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(71) Applicant: VIRGINIA COMMONWEALTH UNIVERSITY [US/US]; 800 East Leigh Street, Suite 3000, Richmond, VA 23219 (US).

(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).

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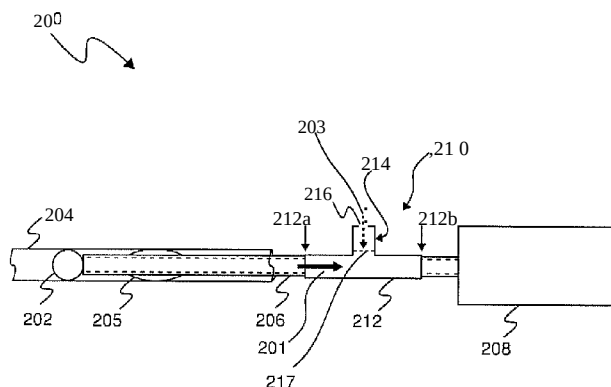


FIGURE 2A

(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 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 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 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 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.

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 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.

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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;

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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;

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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;

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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

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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,

5 "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
10 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
15 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
20 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
25 profile as "dynamic".

Referring now to the drawings, and in particular Figures 1A and IB, 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
30 106 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 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 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 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 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 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 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 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.

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 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 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 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 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, 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.

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 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 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 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 aspirated 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 J 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 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 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 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".

20 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 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 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 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 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 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, 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 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 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 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 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 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 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 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 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 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 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 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 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 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 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.

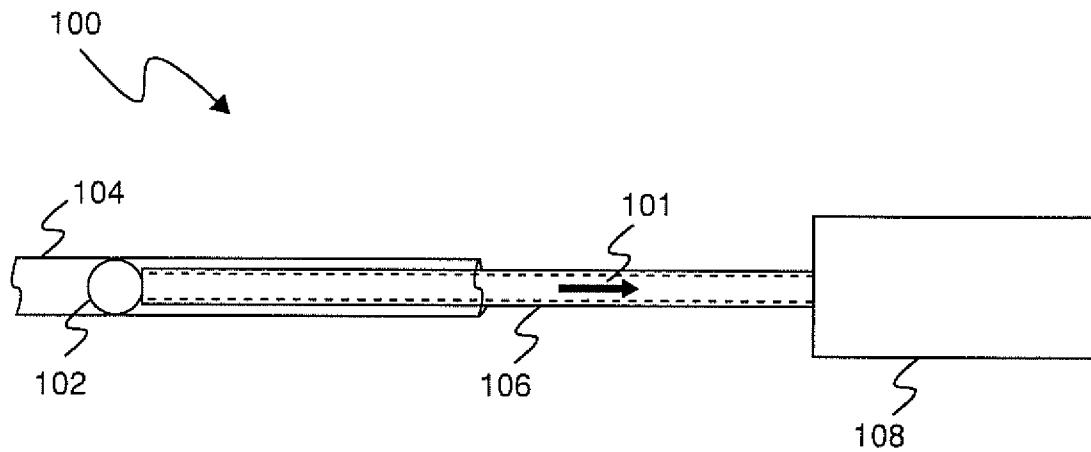


FIGURE 1A

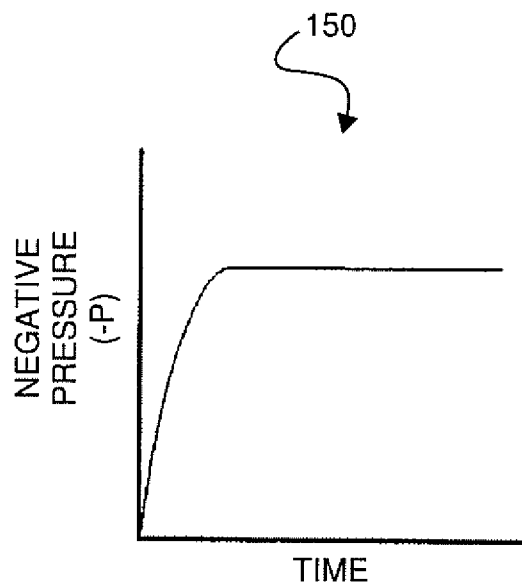


FIGURE 1B

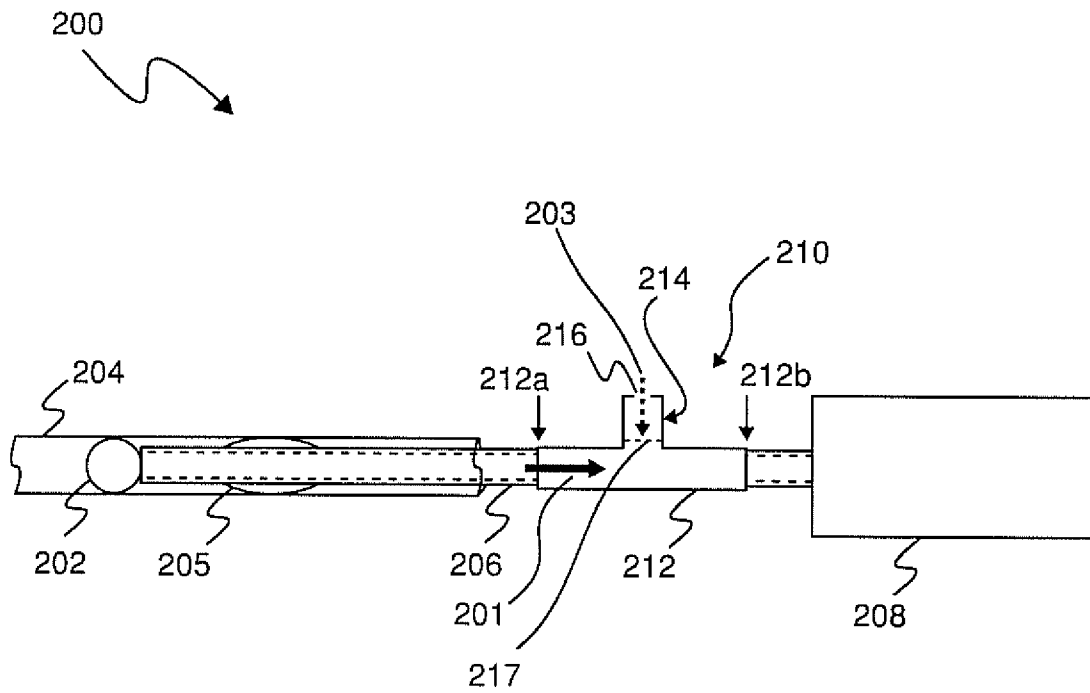


FIGURE 2A

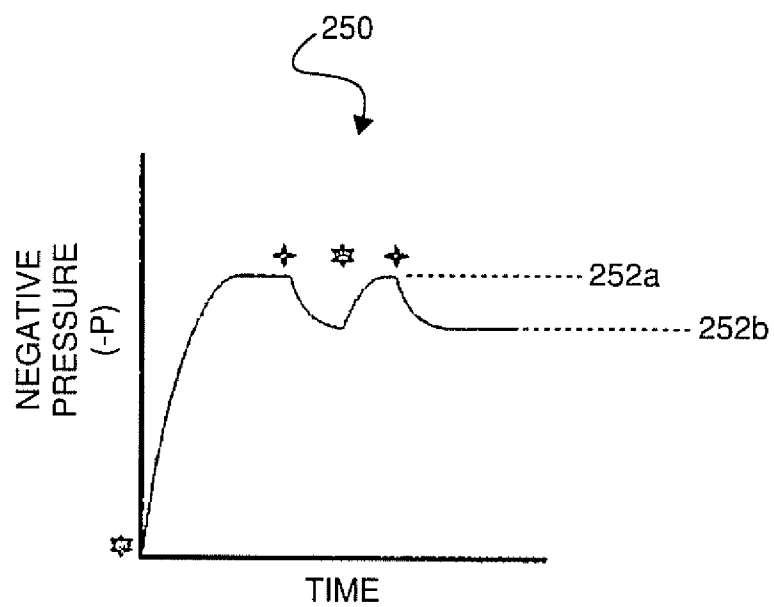


FIGURE 2B

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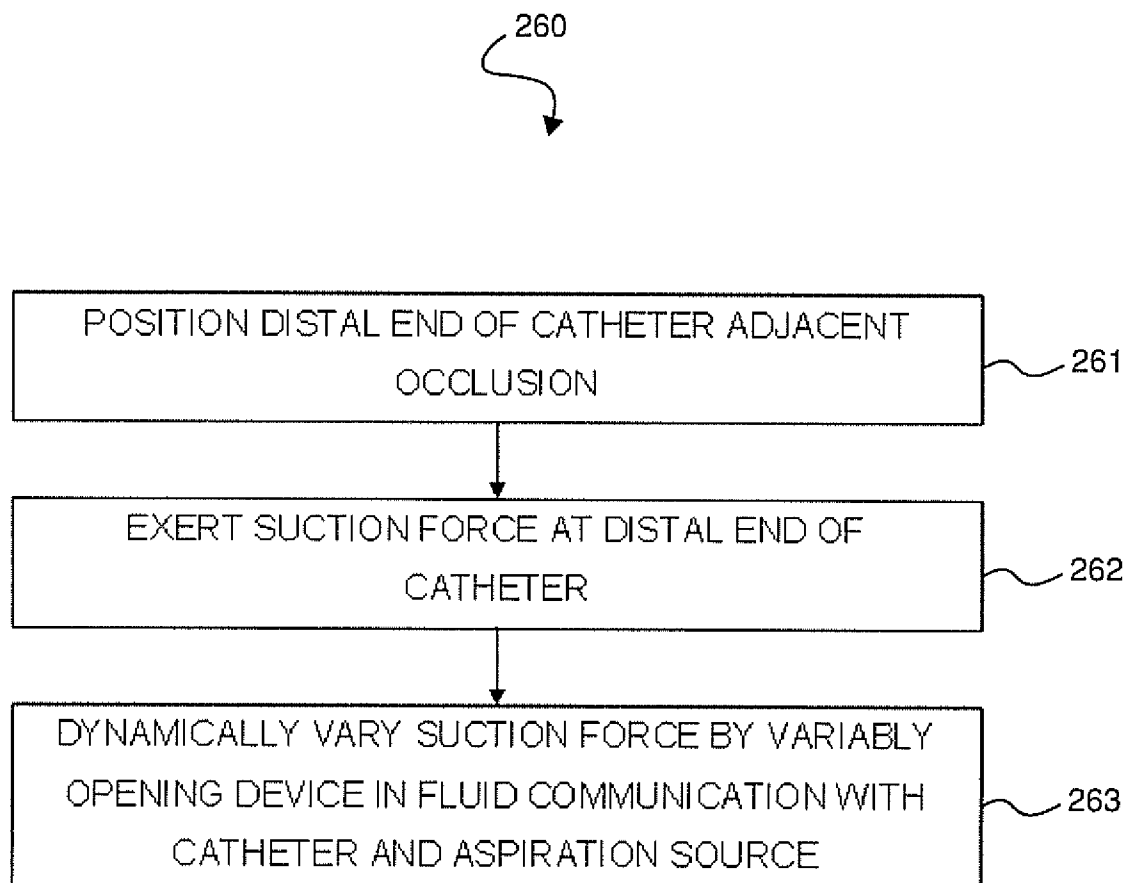


FIGURE 2C

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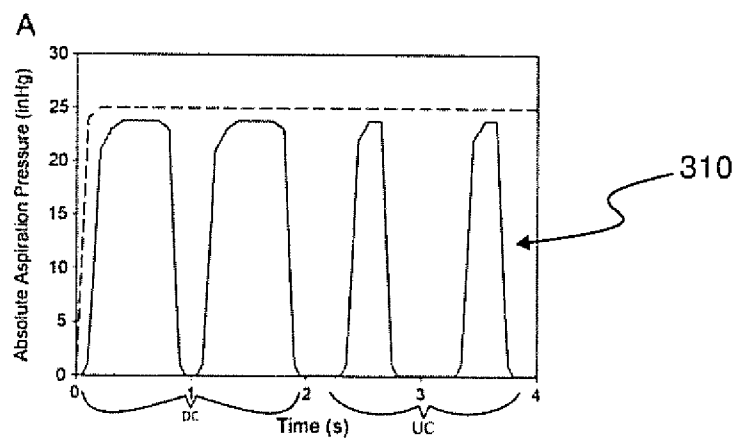


FIGURE 3A

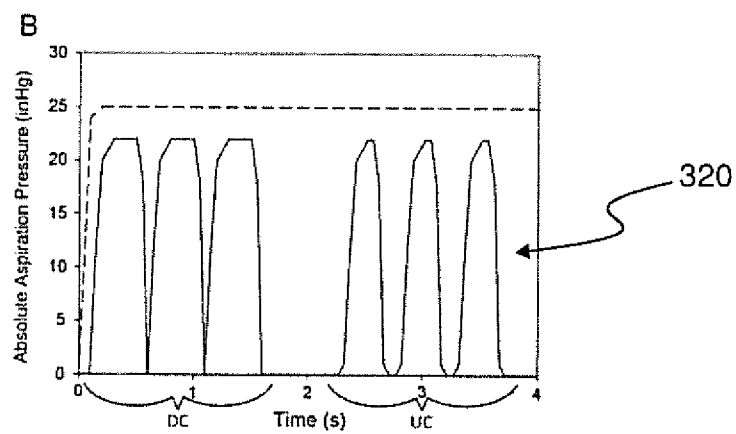


FIGURE 3B

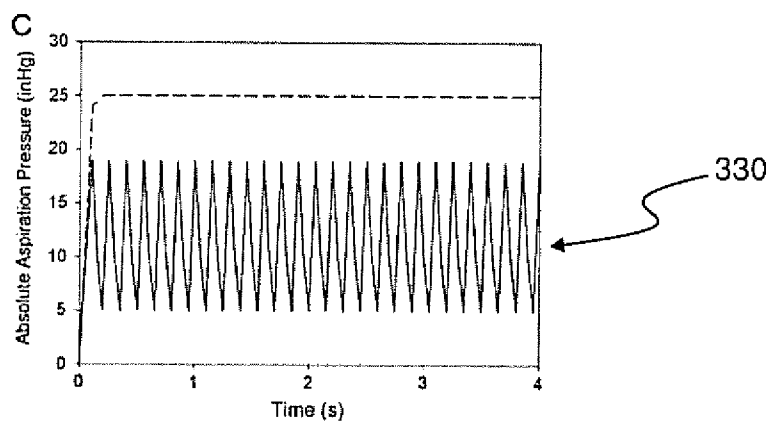


FIGURE 3C

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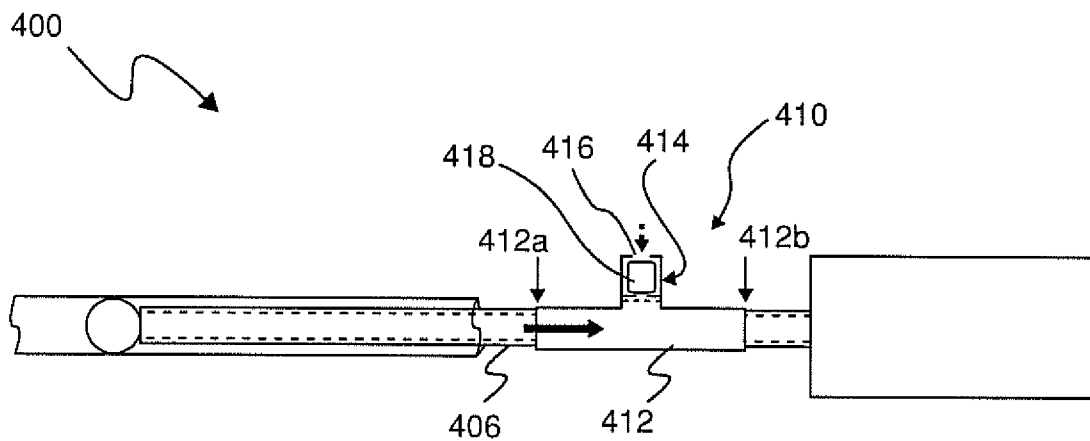


FIGURE 4A

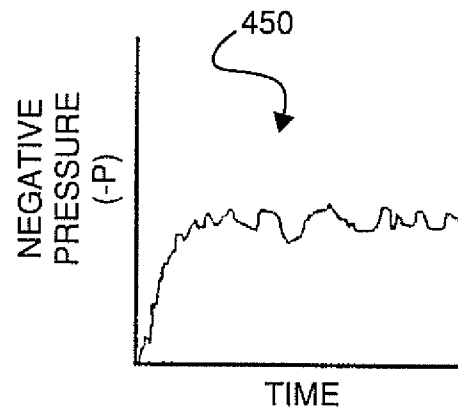


FIGURE 4B

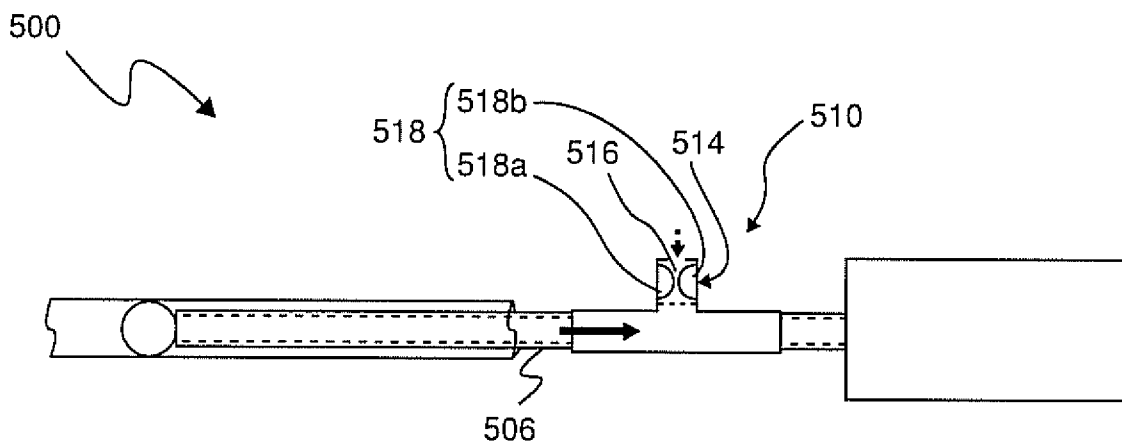


FIGURE 5

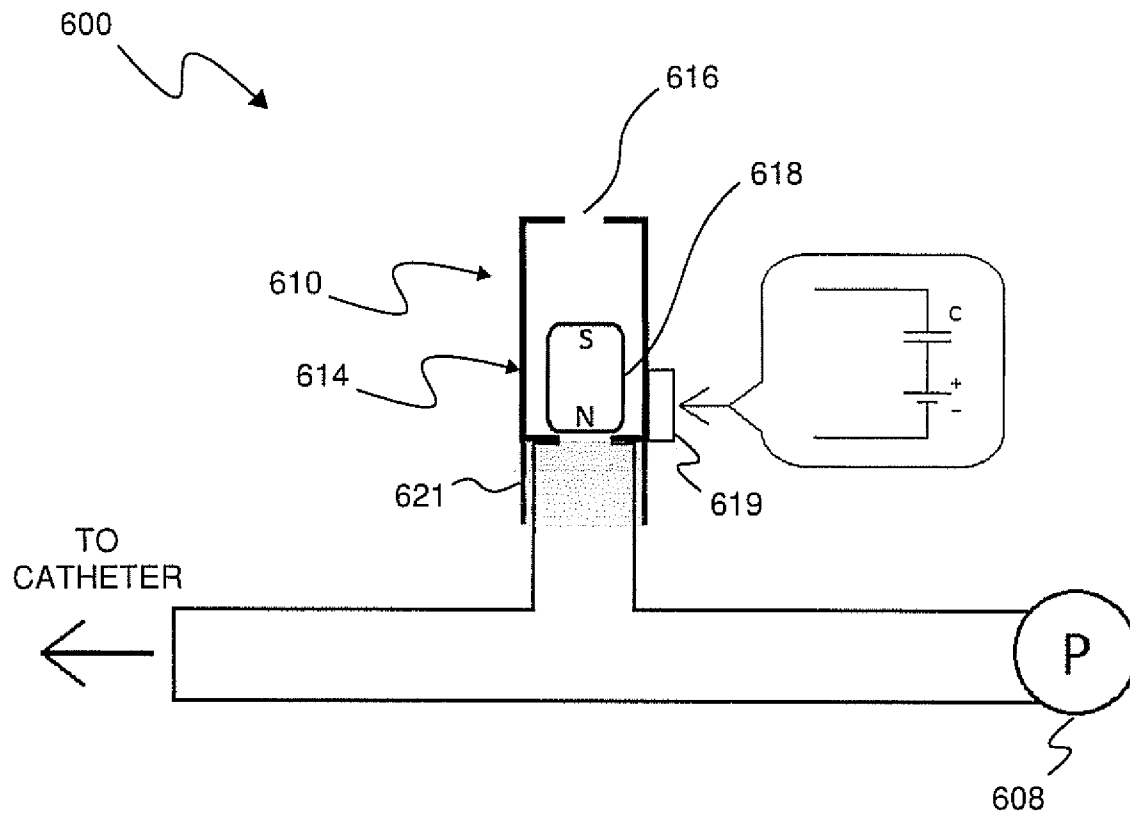


FIGURE 6

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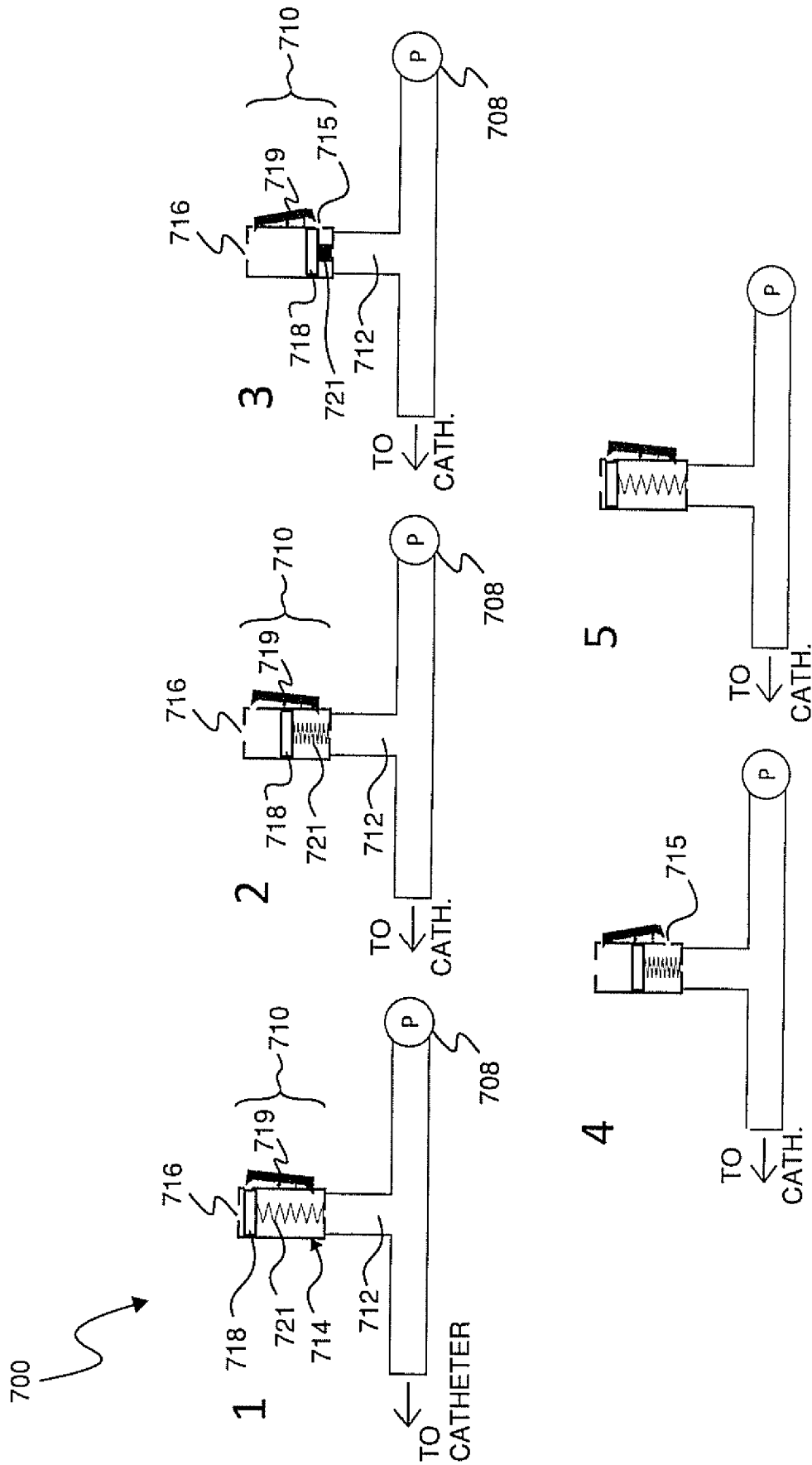


FIGURE 7

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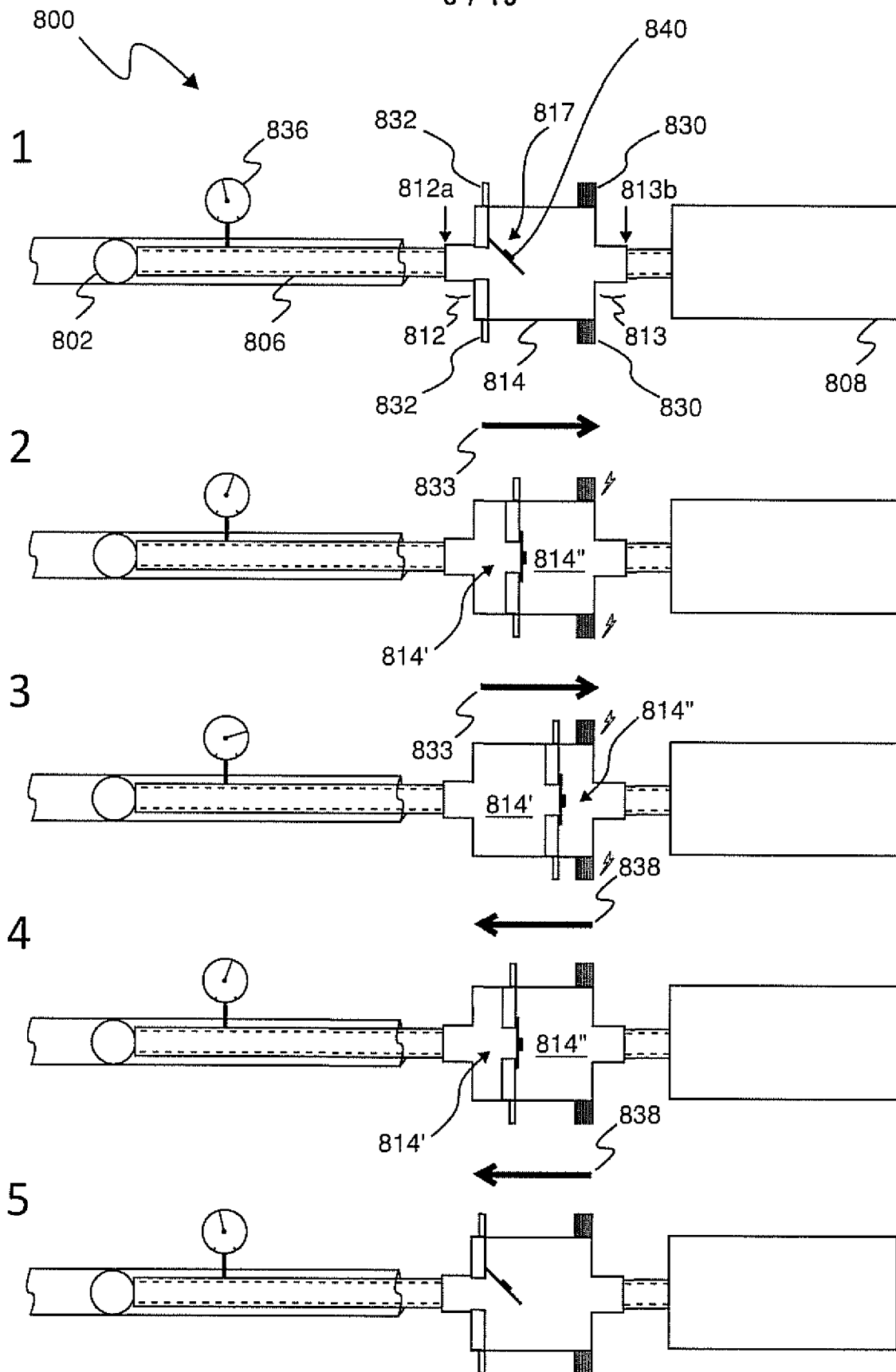


FIGURE 8A

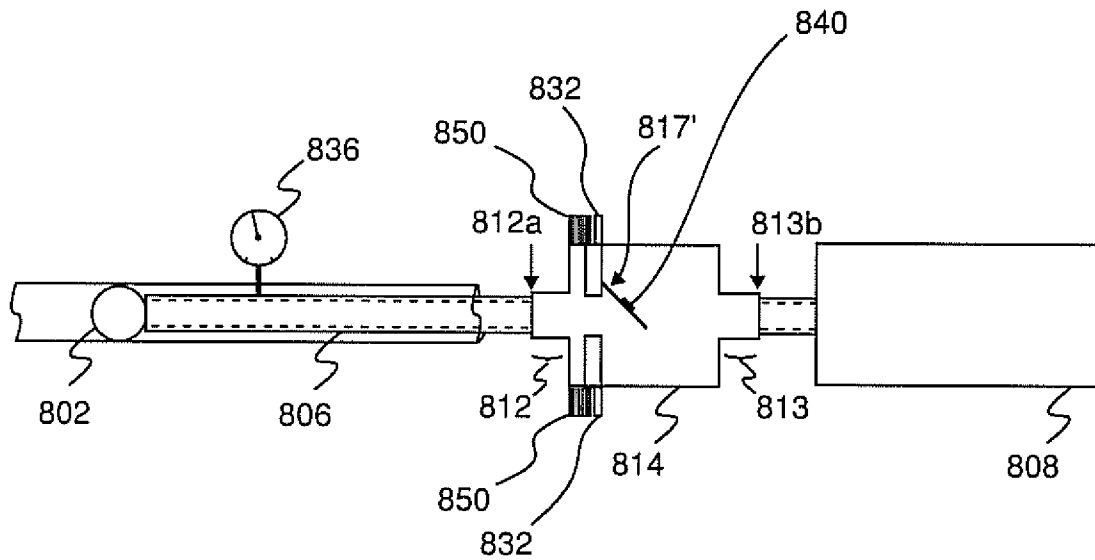


FIGURE 8B

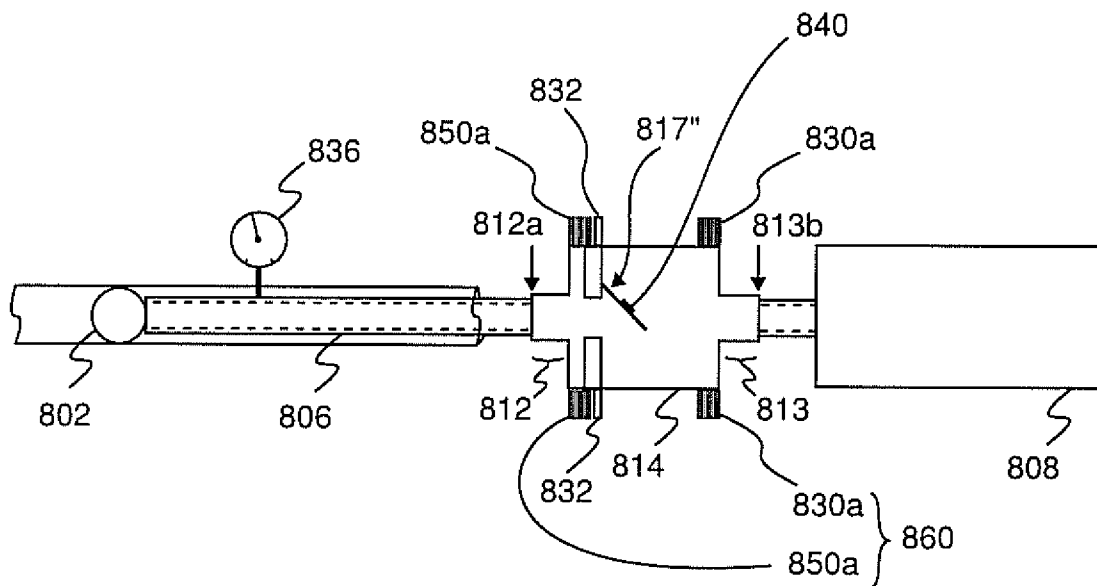


FIGURE 8C

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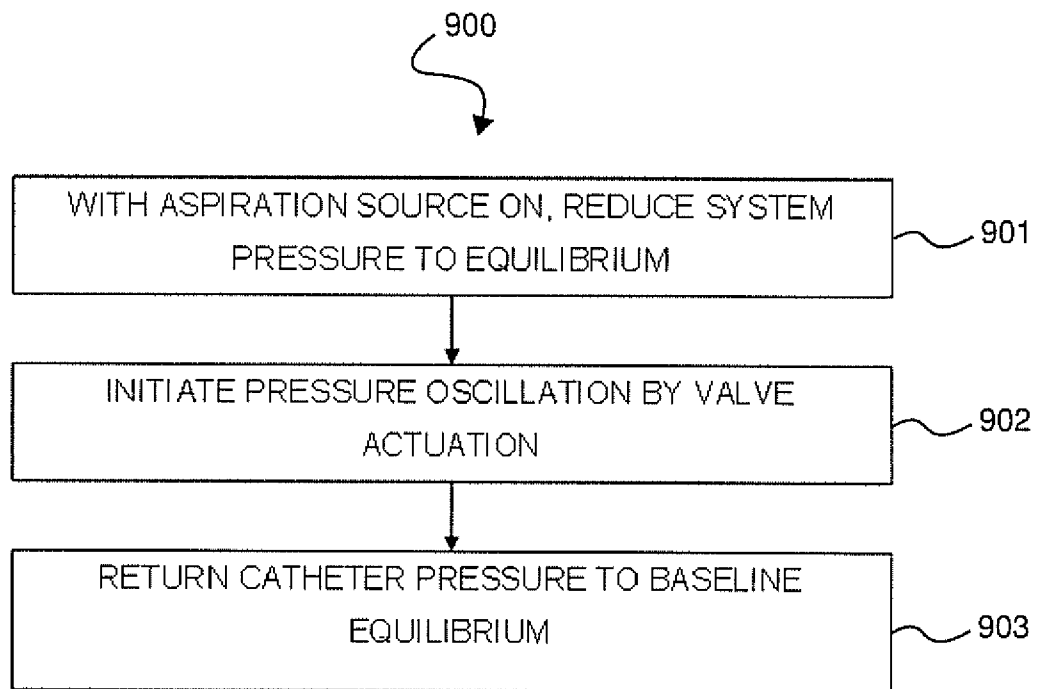


FIGURE 9A

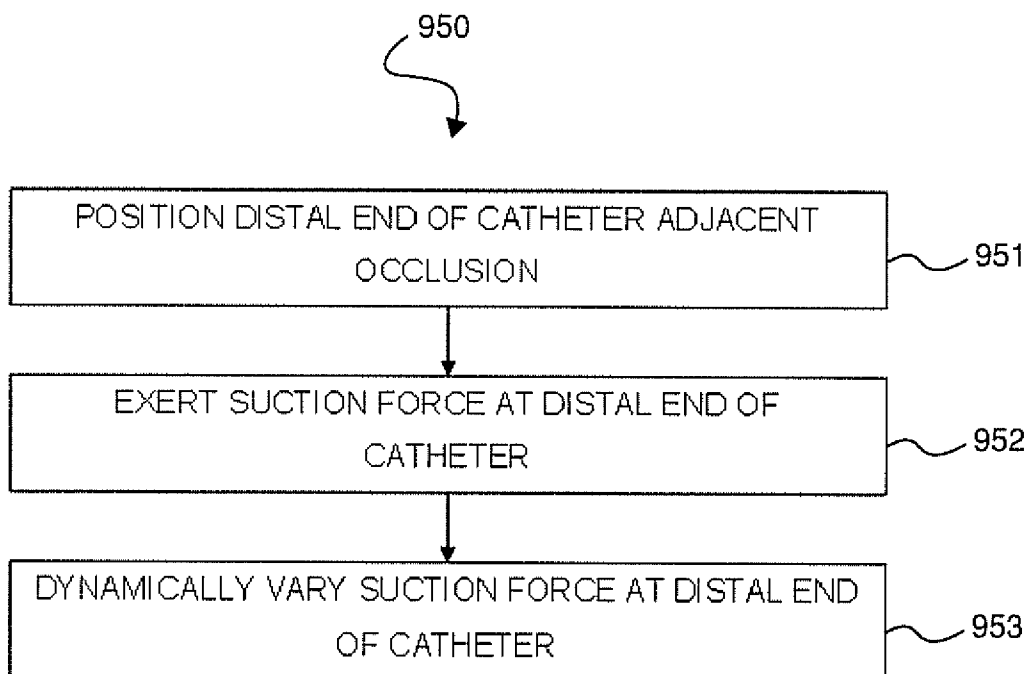


FIGURE 9B

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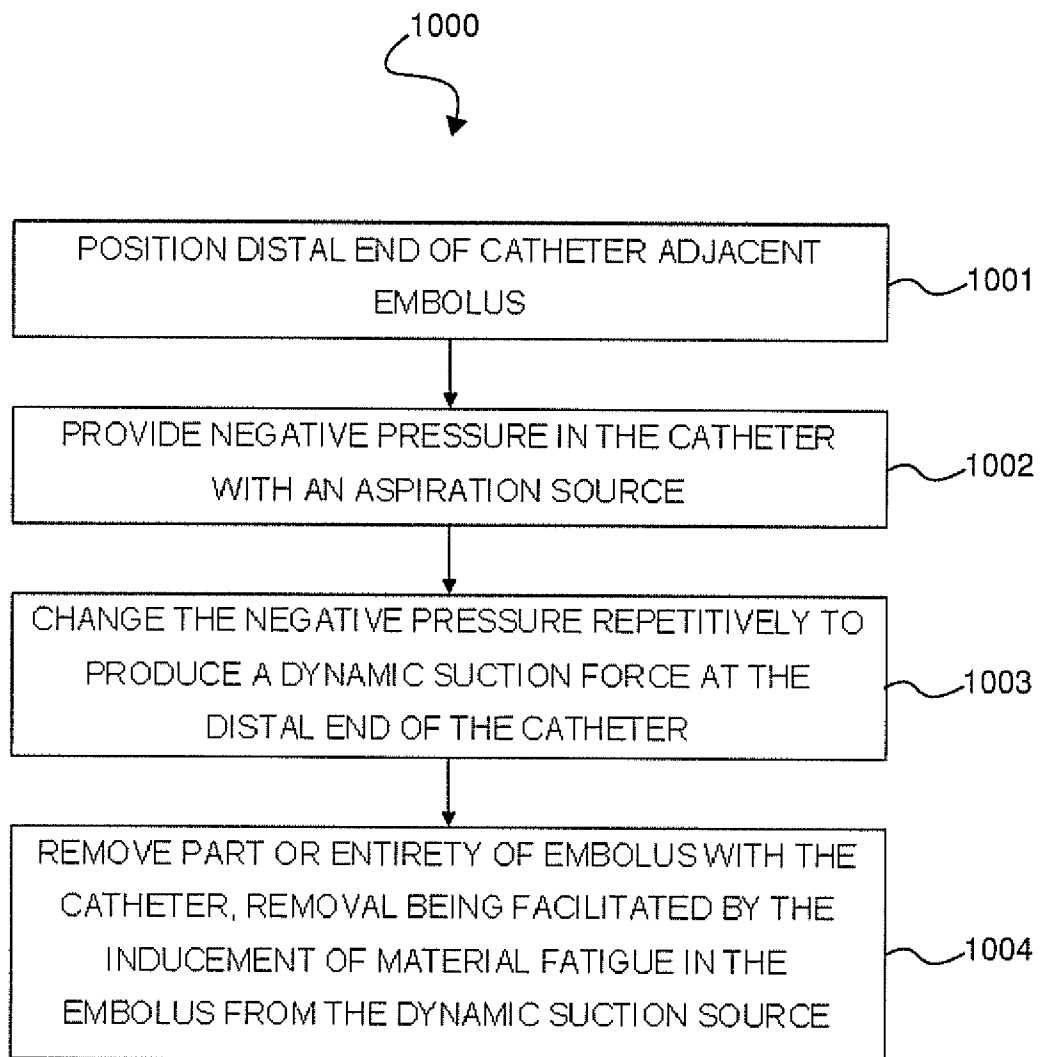
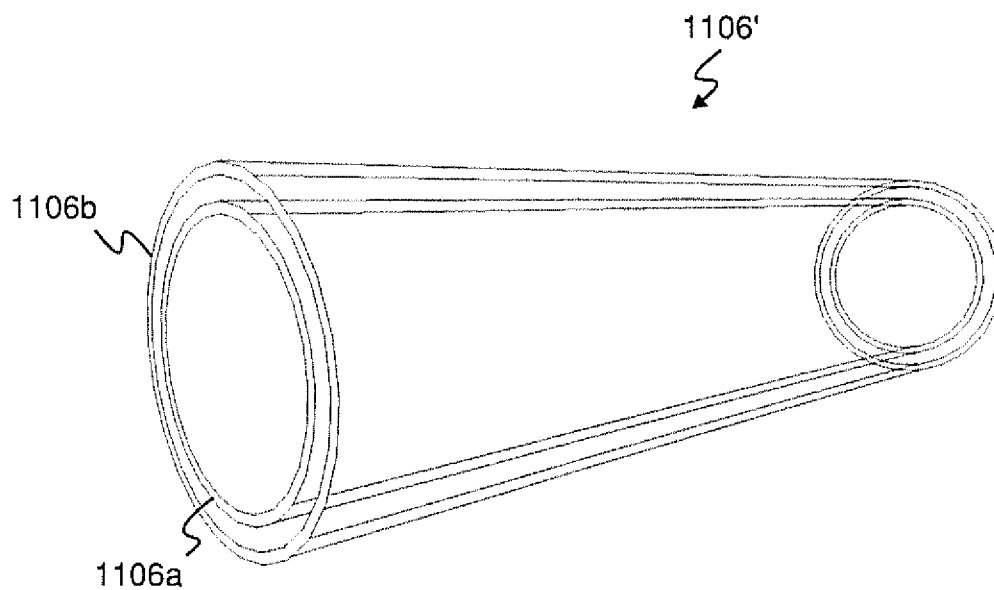
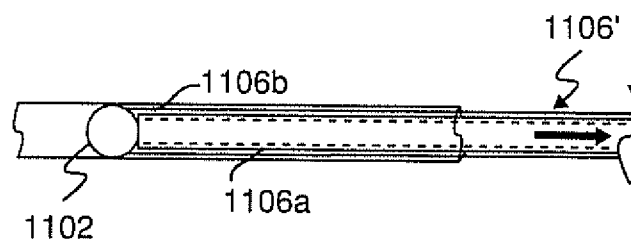
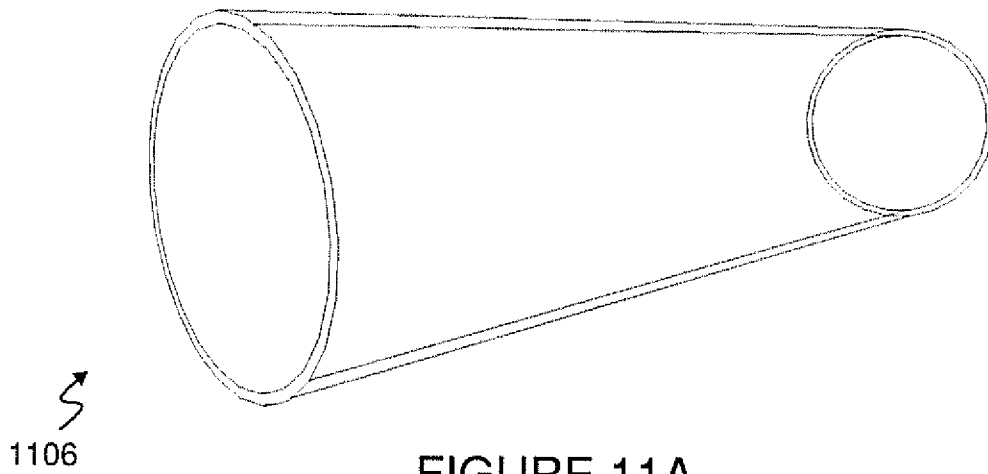


FIGURE 10

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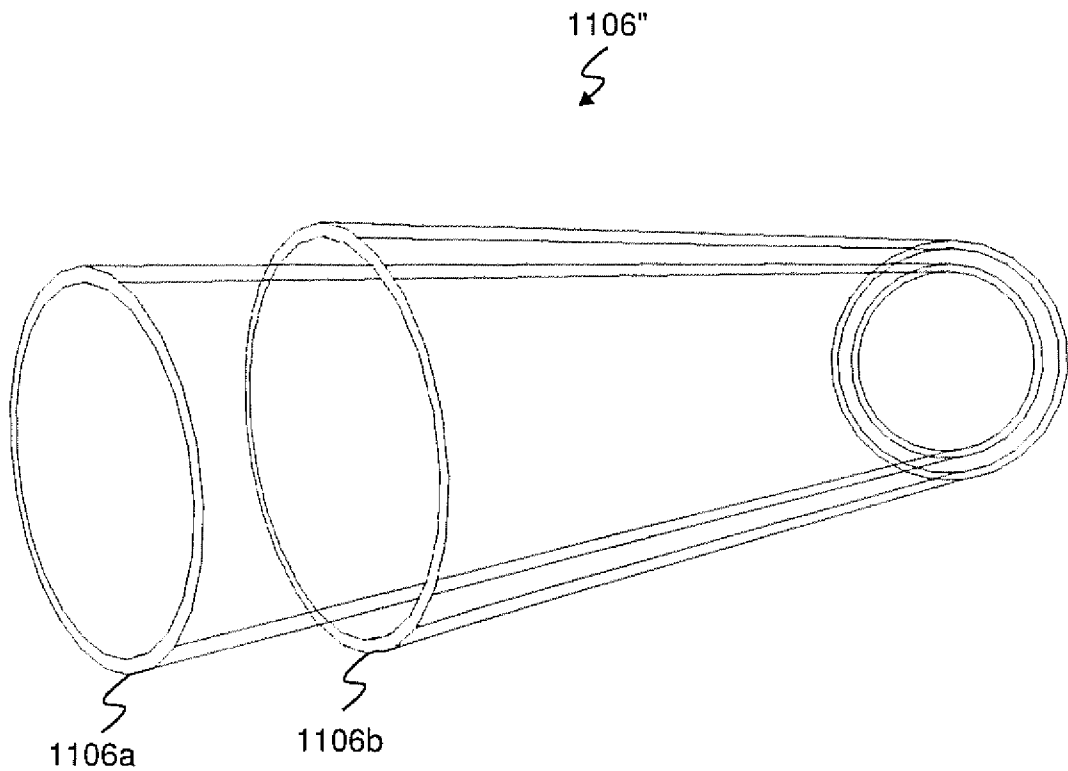


FIGURE 11D

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 SEARCHEDMinimum 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 27/00Documentation 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 modelsElectronic 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 V, 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 (LENNER 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 V, 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

"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

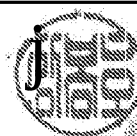
"&" document member of the same patent family

Date of the actual completion of the international search
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
189 Cheongsa-ro, Seo-gu, Daejeon Metropolitan City, 302-701,
Republic of Korea
Facsimile No. +82-42-472-7140

Authorized officer

CHANG, Bong Ho
Telephone No. +82-42-481-3353



INTERNATIONAL SEARCH REPORT

International application No.
PCT/US20 14/0252 11

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.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No.

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