to the outside of the corrugated structure which embeds the helical support to further increase the stiffness of a section of the catheter proximally of the distal end;

Fig. 17 shows steps for manufacture of a corrugated polymer jacketed catheter section;

Fig. 18 shows a catheter portion with a liner, a coil and inner and outer tubular layers respectively and in-fill for increased stiffness;

Fig. 19 shows both the inner and outer tubular layer thickness being increased; in this instance the coil may be floating or constrained between the outer layer and inner liner;

Fig. 20 shows a catheter portion having a liner, an outer jacket layer underneath a coil, and two layers outside the coil; in this instance the coil may be floating or constrained in the jacket material;

Fig. 21 shows, in order to achieve a controlled change in stiffness of the distal tip, multiple layers being overlapped to achieve a precise level of stiffness; in this instance the coil may be floating or constrained in the jacket material;

Fig. 22 is a plot showing results of 3-point bend tests to evaluate stiffness;

Fig. 23 shows the distal-most end of the distal portion finished by inverting an inner liner over the helical support to form a continuous element; in this instance the coil may be floating or constrained in the jacket material;

Fig. 24 shows a distal portion in which softness is improved by extending inner and outer tubular layers beyond the last coil of the helical support; in this instance the coil may be floating or constrained in the jacket material;

Figs. 25A and 25B show further examples of catheter arrangements in which an inner liner is inverted to return as a continuous element; in this instance the coil may be floating or constrained in the jacket material;

Fig. 26 shows in a catheter having a proximal end and an intermediate portion an inner tubular layer of ePTFE material extending along the entire length of the catheter including a distal end, where it is bent back to be continuous;

Fig. 27 shows the inner tubular layer being of ePTFE in a distal portion and of PTFE in a more proximal portion of the catheter; a butt joint is used in which the proximal liner is concentric within the distal liner;

5 Fig. 28 shows the proximal region of rib and recess corrugation having an outer tubular layer comprised of a polymer material and a distal liner transitioning to different material; a lap joint is used in which the distal liner is concentric within the proximal liner;

Fig. 29 shows that for a distance the ePTFE is concentric within the PTFE;

10

Fig. 30 shows a further arrangement of a helical support in the jacket in which the helical support is comprised of a tubular layer of Nitinol or other material over a radiopaque material such as Platinum; in this instance the coil may be floating or embedded;

15 Fig. 31 shows catheters with radiopaque markers at various positions along its length;

Fig. 32 is a series of diagrams showing a typical prior art setup of a balloon guide catheter in a thrombectomy procedure to provide proximal flow occlusion;

20 Fig. 33 shows a balloon catheter with an enhanced flexibility section on the distal tip, and Fig. 34 is a diagram showing layers and lumens of a dual lumen balloon of the catheter of Fig. 33;

Figs. 35 and 36 show corrugated tube tips for enhanced flexibility;

25

Fig. 37 left image shows an Angiogram demonstrating the external carotid, common carotid and internal carotid artery (ICA), including the C1 and C2 segments, and right image shows acceptable positioning of the balloon;

30 Fig. 38 shows the proximal and distal shaft having the same outer diameter, and the proximal shaft having two concentric lumens, in which the central lumen diameter is less than that of the flexible distal tip;

Fig. 39 shows a catheter with a balloon and a distal portion having a smaller outer diameter than the proximal portion;

Fig. 40 shows a catheter with a non-corrugated proximal region of the distal section;

Fig. 41 shows a catheter device with a radiopaque marker at the distal end of the flexible distal tip;

Fig. 42 shows a mother and daughter catheter arrangement wherein the larger catheter is used to occlude inflow to the target vessel, while the smaller catheter is used to retrieve the clot;

Fig. 43, left diagram, shows the use of a small catheter unable to reach a distal target vessel (right) during delivery of a drug or embolic and the resulting undesired delivery to a non-target vessel (top left vessel); and the right hand diagram shows a method wherein a highly flexible large diameter catheter is chosen to effectively occlude the target vessel, and can be placed beyond the non-target vessel, so delivery of the embolic only occurs to the target vessel; it is preferable that the catheter is wedged in the target vessel;

Figs. 44(a) to 44(e) are schematic diagrams outlining relationship between pressure in the catheter lumen, and the clot behaviour, during aspiration;

Fig. 45 shows a setup used for aspiration of a clot or other material from the body using a pump;

Fig. 46 is a flow diagram showing steps including pressure monitoring to establish whether the pump should apply vacuum or pressurize during the aspiration procedure;

Figs. 47(a) to 47(n) are diagrams illustrating operation of the clot removal device in various examples;

Figs. 48(a) to 48(c) show varying pressure signals between two vacuum levels;

Fig. 49 is a flow diagram showing method steps for positive oscillation or shake signals;

Figs. 50(a) and 50(b) are plots showing shake signals;

5 Figs. 51(a) and 51(b) are a flow diagram and an associated plot for vacuum and positive oscillation;

Figs. 52(a) and 52(b) are a flow diagram and an associated plot for positive and negative modulation of aspiration; and

10 Figs. 53(a) and 53(b) are images of a pump and its components, including a housing, a connecting tube, an on-off switch, a battery pack, a pulsatile pump, and a motherboard, in which the pressure sensor is connected to the tube (or “lumen”), which is connected to the catheter, thereby enabling pressure measurement within the catheter.

15 Description of the Embodiments

Various embodiments are depicted in the accompanying drawings for illustrative purposes, and should in no way be interpreted as limiting the scope of the embodiments. Furthermore, various features of different disclosed embodiments can be combined to form additional embodiments, which are part of this disclosure.

20

Terminology

“Jacket” is the wall of the catheter, and these terms are interchangeable. It may be corrugated in all or some regions along the length (longitudinal direction). It may include any or all of a helical support (or “coil”) surrounded by jacket material, and an inner liner. The inner liner, 25 where present, defines the lumen, but otherwise the other jacket material defines the lumen. A liner where present, may be terminated at some location in the catheter.

“Tubular layer” is a layer of material of the jacket.

30 “Pushability” is understood as the transfer of force and/or displacement applied at a proximal portion of a catheter, along a length of the catheter, to a more distal portion of the catheter. The higher the flexural stiffness the greater the pushability.

“Corrugate” is a rib and recess geometry on the outer surface of the catheter, most often in a spiral pattern.

“Distal” means further from a clinician in use, closer to a catheter tip in the longitudinal direction, and “proximal” means closer to the clinician.

Description of the Embodiments

Fig. 1 illustrates an embodiment of a highly flexible, kink resistant catheter 1. The catheter 1 includes a distal portion 3, a proximal portion 2, a central lumen 5 and a reinforcing structure such as a helical support 6 that runs the length of the catheter. The proximal portion and/or a transition between the distal portion and the proximal portion can in various embodiments include any of the corresponding features of the catheters described in U.S. Application No. 15/647,763, filed July 12, 2017, titled “HIGH FLEXIBILITY, KINK RESISTANT CATHETER SHAFT,” which is attached in the Appendix. The inner tubular layer and/or the outer tubular layer can include PTFE, ePTFE, electrospun PTFE, silicone, latex, Tecothane, nylon, PET, Carbothane (Bionate), SIBS, Tecoflex, Pellethane, PGLA, or Kynar, Polyethylene and cyclic olefin copolymers, PEEK.

The inner and outer tubular layers (Fig. 1) in at least the distal portion can be formed from a single section of material or a number different sections of similar or different material. In this embodiment the outer tubular layer 11 of the distal portion is formed from a polyurethane (e.g. Pellethane 80AE) and the inner tubular layer 5 is formed from ePTFE and/or PTFE.

In this case the catheter jacket comprises an inner liner 5 and an outer tubular layer 11 with a helical support 6. The highly flexible distal portion 3 (left side) of the catheter is created by forming corrugations 15 into the outer surface of the outer tubular layer 11. The helical support 6 is encapsulated between the corrugations of the outer tubular layer 11 and the outside of the smooth inner tubular layer 5 as shown in Fig. 1. The formation of a corrugated wall structure during bending provides flexibility while reducing the likelihood of kinking. The corrugated outer surface can also decrease resistance when the outer surface of the catheter contacts a vessel wall. The depth of the corrugations may be tailored to provide a desired variation in stiffness along the length of the catheter as shown in Fig. 2.

As shown in Fig. 1 a parameter “D” is depth of a corrugation and a parameter “W” is the width of a corrugation. The width is not the distance from peak to peak, rather it is the effective width of the valley. In effect for many embodiments this is provided during manufacture by tightening a cinch wire around a tubular layer, heat treating, and removing the cinch wire to provide the corrugated surface. The width W is approximately the diameter of the cinch wire in this case. The depth D is not necessarily uniform because the pressure applied by the cinch wire may vary along the length of the catheter thereby forming deeper indentations in some locations than in others.

Fig. 2 shows a cross section through a wall of a catheter tip 50, having an inner layer 51, a helical coil support structure 52, an outer layer 53 with a corrugated surface 53. The depth A of the corrugations on the left hand side is greater than the depth B on the right hand side. The section with the lower corrugation depth B may function as a transition region before a tip (left hand side) with more flexibility.

In the examples of Figs. 1 and 3 the coil is embedded in the jacket; being constrained from movement relative to the surrounding jacket material.

Additionally, pitch, or corrugation width variations may be used to control the flexibility locally in the corrugated region. Also, flexibility may be set during manufacture by choosing some length of the coil to be embedded in the jacket or to be floating, the region with the floating coil being more flexible. Where the coil is floating it is in the context of the jacket tubular layers being attached in the spaces between corrugation ribs, such as a jacket tubular layer to an inner liner.

The outer tubular layer can extend at least a length of the highly flexible distal portion or extend beyond the distal portion for some distance along the proximal (midsection) length or extend the entire length of the catheter as shown in Figs. 3 and 4 (which shows the catheter of Fig. 1 in its full length). Extending the outer tubular layer at least some length beyond the highly flexible distal portion of the catheter allows for a controlled stiffness transition between the distal and proximal portions of the catheter and for the formation of a robust joint between the outer tubular layer and any additional outer jacket materials. Again, flexibility may be set during manufacture by choosing some length of the coil to be embedded in the jacket or to be floating, as is the case for any of the embodiments described with reference to Figs. 3 or 4.

To form the corrugations in a tubular membrane, the membrane can first be positioned over the helical reinforcing structure. On the application of heat, the outer tubular membrane will reflow such that it forms around the helical structure. A tensioned wire can then be wound around the
5 outside of the tubular membrane such that it forces portions of the membrane into the grooves between each loop of the supporting helical structure. The tubular membrane can then be heat set to fix the corrugations in place. After this process the tensioned wire may be unwound leaving the corrugations behind.

10 The inner tubular layer can extend into the proximal portion of the catheter to provide an uninterrupted lumen and to join or improve the joint strength between the highly flexible distal portion of the catheter and the proximal portion of the catheter. The diameter of the inner tubular layer can be constant (e.g. smooth surface). The inner tubular layer may form at least part of or the entirety of the liner as shown in Figure 4. The inner tubular layer can be made
15 from a low friction material such as ePTFE or PTFE.

As explained above, the outer tubular layer of at least the distal portion is formed from a polyurethane (e.g. Pellethane 80AE) and the inner tubular layer is formed from an ePTFE and/or PTFE liner. It is necessary to attach these layers together and this is not easily achieved as
20 fluoropolymers do not form strong bonds with other materials.

To facilitate bonding between fluoropolymers (e.g. ePTFE and PTFE) and between fluoropolymers and other polymers such as polyurethanes (e.g. Pellethane) the outer or bonding surface of the fluoropolymer(s) may be chemically treated using a sodium-based etching solution
25 such as FluoroEtch. The etching solution removes fluorine atoms from the surface of the fluoropolymer and prepares it for bonding.

The etched fluoropolymer can then be coated with a thin layer of urethane, such as ChronoFlex. On the application of heat, this thin ChronoFlex layer flows and acts to tie the fluoropolymer to a
30 second etched fluoropolymer layer or to a different polymer layer as shown in Fig. 5. This embeds the coil.

This diagram shows part of the cross-section of a catheter at its distal portion 150. This includes a liner 151 of ePTFE or PTFE, a tie layer 152 of urethane or FEP tape or FEP powder. Also,

there is a Nitinol™ coil 153 in an outer jacket 154 of ePTFE, or urethane material. The nitinol coil 153 is encapsulated between the outer tubular corrugated layer and the smooth inner tubular layer 151. The tie layer 151 serves the purpose of attaching the liner 151 to the outer jacket material. If the liner is of ePTFE material then it will need to be etched to strip the fluorine atoms so that it will form a better bond with the tie layer.

Again, flexibility may be set during manufacture by choosing some length of the coil to be embedded in the jacket or to be floating, as is the case for any of the embodiments described below with reference to Figs. 6 and 7.

The ChronoFlex™ tie-layer 152 is so thin it does not cause any significant change in wall thickness. An alternative form of tie-layer involves the use of FEP. The fluoropolymer may be sputter coated with a FEP powder which under heat and pressure forms a bond between the coated fluoropolymer layer and a second layer. An ultra-thin FEP tape may also be used in the same application.

The helical support is encapsulated between the corrugations of the outer tubular layer and the smooth inner tubular layer as shown in Fig. 5. The inner tubular layer and the outer tubular layer are bonded together in the space between the adjacent loops of the helical support by such mechanisms as a tie-layer. The helical support is bonded within the helical channel formed by the corrugated outer tubular layer, i.e., the helical support is molecularly or physically attached to the outer tubular layer. The helical support may also be bonded to the outside surface of the smooth inner tubular layer. The distal portion of the catheter retains highly flexibility and kink resistance because of the advantages inherent in a corrugated outer structure and using materials of appropriate stiffness and thickness.

In the present configuration, the pitch of the helical support may vary over the length of the catheter to influence the flexural stiffness of the catheter. For example, the helical support could have a different pitch at the proximal loops compared to the distal loops.

If the outer tubular layer of the distal portion of the catheter is formed from a fluoropolymer such as ePTFE or PTFE and the outer tubular layer of the proximal portion is formed from a different polymer then achieving a good bond, especially one that resists delamination during tracking, can be difficult. This may be overcome by sandwiching the outer layer of the proximal portion

of the catheter between the inner and outer tubular layers of the distal portion of the catheter as shown in Fig. 6.

Fig. 6 shows a portion 200 of a catheter, having an inner lumen 201 with a liner, an outer layer 203 of Pellethane 80AE material, and Nitinol coils 206. On the right hand side the catheter has a smooth outer surface 203, and distally in a transition section there are corrugations 204 with a small depth, and more distally deeper corrugations 205 for more flexibility. The arrangement of having a transition section between proximal and distal sections may be referred to as a “sandwich arrangement”.

If the inner tubular layer of the distal portion of the catheter is formed from a different material or different section of material from that of the inner tubular layer of the proximal portion then the tubular layers can be joined by creating a small slit or window in one tubular layer and pulling a spliced length of the other tubular layer through it as shown in Fig. 7. The helical support is then wound around the outside of these layers thus keeping them together.

Fig. 7 shows a catheter section 250 with a proximal end 251, a transition section 252, and a distal tip 253, and a spliced proximal layer 260 with a window 261.

In various embodiments the helical support is physically attached by being constrained or embedded in the catheter wall to move with its surrounding wall material. Such embedding might be achieved at an interface between the coil and solely the jacket material, or combination of an interface of the jacket material and the inner liner.

The embedding can be achieved by a very tight fit between the coil and the surrounding material. Generally, there is no gap between the surrounding wall material and the coil. Due to the three-dimensional geometry of the coil, when within a surrounding material, it is unable to move independently.

Due to the manufacturing technique in which the material may be moulded around the coil, there is no play between the coil and jacket, meaning it cannot move independently. That is to say, the coil is immovable without concurrent movement or deformation the surrounding jacket material.

This lack of play, and tightness of fit means there is an interfacial friction between the coil and surrounding material, further providing constraint, and meaning the coil and surrounding material must move together.

5 In other embodiments, the coil may be floating, that is to say there is not a tight fit between the material in the jacket and the helical coil. In these instances, there is some play between the helical support and the jacket. This is particularly the case where the jacket material surrounding the helical support is comprised of ePTFE. In this instance, even in the presence of a relatively tight geometric fit, the material is quite supple and may allow movement of the helical support
10 relative to the ePTFE.

In general, the following are some preferred parameter ranges for aspects of the catheter.

For at least some of the length of the catheter the width of the corrugate is no more than 50% of
15 the pitch of the corrugate.

For at least some of the length of the catheter the width of the corrugate is between 5% and 49% of the pitch of the corrugate, and more preferably the width of the corrugate is between 15% and 45% of the pitch of the corrugate.

20 For at least some of the length of the catheter the width of the corrugate is between 20% and 45% of the pitch of corrugate.

For at least some of the length of the catheter the width of the corrugate is at least 10% of the
25 jacket thickness.

For at least some of the length of the catheter the width of the corrugate is at least 20% of the jacket thickness.

30 At the most distal region of the distal portion the width of the corrugate is at least 60% of the jacket thickness.

At the most distal region of the distal portion the width of the corrugate is at least 60% of the wall thickness and the depth of the corrugate is at least 70% of the wall thickness.

35 The ratio of the width of the corrugate to the depth of the corrugate is at least 0.5 in at least one region of the catheter

In the embodiments described below the coil may be either embedded or floating in some or all regions of the catheter, unless stated otherwise.

Referring again to the construction of the catheter structure, we achieve a catheter with a highly flexible distal tip, to ensure that a smooth transition in flexural stiffness and pushability is achieved between the flexible distal portion and the proximal portion of the catheter, which may be of more conventional construction. A smooth transition prevents areas of stress and strain concentration within the catheter shaft. Such areas have potential for kinking of the catheter, delamination of layers of material, and/or of damage to key bonds within the catheter.

Bench testing demonstrates the large difference between the stiffness of a conventional catheter tip design and a highly flexible corrugated design. Smoothly bridging of this gap presents a technical challenge.

Fig. 8 shows force measured at a 1 mm displacement in a 3-point bend test of a conventional catheter design (0.80A urethane jacket over a 0.005in NiTi coil 0.018in (0.45 mm) pitch over on a 0.001in (0.025mm) PTFE Liner), and highly flexible corrugated ePTFE design (inner and outer 0.002in (0.05 mm) wall ePTFE 0.9g/cm³ density, with a 0.005 in (0.125 mm) NiTi coil, 0.018 in (0.45 mm) pitch.

It should be appreciated that while very good catheter shaft flexibility allows the catheter to navigate extremely tortuous bends at low force and reduced potential for vessel damage, it can also lead to some compromise in pushability. For clarity, pushability is understood as the transfer of force and/or displacement applied at a proximal portion of a catheter, across a length of the catheter, to a more distal portion.

Catheter flexibility may limit the transfer of a displacement applied at a proximal portion of the catheter to a distal portion of the catheter. This implies a portion of the displacement is absorbed through global deformation of the catheter as shown in Fig. 9. Fig. 9 shows behaviour of a conventional catheter under compression when pushed against restriction. In this instance the length of the catheter 600 has not changed. In general, it is this type of shortening which occurs in catheters of conventional construction.

Fig. 10 shows behaviour of a corrugated catheter 650 under compression when pushed against restriction. In the case of a corrugated outer jacket with a thin inner and outer tubular layer, the deformation may be accommodated by the catheter wall. The inner and or outer tubular layers of the catheter can deform locally, particularly in the recess meaning the overall length is reduced.

5 Some of the global deformation of the catheter as shown in Fig. 9 would also be expected.

This soft compressive behaviour is advantageous at the distal tip as the catheter tip is limited in its ability to move forward causing vessel damage or dissection. However, in cases in which the distal tip is very long, some increased pushability in the proximal portion of the tip may be
10 preferable to allow the physician to navigate the catheter distally and proximally as intended.

In one configuration one or more regions of varying pushability and flexibility are present within the catheter tip comprised of one or more of the regions of a rib and recess construction. Fig. 11 shows in a catheter 700 use of progressively more flexible or less pushable sections of catheter
15 wall 701 within the distal tip, distally of a proximal portion 702. In one configuration the most flexible region is on the distal tip of the catheter.

These regions of increased/decreased pushability/flexural stiffness are achieved by a number of features such as embedding of the helical support, alterations to the inner and outer tubular layers
20 (wherein the helical support may or may not be floating between the inner and outer tubular layers), or the use of an in-fill material.

The change in the stiffness or pushability via the transition region may be gradual change or via multiple steps. Where it is stepped or gradually changed it may be achieved by having a
25 particular tubular layer terminated, or by a change to the degree of corrugation or a change in material.

It is envisaged that any or all of these approaches may combined on some or all of the catheter shaft. Examples are as follows:

30 A distal tip in which at least some is of corrugated material which embeds a helical support, wherein the degree of corrugation is altered progressively proximally to achieve in increase in stiffness. The most distal region may or may not have a liner. The liner is ePTFE, transitioning to PTFE in a more proximal region. The most proximal portion may not be corrugated.

5 A distal tip in which at least some is comprised of a floating coil between ePTFE layers with a corrugated design, wherein the thickness of the ePTFE material increases progressively, or in steps proximally. This may be achieved by increasing the wall layer thickness, or by the addition of layers material. The ePTFE liner transitions to PTFE in a more proximal region. The most proximal portion may not be corrugated.

10 A distal region may be comprised of a floating coil between ePTFE layers of corrugate design and more proximally a corrugated embedded portion, and more proximally again of an un-corrugated portion. The ePTFE liner transitions to PTFE in a more proximal region. A distal corrugated region may be combined with a more proximal corrugated region with increasing wall thickness, or the addition of a layer of material to the wall to increase stiffness. The most proximal portion may not be corrugated.

15 In one configuration the helical support is embedded by being bonded to the outer jacket, of for example ePTFE material. This has the effect of stiffening the catheter wall construction, when compared to a floating helical support, thus reducing the flexibility and increasing the pushability.

20 In one configuration, in a catheter portion 750 the helical support 752 is embedded in a matrix 753 of continuous porous flexible material such as ePTFE. The outer wall has corrugated surface, as shown in Fig. 12. An inner tubular layer, or liner 751, as shown in Fig. 12, may not be required.

25 While ePTFE provides a very soft flexible material in the catheter construction it is also compressible due to its porosity. Furthermore, when used as a thin tubular layer which deforms easily locally, macro pushability can be compromised if an area of the catheter becomes impeded particularly if the distal tip meets a resistance. To improve pushability while maintaining high flexibility, an incompressible flexible material may be used for embedding instead of a porous material such as ePTFE. This means it can accommodate deformation more readily than
30 materials which are not porous.

The corrugations allow localised deformation, while a region of continuous incompressible material ensures the efficient transfer of axial force and displacement along the length of the catheter. By reducing the depth of the corrugations, and correspondingly increasing the

thickness of the continuous material, the pushability of the catheter can be increased, while the flexibility is reduced. This may be described as a corrugated jacket design.

- In one embodiment the inner tubular layer is comprised of ePTFE. In one configuration the helical support is transposed from the inner liner such that it is not exposed to the liner. This is to prevent movement or debonding of the helical support, and to prevent it placing local stress or strain on the liner of the catheter. The corrugation geometry may be of semi-circular, U-shaped groove, V-shaped, or square groove.
- In one configuration the width of the corrugate at the surface of the catheter is at least 5% of the wall thickness of the wall. Preferably, in at least one section the width of the corrugate at the surface of the catheter is at least 10% of the wall thickness at the wall. Preferably, in at least one region of the distal tip, the width of the corrugate at the surface of the catheter is at least 30% of the wall thickness at the wall.
- In one embodiment the corrugate depth is between 5% and 95% of the catheter wall thickness. In one configuration the corrugate depth is at least 20% of the catheter wall thickness in at least one section of the catheter.
- In one embodiment, the corrugate depth varies along the corrugated region of the catheter from a larger depth distally to smaller depth proximally. In one embodiment, the corrugate width varies along the corrugated region of the catheter from a larger depth distally to smaller depth proximally. In another embodiment, the corrugate depth varies from a larger depth distally to smaller depth proximally, while the width is substantially constant along the length of the corrugated section of the catheter.
- In one embodiment the corrugate represents the impression of a circular helical wire wound from a depth and width of no impression, i.e. no corrugate, to a depth of at least 50% of the wall thickness. It should be appreciated in that instance that the width of the corrugate is varying from 0 to a maximum width equivalent to the diameter of the helical wire, or impression which remains following removal of the helical wire.

It should be appreciated that a tensile force on the wound cinch helical wire is required to create the corrugations. For example, a 0.005in 304 Stainless Steel circular cross section wire at 1N

tension wound at a force 1N, on an 0.006in wall thickness 80A jacket with an ID of 0.088in will achieve a 10-20% depth of corrugation. Increasing the tension to 1N tension wound at a force 7N will achieve a 40-70% depth of corrugation. Varying levels of force will induce different degrees of corrugation. It should be appreciated that corrugations of high depth D as shown in
5 Fig. 1 will allow the catheter section to flex at a relatively low force. This is because the global bending of the catheter is actually concentrated within the recess of the corrugate.

However, if the corrugation has a very low width, even very deep and numerous corrugations will have a limit to the degree of bending the catheter can accommodate. This is because
10 adjacent corrugations will start to touch one another. Therefore, the flexural stiffness will be low until the adjacent corrugations contact one another, or “bottom-out”, at which point the flexure stiffness will increase. Bending will then be accommodated by deformation of the rest of the catheter wall (and no longer primarily within the recesses)

15 This bottoming-out means the catheter shaft has a lower limit of bend-radius which it can achieve via deformation within the recess. Further bending deformation beyond the bottoming-out limit is achievable but is not accommodated by deformation at the recess of the corrugation; it is accommodated by pressing adjacent corrugations against one another. This is generally at a very high force compared to the deformation which occurs at lower bend radii while the
20 deformation is focused in the recess.

The width of the corrugate should be controlled so as to be large enough to accommodate sufficient deformation within the recess to reach the desired lower limit of bend-radius at relatively low force of bending. This is important as physicians generally wish to be able to
25 navigate catheters at low forces so that the potential for vessel damage is reduced, and the catheters are not deforming the vessels in order to travel forward.

While the width and depth of the corrugation contribute to the flexural stiffness of the catheter, the width can dominate the lower limit of bend-radius to which the catheter can deform.
30 Accordingly a larger corrugate width enables a lower bend radius at a low force of bending.

Consider the example of an 0.088in ID (2.2 mm) catheter with a wall thickness of 0.006in (0.15 mm) with an 0.005in (0.125 mm) diameter Nitinol helical support of 0.018in pitch embedded in 80A, over an ePTFE Liner. A sample with a 0.004in (0.1mm) corrugate width and 0.006in

corrugate depth will yield a force in 3pt bending of 0.05N at 1mm deflection, and a bottom out bend radius of 5mm. A sample with a 0.007in (0.175) corrugate width and 0.006in corrugate depth will yield a similar force in 3pt bending but bottom out bend radius of 3.5mm.

- 5 In order to allow a large catheter to enter the cerebral vessels safely, and to accommodate lower radii bends such as those of the carotid siphon, the width of the corrugate should be of a minimum value relative to the pitch and or wall thickness.

- 10 In one embodiment the width of the corrugate is no more than 50% of the pitch of the corrugate (same as the pitch of the helical support). Preferably the width of the corrugate is between 5% and 49% of the pitch of the corrugate. More preferably the width of the corrugate is between 15% and 45% of the corrugate. More preferably the width of the corrugate is between 20% and 45% of the corrugate.

- 15 In one embodiment the width of the corrugate is at least 10% of the wall thickness. Preferably the width of the corrugate is at least 20% of the wall thickness. In one embodiment at the most distal section of the tip the width of the corrugate it at least 60% of the wall thickness.

- 20 In one embodiment at the most distal section of the tip the width of the corrugate it at least 60% of the wall thickness and the depth of the corrugate is at least 70% of the wall thickness.

- 25 In another embodiment the corrugate represents the impression of a circular helical wire wound from a depth and width of no impression, i.e. no corrugate, to a depth of at least 70% of the wall thickness.

- 30 In one configuration, the inner tubular layer (liner) terminates in a region proximal to the distal end of the catheter. This will further reduce the stiffness of the catheter for a corrugated or uncorrugated configuration. In this instance, particularly in the case wherein the catheter wall is comprised of a material such as a silicone, urethane or pebax, the region without a liner may be tacky. In one embodiment the region of inner lumen of the catheter without a liner has hydrophilic or hydrophobic coating to improve lubricity. This is shown in Fig. 13 for a catheter portion 760 having a helical support 761 embedded in an outer jacket 762, and in which an inner liner 763 extends for part of this length but terminates before the distal end (left side).

In one embodiment the un-lined section is at least 1cm in length, preferably at least 2 cm in length. The termination of the liner is advantageous in allowing a more flexible section of the catheter. However, this can also form a sudden change in flexural stiffness and potential location for kinking or high stress or strain. This may be managed using a change in corrugation parameters, or by skiving the liner. In another embodiment, the termination of the liner is a skive, or angular cut.

In one configuration a section of the un-lined jacket material adjacent to the liner proximally is less corrugated than the section of unlined jacket distally and proximally. This may be achieved by decreasing the depth of the corrugation. In another configuration a corrugated section of the lined jacket adjacent to the unlined jacket has a longer pitch than the section of unlined jacket distally and proximally.

In one configuration the helical support is transposed from the inner liner such that it is not exposed to the inner lumen of the catheter as shown in Fig. 14, having a helical support 771 in an outer jacket 772. This is to prevent pop-out the helical support into the catheter lumen during bend of the catheter. In one embodiment the distance from the inner lumen to the helical support is at least 0.005mm.

Referring to Fig. 15, in a catheter portion 780 there is a helical support 781, and an outer jacket 782 and an inner liner 783. The outer jacket 783 has a proximal part 784 without corrugations, distal part 785 with corrugations. The inner liner 783 terminates proximally of the distal end at 786. This is an example of a configuration in which the most distal section of the distal tip is comprised of a corrugated jacket without a liner, a more proximal section is corrugated and contains a liner, at least one section even more proximally is more corrugated, and at least one section even more proximally again is un-corrugated. In one embodiment all sections of the jacket are of the same material durometer. In one embodiment the material is urethane of durometer 80A. In another embodiment more proximal jackets are of a stiffer urethane or Pebax are present. The liner is comprised of ePTFE. In a more proximal section of the shaft, the liner may transition to PTFE. In one embodiment this transition takes place in a more stiff durometer material than that of the jacket of the corrugated distal tip.

In one embodiment, a catheter portion 800 has a liner 751, a helical support 752, and an outer jacket 753 as for the catheter portion 750. However, in this case there is an outer tubular layer

801 added to the outside of the corrugated structure which embeds the helical support to further increase the stiffness of a section of the catheter proximally of the distal end, as shown in Fig. 16. This layer may be of the same or different material as the material used to encapsulate the helical support. Materials of higher stiffness such as PET or Nylon pr PEEK or other polymer
5 can be used in this instance without significantly adding to the profile. In one embodiment a layer of PET is added which has a thickness of 0.05 mm or less, preferably 0.025 or less, and more preferably 0.0125 mm or less.

In order to manufacture a corrugated polymer jacketed catheter section a number of approaches
10 may be taken. The following steps may be used as shown in Fig. 17:

A conventional catheter construction containing a coil 752 embedded within a polymer jacket 753 is bonded to a PTFE liner 751 is built to form a base assembly.

An outer liner 811 which will not bond to the polymer jacket is then placed over the
15 jacketed coil. Fluoro polymers of high flexibility such as FEP or PTFE or more preferably ePTFE may be used.

A wire 810 is wound in a helix onto the outside of the outer liner under tension imparting a corrugate geometry on the construction. This may be termed a “cinch wire”

The construction is heated to reflow or anneal the material, setting it into the corrugate
20 geometry

The assembly is cooled

The cinch wire 810 is removed

The outer liner 811 is peeled off the assembly to complete the process.

25 An in-fill material may also be used to manage flexibility and increase pushability, and where it is used it embeds the coil. Fig. 18 shows a catheter portion 850 with a liner 851, a coil 852 and inner and outer tubular layers 853 and 854 respectively and in-fill for increased stiffness

In one embodiment the material is used only to partially fill the space around the helical support
30 as shown in Fig. 18. In another embodiment the in-fill material completely fills the helical channel around the helical support between the inner and outer tubular layers. In yet another embodiment the in-fill material is melted to form a layer of material on all surfaces within the helical channel.

35 In one embodiment the outer and inner tubular layer are comprised of ePTFE or PTFE, and the in-fill material is PET, PEEK or FEP

The helical channel may be formed using a helically wound wire (cinch wire) placed temporarily on the outside of the outer tubular layer. To permanently form the helical channel, the construction may then be heated such that the in-fill layer melts to flow between the helical support, the outer tubular layer, and the inner tubular layer. Upon cooling and removal of the helically wound cinch wire on the outer tubular layer, the corrugate configuration is maintained, and an adhesive chemical bond is achieved between the components via the in-fill material.

In one configuration the in-fill material may be a polyurethane, pebax, PET, silicone, latex, Tecothane, Nylon, PET, Carbothane, SIBS, Tecoflex, Pellethane, PGLA or Kynar, Polyethylene and cyclic olefin copolymers, PEEK.

In one configuration the inner tubular layer and outer tubular layer of ePTFE are bonded to one another via sintering. It must be appreciated that in the case of a fluoropolymer, and in particular ePTFE or PTFE for use as the inner and outer tubular layers, the temperature required for the sintering can exceed 500°C. In this instance it may be preferable to use materials for in-fill with a high processing and degradation temperatures such as PET, FEP, or PEEK. Other materials such as urethane or pebax will degrade at lower temperature and are not suitable.

As PET is a relatively stiff material it can be introduced in small volumes to stiffen the corrugate structure without significant impact on catheter profile or completely filling of the helical channel. This may provide regions of floating and of embedded coil.

In one configuration an increase in the pushability or stiffness is achieved by changing the thickness of one or both of the tubular layers. An increase in thickness increases the intrinsic stiffness of the wall. It also means a reduction in the available space for localised material bending and deformation. Therefore, the flexibility may be reduced. Furthermore, as the thickness increases the axial cross-sectional area along the axis of transmission of force and displacement along the catheter increases.

In one embodiment, both the inner and outer tubular layer thickness are increased, as shown in Fig. 19 for the catheter portion 950 as compared to the catheter portion 900. In the catheter portion 900 there is an inner liner 901, a coil 902 and an outer tubular layer 903. In the catheter portion 950 there is a thicker inner liner 951, a coil 952, and a thicker outer tubular layer 953. In

another embodiment the inner tubular layer thickness alone is increased. In yet another embodiment the outer tubular layer thickness alone is increased.

In another configuration the total outer tubular wall thickness may be altered by the addition of one or more layers of the same material. Referring to Fig. 20 a catheter portion 1000 has a liner 1001, an outer jacket layer 1002 underneath a coil 1005, and two layers 1003 and 1004 outside the coil 1005.

The total inner tubular layer wall thickness may be increased by the addition of one or more layers. These layers may be of the same or different materials. In the case of ePTFE, the combined thickness of the inner tubular layers in an unconstrained configuration may be between 0.025 mm to 0.3 mm, preferably between 0.05 mm and 0.2 mm.

In one configuration the inner and outer tubular layers are comprised of multiple layers of ePTFE, wherein there is at least one layer between an outer tubular layer and an inner tubular layer. The total thickness of (for example, ePTFE) tubular layers which are comprised of one or more layers may be between 0.025 mm to 0.3 mm, preferably between 0.05 mm and 0.2 mm. The density of the material (again, such as ePTFE) may be approximately 0.9g/cm^3 . Increasing or decreasing the density of the material will necessitate a bigger or smaller wall thickness to achieve the same effect.

In another embodiment the inner tubular layer thickness is constant along the length of the tip, but the outer tubular layer thickness is larger in at least one region. In another embodiment the outer tubular layer thickness is increased proximally at least once along the length of the catheter tip.

In order to achieve a controlled change in stiffness of the distal tip, multiple layers may be overlapped to achieve a precise level of stiffness as shown in Fig. 21 in which an additional outer layer 1010 is present for part of this catheter portion. This principle may be used for any number of layers, to achieve a desired variation in stiffness. Similarly, single thicker layers may be used proximally, connected to a thinner layer more distally to achieve the same effect.

In one embodiment the tip has one outer tubular layer of 0.025 mm to 0.075 mm across the length of the tip. A second additional outer tubular layer of thickness 0.025 mm to 0.075 mm is present in a region more proximally. A third additional outer tubular layer of thickness 0.025 to

0.075 mm is present in a region even more proximally. A fourth additional layer of thickness 0.025 to 0.075 mm is present in a region even more proximally.

- 5 In one embodiment the distal tip comprises an outer tubular layer of 0.05 mm across the length of the tip. A second additional outer tubular layer of thickness 0.05 mm is present in a region more proximally. A third additional outer tubular layer of thickness 0.05 mm is present in a region even more proximally. A fourth additional layer of thickness 0.05 mm is present in a region even more proximally.
- 10 In one configuration the tubular layers are bonded to one another. The bond may be present across the entire interface of the tubular layers. Alternatively, the bond may only be present at recesses of the corrugations, in the area where the inner and outer tubular layer are in contact. In yet another embodiment, the bond is present between the layers at the rib and recess regions of the corrugations. In another embodiment the material of the inner or outer tubular layer may be
- 15 changed to one with a higher stiffness to increase the stiffness of the wall.

- It should be noted that some variation in the thickness of the tubular layers may be present locally following bonding of inner and outer tubular layers, or their constituent layers, due to the use of local compression (pressure) to ensure a strong bond between tubular layers. This is
- 20 particularly so with ePTFE because it is a porous compressible material. This localised compression may reduce the wall thickness in that area.

- To evaluate a subset of the embodiments described above, 8F catheter samples of inner diameter 0.088in were built and tested in a Three Point Bend Test. The force at a 1mm displacement was
- 25 measured using a 50N Load Cell on a Zwick Roel tensile test machine. The distance between the supports was 20mm. Clear changes in stiffness were achievable using the various configurations outlined above.

- It can be appreciated that the embodiments described above can be used to alter the stiffness of
- 30 the catheter wall as desired. For comparison, a 6F Microvention Sofia Plus catheter indicated for use in neurovasculature is included. Fig. 22 shows results of 3-point bend tests to evaluate stiffness of various embodiments described above.

In the neurovasculature, when entering delicate vessels such as M1, M2, ICA, vertebral and basilar arteries, an atraumatic tip of critical importance. It is preferable that the distal tip has a minimum length of its most flexible section such that the catheter tip will deflect or absorb deformation rather than causing vessel damage.

5

In one embodiment the distal and flexible sections of the catheter of corrugate rib and recess design is a minimum of 1cm in length and is comprised of inner and outer tubular layers in a corrugate configuration, with a floating helical support within a helical channel. In one embodiment for an 8F catheter distal tip, the force in 3-point bend test, for a span of 20mm, at 10 1mm deflection, should not exceed 0.1N.

As shown in Fig. 23, in one configuration, the distal-most end 1050 of the distal portion is finished by inverting an inner tubular layer 1051 over the helical support to form a continuous element.

15

Referring to Fig. 24, in another embodiment, in a distal end 1060 the softness of the distal tip end is improved by extending inner and outer tubular layers 1061 and 1062 beyond the last coil of the helical support.

20

As shown in Fig. 25A, in a distal portion 1070 an inner tubular layer 1071 is inverted at the distal end 1072 to return as a continuous element. Inner and outer tubular layer are comprised of the same piece of material and are continuous. An extension of ePTFE at the end 1072 of the corrugated section is present to improve tip softness. Preferably, an extension beyond the last coil is between 0.5 and 5.0 mm. More preferably the extension beyond the last coil is between 25 1.0 and 0.3 mm. The distal portion 1070 also has an outer tubular layer 1073 terminating before the distal end 1072, and a concentric further outer tubular layer 1074 around the layer 1073 for part of the length of the layer 1073. This staggered overlapping arrangement provides a transition portion with stepped changes in flexural stiffness.

30

Fig. 25B shows a catheter distal portion 1080 with an inner liner 1081 which extends out at the distal tip to form an extension. In this case there are also overlapping staggered outer tubular layers 1083 and 1084.

In the catheter 1070 two or more layers are achieved by using the same piece of material inverted and returned along the length or a portion of the catheter. In one instance two pieces of ePTFE are used to achieve one inner tubular layer, and three outer corrugated tubular layers.

- 5 In the catheter 1080 additional layers are added discretely. In another embodiment, a combination of inverted continuous layers and discrete layers is used. The proximal portion of the catheter (shown un-corrugated) may be corrugated or un-corrugated.

PTFE material is a relatively stiff material compared to ePTFE and so is therefore preferable to
10 avoid the use of PTFE as an inner tubular layer (liner) particularly in areas which will be subject to significant bending during passage through tortuous vessels. In one embodiment, as shown in Fig. 26, in a catheter 1100 having a proximal end 1101 and an intermediate portion 1102 an inner tubular layer is of ePTFE material and this extends along the entire length of the catheter including a distal end 1103, where it is bent back to be continuous with the outer tubular layer.

15

In one configuration, the inner tubular layer is ePTFE in a distal portion and PTFE in a more proximal portion of the catheter as shown in Fig. 27 for a catheter 1150 having a proximal end 1151, an intermediate portion 1152, a distal portion 1153. There is a transition region 1154 in which the outer jacket a layer is merged into and joined with an outer jacket of PTFE material in
20 the intermediate portion and the transition region. The transition from ePTFE to PTFE may be achieved by a "butt" joint, in which the inner tubular layers of PTFE and ePTFE are in contact without overlap.

- 25 In another embodiment, a transition from inner tubular layer of ePTFE to PTFE occurs in a region of the catheter which is not subject to significant bending during use. In one configuration the device dimensions are suitable for placement in the neurovasculature, including M2, M1 and distal internal carotid arteries. Preferably, the transition from ePTFE to PTFE occurs proximal to the petrous segment of the ICA. In one configuration, the transition
30 from an ePTFE to PTFE inner tubular layer occurs between 3 and 40cm from the distal end of the catheter, preferably between 5 and 30cm from the distal end, and more preferably at least 10cm from the distal end.

In one configuration, the transition from inner tubular layer of ePTFE to PTFE occurs in a region
35 proximal to a region of the catheter of rib and corrugation recess. In another configuration the

transition from inner tubular layer of ePTFE to PTFE occurs proximal to the most flexible region of a rib and recess corrugate design, but still within a region of stiffer rib and recess corrugate design.

5 In one embodiment the proximal region of rib and recess corrugate has an outer tubular layer comprised of a polymer material, as shown in Fig. 28. In one configuration the polymer material is a urethane or Pebax. In one embodiment the polymer material is 80A urethane. Fig. 40 shows a catheter 1200 having a proximal end 1201, an intermediate portion 1202, a distal portion 1203, and a transition region 1204. An ePTFE inner tubular layer (liner) 1207 transitions to a PTFE jacket 1205 in the intermediate portion within a corrugated section of the distal tip. A lap joint is used in which the PTFE tubular layer 1208 is concentric within the ePTFE tubular layer 1207.

In another embodiment the transition from ePTFE to PTFE may be achieved via a “lap” joint wherein there is overlap of the tubular layers of ePTFE and PTFE. In one configuration the overlap between the PTFE and ePTFE is between 1mm and 30mm in length. The use of an overlap increases the area of interface for bonding thus improving the bond strength.

In one instance for a distance the ePTFE is concentric within the PTFE, as shown in Fig. 29. In this diagram a catheter 1250 has a proximal end 1251, and intermediate portion 1252, and a distal portion 1253. An inner liner 1260 is bent over at the distal end to form part of the outer jacket of the distal portion 1253. At a transition region between the intermediate portion 1252 and the distal portion 1253 the inner liner 1260 is within a tube of PTFE material 1261 with an overlap length of at least 2mm, preferably at least 5mm. The tubular layer 1261 extends proximally within a jacket material 1262 in the intermediate portion 1252. This provides a configuration with an ePTFE inner tubular layer (liner) transitions to PTFE within a corrugated section of the distal tip. A lap joint is used in which the ePTFE tubular layer 1260 is concentric within the ePTFE tubular layer. 1261

In one configuration, a marker comprised of a helical coil of Platinum is present on the distal tip.

In one embodiment, the helical support may be comprised of a radiopaque material such as Platinum wire. In another embodiment, to leverage the super elastic properties of Nitinol with radiopacity, the helical support may be comprised of drawn Nitinol tubing filled (such as Nitinol#1 DFT, Fort Wayne Metals) with Platinum or other radiopaque material. This would allow the physician to observe the distal tip behaviour under x-ray through the procedure. In one

embodiment the helical support tube is comprised of at least 10% Platinum. Fig. 30 shows such an arrangement in which a catheter portion 1280 has a radiopaque helical coil 1281 around which there is a coating 1282, and there is a tubular layer 1283 over the outer jacket.

- 5 In one configuration, the radiopacity of the distal tip is further enhanced via a region in which the helical support pitch is reduced such that an area of greater density of radiopacity is achieved.

Fig. 31 shows catheters with radiopaque markers 1270 at various positions along its length. Advantages and novel aspects are that allow the physician to ensure that more stiff regions the catheter are not placed in more delicate region of the vasculature. For example, a proximal marker at the start of the flexible distal tip can be used to define the region of the proximal catheter which should not be placed beyond the cervical C1 segment of the internal carotid artery. An intermediate marker can further be used to differentiate the end of a region of intermediate flexibility which should not be placed before, within, or beyond the cavernous segment C4. The region between the intermediate marker and distal marker establishes the region of highest flexibility which is suitable for placement in the C4-C7 regions of the internal carotid artery, and more distal vessels.

In one embodiment, in which the device is suitable for placement in the neurovasculature, the distal flexible tip length is at least 10 cm, and the un-lined distal section is at least 3cm in length. In another embodiment in which the device is suitable for placement in the peripheral vasculature, the

Aspiration Device including the Catheter.

25 A catheter of any example may be used for example for thrombectomy. Recent clinical data has demonstrated that use of flow arrest using a balloon guide catheter can improve outcomes during thrombectomy procedures. This is done by:

30 Reducing flow towards the clot while the balloon is inflated proximal to the clot in the ICA. Reducing the flow reduces the potential for distal emboli to break off, or be carried distally, during the clot retrieval using a stentriever or aspiration catheter.

Providing a lumen for aspiration as the clot enters the BGC after it has been captured by a stentriever or aspiration catheter, and is dragged from the target site.

The prior art setup of balloon guide catheter in a thrombectomy procedure is shown schematically in Fig. 32, with a balloon 1300 and a tip 1301. Balloon guide catheters for use in thrombectomy procedures must facilitate the insertion of a microcatheter, and distal access catheter. In order to do this, the balloon guide must have an inner diameter in the range of 5F or greater. Additionally, the catheter typically has an outer diameter in the range of 8F or 9F.

Existing catheter technology, at the dimensions described above, is extremely stiff. This is due to the catheter materials, design and architecture used. Therefore, the distal tip of the balloon guide catheter cannot be placed beyond the petrous segment. Excessive stiffness means the catheter is not flexible enough to track through the tortuosity of the distal ICA and other target vessels where the clot may be located, and there is a high potential for vessel damage or perforation.

Ideally, the tip of the balloon guide catheter should be as close to the clot as possible. This reduces the distance over which the clot must be dragged from the target vessel to the location of the balloon guide catheter tip. It may also enable the physician to directly aspirate the clot locally as the tip of the catheter can now engage the clot.

In some scenarios, remote aspiration of the clot is being performed using balloon guide catheters, while the balloon is inflated. Remote aspiration is a procedure in which the clot is aspirated without contact of the catheter tip with the clot. This works particularly well in a closed system where alternative flow pathways are not present. The success of this technique is often limited by the fact that the tip of the catheter can be a long distance from the clot.

A balloon catheter, whether used for PTA or embolic protection, is typically of a dual lumen, double layer construction along the length proximal to the balloon. This ensures there are two lumens; one for the passage of guide wires, catheters, or fluids, and one lumen for inflation. This dual layer construction is not always as flexible as desired, and is prone to kinking.

There is therefore a need for a balloon guide catheter which can provide flow arrest, but which also incorporates a very flexible distal portion which can track through a tortuous vessel, such as the distal ICA or as far as the M I or other vasculature.

In one embodiment a shaft or section with enhanced flexibility compared to the proximal section is present distal to the balloon of a balloon catheter. This flexible section enables the tip of the balloon to be placed more distally in the vasculature. This section of enhanced flexibility may be comprised of the types described in U.S. Application No. 15/647763, filed July 12, 2017, titled
5 "HIGH FLEXIBILITY, KINK RESISTANT CATHETER SHAFT," and U.S. Provisional No. 62/599560, filed December 15, 2017, titled "HIGH FLEXIBILITY, KINK RESISTANT CATHETER SHAFT" (both included in the Appendix), corrugate construction or other design.

This device may be designed so that the distal tip is flexible enough to reach and touch the clot
10 for vacuum aspiration. The part which is distal of the flow restrictor (such as the balloon) includes the distal portion and preferably at least some of the transition portion. There may also be some of the transition portion proximally of the flow restrictor.

The length of this flexible section may vary such that it can reach specific anatomical locations,
15 such as the distal internal carotid artery, terminus of the internal carotid artery, proximal MI, distal MI, proximal M2, distal M2, basilar, or vertebral vessels. This length may also help ensure that that while the tip of the catheter can reach the target vessel, the balloon does not pass the cavernous, or petrous segment of the ICA. Inflation of the balloon beyond these segments can cause vessel damage. The length of the flexible section may be between 1cm and 20cm,
20 preferably between 3cm and 15cm.

The outer diameter of this flexible tip may differ from the outer diameter of the proximal section of the catheter. In one embodiment the distal section has a larger diameter than the proximal section. In yet another embodiment the outer diameter has a diameter smaller than the diameter
25 of the proximal section of the catheter. Variations such as a taper in the diameter of the distal section may also be used. Differing diameter distal sections can help to ensure access to specific vessels beyond the area to land the balloon.

Fig. 33 shows a device 350 with a flexible distal catheter tip 1351 extending from a balloon
30 1352, and proximally of which there is a catheter main section 1353 extending from a Y-piece 1354. Fig. 10 shows the balloon 352 inner layer inflation lumen 1360 and the balloon outer layer inflation lumen 1361.

In one configuration, the outer layer of balloon inflation lumen may of enhanced flexibility while the inner layer of the balloon inflation lumen may be of a conventional construction comprising a single layer material, braided extrusion, coiled extrusion or other construction. These layers are shown schematically in Fig. 34, inner layer 1360 and outer layer 1361. In this way the pushability of the catheter may be maintained by the inner layer, while the outer layer mitigates compromise in terms of flexibility. Furthermore this construction will help to prevent kinking, since mechanics dictate that as the ratio of the inner diameter to the outer diameter of a tube increases, kink resistance is reduced. Use of the enhanced flexibility construction for the outer layer, traditionally more prone to kinking will solve this issue.

In another embodiment, a balloon catheter of dual layer construction comprises both inner and outer layer of the balloon inflation lumen of the enhanced flexibility construction. This will represent an ultra-flexible and kink resistant balloon catheter.

In other configurations, the proximal section may utilise other constructions to inflate the balloon such as a single lumen design with a vent hole and teak proof seal, a coaxial lumen or other design.

It should be noted that a balloon guide catheter, with a long distal tip capable of reaching a clot may be used as a thrombectomy device as follows:

Perform an angiogram to determine location of occlusion, and distance between petrous or cavernous carotid, and occlusion

Choose a balloon catheter with distal tip length suitable to reach the clot, while ensuring the balloon inflation does not land beyond the petrous or cavernous carotid

Navigate the distal tip of the catheter to the clot.

Inflate the balloon such that flow arrest is enabled, and alternative flow pathways which could reduce the effectiveness of the aspiration are minimised

Apply a vacuum to the inner lumen of the catheter to aspirate the clot.

If the clot is retrieved, perform another angiogram through the balloon guide catheter or a diagnostic catheter.

Remove the balloon guide catheter.

Procedure is finished.

It may be noted that in the above method, the use of a large diameter distal tip, close to that of the target vessel will maximise the potential of complete clot ingestion.

In yet another embodiment, enhanced catheter shaft flexibility and kink resistance may be achieved without additional helical wire support, but instead using a simple tubular construction with a corrugate architecture. The corrugations may be defined as adjacent circular depressions in the wall thickness of the tube, or as a continuous helical depression as shown in Figs. 35 and 36 respectively. In these diagrams the tip has an outer layer 1400 with corrugations 1401 (Fig. 35) and an outer layer 1450 with more shallow corrugations for desired flexibility.

The device may be designed so that the distal tip is flexible enough to reach and touch a clot for vacuum aspiration. The typical target vessels are the M1, M2, M3, distal ICA.

The distal tip should be long enough to reach the target vessel, while also ensuring that the balloon does not pass the petrous segment of the internal carotid artery (known as C2). This is because the vessels and surrounding tissue beyond the petrous segment are prone to damage which can have catastrophic consequences.

It is preferable to ensure that the location of the balloon when inflated is within C1 segment of the carotid artery. It is also preferable that the balloon be distal to the external carotid artery to ensure effect flow restriction and or flow reversal. The length of the flexible section may be between 1cm and 20cm, preferably between 3cm and 20cm.

Fig. 37 left image shows an Angiogram demonstrating the external carotid, common carotid and internal carotid artery (ICA), including the C1 and C2 segments, and right image shows acceptable positioning of the balloon (2282, in a catheter 2280 proximal of a distal end 2281. It should not be inflated past the C2 segment. The distal tip length of the catheter should be long enough to reach the clot while ensuring safe position within or proximal to the C2 segment of the ICA.

Any or all the embodiments described above to refine the transition from the stiffness of the proximal portion of the distal tip to the most distal portion may be used.

The proximal shaft must serve two functions and have at least two lumens; one for balloon inflation and a main lumen for delivery of fluids and devices, and for aspiration. The flexible tip only requires one lumen, therefore has potential to have a larger lumen than the proximal section. In one embodiment the inner diameter of the flexible tip is the same inner diameter as the proximal shaft.

In another embodiment the proximal and distal shaft have the same outer diameter, and the proximal shaft has two concentric lumens, in which the central lumen diameter is less than that of the flexible distal tip as shown in Fig. 38. This drawing shows a balloon guide catheter 2300 with a flexible corrugated distal tip 2302 and a balloon 2301. In this incidence the inner diameter of a proximal shaft lumen 2303 is less than that of the flexible corrugated distal tip 2302. The proximal and distal shafts have the same outer diameter.

In another embodiment the inner diameter of the proximal shaft is the same as that of the flexible distal tip. In yet another embodiment, the outer diameter of the distal tip is smaller than that of the proximal shaft. The distal tip inner diameter may be the same as, or smaller than, the inner diameter of the proximal shaft. Fig. 39 shows a catheter 1400 with a balloon 2401 and a distal portion 2402 having a smaller outer diameter than the proximal portion 2403.

In one configuration, the distal tip is comprised of a flexible corrugate section distally, and a non-corrugated section proximally. Fig. 40 shows a catheter 1500 with a non-corrugated proximal region 2501 of the distal region 2502.

In one configuration, as shown in Fig. 41 for a catheter device 2600 a radiopaque marker is present at the distal end of the flexible distal tip. Markers are also present immediately distal and or proximal to the balloon to define its location. An additional intermediate distal marker may be present within the distal tip to define a proximal region of increased stiffness unsuitable for placement in distal to the C2 segment of the ICA.

In one configuration, the balloon catheter is suitable for use via direct carotid access. In this case a shorter proximal shaft will improve ergonomics for the physician. In this instance the length of the catheter shaft proximal to the balloon does not exceed 40cm, and preferably does not exceed 30 cm.

Flow Restriction Using Larger Bore Catheter via Near Vessel Occlusion or Wedging

The embodiments described above enable the physician to place larger bore catheters more distally than has been possible using conventional catheter technology. However, it may not be possible to place a larger catheter in the target vessel due to the vessel diameter being smaller than the catheter itself. In this instance a larger catheter may be used to achieve flow restriction.

In some instances, additional vessels are present which perfuse the treatment area. For example, in the case of the anterior cerebral artery, proximal occlusion using a balloon guide catheter placed in the ICA does not prevent inflow to the target treatment site. This is also a problem in posterior stroke where there are two significant inflow vessels (left vertebral artery and right vertebral artery), and the target treatment site is the basilar artery or posterior communicating artery.

In one embodiment a system is comprised of a “mother” and “daughter” catheter, in which significant flow restriction, or flow arrest, may be achieved by placing or wedging a large bore highly flexible mother catheter in a vessel location proximal to the target treatment site. A smaller daughter catheter may then be passed through the parent catheter to the treatment site. In this instance a proximal balloon for flow restriction is not required. Near occlusion of the vessel, without wedging the catheter, will dramatically reduce flow also. This is shown in Fig. 42, in which there is a large catheter 2702 and a smaller catheter 2703 for aspiration of a clot 2701. Large bore highly flexible catheters can enable the most distal flow arrest possible

In other instances, such as embolization, flow restriction using a larger bore catheter may also be advantageous. For example, in embolization, where embolization of non-target vessels is a major concern, additional embolization procedures are often used occlude adjacent non-target vessels. Non-target embolization can cause non-target vessel occlusion, or the delivery of a drug to non-target tissue. This may be avoided if a larger bore highly flexible catheter is placed distally in the vessel feeding the target region of delivery of the embolic such that the catheter tip is wedged. Upon injection of the embolic, the wedged condition prevents retrograde flow of the embolic, thus preventing non-target embolization. Furthermore, the pressure gradient within the vessel is a reflection of the proximal injection pressure, rather than the hemodynamic pressure, giving the physician full control of the delivery of the embolic.

Fig. 43 shows such a configuration, in a catheter 2800 having a distal portion 2801, Left shows the use of a small catheter unable to reach a distal target vessel (right side vessel) during delivery of a drug or embolic and the resulting undesired delivery to a non-target vessel (top left vessel) The right hand diagram shows the use of a method wherein a highly flexible large diameter catheter is chosen to effectively occlude the target vessel, and can be placed beyond the non-target vessel, so delivery of the embolic only occurs to the target vessel. It is preferable that the catheter is wedged in the target vessel.

Furthermore, the distal nature of the vessels targeted in embolization procedures means that often, only microcatheters are capable of entering the vessels today. This limits the type of embolic which can be used (e.g. 018 microcoils may need to be used where larger 035 coils or a plug would be preferred, or the desired particle becomes clogged in the only microcatheter capable of entering the vessel). The technical success of these procedures (in particular embolization for BPH) is also limited by the inability to place larger support catheters distally.

A corrugated catheter section with or without a transition arrangement may be used as a proximal section of a catheter in order to provide flexibility about a particular bend, for example, as an access sheath to provide controlled flexibility about the iliac arch. The configurations may could also be incorporated into a more flexible a urethral stent design or Foley-style catheter, and for a flexible endoscope of corrugate wall.

The device may be used to block blood flow before precise delivery of an embolic agent to region of the vasculature, tumour, or organ.

Aspiration System with Pressure-Controlling Pump

Aspiration has been shown to be safe for the retrieval of clots from the cerebral vasculature. However, technique suffers from a number of limitations. In particular, it is frequently the case that the clot cannot be ingested at the target treatment site. This is particularly the case for harder, larger diameter, and longer clots.

If not completely ingested, the physician will attempt to withdraw catheter and attached clot from the patient under continuous vacuum. This manoeuvre carries risk, is time-consuming, and means the physician has lost access to the target vessel.

If following angiography the physician determines that the target region has not been reperfused, additional attempts must be made to retrieve the clot. Up to five attempts, known as passes are typically required. On average two attempts are required. In 20% to 30% of cases, aspiration is not successful after multiple attempts, and physicians will switch to the use of a stent retriever (Almandoz et al. 2015; Lapergue et al. 2017; Blanc et al. 2017; Mohlenbruch et al. 2016). This further increases procedural time and cost.

As the physician withdraws the catheter proximally towards the access site (typically femoral or radial artery), there is a likelihood that some or all of the clot may break off. These fragments of clot, are known as emboli. Distal emboli lead to poor reperfusion outcomes when assessed under angiography or other imaging. Poor reperfusion, as defined by the TICI scale, is associated with worse patient outcomes.

Another limitation of the aspiration technology is that it is not always possible to advance the catheter tip to the face of the clot. This is due to the extreme tortuosity which may be present in the patient, meaning that often only small diameter catheters such as microcatheters can reach the clot. Larger bore catheters are known to have a greater potential to aspirate the clot, but are frequently too stiff to navigate to the clot face. In this instance, the physician may use a smaller bore catheter, but is less likely to successfully aspirate the clot.

Depending on internal diameter of the catheter, and properties of the clot (diameter, length, hardness/durometer, elasticity etc.), there is a limit to the amount of clot which can be aspirated into the catheter lumen. At this limit the catheter may be described as being clogged. Large lumen catheters can aspirate more clot than small lumen catheters without becoming clogged. During aspiration, the limit to the amount of clot which can be aspirated may be reached before a complete vacuum is reached. This implies that the application of further vacuum does not necessarily increase the amount of clot which is aspirated once a certain limit is reached. This is shown schematically in Figs. 44(a) to 44(e), showing a catheter tip 3500 being used to attempt aspiration of a clot 3501. As illustrated, there is incomplete aspiration. It is a limitation of existing vacuum technology (vacuum pumps and syringes) that the applied vacuum is not engineered to prevent clogging, or maximise efficiency of aspiration.

Based on the problems outlined above, it is desirable to enable the clot to be ingested at the target site in a single manoeuvre. This will save time, reduce procedural complexity, and minimise potential for clot fragmentation during clot retrieval.

- 5 A pump is disclosed, for use in connection with a catheter such as described above in any embodiment, to aspirate clots or other materials from a blood vessel or other region of the body. An aspiration device is shown schematically in Fig. 45, having a catheter 3500, a guide 3502, tubing 3503, and a pump and reservoir assembly 3504.
- 10 The invention utilises control and/or, variation of the vacuum pressure and/or, fluid displacement during aspiration to improve the efficiency of aspiration. Variations in pressure and/or fluid displacement at the catheter tip can help achieve the following:
- Prevent clogging of the catheter
 - Promote maceration and deformation of the clot to enable it to travel through the lumen
- 15 The pump 3504 may provide a negative fluid displacement thereby decreasing pressure (enabling a vacuum) or positive displacement, thereby increasing pressure. The pump is connected to a catheter, enabling application of a positive or negative pressure the catheter lumen. The pump incorporates a sensor which measures the pressure in the catheter lumen.
- 20 The magnitude of this pressure may be used to decide whether a vacuum or pressurizing signal should be applied to the catheter. Based on the measured pressure, the pump may change direction hence altering the pressure and fluid displacement.
- 25 In one embodiment, shown schematically in the form of a state diagram in Fig. 46, the pump uses defined upper and lower limits to decide whether to apply a vacuum or pressurize. These limits enable the catheter to cyclically ingest and if required expel, at least some of the clot. This deformation of the clot improves the efficiency of the aspiration, and prevents clogging of the catheter.
- 30 For the purposes of explanation, the initial pressure is defined as 0 in-Hg in all diagrams before the pump is switched on Fig. 47 (a). In reality, a non-zero pressure is present due to blood pressure. This may be in the region of 60 to 120 mm-Hg (2.4-4.8 in-Hg).

The pump will continuously measure the pressure within the catheter lumen during the procedure. This measurement will be arterial pressure if the pump is switched off. Once the pump is switched on, and it begins to draw some vacuum a negative pressure will be measured, Fig. 47 (b). In the absence of an occlusion or partial occlusion of the catheter tip, this will be a nominal reading, representing free-flow of fluid through the catheter). Once the catheter is advanced and engaged with the clot, an increase in the vacuum is observed, Fig. 47 (c).

Initially when switched on the pump applies a vacuum enabling the catheter to ingest some of the clot, Fig. 47 (d). While further increases in the vacuum ingest more of the clot, Fig. 47 (e), the efficiency of increases in the vacuum pressure in ingesting more clot is reduced, Fig. 47 (f). For this reason, the pump will reverse at some Low Limit of pressure, Fig. 47 (g). The Low Limit is defined such that during vacuum, a portion of the clot has been aspirated but not so much that the clot has become irreversibly clogged. An important aspect is that the lower limit of vacuum can be set well above the full vacuum pressure of -760mmHg to prevent ingestion of too large a clot that could clog the catheter. In one embodiment, the Lower Limit is set to between -100 mm-Hg and -200 mm-Hg. In another embodiment the Lower Limit is set to between -200 mm-Hg and -300 mm-Hg. In another embodiment the Lower Limit is set to between -400 mm-Hg and -500 mm-Hg. In another embodiment the Lower Limit is set to between -600 mm-Hg and -700 mm-Hg.

The direction of fluid displacement of the pump is now reversed. Upon reversal, the catheter will begin to pressurize, thereby increasing the pressure measured, Fig. 47 (g). As the catheter is pressurized (vacuum is reversed), the load which was applied to ingest the clot will be reduced, thereby unloading the clot, and even allowing some or all of the clot to be pushed distally towards the catheter tip Fig. 47(h). During this loading/unloading the clot is being macerated and accordingly becomes more "free" within the catheter.

The pressure is further increased until a High Limit is reached. In one embodiment this High Limit is defined such that the ingested clot may not be completely expelled from the catheter.

Additional cycling of the clot between the Low Limit and high limit (Fig. 47 (i) to (j)) further macerates the clot enabling a greater amount of the clot to be ingested for the same Low Limit of vacuum (Fig. 47 (m)), with eventual complete ingestion of the clot, Fig. 47 (n).

In one embodiment the High Limit is a negative pressure. In another embodiment, the high limit may be 0 mmHg. In yet another preferred embodiment, the High Limit is a positive pressure (Fig. 48 (a) to (c).

- 5 In the absence of a pressure signal from the pump the presence of intra-vascular blood pressure means there is a force present which supports transport of material from the distal tip of the catheter towards the pump. In one embodiment, an initial blood pressure reading may be taken before the procedure is initiated. This reading may be used to calculate the precise High Limit value required. The mean blood pressure, systolic blood pressure, or diastolic blood pressure
- 10 may be used. A novel aspect of this pump system is the incorporation of feedback into the pump algorithm in order to produce more effective pressure cycling. That is to say, the ability of the pump to measure the condition in the pump (e.g. pressure or fluid displacement), and continue or alter its behaviour.
- 15 In one embodiment, the applied pressure signal incorporates an oscillation or "shake" signal. The shake signal implies the application of pulse cycling between two pressure limits as shown in Figs. 50(a) and (b). The signal provides acute aspiration of the clot in order to cause deformation and, or, fragmentation of the clot to improve transport through the catheter. Another aspect is the incorporation of rate based cycling of a negative and positive pressure
- 20 signal. Oscillating frequencies can be defined that may cause the elastic modulus of a clot to be exceeded, thereby, fragmenting the clot in the catheter and promoting easier transport.

The addition of this oscillation is shown in the form of the state diagram in Fig. 49.

- 25 In one embodiment the shake signal may be initiated for a predefined number of cycles. In another embodiment, the shake signal may be used until the pressure has returned to blood pressure. In this instance the material in the catheter can effectively flow without significant resistance. In another embodiment, this shake signal may be initiated based on a specific pressure indicative of catheter occlusion or partial occlusion, and terminated based on
- 30 measurement of pressure within the catheter indicative of free-flow, or partial occlusion.

While the figures generally show a triangular wave form of pressure with respect to time, it should be pointed out that this may not be the case in reality. The graphs are intended to illustrate the directional changes in pressure which are initiated and controlled by the invention.

For example depending on the clot properties, and speed of activation or reversal of the pump, the signals may be more square, saw-tooth, or sinusoidal in form. Furthermore, the resulting pressure - time relationship may not have any repeating unit at all.

- 5 In one embodiment the invention includes both an oscillation or shake signal in the vacuum and positive pressurize signals. This is shown schematically in Figs. 51(a) and 51(b). In yet another embodiment, the system may incorporate only a vacuum oscillation.

- 10 A range of Lower Pressure and Higher-Pressure limit values may improve efficiency of clot transport compared to static aspiration technology. In one embodiment it is preferable to specify a Lower Pressure limit such that the amount of clot which can be ingested is maximised for a single cycle. In another embodiment, it is preferable that the Lower Pressure limit is specified such that the amount of clot which is ingested in a single cycle is not maximised, but instead represents an intermediate condition between a small amount of clot ingestion and maximum clot
15 ingestion. Real numbers will be added in the future based on experiment.

- In another embodiment, the lower limit may be defined in real-time. In one embodiment, a change in the rate of change of the pressure during the vacuum cycle may be used. For example, as the catheter becomes clogged, there is generally a rapid increase in the vacuum pressure. This
20 sudden change in vacuum pressure may be used as a signal to switch the direction of the pump. Similarly, the upper pressure may be defined based on a sudden change in the pressure during the pressurize cycle. In one embodiment this may be defined in order to identify a condition where the catheter is de-clogged.

- 25 It should be appreciated that the upper and lower limits may be defined by a combination of rate of change in pressure, or specific pressure value, or a combination of both.

- In another configuration, a flow displacement, or flow meter is incorporated. This may be used to define upper and lower limits to establish the direction of the pump (aspiration or vacuum). In
30 one embodiment the flow meter can detect if there is no fluid displacement, which is suggestive of catheter clogging.

In another embodiment, the pump may use positive and negative fluid displacement to alternately infuse and aspirate the catheter. In one embodiment, the ratio of the infuse-to-

aspirate cycle may be between 0.01 and 0.99. Preferably the ratio will be between 0.1 and 0.9, or more preferably between 0.4 and 0.9.

5 In one configuration, the pump is a sterile unit, which can be used within the sterile field, or on the patient table adjacent to the patient. This enables the physician to perform all manoeuvres without the requirement of a technician outside the sterile field. The unit may be single use and disposable.

10 In one configuration, the pump incorporates a peristaltic pump mechanism. This ensures that there is no blood contact with the pump parts. The pump may incorporate a reservoir for collection of aspirate. Figs. 53(a) and 53(b) show a pump and components. Shown are a housing connecting a tube, an on-off switch, a battery pack, a pulsatile pump, and a motherboard. The pressure sensor is connected to the tube-lumen, which is connected to the catheter, thereby enabling pressure measurement within the catheter.

15 In one embodiment the pump incorporates a series of LEDs or indicators. These are intended to provide feedback to the physician based on the catheter tip and clot interaction condition. This is provided by the pressure within the catheter. For example, the pressure range associated with free-flow within the catheter, or partial occlusion, or complete occlusion, aspirating or clogged.

20 Furthermore, the indicators may be used to indicate to the physician that the pump is in the oscillation or shake condition.

25 A method is disclosed whereby the physician uses the feedback from the indicators to define the required adjustment of the catheter tip.

30 Place catheter tip adjacent to the clot. Switch on the pump. If the pump indicates free flow is observed the catheter should be moved distally to further engage the clot. If the catheter is aspirating with partial or complete occlusion the physician waits until the pump has free-flow again. The physician again moves the catheter tip distally to engage the next piece of clot. In this way the entire vessel can be cleaned of clot. In the event that the pump becomes clogged, a signal may be provided to the physician that the traditional catheter withdrawal technique may be appropriate.

The embodiments described within this filing are in general aimed at enabling the physician to access regions of the body which provide a challenging anatomy, with highly flexible corrugated catheters. The catheter designs are optimised by way of transitions, and the addition of other elements, such as flow restrictors and a highly effective pump. The ability to make larger
5 catheters while maintaining this type of controlled flexibility enables improved therapy, such as clot removal, embolic delivery to the body.

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

10

Claims

1. A catheter (1) comprising a jacket defining a lumen and comprising a helical support in jacket material along at least some of its length, the catheter comprising at least a proximal portion (2) and a distal portion (3), said distal portion having for at least some of its length a corrugated outer surface (15).
2. A catheter as claimed in claim 1, wherein the catheter comprises a transition portion (53, 54, 204,782) between said proximal portion (1152) and said distal portion (1153), said transition portion (1154) having a flexural stiffness which is less than that of the distal portion and more than that of the proximal portion.
3. A catheter (780) as claimed in claim 2, wherein the transition portion has a corrugated outer surface in which at least some corrugations of the corrugated outer surface have a smaller depth than corrugations of the surface of the distal portion.
4. A catheter as claimed in claims 2 or 3, wherein the transition portion has a higher flexural stiffness than the distal portion by the corrugations having a different pitch.
5. A catheter as claimed in any of claims 2 to 4, wherein the transition portion has a higher flexural stiffness than the distal portion by the corrugations having a larger width.
6. A catheter as claimed in any of claims 2 to 5, wherein the transition portion is configured to provide a gradual controlled stiffness transition between the distal portion and the proximal portion.
7. A catheter as claimed in any of claims 2 to 6, wherein the transition portion has a reduced depth of corrugations which is less than that of the distal portion (782).
8. A catheter as claimed in any of claims 2 to 7, wherein the transition portion includes an additional outer tubular layer (801) along at least some of its length, and said outer tubular layer is not present in the distal portion.
9. A catheter as claimed in claim 8, wherein said outer tubular layer has a thickness of 0.05 mm or less, preferably 0.025mm or less, and more preferably 0.0125 mm or less.

10. A catheter as claimed in claims 8 or 9, wherein said outer tubular layer is of PET composition.
- 5 11. A catheter as claimed in any of claims 2 to 10, wherein in said transition portion an increase in stiffness is achieved by a change in thickness of the jacket.
- 10 12. A catheter as claimed in any of claims 2 to 11, wherein the jacket includes an inner liner (1071) defining said lumen, and in said transition portion an increase in stiffness is achieved by a change in thickness of the outer jacket material (1073, 1074) around the helical support or of the inner liner.
- 15 13. A catheter as claimed in any preceding claim, wherein the jacket includes an inner liner (1071) defining said lumen, and wherein the thickness of the inner liner is between 0.025 mm to 0.3 mm, preferably between 0.05 mm and 0.2 mm.
- 20 14. A catheter as claimed in any preceding claim, wherein the thickness of the jacket is between 0.025 mm to 0.30 mm, preferably between 0.05 mm and 0.2 mm.
- 25 15. A catheter as claimed in any preceding claim, wherein width (W) of the corrugate is at least 10% of the jacket thickness, and preferably the width of the corrugate is at least 20% of the jacket thickness.
- 30 16. A catheter as claimed in any preceding claim, wherein in the distal portion the width of the corrugate is at least 60% of the jacket thickness.
- 35 17. A catheter as claimed in any preceding claim, wherein in the distal portion the width of the corrugate is at least 60% of the jacket thickness and the depth of the corrugate is at least 70% of the jacket thickness.
18. A catheter as claimed in any preceding claim, wherein the jacket includes an inner liner (1071) defining said lumen, and the inner liner thickness is constant along the length of the distal portion, but the outer jacket thickness is larger in at least one region.
19. A catheter as claimed in any of claims 2 to 18, wherein the jacket thickness is increased proximally at least once along the length of the catheter distal portion and/or transition portion.

20. A catheter as claimed in any of claims 2 to 19, wherein the transition portion has a controlled change in stiffness arising from a plurality of layers (1073, 1074) which are overlapped in a staggered configuration with at least one tubular layer terminating proximally of termination of another tubular layer.
- 5 21. A catheter as claimed in any preceding claim, wherein the distal-most end (1050) of the distal portion is provided by an inverted part of a jacket tubular layer forming a continuous surface at the distal end of the distal portion, said layer being folded over at the distal end to overlap itself.
- 10 22. A catheter as claimed in claim 21, wherein said inverted layer (1051) overlies the helical support.
- 15 23. A catheter as claimed in any preceding claim, wherein said distal portion includes an extension (1082) of a tubular layer extending distally of other layers and of the helical support and being folded over to form a distal end edge, thereby providing a distal extension of lower stiffness.
- 20 24. A catheter as claimed in claim 23, wherein the jacket includes an inner liner defining said lumen, and said extension (1072, 1082) is all or part of the inner liner.
- 25 25. A catheter as claimed in claims 23 or 24, wherein said extension has a length in the range of 0.5 mm and 5.0 mm, more preferably between 0.5 mm and 0.3 mm.
26. A catheter as claimed in any of claims 2 to 25, wherein the transition portion includes a region without corrugations.
27. A catheter as claimed in any of claims 2 to 26, wherein the jacket includes an inner liner defining said lumen, and wherein the transition portion includes a joint (1154) between
30 the inner liner and outer jacket material.
28. A catheter as claimed in claim 27, wherein said joint is between an inner liner of ePTFE material and an outer jacket of PTFE material.
- 35 29. A catheter as claimed in any of claims 2 to 28, wherein said transition portion jacket includes a lap joint (1207, 1208) between concentric tubular layers.

30. A catheter as claimed in claim 29, wherein said lap joint is between a tubular layer of ePTFE material and a tubular layer of PTFE material.
- 5 31. A catheter as claimed in claims 29 or 30, wherein said lap joint has a length of between 1mm and 30 mm.
- 10 32. A catheter as claimed in any of claims 2 to 31, wherein the degree of corrugation in the transition portion is altered progressively proximally to achieve an increase in stiffness, the jacket includes an inner liner and said inner liner extends distally and terminates before the most distal region of the distal portion, said inner liner is of ePTFE composition, and at least part of the proximal portion is not corrugated.
- 15 33. A catheter as claimed in any preceding claim, wherein the distal portion includes a region of the helical support being floating in the jacket material.
- 20 34. A catheter as claimed in any preceding claim, wherein the jacket includes material of ePTFE composition surrounding at least part of the helical support, and thickness of the ePTFE material increases distally, and the jacket includes PTFE proximally of the ePTFE material.
- 25 35. A catheter as claimed in any of claims 2 to 34, wherein the transition portion includes a distal region in which the helical support is floating between jacket material ePTFE layers, and a proximal region in which the helical support is embedded in the jacket material.
- 30 36. A catheter as claimed in any preceding claim wherein, at least one region of the helical support (6) is embedded in jacket material, whereby it is constrained from moving relative to said jacket material.
- 35 37. A catheter as claimed in a claim 36, wherein the helical support (752) is embedded in the jacket in a matrix (753) of continuous porous flexible material such as ePTFE, or in a matrix of a non-compressible material such as a urethane.
38. A catheter as claimed in any preceding claim, wherein the jacket includes a liner defining said lumen, and the jacket comprises at least one layer around said liner, and an in-fill

material (851/854) between said inner liner and said jacket layer, or between a plurality of tubular layers of material of said jacket.

- 5 39. A catheter as claimed in claim 38, wherein the in-fill material is used only to partially fill a space around the helical support.
40. A catheter as claimed in claims 38 or 39, wherein the in-fill material completely fills a helical channel around the helical support.
- 10 41. A catheter as claimed in claim 40, wherein the in-fill material is melted to form a layer of material on all surfaces within the helical channel.
- 15 42. A catheter as claimed in any preceding claim, wherein the jacket includes an inner liner defining said lumen, and a helical channel in the jacket includes melted and cooled in-fill material between the helical support and the jacket, and in which there is an adhesive chemical bond at interfaces with the in-fill material.
- 20 43. A catheter as claimed in any preceding claim, wherein the jacket includes an inner liner defining said lumen, and the inner liner and an outer tubular layer of the jacket are bonded to one another by sintering.
44. A catheter as claimed in any preceding claim, wherein the jacket includes an inner liner (5) defining said lumen.
- 25 45. A catheter as claimed in claim 44, and said inner liner extends between the distal portion and the proximal portion.
46. A catheter as claimed in claim 44 or 45, wherein the diameter of the inner liner is constant, with a smooth lumen surface.
- 30 47. A catheter as claimed in any of claims 44 to 46, wherein the inner liner comprises a low friction material such as ePTFE.
- 35 48. A catheter as claimed in any of claims 44 to 47, wherein in at least the distal portion the jacket material comprises polyurethane (e.g. Pellethane 80AE) and the inner liner comprises ePTFE.

49. A catheter as claimed in any of claims 44 to 48, wherein an outer tubular layer of the jacket is bonded to the inner liner or a tie layer around the inner liner.
50. A catheter as claimed in claim 49, wherein the distal portion comprises a tie layer
5 attaching the inner liner to the outer jacket material.
51. A catheter as claimed in claim 50, wherein the tie layer comprises a fluoropolymer which is sputter coated with FEP powder which under heat and pressure forms a bond between the coated fluoropolymer layer and a second layer.
- 10 52. A catheter as claimed in claims 50 or 51, wherein the tie layer comprises FEP or a urethane.
53. A catheter as claimed in any of claims 44 to 52, wherein the helical support is bonded to
15 the outside surface of the inner liner or to a tie layer around said liner.
54. A catheter as claimed in any of claims 44 to 53, wherein an outer tubular layer of the jacket of the proximal portion is sandwiched between the inner liner and another outer tubular layer.
- 20 55. A catheter as claimed in any of claims 44 to 54, wherein the inner liner of the distal portion is formed from a different material from the inner liner of the proximal portion, and the liner materials are joined by creating a small slit or window in one layer and pulling a spliced length of the outer jacket through the slit or window, and the helical
25 support is wound around the outside of these layers thus keeping them together.
56. A catheter as claimed in any of claims 44 to 55, wherein the helical support (771) is spaced apart or transposed from the inner liner such that it is not exposed to the liner.
- 30 57. A catheter as claimed in any preceding claim, wherein the corrugate at the surface of the jacket is at least 5% of the thickness of the jacket.
58. A catheter as claimed in any preceding claim, wherein in at least one region the width of the corrugate at the surface of the catheter is at least 10% of thickness at the jacket.
- 35 59. A catheter as claimed in any preceding claim, wherein in at least one region of the distal portion, the width of the corrugate is at least 30% of the wall thickness.

- 5 60. A catheter as claimed in any preceding claim, wherein the corrugate depth is between 5% and 95% of the jacket thickness in at least one region of the catheter, and preferably the corrugate depth is at least 20% of the catheter wall thickness in at least one region of the catheter.
- 10 61. A catheter as claimed in any preceding claim, wherein the corrugate depth varies along a corrugated region of the catheter from a larger depth distally to a smaller depth proximally.
- 15 62. A catheter as claimed in any preceding claim, wherein the corrugate width varies along a corrugated region of the catheter from a larger depth distally to smaller depth proximally.
63. A catheter as claimed in any of claims 2 to 62, wherein in the transition portion the corrugate depth varies from a larger depth distally to a smaller depth proximally, while the corrugation width is constant in said region.
- 20 64. A catheter as claimed in any preceding claim, wherein the corrugate represents the impression of a circular helical cinch wire wound around jacket material during manufacture.
- 25 65. A catheter as claimed in claim 64, wherein the corrugate represents the impression of a circular helical cinch wire wound from a depth and width of no impression with no corrugate, to a depth of at least 50% of the jacket thickness.
- 30 66. A catheter as claimed in claim 65, wherein the corrugate represents the impression of a circular helical cinch wire wound from a depth and width of no impression with no corrugate, to a depth of at least 70% of the jacket thickness.
- 35 67. A catheter as claimed in claim 66, wherein the corrugate represents the impression of a circular helical wire wound from a depth and width of no impression with no corrugate, to a depth of at least 95% of the jacket thickness.
68. A catheter as claimed in any of claims 44 to 67, wherein the inner liner terminates in a region proximal of the distal end of the distal portion.

69. A catheter as claimed in claim 68, wherein a region (760) of inner lumen of the catheter without said inner liner (763) has hydrophilic or hydrophobic coating to improve lubricity.
- 5 70. A catheter as claimed in claims 68 or 69, wherein the un-lined section is at least 1cm in length, and preferably at least 2 cm in length.
71. A catheter as claimed in any of claims 67 to 70, wherein a sudden change in flexural stiffness at said liner termination is reduced by a change in corrugation parameters, or by
10 skiving the liner with an angular cut.
72. A catheter as claimed in any of claims 68 to 71, wherein a region of the un-lined jacket material adjacent to the liner proximally is less corrugated than in a region of unlined jacket distally and proximally.
- 15 73. A catheter as claimed in any of claims 68 to 72, wherein a corrugated region of the lined jacket adjacent to a region of unlined jacket has a longer pitch than a region of unlined jacket.
- 20 74. A catheter as claimed in any of claims 44 to 73, wherein the jacket (783) has a proximal part (784) in a catheter proximal portion without corrugations, a distal part (785) in the catheter distal portion with corrugations, and the inner liner (783) terminates proximally of the distal end (786).
- 25 75. A catheter as claimed in any of claims 2 to 74, wherein the jacket material comprises regions of different materials having different durometer values.
76. A catheter as claimed in any preceding claim, wherein the catheter has a plurality of radiopaque markers (1270) along its length, and optionally at least part of the helical
30 support comprises a radiopaque marker.
77. A catheter as claimed in claim 76, wherein the helical support comprises a radiopaque material such as Platinum wire.
- 35 78. A catheter as claimed in either of claims 76 or 77, wherein the helical support (6) comprises drawn Nitinol tubing or wire filled with radiopaque material.

79. A catheter as claimed in claim 76 or 77 or 78, wherein the helical support (1281) includes at least 10 w/w % Platinum.
- 5 80. A catheter as claimed in any of claims 76 to 79, wherein radiopacity of the distal portion is enhanced by having a length of reduced helical pitch.
81. A catheter as claimed in any preceding claim, wherein for at least some of the length of the catheter the width of the corrugate is no more than 50% of the pitch of the corrugate.
- 10 82. A catheter as claimed in any preceding claim, wherein for at least some of the length of the catheter the width of the corrugate is between 5% and 49% of the pitch of the corrugate, and more preferably the width of the corrugate is between 15% and 45% of the pitch of the corrugate.
- 15 83. A catheter as claimed in any preceding claim, wherein for at least some of the length of the catheter the width of the corrugate is between 20% and 45% of the pitch of corrugate.
84. A catheter as claimed in any preceding claim, wherein for at least some of the length of the catheter the width of the corrugate is at least 10% of the jacket thickness.
- 20 85. A catheter as claimed in any preceding claim, wherein for at least some of the length of the catheter the width of the corrugate is at least 20% of the jacket thickness.
- 25 86. A catheter as claimed in any preceding claim, wherein at the most distal region of the distal portion the width of the corrugate it at least 60% of the jacket thickness.
87. A catheter as claimed in any preceding claim, wherein at the most distal region of the distal portion the width of the corrugate it at least 60% of the wall thickness and the depth of the corrugate is at least 70% of the wall thickness.
- 30 88. A catheter as claimed in any preceding claim, wherein the ratio of the width of the corrugate to the depth of the corrugate is at least 0.5 in at least one region of the catheter.

89. A method of manufacturing a catheter of any preceding claim, wherein the jacket is formed in at least some regions by positioning a membrane over a helical structure, applying heat so that the membrane reflows such that it forms around the helical structure, winding a tensioned cinch wire around the outside of the membrane such that it forces membrane material into grooves between each loop of the helical structure, heat setting the membrane to fix the corrugations in place, and unwinding the tensioned cinch wire leaving the corrugations behind.
90. A method as claimed in claim 89, wherein the jacket includes fluoropolymers and said fluoropolymers are bonded with each other and/or with other polymers at bonding interfaces.
91. A method as claimed in claims 89 or 90, wherein chemical treatment is applied at said interfaces using an etching solution.
92. A method as claimed in claim 91, wherein the etched fluoropolymer is coated with a thin layer of urethane such as Chornoflex, and on the application of heat, this layer flows and acts to tie the fluoropolymer to a second etched fluoropolymer layer or to a different polymer layer.
93. A method as claimed in any of claims 89 to 92, wherein the method comprises providing the helical support (752) within a polymer jacket (753) which is bonded to a liner (751) to form a base assembly, placing an outer liner (811) which will not bond to the polymer jacket over the jacketed coil, winding the cinch wire (810) in a helix onto the outside of the outer liner under tension thereby imparting a corrugate geometry, heating to reflow or anneal the material to set said material into the corrugate geometry, cooling the assembly, removing the cinch wire (810), and peeling off the outer liner (811).
94. An aspiration device (1350) comprising a catheter (1353) of any of claims 1 to 88 and a flow restrictor (1352), in which the distal portion (1351) is distal of the flow restrictor.
95. An aspiration device as claimed in claim 94 wherein the catheter comprises a transition portion (1400) between said proximal portion and said distal portion, said transition portion having a flexural stiffness which is less than that of the distal portion and more

than that of the proximal portion, and at least part of said transition portion extends distally of the flow restrictor.

- 5 96. An aspiration device as claimed in either of claims 94 or 95, wherein the flow restrictor comprises a balloon (1352) and the balloon is arranged to inflate to block blood flow before aspiration of a clot into the catheter distal portion.
- 10 97. An aspiration device as claimed in any of claims 94 to 96, wherein length of the distal portion (1351) is suited to reach specific anatomical locations such as the distal internal carotid artery, terminus of the internal carotid artery, proximal MI, distal MI, proximal M2, distal M2, basilar, or vertebral vessels, wherein the flow restrictor remains in or proximal of the C1 segment of the ICA.
- 15 98. An aspiration device as claimed in claims 94 to 97, wherein the outer diameter of the distal portion (2402) differs from the outer diameter of the proximal portion (2403) of the catheter.
- 20 99. An aspiration device as claimed in claims 94 to 98, wherein the distal portion (2402) has a larger internal diameter than the proximal portion (2403).
100. An aspiration device as claimed in any of claims 94 to 99, wherein there is a taper in the diameters of the distal and proximal portions.
- 25 101. An aspiration device as claimed in any of claims 94 to 100, further comprising a balloon inflation lumen (2403) and the outer layer of the balloon inflation lumen is of enhanced flexibility in comparison with a balloon inflation lumen inner layer.
- 30 102. An aspiration device as claimed in any of claims 94 to 101, wherein the catheter comprises a proximal portion (2301) having at least two lumens, including a first lumen (2403) for balloon inflation and a second lumen for delivery of fluids and devices, and the distal portion (2302) is for aspiration.
- 35 103. An aspiration device as claimed in any of claims 94 to 102, wherein said distal portion lumen has a larger internal width dimension than the internal width dimension of the second lumen of the proximal portion.

104. An aspiration device as claimed in claims 102 or 103, wherein the proximal portion first and second lumens are concentric.
- 5 105. An aspiration device as claimed in any of claims 94 to 104, wherein the device is for direct carotid access and the length of the catheter proximal of the flow restrictor does not exceed 40 cm, and preferably does not exceed 30 cm.
106. An aspiration device as claimed in any of claims 94 to 105, wherein the flow restrictor comprises part of the catheter proximal portion.
- 10 107. An aspiration device as claimed in any of claims 94 to 106, wherein the catheter comprises first (2702) and second (2703) shafts, in which the first shaft is configured to perform significant flow restriction at a vessel location proximal to a target treatment site, and the second catheter shaft has a smaller diameter and may then be passed through the
- 15 first catheter shaft to the treatment site.
108. An aspiration device as claimed in any of claims 94 to 107, wherein the flow restrictor includes a funnel, open at the distal side.
- 20 109. An aspiration device as claimed in any of claims 94 to 108, wherein the flow restrictor is deployable, or activated, but remains attached to the catheter.
110. An aspiration device as claimed in claim 109, wherein the flow restrictor is a deployable funnel, the open side of the funnel is pointing distally, and the catheter is movable
- 25 proximally with the funnel while the funnel continues to perform flow restriction.
111. A method of use of an aspiration device of any of claims 94 to 110, the method comprising steps of deploying a device of any of claims 94 to 110 in a patient's blood vessel, navigating the distal portion to a clot in the vessel, causing the flow restrictor to
- 30 block blood flow, and applying a vacuum to the catheter so that the clot is aspirated into the distal portion.
112. A method as claimed in claim 111, wherein the method comprises:
- 35 performing an angiogram to determine location of an occlusion, and distance between petrous or cavernous carotid and the occlusion,

- choosing a catheter with a distal portion length suitable to reach a clot causing the occlusion, while ensuring that the flow restrictor does not land beyond the cervical carotid, and with a distal tip with an outer diameter as large as will comfortably fit in the target vessel,
- 5 navigating the distal portion of the catheter to the clot,
- activating the flow restrictor such that flow arrest is enabled, and alternative flow pathways which could reduce the effectiveness of the aspiration are minimised,
- apply a vacuum to the lumen of the catheter to aspirate the clot,
- if the clot is retrieved, perform another angiogram through the balloon guide
- 10 catheter or a diagnostic catheter, and
- removing the catheter.
113. An aspiration system (3500) comprising a catheter of any of claims 1 to 88, a pump (3504) linked with the catheter proximal portion (3503), and a controller configured to
- 15 vary aspiration pressure during aspiration of a clot.
114. An aspiration system as claimed in claim 113, wherein the system comprises a lumen pressure sensor and the controller is configured to vary aspiration pressure according to sensed pressure within the catheter lumen.
- 20 115. An aspiration system as claimed in claims 113 or 114, wherein the system comprises a lumen fluid flow sensor, and the controller is configured to vary aspiration pressure according to sensed fluid displacement in the lumen.
- 25 116. An aspiration system as claimed in any of claims 113 to 115, wherein the controller is configured to improve the efficiency of aspiration by preventing clogging of the catheter, and/or to promote maceration and deformation of a clot to enable it to travel through the lumen.
- 30 117. An aspiration system as claimed in any of claims 113 to 116, wherein the controller is configured to provide a vacuum or a positive pressure based on measured pressure, and to change direction hence altering the pressure and fluid displacement.

118. An aspiration system as claimed in any of claims 113 to 117, wherein the controller has defined upper and lower limits of pressure or displacement to decide whether to apply a vacuum or pressurize.
- 5 119. An aspiration system as claimed in any of claims 113 to 118, wherein the controller is configured to cause the catheter to cyclically ingest and if required expel, at least some of a clot, whereby there is deformation of the clot to improve efficiency of aspiration and prevent clogging of the catheter.
- 10 120. An aspiration system as claimed in any of claims 113 to 119, wherein the controller is configured to begin to draw some vacuum so that a negative pressure is measured and in the absence of an occlusion or partial occlusion of the catheter tip, this will be a nominal reading, representing free-flow of fluid through the catheter, and once the catheter is advanced and engaged with the clot, an increase in the vacuum is observed.
- 15 121. An aspiration system as claimed in any of claims 113 to 120, wherein the controller is configured to increase a vacuum to ingest more of a clot and to reverse at a low limit of pressure defined such that during vacuum, a portion of the clot has been aspirated but not so much that the clot has become irreversibly clogged and the lower limit of vacuum can
20 be set above a full vacuum pressure to prevent ingestion of too large a clot that could clog the catheter.
122. An aspiration system as claimed in claim 121, wherein the controller is configured to set the low limit between -100 mm-HG and -200 mm-Hg, preferably between -200 mm-HG
25 and -300 mm- Hg, more preferably between -400 mm-HG and -500 mm-Hg, and more preferably between -600 mm-HG and -700 mm-Hg.
123. An aspiration system as claimed in any of claims 113 to 122, wherein the controller is configured to cause direction of fluid displacement of the pump to be reversed thereby
30 increasing the pressure measured, and unloading a clot.
124. An aspiration system as claimed in any of claims 113 to 123, wherein the controller is configured to allow some or all of a clot to be pushed distally towards the catheter tip so that the clot is macerated and accordingly becomes more free within the catheter.
- 35 125. An aspiration system as claimed in any of claims 113 to 124, wherein the controller is configured to increase pressure until a sensed pressure high limit is reached.

126. An aspiration system as claimed in claim 125, wherein the controller is configured to set the high limit such that an ingested clot may not be completely expelled from the catheter.
- 5 127. An aspiration system as claimed in either of claims 124 or 126, wherein the controller is configured to store an initial blood pressure reading before a procedure is initiated, and to read this pressure to calculate the high limit value.
- 10 128. An aspiration system as claimed in any of claims 113 to 127, wherein the controller is configured to use patient mean blood pressure, systolic blood pressure, or diastolic blood pressure for pump control.
- 15 129. An aspiration system as claimed in any of claims 113 to 128, wherein the controller is configured to apply pulse cycling between two pressure limits, or rate based cycling of a negative and positive pressure signal, using defined oscillating frequencies that may cause the elastic modulus of a clot to be exceeded, thereby fragmenting the clot in the catheter and promoting easier transport.
- 20 130. An aspiration system as claimed in any of claims 113 to 129, wherein the controller is configured to initiate a shake signal for a predefined number of cycles, or until the pressure has returned to blood pressure.
- 25 131. An aspiration system as claimed in any of claims 121 to 130, wherein the controller is configured to set the low limit in real time, preferably with a change in the rate of change of the pressure.
- 30 132. An aspiration system as claimed in any of claims 113 to 131, wherein the controller is configured to recognize a sudden change in pressure of the catheter as a signal to switch direction of the pump.
- 35 133. An aspiration system as claimed in any of claims 113 to 132, wherein the controller is configured to receive feedback from a flow meter.
134. An aspiration system as claimed in any of claims 113 to 133, wherein the controller is configured to use positive and negative fluid displacement to alternately infuse and aspirate the catheter.

135. An aspiration system as claimed in any of claims 113 to 134, wherein the system comprises an output indicator and the controller is configured to provide feedback to a physician based on the catheter and clot interaction condition, for example pressure within the catheter, pressure range associated with free-flow within the catheter, or partial occlusion, or complete occlusion, aspirating or clogged, to indicate to the physician that the pump is in the oscillation or shake condition.

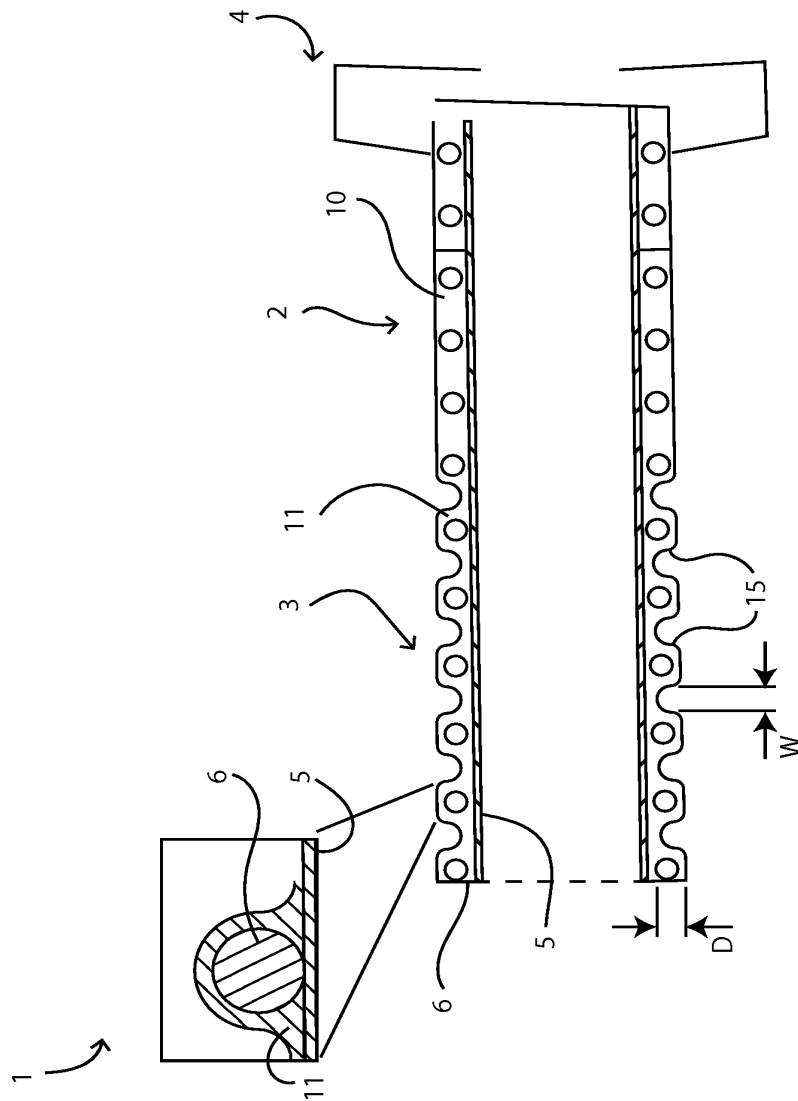


Fig.1

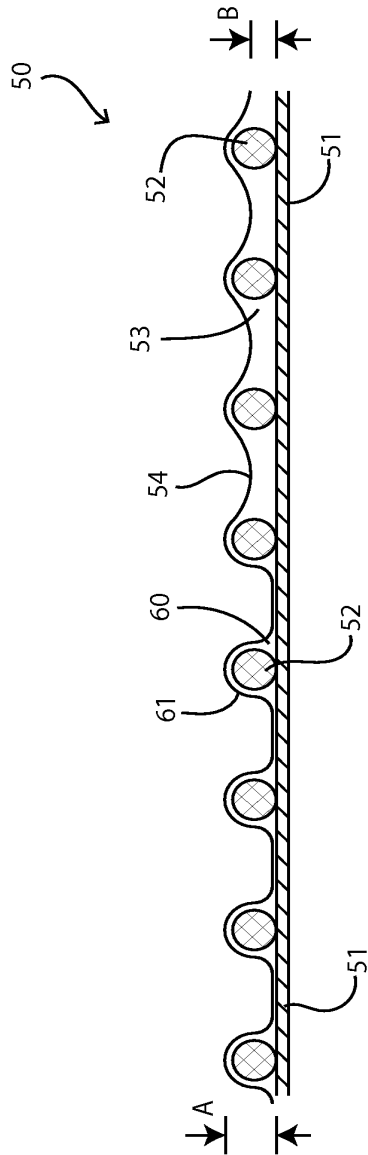


Fig.2

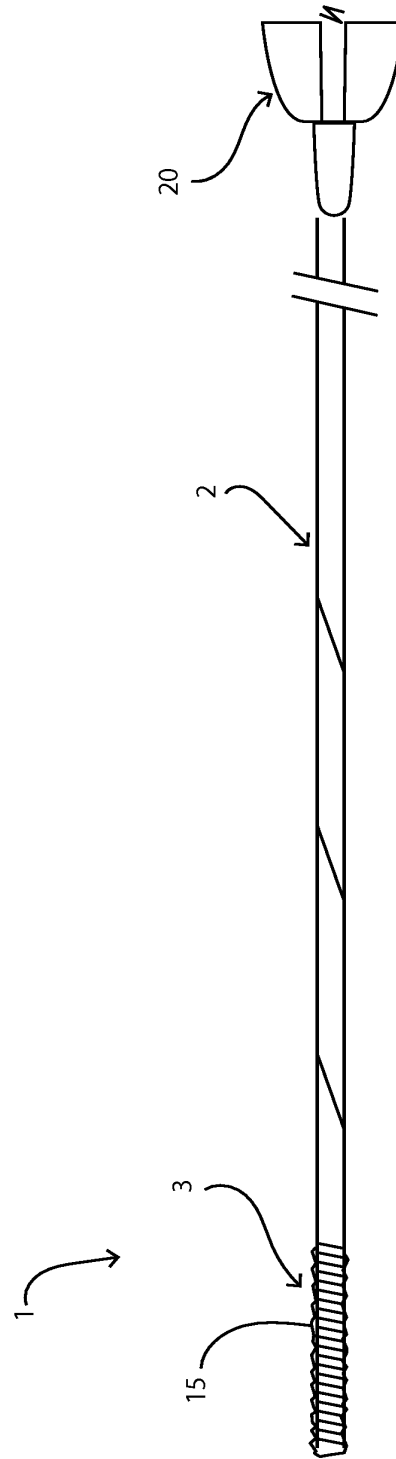


Fig.3

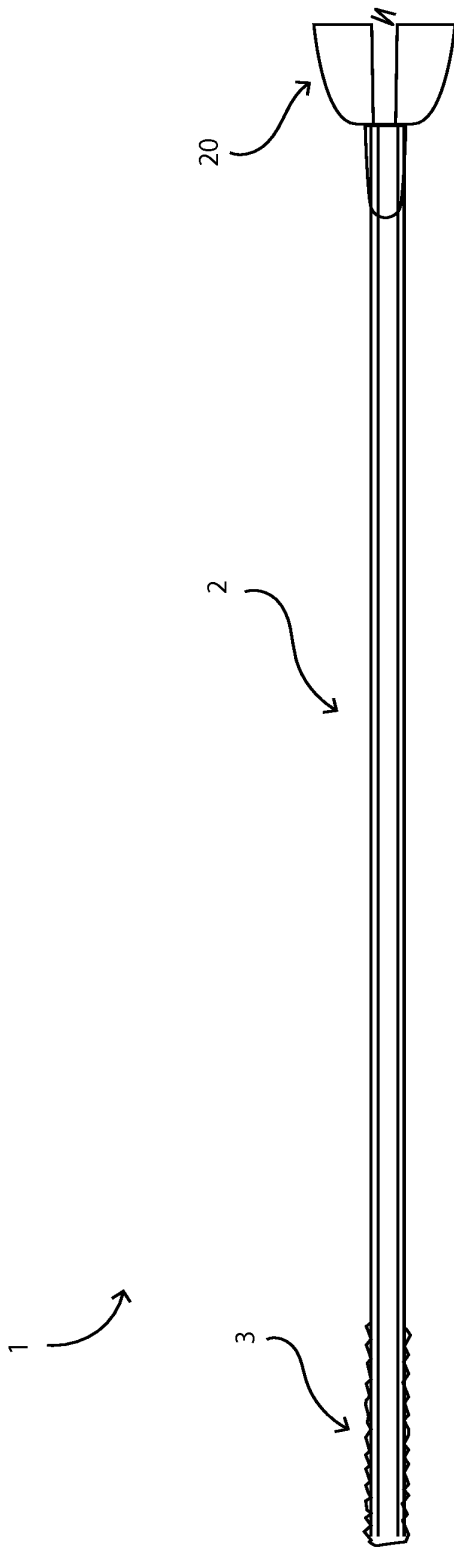


Fig.4

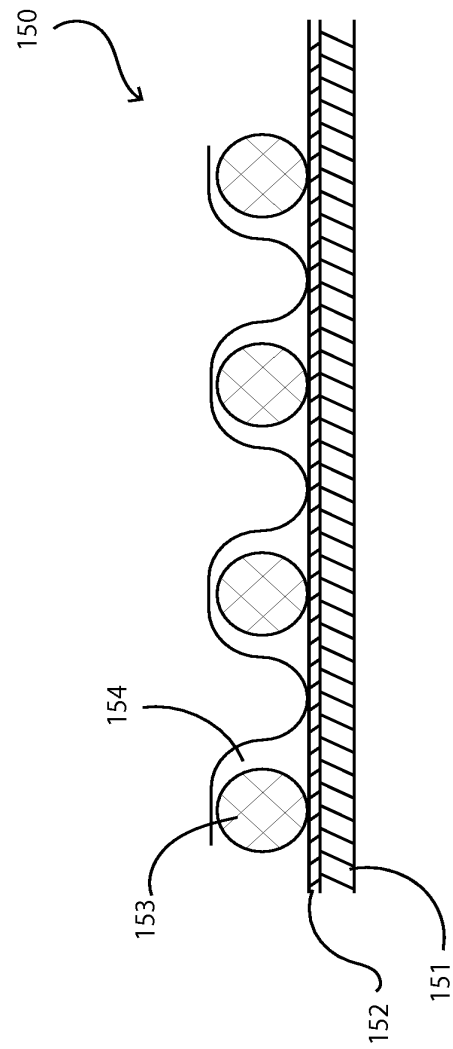


Fig.5

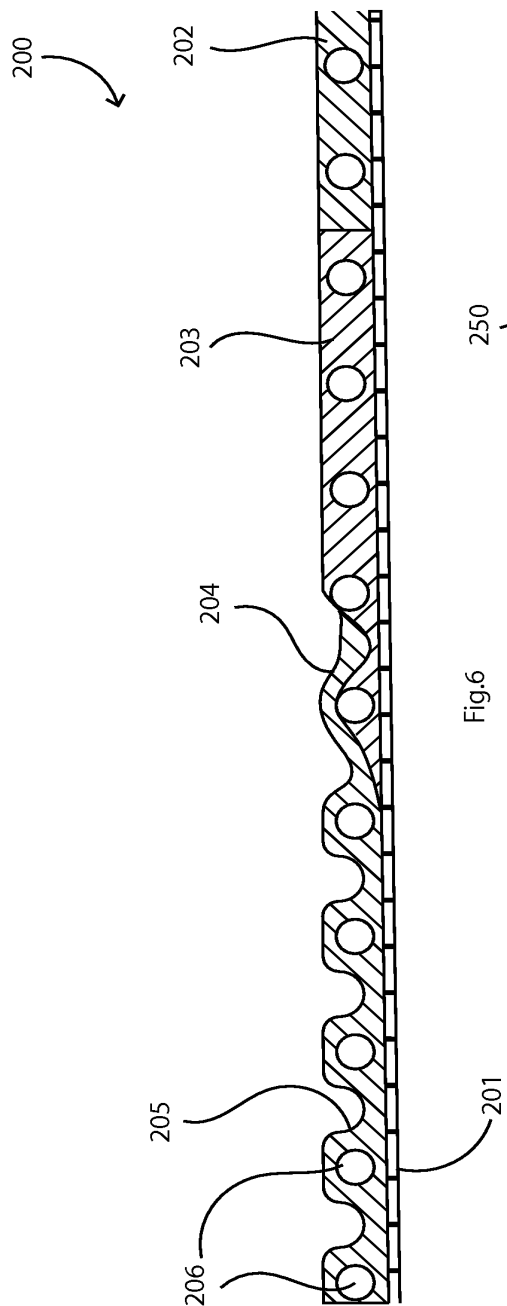


Fig. 6

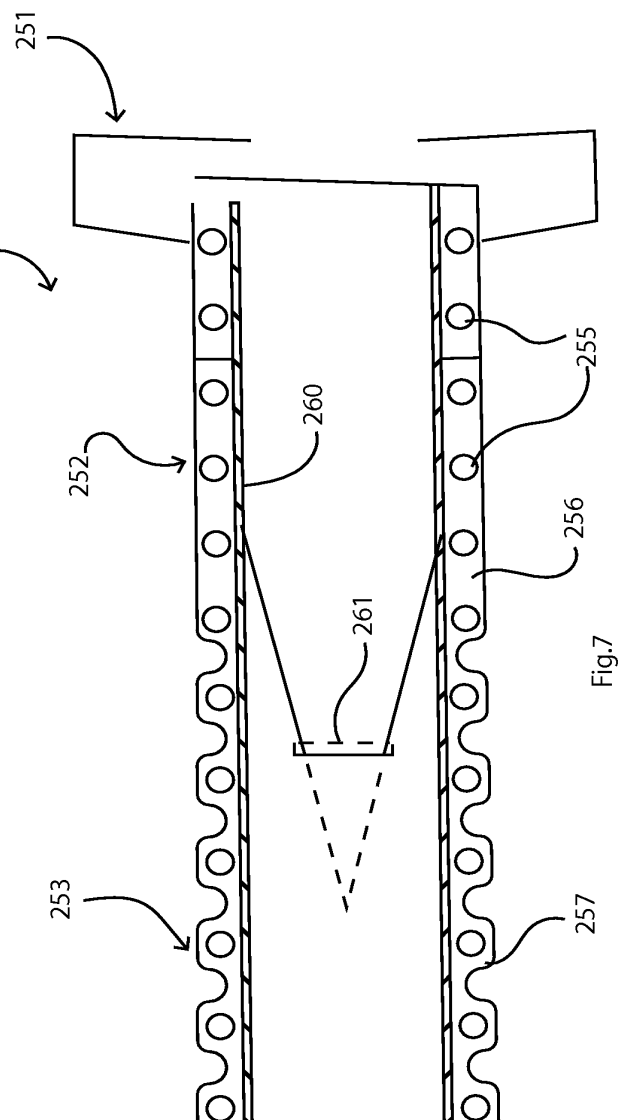


Fig. 7

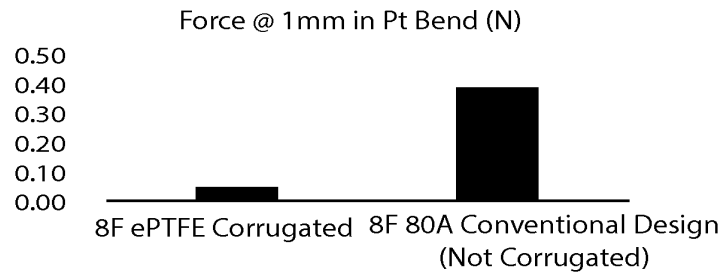


Fig.8

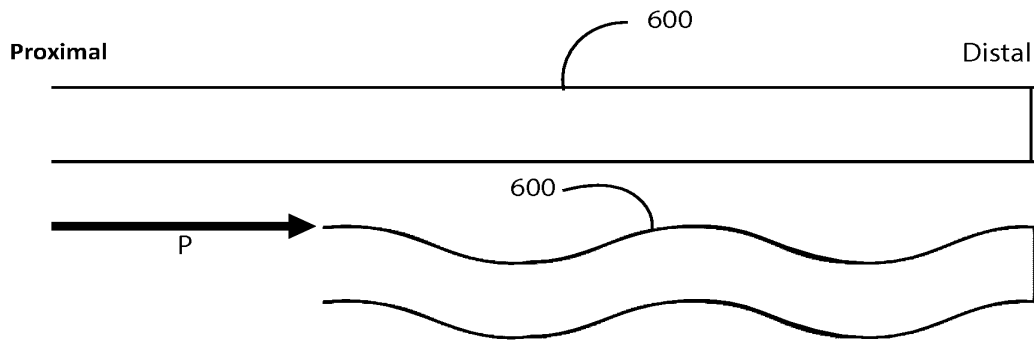


Fig.9

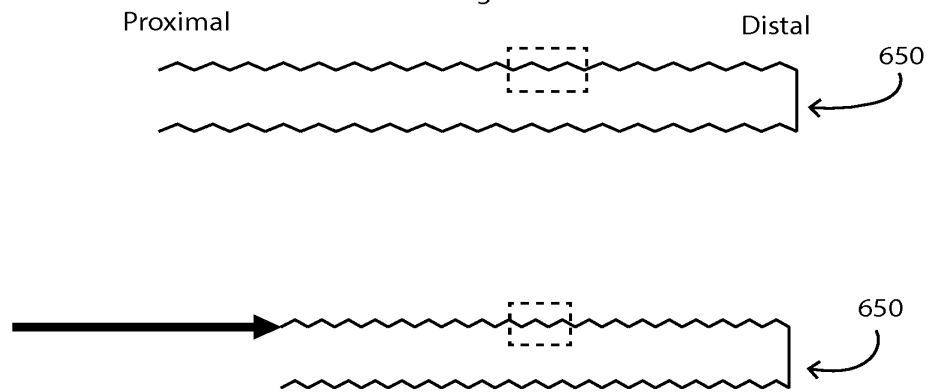
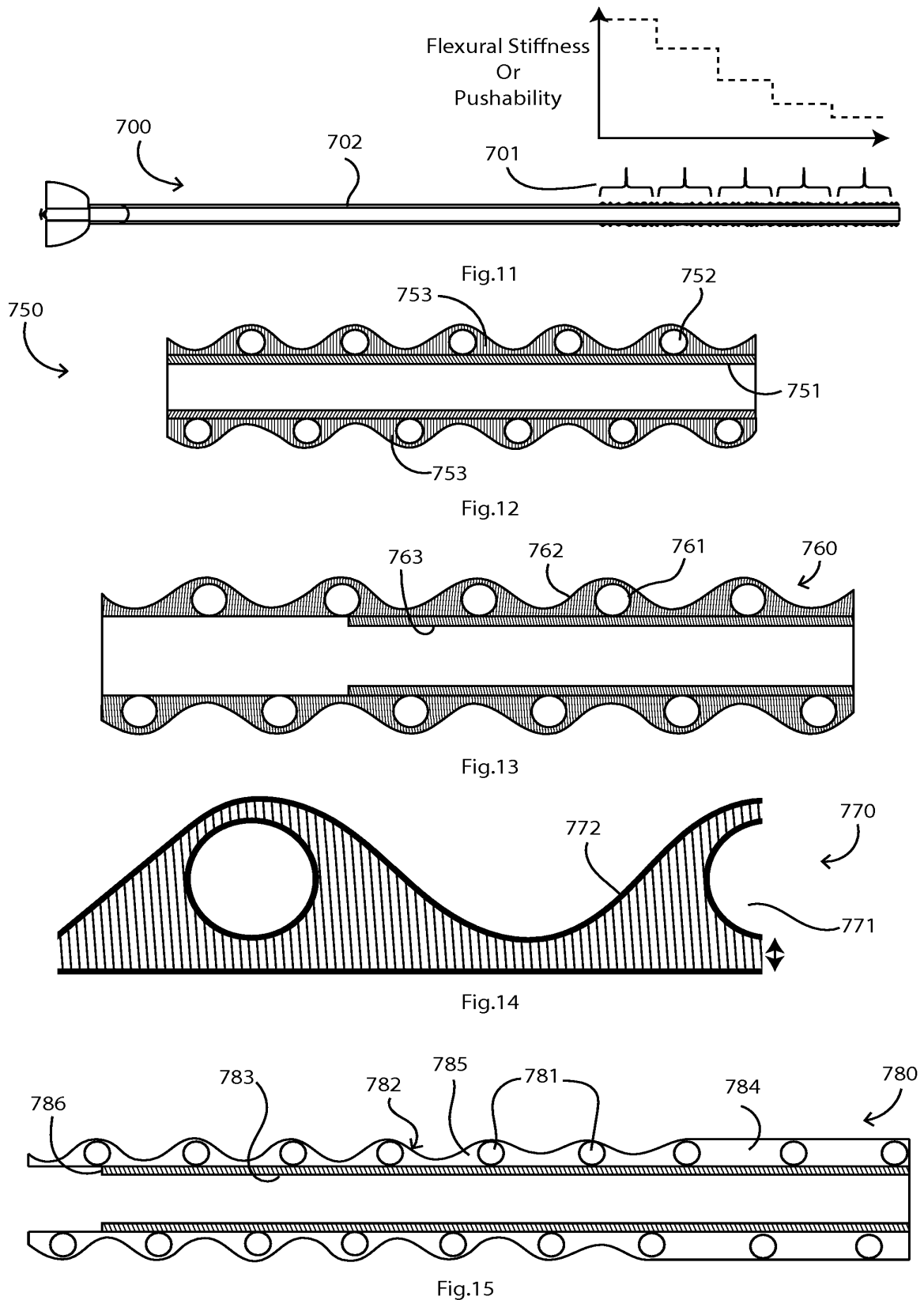


Fig.10



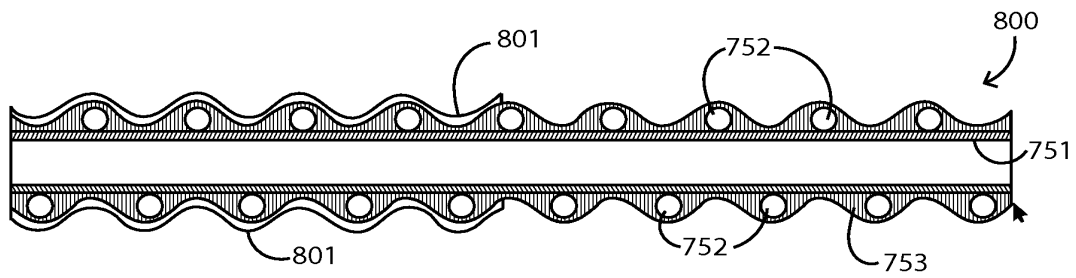


Fig.16

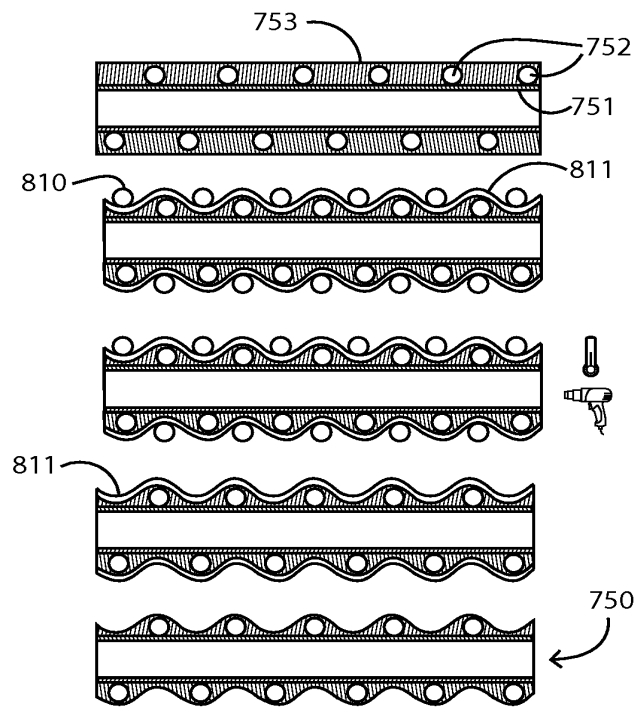


Fig.17

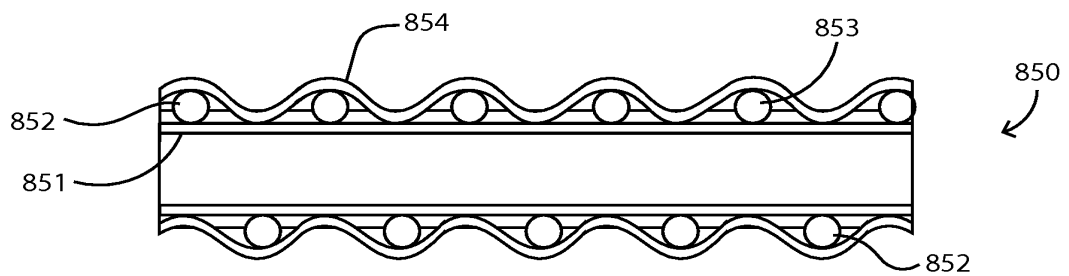


Fig.18

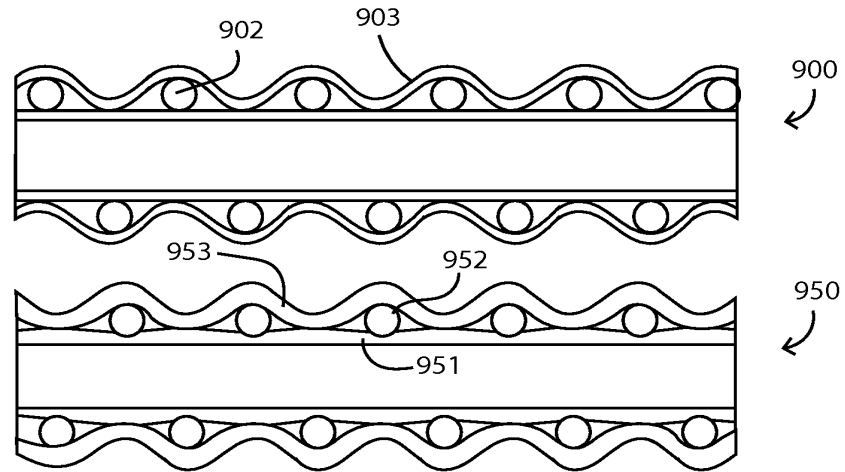


Fig.19

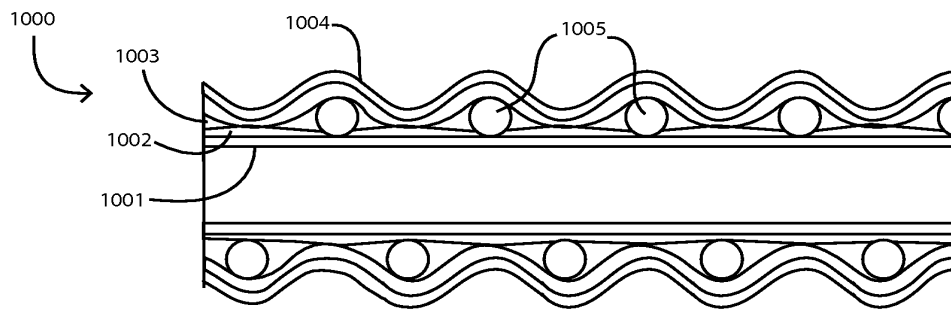


Fig.20

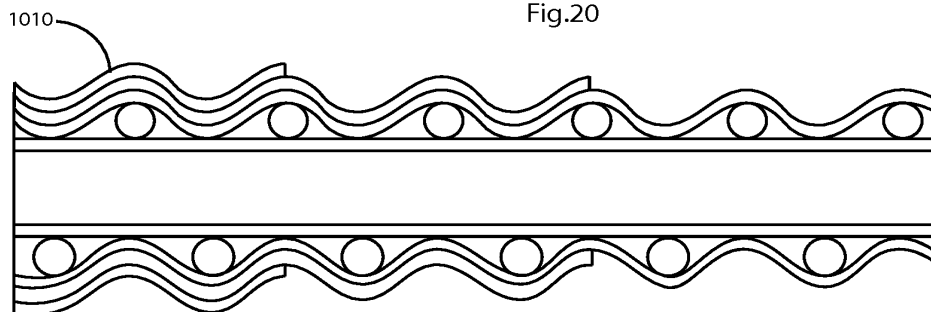


Fig.21

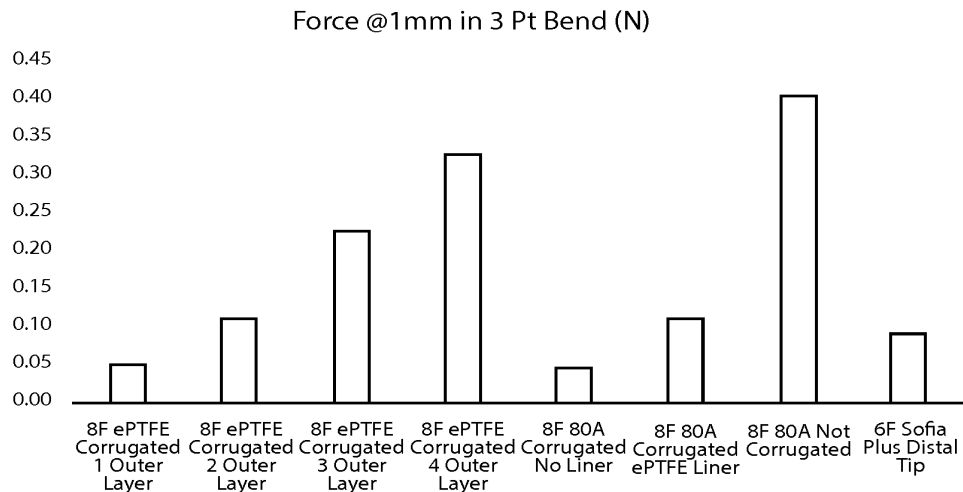
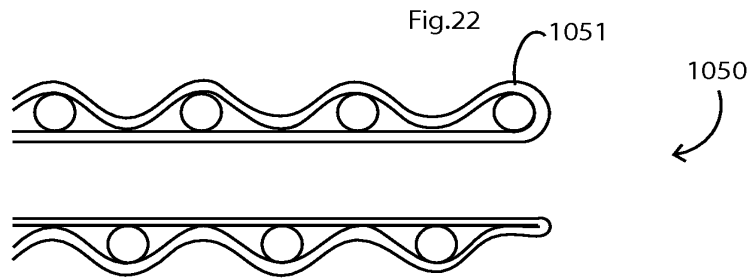
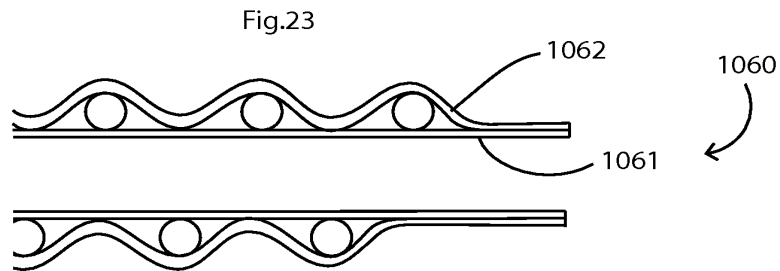
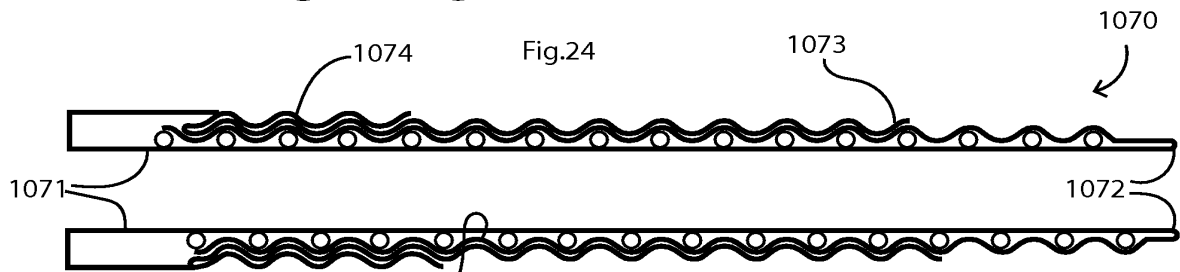
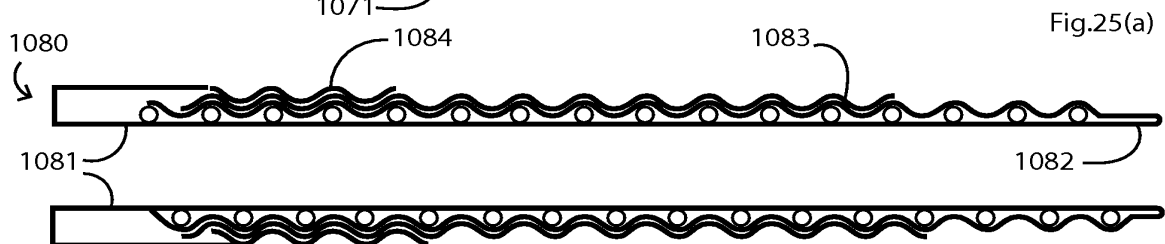


Fig.25(b)

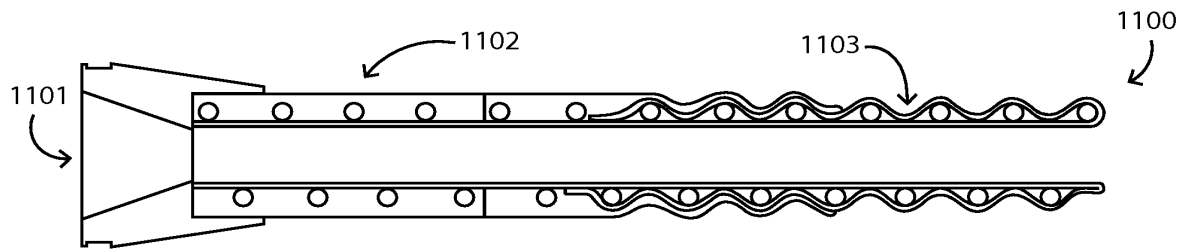


Fig.26

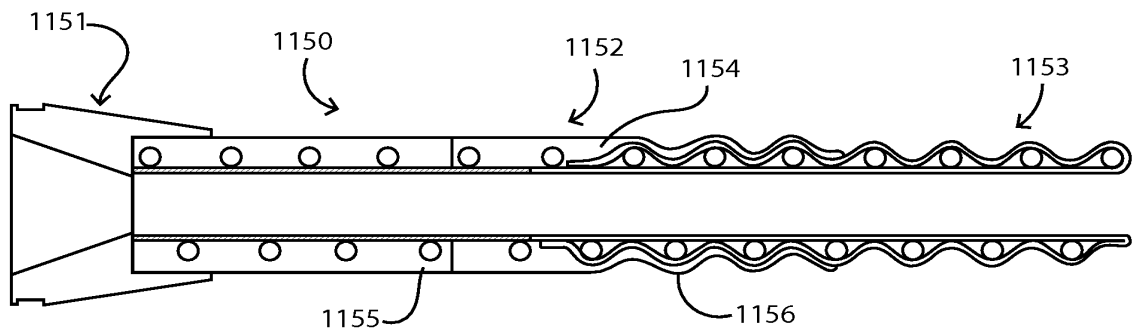


Fig.27

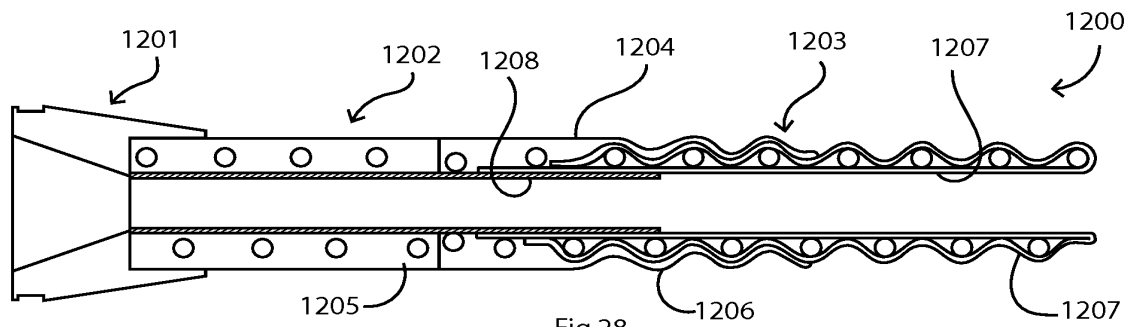


Fig.28

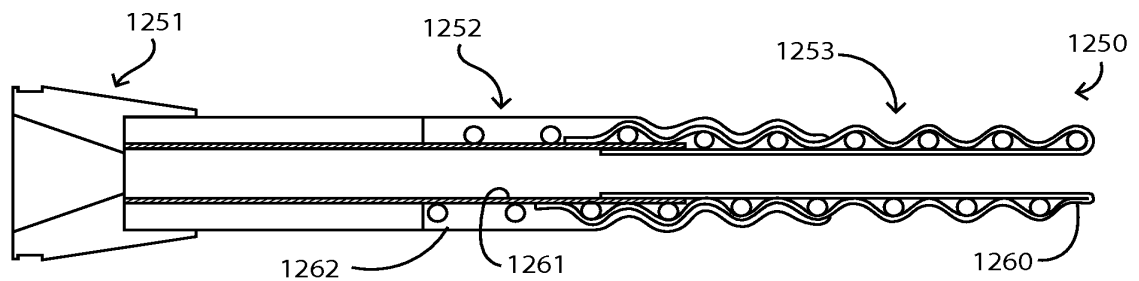


Fig.29

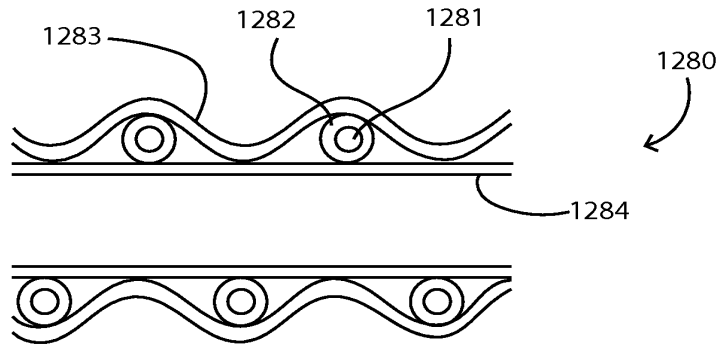


Fig.30

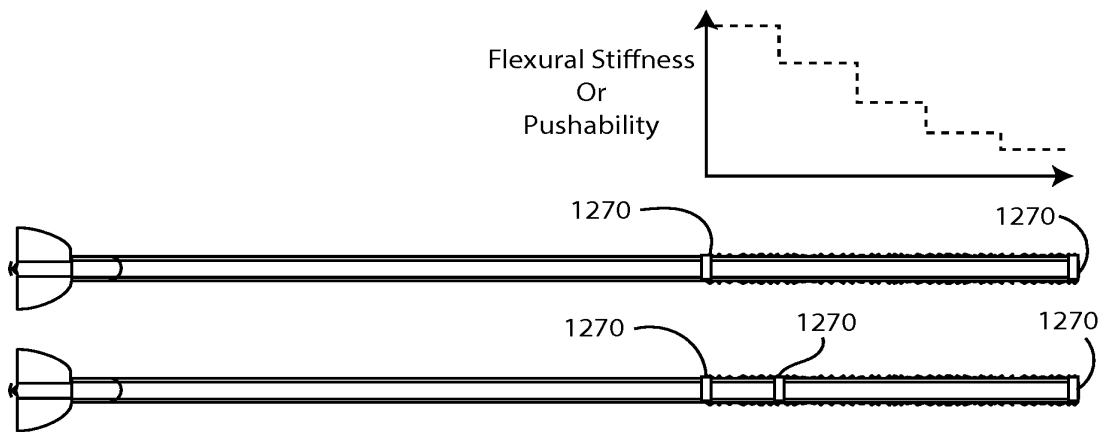


Fig.31

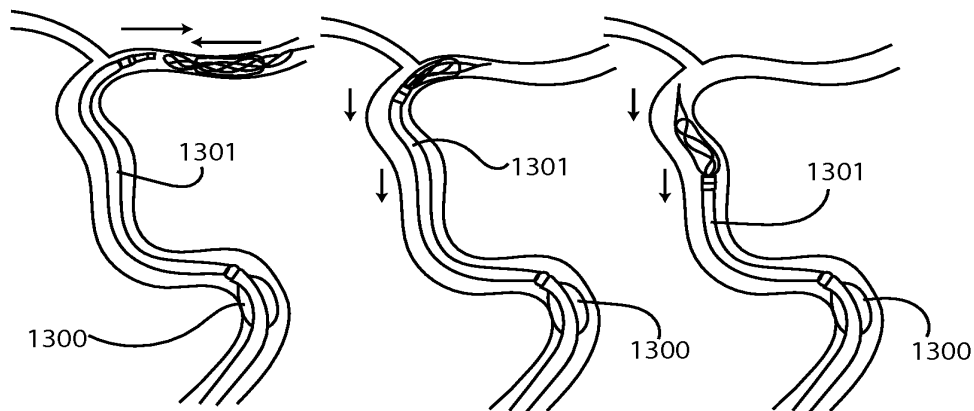
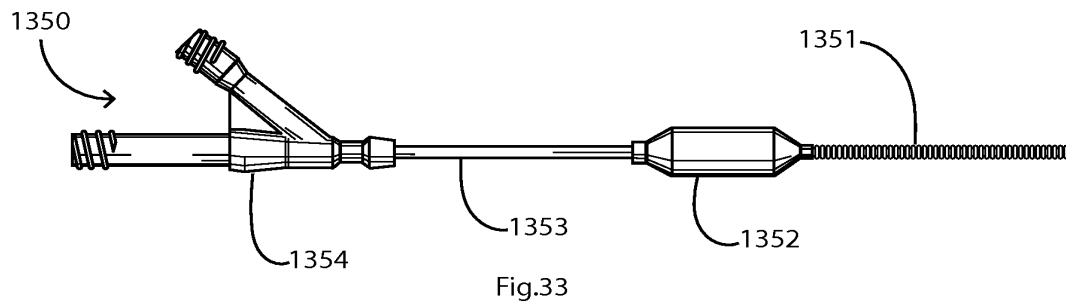
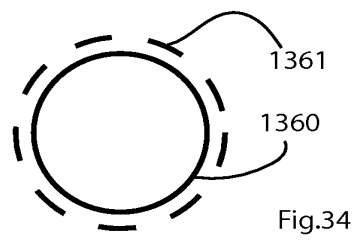
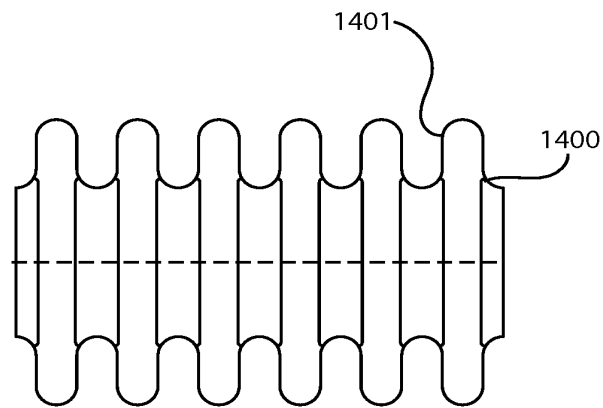
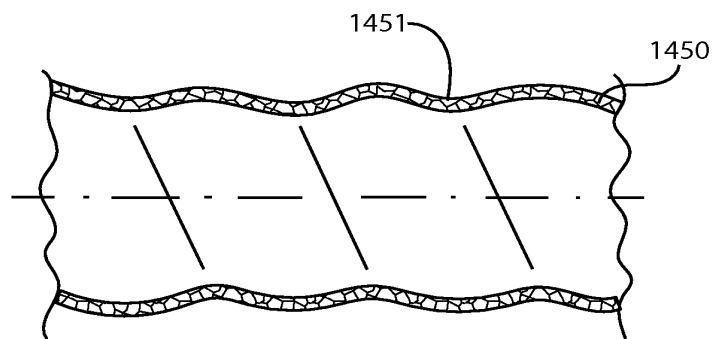


Fig.32 (PRIOR ART)



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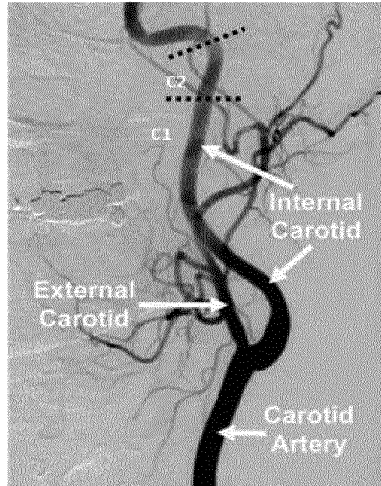
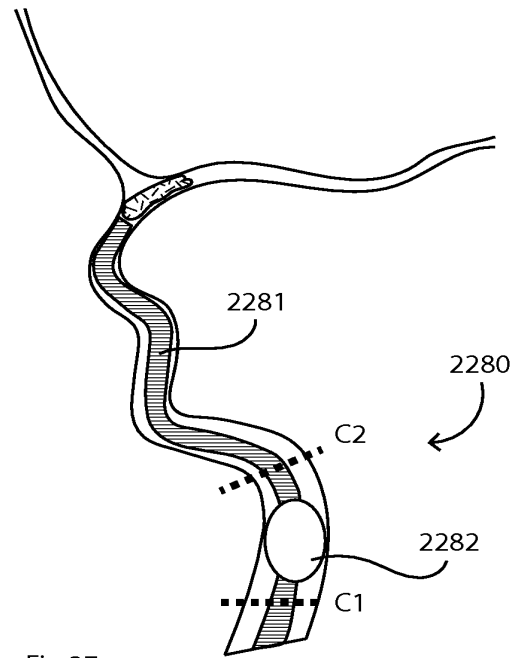


Fig.37

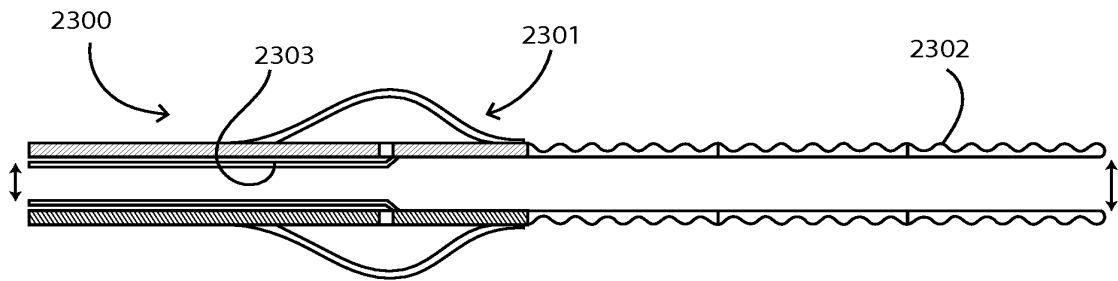


Fig.38

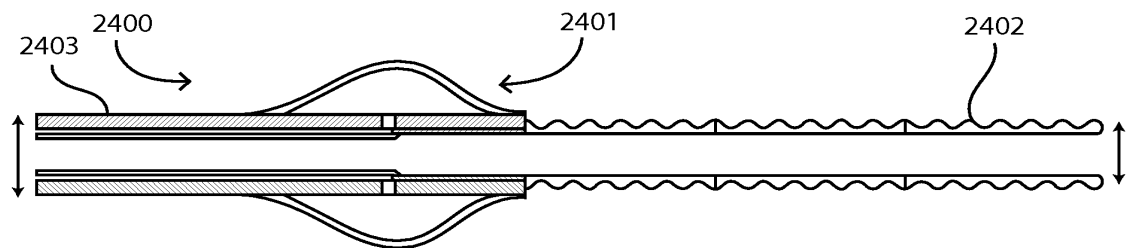


Fig.39

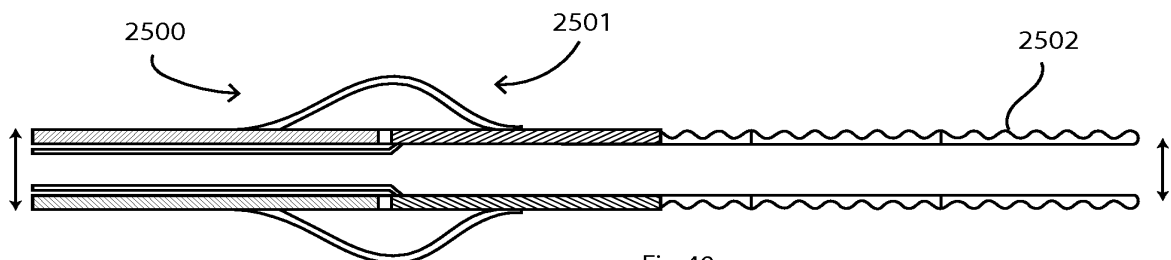


Fig.40

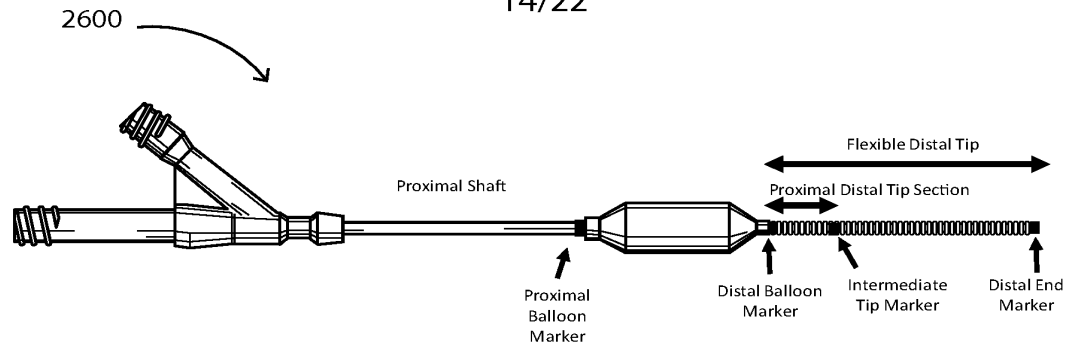


Fig.41

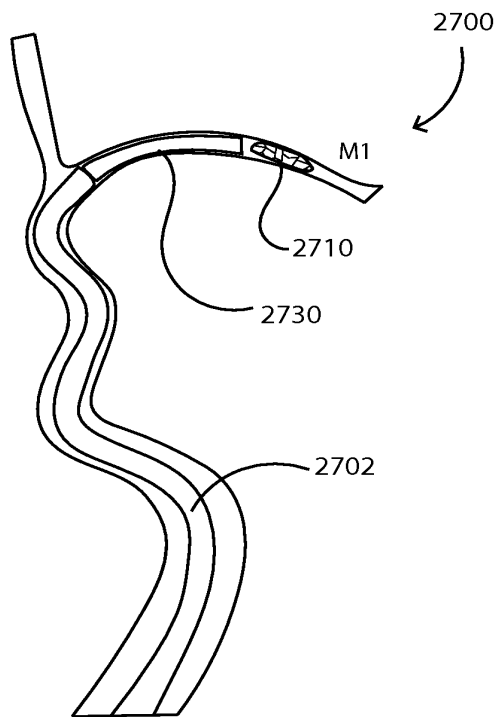


Fig.42

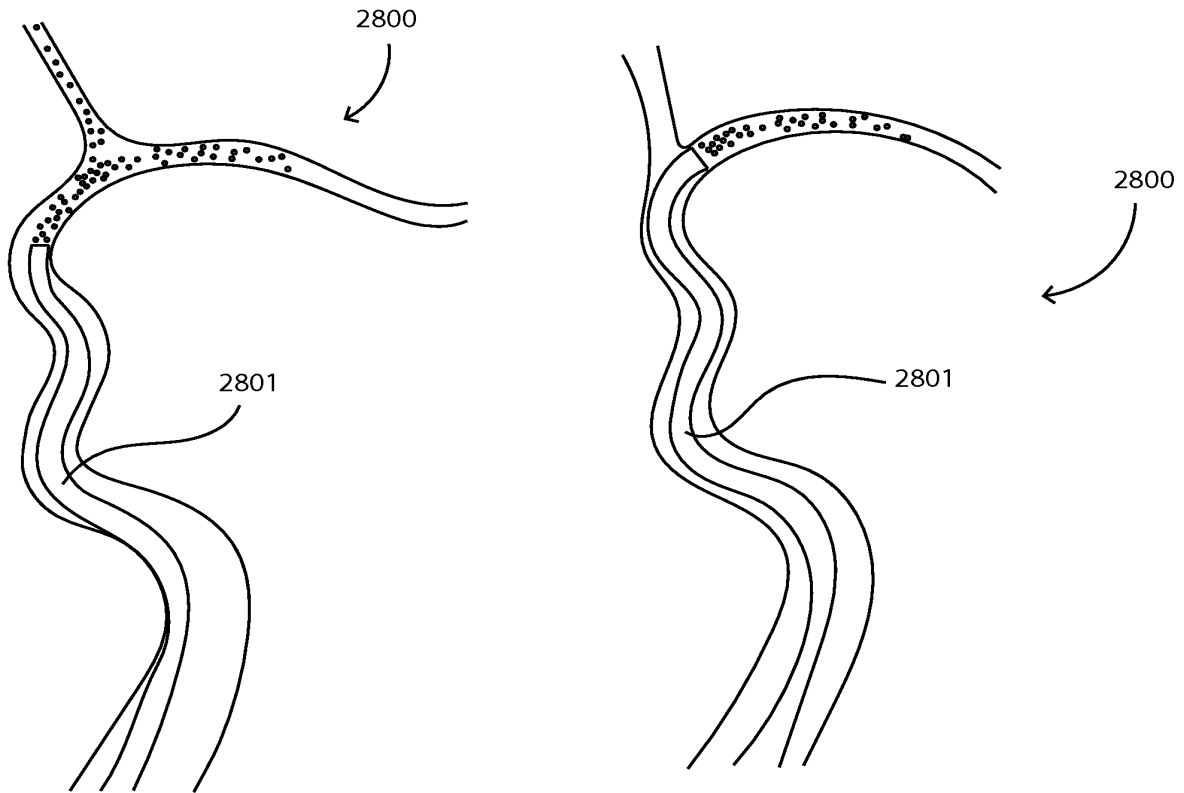


Fig.43

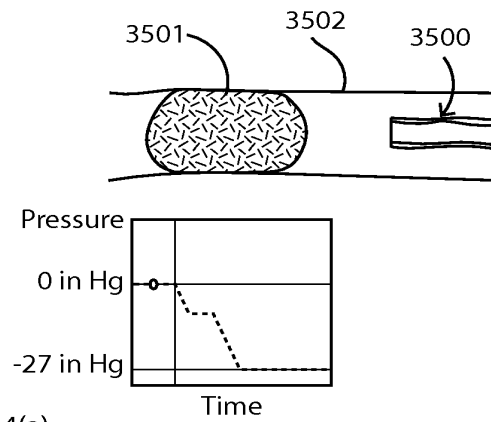


Fig.44(a)

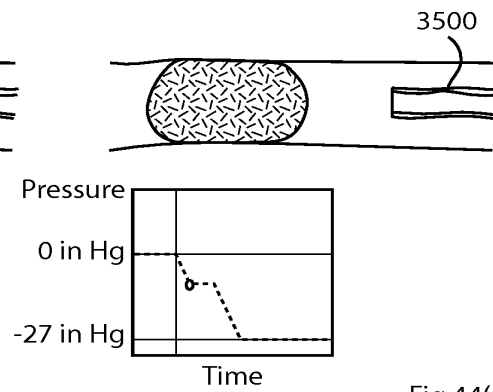


Fig.44(b)

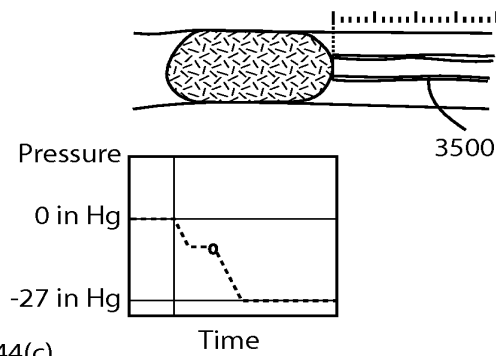


Fig.44(c)

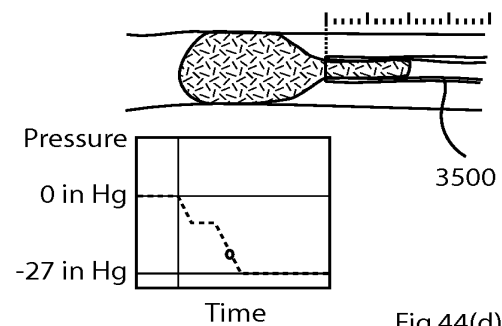


Fig.44(d)

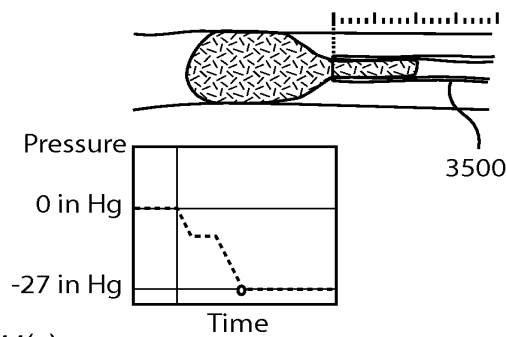


Fig.44(e)

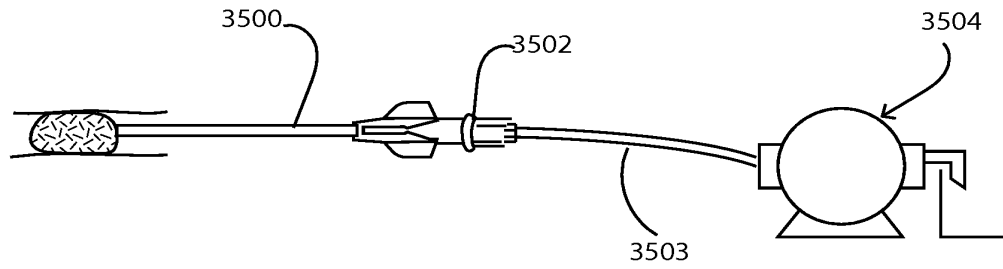


Fig.45

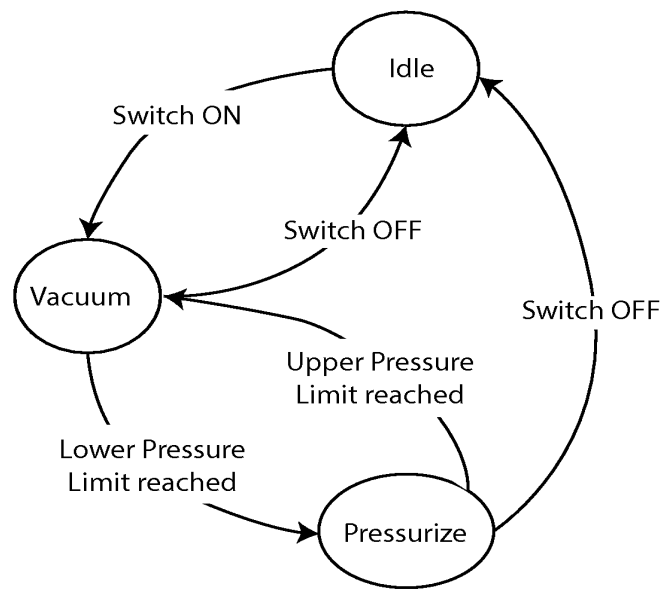


Fig.46

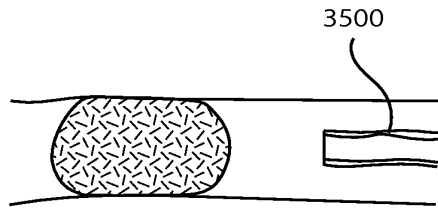
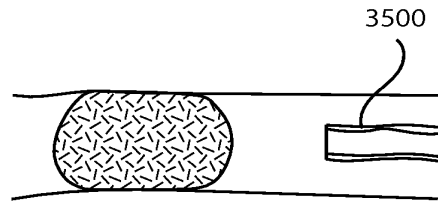
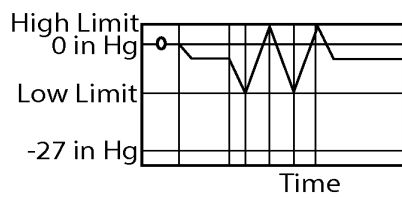


Fig.47(a)

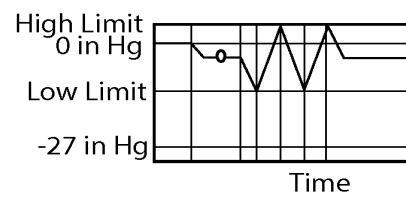


Fig.47(b)

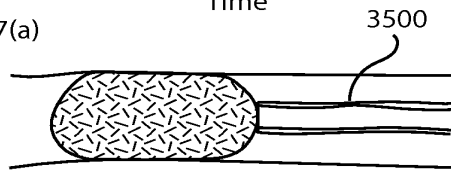
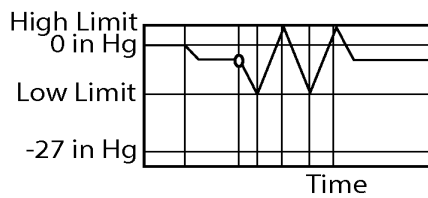


Fig.47(c)

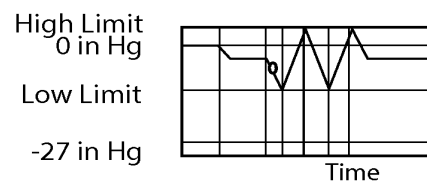
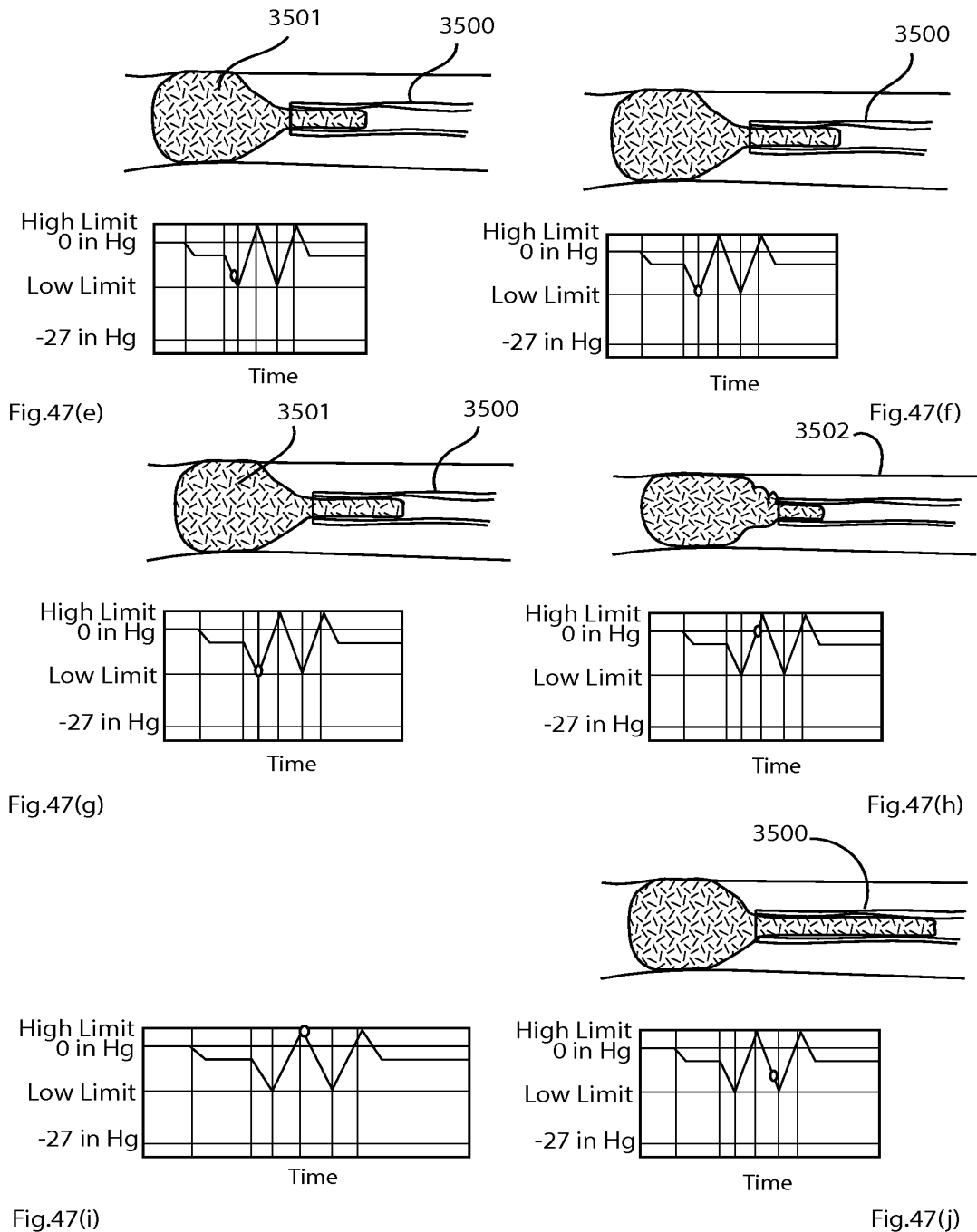


Fig.47(d)



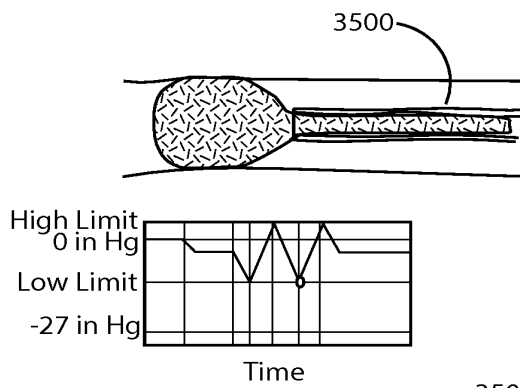


Fig.47(k)

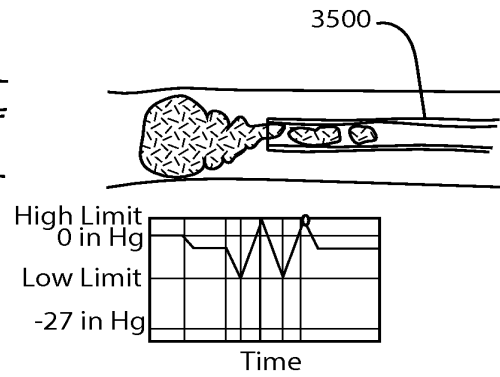


Fig.47(l)

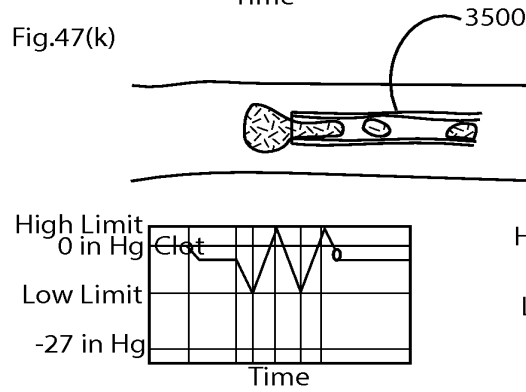


Fig.47(m)

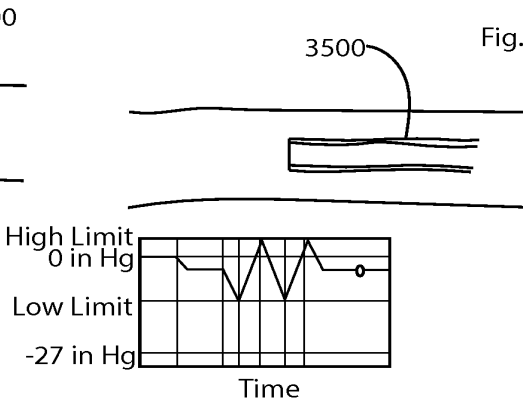


Fig.47(n)

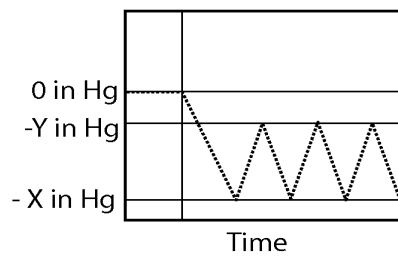


Fig.48(a)

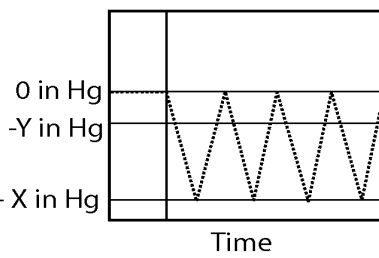


Fig.48(b)

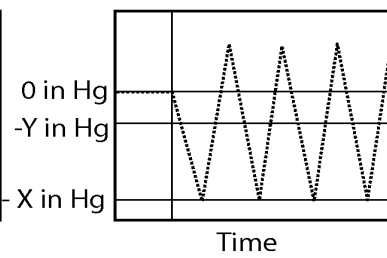


Fig.48(c)

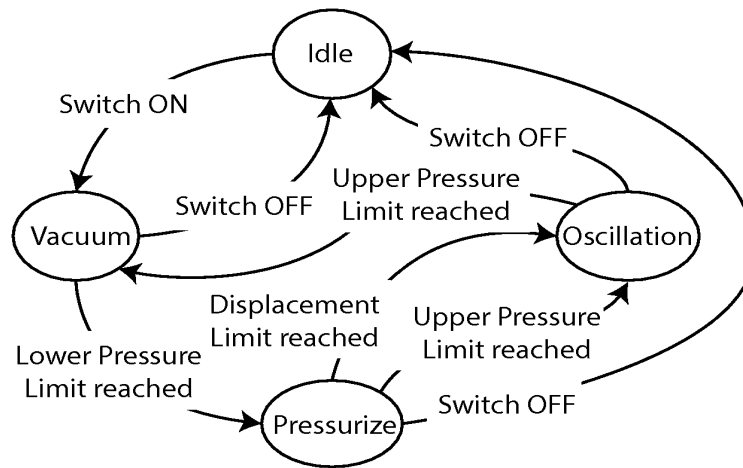


Fig.49

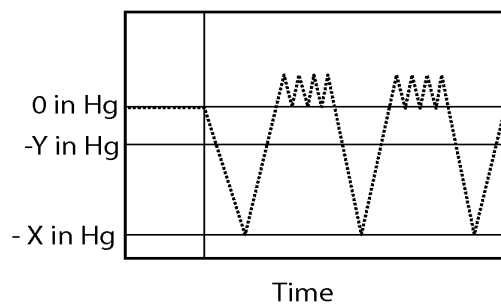


Fig.50(a)

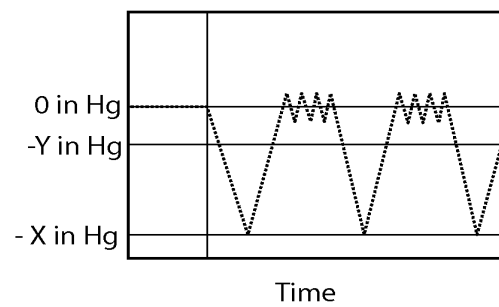


Fig.50(b)

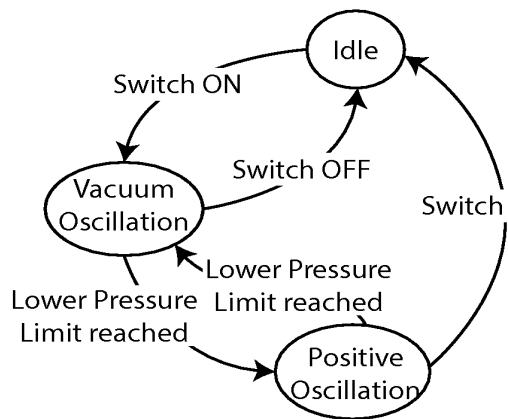


Fig.51(a)

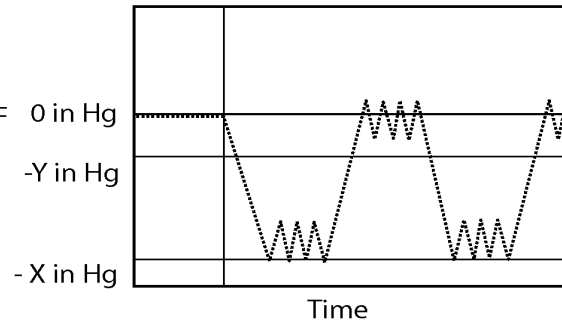


Fig.51(b)

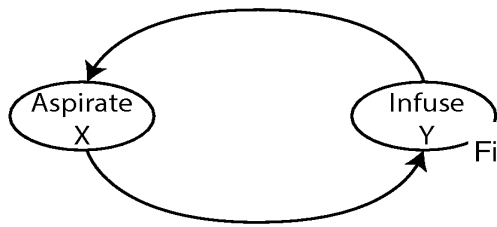


Fig.52(a)

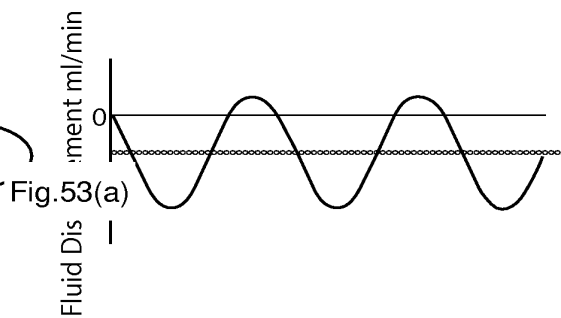


Fig.52(b)

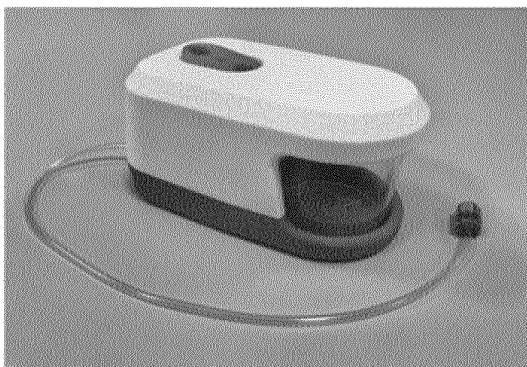


Fig.53(a)

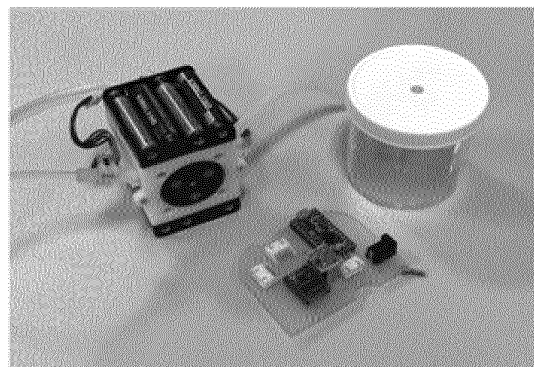


Fig.53(b)

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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Fax: (+31-70) 340-3016

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.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/EP2018/085064

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
wo 9315784 A1	19-08-1993	AU wo 3666393 A 9315784 A1	03-09-1993 19-08-1993

Form PCT/ISA/210 (patent family annex) (April 2005)



(51) International Patent Classification:

A61N 1/00 (2006.01) *A61M 27/00* (2006.01)
A61B 17/22 (2006.01)

(21) International Application Number:

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(22) International Filing Date:

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(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data:

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(72) **Inventors: GREY, Casey**; 800 East Leigh Street, Suite 300, Richmond, VA 23219 (US). **SIMPSON, David**; 800 East Leigh Street, Suite 300, Richmond, VA 23219 (US). **SIMON, Scott**; 800 East Leigh Street, Suite 300, Richmond, VA 23219 (US). **LONGEST, Worth**; 800 East Leigh Street, Suite 300, Richmond, VA 23219 (US). **MASSENZO, Trisha**; 800 East Leigh Street, Suite 300, Richmond, VA 23219 (US).

(74) **Agents:** WHITHAM, Michael E. et al.; Whitham, Curtis, Christofferson & Cook, P.C, 11491 Sunset Hills Road, Suite 340, Reston, VA 20190 (US).

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

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

(84) Designated States (*unless otherwise indicated, for every*

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

Published:

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

(54) Title: DYNAMIC ASPIRATION METHODS AND SYSTEMS

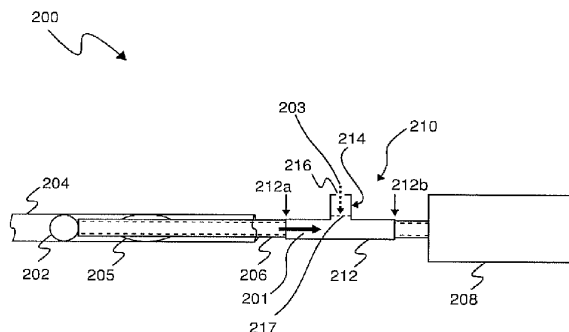


FIGURE 2A

(57) Abstract: Dynamic aspiration, such as in aspiration thrombectomy, provides a changing negative pressure in a catheter such that a dynamic suction force is exerted on a thrombus or occluding element. Various dynamic aspiration profiles may be used. Devices for providing dynamic aspiration may be used with existing catheter-pump systems which currently deliver only static aspiration. A dynamic suction force exerted on a thrombus may induce material fatigue and thereby reduce the clot's load-to-failure and time-to-failure as compared to existing suction thrombectomy techniques.

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DYNAMIC ASPIRATION METHODS AND SYSTEMS

DESCRIPTION

5 *Field of the Invention*

This application generally relates to aspiration methods and systems which allow for dynamically changing suction pressure over time. Certain embodiments of the systems and methods have particular application to surgical procedures including, without limitation, aspiration embolectomy procedures and thrombectomy procedures for improving, for example, ischemic stroke treatment.

BACKGROUND

15 Ischemic stroke is a very serious condition in which the normal flow of blood is partially or completely blocked by an occluding element, resulting in a reduction in blood flow, oxygen delivery, nutrient delivery, and waste exchange in the downstream tissue bed. This is most commonly a clot. It is generally necessary to remove the occluding element as quickly as possible in order to re-establish blood flow to the affected area or areas of the body. Current
20 methods of removing occluding elements focus on applying endovascular disruptive forces. This can involve administration of thrombolytic drugs, mechanical occlusion retrieval, and occlusion removal via intravascular aspiration (suction). Thrombolytic drugs are typically not effective after a predefined window usually defined as 2-3 hours after symptoms arise from an occlusion. Mechanical retrieval usually involves a deployable mesh-like grid such as a stent retriever and is
25 often complicated and dangerous to perform. Aspiration thrombectomy is generally an effective and common treatment for removing an occluding element within the body, especially in the case of ischemic stroke. Traditional aspiration thrombectomy procedures involve application of a constant negative pressure (suction) by either a pump or large gauge syringe to facilitate removal of the occlusion with a catheter. Flow arrest may also be performed using a proximal balloon.
30 However, under conditions such as a strong integration of an occlusion with a vessel wall, such conventional aspiration techniques are unsuccessful. The best thrombectomy technology

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currently only achieves recanalization in approximately 85% of cases. As such, there exists a need for improved techniques for the removal of occlusions and, more particularly, improvements to aspiration thrombectomy.

U.S. Patent Application Publication No. 2013/0267891 teaches a thrombectomy catheter system directed to cutting an occluding element with a fluid jet. Fluid is supplied to the catheter by a source of infusion fluid and a source of positive pressure. The fluid jet is directed into an exhaust lumen to create a suction effect and carry fluid away from the catheter. The suction effect of the fluid jet is intended to draw in occlusive material which may then be cut and removed by the high pressure stream. The catheter tip may be inserted into or through an occlusion to position occlusive material in proximity of the fluid jet. The fluid jet itself may have a variable positive pressure as provided for by a control device which regulates the flow of infusion fluid into the catheter. Suction, as discussed, is achieved passively by the direction of the fluid jet into the exhaust lumen of the catheter. This particular type of design places the fluid jet/aspiration portal in a position that is tangential to the clot or even within the clot itself, resulting in the application of non-uniform forces across the face of the clot.

Ultrasound augmented fibrinolysis delivers ultrasonic oscillations transcranially or via a solid medium of a catheter (usually a metal tip) to increase the penetration of fibrinolytic agents into a clot with the intention of breaking up the clot and permitting the occlusive material to flow distally. Benefits of ultrasound augmented fibrinolysis, however, may not outweigh the increased risk of hemorrhage.

SUMMARY

Embodiments of the invention improves aspiration, especially as used in embolectomy or thrombectomy applications, by providing a dynamic suction force as opposed to a static suction force traditional to aspiration thrombectomy. This can provide improved disruption characteristics. Dynamic suction forces, in contrast to static suction forces, provide repetitive loading to induce material fatigue in an embolus. Subjecting clots to material fatigue via a dynamic aspiration profile (e.g. a cyclic aspiration profile) may reduce the clot's load-to-failure and time-to-failure as compared to existing suction thrombectomy techniques. This has several advantages, notably: the load applied to cause the clot to fail (fracture or break loose) is applied

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in several repetitive loading cycles. The forces applied during any one of these repetitive cycles may be far less than the force necessary to cause the clot to break loose. The additive effect of these repetitive loading cycles causes the clot to fracture and break loose so that it can be removed. This mechanism of failure is commonly referred to as fatigue failure. An everyday
5 example of fatigue failure is observed when a paper clip is repeatedly folded back and forth, and after several cycles the clip easily breaks. While the total load necessary to break a clot free remains constant, when using an exemplary embodiment loading may be applied in smaller incremental steps, and it is the additive effect of these smaller incremental steps resulting in the fatigue of the clot and breaking the clot free from the vessel wall. By applying the load in small
10 incremental “doses” the risk of damage to the surrounding blood vessel is reduced. In existing conventional devices, the suction forces necessary to break a clot free are essentially applied in a “single dose”. Embodiments of the present invention are designed to circumvent this “all or nothing” loading limitation of conventional suction devices and reduce the risk of damage to the surrounding tissues by exploiting fracture mechanics to induce the release of the clot from the
15 surrounding vessel wall. The use of repetitive loading cycles also provides the benefit of removing a greater percentage of clots, including those which are particularly entrenched. A reduction in time-to-failure provides the benefit of reducing the elapsed time to reperfusion of the occluded tissue. Generally, dynamic aspiration shows an improvement in overall clot clearance rate and clot clearance time. By using a catheter that places the suction forces “face
20 on” to the occluding clot a larger surface area of the clot can be engaged than with suction devices that use a tangential approach. This improves the efficiency and efficacy of the process of applying the repetitive loading forces to the clot. Negative pressure and negative pressure oscillations are delivered by a fluid medium which may be, for example, one or more liquids, gases, or a combination thereof.

25 According to one embodiment, an appliance for aspiration control is provided which includes a conduit and a chamber. The conduit has a first end connectable to be in fluid communication with a catheter and a second end connectable to be in fluid communication with a source of suction such that fluid of a first pressure from the source of suction extends through the appliance from second end to the first end. The chamber is connected to the conduit between
30 the first end and the second end and is in fluid communication with the conduit. An opening or hole of the chamber may be selectively opened or closed, or enlarged or narrowed. The opening

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permits fluid of a second pressure which may be different from the fluid of the first pressure to be mixed with the fluid of the first pressure.

According to another embodiment, an appliance for aspiration control may include a first conduit, a second conduit, and a valve. The first conduit has a first end connectable to be in fluid communication with a catheter. The second conduit has a second end connectable to be in fluid communication with a source of suction such that fluid of a first pressure from the source of suction extends through the appliance between the second end and the first end. The chamber may be in fluid communication with and connected to the first conduit and the second conduit. A valve is arranged in the chamber which is selectively operable to reduce or prevent fluid communication between the first conduit and the second conduit and displaceable such that a volume of the chamber between the first end of the first conduit and the valve is selectively variable.

According to yet another embodiment, a method of aspiration is provided which includes steps of positioning a distal end of a catheter adjacent an occlusion, exerting a suction force at the distal end of the catheter with a source of suction in fluid communication with a proximal end of the catheter, and dynamically varying the suction force with a device in fluid communication with the catheter and the source of suction by variably opening the device.

According to yet a further embodiment, there is a method of aspiration which includes steps of positioning a distal end of a catheter adjacent an occlusion, exerting a suction force at the distal end of the catheter with a source of suction in fluid communication with a proximal end of the catheter, and dynamically varying the suction force with a device in fluid communication with the catheter and the source of suction by variably urging a displacement of a valve in the device such that a volume between the distal end of the catheter and the valve is selectively variable.

According to still another embodiment, a method of performing an embolectomy may include steps of positioning a distal end of a catheter adjacent an embolus, providing a negative pressure in the catheter with an aspiration source, changing the negative pressure repetitively with an appliance to produce a dynamic suction force at the distal end of the catheter, and removing at least part of the embolus by aspiration with the catheter. The dynamic suction force provides repetitive loading to induce material fatigue in the embolus.

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According to yet a further embodiment, an aspiration system may comprise a catheter insertable into a body, an aspiration source providing a negative pressure in the catheter, and a device which repetitively changes the negative pressure to produce a dynamic suction force at a distal end of the catheter.

5

BRIEF DESCRIPTION OF THE DRAWINGS

Figures 1A and 1B are, respectively, a schematic of a conventional aspiration system for suction thrombectomy and an aspiration profile;

10 Figures 2A-2C are, respectively, a schematic of an aspiration system for dynamically varying a suction force, an aspiration profile, and an aspiration method;

Figures 3A-3C are cyclic aspiration profiles;

Figures 4A and 4B show, respectively, another aspiration system with an aspiration device for dynamically varying a suction force and a stochastic aspiration profile thereof;

15 Figure 5 shows yet another aspiration system with an aspiration device for dynamically varying a suction force;

Figure 6 shows an aspiration system with an electromagnetically operated aspiration device for dynamically varying a suction force;

20 Figures 7 shows an aspiration system with an aspiration device having an oscillating spring element;

Figures 8A-8C are aspiration systems with aspiration devices having an oscillating valve element; and

Figures 9A and 9B are example dynamic aspiration methods;

Figure 10 is a method of performing an embolectomy; and

25 Figures 11A-11D show catheters usable with all embodiments of the invention.

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DETAILED DESCRIPTION

As a matter of terminology, it should be appreciated that a reduction in positive pressure is equivalent to an increase in negative pressure, and vice versa. As generally used herein, “pressure” (without an indication of being positive or negative), “negative pressure”, and “vacuum pressure” are used interchangeably. “Positive pressure” (with the adjective “positive” explicitly provided) is the opposite of “pressure”, “negative pressure”, and “vacuum pressure”. Positive pressure supplies a pushing force. “Negative pressure”, in contrast, supplies a suction force. However, it should be noted that “pressure-relieving” means a reduction in the magnitude of either positive pressure or negative pressure. “Pressurizing”, on the hand, means an increase in the magnitude of either positive pressure or negative pressure. “Magnitude” means the scalar or absolute value of a parameter.

Furthermore, terms such as “control” and “controlling” do not necessarily imply absolute control, but rather indicate having an influence or effect that is intended and/or predictable. The term “dynamic” does not preclude temporary or brief plateaus or temporary intervals of constant pressure. Rather, over the course of an aspiration procedure (e.g. thrombectomy), the aspiration profile includes a plurality of deliberate variations in the suction force/pressure (this sometimes being referred to as a dynamic suction force). These variations may be repetitive, cyclic, rhythmic, stochastic, or otherwise. A combination of these variation types may also be used together. The terms “dynamic aspiration” and “dynamic suction” may be used interchangeably with the term “impact aspiration”. It is noted that “constant pressure”, particularly as used in describing the prior art, may include incidental perturbations such as caused by adjustments in the position of a catheter tip relative a thrombus. Such incidental perturbations to an aspiration profile or suction force do not alone provide sufficient basis for characterization of an aspiration profile as “dynamic”.

Referring now to the drawings, and in particular Figures 1A and 1B, a schematic representation of a conventional aspiration system 100 is shown for removal of an occlusion 102 from a biological lumen, for example the lumen of an artery 104. After an incision is made and the catheter 106 inserted into the lumen, an aspiration source 108 at a distal end of the catheter 106 applies a negative pressure to a fluid within the catheter. A suction force is indicated by arrow 101. In general, the catheter 106 is placed immediately adjacent the occlusion 102 such

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that the occlusion blocks most or, more typically, the entire distal opening of the catheter 106. The aspiration source 108, for example a pump or syringe, creates a vacuum condition within the catheter of increasing negative pressure until a plateau is reached, as shown in the aspiration profile 150 of Figure 1B. Once a plateau is reached, the occlusion 102 experiences a constant
5 suction force until, ideally, the occlusion or occlusive elements thereof break free of the arterial endothelium and are drawn into the catheter.

In some aspiration systems, a catheter or an extending element thereof is used to pierce or penetrate the occlusion in conjunction with the application of a constant suction force. Although this approach can in some cases aid in the breakup and removal of the occlusion, it has certain
10 drawbacks. One very serious risk is the escape and travel of occlusive material from the initial site of occlusion to a distal portion of the lumen or to another lumen branching therefrom. This is referred to as the distal migration of thrombi and can result in a new clot.

Referring now to Figure 2A, an aspiration system 200 is shown according to an embodiment of the invention. The aspiration system 200 generally comprises a catheter 206, a
15 source of suction 208 (i.e. an aspiration source), and an appliance 210 for affecting the aspiration profile of the catheter. In contrast to the aspiration system 100 of Figure 1A, an appliance 210 for aspiration control is provided in fluid communication with both the catheter 206 and the source of suction 208. Generally, appliance 210 permits alteration of an aspiration profile at the distal end of the catheter 206 and, more specifically, provides for changing the negative pressure in the
20 catheter 206 repetitively to produce a dynamic suction force at the distal end of the catheter. Appliance 210 includes a conduit 212 and a chamber 214 connected to and in fluid communication with the conduit 212. In the embodiment shown, chamber 214 adjoins the conduit 212 between a first end 212a and a second end 212b of the conduit 212. The conduit's first end 212a is connectable to be in fluid communication with the catheter 206, while the
25 second end 212b is connectable to be in fluid communication with the source of suction 208. The connections are such that a fluid of a first pressure from the source of suction 208 extends through the appliance 210 from the second end 212b through the first end 212a. The suction force provided by the negative pressure is indicated at arrow 201.

Chamber 214 has one or more openings 216 which permit fluid of a second pressure to be
30 mixed with the fluid of a first pressure. However, the second fluid is not introduced at a constant volumetric flow rate but rather influenced according to a changing configuration of appliance

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210 or, more specifically, a changing configuration of the opening 216. An opening 216 may be selectively opened and closed or enlarged and narrowed, for example. Variables such as maximum/minimum sizes of the opening 216, a rate of change for enlargement or narrowing of the opening 216, or the pressure differential between the first fluid and the second fluid may be selected or changed to achieve a particular dynamic aspiration profile. Repetitive or redundant variation of these or other variables provides control over the fluid flow (arrow 203) through an opening 216 and thus the negative pressure and aspiration profile at the distal end of the catheter 206.

An aspiration system 200 may further include a stabilizing balloon 205 or similar structure near or at the distal end / tip of the catheter 206. After inflation, a balloon 205 stabilizes the catheter 206 relative the vessel 204 to minimize or eliminate movement of the catheter resulting from dynamic changes in the suction force. This feature, like other features taught herein, is shown with aspiration system 200 by way of example and may optionally be included with other embodiments.

Appliance 210 may include a customized or commercially available valve for regulating the opening/closing or enlarging/narrowing of an opening 216. The valve may be but is not limited to a three-way valve available from companies like Clippard Instrument Laboratory Inc. (Cincinnati, Ohio, USA) or Harvard Apparatus (Holliston, Massachusetts, USA). Other suitable valves will occur to skilled persons in the art in view of the teachings herein.

The first fluid and the second fluid may be respectively referred to as first and second aspiration mediums. The aspiration mediums may be compressible fluids, such as air, or incompressible fluids such as water or saline. Generally, catheter 206, conduit 212, chamber 214, and any connecting tubules are primed with aspiration medium. A biofilter 217 may be provided at a junction of conduit 212 and chamber 214. In some embodiments, the second aspiration fluid may be provided at a positive pressure.

Figure 2B shows an example aspiration profile 250 according to a repetitive alternation of opening 216 between an open state and a closed state. A four-pointed star indicates the opening of opening 216 and six-pointed star indicates a closing of opening 216. In this example, the second fluid which passes through opening 216 during an open state is of a substantially constant pressure. This contributes to controlled maximum and minimum negative pressure equilibriums as indicated at lines 252a and 252b, respectively. Like the first fluid, the second

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fluid may be, for example, ambient air (also referred to simply as “ambient”), water, or saline. A cycle time and fluctuation behavior of a negative pressure in the catheter 206 may be controlled and regulated by changing a state of opening 216. Opening 216 may have two or more discrete states (e.g. fully open and fully closed, such as in the example just described in relation to Figure 5 2B) or may have a continuously variable state.

Figure 2C is a method 260 of aspiration, reference being made to the aspiration system 200 of Figure 2B for illustrative purposes. At step 261, a distal end of catheter 206 is positioned adjacent an occlusion 202. At step 262, a suction force is exerted at the distal end of the catheter 206 with a source of suction 208 in fluid communication with the proximal end of the catheter. 10 At step 263, the suction force is dynamically varied with a device or appliance 210 in fluid communication with the catheter 206 and the source of suction 208. The dynamic variation is achieved by variably opening the device at one or more openings 216.

A variety of different profiles and waveforms may be achieved for the dynamic pressure provided by an aspiration system 200 or other aspiration systems and devices according to 15 embodiments of the invention. Figures 3A-3C show, respectively, example cyclic aspiration profiles 310, 320, and 330 with solid black lines. Generally, aspiration may be characterized by at least a pressure profile and, especially for cyclic aspiration, a frequency profile. Aspiration pressure may be varied for any frequency in at least two general ways. Down-cycling (DC) involves a brief pressure-relieving impulse in each cycle. A majority of time may be spent at 20 maximum treatment pressure. Up-cycling (UC) involves a brief pressurizing impulse in each cycle. In this case, a majority of time may be spent at minimum treatment pressure. Such differences in DC and UC pressure variation are illustrated by way of example in aspiration profiles 310 and 320. UC regulation may be achieved by supplying a plurality of pressurizing pulses to aspirated fluid of a catheter. DC regulation may be achieved by supplying a plurality of 25 pressure-relieving pulses to aspirated fluid of a catheter.

For comparison, Figures 3A-3C include dashed lines representative of constant pressure aspiration profiles. With traditional constant pressure aspiration methods, pressure is increased up to an equilibrium steady-state pressure that is maintained until a thrombus is removed or else the removal is deemed unsuccessful. Dynamic aspiration is found to improve overall clot 30 clearance rate and clot clearance time yet can involve less total loading to an occlusion. In contrast to static loading, dynamic loading from dynamic aspiration supplies repetitive and

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variable loading to induce material fatigue in an embolus. "Material fatigue", or simply "fatigue", is a term used herein according to its meaning in materials science. It involves the progressive weakening of a material as a result of repetitive loading and unloading from, for example, cyclic loading. Over time, a material subject to cyclic loading exhibits localized structural damage. Generally, microscopic cracks begin to form at stress concentrations, for example the surface of a material, sharp edges, or slight structural imperfections. The cracks grow and reach a critical size at which point sudden propagation of the crack causes fracturing of the material.

Many materials exhibit what is referred to as a linear elastic behavior. Under loading a material deforms, and upon removal of such loading the material fully recovers its original conformation. When forces acting upon the material exceed what is called a yield strength, the material begins to deform plastically (as opposed to elastically) and the original conformation cannot be recovered. It is worth noting that fracturing of a material can result from cyclically applied loads which are significantly smaller than the loads associated with or greater than the material's yield strength. For occlusions such as clots, conventional static aspiration applies a constant load to a clot. This can require a suction force which exceeds the yield strength or ultimate tensile strength of the clot. In contrast, dynamic aspiration as taught herein may cause fracture and break-up of a clot applying smaller suction forces which are repetitively varied to induce material fatigue. One possible advantage of using smaller suction forces is a reduction in the risk of damaging a vessel wall and causing hemorrhage. The fracture of a clot, and thus its material failure, may be achieved by loading the clot cyclically, with or without a net fluid flow.

Dynamic aspiration profiles, cyclic or otherwise, may have any one or more of a plurality of parameters changed over time to control/influence the pressure realized in a catheter and to which an occlusion is subjected. Such parameters include but are not limited to static baseline aspiration pressure, frequency, aspiration medium, and pressure waveform. Dynamic aspiration profiles may furthermore have fixed or modulated frequencies and amplitudes. This allows tuning of an aspiration system for optimized treatment efficacy.

Different frequencies of cyclic aspiration may be used to improve clot clearance in comparison to static aspiration. For some embodiments higher frequencies are more effective, particularly frequencies above 1 Hz. In some embodiments, frequencies may be at least 10 Hz and, for still some other embodiments, frequencies may be at least 50 Hz. In comparison to

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ultrasound augmented fibrinolysis, embodiments with dynamic aspiration may employ lower frequency and higher amplitude oscillations aimed at mechanically dislodging and disrupting the clot so that it can be aspirated from the vessel.

In some embodiments, frequency may be varied while aspiration is applied to an occlusion. For example, a method of aspiration may include applying a first frequency and, over the course of an interval of time or at the conclusion of an interval of time, changing to a second frequency. A plurality of frequencies may be used. In an example embodiment, the aspiration frequency may start at a low frequency and progressively stepped up to higher frequencies (e.g. 5 Hz to 10 Hz to 15 Hz to 20 Hz and so forth up to a final operating frequency). Alternatively, aspiration frequency may be stepped down. Occlusions such as clots vary significantly from one patient to another. In addition to possible material property differences between clots (e.g. stiffness, elastic modulus, or the like), the adherence of the occlusive element to the wall of the lumen (e.g. artery) and the material properties of the lumen wall itself will also vary from one patient to another. Embodiments of the invention provide for variation and selection of one or more aspiration profile characteristics including frequency on a patient-by-patient basis.

As previously stated, embodiments such as that illustrated in Figure 2A may provide for a second aspirating medium which has a positive pressure. The value of the positive pressure may be selected according to a desired aspiration profile. A larger magnitude of the positive pressure of the second aspirating medium may be used to increase the rate of change of suction force at the distal end of the catheter. In a single cycle or period of a cyclic aspiration profile, the rate at which the negative pressure increases or decreases is influenced by the pressure differential between the first aspirating medium and the second aspirating medium. Increasing the positive pressure of the second aspirating medium increases this pressure differential and thus increases the rate of change, and vice versa. As a result, for a given cycle/oscillation of a selected time duration, the rate of change of suction/vacuum pressure in the catheter and thus the total change of suction/vacuum pressure in the catheter can be selectively varied. As an example, Figure 3C may show a larger amplitude/total vacuum pressure differential if the second aspirating medium was provided a non-zero/larger positive pressure. This may hold true despite the frequency remaining the same. As illustrated, Figure 3C shows a realized pressure differential (at the catheter tip) of approximately 14inHg resulting from oscillating a source differential (e.g. the aspiration pump at -25 inHg and atmospheric pressure) at a frequency of approximately 6.3 Hz.

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If the second aspirating medium in Figure 3C operated at a positive pressure (e.g. 10 inHg) rather than atmospheric pressure, the rate of pressure change would increase due to the increased pressure differential between aspiration mediums. For example, in this scenario the realized pressure differential may be increased to 20 inHg, up from 14 inHg, while operating at the same frequency (approximately 6.3 Hz). This may be beneficial in cases where the operating frequency of dynamic aspiration must be increased as it would provide a more significant perturbation load onto the occlusion. In a similar way the second aspiration medium could be placed under a vacuum to lower the amplitude of pressure oscillations (e.g. if the vasculature was more sensitive to larger perturbations). Additionally, it will be obvious to one skilled in the art that, along with bulk modulation of aspiration medium operating pressures, the real-time modulation of these pressures is encompassed in this description. This enables the operator to control both the frequency and amplitude of aspiration individually while providing dynamic aspiration treatment.

Generally, frequencies used for dynamic aspiration are lower than frequencies used with ultrasound thrombectomy procedures. For the latter, frequencies employed are typically in the MHz range (i.e. in excess of 1 MHz). The purpose and function of ultrasound has been limited to improving the penetration of thrombolytic agents into clots. A solid metal transducer or probe provides ultrasonic waves adjacent a clot to induce local cavitation. The primary rationale with this technique is that it maintains complete disbursement of the thrombolytic agent onto the clot, rather than letting it settle in the vessel. Provided the very high frequencies and low amplitudes involved, there is effectively no substantial fluid flow and the clot is subjected to static loading conditions. Thus, material fatigue and failure therefrom do not occur. Generally, there is no significant displacement of the clot prior to dissolution by the thrombolytic agents.

In contrast to ultrasound techniques, embodiments of the present invention generally employ frequency ranges well below MHz and, for some embodiments, below KHz. Frequencies in the KHz can undesirably cause heating of the epithelium and vessel damage resulting in increased procedural complications such as hemorrhage. The frequencies employed in some embodiments of the present invention allow for fluid flow, generally back-and-forth according to the aspiration profile. There is no requirement for net fluid flow. However, there may be net fluid flow, particularly if a second aspirating medium is admitted to the system or the occlusion is a partial occlusion which allows for a small amount of luminal fluid to be aspirated from the vessel

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into the catheter. Furthermore, epithelial heating is generally avoided. In some embodiments, a thermocouple may also be included at the tip of the catheter to sense local temperature. If an elevated temperature is detected, chilling of, for example, the catheter may be performed.

Amplitudes of dynamic aspiration profiles may vary between embodiments. Generally,
5 the realized pressure differential (i.e. the magnitude of the difference between the maximum and minimum pressure achieved at the catheter tip) may be between 0 and -100 inHg. In some embodiments, the pressure differential may be between -5 and -20 inHg. Absent an auxiliary source of aspiration, the magnitude of the baseline pressure is preferably maintained above zero (i.e. a vacuum is maintained). An example of this is provided in profile 330 of Figure 3C.
10 Providing a non-zero suction force in the catheter at all times reduces the risk of occlusive material breaking free of a clot and traveling distally in the vessel.

Figure 4A shows an aspiration system 400 for another exemplary embodiment of the invention. Like appliance 210 of aspiration system 200 in Figure 2A, appliance 410 of aspiration system 400 includes a conduit 412 with first and second ends (412a and 412b, respectively) and
15 a chamber 414. Fluid communication is provided among these elements. Arranged within chamber 414 between an opening 416 and conduit 412 is a turbulent element 418. Fluid flow through chamber 414 induces vibratory or chaotic movement of turbulent element 418, resulting in an arrhythmic or stochastic aspiration profile 450 in catheter 406 such as shown in Figure 4B by way of example.

As yet another example variation, an appliance 510 of aspiration system 500 is shown in Figure 5A. Appliance 510 includes within a chamber 514 a vibrational element 518 that restricts fluid flow of a fluid of a second pressure into the appliance 510. A choke point 516 serves a similar function to the opening 216 of aspiration system 200, although vibrational element 518 may be semi-rigid, deformable, and/or displaceable (e.g. displaceable with respect to a wall of
25 chamber 514 or where a first part 518a and at least a second part 518b of vibrational element 518 are displaceable relative to one another). As a fluid is drawn or forced through chamber 514, the geometry of choke point 516 rapidly fluctuates or vibrates, resulting in a vibratory aspiration profile in catheter 506 which may be similar to that as shown in Figure 4B.

Figure 6 shows an exemplary aspiration system 600 which is electromagnetically
30 operated. An appliance 610 is in fluid communication with both a catheter (not shown) and an aspiration source 608. Appliance 610 includes a chamber 614 in which a magnet or magnetic

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element 618 is arranged. A controller 619, which may be attached to chamber 614, controls coil 621. A position of magnetic element 618 within chamber 614 is regulated by controller 619 and coil 621. Specifically, coil 621 may be selectively and repetitively energized by controller 619 such that magnetic element 618 is attracted or repulsed by the electromagnetic force of energized coil 621. Recurrent displacement of magnetic element 618 variably restricts the flow of aspired medium through opening 616. A preselected energizing pattern may be provided by controller 619 to coil 621 such that the aspiration profile of the aspiration system 600 is dynamically (e.g., cyclically) variable.

Figure 7 illustrates an exemplary embodiment with an aspiration system 700. Five schematics, labeled 1 through 5, show aspiration system 700 at various stages of operation. Generally, aspiration system 700 comprises a catheter (not shown), an aspiration source 708, and an appliance 710. Inside of a chamber 714 of appliance 710 is a biasing mechanism 721 such as a spring. A plunger 718 is displaceable in chamber 714 and substantially fills a cross-section thereof. Chamber 714 includes an opening 716 which may be open to an aspirating medium or ambient air. Plunger 718 is arranged such that fluid communication between opening 716 and conduit 712 is restricted or blocked. A second opening 715 of chamber 714 is provided on a side of plunger 718 opposite the first opening 716. A sealing element 719 of appliance 710 selectively seals second opening 715.

Referring now the progression of schematics 1 through 5, schematic 1 shows sealing element 719 sealing the second opening 715. Aspiration source 708 is turned on, establishing a vacuum pressure in conduit 712 which is in fluid communication with chamber 714 up to plunger 718. The resulting suction force exerted on plunger 718 acts in a direction opposite that of the biasing force of biasing mechanism 721. The biasing mechanism 721 exerts an upward force on plunger 718 and a vacuum pressure in conduit 712 and a bottom portion of chamber 714 exerts a downward force on plunger 718. The suction force overcomes the biasing force and pulls the plunger 718 downward toward second opening 715. Schematic 2 of Figure 7 shows an intermediate stage in which the seal on second opening 715 is still intact and the plunger 718 is still being drawn downward by the vacuum pressure overcoming the biasing force of biasing mechanism 721. At schematic 3, plunger 718 releases sealing mechanism 719, opening the second opening 715 to a fluid of a second pressure (e.g. ambient air). In effect, the vacuum is broken. Fluid of a second pressure is drawn into chamber 714, reducing the aspiration pressure in

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conduit 712 and thus in the catheter in fluid communication therewith. The drop in vacuum pressure in a bottom portion of chamber 714 results in a decreased suction force acting on plunger 718. The biasing mechanism 721 is no longer overcome, and the biasing force drives the plunger 718 back toward opening 716, away from second opening 715 as shown in schematic 4.

5 As the plunger 718 returns to its starting position, it causes sealing mechanism 719 to re-establish a seal on second opening 715. This returns the aspiration system 700 to its starting conditions, at which point the cycle repeats. The aspiration profile of the system fluctuates dynamically according to the repetitive opening and sealing of second opening 715 and admission of a second fluid of a lesser pressure through the second opening and into the system.

10 Referring now to Figure 8A, an aspiration system 800 is shown which allows dynamic variation of the suction force at a distal end of a catheter 806. As shown, the distal end of the catheter is placed adjacent to and therefore blocked by occlusion 802. Arranged between the catheter 806 and aspiration source 808 is an appliance 810 for aspiration control. Generally, appliance 810 includes a first conduit 812, a second conduit 813, a chamber 814, and a valve
15 817. First conduit 812 has an end 812a which is connectable to be in fluid communication with a catheter 806. Similarly, second conduit 813 has an end 813b which is connectable to be in fluid communication with aspiration source 808. Chamber 814 is connected to and in fluid communication with both the end 812a of conduit 812 and the end 813b of conduit 813. In some embodiments, conduits 812 and 813 may simply be input and output terminals of the chamber
20 814. Valve 817 is arranged in chamber 814 with conduits 812 and 813 on opposite sides of the valve. In effect, the total volume of chamber 814 may be defined according to a division into two smaller volumes. A first volume of space 814' exists between the end 812a of the first conduit 812 and the valve 817. A second volume of space 814'' exists between the end 813b of the second conduit 813 and the opposite side of valve 817. Although aspiration system 800 shows a
25 configuration in which conduits 812 and 813 are arranged on opposite sides of chamber 814 such that valve 817 is arranged in between the conduits, this is but one example of how the chamber 814 may be divided into at least two volumes of space 814' and 814''.

Valve 817 is selectively operable to reduce or prevent fluid communication between the first conduit 812 and the second conduit 813. Furthermore, the valve 817 is displaceable such
30 that the volume 814' and the volume 814'' may be selectively varied. In cases where force distributions are such that valve 817 remains substantially unmoved during an aspiration force

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oscillation, valve 817 may nevertheless be urged in either of at least two directions, one opposite the other, such that volumes 814' and 814'' are variably subjected to compressive or tensile forces. The effect of these functionalities will now be explained with respect to the five schematics labeled 1 through 5 in Figure 8A, where each numbered schematic represents aspiration system 800 at a different stage of operation. It should be understood that some
5 numeric labels are not repeated for each schematic to avoid cluttering the drawings, but structures which appear substantially identical between schematics should be regarded as the same structures.

The operation of aspiration system 800 of Figure 8A will be explained in connection with
10 the process 900 of Figure 9A. At step 901 and with reference to schematic 1 of Figure 8A, the aspiration source 808 (e.g. a vacuum pump) is turned on. As previously discussed, aspiration system 800 is configured such that fluid communication is provided from the aspiration source 808 through appliance 810 to catheter 806 such that a suction force at the distal end of catheter 806 is supplied to occlusion 802. With the aspiration source 808 turned on and the distal end of
15 catheter 806 occluded by the occluding element of occlusion 802, the pressure inside the tubing, chamber 814, and catheter 806 is reduced to a base operating pressure (e.g. -24 inHg). As the system pumps down (and thus the negative pressure increases), valve 817 allow open communication between volume 814' and 814'' and, correspondingly, catheter 806 and pump 808. With valve 817 open, the enclosed spaces of the entire aspiration system 800 are able to
20 achieve an equilibrium pressure.

At step 902 and with reference to schematic 2 of Figure 8A, a pressure oscillation is initiated. Valve 817, which is displaceable within chamber 814 relative to ends 812a and 813b, may be actively displaced in one or more directions by an actuator 830 such that the volume 814' between the first end 812a and the valve 817 may be increased or decreased. By way of example,
25 aspiration system 800 allows a linear displacement of valve 817 which, according to the embodiment illustrated in Figure 8A, is to the left and to the right. In this case, actuator 830 comprises an electromagnet and valve 817 is fixedly coupled to magnets 832. Actuator 830 may be energized according to two different polarities. In a first polarity, the electromagnet of actuator 830 repulses the one or more magnets 832 and thus urges or drives valve 817 toward
30 end 812a. Urging of valve 817 toward end 812a supplies a compressive force on volume 814' and a tensile force on volume 814''. A displacement of valve 817 toward end 812a may provide a

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minimum value to volume 814' and a maximum value to volume 814''. At step 902, the electromagnetic is switched (from a first polarity or an off state) to a second polarity, whereby magnets 832 are attracted to the electromagnetic coils of actuator 830. That is to say, actuator 830 urges valve 817 away from end 812a and toward end 813b, as indicated by arrow 833.

5 Displacement of valve 817 in the direction 833 (that is, to the right as illustrated), may cause valve 817 to passively close. Alternatively, the valve 817 may be actively closed. Valve 817 closes prior to the completion of displacement in direction 833 such that volume 814' and the volume of the lumen of catheter 806 together form a closed system. Urging of valve 817 in direction 833 (which may or may not be accompanied by displacement in the same direction and
10 an increasing value of volume 814') causes an increase in negative pressure (i.e. an increase in the magnitude of the vacuum pressure) in catheter 806. For example, the negative pressure may increase from an equilibrium pressure of -24 inHg to -28 inHg. Generally, the aspiration source 808 maintains the pressure on the pump side of valve 817, that is the pressure in volume 814'', at the base operating pressure (e.g. -24 inHg).

15 Schematic 3 of Figure 8A is a continuation of schematic 2 and illustrates the increasing value of volume 814' as the valve 817 is urged and displaced in direction 833. The vacuum pressure (VP) dial 836 illustrates the increasing negative pressure in response to the increasing value of volume 814'. Vacuum pressure may increase up to a peak negative pressure (e.g. -30 in Hg).

20 At step 903 of Figure 9A and with reference to schematic 4 of Figure 8A, pressure in volume 814' and catheter 806 may be returned back to the baseline pressure. As illustrated, actuator 830 is de-energized such that it does not act on valve 817 to urge it in direction 833. This allows the valve 817 to passively return to its original starting position according to a displacement in the direction of arrow 838. A force providing such displacement in direction 838
25 derives from the proportionally greater vacuum pressure of volume 814' as compared to the vacuum pressure of volume 814''. Alternatively, actuator 830 may be energized according to its first polarity which repels magnets 832. In this manner, actuator 830 urges valve 817 toward end 812a (in direction 838). Thus valve 817 may be actively displaced in direction 838 by the electromagnetic force of actuator 830. In a fully static situation, e.g. there is no blood flow
30 around the occlusion 802, valve 817 may only open once it returned to its starting position. So

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long as a higher vacuum pressure exists for volume 814' as compared to volume 814'', the valve 817 may stay pulled closed.

As was previously indicated, valve 817 may be actively opened and closed independent of the displacement of valve 817 within chamber 814. In some embodiments, the valve may be
5 selectively maintained in an open state or in a closed state despite a movement of valve 817 in direction 833 or 838 and irrespective of the valve's position relative ends 812a and 813b.

Schematic 5 of Figure 8A shows the aspiration system 800 back in its starting configuration. Process 900 or a similar process according to the teachings herein may be repeated with a selected frequency, resulting in a cyclic oscillation of the one or more forces
10 acting on valve 817 in directions 832 and/or 838. This may in turn supply physical oscillation of the valve 817 in directions 832 and 838 in reaction to such forces. A starting position or a maximum displacement position of valve 817 to either end of chamber 814 may be varied. Valve 817 may be actively (e.g. manually) opened to allow movement of the valve and adjust the values of volumes 814' and 814''.

Figure 9B shows a dynamic aspiration method 950 which is also usable with the aspiration system 800, for example. At step 951, a distal end of a catheter 806 is positioned adjacent an occlusion 802. At step 952, a suction force is exerted at the distal end of the catheter
15 802 with a source of suction 808 in fluid communication with a proximal end of the catheter 806. At step 953, the suction force is dynamically varied with an appliance/device 810 in fluid communication with the catheter 806 and the source of suction 808. The dynamic variance of the suction force may be provided by variably urging a displacement of a valve 817 in the appliance 810 such that a volume 814' between the distal end of the catheter and the valve 817 is selectively variable. Steps 952 and 953 may at times be performed individually or performed
20 simultaneously.

An actuator 830 may comprise one or more electromagnets. In the aspiration system 800 of Figure 8A, actuator 830 includes an electromagnetic coil positioned at a proximal end of chamber 814 adjacent conduit 813. Displacement of valve 817 toward the actuator 830 corresponds with increased vacuum pressure in volume 814' and catheter 806. Figure 8B shows an alternative embodiment in which an electromagnetic-based actuator 850 has an
25 electromagnetic coil arranged at a distal end of chamber 814 adjacent conduit 812. By this arrangement, displacement of valve 817' away from the actuator 850 corresponds with increased
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vacuum pressure in volume 814' and catheter 806. In other words, actuator 850 may provide for a negative pressure pulse by actuating valve 817' such that magnets 832 (and thereby valve 817) is repelled away from the actuator 850. In the example embodiment of Figure 8A, a negative pressure pulse in catheter 806 is created by actuating valve 817 such that magnets 832 and valve
5 817 are attracted toward the actuator 830.

Figure 8C shows an alternative embodiment in which an actuator 860 comprises a first electromagnetic coil 830a and a second electromagnetic coil 850a. The aforementioned operation and details of actuator 830 (Figure 8A) are also applicable to electromagnetic coil 830a. The aforementioned operation and details of actuator 850 (Figure 8B) are also applicable to
10 electromagnetic coil 850a. Actuation of valve 817" can be performed by any one or both of electromagnetic coils 830a and 850a providing individual repulsive and/or attractive forces or paired repulsive and/or attracted forces. Electromagnetic forces exerted by coils 830a and 850a on magnets 832 is inversely proportional to the square of the distance between a coil and the magnet. It will be clear to those of skill in the art that the actuators of embodiments of Figures
15 8A-8C or other embodiments according to the invention may be configured according to the desired electromagnetic force and pressure characteristics. As an example, it may be desirable to ramp a vacuum pressure oscillation as quickly as possible at the start of the oscillation. In this case, arranging the electromagnetic coil and the magnets adjacent one another for the start of a pressure oscillation (such as is provided by actuator 850 in Figure 8B and electromagnetic coil
20 850a in Figure 8C) provides a maximum electromagnetic force at the start of a pressure oscillation.

In some embodiments, an actuator 830, 850, or 860 may take a form other than an electromagnet. For example, the actuator may be a pneumatic or mechanical actuator. These are but some example mechanisms for actuating a valve 817, 817', or 817" to urge it one or more
25 directions in chamber 814 and, in some embodiments, cause its displacement. In some embodiments, valve 817 may be a customized valve or, alternatively, a commercially available valve allowing pressure to either side of the valve to be alternated manually, such as by an actuator 830. Suitable commercially available valves may include but are not limited to motor actuated valves and solenoid valves provided by companies like Sizto Tech Corporation (Palo
30 Alto, California, USA). Other suitable valves and actuation mechanisms will occur to skilled persons in the art in view of the teachings herein.

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For embodiments including those discussed for illustrative purposes herein, the appliance or device providing dynamic aspiration may be located at a distance from a patient on which a medical procedure is being performed. Thus, sterilization requirements may be less rigorous and therefore less expensive than required for a catheter, for example. Alternatively, for some
5 embodiments, regulatory appliances, devices, or actuating mechanisms such as those examples detailed in Figures 2A-2C, 4A-4B, 5, 6, 7, and 8A-8C may be arranged in the catheter such that it operates closer to the target occlusion.

With continued reference to Figures 8A-8C, a valve 817, 817', or 817'' may include a flexible surface to which is attached a stretch sensor 840 for detecting a deflection of the flexible
10 surface. Stretch sensor 840 may be, for example, a piezoelectric strip or film. Deflection readings of a sensor 840 are usable for such purposes as determining catheter placement and the material properties of the aspiration target (e.g. a thrombus or clot). As the device is cycled an output waveform from the sensor 840 may indicate if the catheter 806 is occluded (e.g. by occlusion 802). As valve 817 moves in direction 833 (i.e. to the right as illustrated in Figure 8A), negative
15 pressure develops in catheter 806 more significantly if the catheter 806 is occluded. A greater pressure differential of volume 814' as compared to volume 814'' increases deflection of the flexible surface of valve 817. Furthermore, the material properties of occlusion 802 may also influence the surface deflection and thus be detected by sensor 840. A rigid occlusion material may produce a sharper pressure-development curve as compared to a soft occlusive material
20 which may deform under loading and thus decrease the realized pressure.

Dynamic aspiration may be performed in conjunction with continuous aspiration or as a stand-alone treatment. Generally, maintaining a vacuum throughout the procedure minimizes a risk of distal migration of thrombi. As with current static aspiration techniques, cyclic aspiration may be paired successfully with supplemental treatment methods such as the use of a separator
25 wire.

It is noted that the teachings herein may be effective for any occlusion, including both total and partial occlusions. Occlusions are possible anywhere in the circulatory system, acute ischemic stroke and deep vein thrombosis being two of many examples. Figure 10 shows a method 1000 for performing an embolectomy. At step 1001, the distal end of a catheter is
30 positioned adjacent an embolus. At step 1002, a negative pressure is provided in the catheter with an aspiration source. At step 1003, the negative pressure is repetitively changed with an

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appliance to produce a dynamic suction force at the distal end of the catheter. At step 1004, at least a part of the embolus and preferably an entirety of the embolus is removed with the catheter. The dynamic suction force provides a repetitive loading to induce material fatigue in the embolus, as discussed above.

5 Referring now to Figures 11A-11D, a variety of catheters may be used for various aspiration systems according to the invention. In some exemplary embodiments, ordinary or conventional catheters such as uni-luminal catheter 1106 of Figure 11A may be employed. Alternatively, Figures 11B and 11C shows a catheter 1106' which may be used with any
10 embodiments such as those shown in Figures 2A-2C, 4A-4B, 5, 6, 7, and 8A-8C as well as other exemplary embodiments. Catheter 1106' comprises two coaxial tubes 1106a and 1106b, the former being of a smaller diameter and arranged inside the latter. The primary "dynamic aspiration" tube 1106a is arranged inside a secondary "stabilizing aspiration" tube 1106b. The arrangement of the secondary "stabilization aspiration" catheter 1106b over/around the primary "dynamic aspiration" catheter 1106a helps stabilize the clot 1102 against the catheter 1106' so
15 that the full suction force delivered via the primary tube 1106a acts on the clot 1102. Generally, both tubes 1106a and 1106b may be operated with negative pressure. The principles of dynamic aspiration may be applied to either primary tube 1106a or secondary tube 1106b, or to both. For example, dynamic aspiration through the secondary (outer) tube 1106b may be more effective at disrupting the bonds between the clot 1102 and the vessel wall as compared to a fully-engaged
20 catheter. Utilizing any combination of dynamic and static aspiration with the primary and secondary tubes, along with variable magnitudes of pressure, may be utilized according to alternative exemplary embodiments of the invention.

Figure 11D shows yet another alternative exemplary embodiment for a catheter usable with any embodiment of the invention as taught herein. Catheter 1106'' is similar to catheter
25 1106' and comprises a primary tube 1106a and a secondary tube 1106b. In this case, a terminal end to primary tube 1106a is axially displaced with respect to a terminal end of secondary tube 1106b. More specifically, primary tube 1106a extends beyond a terminal portion of secondary tube 1106b such that a terminal portion of primary tube 1106a is not surrounded or enclosed by the wall of the secondary tube 1106b. Alternatively, secondary tube 1106b may extend beyond a
30 terminal portion of primary tube 1106a such that a terminal portion of secondary tube 1106b

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does not surround or enclose primary tube 1106a. In short, either the primary tube or secondary tube may be axially recessed with respect to the other.

It should be noted that the term “tube”, such as used with respect to elements 1106a and 1106b, may be used interchangeably with the term “catheter”, “tubule”, or the like.

5

Example 1

An example embodiment corresponding with aspiration system 200 of Figure 2A was tested by placing a three-way valve (Harvard Apparatus, Holliston, Massachusetts, USA) between a vacuum source (Penumbra aspiration pump, Penumbra, Alameda, California, USA) and the catheter (Penumbra 5Max reperfusion catheter) to establish open continuity between the vacuum source, the catheter tip, and air (the aspiration medium) when the valve was opened. Temporarily closing the valve to air (e.g., with a finger) allowed the pump to establish a vacuum at the catheter tip. Subsequently removing the finger reopened the system to air and rapidly diminished the vacuum at the catheter tip. Impact aspiration is performed by repeatedly opening and closing the valve to air so that cyclic pressure profiles are developed at the catheter tip. For tests in which water was used as the aspiration medium, the three-way valve was submerged in water. Care was taken to ensure that the system was primed with the aspiration medium before experimentation.

Synthetic polyurethane clots (Concentric Medical, Mountain View, California, USA) were extruded with a cylindrical template cut to a specific clot size using Traceable Digital Calipers (Control Company, Friendswood, Texas, USA). They were then placed in a flow model consisting of a Penumbra SMax reperfusion catheter (1.37 mm tip internal diameter) inside rigid plastic tubing (2.5 mm internal diameter, 4 mm outside diameter) submerged in water. The clots were positioned directly adjacent to the catheter tip and exposed to either suction alone (Penumbra aspiration pump) or cyclic aspiration via the aspiration system 200 shown in Figure 2A. The test was performed until either the clot was removed or 5 minutes had elapsed. If the clot was not completely cleared within 5 min (the standard dwell time of current stent retrievers), the trial was considered unsuccessful. Although not employed in this particular example, what is referred to as the ADAPT technique may be used in accordance with the invention. Per the ADAPT technique, the aspiration catheter is withdrawn after partial engagement of the occlusive element.

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Pressure profiles were generated by placing an Equus 3620 Innova Vacuum Gauge (Equus Products, Irvine, California, USA) distal to the three-way valve during experimentation. Using reduced speed playback of the vacuum gauge fluctuations, recordings were made of the pressures generated during static aspiration and 15 cycles of impact aspiration at frequencies of 1 and 2 Hz, as well as a third group labeled 'Max Hz' where the experimenter cycled the system as fast as possible. The 'Max Hz' category was necessary to capture impact aspiration performance at higher frequencies while acknowledging that accurately reproducing frequencies above 2 Hz is not possible with a manual opening and closing of opening 216. The actual frequency for the 'Max Hz' trials was determined by dividing the number of cycles by the time elapsed.

Statistical analyses were made based on a one-way (static loading vs cyclic loading and UC impact aspiration clot clearance trials) or two-way analysis of variance (all other analyses), Holm-Sidak pairwise multiple comparison procedure ($\alpha = 0.05$).

Example pressure cycle dynamics are provided in Figures 3A-3C. The Penumbra pump acting alone provided an adequate pump-down time, rapidly creating and maintaining a baseline vacuum pressure shown in the Figures by the dotted curve. Both down-cycling (DC) and up-cycling (UC) cyclic aspiration are shown in Figure 3A and 3B.

The Penumbra pump alone—that is without an appliance 210—creates a rapidly developing static pressure curve that reaches a peak value of -24.5 inHg. Cyclic aspiration provided by appliance 210 creates a dynamic pressure curve where the pressure cycles between a maximum and minimum value at a specific frequency (maximum and minimum relating to the magnitude of pressure). Impact aspiration cycles between -23.8 (SD 0.09) inHg and 0 (SD 0) inHg at 1 Hz, between -22.0 (SD 0.11) inHg and 0 (SD 0) inHg at 2 Hz and between -18.9 (SD 0.8) inHg and -5.0 (SD 2.42) inHg at Max Hz (approximately 6.3 Hz). These values are represented in Figures 3A-3C. The relationship between frequency and pressure differential for the three impact aspiration values is remarkably linear with linear curve-fitting yielding an equation of $y = 47.654x - 653.4$ with an r^2 value of 1.

To provide just one illustrative example, a thrombectomy model was created in which static suction alone would be insufficient treatment. A synthetic clot diameter was increased until a static suction Penumbra system was unable to clear the clot from the model.

A comparison was made between a static loading method and cyclic loading method. Aspiration with the Penumbra pump alone failed to clear a single clot ($n=10$) whereas the

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combined clearance rate of impact aspiration was 91.43% (64 cleared, n=70). Impact aspiration was significantly better at clearing clots from the flow model than static aspiration with the Penumbra pump alone ($p<0.001$) despite cyclic loading delivering less total force to the clot than static loading. The discrepancy between total force delivered and experimental outcome indicates
5 that the dynamics of loading play a significant role in the success of the procedure.

Different cyclic frequencies were also evaluated. Impact aspiration had successful clearance rates of 84% (1 Hz, n=25), 100% (2 Hz, n=25) and 90% (Max Hz, n=20) and clearance times of 35.1 (SD 22.8) seconds (1 Hz, n=21), 40.7 (SD 55.4) seconds (2 Hz, n=25), and 7.8 (SD 6.8) seconds (Max Hz, n=18). Aspirating at Max Hz was significantly faster at clearing clots than
10 at 1 Hz ($p<0.001$) or 2 Hz ($p=0.024$). While Max Hz cycling was not 100% successful in this example (noting that all clearance failures occurred with air as the aspirating medium), the downward trend in clot clearance time shown in Figure 3D is a good indicator that increasing frequency is the correct path to more effective treatments. In this example, 6.3 Hz (Max Hz) was the only frequency that maintained uninterrupted net aspiration pressure as both 1 Hz and 2 Hz
15 had minimum pressures of 0 inHg. In many embodiments, a non-zero negative pressure is maintained in the catheter for the duration of an aspiration procedure.

When air was used as the aspirating medium, impact aspiration had an overall clearance rate of 85% (n=40) and an average clearance time of 34.7 (SD 49.3) seconds (n=34). When water was used as the aspirating medium, impact aspiration had an overall clearance rate of 100%
20 (n=30) and an average clearance time of 23.8 (SD 22.7) seconds (n=30). Impact aspiration using water as the aspirating medium was more effective at clearing clots than when air was used as the aspirating medium ($p=0.019$). There were no significant differences between the two aspirating mediums in clearance time. It is likely that the pressure reaches maximum and minimum more quickly with water, providing more total time at maximum pressure, more abrupt
25 pressure perturbations, and steeper pressure development slopes in the ramping phases.

Using DC pressure profiles in impact aspiration resulted in a clearance rate of 60% (n=10) and an average clearance time of 80.7 (SD 94.8) seconds (n=6). Using UC pressure profiles resulted in a clearance rate of 96.67% (n=60) and an average clearance time of 24.3 (SD 24.8) seconds (n=58). Compared with DC, UC pressure profiles were more effective in the
30 general ability to clear clots from the flow model ($p<0.001$) and faster at clearing the clots from the flow model ($p<0.001$). The more efficacious UC method differs from DC impact aspiration

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in that its pressure dynamics are characterized by two rapid perturbations (pressure on and off) with virtually no static loading between them. DC impact aspiration, on the other hand, has a relatively long static loading period between its two perturbations. In this example it appeared that a prolonged static force may decrease the efficacy of the technique.

5 In some embodiments such as those shown in Figures 2A and 8A, the catheter requires only a single port, although additional ports may optionally be used. A single port catheter provides an exhaust lumen independent of additional lumens (e.g. a lumen for supplying positive pressure infusion fluid). A suction force of the catheter/exhaust lumen extends into the vessel in a direction parallel with the distal end of the catheter and the center longitudinal axis of the
10 surrounding vessel walls. This minimizes suction applied to the walls, which can damage or collapse the vessel. In contrast, U.S. Patent App. Pub. No. 2013/0267891 provides a fluid jet parallel with an exhaust lumen of a multi-port catheter, where the fluid jet causes a suction force which is not parallel with a longitudinal axis of the exhaust lumen and the surrounding vessel walls. For example, according to Figure 5 of the publication, a passive suction force caused by
15 the fluid jet is perpendicular to the catheter tip and thus perpendicular to a wall of the vessel in which the catheter is used. Such a configuration may also require rotation of the catheter and penetration of a clot with the catheter for removal thereof. In contrast, embodiments of the present invention may be used without a need to rotate a catheter and without penetration of a thrombus with the catheter. Full engagement of a thrombus may immediately be achieved
20 without penetration of the thrombus.

As shown in exemplary embodiments herein, an appliance (e.g. appliance 210 of Figure 2A or appliance 810 of Figure 8A) is separate but attachable to a source of suction (e.g. aspiration source 208 of Figure 2A or aspiration source 808 of Figure 8A). In some alternative embodiments, an appliance and aspiration source may be integral. An aspiration source may be
25 provided for a dynamic aspiration system where the aspiration source includes an appliance or suction regulatory device which dynamically varies the suction force supplied by the aspiration source to a catheter in fluid communication therewith.

Generally, a fluid communication pathway from the distal end of a catheter to a suction source defines a suction line. A negative pressure is provided in a suction line. In the example
30 embodiments herein, for example aspiration system 200 of Figure 2A or aspiration system 800 of

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Figure 8A, an appliance/device for providing dynamic aspiration is arranged along the suction line.

Although certain features and elements of the invention have been described in relation to particular illustrative embodiments, it should be understood that all features and elements
5 disclosed are not limited to the embodiments shown and described. These serve only as illustrative examples, and features and elements of one embodiment may generally be used with some other embodiment, as will be evident to those of skill in the art.

While some embodiments of the present invention have been disclosed herein, one skilled in the art will recognize that various changes and modifications may be made without
10 departing from the scope of the invention as defined by the following claims.

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CLAIMS

What is claimed is:

1. An appliance for aspiration control, comprising:

a conduit having

a first end connectable to be in fluid communication with a catheter, and

a second end connectable to be in fluid communication with a source of suction

such that fluid of a first pressure from said source of suction extends through said appliance from second end to said first end; and

a chamber connected to said conduit between said first end and said second end and in fluid communication with said conduit, said chamber having an opening which is variably

opened or closed, or

enlarged or narrowed,

wherein said opening permits fluid of a second pressure which is different from said fluid of said first pressure to be mixed with said fluid of said first pressure.

2. The appliance of claim 1, wherein said fluid of a second pressure is ambient air, water, or saline.

3. The appliance of claim 1, wherein said first pressure of said first fluid is more negative than said second pressure of said second fluid.

4. An appliance for aspiration control, comprising:

a first conduit having a first end connectable to be in fluid communication with a catheter;

a second conduit having a second end connectable to be in fluid communication with a source of suction such that fluid of a first pressure from said source of suction extends through said appliance between said second end and said first end;

a chamber in fluid communication with and connected to said first conduit and said second conduit; and

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a valve arranged in said chamber which is selectively operable to reduce or prevent fluid communication between said first conduit and said second conduit and urgeable in at least one direction such that a volume of said chamber or force conditions between said first end of said first conduit and said valve is selectively variable.

5. The appliance of claim 4, further comprising a stretch sensor attached to a flexible surface of said valve, said stretch sensor detecting deflections of said flexible surface.

6. The appliance of claim 4, further comprising an actuator which actively urges said valve in one or more directions in said chamber such that a fluid in said volume of said chamber between said first conduit and said valve is subjected to a pressurizing or pressure-relieving force.

7. The appliance of claim 6, wherein said actuator includes at least one electromagnet that attracts or repels said valve in said chamber when energized.

8. The appliance of claim 4, wherein said valve is operable between an open state and a closed state.

9. A method of aspiration, comprising the steps of:

- positioning a distal end of a catheter adjacent an occlusion;
- exerting a suction force at said distal end of said catheter with a source of suction in fluid communication with a proximal end of said catheter; and
- dynamically varying said suction force with a device in fluid communication with said catheter and said source of suction by variably opening said device.

10. The method of claim 9, further comprising the step of supplying a plurality of pressure-relieving pulses to aspirated fluid of said catheter, said pressure-relieving pulses controlling a frequency of an aspiration profile of said suction force.

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11. The method of claim 9, further comprising the step of supplying a plurality of pressuring pulses to aspired fluid of said catheter, said negatively pressuring pulses controlling a frequency of an aspiration profile of said suction force.

12. The method of claim 9, wherein said dynamically varying step induces a cyclic aspiration profile with a frequency of at least 1 Hz.

13. The method of claim 9, wherein said dynamically varying step induces a cyclic aspiration profile with a frequency of at least 50 Hz.

14. The method of claim 9, wherein said dynamically varying step induces a stochastic aspiration profile for said suction force.

15. A method of aspiration, comprising the steps of:

- positioning a distal end of a catheter adjacent an occlusion;
- exerting a suction force at said distal end of said catheter with a source of suction in fluid communication with a proximal end of said catheter; and
- dynamically varying said suction force with a device in fluid communication with said catheter and said source of suction by variably urging a valve in said device in at least one direction such that a volume or force conditions between said distal end of said catheter and said valve is selectively variable.

16. The method of claim 15, wherein said changing step supplies a plurality of pressure-relieving pulses to aspired fluid of said catheter, said pressure-relieving pulses controlling a frequency of an aspiration profile of said dynamic suction force.

17. The method of claim 15, wherein said changing step supplies a plurality of negatively pressuring pulses to aspired fluid of said catheter, said negatively pressuring pulses controlling a frequency of an aspiration profile of said dynamic suction force.

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18. The method of claim 15, wherein said changing step induces a cyclic aspiration profile with a frequency of at least 1 Hz.

19. The method of claim 15, wherein said changing step induces a cyclic aspiration profile with a frequency of at least 50 Hz.

20. A method of performing an embolectomy, comprising the steps of:

- positioning a distal end of a catheter adjacent an embolus;
- providing a negative pressure in said catheter with an aspiration source;
- changing said negative pressure repetitively with an appliance to produce a dynamic suction force at said distal end of said catheter; and
- removing at least part of said embolus by aspiration with said catheter,

whereby said dynamic suction force provides variable loading to induce material fatigue in said embolus.

21. The method of claim 20, wherein said changing step supplies a plurality of pressure-relieving pulses to aspirated fluid of said catheter, said pressure-relieving pulses controlling a frequency of an aspiration profile of said dynamic suction force.

22. The method of claim 20, wherein said changing step supplies a plurality of negatively pressuring pulses to aspirated fluid of said catheter, said negatively pressuring pulses controlling a frequency of an aspiration profile of said dynamic suction force.

23. The method of claim 20, wherein said changing step induces a cyclic aspiration profile with a frequency of at least 1 Hz.

24. The method of claim 20, wherein said changing step induces a cyclic aspiration profile with a frequency of at least 50 Hz.

25. The method of claim 20, wherein said changing step induces a stochastic aspiration profile for said dynamic suction force.

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26. The method of claim 20, wherein said changing step is performed along a suction line between said catheter and said aspiration source.

27. An aspiration system, comprising:

- a catheter insertable into a body;
- an aspiration source providing a negative pressure in said catheter; and
- a device which repetitively changes said negative pressure to produce a dynamic suction force at a distal end of said catheter.

28. The aspiration system of claim 27, wherein said device supplies a plurality of pressure-relieving pulses to aspirated fluid of said catheter, said pressure-relieving pulses controlling a frequency of an aspiration profile of said dynamic suction force.

29. The aspiration system of claim 27, wherein said device supplies a plurality of negatively pressuring pulses to aspirated fluid of said catheter, said negatively pressuring pulses controlling a frequency of an aspiration profile of said dynamic suction force.

30. The aspiration system of claim 27, wherein said device induces a cyclic aspiration profile with a frequency of at least 1 Hz.

31. The aspiration system of claim 27, wherein said device induces a cyclic aspiration profile with a frequency of at least 50 Hz.

32. The aspiration system of claim 27, wherein said device induces a stochastic aspiration profile for said dynamic suction force.

33. The aspiration system of claim 27, further comprising a suction line connecting said catheter and said aspiration source, wherein said appliance is arranged along said suction line.

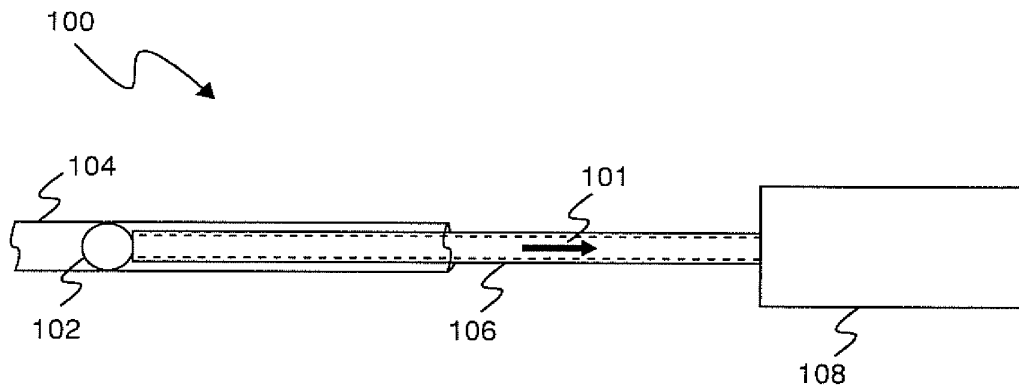


FIGURE 1A

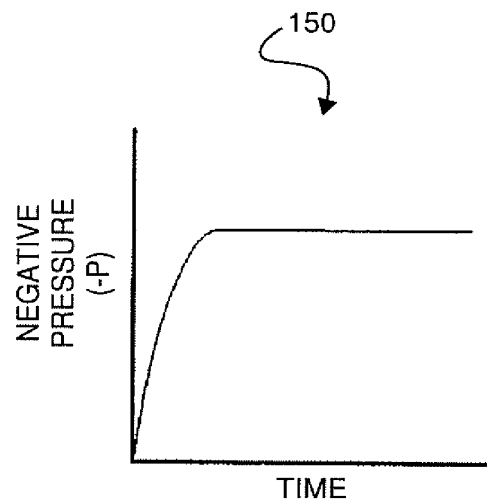


FIGURE 1B

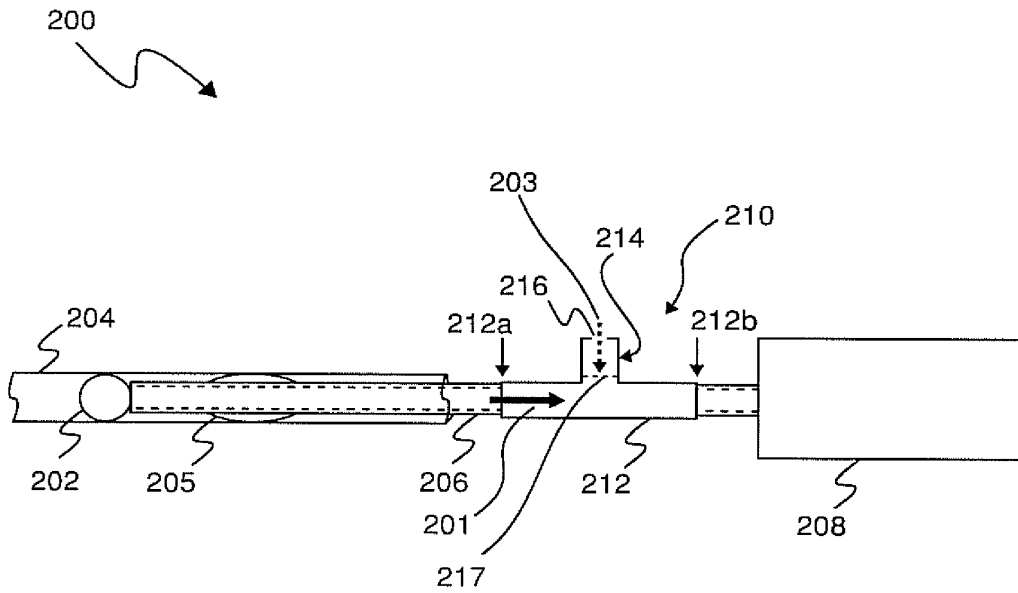


FIGURE 2A

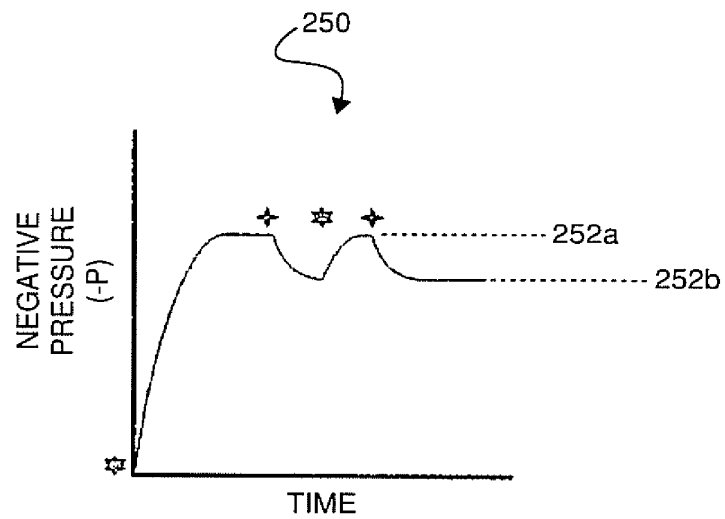


FIGURE 2B

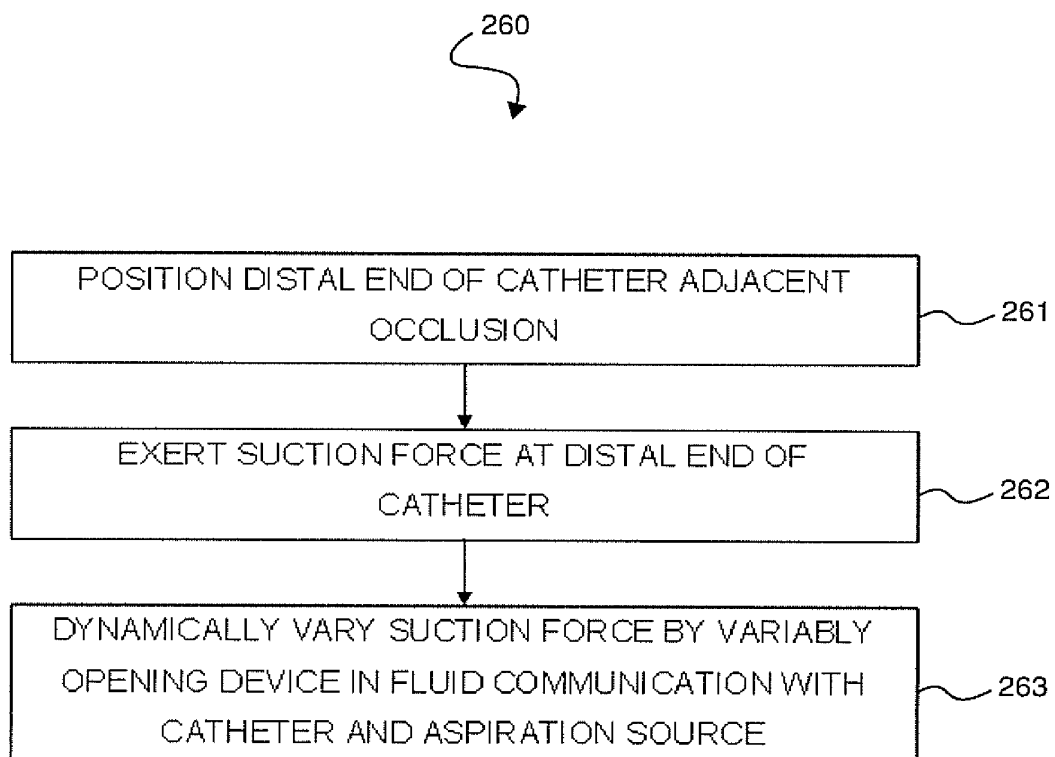


FIGURE 2C

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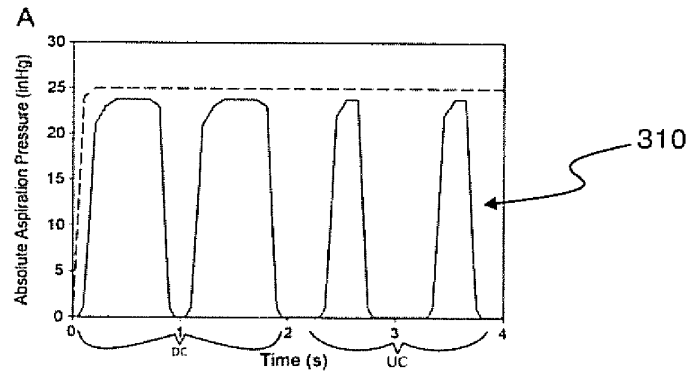


FIGURE 3A

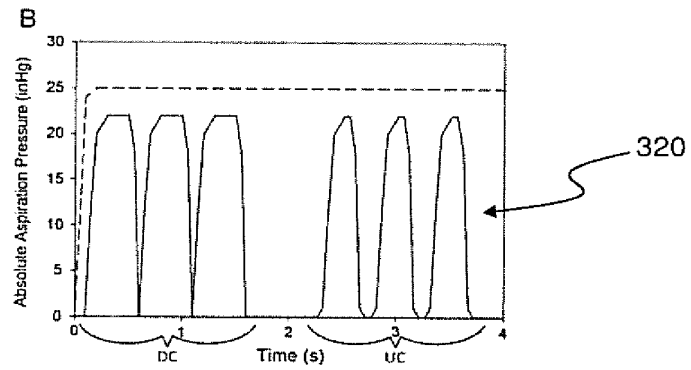


FIGURE 3B

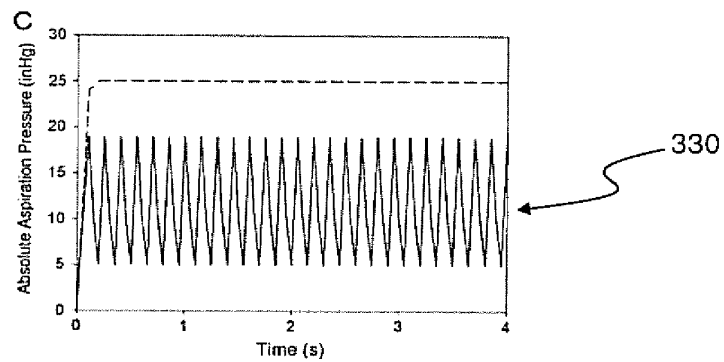


FIGURE 3C

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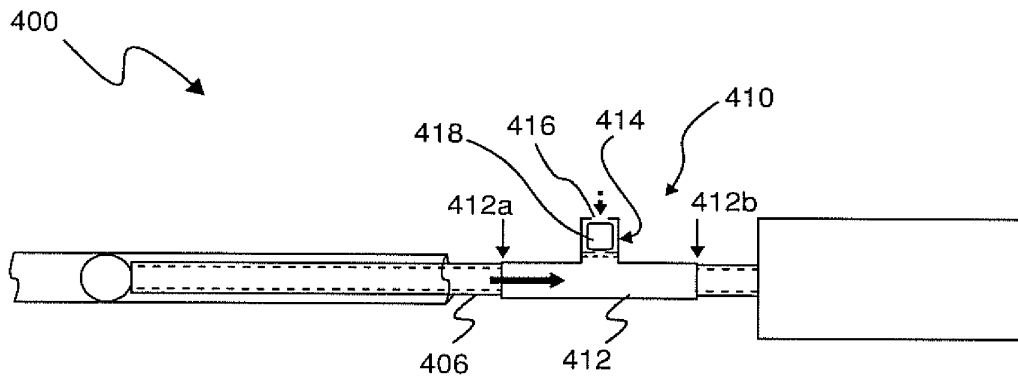


FIGURE 4A

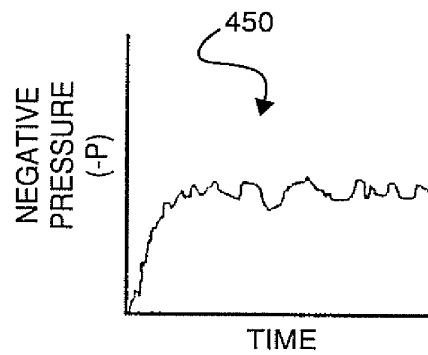


FIGURE 4B

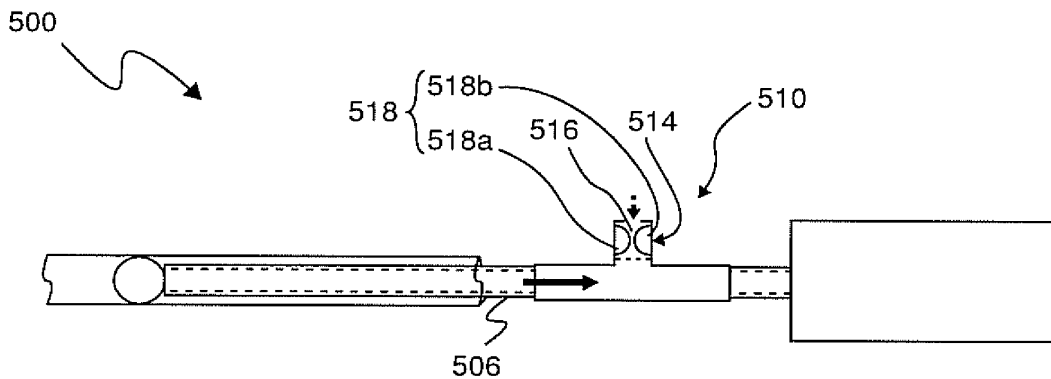


FIGURE 5

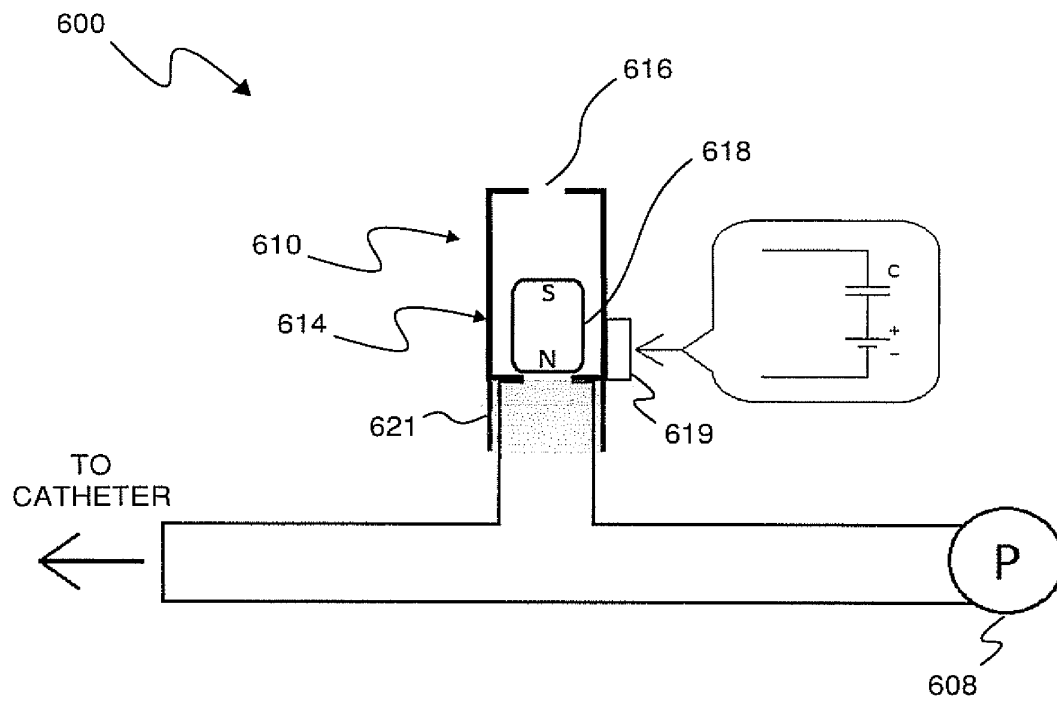


FIGURE 6

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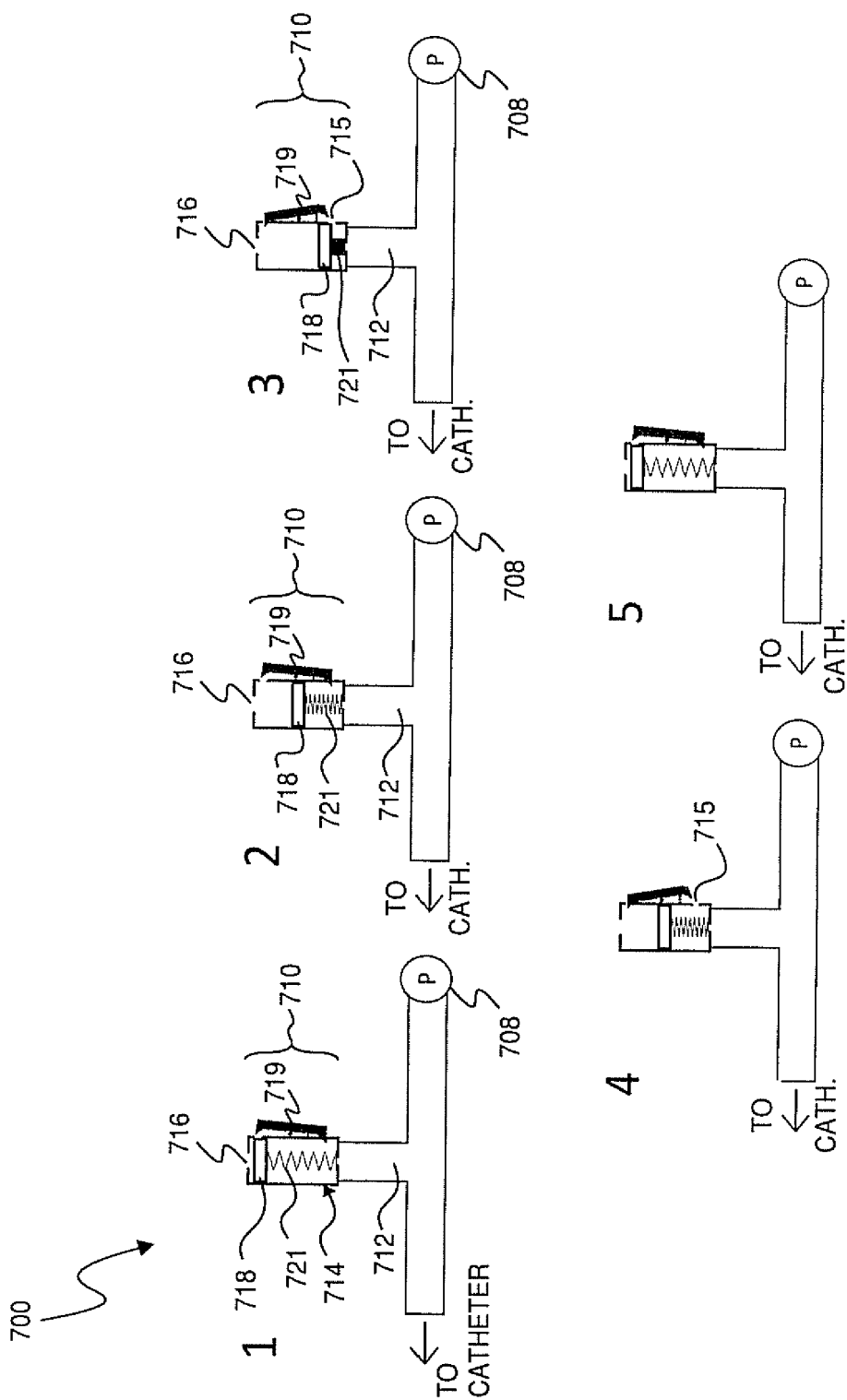


FIGURE 7

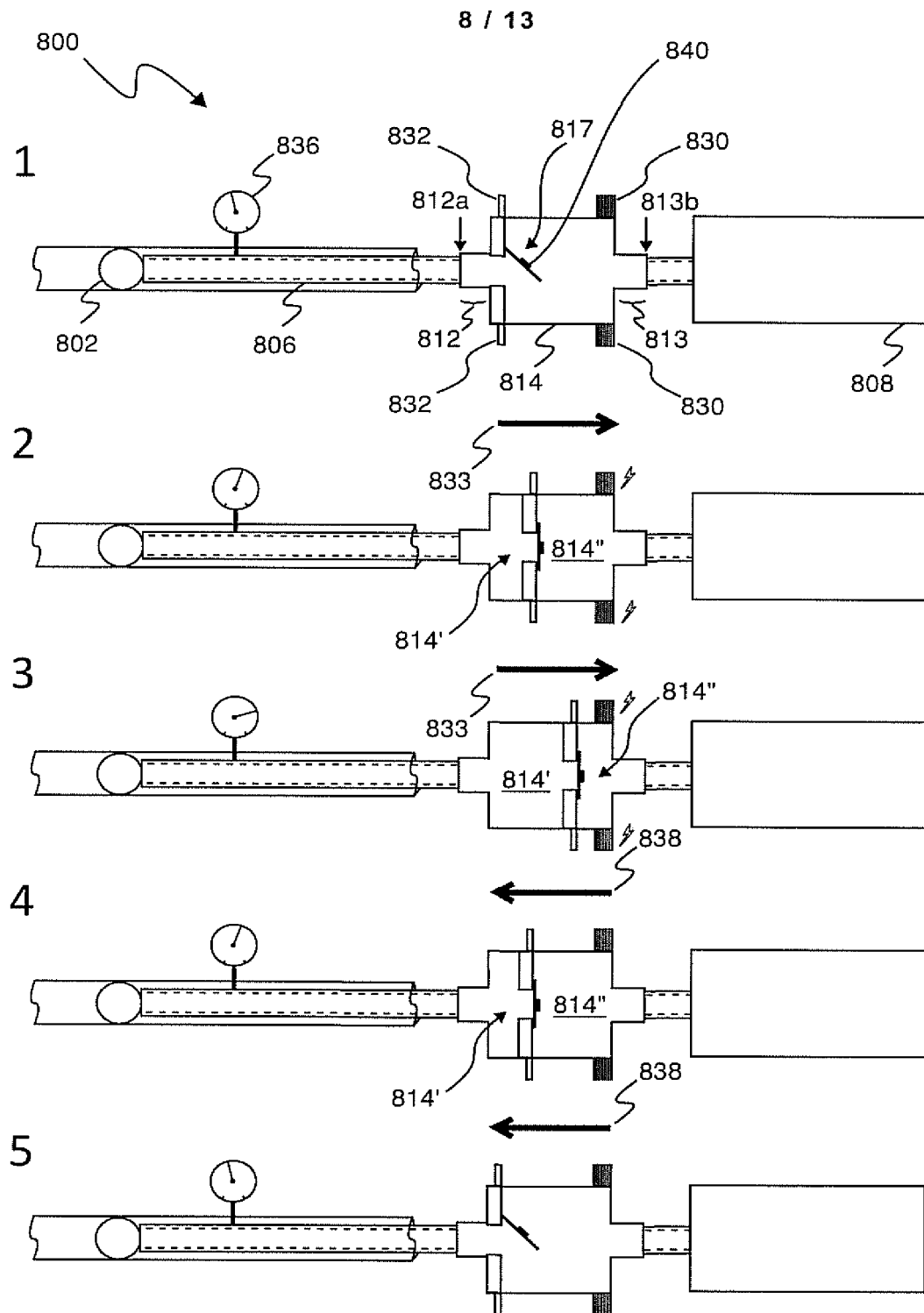


FIGURE 8A

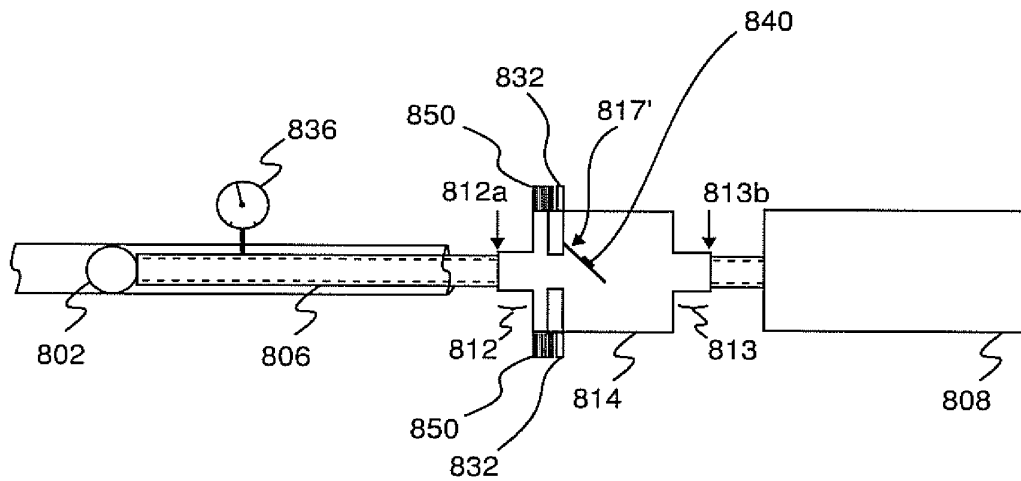


FIGURE 8B

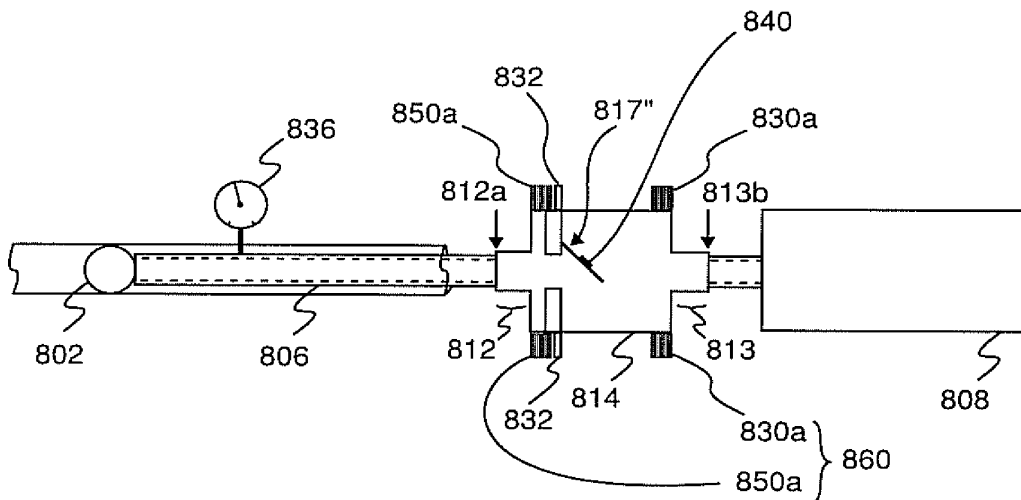


FIGURE 8C

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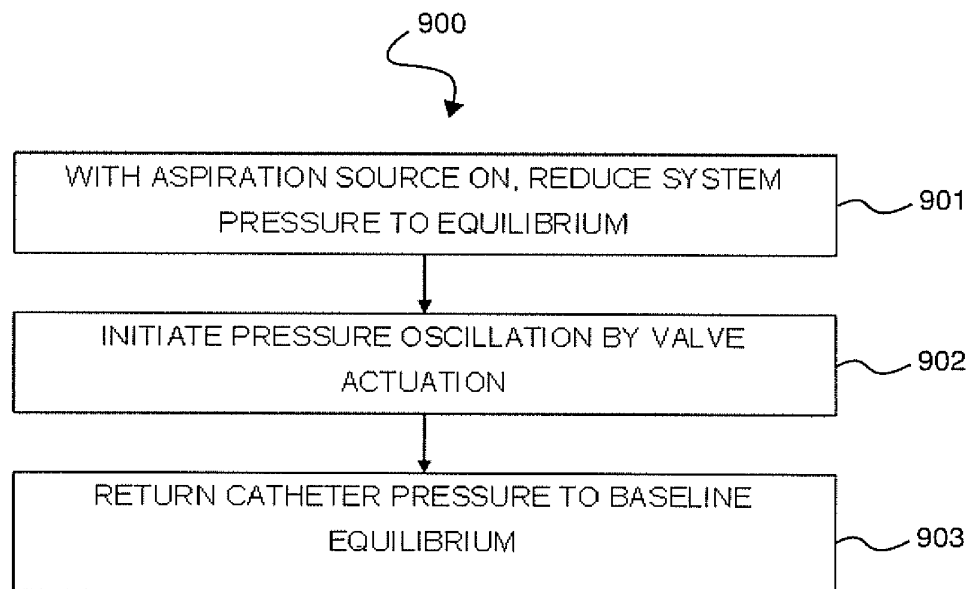


FIGURE 9A

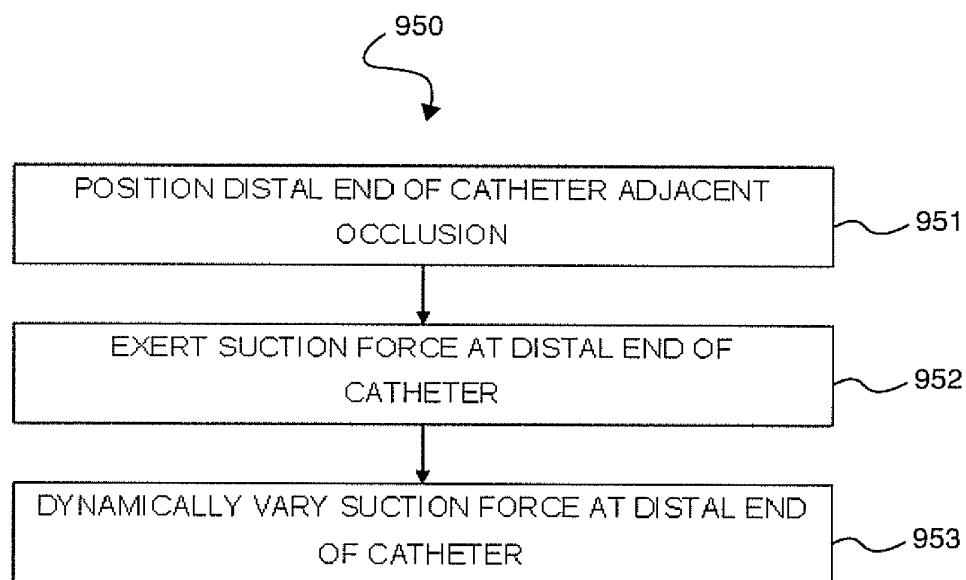


FIGURE 9B

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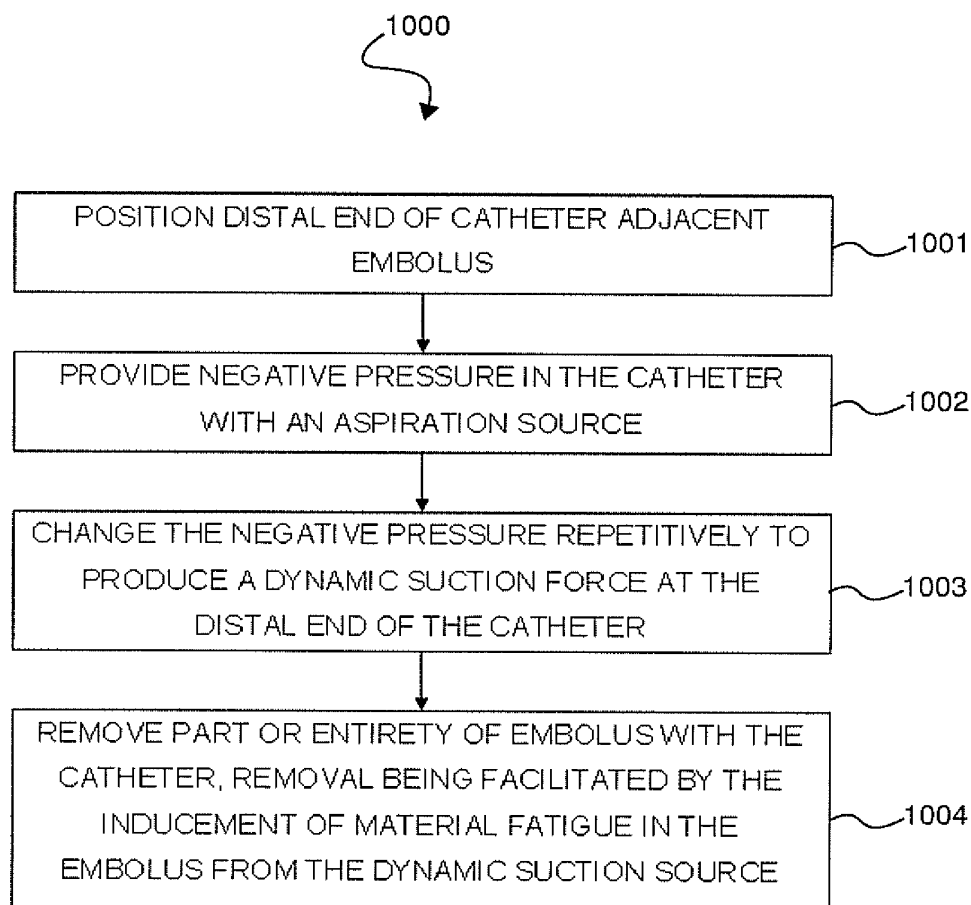


FIGURE 10

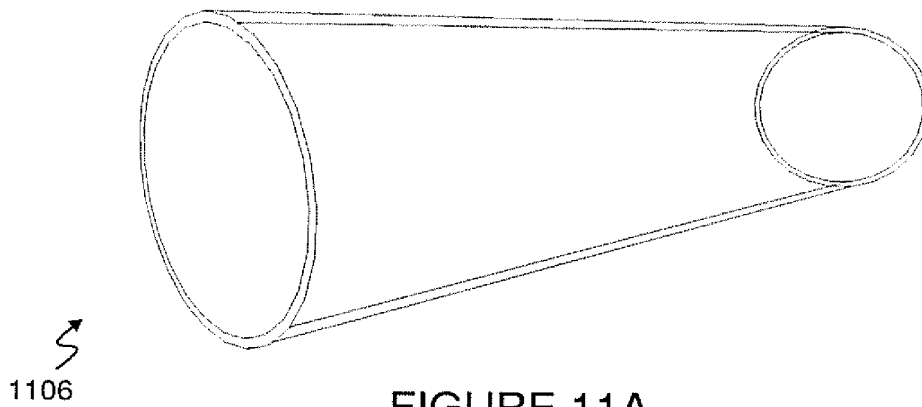


FIGURE 11A

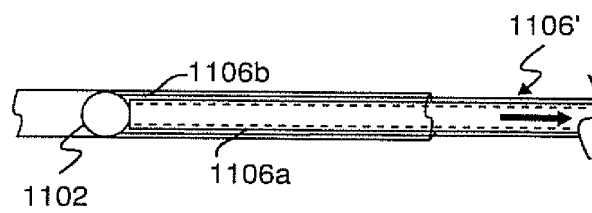


FIGURE 11B

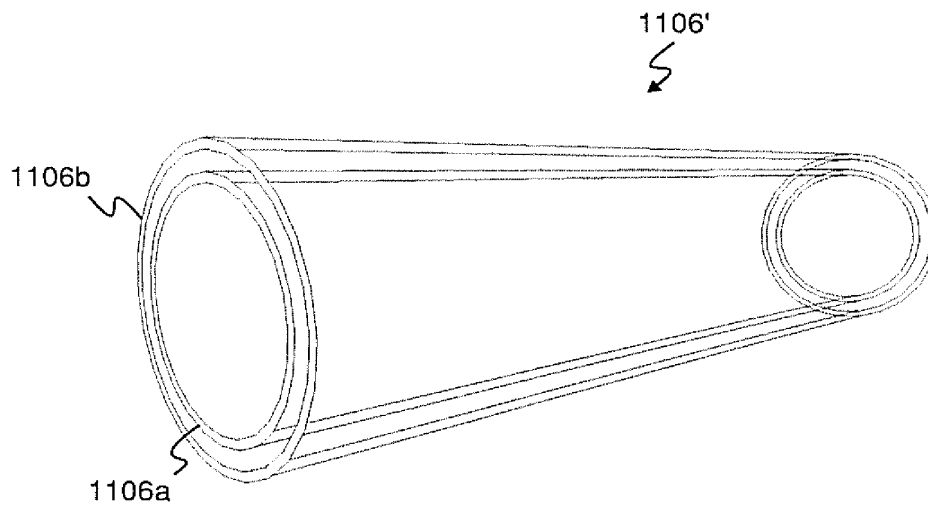


FIGURE 11C

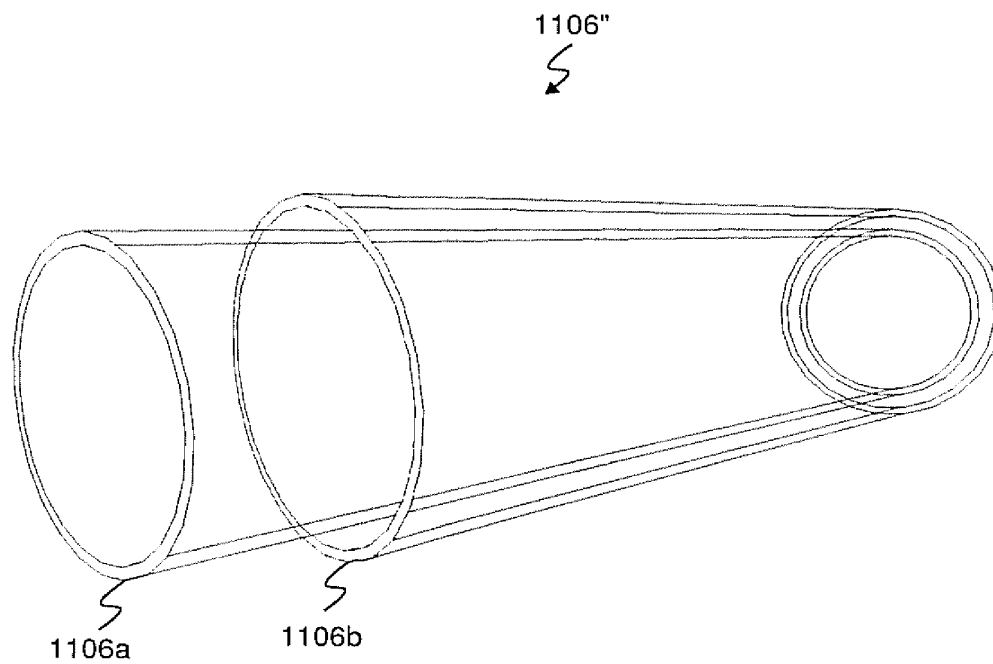


FIGURE 11D

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2014/025211**A. CLASSIFICATION OF SUBJECT MATTER****A61M 1/00(2006.01)i, A61B 17/22(2006.01)i, A61M 27/00(2006.01)i**

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

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

A61M 1/00; A61M 29/00; A61M 5/00; A61M 25/00; A61B 17/22; A61F 2/01; A61M 27/00

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

Korean utility models and applications for utility models

Japanese utility models and applications for utility models

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

eKOMPASS(KIPO internal) & Keywords: aspiration, catheter, valve, suction, thrombectomy, changing negative pressure

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 7004931 B2 (HOGENDIJK, MICHAEL) 28 February 2006 See column 8, line 61 - column 10, line 34; claim 1; and figures 1, 5A and 6C.	1-3
A		4-8, 27-33
X	US 6152909 A (BAGOISAN et al.) 28 November 2000 See column 4, lines 13-17; column 12, line 56 - column 14, line 38; claim 1; and figures 12 and 17.	4-8, 27-33
A	US 2010-0204712 A1 (MALLABY, MARK) 12 August 2010 See paragraphs [0078]-[0080]; claims 1 and 18; and figures 1, 10A and 10B.	1-8, 27-33
A	US 2012-0101510 A1 (LENKER et al.) 26 April 2012 See abstract; claims 1 and 5; and figures 1 and 2.	1-8, 27-33
A	US 2010-0145371 A1 (ROSENBLUTH et al.) 10 June 2010 See abstract; claim 1; and figure 4	1-8, 27-33

☐ 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

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"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

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"&" document member of the same patent family

Date of the actual completion of the international search

27 June 2014 (27.06.2014)

Date of mailing of the international search report

27 June 2014 (27.06.2014)

Name and mailing address of the ISA/KR


 International Application Division
 Korean Intellectual Property Office
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Telephone No. +82-42-481-3353



INTERNATIONAL SEARCH REPORTInternational application No.
PCT/US2014/025211**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.: 9-26
because they relate to subject matter not required to be searched by this Authority, namely:
Claims 9-26 pertain to methods for treatment of the human body by surgery, and thus relate to a subject matter which this ISA is not required, under PCT Article 17(2)(a)(i) and PCT Rule 39.1(iv), to search.
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 any additional fees.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

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)) (July 2009)

INTERNATIONAL SEARCH REPORT
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Electronic Acknowledgement Receipt	
EFS ID:	37288569
Application Number:	16516232
International Application Number:	
Confirmation Number:	6733
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
Receipt Date:	26-SEP-2019
Filing Date:	18-JUL-2019
Time Stamp:	15:30:34
Application Type:	Utility under 35 USC 111(a)

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1	Information Disclosure Statement (IDS) Form (SB08)	2019-09-26_IDS_1.pdf	1039217	no	20
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Warnings:

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2	Foreign Reference	CN101027004A_Penumbra_Inc.pdf	2189457 fa155b9cd41827b7a7b65380240be135309618d	no	53
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National Stage of an International Application under 35 U.S.C. 371

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.

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INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)	Application Number	16516232
	Filing Date	2019-07-18
	First Named Inventor	Derek Dee Deville
	Art Unit	3771
	Examiner Name	Melanie Ruano Tyson
	Attorney Docket Number	Syn2.0/ROAR

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INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)	Application Number	16516232
	Filing Date	2019-07-18
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INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)	Application Number	16516232
	Filing Date	2019-07-18
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	Filing Date	2019-07-18
	First Named Inventor	Derek Dee Deville
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International Application Number:	
Confirmation Number:	6733
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
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Doc code: IDS

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INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)	Application Number	16516232
	Filing Date	2019-07-18
	First Named Inventor	Derek Dee Deville
	Art Unit	3771
	Examiner Name	Melanie Ruano Tyson
	Attorney Docket Number	Syn2.0/ROAR

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INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)	Application Number	16516232
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	Art Unit	3771
	Examiner Name	Melanie Ruano Tyson
	Attorney Docket Number	Syn2.0/ROAR

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NON-PATENT LITERATURE DOCUMENTS

Examiner Initials*	Cite No	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc), date, pages(s), volume-issue number(s), publisher, city and/or country where published.	T ⁵
	1	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	
	2	SAMANIEGO, et al., "Mechanical Thrombectomy: Emerging Technologies and Techniques, Journal of Stroke and Cerebrovascular Diseases, Vol., No., (), 2018: pp1-17	
	3	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	
	4	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	
	5	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	
	6	SIMON, et al., "Hydrodynamic comparison of the Penumbra system and commonly available syringes in forced-suction thrombectomy, J NeuroIntervent surg 2014;6:205-211. doi:10.1136/neurintsurg-2012-010638	
	7	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	
	8	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-2013-010765	

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)	Application Number	16516232
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	First Named Inventor	Derek Dee Deville
	Art Unit	3771
	Examiner Name	Melanie Ruano Tyson
	Attorney Docket Number	Syn2.0/ROAR

9	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
10	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
11	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
12	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
13	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		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.

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INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)	Application Number	16516232
	Filing Date	2019-07-18
	First Named Inventor	Derek Dee Deville
	Art Unit	3771
	Examiner Name	Melanie Ruano Tyson
	Attorney Docket Number	Syn2.0/ROAR

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)	2019-09-26
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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Electronic Acknowledgement Receipt	
EFS ID:	37291167
Application Number:	16516232
International Application Number:	
Confirmation Number:	6733
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
Receipt Date:	26-SEP-2019
Filing Date:	18-JUL-2019
Time Stamp:	17:09:21
Application Type:	Utility under 35 USC 111(a)

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4	Non Patent Literature	Schuhmann_etal_2016_Immunohistochemical_Analysis.pdf	3328870	no	11
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5	Non Patent Literature	Sillanpaa_etal_2012_The_clot_burden_Scores-Sillanpaa.pdf	184259	no	10
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6	Non Patent Literature	Simon_etal_2014_Exploring_the_efficacy.pdf	1154064	no	7
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7	Non Patent Literature	Simon_etal_2014_Hydrodynamic_comparison.pdf	1438020	no	8
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8	Non Patent Literature	Sorimachi_etal_2011_Blood_Pressure.pdf	72086	no	4
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9	Non Patent Literature	Spiotta_etal_2014_Hounsfield_Unit.pdf	1837972	no	6
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11	Non Patent Literature	Turk_etal_2013_Initial_clinical.pdf	643951	no	8
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Warnings:					
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12	Non Patent Literature	Yuki_etal_2012_April_The_Impact_of_Thromboemboli.pdf	2257567	no	6
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13	Non Patent Literature	Zarrinkoob_etal_2015_Blood_Flow.pdf	475938	no	7
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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
16/516,232	07/18/2019	Derek Dee Deville	Syn2.0/ROAR	6733
27316	7590	09/10/2019	EXAMINER	
Mayback & Hoffman, P.A. 350 East Las Olas Blvd Suite 1750 Fort Lauderdale, FL 33301			ART UNIT	PAPER NUMBER
			3771	
			MAIL DATE	DELIVERY MODE
			09/10/2019	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

<i>Decision Granting Request for Prioritized Examination (Track I)</i>	Application No. 16/516,232	Applicant(s) Deville et al.	
	Examiner BRIAN W BROWN	Art Unit OPET	AIA (FITF) Status Yes
<p>1. THE REQUEST FILED <u>18 July 2019</u> IS GRANTED .</p> <p>The above-identified application has met the requirements for prioritized examination</p> <p>A. ☒ for an original nonprovisional application (Track I).</p> <p>B. ☐ for an application undergoing continued examination (RCE).</p> <p>2. The above-identified application will undergo prioritized examination. The application will be accorded special status throughout its entire course of prosecution until one of the following occurs:</p> <p>A. filing a <u>petition for extension of time</u> to extend the time period for filing a reply;</p> <p>B. filing an <u>amendment to amend the application to contain more than four independent claims, more than thirty total claims</u>, or a multiple dependent claim;</p> <p>C. filing a <u>request for continued examination</u> ;</p> <p>D. filing a notice of appeal;</p> <p>E. filing a request for suspension of action;</p> <p>F. mailing of a notice of allowance;</p> <p>G. mailing of a final Office action;</p> <p>H. completion of examination as defined in 37 CFR 41.102; or</p> <p>I. abandonment of the application.</p> <p>Telephone inquiries with regard to this decision should be directed to BRIAN BROWN at (571)272-5338. In his/her absence, calls may be directed to Petition Help Desk at (571) 272-3282.</p>			
/BRIAN W BROWN/ Petitions Examiner, OPET			



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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
16/516,232	07/18/2019	3783	1015	Syn2.0/ROAR	20	4

CONFIRMATION NO. 6733

FILING RECEIPT



0000000110038933

27316

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

Date Mailed: 08/01/2019

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.

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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;

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 appln claims benefit of 62/701,086 07/20/2018
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: 07/31/2019

The country code and number of your priority application, to be used for filing abroad under the Paris Convention, is **US 16/516,232**

Projected Publication Date: 01/23/2020

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

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page 2 of 4

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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 16/516,232				
APPLICATION AS FILED - PART I										
(Column 1)		(Column 2)		SMALL ENTITY		OR OTHER THAN SMALL ENTITY				
FOR	NUMBER FILED	NUMBER EXTRA	RATE(\$)	FEE(\$)		RATE(\$)	FEE(\$)			
BASIC FEE <small>(37 CFR 1.16(a), (b), or (c))</small>	N/A	N/A	N/A	75		N/A				
SEARCH FEE <small>(37 CFR 1.16(k), (j), or (m))</small>	N/A	N/A	N/A	330		N/A				
EXAMINATION FEE <small>(37 CFR 1.16(o), (p), or (q))</small>	N/A	N/A	N/A	380		N/A				
TOTAL CLAIMS <small>(37 CFR 1.16(i))</small>	20	minus 20 = *	x 50 =	0.00	OR					
INDEPENDENT CLAIMS <small>(37 CFR 1.16(h))</small>	4	minus 3 = *	x 230 =	230						
APPLICATION SIZE FEE <small>(37 CFR 1.16(s))</small>	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 <small>(37 CFR 1.16(j))</small>				0.00						
* If the difference in column 1 is less than zero, enter "0" in column 2.				TOTAL		TOTAL				
				1015						
APPLICATION AS AMENDED - PART II										
(Column 1)		(Column 2)		(Column 3)		SMALL ENTITY		OR OTHER THAN SMALL ENTITY		
AMENDMENT A		CLAIMS REMAINING AFTER AMENDMENT		HIGHEST NUMBER PREVIOUSLY PAID FOR	PRESENT EXTRA	RATE(\$)	ADDITIONAL FEE(\$)		RATE(\$)	ADDITIONAL FEE(\$)
	Total <small>(37 CFR 1.16(i))</small>	*	Minus	**	=	x	=	OR	x	=
	Independent <small>(37 CFR 1.16(h))</small>	*	Minus	***	=	x	=	OR	x	=
	Application Size Fee <small>(37 CFR 1.16(s))</small>							OR		
	FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM <small>(37 CFR 1.16(j))</small>							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 <small>(37 CFR 1.16(i))</small>	*	Minus	**	=	x	=	OR	x	=
	Independent <small>(37 CFR 1.16(h))</small>	*	Minus	***	=	x	=	OR	x	=
	Application Size Fee <small>(37 CFR 1.16(s))</small>							OR		
	FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM <small>(37 CFR 1.16(j))</small>							OR		
						TOTAL ADD'L FEE		OR	TOTAL ADD'L FEE	
* If the entry in column 1 is less than the entry in column 2, write "0" in column 3. ** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 20, enter "20". *** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 3, enter "3". The "Highest Number Previously Paid For" (Total or Independent) is the highest found in the appropriate box in column 1.										

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
13756 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 7/12/19

Name M. Sean McBrayer

Telephone

Title Managing Member

This collection of information is required by 37 CFR 1.33, 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.: 16/516,232 Filed/Issue Date: 07/18/2019
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 49796, Frame 914, 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

2019-07-29

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:	36725738
Application Number:	16516232
International Application Number:	
Confirmation Number:	6733
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
Receipt Date:	30-JUL-2019
Filing Date:	
Time Stamp:	12:03:28
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	2019-07-29_Syn20_Roar_Executed_POA_86082-9.pdf	283064 918023767dc275805eb014caed1edd27c05d3640	no	1

Warnings:

Information:					
2	Assignee showing of ownership per 37 CFR 3.73	2019-07-29_Syn20_Roar_State ment373_86082-9.pdf	117939	no	3
			f9160f442791869deeb2f3d74c99a1ffe3bf9 efa		
Warnings:					
Information:					
Total Files Size (in bytes):			401003		
<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: 16516232

Document Date: 07/18/2019

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.

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%;">Attorney Docket No.</td> <td>Syn 2.0/Roar</td> </tr> <tr> <td>First Named Inventor</td> <td>Derek Dee Deville</td> </tr> <tr> <td>Title</td> <td>Aspiration Thrombectomy System and Methods for Thrombus Removal with Aspiration</td> </tr> <tr> <td>Priority Mail Express® Label No.</td> <td>N/A</td> </tr> </table>	Attorney Docket No.	Syn 2.0/Roar	First Named Inventor	Derek Dee Deville	Title	Aspiration Thrombectomy System and Methods for Thrombus Removal with Aspiration	Priority Mail Express® Label No.	N/A
Attorney Docket No.	Syn 2.0/Roar								
First Named Inventor	Derek Dee Deville								
Title	Aspiration Thrombectomy System and Methods for Thrombus Removal with Aspiration								
Priority Mail Express® Label No.	N/A								

APPLICATION ELEMENTS <i>See MPEP chapter 600 concerning utility patent application contents.</i> <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>83</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>6</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) <div style="margin-left: 20px;">☐ Landscape Table on CD</div> 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 	<table border="1" style="width: 100%; border-collapse: collapse;"> <tr> <td colspan="2" style="text-align: center;"> Commissioner for Patents P.O. Box 1450 Alexandria, VA 22313-1450 </td> </tr> <tr> <td colspan="2" style="text-align: center;">ADDRESS TO:</td> </tr> <tr> <td colspan="2" style="text-align: center;">ACCOMPANYING APPLICATION PAPERS</td> </tr> <tr> <td style="vertical-align: top;"> <ol style="list-style-type: none"> 10. ☐ Assignment Papers (cover sheet & document(s)) Name of Assignee _____ 11. ☐ 37 CFR 3.73(c) Statement (when there is an assignee) ☐ Power of Attorney 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 _____ _____ _____ _____ </td> <td style="vertical-align: top;"></td> </tr> </table>	Commissioner for Patents P.O. Box 1450 Alexandria, VA 22313-1450		ADDRESS TO:		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 (when there is an assignee) ☐ Power of Attorney 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 _____ _____ _____ _____ 	
Commissioner for Patents P.O. Box 1450 Alexandria, VA 22313-1450									
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***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	2019-07-18	
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.**

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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.

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
		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	
		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

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	
		Application Number			
Title of Invention	ASPIRATION THROMBECTOMY SYSTEM AND METHODS FOR THROMBUS REMOVAL WITH ASPIRATION CATHETER				
Mailing Address of Inventor:					
Address 1	2268 Acom Palm Road				
Address 2					
City	Boca Raton	State/Province	FL		
Postal Code	33432	Country	US		
All Inventors Must Be Listed - Additional Inventor Information blocks may be generated within this form by selecting the Add button.					

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		
Email Address	mhpateents@dickinsonwright.com	Add Email	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	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.

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
		Application Number	
Title of Invention	ASPIRATION THROMBECTOMY SYSTEM AND METHODS FOR THROMBUS REMOVAL WITH ASPIRATION CATHETER		

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		

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)
	Claims benefit of provisional	62701086	2018-07-20
Prior Application Status	Pending	Remove	
Application Number	Continuity Type	Prior Application Number	Filing or 371(c) Date (YYYY-MM-DD)
	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

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)	Remove
			Access Code ⁱ (if applicable)

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
		Application Number	
Title of Invention	ASPIRATION THROMBECTOMY SYSTEM AND METHODS FOR THROMBUS REMOVAL WITH ASPIRATION CATHETER		
Additional Foreign Priority Data may be generated within this form by selecting the Add button. <div style="text-align: right;"> <input type="button" value="Add"/> </div>			

Statement under 37 CFR 1.55 or 1.78 for AIA (First Inventor to File) Transition Applications

<p>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.</p> <p>☐ 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.</p>
--

Application Data Sheet 37 CFR 1.76		Attorney Docket Number	Syn2.0/ROAR
		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.

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
		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> <div></div> <div></div> </div>			
Name of the Deceased or Legally Incapacitated Inventor: <input type="text"/>			
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
		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)	2018-07-18
First Name	Gregory L.	Last Name	Mayback	Registration Number
				40719
Additional Signature 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
		Application Number	
Title of Invention	ASPIRATION THROMBECTOMY SYSTEM AND METHODS FOR THROMBUS REMOVAL WITH ASPIRATION CATHETER		

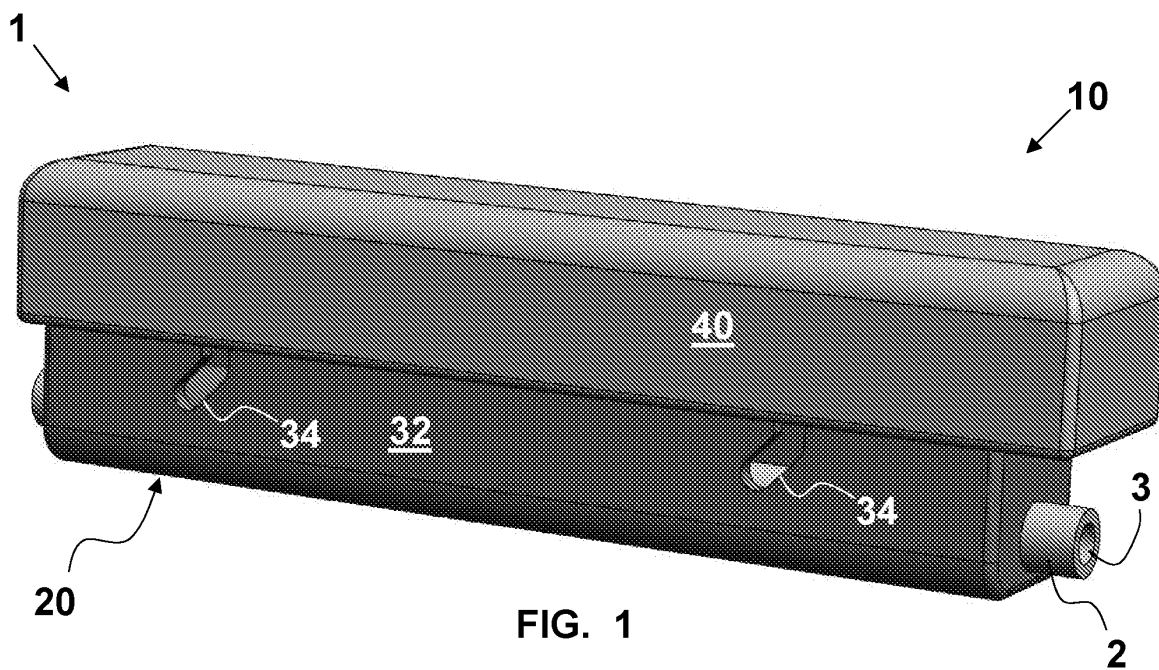
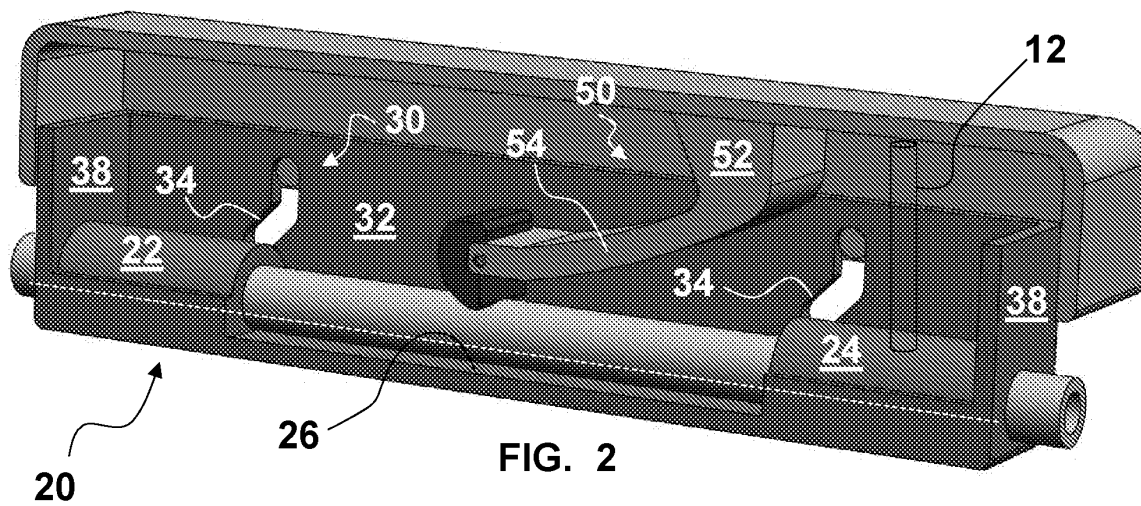
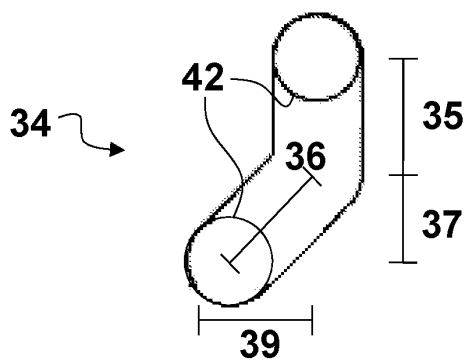
This collection of information is required by 37 CFR 1.76. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 23 minutes 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

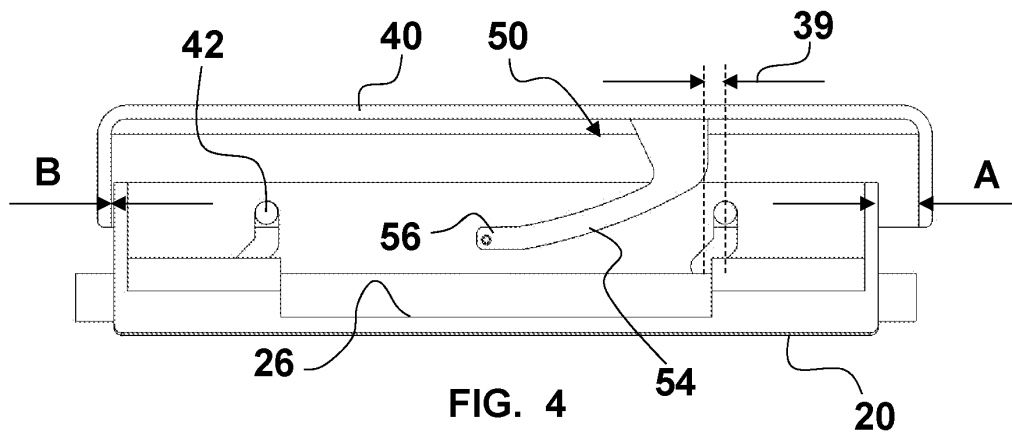
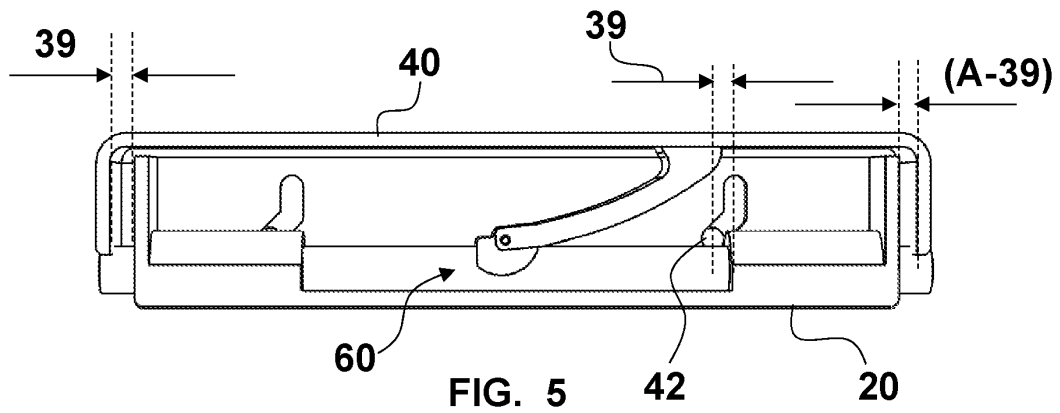
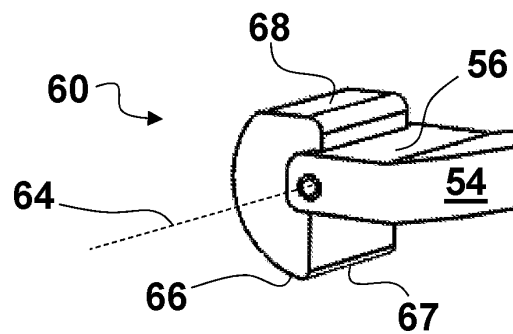
The Privacy Act of 1974 (P.L. 93-579) requires that you be given certain information in connection with your submission of the attached form related to a patent application or patent. Accordingly, pursuant to the requirements of the Act, please be advised that: (1) the general authority for the collection 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.



02/29



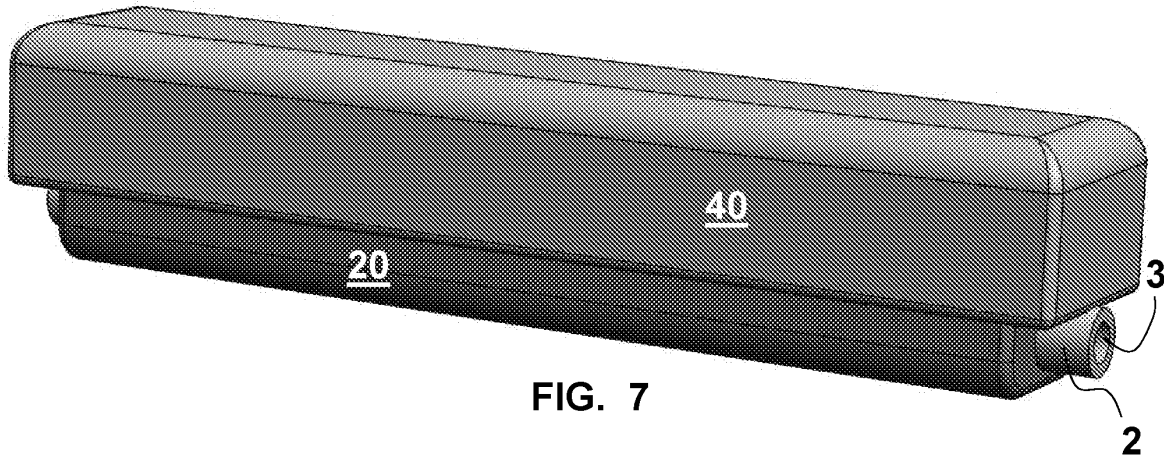
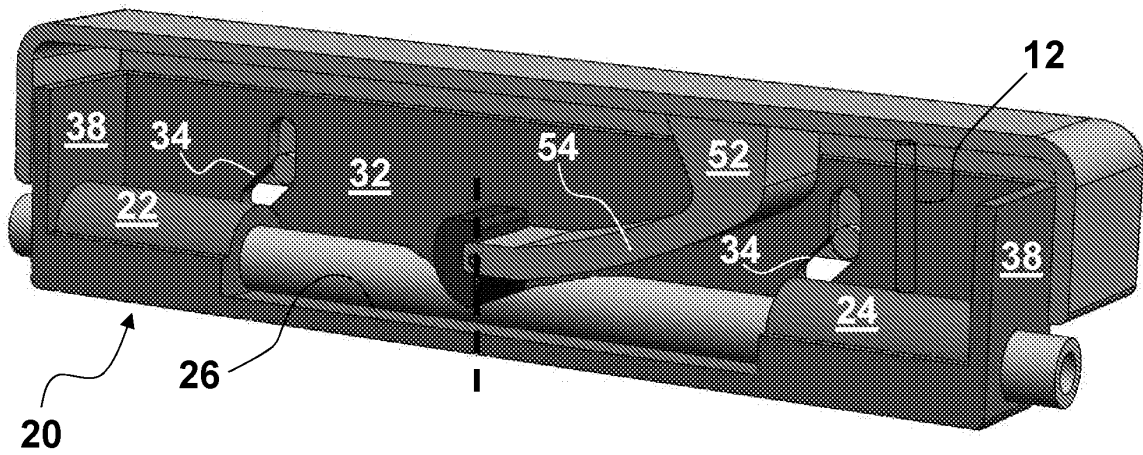
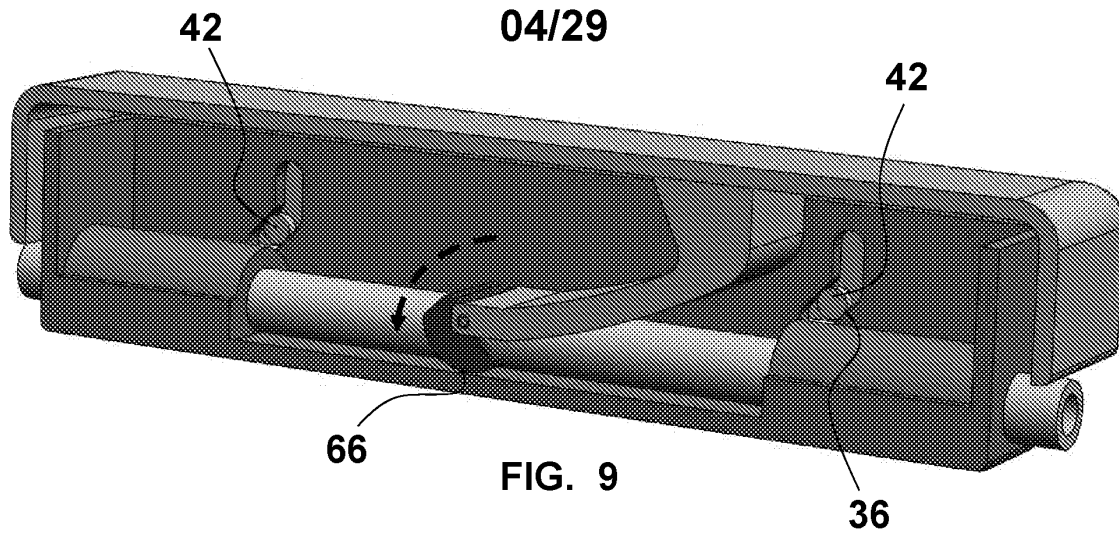
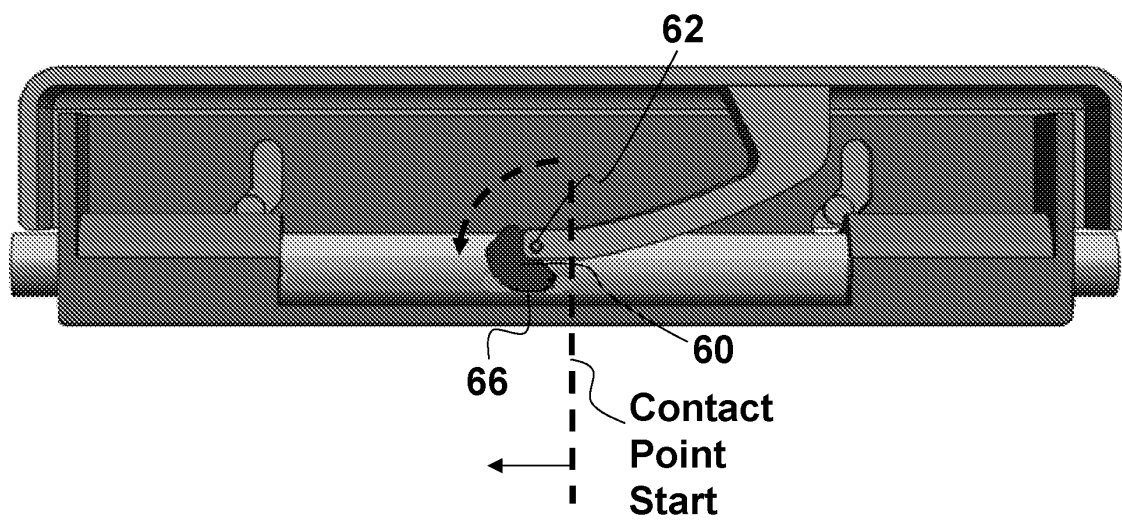
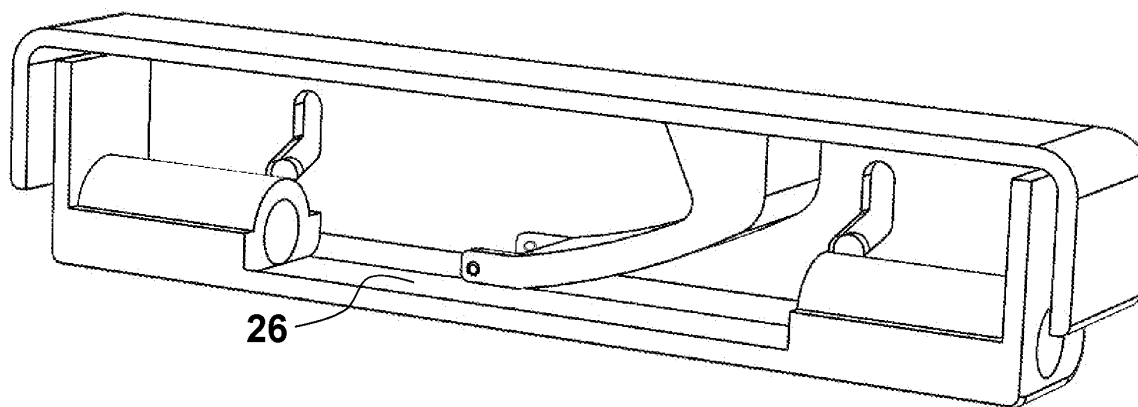
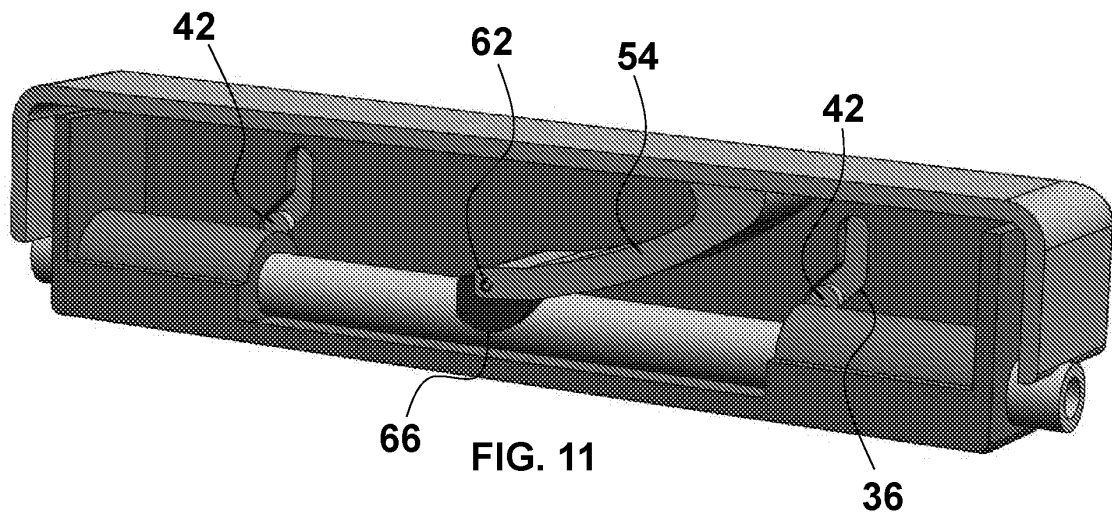
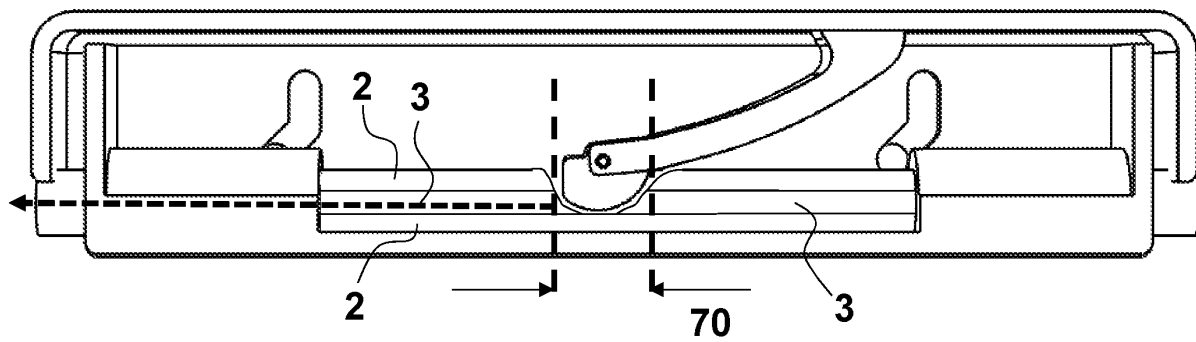
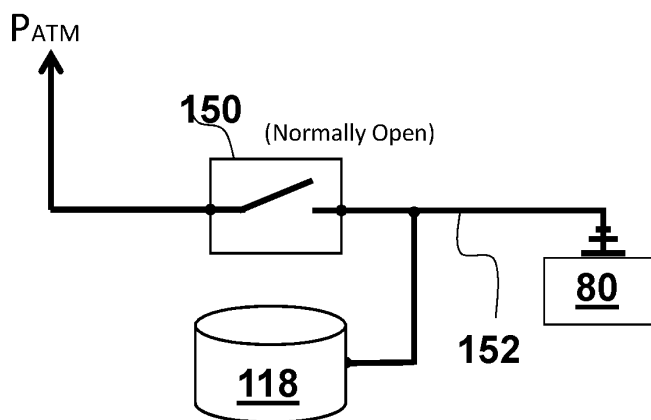
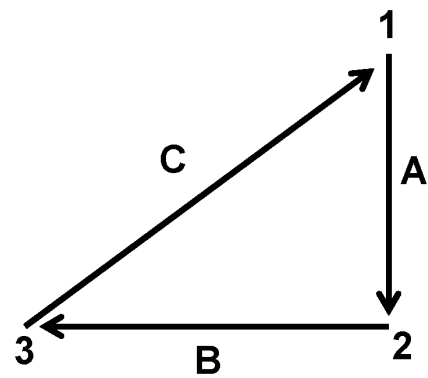


FIG. 8

04/29



05/29



06/29

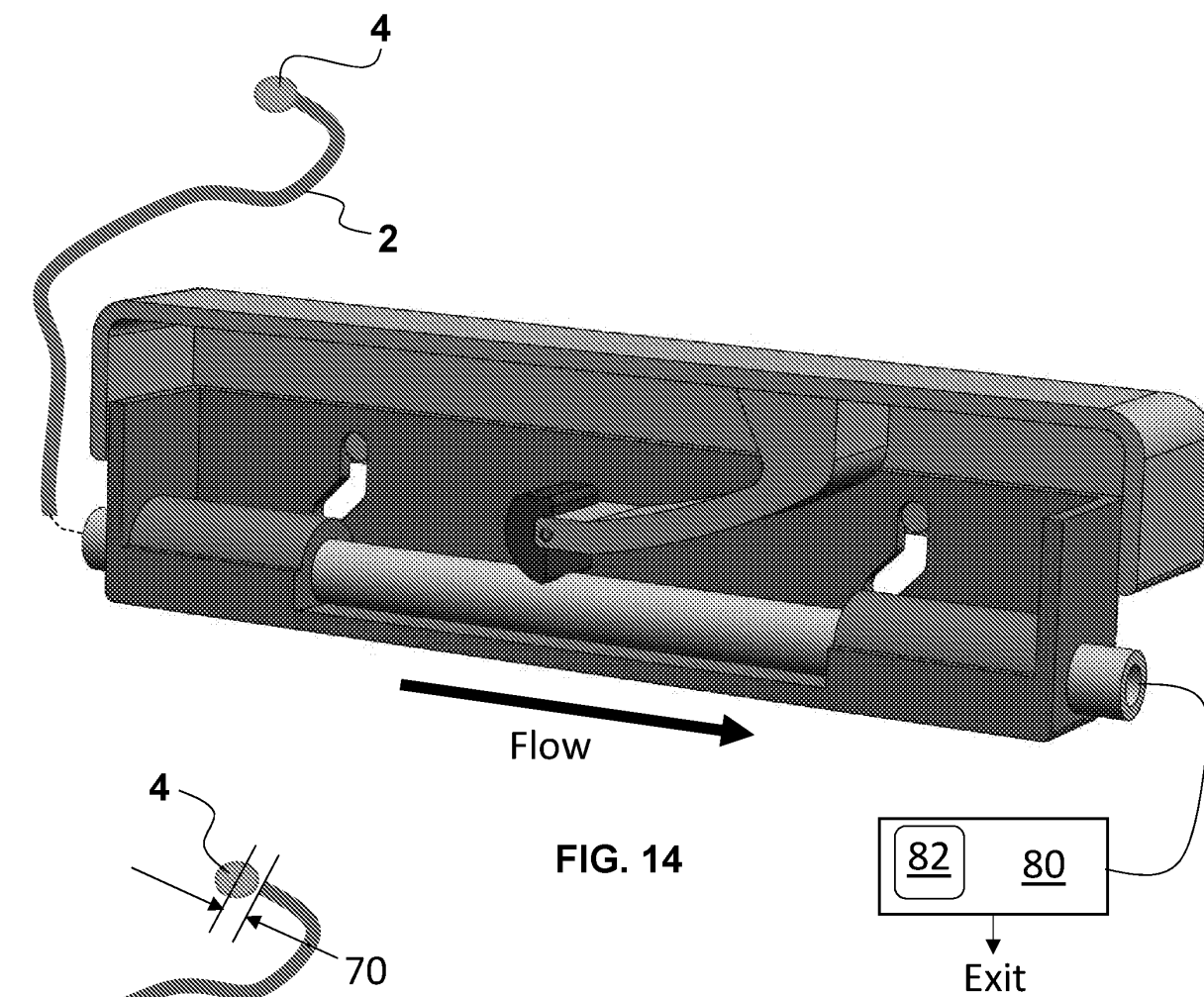
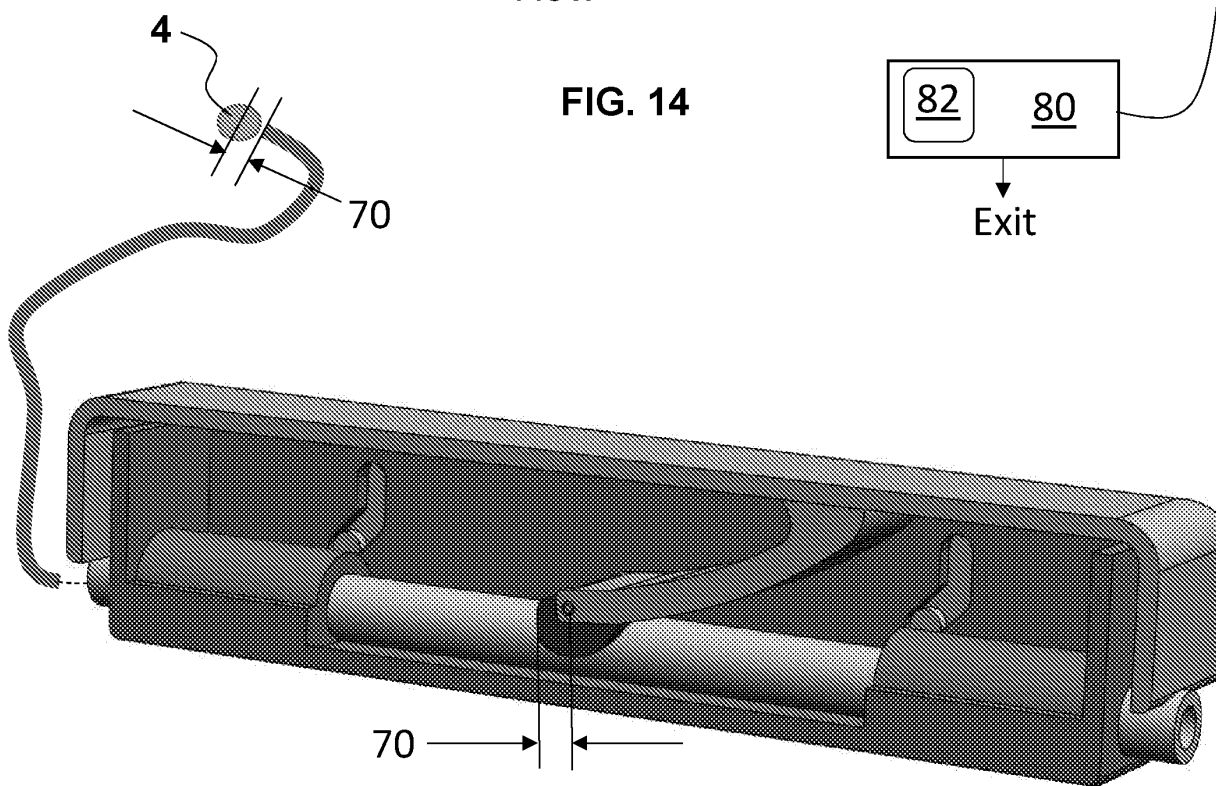
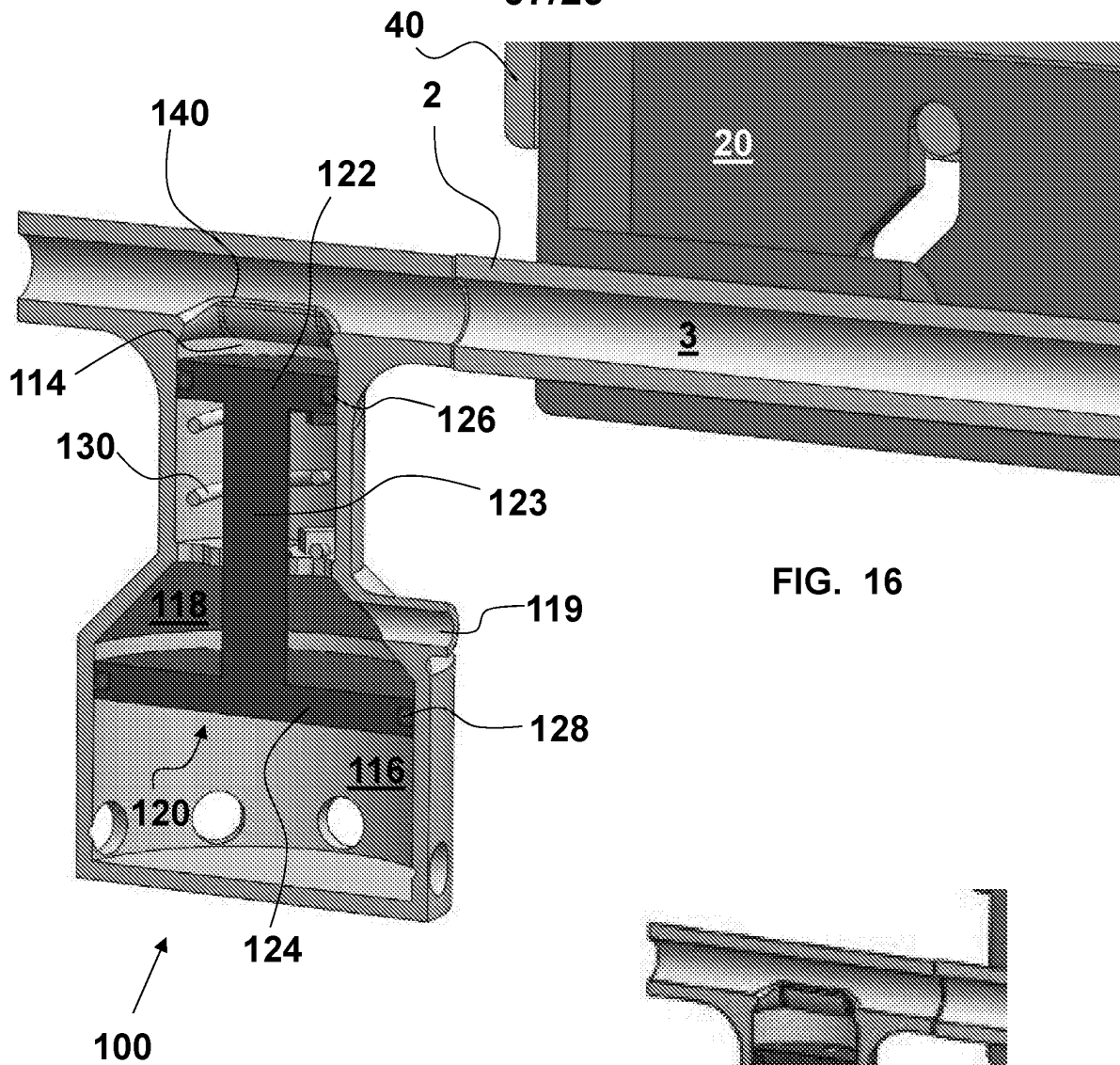
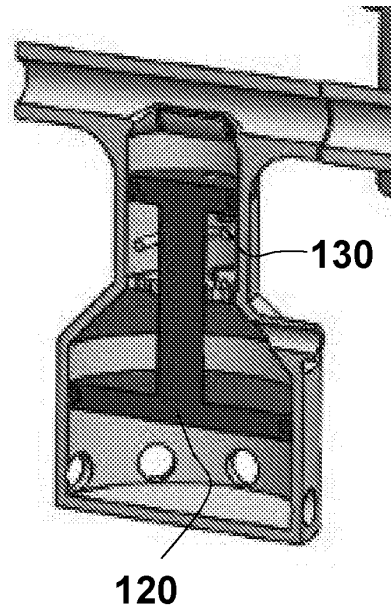
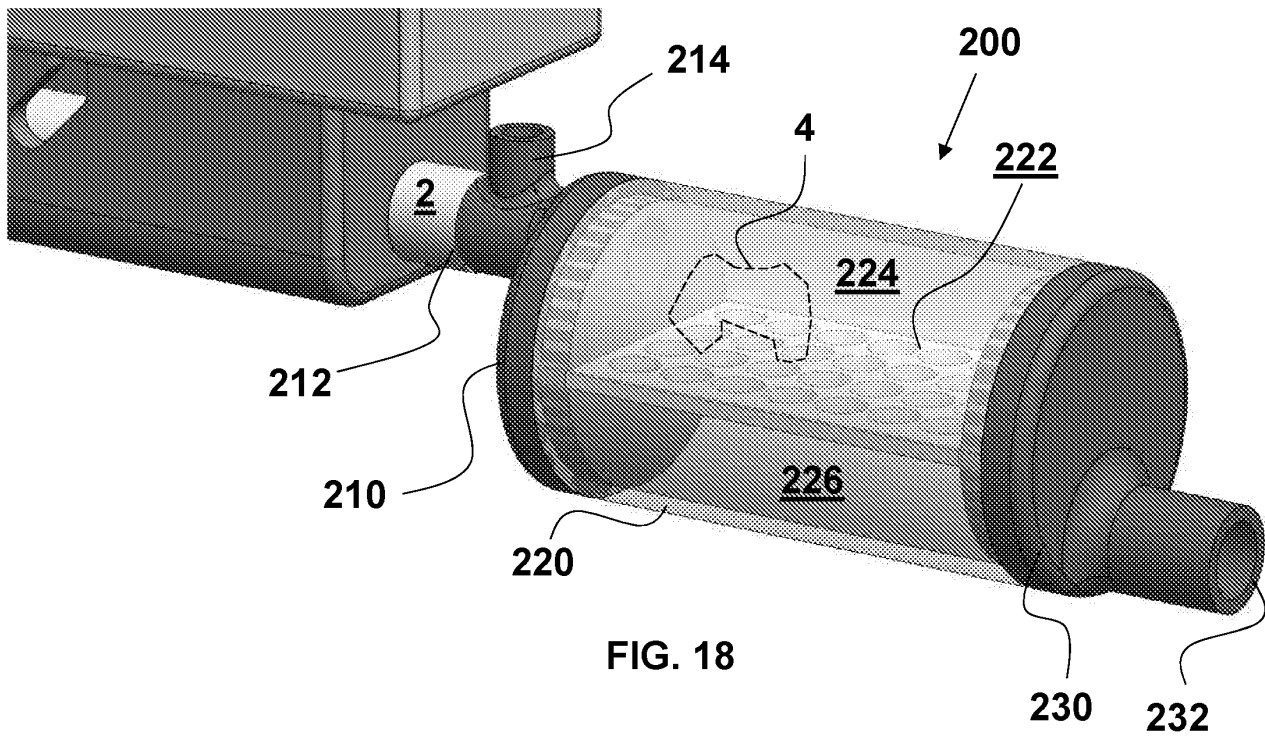
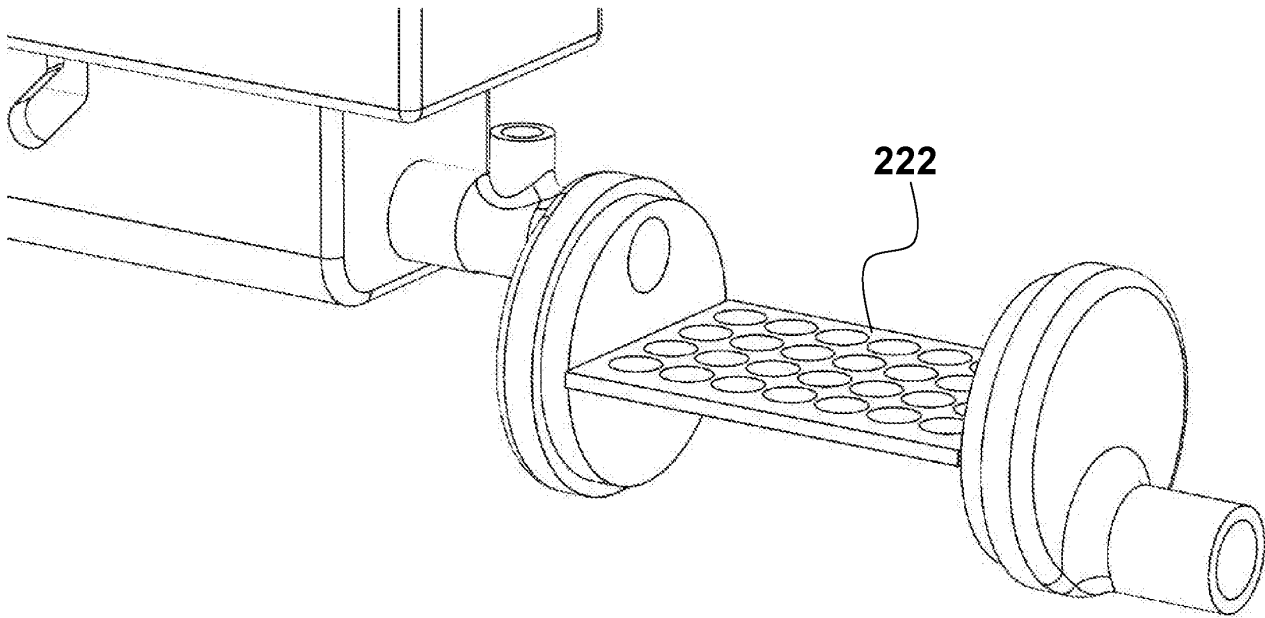


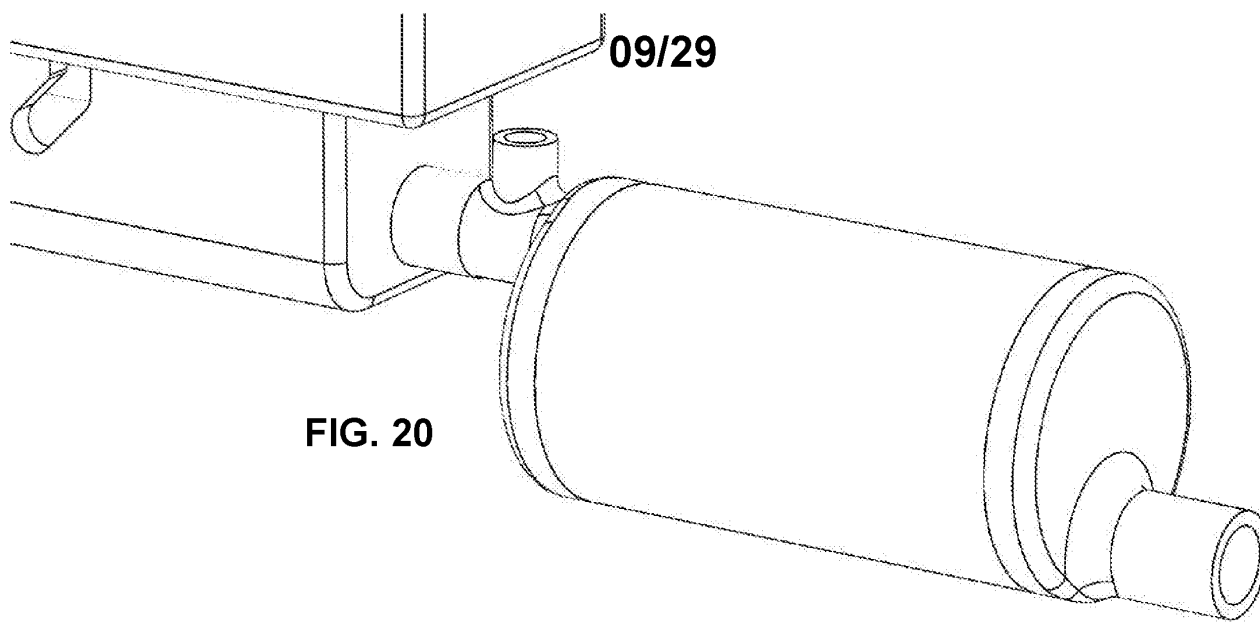
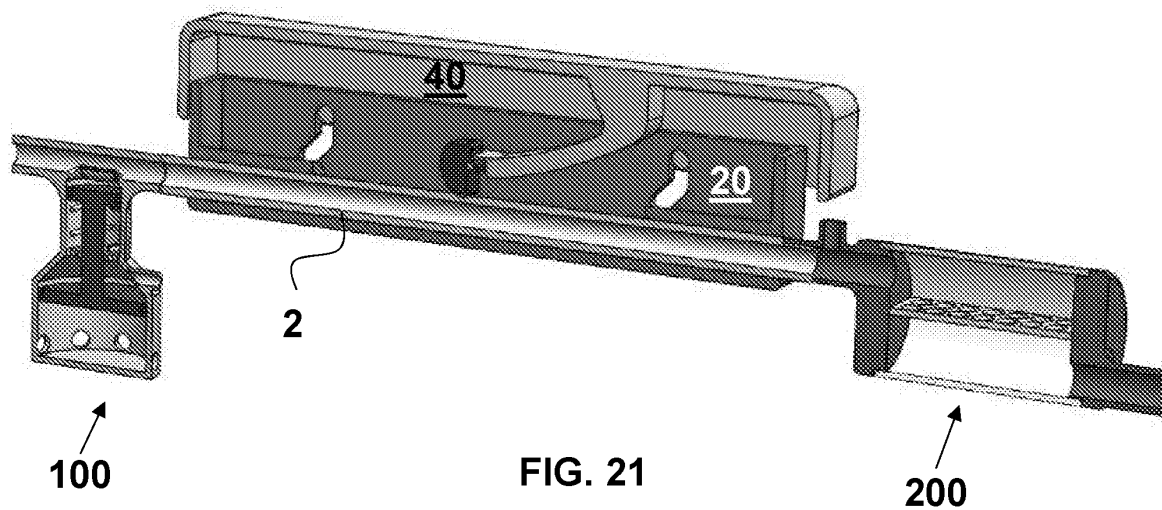
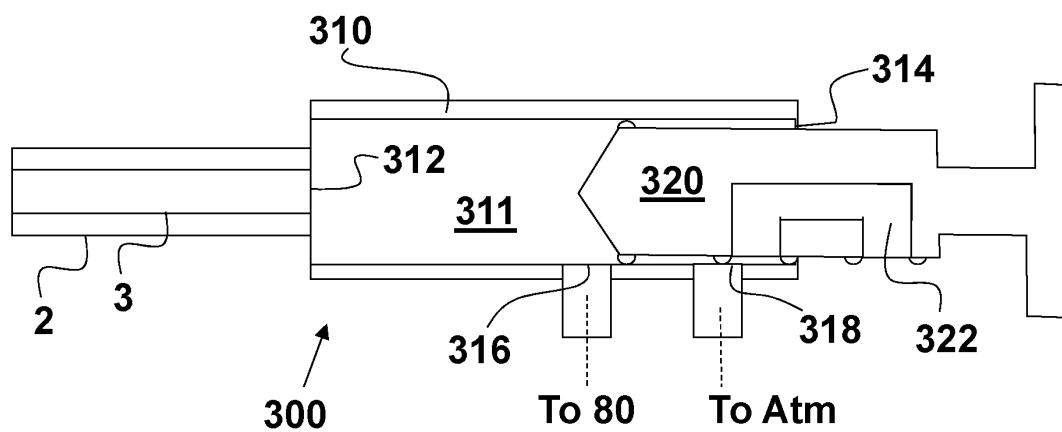
FIG. 15

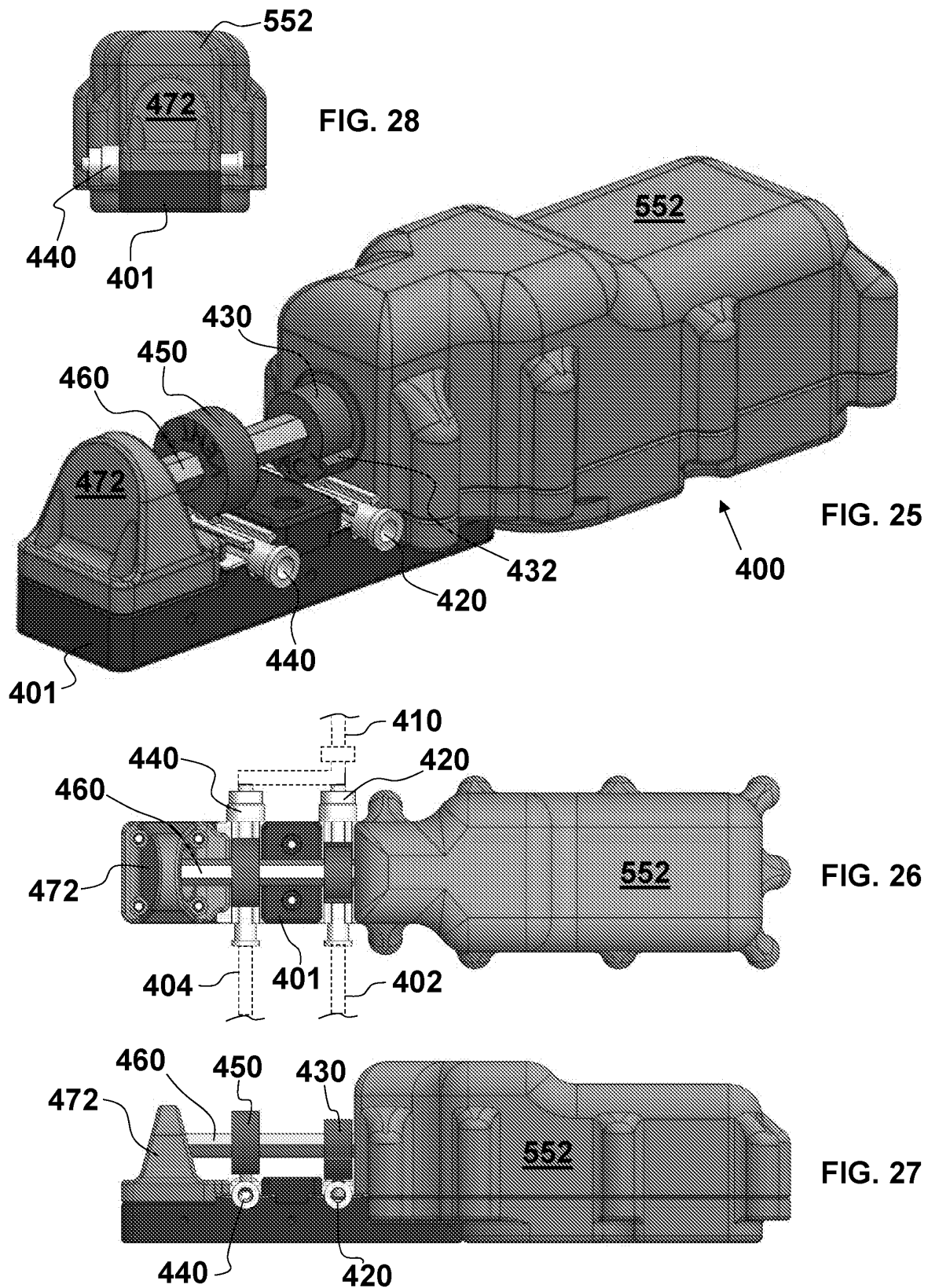
07/29



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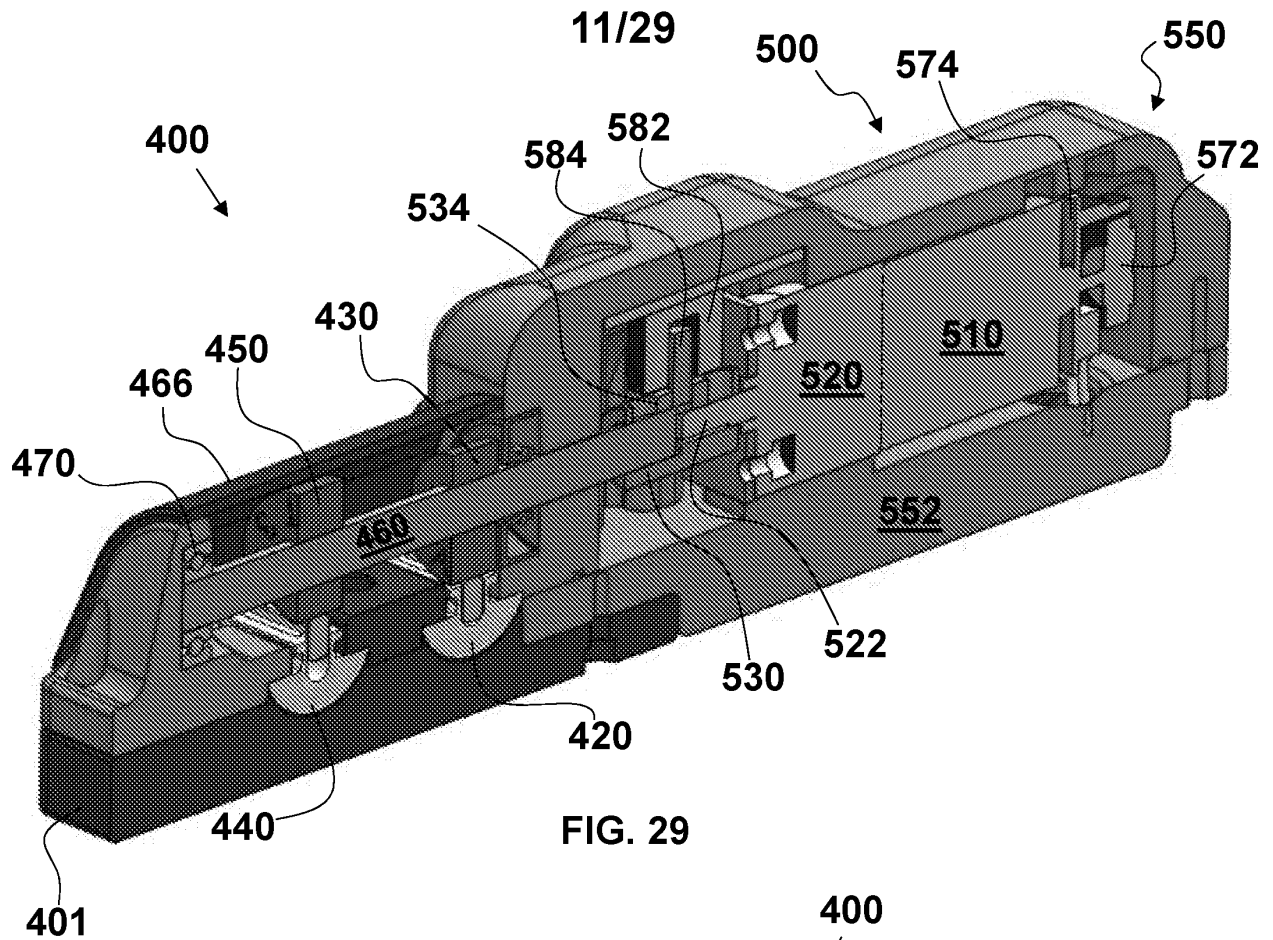


FIG. 29

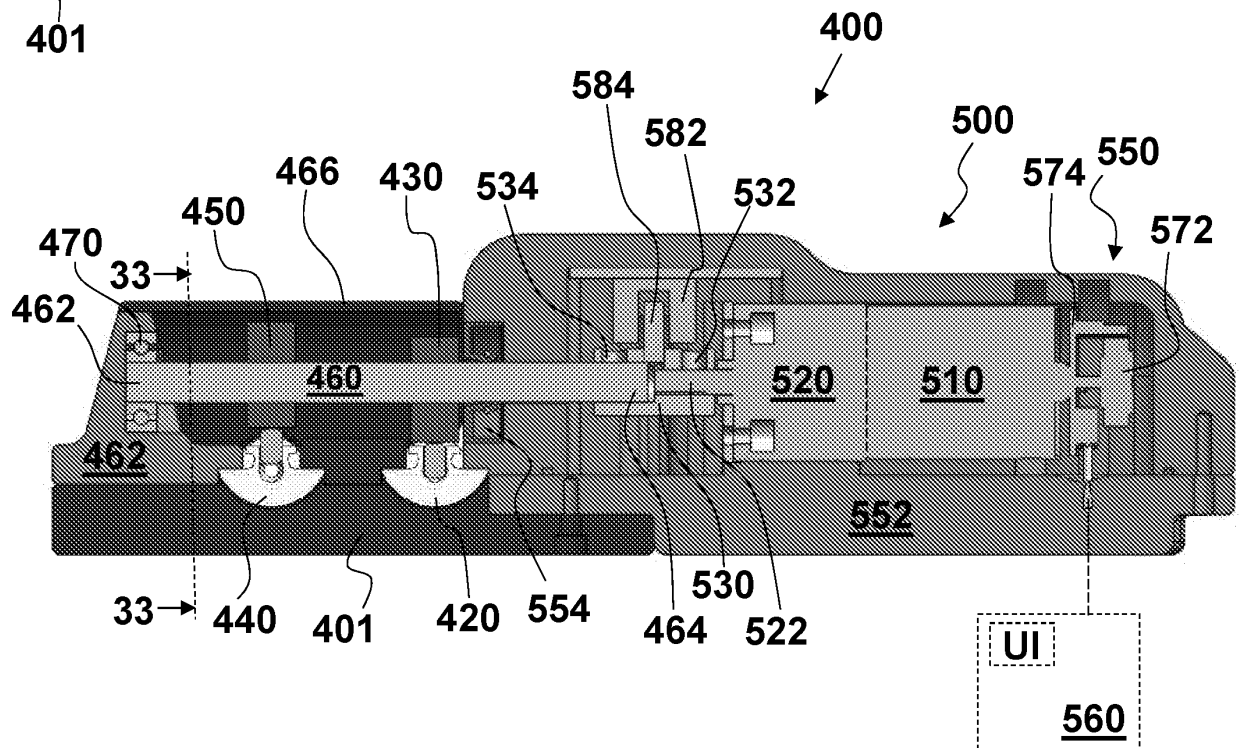
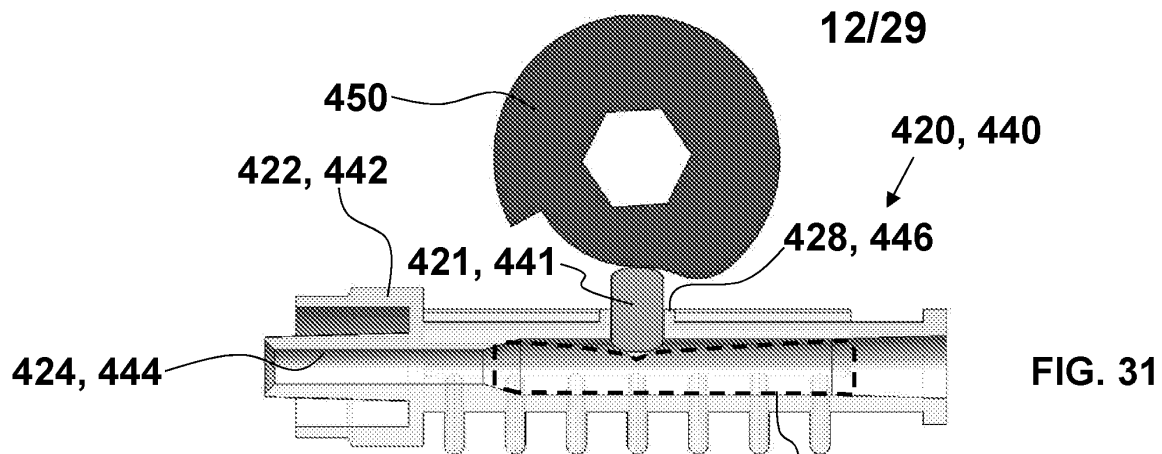
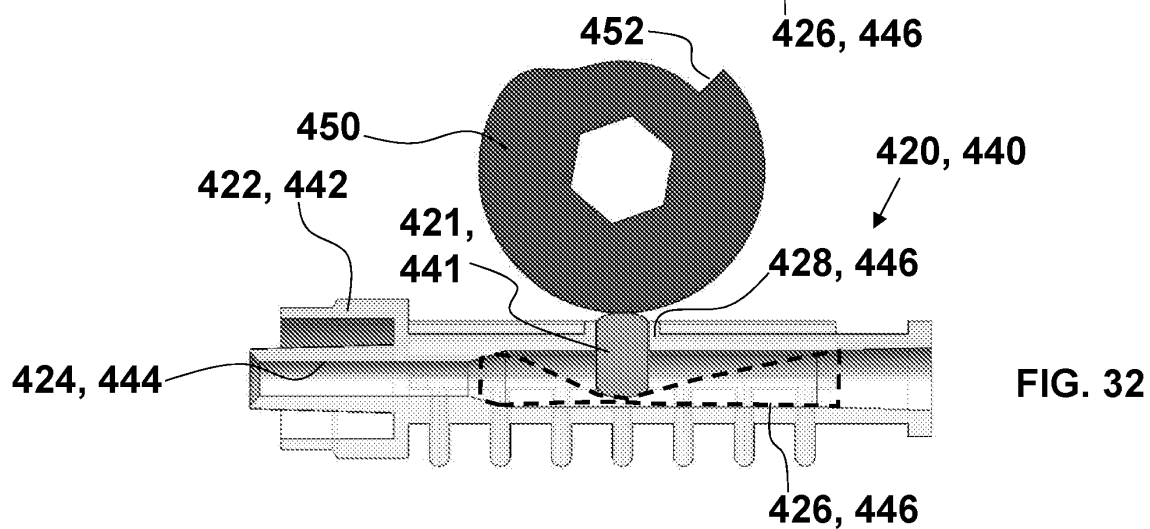
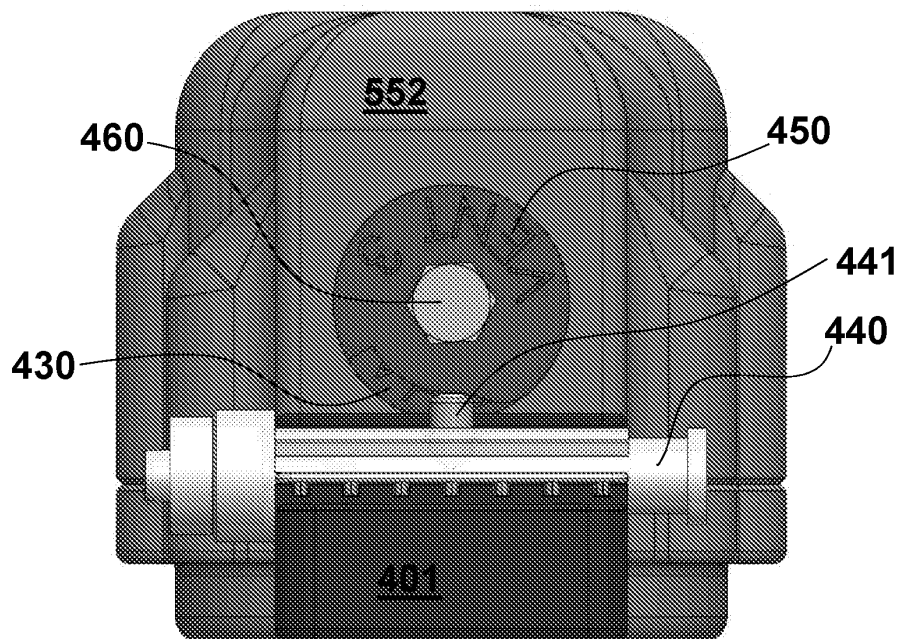
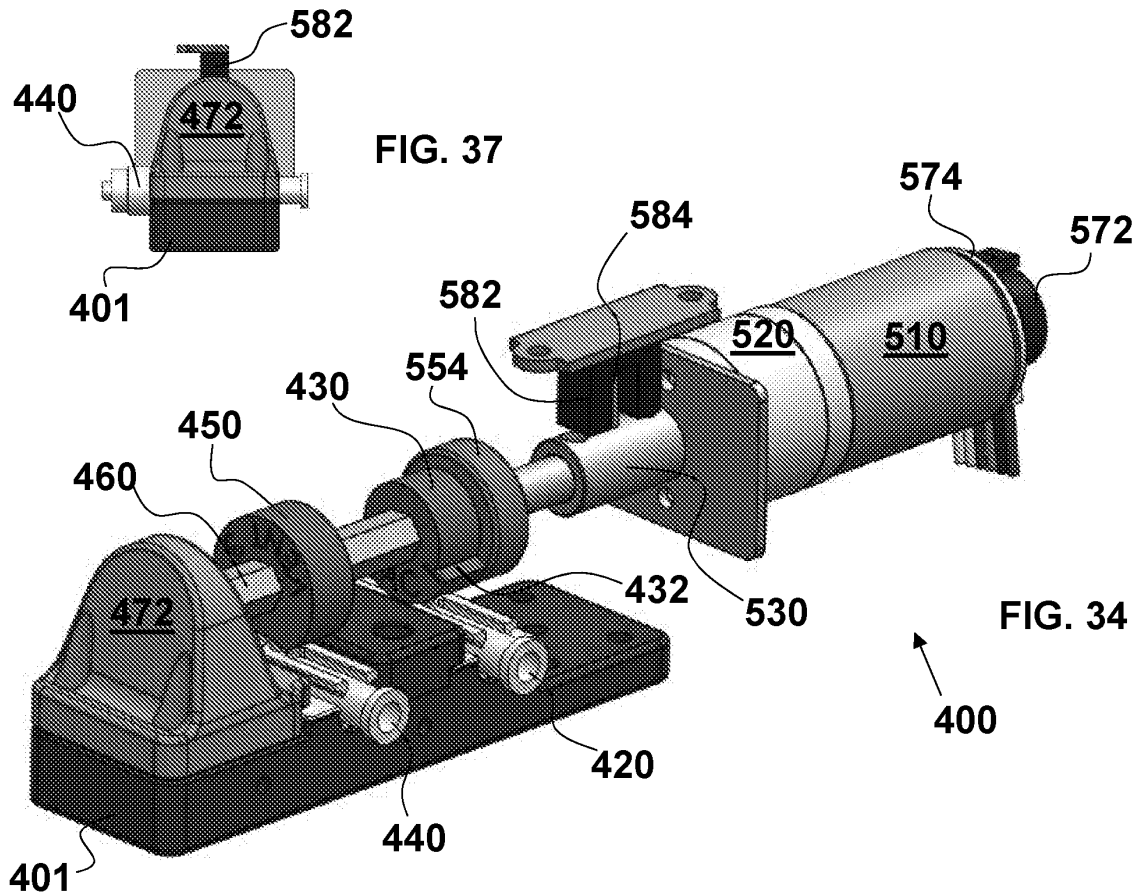
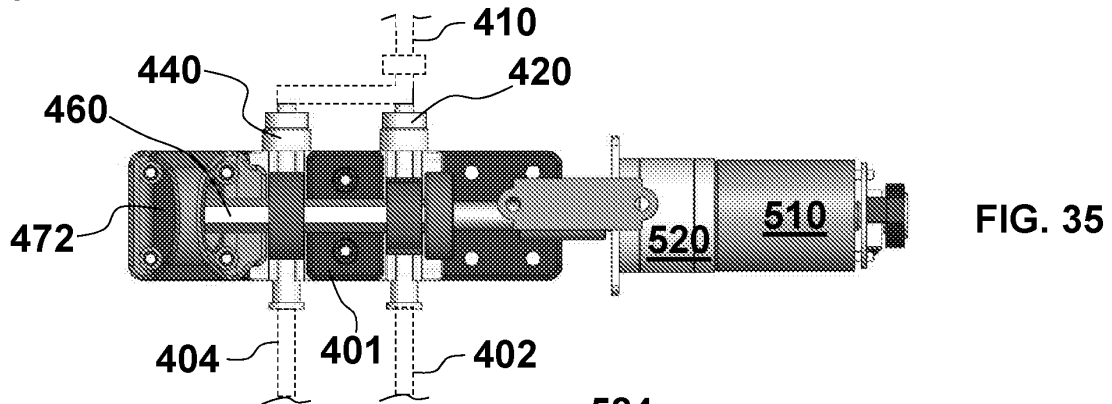
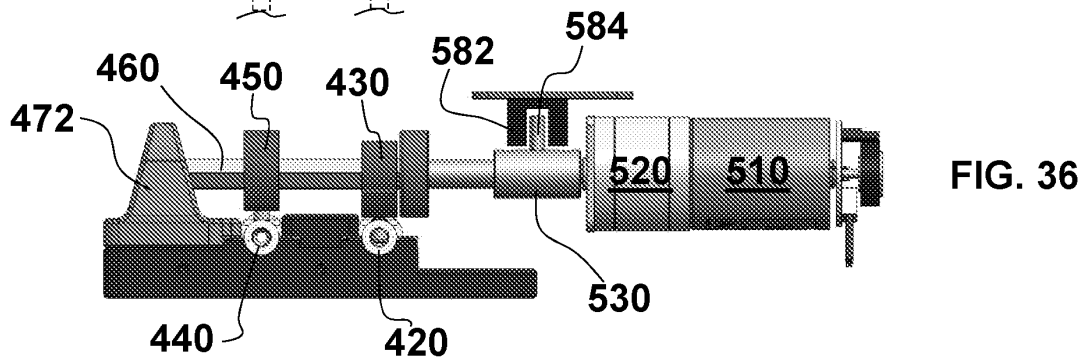
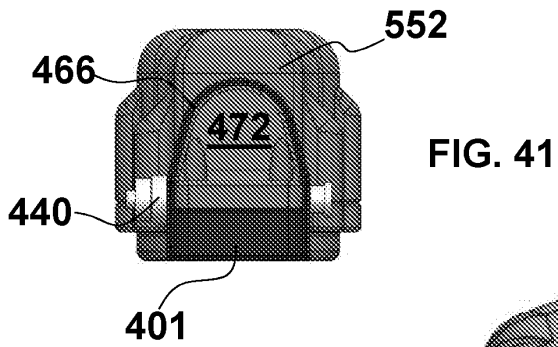
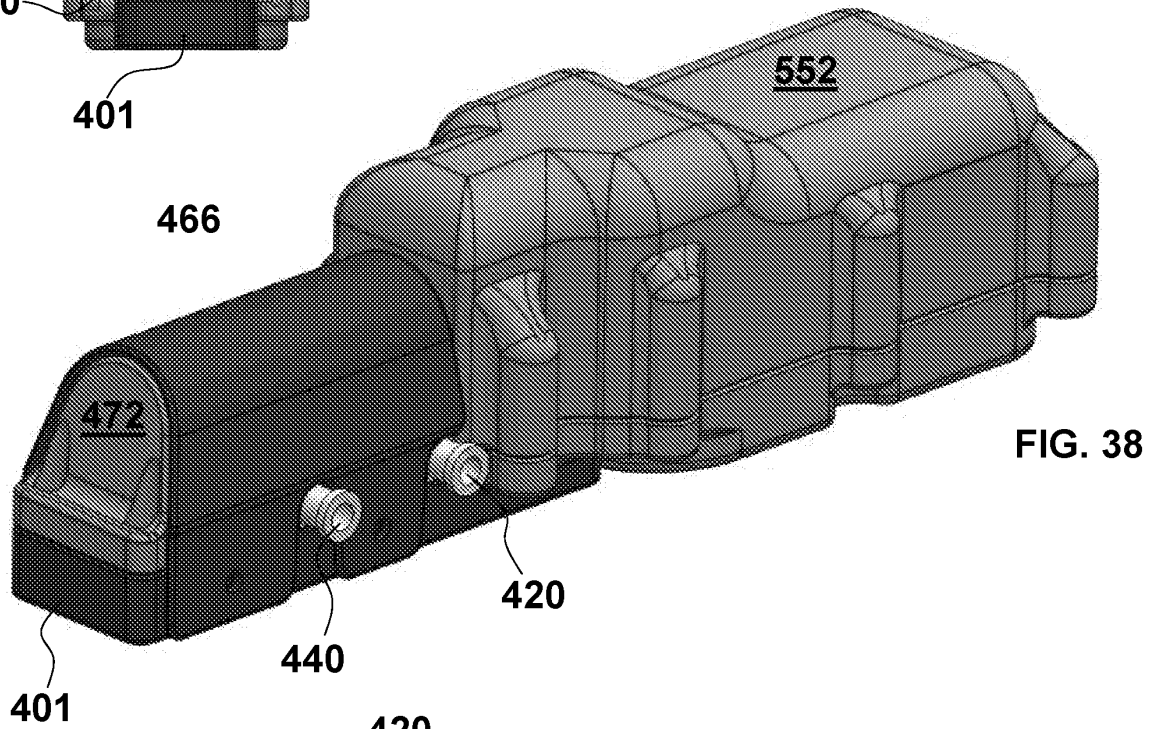
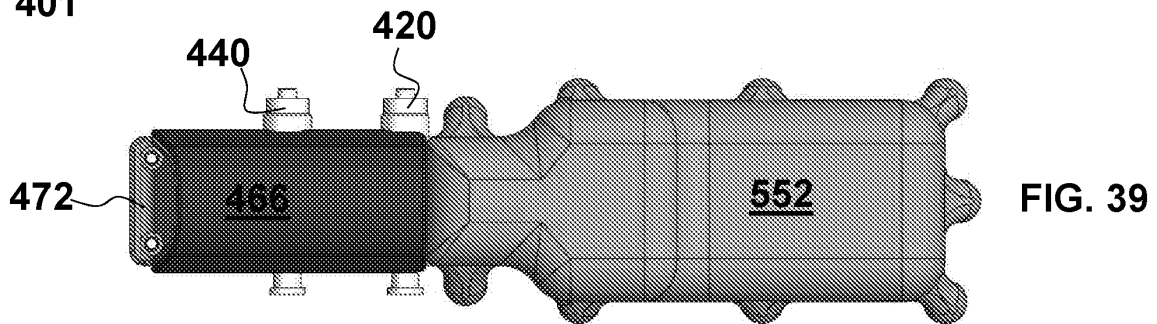
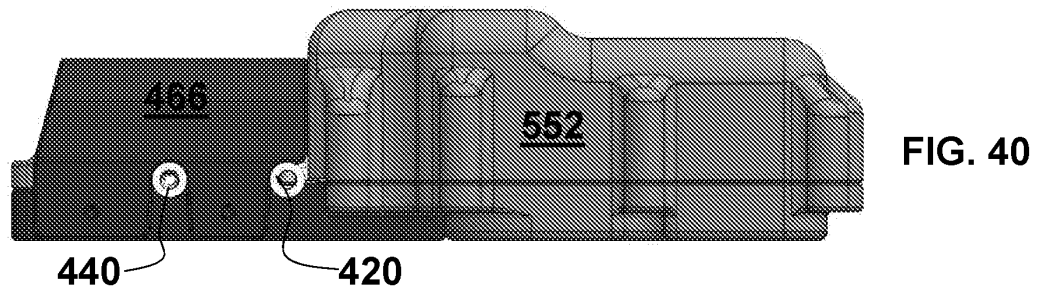


FIG. 30







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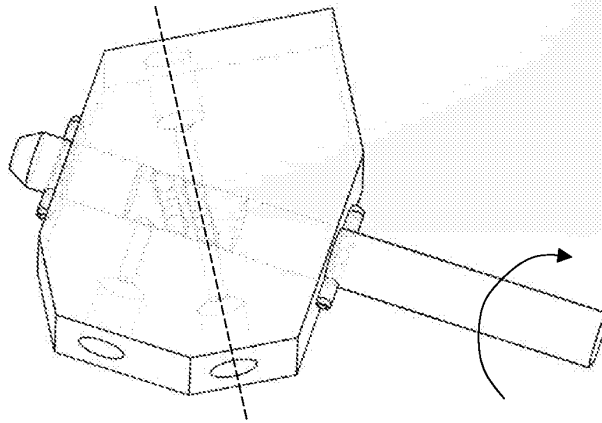


FIG. 42

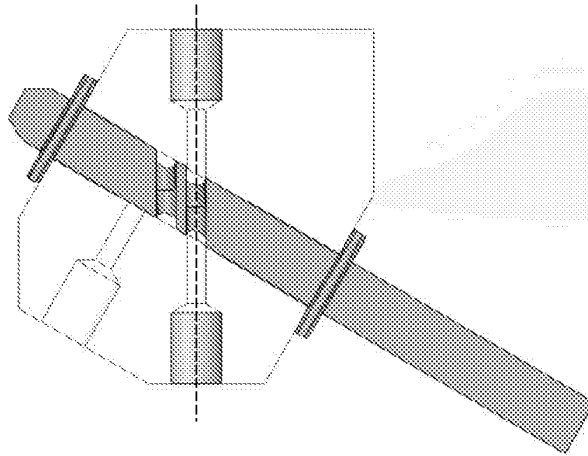


FIG. 43

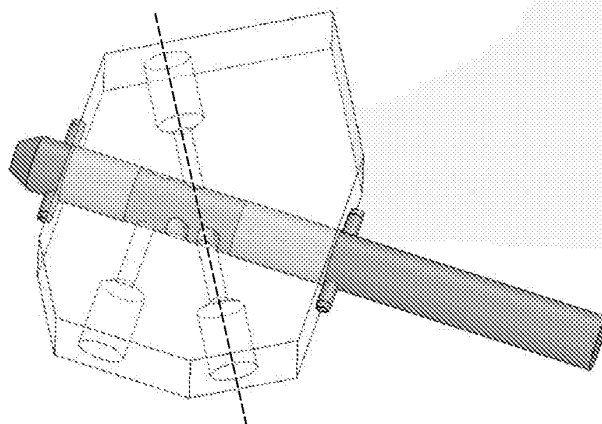


FIG. 44

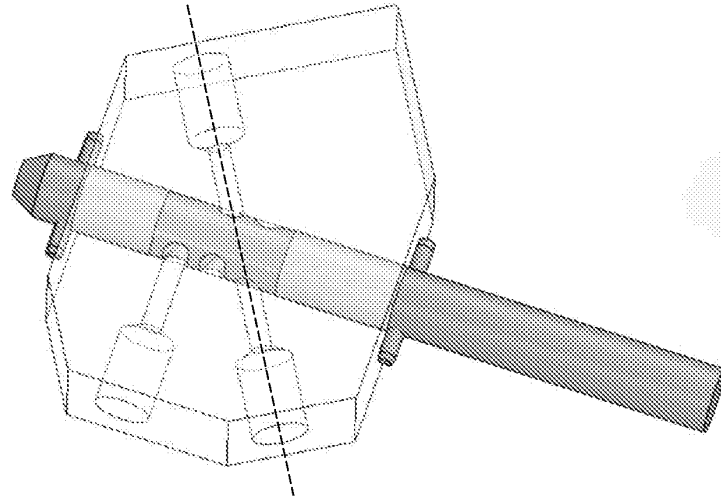


FIG. 45

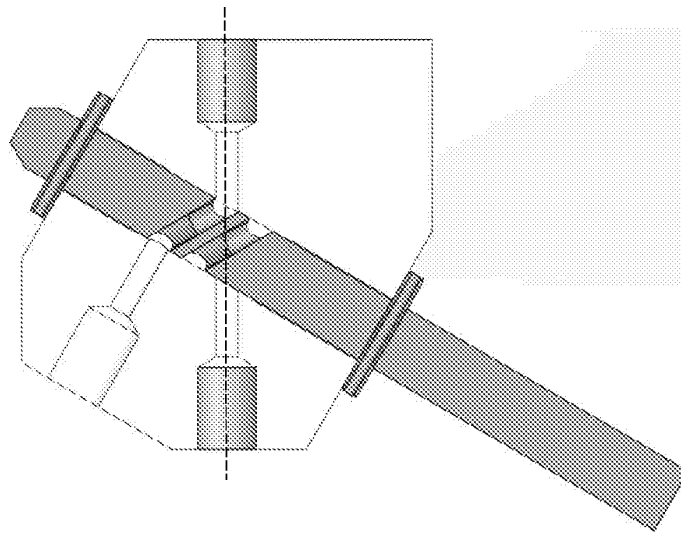


FIG. 46

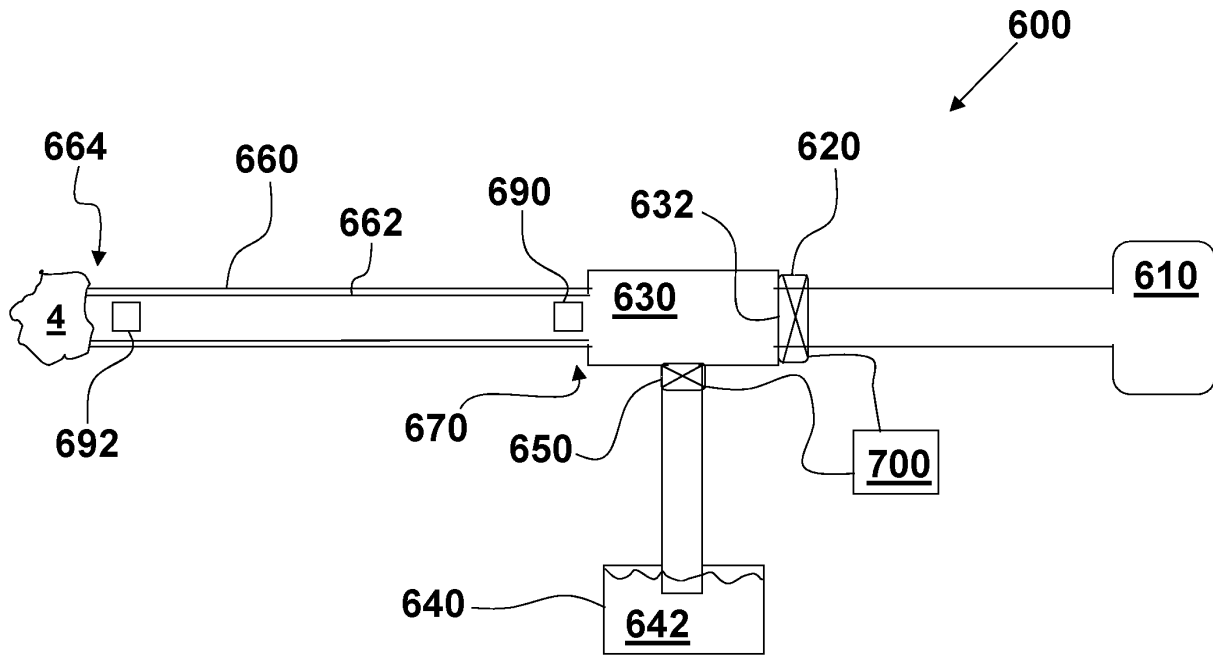


FIG. 47

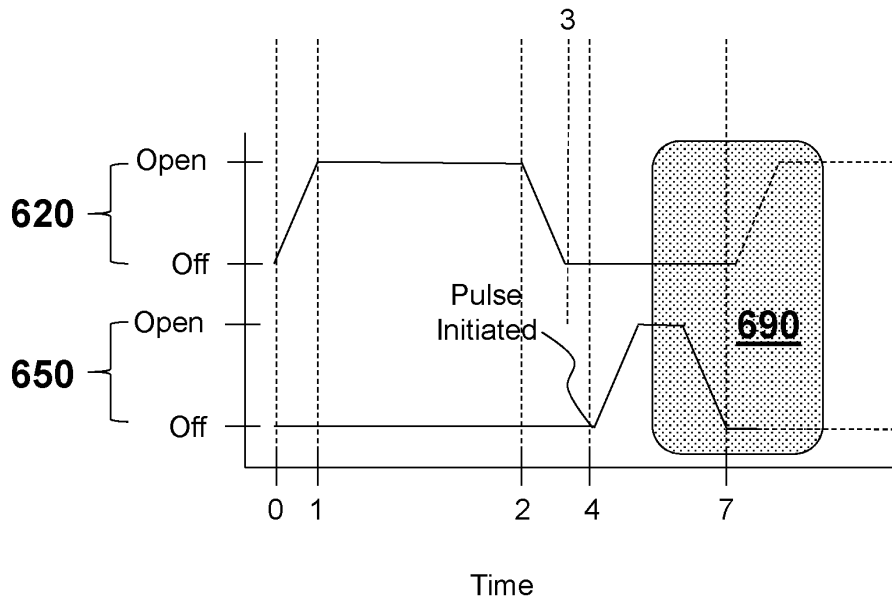
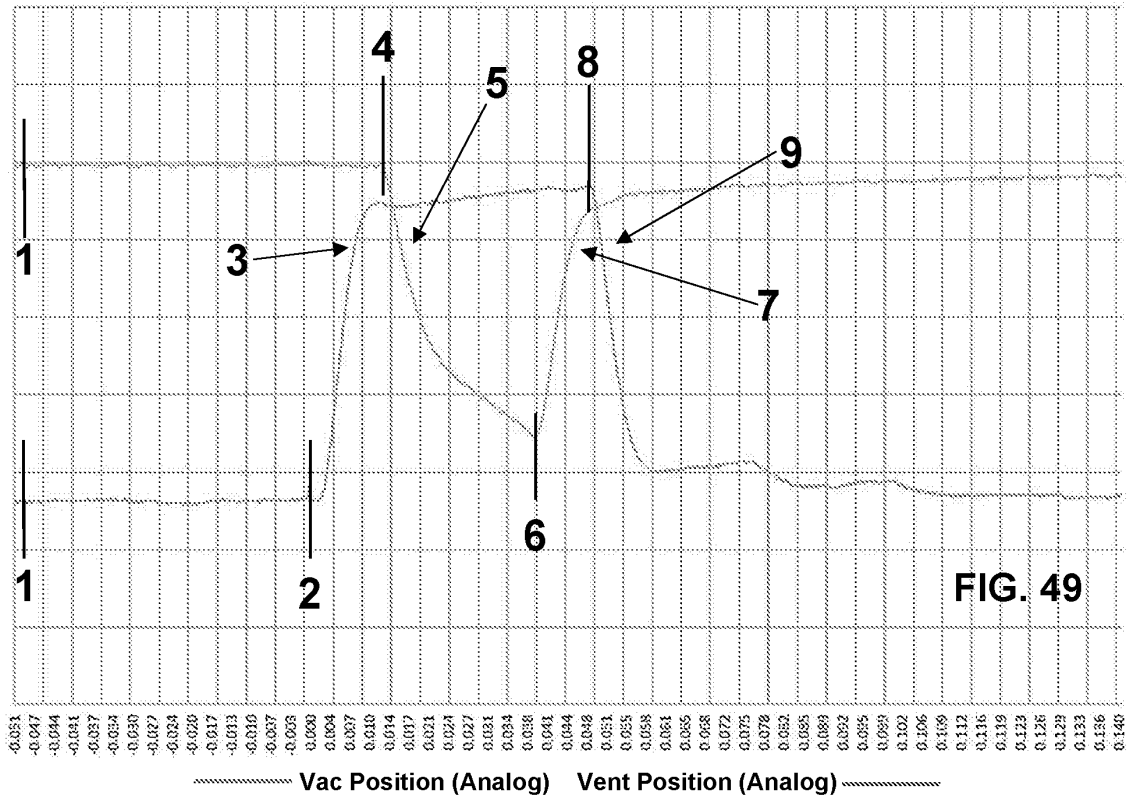
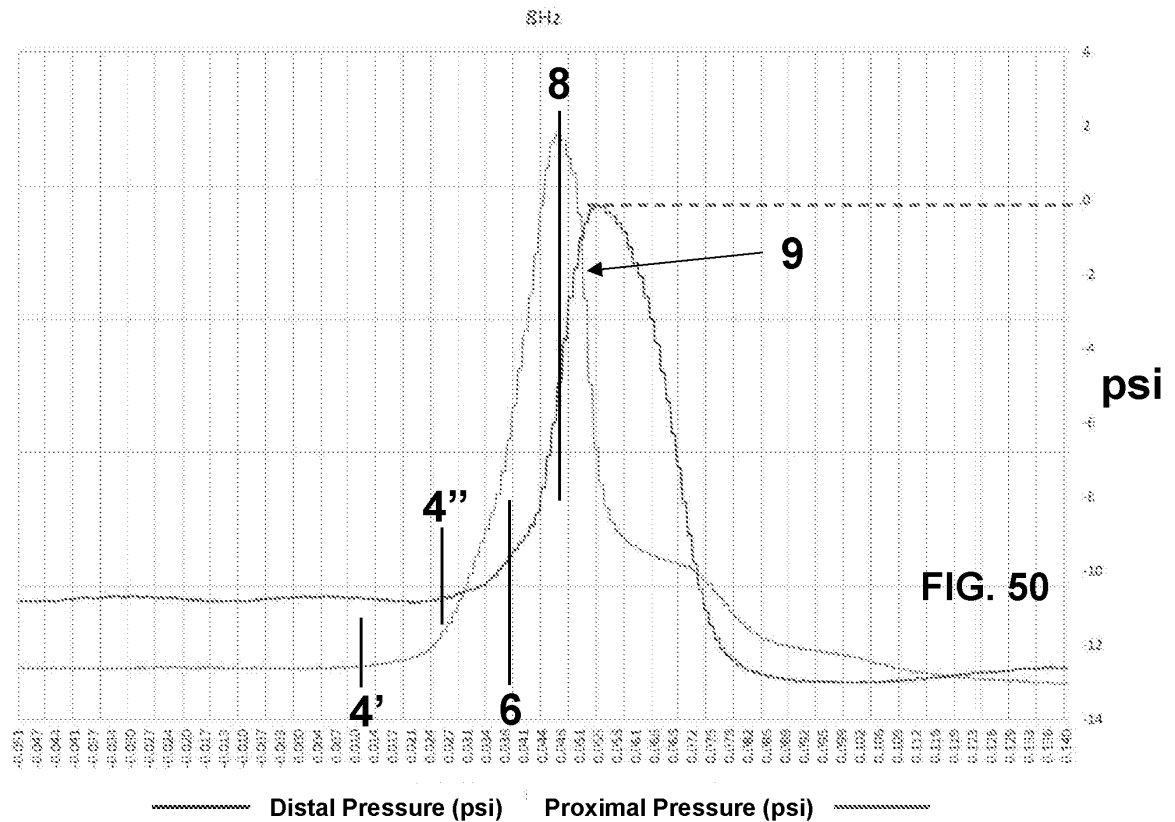


FIG. 48

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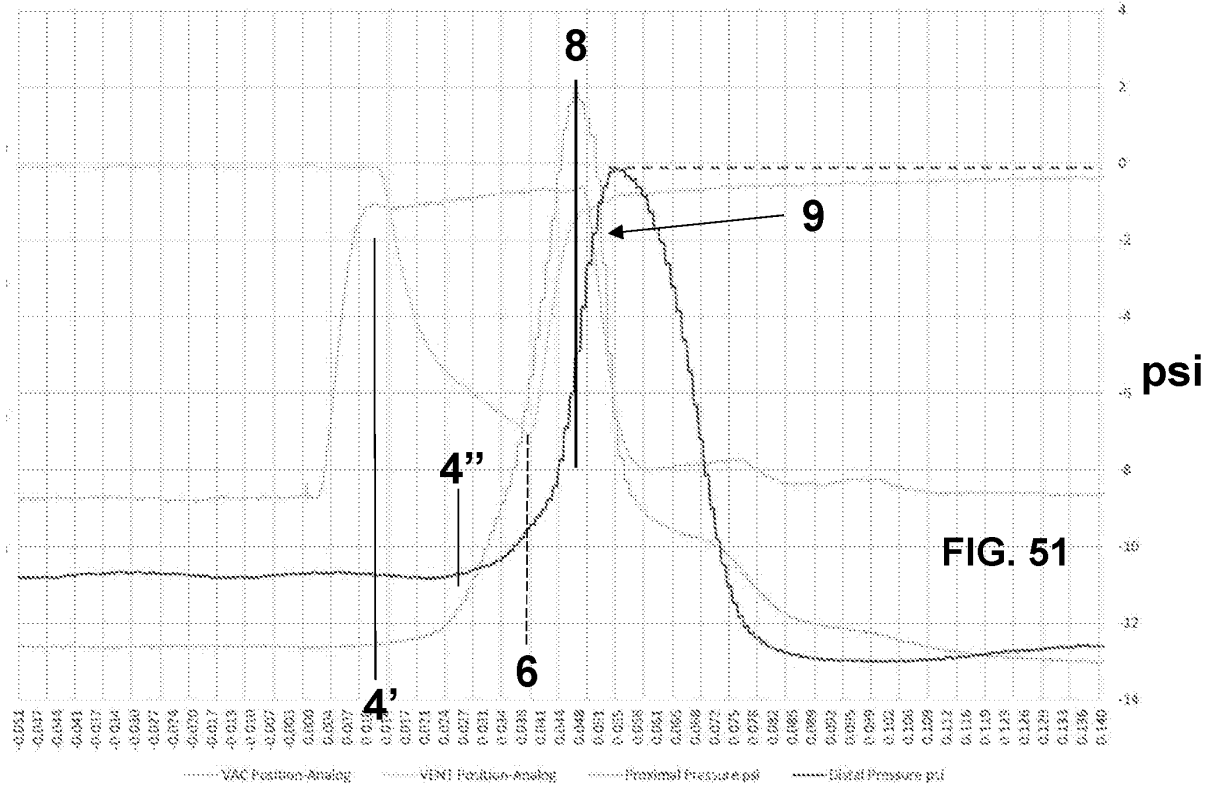
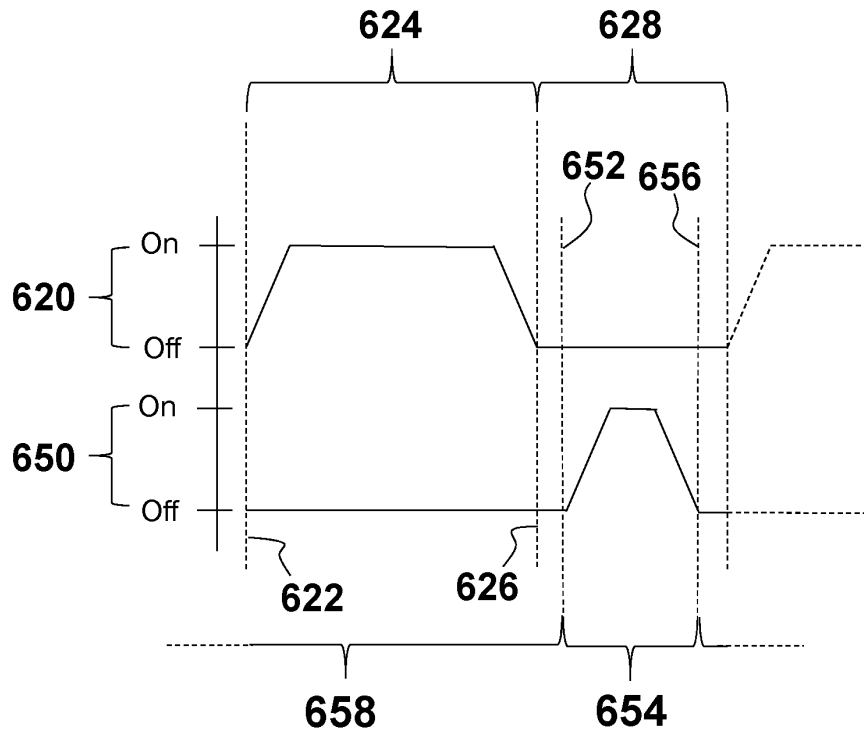
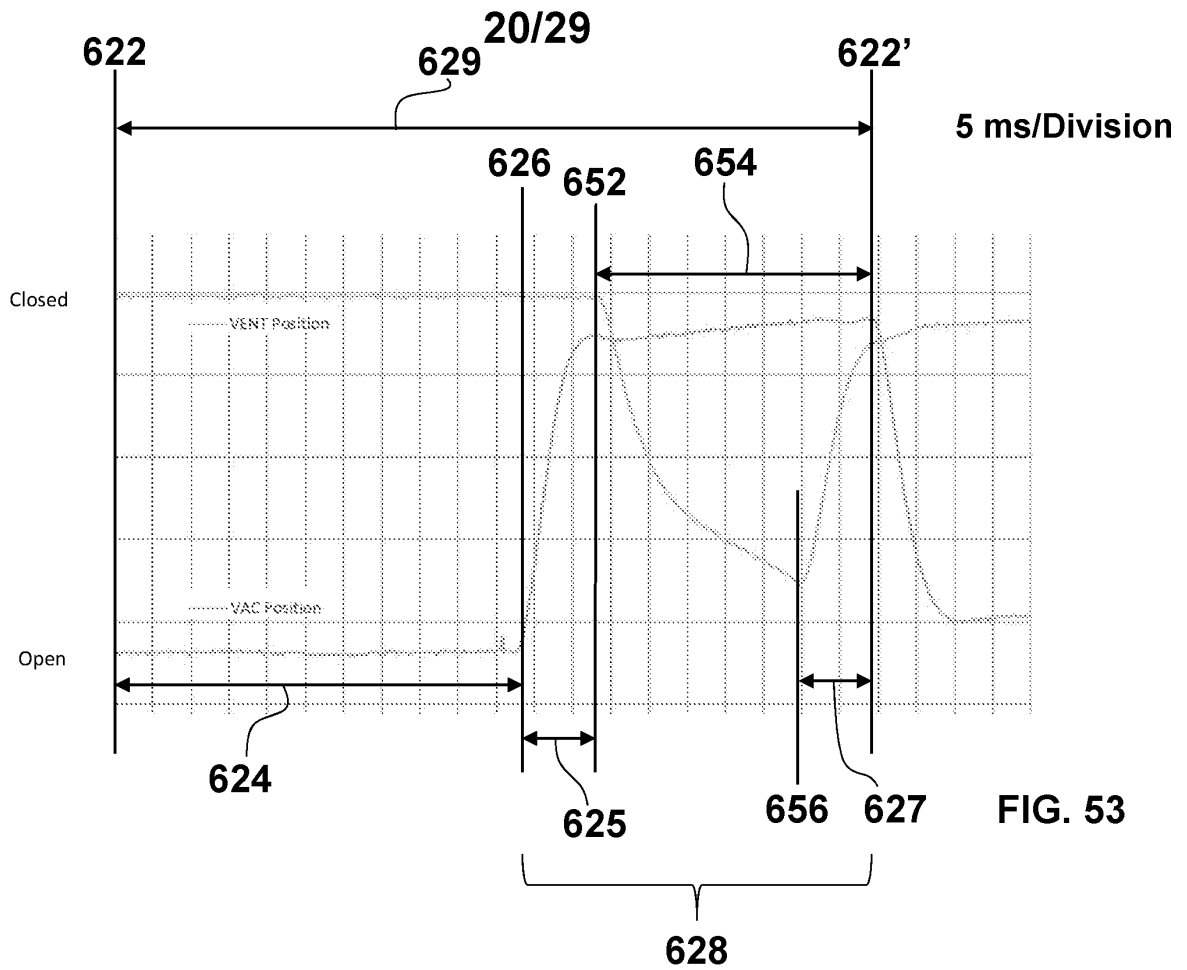
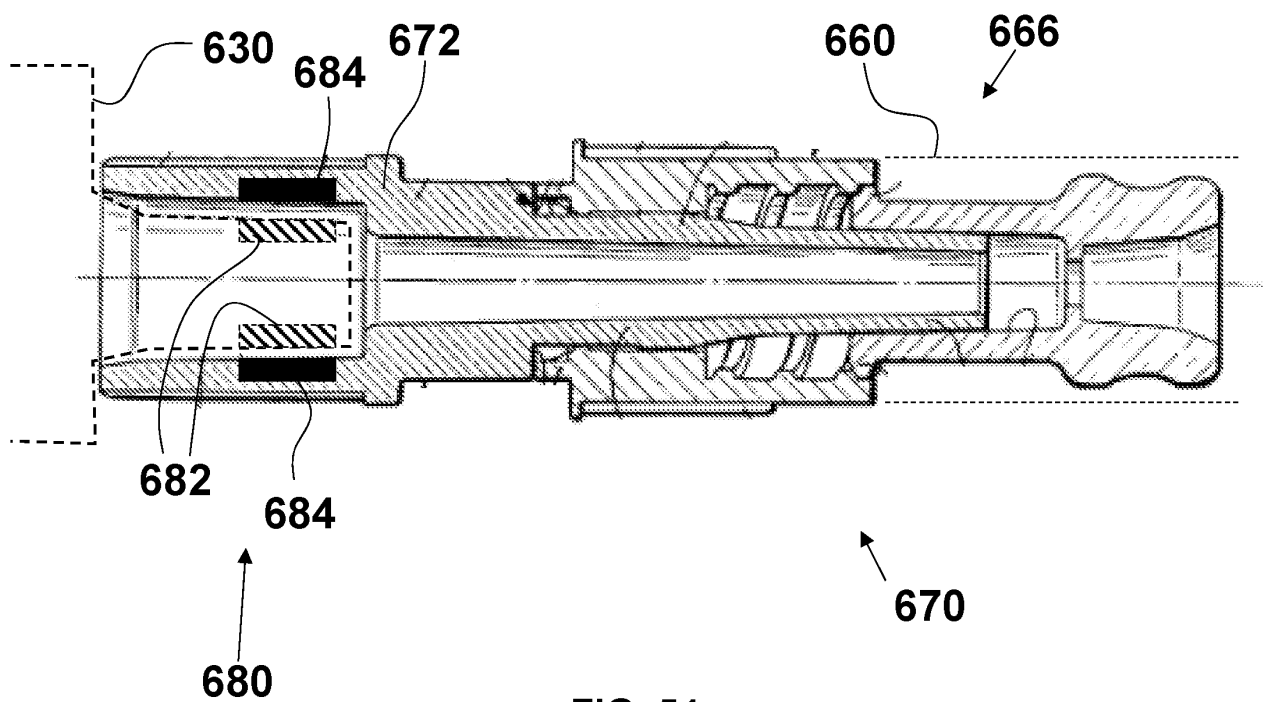


FIG. 52



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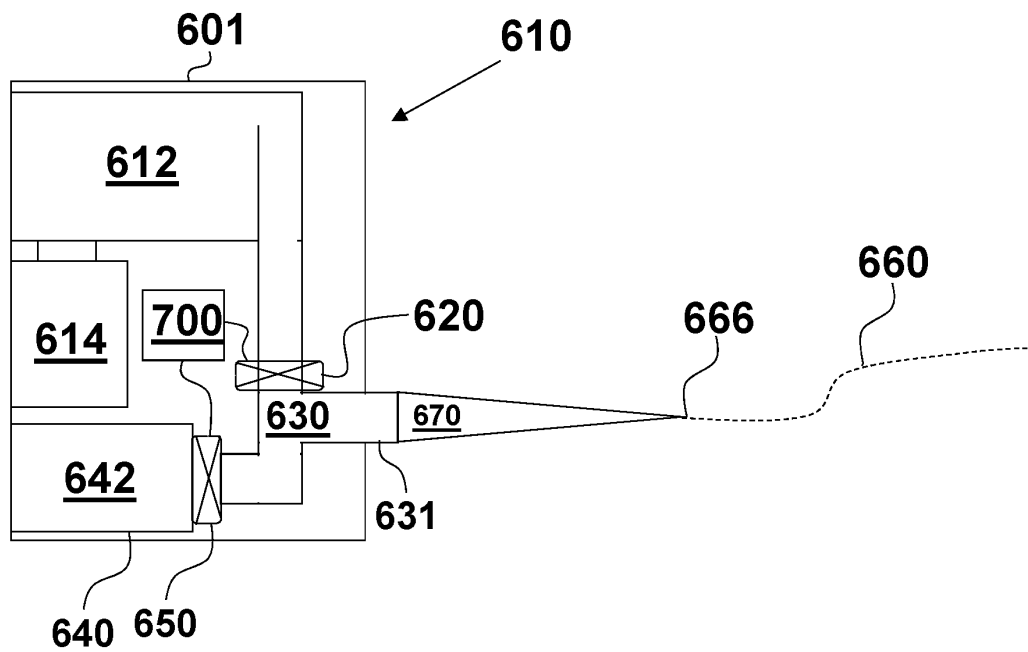


FIG. 55

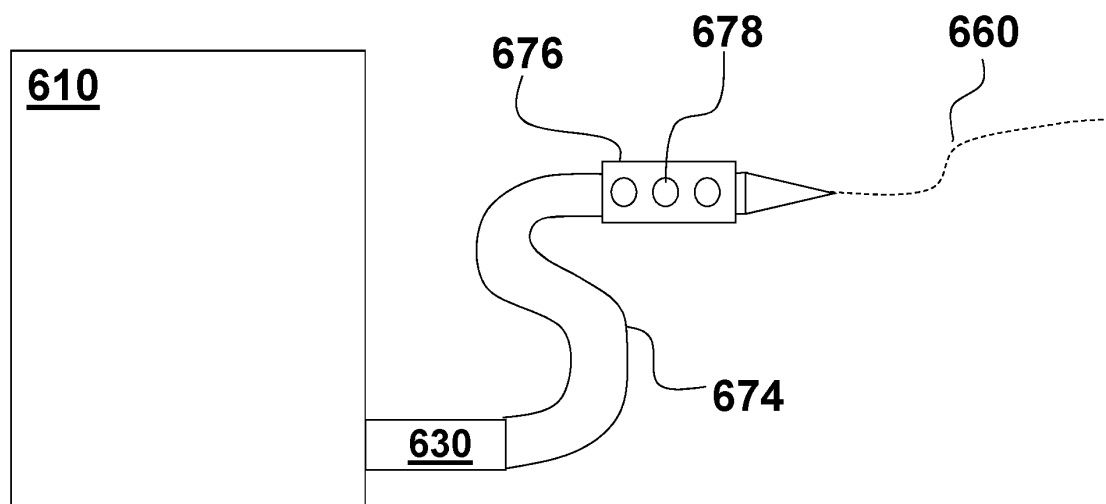


FIG. 56

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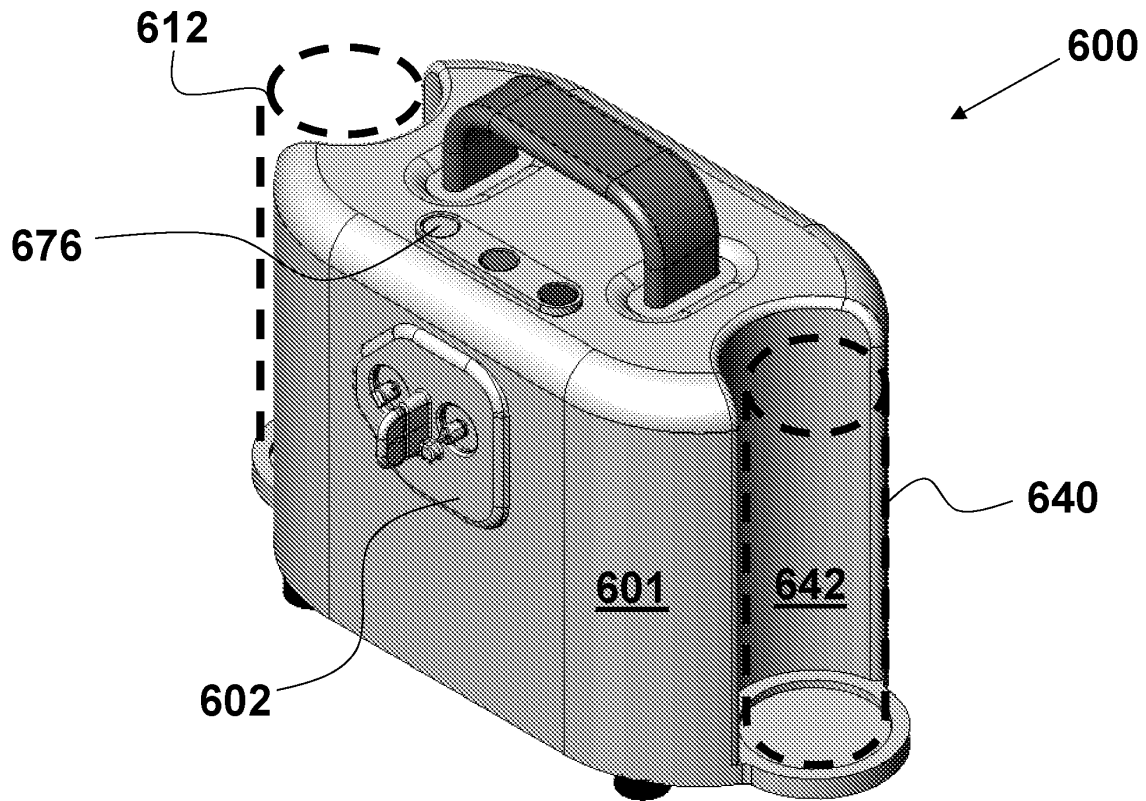


FIG. 57

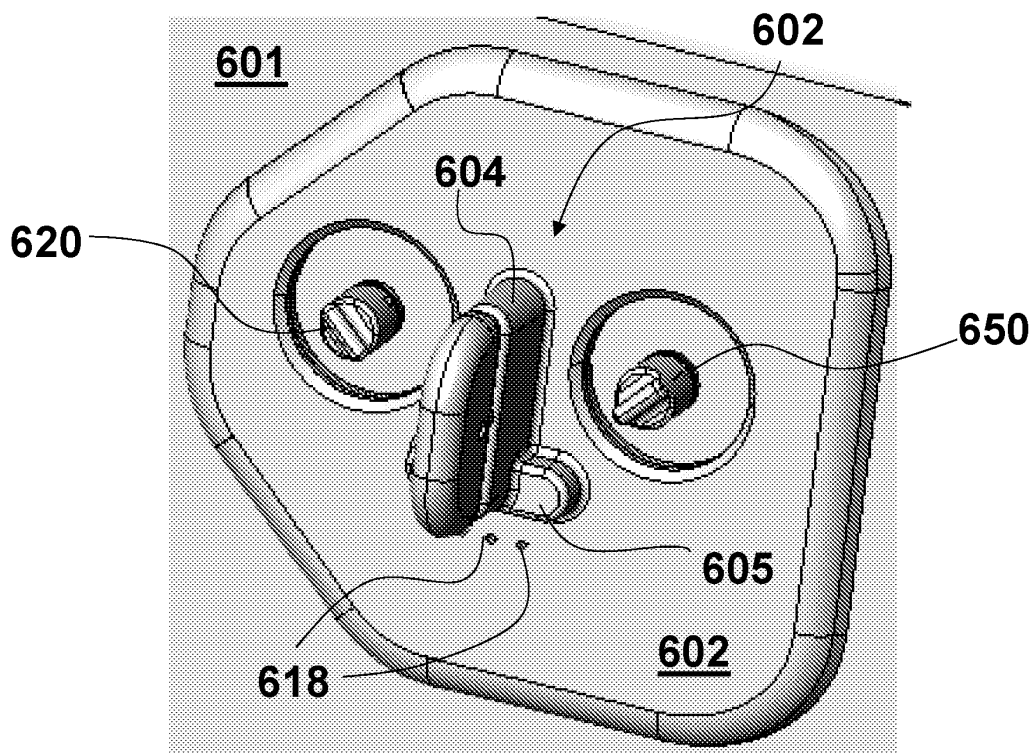


FIG. 58

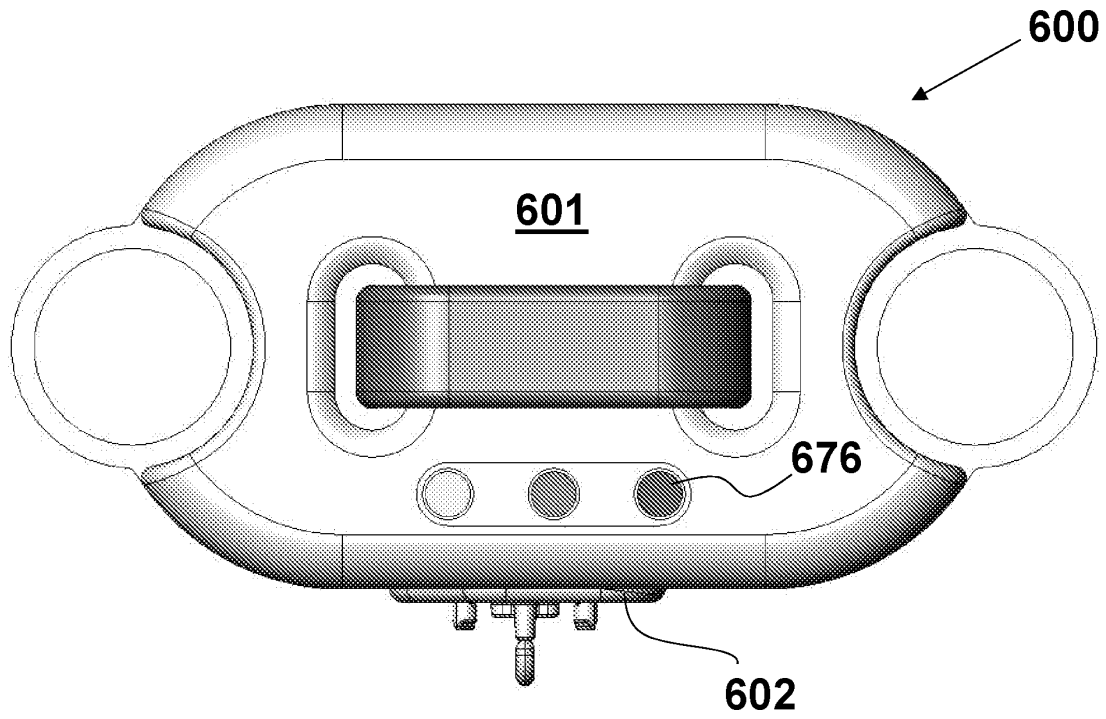


FIG. 59

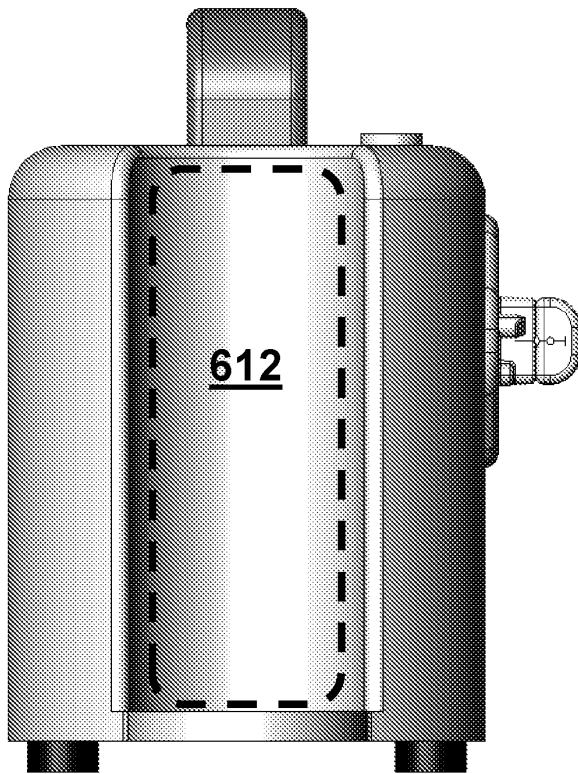


FIG. 60

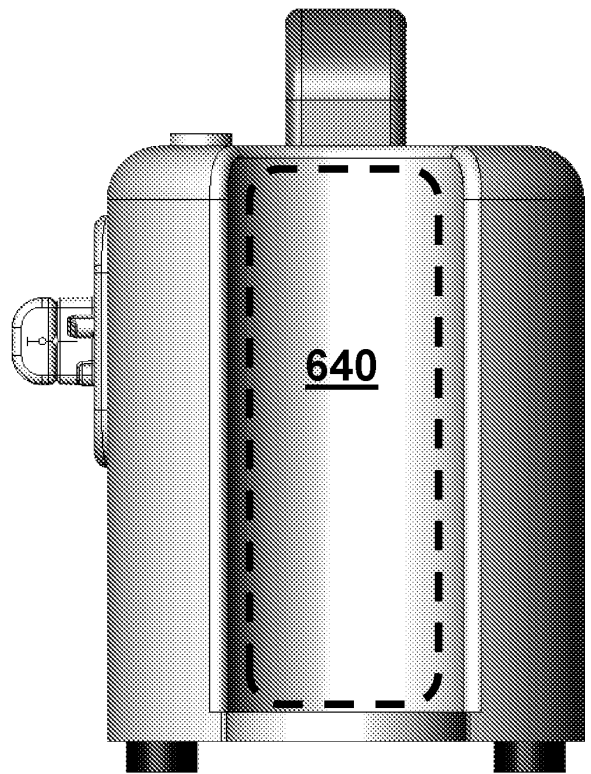


FIG. 61

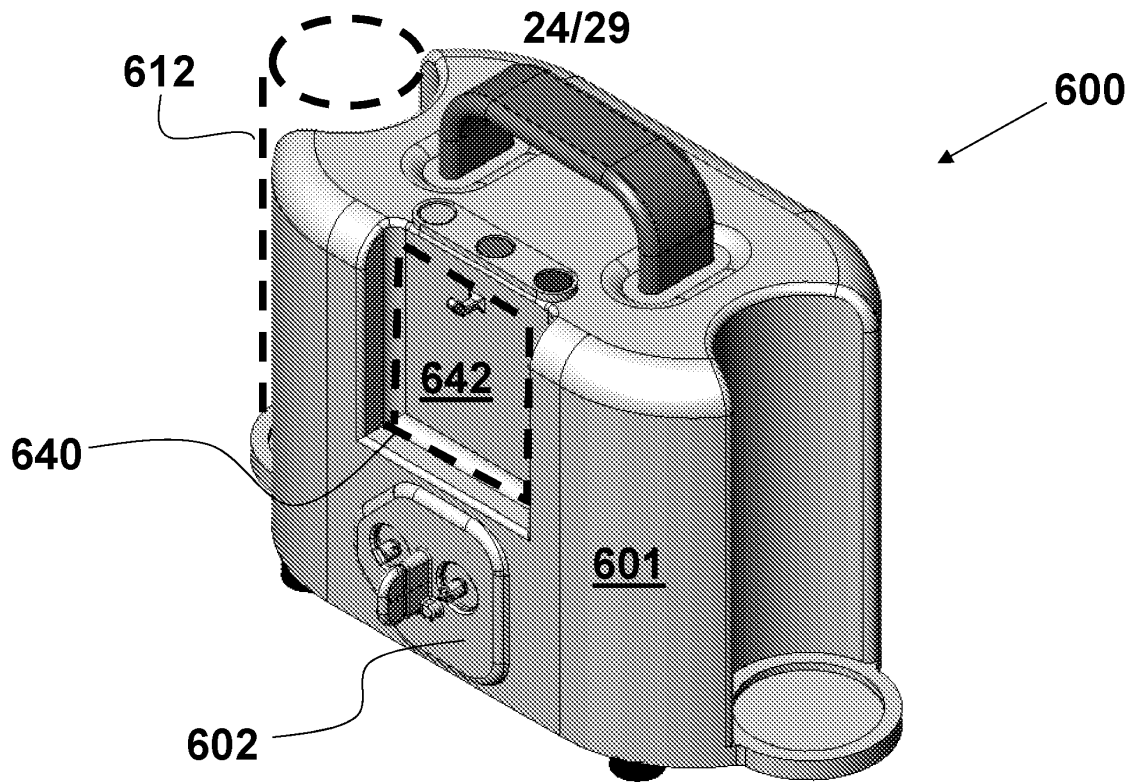


FIG. 62

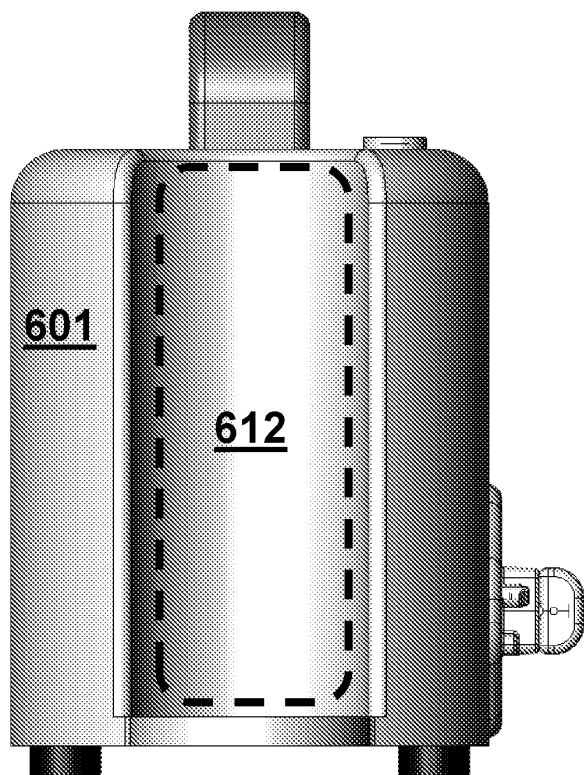


FIG. 63

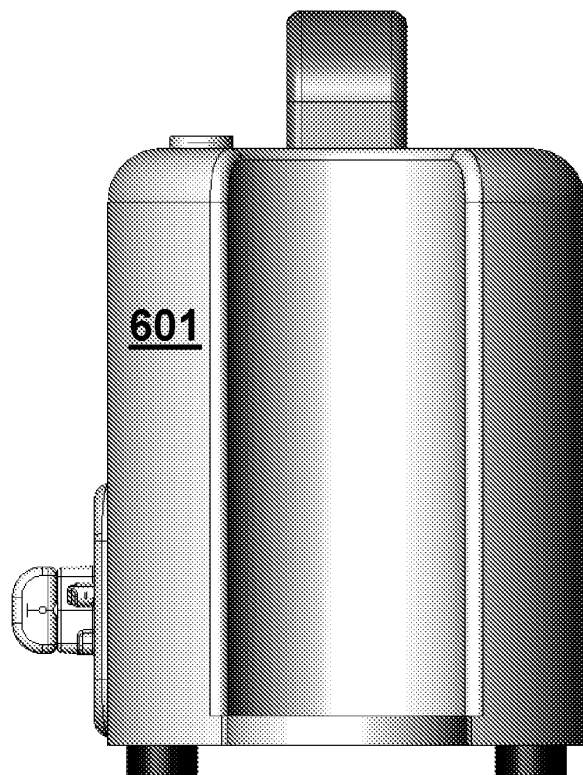


FIG. 64

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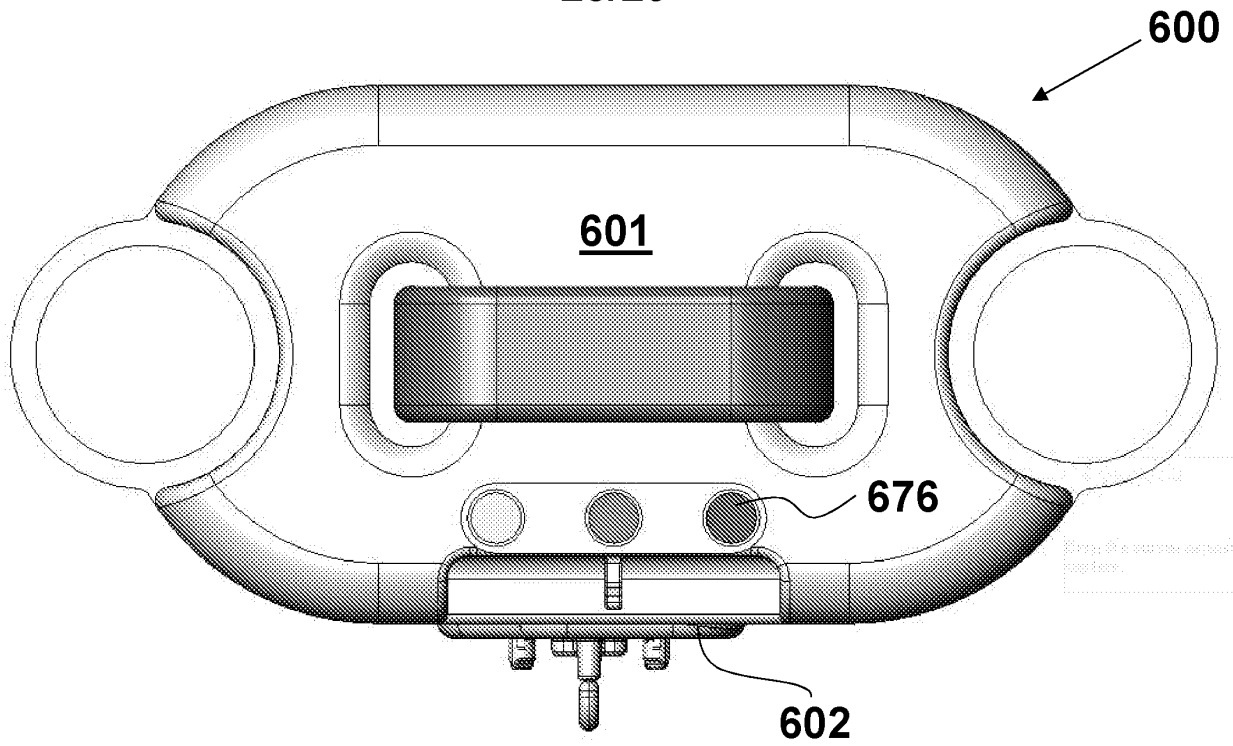


FIG. 65

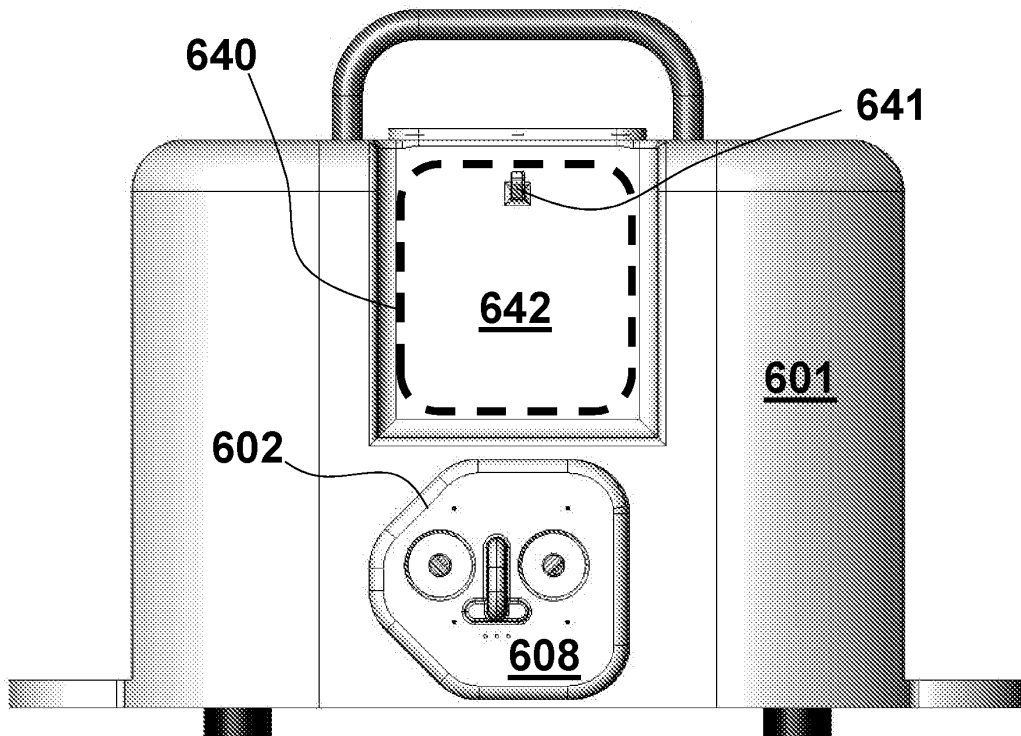


FIG. 66

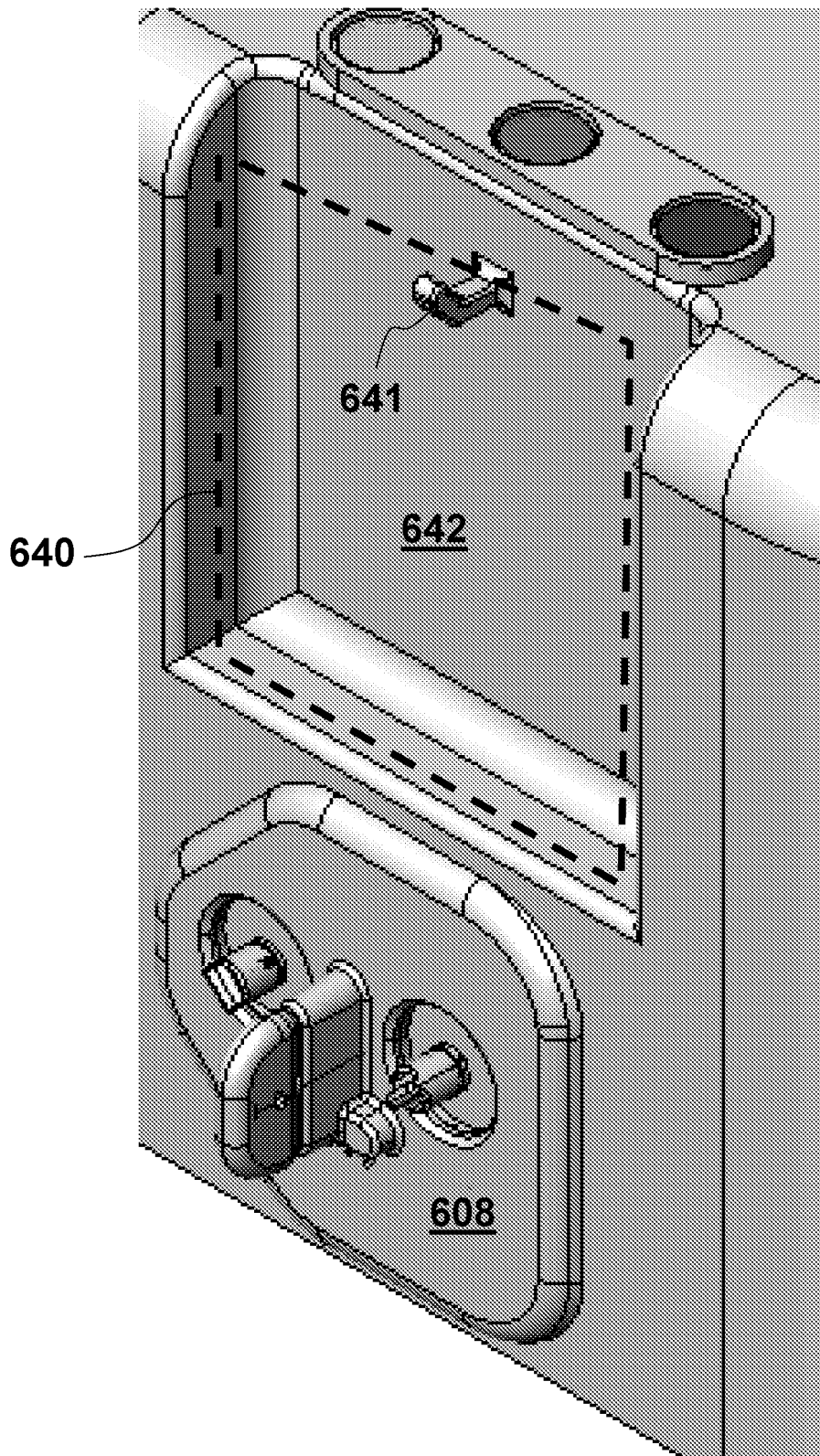


FIG. 67

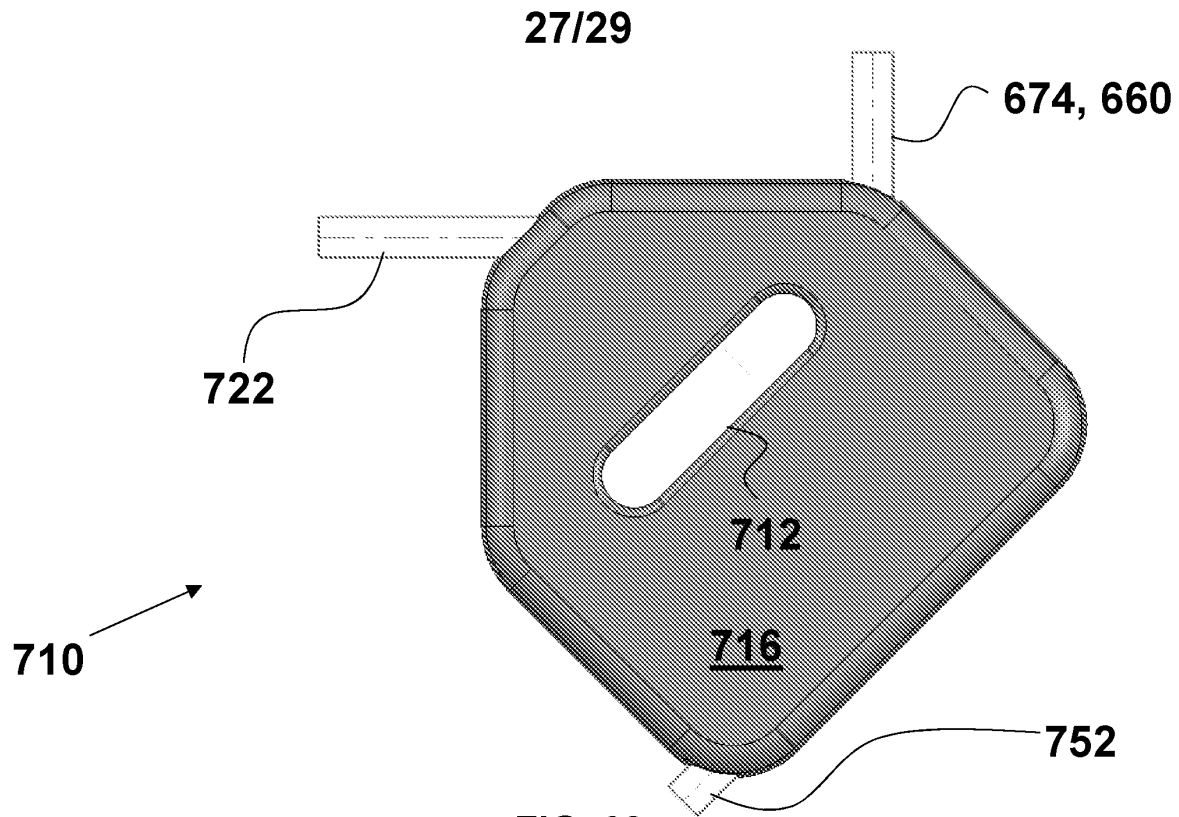


FIG. 68

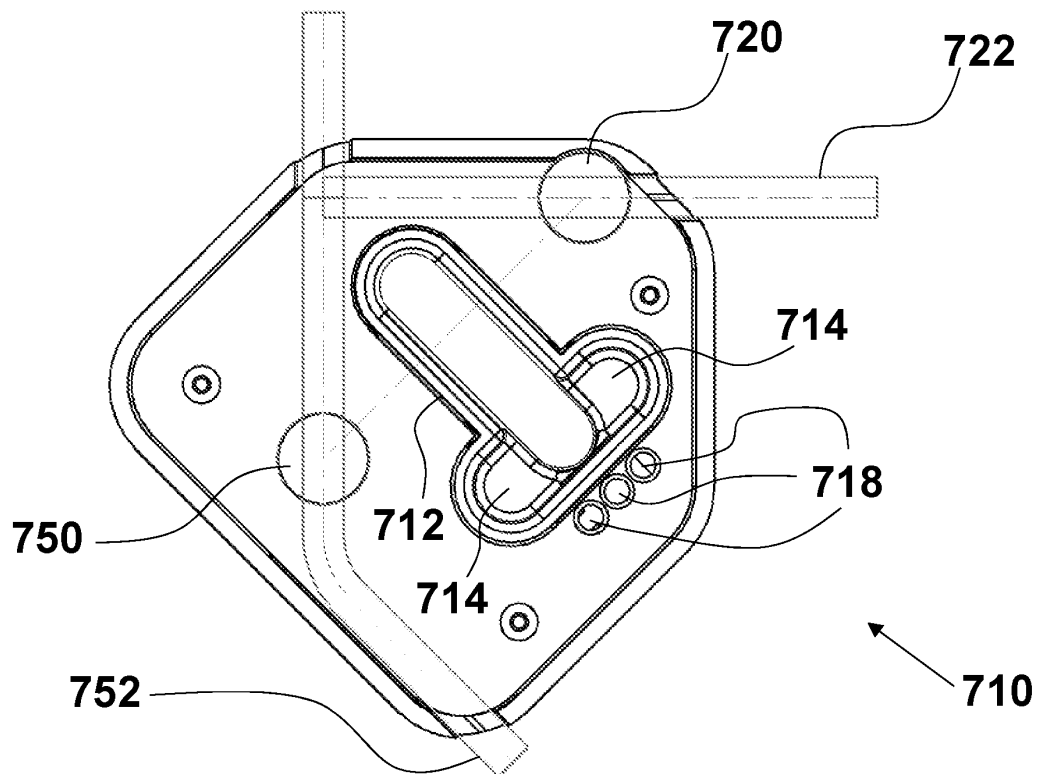


FIG. 69

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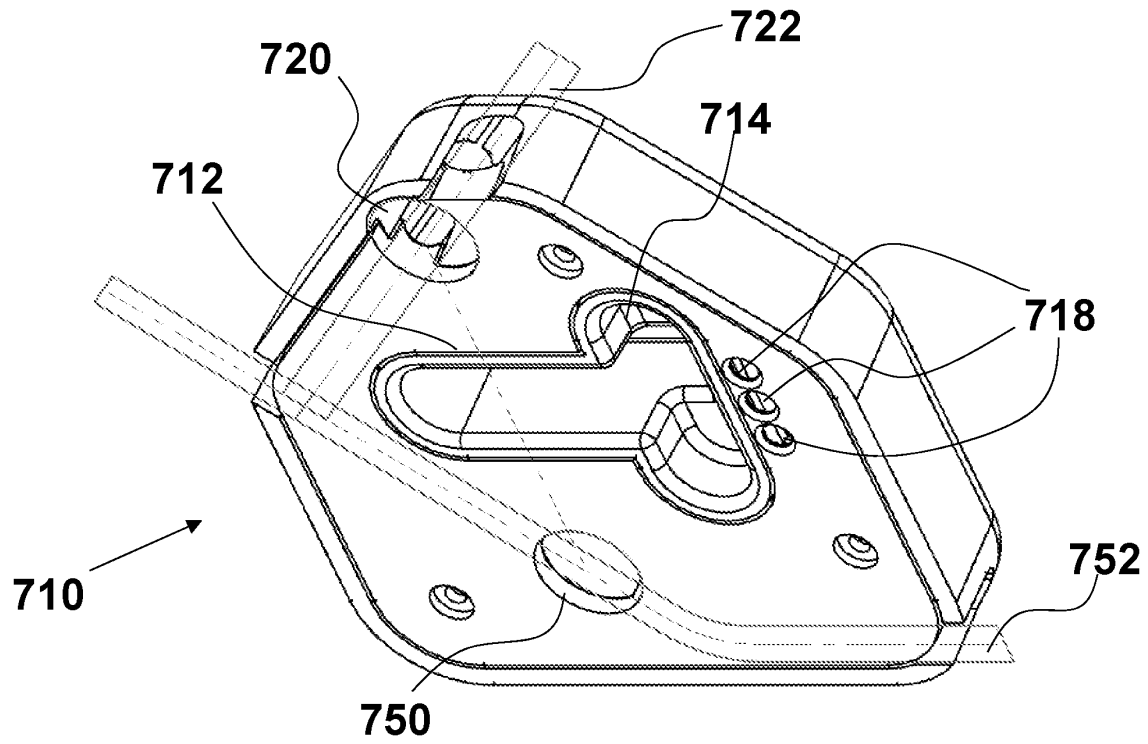


FIG. 70

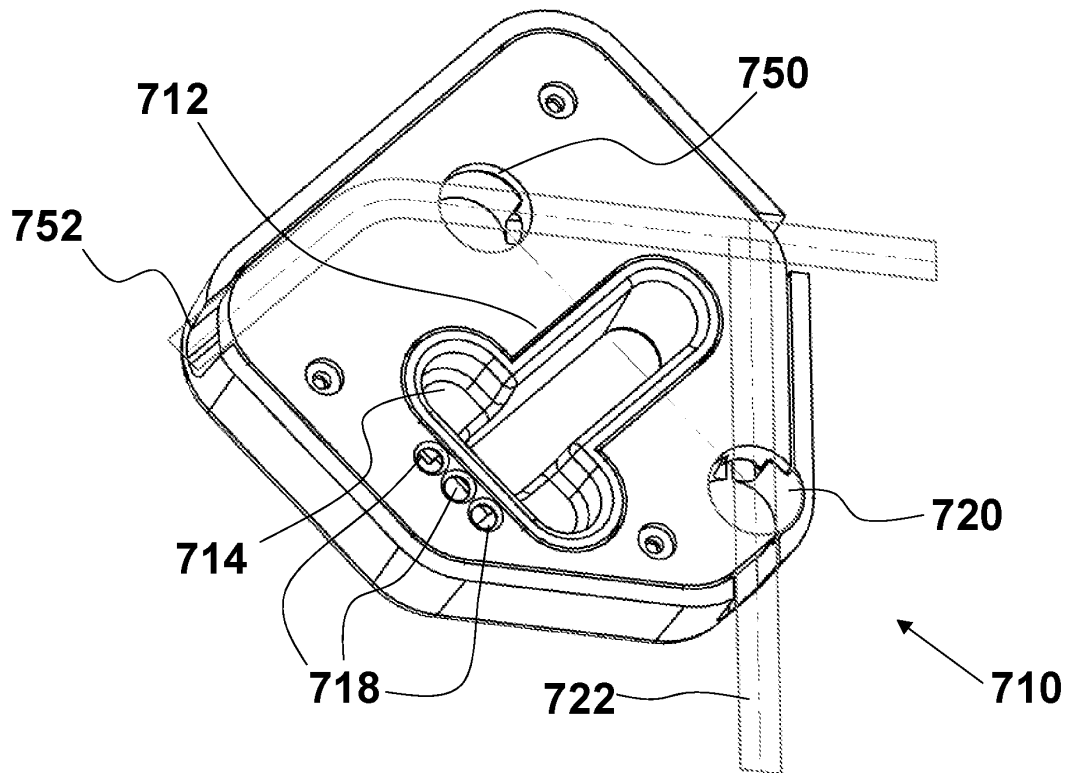
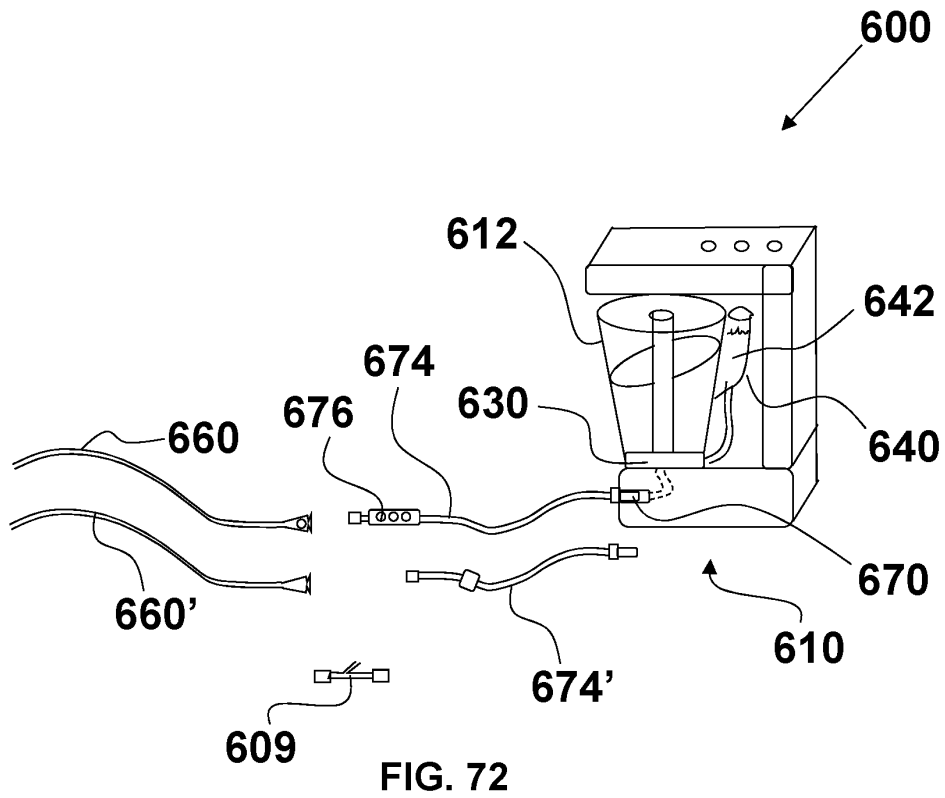


FIG. 71



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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): 7/15/19

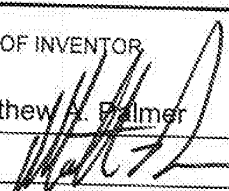
Signature: [Signature]

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.

This collection of information is required by 35 U.S.C. 115 and 37 CFR 1.63. 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 1 minute 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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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
<p>As the below named inventor, I hereby declare that:</p> <p>This declaration is directed to: ☒ The attached application, or ☐ United States application or PCT international application number _____ filed on _____</p> <p>The above-identified application was made or authorized to be made by me.</p> <p>I believe that I am the original inventor or an original joint inventor of a claimed invention in the application.</p> <p>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.</p> <p style="text-align: center;">WARNING:</p> <p>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.</p> <p>LEGAL NAME OF INVENTOR</p> <p>Inventor: <u>Matthew A. Palmer</u> Date (Optional): <u>7-12-19</u></p> <p>Signature: <u></u></p> <p>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.</p>	

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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.

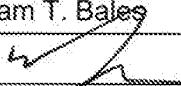
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LEGAL NAME OF INVENTOR

Inventor: William T. Bales Date (Optional): 07/15/2019

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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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.

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WARNING:

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LEGAL NAME OF INVENTOR

Inventor: M. Sean McBrayer Date (Optional): 7/12/19
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
<p>As the below named inventor, I hereby declare that:</p> <p>This declaration is directed to: ☒ The attached application, or ☐ United States application or PCT international application number _____ filed on _____</p> <p>The above-identified application was made or authorized to be made by me.</p> <p>I believe that I am the original inventor or an original joint inventor of a claimed invention in the application.</p> <p>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.</p> <p style="text-align: center;">WARNING:</p> <p>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.</p> <p>LEGAL NAME OF INVENTOR</p> <p>Inventor: <u>Eric Petersen</u> Date (Optional): <u>7/12/19</u></p> <p>Signature: <u><i>Eric Petersen</i></u></p> <p>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.</p>	

This collection of information is required by 35 U.S.C. 115 and 37 CFR 1.63. This 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 1 minute 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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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:**

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LEGAL NAME OF INVENTORInventor: **Richard Cartledge**

Date (Optional): _____

Signature: _____

Note: An application data sheet (PTO/SF/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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**ASPIRATION THROMBECTOMY SYSTEM AND METHODS FOR THROMBUS REMOVAL WITH
ASPIRATION CATHETER**

Abstract of the Disclosure

A thrombectomy removal system includes 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. The vacuum source and the vent source are respectively fluidically connected to the vacuum and vent valves. A manifold connects the proximal portion to the vacuum and vent sources through the valves. Control of the valves prevents forward flow of the distal portion out from the distal end during each cycle. Each cycle can have states including vacuum-only, first double-closed, vent-only, and second double-closed. A time of the double-closed states can be no greater than 30 ms.

CLAIMS

What is claimed is:

1. 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.

2. The system according to claim 1, wherein 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.

3. The system according to claim 2, wherein a time of the double-closed state is no greater than 30 ms.

4. The system according to claim 1, wherein 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.

5. The system according to claim 4, wherein a time of the vent-only state is no greater than 50 ms.

6. The system according to claim 1, wherein 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.

7. The system according to claim 6, 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.

8. The system according to claim 6, wherein a period of the cycle is between approximately 6 Hz and approximately 16 Hz.

9. The system according to claim 6, wherein a period of the cycle is between approximately 8 Hz and 12 Hz.

10. The system according to claim 1, wherein the change in the level of vacuum at the distal end is greater than approximately 15 inHg in no greater than approximately 50 ms.

11. The system according to claim 1, wherein 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

12. The system according to claim 1, wherein the change in the level of vacuum at the distal end is greater than approximately 25 inHg and no greater than approximately 20 ms.

13. The system according to claim 1, wherein:

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.

14. 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 cyclically open and close the vacuum valve and the vent valve at a frequency of between 2 and 16 Hz.

15. The system according to claim 1, wherein 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.

16. The system according to claim 1, wherein 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.

17. The system according to claim 1, which further comprises a shaft and the vacuum valve and the vent valve are mounted together on the shaft.

18. 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.

19. 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

20. 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.

APPLICATION
FOR
UNITED STATES LETTERS PATENT

TITLE OF INVENTION

ASPIRATION THROMBECTOMY SYSTEM AND METHODS FOR
THROMBUS REMOVAL WITH ASPIRATION CATHETER

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CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] This application claims the priority, under 35 U.S.C. § 119, of copending U.S. Provisional Patent Application Nos. 62/701,086, filed July 20, 2018, and 62/750,011, filed October 24, 2018; the prior applications are herewith incorporated by reference herein in their entirety.

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 coked or coking. 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] 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.

[0060] 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.

[0061] 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

[0062] 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:

[0063] FIG. 1 is a fragmentary, perspective view of an exemplary embodiment of a controller for a thrombectomy aspiration catheter in an unactuated state;

[0064] FIG. 2 is a fragmentary, perspective, longitudinal cross-sectional view of the controller of FIG. 1;

[0065] FIG. 3 is an enlarged, diagrammatic, side elevational view of a compression cam assembly of the controller of FIG. 1;

[0066] FIG. 4 is a fragmentary, longitudinal cross-sectional view of the controller of FIG. 1 with a compression roller removed;

[0067] FIG. 5 is a fragmentary, longitudinal cross-sectional view of the controller of FIG. 1 in an actuated state;

[0068] FIG. 6 is a fragmentary, enlarged, perspective view of a portion of an extrusion compressor of the controller of FIG. 1;

[0069] FIG. 7 is a fragmentary, perspective view of the controller of FIG. 1 in the actuated state;

[0070] FIG. 8 is a fragmentary, perspective and partially longitudinal cross-sectional view of the controller of FIG. 7;

[0071] 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;

[0072] FIG. 10 is a fragmentary, longitudinal cross-sectional view of the controller of FIG.

[0073] 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;

[0074] FIG. 12 is a fragmentary, longitudinal cross-sectional view of the controller of FIG. 11;

[0075] FIG. 13 is a longitudinal cross-sectional view of the controller of FIG. 9 with the compression roller and the aspiration catheter removed;

[0076] 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;

[0077] 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;

[0078] 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;

[0079] 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;

[0080] 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;

[0081] 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;

[0082] FIG. 20 is a fragmentary, enlarged, perspective view of the controller and thrombus trap of FIG. 18;

[0083] FIG. 21 is a fragmentary, perspective and longitudinal cross-sectional view of the controller of FIG. 16, and the thrombus trap of FIG. 18;

[0084] FIG. 22 is a fragmentary, longitudinal cross-sectional view of an exemplary embodiment of a volume changing controller;

[0085] FIG. 23 is a vacuum circuit diagram of an exemplary embodiment of a vacuum booster and vacuum booster control device;

[0086] FIG. 24 is a cycle flow diagram of the operation of exemplary embodiments of the controller with the vacuum booster and the thrombus trap;

[0087] 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;

[0088] 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;

[0089] FIG. 27 is an elevational view of a proximal side of the aspiration thrombectomy system of FIG. 25;

[0090] FIG. 28 is an elevational view of a bearing side of the aspiration thrombectomy system of FIG. 25;

[0091] 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;

[0092] FIG. 30 is a longitudinally cross-sectional view of the aspiration thrombectomy system of FIG. 29;

[0093] 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;

[0094] 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;

[0095] 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;

[0096] FIG. 34 is a perspective view of the aspiration thrombectomy system of FIG. 25 with the motor assembly housing removed;

[0097] FIG. 35 is a top plan view of the aspiration thrombectomy system of FIG. 26 with the motor assembly housing removed;

[0098] FIG. 36 is an elevational view of the aspiration thrombectomy system of FIG. 27 with the motor assembly housing removed;

[0099] FIG. 37 is an elevational view of the bearing side of the aspiration thrombectomy system of FIG. 28 with the motor assembly housing removed;

[00100] FIG. 38 is a perspective view of the aspiration thrombectomy system of FIG. 25 with the cam housing;

[00101] FIG. 39 is a top plan view of the aspiration thrombectomy system of FIG. 26 with the cam housing;

[00102] FIG. 40 is an elevational view of the aspiration thrombectomy system of FIG. 27 with the cam housing;

[00103] FIG. 41 is an elevational view of the bearing side of the aspiration thrombectomy system of FIG. 28 with the cam housing;

[00104] 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;

[00105] FIG. 43 is a fragmentary, cross-sectional view of the valve of FIG. 42;

[00106] FIG. 44 is a fragmentary, partially hidden, perspective view of the valve of FIG. 42;

[00107] FIG. 45 is a fragmentary, partially hidden, perspective view of the valve of FIG. 42 in a second valve state;

[00108] FIG. 46 is a fragmentary, cross-sectional view of the valve of FIG. 45;

[00109] FIG. 47 is a diagrammatic, cross-sectional view of an exemplary embodiment of an aspiration thrombectomy system;

[00110] 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;

[00111] 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;

[00112] 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;

[00113] FIG. 51 is a graph illustrating the waveforms of FIG. 49 and 50 combined together in time;

[00114] 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;

[00115] 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;

[00116] FIG. 54 is a fragmentary, longitudinal cross-sectional view of a proximal manifold connector assembly for the system of FIG. 47;

[00117] FIG. 55 is a block diagram of an exemplary embodiment of a self-contained, aspiration thrombectomy system;

[00118] 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;

[00119] 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;

[00120] FIG. 58 is a fragmentary, perspective view of a cassette connection assembly of the system of FIG. 57;

[00121] FIG. 59 is a top plan view of the system of FIG. 57;

[00122] FIG. 60 is a left side elevational view of the system of FIG. 57;

[00123] FIG. 61 is a right side elevational view of the system of FIG. 57;

[00124] 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;

[00125] FIG. 63 is a left side elevational view of the system of FIG. 62;

[00126] FIG. 64 is a right side elevational view of the system of FIG. 62;

[00127] FIG. 65 is a top plan view of the system of FIG. 62;

[00128] FIG. 66 is a front elevational view of the system of FIG. 57;

[00129] FIG. 67 is a fragmentary, front perspective view of cassette connection assembly and the hanging vent liquid reservoir of the system of FIG. 57;

[00130] 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;

[00131] FIG. 69 is a bottom plan view of the valve cassette of FIG. 69;

[00132] FIG. 70 is a bottom perspective view of the valve cassette of FIG. 69;

[00133] FIG. 71 is a bottom perspective view of the valve cassette of FIG. 69; and

[00134] FIG. 72 is a diagrammatic illustrated of an exemplary embodiment of a self-contained, aspiration thrombectomy system.

DETAILED DESCRIPTION OF THE EMBODIMENTS

[00135] 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.

[00136] 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.

[00137] 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.

[00138] 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.

[00139] 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).

[00140] 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).

[00141] 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.

[00142] 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.

[00143] 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.

[00144] 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.

[00145] 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.

[00146] 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.

[00147] 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.

[00148] 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.

[00149] 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.

[00150] 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.

[00151] 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.

[00152] 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.

[00153] 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.

[00154] 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.

[00155] 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 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.

[00156] 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.

[00157] 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.

[00158] 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.

[00159] 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.

[00160] 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.

[00161] 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.

[00162] 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.

[00163] 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.

[00164] 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.

[00165] 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.

[00166] 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.

[00167] 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.

[00168] 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.

[00169] 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.

[00170] 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.

[00171] 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.

[00172] 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.

[00173] 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.

[00174] 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.

[00175] 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.

[00176] 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.

[00177] 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.

[00178] 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.

[00179] 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.

[00180] 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.

[00181] 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.

[00182] 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.

[00183] 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.

[00184] 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.

[00185] 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.

[00186] 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.

[00187] 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.

[00188] 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.

[00189] 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.

[00190] 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.

[00191] 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.

[00192] 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

[00193] 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.

[00194] 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.

[00195] 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

[00196] 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.

[00197] 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.

[00198] 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.

[00199] 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.

[00200] 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.

[00201] 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.

[00202] 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.

[00203] 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 coked during ROAR or not. The surgeon has to turn off ROAR and visualize whether the catheter is coked (in which nothing is being drawn in by the catheter 410) or is not coked (in which blood is being drawn into the catheter 410). With the

different situations of aborting pulse based on flow and pulsing until not coked, it is hard to know when a clot is coked.

[00204] 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 coked from when it is not coked. 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 (uncoked), then a significant flow of blood will exit the system 400. If the catheter 410 is aspirating while coked, then no blood will appear at the vacuum exit. During a ROAR operation and the catheter 410 is uncoked, the user/sensor will detect some blood at the vacuum exit. Finally, during the ROAR operation when the catheter 410 is coked, 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 coked or uncoked.

[00205] 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 coked on the end and the surgeon retracts the entire catheter to drag out the coked 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.

[00206] 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.

[00207] Turning now to embodiments that create maseration 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 1/0). The entire working channel of the aspiration thrombectomy system 600 is to be free from air or other gaseous bubbles during use.

[00208] 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.

[00209] 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” = 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.

[00210] 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.

[00211] 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 corked, 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.

[00212] 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.

[00213] 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.

[00214] 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.

[00215] 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.

[00216] 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.

[00217] 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.

[00218] 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.

[00219] 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.

[00220] 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.

[00221] 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.

[00222] 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.

[00223] 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.

[00224] 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.

[00225] 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.

[00226] 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.

[00227] 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.

[00228] 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.

[00229] 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.

[00230] 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.

[00231] 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.

[00232] 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.

[00233] 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 1-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. [00234] 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.

[00235] 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.

[00236] 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.

[00237] 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.

[00238] 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.

[00239] 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.

[00240] 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.

[00241] 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.

[00242] 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.

[00243] 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.

[00244] 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 purged 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.

[00245] 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.

[00246] 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.

[00247] 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'.

[00248] 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.

[00249] 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.

[00250] 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.

[00251] 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.

[00252] 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.

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:		SYN 2.0/ROAR		
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:				
INDEPENDENT CLAIMS IN EXCESS OF 3	2201	1	230	230
Miscellaneous-Filing:				

Description	Fee Code	Quantity	Amount	Sub-Total in USD(\$)
PUBL. FEE- EARLY, VOLUNTARY, OR NORMAL	1504	1	0	0
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 (\$)				3085

Electronic Acknowledgement Receipt	
EFS ID:	36631243
Application Number:	16516232
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Confirmation Number:	6733
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
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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	2019-07-18_SYN20_Roar_Request_expedited_examination_86082-9.pdf	129132	no	2
			2e038d7ae500ee4b38fa85aa5196e4c3caafb30c		
Warnings:					
Information:					
2	Transmittal of New Application	2019-07-18_SYN20_Roar_Utility_Transmittal_86082-9.pdf	280579	no	2
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3	Application Data Sheet	2019-07-18_SYN20_Roar_ADS_86082-9.pdf	1256583	no	10
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4	Drawings-other than black and white line drawings	2018-07-18_SYN_Roar_drawings_86166-2.pdf	4431370	no	29
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5	Oath or Declaration filed	2019-07-18_SYN20_Roar_Executed_Dec_Deville_86082-9.pdf	324695	no	1
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6	Oath or Declaration filed	2019-07-18_SYN20_Roar_Executed_Dec_Palmer_86082-9.pdf	325871	no	1
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7	Oath or Declaration filed	2019-07-18_SYN20_Roar_Executed_Dec_Bales_86082-9.pdf	323829	no	1
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11		2018-07-18_SYN20_Roar_specification-.pdf	429458	yes	83
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	Document Description		Start	End	
	Abstract		83	83	
	Claims		76	82	
	Specification		1	75	
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12	Fee Worksheet (SB06)	fee-info.pdf	41904	no	2
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Warnings:					

Information:	
Total Files Size (in bytes):	8518015
<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>	

**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 <u>/Gregory L. Mayback/</u>	Date
Name (Print/Typed) <u>Gregory L. Mayback</u>	Practitioner Registration Number <u>40719</u>
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.