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Patent and Trade Mark Attorneys

Our Ref: O237295EP

European Patent No. 3823686
European Patent Application No. 19837037.1
In the name of: RapidPulse, Inc.

This letter contains illustrations using colour.

Authorisation for the payment of the opposition fee (840 euros) is given in the attached form. Please debit this fee from deposit account no. 28050204.

Requests

It is requested that the opposed patent be revoked in its entirety. In the event that the EPO intends not to revoke the opposed patent in its entirety, oral proceedings are requested.

Grounds

The opposition is filed on the grounds of:

- Insufficiency of disclosure (Art. 100(b), Art. 83 EPC)
- Lack of novelty (Art. 100(a), Art. 52(1), Art. 54 EPC)
- Lack of inventive step (Art. 100(a), Art. 52(1), Art. 56 EPC)

Evidence

The following documents are to be included in the proceedings. Documents O1-O18 are cited herein as relevant prior art.

Documents P1-P3 are priority documents of the opposed patent:

- P1** US provisional application No. 62/701,086
- P2** US provisional application No. 62/750,011
- P3** US utility application US 16/516,232

Documents O1-O3 are relevant at least to the novelty of the opposed patent:

- O1** EP 4 461 253 A2 ("Teigen"), published 13 November 2024 (prior art under Art. 54(3) EPC)
- O2** US 2017/0238953 A1 ("Yang"), published 24 August 2017 (prior art under Art. 54(2) EPC)
- O2a** Corrections applied to specification of O2
- O3** WO 2017/214573 A1 ("Ofek"), published 14 December 2017 (prior art under Art. 54(2) EPC)

Documents O4-O18 are relevant for the understanding of the skilled person's common general knowledge and/or are relevant to the inventive step of the opposed patent:

- O4** Exploring the efficacy of cyclic vs static aspiration in a cerebral thrombectomy model: an initial proof of concept study (*Simon S, Grey CP, Massenzo T, et al. J NeuroIntervent Surg 2014; 6: 677–683*); first published 14 November 2013; (prior art under Art. 54(2) EPC)
- O5** SVIN 2018 Annual Meeting Program Overview (prior art under Art. 54(2) EPC)
- O6** Doctor Janardhan (17 March 2019) "Future Stroke Thrombectomy Devices – Promise of Cyclical Aspiration" (available at <https://www.youtube.com/watch?v=d7fv7VqLa5M> and/or <https://youtu.be/d7fv7VqLa5M?si=2DsPLYbGLZJ9QUhl>) (prior art under Art. 54(2) EPC)
- O7** Doctor Janardhan (17 March 2019) "Cyclical Aspiration Improves Clot Ingestion & Reduces Fragmentation - Dr. Marosfoi" (available at <https://www.youtube.com/watch?v=cC3XEisYqvs> and/or <https://youtu.be/cC3XEisYqvs?si=pNlwQv-cguFxAxt>) (prior art under Art. 54(2) EPC)
- O8** US 2016/0375221 A1 ("Panotopoulos"), published 29 December 2016 (prior art under Art. 54(2) EPC)
- O9** WO 2014/151209 A1 ("Grey"), published 25 September 2014 (prior art under Art. 54(2) EPC)
- O10** WO 2019/115809 A1 ("Mullins"), published 20 June 2019 (prior art under Art. 54(2) EPC)
- O11** US 3,955,574 ("Rubinstein"), published 11 May 1976 (prior art under Art. 54(2) EPC)
- O12** US 2012/0138833 A1 ("Matteo"), published 7 June 2012 (prior art under Art. 54(2) EPC)
- O13** US 5,814,064 ("Daniel"), published 29 September 1998 (prior art under Art. 54(2) EPC)
- O14** Mahmood MM, Watt J, Ahmed JM. Thrombus aspiration during primary percutaneous coronary intervention for acute myocardial infarction: A review of clinical evidence and guidelines. *World J Cardiol.* 2015 Dec 26;7(12):889-94. doi: 10.4330/wjc.v7.i12.889. PMID: 26730294; PMCID: PMC4691815. (prior art under Art. 54(2) EPC)
- O15** US 2015/0359549 A1 ("Lenker"), published 17 December 2015 (prior art under Art. 54(2) EPC)
- O16** Jolly SS, Niemela K. Aspiration thrombectomy in ST-elevation myocardial infarction. *EuroIntervention.* 2014 Aug;10 Suppl T:T35-8. doi: 10.4244/EIJV10STA7. PMID: 25256532. (prior art under Art. 54(2) EPC)
- O17** US 2017/0181760 A1 ("Look"), published 29 June 2017 (prior art under Art. 54(2) EPC)
- O18** US 2016/0220741 A1 ("Garrison"), published 4 August 2016 (prior art under Art. 54(2) EPC)

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1. Introduction

1.1. Introduction to the opposed patent and priority documents P1-P3

The opposed patent relates to an aspiration thrombectomy system for removing emboli such as blood clots from vasculature (paragraphs 1 and 2 of the opposed patent).

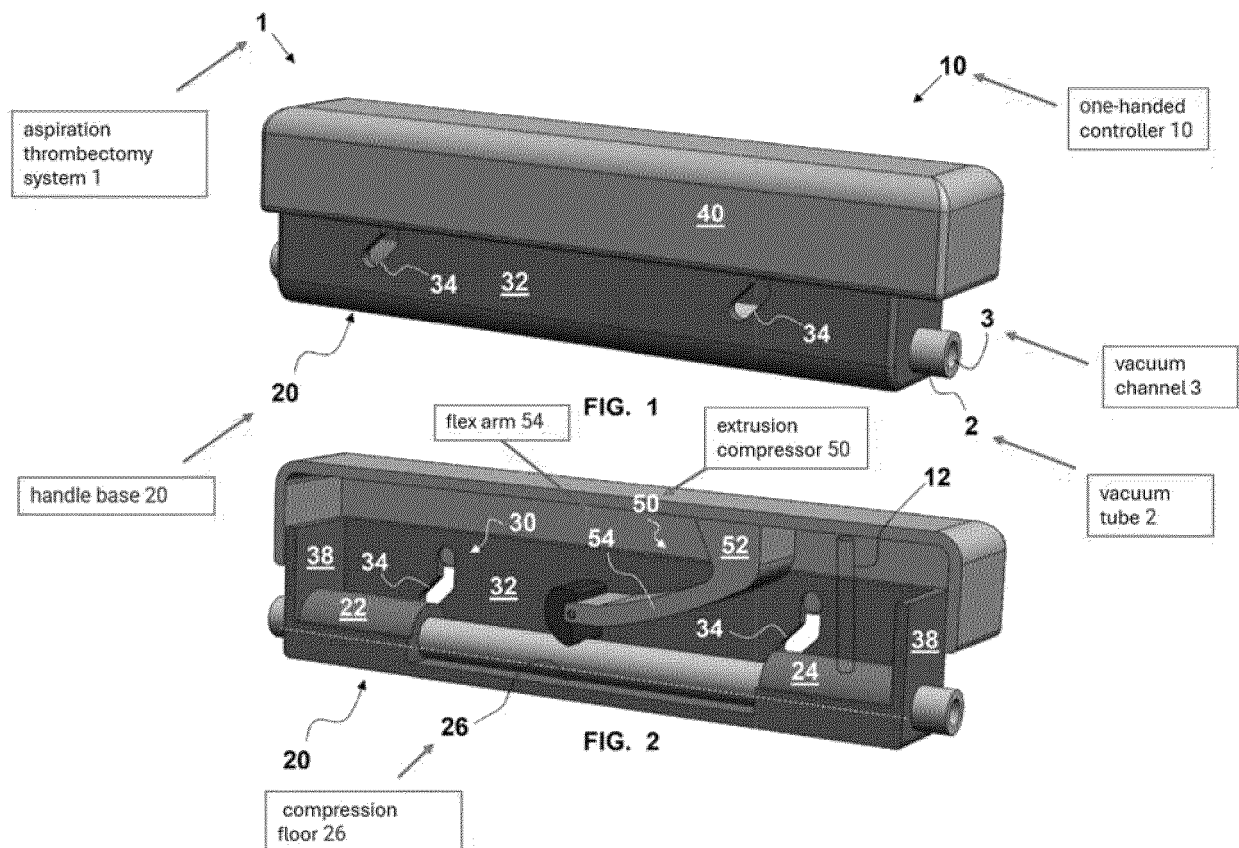
The core concept of aspiration thrombectomy is described in the background of the opposed patent:

[0003] 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.

In such arrangements, it is generally desirable to reduce or avoid obstruction/clogging of the aspiration tube by the embolus (paragraph 11 of the opposed patent).

At a high level, the opposed patent describes three different embodiments:

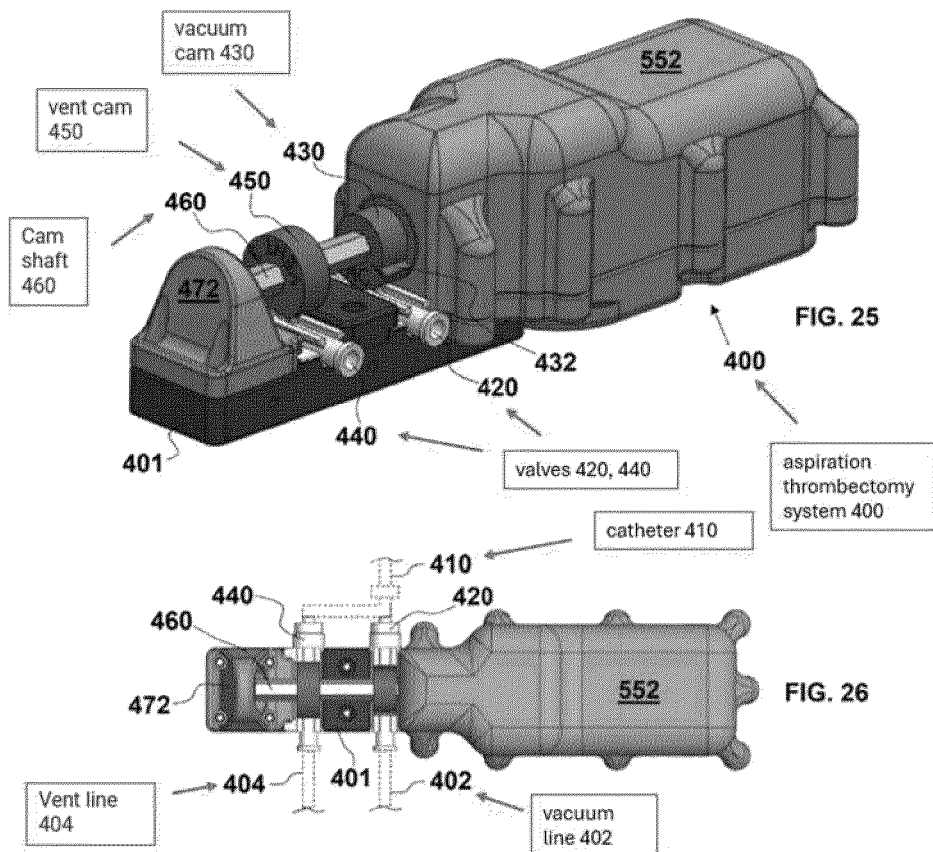
1. The embodiment(s) of Figs. 1-24. This embodiment is introduced in the first priority document (P1). In this embodiment, when a thrombus is trapped at the end of the aspiration catheter, a hand-held controller can be actuated to create a positive amount of “exit flow” to dislodge the thrombus (see paragraph 17).



The operation of this embodiment is described at paragraph 85 of the opposed patent:

[0085] [...] 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.

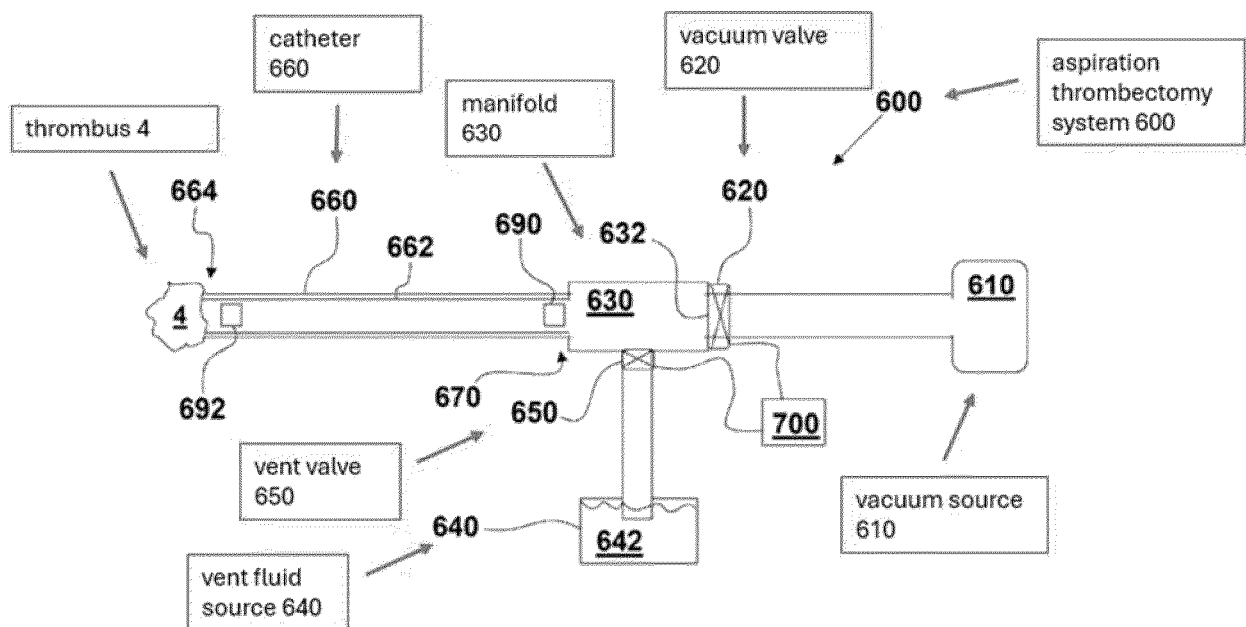
2. The embodiment(s) of Figs. 25-46. This embodiment is first introduced in the second priority document (P2). This embodiment relates to an aspiration thrombectomy system which can operate with an automatic, rapid, and repeated onset of pressure change (see paragraph 110 of opposed patent) and makes use of vacuum and vent cams which can be rotated by a shaft in order to pinch down short sections of tubing.



The operation of this embodiment is described in detail at paragraph 117 of the opposed patent:

[01117] 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. [...] 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.

3. The embodiment of Figs. 47-72. This embodiment is first introduced in the third priority document, P3. This embodiment relates to the “*clot removal system*” claimed in the opposed patent, and comprises a “*catheter*”, a “*controllable vacuum valve*”, a “*vacuum source*”, a “*controllable vent valve*”, a “*vent fluid source*”, a “*manifold connected to the catheter, and to the vacuum valve and to the vent valve*”, and a “*controller connected to the vacuum valve and the vent valve*” (see paragraph 22 of the opposed patent).

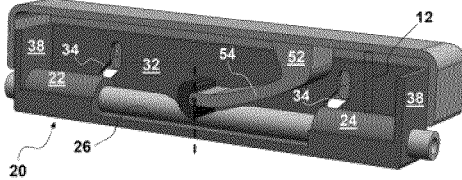
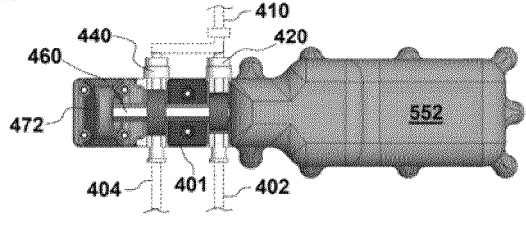
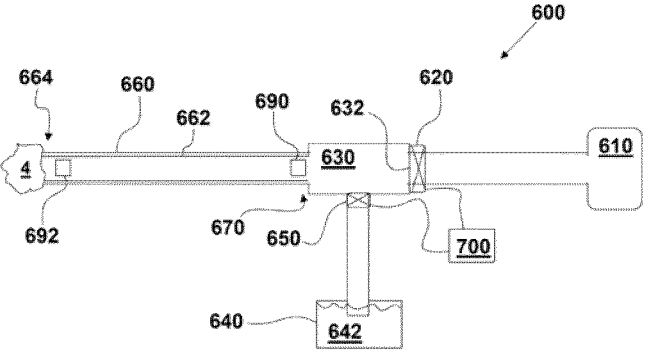


The catheter has a lumen “filled with a liquid column having a proximal portion and a distal portion”, and the system comprises a controller “configured to cyclically open and close the vacuum valve and the vent valve to change a level of vacuum at the distal end and prevent forward flow of the distal portion out from the distal end during each cycle” (see paragraph 22).

The idea of ‘reducing forward flow’ is first introduced with respect to this third main embodiment, and the purpose of reducing forward flow is discussed at paragraph 142 of the opposed patent:

[142] [...] 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.

The following table summarises these three main embodiments of the opposed patent:

<p>“Embodiment 1” Introduced in P1</p>	 <p>FIG. 8</p>
<p>“Embodiment 2” Introduced in P2</p>	 <p>FIG. 26</p>
<p>“Embodiment 3” Introduced in P3</p>	

1.2. Common General Knowledge of the skilled person

The relevant skilled person for the opposed patent is a skilled practitioner in the field of aspiration thrombectomy, consistent with the usual EPO presumption (see e.g., Guidelines for Examination G-VII 3). As a precursor to the comments below regarding the skilled person’s interpretation of the prior art documents, the following remarks address the common general knowledge of the skilled person at the applicable priority date.

1.2.1. The need to prevent distal embolisation was well-known

At the priority date, the skilled person would be well aware that distal embolisation of a thrombus (i.e., downstream movement of a thrombus, or a portion of a thrombus, through a blood vessel) can cause complications during thrombectomy procedures and must be avoided.

As evidence of the common general knowledge, we cite documents O13, O14, O16, O17, as well as O4, O5, O6, and O7. It will be appreciated that these documents are merely examples among others that could be cited.

O13 is a 1997 patent application which describes certain problems in the field of thrombectomy and atherectomy as follows: *“The stenotic debris which is separated from the stenosis is free to flow within the lumen of the vessel. If the debris flows distally, it can occlude distal vasculature and cause significant problems. If it flows proximally, it can enter the circulatory system and form a clot in the neural vasculature, or in the lungs, both of which are highly undesirable”* (see background of O13).

O14 is a study published in 2015 which makes clear that the risk of distal embolization was a known concern in aspiration thrombectomy procedures at that time, noting (for example) that *“Earlier investigations revealed that angiographically distal embolization occurred in around 15% of patients undergoing PPCI. Distal embolization was associated with impaired myocardial reperfusion, larger infarct size and an unfavorable prognosis”* (see introduction).

O16 is a 2014 article in *EuroIntervention* which discusses potential complications of thrombus aspiration, and states that *“Modern primary PCI is very effective in restoring epicardial flow in the infarct artery but a significant limitation is distal embolisation of thrombus and obstruction of the microvasculature”*.

O17 is a patent application published in 2017 which relates to *“relates to an aspiration system for removing, by aspiration, undesired matter such as a thrombus from a fluid carrying cavity, duct, or lumen of the body, such as a blood vessel”* (paragraph 3). The application notes that *“when a device becomes clogged during use, the potential for inadvertent dislodgment of thrombus downstream increases; this is referred to as distal embolism”* (paragraph 65) and that *“Distal embolism may occur if the vacuum pressure is not sufficient, and yet the user is not aware”* (paragraph 67).

O4 is a journal article published in 2013. The Discussion of O4 notes the issue of distal migration and, notably, suggests that preventing forward flow would be one way to mitigate this issue: *“Although none were observed in this study, in the interest of preventing the distal migration of thrombi, impact aspiration would have to be performed either in conjunction with continuous aspiration or as a stand-alone treatment with a minimum frequency such that a vacuum is maintained throughout testing”*.

There are many more documents that could be cited as evidence that this problem was a very well-known issue in the art at the relevant priority date.

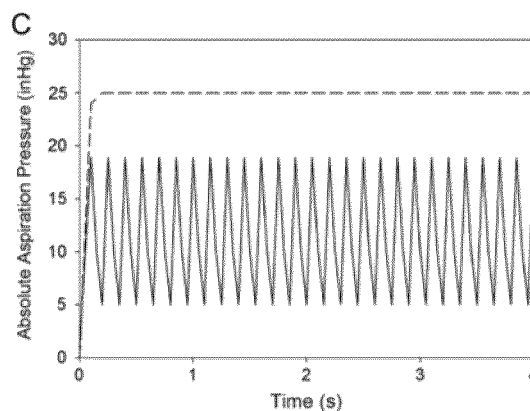
However, it is noted that this point is unlikely to be controversial; in fact it is acknowledged in the background of the opposed patent as follows (emphasis added):

[0004] [...] 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.

In summary: the risk of distal embolization / distal migration of the clot during techniques such as aspiration thrombectomy was extremely well-known at the relevant date. Recognition of this issue has influenced procedural techniques and device development for many years. The skilled person designing a clot removal device at the applicable date would have known that it is essential to mitigate or remove the risk of distal migration when designing or modifying a clot removal device.

1.2.2. Cyclical aspiration was well-known

O4 is an influential journal article published in 2013. The study evaluated the potential of cyclic loading in aspiration thrombectomy in comparison to using static suction (see e.g., abstract). In this context, cyclical loading (also referred to in O4 as 'impact aspiration') means generating cyclical pressure profiles which are applied to the catheter, for example as shown in Fig. 2(c) reproduced below. Fig. 2(c) shows a cyclical loading profile as a solid line, compared with a static loading profile as a dotted line.



According to O4, the logic behind applying a more sophisticated aspiration pressure profile in this way is that it can improve the extraction of clots and improve recanalization rates because “*generally, cyclic changes in force induce material fatigue*” in the clot (see column 2 lines 9-20).

In this way, subjecting clots to material fatigue via cyclic aspiration might reduce their required load-to-failure (theoretically enabling the removal of more entrenched clots) and the time-to-failure given a specific load (theoretically reducing the time to reperfusion) with obvious benefits to the patient.

In line with common knowledge at the time, the authors of O4 were well-aware of the risk of distal migration of emboli. In the first paragraph in the left column of page 682, O4 states (emphasis added):

Distal emboli in cerebral thrombectomy are a significant concern, and not all currently available methods appear to be equal in this regard. As the pressure curves reveal, higher frequency

oscillations were more effective at removing the synthetic clot in this limited experimental model and also never returned to 0 mm Hg. This technique can therefore be optimized to provide uninterrupted net reverse flow to prevent distal migration.

In the conclusion, O4 states:

We demonstrate that cyclic loading with our impact aspiration technique significantly outperforms static loading with the Penumbra pump at clearing synthetic clots in an experimental model. Within our impact aspiration technique, aspirating at a higher frequency (e.g., 6.3 Hz vs 1 Hz) using the UC pressure waveform and water as the aspirating medium is the most effective way to clear synthetic clots from the flow model.

In addition, in the Discussion, O4 teaches that the prevention of forward flow, e.g. by maintaining an overall level of uninterrupted aspiration, will help protect against the risks of distal migration:

Although none were observed in this study, in the interest of preventing the distal migration of thrombi, impact aspiration would have to be performed either in conjunction with continuous aspiration or as a stand-alone treatment with a minimum frequency such that a vacuum is maintained throughout testing. In this study ~6.3 Hz (Max Hz) was the only frequency that maintained uninterrupted net aspiration pressure as both 1 Hz and 2 Hz had minimum pressures of 0 in Hg. Implementing a pressure-controlling device would allow flexibility in aspiration frequency due to the increased control over minimum pressure.

Following publication of this paper, the industry began to develop techniques and products which make use of cyclical aspiration.

As will be explained in greater detail below, document O9, published in 2014, discloses a system for aspiration control based on the following principles:

(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.

O15, published in 2015, discloses a catheter system for removing obstructions, and discloses that:

[179] [...] When continuous or intermittent suction is applied to the distal end of the catheter, the pressure gradient across the occluding lesion increases and thromboembolic material 202 may be dislodged and captured by the aspiration port. The thromboembolic material may thereafter be removed continuous or pulsed suction, thereby reducing the risk of embolization to the basilar artery.

O10, published in 2019, describes an aspiration system that may employ a catheter with a pump which dynamically applies negative or positive pressure to optimally aspirate a clot. At page 42 lines 15 to 21, the document discloses the use of a "shake signal":

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.

O18, published in 2016, relates generally to medical methods and devices for the treatment of acute ischemic stroke, and discloses:

[0114] In yet another aspiration source implementation, the aspiration source 600 provides a cyclic level of aspiration force, for example, an aspiration force that cycles between a high level of vacuum to a lower level of vacuum at a set frequency, or from a high level of vacuum to no vacuum, or from a high level of vacuum to a pressure source. A cyclic aspiration mode may provide a jack-hammer type force on the thrombus and increase the ability to aspirate the thrombus through the catheter. The cyclic aspiration force may be enabled through solenoid valves, a programmable pump motor, or the like. [...]

O5 and related presentations O6 and O7 provide a helpful snapshot of the state of play of innovation in November 2018. O5 is a program showing the schedule for the SVIN (Society of Vascular and Interventional Neurology) annual meeting of 2018. O6 and O7 are presentations from that meeting, evidenced by videos hosted on YouTube. For example, presentation O6 is shown on page 7 of the program (11:45 am – 11:55 am), and O7 is shown on page 9 of the program (8:32 am – 8:40 am).

These presentations each discuss varying the suction pressure in a thrombectomy system and how such systems are more effective than static or uniform suction, whilst also reducing distal embolization and clot fragmentation in use. These presentations refer to other articles and studies which describe the same advantages.

These disclosures show that a hypothetical person skilled in the art would have been aware of the advantages of applying cyclical aspiration in thrombectomy procedures at the applicable date of the opposed patent. Specifically, the skilled person would be aware that cyclical aspiration would reduce the time required to clear a clot, increase the probability of clearing a clot, and reduce the probability of distal embolization.

1.3. Claim labelling

For ease of reference throughout this document, the features of claim 1 are labelled as follows:

Label	Feature
1[Pre]	A clot removal system, comprising:
1[a]	a catheter having a distal end and defining a lumen filled with a liquid column having a proximal portion and a distal portion;
1[b]	a controllable vacuum valve;
1[c]	a vacuum source fluidically connected to the vacuum valve;
1[d]	a controllable vent valve having a vent liquid input;
1[e]	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;
1[f]	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;
1[g]	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,
1[h]	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
1[i]	prevent forward flow of the distal portion out from the distal end during each cycle.

2. Insufficiency of disclosure (Art. 100(b), Art. 83 EPC)

Article 83 EPC requires that a European patent application shall disclose the invention in a manner sufficiently clear and complete for it to be carried out by a person skilled in the art.

The opposed patent does not meet this requirement of the EPC.

2.1. Claim 1

1[i] “prevent forward flow of the distal portion out from the distal end during each cycle”

Claim 1 of the opposed patent defines the system, at least in part and as understood in view of the EPO’s Guidelines for Examination (e.g., F-IV 4.10, F-IV 6.5; and Case Law of the Boards of Appeal II C 8.1), by reference to a result to be achieved. Therefore, the claim extends over an extremely large area, and is not sufficiently disclosed according to the requirements of the EPC.

It is our submission that forward flow, in the manner described in the opposed patent, and as understood in view of general principles at the EPO, is prevented at least during any application of cyclical aspiration in which an overall negative pressure is maintained at the distal end of the catheter. In other words, forward flow is prevented when an overall level of vacuum or ‘suction’ is maintained in the distal end of the catheter. In this way, the risk of distal migration is reduced or eliminated during cyclical aspiration, as suggested in the Discussion of the original and influential “Simon” paper (O4), and as taught by several prior art documents.

If, however, the patentee considers that the term “prevention of forward flow” would be understood in view of general principles at the EPO as implying further technical limitations, for example relating to the provision of a water hammer effect, then it is submitted that the clot removal system of claim 1 is not sufficiently disclosed according to the requirements of the EPC.

The skilled person seeking to implement the invention defined in claim 1 is taught that the system must be “tuned” in order for the system to be optimised for the water hammer effect (see paragraphs 142, 145, 152-159). This tuning depends on many factors of the system, for example “*the density of the fluid, the compliance of the system (the bulk modulus), and the length of the fluid column*” (see paragraph 152). Here, the bulk modulus refers to “*the compliance of the system: both the radial and the longitudinal flexibility of the catheter and the extension tube*” (paragraph 153).

In order for the parameters of the valve switching cycle to be set in a manner such that “*the fluid column does not exit the distal end of the catheter*”, the patent teaches that it is “*important that the catheter, any extension tube that connects to the catheter, the controller, and the valving sequence be tuned as a system*” (paragraph 152).

The opposed patent states:

[0156] 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.

[0157] 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, Vntofftime 656, and Vntoff duration 658. [...]

The teaching of the patent therefore suggests that forward flow that might occur due to the water hammer effect is only prevented when the entire system has been carefully “tuned” for each of several factors (e.g. Vacon time, Vacon duration, Vacoff time, and Vacoff duration, Vnton time, Vnton duration, Vntofftime, and Vntoff). Even once the tuning process has been conducted, the values of the tuned parameters only prevent forward flow for a given catheter and extension tube configuration.

However, claim 1 is not limited to any of these features, and indeed has a much broader scope. Claim 1 does not define any parameters of the cyclical valve cycle, or any relevant aspects of the catheter and extension tube configuration such as the bulk modulus and length of the system.

The description does not teach the skilled person how to put the invention into practice to account for the water hammer effect without first undergoing an involved tuning process, which yields specific valve cycle values relevant only for a given catheter and extension tube configuration.

It is noted that the dependent claims do go on to define at least specific parameters of the valve cycle and the catheter configuration. Taking account of the repercussive effect of these dependent claims on claim 1 it is implicit that claim 1 must cover embodiments in which the parameters have values outside the ranges and values defined in the dependent claims, but which somehow also “prevent forward flow”. However, there is no teaching in the document that would enable the skilled person to put such embodiments into effect.

Therefore, if the prevention of forward flow implies technical limitations beyond, for example, ensuring there is “net” aspiration during the cycle, or avoiding a strong positive pressure in the catheter that might dislodge a coked thrombus, then it is submitted that the skilled person is not provided with sufficient information to enable them to carry out the invention defined in claim 1, which is not limited to any of the essential features which the opposed patent teaches as necessary in order to mitigate for the water hammer effect. Claim 1 is therefore not sufficiently disclosed according to the requirements of the EPC.

2.2. Dependent claims

None of the dependent claims rectify the lack of sufficiency described above, because none of the claims define all the features which would be essential to preventing forward flow which may be created by the water hammer effect. In summary, the teaching of the patent suggests that forward flow that might occur due to the water hammer effect is only prevented when the entire system has been carefully “tuned” for

each of several factors, and none of the dependent claims define timings for each of Vacon time, Vacon duration, Vacoff time, and Vacoff duration, Vnton time, Vnton duration, Vntofftime, and Vntoff, the diameter of the lumen of the catheter, the length of various parts of the system such as the length of the catheter between vent valve and the distal end of the catheter and the lumen diameter, the bulk modulus of the catheter and extension tube, etc.

While additional comments are provided below on specific dependent claims, it is our submission that, depending on the meaning of the term “prevent forward flow” in claim 1, that none of the dependent claims meet the requirements of Article 83.

For example, while some of the dependent claims (e.g., claims 3, 5, and 7-12) define specific parameters and parameter ranges, these provide tunings for only a subset of the factors which the opposed patent teaches must be accounted for in tuning the arrangement. These claims therefore do not meet the requirements of Art. 83 EPC for corresponding reasons as claim 1.

2.2.1.Claim 12

Claim 12 defines that forward flow can be prevented by “regulating timing of the vent valve” of the distal portion out from the distal end during each cycle.

First, the opposed patent gives no details regarding how a controller should be configured or programmed to “regulate” the timing of a vent valve, other than the teaching at e.g. paragraphs 153-157 that certain specific timing values must be used in the valve cycle.

As submitted at section 2.1 with respect to claim 1, the opposed patent makes clear that forward flow via the water hammer effect is only prevented after the entire system has been “tuned” for each of several factors (e.g. Vacon time, Vacon duration, Vacoff time, and Vacoff duration, Vnton time, Vnton duration, Vntofftime, and Vntoff). Even once the tuning process has been conducted, the values of the tuned parameters only prevent forward flow for a given catheter and extension tube configuration.

Therefore, the skilled person is not taught how to prevent forward flow only by “regulating timing of the vent valve”, as defined in claim 12.

Therefore, the skilled person could not build or put the system of claim 12 into effect, such that claim 12 is not sufficiently disclosed according to the requirements of the EPC.

2.2.2.Claim 13

The opposed patent is silent regarding how the subject matter of claim 13 should be achieved. The concept of “physiological pressure” is only mentioned at paragraphs 40 and 149 of the description, and paragraph 40 only repeats the claim wording verbatim.

First, as the skilled person would be aware, “physiological pressure”, i.e. blood pressure, varies between patients.

Second, the patent does not teach how to “retain” a single pressure, i.e. the defined pressure which is “less than physiological pressure”, as required by claim 13, while also changing a level of vacuum, as required by claim 1. Claims 1 and 13 seem to contradict each other in this regard.

Further, the opposed patent makes clear at paragraph 147 that pressure at the distal end is only retained at less than or equal to physiological pressure when the ROAR effect occurs. In turn, paragraph 153 makes clear that the ROAR effect is only optimised after the entire system has been “tuned” for each of several factors (e.g. Vacon time, Vacon duration, Vacoff time, and Vacoff duration, Vnton time, Vnton duration, Vntofftime, and Vntoff). Even once the tuning process has been conducted, the values of the tuned parameters are only relevant for a given catheter and extension tube configuration.

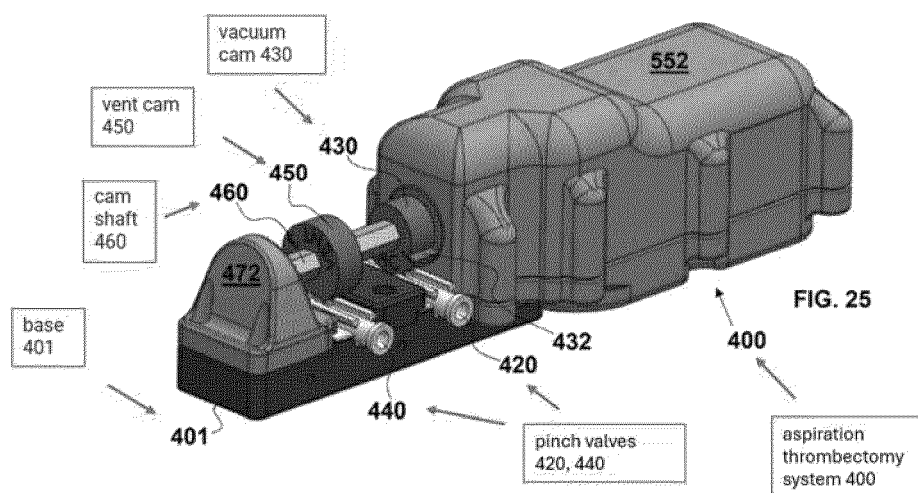
Therefore, the skilled person is not taught how to “retain a level of pressure at the distal end at less than physiological pressure” in the absence of the tuning process and the resulting specific values that process yields. Claim 13 is therefore not sufficiently disclosed according to the requirements of the EPC.

2.3. Claim 14

The subject matter of claim 14 is not disclosed or discussed anywhere in the opposed patent. Therefore, the skilled person is not taught by the opposed patent how to carry out the system defined in claim 14, such that it is not sufficiently disclosed according to the requirements of the EPC.

Paragraph 41 contains a verbatim repetition of the wording of claim 14, but does not contain any additional teaching that might assist the skilled person when putting the invention into practice.

“Embodiment 2”, i.e. the embodiment discussed in relation to Figs. 25-41 of the opposed patent, comprises a shaft in the form of a “cam shaft”. However, no valves are mounted to this cam shaft. Fig. 34 is reproduced below:



As described at paragraph 111, the valves 420, 440 in this embodiment are “mounted to a base 401”. As described at paragraph 114, it is instead the “vacuum and vent cams 430, 450” which are “fixed rotationally to the cam shaft 460”.

Therefore, rather than providing the skilled person with the teaching needed to put the claimed system into effect, it is made explicitly clear in the opposed patent that the valves should not be mounted to a shaft, but should instead be mounted to a base. The opposed patent therefore provides a teaching which is opposed to the subject matter of claim 14.

Even if the vent cams can be considered part of the valves, contrary to the teaching of the opposed patent, this still does not constitute an enabling disclosure of a system in which a vacuum valve and vent valve are “mounted together on the shaft”, as defined in claim 14.

In addition, as set out below at section 3 in relation to the invalidity of the priority claims, “embodiment 2” depicted in Figs. 25-41 does not “prevent forward flow” as required by feature 1[i] of claim 1. Instead, the Figs. 25-41 embodiment *relies* on forward flow in order to create maceration, and therefore forward flow is “*intentional*” (see paragraph 117). Therefore, the skilled person is not provided with any teaching that would enable them to build a functional clot removal system in which forward flow is prevented (as is required by claim 1) and in which two valves are mounted on a shaft (as is defined in claim 14).

Accordingly, the subject matter of claim 14 is not disclosed in a manner sufficiently clear and complete for it to be carried out by a person skilled in the art.

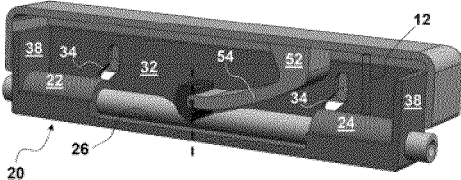
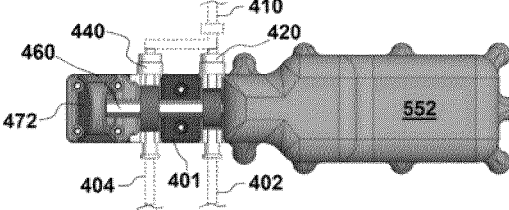
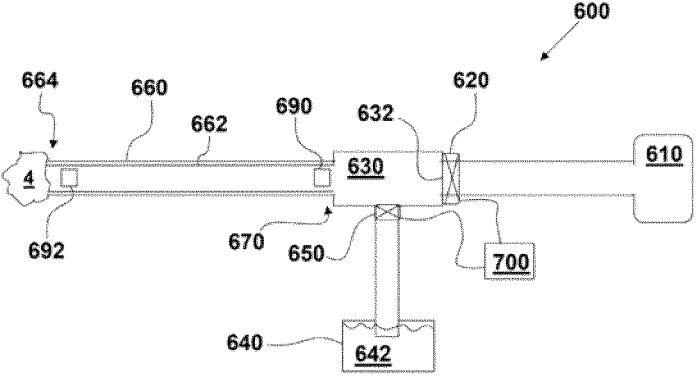
3. Invalidity of Priority Claims

The opposed patent was filed on 19 July 2019, and claims priority to three applications:

1. US provisional application No. 62/701,086 (“document P1”), filed 20 July 2018;
2. US provisional application No. 62/750,011 (“document P2”), filed 24 October 2018; and
3. US utility application US 16/516,232 (“document P3”), filed 18 July 2019.

However, none of the claims of the opposed patent are entitled to either the first, or the second, of these priority claims because the subject matter of the claims is not directly and unambiguously derivable from either document P1 or document P2.

Further to the comments made above in section 1.1, the following table summarises the three main embodiments of the opposed patent, and in which priority document they were first introduced:

<p>“Embodiment 1” Introduced in P1.</p> <p>Corresponds with figures 1-24 and paragraphs 1-109 of the opposed patent.</p>	 <p>FIG. 8</p>
<p>“Embodiment 2” Introduced in P2.</p> <p>Corresponds with figures 25-46 and paragraphs 110-136 of the opposed patent.</p>	 <p>FIG. 26</p>
<p>“Embodiment 3” Introduced in P3.</p> <p>Corresponds with figures 46-72 and paragraphs 137-181 of the opposed patent.</p>	

In the opposed patent, there are very clear delineations between the content introduced in each of the priority documents.

In particular, paragraph 110 marks the introduction of the “P2” content, and introduces Figs. 25 to 41 as describing a different embodiment capable of *“operating with an automatic, rapid, and repeated onset of pressure change”*.

Similarly, paragraph 137 of the opposed patent marks the introduction of the “P3” content, as follows: *“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”*.

3.1. The first priority claim is invalid

At a high level, US provisional application No. 62/701,086 (“P1”) relates to “embodiment 1” of the opposed patent. This embodiment is described above in section 1.1.

Notably, the claims of the opposed patent are directed to ‘embodiment 3’. i.e. the embodiment depicted in Figs. 46-72 of the opposed patent. P1 does not contain any figures or description relating to ‘embodiment 3’.

The wording of the claims of P1 does not align with the wording of the claims of the opposed patent. In fact, there are several clear and evident differences. The wording of the claims of the opposed patent is not present anywhere in P1.

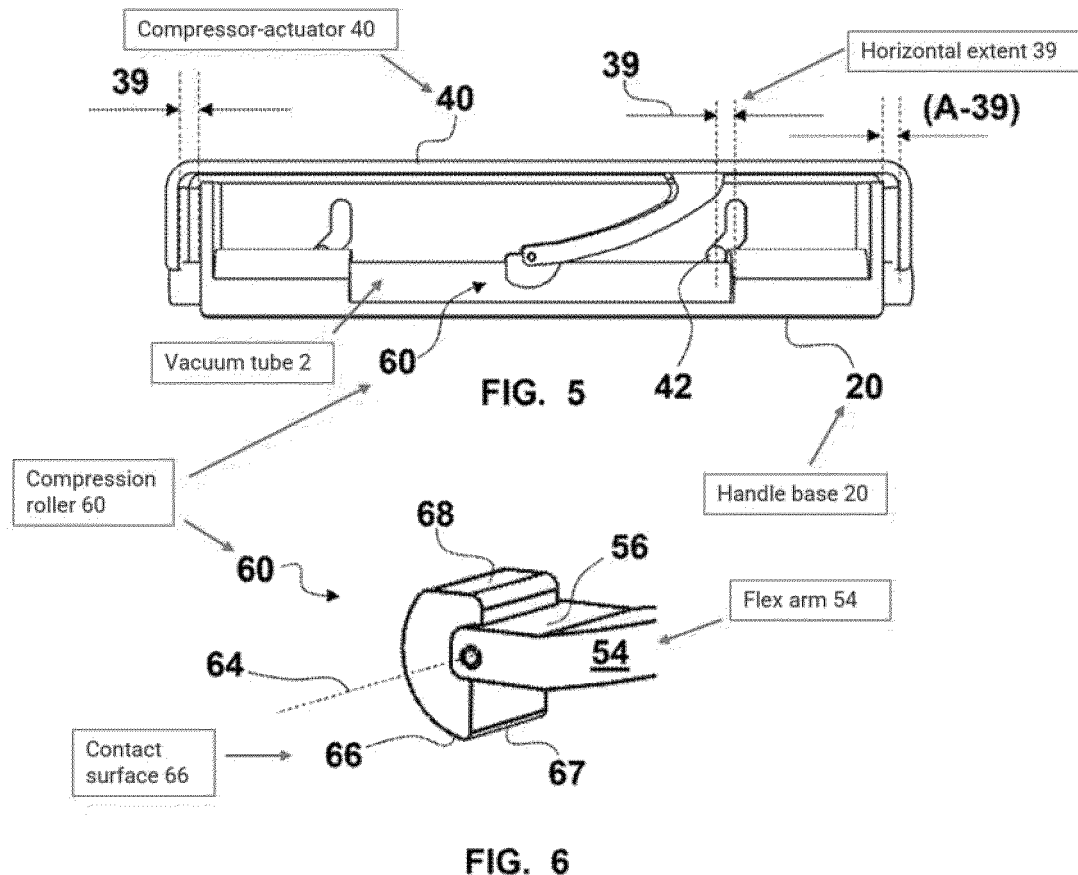
A primary aim of the embodiment disclosed in P1 ('embodiment 1') is to provide an aspiration/suction catheter with a mechanism to "*stop the vacuum*" and which is capable of "*press[ing] the distal fluid column in reverse, i.e., a positive displacement without a check valve, referred to herein as a column shift*" (paragraph 16 of P1). The aim of the column shift is to "*distally dislodge*" a thrombus from a distal opening of the vacuum channel (paragraphs 15, 16, 39, 72-75 of P1).

Selected paragraphs of P1 are reproduced below to assist the Opposition Division (with emphasis added).

[0015] 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.

[0016] 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.

As described in paragraphs 67-68 of P1, a 'column shift' can be effected by providing a compression roller 60 having an exterior contact surface 66 that contacts the vacuum tube 2. This structure is depicted in Figs. 5 and 6 of P1, reproduced below.



As the compressor-actuator 40 is pressed toward the handle base 20, contact point 67 of the exterior surface 66 moves “against the vacuum tube 2 to occlude the vacuum channel 3 completely” (paragraph 68 of P1).

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” and “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” (paragraph 68 of P1).

“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” (paragraph 69 of P1).

In order to effect this column shift, a user can squeeze the hand-held controller to “translate the fluid column in the distal direction of the vacuum tube 2” (paragraph 69 of P1).

3.1.1. Priority document P1 does not disclose the structure required by claim 1

The subject matter of claim 1 of the opposed patent cannot be directly or unambiguously derived from P1.

Regarding features 1[b] and 1[c], P1 does not disclose a “controllable vacuum valve” or a vacuum source “fluidically connected to the vacuum valve”.

The “flex arm 54” and the attached “compression roller 60” cannot be considered as a vacuum valve as required by the claim, at least because it is not “fluidically connected” to a vacuum source.

For example, P1 does not disclose feature 1[d] of the claim, because the P1 document is silent regarding the use of a “vent valve” or a “vent liquid input”.

Regarding features 1[e] and 1[f], P1 also contains no disclosure of a “vent fluid source containing a vent liquid”, nor is there any disclosure of a manifold which meets the requirements of feature 1[f] of the claim.

Regarding features 1[g] and 1[h], P1 discloses a “one-handed controller 10” which the user can “squeeze” to shut off vacuum and “translate a fluid column in the distal direction of the vacuum tube” (paragraph 69 P1). However, this controller is clearly not connected to either a vacuum valve or a vent valve.

In addition, the “one-handed controller 10” of P1 is not *itself* configured to cyclically open and close any valves; instead the user controls the action of the controller by squeezing the handle parts 20, 40 together.

3.1.2. Priority document P1 does not disclose the prevention of forward flow

With respect to feature 1[i], i.e. “prevent forward flow of the distal portion out from the distal end during each cycle”, this feature is also clearly not disclosed in P1.

As set out above, a primary aim of the embodiment disclosed in P1 (‘embodiment 1’) is to provide an aspiration/suction catheter with a mechanism to “stop the vacuum” and which is capable of “press[ing] the distal fluid column in reverse, i.e., a positive displacement without a check valve, referred to herein as a column shift” (paragraph 16 of P1). The aim of the column shift is to “distally dislodge” a thrombus from a distal opening of the vacuum channel (paragraphs 15, 16, 39, 72-75 of P1).

Therefore, the skilled person reading P1 is not taught that forward flow is to be prevented. Instead, P1 teaches the opposite: that forward flow should be intentionally created in order to push the thrombus distally out of the lumen, thereby dislodging it.

Accordingly, feature 1[i] of claim 1 cannot be derived from P1, and certainly not in a direct or unambiguous way. In fact, P1 teaches the use of a system and methodology which is in direct contrast with the system and methodology defined in claim 1 of the opposed patent.

The opposed patent also acknowledges this at paragraph 137, which marks the introduction of the P3 content as follows (emphasis added): “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”.

This paragraph clearly implies that those embodiments referred to before 137, including main embodiment 1, make use of forward flow rather than prevent it.

It follows that claim 1 of the opposed patent is not entitled to its first priority claim, and neither are any of the dependent claims.

3.2. The second priority claim is invalid

US provisional application No. 62/750,011 ("P2") introduces new subject matter relating to "embodiment 2" of the opposed patent. This embodiment is described above in section 1.1.

Much of the content of P2 is also included in document P1. With reference to the content of P2, in comparing the subject matter which P2 adds in comparison with the earlier filed priority document P1, the 'new' subject matter can be summarised as follows:

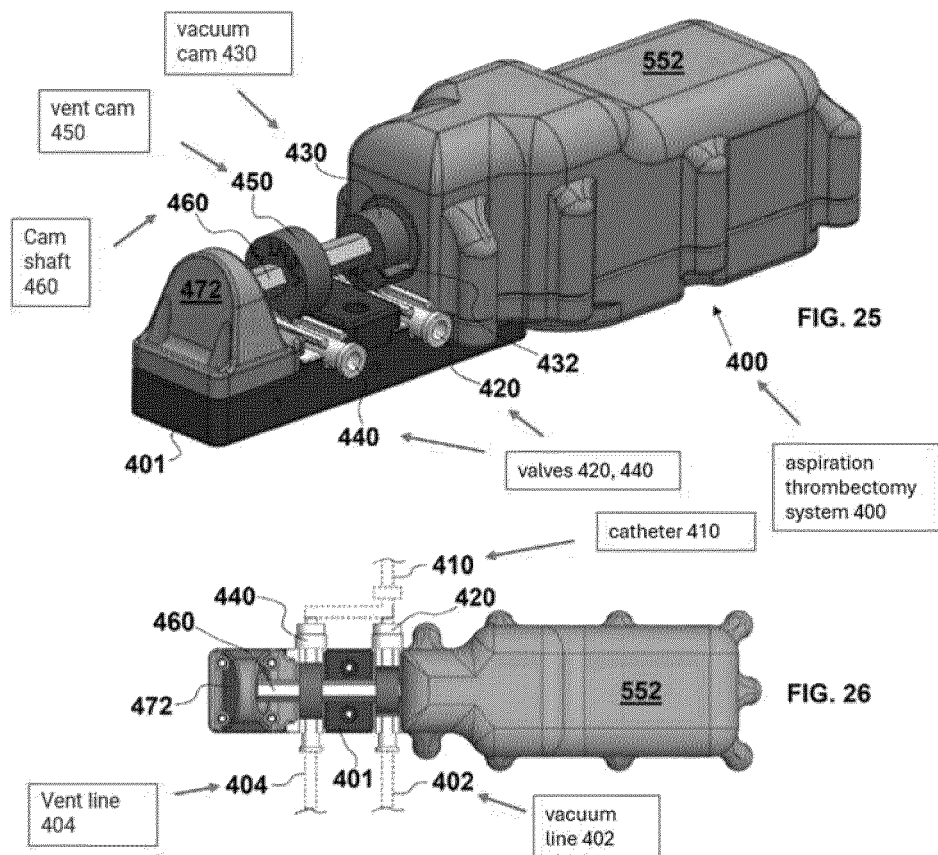
- new figures 25-46; and
- accompanying description of these figures at paragraphs 119-142 of P2.

As with document P1, P2 does not contain any figures or description relating to the claimed 'embodiment 3'.

The wording of the claims of P2 does not align with the wording of the claims of the opposed patent. In fact, there are several clear and evident differences. The wording of the claims of the opposed patent is not present anywhere in P2.

The newly added subject matter includes two alternative implementations. As explained at paragraph 119, newly added 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"*. This implementation includes pinch valves. As explained at paragraph 134, instead of pinch valves, *"In another exemplary alternative, a rotational pintle valve can be used, as shown in Figs. 42 to 46"*.

The first of these implementations is depicted below:



A motor can rotate the cam shaft 460 to move the cam set between open and closed states. Two of these states are depicted in Figs. 31 and 32, reproduced below.

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 (see paragraph 55 of P2):

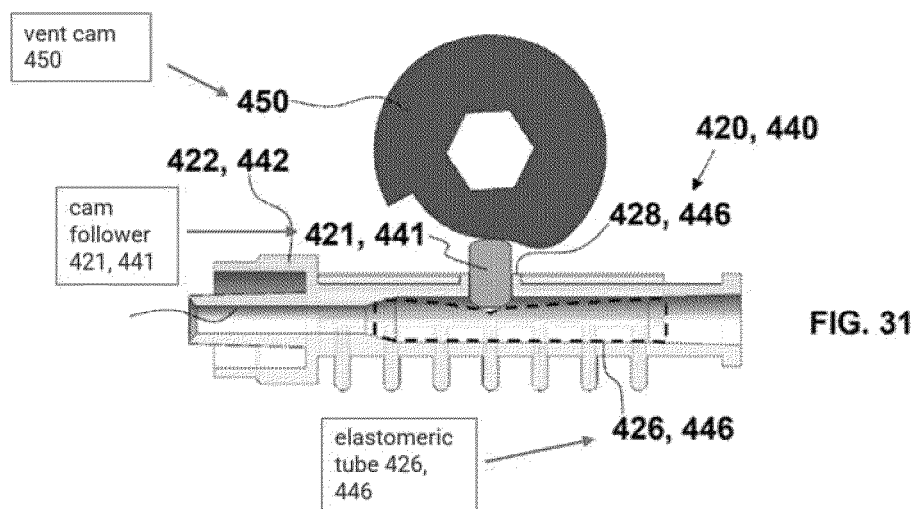
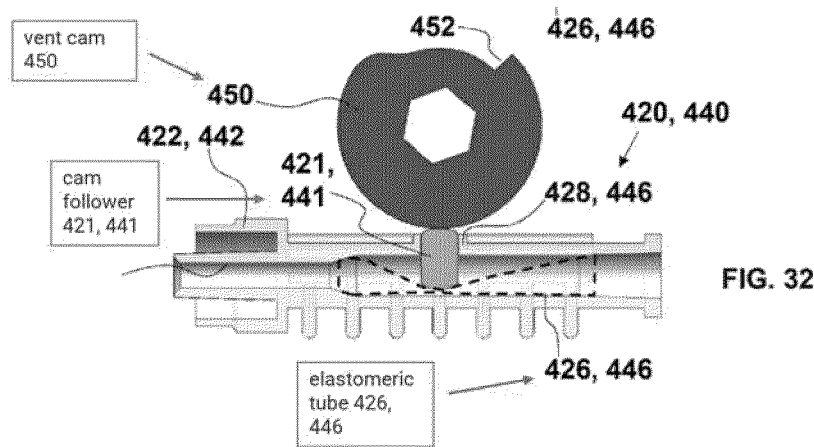


Fig. 32 is an enlarged cross-sectional view of the valve and cam set of Fig. 31 with the cam in a rotational position to close the valve (see paragraph 56 of P2):



3.2.1. Priority document P2 does not disclose the structure required by claim 1

P2 is silent regarding the use of a “controller” which has the features required by feature 1[g].

At paragraphs 122 and 123, P2 discloses the use of a “controller” which can control a motor. The motor is configured to rotate the cam shaft 460, and thereby “*set the valves 420, 440 in whatever state that is desired*” for example those states depicted in Figs. 31 and 32.

However, such a controller is not “connected to the vacuum valve and the vent valve” as required by feature 1[g], but is instead connected to vent and valve cams 420, 440 via the cam shaft 460.

In addition, the controller is not configured to *selectively* open and close the vacuum valve and the vent valve. The valves cannot be individually controlled. The vacuum and vent cams 430, 450 are “fixed rotationally to the cam shaft 460” (paragraph 114). The valves can only be opened and closed together in a way defined by the relative orientations of the vent cams.

3.2.2. Priority document P2 does not disclose the prevention of forward flow

The newly added paragraphs in P2 are also silent regarding any mention of preventing “*forward flow*” as required by claim feature 1[i]. Instead, in a manner consistent with embodiment 1 disclosed in earlier priority document P1, the newly disclosed embodiment *relies* on forward flow to create a distal movement of the clot. For example, P2 states (emphasis added):

[00126] [...] 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. 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 skilled person reading P2 is not taught that forward flow is to be prevented. To the contrary, P2 teaches the opposite: that forward flow should actively and intentionally be created in order to push the thrombus distally out of the lumen, thereby dislodging it.

Accordingly, priority document P2 does not contain any disclosure at all, let alone an enabling disclosure, relating to the subject matter of claim feature 1[i].

The opposed patent also acknowledges this at paragraph 137, which marks the introduction of the P3 content as follows (emphasis added): “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”.

In relation to the embodiment depicted in Fig. 26, i.e. the embodiment introduced for the first time in document P2, the opposed patent states:

[117] [...] 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.

The skilled person is therefore explicitly taught by the priority document P2, and by the opposed patent itself, that the newly introduced embodiment in P2 makes use of forward flow. The use of forward flow is not only intentional, but is in fact essential for the proper working of this embodiment. This is in direct contrast with feature 1 [i] of claim 1 of the granted patent.

In view of the above, it follows that claim 1 of the opposed patent is not entitled to either its first or its second priority claim.

In addition, none of the claims which depend from claim 1 are entitled to the first or second priority claims. This is by virtue of their dependencies on claim 1, but also because the subject matter of these claims cannot be found in either of priority documents P1 or P2.

4. Lack of novelty (Art. 100(a), Art. 52(1), Art. 54 EPC)

4.1. Claim 1

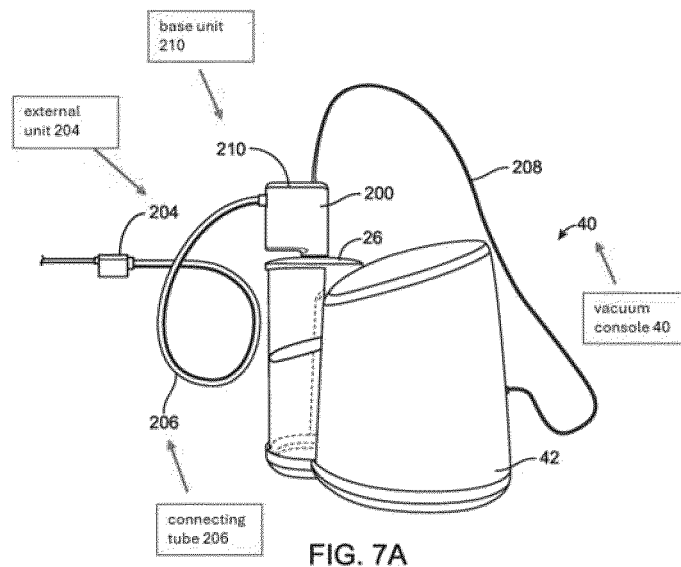
4.1.1. O1 (EP 4 461 253 A2) – “Teigen”

As set out above, the subject matter of claim 1 of the opposed patent is not entitled to either of the earliest claimed priority dates. O1 is a European patent application with a priority date of 24 July 2018. The priority date of O1 pre-dates the effective filing date of the opposed patent. The PCT application from which this EP application derived was published on 30 January 2020 as WO 2020/023541 A1. This PCT application validly entered the EP regional phase. O1 is therefore prior art under Article 54(3) EPC.

To provide a brief overview, O1 discloses devices and methods for controlling clot removal from a patient's vasculature by aspiration thrombectomy (see “field of invention” and paragraph 2 of O1).

In the system of O1, pulsed aspiration may be automatically applied (e.g. when a clogged catheter is detected) or on demand by a user in order to enhance the ingestion of large, tough, or otherwise troublesome occlusions (paragraph 11).

Figs. 7A (reproduced below) and 7B of O1 illustrate a vacuum console and collection canister having a vacuum aspiration control system attached thereto (see ‘brief description of figures’ at paragraph 32).



In use, an aspiration catheter is fitted downstream of this system, e.g. the external unit 204 may be configured to connect directly to a hub or other proximal end of an aspiration catheter (paragraph 44).

Fig. 9 of O1 illustrates an exemplary base unit 200b enclosing an on-off valve and a controller 220. The on-off valve comprises a solenoid actuator 230 and a pinch valve 228 (paragraph 20). The controller 220 includes a printed circuit board (paragraph 47). The base unit 200b is of the type suitable for use in the vacuum aspiration control system depicted in Figs. 7A and 7B:

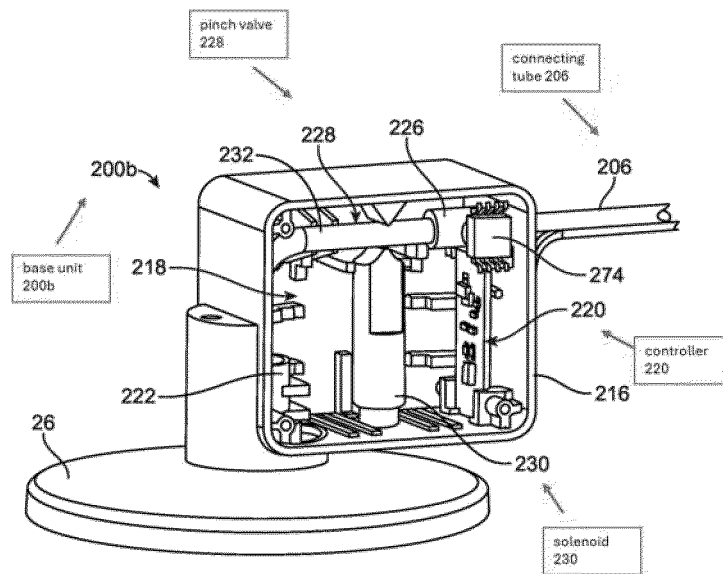


FIG. 9

Fig. 14 illustrates an exemplary pulsed fluid injection assembly suitable for use in the same system (see 'brief description of figures' at paragraph 32).

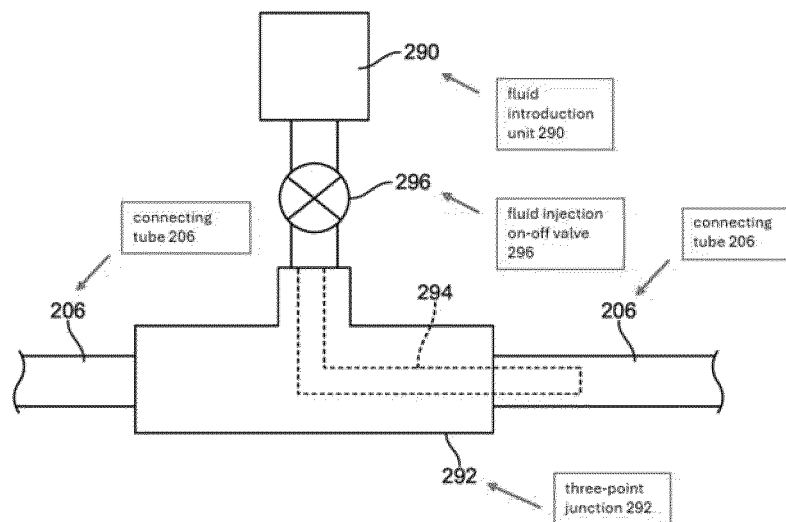
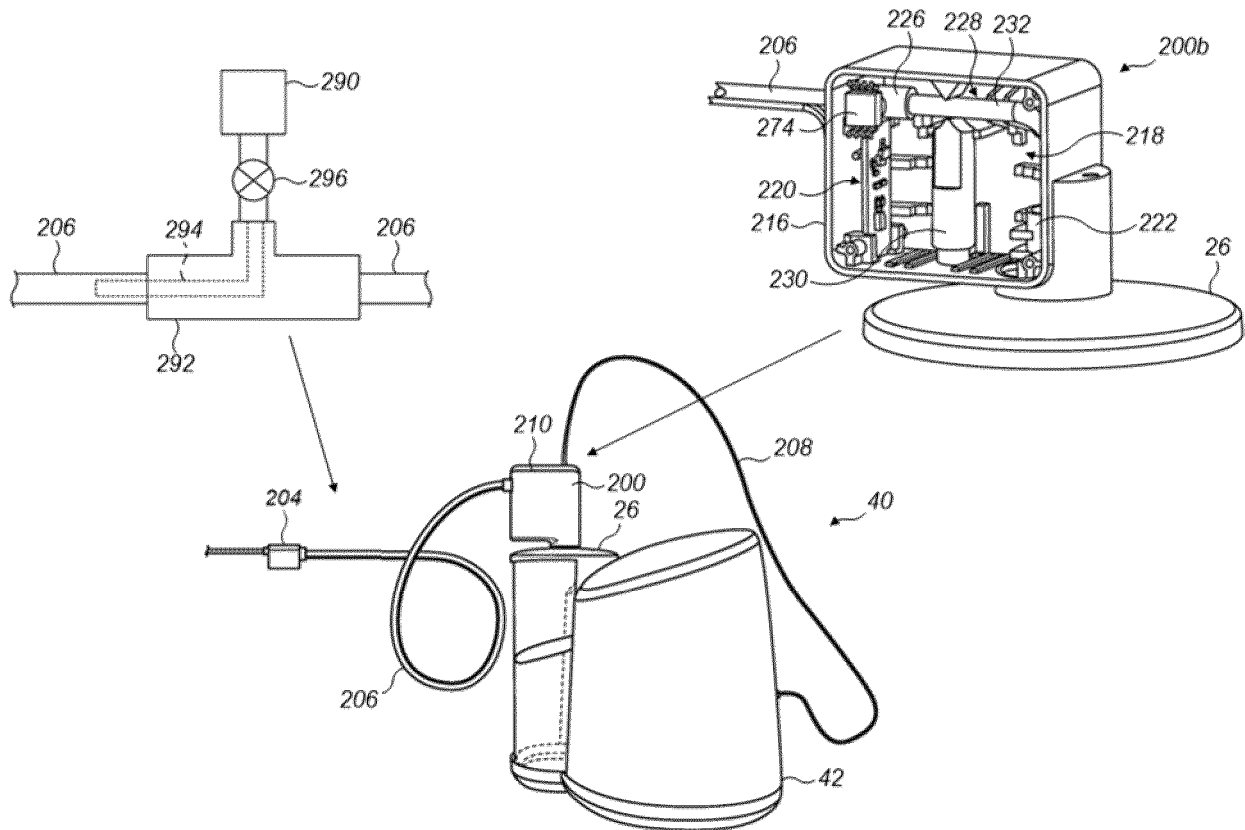


FIG. 14

The controller 220 of O1 generates pressure differentials within a lumen of the aspiration catheter by alternatively opening and closing the vacuum source valve and the pressure source valve (see abstract and claim 1).

The following illustration is a composite figure showing Fig. 14, Fig. 9, and Fig. 7a of O1. This composite figure is not included in O1, and is provided herein solely to enable a quick understanding of the relative locations that each of the above arrangements would take in the relevant embodiment of a dynamic

aspiration system according to O1. It should be noted that figs. 9 and 14 have been “flipped” in order to align with the orientation of the console and collection canister shown in Fig. 7A:



1[Pre] (A clot removal system)

O1 relates to “*devices and methods for controlling clot removal from a patient's vasculature by aspiration thrombectomy*” (see ‘field of the invention’, at paragraph 2 of O1).

O1 states (emphasis added):

[13] [...] The present invention may be useful with any thrombectomy, embolectomy, atherectomy, or other catheter or probe system where blood and clot are withdrawn wholly or partially by application of a vacuum to the proximal end of any reperfusion, aspiration catheter or probe for the purpose of clot extraction.

1[a] (a catheter having a distal end and defining a lumen filled with a liquid column)

O1 clearly discloses the use of a catheter (see e.g. abstract and claim 1).

(abstract) A dynamic aspiration system for use with a vacuum source, a pressure source, and an aspiration catheter includes a connecting tube configured to place the vacuum source, the pressure source, and the aspiration catheter in fluid communication [...]

O1 describes a system for use in an aspiration method. The method is described throughout the application, e.g. at paragraphs 25, 27, 119, and 170, and involves (emphasis added):

[0025] [...] The vacuum aspiration method comprises engaging a distal end of an aspiration catheter against an occlusion in the blood vessel. A vacuum is applied through an aspiration lumen of the aspiration catheter using a vacuum source coupled to a proximal end of the aspiration lumen by a connecting tube. In this way, portions of clot and other occlusive material may be drawn into the aspiration lumen, through the connecting tube, and into a collection receptacle by the vacuum source. Flow through the connecting tube is sensed, and a valve is automatically closed to stop flow through the connecting tube when the sensed flow exceeds a determined value while the vacuum source remains on. Flow through the connecting tube will be later reestablished by opening the valve, and the steps are repeated until a desired amount of clot has been aspirated.

[0027] In some embodiments of the present invention, the controller includes an algorithm that is used to interpret pressure sensor signals to determine whether the contents flowing through a catheter should be characterized as unrestricted, restricted, or clogged. Generally, unrestricted flow is a high flow that may be characterized as excessive and may be primarily or completely comprised of healthy blood, clot-free blood, or blood free of vessel-obstructing clot that is not helpful to aspirate, restricted flow may be comprised of a mix of healthy blood and clot or other occlusive material, and a clog may be caused by a clot or other occlusive material within an aspiration catheter, partially within an aspiration catheter, adjacent to an aspiration catheter, or in other connecting tubing attached to the aspiration catheter [...]

When using the system of O1, blood and portions of the clot are drawn into the collection canister (see e.g. paragraphs 6 and 54). An algorithm is used to make determinations about the “flow” of liquid through the catheter.

Finally, in addition to the above explicit teachings in O1, the opposed patent states, at paragraph 145, that: “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”.

That is, the opposed patent accepts that the fluid column in the catheter comprises aspirated fluid. Clearly, any aspiration thrombectomy system therefore comprises a liquid column in use, at least due to the aspiration of liquid from vasculature.

It follows that, in use, the lumen of the catheter of O1 would be filled with a liquid column having a proximal and a distal portion.

1[b] (a controllable vacuum valve)

The system of O1 comprises a “vacuum source valve” and “a controller configured to modulate the vacuum source valve” (see abstract, claim 1, paragraphs 20-23).

The vacuum source valve is referred to in O1, at times, as an “on-off valve”; for example O1 discloses that the vacuum aspiration system comprises “a base unit which incorporates at least one on-off valve and a controller” (paragraph 24).

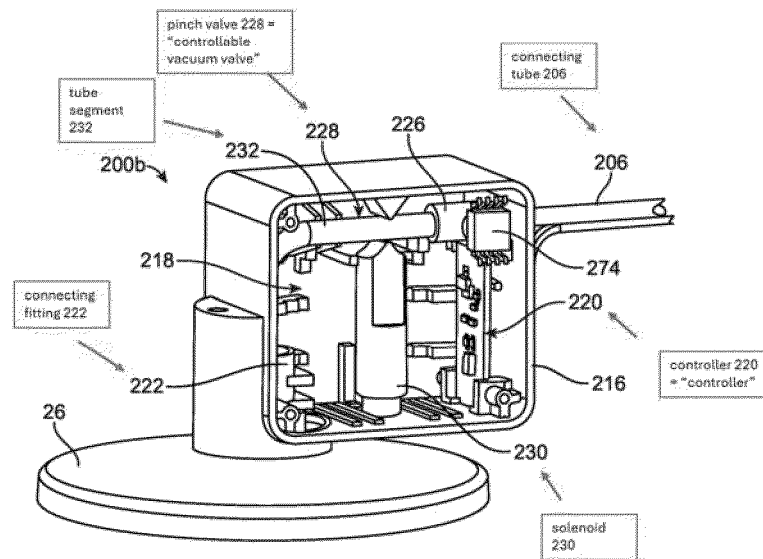


FIG. 9

In relation to Fig. 9, O1 states (emphasis added):

[0047] [...] The tube segment 232 may be collapsible and positioned in a pinch valve 228 which is driven by a solenoid 230. Pinch valve 228 may be biased into a closed position by a compressive spring (not visible), unless it is opened by solenoid 230. The base unit 200b further includes a connecting fitting 222 which is configured to be removably secured to a vacuum fitting (not shown) on the lid 26 of the canister 44. The controller 220 is configured to open and close the pinch valve 228 to allow and prevent, respectively, the flow of clot and blood through the tubing segment 232 from the aspiration catheter into the collection canister. [...]

1[c] (a vacuum source fluidically connected to the vacuum valve)

O1 discloses a system comprising a connecting tube configured to place a vacuum source, a pressure source, and an aspiration catheter in fluid communication (abstract, claim 1).

Paragraph 14 states (emphasis added):

[0014] In a first aspect, the present invention provides a vacuum aspiration control system for use with a vacuum source and an aspiration catheter. The system comprises a flexible connecting tube, an on-off valve, a sensing unit, and a controller. The connecting tube is linear in an unconstrained configuration and is configured to connect the vacuum source to an aspiration lumen in the aspiration catheter. The on-off valve is configured to be operatively connected to the connecting tube, and the sensing unit is configured to determine flow rate within the connecting tube and to produce a signal representative of such flow, typically as either unrestricted flow, restricted flow, or clogged. [...]

And paragraph 24 states (emphasis added):

[0024] In specific embodiments, the vacuum aspiration systems of the present invention comprise a base unit which incorporates at least one on-off valve and the controller. The base unit will typically be configured to be mounted directly on or near a vacuum pump or console and will usually include a connecting cable in order to receive power from the vacuum console or line and optionally exchange information with the controller and the vacuum console. The connecting tube typically has a proximal end configured to connect the vacuum source and distal end configured to connect to the aspiration catheter. [...]

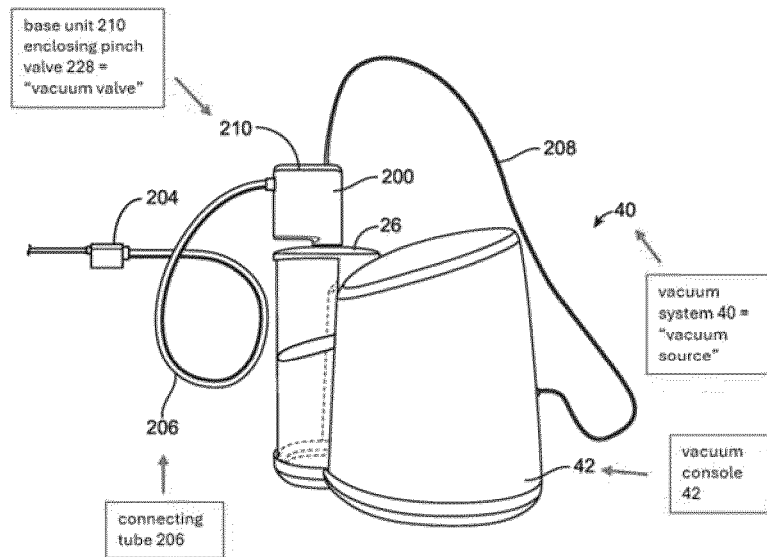


FIG. 7A

The “connecting tube” of O1 is shown in Figs. 7A, 9 and 14, all reproduced above, using reference numeral 206. Because the controllable on-off valve in O1 is positioned along the connecting tube between the vacuum source and the aspiration catheter to open to permit aspiration and close to block aspiration, the skilled person would have recognized that the vacuum source is “fluidically connected” to the on-off valve.

1[d] (a controllable vent valve having a vent liquid input)

Claim 1 of O1 defines a “pressure source valve” which a controller can modulate, along with a vacuum source valve, to generate pressure differentials within the lumen of the aspiration catheter (abstract, claim 1).

Fig. 14 depicts a form which this pressure source valve can take within a pulsed fluid injection assembly. The assembly comprises a vent liquid input in the form of a fluid introduction unit 290 and a controllable vent valve in the form of a “fluid injection on-off valve 296” (paragraph 67).

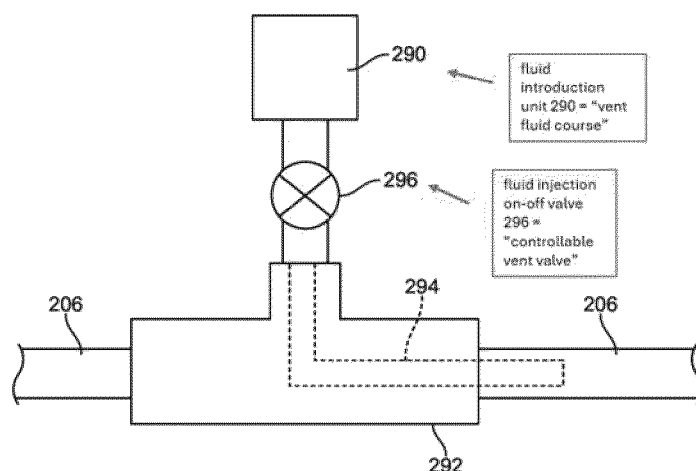


FIG. 14

O1 explains that:

[0067] [...] A fluid injection on-off valve 296 controls the flow of fluid (either liquid or gas) to inject pulses of pressure into the clot flow path that may facilitate the extraction of clot or other occlusive substances. In some instances, the flow of fluid is introduced directly into the connection tubing 206. In other instances, the flow of fluid first traverses an injection tube 294 before entering the connection tubing 206. The injection tubing 294 may direct the pressure pulse towards the catheter, which may optimize the pressure pulse.

The skilled person would have understood the fluid injection valve 296 disclosed by O1 to be a “vent valve”, as that term is used in the opposed patent, because its function is to relieve vacuum pressure by creating a pressure differential via the introduction of fluid into the catheter (see paragraphs 65, 67).

1[e] (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)

Referring again to Fig. 14, the figure depicts a vent fluid source in the form of a fluid introduction unit 290 which is connected to a controllable vent valve in the form of a “fluid injection on-off valve 296” (paragraph 67).

In relation to the Fig. 14 embodiment, O1 discloses that “by introducing fluid into the catheter, where the fluid is at a pressure between full vacuum and ambient pressure, at ambient pressure, at systolic pressure, or above systolic pressure” (paragraph 65).

The skilled person would have recognised that the fluid in the fluid introduction unit 290 is a “vent liquid” and that this fluid is fluidically connected to the fluid injection on-off valve 296, and that when the fluid injection valve 296 is closed, it would retain the fluid within the fluid introduction unit 290 until the valve is reopened to allow the fluid to flow into the three-point junction 292.

1[f] (a manifold connected to the catheter, to the vacuum valve, and to the vent valve)

The “three-point junction 292” shown in Fig. 14 is a manifold connected to the catheter and the vacuum valve (via connecting tube 206) and also to the “fluid injection on-off valve 296”.

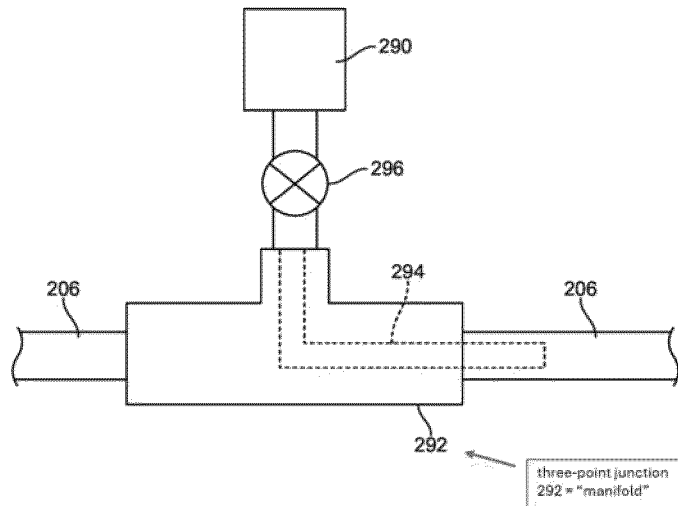


FIG. 14

O1 discloses that the three-point junction may be “positioned between the base unit 210 and the external unit 204 or may be positioned distal to both the base unit 210 and the external unit 204 - i.e. in close proximity to an attached aspiration catheter”.

Because the fluid injection on-off valve 296 “controls the flow of fluid” to “inject pulses of pressure into the clot flow path” (paragraph 67), and because the pinch valve 228 can be controlled by the controller to allow and prevent the flow of clot and blood from the aspiration catheter into a collection canister (paragraph 47), the skilled person would clearly recognise that the three-point junction fluidically connects a proximal portion of the liquid column in the lumen both to the vacuum source through the vacuum valve (e.g. the pinch valve 228), and to the vent fluid source through the vent valve (e.g. the fluid injection on-off valve 296).

1[g] (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)

O1 describes “a controller configured to modulate the vacuum source valve and the pressure source valve, wherein the controller generates pressure differentials within a lumen of the aspiration catheter by alternating between opening and closing the valves” (claim 1, abstract). The dependent claims, in particular claims 2, 3, 8, 10, 11, 12, 13, 14, and 15, disclose further features of the controller and its control of the vacuum source valve and pressure source valve.

As explained at paragraph 47, the tube segment 232 of connecting tube 206 may be collapsible and positioned in the pinch valve 228, which is driven by the solenoid 230. The controller 220 is configured to “open and close the pinch valve 228 to allow and prevent, respectively, the flow of clot and blood through the tubing segment 232 from the aspiration catheter into the collection canister”.

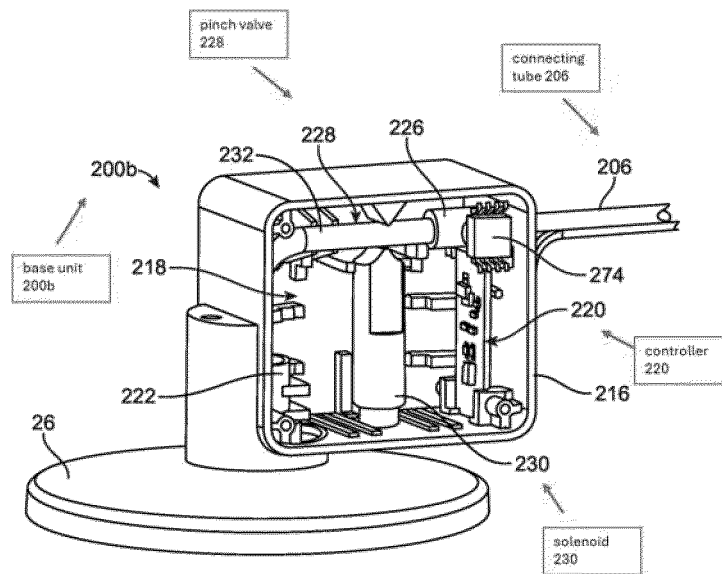


FIG. 9

Accordingly, responsive to opening pinch valve 228, the vacuum source is “fluidically connected to the liquid column in the lumen” of the catheter.

Turning to the vent valve depicted in Fig. 14, when the fluid injection on-off valve 296 is open, fluid is introduced into the catheter (paragraph 65) in order to “inject pulses of pressure into the clot flow path that may facilitate the extraction of clot or other occlusive substances” (paragraph 67).

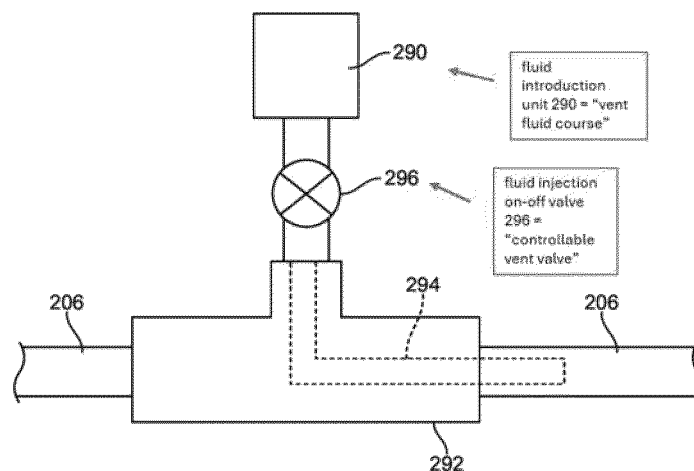


FIG. 14

Accordingly, responsive to opening the fluid injection on-off valve 296, the skilled person would understand that the fluid in the fluid introduction unit is “fluidically connected to the liquid column in the lumen” of the catheter when the fluid injection on-off valve 296 is open.

1[h] (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)

O1 describes "a controller configured to modulate the vacuum source valve and the pressure source valve, wherein the controller generates pressure differentials within a lumen of the aspiration catheter by alternating between opening and closing the valves" (claim 1, abstract).

In describing the high-level method which may be implemented by the system of O1, paragraph 31 states:

[0031] In further embodiments of the method, pressure differentials are generated by closing a valve to a vacuum pump, opening a valve to a source of pressure, wherein the pressure is at least above that of the vacuum, and then re-opening the valve to the vacuum pump. [...]

O1 explains that the controller, e.g. the controller 220 in the base unit depicted in Fig. 9, implements an algorithm (paragraphs 27, and 53-62). When the algorithm detects a clog in the aspiration catheter, e.g. from a thrombus becoming "corked" at the distal end of the catheter, the algorithm may "cause the system to generate a variety of pressure pulses with an extraction cycle" (paragraph 27) to help remove any clogs or occlusions.

Paragraphs 63-66 discuss the use of extraction cycles which are "useful to clear occlusions in an aspiration catheter or to facilitate the aspiration of clot that are large or otherwise hard to aspirate" (paragraph 63). Multiple mechanisms are disclosed which "*facilitate thrombus ingestion into an aspiration catheter*" (paragraph 63).

For example, an extraction cycle may involve alternating "*between providing vacuum aspiration and relative positive pressure*" (paragraph 64). O1 discloses that "*Pressure differentials in the catheter may be generated in a number of ways. In one example, pressure is generated by simply closing off a catheter's access to the vacuum source. In another example, pressure is generated by introducing fluid into the catheter, where the fluid is at a pressure between full vacuum and ambient pressure, at ambient pressure, at systolic pressure, or above systolic pressure (Figs. 14-17)*".

The skilled person would understand that an extraction cycle which alternates between vacuum aspiration and relative positive pressure in the context of an implementation in which the positive pressure may be generated by introducing fluid into the catheter comprises the cyclical opening and closing of the vacuum valve (i.e. the pinch valve 228) and the vent valve (i.e. fluid injection valve 296) in order to change a level of vacuum at the distal end of the catheter.

Fig. 20 of O1 depicts an example pulsation protocol which may be used in an extraction cycle and is reproduced below:

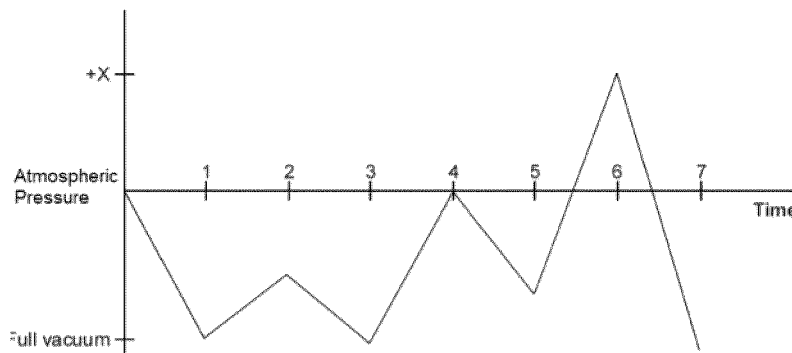


FIG. 20

In relation to Fig. 20, O1 teaches that:

[0077] [...] An extraction cycle may use a pulsation protocol to systemically manipulate the amount of pressure within a catheter to facilitate the extraction of occlusive material . Pressure in a catheter may be manipulated by a variety of methods. For instance, vacuum aspiration may be used to reduce pressure within the catheter and the removal of vacuum suction and/or the introduction of fluid may be used to increase pressure within the catheter. [...]

The skilled person would understand that the graph represents a “change a level of vacuum at the distal end” of the catheter, in order that the “extraction of occlusive material” is facilitated as intended.

1[i] (prevent forward flow of the distal portion out from the distal end)

As set out above, the controller is configured to “modulate the vacuum source valve and the pressure source valve”, and generate pressure differentials within a lumen of the aspiration catheter by “alternating between opening and closing the valves” (at least abstract and claim 1 of O1).

O1 teaches that these pressure differentials may be generated in a number of ways, for example by “introducing fluid into the catheter, where the fluid is at a pressure between full vacuum and ambient pressure” (paragraph 65).

The skilled person would understand that the effect of introducing a fluid into the catheter which is “between full vacuum and ambient pressure” in this way is to increase the relative pressure at the distal end of the aspiration catheter, thereby temporarily partially relieving the “full vacuum”, but while maintaining an overall level of negative pressure (suction).

This interpretation is supported by paragraph 71, which discusses an aim of “allowing a minimal volume of fluid from the pressure source to be introduced into a proximal end of aspiration catheter to increase the relative pressure at a distal end of the aspiration catheter before reverting to vacuum by re-opening vacuum valve and closing pressure valve” (emphasis added).

Partially relieving the vacuum via pulsed aspiration enhances the ingestion of large, tough, or otherwise troublesome occlusions. The skilled person would understand that, by maintaining an overall level of negative pressure (suction) throughout the application of pulsed aspiration, forward flow is prevented.

In addition, the opposed patent is not clear about which specific features give rise to the prevention of forward flow. Any such features are certainly not clearly recited in the claim. At paragraph 139, the opposed patent defines forward flow as follows:

[0139] [...] The term “forward flow” is used herein to define an amount of liquid in the lumen that exits the distal end 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 pL). 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.

At paragraph 43 of the opposed patent, it is stated that “By cycling the vacuum and vent valves at a sufficiently fast rate, a pressure measurement at a rate of one thousand samples per section 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” (emphasis added).

So, the opposed patent teaches that forward flow can be prevented by cycling the vacuum and vent valves at a sufficiently fast rate. The opposed patent discloses an exemplary rate of between approximately 1 Hz and approximately 250 Hz (see paragraph 148) and that an appropriate time between opening the vent valve and a closing of the vent valve is between approximately 10 ms and approximately 50 ms (see paragraph 158 of the opposed patent).

Figure 20 of O1 is a graphical representation of an example pulsation protocol which may be used within an extraction cycle (paragraph 77). O1 discloses that “the time units of figure 20 may be in second, milliseconds, microseconds, or the like” (paragraph 78).

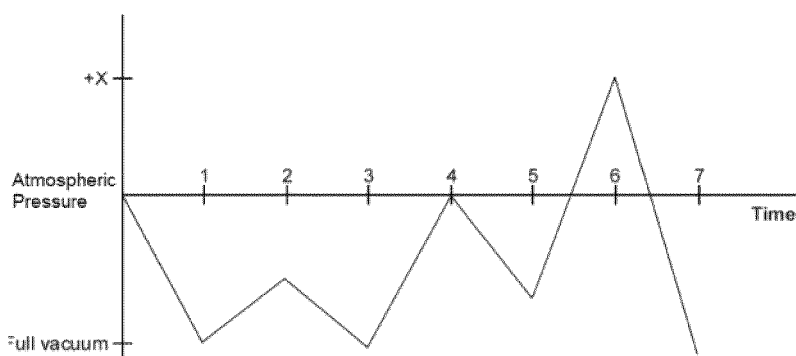


FIG. 20

The skilled person seeking to put the invention disclosed in O1 into effect, and using a time period for the extraction cycle taught by O1 in relation to Fig. 20, in particular when the time units are taken to be seconds or milliseconds, would fall within the preferred operating parameters of the opposed patent. Thereby, according to the opposed patent’s teaching, forward flow would be prevented.

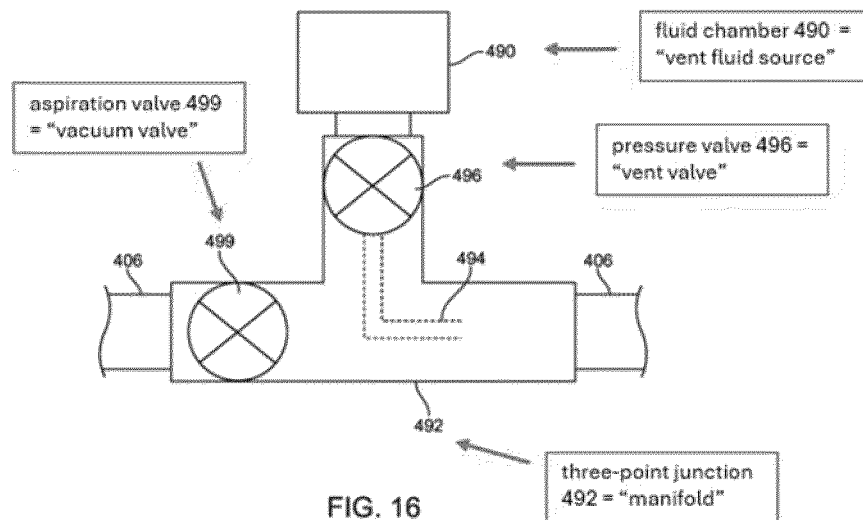
The pulse depicted in fig. 20 of O1 is merely an example extraction cycle. Nevertheless, it will also be appreciated that if the skilled person were to implement the teaching of O1 using exactly this cycle, then at least during units of time 1-5, the pressure is kept “negative”, i.e. there is a degree of suction somewhere between atmospheric pressure and full vacuum. At least via the application of overall negative pressure throughout time units 1-5 of the cycle, forward flow is prevented. At least in this time period, the controller of O1 is selectively opening and closing the vacuum valve and the vent valve such that forward flow is prevented.

Since O1 discloses all the features of claim 1, it follows that claim 1 is not novel over O1.

4.1.1.1. Other embodiments of O1: Fig. 16

The above arguments have focused on a particular embodiment of O1. It is noted that different embodiments of O1 also deprive claim 1 of novelty. The arguments made above in relation to each claim feature apply similarly to these embodiments of O1.

For example, the above arguments focus on an embodiment of O1 which incorporates the three-point junction 292 depicted in Fig. 14. However, an alternative embodiment of O1 incorporates the three-point junction 492 depicted in Fig. 16, reproduced below.



In relation to the implementation depicted in Fig. 16, O1 states:

[0069] [...] The three-point junction 492 has valves to control both vacuum forces and positive pressure pulses. This allows the three-point junction 492 to alternate between applying vacuum aspiration and pulses of pressure, wherein the pressure is above that of the vacuum source. The aspiration valve 499 and the pressure valve 496 may be opened alternatively, simultaneously, with a delay, or in some overlapping sequence. [...]

[0070] In one embodiment, an aspiration valve 499 is positioned between a catheter and an aspiration source to modulate aspiration and a pressure valve 496 is positioned between the catheter and fluid source to modulate fluid injection. The present invention may selectively open and close both aspiration valve 499 and pressure valve 496 to create pressure differentials within the catheter and/or aspiration tubing that result in pressure pulses of a desired amplitude and frequency.

4.1.1.2. Other embodiments of O1: Fig. 17

Figure 17 depicts an embodiment which similarly deprives claim 1 of novelty, in which a connection tubing 706 acts as a common conduit between a vacuum source 700, a pressure source 790, and an aspiration catheter 750 (paragraph 71).

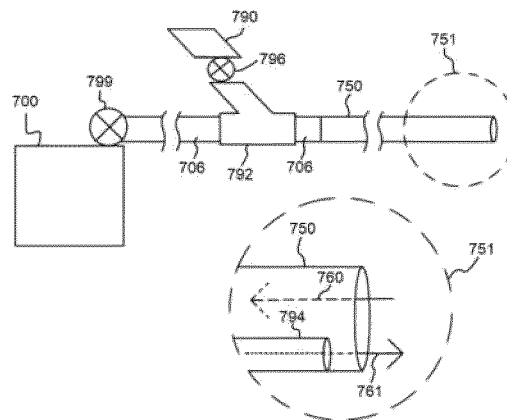


FIG. 17

In relation to this embodiment, paragraph 71 of O1 teaches several ways of modulating the two valves, for example:

[0071] [...] the controller may modulate a vacuum valve 799 and a pressure valve 796, whereby the closing of the vacuum valve 799 and the opening of the pressure valve 796 may result in a relative increase in pressure at a distal tip of an aspiration catheter. Alternatively, the opening of the vacuum valve 799 and the closing of the pressure valve 796 may result in a relative decrease in pressure at the distal tip of the aspiration catheter 750. [...]

As set out above, the skilled person would understand that the effect of introducing a fluid into the catheter which is “between full vacuum and ambient pressure” as described in paragraph 65 is to increase the relative pressure at the distal end of the aspiration catheter, thereby temporarily partially relieving the “full vacuum”, but while maintaining an overall level of negative pressure (suction).

The skilled person would understand that, by adjusting the “relative pressure” via modulation of the two valves depicted in figure 17, an overall level of negative pressure (suction) may be maintained. In this way, forward flow is prevented.

In addition, O1 teaches that the controller may modulate the valves depicted in Fig. 17 as follows:

[0071] [...] In some embodiments, a controller may close vacuum valve 799 and open pressure valve 796 for a small period of time, thus allowing a minimal volume of fluid from the pressure source 790 to be introduced into a proximal end of aspiration catheter 750 to increase the relative pressure at a distal end of the aspiration catheter 750 before reverting to vacuum by re-opening vacuum valve 799 and closing pressure valve 796. [...]

By only providing a minimal volume of fluid into the catheter to increase the relative pressure at the distal end, the suction force in the catheter is maintained and thereby the risk of occlusive material breaking free of a clot and traveling distally in the vessel is reduced. Although O1 does not expressly refer to “forward flow,” the skilled person would have understood that the purpose of O1’s technique and those described in opposed patent are to prevent positive pressure (i.e., a pressure greater than physiological pressure), or maintain a suction force, at the distal end of the catheter to reduce the risk of distal emboli.

Accordingly, the skilled person would understand that forward flow should be prevented when implementing this embodiment of O1.

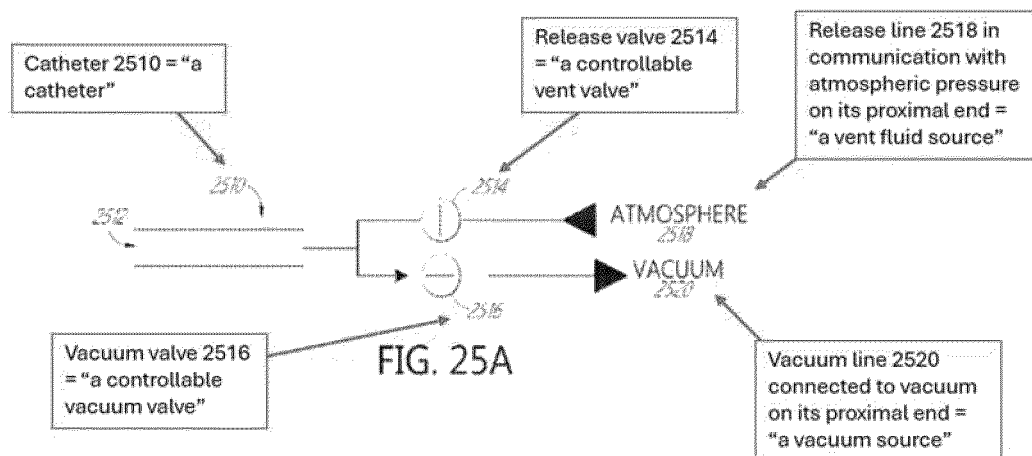
4.1.2.O2 (US 2017/0238953 A1) – “Yang”

O2 is a US patent application having a publication date of 24 August 2017. The publication date of O2 pre-dates the claimed priority dates and the filing date of the opposed patent. O2 is therefore available for the assessment of novelty and inventive step.

In overview, O2 describes to a catheter arrangement which can comprise “a controller for applying intermittent vacuum to the lumen” of the catheter (see e.g., paragraphs [0011], [0014]).

For example, the controller “may be configured to alternate between applying pulses of higher negative pressure and lower negative pressure” (see e.g., paragraph [0014]). In this way, the catheter arrangement of O2 can be used to remove obstructive material from vasculature, and may thereby be used for vascular thrombectomy (see e.g., paragraphs [0063], [0123])

Figs. 25A-25C of O2 depict an arrangement for providing such a pulsed aspiration cycle for aspirating a clot (paragraphs [0040], [0168]). Fig. 25A is reproduced below, annotated to show features corresponding with the claims of the opposed patent.



1[a] (a catheter having a distal end and defining a lumen filled with a liquid column)

As shown above with reference to paragraph [0063], O2 discloses a catheter having a single central lumen. It has been shown that this catheter is used for aspiration thrombectomy. Paragraph [0065] describes that:

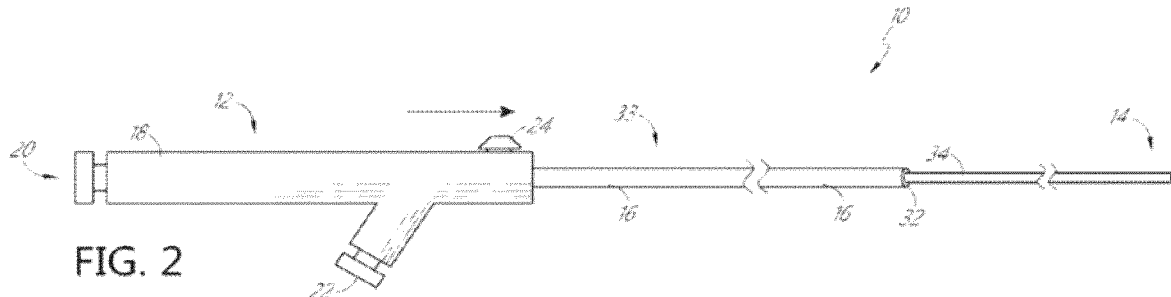
[0065] The catheter 10 generally comprises an elongate tubular body 16 extending between a proximal end 12 and a distal functional end 14.

Paragraph [0067] describes that:

[0067] Distal segment 34 extends between a proximal end 36 and a distal end 38 and defines at least one elongate central lumen 40 extending axially therethrough.

The catheter of O2 therefore clearly has a distal end and a defined lumen.

Fig. 2 of O2, reproduced below, further illustrates the catheter of O2 having a distal end and a defined lumen.



The opposed patent states, at page 54, line 34 to page 55, line 1 of the specification as filed that:

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.

That is, the opposed patent accepts that the fluid column in the catheter comprises aspirated fluid. Clearly, any aspiration thrombectomy system therefore comprises a liquid column in use, at least due to the aspiration of liquid from vasculature. Therefore, O2 comprises a catheter having a distal end filled with a liquid column having a proximal portion and a distal portion as claimed.

In the context of the catheter/lumen in O2 being “fluidically connected” to other system components and in the context of “fluid flow from the catheter” being controlled, the skilled person would recognise that the catheter would need to contain a liquid. For example, O2 describes a “fluid connection” between the catheter and other components of the thrombectomy system. Paragraph [0123] describes:

[0123] ...a pulsatile vacuum pressure aspirator 300 that applies intermittent or pulsatile vacuum to lumen 40. In the illustrated embodiment, the pulsatile vacuum pressure aspirator 300 is in fluid connection with the proximal end 12 of the catheter 10...

Paragraph [0126] describes that:

[0126] ...valve 314 controls the fluid flow from the catheter 10 to the vacuum chamber 310/collection canister 312...

Paragraph [0131] describes that:

[0131] ...the solenoid valve 414 is positioned in and fluidly connects between the air/fluid reservoir 422 at the atmospheric pressure and the aspiration line 424 connecting the catheter 10 to the vacuum chamber 410/collection canister 412.

Additionally, in relation to Figs. 25A-25C, paragraph [0168] of O2 states the “experiments showed that an interrupted vacuum can help aspirating a corked clot stuck at the distal end 2512 of the catheter 2510 by loosening the clot and reshaping it to fit into the catheter 2510 after each vacuum and release cycle”.

The mechanism by which this loosening and reshaping is suggested to be the water hammer effect, described in paragraph 108 as:

[0108] ...an axial reciprocation or water hammer effect, which can further facilitate both transluminal navigation as well as dislodging or breaking up the obstruction. Water hammer, or more generally fluid hammer, is a pressure surge or wave caused when a fluid in motion is forced to stop or change direction suddenly, creating a momentum change [...]

In the context of generating the "water hammer" effect, the skilled person would recognise that the catheter would need to contain a liquid. The water hammer effect relies on the propagation of pressure waves through a fluid medium, which requires the presence of a liquid within the catheter. The skilled reader would therefore understand that the catheter must be filled with a liquid in use to facilitate the transmission of these pressure surges effectively.

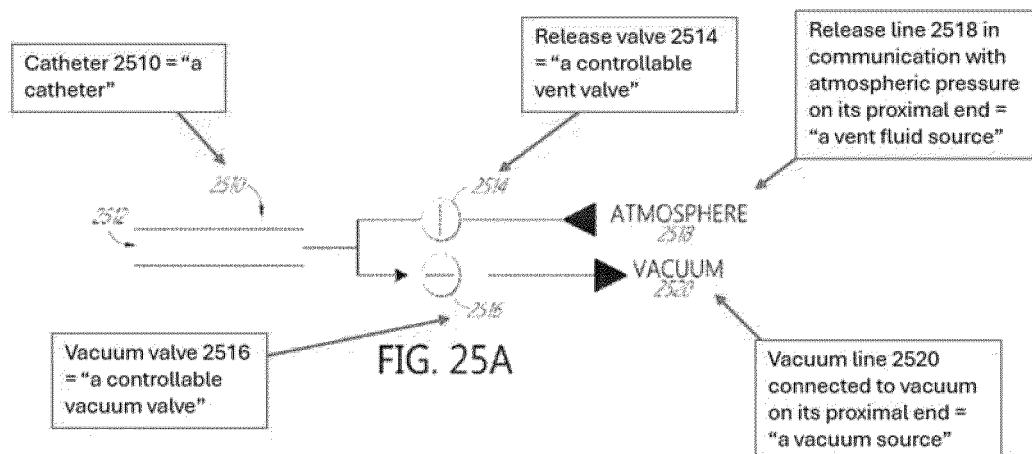
1[b] (a controllable vacuum valve)

O2 discloses (emphasis added):

[0168] Referring to FIGS. 25A-25C, experiments showed that an interrupted vacuum can help aspirating a corked clot stuck at the distal end 2512 of the catheter 2510 by loosening the clot and reshaping it to fit into the catheter 2510 after each vacuum and release cycle. Merely stopping the vacuum is not sufficient to loosen the clot. Completely releasing (venting to atmospheric pressure) the vacuum and allowing the clot to relax before reapplying a vacuum is found to aspirate the corked clot most efficiently.

[0169] FIGS. 25A-25C show a logical progression of the vacuum and release cycle as applied to the catheter 2510. A release line 2518 and a vacuum line 2520 are connected to or near the proximal end of the catheter 2510. The release line 2518 is in communication with atmospheric pressure on its proximal end and has a release valve 2514 configured to open or close the fluid communication between the catheter 2510 and the vacuum. The vacuum line 2520 is connected to vacuum on its proximal end and has a vacuum valve 2516 configured to open or close the fluid communication between the catheter 2510 and the vacuum.

The vacuum valve 2516 of O2 is therefore a controllable vacuum valve as recited by claim 1.



An example of a vacuum valve connected to a vacuum source is also shown in Fig. 13, in relation to which it is stated that:

[0123] ...the pulsatile vacuum pressure aspirator 300 is in fluid connected with the proximal end 12 of the catheter 10 and comprises vacuum generator 302, vacuum chamber 310, collection canister 312, solenoid valve 314...

[0126] Solenoid valve 314 is located in the fluid connection path between a luer or other connector configured to releasably connect to an access port of the catheter 10 and the vacuum chamber 310 /collection canister 312. The solenoid valve 314 controls the fluid flow from the catheter 10 to the vacuum chamber 310 /collection canister 312.

O2 therefore clearly describes a vacuum valve as recited by claim 1.

1[c] (a vacuum source fluidically connected to the vacuum valve)

In relation to Figs. 25A-25C, O2 states that:

[0169] [...] The vacuum line 2520 is connected to vacuum on its proximal end [...]

O2 therefore clearly provides a vacuum source as recited by claim 1. The skilled person would understand that this vacuum source is a vacuum source as described in more detail with respect to Figs. 13 and 14.

In relation to the system of Fig. 13, O2 discloses (emphasis added):

[0123] [...] an embodiment of a pulsatile vacuum pressure aspirator 300 that applies intermittent or pulsatile vacuum to lumen 40. In the illustrated embodiment, the pulsatile vacuum pressure aspirator 300 is in fluid connection with the proximal end 12 of the catheter 10 and comprises vacuum generator 302, vacuum chamber 310, collection canister 312, solenoid valve 314, frequency modulator 316, valve controller 318, and remote controller 320.

[0124] Vacuum generator 302 comprises a vacuum pump 304, a vacuum gauge 306, and a pressure adjustment control 308. The vacuum pump 304 generates vacuum [...]

The vacuum generator 302 therefore provides a vacuum source. The vacuum generator 302 is fluidically connected to solenoid valve 314 via the vacuum chamber 310 and collection canister 312 in order to apply a vacuum to the catheter. The arrangement of Fig. 13 is generally the same arrangement shown in Fig. 14.

The same vacuum generator is used in Fig. 14, and O2 states (emphasis added):

[0131] In another embodiment, shown in FIG. 14, the solenoid valve 414 is positioned in and fluidly connects between the air/fluid reservoir 422 at the atmospheric pressure and the aspiration line 424 connecting the catheter 10 to the vacuum chamber 410/collection canister 412. Unlike the first embodiment in Fig. 13, this system modulates pressure in the catheter 10 by allowing pressure to vary from vacuum to atmospheric pressure.

The vacuum generator 402 therefore provides a vacuum source, in a like manner as the vacuum generator 302 of Fig. 13. For the avoidance of doubt, document O2a shows that the specification of O2 was corrected during prosecution to explicitly refer to the vacuum generator 402. When considering the arrangement shown in Figs. 25A-25C, the skilled reader would appreciate that such a vacuum source is provided.

1[d] (a controllable vent valve having a vent liquid input)

O2 discloses (emphasis added):

[0168] Referring to FIGS. 25A-25C, experiments showed that an interrupted vacuum can help aspirating a corked clot stuck at the distal end 2512 of the catheter 2510 by loosening the clot and reshaping it to fit into the catheter 2510 after each vacuum and release cycle. Merely stopping the vacuum is not sufficient to loosen the clot. Completely releasing (venting to atmospheric pressure) the vacuum and allowing the clot to relax before reapplying a vacuum is found to aspirate the corked clot most efficiently.

[0169] FIGS. 25A-25C show a logical progression of the vacuum and release cycle as applied to the catheter 2510. A release line 2518 and a vacuum line 2520 are connected to or near the proximal end of the catheter 2510. The release line 2518 is in communication with atmospheric pressure on its proximal end and has a release valve 2514 configured to open or close the fluid communication between the catheter 2510 and the vacuum. The vacuum line 2520 is connected to vacuum on its proximal end and has a vacuum valve 2516 configured to open or close the fluid communication between the catheter 2510 and the vacuum.

Paragraph [0170] of O2 provides further detail regarding control of the valve arrangement to provide pulsatile aspiration. It is clear that the release valve 2514 of O2 is therefore a controllable vent valve as recited by claim 1 of the opposed patent.

1[e] (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)

O2 discloses that the release line 2518 is in communication with atmospheric pressure on its proximal end (paragraph [0169]). The atmospheric pressure is a vent fluid source as recited by claim 1.

O2 also describes the operation of the release valve 2514 ('a vent valve') and vacuum valve 2516 ('a vacuum valve'):

[0170] In the first step as shown in FIG. 25A, the release valve 2514 is closed, and the vacuum valve 2516 is open such that the vacuum is applied to the catheter 2510 to aspirate the clot. Then, as shown in FIG. 25B, the release valve 2514 is opened while the vacuum valve 2516 stays open. Because the release line 2518 and the vacuum line 2520 are in fluid communication, either directly or via at least a portion of the catheter 2510, the vacuum is applied mainly through the release line 2518, dropping vacuum applied to the catheter. Finally, as shown in FIG. 25C, the vacuum valve 2516 is shut off, allowing the vacuum to be completely released and the clot to relax. Then, another cycle from FIG. 25A to FIG. 25C begins by closing the release valve 2514 and opening the vacuum valve 2516.

This demonstrates that the release valve 2514 retains fluid at an input until it is opened to allow releasing/venting.

It is clear to the skilled reader that 'releasing' as described in relation to Fig. 25A-2C is the same as venting to atmospheric pressure to modulate pressure in the catheter as described with respect to Fig. 14. For example, paragraph [0168] describes "completely releasing (venting to atmospheric pressure) the vacuum and allowing the clot to relax...".

An atmospheric pressure source 422 connected to a solenoid valve 414 is shown in Fig. 14. O2 states (emphasis added):

[0131] ... the solenoid valve 414 is positioned in and fluidly connects between the air/fluid reservoir 422 at the atmospheric pressure and the aspiration line 424 connecting the catheter 10 to the vacuum chamber 410/collection canister 412. Unlike the first embodiment in Fig. 13, this system modulates pressure in the catheter 10 by allowing pressure to vary from vacuum to atmospheric pressure.

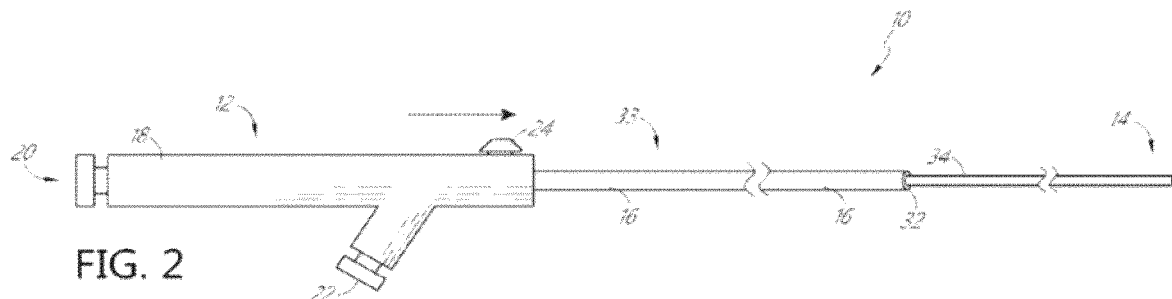
That is, in the arrangement of Fig. 14, the solenoid valve 414 is connected to an atmospheric pressure source and, as shown in the figure, this is "air/fluid at the atmospheric pressure 422". As outlined above with respect to feature **1[a]**, at least for effectiveness of the water hammer effect, the skilled person would recognise that this fluid is a liquid, such that the fluid at the atmospheric pressure is a vent liquid as recited by the claim.

O2 thereby provides a vent fluid source connected to a controllable vent valve and as recited by claim 1 of the opposed patent.

1[f] (a manifold connected to the catheter, to the vacuum valve, and to the vent valve)

Paragraph [0088] of O2 discloses that (emphasis added):

[0088] The proximal end 12 of catheter 10 is additionally provided with a manifold 18 having one or more access ports as is known in the art [...] at least one side port such as aspiration port 22. [...]



The proximal end 12 of the catheter 10 is also shown in Figs. 13 and 14, in relation to which it is described that:

[0123] ...the pulsatile vacuum pressure aspirator 300 is in fluid connection with the proximal end 12 of the catheter 10...

The skilled person would understand that the apparatus shown in Fig. 14 and Figs. 25A-25C fluidically connects to the aspiration port of the manifold shown in Fig. 2. For example, in another arrangement it is described that:

[0167] ...a vacuum port 2416 may be provided near the proximal end 2400 of the catheter 2402 such as on the manifold for releasable connection to a vacuum source to aspirate the clot from the vasculature...

Furthermore, in relation to Figs. 25A-25C, paragraph [0170] states that:

[0170] the release line 2518 and the vacuum line 2520 are in fluid communication, either directly or via at least a portion of the catheter 2510, the vacuum is applied mainly through the release line 2518, dropping vacuum applied to the catheter.

Similarly, it is stated in relation to Fig. 14 that:

[0131] ...the solenoid valve 414 is positioned in and fluidically connects between the air/fluid reservoir 422 at the atmospheric pressure and the aspiration line connecting the catheter 10 to the vacuum chamber 410/collection canister 412...

As there is fluid communication between the interconnected parts to allow vacuum pressure and/or venting pressure to be applied to the catheter, it is clear that there must be a physical body linking them (e.g., piping or another conduit, such as the aspiration line) – that is, a manifold must be present.

O2 therefore provides a manifold which is connected in the manner recited by claim 1.

1[g] (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)

Paragraph [0014] of O2 states that:

[0014] ...the telescoping catheter may further comprise a controller for applying intermittent vacuum to the lumen. The controller may be configured to apply pulses of vacuum to the lumen spaced apart by spaces of neutral pressure. The controller may be configured to alternate between applying pulses of higher negative pressure and lower negative pressure...

The skilled person would understand that this controller is configured to apply pulses as described in relation to Figs. 25A-25C, for example as paragraphs [0168]-[0170] describe the application of intermittent vacuum to the lumen.

Such a controller is also described in more detail with respect to Fig. 13, for controlling solenoid valve 313 fluidically connected to a vacuum generator:

[00128] Valve controller 318 modulates the solenoid valve 314 on and off. The valve controller 318 may be electrically or mechanically connected to the solenoid valve 314... The valve controller 318 may be mechanically controlled by users or may be electrically controlled by the frequency modulator 316.

Fig. 14 shows a similar frequency modulator 416 and valve controller 418 arranged to control the solenoid valve 414 fluidically connected to the air/fluid reservoir 422 ('a vent fluid source'). For the avoidance of doubt, document O2a shows that the specification of O2 was corrected during prosecution to explicitly refer to the frequency modulator 416 and valve controller 418. The skilled reader would appreciate that the valve

controller 418 can be electrically controlled by the frequency modulator 416 in a like manner as described for Fig. 13 (paragraph [0128]), and that such a controller is used in the context of Figs. 25A-25C.

Furthermore, claims of O2 recite:

10. A telescoping catheter as in claim 1, further comprising a controller for applying intermittent vacuum to the lumen.

11. A telescoping catheter as in claim 10, wherein the controller is configured to apply pulses of vacuum to the lumen spaced apart by spaces of neutral pressure.

12. A telescoping catheter as in claim 10, wherein the controller is configured to alternate between applying pulses of higher negative pressure and lower negative pressure.

O2 thereby discloses a controller which is configured to selectively open and close the vacuum and vent valves as recited by claim 1.

1[h] (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)

O2 discusses alternating levels of pressure throughout, and Figs. 25A-C show how this can be achieved using the depicted valve arrangement.

For example, paragraph [0014] states that the controller is:

[0014] [...] configured to apply pulses of vacuum to the lumen spaced apart by spaces of neutral pressure. The controller may be configured to alternate between applying pulses of higher negative pressure and lower negative pressure"

Paragraph [0040] states that:

[0040] FIGS. 25A-25C depict a pulsed aspiration cycle according to an embodiment.

Paragraph [0237] of O2 states that:

[0237] In one aspect of present disclosure, the aspirating thrombus step comprises applying intermittent negative pressure to the first elongate tubular body. In another aspect of present disclosure, the aspirating thrombus step comprises applying alternating negative and positive pressure to the first elongate tubular body.

Paragraph [0108] describes how such pulsatile pressure causes a water hammer effect which can assist in breaking up an obstruction (e.g., a thrombus or clot).

Figs. 25A-25C and the associated description show cyclical control of vacuum and vent valves to achieve the effects described in paragraphs [0014], [0040], [0237], claim 12 and [0108]. In particular, O2 states (emphasis added):

[0168] Referring to FIGS. 25A-25C, experiments showed that an interrupted vacuum can help aspirating a coked clot stuck at the distal end 2512 of the catheter 2510 by loosening the clot and reshaping it to fit into the catheter 2510 after each vacuum and release cycle [...]

[0169] Figs. 25A-25C show a logical progression of the vacuum and release cycle as applied to the catheter 2510 [...]

[0170] In the first step as shown in FIG. 25A, the release valve 2514 is closed, and the vacuum valve 2516 is open such that the vacuum is applied to the catheter 2510 to aspirate the clot. Then, as shown in FIG. 25B, the release valve 2514 is opened while the vacuum valve 2516 stays open. Because the release line 2518 and the vacuum line 2520 are in fluid communication, either directly or via at least a portion of the catheter 2510, the vacuum is applied mainly through the release line 2518, dropping vacuum applied to the catheter. Finally, as shown in FIG. 25C, the vacuum valve 2516 is shut off, allowing the vacuum to be completely released and the clot to relax. Then, another cycle from FIG. 25A to FIG. 25C begins by closing the release valve 2514 and opening the vacuum valve 2516.

O2 thereby provides a controller configured to cyclically open and close the vacuum valve and the vent valve, as recited by claim 1.

It is noted that further analysis of the valve cycle of O2 is provided below in section 4.2.2.

1[i] (prevent forward flow of the distal portion out from the distal end)

Operating an arrangement as described by document O2 would naturally result in the prevention of forward flow, as required by feature **1[i]**.

First, O2 discloses operating parameters which the opposed patent itself teaches leads to the prevention of forward flow.

As discussed above, Figs. 25A-25C show an arrangement comprising a vacuum source and an atmospheric pressure source ('vent fluid source') which can be connected to the catheter in order to provide pulsatile pressure.

Paragraph [0168] of O2 discloses that the period of each vacuum and release cycle may be equal to about 0.1 seconds – that is, a cycling frequency of 10 Hz. Paragraph [0127], describing a frequency modulator for controlling the solenoid valve, suggests that control could take place at frequencies of "*less than about 500Hz, in some modes of operation less than about 20 Hz or less than about 5 Hz*", and paragraph [0130] discloses operating the cycle at a frequency of less than about 260 Hz.

By comparison, the opposed patent discloses that the ROAR effect can retain a level of pressure at the distal end less than or equal to physiological pressure (i.e., to prevent forward flow) when the vacuum valve and vent valve are cycled at a rate of between approximately 1 Hz and approximately 250 Hz (see e.g., page 56, lines 22 to 36). That is, the opposed patent teaches that forward flow can be prevented by cycling the vacuum and vent valves at a sufficiently fast rate.

O2 therefore clearly teaches the use of cycling frequencies which fall in the range which the opposed patent teach as being sufficiently fast to "prevent forward flow". Therefore, operation of the arrangement of

O2 would therefore naturally result in forward flow being prevented, by a similar process as the opposed patent itself describes.

Second, the skilled reader would appreciate that the teaching of O2 is that forward flow is prevented.

Paragraph [0102] of O2 states that pulsatile application of a vacuum may oscillate between:

[0102] "...a first lower negative pressure and a second higher negative pressure. Alternatively, a slight positive pressure may be alternated with a negative pressure, with the application of negative pressure dominating to provide a net aspiration through the lumen".

Similar disclosures are made at paragraph [0014] and claim 12. Clearly, operating an arrangement which cycles between two negative pressure sources cannot lead to forward flow, as no positive pressure would be applied to the catheter at any point. That is, in such an arrangement a vacuum would always be applied through the catheter during operation of the apparatus. As a vacuum is always applied, there is no force which would move the fluid column within the catheter lumen forward and out of the distal end of the catheter. That is, forward flow must inherently be prevented.

Paragraph [0014] and claim 11 also recite that the controller is configured to apply pulses of vacuum to the lumen spaced apart by spaces of neutral pressure. The application of neutral pressure would clearly not provide a positive pressure to cause any forward flow, such that forward flow is prevented.

Furthermore, paragraphs [0168] and [0170] teach that:

[0168] ...experiments showed that an interrupted vacuum can help aspirating a corked clot stuck at the distal end 2512 of the catheter 2510 by loosening the clot and reshaping it to fit into the catheter 2510 after each vacuum and release cycle. Merely stopping the vacuum is not sufficient to loosen the clot. Completely releasing (venting to atmospheric pressure) the vacuum and allowing the clot to relax before reapplying a vacuum is found to aspirate the corked clot most efficiently...

[0170] ...as shown in FIG. 25C, the vacuum valve 2516 is shut off, allowing the vacuum to be completely released and the clot to relax...

That is, the arrangement of O2 is allowing the clot to 'relax' before aspirating the clot. However, the arrangement does not allow the clot to exit the distal end of the catheter (i.e., forward flow is prevented).

The skilled reader would therefore understand that the teaching of O2 is to prevent forward flow.

It has been demonstrated that O2 discloses all of the features of claim 1, and claim 1 therefore lacks novelty.

4.1.3.O3 (WO 2017/214573 A1) – "Ofek"

As set out above, the subject matter of claim 1 of the opposed patent is not entitled to either of the earlier claimed priority dates.

O3 is a PCT application, having a publication date of 9 June 2017. The publication date of O3 pre-dates the filing date of the opposed patent. O3 is therefore available for the assessment of novelty and inventive step.

In overview, O3 describes a pulsatile aspiration system for catheter assemblies, in which occlusions, such as clots, are dislodged by high pressure pulses and aspirated by negative pressure (see e.g., paragraphs [0002], [0003]).

In one particular example:

[00027] ...the patency device 30 provides short-duration, relatively high-pressure impulses through the fluid present in the catheter tube lumen 14 interspersed by relatively longer rest periods 84 of negative baseline pressure provided to the catheter tube lumen. The negative baseline pressure present between impulses enables any occlusion dislodged by the impulses to be sucked proximally up the catheter tube lumen 14 and removed therefrom...

A representative drawing of O3 (Fig. 3) is shown below, and annotated to show features corresponding with those of the claims of the opposed patent, for reference in the following discussion.

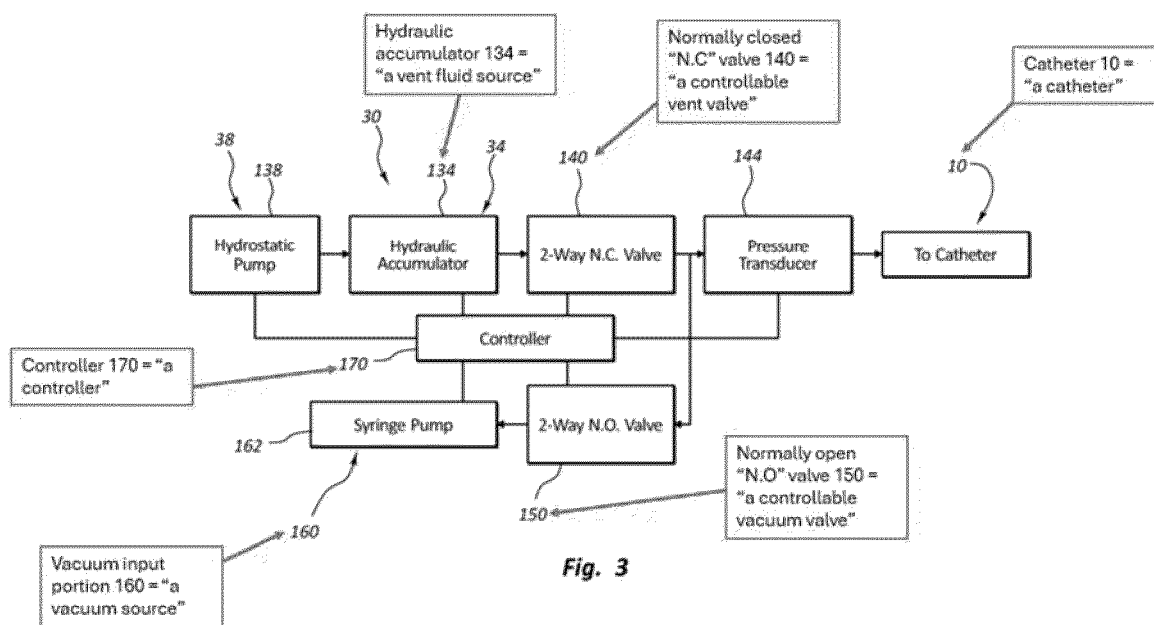


Fig. 3

Claim 1 lacks novelty in view of document O3, as the document discloses all of the features of claim 1.

1[Pre] (A clot removal system)

O3 provides a system that is configured to establish patency of a catheter (i.e., ensure that a catheter is unobstructed) and perform pulsed aspiration of clots at the distal tip of the catheter. In particular, O3 discloses (emphasis added):

[0002] ...a patency device for catheter assemblies and other elongate tubular devices used for establishing access to an interior body portion of a patient. The patency device establishes and/or preserves patency of one or more lumens defined by the catheter assembly by providing impulses of positive pressure to fluid disposed in the lumen of the catheter assembly...

[0003] ...the patency device comprises a fluid reservoir configured to provide a fluid (or establish a fluid path) to at least one lumen of the catheter assembly, and a pressure input portion. The pressure input portion is configured to provide pressure for one or more impulses of positive pressure to a fluid disposed within the lumen. The impulses are configured to dislodge occlusions that may have formed in the lumen. A negative pressure can then be provided to the lumen to aspirate the occlusion and remove it from the catheter assembly.

O3 explains that the system can be used for aspirating occlusions, such as clots, at the distal end of the catheter:

[00022] ...impulses, when performed periodically, are configured to prevent the formation of thrombus or other occlusion in the lumen 14, especially at the distal end thereof...

[00031] ...As noted above, the high-pressure fluid impulses impinge on an occlusion (such as a clot or fibrin sheath) or other obstruction that has formed in the lumen 14, typically at or proximate the distal end 12B of the catheter tube 12... In addition, a suction process can be performed by the patency device 30 to withdraw the clot proximally from the catheter tube 12 and catheter 10 and into the patency device, where it may be disposed of...

O3 also discloses that the system can be used with arterial catheters and components for performing aspiration, which the skilled person would understand allows the system to perform aspiration thrombectomy, for example (emphasis added):

[00021] ...though shown as a PICC, the catheter in other embodiments can include other catheter types, such as dialysis, CVC, PIV, urinary, arterial, balloon catheters, etc. ...

[00040] ... The patency device 30 can further include ports to enable fluids or other substances to be infused into or aspirated from the catheter tube lumen(s) 14, such as antimicrobial agents, etc.

O3 therefore provides a clot removal system as recited by claim 1.

1[a] (a catheter having a distal end and defining a lumen filled with a liquid column)

O3 describes that the system comprises a catheter (emphasis added):

[00020] Reference is first made to FIG. 1, which generally depicts various details of a catheter assembly ("catheter"), generally designated at 10, and a patency device, to be described further below, in accordance with one embodiment. As shown, the catheter 10 includes an elongate catheter tube 12 that defines a lumen 14 extending between a proximal end 12A and a distal end 12B of the catheter tube...

[00021] ...though shown as a PICC, the catheter in other embodiments can include other catheter types, such as dialysis, CVC, PIV, urinary, arterial, balloon catheters, etc. ...

Fig. 1 is reproduced below for reference.

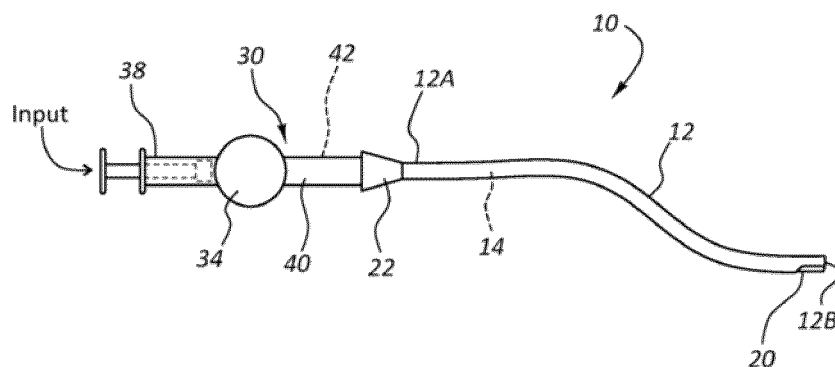


Fig. 1

A catheter is therefore clearly provided by O3, having a distal end and defining a lumen. The skilled reader would also understand that the lumen is filled with a liquid column.

For example, paragraph [00036] describes a catheter lumen being fluid-filled in order to provide a propagation medium for pressure pulses:

[00036] The impulses are propagated distally down the lumen 14, which is fluid-filled prior to commencement of the patency operation so as to provide a propagation medium for the impulses.

The skilled reader would appreciate that a liquid is required to provide such a propagation medium. Indeed, O3 discloses that:

[00031] In one embodiment, the fluid filling the fluid path of the patency device and the catheter tube lumen is a 0.9% saline solution...

It is also noted that the opposed patent states, at page 54, line 34 to page 55, line 1 of the specification as filed that:

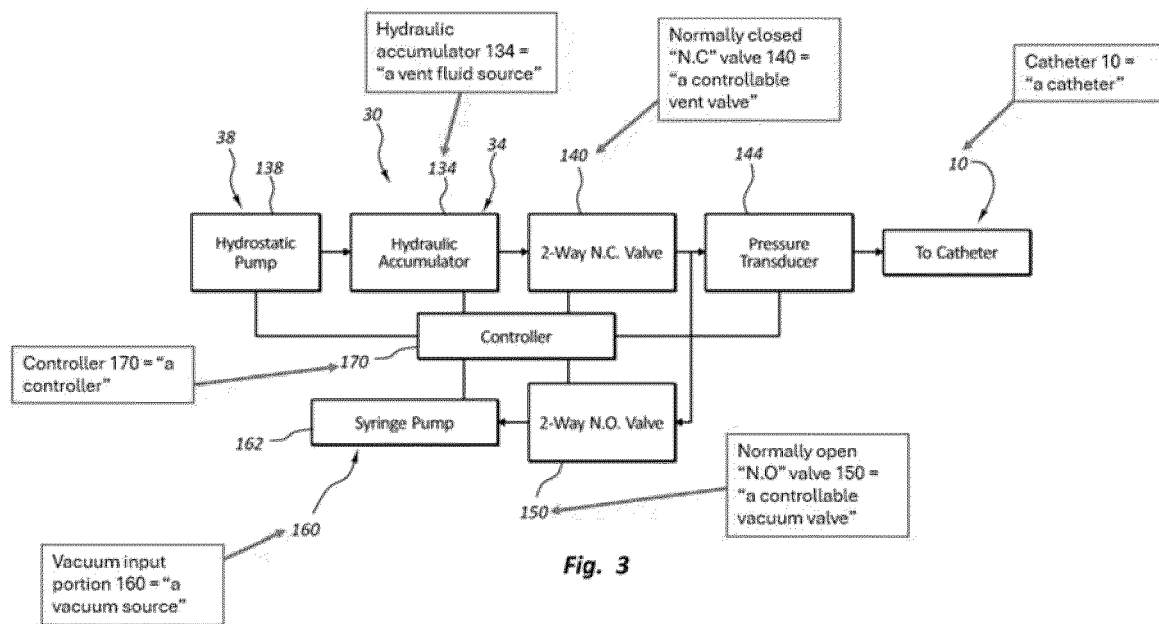
Fluid rushes into the distal end 664 of the catheter 660 and into the canister of the vacuum source 610 while the vacuum valve 620 is open and vacuum is being applied to the fluid column.

That is, the opposed patent accepts that the fluid column in the catheter comprises aspirated fluid. Clearly, any aspiration thrombectomy system therefore comprises a liquid column in use, at least due to the aspiration of liquid from vasculature.

O3 therefore provides a catheter as recited by claim 1.

1[b] (a controllable vacuum valve)

Fig. 3 of O3, reproduced below, shows one example of an aspiration system.



Paragraph [00033] of O3 describes:

[00033] A two-way, normally open ("N.O.") valve 150 is interposed between the N.C. valve 140 and the transducer 144 via a fluid line connected to the N.O. valve fluid inlet. A vacuum input portion 160 for providing negative pressure in the patency device 30 is operably connected to the fluid outlet of the N.C. [sic] valve 150. In the present embodiment, a syringe pump 162 serves as the vacuum input portion 160, though other suitable components can also be employed, such as a vacuum pump... A controller 170 is operably connected to the aforementioned components of the patency device 30 to govern their operation.

That is, as shown in Fig. 3, a vacuum input portion 160 for providing negative pressure in the system is operably connected to the normally open valve 150.

As described at paragraphs [00035] and [00037] of O3, for example, this valve is controllable to apply vacuum pressure when necessary (emphasis added):

[00035] The pressurized fluid is received from the pump 138 by the accumulator 134, which stores the fluid in a pressurized state until needed. The N.O valve 150 is maintained in an open state at the beginning and during the procedure to maintain a negative base pressure in the system except at those times when the N.C. valve 140 is opened to provide the fluid impulses...

[00037] The controller 170 is utilized to precisely control the opening/closing of the N.C. valve 140 and the N.O. valve 150 so as to provide the impulses and the negative baseline pressure to the lumen 14 as desired.

The normally open valve 150 of O3 therefore provides a controllable vacuum valve as recited by claim 1.

1[c] (a vacuum source fluidically connected to the vacuum valve)

As outlined above, Fig. 3 shows a vacuum input portion 160, which is a vacuum source fluidically connected to the normally open valve 150. Paragraph [00033] states:

[00033] In the present embodiment, a syringe pump 162 serves as the vacuum input portion 160, though other suitable components can also be employed, such as a vacuum pump.

In use, the vacuum input portion 160 provides a negative pressure for aspiration, for example as described in paragraph [00037]:

[00037] ...the N.O. valve 150 opens to provide a negative baseline pressure (provided by the syringe pump 162 or other suitable device) in the catheter tube lumen 14 and enable any occlusion dislodged by the impulses to be suctioned proximally out of the lumen, through the N.O. valve to the syringe pump 162.

O3 therefore provides a vacuum source which is fluidically connected to the normally open valve ('vacuum valve'), as required by claim 1.

1[d] (a controllable vent valve)

O3 discloses (emphasis added):

[00032] ...the patency device 30 includes a hydrostatic pump 138 that serves as the pressure input portion 38 for providing hydraulic pressure to fluid contained and maintained at pressure in a hydraulic accumulator ("accumulator") 134 that serves as the fluid reservoir 34. A two-way, normally closed ("N.C.") valve 140 is disposed at and operably connected at its fluid inlet to a fluid outlet of the accumulator 134 via a fluid line.

[00033] A two-way, normally open ("N.O.") valve 150 is interposed between the N.C. valve 140 and the transducer 144 via a fluid line connected to the N.O. valve fluid inlet... A controller 170 is operably connected to the aforementioned components of the patency device 30 to govern their operation.

That is, a normally closed valve 140 is connected to a hydraulic accumulator serving as a pressure input source. This provides a vent valve having a vent liquid input, as outlined in more detail below.

The normally closed valve 140 ('a vent valve') is operated by a controller, for example as described at paragraph [00037] (emphasis added):

[00037] The controller 170 is utilized to precisely control the opening/closing of the N.C. valve 140 and the N.O. valve 150 so as to provide the impulses and the negative baseline pressure to the lumen 14 as desired.

O3 therefore provides a controllable vent valve as recited by claim 1.

1[e] (a vent fluid source containing a vent liquid and fluidically connected to the vent valve)

Paragraph [00032] of O3 states that (emphasis added):

[00032] ...the patency device 30 includes a hydrostatic pump 138 that serves as the pressure input portion 38 for providing hydraulic pressure to fluid contained and maintained at pressure in a hydraulic accumulator ("accumulator") 134 that serves as the fluid reservoir 34. A two-way, normally closed ("N.C.") valve 140 is disposed at and operably connected at its fluid inlet to a fluid outlet of the accumulator 134 via a fluid line.

The hydraulic accumulator thereby provides a vent fluid source, and is fluidically connected to the normally closed valve 140 ('a vent valve').

O3 describes the use of this fluid in relation to helping aspirate a clot:

[00031] ...high-pressure fluid impulses impinge on an occlusion (such as a clot or fibrin sheath) or other obstruction that has formed in the lumen 14, typically at or proximate the distal end 12B of the catheter tube 12. The occlusion is dislodged by the high-pressure impulses, which are strong enough to dislodge the occlusion but are not of sufficient duration to push it out the distal end 12B of the catheter tube 12...

[00036] The N.C. valve 140 is opened and close repeatedly at predetermined time intervals to provide a series of fluid impulses from the accumulator, through the N.C. valve and into the lumen 14 of the catheter 10... The impulses are propagated distally down the lumen 14, which is fluid-filled prior to commencement of the patency operation so as to provide a propagation medium for the impulses.

[00044] ...a method for providing patency to at the lumen(s) 14 the catheter assembly 10 comprises disposing a fluid in the lumen of the catheter tube 12 of the catheter; and propagating a plurality of impulses of positive pressure through the fluid disposed in the lumen...

That is, the fluid provided by the hydraulic accumulator ('a vent fluid source') is used to provide pressure impulses through the catheter by control of the normally closed valve ('a vent valve').

O3 therefore provides a vent fluid source as recited by claim 1.

1[f] (a manifold connected to the catheter, to the vacuum valve, and to the vent valve)

Paragraph [00032] of O2 states:

[00032] A pressure transducer 144 is operably interposed between the fluid outlet of the N.C. valve 140 and the luer connector 22 or other suitable inlet to the catheter. As mentioned above, in this and other embodiments the connector interface 40 (FIG. 1) can be used to operably connect the patency device 30 to the catheter 10. Note that the fluid lines between the various components discussed herein can include tubing or other suitable modes for fluid transport.

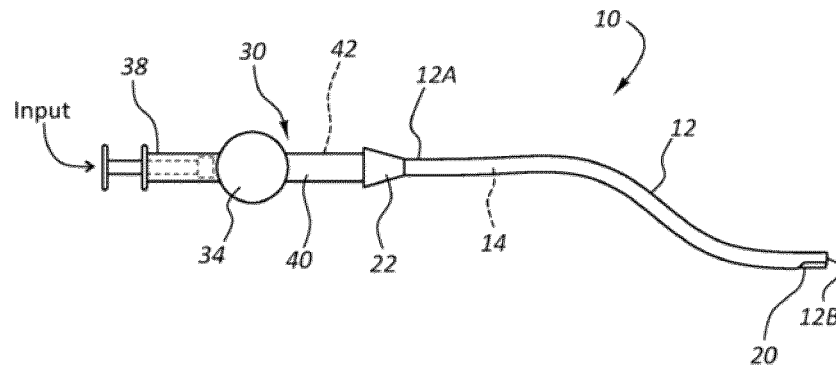


Fig. 1

Paragraph [00025] discloses that:

[00025] A catheter connector interface 40 defining a lumen 42 is included to enable the patency device 30 to operably connect to the luer connector 22 (or other portion) of the catheter 10 and provide a conduit through which the high pressure fluid can pass from the fluid reservoir 34 to the lumen(s) 14 of the catheter tube 12.

That is, the system shown in the schematic drawing of Fig. 3 is provided with a single manifold as shown in Fig. 1. O3 therefore provides a manifold as recited by claim 1.

1[g] (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)

It has been demonstrated above that O3 provides a vent valve and a vacuum valve as recited by claim 1. O3 further discloses:

[00033] A controller 170 is operably connected to the [normally open valve 150 and N.C. valve 140] of the patency device 30 to govern their operation. The controller 170 in one embodiment includes a power source, a printed circuit board including a processor, etc.

[00035] ...The controller 170 or other suitable component can control valve opening/closing.

[00036] The controller 170 determines the number, frequency, rest periods, etc., of the impulses to be delivered by the patency device 30 to the catheter tube lumen(s) 14. The N.C. valve 140 is opened and close repeatedly at predetermined time intervals to provide a series of fluid impulses from the accumulator, through the N.C. valve and into the lumen 14 of the catheter 10. During each impulse when the N.C valve 140 is opened, the N.O valve 150 is shut so as to prevent impulse fluid from entering the N.O. valve and diverting to the syringe pump 162 instead of entering the catheter tube lumen 14 as desired....

Figs. 4A and 4B show further details of control assemblies for the valves, as described at paragraph [00034] (emphasis added):

[00034] FIG. 4A depicts various details regarding a valve control assembly 180 associated with the N.C. valve 140 shown in the patency device 30 of FIG. 3, according to one embodiment... FIG. 4B shows a similar configuration for the valve control assembly 180 associated with the N.O. valve 150... The valve control assemblies 180 for the N.C. valve 140 and the N.O. valve 150 assist in governing operation of the N.C. and N.O. valves during operation of the patency device 30.

O3 therefore provides a controller connected to a vacuum valve and to a vent valve to selectively open and close the valves as recited by claim 1.

1[h] (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)

It has been demonstrated above (e.g., in relation to feature **1[g]**) that O3 discloses a controller configured to cyclically open the vacuum valve and the vent valve.

O3 further discloses that such control changes a level of vacuum at the distal end of the catheter.

Fig. 2 (reproduced below) shows a graph of a pressure profile produced by the device during operation.

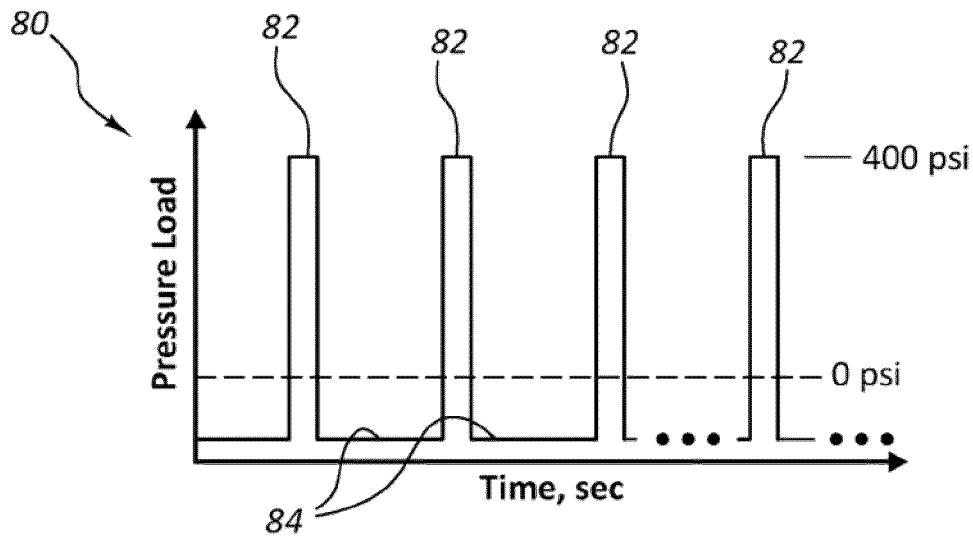


Fig. 2

O3 describes (emphasis added):

[00027] As shown, the patency device 30 provides short-duration, relatively high-pressure impulses through the fluid present in the catheter tube lumen 14 interspersed by relatively longer rest periods 84 of negative baseline pressure provided to the catheter tube lumen. The negative baseline pressure present between impulses enables any occlusion dislodged by the impulses to be sucked proximally up the catheter tube lumen 14 and removed therefrom, thus preventing the dislodged occlusion from entering the bloodstream from the distal end 12B of the catheter tube 12. Note that the rest periods in other embodiments can include a reduction to a neutral pressure or lower (but still positive) pressure or to varying pressures over time as may be desired.

Another example of a series of impulses is also shown in Fig. 10, reproduced below, wherein groups of impulses are separated by rest periods of negative baseline pressure to enable aspiration of any occlusions (paragraph [00053]).

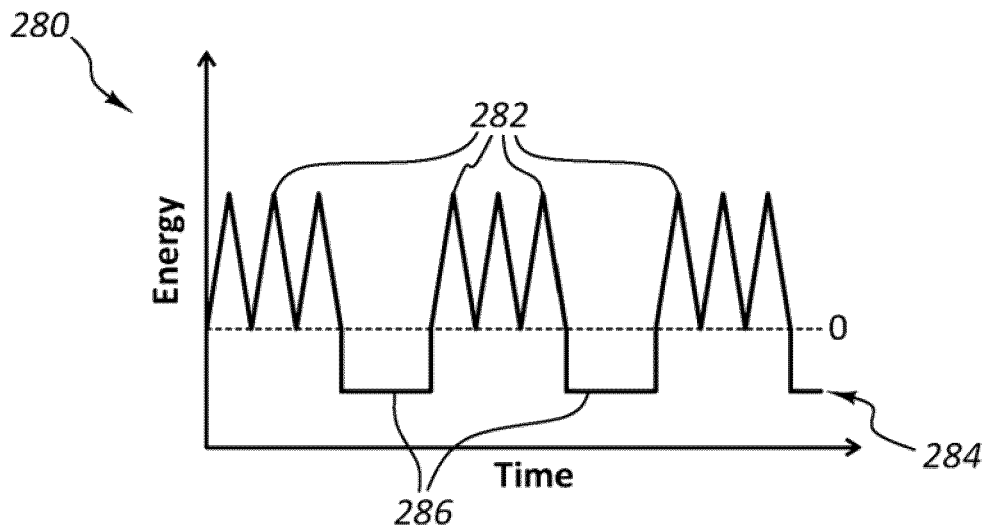


Fig. 10

Clearly, a resulting change in pressure or vacuum level must also occur at the distal end of the catheter in order to affect an occlusion, such as a clot, that is present at that position (e.g., as described at paragraph [00022] – “Such impulses, when performed periodically, are configured to prevent the formation of thrombus or other occlusion in the lumen 14, especially at the distal end thereof”).

1[i] (prevent forward flow of the distal portion out from the distal end)

Generally, the system of O3 is arranged to provide periods of aspiration interspersed with high-pressure bursts, or impulses, in the distal direction. It should be noted that although high-pressure bursts are disclosed, O3 suggests that the high pressure may be measured at the proximal end of the catheter by a pressure transducer 144 (see e.g., paragraph [00039]), and the skilled reader would appreciate that high pressure at this position this is not indicative of positive pressure which could cause forward flow at the distal end of the catheter where the pressure impulses would be weaker.

Indeed, O3 emphasises that any occlusions should not be allowed to re-enter the bloodstream from the distal end of the catheter, and the skilled person would appreciate that this reduces the risk of distal embolization. For example, paragraph [00027] states that (emphasis added):

[00027] ...the patency device 30 provides short-duration, relatively high-pressure impulses through the fluid present in the catheter tube lumen 14 interspersed by relatively longer rest periods 84 of negative baseline pressure...negative baseline pressure present between impulses enables any occlusion dislodged by the impulses to be sucked proximally up the catheter tube lumen 14 and removed therefrom, thus preventing the dislodged occlusion from entering the bloodstream from the distal end 12B of the catheter tube 12.

As the dislodged occlusion is required to not enter the bloodstream, it is clear that the device is operated so as to prevent forward flow of liquid from the catheter.

This is emphasised again at paragraph 31 which states (emphasis added):

[00031] *The occlusion is dislodged by the high-pressure impulses, which are strong enough to dislodge the occlusion but are not of sufficient duration to push it out the distal end 12B of the catheter tube 12. The subsequent negative pressure rest period following each impulse can act to prevent escape of the clot from the catheter tube 12, in one embodiment. In addition, a suction process can be performed by the patency device 30 to withdraw the clot proximally from the catheter tube 12 and catheter 10 and into the patency device, where it may be disposed of In this way, any clot or occlusion present in the catheter 10 can be acceptably removed.*

The system of O3 is therefore operated so as to prevent forward flow of fluid out of the distal end of the catheter, as recited by claim 1.

It has been demonstrated that O3 discloses all of the features of claim 1, and claim 1 therefore lacks novelty.

4.2. Claim 2

Claim 2 recites:

The system according to claim 1, wherein the controller (560) is configured to cyclically open and close the vacuum valve (420) and the vent valve (440) in a repeated cycle comprising a double-closed state in which the vacuum valve (420) is closed and the vent valve (440) is closed.

4.2.1.O1 (EP 4 461 253 A2) – “Teigen”

As set out above in relation to claim 1 of the opposed patent, O1 discloses “a controller configured to modulate the vacuum source valve and the pressure source valve, wherein the controller generates pressure differentials within a lumen of the aspiration catheter by alternating between opening and closing the valves”. O1 describes generating “a variety of pressure pulses with an extraction cycle” (paragraph 27) to help remove any clogs or occlusions (see claim 1 and paragraph 31 of O1). There is clearly disclosure, therefore, of a repeated cycle.

From the wording of the claim alone (*alternating between opening and closing the valves*), as well as the discussion of extraction cycles in O1 at e.g. paragraphs 63-66, the skilled person would understand that the controller is configured to operate the valves in serial, such that both valves are closed at the same time during certain parts of the cycle to achieve the desired generation of pressure differentials.

The skilled person, putting the relevant embodiment of O1 into effect, based solely on the teaching of O1, would naturally conduct the valve operation according to claim 2 of the opposed patent in order to yield effective pulsing. By closing the vacuum valve first before opening the vent valve (i.e. by including a point in the cycle during which both valves are closed), an effective positive pulse is generated according to the teaching in (e.g.) paragraph 63 of O1, which teaches that the pressure pulse should “*introduce an acceleration component*” and create “*a force impulse that breaks static friction momentarily*”.

By contrast, opening the vent valve first before fully closing the vacuum valve would lead to unnecessary loss of the fluid as it would be directly evacuated through the vacuum, and significantly reduce the “acceleration component” and “force impulse” of the pulse.

Also, in relation to the embodiment depicted in Fig. 16, O1 explicitly discloses that:

[0069] [...] The aspiration valve 499 and the pressure valve 496 may be opened alternatively, simultaneously, with a delay, or in some overlapping sequence. In one overlapping sequence, one valve starts to open when the other valve is starting to close, whereby there is a brief period where both valves are at least partially open. In other overlapping sequences, sometimes both valves are open and both valves are closed for at least short periods of time.

The skilled person, interpreting the teachings of O1 as a whole, would understand that this explicit teaching in relation to Fig. 16 is applicable to extraction cycles implemented in every other embodiment of O1. This is not to say that the skilled person would *combine* the teaching provided in relation to the embodiment of Fig. 16 and with teachings made in relation to other embodiments. Instead, the skilled person would understand that the disclosure at paragraph 69 is not limited only to the Fig. 16 embodiment, and would interpret the explicit teachings made in relation to other embodiments (e.g. at paragraphs 63-66) in light of the teaching in paragraph 69. The skilled person would understand the content of paragraphs 63-66 within the context provided by paragraph 69, and would understand that any embodiment of O1 may involve the use of a valve cycle in which the valves may be “opened alternatively, simultaneously, with a delay, or in some overlapping sequence”, i.e. in which the valve cycle comprises a double closed state.

Accordingly, claim 2 is not novel over any of the embodiments of O1 referred to above.

4.2.2.O2 (US 2017/0238953 A1) – “Yang”

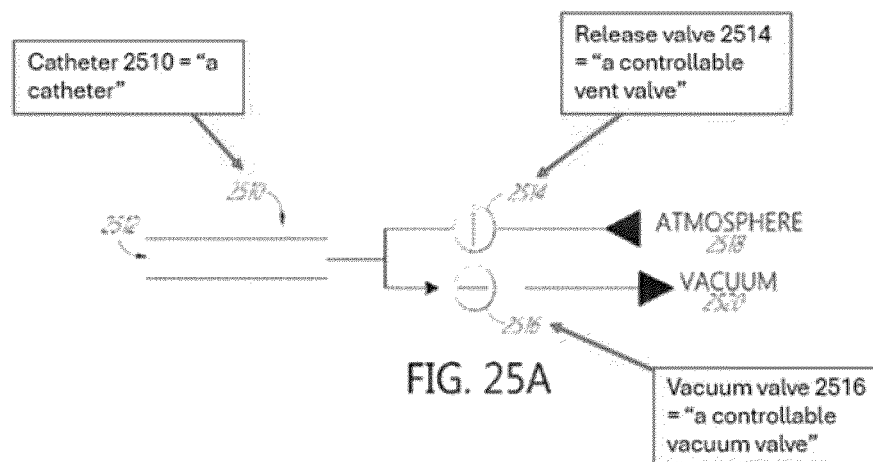
Claim 2 lacks novelty in view of document O2, as the document discloses all of the features of claim 2.

Claim 2 is dependent on claim 1. As demonstrated above in section 4.1.2, O2 discloses all of the features of claim 1.

Paragraph 169 of O2 states that:

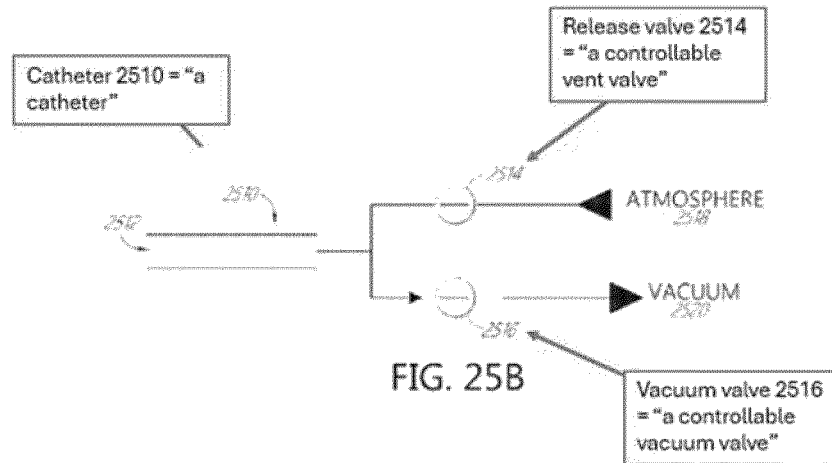
[0169] FIGS. 25a-25c show a logical progression of the vacuum and release cycle as applied to the catheter 2510...

As has been discussed above with respect to Claim 1, O2 clearly discloses that the vacuum valve 2516 and release valve 2514 (‘vent valve’) are cyclically opened and closed in a repeated cycle. The different states of the repeated cycle are shown in Figs. 25A-25C and described in paragraph [0170].



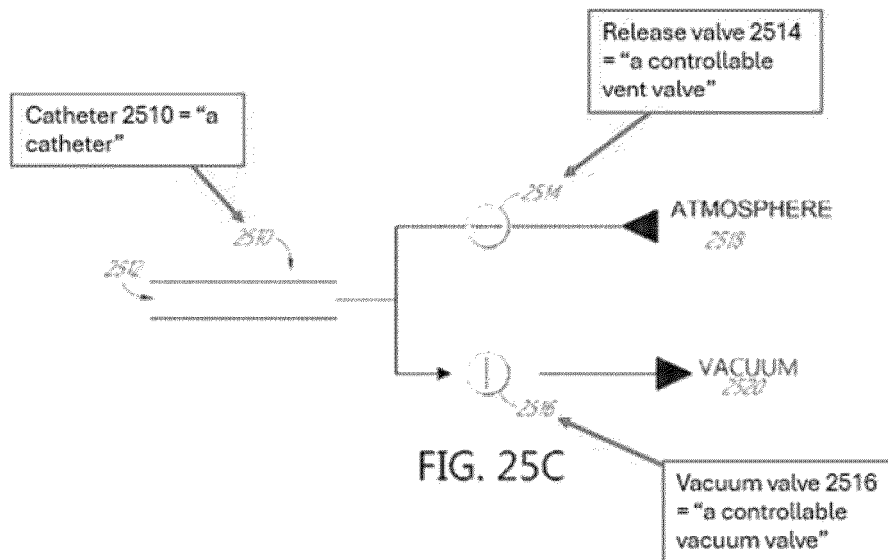
[0170] In the first step as shown in Fig. 25A, the release valve 2514 is closed, and the vacuum valve 2516 is open such that the vacuum is applied to the catheter 2510 to aspirate the clot.

As the vacuum valve 2516 is open and the release valve 2514 ('vent valve') is closed, Fig. 25A shows a 'vacuum only' state.



[0170] ...as shown in Fig. 25B, the release valve 2514 is opened while the vacuum valve 2516 stays open.

Here, only a single valve is operated (i.e., the two valves are operated serially and not in parallel), resulting in a state in which both the release valve 2514 ('vent valve') and the vacuum valve 2516 are both open. Fig. 25B therefore shows a 'double open' state.



[0170] ...as shown in Fig. 25C, the vacuum valve 2516 is shut off allowing the vacuum to be completely released and the clot to relax.

Again, only a single valve is operated, resulting in a state in which the vacuum valve 2516 is closed and the release valve 2514 ('vent valve') is open. Fig. 25C therefore shows a 'vent only' state.

[0170] Then, another cycle from FIG. 25A to FIG. 25C begins by closing the release valve 2514 and opening the vacuum valve 2516.

This passage implicitly discloses a fourth valve state which is present when transitioning from the state of Fig. 25C to the state of Fig. 25A, and this is a 'double-closed state'.

Starting from the 'vent only' state of Fig. 25C and following the instructions of paragraph 170 to "[close] the release valve 2514", would naturally result in a state in which the release valve is closed while the vacuum valve is still closed – i.e., a 'double-closed state' as recited by claim 2.

The skilled person would readily derive the existence of such a 'double-closed' state because it is consistent with the other valve transitions described which, as demonstrated in the passages cited above and the reproduced drawings, each involve operation of only a single valve at a time (i.e., each valve is operated in serial). The skilled person would therefore also transition from the state of Fig. 25C to the state of Fig. 25A by operating a single valve at a time, closing the release valve 2514 before opening the vacuum valve 2516, thereby producing a double-closed state as recited by claim 2.

Operating the arrangement of O2 in accordance with the instructions disclosed therein would therefore naturally provide an arrangement falling within the scope of claim 2. Claim 2 therefore lacks novelty in view of O2.

4.3. Claim 3

Claim 3 recites:

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

4.3.1. O1 (EP 4 461 253 A2) – "Teigen"

As set out above in relation to claim 1, Figure 20 of O1 is a graphical representation of an example pulsation protocol which may be used within an extraction cycle (paragraph 77). O1 discloses that "the time units of figure 20 may be in second, milliseconds, microseconds, or the like" (paragraph 78).

The skilled person seeking to put the invention disclosed in O1 into effect in an implementation in which the time units are milliseconds or microseconds would naturally arrive at an implementation in which the "double-closed" state is less than 30ms, as required by claim 3 of the opposed patent.

4.3.2. O2 (US 2017/0238953 A1) – "Yang"

Claim 3 lacks novelty in view of O2, as the document discloses all of the features of claim 3.

Claim 3 is dependent on claim 2. As demonstrated above in section 4.2.2, O2 discloses all of the features of claim 1.

In relation to the vacuum and release cycle shown in Figs. 25A-25C, paragraph 168 of O2 states that *“the period of each vacuum and release cycle may be equal to or greater than about 0.1... seconds”*.

As outlined above in section 4.2.2, O2 discloses that there are four distinct states involved in each vacuum and release cycle. Paragraph [0168] states that the *“period of each vacuum and release cycle may be equal to or equal to about 0.1... seconds”*. Given a period of 0.1 s, each state would have a duration of approximately 0.025 seconds, or 25 ms. The double-closed state of O2 would therefore have a duration no greater than 30 ms, as required by claim 3.

4.4. Claim 4

Claim 4 recites:

The system according to claim 1, wherein the controller (560) is configured to cyclically open and close the vacuum valve (420) and the vent valve (440) in a repeated cycle comprising a vent-only state in which the vacuum valve (420) is closed and the vent valve (440) is open.

4.4.1. O1 (EP 4 461 253 A2) – “Teigen”

As set out above in relation to claim 1 and claim 2 of the opposed patent, O2 discloses *“a controller configured to modulate the vacuum source valve and the pressure source valve, wherein the controller generates pressure differentials within a lumen of the aspiration catheter by alternating between opening and closing the valves”*. O1 describes generating *“a variety of pressure pulses with an extraction cycle”* (paragraph 27) to help remove any clogs or occlusions (see claim 1 and paragraph 31 of O1). There is clearly disclosure, therefore, of a repeated cycle.

From the wording of the claim alone (*alternating between opening and closing the valves*), as well as the discussion of extraction cycles in O1 at, e.g., paragraphs 63-66, the skilled person would understand that the controller is configured to operate the valves in serial such that the vacuum valve is closed and the vent valve is open during certain parts of the cycle to achieve the desired generation of pressure differentials.

The skilled person, putting the relevant embodiment of O1 into effect, based solely on the teaching of O1, would naturally conduct the valve operation according to claim 4 of the opposed patent. By including a point in the cycle during which the vent valve (only) is open, an effective positive pulse is generated according to the teaching in (e.g.) paragraph 63 of O1, which teaches that the pressure pulse should *“introduce an acceleration component”* and create *“a force impulse that breaks static friction momentarily”*.

By contrast, leaving the vacuum valve open during application of the positive pulse would lead to unnecessary loss of the fluid as it would be directly evacuated through the vacuum, and significantly reduce the *“acceleration component”* and *“force impulse”* of the pulse.

In relation to the embodiment depicted in figure 16, O1 explicitly discloses that:

[0069] [...] The aspiration valve 499 and the pressure valve 496 may be opened alternatively, simultaneously, with a delay, or in some overlapping sequence. In one overlapping sequence, one valve starts to open when the other valve is starting to close, whereby there is a brief period where both valves are at least partially open. In other overlapping sequences, sometimes both valves are open and both valves are closed for at least short periods of time.

If the valves are opened alternatively, as described in paragraph 69 and defined in claim 1, there will be a point during the cycle when the vacuum valve is closed and the vent valve is open.

For completeness, it is noted that while paragraph 69 refers to the embodiment depicted in figure 16, the skilled person would read the content of the other embodiments of O2 e.g. at paragraphs 63-66 within the context provided by paragraph 69, and would understand that any embodiment of O1 may involve the use of a “vent-only state” as required by claim 4.

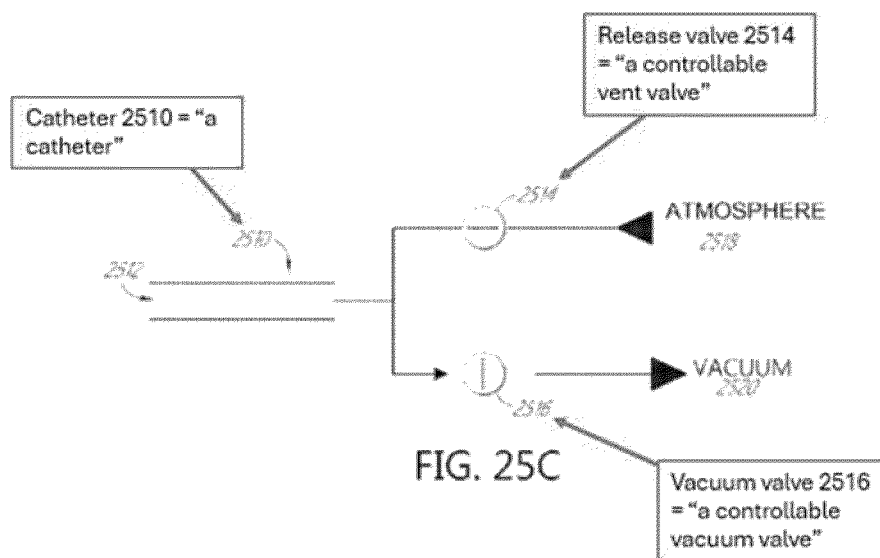
Therefore, claim 4 is not novel over O1.

4.4.2. O2 (US 2017/0238953 A1) – “Yang”

Claim 4 lacks novelty in view of O2, as the document discloses all of the features of claim 4.

Claim 4 is dependent on claim 1. As demonstrated above in section 4.1.2, O2 discloses all of the features of claim 1.

The discussion above in section 4.2.2 also demonstrates that the features of claim 4 are disclosed by O2. In particular, a ‘vent only’ state is shown in Fig. 25C of O2, reproduced below.



[0170] ...as shown in Fig. 25C, the vacuum valve 2516 is shut off allowing the vacuum to be completely released and the clot to relax.

4.4.3.O3 (WO 2017/214573 A1) – “Ofek”

Claim 4 lacks novelty in view of O3, as the document discloses all of the features of claim 4.

Claim 4 is dependent on claim 1. As demonstrated above in section 4.1.3, O3 discloses all of the features of claim 1.

The operation of the valves of O3 are described above with respect to claim 1 in section 4.1.3, and it has been shown that the controller of O3 is configured to cyclically open a vacuum valve and a vent valve. O3 further discloses that (emphasis added):

[00035] The pressurized fluid is received from the pump 138 by the accumulator 134, which stores the fluid in a pressurized state until needed. The N.O valve 150 is maintained in an open state at the beginning and during the procedure to maintain a negative base pressure in the system except at those times when the N.C. valve 140 is opened to provide the fluid impulses.

That is, paragraph [00035] of O3 describes a state wherein the N.O. valve 150 (vacuum valve) is closed and the N.C. valve (vent valve) is open, i.e., a vent-only state as recited by claim 4.

4.5. Claim 5

Claim 5 recites:

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

4.5.1.O1 (EP 4 461 253 A2) – “Teigen”

As set out above in relation to claim 1 and claim 3, Figure 20 of O1 is a graphical representation of an example pulsation protocol which may be used within an extraction cycle (paragraph 77). O1 discloses that “the time units of figure 20 may be in second, milliseconds, microseconds, or the like” (paragraph 78).

The skilled person seeking to put the invention disclosed in O1 into effect and using an implementation in which the time units are milliseconds or microseconds would naturally arrive at an implementation in which the “vent-only” state is less than 50 ms, as required by claim 5 of the opposed patent.

4.5.2.O2 (US 2017/0238953 A1) – “Yang”

Claim 5 is dependent on claim 4. As demonstrated above in section 4.4.2, O2 discloses all of the features of claim 1.

In relation to the vacuum and release cycle shown in Figs. 25A-25C, paragraph 168 of O2 states that “*the period of each vacuum and release cycle may be equal to or greater than about 0.1... seconds*”.

As outlined above in section 4.2.2, O2 discloses that there are four distinct states involved in each vacuum and release cycle. Paragraph [0168] states that the “*period of each vacuum and release cycle may be equal to or equal to about 0.1... seconds*”. Given a period of 0.1 s, each state would have a duration of

approximately 0.025 seconds, or 25 ms. The vent-only state of O2 would therefore have a duration no greater than 50 ms, as required by claim 5.

4.5.3.O3 (WO 2017/214573 A1) – “Ofek”

Claim 5 lacks novelty in view of O3, as the document discloses all of the features of claim 5.

Claim 5 is dependent on claim 4. As demonstrated above in section 4.4.3, O3 discloses all of the features of claim 1.

Furthermore, paragraph [00039] of O3 states that the frequency of the pressure impulses can range “*from about 1 to over 150 Hz*”. In a specific example, the frequency given is about 30 Hz. Noting that each pressure pulse is provided by a vent-only state as described above with respect to claim 4, this suggests that each pressure pulse last must last for less than 0.033 seconds, or 33 ms. The vent-only state of O3 therefore has a duration no greater than 50 ms, as required by claim 5.

4.6. Claim 6

Claim 6 recites:

The system according to claim 1, wherein the controller (560) is configured to selectively open and close the vacuum valve (420) and the vent valve cycle in a repeated cycle comprising:
a vacuum-only state in which the vacuum valve (420) is open and the vent valve (440) is closed;
a first double-closed state in which the vacuum valve (420) is closed and the vent valve (440) is closed;
a vent-only state in which the vacuum valve (420) is closed and the vent valve (440) is open; and
a second double-closed state in which the vacuum valve (420) is closed and the vent valve (440) is closed.

4.6.1.O1 (EP 4 461 253 A2) – “Teigen”

As set out above in relation to claims 1, 2, and 4 of the opposed patent, O1 discloses “*a controller configured to modulate the vacuum source valve and the pressure source valve, wherein the controller generates pressure differentials within a lumen of the aspiration catheter by alternating between opening and closing the valves*”. O1 describes generating “*a variety of pressure pulses with an extraction cycle*” (paragraph 27) to help remove any clogs or occlusions (see claim 1 and paragraph 31 of O1). There is clearly disclosure, therefore, of a repeated cycle.

From the wording of the claims of O1 alone (*alternating between opening and closing the valves*), as well as the discussion of extraction cycles in O1 at e.g. paragraphs 63-66, the skilled person would understand that the controller is configured to operate the valves in serial, such that the vacuum valve is closed and the vent valve is open during certain parts of the cycle, and vice-versa, to achieve the desired generation of pressure differentials.

In relation to the embodiment depicted in figure 16, O1 explicitly discloses that:

[0069] [...] The aspiration valve 499 and the pressure valve 496 may be opened alternatively, simultaneously, with a delay, or in some overlapping sequence. In one overlapping sequence, one valve starts to open when the other valve is starting to close, whereby there is a brief period where both valves are at least partially open. In other overlapping sequences, sometimes both valves are open and both valves are closed for at least short periods of time.

If the valves are opened alternatively, as described in paragraph 69 and defined in claim 1 of O1, in a way which will “*alternate between applying vacuum aspiration and pulses of pressure*” as desired, there will be points during the cycle when each of the conditions defined in claim 6 of the opposed patent are met.

In addition, while paragraph 69 refers to the embodiment depicted in Fig. 16, the skilled person would read the content of the other embodiments of O1 e.g. at paragraphs 63-66 within the context provided by paragraph 69, and would understand that any embodiment of O1 may involve the use of a valve cycle in which the valves may be “opened alternatively, simultaneously, with a delay, or in some overlapping sequence”, i.e. in which the valve cycle comprise both a first and a second double-closed state.

Therefore, claim 6 lacks novelty over O1.

4.6.2.O2 (US 2017/0238953 A1) – “Yang”

Claim 6 lacks novelty in view of O2, as the document discloses all of the features of claim 6.

Claim 6 is dependent on claim 1. As demonstrated above in section 4.1.2, O2 discloses all of the features of claim 1.

Claim 6 recites that the controller is configured to selectively open and close the vacuum valve and the vent valve in a repeated cycle comprising a vacuum-only state, a first double-closed state, a vent-only state, and a second double-closed state.

There is nothing in claim 6 to suggest that these states are in a particular order (for example, that the four states immediately succeed one another). Furthermore, claim 6 specifies only that there is a repeated cycle ‘comprising’ these steps – that is, the repeated cycle includes these steps, but does not exclude the presence of other steps (see e.g., Guidelines for Examination F-IV 4.20).

Paragraphs 169 and 170 of O2 state:

[0169] FIGS. 25a-25c show a logical progression of the vacuum and release cycle as applied to the catheter 2510...

[0170] In the first step as shown in FIG. 25A, the release valve 2514 is closed, and the vacuum valve 2516 is open such that the vacuum is applied to the catheter 2510... Then, as shown in FIG. 25B, the release valve 2514 is opened while the vacuum valve 2516 stays open... Finally, as shown in FIG. 25C, the vacuum valve 2516 is shut off... Then, another cycle from FIG. 25A to FIG. 25C begins by closing the release valve 2514 and opening the vacuum valve 2516.

O2 therefore clearly discloses that the vacuum valve and release valve (‘vent valve’) are cyclically opened and closed in a repeated cycle.

As outlined above in section 4.2.1, O2 discloses a vacuum-only state in which a vacuum valve 2516 is open and a vent valve 2514 is closed (Fig. 25A), a 'double open' state in which both the vacuum valve 2516 and vent valve 2514 are open (Fig. 25B) a 'vent-only' state in which the vacuum valve 2516 is closed and the vent valve 2514 is open (Fig. 25C), and a 'double-closed' state in which the vacuum valve 2516 is closed and the vent valve 2514 is closed (implicitly disclosed by transitioning from the state of Fig. 25C to the state of Fig. 25A while operating a single valve at a time).

When the apparatus of O2 is operated, the controller will open and close the vacuum valve and vent valve to repeatedly pass through the states of Figs. 25A-25C. In particular, the controller operates the valves in a repeated cycle comprising, in order:

- i. A first vacuum-only state (Fig. 25A);
- ii. A first double open state (Fig. 25B);
- iii. A first vent-only state (Fig. 25C);
- iv. A first double-closed state (transition from Fig. 25C to Fig. 25A);
- v. A second vacuum-only state (Fig. 25A);
- vi. A second double open state (Fig. 25B);
- vii. A second vent-only state (Fig. 25C); and
- viii. A second double-closed state (transition from Fig. 25C to Fig. 25A).

O2 thereby provides a repeated cycle comprising a first double-closed state (in a first transition from Fig. 25C to Fig. 25A) and a second double-closed state (in a second transition from Fig. 25C to Fig. 25A), among other states, as recited by claim 6.

4.7. Claim 7

Claim 7 recites:

The system according to claim 6, wherein a time between an opening of the vent valve (440) and a closing of the vent valve (440) is between approximately 10 ms and approximately 50 ms.

4.7.1. O2 (US 2017/0238953 A1) – “Yang”

Claim 7 is dependent on claim 6. As demonstrated above in section 4.6.2, O2 discloses all of the features of claim 6.

In relation to the vacuum and release cycle shown in Figs. 25A-25C, paragraph 168 of O2 states that “*the period of each vacuum and release cycle may be equal to or greater than about 0.1... seconds*”.

As outlined above in section 4.2.2, O2 discloses that there are four distinct states involved in each vacuum and release cycle. Paragraph [0168] states that the “*period of each vacuum and release cycle may be equal to or equal to about 0.1... seconds*”. Given a period of 0.1 s, each state would have a duration of approximately 0.025 seconds, or 25 ms. The vent-only state of O2 would therefore have a duration no greater than 50 ms, as required by claim 7.

4.8. Claim 9

Claim 9 recites:

The system according to claim 1, wherein the change in the level of vacuum at the distal end is:

greater than approximately 51 kPa (15 inHg) in no greater than approximately 50 ms; or greater than approximately 68 kPa (20 inHg) and no greater than approximately 30 ms; or greater than approximately 85 kPa (25 inHg) and no greater than approximately 20 ms.

4.8.1.O3 (WO 2017/214573 A1) – “Ofek”

Claim 9 lacks novelty in view of O3, as the document discloses all of the features of claim 9.

Claim 9 is dependent on claim 1. As demonstrated above in section 4.1.2, O3 discloses all of the features of claim 1.

Fig. 2 of O3 (reproduced below) shows a graph of a pressure profile produced by the device during operation.

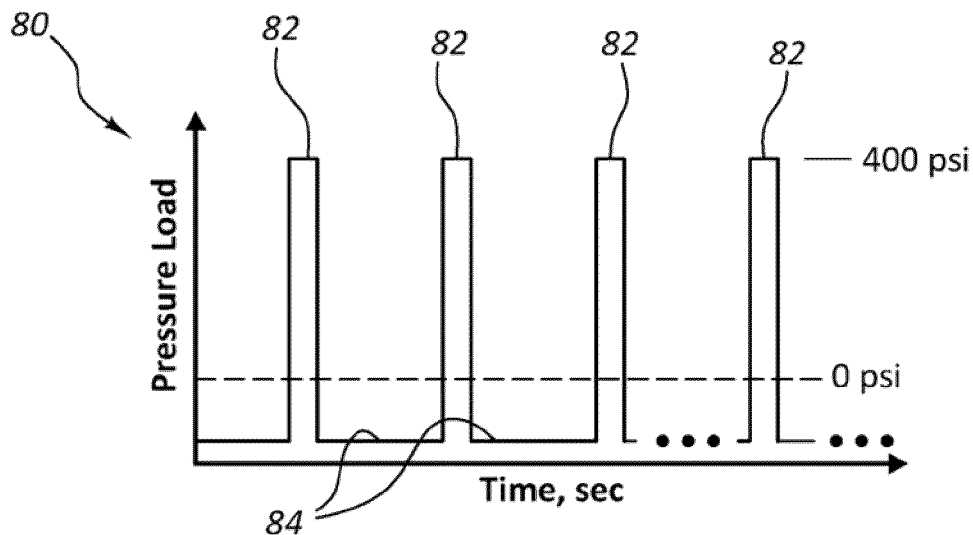


Fig. 2

In particular, Fig. 2 shows an example in which (emphasis added):

[00028] In the present embodiment, the pressure peaks 82 are each characterized by a rise-time phase of about 30 milliseconds, a holding high-pressure phase of about 200 milliseconds, and a pressure reduction phase of about 40 milliseconds.

[00030] In the present embodiment, the maximum pressure achieved by the impulses is about 400 psi, though this can vary according to desired application, catheter lumen design, type or size of occlusion, catheter tube length, etc. In one embodiment, it is appreciated that the maximum pressure of the impulses may exceed the burst pressure strength rating of the catheter tube 12 in one embodiment, but as the impulses are of relatively short duration, no rupturing or failure of the catheter 10 occurs.

A pressure of 400 psi corresponds to ~814 inHg, or ~2760 kPa. As this pressure change occurs in a time period of about 30 ms, O3 clearly discloses an arrangement in which the change in the level of vacuum at the distal end greater than approximately 51 kPa (15 inHg) in no greater than approximately 50 ms, as recited by claim 9.

Claim 9 therefore lacks novelty in view of O3.

4.9. Claim 10

Claim 10 recites:

The system according to claim 1, wherein:

the lumen has an internal diameter of between approximately 0.965 mm (0.038") and approximately 2.692 mm (0.106"); and

the controller (560) is configured to cyclically open and close the vacuum valve (420) and the vent valve (440) at a frequency of between 2 and 16 Hz.

4.9.1. O2 (US 2017/0238953 A1) – "Yang"

Claim 10 lacks novelty in view of O2, as the document discloses all of the features of claim 10.

Claim 10 is dependent on claim 1. As demonstrated above in section 4.1.2, O2 discloses all of the features of claim 1.

O2 describes the catheter as follows (emphasis added):

[0065] The catheter 10 generally comprises an elongate tubular body 16 extending between a proximal end 12 and a distal functional end 14...

[0066] In the illustrated embodiment, the tubular body 16 is divided into at least a fixed proximal section and an axially extendable and retractable distal section 34 separated at a transition 32.

[0068] The inner diameter of the distal section 34 may be between about 0.030 inches and about 0.112 inches, between about 0.040 inches and about 0.102 inches, between about 0.045 inches and about 0.097 inches, between about 0.050 inches and about 0.092 inches, between about 0.055 inches and about 0.087 inches, between about 0.060 inches and about 0.082 inches, between about 0.062 inches and about 0.080 inches, between about 0.064 inches and about 0.078 inches, between about 0.066 inches and about 0.076 inches, between about 0.068 inches and about 0.074 inches, or between about 0.070 inches and about 0.072 inches.

That is, the catheter described in O2 and shown in Fig. 14 is provided with a lumen having a diameter which falls within the claimed range.

In addition, paragraph [0168] of O2 discloses that the period of each vacuum and release cycle may be equal to about 0.1 seconds – that is, a cycling frequency of 10 Hz. This would naturally result in opening and closing of the valves at a frequency that is between 2 and 16 HZ as recited by claim 10.

Claim 10 therefore lacks novelty in view of O2.

4.10. Claim 11

Claim 11 recites:

The system according to claim 1, wherein:

the lumen has an internal diameter of between approximately 1.73 mm (0.068") and approximately 2.24 mm (0.088"); and

the controller (560) is configured to cyclically open and close the vacuum valve (420) and the vent valve (440) at a frequency of between 2 and 16 Hz.

4.10.1. O2 (US 2017/0238953 A1) – “Yang”

Claim 11 lacks novelty in view of O2, as the document discloses all of the features of claim 11.

Claim 11 is dependent on claim 1. As demonstrated above in section 4.1.2, O2 discloses all of the features of claim 1.

O2 describes the catheter as follows:

[0065] The catheter 10 generally comprises an elongate tubular body 16 extending between a proximal end 12 and a distal functional end 14...

[0066] In the illustrated embodiment, the tubular body 16 is divided into at least a fixed proximal section and an axially extendable and retractable distal section 34 separated at a transition 32.

[0068] The inner diameter of the distal section 34 may be between about 0.030 inches and about 0.112 inches, between about 0.040 inches and about 0.102 inches, between about 0.045 inches and about 0.097 inches, between about 0.050 inches and about 0.092 inches, between about 0.055 inches and about 0.087 inches, between about 0.060 inches and about 0.082 inches, between about 0.062 inches and about 0.080 inches, between about 0.064 inches and about 0.078 inches, between about 0.066 inches and about 0.076 inches, between about 0.068 inches and about 0.074 inches, or between about 0.070 inches and about 0.072 inches.

That is, the catheter described in O2 and shown in Fig. 14 is provided with a lumen having a diameter which falls within the claimed range.

In addition, paragraph [0168] of O2 discloses that the period of each vacuum and release cycle may be equal to about 0.1 seconds – that is, a cycling frequency of 10 Hz. This would naturally result in opening and closing of the valves at a frequency that is between 2 and 16 HZ as recited by claim 11.

Claim 11 therefore lacks novelty in view of O2.

4.11. Claim 12

Claim 12 recites:

The system according to claim 1, wherein the controller (560) is configured to cyclically open and close the vacuum valve (420) and the vent valve (440) 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 (440).

4.11.1. O1 (EP 4 461 253 A2) – “Teigen”

As set out in relation to claim 1, the controller in O1 is configured to “*modulate the vacuum source valve and the pressure source valve*”, and generate pressure differentials within a lumen of the aspiration catheter by “*alternating between opening and closing the valves*” (at least abstract and claim 1 of O1).

O1 discloses the use of extraction cycles which may employ one or more pulsation protocols to systemically manipulate the amount of pressure within the catheter (paragraphs 63-66, 77). O1 further teaches that these pressure differentials may be generated in a number of ways, for example by “*introducing fluid into the catheter, where the fluid is at a pressure between full vacuum and ambient pressure*” (paragraph 65).

In order for the pressure to be systematically manipulated via regular pressure pulses, the skilled person would recognise that the introduction of fluid into the catheter must be controlled, and therefore that the timing of the vent valve in O1 must also be controlled, i.e. regulated.

Further, as explained above, forward flow would be prevented in implementations of O1, in particular implementations in which fluid is introduced which is “*at a pressure between full vacuum and ambient pressure*”. In these implementations, the full vacuum is temporarily partially relieved, while maintaining an overall level of negative pressure (suction) in the catheter.

The skilled person carrying out this teaching of O1 would inevitably arrive at a result in which the timing of the fluid injection on-off valve 296 is regulated, and in which forward flow is prevented.

4.11.2. O2 (US 2017/0238953 A1) – “Yang”

Claim 12 lacks novelty in view of O2, as the document discloses all of the features of claim 12.

Claim 12 is dependent on claim 1. As demonstrated above in section 4.1.2, O2 discloses all of the features of claim 1.

As discussed in section 4.1.2, Figs. 14 and 25A-25C of O2 show arrangements comprising a vacuum source and an atmospheric pressure source (‘vent fluid source’) which can be connected to the catheter in order to provide pulsatile pressure.

Paragraph [0168] of O2 discloses that the period of each vacuum and release cycle may be equal to about 0.1 seconds – that is, a cycling frequency of 10 Hz. Paragraph [0127], describing a frequency modulator for controlling the solenoid valve, suggests that control could take place at frequencies of “less than about 500Hz, in some modes of operation less than about 20 Hz or less than about 5 Hz”, and paragraph [0130] discloses operating the cycle at a frequency of less than about 260 Hz.

By comparison, the opposed patent discloses that the ROAR effect can retain a level of pressure at the distal end less than or equal to physiological pressure (i.e., to prevent forward flow) when the vacuum valve and vent valve are cycled at a rate of between approximately 1 Hz and approximately 250 Hz (see e.g., page 56, lines 22 to 36). In particular, the opposed patent states (page 9, lines 26 to 32):

By cycling the vacuum and vent valves at a sufficiently fast rate, a pressure measurement at a rate of one thousand samples per section 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 coked condition.

That is, the opposed patent equates cycling at a sufficiently fast rate with timing of the valves. O2 discloses cycling valves at a sufficiently fast rate (i.e., at frequencies considered suitable by the opposed patent itself), and is therefore also considered to disclose regulating timing of the release valve 2514 (‘vent valve’) in the same manner as claim 12.

Claim 12 therefore lacks novelty in view of O2.

4.11.3. O3 (WO 2017/214573 A1) – “Ofek”

Claim 12 lacks novelty in view of O3, as the document discloses all of the features of claim 12.

Claim 12 is dependent on claim 1. As demonstrated above in section 4.1.3, O3 discloses all of the features of claim 1.

It has been demonstrated above that O3 shows a system in which a controller is configured to cyclically open and close a vacuum valve and a vent valve in a repeated cycle and prevent forward flow. The cycles of opening and closing the valves provide high pressure pulses.

Paragraph [00039] of O3 discloses that the frequency of high pressure impulses can vary in a range of about 1 to over about 150 Hz. This paragraph goes on to say that the impulse frequency may be set to match a resonant frequency of a catheter, and so may be about 30 Hz in one example, or may vary from about 15 Hz to about 50 Hz.

By comparison, the opposed patent discloses that the ROAR effect can retain a level of pressure at the distal end less than or equal to physiological pressure (i.e., to prevent forward flow) when the vacuum valve and vent valve are cycled at a rate of between approximately 1 Hz and approximately 250 Hz (see e.g., page 56, lines 22 to 36). In particular, the opposed patent states (page 9, lines 26 to 32):

By cycling the vacuum and vent valves at a sufficiently fast rate, a pressure measurement at a rate of one thousand samples per section 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 coked condition.

That is, the opposed patent equates cycling at a sufficiently fast rate with timing of the valves. O3 discloses cycling valves at a sufficiently fast rate (i.e., at frequencies considered suitable by the opposed patent itself), and is therefore also considered to disclose regulating timing of the normally closed valve 140 ('vent valve') in the same manner as claim 12.

Furthermore, O3 states that (emphasis added):

[00038] In one embodiment, the response time of the valves 140 and 150 is sufficiently fast to enable the positive pressure impulses to be followed in quick succession by the negative baseline pressure or negative pressure impulse.

In the context of providing high-pressure impulses which are "strong enough to dislodge an occlusion but are not of sufficient duration to push it out the distal end 12B of the catheter tube 12" (paragraph [00031]), the skilled person would understand that 'sufficiently fast' response time refers to ensuring that timing of the valves is suitable for preventing forward flow, as recited by claim 12.

Claim 12 therefore lacks novelty in view of O3.

4.12. Claim 13

Claim 13 recites:

The system according to claim 1, wherein the controller (560) is configured to cyclically open and close the vacuum valve (420) and the vent valve (440) to retain a level of pressure at the distal end at less than physiological pressure.

4.12.1. O1 (EP 4 461 253 A2) – “Teigen”

Claim 13 lacks novelty in view of O1, as the document discloses all of the features of claim 13.

O1 discloses this e.g. by teaching that the pressure differentials may be generated by “*introducing fluid into the catheter, where the fluid is at a pressure between full vacuum and ambient pressure*” (paragraph 65).

O1 explicitly teaches that the fluid provided by the fluid injection device may be at the appropriate pressure as required by the implementation e.g. stating that the fluid may be “*at a pressure above that of the vacuum aspiration system, between full vacuum pressure and ambient pressure, at ambient pressure, between ambient pressure and systolic pressure, at systolic pressure, or above systolic pressure*” (paragraph 26).

4.12.2. O2 (US 2017/0238953 A1) – “Yang”

Claim 13 lacks novelty in view of O2, as the document discloses all of the features of claim 13.

Claim 13 is dependent on claim 1. As demonstrated above in section 4.1.2, O2 discloses all of the features of claim 1.

Paragraph 102 of O2 states that pulsatile application of a vacuum may oscillate between (emphasis added):

[0102] ...a first lower negative pressure and a second higher negative pressure...

Clearly, in such an arrangement the level of pressure at the distal end of the lumen must be less than physiological pressure whichever pressure source is connected to the catheter via the valve arrangement at a given time.

Claim 13 therefore lacks novelty in view of O2.

4.12.3. O3 (WO 2017/214573 A1) – “Ofek”

Claim 13 lacks novelty in view of O3, as the document discloses all of the features of claim 13.

Claim 13 is dependent on claim 1. As demonstrated above in section 4.1.3, O3 discloses all of the features of claim 1.

As described above with respect to claim 1, O3 teaches that pressure pulses applied through the catheter are interspersed with baseline negative pressure to ensure that the dislodged occlusion is prevented from entering the bloodstream from a distal end of the catheter. For example, paragraph [00027] states that (emphasis added):

[00027] ...the patency device 30 provides short-duration, relatively high-pressure impulses through the fluid present in the catheter tube lumen 14 interspersed by relatively longer rest periods 84 of negative baseline pressure...negative baseline pressure present between impulses enables any occlusion dislodged by the impulses to be sucked proximally up the catheter tube lumen 14 and removed therefrom, thus preventing the dislodged occlusion from entering the bloodstream from the distal end 12B of the catheter tube 12.

It therefore follows that the level of pressure at the distal end of the catheter must always be less than physiological pressure, as if that were not the case then the arrangement would risk the occlusion entering the bloodstream.

Claim 14 therefore lacks novelty in view of O3.

4.13. **Claim 14**

Claim 14 recites:

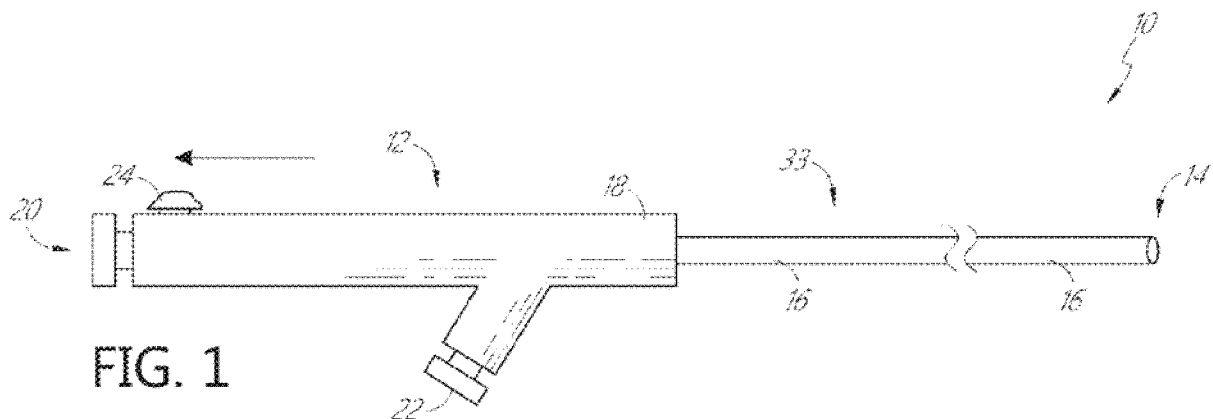
The system according to claim 1, which further comprises a shaft and the vacuum valve (420) and the vent valve (440) are mounted together on the shaft.

4.13.1. O2 (US 2017/0238953 A1) – “Yang”

Claim 14 lacks novelty in view of O2, as the document discloses all of the features of claim 14.

Claim 14 is dependent on claim 1. As demonstrated above in section 4.1.2, O2 discloses all of the features of claim 1.

An example of a manifold connected to the proximal end of a catheter is shown in Fig. 1 of O2 (reproduced below). The manifold 18 comprises an aspiration port 22 as described in paragraph 88. As will be appreciated from Fig. 1, the manifold 18 is a generally elongate, narrow body - i.e., a shaft.



Paragraph 131 describes that the solenoid valve 414 (which may be replaced with two valves as shown in Fig. 25A-25C as described in section 4.1.2) is connected to the aspiration line connecting to the catheter. That is, the two valves are connected to the aspiration port 22 of the manifold 18 of Fig. 1.

That is, the vacuum and release valves of O2 would be connected to, and therefore 'mounted together on', a shaft (manifold 18) as recited by claim 14.

prior art, the objective technical problem, and/or the selection of other documents for combination with the closest prior art) would be dependent upon the Opposition Division's reasoning. This is also the case for each of the dependent claims.

For example, should the Opposition Division decide that any of the documents discussed above with respect to novelty does not disclose all of the features of claim 1, we would intend to use that document as a starting point for demonstrating that the claim lacks an inventive step (e.g., in combination with any other prior art discussed herein). This is also the case for each of the dependent claims – if any of the documents discussed above with respect to novelty (specifically, either of O2 or O3 as prior art available for the assessment of novelty and inventive step) does not disclose all of the features of a particular dependent claim, then we may use that document as a suitable starting point for an objection that the claim lacks an inventive step, even if that document has not been explicitly included as a reference for the consideration of novelty and/or inventive step of any one or more claims herein.

5.0.2. Lack of 'technical effect' across the scope of the claim(s)

As an initial comment before discussing the prior art in relation to Art. 56 EPC, it is respectfully requested that, should the Opposition Division find it necessary to conduct a 'problem-solution analysis' in line with usual EPO practice, it be mindful of the EPO's general principle that the specific 'technical effect' (as understood according to usual EPO practice) underlying a specific technical problem should be achieved across the whole scope of the claim (e.g., as set out in Case Law of the Boards of Appeal I D 4.1.3).

As the Division will know, the Enlarged Board of Appeal commented as follows in G 0001/19:

82. It is a general principle that the question whether a feature contributes to the technical character of the claimed subject-matter is to be assessed in view of the whole scope of the claim. Using the problem-solution approach, the analysis under Article 56 EPC may reveal that a specific problem is not solved (i.e. a specific effect is not achieved) over the whole scope of the claim. In such cases, the aforementioned specific problem may not be considered as the basis for the inventive step analysis unless the claim is limited in such a way that substantially all embodiments encompassed by it show the desired effect (see, for example, T 939/92, OJ EPO 1996, 309, Reasons, point 2.6, where the board was not satisfied that substantially all claimed chemical compounds were likely to be herbicidally active). Such limitation is typically achieved by narrowing one or more features (e.g. a temperature or concentration range within a chemical process) and/or by adding one or more limiting features. The above principle, as it was elaborated in the often-cited decision T 939/92, just specifies the further general principle that the entire or substantially the entire claimed subject-matter must fulfil the patentability requirements. [...]

In this regard, it is submitted that many conceivable 'technical effects' (as understood according to usual EPO practice) which might be naively attributed to the subject matter of claim 1 and its dependent claims are in fact not suitable as the basis of a problem-solution analysis.

For example, the prevention of forward flow as a 'technical effect' cannot form the basis of a problem-solution analysis according to usual EPO practice, at least without significant amendment of claim 1. This is because the opposed patent makes clear that the 'technical effect' of "preventing forward flow" is not achieved by simply any cyclical opening and closing of a vacuum and vent valve. Indeed, this would also be obvious to the skilled person.

Clearly, for example, if the vent valve is left open for too long there will be forward flow. This is made clear in the opposed patent itself, with paragraph 147 teaching that “[...] subsequent opening of the vent valve 650 causes vent liquid 642 to enter the manifold 630 [...] 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”.

Similarly, the prevention of forward flow by optimising and/or mitigating for the water hammer effect cannot form the basis of the EPO’s usual problem-solution analysis with the claim in its current form. This is because, according to the opposed patent, the system must be “tuned” in order for the system to prevent forward flow in this manner (see paragraphs 42, 152-159). In particular, paragraph 42 states that “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”. This tuning depends on many factors of the system, for example “the density of the fluid, the compliance of the system (the bulk modulus), and the length of the fluid column” (see paragraph 152). Here, the bulk modulus refers to “the compliance of the system: both the radial and the longitudinal flexibility of the catheter and the extension tube” (paragraph 153).

In order for the parameters of the valve switching cycle to be set in a manner such that “the fluid column does not exit the distal end of the catheter”, it is “important that the catheter, any extension tube that connects to the catheter, the controller, and the valving sequence be tuned as a system” (paragraph 152).

Paragraph 156 of the opposed patent states:

[0156] 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.

[0157] 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, Vntofftime 656, and Vntoff duration 658. [...]

It is therefore clear from the teaching of the patent that the water hammer effect is only controlled or optimised to prevent forward flow when the entire system has been carefully “tuned” for each of several factors (e.g. Vacon time, Vacon duration, Vacoff time, and Vacoff duration, Vnton time, Vnton duration, Vntofftime, and Vntoff duration). Even once the tuning process has been conducted, the values of the tuned parameters only quell movement of the fluid to prevent the fluid from exiting the distal end of the catheter for a given catheter and extension tube configuration.

Accordingly, the ‘technical effect’ of the prevention of forward flow cannot form the basis of an inventive step analysis under the EPO’s problem-solution framework, at least without significant amendment of the claims to specify, for example, the values of the tuned parameters and the specifics of the given catheter and extension tube configuration.

Additional comments are provided below in respect of certain dependent claims, however we ask that the Opposition Division bear this general principle in mind while assessing the inventive step of any dependent claim.

5.1. Claim 1

Claim 1 is recited in section 1.3 of this letter, with our suggested labelling scheme.

5.1.1.O18 (US 2016/0220741 A1) - "Garrison"

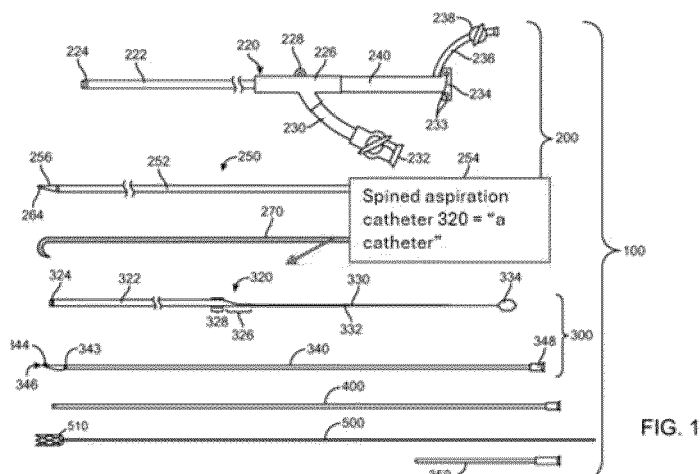
O18 is a US patent application published 4 August 2016, before the earliest claimed priority date of the opposed patent. O18 is therefore prior art under Art. 54(2) EPC, available for the assessment of novelty and inventive step.

O18 discloses an intravascular access system comprising an aspiration catheter (see e.g. abstract).

A general purpose of O18, as set out in the background section, is to improve on the prior art in the following respects:

[0008] [...] There is a need for a system of devices and methods that enable rapid access, optimized aspiration of the clot, distal protection throughout all stages of the procedure, which potentially liberate emboli, and safe and rapid exchange of devices as needed to fully restore flow to the blocked cerebral vessel.

Fig. 1 of O18 (reproduced below) shows a system of devices for accessing and removing a cerebral occlusion including an access sheath 220 having a sheath body 222, and a spined aspiration catheter 320 (see paragraph 44):



In use, as can be seen in Fig. 2B (reproduced in part below), the lumen of the aspiration catheter is fluidly connected to the lumen of the access sheath such that fluid flow into and/or out of the system is possible, such as by applying suction from an aspiration source coupled to the system (paragraph 47). An overlapping region 120 provides a seal between catheter and access sheath:

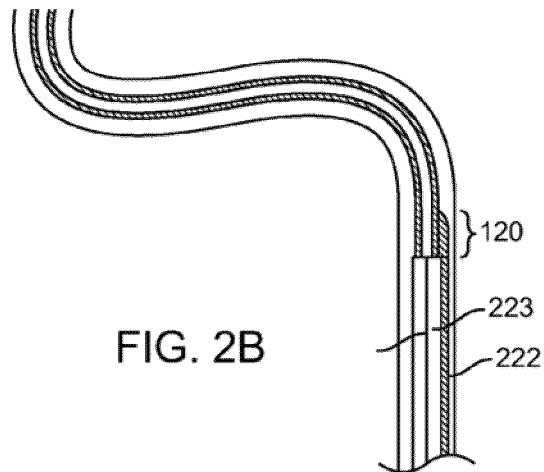


Fig. 11 of O18 shows an implementation of an aspiration system which includes an aspiration source 600, for use with the system of devices shown in Fig. 1 (paragraph 32 of O18):

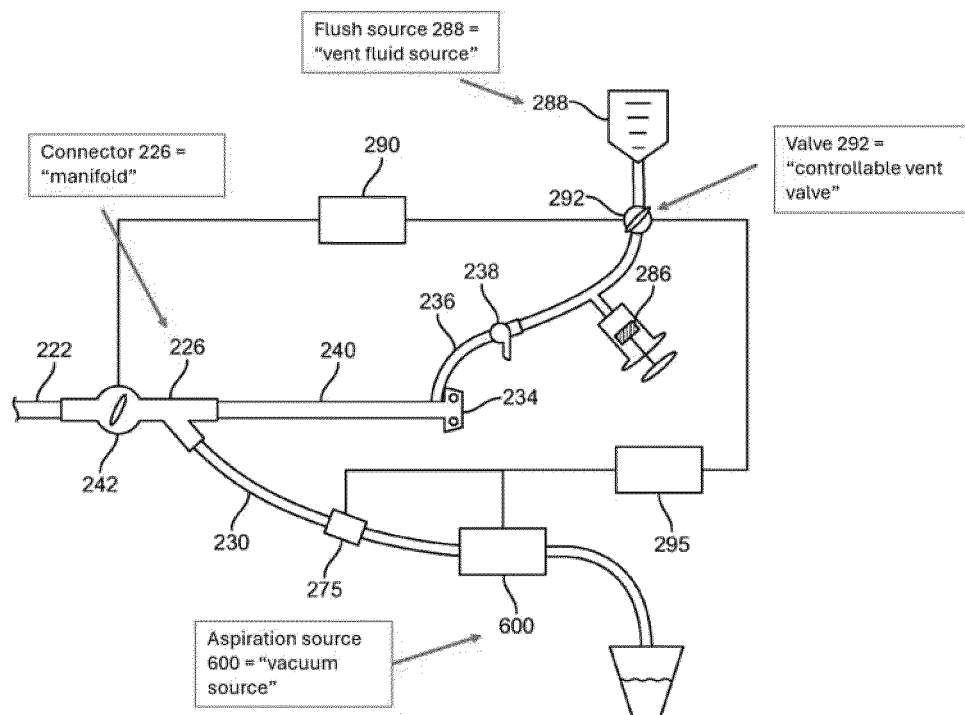


FIG. 11

In the system of fig. 11, an aspiration source 600 provides “a cyclic level of aspiration force, for example, an aspiration force that cycles between a high level of vacuum to a lower level of vacuum at a set frequency”. This cyclic aspiration mode may “provide a jack-hammer type force on the thrombus and increase the ability to aspirate the thrombus through the catheter”. The cyclic aspiration force may be enabled “through solenoid valves, a programmable pump motor, or the like. In an implementation, cyclic aspiration is applied only when clogged or restricted flow is detected in the aspiration line” and may be “controlled automatically via a feedback loop to the aspiration source” for example (see paragraph 114).

In this system, a controllable valve 292 can “control flow from the flush source 288 to the flush line 236.” (see paragraph 116).

Since O18 relates to a aspiration thrombectomy system and method in which a cyclic level of aspiration force is applied to a thrombus, and has many structural similarities to the claimed clot removal system, it follows that O18 is an appropriate starting point for the assessment of inventive step.

1[Pre] (A clot removal system)

O18 relates to a rapid aspiration thrombectomy system and method (see title).

O18 relates to methods and systems for “navigating complex anatomy to perform rapid and safe aspiration and removal of cerebral occlusions” (see paragraph 3) and describes a thrombectomy procedure as follows (emphasis added):

[127] Once the distal tip of the spined aspiration catheter 320 is at the face of the clot, aspiration is initiated at a level suitable for aspiration thrombectomy, which is a higher level than for distal embolic protection. The catheter 320 may remain in aspiration mode against the clot for some period of time, as deemed suitable by the user. Depending on the results of the aspiration thrombectomy maneuver (as observed by flow through the aspiration line and/or resistance to backwards force on the spine of the catheter), the user may determine that the clot has been completely aspirated, or if not, the user may choose to move the catheter 320 back and forth to aspirate the clot in situ, or to slowly retract the catheter 320 into the sheath 220.

When providing a cyclical level of aspiration force, the cyclic aspiration mode may “provide a jack-hammer type force on the thrombus and increase the ability to aspirate the thrombus through the catheter” (see paragraph 114).

The skilled person would therefore understand that the system of O18 is a clot removal system.

1[a] (a catheter having a distal end and defining a lumen filled with a liquid column having a proximal portion and a distal portion)

The system of O18 comprises an “aspiration catheter” which is depicted using reference numeral 320 in Fig. 1 reproduced above. The aspiration catheter has a distal tip which can be “positioned [...] at the face of the occlusion in the artery” (paragraphs 43, 45) and a “distal end region”.

O18 inherently discloses that the catheter lumen is “filled with a liquid column having a proximal portion and a distal portion”, at least because the skilled person would have recognised that all catheters used in aspiration thrombectomy define a lumen filled with a liquid column contained within the proximal and distal ends of the catheter, or that it would have been obvious to use the catheter in a manner such that it includes a lumen having opposing distal and proximal ends filled with a liquid column, because the purpose of the catheter in O18 is to act as a conduit to collect liquid, including blood and clot material from a patient’s blood vessel.

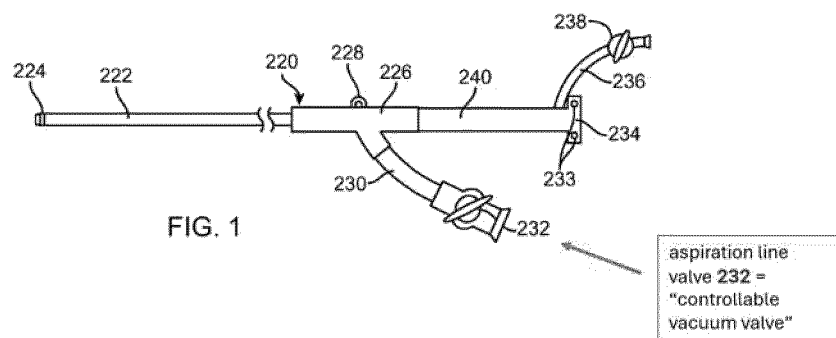
O18 clearly contemplates that the catheter lumen’s purpose is to be filled with flowing liquid, stating for example that “*The contiguous aspiration lumen can be used to aspirate fluid and debris from the distal opening of the luminal portion*” (at paragraph 12, emphasis added) and that the lumens of the catheter and access sheath are “*fluidly connected and contiguous such that fluid flow into and/or out of the system is possible, such as by applying suction from an aspiration source [...]*”.

In addition, the opposed patent states, at paragraph 145, that: “*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*”. That is, the opposed patent accepts that the fluid column in the catheter comprises aspirated fluid. According to the teaching of the patent, therefore, any aspiration thrombectomy system comprises a liquid column in use, at least due to the aspiration of liquid from vasculature.

1[b] (a controllable vacuum valve)

O18 contemplates several possible implementations of a controllable vacuum valve.

With reference to Fig. 1, part of which is reproduced below, paragraph 60 of O18 discloses that “*The aspiration line 230 can terminate in a stopcock, female Luer connector, or other connector 232 that allows connection to an aspiration source*” and goes on to describe connector 232 as an “*aspiration line valve 232*” which “*enables the line 230 to be opened or closed*”.



With reference to the aspiration source 600 shown in Fig. 11, paragraph 113 of O18 describes that the system may further include “*a flow sensor 275 that senses flow in the aspiration line 230, coupled to a controller that controls the level of aspiration*” and that the use of a cyclic aspiration force may be enabled “*through solenoid valves, a programmable pump motor, or the like*” (paragraph 114, emphasis added).

In addition, paragraph 112 of O18 makes clear that several implementations of the vacuum source are contemplated, including implementations in which the aspiration rate may be varied “*by providing an element with variable resistance to flow, for example parallel flow paths that can switch between a high and low flow resistance path, flow orifices or lumens that can be variably opened, or other means to vary flow resistance*”.

1[c] (a vacuum source fluidically connected to the vacuum valve)

The system of O18 includes an aspiration source 600, as shown e.g. in Fig. 2A, Fig. 3, and Fig. 11.

As described at paragraph 111, the aspiration source 600 can be “*attached to the aspiration line 230 on the access sheath 220*” (see paragraph 111).

The skilled person would understand that, to enable the vacuum valve to function to “*control the level of aspiration*” and/or enable cyclical aspiration as described at paragraphs 113 and 114, it must be “*fluidically connected to the vacuum valve*”.

1[d] (a controllable vent valve having a vent liquid input)

&

1[e] (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)

Fig. 11 shows a valve 292 and flush source 288:

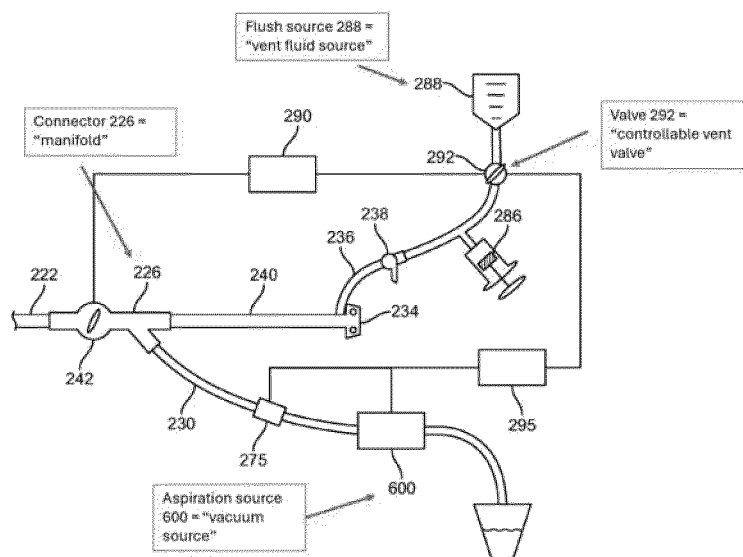


FIG. 11

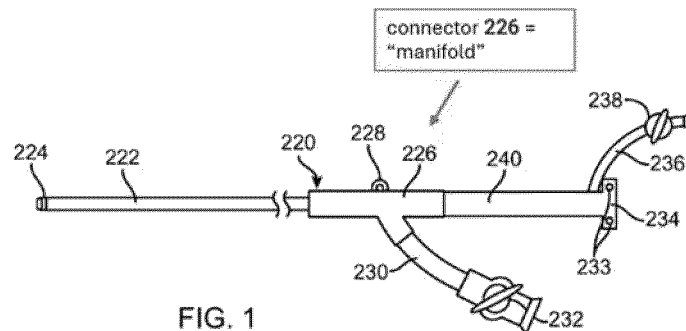
O18 describes Fig. 11 as follows:

[0116] [...] Additionally the flush line 236 may be connected to a flush source 288, for example, a pressurized bag of saline. A valve 292 can control flow from the flush source 288 to the flush line 236. When the valve 292 is opened to the flush line 236 a pressurized source of fluid is provided. In an implementation, the valve 292 is coupled via a mechanical or electromechanical coupler 295 to the aspiration source 600 such that the valve 292 is only open when the aspiration source 600 is on. Alternately, the valve 292 is coupled to a flow sensor 275 in the aspiration line 230, such that the valve 292 is only on when there is flow in the direction towards the aspiration source 600 [...]

A vent liquid is therefore clearly provided by O18 in the form of pressurised saline, such that flush source 288 provides a vent fluid source as recited by claim 1. The valve 292 controls flow of saline into the flush line 236 and thereby provides a controllable vent valve as recited by claim 1.

1[f] (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)

The connector 226 depicted in Fig. 11, optionally in combination with any appropriate number of additional connectors and/or connecting structures, is a “manifold” as defined in feature 1[f] of the opposed patent.



Paragraph 47 makes clear that the lumens of the catheter and access sheath are “fluidly connected and contiguous such that fluid flow into and/or out of the system is possible, such as by applying suction from an aspiration source coupled to the system via a connector 226 on the access sheath 220”. The connector 226 is connected to the sheath body 222 of the access sheath 220, as can be appreciated from Fig. 11 and as described in paragraph 60.

Therefore, the connector 226 is “connected to the catheter” (via access sheath 220) as required by 1[f].

Paragraph 60 describes the connector 226 as follows:

[0060] [...] the access sheath 220 also can include a connector 226 that connects a proximal end of the sheath body 222 to the proximal hemostasis valve 234, and also provides a connection to the aspiration line 230. This connector 226 can have a large bore inner lumen, and connects to a large-bore aspiration line 230.

Therefore the connector 226 is connected to the aspiration line 230. Since the vacuum valve forms part of the vacuum source 600 (as described in paragraph 112), or else is positioned between the connector 226 and the source of aspiration (as shown in Fig.1), it follows that O18 teaches that the connector 226 is “connected to the vacuum valve” in the manner defined in **1[f]**.

As can be appreciated from Fig. 11, the connector 236 is connected to the valve 292 (via proximal extension portion 240 and flush line 236).

Finally, as there must be fluid communication between the interconnected parts to allow cyclical and/or variable vacuum pressure to be applied to the catheter (as described e.g. at paragraph 114), and to allow the sheath to be “flushed with saline” during the procedure “as desired”, it is clear that the connector 226 “fluidically connects a proximal portion of the liquid column in the lumen” to the vacuum source through the vacuum valve, as further defined in **1[f]**.

***1[g] (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)***

O18 discloses an aspiration source 600 comprising e.g. a solenoid valve (see analysis of feature 1[b] above). Cyclic aspiration is applied when “*clogged or restricted flow is detected in the aspiration line*” and the configuration may be “*controlled automatically via a feedback loop to the aspiration source*” (paragraph 114).

Because the aspiration source is configured to provide a cyclic level of aspiration force e.g. via control of the solenoid valve, and because this mode can be entered “automatically”, it is implicit that there is a controller connected to the solenoid valve which is configured to “selectively open and close the vacuum valve” such that “responsive to opening the vacuum valve, the vacuum source is fluidically connected to the liquid column in the lumen”.

With regard to the vent valve, O18 teaches that:

[0116] [...] In an implementation, the valve 292 is coupled via a mechanical or electromechanical coupler 295 to the aspiration source 600 such that the valve 292 is only open when the aspiration source 600 is on. Alternately, the valve 292 is coupled to a flow sensor 275 in the aspiration line 230, such that the valve 292 is only on when there is flow in the direction towards the aspiration source 600. [...].

Again, it is implicit that the arrangement of O18 comprises a controller connected to the vent valve and configured to selectively open and close the vent valve.

There is some ambiguity regarding whether this is the same controller as controls the vacuum source, however this is an obvious modification.

1[h] (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)

Paragraph 114 teaches the use of cyclical aspiration that provides “an aspiration force that cycles between a high level of vacuum to a lower level of vacuum at a set frequency”, or which cycles from “a high level of vacuum to no vacuum”.

O18 teaches cyclically opening and closing a vacuum valve to change a level of vacuum at the distal end of the catheter, e.g. in order to “provide a jack-hammer type force on the thrombus and increase the ability to aspirate the thrombus through the catheter” (paragraph 114).

However, O18 does not disclose the cyclical opening and closing of both a vacuum valve and a vent valve to create this cyclical aspiration force.

1[i] (prevent forward flow of the distal portion out from the distal end during each cycle).

O18 is very clear in its teaching regarding the risk of “distal emboli”. The occurrence of distal emboli during the procedure has “potentially negative neurologic effect and procedural complications such as perforation and intracerebral haemorrhage” (paragraph 8). In this regard, O18 teaches that “The higher efficiency of aspiration force through the systems described herein reduces distal embolic debris and increases the rate of “one-pass” thrombectomy” (paragraph 42) and that “by providing the ability to maintain aspiration continuously from either the catheter tip or the sheath tip or the sheath distal region, and providing the means to change aspiration levels and maintain asp, the procedure optimizes the ability to aspiration clot while minimizing distal emboli and minimizing blood loss from aspiration” (paragraph 128).

Paragraph 114 teaches the use of cyclical aspiration that provides “an aspiration force that cycles between a high level of vacuum to a lower level of vacuum at a set frequency”, or which cycles from “a high level of vacuum to no vacuum”. In such implementations, an overall level of aspiration would be maintained in the catheter, and in this way forward flow would be prevented.

5.1.1.1. Establishing the ‘objective technical problem’ to be solved

In summary, the distinguishing features of claim 1 of the opposed patent over O18 are that O18 does not explicitly teach the use of the same controller connected to both the vacuum valve and the vent valve, and O18 does not disclose the cyclical opening and closing of both a vacuum valve and a vent valve to change a level of vacuum at the distal end of the catheter (feature 1[h]).

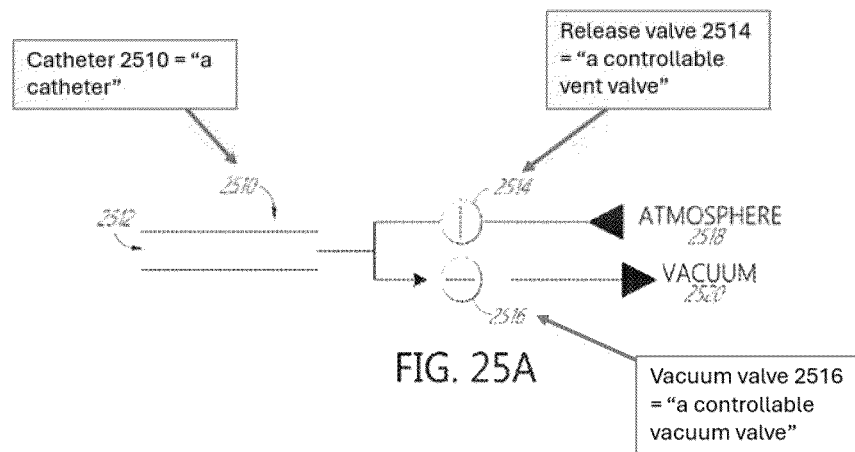
Forward flow is already prevented during the application of cyclical aspiration in O18, for example in an implementation in which an aspiration force is applied that cycles between a high level of vacuum to a lower level of vacuum at a set frequency.

A 'technical effect', as understood according to usual EPO practice, of these differences is that an alternative method of providing cyclical aspiration is provided. An objective technical problem can be framed as "how to provide an alternative method of cyclical aspiration".

The skilled person seeking to solve this problem would turn to other documents in the field, for example those described herein, including those set out above at section 1.2.2. Examples of combination with O2 and O3 are outlined in more detail below, but it will be understood that other documents described herein could be used in their place.

5.1.1.2. Combination of O18 with O2 ("Yang")

For example, as set out above at section 4.1.2, Figs. 25A-C of O2 ("Yang") show a vacuum and release cycle which can be applied to a catheter to create pulsed aspiration (paragraphs 40, 168-169 of O2). Fig. 25A shows the first valve state or 'step' in the cycle:



Since the system of O18 already has a catheter, vent fluid source, vent valve, vacuum source, vacuum valve, and a manifold, the skilled person would appreciate that the valve cycle taught by O2 could be incorporated into the system of O18 in a straightforward manner.

In this way, the teaching of O2 would have prompted the skilled person, faced with the objective technical problem, to modify the arrangement of O18 in such a way as to arrive at a modified arrangement which falls within the terms of claim 1.

As set out above at section 4.1.2, in relation to cyclical aspiration, O2 teaches the use of a controller that is:

[0014] [...] configured to apply pulses of vacuum to the lumen spaced apart by spaces of neutral pressure. The controller may be configured to alternate between applying pulses of higher negative pressure and lower negative pressure.

This aligns with the teaching of O18:

[0114] In yet another aspiration source implementation, the aspiration source 600 provides a cyclic level of aspiration force, for example, an aspiration force that cycles between a high level of vacuum to a lower level of vacuum at a set frequency, or from a high level of vacuum to no vacuum, or from a high level of vacuum to a pressure source.

In relation to the water hammer effect, paragraph 114 of O18 states that cyclical aspiration may provide a jack-hammer type force on the thrombus and increase the ability to aspirate the thrombus through the catheter. Paragraph 108 of O2 similarly teaches that pulsatile pressure causes a water hammer effect which can assist in breaking up a thrombus or clot.

It follows that the skilled person would clearly understand that the approaches taught by O18 and O2 are technically compatible alternatives to one another. The skilled person would understand that the valve cycle taught by O2 would provide an effective method of cyclical aspiration if incorporated into the system of O2.

In making such a modification, the skilled person would be mindful of their own common general knowledge that distal migration of the clot must be avoided. This is re-iterated in O18, which states (for example) that “*distal protection*” must be enabled “*throughout all stages of the procedure*” (see paragraph 8). Therefore, the skilled person would seek to avoid forward flow when making the modifications to O18.

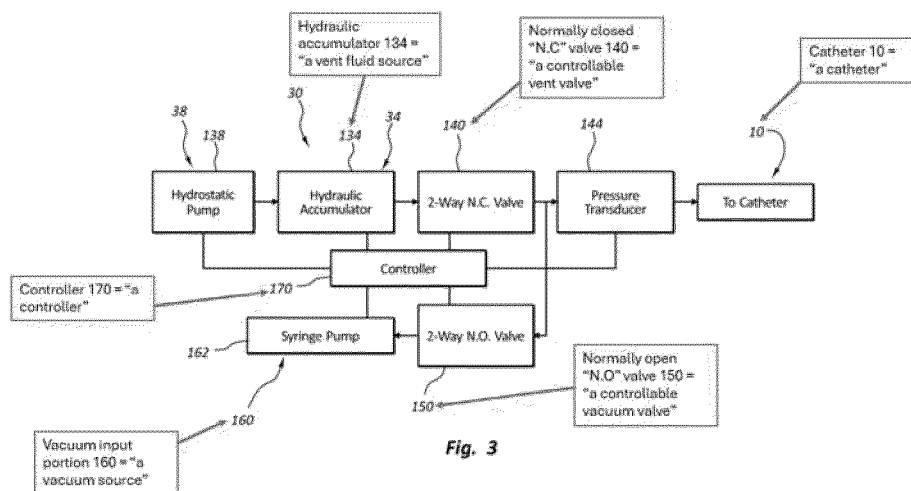
In any case, the incorporation of the valve cycle of O2 into the system of O18 would naturally result in the prevention of forward flow. Both O18 and O2 teach the application of a first negative and a second negative pressure (paragraph 117 in O18 and 102 in O2).

Clearly, operating an arrangement which cycles between two negative pressures cannot lead to forward flow, as no positive pressure would be applied to the catheter at any point. That is, in such an arrangement a vacuum would always be applied through the catheter during operation of the apparatus. As a vacuum is always applied, there is no force which would move the fluid column within the catheter lumen forward and out of the distal end of the catheter. That is, forward flow must inherently be prevented.

Accordingly, the claimed invention would have been obvious to the skilled person starting from O18 and considering the teachings of O2.

5.1.1.3. Combination of O18 with O3 (“Ofek”)

As set out above at section 4.1.3, O3 discloses the structure and functionality defined in claim 1. The skilled person would appreciate from consulting O3 that the arrangements of O3 share many similarities with the arrangements disclosed in O18. For example, O18 has a catheter, vent fluid source, vent valve, vacuum source, vacuum valve, and a manifold, in a manner not dissimilar to the block diagram depicted in Fig. 3 of O3.



In O3, as detailed at point 4.1.3, the controller 170 is operably connected to both the normally open valve 150 and N.C. valve 140. The fluid provided by the hydraulic accumulator ('a vent fluid source') is used to provide pressure impulses through the catheter by control of the normally closed valve ('a vent valve').

O3 describes (emphasis added):

[00027] As shown, the patency device 30 provides short-duration, relatively high-pressure impulses through the fluid present in the catheter tube lumen 14 interspersed by relatively longer rest periods 84 of negative baseline pressure provided to the catheter tube lumen. The negative baseline pressure present between impulses enables any occlusion dislodged by the impulses to be sucked proximally up the catheter tube lumen 14 and removed therefrom, thus preventing the dislodged occlusion from entering the bloodstream from the distal end 12B of the catheter tube 12. Note that the rest periods in other embodiments can include a reduction to a neutral pressure or lower (but still positive) pressure or to varying pressures over time as may be desired.

The teaching of O3 would have prompted the skilled person, faced with the objective technical problem, to modify the arrangement of O18 in such a way as to include such impulses provided by a vent fluid, for example via the "flush source 288" already present in the arrangement of O18, and therefore to arrive at a modified arrangement which falls within the terms of claim 1.

Since the skilled person is well-aware of the need to avoid distal embolization, and since, as detailed above, the arrangements of both O18 and O3, when operated, will prevent forward flow, the resulting modified arrangement will prevent forward flow out from the distal end of the catheter.

5.1.2.O8 (US 20160375221 A1) - "Panotopoulos"

O8 is a US patent application published 29 December 2016, before the earliest claimed priority date of the opposed patent. O8 is therefore prior art under Art. 54(2) EPC, available for the assessment of novelty and inventive step.

O8 describes a fluid exchange catheter system which is suitable for the removal of substances from the body such as blood, coagulated blood, blood clot(s) (thrombus/thrombi) etc. (see e.g., Abstract, paragraph [0058]).

The system of O8 is configured to help keep the catheter free from blockages, and to remove blockages from the body, by changing the fluid pressure within the catheter (see e.g., Abstract). For example, O8 states (emphasis added):

[0016] ...the inventor of the present invention has developed a fluid exchange catheter which provides a stable fluid exchange performance without the risk of prolonged blockage of the catheter... unblocking of the catheter is effected by altering the width of the at least one lumen opening by changing the infusion and/or aspiration fluid pressure of the catheter, the infusion and/or aspiration fluid pressure being different from an outer pressure acting on the outside of the distal wall portion of the obligatory lumen. Thereby, a stable fluid flow through the catheter can be achieved...

[0058] In particular embodiments, the catheter of the invention is used for the removal of substances, such as undesired substances from the body. Preferred examples of such substances are selected from the group consisting of blood, coagulated blood, blood clot(s) (thrombus/thrombi)...

Fig. 1 of O8 (reproduced below, annotated relative to the opposed patent) shows an example of the system including a catheter (which in the depicted example comprises two lumen tubes 1 and 2), an infusion device 3 for introducing fluid to the catheter, and an aspiration device 4 for removing fluid from the catheter:

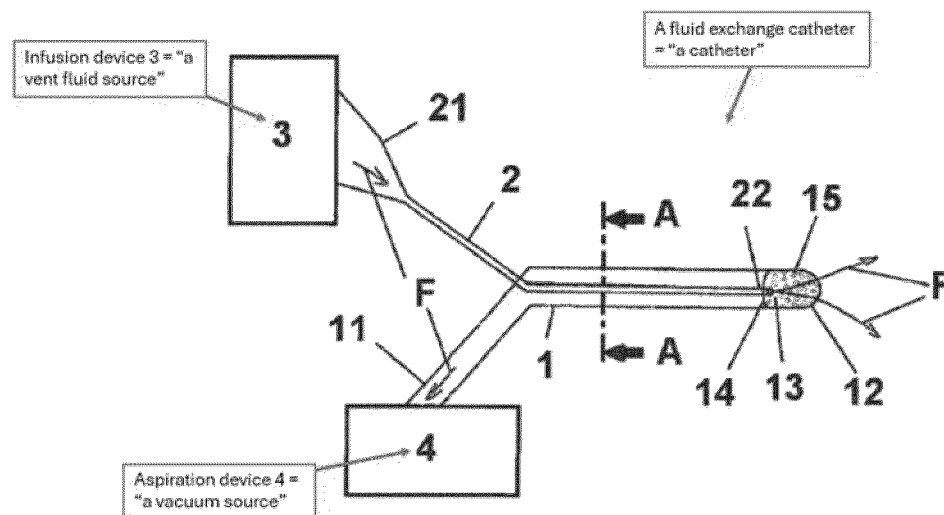


Fig. 1

O8 has many structural similarities with the arrangement claimed by the opposed patent, and so represents a suitable starting point for the assessment of inventive step.

1[Pre] (A clot removal system)

O8 discloses (emphasis added):

[0001] ...a fluid exchange catheter, for example for drug delivery into a body, i.e. human or animal tissue. Particularly, the proposed invention provides a fluid exchange catheter being able to prevent or remove blockage of the catheter, which can occur due to different causes, such as clogging by a blood clot, pus or the like. Further, the proposed invention provides a process for unblocking such a fluid exchange catheter... can be used in any other suitable surgical field.

The principal application of the arrangement of O8 is therefore use as a fluid exchange catheter. However, the document also discloses that the system can be used in other suitable surgical field, and in fact teaches that (emphasis added):

[0058] In particular embodiments, the catheter of the invention is used for the removal of substances, such as undesired substances, from the body. Preferred examples of such substances are selected from the group consisting of blood, coagulated blood, blood clot(s) (thrombus/thrombi)...

A method for removing clots using the system is also described in claims 27 and 28.

O8 therefore provides a clot removal system.

1[a] (a catheter having a distal end and defining a lumen filled with a liquid column)

Fig. 1, reproduced above, shows a fluid exchange catheter system as described by O8 (see e.g., paragraph [0069]). The system comprises:

[0073] ...a fluid exchange catheter... which consists of two lumen or lumen tubes 1 and 2, namely an obligatory lumen or outer lumen 1 and an additional lumen or inner lumen 2, wherein the additional lumen 2 is provided inside the obligatory lumen 1 in a concentric manner...

Suitable cross-sections of suitable catheters are shown in Figs. 2a-2e.

O8 further states that (emphasis added):

[0079] Alternatively to the above mentioned structure, it is possible to merely use one single obligatory lumen 1 comprising an opening, for example an oval slit opening, at its proximal end 11 and its distal end 12, respectively, wherein the proximal end 11 of the obligatory lumen 1 is alternately connected to the infusion device 3, the aspiration device 4 and/or a stop mechanism in between...

That is, O8 also discloses the use of a catheter having a single lumen which is connected to an infusion device and an aspiration device at its proximal end. In the context of aspiration of blood, the skilled person would appreciate that the lumen would be filled with a liquid column in use, and O8 teaches that the system can be used for infusion of various liquids (see e.g., paragraphs [0074]-[0076]).

O8 therefore provides a catheter as recited by claim 1.

1[b] (a controllable vacuum valve)

In relation to an embodiment wherein the catheter comprises a single lumen, O8 discloses (emphasis added):

[0079] ... the proximal end 11 of the obligatory lumen 1 is alternately connected to the infusion device 3, the aspiration device 4 and/or a stop mechanism in between. Such an embodiment could be implemented by a device adapted for a pendulum movement, including two separate tubes corresponding to an aspiration pump or fluid container and an infusion pump or fluid container or connected thereto, respectively, wherein the pendulum device is constructed to connect the obligatory lumen 1 with one of the two tubes by a pendulum or oscillation movement. Here, due to the controlled movement of the pendulum and, thus, the controlled connection between the obligatory lumen 1 and one of the two tubes (or the stop in between), the single lumen catheter acts as infusion means or aspiration means depending on the respective connected opening of the pendulum, while any infusion or aspiration is stopped in between opening.

Clearly, in such an arrangement the pendulum device controls the flow of liquid through the lumen by selectively connecting an aspiration pump or infusion pump. That is, the pendulum device provides a controllable valve.

The pendulum device is used to connect the catheter to the aspiration device ('a vacuum source', see below). The pendulum device of O8 therefore provides a controllable vacuum valve as recited by claim 1.

For completeness, it is noted that O8 also provides a controllable vacuum valve in relation to the multi-lumen embodiment (emphasis added):

[0075] ...a process can consist of alternating steps of an infusion period of several seconds or even minutes with a particular infusion pressure, followed by an aspiration period of several seconds or even minutes with a particular aspiration pressure. In order to achieve such a pattern, it is desirable to provide blocking means, which are in the position to block a connection between the infusion device 3 and the additional lumen 2, or the connection between the aspiration device 4 and the obligatory lumen 1...

The duration of aspiration can be controlled (see e.g., paragraphs [0027], [0074]) , and so the skilled reader would understand that the blocking device must be controllable accordingly.

1[c] (a vacuum source fluidically connected to the vacuum valve)

O8 discloses:

[0073] ... the obligatory lumen 1 is connected to an aspiration device 4 at its proximal tip or proximal end 11...

[0074] ...negative pressures of the aspiration device 4, such as a pump...

As the aspiration device provides a negative pressure, it provides a vacuum source as recited by the claim. It has been demonstrated above that a vacuum valve is provided by O8, and it is clear at least from those

passages of O8 that the aspiration device ('a vacuum source') is fluidically connected to the valve (e.g., in order to provide control of the application of negative pressure).

1[d] (a controllable vent valve having a vent liquid input)

As noted above, in relation to an embodiment wherein the catheter comprises a single lumen, O8 discloses (emphasis added):

[0079] ... the proximal end 11 of the obligatory lumen 1 is alternately connected to the infusion device 3, the aspiration device 4 and/or a stop mechanism in between. Such an embodiment could be implemented by a device adapted for a pendulum movement, including two separate tubes corresponding to an aspiration pump or fluid container and an infusion pump or fluid container or connected thereto, respectively, wherein the pendulum device is constructed to connect the obligatory lumen 1 with one of the two tubes by a pendulum or oscillation movement. Here, due to the controlled movement of the pendulum and, thus, the controlled connection between the obligatory lumen 1 and one of the two tubes (or the stop in between), the single lumen catheter acts as infusion means or aspiration means depending on the respective connected opening of the pendulum, while any infusion or aspiration is stopped in between opening.

Clearly, in such an arrangement the pendulum device controls the flow of liquid through the lumen by selectively connecting an aspiration pump or infusion pump. That is, the pendulum device provides a controllable valve.

The pendulum device is used to connect the catheter to the infusion device ('a vent fluid source', see below). The pendulum device of O8 therefore *also* provides a controllable vent valve as recited by claim 1.

The pendulum device is considered to provide both the controllable vacuum valve and controllable vent valve recited by claim 1. This understanding is consistent with claim 1 and the opposed patent. In particular, there is nothing in the wording of claim 1 as granted which the skilled person would understand as requiring the vacuum valve and vent valve to be independently controllable one another.

The opposed patent describes an example (e.g., in relation to Figs. 25 and 26) wherein a rotation pintle valve can be used to provide a vacuum valve and a vent valve. In this arrangement, a motor can rotate a cam shaft to move a cam set comprising vacuum and vent cams between open and closed states, wherein the cam set is used to pinch down short sections of tubing.

In this example of the opposed patent, it is not possible to independently control the vacuum valve and the vent valve, as both valves are controlled by a single cam shaft.

If the rotational pintle valve described in the opposed patent is considered to provide both a controllable vacuum valve and a controllable vent valve (despite not providing independent valves), then the pendulum device of O8 therefore also provides both a controllable vacuum valve and a controllable vent valve.

1[e] (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)

O8 discloses a source of fluid for delivery through the catheter (emphasis added):

[0027] ...the proximal end of one lumen of the catheter is connected to at least one infusion device, such as a fluid container or a peristaltic pump or the like, for infusion of fluid into the body through the lumen...

[0073] ...The additional lumen 2 is connected to an infusion device 3 such as a pump or a fluid container or the like, at its proximal tip or proximal end 21...

The skilled reader would understand that the infusion device provides a vent fluid source as recited by the claim because O8 uses this fluid to change the pressure in the catheter in order to remove blockages, and it is not solely provided to provide drugs or the like (emphasis added):

[0027] ...the infusion device and the aspiration device can be configured to create programmable changes of pressure in the lumens. Thereby, it is possible to carry out a process for unblocking a fluid exchange catheter...

[0074] The infusion and aspiration devices 3, 4 periodically and/or continuously change liquid pressure gradients in the catheter system in order to create non-linear currents of fluid F that exits into the distal wall portion 13 of the obligatory lumen 1, i.e. inside the distal end 12 of the obligatory lumen 1, and wash the catheter's tips 12, 22 clean and keep the fluid exchange between the catheter and the tissue unobstructed, without the need of any moving parts.

As outlined above, the blocking means of O8 is used to control the delivery of fluid from the infusion device, and so the infusion device ('vent fluid source') is fluidically connected to the blocking device ('vent valve').

1[f] (a manifold connected to the catheter, to the vacuum valve, and to the vent valve)

The comments above regarding the provision of a vacuum valve in O8 notwithstanding, the skilled reader would understand that a manifold is at least implicitly disclosed by the document.

O8 discloses an embodiment in which the catheter comprises a single lumen:

[0079] ...wherein the proximal end 11 of the obligatory lumen 1 is alternately connected to the infusion device 3, the aspiration device 4, and/or a stop mechanism in between. Such an embodiment could be implemented by a device adapted for a pendulum movement, including two separate tubes corresponding to an aspiration pump or fluid container and an infusion pump or fluid container or connected thereto, respectively, wherein the pendulum device is constructed to connect the obligatory lumen 1 with one of the two tubes by a pendulum or oscillation movement...

The proximal end of this lumen must therefore be fluidically connected to the aspiration device ('vacuum source') and to the infusion device ('vent fluid source') through the pendulum device ('vacuum valve'). Such a fluidic connection can only be provided by a physical structure connecting these parts together. This physical structure provides a manifold as recited by claim 1.

1[g] (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)

O8 discloses that operation of the fluid exchange catheter system can be controlled and programmed in order to provide a desired cycle of infusion and aspiration.

For example, O8 states that (emphasis added):

[0027] ...different functions of the respective lumens can be achieved and controlled, such as, for example, infusion, aspiration, or alternating patterns of infusion and aspiration... the infusion device and the aspiration device can be configured to create programmable changes of pressure in the lumens. Thereby, it is possible to carry out a process for unblocking a fluid exchange catheter, the fluid exchange catheter having a configuration as described above, and the process comprising the step of controlling infusion and/or aspiration through the obligatory lumen...The catheter as used in the above described process can further comprise the step of controlling infusion and/or aspiration through the additional lumen for creating a non-linear motion of the fluid flowing through the at least one additional lumen, and into the distal end of the obligatory lumen.

[0029] ...it is preferable for the catheter system that the controlling mechanism further comprises blockage means for blocking the at least one additional lumen and/or blockage means for blocking the obligatory lumen. For example, the blockage means for blocking the additional lumen can block the same for a first time interval followed by a second time interval of free flow of the fluid through the additional lumen. Also, the blockage means for blocking the obligatory lumen can block the same for a first time interval, optionally followed by a second time interval of free flow of the fluid through the obligatory lumen...

[0079] ...the proximal end 11 of the obligatory lumen 1 is alternately connected to the infusion device 3, the aspiration device 4 and/or a stop mechanism in between. Such an embodiment could be implemented by a device adapted for a pendulum movement, including two separate tubes corresponding to an aspiration pump or fluid container and an infusion pump or fluid container or connected thereto, respectively, wherein the pendulum device is constructed to connect the obligatory lumen 1 with one of the two tubes by a pendulum or oscillation movement. Here, due to the controlled movement of the pendulum and, thus, the controlled connection between the obligatory lumen 1 and one of the two tubes (or the stop in between), the single lumen catheter acts as infusion means or aspiration means depending on the respective connected opening of the pendulum...

The skilled reader would therefore appreciate that a controller is provide in O8 in order to allow such control of the pendulum device ('vacuum valve') and thereby provide control over the changes in pressure for unblocking the catheter.

1[h] (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)

The comments above regarding the provision of a vacuum valve in O8 notwithstanding, the skilled reader would understand that cyclically alternating connection of an infusion device ('vent fluid source') and an aspiration device ('vacuum source') is equivalent to the cyclical control of a vacuum valve and a vent valve as recited by claim 1.

O8 states that:

[0079] ... the proximal end 11 of the obligatory lumen 1 is alternately connected to the infusion device 3, the aspiration device 4 and/or a stop mechanism in between... due to the controlled movement of the pendulum and, thus, the controlled connection between the obligatory lumen 1 and one of the two tubes (or the stop in between), the single lumen catheter acts as infusion means or aspiration means depending on the respective connected opening of the pendulum, while any infusion or aspiration is stopped in between opening.

That is, the controller described above controls the pendulum device ('vacuum valve') so as to cyclically alternate between connecting the infusion device ('vent fluid source') to the lumen, and connecting the aspiration device ('vacuum source') to the lumen. O8 therefore discloses cyclical control as recited by claim 1.

The skilled reader would understand that alternating between an infusion device ('vent fluid source') and an aspiration device ('vacuum source') in this way would inherently change the level of vacuum at the distal end of the catheter. However, for the avoidance of doubt, it is noted that O8 itself teaches that this may be done to change a pressure (i.e., a vacuum level) within the catheter (emphasis added):

[0016] ...any lumen can be adapted for fluid infusion and/or fluid aspiration, and an unblocking of the catheter is effected by altering the width of the at least one lumen opening by changing the infusion and/or aspiration fluid pressure of the catheter, the infusion and/or aspiration fluid pressure being different from an outer pressure acting on the outside of the distal wall portion of the obligatory lumen. Thereby, a stable fluid flow through the catheter can be achieved...

[0021] ...unblocking of the catheter can also be effected by generally altering the width of the at least one lumen opening by changing the infusion and/or aspiration fluid pressure of the catheter, wherein the infusion and/or aspiration fluid pressure is different from an outer pressure acting on the outside of the distal wall portion of the obligatory lumen...

[0074] ...The pressure differences in the system are created by any pattern of positive pressures of the infusion device 3, such as a pump or fluid container, and the accordingly synchronized pattern of negative pressures of the aspiration device 4, such as a pump or fluid container. Here the expression "pressures" always refer to the pressure at the catheter's tip surrounding tissue. The described system allows a fully and safely controllable infusion-aspiration rate and unobstructed fluid exchange...

[0076] As one particular example, in one of the many possible system's versions regarding construction and operational mode, a peristaltic pump as infusion device 3 is programmed to infuse the liquid with a +200 mmHg pressure... a peristaltic pump as aspiration device 4 is programmed to aspirate with a -100 mmHg pressure...

It is therefore clear that the level of vacuum at the distal end is changed as a result of the control of the device, as recited by claim 1.

5.1.2.1. Establishing the ‘objective technical problem’ to be solved

O8 differs from claim 1 in that O8 does not explicitly disclose the prevention of forward flow of fluid out from the distal end of the catheter. However, this feature cannot lead to an inventive step at least for the reasons given above in section 5.1.2, in addition to the reasons given below.

O8 describes the provision of a fluid exchange catheter in which fluid is provided from the distal end of the catheter (see e.g., fluid flow ‘F’ in Fig. 1, reproduced above). However, the system of O8 is suitable for and intended for such a use as a clot removal system as described at paragraph [0058], for example:

[0058] ...the catheter of the invention is used for the removal of substances, such as undesired substances, from the body. Preferred examples of such substances are selected from the group consisting of blood, coagulated blood, blood clot(s) (thrombus/thrombi)...

When using the system in this way, the skilled person would understand (e.g., as a matter of their common general knowledge expanded in detail above) that forward flow of fluid should be avoided when aspirating a clot or the like in order to reduce the risk of distal embolization.

Although O8 does describe infusing fluid into the body from the distal end of the catheter, this would not teach the skilled person away from arrangements in which forward flow is prevented. The skilled reader would appreciate that when the system is used to remove substances such as clots from the body, fluid may not need to be infused from the distal end of the catheter, and different considerations apply as compared with where the system is used for fluid exchange.

A ‘technical effect’, determined according to usual EPO practice, of the differences between O8 and claim 1 is that the risk of distal embolization is reduced and a more effective aspiration system is provided. An objective technical problem can therefore be framed as “how to provide an improved clot aspiration system”.

The skilled person seeking to solve this this problem would turn to other documents in the field, for example those described herein, including those set out above at section 1.2.2. Examples of combination with O2 and O3 are outlined in more detail below, but it will be understood that other documents described herein could be used in their place.

5.1.2.2. Combination of O8 with O2 (“Yang”)

As set out above at section 4.1.2, O2 describes a catheter arrangement comprising “a controller for applying intermittent vacuum to the lumen” of the catheter (see e.g., paragraphs [0011], [0014]).

The systems of O8 and O2 share a catheter, vent fluid source, vent valve, vacuum source, vacuum valve, controller, and a manifold, and so the skilled person would appreciate that they are technically compatible with one another, and no substantial modification is required to make the apparatus of O8 suitable for use with the apparatus and mode of operation described in O2.

O2 teaches that:

[0123] A pulsatile vacuum aspirator may be used in order to improve effectiveness of aspiration for vascular thrombectomy...

The skilled person would appreciate that this improvement is due to the water hammer effect which O2 describes:

[0108] The intensity of intermittent or pulsatile vacuum applied to lumen 40 may be adjusted to cause the distal tip 38 of the catheter 10 to experience an axial reciprocation or water hammer effect, which can further facilitate both transluminal navigation as well as dislodging or breaking up the obstruction...

When searching for a solution to the objective technical problem posed, the skilled person would therefore turn to O2 for an alternative operating method which can be applied to the apparatus of O8.

To provide the effects described, O2 discloses that the period of each vacuum and release cycle may be equal to about 0.1 seconds – that is, a cycling frequency of 10 Hz (see e.g., paragraph [0168]). Paragraph [0127], describing a frequency modulator for controlling the solenoid valve, suggests that control could take place at frequencies of “less than about 500Hz, in some modes of operation less than about 20 Hz or less than about 5 Hz”, and paragraph [0130] discloses operating the cycle at a frequency of less than about 260 Hz. That is, as discussed above, O2 teaches the use of cycling frequencies which fall in the range which the opposed patent teaches as being sufficiently fast to “prevent forward flow”.

The skilled person, implementing the teaching of O2 in the arrangement of O8 in order to provide an improved aspiration system, would thereby arrive at a system in which forward flow is prevented.

Accordingly, the claimed invention would have been obvious to the skilled person starting from O8 and considering the teachings of O2.

5.1.2.3. Combination of O8 with O3 (“Ofek”)

As set out above in section 4.1.3, O3 discloses a pulsatile aspiration system for catheter assemblies, in which occlusions, such as clots, are dislodged by high pressure pulses and aspirated by negative pressure (see e.g., paragraphs [0002], [0003]).

The systems of O8 and O3 share a catheter, vent fluid source, vent valve, vacuum source, vacuum valve, controller, and a manifold, and so the skilled person would appreciate that they are technically compatible with one another, and no substantial modification is required to make the apparatus of O8 suitable for use with the apparatus and mode of operation described in O3.

Generally, O3 teaches an arrangement which “establishes and/or preserves patency of one or more lumens defined by the catheter assembly by providing impulses of positive pressure to fluid disposed in the lumen of the catheter assembly” (paragraph [0002]).

This is generally the same as document O8 which provides “a fluid exchange catheter being able to prevent or remove blockage of the catheter, which can occur due to different causes, such as clogging by a blood clot, pus or the like. Further, the proposed invention provides a process for unblocking such a fluid exchange catheter” (paragraph [0001]). The documents are clearly closely related, such that the skilled

person would naturally turn to document O3 when starting from O8 and considering the objective technical problem posed.

O3 specifically teaches that occlusions should not be allowed to re-enter the bloodstream from the distal end of the catheter. For example, paragraph [00027] states that (emphasis added):

[00027] ...the patency device 30 provides short-duration, relatively high-pressure impulses through the fluid present in the catheter tube lumen 14 interspersed by relatively longer rest periods 84 of negative baseline pressure...negative baseline pressure present between impulses enables any occlusion dislodged by the impulses to be sucked proximally up the catheter tube lumen 14 and removed therefrom, thus preventing the dislodged occlusion from entering the bloodstream from the distal end 12B of the catheter tube 12.

The skilled person, implementing the teaching of O3 in the arrangement of O8 in order to provide an improved aspiration system, would thereby arrive at a system in which forward flow is prevented.

Accordingly, the claimed invention would have been obvious to the skilled person starting from O8 and considering the teachings of O3.

5.1.3. Other Documents

Other documents could also be used to demonstrate that claim 1 lacks an inventive step, either as a starting point or as a document that the skilled person would turn to in combination with a suitable starting document.

5.1.3.1. O9 (WO 2014/151209 A1) - "Grey"

O9 is a PCT application, having a publication date of 25 September 2014. The publication date of O9 pre-dates the filing date of the opposed patent. O9 is therefore available for the assessment of novelty and inventive step.

A representative drawing of O9 (Fig. 2A) is shown below, and annotated to show features corresponding with those of the claims of the opposed patent, for reference in the following discussion.

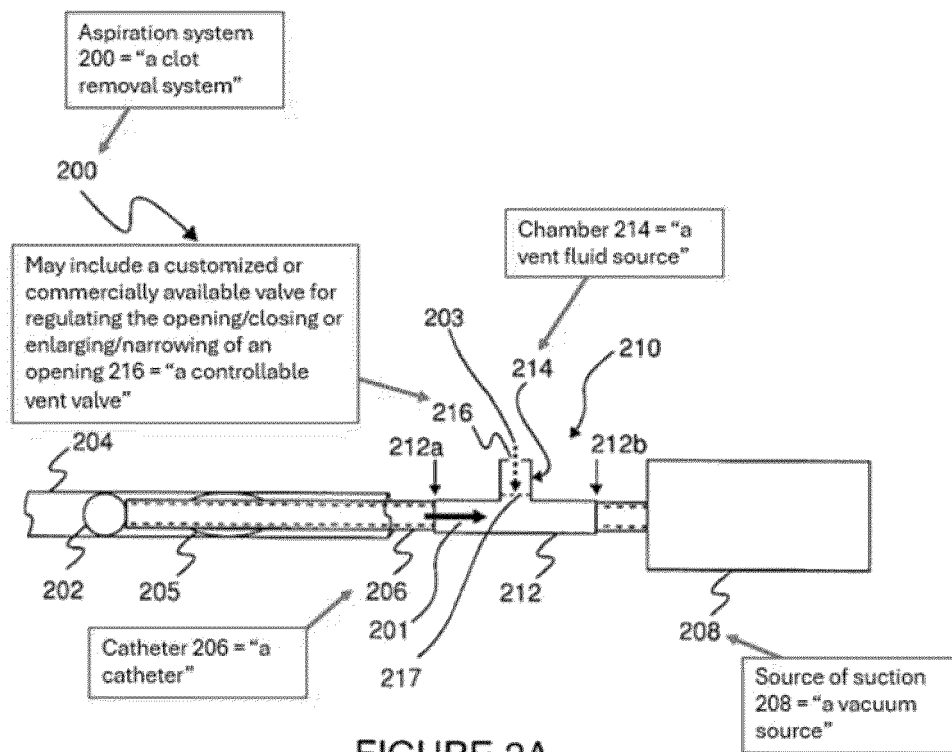


FIGURE 2A

Generally, O9 describes "an aspiration system comprising 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" (page 5, lines 1 to 4). The system is provided to improve efficiency of aspiration of clots, as the dynamic (i.e., changing) suction force in the catheter induces material fatigue in a clot, thereby breaking the clot apart so that it can be removed (see e.g., page 3, lines 1 to 24). Dynamic suction is achieved by introducing fluid at a second pressure into the catheter (see e.g., page 3, line 25 to page 4, line 2).

If certain features of claim 1 are believed to be a distinguishing feature, then those features lack an inventive step because they are disclosed by O9.

1[Pre] (A clot removal system)

O9 states that (page 1, lines 7 to 11, emphasis added):

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.

The background section of O9 (particular at page 1, line 15 to page 2, line 3) describes the use of aspiration thrombectomy as a treatment for removing occlusions in the body, especially in the case of ischemic stroke, and presents the systems and methods disclosed therein as "improvements for the

removal of occlusions and, more particularly, improvements to aspiration thrombectomy” (page 2, lines 1 to 3).

An example of such a system is shown in Figure 2A (page 7, lines 13 to 160):

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.

A method of using this system is illustrated in Figure 2C, which shows (page 9, lines 6 to 12, emphasis added):

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.

O9 therefore clearly provides a clot removal system.

1[a] (a catheter having a distal end and defining a lumen filled with a liquid column)

See, e.g., Figure 2A, reproduced above, showing that the system of O9 comprises a catheter 206. In use, it is stated that “a distal end of catheter 206 is positioned adjacent an occlusion 202” (page 9, lines 7 to 8) such that a suction force can be applied through to the distal end of the catheter to aspirate the clot (see e.g., page 4, lines 14 to 20).

It is at least implicit that aspiration will result in the collection of liquid (e.g., blood) to fill the catheter with a liquid column. See also page 3, lines 22 to 24 which states that (emphasis added):

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.

In addition, at page 8, lines 20 to 25 it is stated that:

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.

O9 therefore discloses that the catheter defines a lumen filled with a liquid column as recited by claim 1.

1[c] (a vacuum source fluidically connected to the vacuum valve)

O9 does not explicitly disclose that the arrangement comprises a vacuum valve. However, a vacuum source is present.

See e.g., Fig. 2A, reproduced above, and the associated description (page 7, lines 14 to 28) which states that:

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...

...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.

The source of suction 208 therefore provides a vacuum source as recited by claim 1.

1[d] (a controllable vent valve)

The clot removal system of O9 includes a conduit (e.g., conduit 212 in Figure 2A) and a chamber (e.g., chamber 214 in Fig. 2A) connected to the proximal end of the catheter. The chamber has an opening (e.g., opening 216 in Fig. 2A), wherein (page 3, line 30 to page 4, line 2; emphasis added):

An opening or hole of the chamber may be selectively opened or closed, or enlarged or narrowed. The opening 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.

Page 8, lines 15 to 19 of O9 further states:

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 valve for regulating the opening/closing or enlarging/narrowing of the opening 216 thereby provides a controllable vent valve.

1[e] (a vent fluid source containing a vent liquid and fluidically connected to the vent valve)

As alluded to above in relation to feature **1[d]**, O9 discloses a vent liquid which is introduced to the proximal end of the catheter through the opening 216, for example as described at page 3, line 30 to page 4, line 2:

An opening or hole of the chamber may be selectively opened or closed, or enlarged or narrowed. The opening 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.

O9 describes control of the opening 216 (e.g., as a vent valve) to control introduction of this fluid from the chamber at page 7, line 29 to page 8, line 8, for example, which recites (emphasis added):

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 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.

O9 also describes the second fluid (page 8, lines 20 to 25; emphasis added):

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.

This fluid of a second pressure is provided from the chamber by control of the opening to repeatedly change the pressure within the catheter (page 8, lines 26 to 31; emphasis added):

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.

The chamber is therefore a vent fluid source as recited by claim 1.

1[f] (a manifold connected to the catheter, to the vacuum valve, and to the vent valve)

Notwithstanding that O9 does not explicitly describe an independent vacuum valve, a manifold connected to (and fluidically connecting) all of the other components is described. This manifold is provided as conduit 212, shown in Fig. 2A reproduced above.

Page 7, lines 21 to 25 describes the conduit 212:

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.

Thus, O9 describes a manifold which is connected to a catheter and to a vent valve (provided as a valve in opening 216 to the chamber 214). The manifold thereby fluidically connects the liquid column in the catheter to the source of suction 208 ('the vacuum source') and the chamber 214 ('vent fluid source') as recited by claim 1.

1[g] (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)

Notwithstanding that O9 does not explicitly describe an independent vacuum valve, a controller is provided, and the opening 216 ('vent valve') is controlled to cyclically open and close to change a level of vacuum at the distal end of the catheter.

O9 states that (page 8, lines 1 to 8; emphasis added):

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.

In addition, Figure 2C shows a method of aspiration, using the apparatus shown in Fig. 2A. Page 9, lines 7 to 12 states (emphasis added):

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.

Figs. 3A to 3C show examples of cyclically varying pressure profiles achieved by such control, and it is stated that (page 12, lines 9 to 13):

...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.

That is, it is clear from these disclosures that a controller is provided in order to allow an operator to have control over the valve arrangement of O9.

Furthermore, Figure 6 of O9 shows another example aspiration system which operates in the same manner, having a valve arrangement for the vent fluid in the form of a magnet or magnetic element 618. The magnetic element 618 provides a valve which is controlled by a controller 619 to vary the flow of vent fluid (see e.g., page 13, line 31 to page 14, line 8; emphasis added):

Appliance 610 includes a chamber 614 in which a magnet or magnetic 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 5 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.

O9 therefore provides a controller as recited by claim 1.

1[h] (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)

Notwithstanding that O9 does not explicitly describe an independent vacuum valve, the controller provides control such that the opening 216 ('vent valve') is cyclically opened and closed to change a level of vacuum at the distal end of the catheter.

For example, O9 states that (page 9, lines 13 to 17; emphasis added):

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.

By providing cyclical aspiration profiles in which the pressure is changed over time and is not constant, dynamic loading (or repetitive loading) is applied to an aspirated clot to break up the clot by inducing material fatigue, thereby improving aspiration efficiency (page 9, line 31 to page 10, line 4):

...dynamic loading from dynamic aspiration supplies repetitive and 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.

Such dynamic or repetitive loading clearly requires the cyclical opening and closing of the opening 216 by a vent valve, as outlined above. For example, page 8, lines 2 to 8 states that (emphasis added):

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.

O9 also teaches that parameters of the dynamic (i.e., cyclical) aspiration profile may be adjusted to enhance treatment (page 10, lines 22 to 29):

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.

The controller of O9 is therefore configured as recited by claim 1.

1[i] (prevent forward flow of the distal portion out from the distal end)

In O9, Figs. 1A and 1B show a schematic representation of a *conventional* aspiration system 100, and an aspiration/suction profile that is used with such a system (page 7, lines 2 to 12, emphasis added):

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 experiences a constant suction 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.

O9 therefore describes the problems of conventional thrombectomy techniques utilising static aspiration at a single pressure, including the well-known and serious risk of distal embolization. The new arrangements described in O9 are provided to address this risk, utilising varying suction profiles as discussed above.

For example, page 13, lines 4 to 11 states that (emphasis added):

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.

Similarly, page 20, lines 21 to 23 states that:

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.

O9 therefore discloses that a vacuum pressure be maintained at all times, such that forward flow of liquid from the catheter is not possible, thereby reducing the risk of distal embolization. Fig. 3C of O9 is reproduced below for reference, where the cyclic aspiration cycle 330 is shown with a solid black line.

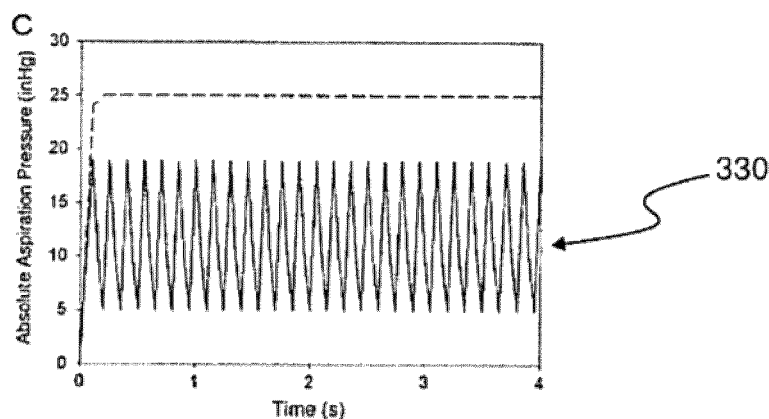


FIGURE 3C

The arrangement of O9 therefore prevents forward flow out of the distal end of the catheter as required by claim 1.

5.1.3.2. O10 (WO 2019/115809 A1) – “Mullins”

O10 is a PCT application, having a publication date of 20 June 2019. The publication date of O10 pre-dates the filing date of the opposed patent. O10 is therefore available for the assessment of novelty and inventive step.

A representative drawing of O10 (Fig. 45) is shown below, and annotated to show features corresponding with those of the claims of the opposed patent, for reference in the following discussion.

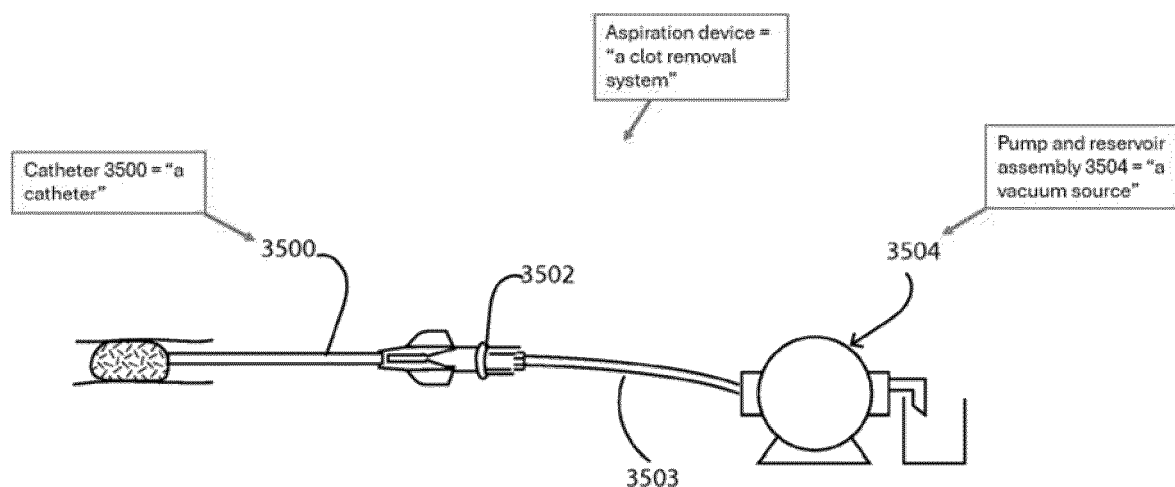


Fig.45

Mullins is particularly relevant for the consideration of inventive step of features **1[h]** and **1[i]**, as it explicitly teaches changing a vacuum level at the distal end of a catheter to prevent clogging, and preventing forward flow to reduce the risk of distal embolization. The skilled person would therefore contemplate the teaching of Mullins and apply it to other documents cited herein and, in doing so, arrive at an arrangement falling within the scope of claim 1.

The drawbacks of known arrangements, and the comparative advantages of O10 are described at page 39, line 29 to page 40, line 3 of O10:

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.

Page 40, lines 5 to 14 of O10 further states (emphasis added):

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.

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

The process of aspirating a clot using a varying pressure is described in O10 with respect to Figs. 47(a) to 47(n), which describes how a clot is engaged by the catheter and aspirated using a pressure which cycles between a high limit and a low limit. As stated at page 42, line 1 “*In one embodiment the High Limit is a negative pressure*” (as shown in Fig. 48(a), reproduced below) – that is, a net negative pressure is always applied, such that forward flow cannot occur. Indeed, page 41, lines 28 to 29 recites (emphasis added):

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.

Forward flow is clearly prevented in such arrangements.

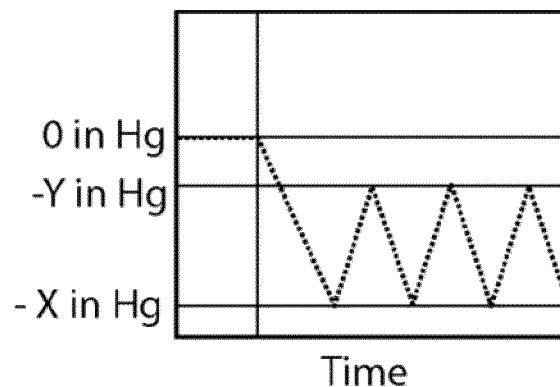


Fig.48(a)

The motivation for preventing forward flow is outlined at page 39, lines 8 to 12:

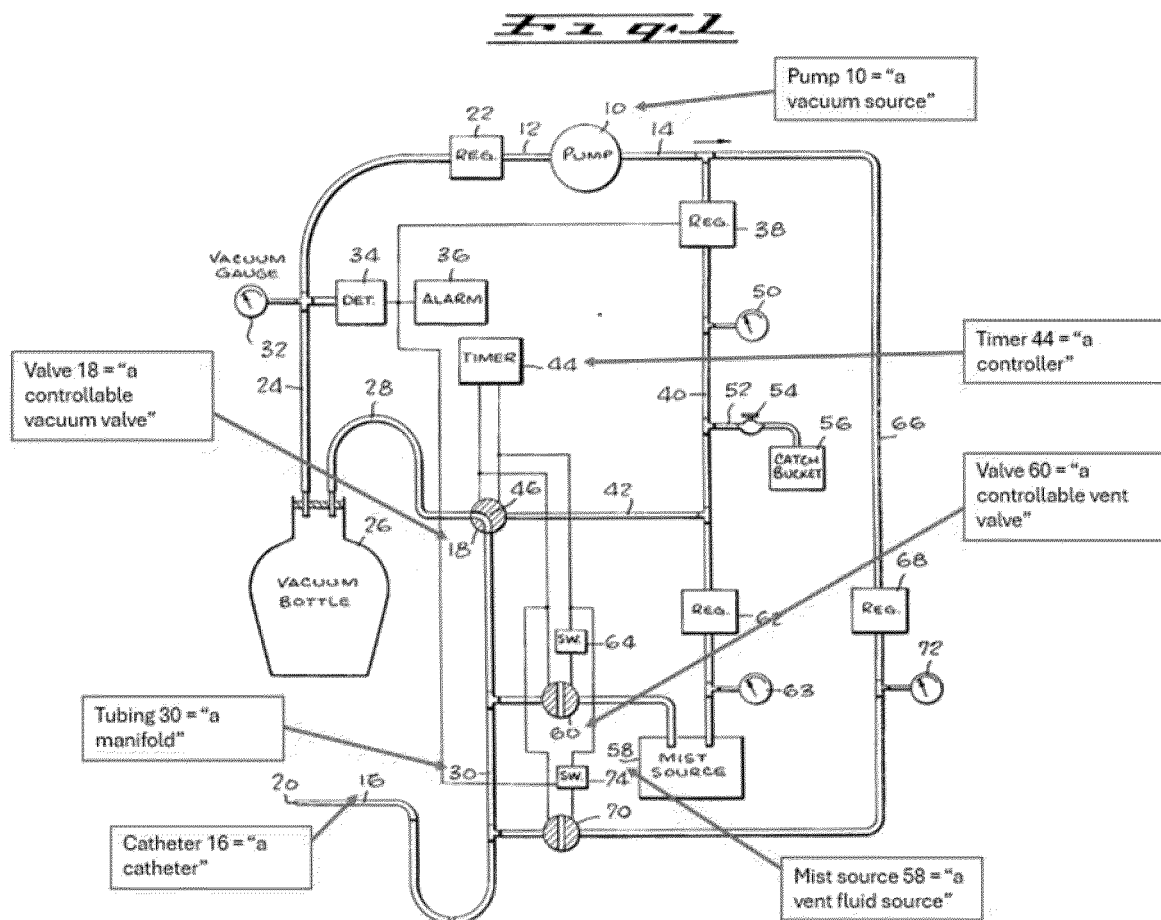
As the physician withdraws the catheter proximally towards the access site (typically femoral or radial artery), there is a likelihood that some or all of the clot may break off. These fragments of clot, are known as emboli. Distal emboli lead to poor reperfusion outcomes when assessed under angiography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

The skilled person would therefore be motivated to operate a clot removal system with no forward flow, and by applying varying pressure, in the manner described by O10, in order to avoid worse patient outcomes and to improve aspiration of clots.

5.1.3.3. O11 (US 3,955,574) - "Rubinstein"

O11 is a US patent application, having a publication date of 11 May 1976. The publication date of O11 pre-dates the filing date of the opposed patent. O11 is therefore available for the assessment of novelty and inventive step.

A representative drawing of O11 (Fig. 1) is shown below, and annotated to show features corresponding with those of the claims of the opposed patent, for reference in the following discussion.



O11 describes a pumping system and catheter for drawing material from a body during medical procedures. In particular, the pumping system is configured to cyclically alternate between negative and positive pressure in order to improve suction efficiency by ensuring that the catheter does not become blocked (see e.g., column 1, lines 7 to 14, and column 5, lines 10 to 15).

If certain features of claim 1 are believed to be a distinguishing feature, then those features lack an inventive step because they are disclosed by O11.

1[Pre] (A clot removal system)

O11 provides a pumping system and a catheter (emphasis added):

...for drawing fluids and other viscous materials from a body, such as may be required during certain medical procedures. More specifically, the present invention concerns a pumping system wherein cyclical reversals of pumping pressure are applied to the catheter connected thereto to have negative and positive pressure cyclically alternated. (column 1, lines 6 to 14)

As such, the skilled person would recognise that the system of O11 would be suitable as a clot removal system.

1[a] (a catheter having a distal end and defining a lumen filled with a liquid column)

See e.g., Fig. 1, reproduced above. It is at least implicit that aspiration would result in the collection of liquid, from the distal end of the catheter, to fill the catheter with a liquid column. For example, column 1, lines 21 to 24 recites that:

...fluids in which the tip of the catheter is immersed are thereby drawn through the catheter into a vacuum bottle or other reservoir provided as a collector...

It is further stated at column 2, lines 37 to 41 that:

Fluids and other viscous materials drawn through the catheter 16, the tubing 30, the valve 18, and the tubing 28 during suction are deposited in the vacuum bottle 26 which is maintained under a predetermined vacuum

At columns 3, lines 57 to 62 describe the draining of excess liquid from the system:

Moisture is oftentimes transmitted through the pump 10 and the tubing used in a suction unit. It is desirable that such moisture be drained or bled from the system. To this end, a bleed line 52 having an appropriate stopcock 54 is provided to allow and control draining of moisture into a catch bucket 56, or the like.

It is therefore clear to the skilled reader that that the catheter is filled with a liquid column in use.

1[b] (a controllable vacuum valve)

O11 discloses at column 2, lines 28 to 24 (emphasis added):

...negative pressure when applied to a catheter 16 via a valve 18 causes suction of fluids and other viscous materials situated at or in close proximity to a tip 20 of the catheter 16. As shown, the inlet port 12 of the pump 10 is connected to the catheter 16 via a vacuum regulator 22, tubing 24, a vacuum bottle 26, tubing 28, valve 18, and tubing 30...

That is, the pump ('a vacuum source', see below) is connected to the catheter ('a catheter') via a valve 18. This valve can be controlled as described at column 2, lines 60 to 63:

Position control or switching of the valve 18 may be readily accomplished by use of a timer 44 having any conventional design...

Control of the valve is described in more detail at column 3, lines 21 to 36 (emphasis added):

The valve 18 simply may involve a movable plug 46 having a connecting channel 48 and which is alternately rotated under the control of the timer 44 to have the channel 48 connect the tubing 30 to either the tubing 28 or the tubing 42 which would be connected to the standard parts of the valve 18. Referring to FIG. 2, diagram A illustrates the movable plug 46 of the valve 18 as being positioned to have the channel 48 permit fluid flow between the tubing 28 and the tubing 30 such that negative pressure is applied through the tubing 30 to the catheter 16. By comparison, diagram B illustrates the movable plug 46 as having been rotated to have the channel 48 positioned to permit fluid flow between the tubing 42 and the tubing 30 such that positive pressure is applied to the catheter 16 connected to the hose 30.

Valve 18 therefore provides a controllable vacuum valve as recited by claim 1.

1[c] (a vacuum source fluidically connected to the vacuum valve)

Generally, O11 describes to "a pumping system for catheter suction units wherein suction and pressure are cyclically alternated" (column 1, lines 64 to 65). As outlined above, valve 18 ('a vacuum valve') connects a pump to the catheter (see e.g., Fig. 1, reproduced above). Column 2, lines 23 to 34 recites (emphasis added):

a pumping system for catheter suction units in accordance with the present invention essentially includes a pump 10 for providing negative pressure at an inlet port 12 and positive pressure at an outlet port 14.

The negative pressure when applied to a catheter 16 via a valve 18 causes suction of fluids and other viscous materials situated at or in close proximity to a tip 20 of the catheter 16. As shown, the inlet port 12 of the pump 10 is connected to the catheter 16 via a vacuum regulator 22, tubing 24, a vacuum bottle 26, tubing 28, valve 18, and tubing 30.

The pump thereby allows the system to draw "fluids and other viscous materials from the body" (column 1, lines 7 to 10). O11 therefore discloses a vacuum source as recited by claim 1.

1[d] (a controllable vent valve)

O11 discloses (column 4, lines 2 to 8, emphasis added):

...a mist source or container 58 for detergent, enzymatic fluid, or other fluid is connected via a valve 60 to the tubing 30 to have the detergent or other enzymatic fluid contained in the mist source 58 ejected through the catheter 16 whenever the valve 60 is operated to have the mist source 58 connected to the tubing 30.

That is, a mist source ('a vent fluid source', see below), is connected to the catheter via a valve 60 (see e.g., Fig. 1 reproduced above). This valve can be controlled as described at column 4, lines 17 to 35:

...valve 60 may be of the same type as the valve 46 except that only two parts would be required. Referring to FIG. 2, diagram C illustrates a movable plug 65 as being positioned to prohibit fluid flow through the valve 60. By comparison, diagram D illustrates the movable plug 65 as being positioned to allow fluid flow through the valve 60.

Referring once again to FIG. 1, the valve 60 is connected to be controlled by the timer 44 when electrically connected thereto via a switch 64. Accordingly, the valve 60 is operated, when actuated, in synchronization with the valve 46 such that the mist source 58 is connected to the tubing 30 via the valve 60 only during blowing periods when positive pressure is being provided to the catheter 16...

Valve 60 therefore provides a controllable vent valve as recited by claim 1.

For completeness, and noting that there is nothing in claim 1 which requires the vent valve and vacuum valve to be independent of one another, it is noted that valve 18 may be considered to provide a controllable vacuum valve and a controllable vent valve.

Operation of valve 18 to connect the pump ('a vacuum source') has been demonstrated above. However, O11 further discloses that (column 2, lines 56 to 60):

Positive pressure provided at the outlet port 14 of the pump 10 may be provided to the catheter 16 via a pressure regulator 38, tubing 40 and 42, the valve 18, and the tubing 30, whenever the valve 18 is positioned to connect the tubing 42 to the tubing 30...

In relation to Fig. 2, it is also noted that valve 18 can be operated in the following manner (column 3, lines 31 to 35):

...diagram B illustrates the movable plug 46 as having been rotated to have the channel 48 positioned to permit fluid flow between the tubing 42 and the tubing 30 such that positive pressure is applied to the catheter 16 connected to the hose 30...

As valve 18 is also operable (i.e., additionally to valve 60) to control application of a positive pressure to the catheter, it may also be considered to provide a vent valve.

1[e] (a vent fluid source containing a vent liquid and fluidically connected to the vent valve)

O11 describes (e.g., at column 3, line 63 to column 4, line 8) that a detergent or other enzymatic fluid may be applied to the catheter at a positive pressure:

For this purpose, a mist source or container 58 for detergent, enzymatic fluid, or other fluid is connected via a valve 60 to the tubing 30 to have the detergent or other enzymatic fluid contained in the mist source 58 ejected through the catheter 16 whenever the valve 60 is operated to have the mist source 58 connected to the tubing 30.

It is further stated that (column 4, lines 26 to 32):

...the valve 60 is operated, when actuated, in synchronization with the valve 46 such that the mist source 58 is connected to the tubing 30 via the valve 60 only during blowing periods when positive pressure is being provided to the catheter 16.

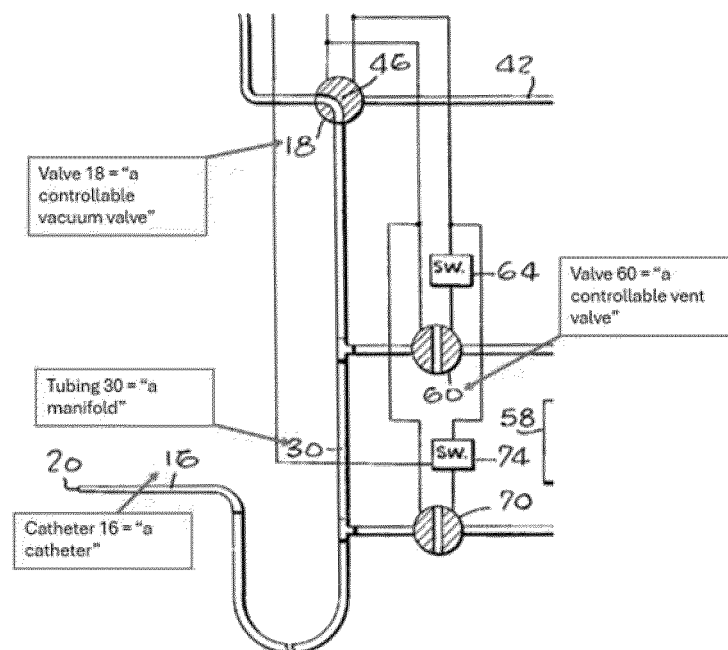
The mist source 58 thereby provides a source of fluid which can be introduced into the catheter at a positive pressure via valve 60 ('a vent valve'), which the valve 60 is appropriately operated. The mist source 58 is therefore considered as a vent fluid source.

For completeness, and following the discussion above regarding the alternative understanding of valve 18 as a vent valve within the scope of claim 1, it is further noted that when positive pressure is provided via valve 18, fluid which is present in tubing 42 may be considered to provide a vent fluid as recited by claim 1. For example, in relation to valve 18 Fig. 2 it is stated that (column 3, lines 31 to 36):

...diagram B illustrates the movable plug 46 as having been rotated to have the channel 48 positioned to permit fluid flow between the tubing 42 and the tubing 30 such that positive pressure is applied to the catheter 16 connected to the hose 30.

1[f] (a manifold connected to the catheter, to the vacuum valve, and to the vent valve)

An enlarged portion of Fig. 1 of O11, annotated with respect to claim 1, is included below for reference.



From Fig. 1 and the associated description, it will be appreciated that tubing 30 provides a pipe which is connected to the catheter 16 ('a catheter'), valve 18 ('a vacuum valve'), and to the valve 60 ('a vent valve'). The valves are operated to fluidically connected vacuum and vent sources (as described above) to the catheter.

For example, O11 discloses that (column 2, lines 37 to 41, emphasis added):

Fluids and other viscous materials drawn through the catheter 16, the tubing 30, the valve 18, and the tubing 28 during suction are deposited in the vacuum bottle 26 which is maintained under a predetermined vacuum...

It is also disclosed that (column 2, lines 57 to 60):

Positive pressure provided at the outlet port 14 of the pump 10 may be provided to the catheter 16 via a pressure regulator 38, tubing 40 and 42, the valve 18, and the tubing 30, whenever the valve 18 is positioned to connect the tubing 42 to the tubing 30.

The mist source ('a vent fluid source') is also fluidically connected to the catheter via the tubing 30 (column 4, lines 28 to 29):

...the valve 60 is operated, when actuated, in synchronization with the valve 46 such that the mist source 58 is connected to the tubing 30 via the valve 60...

Tubing 30 of O11 therefore provides a manifold as recited by claim 1.

1[g] (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)

As outlined above, timer 44 is provided in O11 so as to control the operation of valves 18 ('a vacuum valve') and 60 ('a vent valve') in the manner recited by claim 1.

For example, O11 states that (e.g., at column 3, line 63 to column 4, line 8):

...a mist source or container 58 for detergent, enzymatic fluid, or other fluid is connected via a valve 60 to the tubing 30 to have the detergent or other enzymatic fluid contained in the mist source 58 ejected through the catheter 16 whenever the valve 60 is operated to have the mist source 58 connected to the tubing 30.

In relation to valve 18, it is disclosed that that valve comprises a movable plug rotated under control of the timer, wherein (column 3, lines 21 to 36):

Referring to FIG. 2, diagram A illustrates the movable plug 46 of the valve 18 as being positioned to have the channel 48 permit fluid flow between the tubing 28 and the tubing 30 such that negative pressure is applied through the tubing 30 to the catheter 16. By comparison, diagram B illustrates the movable plug 46 as having been rotated to have the channel 48 positioned to permit fluid flow between the tubing 42 and the tubing 30 such that positive pressure is applied to the catheter 16 connected to the hose 30.

The timer therefore provides a controller as recited by claim 1.

1[h] (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)

Generally, O11 discloses a system in which (column 1, lines 12 to 14, emphasis added):

... cyclical reversals of pumping pressure are applied to the catheter connected thereto to have negative and positive pressure cyclically alternated.

In particular (column 2, lines 1 to 12, emphasis added):

the subject pumping system includes a time controlled valve which is operated at predetermined time intervals to have suction through the catheter interrupted by a predetermined period of positive pressure to cause a reversal of the fluid flow therethrough. A source of mist is connected to allow controlled injection of detergent or enzymatic fluid through the catheter. Extreme clogging of the catheter is remedied by a super-ejection mode during which bursts of positive pressure are applied to the catheter to blow free whatever materials are caught in the catheter and thereby eliminate the blockage.

This operation provides a system which (column 5, lines 12 to 15):

...is essentially self-cleaning such that blockages of a catheter used therewith are substantially reduced, thereby allowing single aperture catheters having greater suction efficiency to be used.

It is therefore clear that O11 provides a system in which the level of vacuum at a distal end of a catheter is changed. This is achieved by operating the valves under control of a timer 44 ('a controller'). For example, column 3, lines 1 to 20, which recites:

In order that negative pressure and positive pressure be alternately applied to the catheter 16, the valve 18 is controlled by the timer 44 to alternately connect tubing 28 to tubing 30 during a period of suction and connect tubing 42 to tubing 30 during a period of blowing. The flow of fluid through the catheter 16 is thereby cyclically reversed to produce a self-cleaning action as a result of the continuous back and forth movement of materials that may otherwise become wedged within the catheter 16 when moved in a single direction through the catheter 16.

Furthermore, column 4, lines 24 to 31 states:

...the valve 60 is connected to be controlled by the timer 44 when electrically connected thereto via a switch 64. Accordingly, the valve 60 is operated, when actuated, in synchronization with the valve 46 such that the mist source 58 is connected to the tubing 30 via the valve 60 only during blowing periods when positive pressure is being provided to the catheter 16.

That is, the fluid provided by the mist source 58 ('a vent fluid') is applied during periods of positive pressure.

O11 therefore clearly describes cyclical valve control to change a level of vacuum at the distal end of the catheter.

5.2. Claim 2

Claim 2 recites:

The system according to claim 1, wherein the controller (560) is configured to cyclically open and close the vacuum valve (420) and the vent valve (440) in a repeated cycle comprising a double-closed state in which the vacuum valve (420) is closed and the vent valve (440) is closed.

5.2.1. Lack of technical effect

It is noted that no 'technical effect', determined in line with usual EPO practice, or advantage is attributed to the double-closed state in the opposed patent.

Particularly, further to the comments made above at point 5.0.2, it is again noted that the specific 'technical effect', determined in line with usual EPO practice and with respect to the EPO's problem-solution approach for assessing inventive step, underlying a specific technical problem should be achieved across the whole scope of the claim.

In this regard, it is unclear what 'technical effect' for the EPO's problem-solution approach could be ascribed to the provision of a double-closed state as defined in claim 2. As is clear from inspection of Figs. 49 and 50, and as made explicitly clear from the description of the opposed patent at paragraph 151, if both a vent valve and a vacuum valve are left closed for too long then the pressure at the distal end of the catheter will rise until forward flow occurs.

More generally, it would be clear to the skilled person that providing a double-closed state which is either too long, or too short, would render the clot removal system fundamentally unsuitable for its purpose.

Accordingly, it is submitted that if claim 2 is believed to provide a distinguishing feature, then those features lack an inventive step by virtue of not giving rise to a 'technical effect', determined in line with usual EPO practice, which is achieved across the scope of the claim.

Even if the Opposition Division disagrees with the above analysis and considers the subject matter of claim 2 to give rise to a 'technical effect' across the scope of the claim, the subject matter is still fundamentally obvious because it is a simple, obvious design choice. The design choice is obvious because, with only two valves, there are merely four possible valve states: open-open, open-closed, closed-open, and closed-closed. Selecting the double-closed state from this limited set does not represent any undue burden or require inventive thought - it is simply one of the limited options available when cycling through valve states, such that implementing or using it would be an obvious design choice for the skilled person.

In addition, the skilled person would implement a double-closed state in any prior art arrangement comprising two valves (e.g., as disclosed in various documents cited herein), because they would understand that a state in which both valves are simultaneously open leads to pressure losses or lack of control of pressure in the catheter. In such an arrangement in which both valves are open at the same time, it is obvious that fluid provided from the vent fluid source will pass directly to the vacuum source and not through the catheter. Therefore, providing a double-closed state would be an obvious choice to avoid this situation.

5.2.2.O8 (US 20160275221 A1) – “Panotopoulos”

If claim 2 is believed to provide a distinguishing feature, then those features lack an inventive step because they are disclosed by O8.

It has been demonstrated above (see section 5.1.2) that O8 describes a controller configured to cyclically open a vacuum valve and a vent valve. For example, O8 states that:

[0079] ... the proximal end 11 of the obligatory lumen 1 is alternately connected to the infusion device 3, the aspiration device 4 and/or a stop mechanism in between... due to the controlled movement of the pendulum and, thus, the controlled connection between the obligatory lumen 1 and one of the two tubes (or the stop in between), the single lumen catheter acts as infusion means or aspiration means depending on the respective connected opening of the pendulum, while any infusion or aspiration is stopped in between opening.

In particular, in this arrangement, the pendulum device is considered to provide both the controllable vacuum valve and controllable vent valve recited by claim 1. This understanding is consistent with claim 1 and the opposed patent.

However, in relation to embodiments comprising multiple lumens, O8 also discloses independent blocking means (i.e., valves) for each of the infusion pathway and the aspiration pathway (emphasis added):

[0075] ...it is desirable to provide blocking means, which are in the position to block a connection between the infusion device 3 and the additional lumen 2, or the connection between the aspiration device 4 and the obligatory lumen 1. For example, a blocking means can block the additional lumen 2 for a first time interval followed by a second time interval of free flow of the fluid through the additional lumen 2, or another blocking means can block the obligatory lumen 1 for a first time interval followed by a second time interval of free flow of the fluid through the obligatory lumen 1. Thereby, it is possible to achieve a pattern in which liquid is infused through the additional lumen 2 with a first pressure for a first time interval followed by a second time interval of stop, wherein the obligatory lumen 1 is blocked during the first and second time intervals, and in which fluid is aspirated through the obligatory lumen 1 with a second pressure being lower than the first pressure during a third time interval, wherein the additional lumen 2 is blocked during the third time interval...

O8 therefore additionally discloses cyclically opening and closing of independent blocking means for an aspiration channel and an infusion channel. These blocking means therefore provide a controllable vacuum valve (as a blocking means in an aspiration channel) and a controllable vent valve (as a blocking means in an infusion channel).

In such an arrangement, O8 further discloses:

[0075] ... a fourth time interval during which all lumens 1 and 2 are blocked.

That is, O8 explicitly describes an operating interval during which both a vacuum valve and a vent valve are in closed states, such that neither aspiration or infusion are provided. This therefore provides a double-closed state as recited by claim 2.

The skilled person would appreciate that implementing such a further time interval in relation to the single-lumen embodiment, comprising the pendulum device, would similarly be desirable. Doing so would provide a state in which no aspiration or infusion is applied, i.e., a double-closed state. Such an arrangement would not require any inventive skill.

Indeed, O8 discloses a stop mechanism (emphasis added):

[0079] ... it is possible to merely use one single obligatory lumen 1 comprising an opening, for example an oval slit opening, at its proximal end 11 and its distal end 12, respectively, wherein the proximal end 11 of the obligatory lumen 1 is alternately connected to the infusion device 3, the aspiration device 4 and/or a stop mechanism in between... due to the controlled movement of the pendulum and, thus, the controlled connection between the obligatory lumen 1 and one of the two tubes (or the stop in between), the single lumen catheter acts as infusion means or aspiration means depending on the respective connected opening of the pendulum, while any infusion or aspiration is stopped in between opening...

The skilled reader would understand (e.g., given the context of the fourth time interval described in paragraph [0075], and the description of *stopping* aspiration or infusion in paragraph [0079]) that the stop mechanism represents a position in which the pendulum device does not connect either of the infusion device 3 ('a vent fluid source') or the aspiration device 4 ('a vacuum source') to the lumen 1. The stop mechanism therefore provides a 'double-closed state' within the scope of claim 2.

5.2.3. O11 (US 3,955,574) – "Rubinstein"

If claim 2 is believed to provide a distinguishing feature, then those features lack an inventive step because they are disclosed by O11.

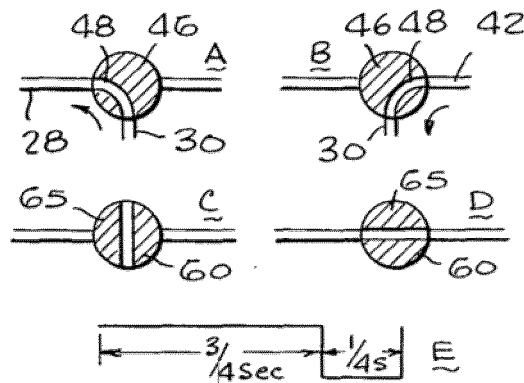
It has been demonstrated above (see section 5.1.3.3) that O11 describes a controller which is configured to cyclically open and close a vacuum valve and a vent valve, such that the system of O11 provides (column 1, lines 64 to 68):

...a pumping system for catheter suction units wherein suction and pressure are cyclically alternated to have the flow of fluid through a catheter cyclically reserved and thereby self-cleaning.

O11 further discloses that the cyclical operation of a vacuum valve and a vent valve comprises a double-closed state in which the vacuum valve is closed and the vent valve is closed, as recited by claim 2.

In a double-closed state, neither of a vacuum source or a vent fluid source are fluidically connected to the catheter.

Operation of the valves is described in relation to Fig. 2 of O11, reproduced below for reference.



Each valve in O11 comprises a rotatable plug, where the rotational position of the plug determines whether the valve is open or closed, and/or which conduits are fluidically connected through the valve. For example, in relation to valve 18 ('a vacuum valve'), it is stated that (column 3, lines 21 to 36):

The valve 18 simply may involve a movable plug 46 having a connecting channel 48 and which is alternately rotated under the control of the timer 44 to have the channel 48 connect the tubing 30 to either the tubing 28 or the tubing 42 which would be connected to the standard parts of the valve 18. Referring to FIG. 2, diagram A illustrates the movable plug 46 of the valve 18 as being positioned to have the channel 48 permit fluid flow between the tubing 28 and the tubing 30 such that negative pressure is applied through the tubing 30 to the catheter 16. By comparison, diagram B illustrates the movable plug 46 as having been rotated to have the channel 48 positioned to permit fluid flow between the tubing 42 and the tubing 30 such that positive pressure is applied to the catheter 16 connected to the hose 30.

Similarly, in relation to valve 60 ('a vent valve'), it is stated that (column 4, lines 17 to 31):

The valve 60 may be of the same type as the valve 46 except that only two parts would be required. Referring to FIG. 2, diagram C illustrates a movable plug 65 as being positioned to prohibit fluid flow through the valve 60. By comparison, diagram D illustrates the movable plug 65 as being positioned to allow fluid flow through the valve 60.

Referring once again to FIG. 1, the valve 60 is connected to be controlled by the timer 44 when electrically connected thereto via a switch 64. Accordingly, the valve 60 is operated, when actuated, in synchronization with the valve 46 such that the mist source 58 is connected to the tubing 30 via the valve 60 only during blowing periods when positive pressure is being provided to the catheter 16.

The skilled reader would therefore appreciate that the valves 18, 60 ('a vacuum valve' and 'a vent valve') of O11 rotate between the positions shown in Fig. 2. In particular, the valves 18, 60 cannot instantaneously transition between the different states described.

The rotary valves of O11 are therefore at least implicitly in a double-closed state when they are rotating between the positions outlined above, as will be demonstrated.

Initially, valve 18 ('a vacuum valve') is in the state shown in diagram A of Fig. 2, positioned so as to connect the pump ('a vacuum source') to the catheter. At the same time, valve 60 ('a vent valve') is in the state shown in diagram C of Fig. 2, wherein the mist source 58 ('a vent fluid source') is not fluidically connected to the catheter.

The timer 44 ('a controller') then operates the valves such that the plugs are rotated to respective second positions, wherein valve 18 is in the state shown in diagram B of Fig. 2, and valve 60 is in the state shown in diagram D of Fig. 2.

Clearly, during this transition no fluid connections are possible through either valve, as the channel 48 through each plug 46 is not aligned with any section of tubing. This therefore presents a 'double-closed state', as neither of the pump ('a vacuum source') or the mist source ('a vent fluid source') is fluidically connected to the catheter.

During cyclical operation of the system of O11, such a double-closed state would naturally be repeated to provide alternating cycles of negative and positive pressure as described therein.

O11 therefore provides a double-closed state as recited by claim 2.

5.3. **Claim 3**

Claim 3 recites:

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

If it is considered that claim 3 provides a distinguishing feature, then it lacks an inventive step. Claim 3 recites a selection of a parameter that the skilled person would naturally arrive at by routine trial and error or by applying normal design procedures. It is also noted that no particular 'technical effect', as determined according to usual EPO practice, is attributed to a double-closed state of no greater than 30 ms, and the effects of this feature amount to nothing more than would be expected by the skilled person based on their common general knowledge.

First, the skilled person would naturally consider varying such parameters to ensure that a clot removal system is optimised and fit for purpose. For example, several of the cited documents explicitly teach and/or suggest to the skilled person that such parameters should be adjusted or optimised.

For example, document O4 suggests the principle of adjusting parameters to enable a desired effect, for example (page 680, right column; emphasis added):

While Max Hz cycling was not 100% successful in this study (it is worthwhile to note that all clearance failures occurred with air as the medium), the downward trend in clot clearance time shown in figure 3 is a good indicator that increasing frequency is the correct path to more effective treatments. We believe that additional dimensions of frequency and amplitude modulation may be added to this technique in which their values are temporally adjusted to increase treatment efficacy.

Indeed, O4 suggests further exploration in this area (page 682, left column; emphasis added):

...with these pilot data established, does it seem prudent to embark on future research to classify further how the many variables involved—for example, frequency, differential amplitude range, pressure waveform—can be optimized. Furthermore, these data make it worthwhile to develop a device that can vary the frequency and pressure more precisely. This will allow much more detailed examination of suction variation that might be able to be a stand-alone technique or to augment current techniques by replacing flow arrest or static suction...

At page 10, lines 22 to 27 of O9 it is stated that (emphasis added):

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.

With respect to O9, it is also noted that page 10, lines 28 to 31 of O9 discloses that (emphasis added):

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.

By suggesting operation at a frequency of at least 50 Hz, O9 therefore clearly discloses arrangements wherein the entire valve cycle should have a duration of no more than 20 ms (i.e., 1/50 s), which would naturally lead the skilled person to provide a double-closed state having a duration no greater than 30 ms.

O11 also states, at column 3, lines 37 to 39, that “Any time periods can be employed for the periods of suction and blowing as well as for the total cycle by adjustment of the timer 44”, and so the skilled person would therefore modify such periods as required and, in doing so, would naturally consider operating within the claimed area.

These citations evidence that the skilled person would naturally consider varying such parameters to ensure that a clot removal system is optimised. In performing such optimisation the skilled person would naturally arrive at an arrangement wherein the time of the double-closed state is no greater than 30 ms.

Second, the skilled person is taught by the prior art to optimise the system for a given catheter. For example, paragraph 39 of O3 states that (emphasis added):

[00039] As mentioned, the pressure level of the impulses can be varied or determined according to a variety of factors, including catheter length, catheter lumen size, burst strength, impulse duration, rest period duration, other catheter configuration, etc. In one embodiment, the pressure of each impulse can be chosen from a range of from about 30 psi to about 120 psi, though other pressure below and above this are possible. Also, frequency of the impulses, or impulse frequency, can be set according to a predetermined pattern and can vary according to a number of factors such as those described immediately above...

Similarly, paragraph 130 of O2 states that:

[0130] By tuning frequency, duty cycle, and wave form, one skilled in the art may match or approximate the resonating frequency to the natural frequency of the catheter. This may further enhance the efficacy of aspiration.

It is acknowledged in the opposed patent itself that the timing depends on the choice of a given catheter and extension tube configuration (page 53, lines 15 to 18):

...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 addition, at page 61, lines 30 to 31 it is stated that “*the cycle time is optimized by the dynamics or the resonance of a particular catheter 660*”. Conversely, it is noted that this suggests that the claimed duration of a double-closed state would not result in the prevention of forward flow for all catheters.

This shows that the prior art and the opposed patent provide generally the same teaching about varying parameters and tuning a clot removal system to suit a catheter that is selected for use with the system. Therefore, when the same catheter is used in a prior art system as is used in a system as provided by the opposed patent, the skilled person would naturally arrive at the same set of optimised parameters, or at least consider those parameters during a tuning process.

As detailed above at point 1.2.1, the need to prevent distal embolization is well-known. For example, the skilled person is aware that when a device becomes clogged by a thrombus during use the potential for inadvertent dislodgment of the thrombus downstream increases. The skilled person would have been aware of the need to mitigate for the risk of distal embolization, and that the presence of so-called “forward flow” may increase this risk.

Given their common general knowledge relating to distal embolization and the teachings of the various prior art documents cited herein, it would be obvious to the skilled person that when modifying various parameters to optimise the system, for example in view of a particular catheter that is connected to the device, it should be ensured that forward flow is prevented.

For example, O3 teaches that:

[00031] The occlusion is dislodged by the high-pressure impulses, which are strong enough to dislodge the occlusion but are not of sufficient duration to push it out the distal end 12B of the catheter tube 12. The subsequent negative pressure rest period following each impulse can act to prevent escape of the clot from the catheter tube 12, in one embodiment. In addition, a suction process can be performed by the patency device 30 to withdraw the clot proximally from the catheter tube 12 and catheter 10 and into the patency device, where it may be disposed of In this way, any clot or occlusion present in the catheter 10 can be acceptably removed.

O18 discloses that:

[00128] ...by providing the ability to maintain aspiration continuously from either the catheter tip or the sheath tip or the sheath distal region, and providing the means to change aspiration levels and maintain asp, the procedure optimizes the ability to aspiration clot while minimizing distal emboli and minimizing blood loss from aspiration...

Paragraph 114 O14 also teaches the use of cyclical aspiration that provides “an aspiration force that cycles between a high level of vacuum to a lower level of vacuum at a set frequency”, or which cycles from “a high level of vacuum to no vacuum”. In such implementations, an overall level of aspiration would be maintained in the catheter, and in this way forward flow would be prevented.

Therefore, in optimising the device the skilled person would seek to ensure that distal migration is prevented.

It would be part of the skilled person’s common general knowledge that controlling the length of time that valves are open or closed would be one way to ensure that distal migration and forward flow are prevented, for example at least because it is obvious that not applying suction, or applying positive pressure pulses for a prolonged duration, would increase the risk forward flow and distal migration occurring.

The skilled person would therefore seek to preserve an overall negative pressure in the catheter, and also increase the efficiency with which a thrombus is aspirated, by optimising the frequency and duration of the operating states of a valve arrangement. This would include optimising the duration of a double-closed state, and would naturally lead the skilled person to limit the duration of the double-closed state, for example to less than 30 ms, to prevent forward flow and distal migration. In particular, the selection of no greater than 30 ms does not have any unexpected technical advantage and would naturally be considered by the skilled person.

The prior art therefore provides a variety of teachings that would lead the skilled person to modify and optimize various operating parameters of the clot removal systems described therein. In performing such modification, the skilled person would naturally arrive at an arrangement which falls within the scope of claim 3.

It is also noted that claim 3 merely defines selecting a particular duration of a double-closed state from a limited range of possibilities and parameters, and it is clear that these parameters could be arrived at by routine trial and error or by applying normal design procedures to prevent forward flow (e.g., to choose suitable parameters to optimise operation of the device, such as for a given catheter in the manner taught by the opposed patent and the prior art as outlined above). It is generally accepted that achieving a known ‘technical effect’ by means of modifications of the closest prior art which would be obvious to the skilled person cannot be considered inventive (Case Law of the Boards of Appeal I.D. 9.21.2). Indeed, based at least on these disclosures in the prior art documents, the skilled person would have a reasonable expectation of successfully improving the operation of a clot removal system, such that modifying these parameters should are not considered to involve an inventive step (Case Law of the Boards of Appeal I.D. 7.1).

Claim 3 therefore lacks an inventive step.

5.4. Claim 4

Claim 4 recites:

The system according to claim 1, wherein the controller (560) is configured to cyclically open and close the vacuum valve (420) and the vent valve (440) in a repeated cycle comprising a vent-only state in which the vacuum valve (420) is closed and the vent valve (440) is open.

5.4.1. Lack of technical effect

It is noted that no ‘technical effect’ or advantage as determined according to usual EPO practice is attributed to the vent-only state in the opposed patent.

Particularly, further to the comments made above at point 5.0.2, it is again noted that the specific ‘technical effect’, with respect to the EPO’s usual ‘problem-solution’ approach to assessing inventive step, underlying a specific technical problem should be achieved across the whole scope of the claim.

In this regard, it is unclear what ‘technical effect’ under the EPO’s ‘problem-solution’ analysis could be ascribed to the provision of a vent-only state as defined in claim 4. As is clear from inspection of Figs. 49 and 50, and as made explicitly clear from the description of the opposed patent at paragraph 151, if both a vent valve is left open for too long then the pressure at the distal end of the catheter will rise until forward flow occurs.

More generally, it would be clear to the skilled person that providing a vent-only state which is either too long, or too short, would render the clot removal system fundamentally unsuitable for its purpose.

Accordingly, it is submitted that if claim 4 is believed to provide a distinguishing feature, then those features lack an inventive step by virtue of not giving rise to a ‘technical effect’, as determined according to usual EPO practice, which is achieved across the scope of the claim.

Even if the Opposition Division disagrees with the above analysis and considers the subject matter of claim 4 to give rise to a ‘technical effect’ across the scope of the claim, the subject matter is still fundamentally obvious because it is a simple, obvious design choice. The design choice is obvious because, with only two valves, there are merely four possible valve states: open-open, open-closed, closed-open, and closed-closed. Selecting the vent-only state from this limited set does not represent any undue burden or require inventive thought - it is simply one of the limited options available when cycling through valve states, such that implementing or using it would be an obvious design choice for the skilled person.

In addition, the skilled person would implement a vent-only state in any prior art arrangement comprising two valves (e.g., as disclosed in various documents cited herein), because they would understand that a state in which both valves are simultaneously open leads to pressure losses or lack of control of pressure in the catheter. In such an arrangement in which both valves are open at the same time, it is obvious that fluid provided from the vent fluid source will pass directly to the vacuum source and not through the catheter. Therefore, providing a vent-only state would be an obvious choice to avoid this situation.

5.4.2. O11 (US 3,955,574) – “Rubinstein”

If claim 4 is believed to provide a distinguishing feature, then those features lack an inventive step because they are disclosed by O11.

Column 3, lines 1 to 20 of O11 describes operation of valve 18, which is considered a vacuum valve as outlined above in section 5.1.3.3:

In order that negative pressure and positive pressure be alternately applied to the catheter 16, the valve 18 is controlled by the timer 44 to alternately connect tubing 28 to tubing 30 during a period of suction and connect tubing 42 to tubing 30 during a period of blowing.

The skilled person would appreciate from the opposed patent that a state in which the vacuum valve is closed means that there is a valve state in which no vacuum is applied to the catheter. It is clear from at least the above-referenced section of O11 that suction is only applied when the valve 18 ('a vacuum valve') connects tubing 28 (leading to the vacuum bottle 26 and the pump 10 ('a vacuum source')) is connected to tubing 30 (leading to the catheter 16). Suction is not applied when the valve 18 connects tubing 52 to the catheter 16, and so this is considered to be a closed state of the vacuum valve.

Furthermore, column 4, lines 24 to 31 states:

the valve 60 is connected to be controlled by the timer 44 when electrically connected thereto via a switch 64. Accordingly, the valve 60 is operated, when actuated, in synchronization with the valve 46 such that the mist source 58 is connected to the tubing 30 via the valve 60 only during blowing periods when positive pressure is being provided to the catheter 16.

That is, when the valve 18 ('a vacuum valve') does not fluidically connect the vacuum bottle 26 and the pump 10 ('a vacuum source') to the catheter, valve 60 ('a vent valve') fluidically connects the mist source 58 ('a vent fluid source') to the catheter. This therefore provides a vent-only state as recited by claim 4.

The timer 44 ('a controller') cycles through these states as described in O11, thereby operating cyclically as recited by claim 4.

For completeness, and noting that there is nothing in claim 1 which requires the vent valve and vacuum valve to be independent of one another, it is noted that valve 18 may be considered to provide a controllable vacuum valve and a controllable vent valve (see above in section 5.1.3.3).

As outlined above, the valve 18 can be used to alternate between periods of suction and blowing (see e.g., column 3, lines 1 to 20 of O11). To achieve this effect (column 3, lines 21 to 24):

...valve 18 may simply involve a movable plug 46 having a connecting channel 48 and which is alternately rotated under the control of the timer 44 to have the channel connect the tubing 30 to either the tubing 29 or the tubing 42...

It is therefore clear to the skilled person that when the valve 18 is positioned such that the tubing 30 is connected to the tubing 42, it is not possible for suction to also be applied, such that this position represents a vent-only state as recited by claim 4.

5.5. Claim 5

Claim 5 recites:

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

If it is considered that claim 5 provides a distinguishing feature, then it lacks inventive step. Claim 5 recites a selection of a parameter that the skilled person would naturally arrive at by routine trial and error or by

applying normal design procedures. It is also noted that no particular ‘technical effect’, determined according to usual EPO practice, is attributed to a vent-only state of no greater than 50 ms, and the effects of this feature amount to nothing more than would be expected by the skilled person based on their common general knowledge.

First, the skilled person would naturally consider varying such parameters to ensure that a clot removal system is optimised and fit for purpose. For example, several of the cited documents explicitly teach and/or suggest to the skilled person that such parameters should be adjusted or optimised.

For example, document O4 suggests the principle of adjusting parameters to enable a desired effect, for example (page 680, right column; emphasis added):

While Max Hz cycling was not 100% successful in this study (it is worthwhile to note that all clearance failures occurred with air as the medium), the downward trend in clot clearance time shown in figure 3 is a good indicator that increasing frequency is the correct path to more effective treatments. We believe that additional dimensions of frequency and amplitude modulation may be added to this technique in which their values are temporally adjusted to increase treatment efficacy.

Indeed, O4 suggests further exploration in this area (page 682, left column; emphasis added):

...with these pilot data established, does it seem prudent to embark on future research to classify further how the many variables involved—for example, frequency, differential amplitude range, pressure waveform—can be optimized. Furthermore, these data make it worthwhile to develop a device that can vary the frequency and pressure more precisely. This will allow much more detailed examination of suction variation that might be able to be a stand-alone technique or to augment current techniques by replacing flow arrest or static suction...

At page 10, lines 22 to 27 of O9 it is stated that (emphasis added):

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.

With respect to O9, it is also noted that page 10, lines 28 to 31 of O9 discloses that (emphasis added):

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.

By suggesting operation at a frequency of at least 50 Hz, O9 therefore clearly discloses arrangements wherein the entire valve cycle should have a duration of no more than 20 ms (i.e., 1/50 s), which would naturally lead the skilled person to provide a vent-only state having a duration no greater than 50 ms.

O11 also states, at column 3, lines 37 to 39, that “Any time periods can be employed for the periods of suction and blowing as well as for the total cycle by adjustment of the timer 44”, and so the skilled person would therefore modify such periods as required and, in doing so, would naturally consider operating within the claimed area.

These citations evidence that the skilled person would naturally consider varying such parameters to ensure that a clot removal system is optimised. In performing such optimisation the skilled person would naturally arrive at an arrangement wherein the time of the vent-only state is no greater than 50 ms.

Second, the skilled person is taught by the prior art to optimise the system for a given catheter. For example, paragraph 39 of O3 states that (emphasis added):

[00039] As mentioned, the pressure level of the impulses can be varied or determined according to a variety of factors, including catheter length, catheter lumen size, burst strength, impulse duration, rest period duration, other catheter configuration, etc. In one embodiment, the pressure of each impulse can be chosen from a range of from about 30 psi to about 120 psi, though other pressure below and above this are possible. Also, frequency of the impulses, or impulse frequency, can be set according to a predetermined pattern and can vary according to a number of factors such as those described immediately above...

Similarly, paragraph 130 of O2 states that:

[0130] By tuning frequency, duty cycle, and wave form, one skilled in the art may match or approximate the resonating frequency to the natural frequency of the catheter. This may further enhance the efficacy of aspiration.

It is acknowledged in the opposed patent itself that the timing depends on the choice of a given catheter and extension tube configuration (page 53, lines 15 to 18):

...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 addition, at page 61, lines 30 to 31 it is stated that “the cycle time is optimized by the dynamics or the resonance of a particular catheter 660”. Conversely, it is noted that this suggests that the claimed duration of a vent-only state would not result in the prevention of forward flow for all catheters.

This shows that the prior art and the opposed patent provide generally the same teaching about varying parameters and tuning a clot removal system to suit a catheter that is selected for use with the system. Therefore, when the same catheter is used in a prior art system as is used in a system as provided by the opposed patent, the skilled person would naturally arrive at the same set of optimised parameters, or at least consider those parameters during a tuning process.

As detailed above at point 1.2.1, the need to prevent distal embolization is well-known. For example, the skilled person is aware that when a device becomes clogged by a thrombus during use the potential for inadvertent dislodgment of the thrombus downstream increases. The skilled person would have been aware of the need to mitigate for the risk of distal embolization, and that the presence of so-called “forward flow” may increase this risk.

Given their common general knowledge relating to distal embolization and the teachings of the various prior art documents cited herein, it would be obvious to the skilled person that when modifying various parameters to optimise the system, for example in view of a particular catheter that is connected to the device, it should be ensured that forward flow is prevented.

For example, O3 teaches that:

[00031] The occlusion is dislodged by the high-pressure impulses, which are strong enough to dislodge the occlusion but are not of sufficient duration to push it out the distal end 12B of the catheter tube 12. The subsequent negative pressure rest period following each impulse can act to prevent escape of the clot from the catheter tube 12, in one embodiment. In addition, a suction process can be performed by the patency device 30 to withdraw the clot proximally from the catheter tube 12 and catheter 10 and into the patency device, where it may be disposed of. In this way, any clot or occlusion present in the catheter 10 can be acceptably removed.

O18 discloses that:

[00128] ...by providing the ability to maintain aspiration continuously from either the catheter tip or the sheath tip or the sheath distal region, and providing the means to change aspiration levels and maintain asp, the procedure optimizes the ability to aspiration clot while minimizing distal emboli and minimizing blood loss from aspiration...

Paragraph 114 O14 also teaches the use of cyclical aspiration that provides “an aspiration force that cycles between a high level of vacuum to a lower level of vacuum at a set frequency”, or which cycles from “a high level of vacuum to no vacuum”. In such implementations, an overall level of aspiration would be maintained in the catheter, and in this way forward flow would be prevented.

Therefore, in optimising the device the skilled person would seek to ensure that distal migration is prevented.

It would be part of the skilled person’s common general knowledge that controlling the length of time that valves are open or closed would be one way to ensure that distal migration and forward flow are prevented, for example at least because it is obvious that not applying suction, or applying positive pressure pulses for a prolonged duration (e.g., such as in a vent-only state), would increase the risk forward flow and distal migration occurring.

The skilled person would therefore seek to preserve an overall negative pressure in the catheter, and also increase the efficiency with which a thrombus is aspirated, by optimising the frequency and duration of the operating states of a valve arrangement. This would include optimising the duration of a vent-only state, and would naturally lead the skilled person to limit the duration of the vent-only state, for example to less than 50 ms, to prevent forward flow and distal migration. In particular, the selection of no greater than 50 ms does not have any unexpected technical advantage and would naturally be considered by the skilled person.

The prior art therefore provides a variety of teachings that would lead the skilled person to modify and optimize various operating parameters of the clot removal systems described therein. In performing such modification, the skilled person would naturally arrive at an arrangement which falls within the scope of claim 5.

It is also noted that claim 5 merely defines selecting a particular duration of a vent-only state from a limited range of possibilities and parameters, and it is clear that these parameters could be arrived at by routine trial and error or by applying normal design procedures to prevent forward flow (e.g., to choose suitable parameters to optimise operation of the device, such as for a given catheter in the manner taught by the opposed patent and the prior art as outlined above). It is generally accepted that achieving a known 'technical effect' by means of modifications of the closest prior art which would be obvious to the skilled person cannot be considered inventive (Case Law of the Boards of Appeal I.D. 9.21.2). Indeed, based at least on these disclosures in the prior art documents, the skilled person would have a reasonable expectation of successfully improving the operation of a clot removal system, such that modifying these parameters should not be considered to involve an inventive step (Case Law of the Boards of Appeal I.D. 7.1).

Claim 5 therefore lacks an inventive step.

5.6. Claim 6

Claim 6 recites:

The system according to claim 1, wherein the controller (560) is configured to selectively open and close the vacuum valve (420) and the vent valve cycle in a repeated cycle comprising:
a vacuum-only state in which the vacuum valve (420) is open and the vent valve (440) is closed;
a first double-closed state in which the vacuum valve (420) is closed and the vent valve (440) is closed;
a vent-only state in which the vacuum valve (420) is closed and the vent valve (440) is open; and
a second double-closed state in which the vacuum valve (420) is closed and the vent valve (440) is closed.

It will be appreciated that the comments made above with respect to claims 2 and 4 (e.g., in sections 5.2 and 5.4) also apply here, as claim 6 merely relates to the combination of different valve states in a repeated cycle. Similarly, comments below may apply *mutatis mutandis* to those claims.

If it is considered that claim 6 provides a distinguishing feature, then it lacks an inventive step for at least the following reasons.

Claim 6 recites that the controller is configured to selectively open and close the vacuum valve and the vent valve in a repeated cycle comprising a vacuum-only state, a first double-closed state, a vent-only state, and a second double-closed state.

However, there is nothing in claim 6 to suggest that these states are in a particular order (for example, that the four states immediately succeed one another). Furthermore, claim 6 specifies only that there is a repeated cycle 'comprising' these steps – that is, the repeated cycle includes these steps, but does not exclude the presence of other steps (see e.g., Guidelines for Examination F-IV 4.20).

Therefore, for any disclosure referenced herein which teaches or suggests the use of a double-closed state, a vacuum-only state, and a vent-only state, a repeated cycle can be arbitrarily chosen or defined which includes two double-closed states, as required by claim 6.

Additionally, the fact that opening the vent valve and the vacuum valve at the same time would reduce the applied pressure or aspiration would be obvious to the skilled person. It is merely a natural consequence of how fluid flows in such clot removal systems and the fact that both the vent source and the vacuum source need to be connected to a proximal end of a catheter system. In such an arrangement it is obvious that fluid provided from a vent fluid source will pass directly to a vacuum source and not through the catheter if both valves are open at the same time, reducing the efficacy of both the vent source and the vacuum source.

Secondly, the skilled person would understand that operating the valves serially, i.e. in turn, would reduce this risk. Operating the valves in parallel would increase the risk of both valves being open at the same time, reducing efficacy of vent or vacuum application. Therefore, the skilled person would implement serial control, wherein a first valve is closed before a second valve is opened, with the delay (e.g., to confirm that the first valve is closed) between these steps providing a double-closed state.

For example, to apply aspiration, the skilled person would logically:

1. Close the vent valve first to cut off the positive pressure source, then
2. Open the vacuum valve to allow full vacuum force to be applied.

This provides a vacuum-only state.

Similarly, to apply venting, the skilled person would logically:

1. Close the vacuum valve first to cut off the negative pressure source, then
2. Open the vent valve to allow full positive pressure to be applied.

This provides a vent-only state.

In this operation, a double-closed state is necessarily created due to the delay between the valve actuations and, in any case, the skilled person would understand that an overlap between valve actuations is undesirable for the reasons noted above.

The skilled person would therefore implement double-closed states in any prior art arrangement comprising two valves. Claim 6 therefore lacks an inventive step.

In addition to the discussion of valve states described by documents elsewhere herein, and for the avoidance of doubt, it is noted here that at least documents O3, O8 and O11 provide a vacuum-only state as recited by claim 6.

For example, O3 discloses a state in which the normally open valve ('a vacuum valve' is open and the normally closed valve ('a vent valve') is closed. For example, see paragraph [0037] which states that *"Between each impulse and after the series of impulses has ended, the N.C. valve 140 closes and the N.O. valve 150 opens to provide a negative baseline pressure"*.

O8 discloses that flow in only one direction may take place at a time (i.e., either vacuum only or vent only; emphasis added):

[0029] ...it is preferable for the catheter system that the controlling mechanism further comprises blockage means for blocking the at least one additional lumen and/or blockage means for blocking the obligatory lumen. For example, the blockage means for blocking the additional lumen can block the same for a first time interval followed by a second time interval of free flow of the fluid through the additional lumen. Also, the blockage means for blocking the obligatory lumen can block the same for a first time interval, optionally followed by a second time interval of free flow of the fluid through the obligatory lumen...

[0079] ...the proximal end 11 of the obligatory lumen 1 is alternately connected to the infusion device 3, the aspiration device 4 and/or a stop mechanism in between. Such an embodiment could be implemented by a device adapted for a pendulum movement, including two separate tubes corresponding to an aspiration pump or fluid container and an infusion pump or fluid container or connected thereto, respectively, wherein the pendulum device is constructed to connect the obligatory lumen 1 with one of the two tubes by a pendulum or oscillation movement. Here, due to the controlled movement of the pendulum and, thus, the controlled connection between the obligatory lumen 1 and one of the two tubes (or the stop in between), the single lumen catheter acts as infusion means or aspiration means depending on the respective connected opening of the pendulum...

As outlined above in section 5.1.3.3, O11 discloses a system in which (column 1, lines 12 to 14, emphasis added):

... cyclical reversals of pumping pressure are applied to the catheter connected thereto to have negative and positive pressure cyclically alternated.

5.7. Claim 7

Claim 7 recites:

The system according to claim 6, wherein a time between an opening of the vent valve (440) and a closing of the vent valve (440) is between approximately 10 ms and approximately 50 ms.

If it is considered that claim 7 provides a distinguishing feature, then it lacks an inventive step. Claim 7 recites a selection of a parameter that the skilled person would naturally arrive at by routine trial and error or by applying normal design procedures. It is also noted that no particular 'technical effect', determined according to usual EPO practice, is attributed to an open state of the vent valve having a duration of between 10 ms and 50 ms, and the effects of this feature amount to nothing more than would be expected by the skilled person based on their common general knowledge.

First, the skilled person would naturally consider varying such parameters to ensure that a clot removal system is optimised and fit for purpose. For example, several of the cited documents explicitly teach and/or suggest to the skilled person that such parameters should be adjusted or optimised.

For example, document O4 suggests the principle of adjusting parameters to enable a desired effect, for example (page 680, right column; emphasis added):

While Max Hz cycling was not 100% successful in this study (it is worthwhile to note that all clearance failures occurred with air as the medium), the downward trend in clot clearance time shown in figure 3 is a good indicator that increasing frequency is the correct path to more effective treatments. We believe that additional dimensions of frequency and amplitude modulation may be added to this technique in which their values are temporally adjusted to increase treatment efficacy.

Indeed, O4 suggests further exploration in this area (page 682, left column; emphasis added):

...with these pilot data established, does it seem prudent to embark on future research to classify further how the many variables involved—for example, frequency, differential amplitude range, pressure waveform—can be optimized. Furthermore, these data make it worthwhile to develop a device that can vary the frequency and pressure more precisely. This will allow much more detailed examination of suction variation that might be able to be a stand-alone technique or to augment current techniques by replacing flow arrest or static suction...

At page 10, lines 22 to 27 of O9 it is stated that (emphasis added):

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.

With respect to O9, it is also noted that page 10, lines 28 to 31 of O9 discloses that (emphasis added):

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.

By suggesting operation at a frequency of at least 50 Hz, O9 therefore clearly discloses arrangements wherein the entire valve cycle should have a duration of no more than 20 ms (i.e., 1/50 s). Operation at a frequency of 10 Hz would result in a duration of the valve cycle being no more than 100 ms (i.e., 1/10 s). Operating in accordance with the ranges disclosed by O9 would naturally lead the skilled person to open the vent valve for a time of between 10 ms and 50 ms in order to maintain the valve cycle duration proposed.

O11 also states, at column 3, lines 37 to 39, that “Any time periods can be employed for the periods of suction and blowing as well as for the total cycle by adjustment of the timer 44”, and so the skilled person would therefore modify such periods as required and, in doing so, would naturally consider operating within the claimed area.

These citations evidence that the skilled person would naturally consider varying such parameters to ensure that a clot removal system is optimised. In performing such optimisation the skilled person would naturally arrive at an arrangement wherein the open state of the vent valve has a duration of between 10 ms and 50 ms.

Second, the skilled person is taught by the prior art to optimise the system for a given catheter. For example, paragraph 39 of O3 states that (emphasis added):

[00039] As mentioned, the pressure level of the impulses can be varied or determined according to a variety of factors, including catheter length, catheter lumen size, burst strength, impulse duration, rest period duration, other catheter configuration, etc. In one embodiment, the pressure of each impulse can be chosen from a range of from about 30 psi to about 120 psi, though other pressure below and above this are possible. Also, frequency of the impulses, or impulse frequency, can be set according to a predetermined pattern and can vary according to a number of factors such as those described immediately above...

Similarly, paragraph 130 of O2 states that:

[0130] By tuning frequency, duty cycle, and wave form, one skilled in the art may match or approximate the resonating frequency to the natural frequency of the catheter. This may further enhance the efficacy of aspiration.

It is acknowledged in the opposed patent itself that the timing depends on the choice of a given catheter and extension tube configuration (page 53, lines 15 to 18):

...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 addition, at page 61, lines 30 to 31 it is stated that “the cycle time is optimized by the dynamics or the resonance of a particular catheter 660”. Conversely, it is noted that this suggests that the claimed duration of an open state for the vent valve would not result in the prevention of forward flow for all catheters.

This shows that the prior art and the opposed patent provide generally the same teaching about varying parameters and tuning a clot removal system to suit a catheter that is selected for use with the system. Therefore, when the same catheter is used in a prior art system as is used in a system as provided by the opposed patent, the skilled person would naturally arrive at the same set of optimised parameters, or at least consider those parameters during a tuning process.

As detailed above at point 1.2.1, the need to prevent distal embolization is well-known. For example, the skilled person is aware that when a device becomes clogged by a thrombus during use the potential for inadvertent dislodgment of the thrombus downstream increases. The skilled person would have been aware of the need to mitigate for the risk of distal embolization, and that the presence of so-called “forward flow” may increase this risk.

Given their common general knowledge relating to distal embolization and the teachings of the various prior art documents cited herein, it would be obvious to the skilled person that when modifying various parameters to optimise the system, for example in view of a particular catheter that is connected to the device, it should be ensured that forward flow is prevented.

For example, O3 teaches that:

[00031] The occlusion is dislodged by the high-pressure impulses, which are strong enough to dislodge the occlusion but are not of sufficient duration to push it out the distal end 12B of the catheter tube 12. The subsequent negative pressure rest period following each impulse can act to prevent escape of the clot from the catheter tube 12, in one embodiment. In addition, a suction process can be performed by the patency device 30 to withdraw the clot proximally from the catheter tube 12 and catheter 10 and into the patency device, where it may be disposed of. In this way, any clot or occlusion present in the catheter 10 can be acceptably removed.

O18 discloses that:

[00128] ...by providing the ability to maintain aspiration continuously from either the catheter tip or the sheath tip or the sheath distal region, and providing the means to change aspiration levels and maintain asp, the procedure optimizes the ability to aspiration clot while minimizing distal emboli and minimizing blood loss from aspiration...

Paragraph 114 O14 also teaches the use of cyclical aspiration that provides “an aspiration force that cycles between a high level of vacuum to a lower level of vacuum at a set frequency”, or which cycles from “a high level of vacuum to no vacuum”. In such implementations, an overall level of aspiration would be maintained in the catheter, and in this way forward flow would be prevented.

Therefore, in optimising the device the skilled person would seek to ensure that distal migration is prevented.

It would be part of the skilled person’s common general knowledge that controlling the length of time that valves are open or closed would be one way to ensure that distal migration and forward flow are prevented, for example at least because it is obvious that not applying suction, or applying positive pressure pulses for a prolonged duration, would increase the risk forward flow and distal migration occurring.

The skilled person would therefore seek to preserve an overall negative pressure in the catheter, and also increase the efficiency with which a thrombus is aspirated, by optimising the frequency and duration of the operating states of a valve arrangement. This would include optimising the length of time for which the vent valve is open, and would naturally lead the skilled person to limit this duration, for example to between 10 ms and 50 ms, to prevent forward flow and distal migration. In particular, the selection of between 10 ms and 50 ms does not have any unexpected technical advantage and would naturally be considered by the skilled person.

The prior art therefore provides a variety of teachings that would lead the skilled person to modify and optimize various operating parameters of the clot removal systems described therein. In performing such modification, the skilled person would naturally arrive at an arrangement which falls within the scope of claim 7.

It is also noted that claim 7 merely defines selecting a particular duration of an open state of the vent valve from a limited range of possibilities and parameters, and it is clear that these parameters could be arrived at by routine trial and error or by applying normal design procedures to prevent forward flow (e.g., to choose suitable parameters to optimise operation of the device, such as for a given catheter in the manner taught by the opposed patent and the prior art as outlined above). It is generally accepted that achieving a known ‘technical effect’ by means of modifications of the closest prior art which would be obvious to the skilled person cannot be considered inventive (Case Law of the Boards of Appeal I.D. 9.21.2). Indeed, based at least on these disclosures in the prior art documents, the skilled person would have a reasonable

expectation of successfully improving the operation of a clot removal system, such that modifying these parameters should not be considered to involve an inventive step (Case Law of the Boards of Appeal I.D. 7.1).

Claim 7 therefore lacks an inventive step.

5.8. Claim 8

Claim 8 recites:

*The system according to claim 6, wherein a period of the cycle is:
between approximately 6 Hz and approximately 16 Hz; or
between approximately 8 Hz and 12 Hz.*

If it is considered that claim 8 provides a distinguishing feature, then it lacks an inventive step. Claim 8 recites a selection of a parameter that the skilled person would naturally arrive at by routine trial and error or by applying normal design procedures. It is also noted that no particular 'technical effect', determined according to usual EPO practice, is attributed to the frequency ranges given in the claim.

First, the skilled person would naturally consider varying such parameters to ensure that a clot removal system is optimised and fit for purpose. For example, several of the cited documents explicitly teach and/or suggest to the skilled person that such parameters should be adjusted or optimised.

For example, document O4 suggests the principle of adjusting parameters to enable a desired effect, for example (page 680, right column; emphasis added):

While Max Hz cycling was not 100% successful in this study (it is worthwhile to note that all clearance failures occurred with air as the medium), the downward trend in clot clearance time shown in figure 3 is a good indicator that increasing frequency is the correct path to more effective treatments. We believe that additional dimensions of frequency and amplitude modulation may be added to this technique in which their values are temporally adjusted to increase treatment efficacy.

Indeed, O4 suggests further exploration in this area (page 682, left column; emphasis added):

...with these pilot data established, does it seem prudent to embark on future research to classify further how the many variables involved—for example, frequency, differential amplitude range, pressure waveform—can be optimized. Furthermore, these data make it worthwhile to develop a device that can vary the frequency and pressure more precisely. This will allow much more detailed examination of suction variation that might be able to be a stand-alone technique or to augment current techniques by replacing flow arrest or static suction...

At page 10, lines 22 to 27 of O9 it is stated that (emphasis added):

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.

With respect to O9, it is also noted that page 10, lines 28 to 31 of O9 discloses that (emphasis added):

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....

O9 therefore clearly teaches towards operating at frequencies within the range recited by claim 8.

O11 also states, at column 3, lines 37 to 39, that “Any time periods can be employed for the periods of suction and blowing as well as for the total cycle by adjustment of the timer 44”, and so the skilled person would therefore modify such periods as required and, in doing so, would naturally consider operating within the claimed area.

These citations evidence that the skilled person would naturally consider varying such parameters to ensure that a clot removal system is optimised. In performing such optimisation the skilled person would naturally arrive at the claimed cycle frequency.

Second, the skilled person is taught by the prior art to optimise the system for a given catheter. For example, paragraph 39 of O3 states that (emphasis added):

[00039] As mentioned, the pressure level of the impulses can be varied or determined according to a variety of factors, including catheter length, catheter lumen size, burst strength, impulse duration, rest period duration, other catheter configuration, etc. In one embodiment, the pressure of each impulse can be chosen from a range of from about 30 psi to about 120 psi, though other pressure below and above this are possible. Also, frequency of the impulses, or impulse frequency, can be set according to a predetermined pattern and can vary according to a number of factors such as those described immediately above...

Similarly, paragraph 130 of O2 states that:

[0130] By tuning frequency, duty cycle, and wave form, one skilled in the art may match or approximate the resonating frequency to the natural frequency of the catheter. This may further enhance the efficacy of aspiration.

It is acknowledged in the opposed patent itself that the timing depends on the choice of a given catheter and extension tube configuration (page 53, lines 15 to 18):

...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 addition, at page 61, lines 30 to 31 it is stated that “*the cycle time is optimized by the dynamics or the resonance of a particular catheter 660*”. Conversely, it is noted that this suggests that the claimed cycle frequencies would not result in the prevention of forward flow for all catheters.

This shows that the prior art and the opposed patent provide generally the same teaching about varying parameters and tuning a clot removal system to suit a catheter that is selected for use with the system. Therefore, when the same catheter is used in a prior art system as is used in a system as provided by the opposed patent, the skilled person would naturally arrive at the same set of optimised parameters, or at least consider those parameters during a tuning process.

As detailed above at point 1.2.1, the need to prevent distal embolization is well-known. For example, the skilled person is aware that when a device becomes clogged by a thrombus during use the potential for inadvertent dislodgment of the thrombus downstream increases. The skilled person would have been aware of the need to mitigate for the risk of distal embolization, and that the presence of so-called “forward flow” may increase this risk.

Given their common general knowledge relating to distal embolization and the teachings of the various prior art documents cited herein, it would be obvious to the skilled person that when modifying various parameters to optimise the system, for example in view of a particular catheter that is connected to the device, it should be ensured that forward flow is prevented.

For example, O3 teaches that:

[00031] The occlusion is dislodged by the high-pressure impulses, which are strong enough to dislodge the occlusion but are not of sufficient duration to push it out the distal end 12B of the catheter tube 12. The subsequent negative pressure rest period following each impulse can act to prevent escape of the clot from the catheter tube 12, in one embodiment. In addition, a suction process can be performed by the patency device 30 to withdraw the clot proximally from the catheter tube 12 and catheter 10 and into the patency device, where it may be disposed of. In this way, any clot or occlusion present in the catheter 10 can be acceptably removed.

O18 discloses that:

[00128] ...by providing the ability to maintain aspiration continuously from either the catheter tip or the sheath tip or the sheath distal region, and providing the means to change aspiration levels and maintain asp, the procedure optimizes the ability to aspiration clot while minimizing distal emboli and minimizing blood loss from aspiration...

Paragraph 114 of O14 also teaches the use of cyclical aspiration that provides “*an aspiration force that cycles between a high level of vacuum to a lower level of vacuum at a set frequency*”, or which cycles from “*a high level of vacuum to no vacuum*”. In such implementations, an overall level of aspiration would be maintained in the catheter, and in this way forward flow would be prevented.

Therefore, in optimising the device the skilled person would seek to ensure that distal migration is prevented.

It would be part of the skilled person's common general knowledge that controlling the length of time that valves are open or closed would be one way to ensure that distal migration and forward flow are prevented, for example at least because it is obvious that not applying suction, or applying positive pressure pulses for a prolonged duration, would increase the risk forward flow and distal migration occurring.

The skilled person would therefore seek to preserve an overall negative pressure in the catheter, and also increase the efficiency with which a thrombus is aspirated, by optimising the frequency and duration of the operating states of a valve arrangement. This would include optimising the cycle frequency so as to prevent forward flow and distal migration. In particular, the selection of cycle frequencies in the range of 6 to 16 Hz does not have any unexpected technical advantage and would naturally be considered by the skilled person.

The prior art therefore provides a variety of teachings that would lead the skilled person to modify and optimize various operating parameters of the clot removal systems described therein. In performing such modification, the skilled person would naturally arrive at an arrangement which falls within the scope of claim 8.

It is also noted that claim 8 merely defines selecting a particular cycle frequency from a limited range of possibilities and parameters, and it is clear that these parameters could be arrived at by routine trial and error or by applying normal design procedures to prevent forward flow (e.g., to choose suitable parameters to optimise operation of the device, such as for a given catheter in the manner taught by the opposed patent and the prior art as outlined above). It is generally accepted that achieving a known 'technical effect' by means of modifications of the closest prior art which would be obvious to the skilled person cannot be considered inventive (Case Law of the Boards of Appeal I.D. 9.21.2). Indeed, based at least on these disclosures in the prior art documents, the skilled person would have a reasonable expectation of successfully improving the operation of a clot removal system, such that modifying these parameters should be not considered to involve an inventive step (Case Law of the Boards of Appeal I.D. 7.1).

Claim 8 therefore lacks an inventive step.

5.9. Claim 9

Claim 9 recites:

*The system according to claim 1, wherein the change in the level of vacuum at the distal end is:
greater than approximately 51 kPa (15 inHg) in no greater than approximately 50 ms; or
greater than approximately 68 kPa (20 inHg) and no greater than approximately 30 ms; or
greater than approximately 85 kPa (25 inHg) and no greater than approximately 20 ms.*

If it is considered that claim 9 provides a distinguishing feature, then it lacks an inventive step. Claim 9 recites a selection of parameters that the skilled person would naturally arrive at by routine trial and error or by applying normal design procedures. It is also noted that no particular 'technical effect', determined according to usual EPO practice, is attributed to the combination of vacuum level changes and timings recited by claim 9 in the specification as filed, nor do these vacuum level changes and timings have a synergistic or unexpected effect on one another such that claim 9 represents merely an aggregation of two parameter ranges.

First, the skilled person would naturally consider varying such parameters to ensure that a clot removal system is optimised and fit for purpose. For example, several of the cited documents explicitly teach and/or suggest to the skilled person that such parameters should be adjusted or optimised.

For example, document O4 suggests the principle of adjusting parameters to enable a desired effect, for example (page 680, right column; emphasis added):

While Max Hz cycling was not 100% successful in this study (it is worthwhile to note that all clearance failures occurred with air as the medium), the downward trend in clot clearance time shown in figure 3 is a good indicator that increasing frequency is the correct path to more effective treatments. We believe that additional dimensions of frequency and amplitude modulation may be added to this technique in which their values are temporally adjusted to increase treatment efficacy.

Indeed, O4 suggests further exploration in this area (page 682, left column; emphasis added):

...with these pilot data established, does it seem prudent to embark on future research to classify further how the many variables involved—for example, frequency, differential amplitude range, pressure waveform—can be optimized. Furthermore, these data make it worthwhile to develop a device that can vary the frequency and pressure more precisely. This will allow much more detailed examination of suction variation that might be able to be a stand-alone technique or to augment current techniques by replacing flow arrest or static suction...

In the context of O4, the skilled person would appreciate that the term ‘amplitude’ refers to the aspiration pressure that is used (for example, see Figure 2), such that O4 clearly teaches the skilled person to adjust parameters including (but not limited to) the pressure change, and the time over which the pressure is changed (e.g., by varying the frequency and pressure waveform).

At page 10, lines 22 to 27 of O9 it is stated that (emphasis added):

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.

With respect to O9, it is also noted that page 10, lines 28 to 31 of O9 discloses that (emphasis added):

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.

By suggesting operation at a frequency of at least 50 Hz, O9 therefore clearly discloses arrangements wherein the entire valve cycle should have a duration of no more than 20 ms (i.e., 1/50 s), which would naturally lead the skilled person to provide an arrangement wherein pressure is changed in no greater than approximately 50 ms as recited by claim 9.

O11 also states, at column 3, lines 37 to 39, that “Any time periods can be employed for the periods of suction and blowing as well as for the total cycle by adjustment of the timer 44”, and so the skilled person would therefore modify such periods as required and, in doing so, would naturally consider operating within the claimed area.

These citations evidence that the skilled person would naturally consider varying such parameters to ensure that a clot removal system is optimised. In performing such optimisation the skilled person would naturally arrive at an arrangement as recited by claim 9.

Second, the skilled person is taught by the prior art to optimise the system for a given catheter. For example, paragraph 39 of O3 states that (emphasis added):

[00039] As mentioned, the pressure level of the impulses can be varied or determined according to a variety of factors, including catheter length, catheter lumen size, burst strength, impulse duration, rest period duration, other catheter configuration, etc. In one embodiment, the pressure of each impulse can be chosen from a range of from about 30 psi to about 120 psi, though other pressure below and above this are possible. Also, frequency of the impulses, or impulse frequency, can be set according to a predetermined pattern and can vary according to a number of factors such as those described immediately above...

Similarly, paragraph 130 of O2 states that:

[0130] By tuning frequency, duty cycle, and wave form, one skilled in the art may match or approximate the resonating frequency to the natural frequency of the catheter. This may further enhance the efficacy of aspiration.

The skilled person would appreciate that tuning of a wave form disclosed by O3 encompasses tuning of the amplitude of a wave form, i.e., aspiration pressure, in this context. For example, this is also guided by the suggestion that the pressure of the impulses can be chosen from a range of about 30 psi to about 120 psi, as considered in more detail below.

It is acknowledged in the opposed patent itself that the timing depends on the choice of a given catheter and extension tube configuration (page 53, lines 15 to 18):

...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 addition, at page 61, lines 30 to 31 it is stated that “the cycle time is optimized by the dynamics or the resonance of a particular catheter 660”. Conversely, it is noted that this suggests that the claimed vacuum level changes and timings thereof would not prevent forward flow for all catheters.

This shows that the prior art and the opposed patent provide generally the same teaching about varying parameters and tuning a clot removal system to suit a catheter that is selected for use with the system. Therefore, when the same catheter is used in a prior art system as is used in a system as provided by the opposed patent, the skilled person would naturally arrive at the same set of optimised parameters, or at least consider those parameters during a tuning process.

As detailed above at point 1.2.1, the need to prevent distal embolization is well-known. For example, the skilled person is aware that when a device becomes clogged by a thrombus during use the potential for inadvertent dislodgment of the thrombus downstream increases. The skilled person would have been aware of the need to mitigate for the risk of distal embolization, and that the presence of so-called “forward flow” may increase this risk.

Given their common general knowledge relating to distal embolization and the teachings of the various prior art documents cited herein, it would be obvious to the skilled person that when modifying various parameters to optimise the system, for example in view of a particular catheter that is connected to the device, it should be ensured that forward flow is prevented.

For example, O3 teaches that:

[00031] The occlusion is dislodged by the high-pressure impulses, which are strong enough to dislodge the occlusion but are not of sufficient duration to push it out the distal end 12B of the catheter tube 12. The subsequent negative pressure rest period following each impulse can act to prevent escape of the clot from the catheter tube 12, in one embodiment. In addition, a suction process can be performed by the patency device 30 to withdraw the clot proximally from the catheter tube 12 and catheter 10 and into the patency device, where it may be disposed of. In this way, any clot or occlusion present in the catheter 10 can be acceptably removed.

O18 discloses that:

[00128] ...by providing the ability to maintain aspiration continuously from either the catheter tip or the sheath tip or the sheath distal region, and providing the means to change aspiration levels and maintain asp, the procedure optimizes the ability to aspiration clot while minimizing distal emboli and minimizing blood loss from aspiration...

Paragraph 114 O14 also teaches the use of cyclical aspiration that provides “an aspiration force that cycles between a high level of vacuum to a lower level of vacuum at a set frequency”, or which cycles from “a high level of vacuum to no vacuum”. In such implementations, an overall level of aspiration would be maintained in the catheter, and in this way forward flow would be prevented.

Therefore, in optimising the device the skilled person would seek to ensure that distal migration is prevented.

It would be part of the skilled person’s common general knowledge that controlling the length of time that valves are open or closed would be one way to ensure that distal migration and forward flow are prevented, for example at least because it is obvious that not applying suction, or applying positive pressure pulses for a prolonged duration, would increase the risk forward flow and distal migration occurring.

The skilled person would therefore seek to preserve an overall negative pressure in the catheter, and also increase the efficiency with which a thrombus is aspirated, by optimising the frequency and duration of the operating states of a valve arrangement. This would include optimising the duration of valve states and the pressure which is applied to the catheter, and would naturally lead the skilled person to control the time over which the vacuum level is changed to prevent forward flow and distal migration. In particular, the selection of the claimed parameters does not have any unexpected technical advantage and would naturally be considered by the skilled person.

The prior art therefore provides a variety of teachings that would lead the skilled person to modify and optimize various operating parameters of the clot removal systems described therein. In performing such modification, the skilled person would naturally arrive at an arrangement which falls within the scope of claim 9.

It is also noted that claim 9 merely defines selecting a particular magnitude and duration of a vacuum level change from a limited range of possibilities and parameters, and it is clear that these parameters could be arrived at by routine trial and error or by applying normal design procedures to prevent forward flow (e.g., to choose suitable parameters to optimise operation of the device, such as for a given catheter in the manner taught by the opposed patent and the prior art as outlined above). It is generally accepted that achieving a known 'technical effect' by means of modifications of the closest prior art which would be obvious to the skilled person cannot be considered inventive (Case Law of the Boards of Appeal I.D. 9.21.2). Indeed, based at least on these disclosures in the prior art documents, the skilled person would have a reasonable expectation of successfully improving the operation of a clot removal system, such that modifying these parameters should be not considered to involve an inventive step (Case Law of the Boards of Appeal I.D. 7.1).

Indeed, certain of these parameters are explicitly considered by the cited prior art as disclosed elsewhere herein, and below.

For example, paragraph 39 of O3 states that (emphasis added):

[00039] As mentioned, the pressure level of the impulses can be varied or determined according to a variety of factors, including catheter length, catheter lumen size, burst strength, impulse duration, rest period duration, other catheter configuration, etc. In one embodiment, the pressure of each impulse can be chosen from a range of from about 30 psi to about 120 psi, though other pressure below and above this are possible...

30 psi corresponds to approximately 210 kPa and 120 psi corresponds to approximately 830 kPa. O3 therefore clearly discloses utilises pressure changes greater than approximately 51 kPa as recited by claim 9.

O10 discloses in relation to Fig. 47 that a lower pressure limit may set at between -600 mmHg and -700 mmHg (that is, between approximately 24 inHg and 28 inHg, where the initial pressure is 0 inHg. O10 therefore discloses a change in the level of vacuum pressure of greater than 15 inHg as recited by claim 9.

O18 an arrangement wherein a lumen used to aspirate fluid can be formed in a luminal portion and a sheath body, which are arranged to have an overlapping region. A seal at this overlapping region is intended to "enable sealing against a vacuum of up to 25 inHg, or up to 28 inHg" (paragraph [0012]). That is, O18 at least implicitly suggests utilising a vacuum pressure greater than 15 inHg, as recited by claim 9.

These teachings could be combined with any other suitable prior art document to arrive at an arrangement as recited by claim 9.

5.9.1.O9 (WO 2014/151209 A1) - "Grey"

If it is considered that claim 9 provides a distinguishing feature, then it lacks an inventive step in view of document O9.

Page 13, lines 4 to 9 of O9 discloses that (emphasis added):

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).

O9 therefore clearly discloses arrangements wherein the change in the level of vacuum at the distal end is greater than approximately 15 inHg as recited by claim 9.

Page 10, lines 28 to 31 of O9 discloses that (emphasis added):

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.

By suggesting operation at a frequency of at least 50 Hz, O9 clearly discloses arrangements wherein the change in the level of vacuum at the distal end occurs in no greater than approximately 20 ms as recited by claim 9.

O9 would therefore lead the skilled person to operate within the parameters as defined by claim 9.

5.10. Claim 10

Claim 10 recites:

*The system according to claim 1, wherein:
the lumen has an internal diameter of between approximately 0.965 mm (0.038") and approximately 2.692 mm (0.106"); and
the controller (560) is configured to cyclically open and close the vacuum valve (420) and the vent valve (440) at a frequency of between 2 and 16 Hz.*

If it is considered that claim 10 provides a distinguishing feature, then it lacks an inventive step. Claim 10 recites a selection of parameters that the skilled person would naturally arrive at by routine trial and error or by applying normal design procedures. In particular, claim 10 merely relates to selection of a parameter (i.e., valve cycle frequency) based on the choice of a particular catheter, according to normal design procedures known to the person skilled in the art.

First, the skilled person would naturally consider varying such parameters to ensure that a clot removal system is optimised and fit for purpose. For example, several of the cited documents explicitly teach and/or suggest to the skilled person that such parameters should be adjusted or optimised.

For example, document O4 suggests the principle of adjusting parameters to enable a desired effect, for example (page 680, right column; emphasis added):

While Max Hz cycling was not 100% successful in this study (it is worthwhile to note that all clearance failures occurred with air as the medium), the downward trend in clot clearance time shown in figure 3 is a good indicator that increasing frequency is the correct path to more effective treatments. We believe that additional dimensions of frequency and amplitude modulation may be added to this technique in which their values are temporally adjusted to increase treatment efficacy.

Indeed, O4 suggests further exploration in this area (page 682, left column; emphasis added):

...with these pilot data established, does it seem prudent to embark on future research to classify further how the many variables involved—for example, frequency, differential amplitude range, pressure waveform—can be optimized. Furthermore, these data make it worthwhile to develop a device that can vary the frequency and pressure more precisely. This will allow much more detailed examination of suction variation that might be able to be a stand-alone technique or to augment current techniques by replacing flow arrest or static suction...

At page 10, lines 22 to 27 of O9 it is stated that (emphasis added):

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.

With respect to O9, it is also noted that page 10, lines 28 to 31 of O9 discloses that (emphasis added):

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.

That is, O9 explicitly contemplates operating in the frequency range as recited by claim 10.

O11 also states, at column 3, lines 37 to 39, that “Any time periods can be employed for the periods of suction and blowing as well as for the total cycle by adjustment of the timer 44”, and so the skilled person would therefore modify such periods as required and, in doing so, would naturally consider operating within the claimed area.

These citations evidence that the skilled person would naturally consider varying parameters such as cycle frequency to ensure that a clot removal system is optimised. In performing such optimisation the skilled person would naturally arrive at an arrangement as recited by claim 10.

Second, the skilled person is taught by the prior art to optimise the system for a given catheter. For example, paragraph 39 of O3 states that (emphasis added):

[00039] As mentioned, the pressure level of the impulses can be varied or determined according to a variety of factors, including catheter length, catheter lumen size, burst strength, impulse duration, rest period duration, other catheter configuration, etc. In one embodiment, the pressure of each impulse can be chosen from a range of from about 30 psi to about 120 psi, though other pressure below and above this are possible. Also, frequency of the impulses, or impulse frequency, can be set according to a predetermined pattern and can vary according to a number of factors such as those described immediately above...

Similarly, paragraph 130 of O2 states that:

[0130] By tuning frequency, duty cycle, and wave form, one skilled in the art may match or approximate the resonating frequency to the natural frequency of the catheter. This may further enhance the efficacy of aspiration.

It is acknowledged in the opposed patent itself that the timing depends on the choice of a given catheter and extension tube configuration (page 53, lines 15 to 18):

...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 addition, at page 61, lines 30 to 31 it is stated that “*the cycle time is optimized by the dynamics or the resonance of a particular catheter 660*”.

This shows that the prior art and the opposed patent provide generally the same teaching about varying parameters and tuning a clot removal system to suit a catheter that is selected for use with the system. Therefore, when the same catheter is used in a prior art system as is used in a system as provided by claim 10, the skilled person would naturally arrive at the same set of optimised parameters, or at least consider those parameters during a tuning process.

As detailed above at point 1.2.1, the need to prevent distal embolization is well-known. For example, the skilled person is aware that when a device becomes clogged by a thrombus during use the potential for inadvertent dislodgment of the thrombus downstream increases. The skilled person would have been aware of the need to mitigate for the risk of distal embolization, and that the presence of so-called “forward flow” may increase this risk.

Given their common general knowledge relating to distal embolization and the teachings of the various prior art documents cited herein, it would be obvious to the skilled person that when modifying various parameters to optimise the system, for example in view of a particular catheter that is connected to the device, it should be ensured that forward flow is prevented.

For example, O3 teaches that:

[00031] The occlusion is dislodged by the high-pressure impulses, which are strong enough to dislodge the occlusion but are not of sufficient duration to push it out the distal end 12B of the catheter tube 12. The subsequent negative pressure rest period following each impulse can act to prevent escape of the clot from the catheter tube 12, in one embodiment. In addition, a suction process can be performed by the patency device 30 to withdraw the clot proximally from the catheter tube 12 and catheter 10 and into the patency device, where it may be disposed of In this way, any clot or occlusion present in the catheter 10 can be acceptably removed.

O18 discloses that:

[00128] ...by providing the ability to maintain aspiration continuously from either the catheter tip or the sheath tip or the sheath distal region, and providing the means to change aspiration levels and maintain asp, the procedure optimizes the ability to aspiration clot while minimizing distal emboli and minimizing blood loss from aspiration...

Paragraph 114 O14 also teaches the use of cyclical aspiration that provides “an aspiration force that cycles between a high level of vacuum to a lower level of vacuum at a set frequency”, or which cycles from “a high level of vacuum to no vacuum”. In such implementations, an overall level of aspiration would be maintained in the catheter, and in this way forward flow would be prevented.

Therefore, in optimising the device the skilled person would seek to ensure that distal migration is prevented.

It would be part of the skilled person’s common general knowledge that controlling the length of time that valves are open or closed for, and hence the frequency at which valves are open or closed, would be one way to ensure that distal migration and forward flow are prevented, for example at least because it is obvious that not applying suction, or applying positive pressure pulses for a prolonged duration, would increase the risk forward flow and distal migration occurring.

The skilled person would therefore seek to preserve an overall negative pressure in the catheter, and also increase the efficiency with which a thrombus is aspirated, by optimising the frequency and duration of the operating states of a valve arrangement. In particular, the selection of the claimed parameters does not have any unexpected technical advantage and would naturally be considered by the skilled person.

The prior art therefore provides a variety of teachings that would lead the skilled person to modify and optimize various operating parameters of the clot removal systems described therein. In performing such modification, the skilled person would naturally arrive at an arrangement which falls within the scope of claim 10.

It is also noted that claim 10 merely defines selecting a particular valve cycle frequency based on the particular selection of a catheter, and it is clear that such frequencies could be arrived at by routine trial and error or by applying normal design procedures to prevent forward flow (e.g., to choose suitable parameters to optimise operation of the device, such as for a given catheter in the manner taught by the opposed patent and the prior art as outlined above). It is generally accepted that achieving a known ‘technical effect’ by means of modifications of the closest prior art which would be obvious to the skilled person cannot be considered inventive (Case Law of the Boards of Appeal I.D. 9.21.2). Indeed, based at least on these disclosures in the prior art documents, the skilled person would have a reasonable expectation of successfully improving the operation of a clot removal system, such that modifying these parameters should are not considered to involve an inventive step (Case Law of the Boards of Appeal I.D. 7.1).

Further, the selection of such catheter sizes is explicitly considered by the cited prior art as disclosed elsewhere herein, and below.

For example, O17 discloses an aspiration system in which (emphasis added)

[0068] ... The aspiration lumen 18 may be sized for aspiration of thrombus, and in some embodiments may have an inner diameter of between about 0.38 millimeter (0.015 inches) and about 2.54 millimeters (0.100 inches)...

O18 discloses an arrangement wherein emphasis added):

[0056] The diameter of the sheath body 222 is suitable for insertion into the carotid artery, with an inner lumen 223 that is suitably sized for providing a passageway for catheters to treat the occlusion. In an implementation, the sheath body 222 can have an inner diameter of about 0.074" and an outer diameter of about 0.090", corresponding to a 5 French sheath size, an inner diameter of about 0.087" and an outer diameter of about 0.104", corresponding to a 6 French sheath size, or an inner diameter of about 0.100" and an outer diameter of about 0.177", corresponding to a 7 French sheath size...

These teachings could be combined with any other suitable prior art document to arrive at an arrangement as recited by claim 10.

5.10.1. O4 (Exploring the efficacy of cyclic vs static aspiration in a cerebral thrombectomy model: an initial proof of concept study) – "Simon"

If it is considered that claim 10 provides a distinguishing feature, then it lacks an inventive step in view of document O4.

O4 discloses that the test apparatus comprises (page 678, left hand column; emphasis added):

...a flow model consisting of a Penumbra 5Max reperfusion catheter (1.37 mm tip internal diameter) inside rigid plastic tubing (2.5 mm internal diameter, 4 mm outside diameter) submerged in water...

That is, O4 utilises a catheter having an internal lumen diameter within the range recited by claim 10.

In addition, in the Discussion, O4 states that a frequency of ~6.3 Hz was the most effective in this set up:

Although none were observed in this study, in the interest of preventing the distal migration of thrombi, impact aspiration would have to be performed either in conjunction with continuous aspiration or as a stand-alone treatment with a minimum frequency such that a vacuum is maintained throughout testing. In this study ~6.3 Hz (Max Hz) was the only frequency that maintained uninterrupted net aspiration pressure as both 1 Hz and 2 Hz had minimum pressures of 0 in Hg. Implementing a pressure-controlling device would allow flexibility in aspiration frequency due to the increased control over minimum pressure.

O4 therefore explicitly teaches a combination of lumen diameter and frequency which falls within the scope of claim 10. This teaching could be combined with any other suitable prior art document to arrive at an arrangement as recited by claim 10.

5.10.2. O9 (WO 2014/151209 A1) – “Grey”

If it is considered that claim 10 provides a distinguishing feature, then it lacks an inventive step in view of document O9.

O9 discloses an example utilising the aspiration system shown in Figure 2A, in which synthetic clots (page 22, lines 21 to 23; emphasis added):

...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...

This apparatus was tested at different cycle frequencies, including (page 23, lines 19 to 23; emphasis added):

...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 -72.0 (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)...

O9 therefore explicitly teaches a combination of lumen diameter and frequency which falls within the scope of claim 10. This teaching could be combined with any other suitable prior art document to arrive at an arrangement as recited by claim 10.

5.11. Claim 11

Claim 11 recites:

*The system according to claim 1, wherein:
the lumen has an internal diameter of between approximately 1.73 mm (0.068") and approximately 2.24 mm (0.088"); and
the controller (560) is configured to cyclically open and close the vacuum valve (420) and the vent valve (440) at a frequency of between 2 and 16 Hz.*

If it is considered that claim 11 provides a distinguishing feature, then it lacks an inventive step. Claim 11 recites a selection of parameters that the skilled person would naturally arrive at by routine trial and error or by applying normal design procedures. In particular, claim 11 merely relates to selection of a parameter

(i.e., valve cycle frequency) based on the choice of a particular catheter, according to normal design procedures known to the person skilled in the art.

First, the skilled person would naturally consider varying such parameters to ensure that a clot removal system is optimised and fit for purpose. For example, several of the cited documents explicitly teach and/or suggest to the skilled person that such parameters should be adjusted or optimised.

For example, document O4 suggests the principle of adjusting parameters to enable a desired effect, for example (page 680, right column; emphasis added):

While Max Hz cycling was not 100% successful in this study (it is worthwhile to note that all clearance failures occurred with air as the medium), the downward trend in clot clearance time shown in figure 3 is a good indicator that increasing frequency is the correct path to more effective treatments. We believe that additional dimensions of frequency and amplitude modulation may be added to this technique in which their values are temporally adjusted to increase treatment efficacy.

Indeed, O4 suggests further exploration in this area (page 682, left column; emphasis added):

...with these pilot data established, does it seem prudent to embark on future research to classify further how the many variables involved—for example, frequency, differential amplitude range, pressure waveform—can be optimized. Furthermore, these data make it worthwhile to develop a device that can vary the frequency and pressure more precisely. This will allow much more detailed examination of suction variation that might be able to be a stand-alone technique or to augment current techniques by replacing flow arrest or static suction...

At page 10, lines 22 to 27 of O9 it is stated that (emphasis added):

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.

With respect to O9, it is also noted that page 10, lines 28 to 31 of O9 discloses that (emphasis added):

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.

That is, O9 explicitly contemplates operating in the frequency range as recited by claim 10.

O11 also states, at column 3, lines 37 to 39, that “Any time periods can be employed for the periods of suction and blowing as well as for the total cycle by adjustment of the timer 44”, and so the skilled person would therefore modify such periods as required and, in doing so, would naturally consider operating within the claimed area.

These citations evidence that the skilled person would naturally consider varying parameters such as cycle frequency to ensure that a clot removal system is optimised. In performing such optimisation the skilled person would naturally arrive at an arrangement as recited by claim 10.

Second, the skilled person is taught by the prior art to optimise the system for a given catheter. For example, paragraph 39 of O3 states that (emphasis added):

[00039] As mentioned, the pressure level of the impulses can be varied or determined according to a variety of factors, including catheter length, catheter lumen size, burst strength, impulse duration, rest period duration, other catheter configuration, etc. In one embodiment, the pressure of each impulse can be chosen from a range of from about 30 psi to about 120 psi, though other pressure below and above this are possible. Also, frequency of the impulses, or impulse frequency, can be set according to a predetermined pattern and can vary according to a number of factors such as those described immediately above...

Similarly, paragraph 130 of O2 states that:

[0130] By tuning frequency, duty cycle, and wave form, one skilled in the art may match or approximate the resonating frequency to the natural frequency of the catheter. This may further enhance the efficacy of aspiration.

It is acknowledged in the opposed patent itself that the timing depends on the choice of a given catheter and extension tube configuration (page 53, lines 15 to 18):

...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 addition, at page 61, lines 30 to 31 it is stated that “the cycle time is optimized by the dynamics or the resonance of a particular catheter 660”.

This shows that the prior art and the opposed patent provide generally the same teaching about varying parameters and tuning a clot removal system to suit a catheter that is selected for use with the system. Therefore, when the same catheter is used in a prior art system as is used in a system as provided by claim 10, the skilled person would naturally arrive at the same set of optimised parameters, or at least consider those parameters during a tuning process.

As detailed above at point 1.2.1, the need to prevent distal embolization is well-known. For example, the skilled person is aware that when a device becomes clogged by a thrombus during use the potential for inadvertent dislodgment of the thrombus downstream increases. The skilled person would have been aware of the need to mitigate for the risk of distal embolization, and that the presence of so-called “forward flow” may increase this risk.

Given their common general knowledge relating to distal embolization and the teachings of the various prior art documents cited herein, it would be obvious to the skilled person that when modifying various parameters to optimise the system, for example in view of a particular catheter that is connected to the device, it should be ensured that forward flow is prevented.

For example, O3 teaches that:

[00031] The occlusion is dislodged by the high-pressure impulses, which are strong enough to dislodge the occlusion but are not of sufficient duration to push it out the distal end 12B of the catheter tube 12. The subsequent negative pressure rest period following each impulse can act to prevent escape of the clot from the catheter tube 12, in one embodiment. In addition, a suction process can be performed by the patency device 30 to withdraw the clot proximally from the catheter tube 12 and catheter 10 and into the patency device, where it may be disposed of In this way, any clot or occlusion present in the catheter 10 can be acceptably removed.

O18 discloses that:

[00128] ...by providing the ability to maintain aspiration continuously from either the catheter tip or the sheath tip or the sheath distal region, and providing the means to change aspiration levels and maintain asp, the procedure optimizes the ability to aspiration clot while minimizing distal emboli and minimizing blood loss from aspiration...

Paragraph 114 O14 also teaches the use of cyclical aspiration that provides “an aspiration force that cycles between a high level of vacuum to a lower level of vacuum at a set frequency”, or which cycles from “a high level of vacuum to no vacuum”. In such implementations, an overall level of aspiration would be maintained in the catheter, and in this way forward flow would be prevented.

Therefore, in optimising the device the skilled person would seek to ensure that distal migration is prevented.

It would be part of the skilled person’s common general knowledge that controlling the length of time that valves are open or closed for, and hence the frequency at which valves are open or closed, would be one way to ensure that distal migration and forward flow are prevented, for example at least because it is obvious that not applying suction, or applying positive pressure pulses for a prolonged duration, would increase the risk forward flow and distal migration occurring.

The skilled person would therefore seek to preserve an overall negative pressure in the catheter, and also increase the efficiency with which a thrombus is aspirated, by optimising the frequency and duration of the operating states of a valve arrangement. In particular, the selection of the claimed parameters does not have any unexpected technical advantage and would naturally be considered by the skilled person.

The prior art therefore provides a variety of teachings that would lead the skilled person to modify and optimize various operating parameters of the clot removal systems described therein. In performing such modification, the skilled person would naturally arrive at an arrangement which falls within the scope of claim 11.

It is also noted that claim 11 merely defines selecting a particular valve cycle frequency based on the particular selection of a catheter, and it is clear that such frequencies could be arrived at by routine trial and error or by applying normal design procedures to prevent forward flow (e.g., to choose suitable parameters to optimise operation of the device, such as for a given catheter in the manner taught by the opposed patent and the prior art as outlined above). It is generally accepted that achieving a known ‘technical effect’ by means of modifications of the closest prior art which would be obvious to the skilled person cannot be considered inventive (Case Law of the Boards of Appeal I.D. 9.21.2). Indeed, based at least on these disclosures in the prior art documents, the skilled person would have a reasonable expectation of successfully improving the operation of a clot removal system, such that modifying these parameters should are not considered to involve an inventive step (Case Law of the Boards of Appeal I.D. 7.1).

Further, the selection of such catheter sizes are at least implicitly considered by the cited prior art as disclosed elsewhere herein, and below.

For example, O17 discloses an aspiration system in which (emphasis added)

[0068] ... The aspiration lumen 18 may be sized for aspiration of thrombus, and in some embodiments may have an inner diameter of between about 0.38 millimeter (0.015 inches) and about 2.54 millimeters (0.100 inches)...

O18 discloses an arrangement wherein emphasis added):

[0056] The diameter of the sheath body 222 is suitable for insertion into the carotid artery, with an inner lumen 223 that is suitably sized for providing a passageway for catheters to treat the occlusion. In an implementation, the sheath body 222 can have an inner diameter of about 0.074" and an outer diameter of about 0.090", corresponding to a 5 French sheath size, an inner diameter of about 0.087" and an outer diameter of about 0.104", corresponding to a 6 French sheath size, or an inner diameter of about 0.100" and an outer diameter of about 0.177", corresponding to a 7 French sheath size...

These teachings could be combined with any other suitable prior art document to arrive at an arrangement as recited by claim 10.

5.12. Claim 12

Claim 12 recites:

The system according to claim 1, wherein the controller (560) is configured to cyclically open and close the vacuum valve (420) and the vent valve (440) 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 (440).

If it is considered that claim 12 provides a distinguishing feature, then it lacks an inventive step.

As detailed above at point 1.2.1, the need to prevent distal embolization is well-known. For example, the skilled person is aware that when a device becomes clogged by a thrombus during use the potential for inadvertent dislodgment of the thrombus downstream increases. The skilled person would have been aware of the need to mitigate for the risk of distal embolization, and that the presence of so-called "forward flow" may increase this risk.

Given their common general knowledge relating to distal embolization and the teachings of the various prior art documents cited herein, it would be obvious to the skilled person that when modifying various parameters, such as the frequency of a valve cycle and the duration of valve states within the cycle, to optimise the system, for example in view of a particular catheter that is connected to the device, it should be ensured that forward flow is prevented.

For example, O3 teaches that:

[00031] The occlusion is dislodged by the high-pressure impulses, which are strong enough to dislodge the occlusion but are not of sufficient duration to push it out the distal end 12B of the catheter tube 12. The subsequent negative pressure rest period following each impulse can act to prevent escape of the clot from the catheter tube 12, in one embodiment. In addition, a suction process can be performed by the patency device 30 to withdraw the clot proximally from the catheter tube 12 and catheter 10 and into the patency device, where it may be disposed of In this way, any clot or occlusion present in the catheter 10 can be acceptably removed.

O18 discloses that:

[00128] ...by providing the ability to maintain aspiration continuously from either the catheter tip or the sheath tip or the sheath distal region, and providing the means to change aspiration levels and maintain asp, the procedure optimizes the ability to aspiration clot while minimizing distal emboli and minimizing blood loss from aspiration...

Paragraph 114 O14 also teaches the use of cyclical aspiration that provides “an aspiration force that cycles between a high level of vacuum to a lower level of vacuum at a set frequency”, or which cycles from “a high level of vacuum to no vacuum”. In such implementations, an overall level of aspiration would be maintained in the catheter, and in this way forward flow would be prevented.

Therefore, in optimising the device the skilled person would seek to ensure that distal migration is prevented.

It would be part of the skilled person’s common general knowledge that controlling the length of time that valves are open or closed would be one way to ensure that distal migration and forward flow are prevented, for example at least because it is obvious that not applying suction, or applying positive pressure pulses for a prolonged duration, would increase the risk forward flow and distal migration occurring.

The skilled person would therefore seek to preserve an overall negative pressure in the catheter, and also increase the efficiency with which a thrombus is aspirated, by optimising the frequency and duration of the operating states of a valve arrangement. This would include regulating the timing of a vent valve to prevent forward flow and distal migration.

The prior art provides a variety of teachings that would lead the skilled person to modify and optimize various operating parameters of the clot removal systems described therein. In performing such modification, the skilled person would naturally arrive at an arrangement which falls within the scope of claim 12.

5.12.1. Other Documents

Other documents could also be used to demonstrate that claim 12 lacks an inventive step, either as a starting point or as a document that the skilled person would turn to in combination with a suitable starting document.

In particular, it is believed that claim 12 would be obvious in view of any of the documents referred to above with respect to claim 1 (e.g., documents O18, O8, O9, O10 and O11). It has been demonstrated that those documents disclose systems in which a controller may be configured to cyclically control valve arrangements to prevent forward flow. It therefore follows, as a natural consequence of this operation, that

these controllers regulate the timing of a vent valve to prevent forward flow, in the manner required by claim 12.

5.13. Claim 13

Claim 13 recites:

The system according to claim 1, wherein the controller (560) is configured to cyclically open and close the vacuum valve (420) and the vent valve (440) to retain a level of pressure at the distal end at less than physiological pressure.

If it is considered that claim 13 provides a distinguishing feature, then it lacks an inventive step. As outlined above in section 1.2.1 the common general knowledge of the skilled person would lead them to seek to avoid forward flow in order to prevent distal embolization. Therefore, even if documents cited herein do not explicitly discuss retaining a level of pressure at the distal end at less than physiological pressure, the skilled person would have found it obvious to implement such a feature as they would recognise that if the pressure at the distal end is above physiological pressure there would be an increased risk of forward flow and distal embolization. Therefore, ensuring that the level of pressure at a distal end is less than physiological pressure is a trivial solution to ensure that forward flow and distal embolization are prevented.

Similarly, for any document cited herein which suggests that forward flow must be prevented, it follows as a logical consequence that the level of pressure at the distal end is less than physiological pressure, as if that were not the case then forward flow would occur.

5.13.1. O10 (WO 2019/115809 A1) – “Mullins”

If it is considered that claim 13 provides a distinguishing feature, then it lacks inventive step in view of document O10.

O10 teaches that distal embolization is a known problem to be addressed. For example, at page 39, lines 9 to 12 it is stated that:

...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.

To address this problem, and also to prevent clogging of the catheter and promote maceration and deformation of a clot to enable it to travel through a catheter (see e.g., page 40, lines 1 to 14), O10 teaches the use of pulsatile aspiration, where applied pressure is varied.

In particular, O10 teaches that pressure is varied between a Low Limit and a High Limit. Page 42, line 1 of O10 states that “*In one embodiment the High Limit is a negative pressure*” (as shown in Fig. 48(a), reproduced below).

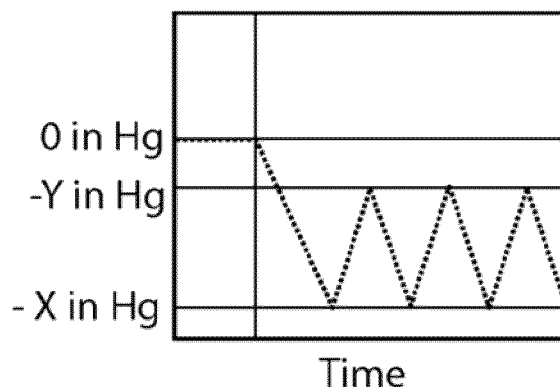


Fig.48(a)

For reference in this image, it is noted at page 40, lines 31 to 33 that:

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).

That is, 0 inHg shown in Fig. 48(a) is representative of blood pressure, i.e., physiological pressure. Fig. 48(a) therefore clearly shows that the pulsatile vacuum which is applied to a catheter is always less than physiological pressure, as recited by claim 13.

O10 therefore clearly teaches the retention of a level of pressure at the distal end which is less than physiological pressure (as both the high level and low level of pressure are negative). This teaching would be implemented in any of the documents discussed herein, for example to reduce the risk of distal embolization.

5.14. Claim 14

Claim 14 recites:

The system according to claim 1, which further comprises a shaft and the vacuum valve (420) and the vent valve (440) are mounted together on the shaft.

5.14.1. O12 (US 2012/0138833 A1) – “Matteo”

O12 is a US patent application, having a publication date of 7 June 2012. The publication date of O12 pre-dates the filing date of the opposed patent. O12 is therefore available for the assessment of novelty and inventive step.

If claim 14 is believed to introduce a distinguishing feature, then that feature lacks an inventive step because it is disclosed by O12.

Matteo discloses a system “to control multiple microvalves” for use in a variety of chemical, biological, and biomedical applications, including “medical and scientific instrumentation” (see e.g., paragraphs 6 and 12).

Matteo therefore falls within the same technical field as other documents cited herein, which relate to medical instruments.

In general, O12 relates to a valve arrangement wherein a cam is driven by a position-control mechanism to move an actuator and thereby close/open a channel (see e.g., Fig. 1 and paragraph [0043]).

A representative drawing of O12 (Fig. 10A) is shown below, for reference.

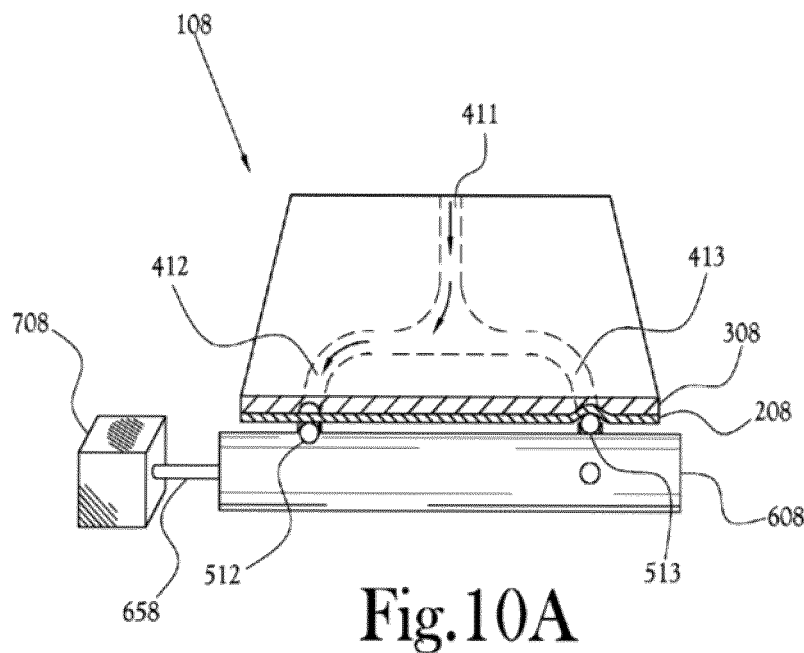


Fig.10A

Paragraph 49 of O12 recites (emphasis added):

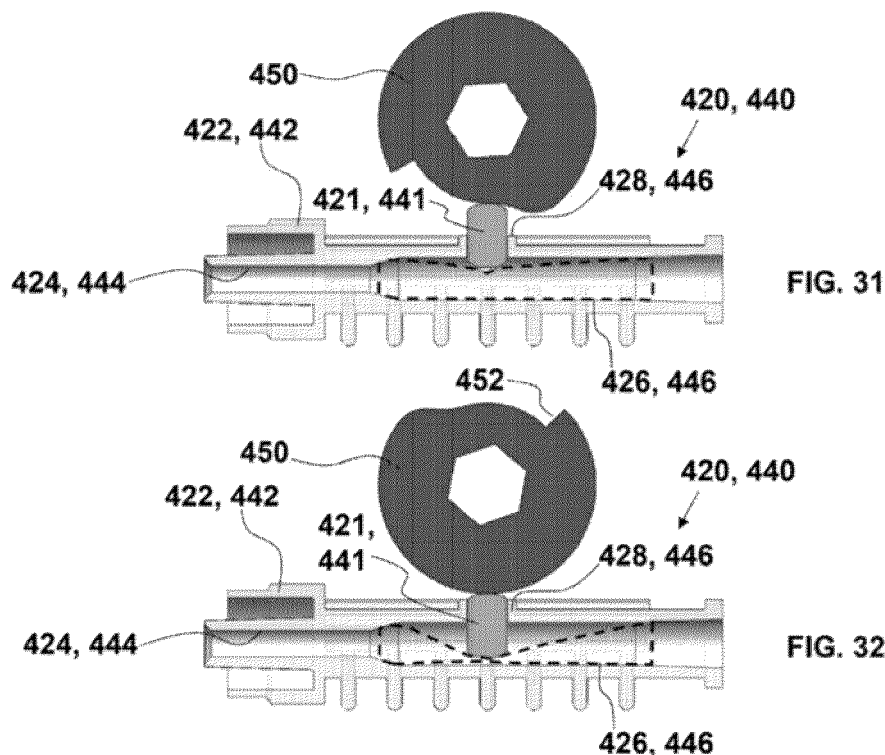
[0049] ...system 108 includes a cylindrical cam 608 and two actuator balls 512 and 513. The actuator ball 512 is positioned to pinch channel 412, and the actuator ball 513 is positioned to pinch channel 413. In this embodiment, the cylindrical cam 608 has a number of detents, which allow for multiple settings of the actuator balls 512 and 513. In the first setting, seen in FIG. 10A, the first actuator ball 512 is resting in a detent, while the second actuator ball 513 is not in a detent and therefore is pinching the second channel 413. With the second channel 413 in the closed state, the fluid from the input channel 411 flows through the first distribution channel 412. In the second setting, seen in FIG. 10B, the cam 608 has been rotated so that now the second actuator ball 513 is resting in a detent, while the first actuator ball 512 is not in a detent and therefore is pinching the first channel 412. With the first channel 412 in the closed state, the fluid from the input channel 411 flows through the second distribution channel 413. Finally, in the third setting, seen in FIG. 10C, the cam 608 has been rotated yet again so that now both actuator balls 512 and 513 are resting in detents, and both distribution channels 412 and 413 are in an open state.

The arrangement shown in Fig. 10A of O10 thereby provides a shaft in the form of a cylindrical cam 608. The detents in the cam shaft provide valve components which are set in (i.e., mounted on) the cylindrical cam. The arrangement of Fig. 10A thereby provides two valves (comprising the actuator balls 512 and 513,

positioned to pinch channels 412 and 413, respectively), which may, for example, correspond to a vacuum valve and a vent valve in arrangements disclosed in the other cited documents. These valves are mounted together on a shaft (cylindrical cam 608), whereby rotation of that shaft provides control over the opening and closing of the valves by detents formed in the shaft.

When seeking an alternative to the valve arrangements disclosed by the cited documents, the skilled person would consider utilising valves as described by O12, and in doing so arrive at an arrangement falling within the scope of claim 14.

For reference, Figs. 31 and 32 of the opposed patent are reproduced below.



The opposed patent states that “the vacuum and vent cams 430, 450 are fixed rotationally to the cam shaft 460” (page 41, line 23 specification as filed). Figs. 31 and 32 show a pinch valve, wherein “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” (page 42, lines 29 to 32 specification as filed).

It will therefore be appreciated that O12 discloses a valve arrangement which is functionally and structurally identical to the pinch valve arrangement considered by the opposed patent itself (with detents in a cylindrical cam as described by O12 providing a valve cam as described by the opposed patent, and actuator balls as described by O12 providing a cam follower as described by the opposed patent), such that O12 discloses a valve arrangement within the scope of claim 14.

6. Conclusion

For the reasons set out above, the opposed patent should be revoked in its entirety. If oral proceedings are held we will speak in English and will require translation into English from any other language used at the oral proceedings.

Yours faithfully,

/Signed electronically/

Thomas Daniel Hamer
Professional Representative
For and on behalf of Kilburn & Strobe LLP (Professional association no. 1016)



US 20170238953A1

(19) **United States**

(12) **Patent Application Publication**
Yang et al.

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(43) **Pub. Date: Aug. 24, 2017**

(54) **TELESCOPING NEUROVASCULAR
CATHETER WITH ACTIVE DISTAL TIP**

A61M 1/00 (2006.01)

A61M 25/06 (2006.01)

(71) Applicant: **INCEPT, LLC**, Sunnyvale, CA (US)

(52) **U.S. Cl.**

CPC *A61B 17/22012* (2013.01); *A61M 1/0035*
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25/0023 (2013.01); *A61M 25/0102* (2013.01);
A61M 25/0108 (2013.01); *A61M 25/005*
(2013.01); *A61M 25/0662* (2013.01); *A61M*
25/0009 (2013.01); *A61M 1/32* (2013.01);
A61F 2/95 (2013.01); *A61F 7/12* (2013.01);
A61M 39/06 (2013.01); *A61B 17/22031*
(2013.01); *A61B 17/3203* (2013.01); *A61F*
2007/126 (2013.01); *A61B 2017/00862*
(2013.01)

(72) Inventors: **Yi Yang**, San Francisco, CA (US); **Fred
Khosravi**, Mountain View, CA (US);
Joseph Rimsa, Palo Alto, CA (US)

(21) Appl. No.: **15/443,874**

(22) Filed: **Feb. 27, 2017**

Related U.S. Application Data

(63) Continuation of application No. 15/442,393, filed on
Feb. 24, 2017.

(60) Provisional application No. 62/443,595, filed on Jan.
6, 2017, provisional application No. 62/299,418, filed
on Feb. 24, 2016.

Publication Classification

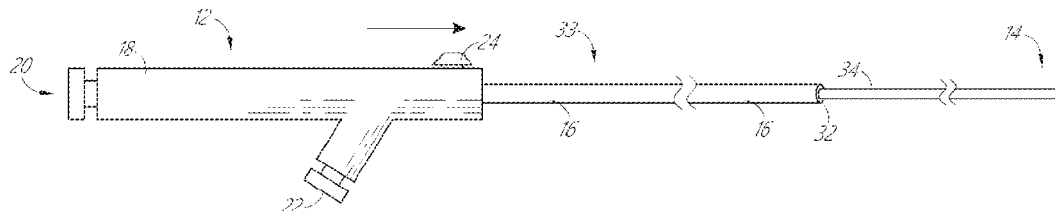
(51) **Int. Cl.**

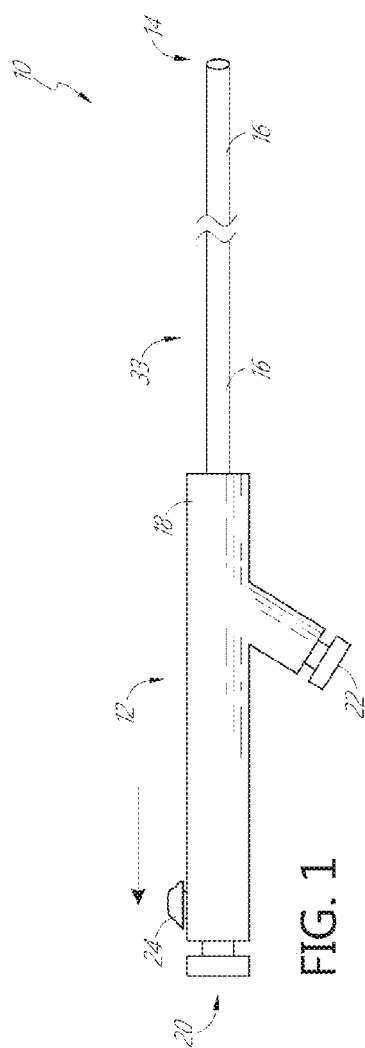
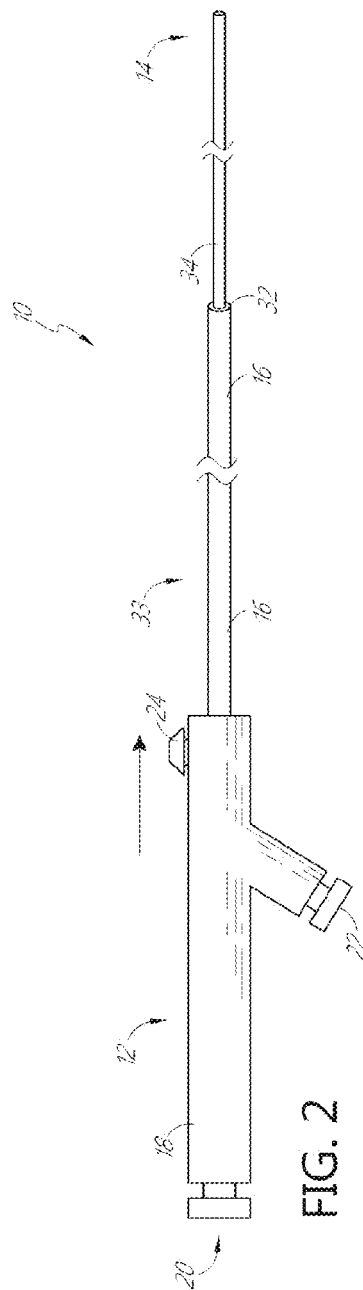
A61B 17/22 (2006.01)
A61M 25/01 (2006.01)
A61M 25/00 (2006.01)
A61B 17/3203 (2006.01)
A61M 1/32 (2006.01)
A61F 2/95 (2006.01)
A61F 7/12 (2006.01)
A61M 39/06 (2006.01)

(57)

ABSTRACT

A telescoping catheter is provided such as for distal neuro-vascular aspiration or access. The catheter includes an elongate, flexible tubular body, having a proximal section with at least one lumen and a distal section which is axially movably positioned within the lumen. A control is provided for advancing the distal section from a first, proximally retracted position within the proximal section to a second extended position, extending distally beyond the proximal section. The distal end of at least one of the proximal and distal sections may be provided with at least one active feature, such as at least one movable jaw or rotatable agitator, to assist in the capture of vascular obstruction. The jaw may be operable in response to application of pulsatile negative pressure through the catheter.





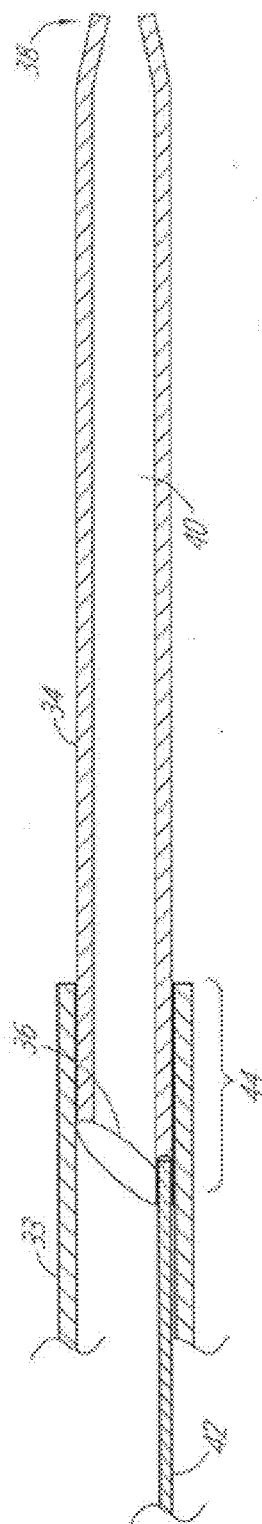


FIG. 3A

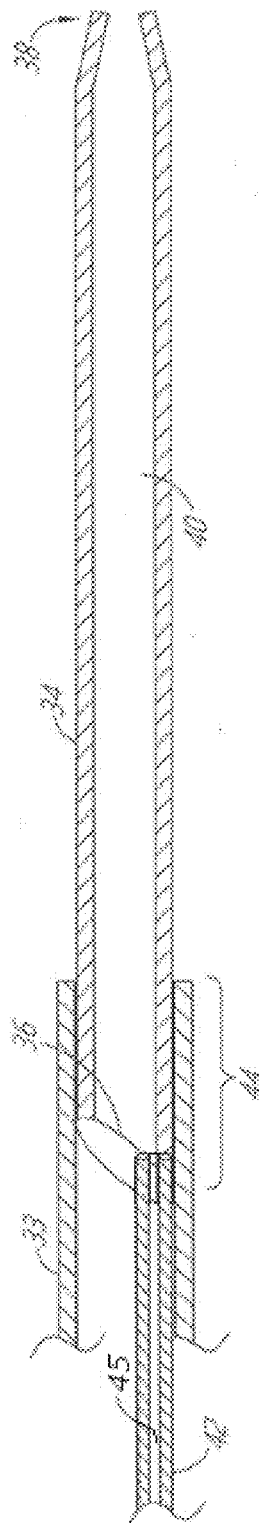


FIG. 3B

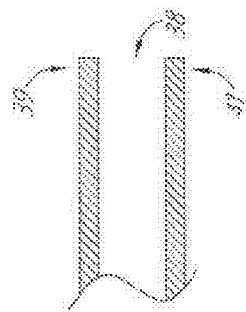


FIG. 4A

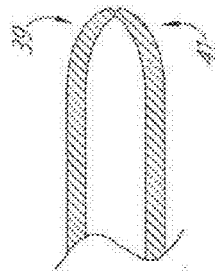


FIG. 4B

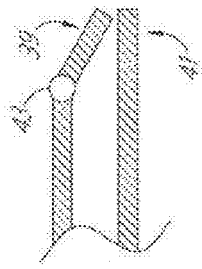


FIG. 4C

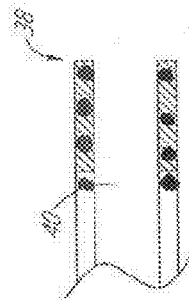


FIG. 4J

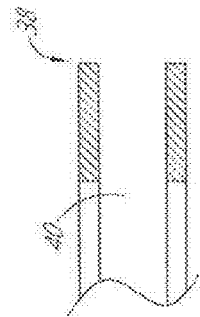


FIG. 4D

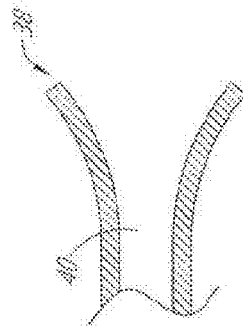


FIG. 4E



FIG. 4K

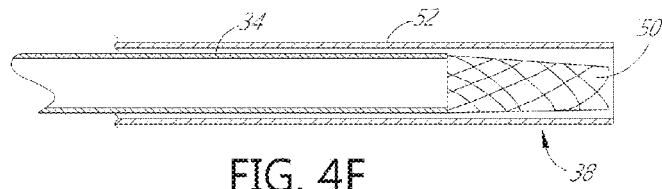


FIG. 4F

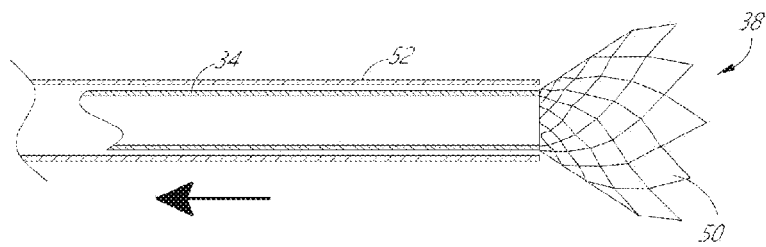


FIG. 4G

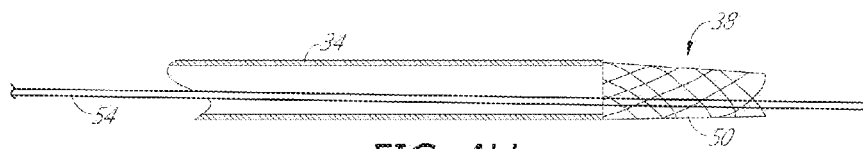


FIG. 4H

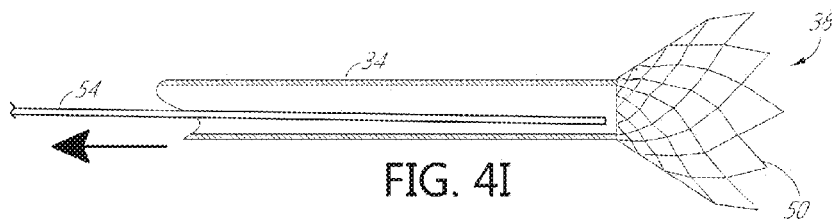
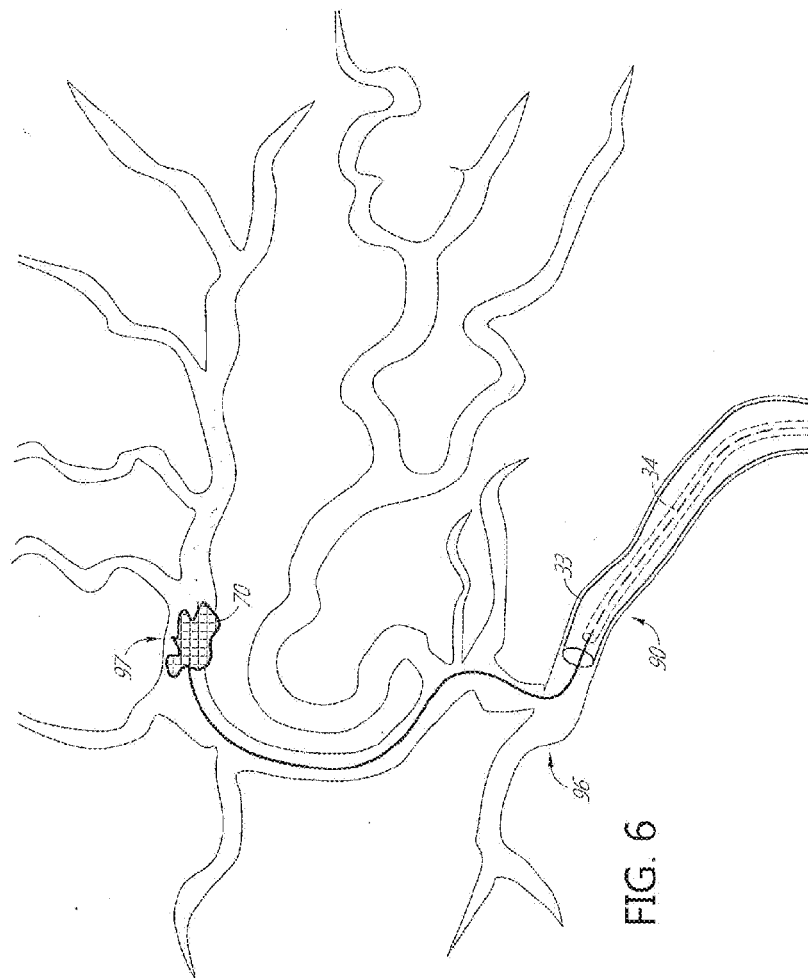
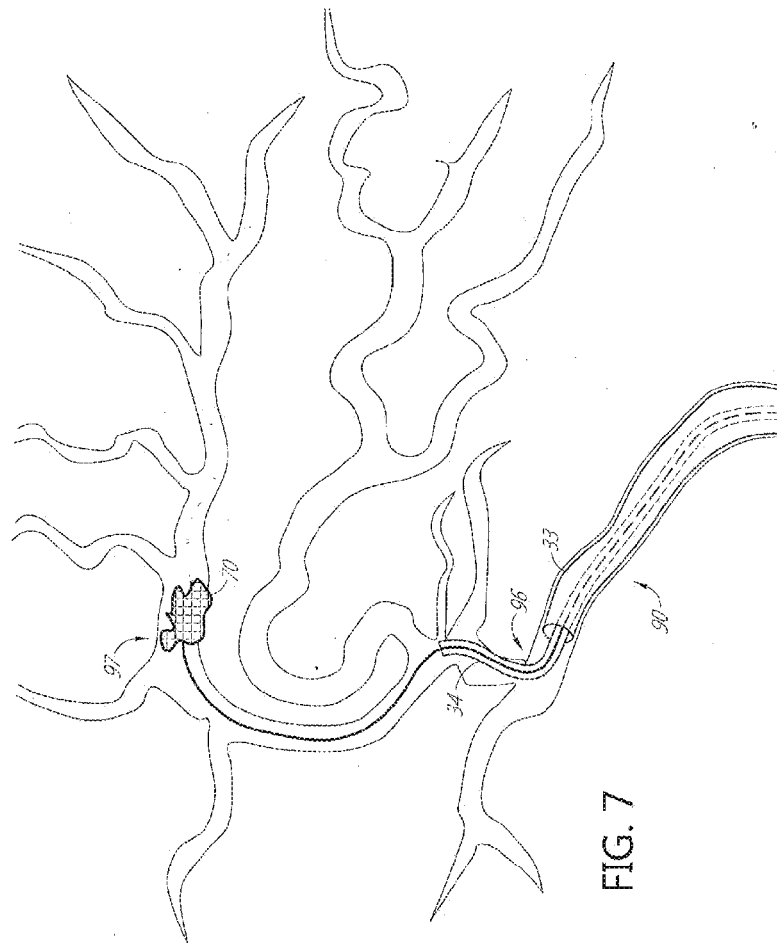


FIG. 4I





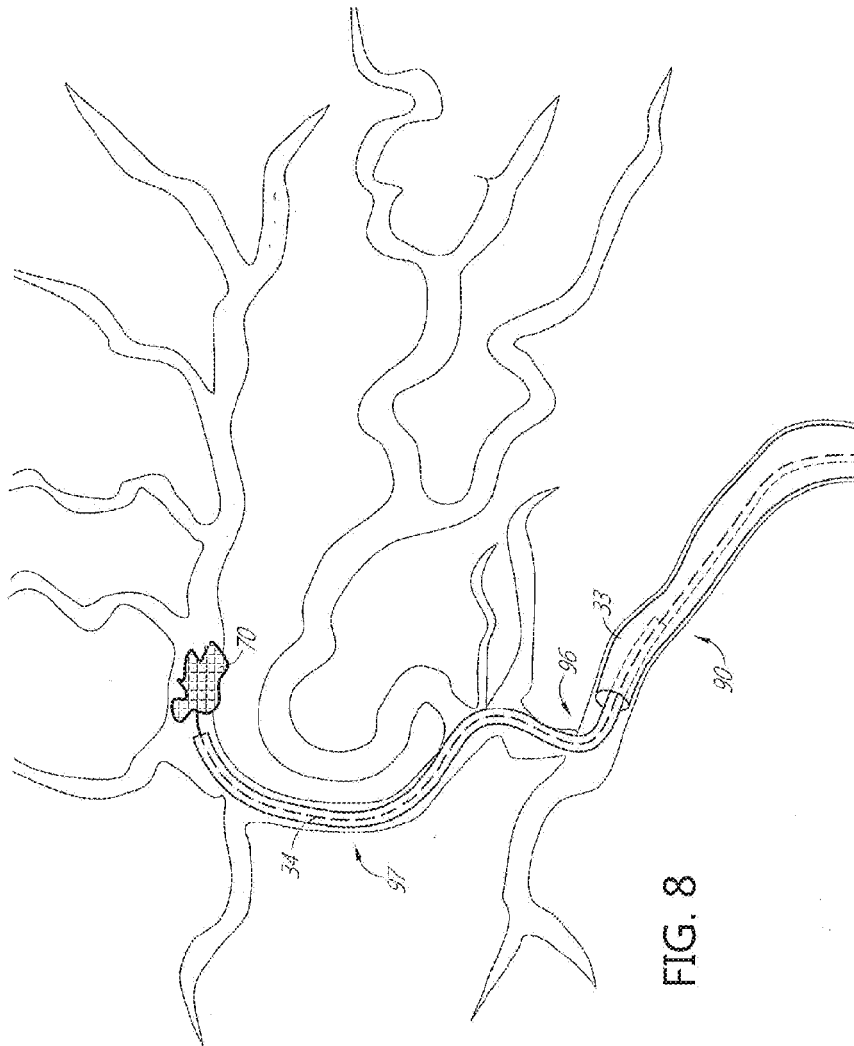
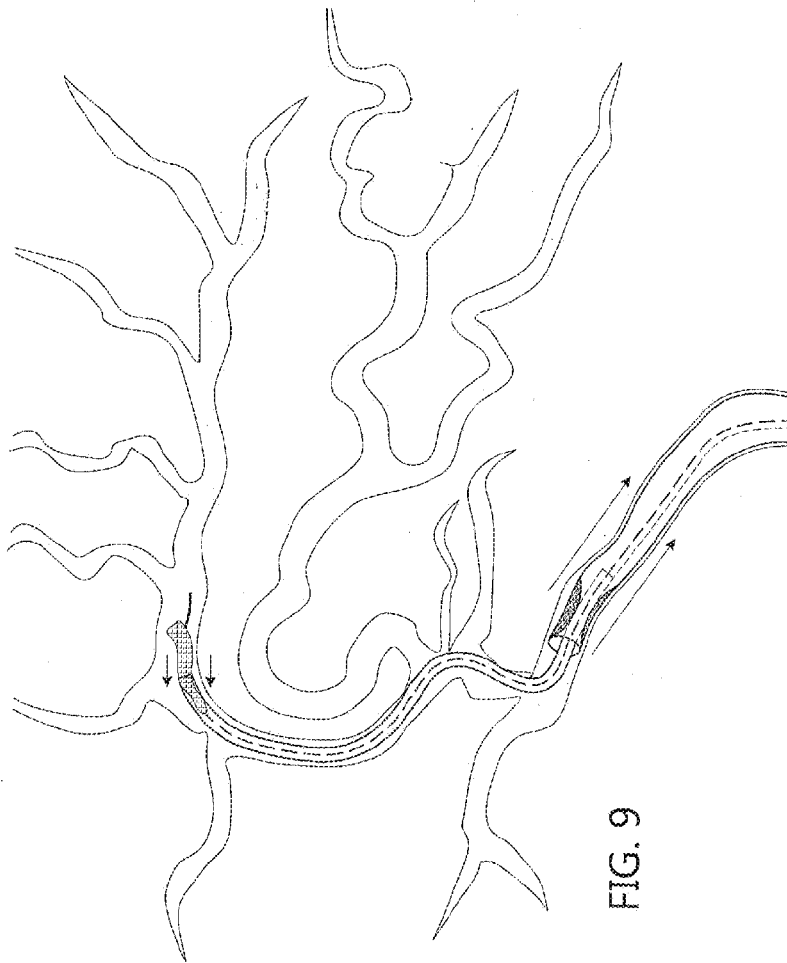
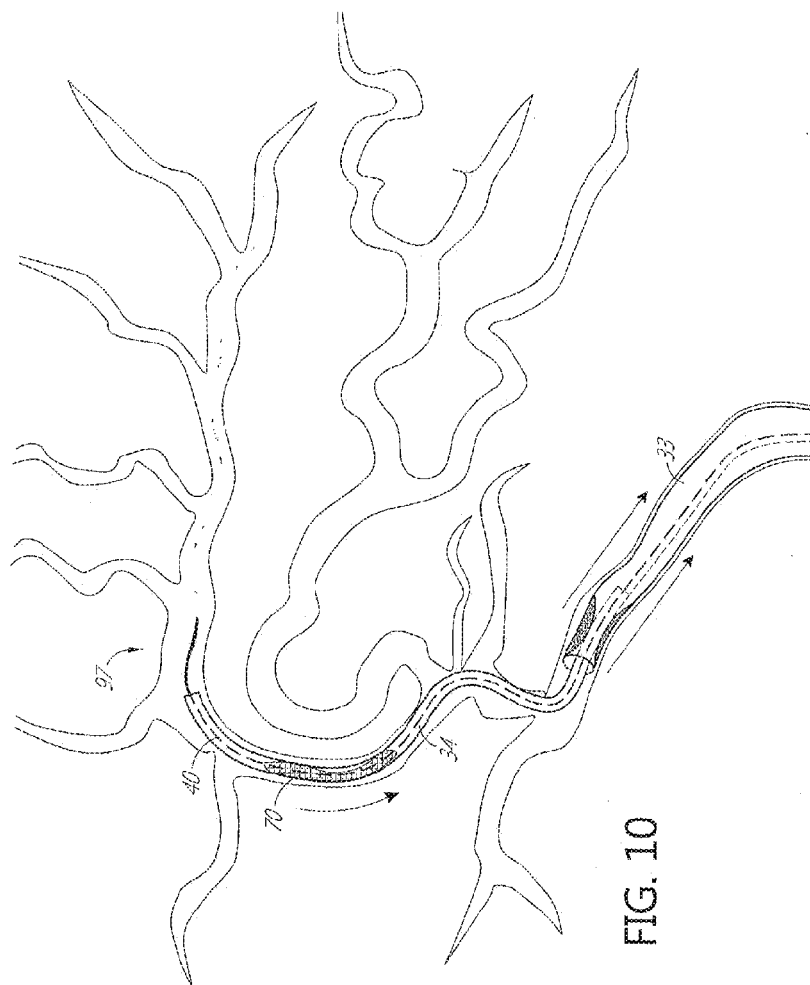
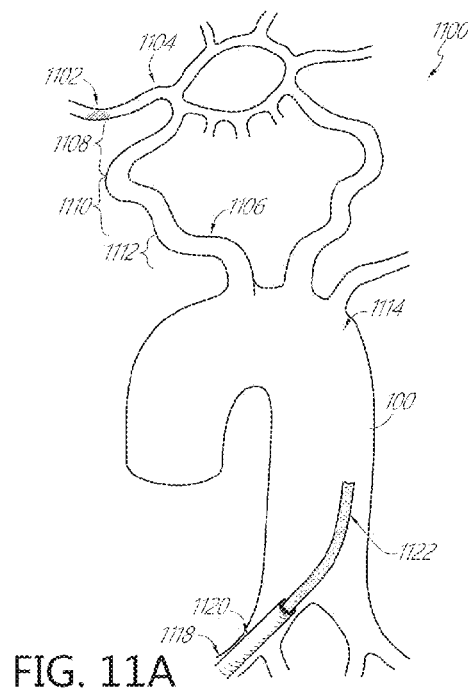
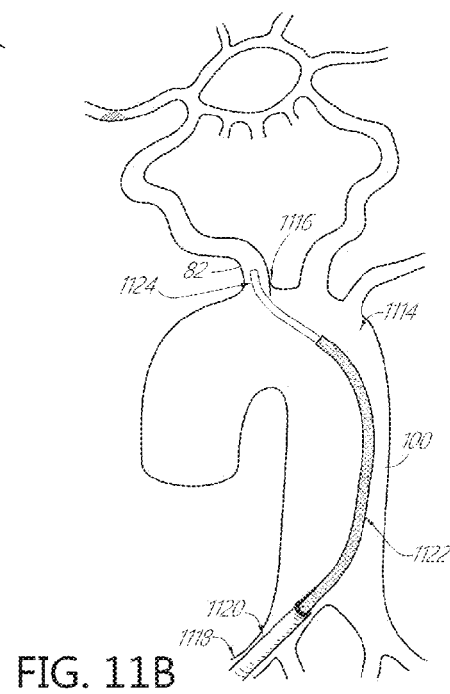
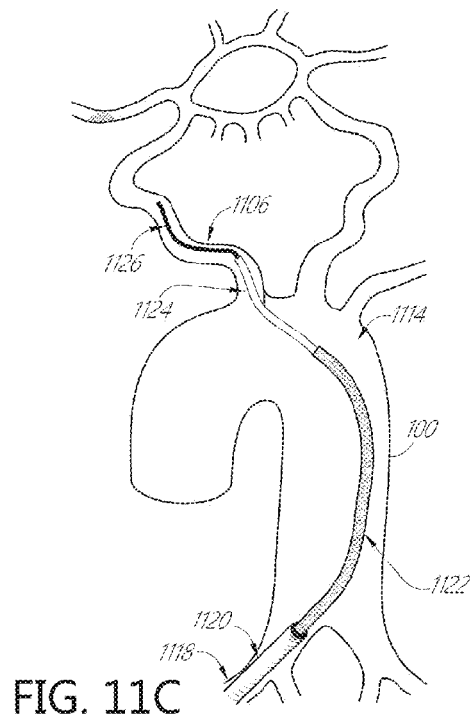
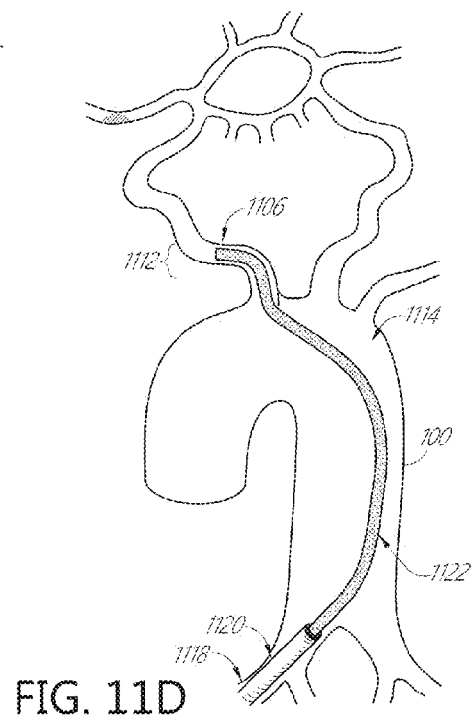


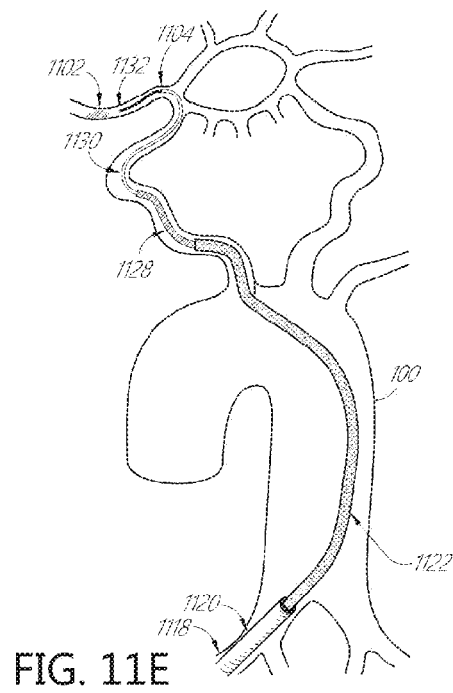
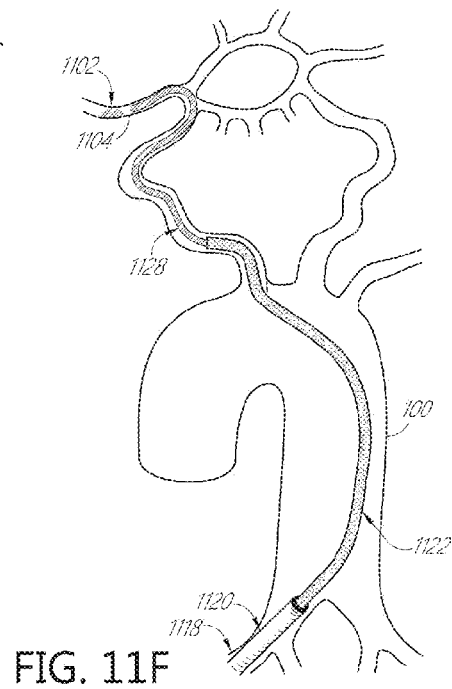
FIG. 8

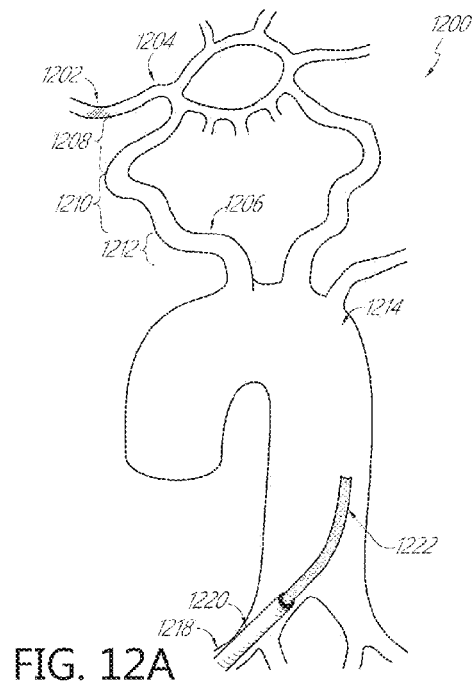
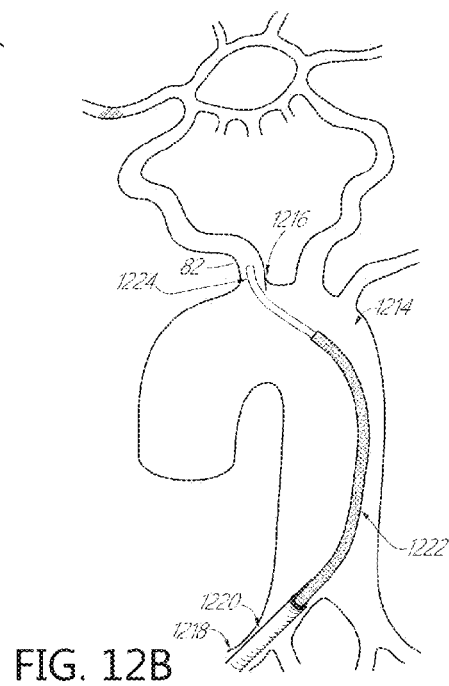


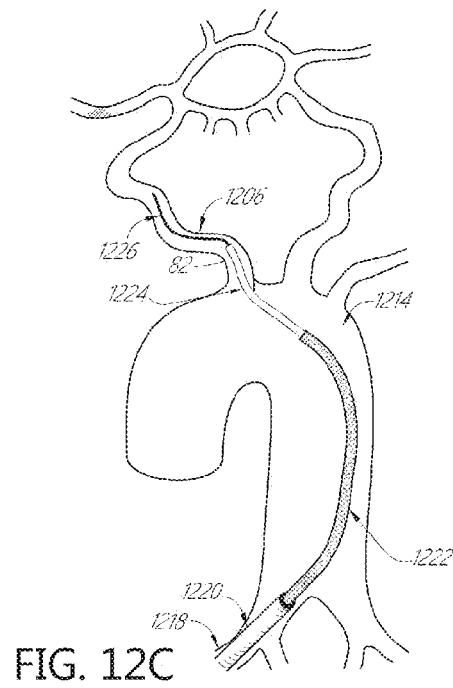
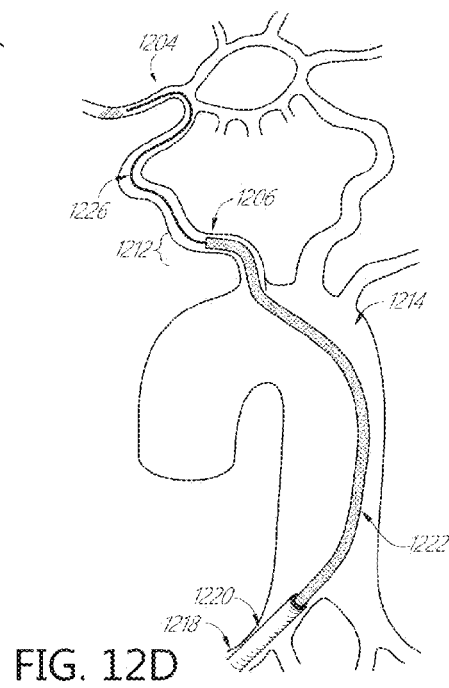


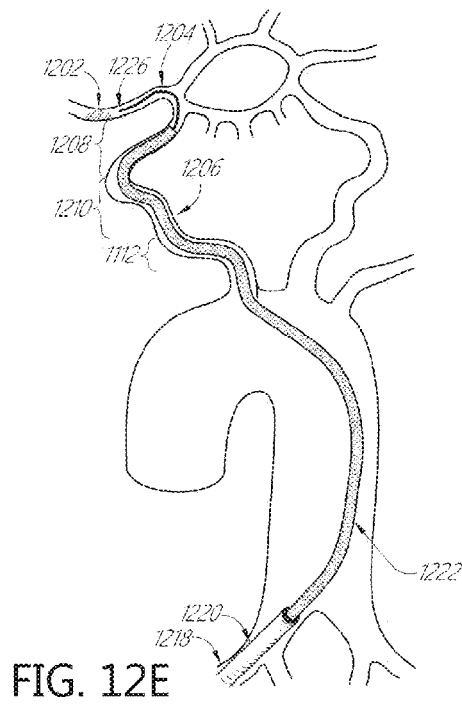
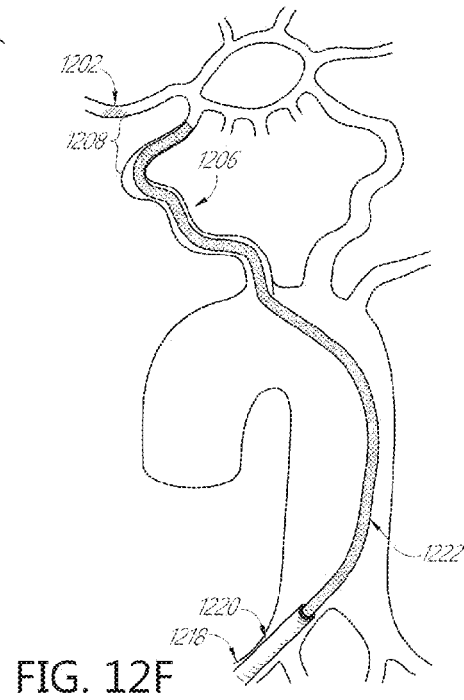












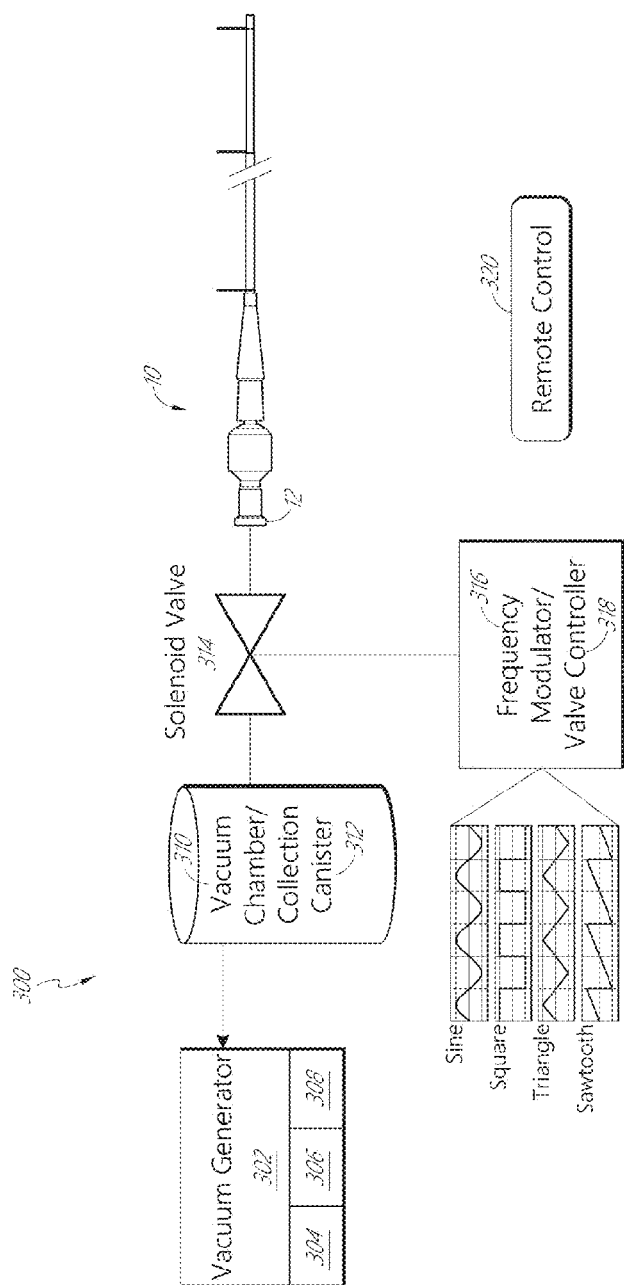


FIG. 13

FIG. 14

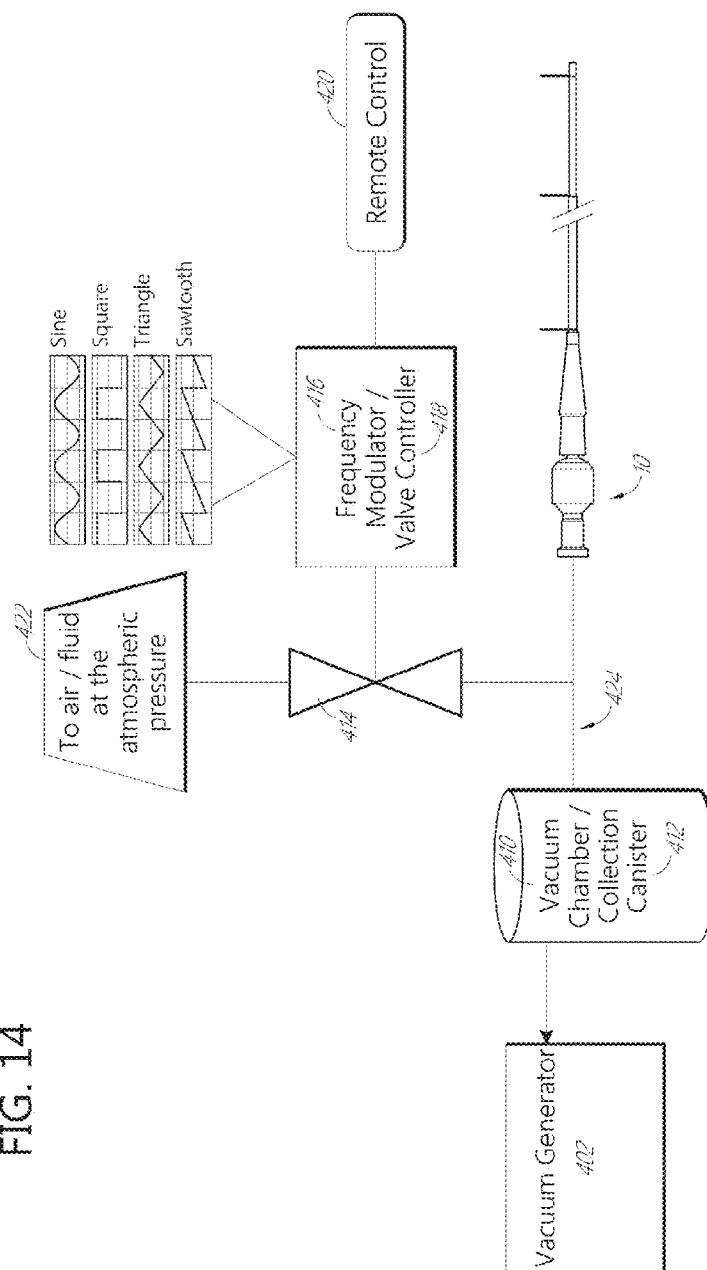
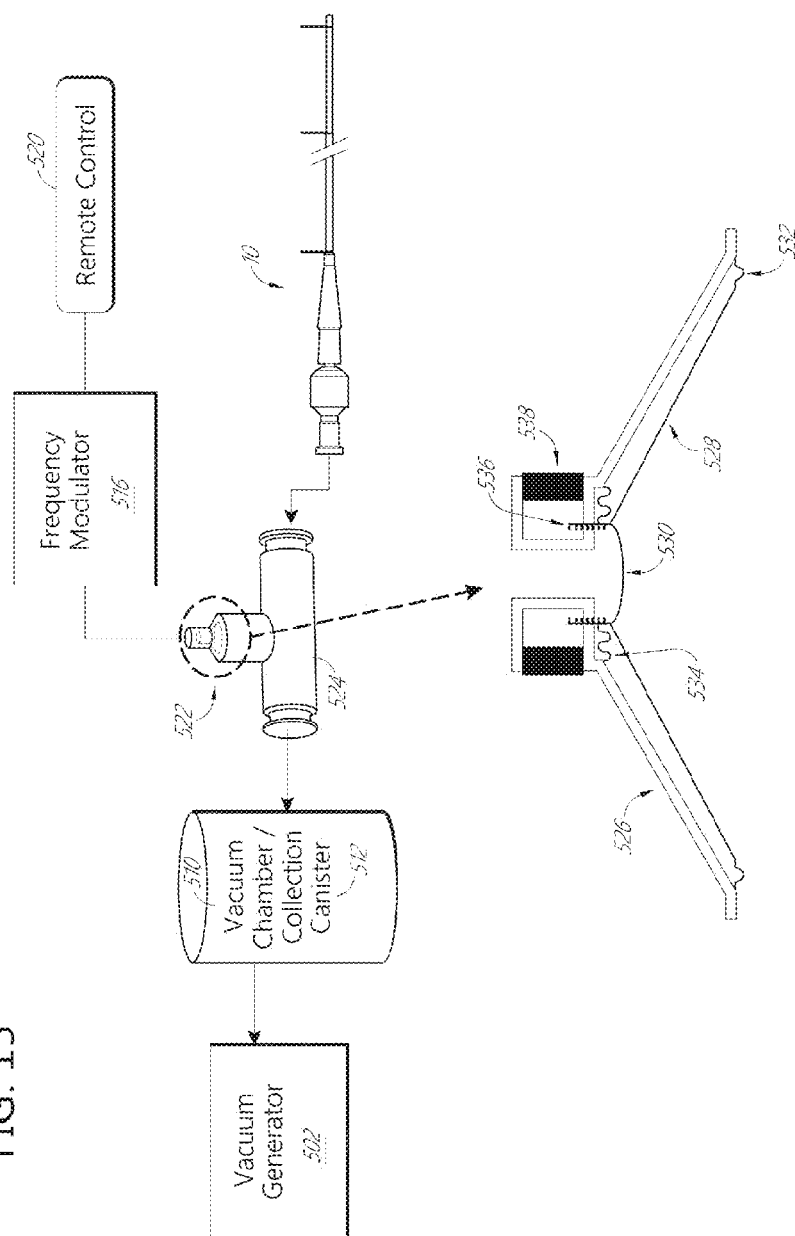


FIG. 15



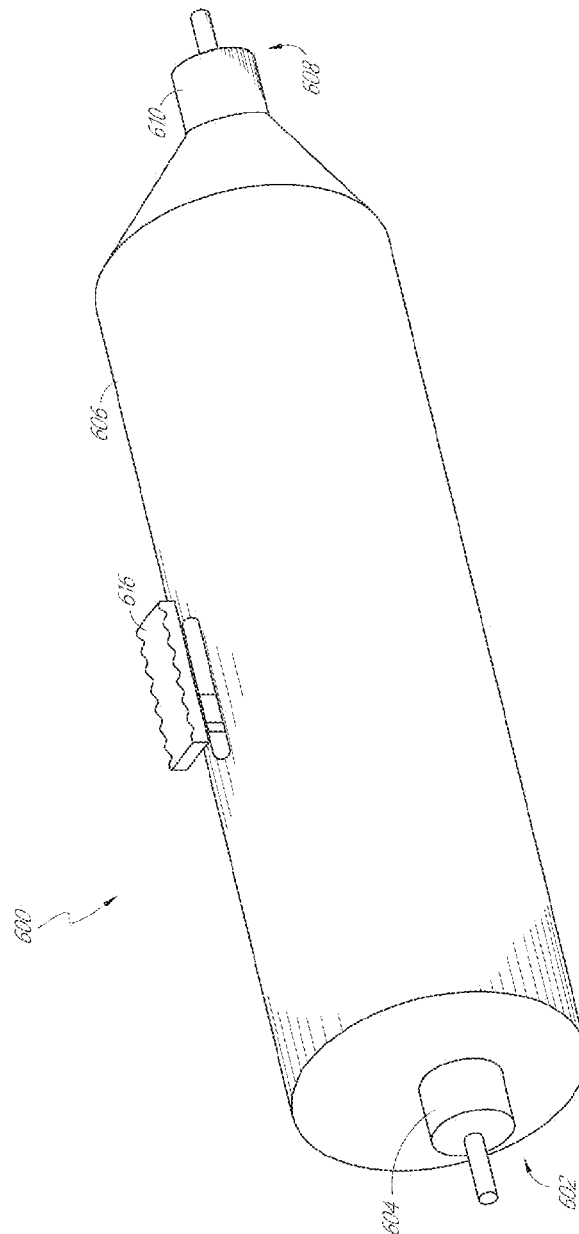


FIG. 16

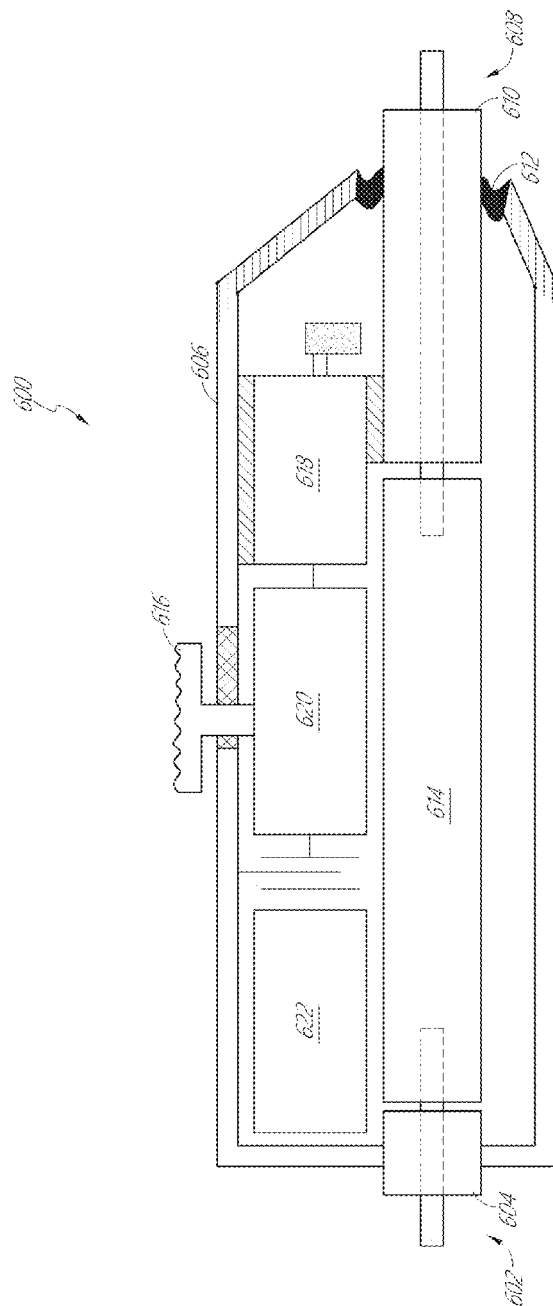


FIG. 17

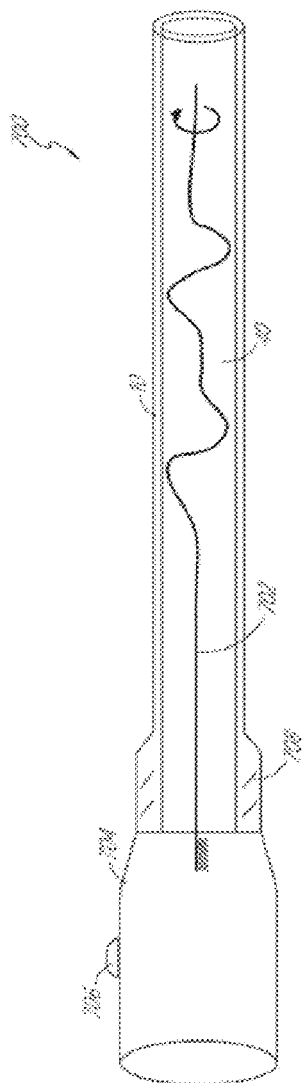


FIG. 18

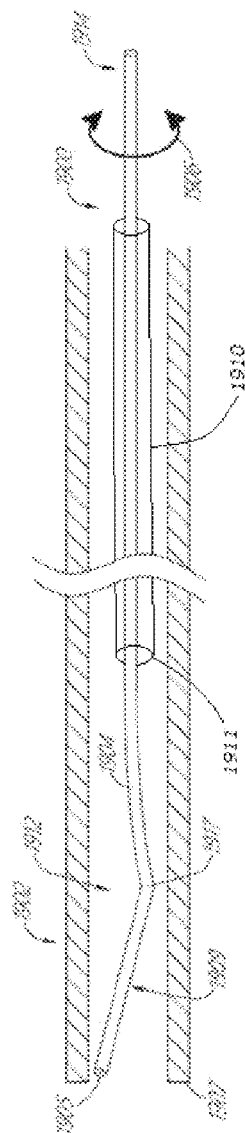


FIG. 19

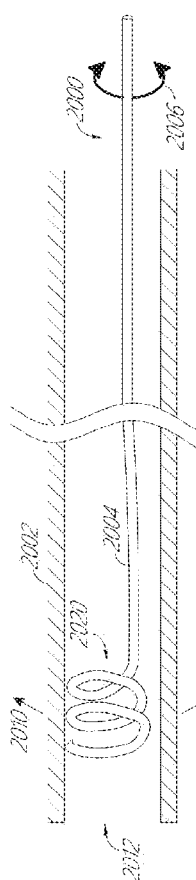


FIG. 20A

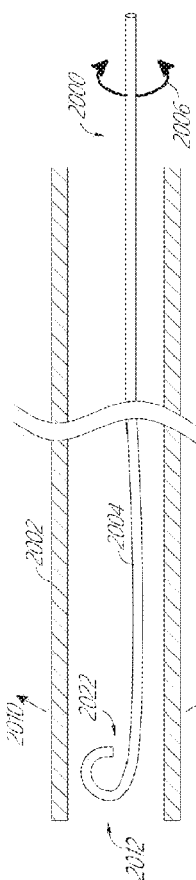


FIG. 20B

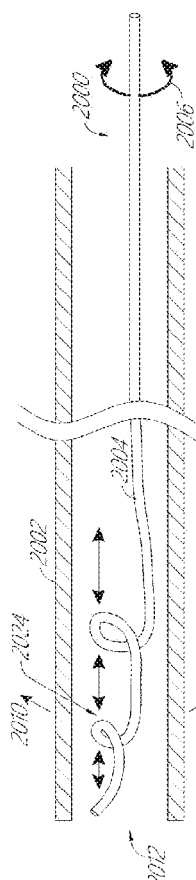


FIG. 20C

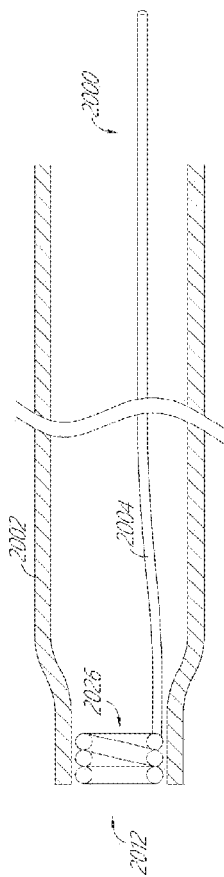


FIG. 20D

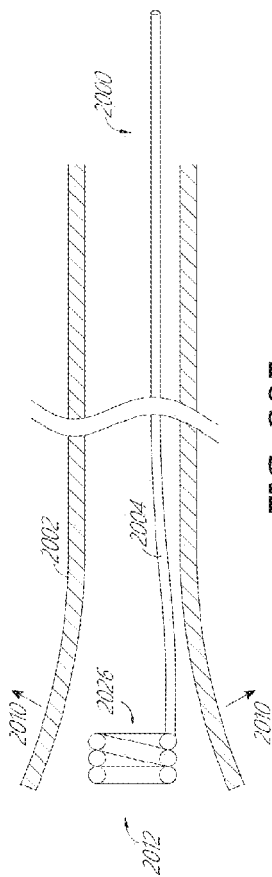


FIG. 20E

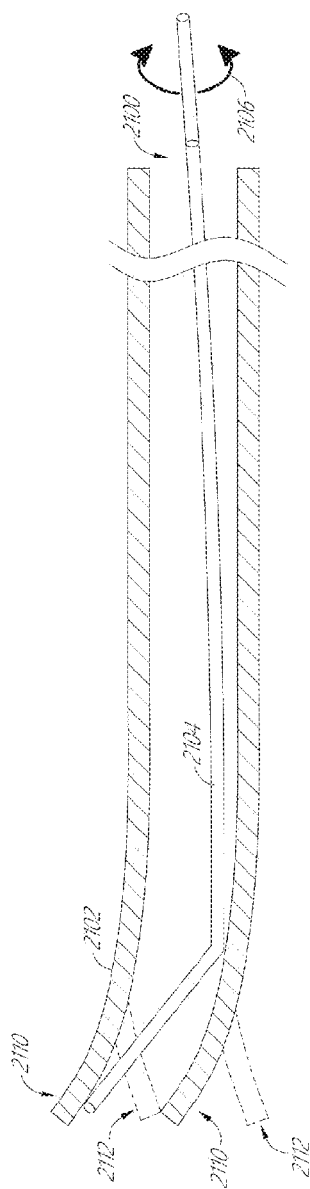


FIG. 21A

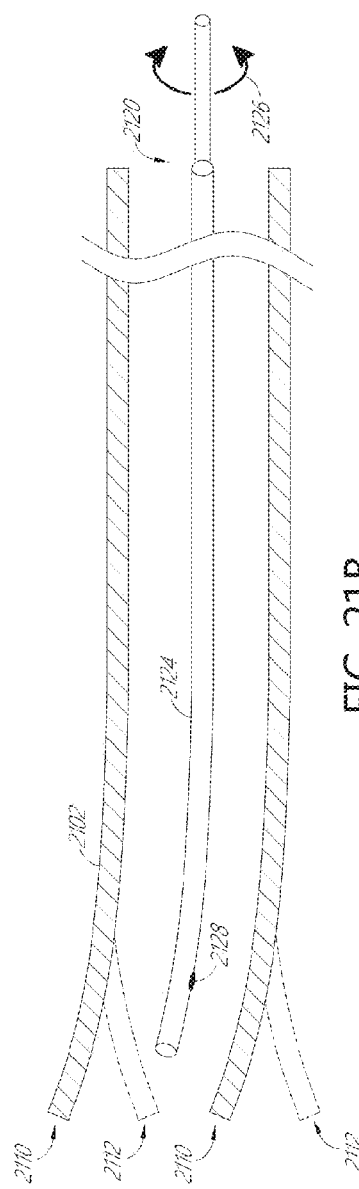


FIG. 21B

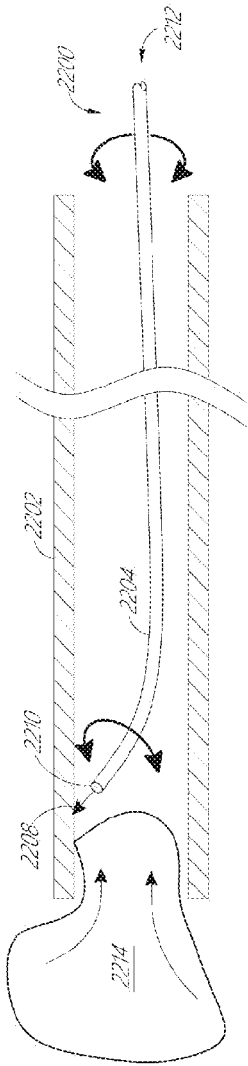


FIG. 22A

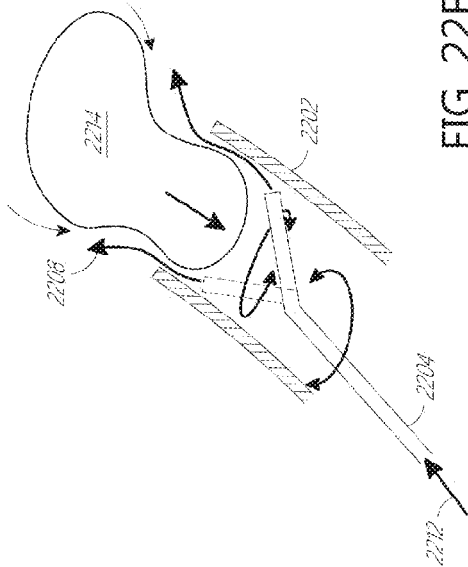


FIG. 22B

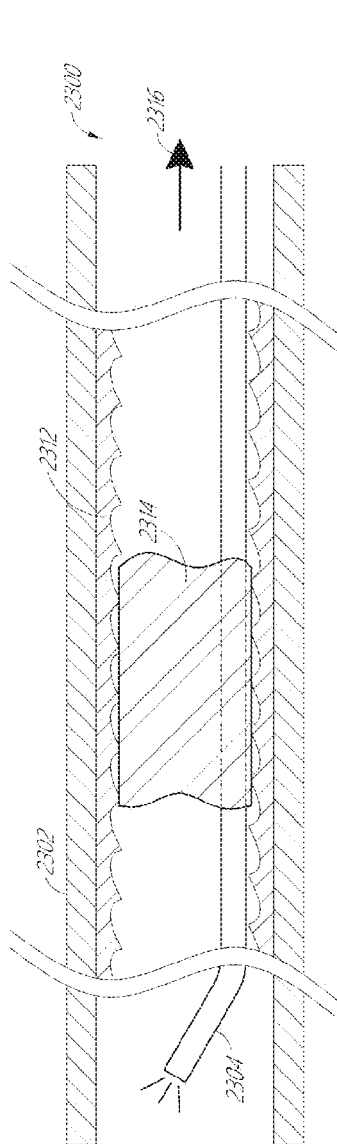


FIG. 23A

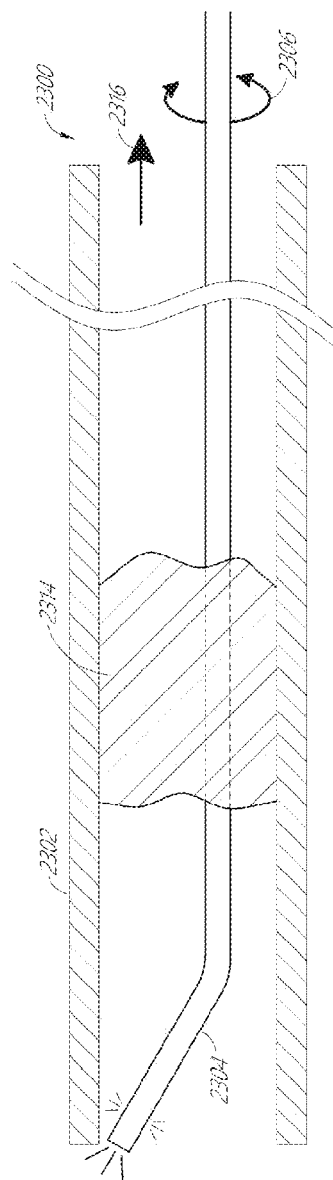


FIG. 23B

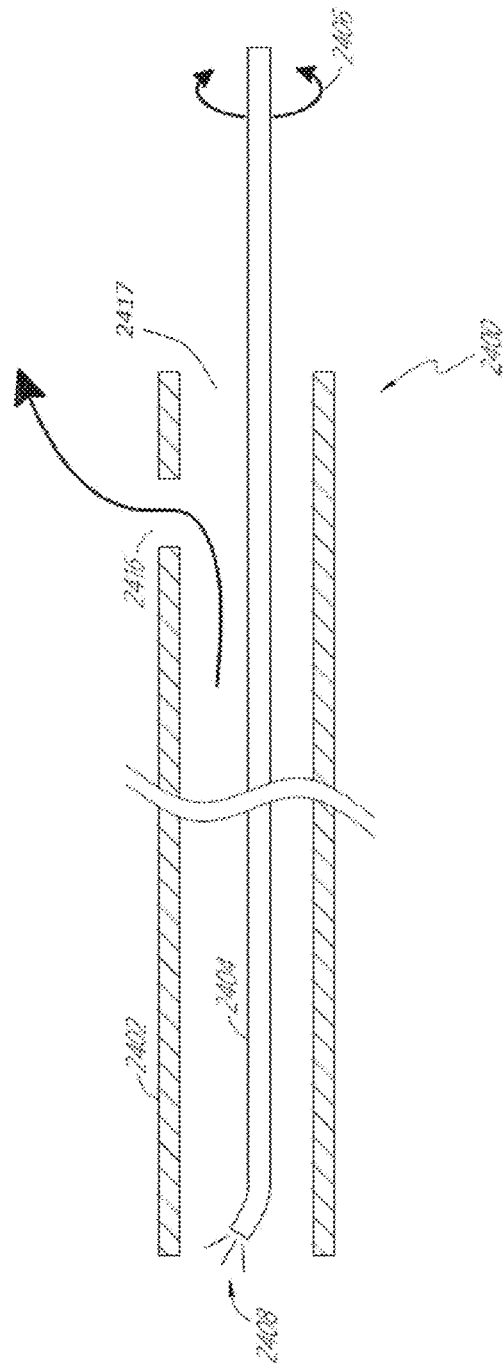
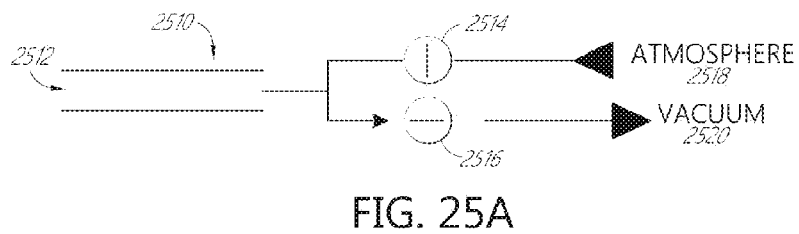
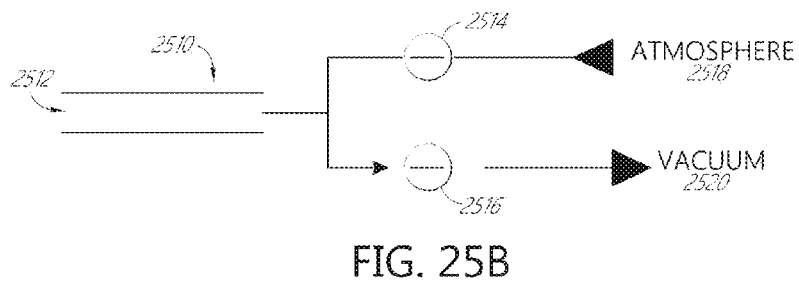
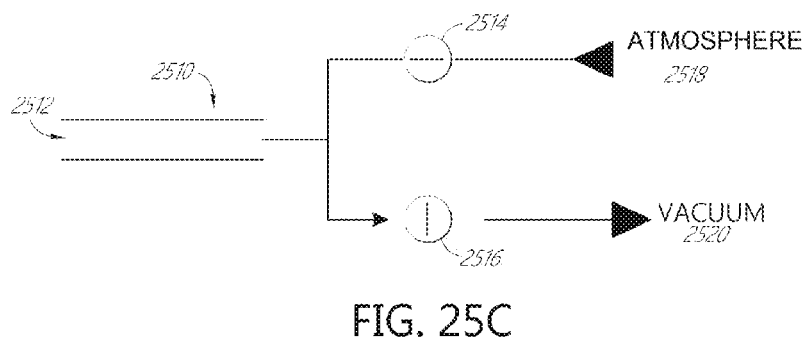


FIG. 24



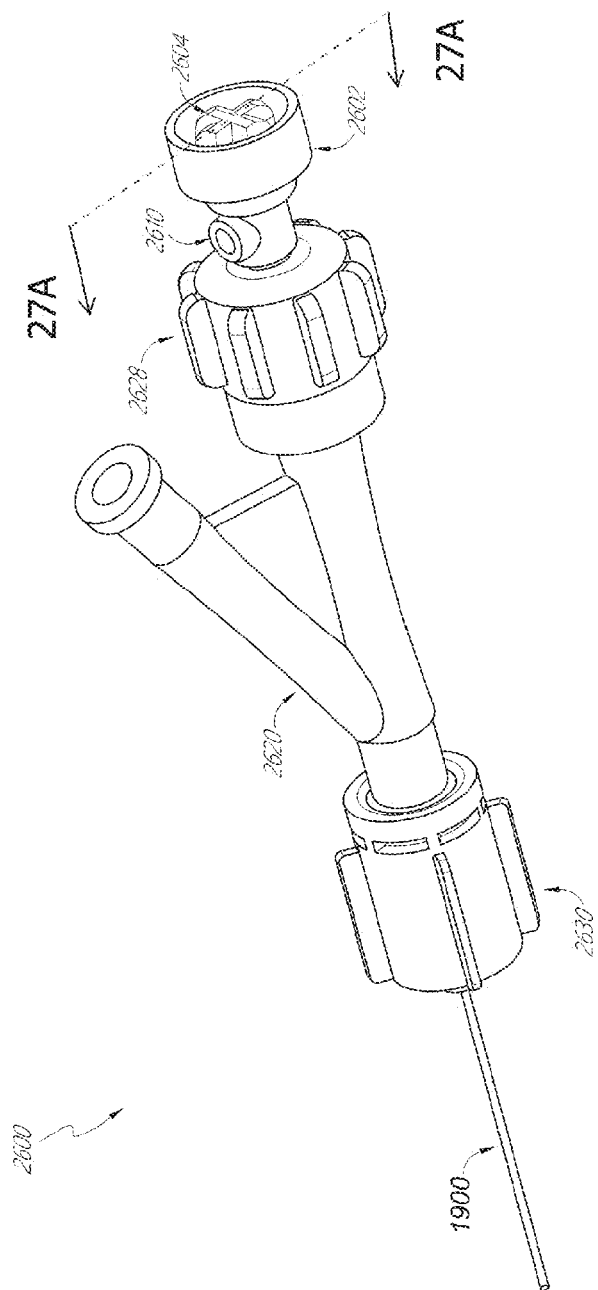


FIG. 26

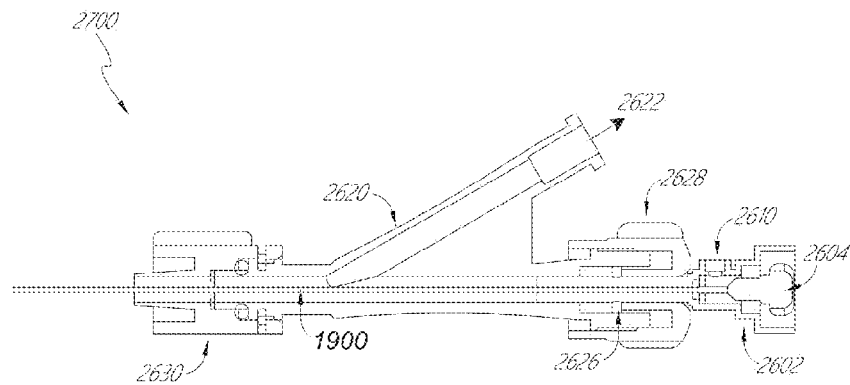


FIG. 27A

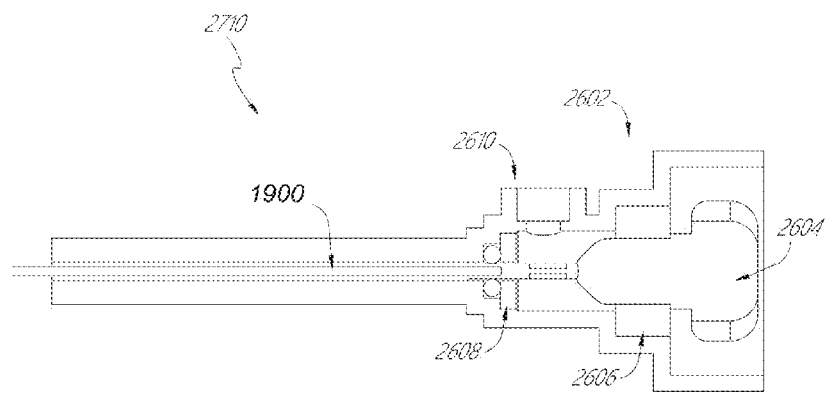


FIG. 27B

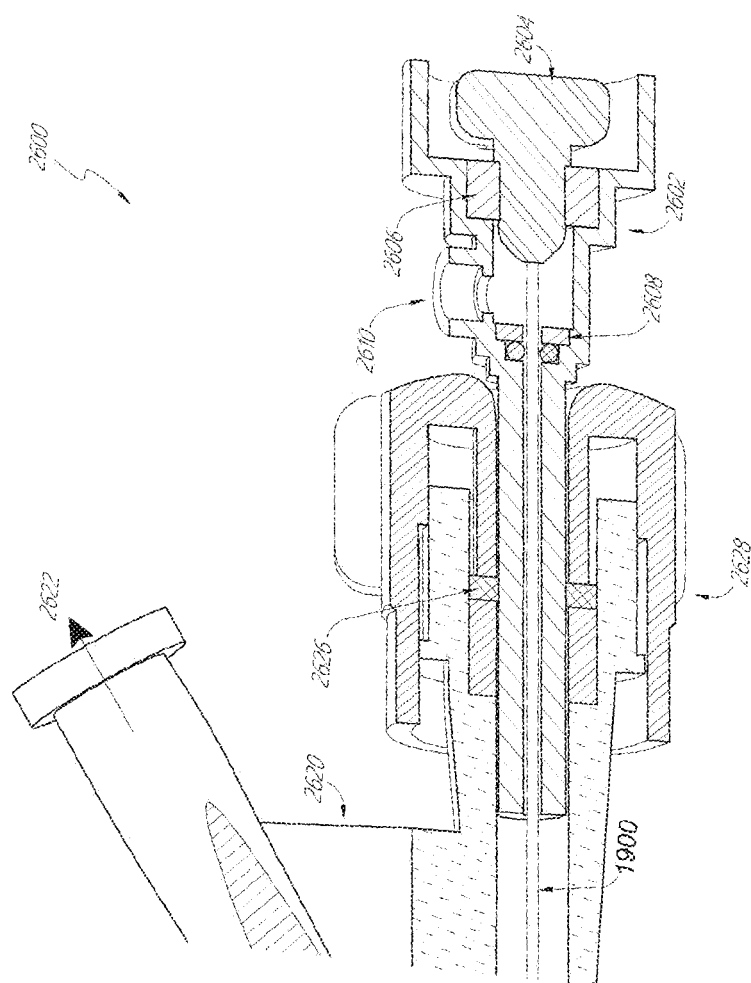


FIG. 28

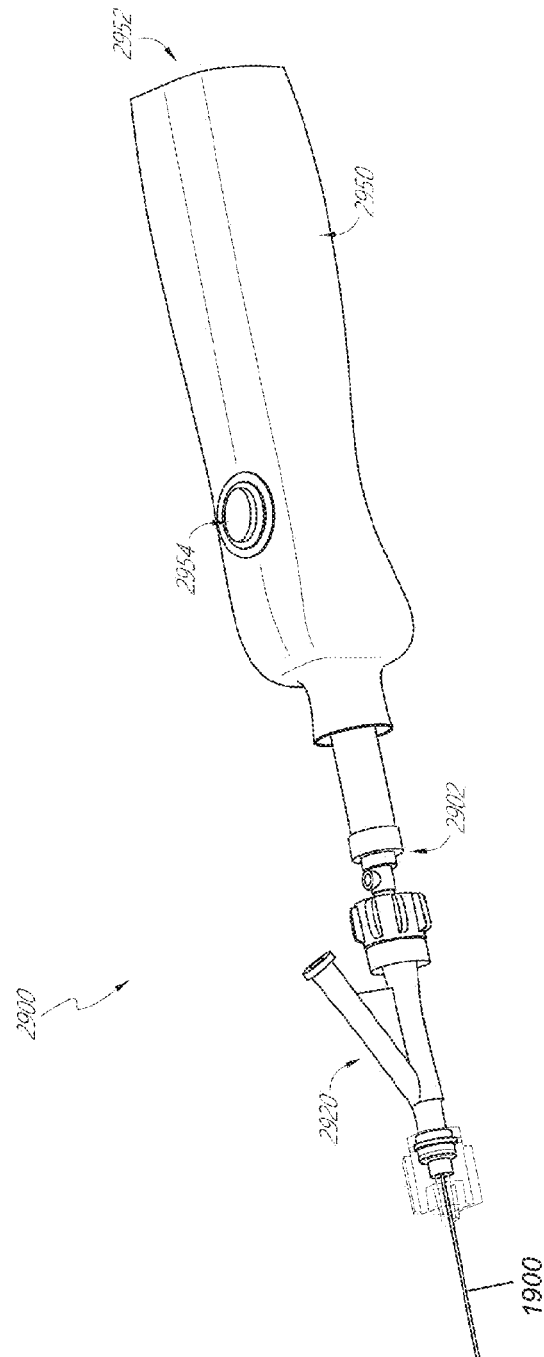


FIG. 29

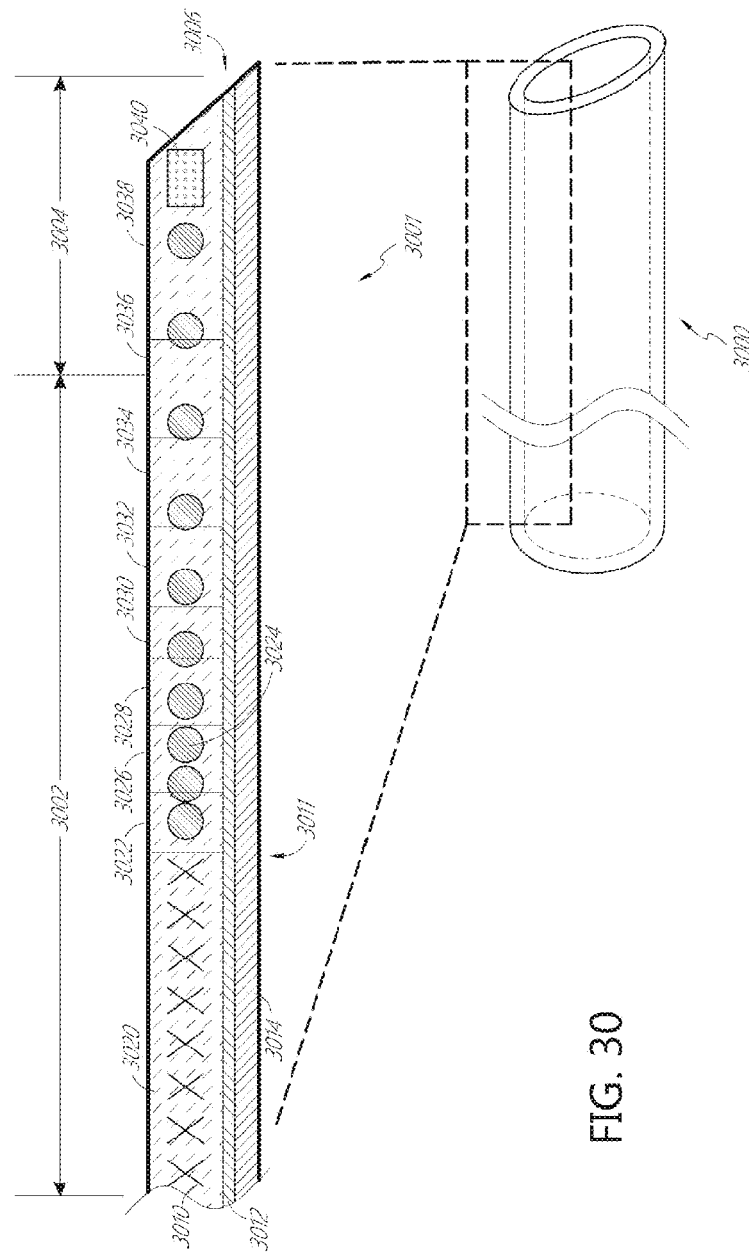


FIG. 30

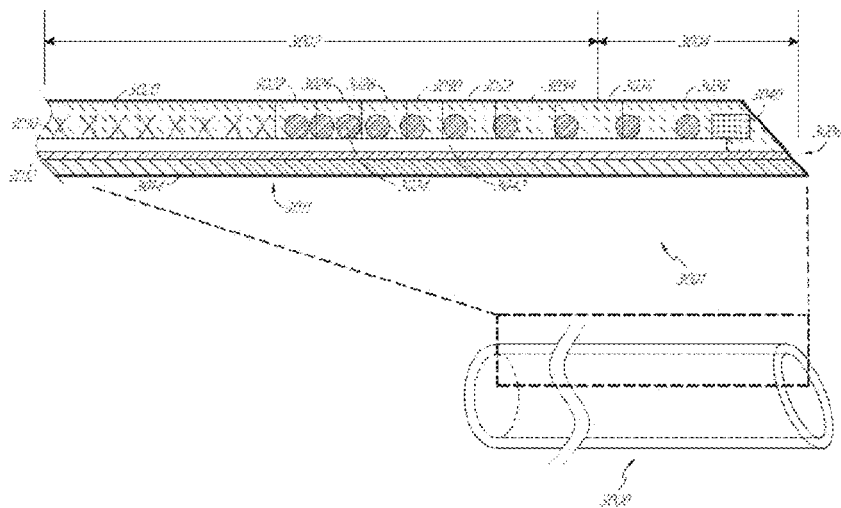


FIG. 31A

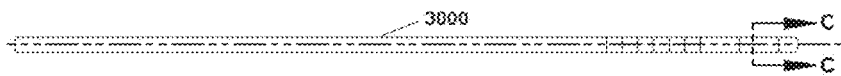


FIG. 31B

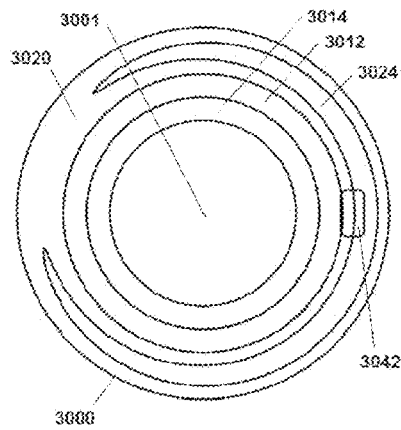


FIG. 31C

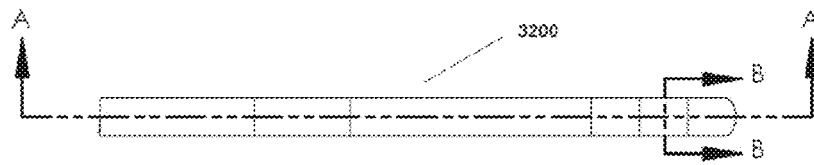


FIG. 32A

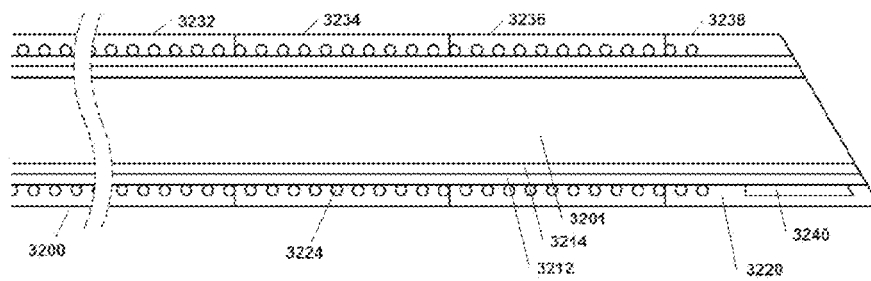


FIG. 32B

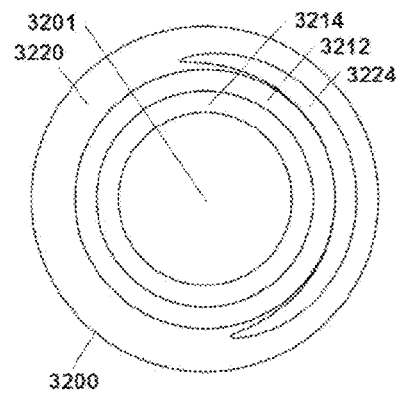


FIG. 32C

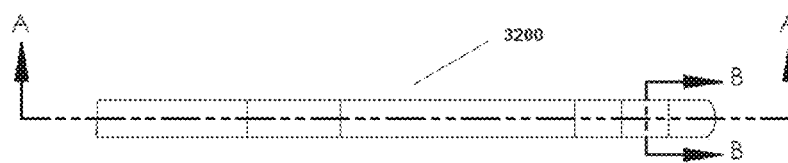


FIG. 33A

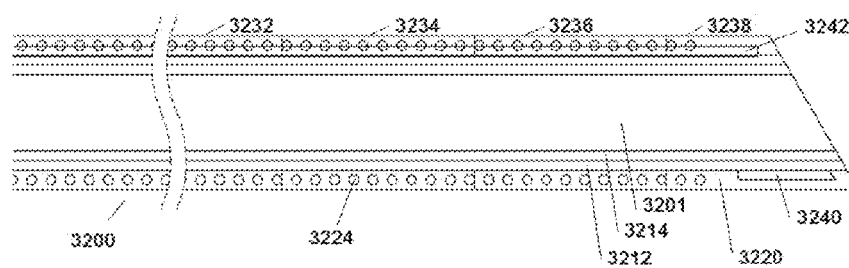


FIG. 33B

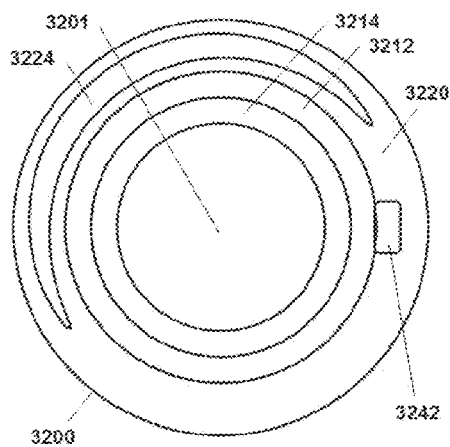
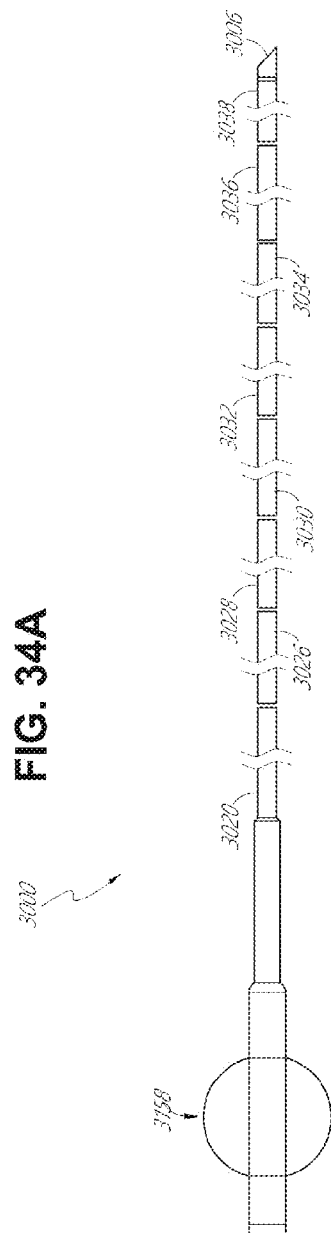
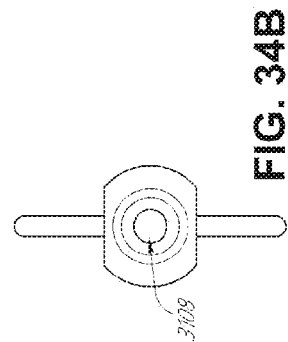


FIG. 33C



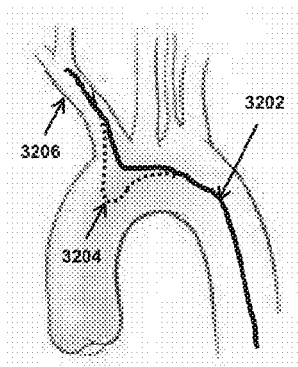


FIG. 35

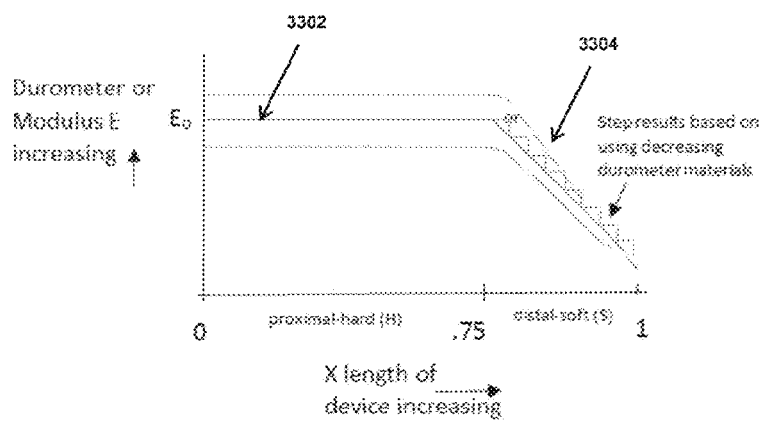
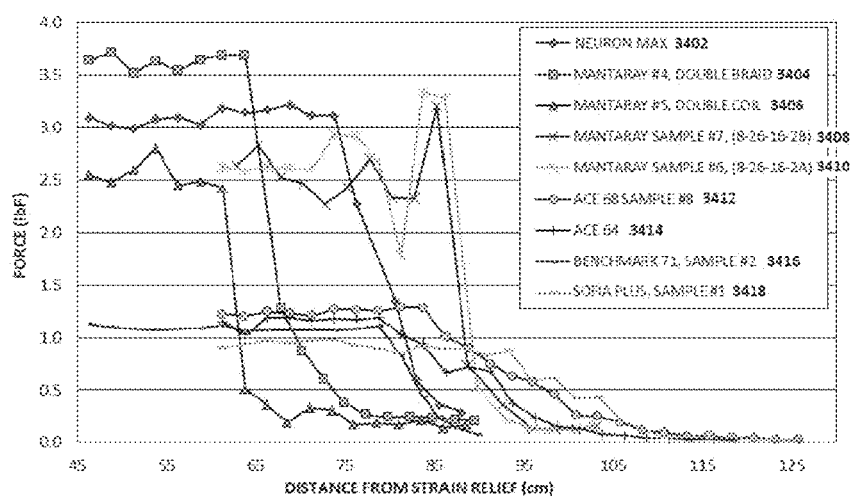
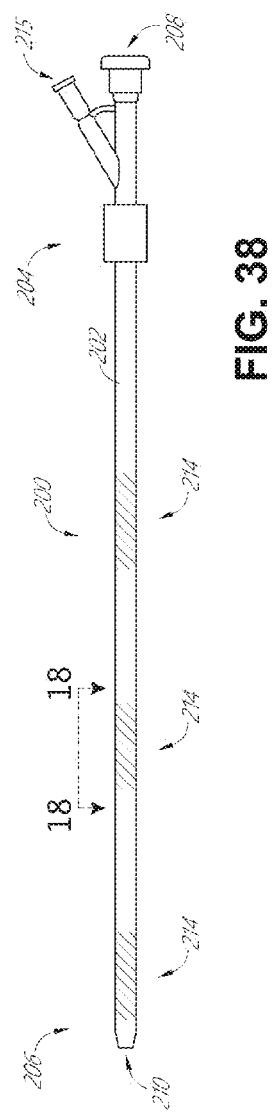
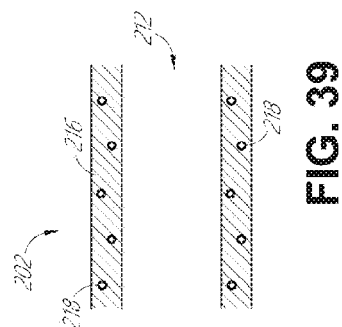


FIG. 36





**TELESCOPING NEUROVASCULAR
CATHETER WITH ACTIVE DISTAL TIP****CROSS-REFERENCE TO RELATED
APPLICATIONS**

[0001] This application is a continuation application of U.S. patent application Ser. No. 15/442,393, filed Feb. 24, 2017, which claims the benefit of U.S. Provisional Application No. 62/299,418, filed Feb. 24, 2016, and U.S. Provisional Application No. 62/443,595, filed Jan. 6, 2017, the entirety of these applications are hereby incorporated by reference herein.

BACKGROUND OF THE INVENTION

[0002] Stroke is the third most common cause of death in the United States and the most disabling neurologic disorder. Approximately 700,000 patients suffer from stroke annually. Stroke is a syndrome characterized by the acute onset of a neurological deficit that persists for at least 24 hours, reflecting focal involvement of the central nervous system, and is the result of a disturbance of the cerebral circulation. Its incidence increases with age. Risk factors for stroke include systolic or diastolic hypertension, hypercholesterolemia, cigarette smoking, heavy alcohol consumption, and oral contraceptive use.

[0003] Hemorrhagic stroke accounts for 20% of the annual stroke population. Hemorrhagic stroke often occurs due to rupture of an aneurysm or arteriovenous malformation bleeding into the brain tissue, resulting in cerebral infarction. The remaining 80% of the stroke population are ischemic strokes and are caused by occluded vessels that deprive the brain of oxygen-carrying blood. Ischemic strokes are often caused by emboli or pieces of thrombotic tissue that have dislodged from other body sites or from the cerebral vessels themselves to occlude in the narrow cerebral arteries more distally. When a patient presents with neurological symptoms and signs which resolve completely within 1 hour, the term transient ischemic attack (TIA) is used. Etiologically, TIA and stroke share the same pathophysiologic mechanisms and thus represent a continuum based on persistence of symptoms and extent of ischemic insult.

[0004] Emboli occasionally form around the valves of the heart or in the left atrial appendage during periods of irregular heart rhythm and then are dislodged and follow the blood flow into the distal regions of the body. Those emboli can pass to the brain and cause an embolic stroke. As will be discussed below, many such occlusions occur in the middle cerebral artery (MCA), although such is not the only site where emboli come to rest.

[0005] When a patient presents with neurological deficit, a diagnostic hypothesis for the cause of stroke can be generated based on the patient's history, a review of stroke risk factors, and a neurologic examination. If an ischemic event is suspected, a clinician can tentatively assess whether the patient has a cardiogenic source of emboli, large artery extracranial or intracranial disease, small artery intraparenchymal disease, or a hematologic or other systemic disorder. A head CT scan is often performed to determine whether the patient has suffered an ischemic or hemorrhagic insult. Blood would be present on the CT scan in subarachnoid hemorrhage, intraparenchymal hematoma, or intraventricular hemorrhage.

[0006] Traditionally, emergent management of acute ischemic stroke consisted mainly of general supportive care, e.g. hydration, monitoring neurological status, blood pressure control, and/or anti-platelet or anti-coagulation therapy. In 1996, the Food and Drug Administration approved the use of Genentech Inc.'s thrombolytic drug, tissue plasminogen activator (t-PA) or Activase®, for treating acute stroke. A randomized, double-blind trial, the National Institute of Neurological Disorders and t-PA Stroke Study, revealed a statistically significant improvement in stroke scale scores at 24 hours in the group of patients receiving intravenous t-PA within 3 hours of the onset of an ischemic stroke. Since the approval of t-PA, an emergency room physician could, for the first time, offer a stroke patient an effective treatment besides supportive care.

[0007] However, treatment with systemic t-PA is associated with increased risk of intracerebral hemorrhage and other hemorrhagic complications. Patients treated with t-PA were more likely to sustain a symptomatic intracerebral hemorrhage during the first 36 hours of treatment. The frequency of symptomatic hemorrhage increases when t-PA is administered beyond 3 hours from the onset of a stroke. Besides the time constraint in using t-PA in acute ischemic stroke, other contraindications include the following: if the patient has had a previous stroke or serious head trauma in the preceding 3 months, if the patient has a systolic blood pressure above 185 mm Hg or diastolic blood pressure above 110 mmHg, if the patient requires aggressive treatment to reduce the blood pressure to the specified limits, if the patient is taking anticoagulants or has a propensity to hemorrhage, and/or if the patient has had a recent invasive surgical procedure. Therefore, only a small percentage of selected stroke patients are qualified to receive t-PA.

[0008] Obstructive emboli have also been mechanically removed from various sites in the vasculature for years. Mechanical therapies have involved capturing and removing the clot, dissolving the clot, disrupting and suctioning the clot, and/or creating a flow channel through the clot. One of the first mechanical devices developed for stroke treatment is the MERCI Retriever System (Concentric Medical, Redwood City, Calif.). A balloon-tipped guide catheter is used to access the internal carotid artery (ICA) from the femoral artery. A microcatheter is placed through the guide catheter and used to deliver the coil-tipped retriever across the clot and is then pulled back to deploy the retriever around the clot. The microcatheter and retriever are then pulled back, with the goal of pulling the clot, into the balloon guide catheter while the balloon is inflated and a syringe is connected to the balloon guide catheter to aspirate the guide catheter during clot retrieval. This device has had initially positive results as compared to thrombolytic therapy alone.

[0009] Other thrombectomy devices utilize expandable cages, baskets, or snares to capture and retrieve clot. Temporary stents, sometimes referred to as stentrievors or revascularization devices, are utilized to remove or retrieve clot as well as restore flow to the vessel. A series of devices using active laser or ultrasound energy to break up the clot have also been utilized. Other active energy devices have been used in conjunction with intra-arterial thrombolytic infusion to accelerate the dissolution of the thrombus. Many of these devices are used in conjunction with aspiration to aid in the removal of the clot and reduce the risk of emboli. Suctioning of the clot has also been used with single-lumen catheters and syringes or aspiration pumps, with or without adjunct

disruption of the clot. Devices which apply powered fluid vortices in combination with suction have been utilized to improve the efficacy of this method of thrombectomy. Finally, balloons or stents have been used to create a patent lumen through the clot when clot removal or dissolution was not possible.

[0010] Notwithstanding the foregoing, there remains a need for new devices and methods for treating vasculature occlusions in the body, including acute ischemic stroke and occlusive cerebrovascular disease.

SUMMARY OF THE INVENTION

[0011] There is provided in accordance with one aspect, a telescoping catheter, comprising: an elongate, flexible tubular body, comprising a proximal section having at least one lumen and a distal section axially movably positioned within the lumen; and a control for advancing the distal section from a first, proximally retracted position within the proximal section to a second, extended position, extending distally beyond the proximal section; and an active tip on the distal end of the distal section, comprising a distal opening that is movable between a smaller and a larger configuration.

[0012] In one aspect of present disclosure, the control comprises a pull wire extending through the proximal section. In another aspect of present disclosure, the distal section is distally advanceable to extend beyond the proximal section for a distance of at least about 10 cm. In yet another aspect of present disclosure, the distal section is distally advanceable to extend beyond the proximal section for a distance of at least about 25 cm.

[0013] In one aspect of present disclosure, the distal opening is movable in response to movement of a control wire. In another aspect of present disclosure, the distal opening is movable between a smaller and a larger configuration in response to application of vacuum to the lumen. In yet another aspect of present disclosure, the size of the distal opening is changed by lateral movement of a side wall on the distal section. In yet another aspect of present disclosure, the distal opening comprises at least one movable jaw. In another aspect of present disclosure, the distal end of the distal section comprises a duck bill valve configuration.

[0014] In one aspect of present disclosure, the telescoping catheter may further comprise a controller for applying intermittent vacuum to the lumen. The controller may be configured to apply pulses of vacuum to the lumen spaced apart by spaces of neutral pressure. The controller may be configured to alternate between applying pulses of higher negative pressure and lower negative pressure. The distal tip of the catheter may axially reciprocate in response to application of pulses of vacuum to the lumen.

[0015] Any feature, structure, or step disclosed herein can be replaced with or combined with any other feature, structure, or step disclosed herein, or omitted. Further, for purposes of summarizing the disclosure, certain aspects, advantages, and features of the embodiments have been described herein. It is to be understood that not necessarily any or all such advantages are achieved in accordance with any particular embodiment disclosed herein. No individual aspects of this disclosure are essential or indispensable. Further features and advantages of the embodiments will become apparent to those of skill in the art in view of the Detailed Description which follows when considered together with the attached drawings and claims.

BRIEF DESCRIPTION OF THE DRAWINGS

[0016] FIG. 1 is a side elevational schematic view of an intracranial aspiration catheter in accordance with the present invention, with a distal segment in a proximally retracted configuration.

[0017] FIG. 2 is a side elevational view as in FIG. 1, with the distal segment in a distally extended configuration.

[0018] FIGS. 3A-3B are cross-sectional elevational views of a distal end of catheter 10, with the distal section 34 fully extended.

[0019] FIGS. 4A-4C schematically illustrate different cutting tip configurations.

[0020] FIGS. 4D-4E and 4J-4K schematically illustrate a distal dynamic funnel tip configuration.

[0021] FIGS. 4F-4G illustrate a dynamic flared tip having a first restraint system.

[0022] FIGS. 4H-4I illustrate a dynamic flared tip having an alternative restraint system.

[0023] FIG. 5 depicts cerebral arterial vasculature including the Circle of Willis, and an access catheter positioned at an occlusion in the left carotid siphon artery.

[0024] FIGS. 6 through 9 show a sequence of steps involved in positioning of the catheter and aspirating obstructive material from the middle cerebral artery.

[0025] FIG. 10 illustrates removal of the catheter following aspiration of obstructive material.

[0026] FIGS. 11A-11F depict a sequence of steps to access a neurovascular occlusion for aspiration.

[0027] FIGS. 12A-12F depict an alternative sequence of steps in accordance with an aspect of the present invention involved in accessing a neurovascular occlusion for aspiration.

[0028] FIG. 13 illustrates an aspiration system configured to apply pulsatile negative pressure through the aspiration catheter.

[0029] FIG. 14 illustrates an alternative aspiration system configured to apply pulsatile negative pressure through the aspiration catheter.

[0030] FIG. 15 illustrates a further alternative aspiration system configured to apply mechanical vibration through the aspiration catheter.

[0031] FIGS. 16 and 17 illustrate a further alternative aspiration system configured to apply mechanical vibration through the aspiration catheter.

[0032] FIG. 18 illustrates a further alternative aspiration system having an agitator configured to apply mechanical vibration at a vibration zone on the aspiration catheter.

[0033] FIG. 19 depicts a simplified agitator such as a hypo tube supported wire placed in a catheter to create a vibration zone.

[0034] FIGS. 20A-20C depict agitators with various distal tip configurations.

[0035] FIGS. 20D-20E depict an agitator positioned within a swellable polymer distal funnel tip.

[0036] FIGS. 21A-21B illustrate a moving or wiggling distal tip of a catheter in response to activating the agitator.

[0037] FIGS. 22A-22B illustrate media injection from a moving or wiggling distal tip of an agitator.

[0038] FIGS. 23A-23B illustrate media injection from a distal tip of an agitator to assist aspiration.

[0039] FIG. 24 depicts a proximal aspiration port carried by a catheter.

[0040] FIGS. 25A-25C depict a pulsed aspiration cycle according to an embodiment.

[0041] FIG. 26 depicts a perspective view of a rotating hemostasis valve and a proximal drive assembly.

[0042] FIG. 27A illustrates a longitudinal cross-sectional elevational view taken along the line 27A-27A in FIG. 26.

[0043] FIG. 27B illustrates an enlarged longitudinal cross-sectional elevational view of the proximal drive assembly 2602 from FIG. 27A.

[0044] FIG. 28 depicts a cross-sectional perspective view of the proximal portion of FIG. 26.

[0045] FIG. 29 depicts a perspective view of an agitator driver, a proximal drive assembly, and a rotating hemostasis valve.

[0046] FIG. 30 illustrates a cross-sectional elevational view of a catheter wall according to an embodiment.

[0047] FIG. 31A illustrates a cross-sectional elevational view of a catheter wall according to another embodiment, showing one or more axially extending filaments.

[0048] FIG. 31B describes a side elevational view of the catheter of FIG. 31A.

[0049] FIG. 31C illustrates a cross-sectional view taken along the line C-C of FIG. 31B, showing one or more axially extending filaments.

[0050] FIG. 32A depicts a side elevational view of a catheter according to one embodiment.

[0051] FIG. 32B describes a cross-sectional elevational view taken along the line A-A of FIG. 32A.

[0052] FIG. 32C illustrates a cross-sectional view taken along the line B-B of FIG. 32A.

[0053] FIG. 33A depicts a side elevational view of a catheter according to another embodiment.

[0054] FIG. 33B describes a cross-sectional elevational view taken along the line A-A of FIG. 33A, showing one or more axially extending filaments.

[0055] FIG. 33C illustrates a cross-sectional view taken along the line B-B of FIG. 33A, showing one or more axially extending filaments.

[0056] FIG. 34A illustrates a side elevational view of a progressively enhanced flexibility catheter according to an embodiment.

[0057] FIG. 34B is a proximal end view of the enhanced flexibility catheter of FIG. 34A.

[0058] FIG. 35 illustrates back-up support of the catheter in accordance with the present invention.

[0059] FIG. 36 depicts a graph of modulus or durometer of the catheter along the length of the catheter, from the proximal end to the distal end.

[0060] FIG. 37 depicts a graph of flexure test profiles of catheters in accordance with the present invention compared with conventional catheters.

[0061] FIG. 38 is a side elevational schematic view of a transformable catheter in accordance with the present invention.

[0062] FIG. 39 is a cross-sectional view taken along the lines 18-18 of FIG. 38, showing heating elements within the catheter sidewall.

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENT

[0063] Referring to FIG. 1, there is disclosed a catheter 10 in accordance with one aspect of the present invention. Although primarily described in the context of an axially extendable distal segment aspiration catheter with a single central lumen, catheters of the present invention can readily be modified to incorporate additional structures, such as

permanent or removable column strength enhancing mandrels, two or more lumen such as to permit drug, contrast or irrigant infusion or to supply inflation media to an inflatable balloon carried by the catheter, or combinations of these features, as will be readily apparent to one of skill in the art in view of the disclosure herein. In addition, the present invention will be described primarily in the context of removing obstructive material from remote vasculature in the brain, but has applicability as an access catheter for delivery and removal of any of a variety of diagnostics or therapeutic devices with or without aspiration.

[0064] The catheters disclosed herein may readily be adapted for use throughout the body wherever it may be desirable to distally advance a low profile distal catheter segment from a larger diameter proximal segment. For example, axially extendable catheter shafts in accordance with the present invention may be dimensioned for use throughout the coronary and peripheral vasculature, the gastrointestinal tract, the urethra, ureters, Fallopian tubes and other lumens and potential lumens, as well. The telescoping structure of the present invention may also be used to provide minimally invasive percutaneous tissue access, such as for diagnostic or therapeutic access to a solid tissue target (e.g., breast or liver or brain biopsy or tissue excision), delivery of laparoscopic tools or access to bones such as the spine for delivery of screws, bone cement or other tools or implants.

[0065] The catheter 10 generally comprises an elongate tubular body 16 extending between a proximal end 12 and a distal functional end 14. The length of the tubular body 16 depends upon the desired application. For example, lengths in the area of from about 120 cm to about 140 cm or more are typical for use in femoral access percutaneous transluminal coronary applications. Intracranial or other applications may call for a different catheter shaft length depending upon the vascular access site, as will be understood in the art.

[0066] In the illustrated embodiment, the tubular body 16 is divided into at least a fixed proximal section 33 and an axially extendable and retractable distal section 34 separated at a transition 32.

[0067] Referring to FIGS. 3A and 3B, there is illustrated a cross-sectional view of the distal segment 34 shown extended distally from the proximal segment 33 in accordance with the present invention. Distal segment 34 extends between a proximal end 36 and a distal end 38 and defines at least one elongate central lumen 40 extending axially therethrough. Distal end 38 may be provided with one or more movable side walls or jaws 39, which move laterally in the direction of an opposing side wall or jaw 41 under the influence of aspiration, to enable the distal end 38 to bite or break thrombus or other material into smaller particles, to facilitate aspiration through lumen 40. Both walls 39 and 41 may be movable towards and away from each other to break up thrombus as is discussed further below. For certain applications, the proximal section 33 may also or alternatively be provided with one or two opposing jaws, also responsive to vacuum or mechanical actuation to break up thrombus.

[0068] The inner diameter of the distal section 34 may be between about 0.030 inches and about 0.112 inches, between about 0.040 inches and about 0.102 inches, between about 0.045 inches and about 0.097 inches, between about 0.050 inches and about 0.092 inches, between about 0.055 inches

and about 0.087 inches, between about 0.060 inches and about 0.082 inches, between about 0.062 inches and about 0.080 inches, between about 0.064 inches and about 0.078 inches, between about 0.066 inches and about 0.076 inches, between about 0.068 inches and about 0.074 inches, or between about 0.070 inches and about 0.072 inches.

[0069] The inner diameter and the outer diameter of the distal section **34** may be constant or substantially constant along its longitudinal length. Alternatively, the distal section **34** may be tapered near its distal end. The distal section **34** may be tapered at less than or equal to about 5 cm, about 10 cm, about 15 cm, about 20 cm, about 23 cm, about 25 cm, about 30 cm, about 31 cm, about 35 cm, about 40 cm, about 45 cm, about 50 cm, about 60 cm, or about 70 cm from its distal end.

[0070] The inner diameter of the distal section **34** may be tapered or decreased near the distal end by less than or equal to about 95%, about 90%, about 85%, about 80%, about 75%, about 70%, about 65%, about 60%, about 55%, about 50%, about 45%, about 40%, about 35%, about 30%, about 25%, about 20%, about 10%, or about 5%. The inner diameter of the distal section **34** may be tapered or decreased near the distal end by greater than or equal to about 95%, about 90%, about 85%, about 80%, about 75%, about 70%, about 65%, about 60%, about 55%, about 50%, about 45%, about 40%, about 35%, about 30%, about 25%, about 20%, about 10%, or about 5%. The tapered inner diameter of the distal section **34** may be by less than or equal to about 0.11 inches, about 0.1 inches, about 0.090 inches, about 0.080 inches, about 0.070 inches, about 0.065 inches, about 0.060 inches, about 0.055 inches, about 0.050 inches, about 0.045 inches, about 0.040 inches, about 0.035 inches, about 0.030 inches, about 0.025 inches, about 0.020 inches, about 0.015 inches, or about 0.010 inches.

[0071] The length of the distal section **34** may be between about 13 cm and about 53 cm, between about 18 cm and about 48 cm, between about 23 cm and about 43 cm, or between about 28 cm and about 38 cm. The length of the distal section **34** may be less than or equal to about 20 cm, about 25 cm, about 30 cm, about 33 cm, about 35 cm, about 40 cm, about 41 cm, about 45 cm, about 50 cm, about 55 cm, about 60 cm, about 70 cm, or about 80 cm. The length of the distal section **34** may depend on the degree of tapering of the internal diameter of the distal section **34**.

[0072] The proximal end **36** of distal section **34** is provided with a proximally extending pull wire **42**. Pull wire **42** extends proximally throughout the length of the tubular body **16**, to control **24** which may be carried by manifold **18**. Axial movement of control **24** produces a corresponding axial movement of distal section **34** with respect to proximal section **33** as has been discussed. Alternatively, the proximal end of pull wire **42** may exit through a port on manifold **18**, such that it may be manually grasped and pulled or pushed by the clinician to extend or retract the distal section **34**. The length of the pull wire **42** may be between about 700 mm and about 1556 mm, between about 800 mm and about 1456 mm, between about 850 mm and about 1406 mm, between about 900 mm and about 1356 mm, between about 950 mm and about 1306 mm, between about 1000 mm and about 1256 mm, between about 1020 mm and about 1236 mm, between about 1040 mm and about 1216 mm, between about 1060 mm and about 1196 mm, between about 1080 mm and about 1176 mm, between about 1100 mm and about 1156

mm, between about 1110 mm and about 1146 mm, or between about 1120 mm and about 1136 mm.

[0073] Upon distal advance of pull wire **42** to its limit of travel, an overlap **44** remains between the proximal end **36** of distal section **34** and the proximal section **33**. This overlap **44** is configured to provide a seal to enable efficient transmission of vacuum from proximal section **33** to distal section **34**. Overlap **44** may be provided with any of a variety of additional features to facilitate a seal, such as a gasket, coating or tightly toleranced sliding fit. Preferably the clearance between the OD of the distal section **34** and ID of the proximal section **33**, at least in the vicinity of transition **32**, will be no more than about 0.005 inches and preferably no more than about 0.003 inches to provide an effective seal in a blood environment.

[0074] Following positioning of the distal end of proximal section **33** within the vasculature, such as within the cervical carotid artery, the control **24** is manipulated to distally advance distal section **34** deeper into the vasculature. For this purpose, the pull wire **42** will be provided with sufficient column strength to enable distal advance of the distal tip **38** as will be discussed below.

[0075] The pull wire **42** and distal section **34** may be integrated into a catheter as illustrated in FIGS. **1** and **2**. Alternatively, distal section **34** and pull wire **42** may be configured as a stand-alone catheter extension device as is discussed in greater detail below. The catheter extension device may be introduced into the proximal end of proximal section **33** after placement of proximal section **33** and advanced distally there through as illustrated in FIG. **3A**, to telescopically extend the reach of the aspiration system.

[0076] Referring to FIG. **3B**, the pull wire **42** may comprise a tubular wall having an axially extending central lumen **45**. The central lumen **45** permits introduction of media such as lubricants, drugs, contrast agents or others into the distal section **34**. In addition, the central lumen **45** extending through pull wire **42** permits introduction of an agitator as is discussed in greater detail below.

[0077] Referring to FIGS. **4A** through **4C**, the distal tip **38** may be provided any of a variety of structures which produce an active movement such as a biting action in response to the application of an activation force such as a vacuum in lumen **40**. Alternatively, an axially movable control wire may be connected with respect to a side wall of the distal tip **38**, to enable cutting action under positive mechanical force. FIG. **4A** illustrates a distal tip **38** in an open configuration, while FIG. **4B** illustrates distal tip **38** with opposing side walls **39** and **41** drawn together by the negative pressure in aspiration lumen **40**. This may be accomplished by providing a tapered thickness in side walls **39** and **41**, or a groove or living hinge which facilitates lateral movement of at least one of side wall **39** or **41**.

[0078] Alternatively, referring to FIG. **4C**, a pivot point or hinge **43** may be provided to enable lateral movement of side wall **39** to operate as a jaw. Two opposing side walls may be moveable medially and laterally with bilateral symmetry like a duck bill valve. Three or more jaws may be provided, such as three triangular jaws separated at about 120° spacing which under an aspiration pulse close to form a pyramid closed tip.

[0079] In some implementations of the present invention, the distal tip **14** is preferably provided with the capability to dilate beyond the nominal diameter of distal section **34**. This provides a conical funnel like tip with an enlarged distal

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

[0080] The flexible petals may be retained in a radially inwardly inclined configuration such as by application of negative pressure via lumen 40 during transluminal navigation of the distal section 34. Upon removal of the negative pressure, the panels may incline radially outwardly in response to a preset bias. Application of pulsatile vacuum may thereafter cause the panels to close radially inwardly to perform the biting function described previously.

[0081] The distal funnel opening may be actuated in a variety of other ways as will be apparent to those of skill in the art, such as by providing a pull wire or axially slideable outer or inner sleeve to open and close the funnel in response to mechanical movement of the wire or sleeve. Alternatively the funnel opening may be controlled by rotation of a control wire or tubular sleeve relative to the distal section 34, to activate an iris or spiral mechanism such as a helical ribbon or wire carried by the distal tip.

[0082] The normal state of the distal funnel may be a cylindrical configuration, and a mechanical, thermal or electrical actuator may be utilized to enlarge the distal funnel opening. Alternatively, the normal state of the funnel may be conical, and a mechanical, thermal or electrical actuator may be utilized to reduce the diameter such as for transluminal navigation. The petals or other wall of the funnel or elements disposed within the wall of the funnel may comprise a shape memory material such as a shape memory polymer or metal alloy such as nitinol, which may be laser cut from tube stock or woven into a fine mesh. The geometry of the funnel may be transformed by application of heat, such as body heat, or heat from a heat source carried by the catheter such as an electrical resistance wire within the wall or adjacent the catheter tip. Heat may alternatively be applied from a heat source introduced by way of central lumen 40, such as a heated fluid, or a removable heater such as an elongate flexible body carrying a resistance coil. Transformation of the funnel from one configuration to the other may alternatively be accomplished by reducing the temperature of the funnel below body temperature such as by introducing a cooled fluid into thermal communication with the funnel tip or providing the catheter or a removable cooling catheter with a Joule-Thomson expansion chamber located near the distal end.

[0083] In an alternate configuration, the sidewall of the funnel is provided with an inflatable balloon in the form of a ring or hoop, in communication with an inflation lumen extending throughout the length of the catheter. Introduction of inflation media inflates the annular balloon, transforming the configuration of the funnel tip from a reduced diameter to an enlarged diameter.

[0084] In an alternate configuration, the distal tip is biased into the funnel configuration, and restrained into a cylindrical configuration such as for transluminal navigation. When

the funnel tip is desired to be enlarged, the restraint can be removed. The restraint may comprise an outer tubular covering membrane or loop configured to be removed by pulling a pull wire in a proximal direction. Alternatively, the restraint may be a bioabsorbable material, which dissolves following a preset amount of time that exceeds the anticipated time from vascular access to reach the final intravascular position.

[0085] Referring to FIGS. 4J-4K, the distal flared tip may comprise embedded elastic elements (e.g., a coil, struts or cage) such as spring steel, Nitinol or others known in the art that bias the tip into the flared configuration. The elastic elements such as in the form of a Nitinol cage may alternatively reside on the ID of the catheter. The polymer tip restrains the elastic elements to provide a cylindrical exterior configuration for transluminal navigation as seen in FIG. 4J. Softening the polymer (e.g., a hydrophilic blend) such as by body heat or moisture allows the elastic elements to transform the tip into the funnel configuration as seen in FIG. 4K. Alternatively, a conical NiTi cage at the tip is coated with a double hydrophilic non-cross linked glue. As the catheter advances the glue dissolves and gradually flares the tip into a funnel. The polymer tip may be formed without embedded elastic components and instead comprise a coextrusion with multiple layers, varying thickness in multiple layers, blending hydrophilic components at different ratios to control flaring. Multiple axially extending pull wires may be embedded through extruded lumen extending axially throughout the catheter wall. The wires are pushed or pulled to open/close the catheter distal end to flare or collapse. Funnel-shaped, underexpanded NiTi stent can be deployed at the tip area straddling between high and low durometer regions but greater length into high durometer region. Once ready to engage a clot, the stent can be pushed distally further into the low durometer tip. After complete clot retrieval the stent is pulled back into high durometer region, collapsing the funnel. This is an example of an active on-demand funneling tip.

[0086] Referring to FIG. 4F, there is illustrated a cross-sectional view of a distal end of a tubular catheter body such as distal section 34. The tubular body is provided with a distal tip 38 in the form of a self expandable (e.g., Nitinol) mesh 50, constrained by an outer tubular restraint 52. Restraint 52 may comprise a proximally retractable tubular body extending proximally to a control on the proximal manifold; a peel away sheath carried by an elongate proximally retractable pull wire, or other mechanism disclosed elsewhere herein. As shown in FIG. 4G, proximal retraction of tubular restraint 52 with respect to tubular body 34, or distal advance of tubular body 34 with respect to restraint 52 exposes and releases the mesh 50 to self expand to a funnel shape to facilitate capture and removal of intravascular debris.

[0087] Referring to FIGS. 4H and 4I, the self expandable conical mesh 50 is restrained by interweaving an internal restraint wire 54. Restraint wire 54 may be a procedure guide wire, or a dedicated restraint wire. Proximal retraction of the restraint wire 54 releases the mesh 50, to self expand to a final, funnel configuration. Release of the mesh 50 may be accomplished in a variety of alternative ways, such as bio absorbable materials, and electrolytic detachment.

[0088] The proximal end 12 of catheter 10 is additionally provided with a manifold 18 having one or more access ports

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

[0089] Manifold **18** may additionally be provided with a control **24**, for controlling the axial position of the distal segment **34** of the catheter. Control **24** may take any of a variety of forms depending upon the mechanical structure and desired axial range of travel of the distal segment **34**. In the illustrated embodiment, control **24** comprises a slider switch which is mechanically axially movably linked to the distal segment such that proximal retraction of the slider switch **24** produces a proximal movement of the distal segment **34**. This retracts the distal segment **34** into the proximal section **33** as illustrated in FIG. 1. Distal axial advancement of the slider switch **24** produces a distal axial advance of the distal segment **34**, as illustrated in FIGS. 2 and 3.

[0090] Any of a variety of controls may be utilized, including switches, buttons, levers, rotatable knobs, pull/push wires, and others which will be apparent to those of skill in the art in view of the disclosure herein. The control will generally be linked to the distal segment by a control wire **42**.

[0091] Alternatively, the proximal section **33** and distal section **34** maybe provided as separate devices, in which construction the proximal control may be omitted. The distal end of proximal section **33** may be provided with one or more jaws as has been discussed previously herein, for morcellating or otherwise breaking thrombus or other obstruction into pieces or otherwise facilitating aspiration. The proximal section **33** may additionally be mechanically coupled to or adapted for coupling to a source of vibrational or rotational movement, such as to provide the intermittent or pulsatile movement discussed elsewhere herein to facilitate navigation into the vasculature.

[0092] Using axial reciprocation, and/or rotation, and/or biting action of the distal jaws, the clinician may be able to reach the obstruction using proximal section **33**. See, for example, FIG. 5 in which proximal section **33** is able to reach an obstruction in the left carotid siphon. If, however, the proximal section **33** is not able to advance sufficiently close to the obstruction, a separate telescoping distal section **34** may be introduced into the proximal section **33** and advanced therethrough and beyond, as illustrated in FIGS. 2 and 6-10, to reach the obstruction.

[0093] The cerebral circulation is regulated in such a way that a constant total cerebral blood flow (CBF) is generally maintained under varying conditions. For example, a reduction in flow to one part of the brain, such as in acute ischemic stroke, may be compensated by an increase in flow to another part, so that CBF to any one region of the brain remains unchanged. More importantly, when one part of the brain becomes ischemic due to a vascular occlusion, the

brain compensates by increasing blood flow to the ischemic area through its collateral circulation.

[0094] FIG. 5 depicts cerebral arterial vasculature including the Circle of Willis. Aorta **100** gives rise to right brachiocephalic artery **82**, left common carotid artery (CCA) **80**, and left subclavian artery **84**. The brachiocephalic artery **82** further branches into right common carotid artery **85** and right subclavian artery **83**. The left CCA gives rise to left internal carotid artery (ICA) **90** which becomes left middle cerebral artery (MCA) **97** and left anterior cerebral artery (ACA) **99**. Anteriorly, the Circle of Willis is formed by the internal carotid arteries, the anterior cerebral arteries, and anterior communicating artery **91** which connects the two ACAs. The right and left ICA also send right posterior communicating artery **72** and left posterior communicating artery **95** to connect, respectively, with right posterior cerebral artery (PCA) **74** and left PCA **94**. The two posterior communicating arteries and PCAs, and the origin of the posterior cerebral artery from basilar artery **92** complete the circle posteriorly.

[0095] When an occlusion occurs acutely, for example, in left carotid siphon **70**, as depicted in FIG. 5, blood flow in the right cerebral arteries, left external carotid artery **78**, right vertebral artery **76** and left vertebral artery **77** increases, resulting in directional change of flow through the Circle of Willis to compensate for the sudden decrease of blood flow in the left carotid siphon. Specifically, blood flow reverses in right posterior communicating artery **72**, right PCA **74**, left posterior communicating artery **95**. Anterior communicating artery **91** opens, reversing flow in left ACA **99**, and flow increases in the left external carotid artery, reversing flow along left ophthalmic artery **75**, all of which contribute to flow in left ICA **90** distal the occlusion to provide perfusion to the ischemic area distal to the occlusion.

[0096] As illustrated in FIG. 5, the proximal segment of catheter **10** is transluminally navigated along or over the guidewire, to the proximal side of the occlusion. Transluminal navigation may be accomplished with the distal section **34** of the catheter in the first, proximally retracted configuration. This enables distal advance of the proximal section **33** until further progress is inhibited by small and/or tortuous vasculature. Alternatively, the distal section **34** is a separate device, and is not inserted into the proximal section **33** until it is determined that the proximal section **33** cannot safely reach the occlusion. In the example illustrated in FIG. 5, the occlusion may be safely reached by the proximal section **33**, without the need to insert or distally extend a distal section **34**.

[0097] The distal end of the proximal section **33** of aspiration catheter **10** is inserted typically through an incision on a peripheral artery over a guidewire and advanced as far as deemed safe into a more distal carotid or intracranial artery, such as the cervical carotid, terminal ICA, carotid siphon, MCA, or ACA. The occlusion site can be localized with cerebral angiogram or IVUS. In emergency situations, the catheter can be inserted directly into the symptomatic carotid artery after localization of the occlusion with the assistance of IVUS or standard carotid doppler and TCD.

[0098] If it does not appear that sufficient distal navigation of the proximal section **33** to reach the occlusion can be safely accomplished, the distal section **34** is inserted into the proximal port **20** and/or distally extended beyond proximal

section 33 until distal tip 38 is positioned in the vicinity of the proximal edge of the obstruction.

[0099] Referring to FIG. 6, an obstruction 70 is lodged in the middle cerebral artery 97. Proximal section 33 is positioned in the ICA and not able to navigate beyond a certain point such as at the branch 96 to the MCA artery 97. The proximal section 33 may be provided with a distal section 34 carried there in. Alternatively, a separate distal section 34 may be introduced into the proximal end of proximal section 33 once the determination has been made that the obstruction 70 cannot be reached directly by proximal section 33 alone. As seen in FIGS. 7 and 8, the distal section 34 may thereafter be transluminally navigated through the distal tortuous vasculature between proximal section 33 and the obstruction 70.

[0100] Referring to FIG. 9, the obstruction 70 may thereafter be drawn into distal section 34 upon application of constant or pulsatile negative pressure with or without the use of jaws or other activation on the distal end of distal section 34 as discussed elsewhere herein. Once the obstruction 70 has either been drawn into distal section 34, or drawn sufficiently into distal section 34 that it may be proximately withdrawn from the body, proximal section 33 and distal section 34 are thereafter proximally withdrawn.

[0101] Aspiration may be applied via lumen 40, either in a constant mode, or in a pulsatile mode. Preferably, pulsatile application of vacuum will cause the distal tip 38 to open and close like a jaw, which facilitates reshaping the thrombus or biting or nibbling the thrombus material into strands or pieces to facilitate proximal withdrawal under negative pressure through lumen 40. Application of aspiration may be accompanied by distal advance of the distal tip 38 into the thrombotic material.

[0102] Pulsatile application of a vacuum may oscillate between positive vacuum and zero vacuum, or between a first lower negative pressure and a second higher negative pressure. Alternatively, a slight positive pressure may be alternated with a negative pressure, with the application of negative pressure dominating to provide a net aspiration through the lumen 40. Pulse cycling is discussed in greater detail in connection with FIG. 25.

[0103] The proximal manifold and/or a proximal control unit (not illustrated) connected to the manifold may enable the clinician to adjust any of a variety of pulse parameters including pulse rate, pulse duration, timing between pulses as well as the intensity of the pulsatile vacuum.

[0104] The distal section may thereafter be proximally retracted into proximal section 33 and the catheter proximally retracted from the patient. Alternatively, proximal retraction of the catheter 10 may be accomplished with the distal section 34 in the distally extended position. A vasodilator, e.g., nifedipine or nitroprusside, may be injected through a second lumen to inhibit vascular spasm induced as a result of instrumentation.

[0105] Pressure may be monitored by a manometer carried by the catheter or a wire positioned in a lumen of the catheter. A pressure control and display may be included in the proximal control unit or proximal end of the catheter, allowing suction within the vessel to be regulated.

[0106] Focal hypothermia, which has been shown to be neuroprotective, can be administered by perfusing hypothermic oxygenated blood or fluid. Moderate hypothermia, at approximately 32 to 34° C., can be introduced during the fluid infusion. Perfusion through a port on manifold 18 can

be achieved by withdrawing venous blood from a peripheral vein and processing through a pump oxygenator, or by withdrawing oxygenated blood from a peripheral artery, such as a femoral artery, and pumping it back into the carotid artery.

[0107] If continuous and/or intermittent suction fails to dislodge the occlusion, a thrombolytic agent, e.g., t-PA, can be infused through central lumen 40 or a second lumen to lyse any thrombotic material with greater local efficacy and fewer systemic complications. Administration of thrombolytic agent, however, may not be recommended for devices which are inserted directly into the carotid artery due to increased risk of hemorrhage.

[0108] The intensity of intermittent or pulsatile vacuum applied to lumen 40 may be adjusted to cause the distal tip 38 of the catheter 10 to experience an axial reciprocation or water hammer effect, which can further facilitate both transluminal navigation as well as dislodging or breaking up the obstruction. Water hammer, or more generally fluid hammer, is a pressure surge or wave caused when a fluid in motion is forced to stop or change direction suddenly, creating a momentum change. A water hammer commonly occurs when a valve closes suddenly at the end of a pipeline system, and a pressure wave propagates in the pipe. A pressure surge or wave is generated inside the lumen 40 of the aspiration catheter 10 when a solenoid or valve closes and stops the fluid flow suddenly, or other pulse generator is activated. As the pressure wave propagates in the catheter 10, it causes the catheter 10 to axially vibrate. Since vibration can reduce surface friction between the outer diameter of the catheter 10 and the inner diameter of the vessel wall, it enables catheter to track through tortuous anatomies as well as assist capturing thrombus.

[0109] Referring to FIGS. 11A-11F, the cerebral circulation 1100 is simplified for the ease of demonstrating procedural steps. A thrombotic occlusion 1102 is in the right middle cerebral artery (RMCA) 1104. The RMCA 1104 branches from the right internal carotid artery (RICA) 1106. The RICA 1106 branches from the right common carotid artery (RCCA) (not shown). The RICA 1106 comprises cerebral 1108 (most distal from the aorta 100), cavernous 1110, and petrous 1112 (most proximal from the aorta 100) segments. The RCCA branches from the brachiocephalic artery. The brachiocephalic artery branches from the arch 1114 of the aorta 100.

[0110] The procedural steps for aspirating a thrombotic occlusion are described as follows. Referring to FIG. 11A, an introducer sheath 1120 is introduced at the femoral artery 1118. The outer diameter of the introducer sheath 1120 may be equal to or less than about 12F, 11F, 10F, 9F, 8F, 7F, or 6F. Then, a guide sheath 1122 is inserted through the introducer sheath 1120. The outer diameter of the guide sheath 1122 may be equal to or less than about 9F, 8F, 7F, 6F, 5F, 4F, or 3F, and the inner diameter of the introducer sheath 1120 may be greater than the outer diameter of the guide sheath 1122.

[0111] Referring to FIG. 11B, an insert catheter 1124 is inserted through the guide sheath 1122. The outer diameter of the insert catheter 1124 may be equal to or less than about 9F, 8F, 7F, 6F, 5F, 4F, or 3F, and the inner diameter of the guide sheath 1122 may be greater than the outer diameter of the insert catheter 1124. In some cases, a first guidewire 1126 may be introduced through the insert catheter 1124 (not shown in FIG. 11B). Then, the guide sheath 1122, the insert

catheter **1124**, and optionally the first guidewire **1126** are tracked up to the aortic arch **1114**. The insert catheter **1124** is used to engage the origin of a vessel. In FIG. **11B**, the insert catheter **1124** engages the origin **1116** of the brachiocephalic artery **82**. An angiographic run is performed by injecting contrast media through the insert catheter **1124**. In the cases where the first guidewire **1126** is used before the angiographic run, the first guidewire **1126** is removed prior to injecting the contrast media.

[0112] Referring to FIG. **11C**, the first guidewire **1126** is inserted through the lumen of the insert catheter **1124**. Then, the first guidewire **1126**, the insert catheter **1124**, and the guide sheath **1122** are advanced together to the ICA **1106**. Referring to FIG. **11D**, due to the stiffness of a typical guide sheath **1122** currently available in the market (e.g., Neuron MAX System produced by Penumbra Inc.), the most distal vessel that the guide sheath **1122** could navigate to is the petrous segment **1112** of the ICA **1106**. Once the first guidewire **1126**, the insert catheter **1124**, and the guide sheath **1122** are advanced to the ICA **1106**, both the first guidewire **1126** and the insert catheter **1124** are removed.

[0113] Referring to FIG. **11E**, a second guidewire **1132** loaded inside the central lumen of a reperfusion catheter **1130** (e.g., 3Max), which is loaded inside the central lumen of an aspiration catheter **1128** (e.g., ACE 68), are introduced through the guide sheath **1122**. The diameter of the second guidewire **1132** may be equal to or less than about 0.03", about 0.025", about 0.02", about 0.016", about 0.014", about 0.01", or about 0.005". The inner diameter of the reperfusion catheter **1130** may be greater than the outer diameter of the second guidewire **1132**. The inner diameter of the aspiration catheter **1128** may be greater than the outer diameter of the reperfusion catheter **1130**. The inner diameter of the guide sheath **1122** may be greater than the outer diameter of the aspiration catheter **1128**. Then, the second guidewire **1132** is advanced distally and positioned at the proximal end of the clot **1102** in the MCA **1104**.

[0114] Referring to FIG. **11F**, the aspiration catheter **1128** is tracked over the reperfusion catheter **1130** and the second guidewire **1132** to the proximal end of the clot **1102** in the MCA **1104**. Both the second guidewire **1132** and the reperfusion catheter **1130** are removed. A vacuum pressure is then applied at the proximal end of the aspiration catheter **1128** to aspirate the clot **1102** through the central lumen of the aspiration catheter **1128**.

[0115] A preferable, simplified method for aspirating a thrombotic occlusion in accordance with the present invention is described in connection with FIGS. **12A-12F**. The alternative steps for aspirating a thrombotic occlusion make use of a transitional guidewire and a transitional guide sheath. The transitional guidewire has a soft and trackable distal segment with a smaller diameter so that the transitional guidewire may be advanced deeper than the guidewire **1126** described in FIG. **11C**. In addition, the transitional guide sheath has a soft and trackable distal segment such that the transitional guide sheath may be advanced deeper than the guide sheath **1122** described in FIG. **11D**. Using a transitional guidewire and a transitional guide sheath that can be advanced to an area near the clot eliminates the need to use a second guidewire or a reperfusion catheter to reach the clot.

[0116] Referring to FIG. **12A**, an introducer sheath **1220** is introduced at the femoral artery **1218**. The outer diameter of the introducer sheath **1220** may be equal to or less than about

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

[0117] The transitional guide sheath **1222**, the insert catheter **1224**, and optionally the first guidewire are tracked up to the aortic arch **1214**. See FIG. **12B**. The insert catheter **1224** may be used to select the origin of a vessel. In FIG. **12B**, the insert catheter **1224** engages the origin **1216** of the brachiocephalic artery **82**. An angiographic run may be performed by injecting contrast media through the insert catheter **1224**. In the cases where the first guidewire is used before the angiographic run, the first guidewire is preferably removed prior to injecting the contrast media.

[0118] Referring to FIG. **12C**, the transitional guidewire **1226** is inserted through the lumen of the insert catheter **1224** or guide sheath **1222**. The diameter of at least a portion of the transitional guidewire **1226** (e.g., proximal diameter) is substantially similar to that of the first guidewire **1126**. The diameter of at least a portion of the transitional guidewire **1226** (e.g., distal diameter) may be smaller than that of the first guidewire **1126** and may have a diameter along a proximal segment of at least about 0.030" and in one implementation about 0.038". A transition begins within the range of from about 15 cm-30 cm from the distal end, and typically no more than about 20 cm or 25 cm from the distal end, distally of which the diameter tapers down to no more than about 0.018" and in one implementation about 0.016". Referring to FIG. **12D**, if utilized, the insert catheter **1224** may be removed because it is too stiff to be advanced to the MCA **1204**. In certain implementations of the invention, the transitional guidewire **1226** provides sufficient back up support that the combination access and aspiration catheter **1224** may be advanced directly over the transitional guidewire without any intervening devices. Then, the transitional guidewire **1226** is advanced to the MCA **1204**. The transitional guidewire **1226** has a distal segment that has a smaller diameter than that of the first guidewire **1126** described in FIG. **11C**. The distal segment of the transitional guidewire **1226** comprises a soft and atraumatic tip and can be tracked to the remote neurovasculature such as the MCA **1204**, which is distal to the petrous segment **1212** of the ICA **1206**.

[0119] Referring to FIG. **12E**, the transitional guide sheath **1222** is advanced to or beyond the cavernous segment **1210** or the cerebral **1208** segment of the ICA **1206**. Unlike the guide sheath **1122** described in FIG. **11D**, the transitional guide sheath **1222** may be advanced to the cavernous segment **1210** or the cerebral **1208** segment of the ICA **1206** beyond the petrous segment **1212** because the transitional guide sheath **1222** has a soft yet trackable distal segment described in further detail below, for example in connection

with FIG. 30. The larger proximal diameter and stiffer body of the transitional guidewire 1226 may provide better support for the transitional guide sheath 1222 to track through the vasculature.

[0120] Referring to FIG. 12F, after the transitional guide sheath 1222 is advanced to the cerebral segment 1208 of the ICA 1206, the transitional guidewire 1226 is removed. Then, a vacuum pressure is applied at the proximal end of the transitional guide sheath 1222 to aspirate the clot 1202 through the central lumen of the transitional guide sheath 1222. The inner diameter of the transitional guide sheath 1222 may be equal to about or greater than about 0.100", about 0.088", about 0.080", about 0.070", or about 0.060". The inner diameter of the transitional guide sheath 1222 is larger than the aspiration catheter 1128 described in FIG. 11E, which translates to more effective aspiration. The cross-sectional area of the central lumen of the transitional guide sheath 1222 may be almost twice as large as that of the largest aspiration catheter 1128 currently available.

[0121] If the guide sheath 1222 is not able to track deep enough into the distal vasculature to reach the clot or other desired target site, a telescopic extension segment as discussed elsewhere herein may be introduced into the proximal end of sheath 1222 and advanced distally to extend beyond the distal end of the sheath 1222 and thereby extend the reach of the aspiration system. In one implementation of the invention, the extension segment has an ID of about 0.070".

[0122] If thrombotic material is not able to be drawn into the sheath 1222 or extension segment under constant vacuum, pulsatile vacuum may be applied as discussed below. If pulsatile vacuum does not satisfactorily capture the clot, an agitator may be advanced through the sheath 1222 and extension segment to facilitate drawing the clot into the central lumen. Additional details of the agitator and its use are disclosed below.

[0123] A pulsatile vacuum pressure aspirator may be used in order to improve effectiveness of aspiration for vascular thrombectomy and to improve catheter trackability through tortuous vasculatures. FIG. 13 shows an embodiment of a pulsatile vacuum pressure aspirator 300 that applies intermittent or pulsatile vacuum to lumen 40. In the illustrated embodiment, the pulsatile vacuum pressure aspirator 300 is in fluid connection with the proximal end 12 of the catheter 10 and comprises vacuum generator 302, vacuum chamber 310, collection canister 312, solenoid valve 314, frequency modulator 316, valve controller 318, and remote controller 320.

[0124] Vacuum generator 302 comprises a vacuum pump 304, a vacuum gauge 306, and a pressure adjustment control 308. The vacuum pump 304 generates vacuum. The vacuum gauge 306 is in fluid connection with the vacuum pump 304 and indicates the vacuum pressure generated by the pump 304. The pressure adjustment control 308 allows the user to set to a specific vacuum pressure. Any of a variety of controls may be utilized, including switches, buttons, levers, rotatable knobs, and others which will be apparent to those of skill in the art in view of the disclosure herein.

[0125] Vacuum chamber 310 is in fluid connection with the vacuum generator 302 and acts as a pressure reservoir and/or damper. Collection canister 312 is in fluid connection with the vacuum chamber 310 and collects debris. The collection canister 312 may be a removable vial that collects debris or tissues, which may be used for pathologic diag-

nosis. Vacuum chamber 310 and collection canister 312 may be separate components that are in fluid connection with each other or a merged component. In the illustrated embodiment, the vacuum chamber 310 and the collection canister 312 is a merged component and is in fluid connection with the vacuum generator 302.

[0126] Solenoid valve 314 is located in the fluid connection path between a luer or other connector configured to releasably connect to an access port of the catheter 10 and the vacuum chamber 310/collection canister 312. The solenoid valve 314 controls the fluid flow from the catheter 10 to the vacuum chamber 310/collection canister 312.

[0127] Pulsatile vacuum pressure aspirator 300 may comprise frequency modulator 316 for control of the solenoid valve 314. The frequency modulator 316 generates different electrical wave frequencies and forms, which are translated into the movement of the solenoid valve 314 by the valve controller 318. The wave forms generated from the frequency modulator 316 comprise sinusoidal, square, and sawtooth waves. The wave forms generated from the frequency modulator 316 typically have frequencies less than about 500 Hz, in some modes of operation less than about 20 Hz or less than about 5 Hz. The wave forms have duty cycles ranging from 0%, in which the solenoid valve 314 is fully shut, to 100%, in which the solenoid valve 314 is fully open.

[0128] Valve controller 318 modulates the solenoid valve 314 on and off. The valve controller 318 may be electrically or mechanically connected to the solenoid valve 314. Any of a variety of controls may be utilized, including electrical controllers, switches, buttons, levers, rotatable knobs, and others which will be apparent to those of skill in the art in view of the disclosure herein. The valve controller 318 may be mechanically controlled by users or may be electrically controlled by the frequency modulator 316. The frequency modulator 316 and the valve controller 318 may be separate components that are electrically or mechanically connected or a merged component.

[0129] Remote control 320 enables physicians to control the frequency modulator 316 and/or the valve controller 318 for various purposes, such as turning the valve on/off, selecting different wave frequencies, and selecting different wave forms, while manipulating the catheter 10 at the patient side. Remote control 320 may be in wired or wireless communication with aspirator 300.

[0130] By tuning frequency, duty cycle, and wave form, one skilled in the art may match or approximate the resonating frequency to the natural frequency of the catheter. This may further enhance the efficacy of aspiration. The natural frequency of the catheter is typically less than about 260 Hz.

[0131] In another embodiment, shown in FIG. 14, the solenoid valve 414 is positioned in and fluidly connects between the air/fluid reservoir 422 at the atmospheric pressure and the aspiration line 424 connecting the catheter 10 to the vacuum chamber 410/collection canister 412. Unlike the first embodiment in FIG. 13, this system modulates pressure in the catheter 10 by allowing pressure to vary from vacuum to atmospheric pressure. When the solenoid valve 414 is open to the air/fluid reservoir 422 at the atmospheric pressure, the vacuum pressure in the aspiration line 424 decreases to the atmospheric pressure. When the solenoid valve 414 is closed, it increases the vacuum pressure in the aspiration line 424.

[0132] In yet another embodiment, shown in FIG. 15, an electro-magnetic actuated diaphragm 522 is attached to the aspiration line 524 connecting the catheter 10 to the vacuum chamber 510/collection canister 512. The electromagnetic actuated diaphragm 522, which is similar to that of a speaker driver, generates acoustic pressure waves in the catheter 10. The diaphragm 522 typically has a structure similar to a speaker driver and comprises frame 526, cone 528, dust cap 530, surround 532, spider or damper 534, voice coil 536 and magnet 538. Strength of the acoustic pressure waves may be modulated by the strength of the magnet 538. The frequency modulator 516 connected to the remote control 520 is electrically connected to the diaphragm 522 and generates different electrical wave frequencies and forms, which are translated by the diaphragm 522 into acoustic pressure waves in the aspiration line 524 and the catheter 10.

[0133] Tortuous vasculature is a common reason for failure to treat vasculature occlusions in the body due to inability to track the catheter to the location of the disease. Navigating catheters through tortuous anatomy such as neurovasculature can be a challenge. The catheter has to be very soft as not to damage the vessel wall. At the same time, it also has to be able to negotiate multiple tight turns without kinking. In addition, it has to have sufficient column strength to transmit force axially for advancing through the vasculature. All these performance characteristics are competing design requirements. It is difficult to optimize one performance characteristic without sacrificing the others.

[0134] Reducing friction between the inner diameter of the vessel and the outer diameter of the catheter can minimize axial force required to advance catheter through tortuous vasculature. Therefore, the column strength of the catheter may be traded off for optimizing other performance requirements of the catheter. An example of a method to reduce friction between the inner diameter of the blood vessel and the outer diameter of the catheter is to apply a thin layer of coating, usually hydrophilic in nature, to the outer diameter of the catheter to reduce its surface friction coefficient while in vivo.

[0135] In addition or as an alternative to the water hammer construction discussed above, axial mechanical vibration or shock waves may be propagated to or generated at the distal end of the catheter using a variety of vibration generators, such as spark gap generators, piezoelectric pulse generators, electric solenoids, rotational shaft (wire) having one or more bends or carrying an eccentric weight, or any of a variety of other impulse generating sources well understood for example in the lithotripsy arts. Mechanical shock wave or pulse generators may be built into the proximal manifold 18, and/or mechanically coupled to the manifold or proximal catheter shaft as desired. Preferably, controls are provided on the manifold or on a proximal control coupled to the manifold, to enable the clinician to vary the intensity and time parameters of the mechanical pulses. Shock waves may be propagated along the proximal section 33 to assist in transluminal advance, and/or distal section 34 by way of pull wire 42, depending upon the desired clinical performance.

[0136] In an embodiment shown in FIGS. 16 and 17, the distal end 608 of a vibrating device 600 is placed in fluid connection with the proximal end 12 of the catheter 10 (not illustrated) and generates transverse and/or longitudinal vibration in the catheter 10. By inducing transverse vibration in the catheter 10, it reduces effective contact surface area

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

[0137] In the illustrated embodiment, the proximal end 602 of the vibrating device 600 may be connected to a vacuum pressure source such as a vacuum generator. The proximal connector 604 is attached to the housing 606. In at least one embodiment, the proximal connector 604 may be a luer connector. The distal end 608 of the vibrating device 600 is connected to the catheter 10. The distal connector 610 is held in place by a flexible seal 612 that is attached to the housing 606. In at least one embodiment, the distal connector 610 may be a luer connector. The flexible seal 612 allows the distal connector 610 to move longitudinally as well as transversely. The flexible tubing links the proximal connector 604 and the distal connector 610, creating an aspiration channel 614 for the fluid to travel through.

[0138] The vibrating device has a controller 616 to turn on/off the vibrating action as well as to vary its frequency. In this embodiment, the controller 616 is drawn as a sliding switch. Any of a variety of controls may be utilized, including electrical controllers, switches, buttons, levers, rotatable knobs, and others which will be apparent to those of skill in the art in view of the disclosure herein.

[0139] A vibration generator such as a motor 618 has an eccentrically mounted inertial weight on its shaft generating vibration. Any of a variety of motors may be used, including an electric motor, an electro-magnetic actuator, and a piezo-electric transducer. The frequency of the vibration is related to the RPM of the motor 618. A driving circuit 620 is connected to the motor 618 and the controller 616 and drives the motor 618 at different RPMs based on the manipulation of the controller 616. In the illustrated embodiment, the circuit 620 drives the motor 618 at different RPMs based on the position of the sliding switch. A battery 622 is connected to and powers the driving circuit 620 and the motor 618.

[0140] The motor 618 may be mounted perpendicularly to the length of the aspiration channel 614 to create longitudinal vibration. Also, a mechanical cam may be attached to the motor 618 to create larger magnitude longitudinal reciprocating motion. The frequency range generated by the electric motor is typically less than about 85 Hz. To achieve sonic frequencies in the range from about 85 Hz to about 260 Hz, one might replace the electric motor with an electro-magnetic actuator. To achieve ultrasonic frequencies in the range of about 20 Hz to about 1.6 MHz, one might employ a piezoelectric transducer.

[0141] In yet another embodiment, shown in FIG. 18, an agitator such as stylet 702 is permanently or removably inserted into a lumen 40 of the catheter 10 and rotated to generate vibration in the catheter 10 and thus improve catheter trackability through tortuous vasculatures. The stylet 702, whose outer diameter is within the range of from about 0.005 inches (about 0.127 mm) to about 0.035 inches (about 0.889 mm), may have at least one bend or at least one weight. The peak to peak transverse distance between the

bends will be less than the inner diameter of the catheter **10** when positioned within the catheter. The bends or weights of the stylet **702** may be positioned at different locations along the entire length of the catheter **10** or contained within a vibration zone within the distal most 50% or 30% or 10% of the length of the catheter depending upon desired performance, with the purpose to create the most desirable vibration when tracking the catheter **10** through the distal vasculature.

[0142] Alternatively, the stylet **702** may have an asymmetric weight such as a bead at a distal vibration zone or at its distal end. The stylet **702** may comprise a monofilament or braided or woven filaments or wires.

[0143] In another alternative, the stylet **702** may have a heater (e.g., an electric coil) at its distal end that facilitates the dissolution of the thrombus or changes the size of the thrombus that is aspirated into the catheter.

[0144] The proximal end of the stylet is attached to a motor driver **704** capable of generating rotational and/or axially reciprocating motion at various frequencies to form a motor driver-stylet assembly **700**. The assembly **700** has a controller **706** to turn on/off the rotating action as well as to vary its frequency. In this embodiment, the controller **706** is drawn as an on/off button. Any of a variety of controls may be utilized, including electrical controllers, switches, buttons, levers, rotatable knobs, and others which will be apparent to those of skill in the art in view of the disclosure herein. The proximal luer **708** or other connector of the catheter **10** reversibly attaches the catheter **10** to the motor driver **804**.

[0145] Once the catheter **10** has reached its intended location, the entire motor driver-stylet assembly **700** may be detached and removed from the catheter **10** leaving a central aspiration lumen.

[0146] In patients with vertebral artery occlusions, treatment with angioplasty can result in complications due to embolization of the occlusive lesion downstream to the basilar artery. Emboli small enough to pass through the vertebral arteries into the larger basilar artery are usually arrested at the top of the basilar artery, where it bifurcates into the posterior cerebral arteries. The resulting reduction in blood flow to the ascending reticular formation of the midbrain and thalamus produces immediate loss of consciousness. The devices described herein can be used to remove thromboembolic material from the vertebral artery or more distally such as in M1, M2, or M3 arteries.

[0147] Agitators for providing vibratory assistance for navigation and/or assisting in the capture and aspiration of debris are described further in connection with FIGS. 19-24. Referring to FIG. 19, an agitator **1900** may comprise an elongate, flexible body such as a wire or hypo tube having a proximal, control end and a distal, active zone or end. The hypo tube agitator has an inside lumen extending longitudinally that allows infusion of media. Referring to FIG. 19, an agitator **1900** comprises a wire or hypo tube **1904**, introduced into the proximal end of a catheter **1902** and advanced to the distal end **1907** of the catheter **1902**. The distal tip **1905** of the agitator **1900** may be placed at, beyond, or inside the distal end of the catheter **1902**. The agitator **1900** can be either preloaded into the catheter **1902** and inserted into the patient's body together with the catheter **1902** or added after the catheter **1902** has been placed. When loaded inside the catheter **1902**, the agitator **1900** may extend substantially longitudinally along the length of the

catheter **1902**. The agitator **1900** may further comprise a controller at the proximal end to axially adjust the distal tip position. The controller of the agitator **1900** may be used to axially adjust the position of the distal tip **1905** when the agitator **1900** is introduced into a variable length catheter such as that discussed in connection with FIG. 3.

[0148] In one implementation of the invention, the agitator and drive system are configured as a stand-alone device. Once the distal section **34** (FIG. 3B) has been positioned within a few (e.g., no more than about 3 or 2) centimeters of the obstruction, the distal end of agitator **1900** maybe introduced into the proximal end of central lumen **45** of pull wire **42**. Agitator **1900** may thereafter be distally advanced so that a distal segment of agitator **1900** extends beyond the distal end of pull wire **42**, and into the distal section **34**. The portion of the agitator **1900** contained within lumen **45** of pull wire **42** is restrained from any significant lateral motion. However, the distal portion of agitator **1900** which extends beyond the distal end of pull wire **42** is relatively laterally unconstrained and is able to agitate thrombus to facilitate drawing the thrombus into and through the distal section **34**. Once the thrombus has been drawn proximally under vacuum and with activation of the agitator as needed, to reach the step up in ID at the proximal end of distal section **34**, the risk of clogging is greatly reduced.

[0149] The agitator **1900** may be rotated manually or via a motor **1906** driven from the catheter **1902**'s proximal end to rotate or translate the distal end of the agitator **1900**. The driver **1906** may be connected to the proximal end of the agitator **1900** either permanently or removably. The driver **1906** may be a manual driver that is manually controlled such as a guidewire torquer. The driver **1906** may be a motorized driver. The motorized driver may be manually controlled with respect to one or more factors such as rotational direction (CCW/CW), speed, duration, etc. The motorized driver may be automatically controlled with respect to one or more factors such as direction (CCW/CW), speed, duration, etc. In one mode, the rotational direction of the agitator is periodically reversed.

[0150] The automatically controlled driver may comprise an actuator, and actuating the actuator may execute a pre-programmed series of steps. The actuator may be a button, a dial, a knob, a switch, a lever, a valve, a slide, a keypad, or any combinations thereof. The driver **1906** may also be under synchronized control, in which the driver **1906** drives the agitator **1900** in synchronization with aspiration and media injection. The agitator **1900** may be configured to promote motion at the distal end to help engage and move the clot.

[0151] Media may be infused into/around the clot area to help liberate the clot from the vasculature.

[0152] The agitator **1900** comprises a distal end **1912**, a proximal end **1914** and a distal tip **1905**. The proximal end **1914** of the agitator **1900** has a cross-section and/or wall thickness that is large enough to transmit the torque required to rotate the distal end **1912** of the agitator **1900** when placed in the catheter **1902**, within the curved vasculature. The outer diameter of the agitator **1900** may be from about 0.25 mm to about 0.65 mm, from about 0.3 mm to about 0.6 mm, from about 0.35 mm to about 0.55 mm, from about 0.4 mm to about 0.5 mm, from about 0.42 mm to about 0.48 mm, or from about 0.44 mm to about 0.46 mm. In case of the hypo tube **1904**, the wall thickness of the hypo tube **1904** may be from about 0.01 mm to about 0.29 mm, from about 0.05 mm

to about 0.25 mm, from about 0.1 mm to about 0.2 mm, from about 0.12 mm to about 0.18 mm, from about 0.13 mm to about 0.17 mm, or from about 0.14 mm to about 0.16 mm.

[0153] The agitator **1900** may additionally be provided with a guide tube **1910**, such as a hypo tube, to allow the agitator to spin, or axially or rotationally reciprocate, while constraining a proximal drive segment of the agitator **1900** against lateral motion. A distal end **1911** of guide tube **1910** may be positioned within about 25 cm or within about 20 cm or 15 cm or less of the distal end of the agitator **1900**, depending upon desired performance. The distal section of the agitator **1900**, extending beyond distal end **1911** of guide tube **1910**, is laterally unconstrained within the ID of distal segment **34** and available to agitate and facilitate aspiration of material into and through the central lumen.

[0154] The diameter of the agitator **1900** may be constant along its longitudinal length. The diameter of the agitator **1900** may increase or decrease along its longitudinal length to coincide with features of the catheter **1902**. In one implementation, the diameter of the agitator **1900** decreases in the distal direction along its longitudinal length by at least one step or tapered zone to provide increasing flexibility.

[0155] The distal end **1912** of the agitator **1900** may be straight. Alternatively, the distal end **1912** of the agitator **1900** may be curved or formed into different shapes to interact with the clot. FIG. **19** illustrates a bend **1917** spaced apart from the distal tip **1905** by a motion segment **1909** having a length of from about 1 mm to about 15 mm. FIGS. **20A-20C** depict more complex exemplary shapes of the motion segment **1909** of the agitator **1900**. FIGS. **20D-20E** depict an agitator positioned within a swellable polymer distal funnel tip.

[0156] The agitator **1900** may comprise a single, uniform material or multiple materials. The materials of the agitator **1900** may be processed (e.g., heat treatment/annealing) to give varying properties for the local performance requirements. The agitator **1900** may be structured to provide flexibility while exhibiting high torque transmission. The agitator **1900** may be made of Nitinol, 304 Stainless Steel, 316 LVM Stainless Steel, PTFE, Parylene, or any combinations thereof. At least a portion of the surface of the agitator **1900** may be coated. The entire length of the agitator **1900** may be coated. The coating on the agitator **1900** may provide lubrication between the ID wall of the catheter **1902** and the agitator **1900**. In a case that an intermediate hypotube is placed between the wall of the catheter **1902** and the agitator **1900**, e.g., constraining tube **1910** or tubular pull wire **42**, the coating on the agitator **1900** may provide lubrication between the intermediate hypotube and the proximal drive portion of the agitator **1900**. The coating materials of the wire or hypo tube **1904** include PTFE, Parylene, Teflon, or any combinations thereof.

[0157] Any of the ID or OD of any of the catheter shafts or other catheter components disclosed herein may be provided with a lubricious coating or may be made from a lubricious material. For example, a hydrophilic polymer such as Polyacrylamide, PEO, thermoplastic starch, PVP, copolymers of hydrophilic polymer can be extruded with hydrophobic polymers such as PEO soft segmented polyurethane blended with Tecoflex. The lubricious coating or the lubricious material may include surface modifying additive (SMA) during melt processing. The lubricious coating or the lubricious material contributes to at least ease of navigation, lower ID skin friction, or better clot removal. In

some embodiments, post processing wire ebeam, Gamma, UV, etc. additionally may be desirable to expose to moisture, temperature, etc. Catheters may be made from PEO impregnated polyurethanes such as Hydrothane, Tecophilic polyurethane for both OD and ID lubricity and inherent thromboresistant property without requiring a secondary coating process.

[0158] Referring to FIG. **20A**, the distal end **2012** of the agitator **1900** may comprise a coil **2020** to grip a caked clot and wiggle the distal end **2010** of the catheter **2002** and the clot during rotation **2006**. The coil **2020** may be a tight, offset coil, and may comprise at least one and optionally two or three or more complete revolutions.

[0159] Referring to FIG. **20B**, the distal end **2012** of the agitator **1900** may comprise a hook **2022** to grip and emulsify a clot. The hook **2022** may be concave proximally, or may extend transversely to the axis of the agitator body, extending in a circumferential orientation. Referring to FIG. **20C**, the distal end **2012** of the agitator **1900** may comprise a loose coil or spring **2024**. The loose coil or spring **2024** may expand (lengthen) and contract (shorten) with a change in direction of rotation.

[0160] Referring to FIGS. **20D-20E**, the distal end **2012** of the agitator **2000** may comprise a coil **2026** to grip a caked clot and wiggle the distal end **2010** of the catheter **2002** and the clot during rotation. In addition, the distal end **2010** of the catheter **2002** may include a polymer sidewall that reforms by hydration. The coil **2026** maintains a guide wire lumen during placement of the catheter. The polymer enables the distal end **2010** of the catheter **2002** to expand to a funnel shape after absorption of serum from blood. See FIG. **20E**.

[0161] Referring to FIGS. **21A-21B**, the distal tip **2110** of the catheter **2102** may move or wiggle by interacting with the agitator **1900**. When the distal end of the agitator **1900** rotates (e.g., via a driver **2106**), the motion segment **1909** and distal tip **1905** of the agitator interact with the side wall of the catheter **2102** which wiggles as shown by broken lines **2112**. The length of the motion segment, stiffness of the agitator **1900** and rotational velocity determines the interaction with the wall of the catheter **2102** and the amount of wiggle transmitted to the catheter **2101** with rotation of the agitator **1900**.

[0162] Alternatively, the distal tip **2110** of the catheter **2102** may move or wiggle by pulsed media jets existing one or more holes near the distal end of the hypo tube **2124**. The hypo tube **2124** has an inside lumen extending along the longitudinal length of the hypo tube **2124**. One or more side holes **2128** may be placed near the distal end of the hypo tube **2124** and allow fluid communication between the lumen of the hypo tube **2124** and the outside of the hypo tube **2124** (i.e., the lumen of the catheter **2102**). Media (e.g. saline) may be introduced under pressure into the proximal end of the hypo tube **2124**, through the lumen of the hypo tube **2124**, and then through the one or more holes of the hypo tube **2124**. When media is injected into the hypo tube **2124** in a pulsed manner, pulsed media jets eject from the holes of the hypo tube **2124** and transmit forces on the wall of the catheter **2102**, resulting in a wiggle motion of the catheter **2102**. The hypo tube **2124** may additionally rotate (e.g., via a driver **2106**) to facilitate a wiggle motion of the catheter **2102**.

[0163] Referring to FIGS. **22A-22B**, the hypo tube **2204** may have one or more holes **2210** and is bent near its distal

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

[0164] As the hypo tube 2204 rotates, the hypo tube 2204 ejects media and simultaneously makes the distal tip of the catheter 2202 wriggle. When the distal tip of the catheter 2202 wriggles by the rotation of the hypo tube 2204, the wriggle of the catheter 2202 may push the clot 2214 from side to side, and the hypo tube 2204 simultaneously ejects media at the interface between the clot 2214 and the catheter 2202, providing a lubricious avenue for the clot 2214 to release and flow into the catheter 2202.

[0165] With or without injection of media, rotation of the motion segment 1909 helps to break up or reshape the thrombus and facilitate entry into the aspiration lumen. In certain situations, the clot can be aspirated completely within the central lumen. In other situations, the clot may only be able to be partially drawn into the central lumen, such as illustrated in FIG. 22B. In this situation, rotation of the agitator may be stopped with application of vacuum remaining on to retain the clot on the distal end of the catheter. The catheter may then be proximally withdrawn, pulling the clot along with it, into the access sheath and out of the proximal vascular access point.

[0166] Referring to FIGS. 23A-23B, the hypo tube 2304 may have one or more holes along its surface more proximal from the distal end to facilitate the movement or flow of the clot 2314 inside the catheter 2302 toward its proximal end 2300. Vacuum 2316 is applied at the proximal end 2300 of the catheter 2302 to move the removed clot 2314 from the distal end to the proximal end 2300 of the catheter 2302. As shown in FIG. 23A, the holes may provide a thin film 2312 around the inside of the wall of the catheter 2302 to facilitate the flow of media and/or the clot 2314 and minimize any clogging of the clot 2314. As shown in FIG. 23B, the hypo tube 2304 may have one or more holes to provide media jets ejecting radially from the hypo tube 2304 to grab, pull, and/or emulsify the clot 2314 as the clot 2314 passes by the one or more holes on the surface of the hypo tube 2304.

[0167] Referring to FIG. 24, a vacuum port 2416 may be provided near the proximal end 2400 of the catheter 2402 such as on the manifold for releasable connection to a vacuum source to aspirate the clot from the vasculature. This allows the vacuum port 2416 to be distinct from the proximal port 2417 for receiving the agitator 1900. This can minimize the risk that the movement or control of the wire or hypo tube 2404 at its proximal end may be adversely affected by vacuum, aspirated clot, and/or media. The vacuum port may be connected to the catheter 2400 via a rotating hemostasis valve, discussed below.

[0168] Referring to FIGS. 25A-25C, experiments showed that an interrupted vacuum can help aspirating a corked clot stuck at the distal end 2512 of the catheter 2510 by loosening the clot and reshaping it to fit into the catheter 2510 after each vacuum and release cycle. Merely stopping the vacuum is not sufficient to loosen the clot. Completely releasing (venting to atmospheric pressure) the vacuum and allowing the clot to relax before reapplying a vacuum is found to

aspirate the corked clot most efficiently. The period of each vacuum and release cycle may be equal to or greater than about 0.1, 0.5, 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 seconds.

[0169] FIGS. 25A-25C show a logical progression of the vacuum and release cycle as applied to the catheter 2510. A release line 2518 and a vacuum line 2520 are connected to or near the proximal end of the catheter 2510. The release line 2518 is in communication with atmospheric pressure on its proximal end and has a release valve 2514 configured to open or close the fluid communication between the catheter 2510 and the vacuum. The vacuum line 2520 is connected to vacuum on its proximal end and has a vacuum valve 2516 configured to open or close the fluid communication between the catheter 2510 and the vacuum.

[0170] In the first step as shown in FIG. 25A, the release valve 2514 is closed, and the vacuum valve 2516 is open such that the vacuum is applied to the catheter 2510 to aspirate the clot. Then, as shown in FIG. 25B, the release valve 2514 is opened while the vacuum valve 2516 stays open. Because the release line 2518 and the vacuum line 2520 are in fluid communication, either directly or via at least a portion of the catheter 2510, the vacuum is applied mainly through the release line 2518, dropping vacuum applied to the catheter. Finally, as shown in FIG. 25C, the vacuum valve 2516 is shut off, allowing the vacuum to be completely released and the clot to relax. Then, another cycle from FIG. 25A to FIG. 25C begins by closing the release valve 2514 and opening the vacuum valve 2516.

[0171] Referring to FIG. 26, there is illustrated a proximal drive assembly and/or the rotating hemostasis valve to provide the interface for driving the agitator 1900, providing the port for injecting media, and the aspiration port. Referring to FIGS. 26, 27A, 27B, and 28, the proximal drive assembly 2602 and the rotating hemostasis valve 2620 may be releasably or permanently coupled to the proximal end of the agitator 1900. The proximal portion of the agitator 1900 passes proximally through a lumen of the rotating hemostasis valve 2620 and then that of the proximal drive assembly 2602. The proximal end of the agitator 1900 may terminate inside the lumen of the proximal drive assembly 2602. The distal portion of the proximal drive assembly 2602 is inserted into the proximal end of the rotating hemostasis valve 2620. In another embodiment, the proximal drive assembly 2602 may be integrated into the rotating hemostasis valve 2620.

[0172] The rotating hemostasis valve (RHV) 2620 comprises a distal connector 2630 at its distal end, which is configured to couple the rotating hemostasis valve to the proximal end of the catheter (not shown). The distal connector 2630 may be a luer connector. The rotating hemostasis valve 2620 comprises a central lumen along its longitudinal length, through which a proximal section of agitator 1900 passes. The rotating hemostasis valve 2620 further comprises an aspiration port 2622, which bifurcates from the central lumen of the rotating hemostasis valve 2620 and provides the aspiration flow path. The rotating hemostasis valve 2620 comprises a RHV seal 2626 and a proximal rotating collar 2628 at its proximal end. The proximal rotating collar 2628 controls the opening and closing of the RHV seal 2626. The user (e.g., physician) can either open or close the RHV seal 2626 by rotating the proximal rotating collar 2628. The RHV seal 2626, when closed, does not allow fluid communication between the inside lumen distal of the RHV seal 2626 and the inside lumen proximal of the

RHV seal **262**. At the same time, the RHV seal **262** does not hamper the longitudinal movement of the distal portion of the proximal drive assembly **2602** inside the rotating hemostasis valve **2629**.

[0173] Experiments showed that as the wire or hypo tube **1900** is rotated back and forth (i.e., oscillating), the distal end of the agitator **1900** changes its position relative to the catheter. The distal end of the agitator **1900** was shown to foreshorten/lengthen as the wire or hypo tube **2624** wound/unwound within the catheter due to the rotation of the agitator **1900** or the increase/decrease in media injection pressure. The proximal rotating collar **2628** and the RHV seal **2626** permit the user (e.g., physician) to account for this variance in length and advance/withdraw the agitator **1900** relative to the catheter and fix it in place by simply moving the proximal drive assembly **2602** in/out of the rotating hemostasis valve **2629**. If the agitator **1900** is preloaded into the catheter, the distance may be initially set at a nominal position. In another embodiment, the proximal rotating collar **2628** of the rotating hemostasis valve **2620** may be part of the proximal drive assembly **2602**.

[0174] The proximal drive assembly **2602** comprises a proximal drive connector **2604**, to which the driver is connected, and a media injection port **2610**, into which media is injected. The proximal drive assembly also comprises a bearing **2606**, which allows free rotation of the proximal drive connector **2604** with respect to the proximal drive assembly **2602**. The proximal drive connection **2604** may be coupled to the proximal end of the agitator **1900** such that the rotation of the proximal drive connector **2604** is translated to the rotation of the wire or hypo tube **1900**. The proximal drive assembly further comprises a drive tube seal **2608**, which prevents fluid communication between the inside lumen (of the proximal drive assembly **2602**) distal of the drive tube seal **2608** and the inside lumen proximal of the drive tube seal **2608**.

[0175] Referring to FIG. 29, the driver **2950** is removably connected to the proximal end of the proximal drive assembly **2902** via the proximal drive connection **2604**. The driver **2950** is configured to drive the agitator **1900**. The driver **2950** is a motorized driver that is automatically controlled with respect to one or more factors such as direction (CCW/CW), speed, duration, etc. The driver **2950** comprises a control **2954** such as a button, which executes a pre-programmed series of steps when pushed. The driver **2954** may be under synchronized control, in which the driver **2954** drives the agitator **1900** in synchronization with aspiration and media injection, when the back of the driver **2950** is plugged into the synchronization port **2952**.

[0176] The system for retrieving clots comprises the aspiration catheter; the agitator **1900** longitudinally extendable inside the lumen of the aspiration catheter; and the driver connectable to the proximal end of the agitator **1900** (e.g., via the rotating hemostasis valve or the proximal drive assembly) with or without a synchronization port. The system may allow impulse aspiration and/or impulse injection of media. The media may comprise water, saline solution, or media with an effective amount of drug (e.g., drug therapy such as heparin, plavix, tPA). The components may be manipulated individually or in a synchronized manner using predetermined operating parameters (e.g., for synchronized aspiration, injection, and rotation).

[0177] The method of retrieving a clot may comprise providing the aspiration catheter, the agitator longitudinally

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

[0178] In order to detach a more stubborn clot, aspiration, media injection, and/or rotation of the wire or hypo tube may be timed. Building up a surplus of media around the clot will form a plug. When aspiration is activated and/or pulsed, the vacuum can draw the “plug” proximally inside the lumen of the wire or hypo tube like a syringe plunger. A higher local vacuum around the clot is maintained, and more momentum is added to the “plug” as more media is added. Timing the rotation of the wire or hypo tube with aspiration and media injection may help wiggle or fatigue the clot and detach it out of the vasculature.

[0179] Any of the catheter shaft or sections of the catheter shaft or telescoping extensions in accordance with the present invention may comprise a multi-layer construct having a high degree of flexibility and sufficient push ability to reach deep into the cerebral vasculature, such as at least as deep as the petrous, cavernous, or cerebral segment of the internal carotid artery (ICA).

[0180] In one example, referring to FIG. 30, the catheter **3000** may have an effective length from the manifold to distal tip from about 70 cm to about 150 cm, from about 80 cm to about 140 cm, from about 90 cm to about 130 cm, from about 100 cm to about 120 cm, or from about 105 cm to about 115 cm. The outer diameter of the catheter **3000** may be from about 0.07 inches to about 0.15 inches, from about 0.08 inches to about 0.14 inches, from about 0.09 inches to about 0.13 inches, from about 0.1 inches to about 0.12 inches, or from about 0.105 inches to about 0.115 inches, and may be lower in a distal segment than in a proximal segment. The inner diameter **3108** of the catheter **3000** in a single central lumen embodiment may be greater than or equal to about 0.11 inches, greater than or equal to about 0.1 inches, greater than or equal to about 0.09 inches, greater than or equal to about 0.088 inches, greater than or equal to about 0.08 inches, greater than or equal to about 0.07 inches, greater than or equal to about 0.06 inches, or greater than or equal to about 0.05 inches. The inner diameter **3108** of the catheter **3000** in a single central lumen embodiment may be less than or equal to about 0.11 inches, less than or equal to about 0.1 inches, less than or equal to about 0.09 inches, less than or equal to about 0.088 inches, less than or equal to about 0.08 inches, less than or equal to about 0.07 inches, less than or equal to about 0.06 inches, or less than or equal to about 0.05 inches. Referring to FIG. 30, an inner liner **3014** may be formed by dip coating a mandrel (not shown) to provide a thin walled tubular inside layer of the catheter body **3000**. The dip coating may be produced by coating a wire such as a silver coated copper wire in PTFE. The mandrel may thereafter be axially elongated to reduce diameter, and removed to leave the tubular inner liner. The outside surface of the tubular inner liner **3014** may thereafter

be coated with a soft tie layer **3012** such as polyurethane (e.g., Tecoflex™), to produce a layer having a thickness of no more than about 0.005 inches, and in some implementations approximately 0.001 inches. The tie layer **3012** will generally extend along at least about the most distal 10 cm or 20 cm of the catheter shaft **3000** generally less than about 50 cm and may in one implementation extend approximately the distal 30 cm of the catheter shaft **3000**, **3100**.

[**0181**] A braid such as a 75 ppi stainless steel braid **3010** may thereafter be wrapped around the inner liner **3014** through a proximal zone up to a distal transition **3011**. From the distal transition **3011** to the distal end of the catheter **3000**, a coil **3024** comprising a shape memory material such as a Nitinol alloy may thereafter be wrapped around the inner liner **3014**. In one implementation, the Nitinol coil has a transition temperature below body temperature so that the Nitinol reside in the austenite (springy) state at body temperature. Adjacent loops or filars of the coil may be closely tightly wound in a proximal zone with a distal section having looser spacing between adjacent loops. In an embodiment having a coil section **3024** with an axial length of between about 20% and 30% of the overall catheter length, (e.g., 28 cm coil length in a 110 cm catheter shaft **3000**), at least the distal 1 or 2 or 3 or 4 cm of the coil will have a spacing that is at least about 130%, and in some implementations at least about 150% or more than the spacing in the proximal coil section. In a 110 cm catheter shaft **3000** having a Nitinol coil the spacing in the proximal coil may be about 0.004 inches and in the distal section may be at least about 0.006 inches or 0.007 inches or more.

[**0182**] The distal end of the coil **3024** is spaced proximally from the distal end of the inner liner **3014** to provide room for an annular radiopaque marker **3040**. In one embodiment, the distal end of the catheter **3000** is provided with a beveled distal surface **3006** residing on a plane having an angle of at least about 10° or 20° and in one embodiment about 30° with respect to a longitudinal axis of the catheter **3000**. The radiopaque marker **3040** may reside in a plane that is transverse to the longitudinal axis. Alternatively, at least the distally facing edge of the annular radiopaque marker **3040** may be an ellipse, residing on a plane which is inclined with respect to the longitudinal axis to complement the bevel angle of the distal surface **3006**.

[**0183**] After applying the proximal braid **3010**, the distal coil **3024** and the RO marker **3040** an outer Jacket **3020** maybe applied such as a shrink wrap tube to enclose the catheter body **3000**. The outer shrink-wrapped sleeve **3020** may comprise any of a variety of materials, such as polyethylene, polyurethane, PEBAX, nylon or others known in the art. Sufficient heat is applied to cause the polymer to flow into and embed the proximal braid and distal coil.

[**0184**] In one implementation, the outer shrink wrap jacket **3020** is formed by sequentially advancing a plurality of short tubular segments **3022**, **3026**, **3028**, **3030**, **3032**, **3034**, **3036**, **3038** concentrically over the catheter shaft subassembly, and applying heat to shrink the sections on to the catheter **3000** and provide a smooth continuous outer tubular body. The foregoing construction may extend a long at least the most distal 10 cm, and preferably at least about the most distal 20 or 25 cm of the catheter body **3000**.

[**0185**] The durometer of the outer wall segments may decrease in a distal direction. For example, proximal segments such as **3022** and **3026**, may have a durometer of at least about 60 or 70D, with gradual decrease in durometer of

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

[**0186**] Referring to FIGS. 31A-31C, the catheter may further comprise a tension support for increasing the tension resistance in the distal zone. The tension support may comprise a filament and, more specifically, may comprise one or more axially extending filaments **3042**. The one or more axially extending filaments **3042** may be axially placed inside the catheter wall near the distal end of the catheter. The one or more axially extending filaments **3042** serve as a tension support and resist elongation of the catheter wall under tension (e.g., when the catheter is being proximally retracted through tortuous vasculature). At least one of the one or more axially extending filaments **3042** may proximally extend along the length of the catheter wall from near the distal end of the catheter to less than about 5 cm from the distal end of the catheter, less than about 10 cm from the distal end of the catheter, less than about 15 cm from the distal end of the catheter, less than about 20 cm from the distal end of the catheter, less than about 25 cm from the distal end of the catheter, less than about 30 cm from the distal end of the catheter, less than about 35 cm from the distal end of the catheter, less than about 40 cm from the distal end of the catheter, or less than about 50 cm from the distal end of the catheter. The one or more axially extending filaments **3042** may have a length greater than or equal to about 50 cm, greater than or equal to about 40 cm, greater than or equal to about 35 cm, greater than or equal to about 30 cm, greater than or equal to about 25 cm, greater than or equal to about 20 cm, greater than or equal to about 15 cm, greater than or equal to about 10 cm, or greater than or equal to about 5 cm. At least one of the one or more axially extending filaments **3042** may have a length less than or equal to about 50 cm, less than or equal to about 40 cm, less than or equal to about 35 cm, less than or equal to about 30 cm, less than or equal to about 25 cm, less than or equal to about 20 cm, less than or equal to about 15 cm, less than or equal to about 10 cm, or less than or equal to about 5 cm. At least one of the one or more axially extending filaments **3042** may extend at least about the most distal 50 cm of the length of the catheter, at least about the most distal 40 cm of the length of the catheter, at least about the most distal 35 cm of the length of the catheter, at least about the most distal 30 cm of the length of the catheter, at least about the most distal 25 cm of the length of the catheter, at least about the most distal 20 cm of the length of the catheter, at least about the most distal 15 cm of the length of the catheter, at least about the most distal 10 cm of the length of the catheter, or at least about the most distal 5 cm of the length of the catheter.

[**0187**] The one or more axially extending filaments **3042** may be placed near or radially outside the tie layer **3012** or the inner liner **3014**. The one or more axially extending

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

[0188] When more than one axially extending filaments **3042** are placed in the catheter wall, the axially extending filaments **3042** may be placed in a radially symmetrical manner. For example, the angle between the two axially extending filaments **3042** with respect to the radial center of the catheter may be about 180 degree. Alternatively, depending on desired clinical performances (e.g., flexibility, trackability), the axially extending filaments **3042** may be placed in a radially asymmetrical manner. The angle between any two axially extending filaments **3042** with respect to the radial center of the catheter may be less than about 180 degree, less than or equal to about 165 degree, less than or equal to about 150 degree, less than or equal to about 135 degree, less than or equal to about 120 degree, less than or equal to about 105 degree, less than or equal to about 90 degree, less than or equal to about 75 degree, less than or equal to about 60 degree, less than or equal to about 45 degree, less than or equal to about 30 degree, less than or equal to about 15 degree, less than or equal to about 10 degree, or less than or equal to about 5 degree.

[0189] The one or more axially extending filaments **3042** may be made of materials such as Kevlar, Polyester, Meta-Para-Aramid, or any combinations thereof. At least one of the one or more axially extending filaments **3042** may comprise a single fiber or a multi-fiber bundle, and the fiber or bundle may have a round or rectangular cross section. The terms fiber or filament do not convey composition, and they may comprise any of a variety of high tensile strength polymers, metals or alloys depending upon design considerations such as the desired tensile failure limit and wall thickness. The cross-sectional dimension of the one or more axially extending filaments **3042**, as measured in the radial direction, may be no more than about 1%, 2%, 3%, 4%, 5%, 6%, 7%, 8%, 9%, 10%, 11%, 12%, 13%, 14%, 15%, 20%, 25%, or 30% of that of the catheter **3000**. The cross-sectional dimension of the one or more axially extending filaments **3042**, as measured in the radial direction, may be no more than about 0.001 inches, about 0.002 inches, about 0.003 inches, about 0.004 inches, about 0.005 inches, about 0.006 inches, about 0.007 inches, about 0.008 inches, about 0.009 inches, about 0.010 inches, about 0.015 inches, about 0.020 inches, about 0.025 inches, or about 0.030 inches.

[0190] The one or more axially extending filaments **3042** may increase the tensile strength of the distal zone of the catheter to at least about 1 pound, at least about 2 pounds, at least about 3 pounds, at least about 4 pounds, at least about 5 pounds, at least about 6 pounds, at least about 7 pounds, at least about 8 pounds, or at least about 10 pounds or more.

[0191] Referring to FIGS. 32A-32C, depending on whether the catheter **3000** is able to navigate sufficiently distally to reach the target site, an intraluminal catheter **3200** such as a telescopic extension segment having a proximally extending control wire as has been described elsewhere herein (e.g., distal segment **34** in FIGS. 3A and 3B) may be inserted through the catheter **3000** from the proximal end of the catheter **3000**. The intraluminal catheter **3200** is inserted such that the distal end of the intraluminal catheter **3200** reaches further distally beyond the distal end of the catheter **3000**. The outer diameter of the intraluminal catheter **3200**

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

[0192] The intraluminal catheter **3200** incorporates characteristics of the side wall construction of the catheter **3000** described herein. The axial length of the tubular extension segment may be less than about 50% and typically less than about 25% of the length of the catheter **3000**. The axial length of the tubular extension segment will generally be at least about 10 cm or 15 cm or 20 cm or 25 cm or more but generally no more than about 70 cm or 50 cm or 30 cm.

[0193] Referring to FIGS. 33A-33C, the intraluminal catheter **3200** may have one or more axially extending filaments **3242**. The one or more axially extending filaments **3242** incorporate characteristics of the one or more axially extending filaments **3042** of the catheter **3000**, except the cross-sectional dimension as measured in the radial direction of the one or more axially extending filaments **3242** of the intraluminal catheter **3200** may be less than the corresponding dimension of the filament **3042** in the catheter **3000**.

[0194] Referring to FIGS. 34A-34B, there is illustrated one example of an outer jacket segment stacking pattern for a progressive flexibility catheter of the type discussed in connection with FIG. 30. A distal segment **3038** may have a length within the range of about 1-3 cm, and a durometer of less than about 35D or 30D. An adjacent proximal segment **3036** may have a length within the range of about 4-6 cm, and a durometer of less than about 35D or 30D. An adjacent proximal segment **3034** may have a length within the range of about 4-6 cm, and a durometer of about 35D or less. An adjacent proximal segment **3032** may have a length within the range of about 1-3 cm, and a durometer within the range of from about 35D to about 45D (e.g., 40D). An adjacent proximal segment **3030** may have a length within the range of about 1-3 cm, and a durometer within the range of from about 50D to about 60D (e.g., about 55D). An adjacent proximal segment **3028** may have a length within the range of about 1-3 cm, and a durometer within the range of from about 35D to about 50D to about 60D (e.g., about 55D). An adjacent proximal segment **3026** may have a length within the range of about 1-3 cm, and a durometer of at least about 60D and typically less than about 75D. More proximal segments may have a durometer of at least about 65D or 70D. The distal most two or three segments may comprise a material such as Tecothane, and more proximal segments may comprise PEBAX or other catheter jacket materials known in the art. At least three or five or seven or nine or more discrete segments may be utilized, having a change in durometer between highest and lowest along the length of the catheter shaft of at least about 10D, preferably at least about 20D and in some implementations at least about 30D or 40D or more.

[0195] Performance metrics of a catheter include back-up support, trackability, pushability, and kink resistance. Back-up support means ability of the catheter to remain in position within anatomy and provide a stable platform through which endoluminal devices may advance. Referring to FIG. 35, when the devices are pushed through the catheter **3202**, if there is not enough back-up support in the catheter **3202**, the distal portion **3204** of the catheter **3202** may prolapse, pull out, or back out of a vessel **3206** that branches out of a main blood vessel (e.g., brachiocephalic artery **82**, common carotid artery **80**, or subclavian artery **84**). Back-up support for the catheter **3202** may be improved by providing a

proximal region with high durometer or modulus and a distal region with low durometer or modulus. Durometer or modulus of the proximal region of the catheter 3202 may be improved by braid reinforcement. The region of the catheter at which durometer or modulus is strengthened may be placed near branching points at which the aortic arch 1114, 1214 branches into brachiocephalic artery 82, common carotid artery 80, or subclavian artery 84 or near other anatomical structures (i.e., branching points) at which a main vessel branches into one or more smaller vessels, providing an opportunity for a catheter with poor back-up support to prolapse. For example, the region of the catheter at which durometer or modulus is strengthened may be placed within about 0.5 cm, about 1 cm, about 2 cm, about 3 cm, about 4 cm, about 5 cm, or about 6 cm from a branching point at which a main vessel branches into one or more smaller vessels.

[0196] Trackability means ability of the catheter to track further distally than other catheters (e.g., to M1). For example, a catheter that can reach a cerebral segment of the internal carotid artery (ICA) has better trackability than a catheter that can reach a cavernous or petrous segment of the ICA. Trackability of the catheter may be improved by using a catheter wall with low durometer or modulus or by adding a coating (e.g., a hydrophilic coating) on at least a portion of the catheter wall. In one embodiment, the hydrophilic coating may be placed along the distal most region of the catheter. The hydrophilic coating on the catheter may extend to about 1 cm, about 5 cm, about 10 cm, about 15 cm, or about 20 cm from the distal end of the catheter. The region with lower durometer or modulus may locate at the distal most region of the catheter. The region with lower durometer or modulus may extend to about 1 cm, about 5 cm, about 10 cm, about 15 cm, or about 20 cm from the distal end of the catheter.

[0197] Pushability means rigidity of the catheter sufficient to push through anatomy without “buckling”. Pushability of the catheter may be improved by increasing its durometer or modulus. Pushability of the catheter may also be improved by providing a proximal region with high durometer or modulus and a distal region with low durometer or modulus. A transition region of the catheter in which durometer or modulus changes along its longitudinal length (e.g., decreasing durometer or modulus from the proximal end to the distal end) may begin at about 50%, 60%, 70%, 75%, 80%, or more of the length of the catheter from its proximal end.

[0198] Kink resistance means resistance of the catheter to kinking. In addition, if the catheter does kink, kink resistance of the catheter helps it return to its original shape. Kink resistance is important in the distal segment of the catheter, which is more prone to kinking than the proximal segment. Kink resistance of the catheter may be improved by adding one or more NiTi coils (or a coil at least portion of which is Nitinol) to the catheter wall.

[0199] FIG. 36 describes a graph of durometer or modulus of a catheter in accordance with the present invention along the length of the catheter, from the proximal end ($x=0$) to the distal end ($x=1$). The catheter according to an embodiment may have a decreasing durometer or modulus (E) approaching its distal end. The proximal end of the catheter has higher durometer or modulus than that of the distal end of the catheter. High durometer or modulus near the proximal end provides superior back-up support of the catheter. Durometer or modulus of the catheter is substantially constant

along its length near the proximal end 3302 of the catheter. Then, durometer or modulus of the catheter decreases near the distal end 3304 of the catheter. Durometer or modulus of the catheter may begin to decrease (i.e., transition region) at about 50%, 70%, 75%, 80%, or 90% of the length of the catheter from its proximal end. The catheter may have successively decreasing durometer or modulus near its distal end by using materials with less durometer or modulus or having a thinner catheter wall near the distal end. Decreased durometer or modulus near the distal end provides superior trackability of the catheter.

[0200] FIG. 37 describes flexibility test profiles of catheters in accordance with the present invention compared with conventional catheters. Flexibility of a catheter was measured by the three point flexural test with a span of one inch and a displacement of 2 mm. In other words, FIG. 37 describes a force (i.e., flexural load) necessary to vertically displace an one-inch-long catheter segment by 2 mm with respect to distance from strain relief (i.e., proximal end of the catheter) to the point of force application. All catheters tested in FIG. 37 show modulus or flexibility profiles similar to one shown in FIG. 36. Modulus of the catheters stays substantially constant along its length near the proximal end and then gradually decreases near the distal end.

[0201] Catheters according to the present invention have a flexural load that is substantially constant along the longitudinal length near the proximal end and a rapidly decreasing flexural load near the distal end. In a catheter having a length of about 125 cm, the catheters may have a flexural load greater than or equal to about 1.0 lbF, about 1.5 lbF, about 2.0 lbF, about 2.5 lbF, about 3.0 lbF, or about 3.5 lbF at about 85 cm from the proximal end. The catheters may have a flexural load less than or equal to about 2.5 lbF, about 2.0 lbF, about 1.5 lbF, about 1.0 lbF, or about 0.5 lbF at about 95 cm from the proximal end. The catheters may have a flexural load less than or equal to about 1.5 lbF, about 1.0 lbF, about 0.75 lbF, about 0.5 lbF, about 0.25 lbF, or about 0.1 lbF at about 105 cm from the proximal end. The catheters may have a flexural load less than or equal to about 1.0 lbF, about 0.75 lbF, about 0.5 lbF, about 0.4 lbF, about 0.3 lbF, about 0.2 lbF, or about 0.1 lbF at about 115 cm from the proximal end. For catheters having different lengths, the foregoing dimensions can be scaled from the distal end of the catheter as a percentage of catheter length.

[0202] In certain implementations constructed in accordance with FIG. 30, the flexural load is less than about 3.0 or 3.25 lbF at 65 cm from the proximal end and greater than about 2.25 or 2.5 lbF on average from 65 cm to 85 cm from the proximal end. Flexural load drops to no more than about 1.0 and preferably no more than about 0.5 lbF at about 95 cm from the proximal end. This provides enhanced backup support in the aorta while maintaining enhanced trackability into the distal vasculature.

[0203] In other embodiments, the catheters may have a flexural load greater than or equal to about 1.0 lbF, about 1.5 lbF, about 2.0 lbF, about 2.5 lbF, about 3.0 lbF, or about 3.5 lbF at about 60 cm from the proximal end. The catheters may have a flexural load less than or equal to about 2.0 lbF, about 1.5 lbF, about 1.0 lbF, or about 0.5 lbF at about 70 cm from the proximal end. The catheters may have a flexural load less than or equal to about 1.0 lbF, about 0.75 lbF, about 0.5 lbF, about 0.4 lbF, about 0.3 lbF, about 0.2 lbF, or about 0.1 lbF at about 80 cm from the proximal end. The catheters may have a flexural load less than or equal to about 1.0 lbF, about

0.75 lbF, about 0.5 lbF, about 0.4 lbF, about 0.3 lbF, about 0.2 lbF, or about 0.1 lbF at about 90 cm from the proximal end.

[0204] The catheters may have a transition region, in which its flexural load changes by greater than or equal to about 1.0 lbF, about 1.5 lbF, about 2.0 lbF, about 2.5 lbF, about 3.0 lbF, or about 3.5 lbF. The longitudinal length of the transition region may be less than or equal to about 20 cm, about 15 cm, about 10 cm, about 5 cm, about 3 cm, or about 1 cm.

[0205] Compared to Neuron Max (Penumbra, Inc.) **3402**, catheters according to the present invention (e.g., **3404**, **3406**, **3408**, **3410**) have comparable modulus near its proximal end. This way, the catheters according to the present invention provide back-up support comparable to that of Neuron Max. In addition, the catheters have modulus that falls more rapidly near the transition region (between the proximal end and the distal end) than that of Neuron Max.

[0206] Compared to Ace 68 catheter (Penumbra) **3412**, Ace 64 catheter (Penumbra) **3414**, Benchmark 71 catheter (Penumbra) **3416**, and Sofia Plus (MicroVention) **3418**, the catheters according to the present inventions have greater modulus near its proximal end and comparable modulus near its distal end. This way, the catheters according to the present invention provide superior back-up support with comparable trackability compared to conventional catheters. The catheters according to the present invention may achieve this modulus profile even when their inner diameters (and thus lumen volumes) are greater than or equal to those of Ace 68, Ace 64, Benchmark 71, and Sofia Plus, which range from 0.064 inch to 0.071 inch.

[0207] Referring to FIG. 38, there is illustrated a transformable access sheath **200**. The access sheath **200** comprises an elongate flexible tubular body **202** extending between a proximal end **204** and a distal end **206**. A proximal access port **208** is in communication with a distal port **210** on the distal end **206** by way of a central lumen **212**. See FIG. 39.

[0208] At least one transition zone **214** is provided on the tubular body **202**. Transition zone **214** is controllably transformable between a relatively stiff configuration and a relatively flexible configuration. The access sheath **200** may be distally advanced through tortuous anatomy with at least one transition zone **214** in a relatively stiff configuration as desired such as to provide column strength or to facilitate the introduction of instruments therethrough. The transition zone **214** may be controllably transformed to a relatively flexible configuration as desired, such as to navigate tight bends in the vasculature.

[0209] In the illustrated embodiment, three transition zones **214** are shown. However, one or two or three or four or more transition zones may be utilized, depending upon the desired clinical performance. The transition zone **214** may be from about 1 cm to about 20 or 30 cm or more in length. In certain embodiments, the transition zones will be within the range of from about 2 cm to about 10 cm in length. The length and location of the transition zones may depend upon the target anatomy for the access catheter, and can be located accordingly.

[0210] Referring to FIG. 39, there is illustrated a cross-sectional view taken along the lines 18-18 of FIG. 38, through a transition zone **214**. The tubular body **202** comprises a sidewall **216** having at least one heating element **218** carried by or embedded within the sidewall **216**. In the

illustrated embodiment, the heater **218** may be an electrically conductive filament, such as a filar on an electrically conductive helical coil or braid. The electrically conductive filament may be placed within or laminated within an inner layer and an outer layer of the sidewall **216**. In at least one embodiment, an inner layer of the sidewall **216** may comprise polytetrafluoroethylene (PTFE) for lubricity. In at least one embodiment, an outer layer of the sidewall **216** may comprise biocompatible material preferably with a glass transition temperature from about 40° C. to about 80° C.

[0211] Alternatively, an electrically conductive polymer may be utilized to form the sidewall **216**. Electrically conductive coatings may alternatively be printed, laminated, embedded or otherwise applied to the outside, the inside, or laminated within an inner layer and an outer layer of the sidewall **216**. In at least one embodiment, the resistance of the heater **218** may be calibrated to a specific heating temperature, such as 40-80° C., for a predetermined voltage level of the power source. This may eliminate the need for a thermocouple and prevent potential overheating.

[0212] One or more electrical conductors may extend between the transition zone **214** and a proximal activation port **215**, adapted for coupling to a source of electricity from an external controller. In a mono polar construction, a single conductor for each transition zone **214** may extend proximally to the activation port **215**. A second conductor may lead to or comprise an electrically conductive surface on the tubular body **202**, for conducting electricity through the body of the patient to an external electrode as is understood in the art. Alternatively, in a bipolar embodiment, each transition zone **214** may be provided with at least two electrical conductors extending proximally to the activation port **215**.

[0213] At least the transition zone comprises a biocompatible material that is relatively firm at body temperature (e.g., 37° C.) but transitions to a relatively soft, flexible material upon application of heat. Typical suitable materials have a relatively low melting point so as to be softenable at temperatures not so high as to damage living vessels. In any event the material will have a softening point or a glass transition temperature above body temperature, with a melting point significantly above body temperature and above the temperature reached by activating the heating element **218**. In one embodiment, the biocompatible material preferably has a glass transition temperature from about 40° C. to about 80° C. Suitable materials may include polymers with a polymer chain orientation that causes the polymer to break when heated.

[0214] Examples of suitable biostable materials are polymers, typically thermoplastic polymers such as polyolefins and polyurethanes and most other biocompatible polymers. Typical suitable bioabsorbable materials include polyglycolide (PGA), poly(L-lactide) (PLLA), poly(epsilon-caprolactone) (PCL), and blends or combinations thereof. Polyglycolide for example has a glass transition temperature between 35-40° C., such having a considerably higher melting point.

[0215] Typical operating (softening) temperatures in this regard are on the order of between about 40 and 80° C., often between about 40° C. and 60° C. to cause a softening transition of the transition zone **214**, and allow a transition back to a firm state upon removal of power and reversion of the transition zone **214** back to body temperature. A temperature higher than about 80° C. may be acceptable for a

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

[0216] Upon being heated, the biocompatible energy-activated transition zone **214** softens so that it may be navigated through a tight bend for example. The material is to be softened enough by the energy application so that it increases in flexibility, but retains the structural integrity necessary for navigation and retains its shape so that upon interruption of the heat source it will harden back to its original configuration. To maintain the integrity of the tubular body, side wall **216** may be provided with flexible reinforcing structures such as a helically wrapped wire, ribbon or polymeric strand such as polyimide, or other braid or weave as is understood in the neurovascular catheter arts. A resistance coil or other resistance filaments may also provide the mechanical reinforcing function while the transition zone is in the softened state.

[0217] Heating may alternatively be provided by positioning a heat source such as a resistance heat element carried by a heater catheter within the central lumen **212**. Once the catheter has reached its final position in the vasculature, the heater catheter may be proximally withdrawn from the central lumen **212**, which is now available for aspiration or to receive a distal section **34** therethrough. In either heater configuration, a power source may be provided within or electrically coupled to a proximal manifold on the aspiration catheter or heater catheter.

[0218] Access for the catheter of the present invention can be achieved using conventional techniques through an incision on a peripheral artery, such as right femoral artery, left femoral artery, right radial artery, left radial artery, right brachial artery, left brachial artery, right axillary artery, left axillary artery, right subclavian artery, or left subclavian artery. An incision can also be made on right carotid artery or left carotid artery in emergency situations.

[0219] Avoiding a tight fit between the guidewire **40** and inside diameter of guidewire lumen **28** enhances the slidability of the catheter over the guidewire. In ultra small diameter catheter designs, it may be desirable to coat the outside surface of the guidewire **40** and/or the inside surface of the wall defining lumen **38** with a lubricous coating to minimize friction as the catheter **10** is axially moved with respect to the guidewire **40**. A variety of coatings may be utilized, such as Paralene, Teflon, silicone, polyimide-polytetrafluoroethylene composite materials or others known in the art and suitable depending upon the material of the guidewire or inner tubular wall **38**.

[0220] Aspiration catheters of the present invention which are adapted for intracranial applications generally have a total length in the range of from 60 cm to 250 cm, usually from about 135 cm to about 175 cm. The length of the proximal segment **33** will typically be from 20 cm to 220 cm, more typically from 100 cm to about 120 cm. The length of the distal segment **34** will typically be in the range from 10 cm to about 60 cm, usually from about 25 cm to about 40 cm.

[0221] The catheters of the present invention may be composed of any of a variety of biologically compatible polymeric resins having suitable characteristics when formed into the tubular catheter body segments. Exemplary materials include polyvinyl chloride, polyethers, polyamides, polyethylenes, polyurethanes, copolymers thereof, and the like. In one embodiment, both the proximal body segment **33** and distal body segment **34** will comprise a polyvinyl chloride (PVC), with the proximal body segment being formed from a relatively rigid PVC and the distal body segment being formed from a relatively flexible, supple PVC. Optionally, the proximal body segment may be reinforced with a metal or polymeric braid or other conventional reinforcing layer.

[0222] The proximal body segment will exhibit sufficient column strength to permit axial positioning of the catheter through a guide catheter with at least a portion of the proximal body segment **33** extending beyond the guide catheter and into the patient's vasculature. The proximal body segment may have a shore hardness in the range from 50 D to 100 D, often being about 70 D to 80 D. Usually, the proximal shaft will have a flexural modulus from 20,000 psi to 1,000,000 psi, preferably from 100,000 psi to 600,000 psi. The distal body segment **34** will be sufficiently flexible and supple so that it may navigate the patient's more narrow distal vasculature. In highly flexible embodiments, the shore hardness of the distal body segment **34** may be in the range of from about 20 A to about 100 A, and the flexural modulus for the distal segment **34** may be from about 50 psi to about 15,000 psi.

[0223] The catheter body may further comprise other components, such as radiopaque fillers; colorants; reinforcing materials; reinforcement layers, such as braids or helical reinforcement elements; or the like. In particular, the proximal body segment may be reinforced in order to enhance its column strength and torqueability (torque transmission) while preferably limiting its wall thickness and outside diameter.

[0224] Usually, radiopaque markers will be provided at least at the distal end **14** and the transition region **32** at the distal end of proximal segment **33**. One radiopaque marker comprises a metal band which is fully recessed within or carried on the outside of the distal end of the proximal body segment **33**. Suitable marker bands can be produced from a variety of materials, including platinum, gold, and tungsten/rhenium alloy. Preferably, the radiopaque marker band will be recessed in an annular channel to produce a smooth exterior surface.

[0225] The proximal section **33** of tubular body **16** may be produced in accordance with any of a variety of known techniques for manufacturing interventional catheter bodies, such as by extrusion of appropriate biocompatible polymeric materials. Alternatively, at least a proximal portion or all of the length of tubular body **16** may comprise a polymeric or metal spring coil, solid walled hypodermic needle tubing, or braided reinforced wall, as is known in the microcatheter arts.

[0226] In a catheter intended for neurovascular applications, the proximal section **33** of body **16** will typically have an outside diameter within the range of from about 0.117 inches to about 0.078 inches. In one implementation, proximal section **33** has an OD of about 0.104 inches and an ID of about 0.088 inches. The distal section **34** has an OD of about 0.085 inches and an ID of about 0.070 inches.

[0227] Diameters outside of the preferred ranges may also be used, provided that the functional consequences of the diameter are acceptable for the intended purpose of the catheter. For example, the lower limit of the diameter for any portion of tubular body 16 in a given application will be a function of the number of fluid or other functional lumen contained in the catheter, together with the acceptable minimum aspiration flow rate and collapse resistance.

[0228] Tubular body 16 must have sufficient structural integrity (e.g., column strength or “pushability”) to permit the catheter to be advanced to distal locations without buckling or undesirable bending of the tubular body. The ability of the body 16 to transmit torque may also be desirable, such as to avoid kinking upon rotation, to assist in steering. The tubular body 16, and particularly the distal section 34, may be provided with any of a variety of torque and/or column strength enhancing structures. For example, axially extending stiffening wires, spiral wrapped support layers, braided or woven reinforcement filaments may be built into or layered on the tubular body 16. See, for example, U.S. Pat. No. 5,891,114 to Chien, et al., the disclosure of which is incorporated in its entirety herein by reference.

[0229] In many applications, the proximal section 33 will not be required to traverse particularly low profile or tortuous arteries. For example, the proximal section 33 will be mostly or entirely within the relatively large diameter guide catheter. The transition 32 can be located on the catheter shaft 16 to correspond approximately with or beyond the distal end of the guide catheter.

[0230] For certain applications, such as intracranial catheterizations, the distal section 34 is preferably at least about 5 cm or 10 cm long and small enough in diameter to pass through vessels as low as 3 mm or 2 mm or lower. The distal section may have a length of at least about 20 cm or 30 cm or 40 cm or more, depending upon the intended target vessel or treatment site.

[0231] The distal section, whether carried within the proximal section as an integrated device, or is a separate device to be inserted into the proximal section during a procedure, is substantially shorter than the proximal section. When the distal end of the distal section and the distal end of the proximal section are axially aligned, the proximal end of the distal section is spaced distally apart from the proximal end of the proximal section. The control element such as a control wire or tube spans the distance between the proximal end of the distal section and the proximal manifold or proximal control.

[0232] In the foregoing configuration, the proximal end of the distal section will generally be spaced apart distally from the proximal end of the proximal section by at least about 25%, and in some embodiments at least about 50% or 70% or more of the length of the proximal section.

[0233] In accordance with one aspect, there is provided a method of aspirating a vascular occlusion from a remote site, comprising the steps of: advancing a first elongate tubular body through a vascular access site and into a body vessel; thereafter advancing a second tubular body distally to extend beyond the first elongate tubular body to reach the remote site, the second tubular body having a lumen and a length that is shorter than the first elongate tubular body; and aspirating thrombus from the site into the lumen by applying pulsatile vacuum to the first elongate tubular body.

[0234] In one aspect of present disclosure, the aspirating step comprises biting the thrombus by changing the size of a distal opening on the catheter. The changing the size of the opening may be accomplished in response to application of intermittent vacuum to the lumen. In another aspect of present disclosure, the method of aspirating a vascular occlusion further comprises vibrating the first elongate tubular body during the advancing a first elongate tubular body step. In yet another aspect of present disclosure, the method of aspirating a vascular occlusion further comprises vibrating the second tubular body during the advancing a second tubular body step. In yet another aspect of present disclosure, the method of aspirating a vascular occlusion further comprises vibrating at least the distal section of the second tubular body during the aspirating step.

[0235] In one aspect of present disclosure, the second tubular body has a proximal opening, and the proximal opening is positioned within the first elongate tubular body within about 25 cm of the distal end of the first elongate tubular body following the advancing the second tubular body distally step. In another aspect of present disclosure, the second tubular body is introduced into the first elongate tubular body following the advancing the first elongate tubular body step. In yet another aspect of present disclosure, the second tubular body is carried within the first elongate tubular body during the advancing the first elongate tubular body step.

[0236] In one aspect of present disclosure, the method of aspirating a vascular occlusion may further comprise advancing an agitator into the second tubular body following the advancing a second tubular body step. The method of aspirating a vascular occlusion may further comprise rotating the agitator to assist the aspirating thrombus step. The method of aspirating a vascular occlusion may further comprise introducing a lubricant through the agitator to assist the aspirating thrombus step. More specifically, the method of aspirating a vascular occlusion may further comprise introducing polyethylene glycol through the agitator to assist the aspirating thrombus step.

[0237] In one aspect of present disclosure, the aspirating thrombus step comprises applying intermittent negative pressure to the first elongate tubular body. In another aspect of present disclosure, the aspirating thrombus step comprises applying alternating negative and positive pressure to the first elongate tubular body. In yet another aspect of present disclosure, the advancing a second tubular body distally step comprises distally advancing a control wire extending proximally from a proximal end of the second tubular body. The control wire may be tubular, and the method of aspirating a vascular occlusion may further comprise the step of advancing an agitator through the control wire such that a distal segment of the agitator is exposed beyond the control wire and within the second tubular body.

[0238] In accordance with one aspect, there is provided a system for aspirating a vascular occlusion from a remote site, comprising: an elongate, flexible tubular body, comprising at least one central lumen extending along its longitudinal length; an agitator extendable through the central lumen of the tubular body to position a distal end of the agitator near a distal end of the tubular body; a driver connectable to a proximal end of the agitator and configured to actuate the agitator; and a vacuum port near the proximal

end of the tubular body and in fluid communication with the central lumen of the tubular body.

[0239] In one aspect of present disclosure, the agitator comprises an elongate tube. The agitator may comprise a wire extending through the elongate tube and having at least one bend near its distal end. In another aspect of present disclosure, the agitator comprises a proximal end, a distal end, and a loop at the distal end. In yet another aspect of present disclosure, the driver is configured to rotate the agitator cyclically in alternating directions.

[0240] In one aspect of present disclosure, the agitator comprises: at least one lumen along its longitudinal length, an influent port near its proximal end configured to allow fluid communication between the lumen of the agitator and a source of media, and at least one effluent port configured to allow fluid communication between the lumen of the agitator and the central lumen of the tubular body. The system for aspirating a vascular occlusion may further comprise a control, for expressing media from the effluent port of the agitator into the central lumen of the tubular body. The distal portion of the tubular body may be configured to vibrate in a transverse direction in response to the injection of media.

[0241] In one aspect of present disclosure, the system for aspirating a vascular occlusion further comprises a controller for applying a pulsatile vacuum cycle to the central lumen. In another aspect of present disclosure, the system for aspirating a vascular occlusion further comprises a rotating hemostasis valve coupled to the proximal end of the tubular body, the rotating hemostasis valve comprising: at least one main lumen along its longitudinal length, through which the proximal portion of the agitator is configured to pass, and an aspiration lumen bifurcating from the main lumen and provided with a vacuum port. In yet another aspect of present disclosure, the system further comprises a proximal drive assembly coupled to the proximal end of the tubular body, the proximal drive assembly comprising: at least one main lumen along its longitudinal length for receiving the agitator; a media injection port, into which media is injected, in fluid communication with the central lumen of the tubular body, and a proximal drive connection at the proximal end, which operably connects between the agitator and the driver.

[0242] In accordance with another aspect, there is provided a method of aspirating a vascular occlusion from a remote site, comprising: providing the system for aspirating a vascular occlusion; placing the tubular body adjacent to the occlusion; activating the driver to actuate the agitator and loosen the occlusion; and drawing occlusive material into the central lumen by applying vacuum to the central lumen. In one aspect of present disclosure, there is provided a method of aspirating a vascular occlusion from a remote site, comprising: providing the system for aspirating a vascular occlusion; placing the tubular body adjacent to the occlusion; activating the driver to cause the distal tip of the agitator to rotate; injecting media through the influent port; and aspirating occlusive material into the central lumen by applying vacuum to the central lumen. Actuation of the driver, aspiration, and media injection may be synchronized to facilitate the removal and/or aspiration of the occlusion.

[0243] In accordance with one aspect, there is provided a method of aspirating a vascular occlusion from a remote site, comprising: advancing a guidewire to a site at least as distal as the cavernous segment of the internal carotid artery;

advancing a tubular body directly over the guidewire to a site at least as distal as the cavernous segment; removing the guidewire from the tubular body; and aspirating thrombus into the tubular body by applying vacuum to the tubular body. In one aspect of present disclosure, the method of aspirating a vascular occlusion comprises advancing the tubular body at least as distal as the cerebral segment of the internal carotid artery. In another aspect of present disclosure, the method of aspirating a vascular occlusion comprises advancing the guidewire at least as distal as the middle cerebral artery.

[0244] In yet another aspect of present disclosure, the method of aspirating a vascular occlusion further comprises providing sufficient back up support to the tubular body to resist prolapse of the tubular body into the aorta. In one aspect, the back up support may be provided by advancing the tubular body over a guidewire having a distal end positioned at least as distal as the cavernous segment of the internal carotid artery, and a diameter at the point the guidewire enters the brachiocephalic artery of at least about 0.030 inches. In another aspect, the back up support may be provided by advancing the tubular body over a guidewire having a distal end positioned at least as distal as the cavernous segment of the internal carotid artery, and a diameter at the point the guidewire enters the brachiocephalic artery of about 0.038 inches. The guidewire may be navigable to at least the cerebral segment of the internal carotid artery by having a distal segment having a diameter of no more than about 0.020 inches. The guidewire may be navigable to at least the cerebral segment of the internal carotid artery by having a distal segment having a diameter of about 0.016 inches. The distal segment may have a length of no more than about 25 cm. The distal segment may have a length of no more than about 20 cm.

[0245] In accordance with another aspect, there is provided a method of tracking an aspiration catheter from a femoral access site to at least as distal as the cavernous segment of the internal carotid artery, comprising the steps of: advancing a guidewire from the femoral access site to at least as distal as the cerebral segment of the internal carotid artery, the guidewire having a proximal section having a diameter of at least about 0.030 inches and a distal section having a length of no more than about 25 cm and a diameter of no more than about 0.020 inches; tracking an aspiration catheter directly over the guidewire and to a site at least as distal as the cavernous segment, the aspiration catheter having a distal end and a central lumen at the distal end with a diameter of at least about 0.080 inches and a beveled distal tip. In one aspect of present disclosure, the diameter of the proximal section of the guidewire is about 0.038 inches, and the diameter of the distal section is about 0.016 inches.

[0246] In another aspect of present disclosure, a distal segment of the catheter comprises a side wall defining the central lumen, the side wall comprising: a tubular inner liner; a soft tie layer separated from the lumen by the inner liner; a helical coil surrounding the tie layer, adjacent windings of the coil spaced progressively further apart in the distal direction; and an outer jacket surrounding the helical coil, the outer jacket formed from a plurality of tubular segments positioned coaxially about the coil; wherein a proximal one of the tubular segments has a durometer of at least about 60D and a distal one of the tubular segments has a durometer of no more than about 35D. The tubular liner may be formed by dip coating a removable mandrel and may

comprise PTFE. The tie layer may comprise polyurethane. The tie layer may have a wall thickness of no more than about 0.005 inches and may extend along at least the most distal 20 cm of the flexible body. The coil may comprise a shape memory material.

[0247] In accordance with one aspect, there is provided an enhanced flexibility neurovascular catheter, comprising: an elongate flexible body, having a proximal end, a distal end and a side wall defining a central lumen, a distal zone of the side wall comprising: a tubular inner liner; a soft tie layer separated from the lumen by the inner liner; a helical coil surrounding the tie layer, adjacent windings of the coil spaced progressively further apart in the distal direction; and an outer jacket surrounding the helical coil, the outer jacket formed from a plurality of tubular segments positioned coaxially about the coil; wherein a proximal one of the tubular segments has a durometer of at least about 60D and a distal one of the tubular segments has a durometer of no more than about 35D. In one aspect of present disclosure, the tubular liner is formed by dip coating a removable mandrel. In another aspect of present disclosure, the tubular liner comprises PTFE.

[0248] In yet another aspect of present disclosure, the tie layer comprises polyurethane. The tie layer may have a wall thickness of no more than about 0.005 inches and may extend along at least the most distal 20 cm of the flexible body. In one aspect of present disclosure, the coil comprises a shape memory material. The coil may comprise Nitinol, and the Nitinol may comprise an Austenite state at body temperature.

[0249] In one aspect of present disclosure, the outer jacket is formed from at least five discrete tubular segments. The outer jacket may be formed from at least nine discrete tubular segments. The difference in durometer between a proximal one of the tubular segments and a distal one of the tubular segments may be at least about 20D. The difference in durometer between a proximal one of the tubular segments and a distal one of the tubular segments may be at least about 30D.

[0250] In another aspect of present disclosure, the enhanced flexibility neurovascular catheter, further comprises a tension support for increasing the tension resistance in the distal zone. The tension support may comprise a filament and may comprise an axially extending filament. The axially extending filament may be carried between the inner liner and the helical coil. The axially extending filament may increase the tensile strength to at least about 5 pounds.

[0251] In accordance with one aspect, there is provided an enhanced flexibility neurovascular catheter, comprising: an elongate flexible body, having a proximal end, a distal end and a side wall defining a central lumen, a distal zone of the side wall comprising: an outer jacket surrounding a helical coil, the outer jacket formed from a plurality of tubular segments positioned coaxially about the coil; wherein a proximal one of the tubular segments has a durometer of at least about 60D and a distal one of the tubular segments has a durometer of no more than about 35D; and an axially extending filament within the side wall, extending at least about the most distal 10 cm of the length of the catheter. The filament may extend at least about the most distal 15 cm of the length of the catheter. The filament may extend at least about the most distal 20 cm of the length of the catheter. The

filament may comprise multiple fibers and may extend axially in between the coil and the inner liner.

[0252] In one aspect of present disclosure, the side wall further comprises: a tubular inner liner; a soft tie layer separated from the lumen by the inner liner; wherein the helical coil surrounds the tie layer, and adjacent windings of the coil are spaced progressively further apart in the distal direction. The tubular liner may be formed by dip coating a removable mandrel and may comprise PTFE. The tie layer may comprise polyurethane and may have a wall thickness of no more than about 0.005 inches. The tie layer may extend along at least the most distal 20 cm of the flexible body. The coil may comprise a shape memory material and may comprise Nitinol. The Nitinol may comprise an Austenite state at body temperature.

[0253] In one aspect of present disclosure, the outer jacket may be formed from at least five discrete tubular segments. In another aspect of present disclosure, the outer jacket may be formed from at least nine discrete tubular segments. The difference in durometer between a proximal one of the tubular segments and a distal one of the tubular segments may be at least about 20D. The difference in durometer between a proximal one of the tubular segments and a distal one of the tubular segments may be at least about 30D. In another aspect of present disclosure, the catheter can withstand at least about 3.5 pounds tension before failure. In yet another aspect, the catheter can withstand at least about 5 pounds tension before failure.

[0254] In accordance with one aspect, there is provided a method of making a high flexibility distal zone on a neurovascular catheter, comprising the steps of: dip coating a removable mandrel to form a tubular inner layer on the mandrel; coating the tubular inner layer with a soft tie layer; applying a helical coil to the outside of the tie layer; positioning a plurality of tubular segments on the helical coil; the plurality of segments having durometers that decrease in a distal direction; heating the tubular segments to form the high flexibility distal zone on the neurovascular catheter; and removing the mandrel. In one aspect of present disclosure, removing the mandrel step includes axially elongating the mandrel. In another aspect of present disclosure, the method of making a high flexibility distal zone on a neurovascular catheter comprises positioning at least seven segments on the helical coil. In yet another aspect of present disclosure, the method of making a high flexibility distal zone on a neurovascular catheter comprises positioning at least nine segments on the helical coil.

[0255] In one aspect of present disclosure, the difference in durometer between a proximal one of the tubular segments and a distal one of the tubular segments is at least about 20D. The difference in durometer between a proximal one of the tubular segments and a distal one of the tubular segments may be at least about 30D. The tubular inner layer may comprise PTFE. In another aspect of present disclosure, the tie layer comprises polyurethane. The tie layer may have a wall thickness of no more than about 0.005 inches. The tie layer may extend along at least the most distal 20 cm of the flexible body.

[0256] In one aspect of present disclosure, the coil comprises a shape memory material. The coil may comprise Nitinol. The Nitinol may comprise an Austenite state at body temperature. In another aspect of present disclosure, the method of making a high flexibility distal zone on a neurovascular catheter further comprises the step of positioning at

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

[0257] In accordance with one aspect, there is provided a method of aspirating a vascular occlusion from a remote site, comprising the steps of: advancing an elongate tubular body through a vascular access site and into a body vessel, the tubular body comprising a proximal end, a distal end and a central lumen; positioning the distal end at least as far distally as the cavernous segment of the middle cerebral artery; applying vacuum to the lumen to draw thrombus into the lumen; and mechanically disrupting the thrombus to facilitate entry into the lumen.

[0258] In one aspect of present disclosure, the mechanically disrupting step comprises introducing vibration at the distal end of the tubular body. The vibration may be introduced by rotating an agitator within the tubular body. The method of aspirating a vascular occlusion may comprise rotating a wire within the tubular body. The method of aspirating a vascular occlusion may comprise rotating a tube within the tubular body and may further comprise the step of introducing media through the tube. The method of aspirating a vascular occlusion may comprise the step of introducing a lubricant through the tube to facilitate advancing thrombus through the lumen and may comprise the step of introducing polyethylene glycol through the tube.

[0259] In another aspect of present disclosure, the applying vacuum step comprises applying pulsatile vacuum. In yet another aspect of present disclosure, the advancing an elongate tubular body step is accomplished directly over a guidewire without any intervening tubular bodies. The method of aspirating a vascular occlusion may comprise advancing the tubular body at least as distal as the cavernous segment of the internal carotid artery. The method of aspirating a vascular occlusion may comprise advancing the tubular body at least as distal as the cerebral segment of the internal carotid artery. The method of aspirating a vascular occlusion may comprise advancing the guidewire at least as distal as the middle cerebral artery.

[0260] In one aspect of present disclosure, the method of aspirating a vascular occlusion further comprises providing sufficient back up support to the tubular body to resist prolapse of the tubular body into the aorta. The back up support may be provided to the tubular body by advancing the tubular body over a guidewire having a distal end positioned at least as distal as the cavernous segment of the internal carotid artery, and a diameter at the point the guidewire enters the brachiocephalic artery of at least about 0.030 inches. The back up support may be provided to the tubular body by advancing the tubular body over a guidewire having a distal end positioned at least as distal as the cavernous segment of the internal carotid artery, and a diameter at the point the guidewire enters the brachiocephalic artery of about 0.038 inches.

[0261] In one aspect of present disclosure, the guidewire is navigable to at least the cerebral segment of the internal

carotid artery by having a distal segment having a diameter of no more than about 0.020 inches. The guidewire may be navigable to at least the cerebral segment of the internal carotid artery by having a distal segment having a diameter of about 0.016 inches. In yet another aspect of present disclosure, the method of aspirating a vascular occlusion further comprises the step of introducing an agitator into the tubular body subsequent to the positioning step. A proximal section of the agitator may extend through a constraint tube, and a distal section of the agitator may extend beyond a distal end of the constraint tube.

[0262] In accordance with one aspect, there is provided a method of aspirating a vascular occlusion from a remote site, comprising: advancing a guidewire through a vascular access point and transvascularly to a site at least as distal as the cavernous segment of the internal carotid artery; accessing a site at least as distal as the cavernous segment by advancing a combined access and aspiration catheter directly over the guidewire; removing the guidewire; and aspirating thrombus through the combined access and aspiration catheter. In one aspect of present disclosure, the method of aspirating a vascular occlusion comprises advancing the combined access and aspiration catheter at least as distal as the cerebral segment of the internal carotid artery. In another aspect of present disclosure, the method of aspirating a vascular occlusion comprises advancing the guidewire at least as distal as the middle cerebral artery.

[0263] In yet another aspect of present disclosure, the method of aspirating a vascular occlusion further comprises providing sufficient back up support to the combined access and aspiration catheter to resist prolapse of the catheter into the aorta. The back up support may be provided to the combined access and aspiration catheter by advancing the combined access and aspiration catheter over a guidewire having a distal end positioned at least as distal as the cavernous segment of the internal carotid artery, and a diameter at the point the guidewire enters the brachiocephalic artery of at least about 0.030 inches. The back up support is provided to the combined access and aspiration catheter by advancing the combined access and aspiration catheter over a guidewire having a distal end positioned at least as distal as the cavernous segment of the internal carotid artery, and a diameter at the point the guidewire enters the brachiocephalic artery of about 0.038 inches.

[0264] In one aspect of present disclosure, the guidewire is navigable to at least the cerebral segment of the internal carotid artery by having a distal segment having a diameter of no more than about 0.020 inches. The guidewire may be navigable to at least the cerebral segment of the internal carotid artery by having a distal segment having a diameter of about 0.016 inches. The diameter of the proximal section of the guidewire may be about 0.038 inches, and the diameter of the distal section may be about 0.016 inches.

[0265] In another aspect of present disclosure, a distal segment of the combined access and aspiration catheter comprises a side wall defining a central lumen, the side wall comprising: a tubular inner liner; a tie layer separated from the lumen by the inner liner; a helical coil surrounding the tie layer, adjacent windings of the coil spaced progressively further apart in the distal direction; and an outer jacket surrounding the helical coil, the outer jacket formed from a plurality of tubular segments positioned coaxially about the coil; wherein a proximal one of the tubular segments has a durometer of at least about 60D and a distal one of the

tubular segments has a durometer of no more than about 35D. The tubular liner may be formed by dip coating a removable mandrel. The tubular liner may comprise PTFE. The tie layer may comprise polyurethane, and may have a wall thickness of no more than about 0.005 inches. The tie layer may extend along at least the most distal 20 cm of the flexible body.

[0266] In one aspect of present disclosure, the coil comprises a shape memory material. In another aspect of present disclosure, the method of aspirating a vascular occlusion further comprises introducing an agitator into the combined access and aspiration catheter. The method of aspirating a vascular occlusion may further comprise vibrating a distal portion of the agitator during the aspirating step. The method of aspirating a vascular occlusion may further comprise introducing a fluid media through the agitator during the aspirating step. The method of aspirating a vascular occlusion may further comprise introducing polyethylene glycol through the agitator during the aspirating step.

[0267] In accordance with one aspect, there is provided a neurovascular catheter, comprising: an elongate flexible tubular body, having a proximal end, a distal end and a side wall defining a central lumen, a distal zone of the tubular body comprising: a tubular inner liner; a tie layer separated from the lumen by the inner liner; a helical coil surrounding the tie layer, adjacent windings of the coil spaced progressively further apart in the distal direction; an outer jacket surrounding the helical coil, and an opening at the distal end which is enlargeable from a first inside diameter for transluminal navigation to a second, larger inside diameter to facilitate aspiration of thrombus into the lumen. In one aspect of present disclosure, the distal opening is enlargeable in response to exposure to blood. In another aspect of present disclosure, the distal opening is enlargeable in response to exposure to body temperature. In yet another aspect of present disclosure, the distal opening is enlargeable in response to removal of a constraint. The constraint may comprise a polymer having a structural integrity that decreases in the intravascular environment.

[0268] In one aspect of present disclosure, the catheter body adjacent the distal opening comprises a radially outwardly biased embedded support. The catheter body adjacent the distal opening may comprise an embedded Nitinol frame. The support may comprise a wire mesh. The support may comprise a stent. In another aspect of present disclosure, the catheter body adjacent the distal opening comprises a hydrophilic blend. In yet another aspect of present disclosure, the tubular liner is formed by dip coating a removable mandrel. The tubular liner may comprise PTFE.

[0269] In one aspect of present disclosure, the tie layer comprises polyurethane. The tie layer may have a wall thickness of no more than about 0.005 inches. The tie layer may extend along at least the most distal 20 cm of the flexible body. In another aspect of present disclosure, the coil comprises a shape memory material. The coil may comprise Nitinol. The Nitinol may comprise an Austenite state at body temperature. In one aspect of present disclosure, the outer jacket is formed from at least five discrete tubular segments. The outer jacket may be formed from at least nine discrete tubular segments. The difference in durometer between a proximal one of the tubular segments and a distal one of the tubular segments may be at least about

20D. The difference in durometer between a proximal one of the tubular segments and a distal one of the tubular segments may be at least about 30D.

[0270] In accordance with one aspect, there is provided a neurovascular catheter extension segment, comprising: an elongate flexible control wire, having a proximal end and a distal end; a tubular extension segment having a side wall defining a central lumen carried by the distal end of the control wire, the side wall comprising: a tubular inner liner; a tie layer separated from the lumen by the inner liner; a helical coil surrounding the tie layer; and an outer jacket surrounding the helical coil. In one aspect of present disclosure, the outer jacket is formed from a plurality of tubular segments positioned coaxially about the coil. A proximal one of the tubular segments may have a durometer of at least about 60D, and a distal one of the tubular segments may have a durometer of no more than about 35D.

[0271] In another aspect of present disclosure, the tubular liner is formed by dip coating a removable mandrel. The tubular liner may comprise PTFE. In yet another aspect of present disclosure, the tie layer comprises polyurethane. The tie layer may have a wall thickness of no more than about 0.005 inches. The tie layer may extend along at least the most distal 20 cm of the tubular extension segment. In one aspect of present disclosure, the coil comprises a shape memory material. The coil may comprise Nitinol. The Nitinol may comprise an Austenite state at body temperature.

[0272] In one aspect of present disclosure, the outer jacket is formed from at least five discrete tubular segments. The outer jacket may be formed from at least nine discrete tubular segments. The difference in durometer between a proximal one of the tubular segments and a distal one of the tubular segments may be at least about 20D. The difference in durometer between a proximal one of the tubular segments and a distal one of the tubular segments may be at least about 30D. In another aspect of present disclosure, the control wire comprises a central lumen. The control wire central lumen may be in communication with the central lumen of the tubular extension segment. In yet another aspect of present disclosure, the inside diameter of the neurovascular catheter extension segment is at least 2× the inside diameter of the control wire central lumen. The inside diameter of the neurovascular catheter extension segment may be at least 3× the inside diameter of the control wire central lumen.

[0273] In accordance with another aspect, there is provided a neurovascular catheter extension segment system, comprising the neurovascular catheter extension segment described above and an agitator configured to extend through the control wire central lumen and into the central lumen of the tubular extension segment.

[0274] Although the present invention has been described in terms of certain preferred embodiments, it may be incorporated into other embodiments by persons of skill in the art in view of the disclosure herein. The scope of the invention is therefore not intended to be limited by the specific embodiments disclosed herein, but is intended to be defined by the full scope of the following claims.

What is claimed is:

1. A telescoping catheter, comprising:

an elongate, flexible tubular body, comprising a proximal section having at least one lumen and a distal section axially movably positioned within the lumen; and

- a control for advancing the distal section from a first, proximally retracted position within the proximal section to a second, extended position, extending distally beyond the proximal section; and
- an active tip on the distal end of the distal section, comprising a distal opening that is movable between a smaller and a larger configuration.
2. A telescoping catheter as in claim 1, wherein the control comprises a pull wire extending through the proximal section.
3. A telescoping catheter as in claim 1, wherein the distal section is distally advanceable to extend beyond the proximal section for a distance of at least about 10 cm.
4. A telescoping catheter as in claim 1, wherein the distal section is distally advanceable to extend beyond the proximal section for a distance of at least about 25 cm.
5. A telescoping catheter as in claim 1, wherein the distal opening is movable in response to movement of a control wire.
6. A telescoping catheter as in claim 1, wherein the distal opening is movable between a smaller and a larger configuration in response to application of vacuum to the lumen.
7. A telescoping catheter as in claim 1, wherein the size of the distal opening is changed by lateral movement of a side wall on the distal section.
8. A telescoping catheter as in claim 1, wherein the distal opening comprises at least one movable jaw.
9. A telescoping catheter as in claim 1, wherein the distal end of the distal section comprises a duck bill valve configuration.
10. A telescoping catheter as in claim 1, further comprising a controller for applying intermittent vacuum to the lumen.
11. A telescoping catheter as in claim 10, wherein the controller is configured to apply pulses of vacuum to the lumen spaced apart by spaces of neutral pressure.
12. A telescoping catheter as in claim 10, wherein the controller is configured to alternate between applying pulses of higher negative pressure and lower negative pressure.
13. A telescoping catheter as in claim 10, wherein the distal tip of the catheter axially reciprocates in response to application of pulses of vacuum to the lumen.
- * * * * *

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than or equal to about 0.06 inches, or less than or equal to about 0.05 inches. Referring to FIG. 30, an inner liner 3014 may be formed by dip coating a mandrel (not shown) to provide a thin walled tubular inside layer of the catheter body 3000. The dip coating may be produced by coating a wire such as a silver coated copper wire in PTFE. The mandrel may thereafter be axially elongated to reduce diameter, and removed to leave the tubular inner liner. The outside surface of the tubular inner liner 3014 may thereafter be coated with a soft tie layer 3012 such as polyurethane (e.g., TecoflexTM), to produce a layer having a thickness of no more than about 0.005 inches, and in some implementations approximately 0.001 inches. The tie layer 3012 will generally extend along at least about the most distal 10 cm or 20 cm of the catheter shaft 3000 generally less than about 50 cm and may in one implementation extend approximately the distal 30 cm of the catheter shaft 3000, 3100.

Change(s) applied
to document,
/T.D.R./
9/16/2020

5~16

Please amend page 42, lines 18 to 29 of the Specification as follows:

The durometer of the outer wall segments may decrease in a distal direction. For example, proximal segments such as 3022 and 3026, may have a durometer of at least about 60 or 70D, with gradual decrease in durometer of successive segments in a distal direction to a durometer of no more than about 35D or 25D or lower. A 25 cm section may have at least about 3 or 5 or 7 or more segments and the catheter 3000 overall may have at least about 6 or 8 or 10 or more distinct flexibility zones. The distal 1 or 2 or 4 or more segments 3036, 3038, may have a smaller OD following shrinking than the more proximal segments 3022-3034 within a larger OD section 3002, as illustrated in FIGS. 30 and 31A, to produce a step down in OD for the finished catheter body 3000. The length of the lower OD section 3004 may be within the range of from about 3 cm to about 15 cm and in some embodiments is within the range of from about 5 cm to about 10 cm such as about 7 or 8 cm, and may be accomplished by providing the distal segments 3036, 3038 with a lower wall thickness.

3~8

Please amend page 45, lines 18 to 23 of the Specification as follows:

The intraluminal catheter 3200 incorporates characteristics of the side wall construction of the catheter 3000 described herein. For example, as illustrated in FIGS. 32A-32C, the intraluminal catheter may comprise a plurality of short tubular segments 3232, 3234, 3236, 3238;

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corked clot and wiggle the distal end 2010 of the catheter 2002 and the clot during rotation 2006. The coil 2020 may be a tight, offset coil, and may comprise at least one and optionally two or three or more complete revolutions.

Change(s) applied

13-19

to document, **Please amend page 34, line 29 to page 35, line 5 of the Specification as follows:**

/T.D.R./

9/16/2020

Referring to FIGS. 21A–21B, the distal tip 2110 of the catheter 2102 may move or wiggle by interacting with the agitator 1900. As illustrated in the figures, the agitator 1900 comprises a wire or hypo tube 2104. When the distal end of the agitator 1900 rotates (e.g., via a driver 2106), the motion segment 1909 and distal tip 1905 of the agitator interact with the side wall of the catheter 2102 which wiggles as shown by broken lines 2112. The length of the motion segment, stiffness of the agitator 1900 and rotational velocity determines the interaction with the wall of the catheter 2102 and the amount of wiggle transmitted to the catheter 2101 with rotation of the agitator 1900.

3-29

Please amend page 40, line 17 to page 41, line 13 of the Specification as follows:

In one example, referring to FIG. 30, the catheter 3000 may have an effective length from the manifold to distal tip from about 70cm to about 150cm, from about 80cm to about 140cm, from about 90cm to about 130cm, from about 100cm to about 120cm, or from about 105cm to about 115cm. The outer diameter of the catheter 3000 may be from about 0.07 inches to about 0.15 inches, from about 0.08 inches to about 0.14 inches, from about 0.09 inches to about 0.13 inches, from about 0.1 inches to about 0.12 inches, or from about 0.105 inches to about 0.115 inches, and may be lower in a distal segment than in a proximal segment. The inner diameter 3108 of the catheter 3000 in a single central lumen 3001 embodiment may be greater than or equal to about 0.11 inches, greater than or equal to about 0.1 inches, greater than or equal to about 0.09 inches, greater than or equal to about 0.088 inches, greater than or equal to about 0.08 inches, greater than or equal to about 0.07 inches, greater than or equal to about 0.06 inches, or greater than or equal to about 0.05 inches. The inner diameter 3108 of the catheter 3000 in a single central lumen 3001 embodiment may be less than or equal to about 0.11 inches, less than or equal to about 0.1 inches, less than or equal to about 0.09 inches, less than or equal to about 0.088 inches, less than or equal to about 0.08 inches, less than or equal to about 0.07 inches, less

Change(s) applied
to document,

/T.D.R./

9/16/2020

AMENDMENTS TO THE SPECIFICATION

21

27

Please amend page 22, lines 15 to 24 of the Specification as follows:

A preferable, simplified method for aspirating a thrombotic occlusion in accordance with the present invention is described in connection with FIGS. 12A—12F. As illustrated in FIGS. 12A-12F, the cerebral circulation 1200 is simplified for the ease of demonstrating procedural steps. The alternative steps for aspirating a thrombotic occlusion make use of a transitional guidewire and a transitional guide sheath. The transitional guidewire has a soft and trackable distal segment with a smaller diameter so that the transitional guidewire may be advanced deeper than the guidewire 1126 described in FIG. 11C. In addition, the transitional guide sheath has a soft and trackable distal segment such that the transitional guide sheath may be advanced deeper than the guide sheath 1122 described in FIG. 11D. Using a transitional guidewire and a transitional guide sheath that can be advanced to an area near the clot eliminates the need to use a second guidewire or a reperfusion catheter to reach the clot.

10--17

Please amend page 26, line 27 to page 27, line 4 of the Specification as follows:

In another embodiment, shown in FIG. 14, an alternative aspiration system may comprises a vacuum generator 402, a frequency modulator 416, a valve controller 418, and a remote controller 420. In this embodiment, the solenoid valve 414 is positioned in and fluidly connects between the air/fluid reservoir 422 at the atmospheric pressure and the aspiration line 424 connecting the catheter 10 to the vacuum chamber 410 / collection canister 412. Unlike the first embodiment in FIG. 13, this system modulates pressure in the catheter 10 by allowing pressure to vary from vacuum to atmospheric pressure. When the solenoid valve 414 is open to the air/fluid reservoir 422 at the atmospheric pressure, the vacuum pressure in the aspiration line 424 decreases to the atmospheric pressure. When the solenoid valve 414 is closed, it increases the vacuum pressure in the aspiration line 424.

33

26-29

Please amend page 34, lines 13 to 16 of the Specification as follows:

Referring to FIG. 20A, an agitator 1900 comprises a wire or hypo tube 2004, as illustrated in the figure, and the distal end 2012 of the agitator 1900 may comprise a coil 2020 to grip a



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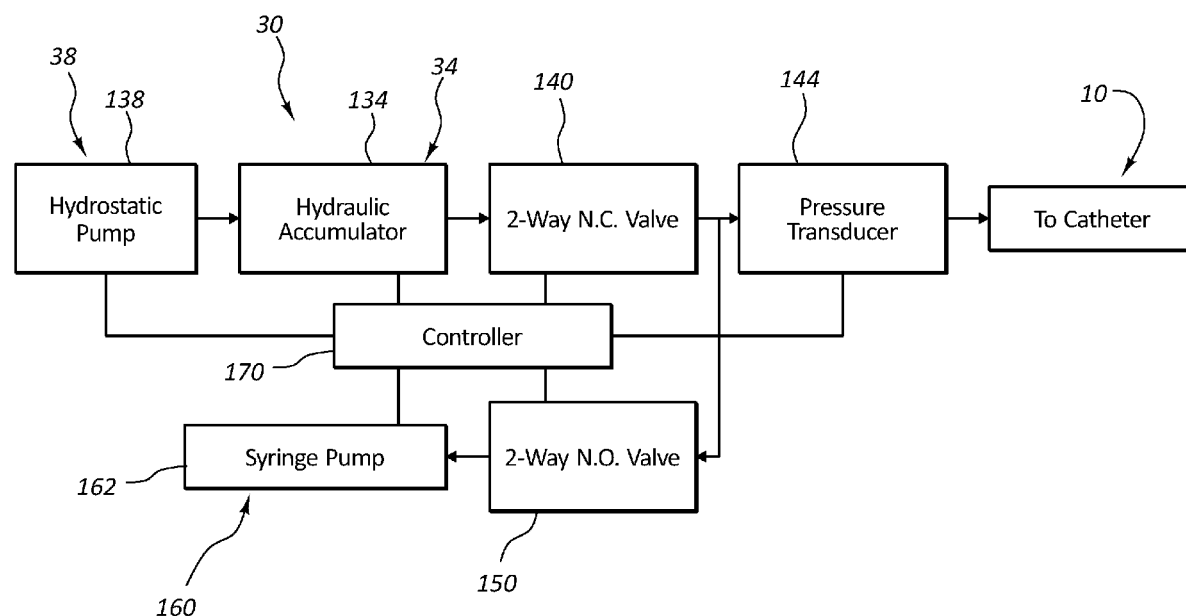


Fig. 3

(57) Abstract: A patency device for catheter assemblies and other elongate tubular devices used for establishing access to an interior body portion of a patient is disclosed. The patency device establishes and preserves patency of one or more lumens defined by the catheter assembly by providing impulses of positive pressure to fluid disposed in the lumen of the catheter assembly. In one embodiment, the patency device comprises a fluid reservoir configured to provide a fluid path to at least one lumen of the catheter assembly, and a pressure input portion. The pressure input portion is configured to provide pressure for one or more impulses of positive pressure to a fluid disposed within the lumen. The impulses are configured to dislodge occlusions that may have formed in the lumen. A negative pressure can then be provided to the lumen to aspirate the occlusion.



SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN,
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SYSTEMS AND METHODS FOR CORRECTING AND PREVENTING OCCLUSION IN A CATHETER

CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] This application claims the benefit of U.S. Provisional Patent Application No. 62/348,082, filed June 9, 2016, and titled “Systems and Methods for Correcting and Preventing Occlusion in a Catheter,” which is incorporated herein by reference in its entirety.

BRIEF SUMMARY

[0002] Briefly summarized, embodiments of the present invention are directed to a patency device for catheter assemblies and other elongate tubular devices used for establishing access to an interior body portion of a patient. The patency device establishes and/or preserves patency of one or more lumens defined by the catheter assembly by providing impulses of positive pressure to fluid disposed in the lumen of the catheter assembly.

[0003] In one embodiment, the patency device comprises a fluid reservoir configured to provide a fluid (or establish a fluid path) to at least one lumen of the catheter assembly, and a pressure input portion. The pressure input portion is configured to provide pressure for one or more impulses of positive pressure to a fluid disposed within the lumen. The impulses are configured to dislodge occlusions that may have formed in the lumen. A negative pressure can then be provided to the lumen to aspirate the occlusion and remove it from the catheter assembly.

[0004] These and other features of embodiments of the present invention will become more fully apparent from the following description and appended claims, or may be learned by the practice of embodiments of the invention as set forth hereinafter.

BRIEF DESCRIPTION OF THE DRAWINGS

[0005] A more particular description of the present disclosure will be rendered by reference to specific embodiments thereof that are illustrated in the appended drawings. It is appreciated that these drawings depict only typical embodiments of the invention and are therefore not to be considered limiting of its scope. Example embodiments of the invention will be described and explained with additional specificity and detail through the use of the accompanying drawings in which:

[0006] FIG. 1 is a simplified view of a catheter assembly and a patency device attached thereto according to one embodiment;

[0007] FIG. 2 is a graph showing a pressure profile for the patency device of FIG. 1;

[0008] FIG. 3 is a block diagram of a patency device according to one embodiment;

[0009] FIGS. 4A and 4B are schematic diagrams of valve assemblies for the patency device of FIG. 3;

[00010] FIG. 5 is a block diagram of a patency device according to one embodiment;

[00011] FIG. 6 is a block diagram of a patency device according to one embodiment;

[00012] FIG. 7 is a block diagram of a patency device according to one embodiment;

[00013] FIG. 8 is a pressure profile for a patency device according to one embodiment;

[00014] FIG. 9 is a pressure profile for a patency device according to one embodiment;

[00015] FIG. 10 is a pressure profile for a patency device according to one embodiment; and

[00016] FIG. 11 is a block diagram of a patency device according to one embodiment.

DETAILED DESCRIPTION OF SELECTED EMBODIMENTS

[00017] Reference will now be made to figures wherein like structures will be provided with like reference designations. It is understood that the drawings are diagrammatic and schematic representations of exemplary embodiments of the present invention, and are neither limiting nor necessarily drawn to scale.

[00018] For clarity it is to be understood that the word “proximal” refers to a direction relatively closer to a clinician using the device to be described herein, while the word “distal” refers to a direction relatively further from the clinician. For example, the end of a catheter placed within the body of a patient is considered a distal end of the catheter, while the catheter end remaining outside the body is a proximal end of the catheter. Also, the words “including,” “has,” and “having,” as used herein, including the claims, shall have the same meaning as the word “comprising.”

[00019] Embodiments of the present invention are generally directed to catheter assemblies and other elongate tubular devices used for establishing access to an interior body portion of a patient. A peripherally inserted central catheter (“PICC”) is one example of such a catheter assembly. In particular, solutions and methods for establishing and preserving the patency of one or more lumens defined by the catheter assembly are disclosed. Examples of patency devices that may be employed are disclosed according to particular embodiments, discussed below.

[00020] Reference is first made to FIG. 1, which generally depicts various details of a catheter assembly (“catheter”), generally designated at 10, and a patency device, to be described further below, in accordance with one embodiment. As shown, the catheter 10 includes an elongate catheter tube 12 that defines a lumen 14 extending between a proximal end 12A and a distal end 12B of the catheter tube. A luer connector 22 or other suitable connector is included at the proximal end 12A of the catheter tube 12. In other embodiments, the catheter can include a bifurcation hub at the proximal end of the catheter tube, with one or more extension legs proximally extending therefrom.

[00021] Though shown here as defining a single lumen 14, the catheter 10 in other embodiments can define two or more lumens. Also, though shown as a PICC, the catheter in other embodiments can include other catheter types, such as dialysis, CVC, PIV, urinary, arterial, balloon catheters, etc. Thus, the discussion herein is not intended to be limiting.

[00022] FIG. 1 further shows details regarding a patency device 30 configured to operably connect on a temporary basis with the catheter 10 and provide patency to the catheter tube lumen 14, according to one embodiment. Generally, the patency device 30 includes a fluid reservoir 34 that is configured, together with a pressure input portion 38, to provide one or more relatively short-duration impulses, also referred to herein as positive pressure impulses, of high-pressure fluid to the lumen 14 of the catheter tube 12. Such impulses, when performed periodically, are configured to prevent the formation of thrombus or other occlusion in the lumen 14, especially at the distal end thereof. These short-duration, high pressure impulses can also be used to clear the lumen after occlusions have formed therein.

[00023] In greater detail, the pressure input portion 38 of the patency device 30 includes a mechanical input, such as a manual or motor-controlled plunger-type syringe, to impart pressure impulses to fluid contained in the fluid reservoir 34. The fluid reservoir 34 is

configured to hold an amount of fluid that can be directed into the lumen(s) 14 of the catheter tube 12 prior to or in conjunction with the pressure impulses produced by the pressure input portion 38. In one embodiment and as seen below, the fluid reservoir 34 serves as a hydraulic accumulator to store pressurized fluid, produced by the pressure input portion 38, before its release to the lumen(s) 14.

[00024] It is noted that other types of pressure input portions can be utilized to provide high-pressure fluid impulses, including electrical and acoustic actuators, voice coil actuators, linear actuators, piezoelectric motors, vibrational drums and membrane, etc., for instance.

[00025] A catheter connector interface 40 defining a lumen 42 is included to enable the patency device 30 to operably connect to the luer connector 22 (or other portion) of the catheter 10 and provide a conduit through which the high pressure fluid can pass from the fluid reservoir 34 to the lumen(s) 14 of the catheter tube 12. Note that in one embodiment the connector interface 40 is a sterile item to bridge between the non-sterile patency device 30 and the catheter 10. In this way, the connector interface 40 can be manufactured as a disposable, sterile item, while the patency device 30 is reusable.

[00026] In operation, the patency device 30 emits periodic, relatively short-duration, relatively high-pressure bursts, or impulses, in the distal direction through the fluid-filled lumen 14 of the catheter tube 12. These impulses are produced by the pressure input portion 38 in conjunction with the pressure portion 34 and transmitted through the lumen 42 of the patency device 30 to the catheter tube lumen 14 via the connector interface 40 luer connector 22. It is appreciated that the pressure of the impulses, the impulse duration, the rest period between impulses, the frequency of successive impulses, etc., can be adjusted and varied according to the particular patency procedure being performed for the catheter 10.

[00027] FIG. 2 depicts a graph of a pressure profile 80 (including fluid pressure vs. time) produced by the patency device 30 during operation. The pressure profile 80 includes time on the x-axis and impulse pressure on the y-axis for operation of the patency device 30. As shown, the patency device 30 provides short-duration, relatively high-pressure impulses through the fluid present in the catheter tube lumen 14 interspersed by relatively longer rest periods 84 of negative baseline pressure provided to the catheter tube lumen. The negative baseline pressure present between impulses enables any occlusion dislodged by the impulses to be sucked proximally up the catheter tube lumen 14 and removed therefrom, thus preventing the

dislodged occlusion from entering the bloodstream from the distal end 12B of the catheter tube 12. Note that the rest periods in other embodiments can include a reduction to a neutral pressure or lower (but still positive) pressure or to varying pressures over time as may be desired.

[00028] FIG. 2 further shows that successive impulse peaks 82 that represent the short-duration high-pressure fluid impulses are shown on the graph of the pressure profile 80. In the present embodiment, the pressure peaks 82 are each characterized by a rise-time phase of about 30 milliseconds, a holding high-pressure phase of about 200 milliseconds, and a pressure reduction phase of about 40 milliseconds. It is appreciated that these phases of the pressure peaks 82 can vary from the values given herein, and each pressure peak can vary in phase characteristics from previous and/or subsequent peaks. Also, the magnitude and duration of the impulses can vary from what is described herein and from one another.

[00029] In one embodiment, the pressure peaks 82 are modified by a controller of the patency device 30 so as to be customizable by the user. The rest periods 84 between the high-pressure fluid impulses (represented by the pressure peaks 82) can also be varied in duration, baseline pressure, etc.

[00030] In the present embodiment, the maximum pressure achieved by the impulses is about 400 psi, though this can vary according to desired application, catheter lumen design, type or size of occlusion, catheter tube length, etc. In one embodiment, it is appreciated that the maximum pressure of the impulses may exceed the burst pressure strength rating of the catheter tube 12 in one embodiment, but as the impulses are of relatively short duration, no rupturing or failure of the catheter 10 occurs.

[00031] As mentioned above, the high-pressure fluid impulses travel from the patency device 30 and into the catheter 10 so as to travel down the fluid-filled lumen 14 of the catheter tube 12. In one embodiment, the fluid filling the fluid path of the patency device and the catheter tube lumen 14 is a 0.9% saline solution, though other fluids may also be acceptably used. Note that the use of other fluids can necessitate altering the impulse characteristics (e.g., impulse pressure, impulse duration, rest period duration, etc.). As noted above, the high-pressure fluid impulses impinge on an occlusion (such as a clot or fibrin sheath) or other obstruction that has formed in the lumen 14, typically at or proximate the distal end 12B of the catheter tube 12. The occlusion is dislodged by the high-pressure impulses, which are strong enough to dislodge the occlusion but are not of sufficient duration to push it out the distal end

12B of the catheter tube 12. The subsequent negative pressure rest period following each impulse can act to prevent escape of the clot from the catheter tube 12, in one embodiment. In addition, a suction process can be performed by the patency device 30 to withdraw the clot proximally from the catheter tube 12 and catheter 10 and into the patency device, where it may be disposed of. In this way, any clot or occlusion present in the catheter 10 can be acceptably removed.

[00032] FIG. 3 depicts the patency device 30 according to one embodiment. As shown, the patency device 30 includes a hydrostatic pump 138 that serves as the pressure input portion 38 for providing hydraulic pressure to fluid contained and maintained at pressure in a hydraulic accumulator (“accumulator”) 134 that serves as the fluid reservoir 34. A two-way, normally closed (“N.C.”) valve 140 is disposed at and operably connected at its fluid inlet to a fluid outlet of the accumulator 134 via a fluid line. A pressure transducer 144 is operably interposed between the fluid outlet of the N.C. valve 140 and the luer connector 22 or other suitable inlet to the catheter. As mentioned above, in this and other embodiments the connector interface 40 (FIG. 1) can be used to operably connect the patency device 30 to the catheter 10. Note that the fluid lines between the various components discussed herein can include tubing or other suitable modes for fluid transport.

[00033] A two-way, normally open (“N.O.”) valve 150 is interposed between the N.C. valve 140 and the transducer 144 via a fluid line connected to the N.O. valve fluid inlet. A vacuum input portion 160 for providing negative pressure in the patency device 30 is operably connected to the fluid outlet of the N.C. valve 150. In the present embodiment, a syringe pump 162 serves as the vacuum input portion 160, though other suitable components can also be employed, such as a vacuum pump. A controller 170 is operably connected to the aforementioned components of the patency device 30 to govern their operation. The controller 170 in one embodiment includes a power source, a printed circuit board including a processor, etc.

[00034] FIG. 4A depicts various details regarding a valve control assembly 180 associated with the N.C. valve 140 shown in the patency device 30 of FIG. 3, according to one embodiment. As shown, the valve control assembly 180 includes a relay 182 and a power diode operably interconnected with the N.C. valve 140. A power supply 186 is included for the N.C. valve 140, as is a power supply 188 for the relay 182. FIG. 4B shows a similar configuration for the valve control assembly 180 associated with the N.O. valve 150 of the

patency device 30 of FIG. 3, including a relay 182 and a power diode operably interconnected with the N.O. valve. A power supply 186 is included for the N.O. valve 150, as is a power supply 188 for the relay 182. The valve control assemblies 180 for the N.C. valve 140 and the N.O. valve 150 assist in governing operation of the N.C. and N.O. valves during operation of the patency device 30. In the present embodiment, the N.C. valve 140 and the N.O. valve 150 are gate-valve types of valves, though it is appreciated that other suitable types of valves can be utilized. In another embodiment, the functionality of the N.C. valve 140 and the N.O. valve 150 can be combined into a single valve, such as a three-way valve, with the fluid lines being arranged so as to provide such an embodiment. In such a single valve embodiment, the single three-way valve is operated to alternately provide the impulses of positive pressures as well as the negative baseline pressures/negative impulses.

[00035] The patency device 30 of FIG. 3 is operably attached to luer connector 22 of the catheter 10 when a patency procedure (a procedure to clear the catheter tube lumen(s) 14 of an occlusion or to prevent formation thereof) is desired by a clinician or catheter user. In operation, the patency device 30 first provides fluid pressure via actuation – either manually or by automatic/motor modes – of the hydrostatic pump 138. The pressurized fluid is received from the pump 138 by the accumulator 134, which stores the fluid in a pressurized state until needed. The N.O. valve 150 is maintained in an open state at the beginning and during the procedure to maintain a negative base pressure in the system except at those times when the N.C. valve 140 is opened to provide the fluid impulses. The controller 170 or other suitable component can control valve opening/closing.

[00036] The controller 170 determines the number, frequency, rest periods, etc., of the impulses to be delivered by the patency device 30 to the catheter tube lumen(s) 14. The N.C. valve 140 is opened and close repeatedly at predetermined time intervals to provide a series of fluid impulses from the accumulator, through the N.C. valve and into the lumen 14 of the catheter 10. During each impulse when the N.C valve 140 is opened, the N.O valve 150 is shut so as to prevent impulse fluid from entering the N.O. valve and diverting to the syringe pump 162 instead of entering the catheter tube lumen 14 as desired. The impulses are propagated distally down the lumen 14, which is fluid-filled prior to commencement of the patency operation so as to provide a propagation medium for the impulses.

[00037] Between each impulse and after the series of impulses has ended, the N.C. valve 140 closes and the N.O. valve 150 opens to provide a negative baseline pressure (provided by

the syringe pump 162 or other suitable device) in the catheter tube lumen 14 and enable any occlusion dislodged by the impulses to be suctioned proximally out of the lumen, through the N.O. valve to the syringe pump 162. An appropriate capture reservoir or the like can be operably connected to the syringe pump to provide for retention of occlusions and fluid if needed. The controller 170 is utilized to precisely control the opening/closing of the N.C. valve 140 and the N.O. valve 150 so as to provide the impulses and the negative baseline pressure to the lumen 14 as desired.

[00038] In one embodiment, it is appreciated that the baseline negative pressure periods existing between the positive pressure impulses can be replaced or supplemented with relatively short-duration impulses of negative pressure to further assist in occlusion dislodgement. Subsequent negative baseline pressure can then be used to remove the occlusion to the lumen 14. In one embodiment, the response time of the valves 140 and 150 is sufficiently fast to enable the positive pressure impulses to be followed in quick succession by the negative baseline pressure or negative pressure impulse.

[00039] The pressure transducer 144 is utilized and controlled by the processor 170 to measure the pressure of the impulses delivered to the catheter tube lumen 14 by the patency device 30. As mentioned, the pressure level of the impulses can be varied or determined according to a variety of factors, including catheter length, catheter lumen size, burst strength, impulse duration, rest period duration, other catheter configuration, etc. In one embodiment, the pressure of each impulse can be chosen from a range of from about 30 psi to about 120 psi, though other pressure below and above this are possible. Also, frequency of the impulses, or impulse frequency, can be set according to a predetermined pattern and can vary according to a number of factors such as those described immediately above and can range in one embodiment from about 1 to over about 150 Hz, though other frequency ranges are also possible. In one embodiment, the impulse frequency is set to match the resonant frequency of the catheter 10 itself, thus enabling improved propagation of the impulses distally through the lumen 14. In one example, for instance, the resonant frequency of a 3 Fr single lumen catheter assembly was found to be about 30 Hz for catheter tube lengths of from about 35 cm to about 55 cm. The resonant frequency will vary according to a number of catheter characteristics. In one embodiment, for instance, resonant frequencies for various catheters vary from about 15 Hz to about 50 Hz, though other frequencies are possible.

[00040] In one embodiment, the impulse frequency is above about 20 KHz, thus performing as an ultrasound impulse signal to dislodge lumen occlusions or maintain lumen patency. These ultrasonic signals are of sufficient frequency, intensity, and duty cycle as to dislodge the occlusion(s) present in the lumen(s) 14. In one embodiment, the patency device 30 can include an ultrasound module operably connectable to the luer connector 22 or extension leg of the catheter 10 and further includes an ultrasound transducer for providing ultrasonic impulses to the fluid-filled lumen 14. The patency device 30 can further include ports to enable fluids or other substances to be infused into or aspirated from the catheter tube lumen(s) 14, such as antimicrobial agents, etc.

[00041] Note that the patency device 30 is either externally powered or can include its own power source, such as a battery. Note further that in one embodiment that the controller 170 can enable customization of the characteristics of the impulses, rest periods, baseline pressure, etc. by the user.

[00042] It is appreciated that periodic use of the patency devices described herein can also serve to prevent the formation of an occlusion by preventing initial adherence and growth of the occlusion in the first place, as mentioned herein. In one embodiment, the patency device is self-operating, thus serving as a passive solution to preventing occlusions.

[00043] Note that in one embodiment a pressure regulator can be employed to provide and/or maintain pressurized fluid in the patency device 30. Note also that it is appreciated that adjustments may be made to the pressure of the impulses to compensate for pressure loss/attenuation as a function of the distance the impulse travels distally through the catheter tube lumen 14.

[00044] In light of the above, it is appreciated that in one embodiment, a method for providing patency to at the lumen(s) 14 the catheter assembly 10 comprises disposing a fluid in the lumen of the catheter tube 12 of the catheter; and propagating a plurality of impulses of positive pressure through the fluid disposed in the lumen, noting that the impulses are propagated in a predetermined pattern.

[00045] The patency device of FIG. 5 replaces the gate valve-type of valves with tubing pinch valves for the N.C valve 140 and the N.O. valve 150. Such valves operate by pinching off a portion of the tubing that comprises the fluid lines, such as the illustrated high pressure tubing 194 proximate the N.O. pinch valve 150, so as to stop fluid flow therethrough. The

valve releases the pinch-off of the tubing to enable fluid flow anew therethrough. These and other valve types are therefore contemplated.

[00046] FIG. 6 depicts details of the patency device 30 according to another embodiment, wherein the pressure input portion 38 includes an actuator, such as a voice coil actuator 200 configured to provide mechanical movement for the formation of the desired fluid pressure impulses. A servo drive 214 is operably connected to the voice coil actuator 200 to assist in actuator function. A piston 202 (or plunger or the like) is operably connected to the voice coil actuator 200, which in turn is operably connected to the fluid reservoir 34, here a fluid-containing syringe 206. The syringe 206 in the present embodiment is a high pressure syringe. The piston 202 is sized to be received within a proximal end of the syringe 206 so as to enable the piston to transfer the mechanical movements of the voice coil actuator to the fluid present in the syringe to create the desired impulses. Impulses produced in the fluid of the syringe 206 are forwarded past a valve 210 and into the lumen 14 of the catheter tube 12. A hub adapter 208 is included in the present embodiment to enable the valve 210 to operably connect to the catheter 10.

[00047] The valve 210 is operable, such as by 170 controller, to selectively open to enable the impulses produced by the aforementioned components to pass through to the catheter lumen 14. At all other times during a patency procedure, the valve 210 is switched to enable a negative baseline pressure to be imparted to the catheter lumen 14 via the syringe pump 162 in manner similar to embodiments discussed above. In one embodiment, pressure of the impulses produced by the patency device 30 of FIG. 6 are measured from about 60 psi to more than about 100 psi, though this can vary according to system design.

[00048] FIG. 7 depicts details of the patency device 30 according to another embodiment, wherein the pressure input portion 38 includes a wave generator 220, such as a loudspeaker, to produce energy for the formation of the desired fluid impulses. A signal generator 224 produces voltage waveforms, or driving signals, to actuate the wave generator in a desired pattern for the impulses, the signals of the signal generator being amplified by an amplifier 226. In one embodiment, pressure of the impulses produced by the patency device 30 of FIG. 7 are measured at about 40 psi or less, though this can vary according to system design.

[00049] A piston, such as a plunger, is operably connected to the movable cone of the loudspeaker of the wave generator 220 is received within the fluid-containing syringe 206,

serving as the fluid reservoir 34. Operation of the loudspeaker moves the cone thereof in accordance with the driving signals received and amplified by the signal generator 224 and amplifier 226, which in turn moves the plunger in accordance with the driving signals. The fluid contained in syringe 106 is moved by the plunger, which produces the desired fluid impulses that are propagated distally through the lumen 14 of the catheter 10 via the hub adapter 208. In one embodiment, the impulses produced by the patency device of FIG. 7 are in a frequency range of from about 1 to about 200 Hz, though a variety of other frequencies are possible.

[00050] The embodiments of the patency device 30 shown and described in connection with FIGS. 3, 5, 6, and 7 are therefore representative of a multitude of a variety of patency devices that can be employed to provide fluid impulses for the dislodgement of occlusive material within the lumen of a catheter and/or to maintain the patency of the lumen, free from occlusions.

[00051] FIGS. 8-10 depict various operation cycles for the positive pressure impulses produced by the present patency device, such as the patency device 30 shown in FIG. 6, for instance. FIG. 8 shows a pulse profile 280 including a continuous series of equal (in terms of energy, pressure) impulses delivered to the catheter tube lumen 14 (FIG. 1) at a set impulse frequency and returning to a baseline pressure 284 before starting the next impulse. The frequency can be any one or more of a variety of impulse frequencies, including ultrasonic frequencies (*e.g.*, above 20 KHz).

[00052] In FIG. 9, a series of groups of impulses is shown, wherein groups of impulses are separated by rest periods 286 of nominal baseline pressure 284, such as a low positive pressure, which pattern is useful for when no occlusion is present but impulses are used to keep the lumen 14 patent.

[00053] In FIG. 10, a series of groups of impulses is shown, wherein groups of impulses are separated by rest periods 286 of negative baseline pressure 284 to enable aspiration from the catheter 10 of any occlusions dislodged by the impulses, as discussed further above. In these and the other examples herein, note that the number of impulses in each group can vary according to user desire and/or a pre-set predetermined pattern, as can the pressure, frequency, etc. Note that frequency use of the patency device 30 can vary from continuously, hourly,

daily, weekly, occasionally, etc., depending on whether the intended use is prophylactic or corrective, the amount of occlusion present, etc.

[00054] FIG. 11 depicts details of the patency device 30 including the pressure input portion 38, including a hydrostatic pump or other suitable component as described herein or appreciated. A membrane 290 is included and configured to move/vibrate when acted upon by the positive pressure produced by the pressure input portion 38, thus producing impulses of positive pressure that are propagated through fluid disposed in a valve 294, such as a three-way valve, before travelling through the fluid-filled luer connector 22 and the lumen 14 of the catheter 10 to provide patency thereto. A vacuum input portion 160 is provided to supply negative baseline pressure/negative pressure impulses to fluid in the lumen 14 when the valve 294 is actuated to provide fluid communication therebetween. It is appreciated that no fluid reservoir 34 is included in the present embodiment. The embodiment shown in FIG. 11 can include a T-connector to provide the illustrated structure, in one embodiment.

[00055] Embodiments of the invention may be embodied in other specific forms without departing from the spirit of the present disclosure. The described embodiments are to be considered in all respects only as illustrative, not restrictive. The scope of the embodiments is, therefore, indicated by the appended claims rather than by the foregoing description. All changes that come within the meaning and range of equivalency of the claims are to be embraced within their scope.

CLAIMS

What is claimed is:

1. A patency device for providing patency to at least one lumen of a catheter assembly, the patency device comprising:
 - a fluid reservoir configured to provide a fluid path to the at least one lumen of the catheter assembly;
 - a pressure input portion configured to provide pressure for at least one impulse of positive pressure to a fluid disposed within the at least one lumen; and
 - an interface portion configured to operably connect the patency device to the at least one lumen.
2. The device as defined in claim 1, wherein the at least one impulse is configured to dislodge an occlusion disposed in the at least one lumen.
3. The device as defined in claim 1, wherein the patency device is further configured to provide a temporary negative pressure to the fluid disposed in the at least one lumen.
4. The device as defined in claim 3, wherein the temporary negative pressure is provided by a vacuum input portion of the patency device.
5. The device as defined in claim 4, wherein the vacuum input portion includes at least one of a syringe pump and a vacuum pump.
6. The device as defined in claim 4, wherein a normally open valve is included with the vacuum input portion.
7. The device as defined in claim 6, wherein a normally closed valve is included with the pressure input portion.
8. The device as defined in claim 7, wherein the normally open valve is configured to provide the temporary negative pressure to the fluid disposed in the at least one lumen, the normally open valve configured to close upon opening of the normally closed valve, the normally closed valve configured to provide the at least one impulse to the fluid disposed in the at least one lumen.

9. The device as defined in claim 1, wherein the at least one impulse includes a series of impulses at a predetermined impulse frequency and wherein the interface portion is disposable and provides a sterile barrier between the catheter assembly and the patency device.

10. The device as defined in claim 9, wherein the predetermined impulse frequency is at least 20 KHz.

11. The device as defined in claim 1, wherein the pressure input portion provides multiple series of the impulses in a predetermined impulse pattern, each series including at least one impulse.

12. The device as defined in claim 11, wherein each of the series of the impulses is separated by a rest period.

13. The device as defined in claim 12, wherein the patency device is configured to provide a negative pressure to the fluid disposed within the at least one lumen during each rest period.

14. The device as defined in claim 1, wherein the patency device is configured to provide the at least one impulse at a pressure of at least 30 psi.

15. The device as defined in claim 1, wherein the patency device is configured to provide the at least one impulse at a pressure that exceeds a burst pressure strength rating of a catheter tube of the catheter assembly.

16. The device as defined in claim 1, further comprising a pressure transducer configured to provide data relating to a pressure within a fluid line of the patency device.

17. The device as defined in claim 1, further comprising a controller configured to govern operation of the patency device, the controller including a processor.

18. The device as defined in claim 1, wherein the pressure input portion includes at least one of a hydrostatic pump, an actuator, and a wave generator.

19. The device as defined in claim 1, wherein the fluid reservoir includes at least one of a hydraulic accumulator and a syringe.

20. The device as defined in claim 1, wherein the at least one impulse includes a rise-time phase of about 30 milliseconds, a holding high-pressure phase of about 200 milliseconds, and a pressure reduction phase of about 40 milliseconds.

21. A patency device for providing patency to at least one lumen of a catheter assembly, the patency device comprising:

- a fluid path to the at least one lumen of the catheter assembly;
- a pressure input portion configured to provide pressure for at least one impulse of positive pressure to a fluid disposed within the at least one lumen; and
- a vacuum input portion configured to provide a temporary negative pressure to the fluid disposed in the at least one lumen.

22. The device as defined in claim 21, wherein the vacuum input portion includes at least one of a syringe pump and a vacuum pump.

23. The device as defined in claim 21, wherein a normally open valve is included with the vacuum input portion.

24. The device as defined in claim 23, wherein a normally closed valve is included with the pressure input portion.

25. The device as defined in claim 24, wherein the normally open valve is configured to provide the temporary negative pressure to the fluid disposed in the at least one lumen, the normally open valve configured to close upon opening of the normally closed valve, the normally closed valve configured to provide the at least one impulse to the fluid disposed in the at least one lumen.

26. The device as defined in claim 21, wherein the pressure input portion includes one of a hydrostatic pump and an actuator, and wherein the fluid path includes a hydraulic accumulator operably connected to the hydrostatic pump.

27. The device as defined in claim 21, wherein the at least one impulse includes a series of impulses at a predetermined impulse frequency.

28. A method for providing patency to at least one lumen of a catheter assembly, the method comprising:

disposing a fluid in the at least one lumen of a catheter tube of the catheter; and propagating a plurality of impulses of positive pressure through the fluid disposed in the at least one lumen, the impulses propagated in a predetermined pattern.

29. The method as defined in claim 28, wherein propagating the plurality of impulses comprises propagating at least one series of impulses at a predetermined impulse frequency.

30. The method as defined in claim 29, further comprising propagating a first series of impulses followed by a rest period, and propagating a subsequent series of impulses.

31. The method as defined in claim 28, wherein propagating the plurality of impulses further comprises propagating the impulses at a pulse frequency of at least about 20KHz.

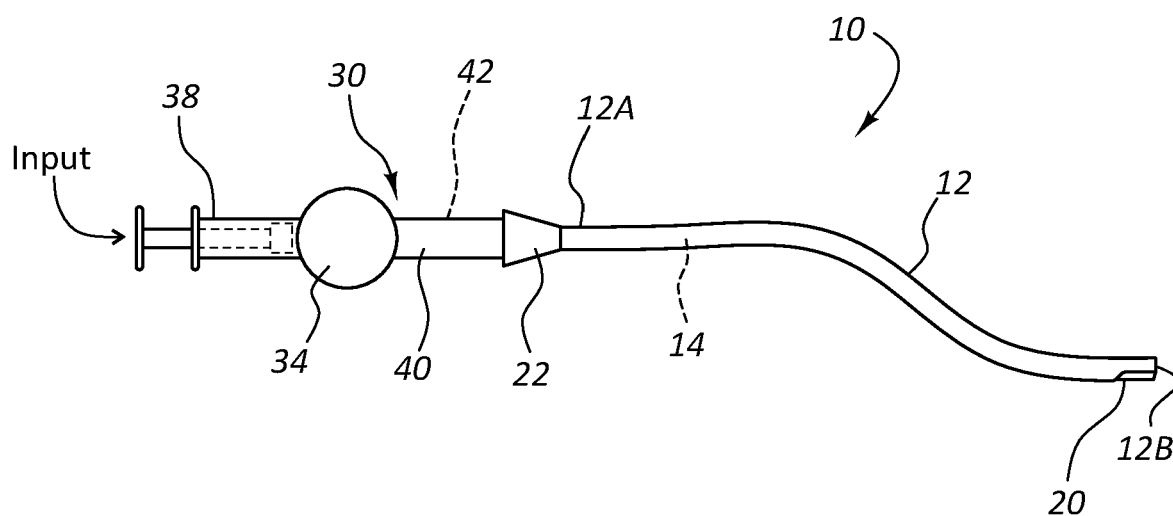
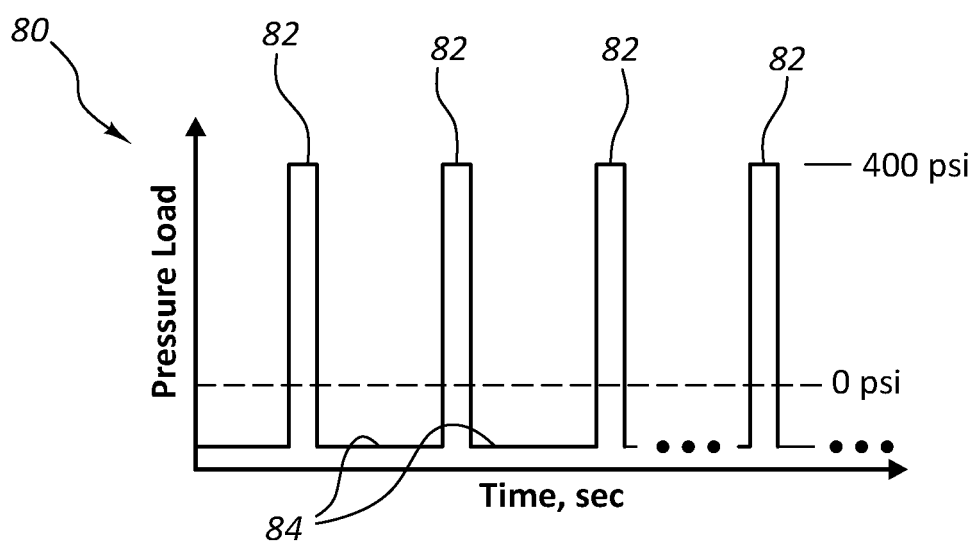
32. The method as defined in claim 28, further comprising providing a negative pressure to the fluid disposed in the at least one lumen to aspirate occlusions dislodged by the plurality of impulses.

33. The method as defined in claim 28, further comprising providing a negative pressure to the fluid disposed in the at least one lumen between impulses of positive pressure to aspirate occlusions dislodged by the plurality of impulses.

34. The method as defined in claim 28, wherein propagating the impulses includes propagating the impulses in a distal direction with respect to the at least one lumen of the catheter tube.

35. The method as defined in claim 28, wherein propagating the plurality of impulses comprises propagating at least one series of impulses at a predetermined impulse frequency, the impulse frequency substantially matching a resonant frequency of the catheter assembly.

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**Fig. 1****Fig. 2**

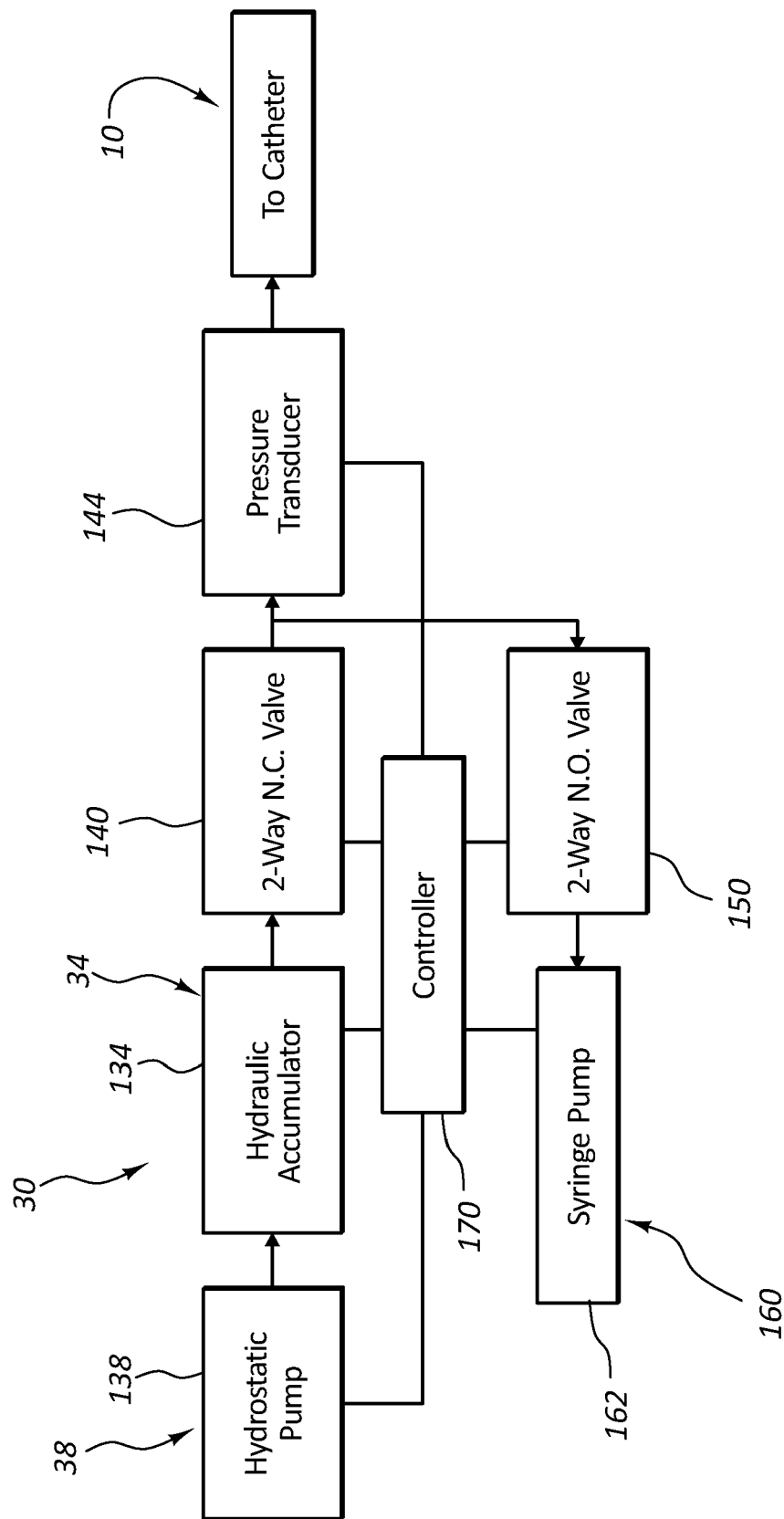
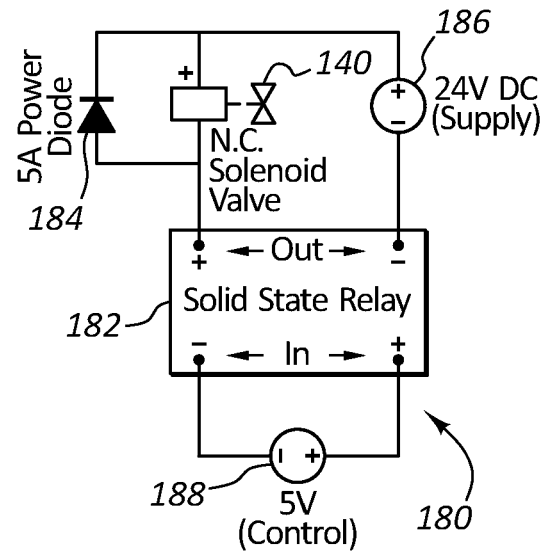
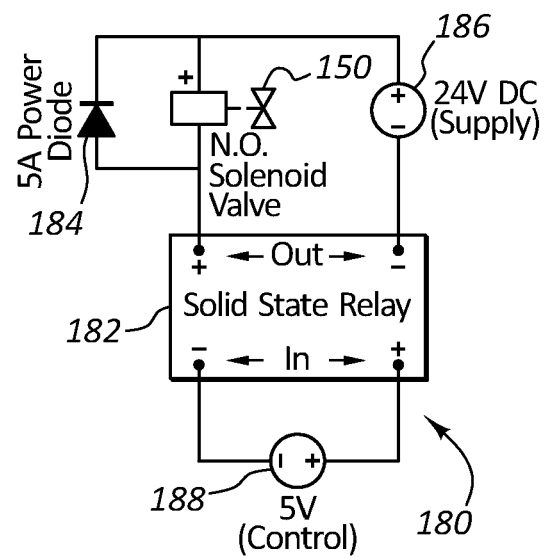


Fig. 3

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**Fig. 4A****Fig. 4B**

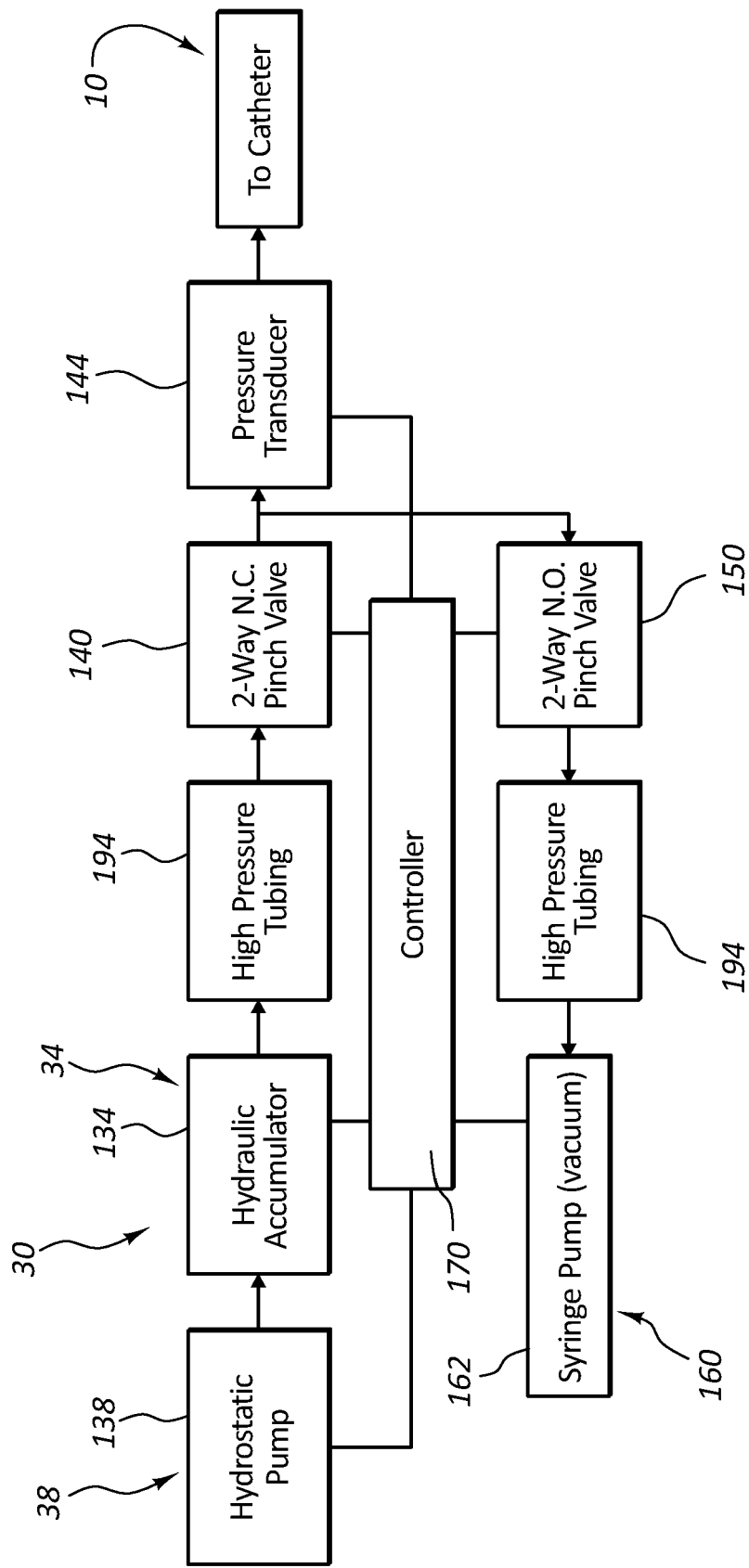


Fig. 5

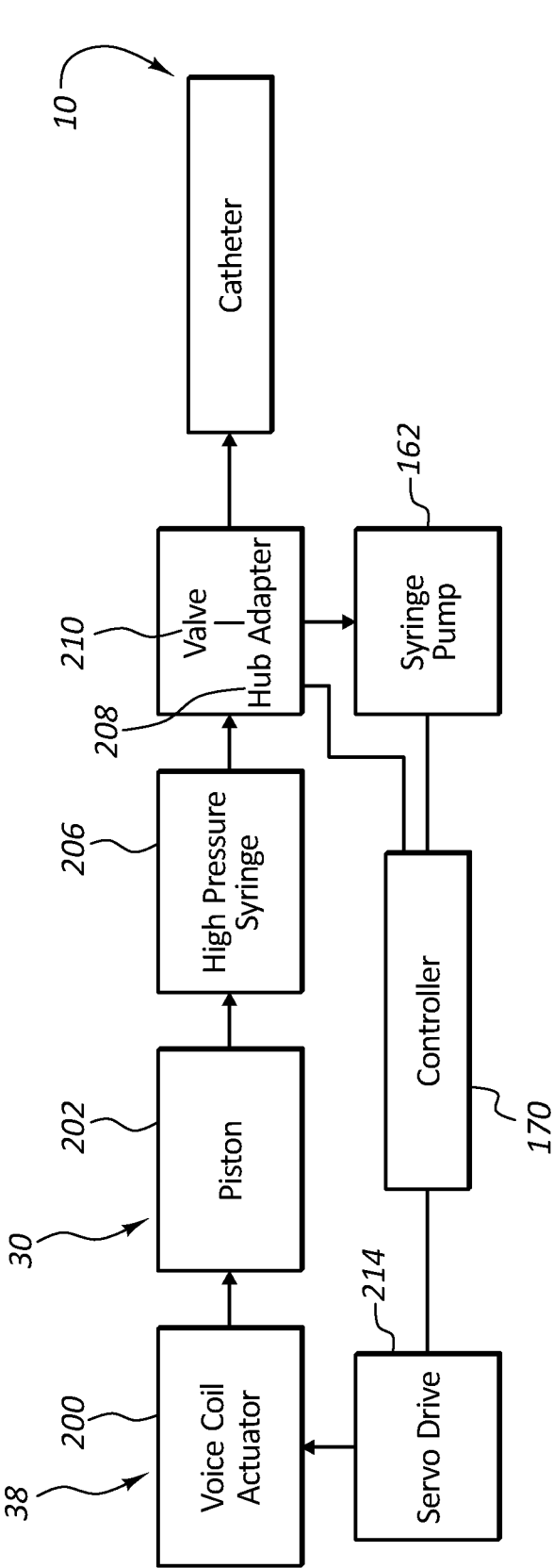


Fig. 6

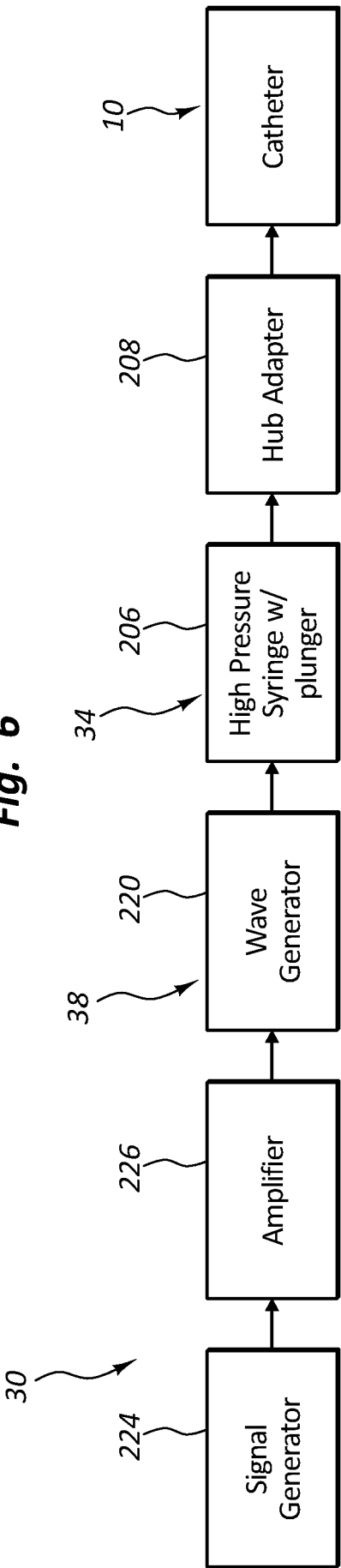


Fig. 7

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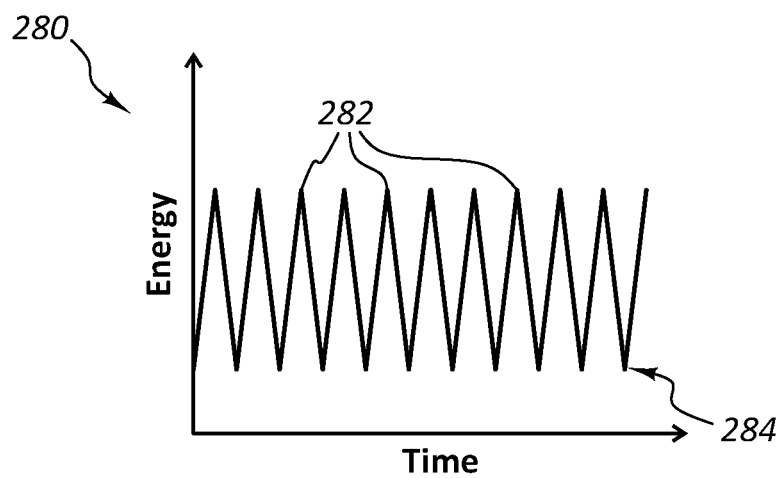


Fig. 8

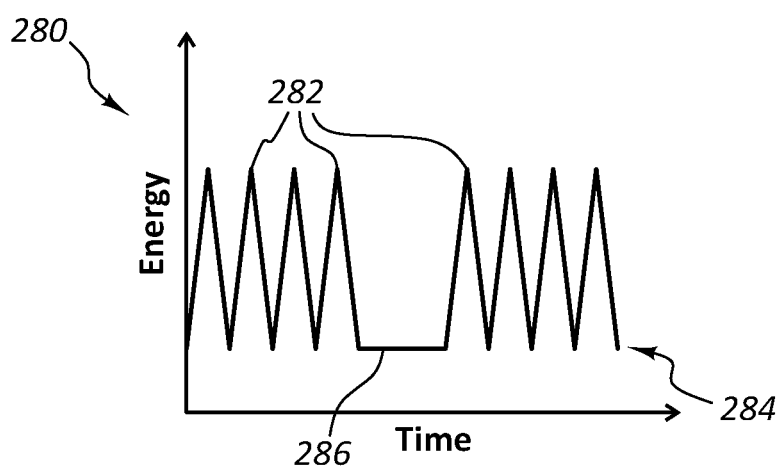


Fig. 9

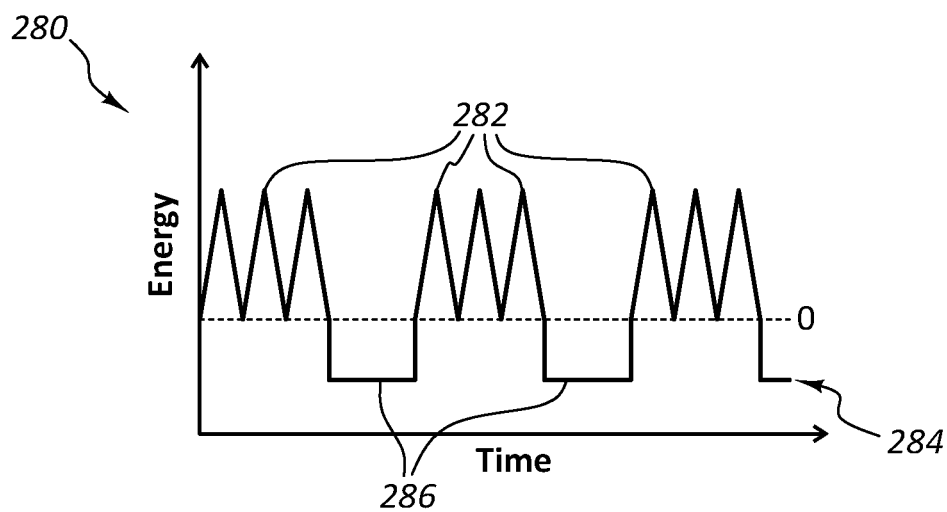


Fig. 10

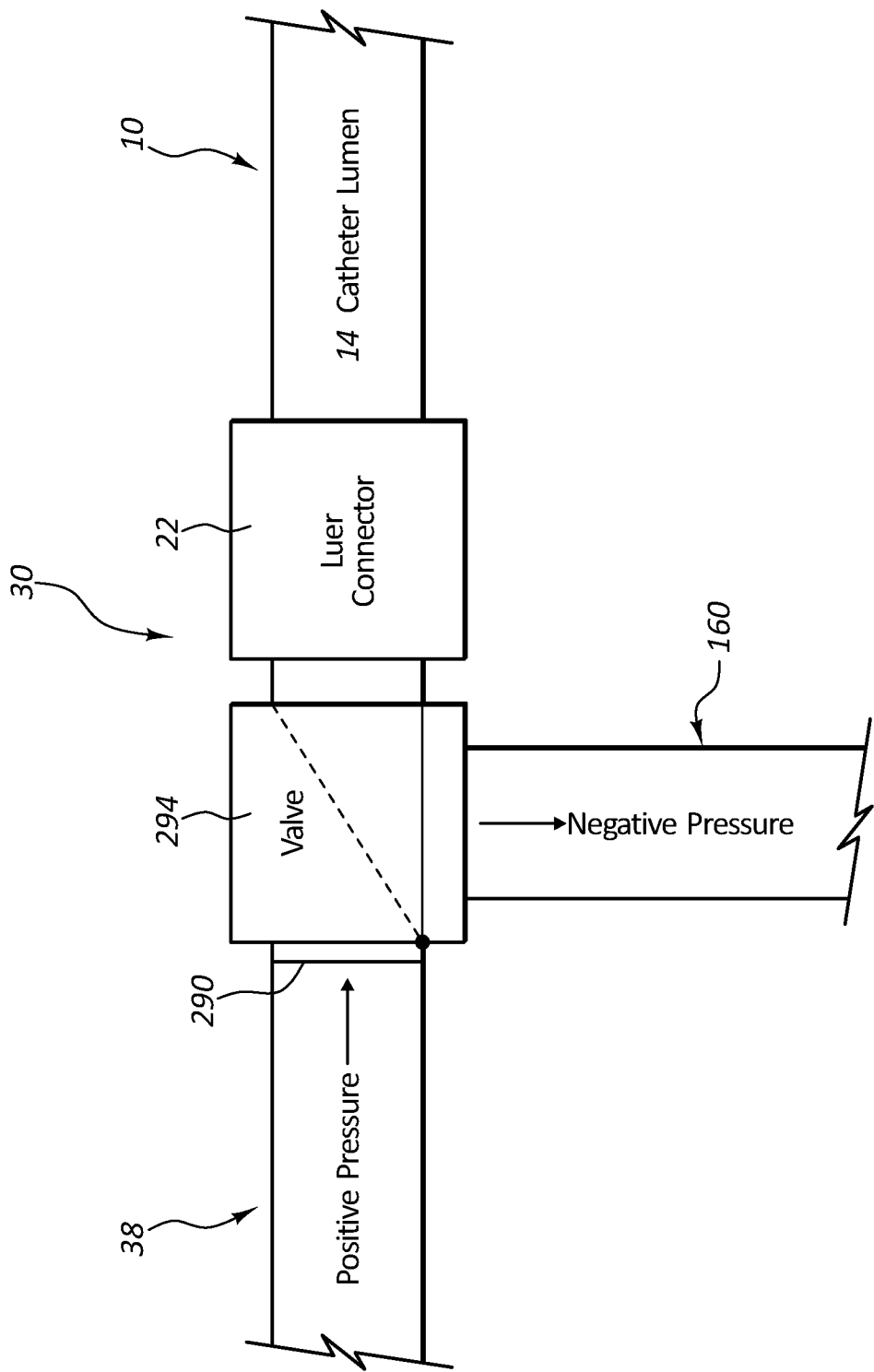


Fig. 11

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US2017/036866

A. CLASSIFICATION OF SUBJECT MATTER

IPC(8) - A61B 17/00; A61F 2/00; A61M 1/00; A61M 5/142; A61M 5/168; A61M 25/00 (2017.01)

CPC - A61M 1/00; A61M 1/106; A61M 5/00; A61M 5/142; A61M 25/00; A61M 25/0068; A61M 25/007 (2017.05)

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

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

See Search History document

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

USPC - 604/27; 604/28; 604/131; 604/151; 604/506; 604/508; 604/890.1; 604/891.1 (keyword delimited)

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

See Search History document

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 6,471,689 B1 (JOSEPH et al) 29 October 2002 (29.10.2002) entire document	1-35
A	US 2009/0088724 A1 (CHEBATOR et al) 02 April 2009 (02.04.2009) entire document	1-35
A	US 4,929,242 A (DESECKI et al) 29 May 1990 (29.05.1990) entire document	1-35
A	US 8,876,795 B2 (FIERING et al) 04 November 2014 (04.11.2014) entire document	1-35
A	US 7,255,690 B2 (GRAY et al) 14 August 2007 (14.08.2007) entire document	1-35

☐ 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

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"P" document published prior to the international filing date but later than the priority date claimed

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"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

26 July 2017

Date of mailing of the international search report

16 AUG 2017

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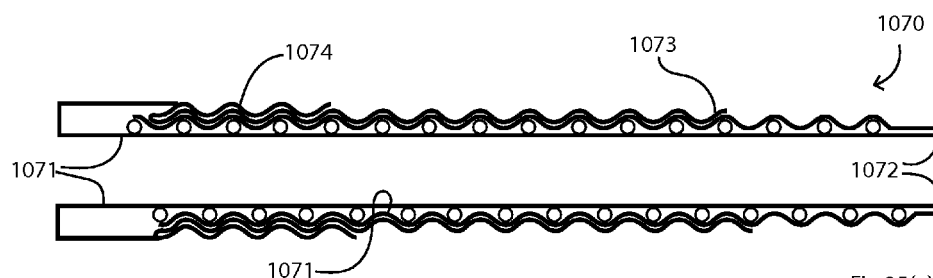


Fig.25(a)

(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.

“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.

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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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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.

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.

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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 M1, distal M1, 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;

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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;

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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;

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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 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.

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 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 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 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 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 it at least 60% of the jacket thickness.

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.

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 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 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)

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 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 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. 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 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 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 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 geometry

The assembly is cooled

The cinch wire 810 is removed

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

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 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.

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.

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.

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 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 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 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 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.

10 PTFE material is a relatively stiff material compared to ePTFE and so is therefore preferable to 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 the intermediate portion and the transition region. The transition from ePTFE to PTFE may be
20 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
10 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
15 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
20 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:

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
30 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 "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 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, 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, 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 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 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 also be incorporated into a more flexible 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
5 (Almandoz et al. 2015; Lapergue et al. 2017; Blanc et al. 2017; Möhlenbruch 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
10 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
15 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.
20 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
25 existing vacuum technology (vacuum pumps and syringes) that the applied vacuum is not engineered to prevent clogging, or maximise efficiency of aspiration.
30

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.

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.

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.

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.

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

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

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 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.

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.
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.
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.
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.
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.
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.
16. A catheter as claimed in any preceding claim, wherein in the distal portion the width of the corrugate it at least 60% of the jacket thickness.
17. A catheter as claimed in any preceding claim, wherein in the distal portion the width of the corrugate it 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.
- 15 53. A catheter as claimed in any of claims 44 to 52, wherein the helical support is bonded to 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 support is wound around the outside of these layers thus keeping them together.
- 25 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.

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.

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.

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.

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.

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.

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.

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:
performing an angiogram to determine location of an occlusion, and distance
35 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,

10 if the clot is retrieved, perform another angiogram through the balloon guide 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.
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.
- 35 134. 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.

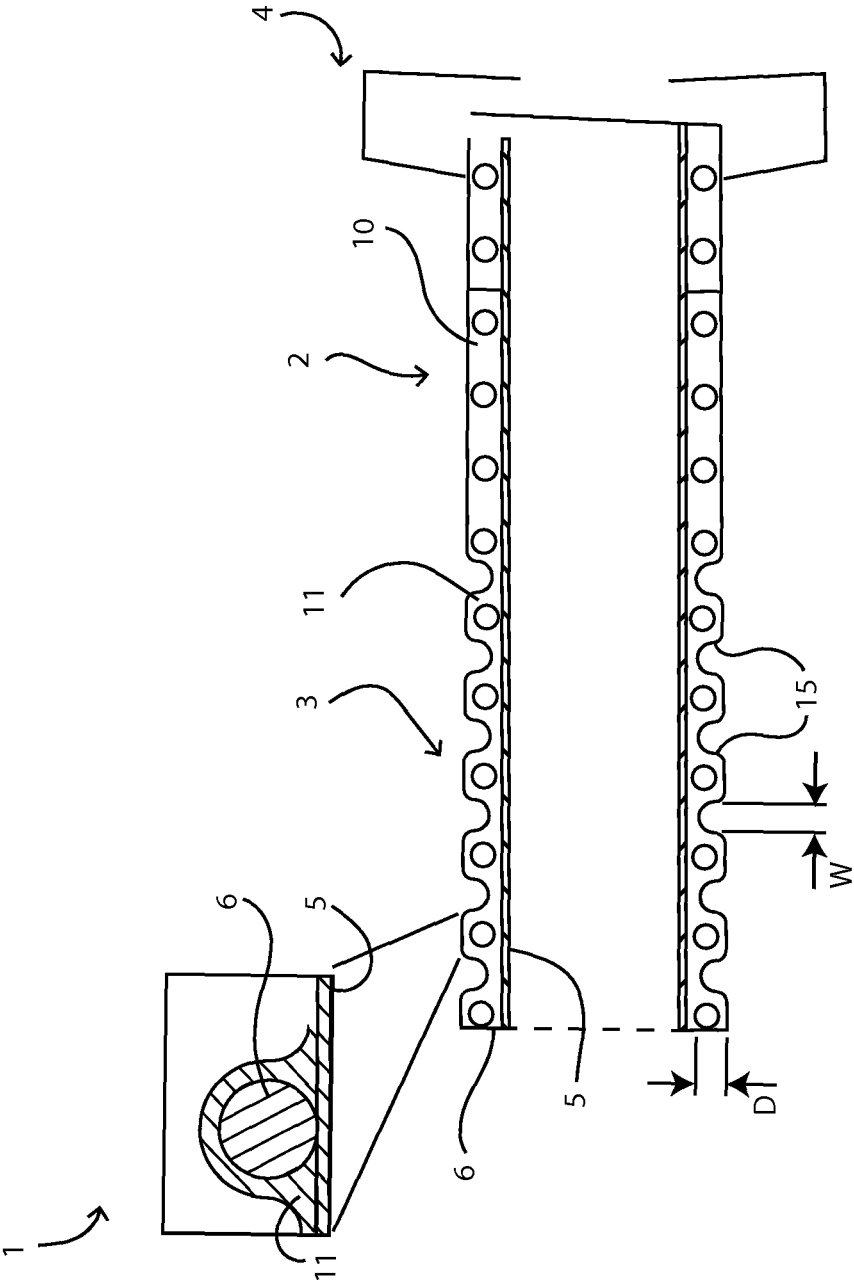


Fig.1

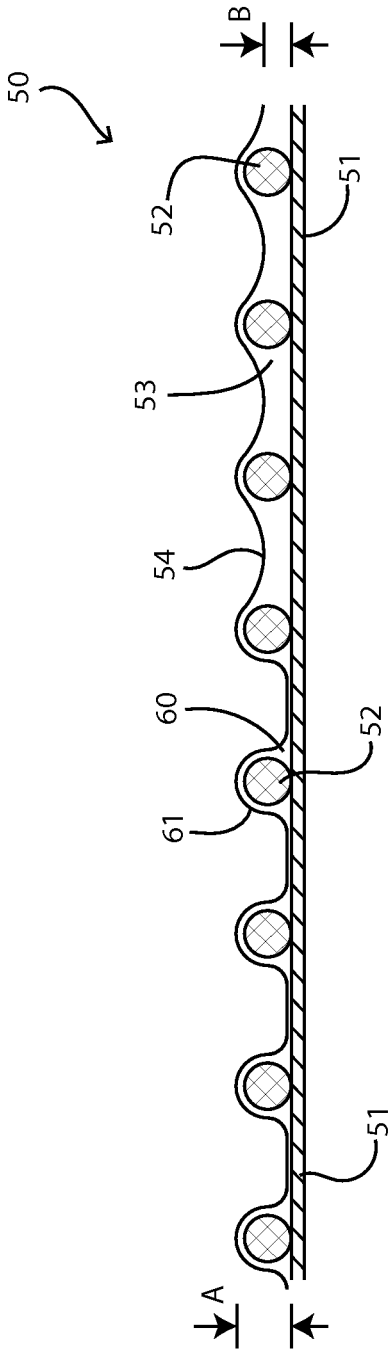


Fig.2

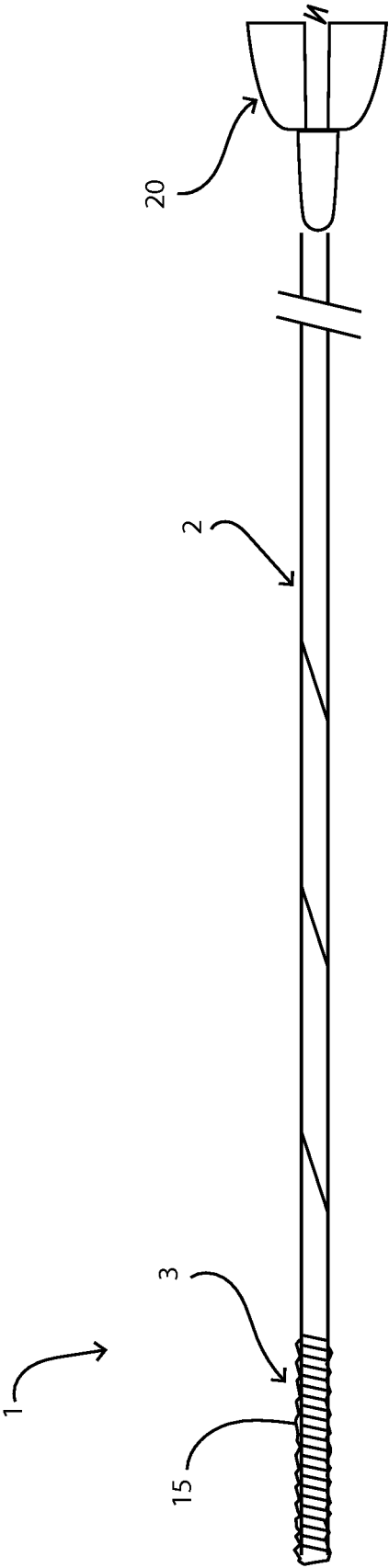


Fig.3

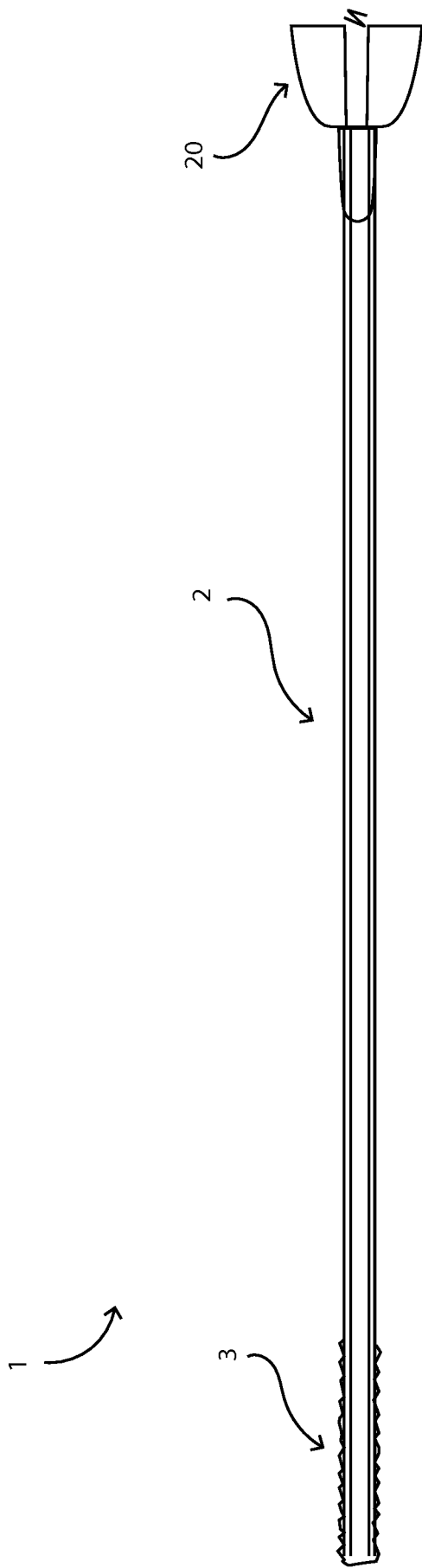


Fig. 4

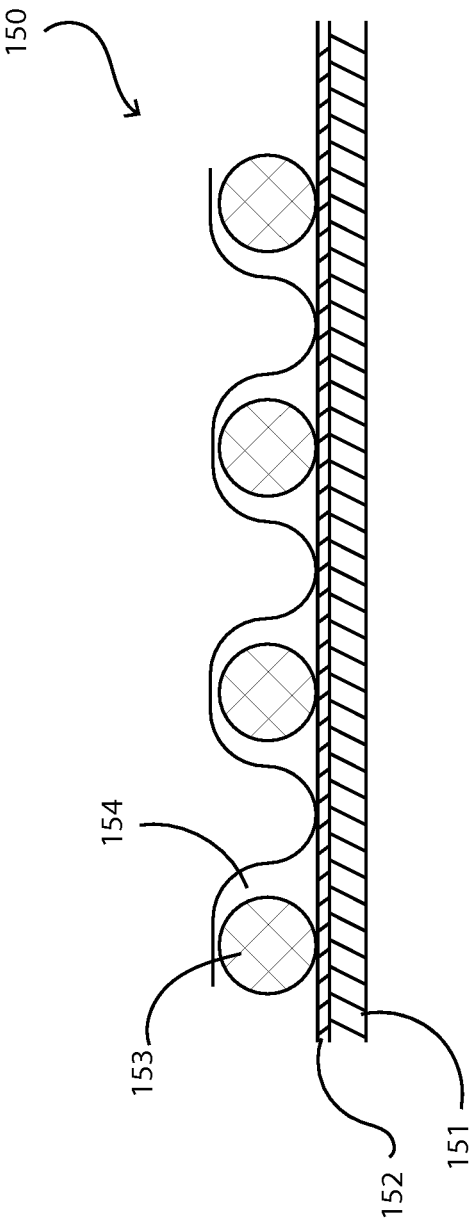


Fig. 5

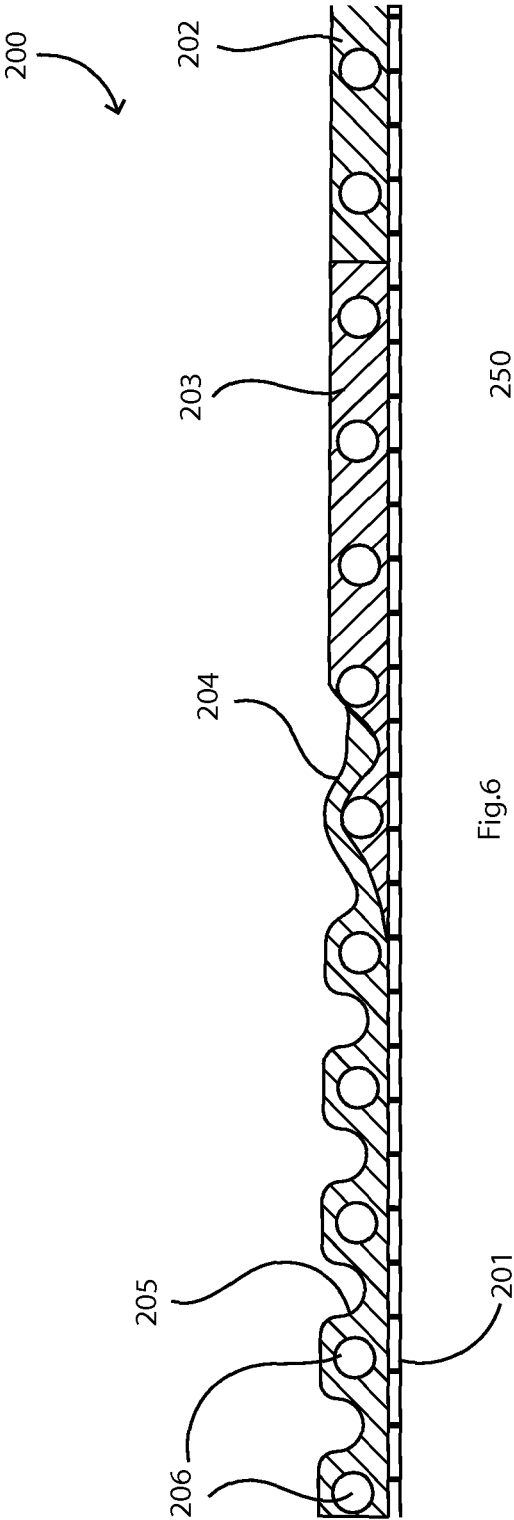


Fig. 6

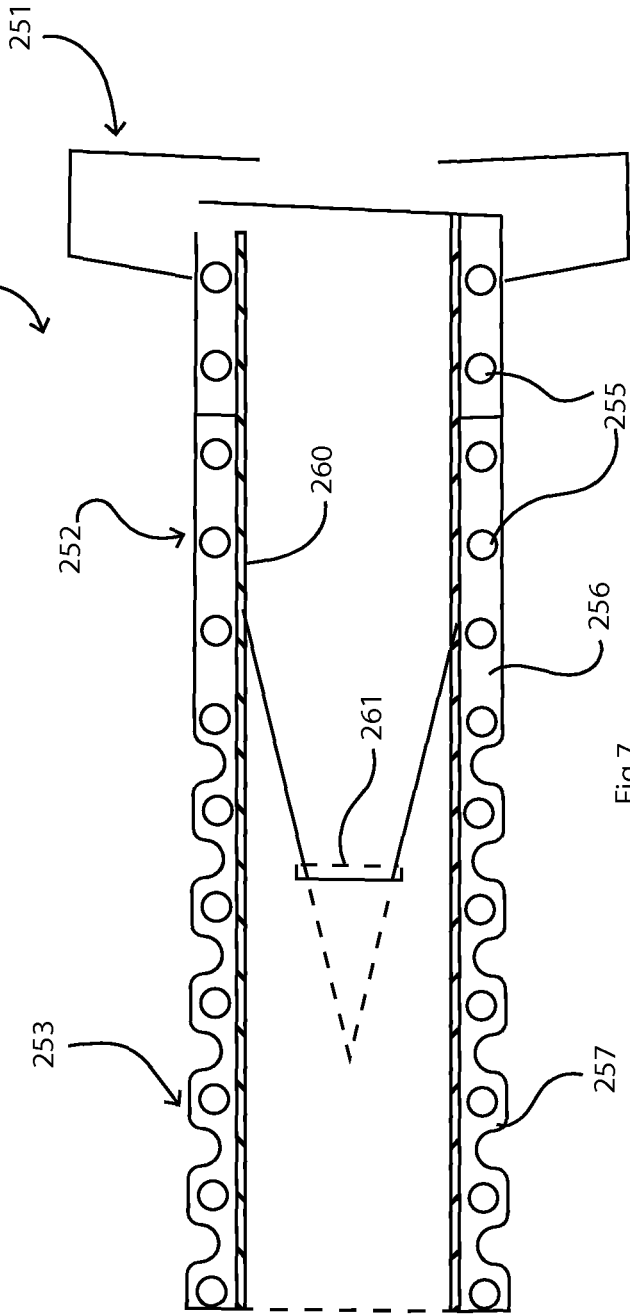


Fig. 7

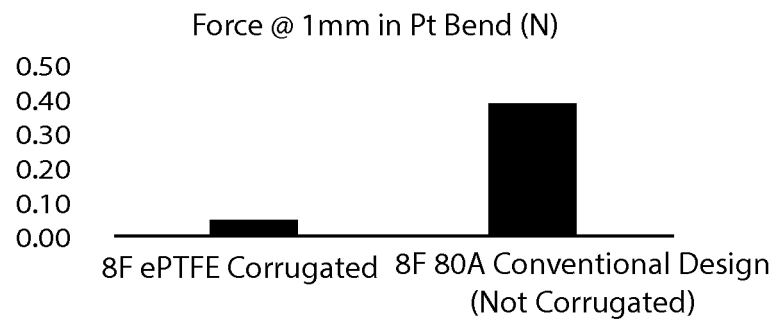


Fig.8

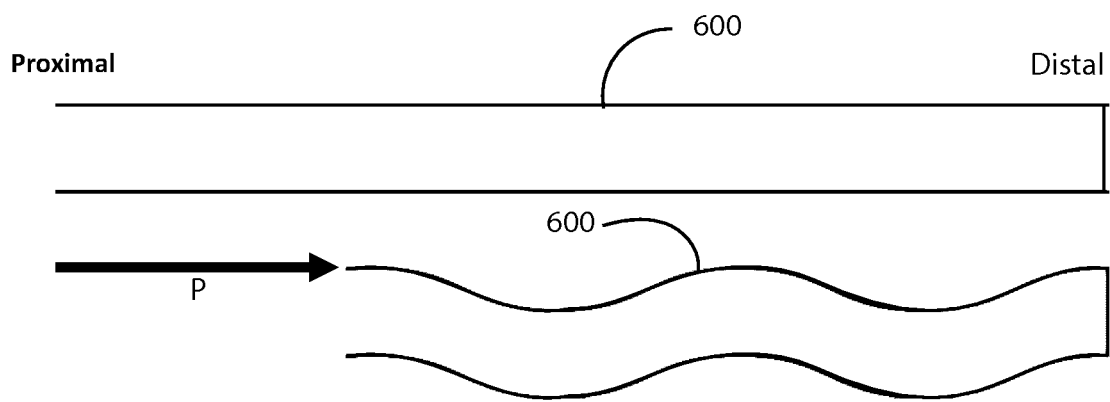


Fig.9

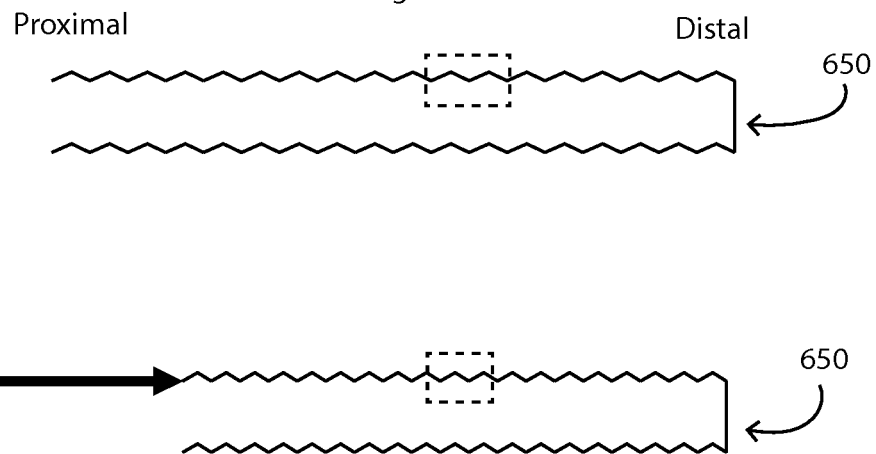
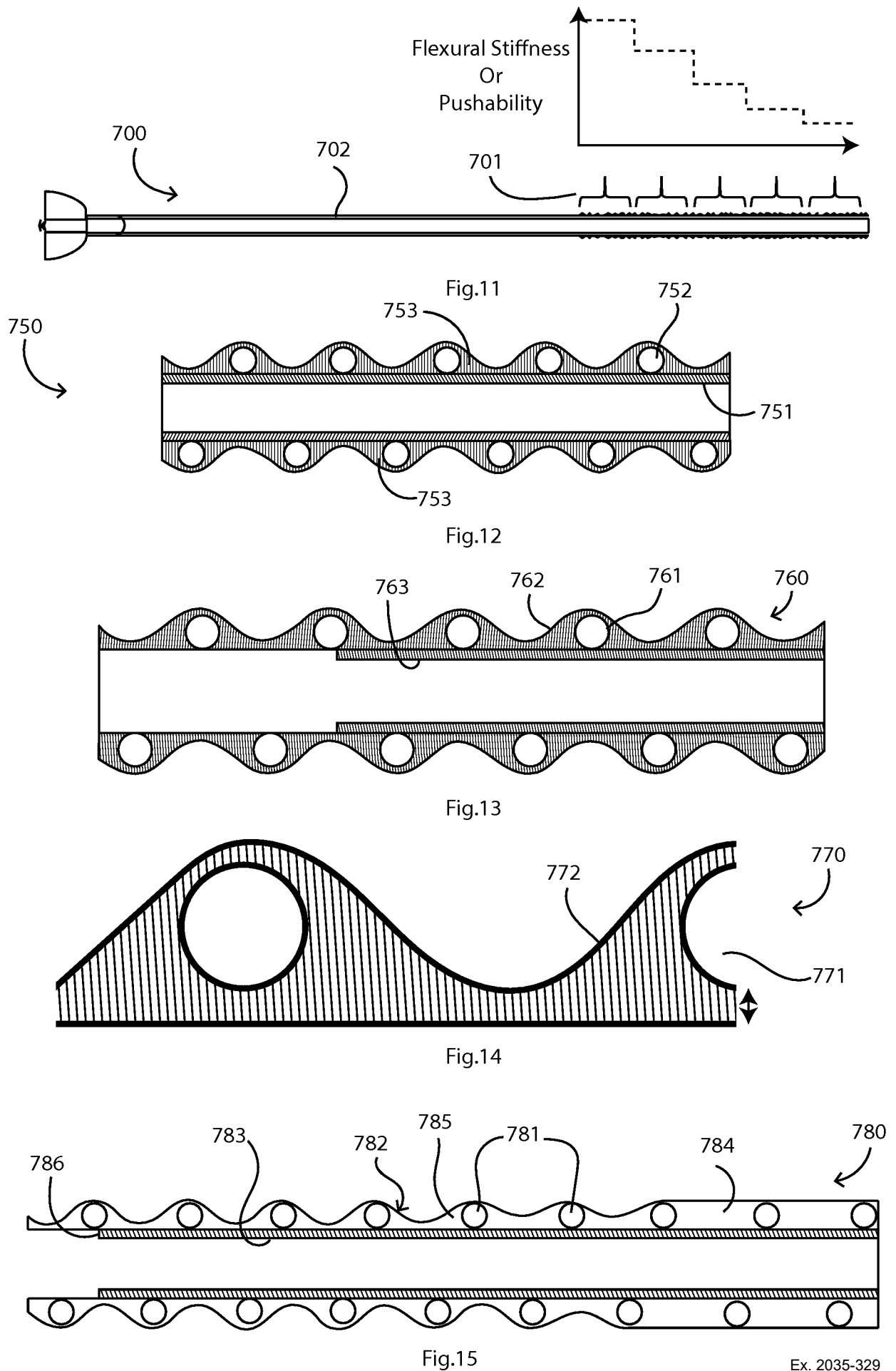


Fig.10



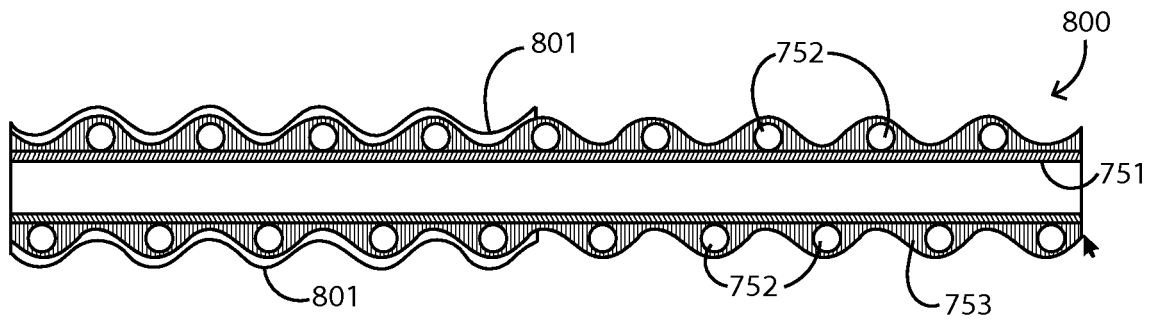


Fig.16

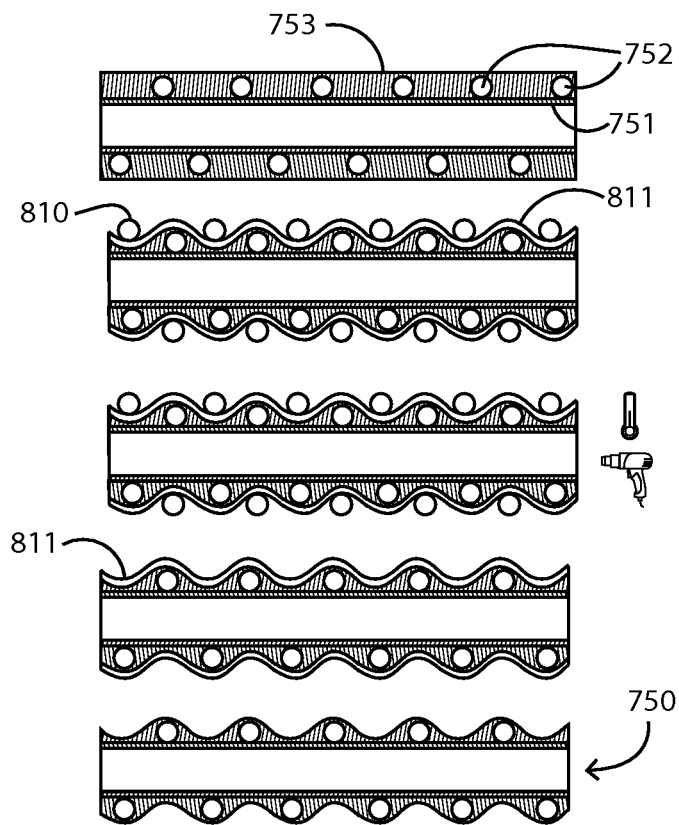


Fig.17

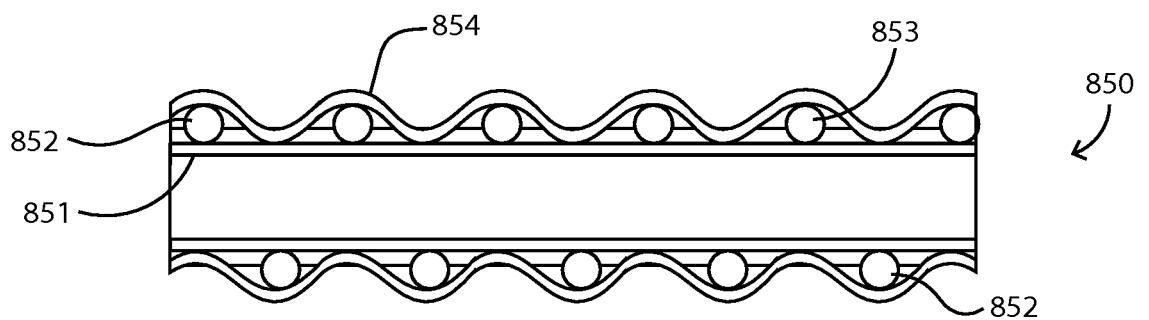


Fig.18

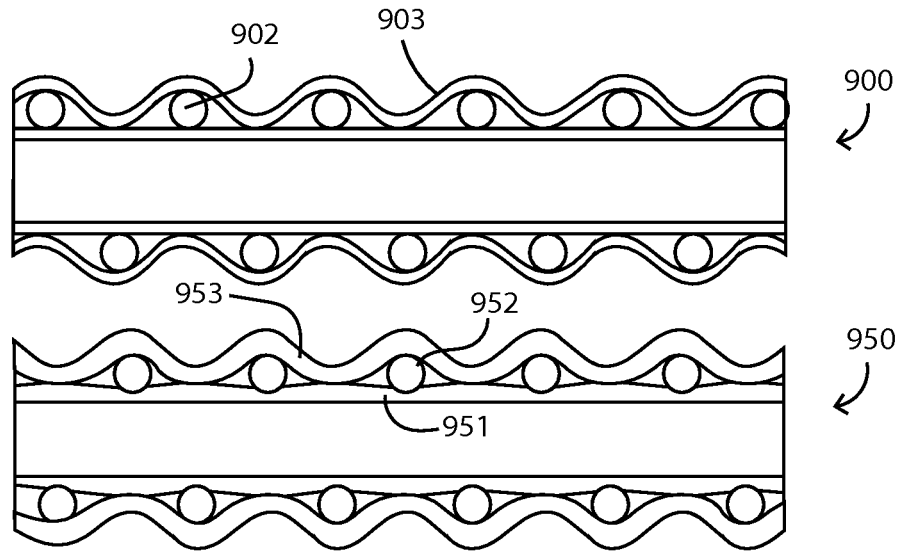


Fig.19

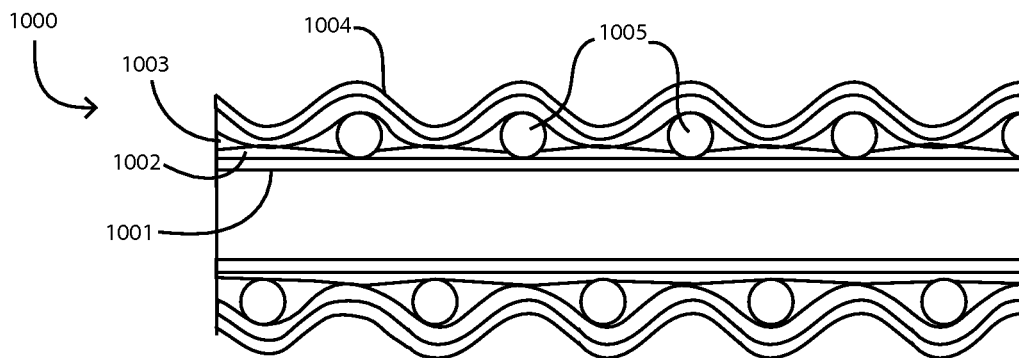


Fig.20

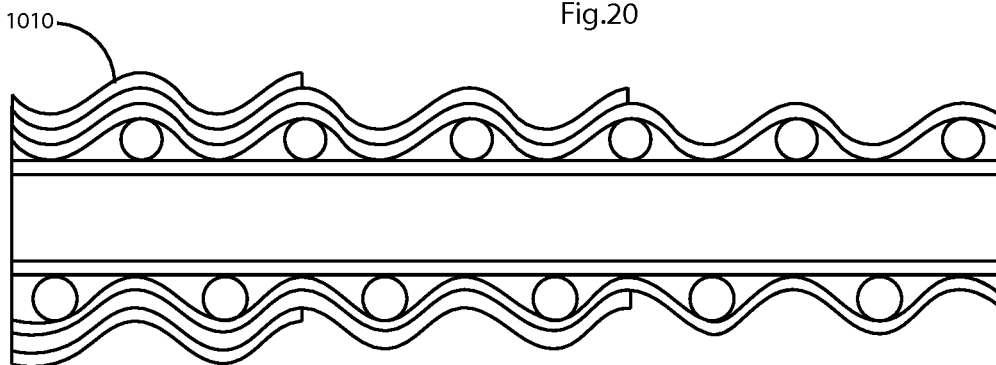
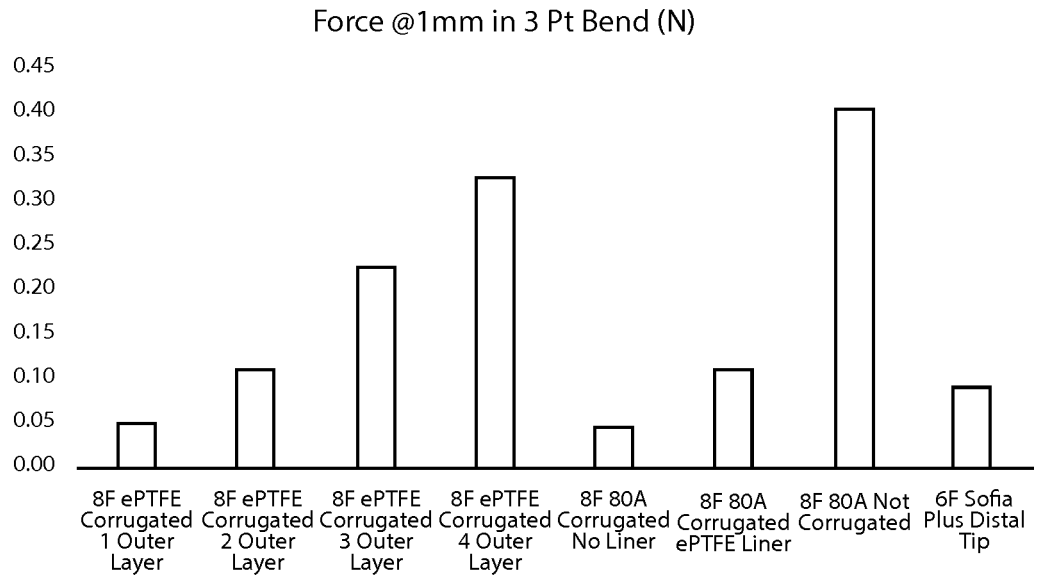
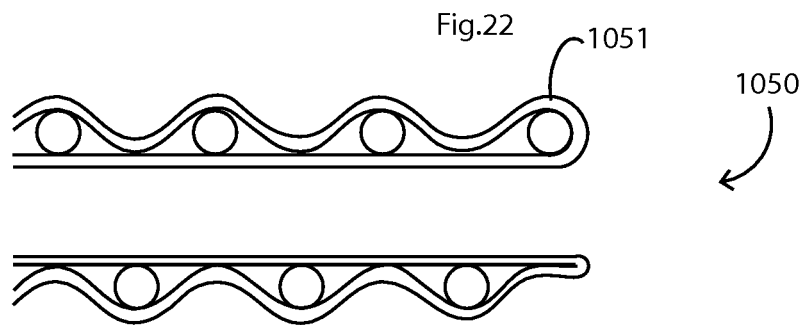
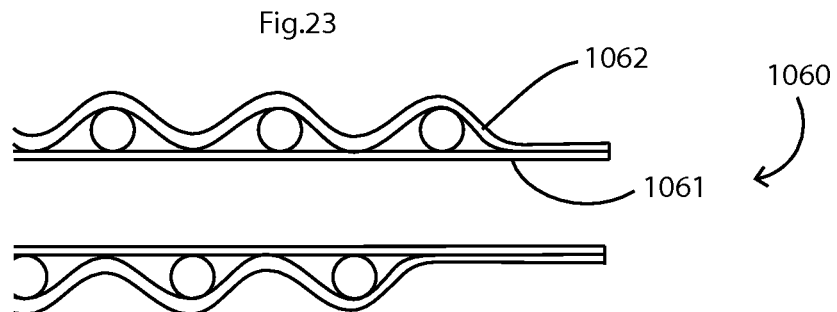
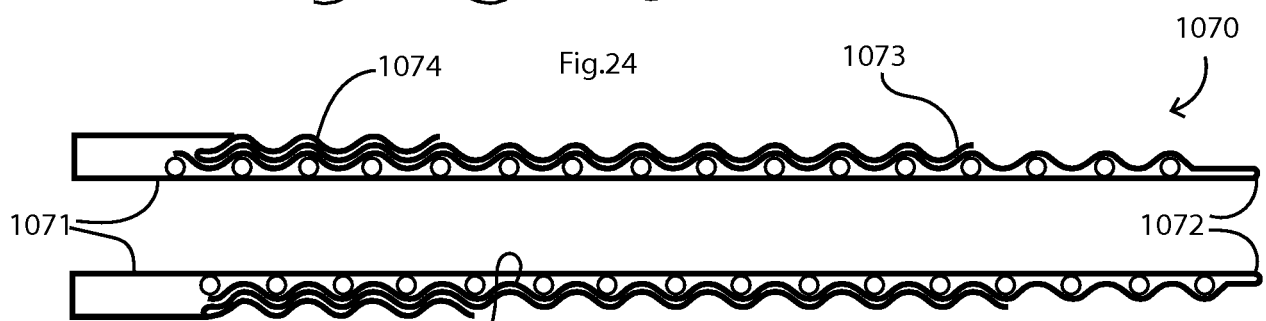
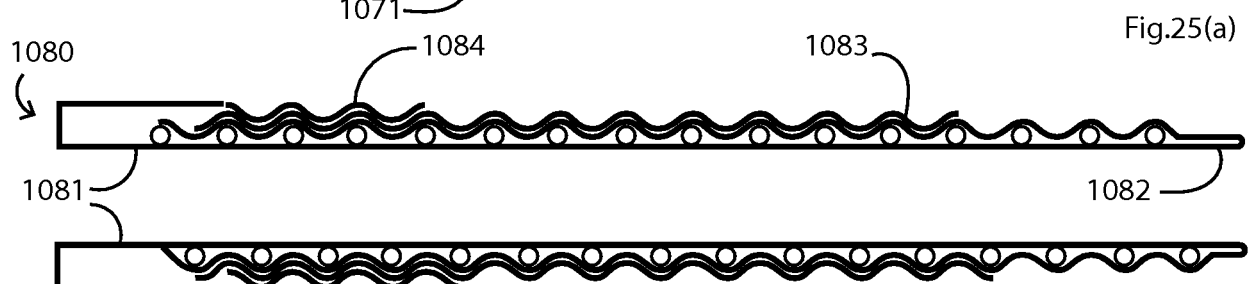


Fig.21



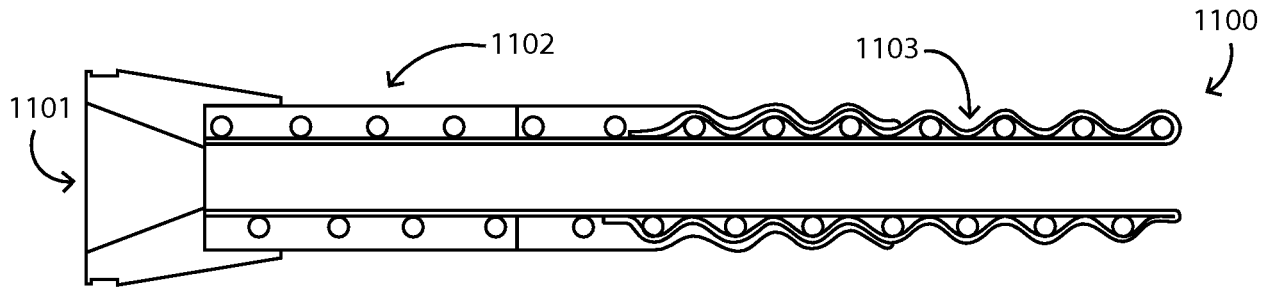


Fig.26

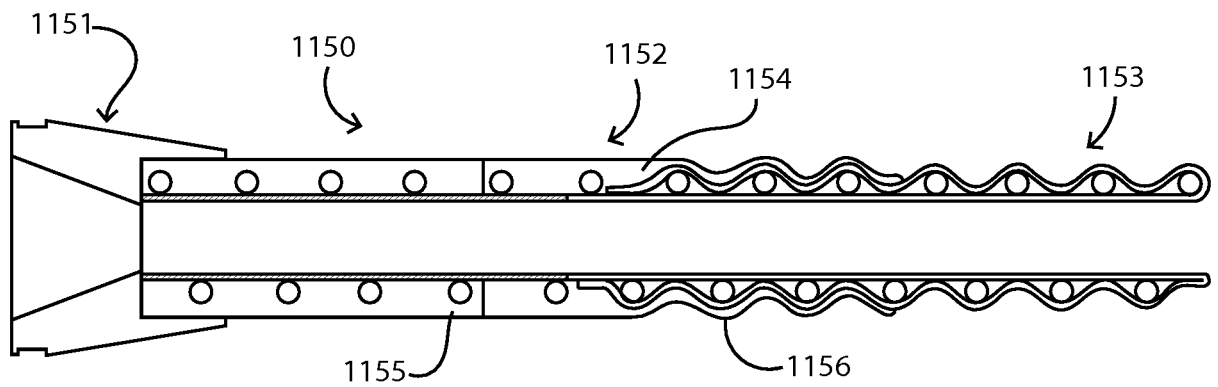


Fig.27

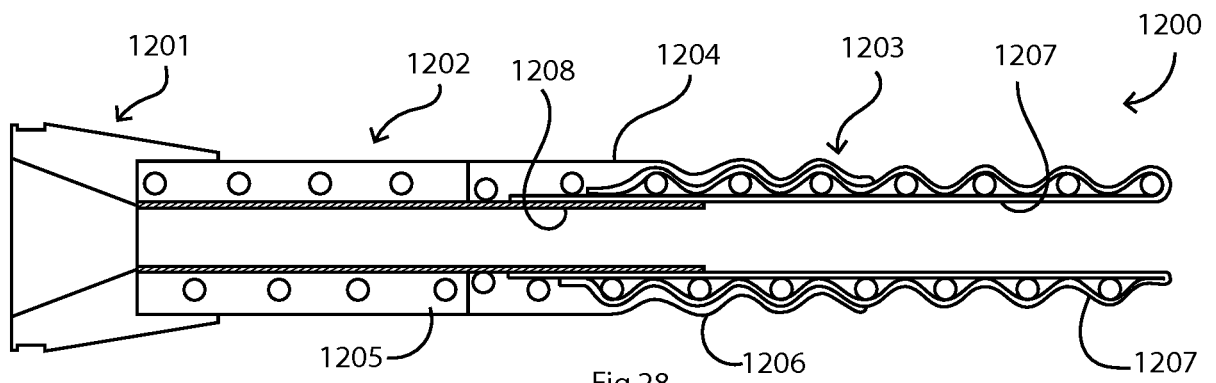


Fig.28

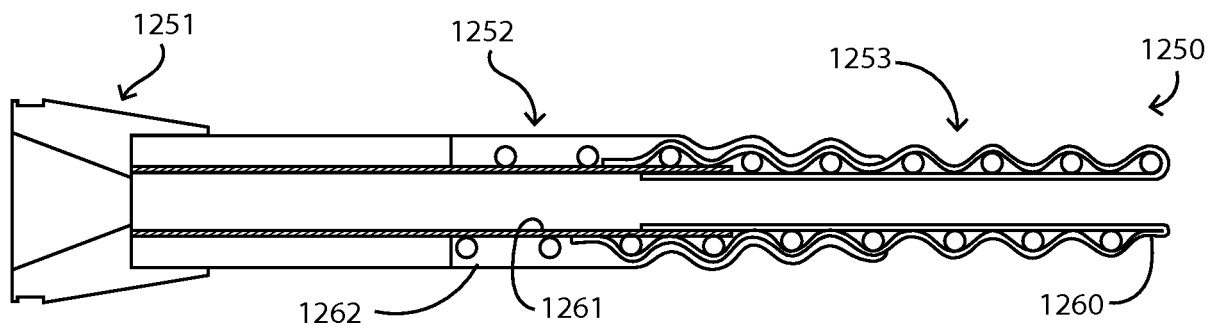


Fig.29

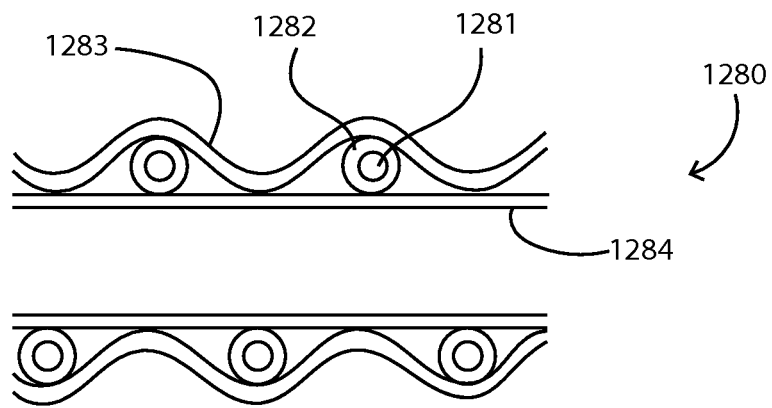


Fig.30

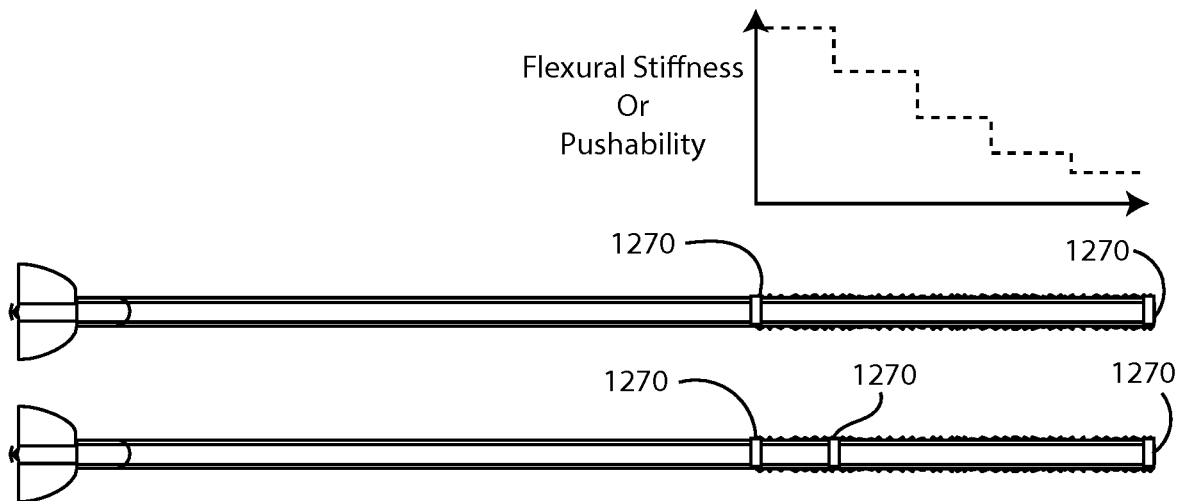


Fig.31

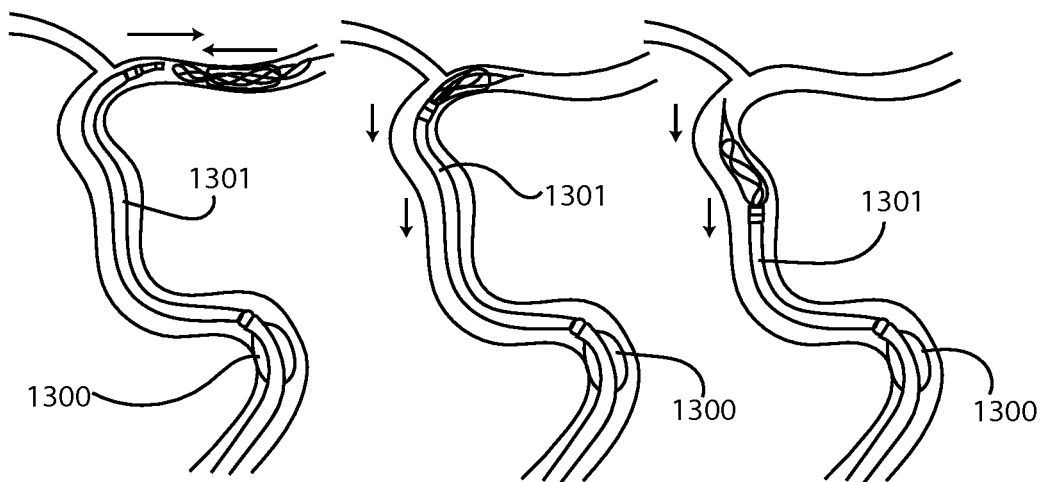


Fig.32 (PRIOR ART)

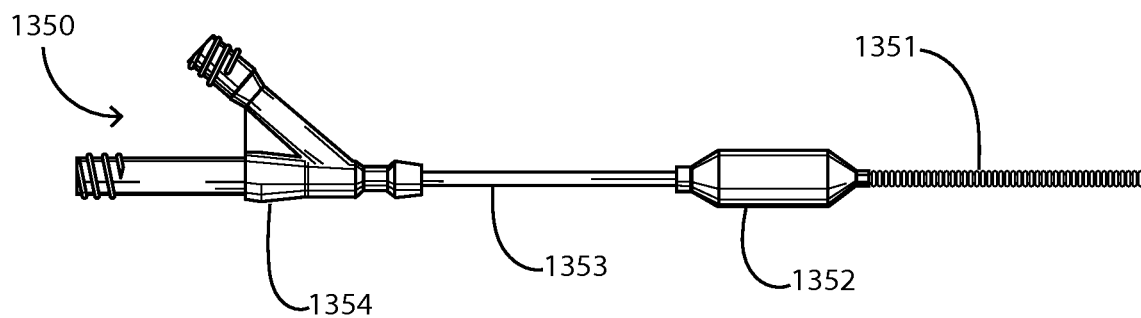


Fig.33

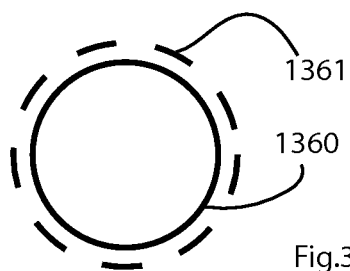


Fig.34

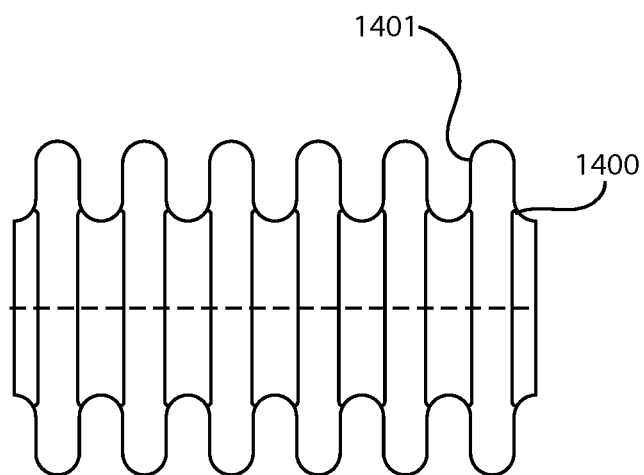


Fig.35

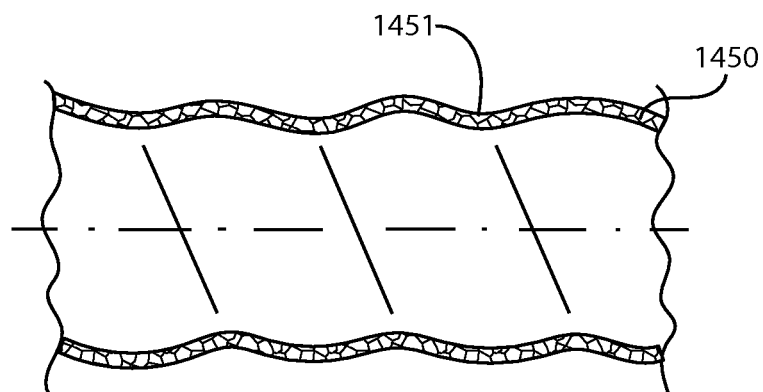


Fig.36

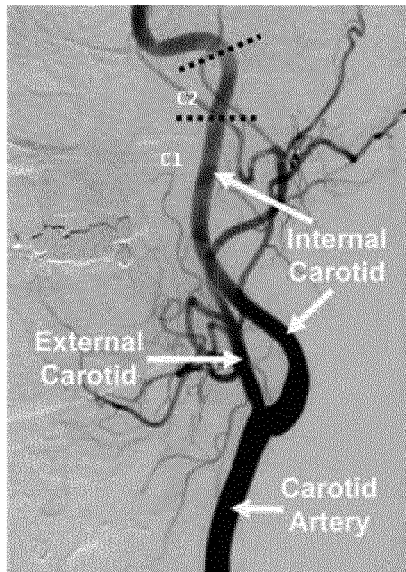
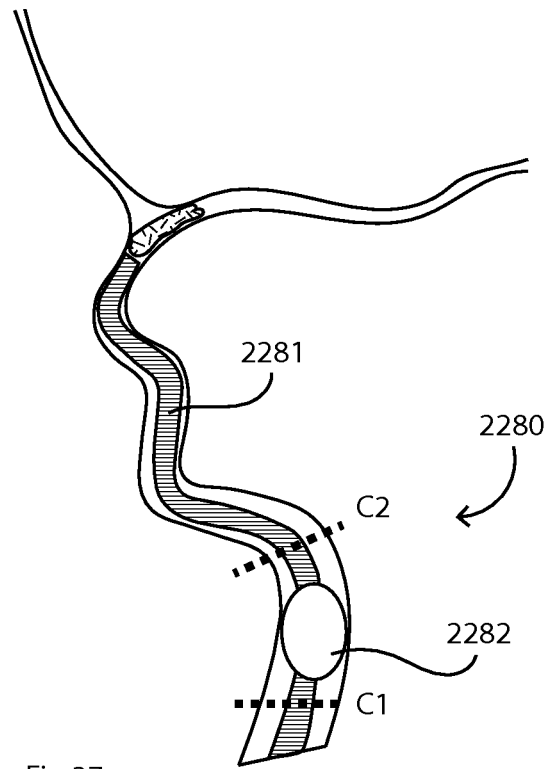


Fig.37

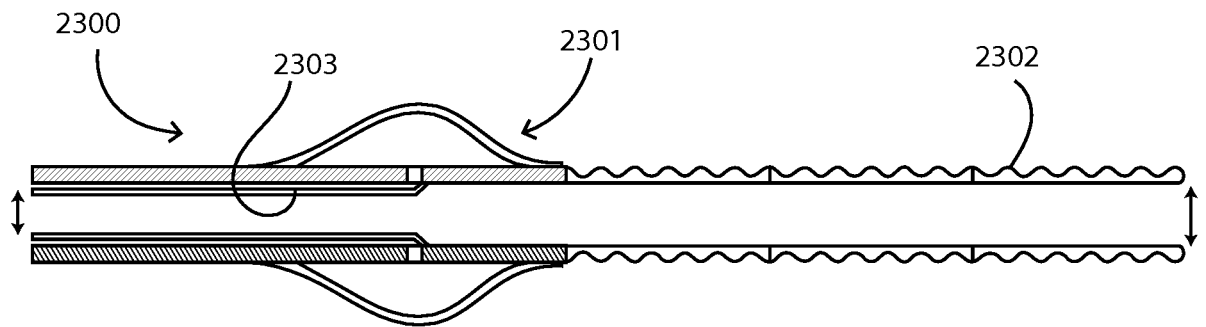


Fig.38

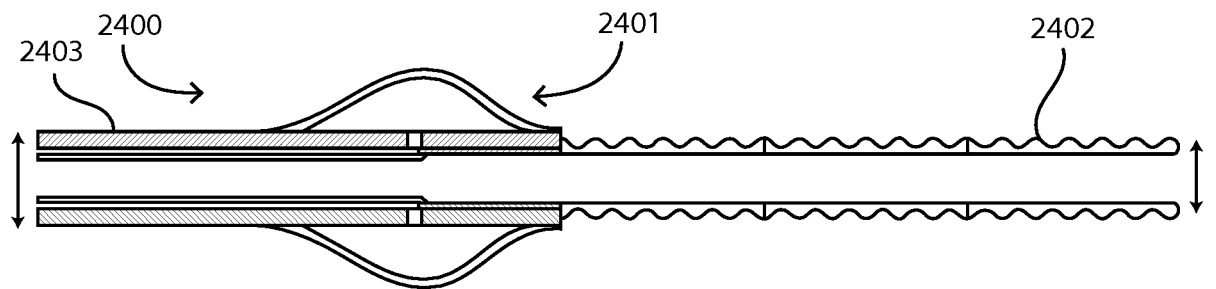


Fig.39

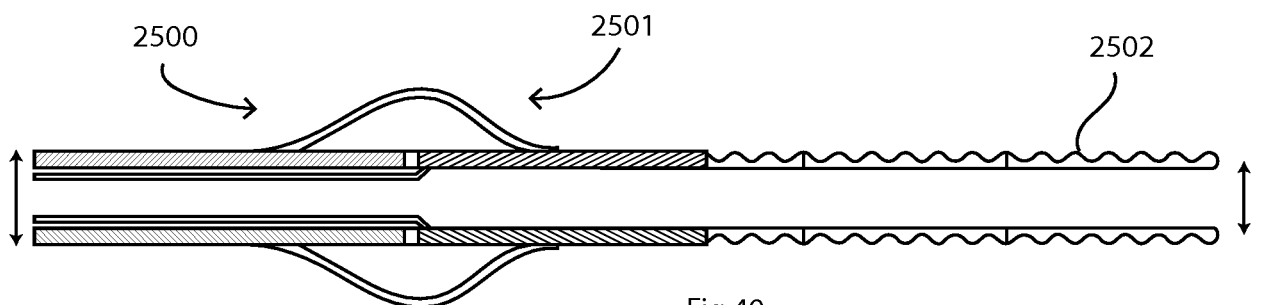


Fig.40

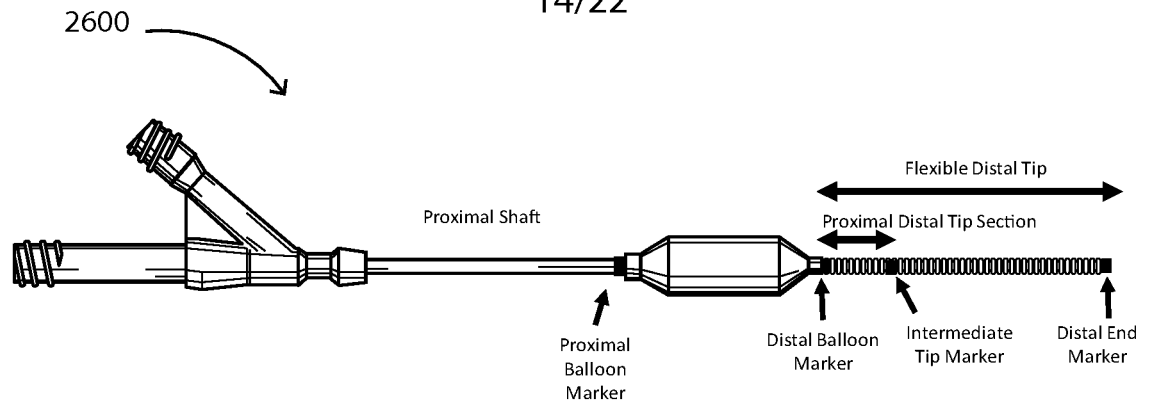


Fig.41

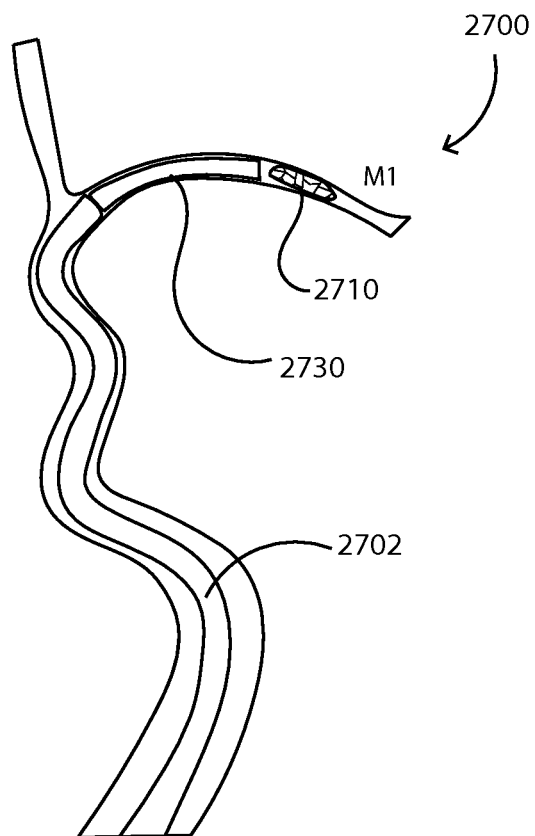


Fig.42

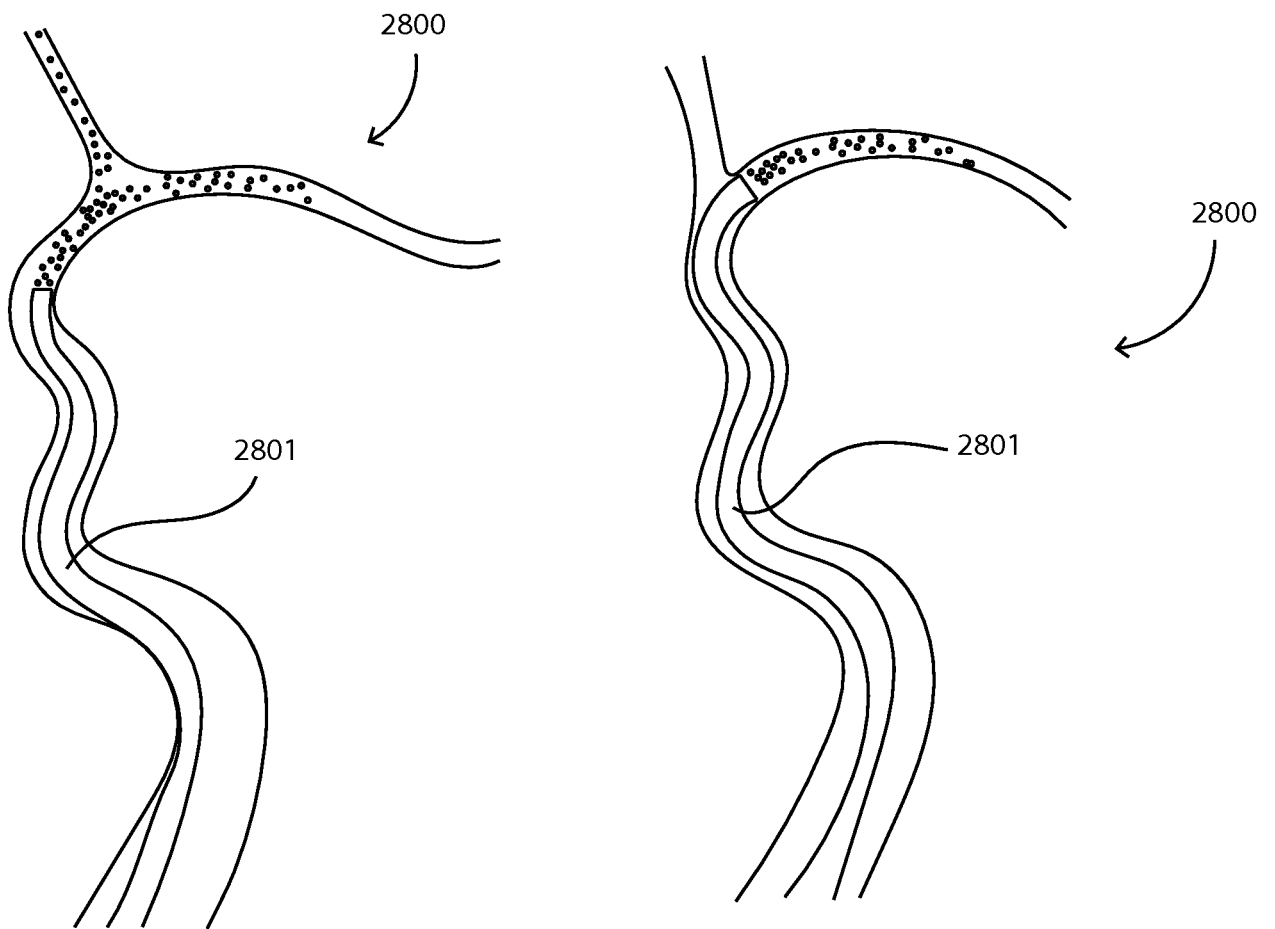


Fig.43

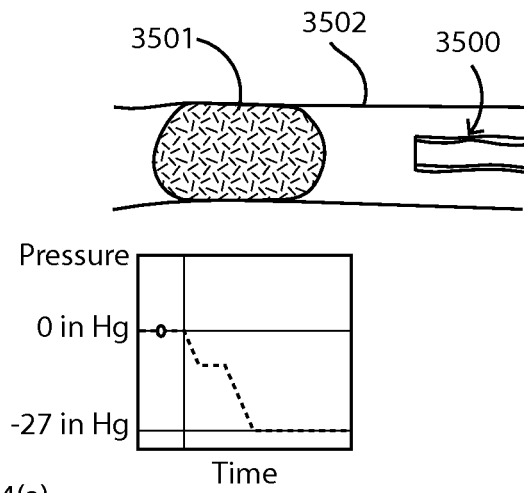


Fig.44(a)

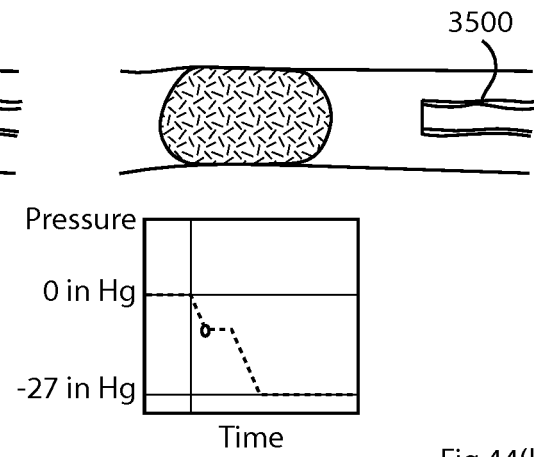


Fig.44(b)

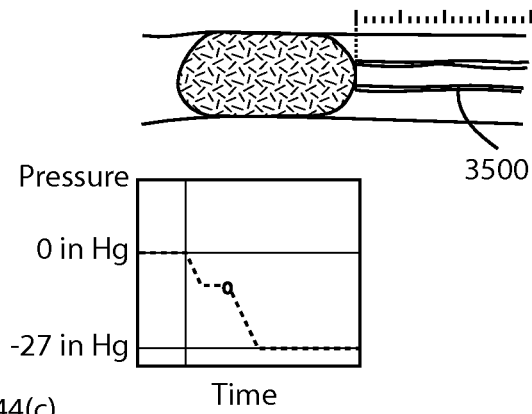


Fig.44(c)

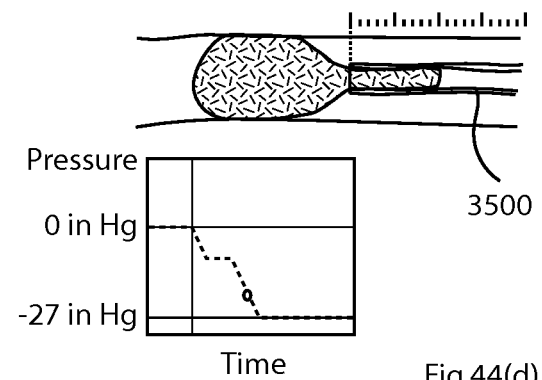


Fig.44(d)

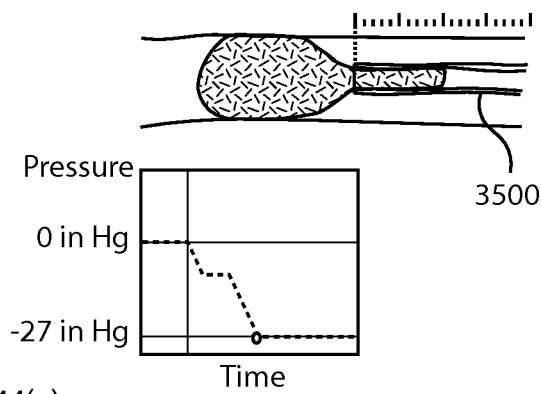


Fig.44(e)

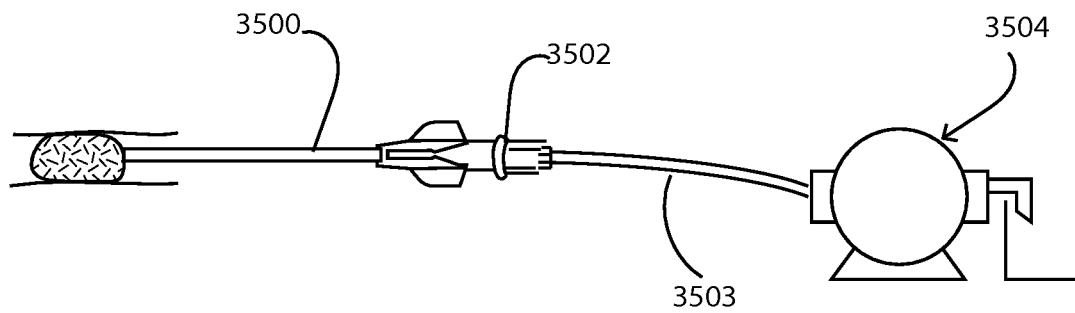


Fig.45

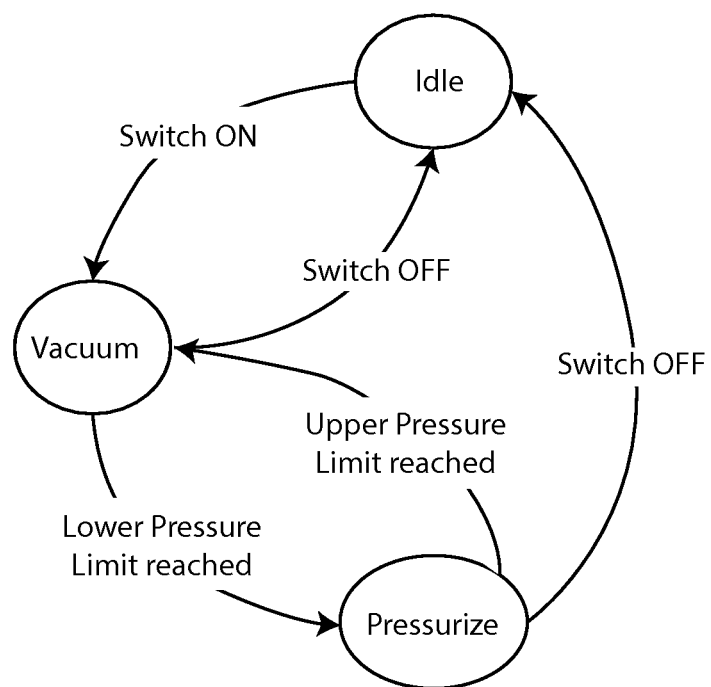
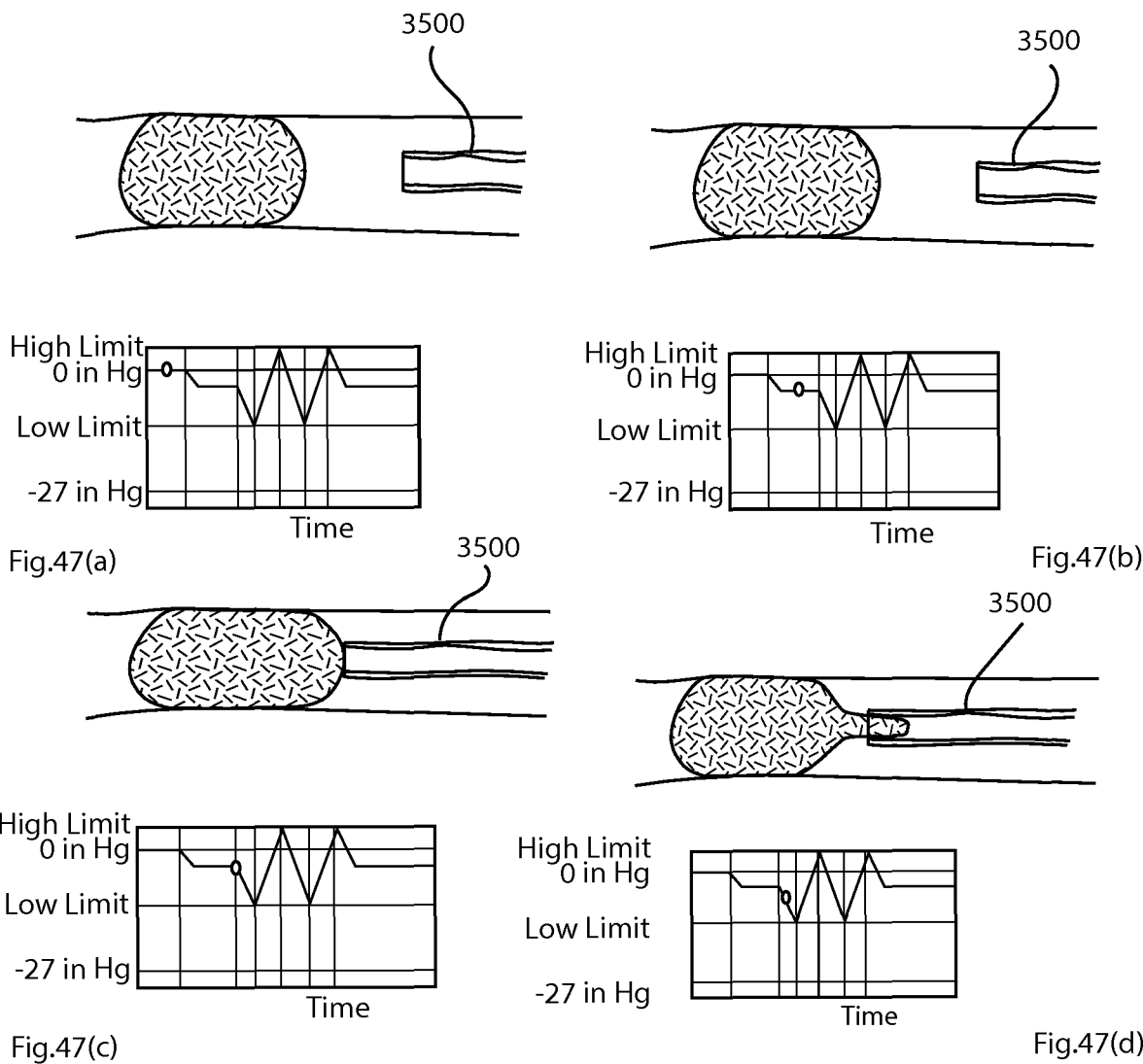


Fig.46



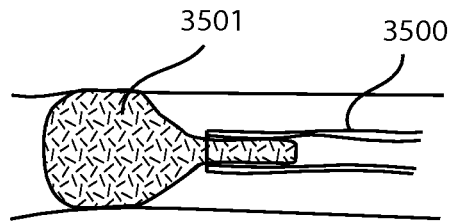
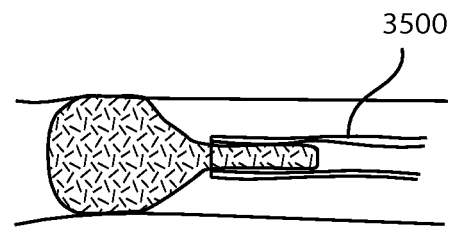
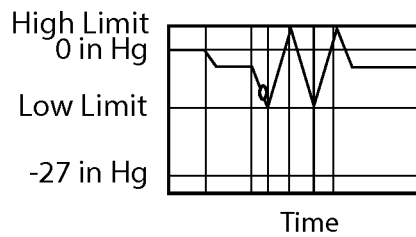
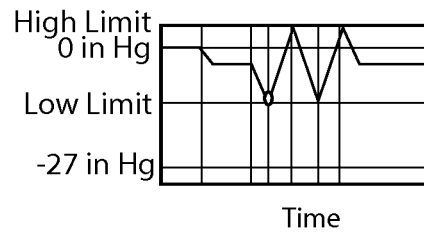


Fig.47(e)

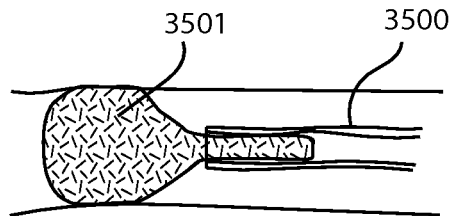
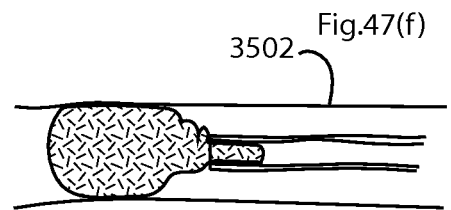


Fig.47(f)

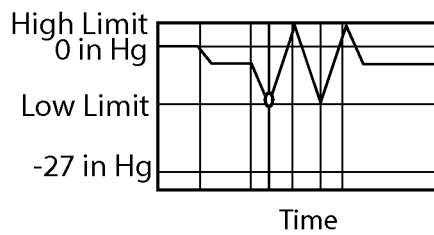
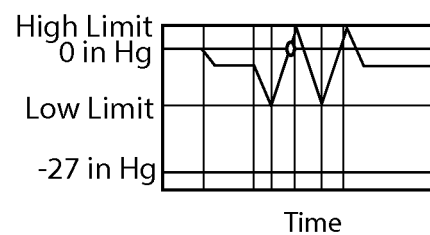


Fig.47(g)

Fig.47(h)

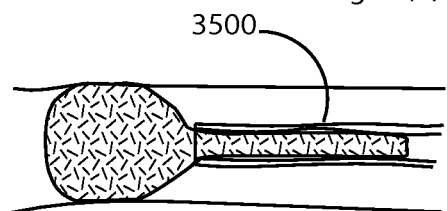
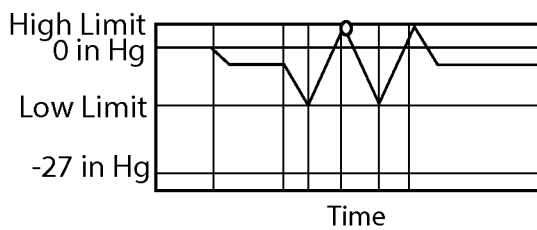
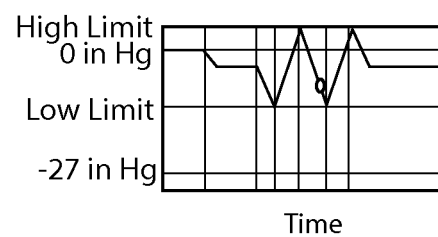


Fig.47(i)

Fig.47(j)

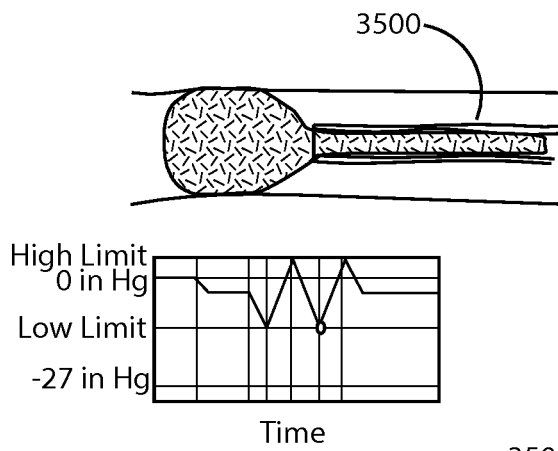
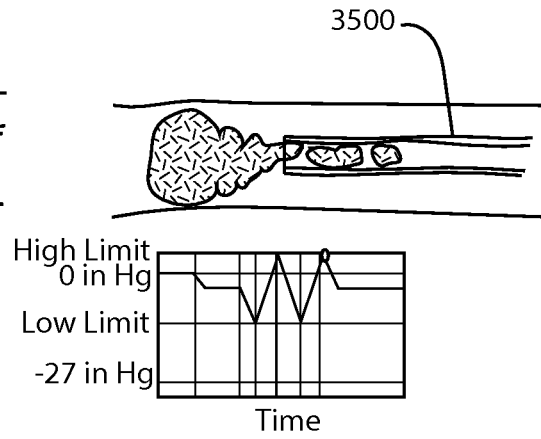
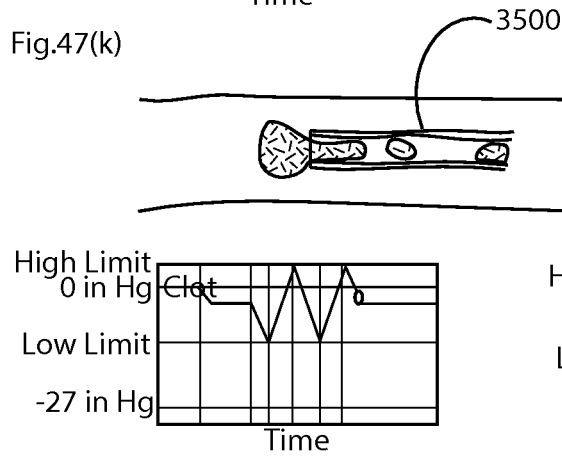
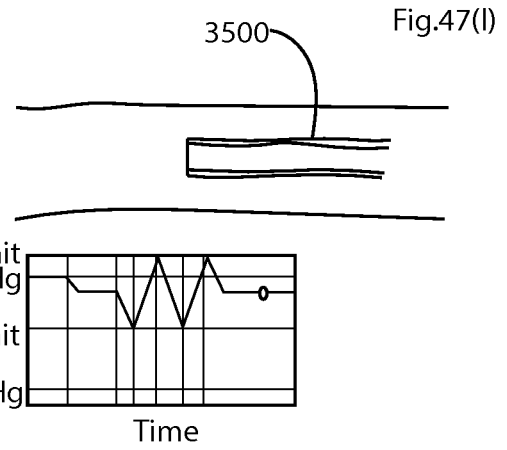
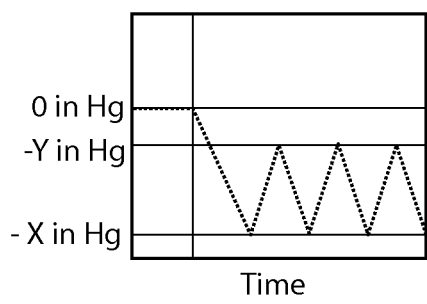


Fig. 48(a)

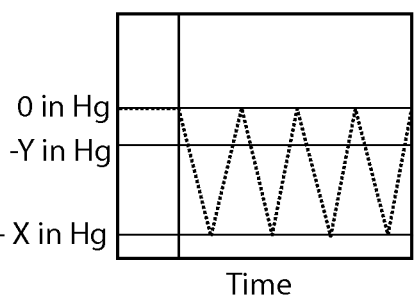


Fig. 48(b)

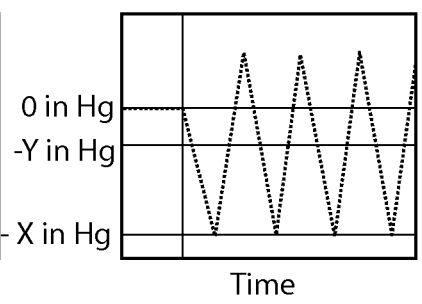


Fig. 48(c)

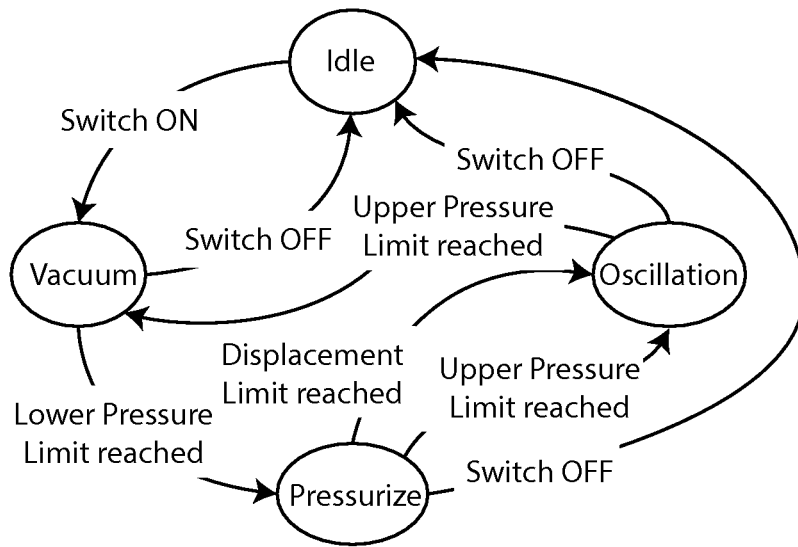


Fig.49

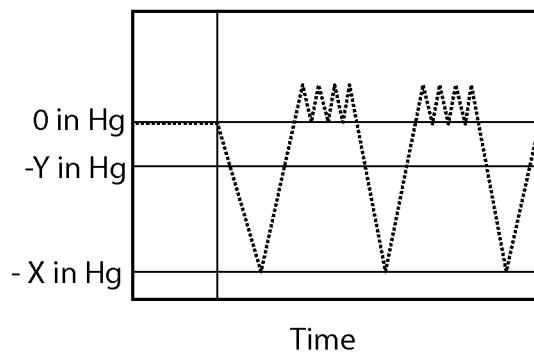


Fig.50(a)

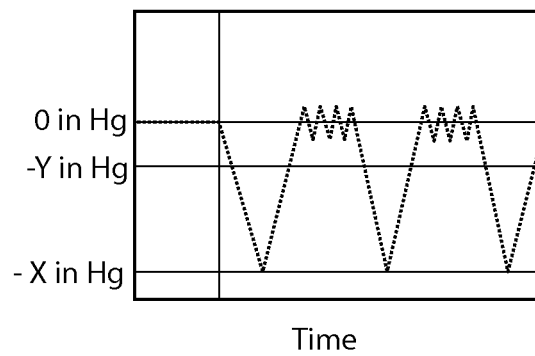


Fig.50(b)

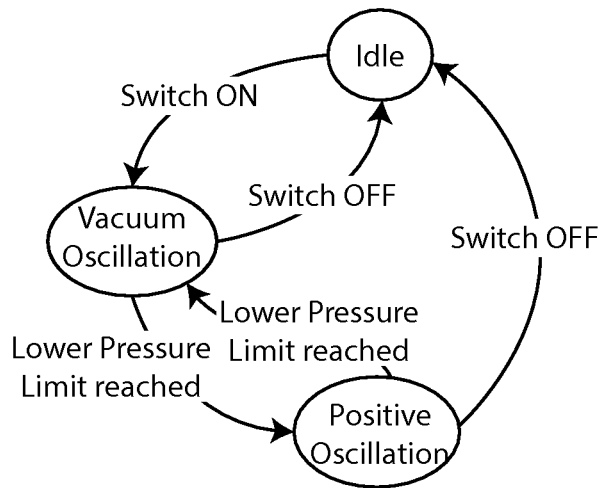


Fig.51(a)

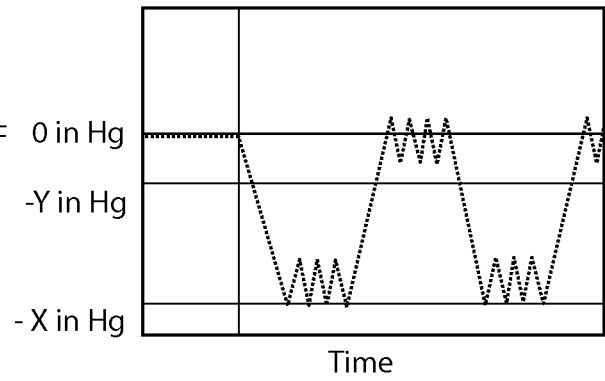


Fig.51(b)

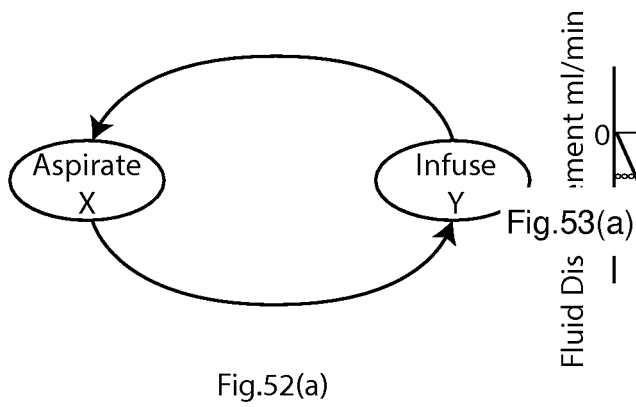


Fig.52(a)

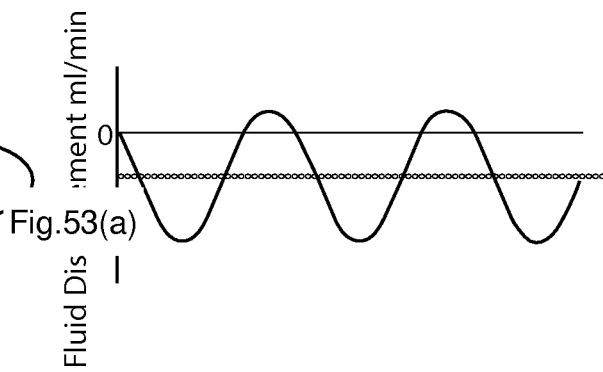


Fig.52(b)

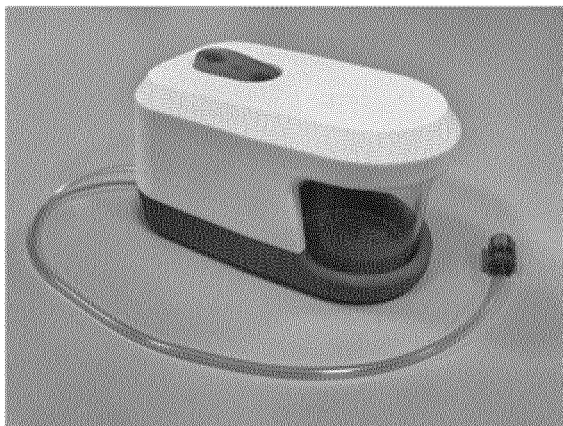


Fig.53(a)

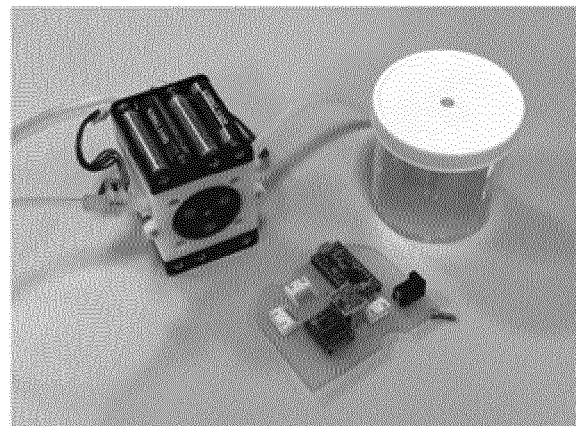


Fig.53(b)

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 3666393 A WO 9315784 A1	03-09-1993 19-08-1993
