

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

PENUMBRA, INC.
Petitioner

v.

RAPIDPULSE, INC.
Patent Owner

U.S. Patent No. 11,406,402

**PETITION FOR *INTER PARTES* REVIEW
OF U.S. PATENT NO. 11,406,402**

DECLARATION OF BRIAN BROWN

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I. LIST OF EXHIBITS

1001	U.S. Patent No. 11,406,402 (“the ’402 Patent”)
1002	U.S. Provisional Application No. 62/701,086 (“Deville-Prov1”)
1003	U.S. Provisional Application No. 62/750,011 (“Deville-Prov2”)
1004	Prosecution File History of the ’402 Patent
1005	Expert Declaration of Brian Brown
1006	CV of Brian Brown
1007	U.S. Patent No. 10,322,230 (“Ofek”)
1008	U.S. Patent No. 11,197,977 (“Mullins”)
1009	Prosecution File History of U.S. Patent No. 11,197,977 (“Mullins”)
1009.1	U.S. Provisional Application No. 62/599,560 (“Mullins-Prov1”)
1009.2	U.S. Provisional Application No. 62/599,573 (“Mullins-Prov2”)
1009.3	U.S. Provisional Application No. 62/616,188 (“Mullins-Prov3”)
1010	International Application No. WO 2014/151209 A1 (“Grey”)
1011	U.S. Patent No. 3,955,574 (“Rubenstein”)
1012	U.S. Patent Publication No. 2017/0238953 A1 (“Yang”)
1013	U.S. Patent Publication No. 2012/0138833 A1 (“Matteo”)
1014	Patricia E. Thorpe & Francisco J. Osse, <i>Endovenous Management of Iliocaval Occlusion</i> , in THE VEIN BOOK, 2007 MECHANICAL THROMBECTOMY
1015	Dave Fornell, <i>Catheter-Based Clot Busting Therapies</i> , DIAGNOSTIC AND INTERVENTIONAL CARDIOLOGY (Feb. 4, 2013),

	https://www.dicardiology.com/article/catheter-based-clot-busting-therapies
1016	International Application No. WO 2018/019829 A1 (“Brady”)
1017	Gilles Rioufol, et al., <i>Large Tube Section Is the Key to Successful Coronary Thrombus Aspiration: Findings of a Standardized Bench Test</i> , 67 CATHETERIZATION & CARDIOVASCULAR INTERVENTIONS 254-257 (Dec. 5, 2005), https://onlinelibrary.wiley.com/doi/10.1002/ccd.20471
1018	Michael Haude, <i>Mechanical Thrombectomy Catheter Systems</i> , 2 INTERVENTIONAL CARDIOLOGY 58-60 (2007), https://www.icrjournal.com/articles/thrombectomy-catheter-systems
1019	U.S. Patent No. 3,086,528 (“Eichelman”)
1020	U.S. Patent No. 3,659,605 (“Sielaff”)
1021	U.S. Patent No. 3,042,042 (“Blanck”)
1022	Scott Simon, et al., <i>Exploring the Efficacy of Cyclic vs. Static Aspiration in a Cerebral Thrombectomy Model: An Initial Proof of Concept Study</i> , 6 J. NEUROINTERVENT. SURG. 677 (Dec. 14, 2014)
1023	Expert Declaration of Ian Ross, MD
1024	CV of Ian Ross, MD
1025	U.S. Patent Publication No. 2010/0204672 A1 (“Lockhart”)
1026	U.S. Patent No. 4,634,435 (“Ingraham”)
1027	Stephan A. Munich, et al., <i>Overview of Mechanical Thrombectomy Techniques</i> , 85 NEUROSURGERY S60-S67 (June 14, 2019) https://academic.oup.com/neurosurgery/article/85/suppl_1/S60/5512732
1028	U.S. Patent No. 10,531,883 (“the ’883 Patent”)

1029	Prosecution File History of the '883 Patent
1030	U.S. Patent No. 10,722,253 (“the '253 Patent”)
1031	Prosecution File History of the '253 Patent
1032	Troy D. Long, et al., <i>Novel Aspiration Catheter Design for Acute Stroke Thrombectomy</i> , 11 JOURNAL OF NEUROINTERVENTIONAL SURGERY 2 (July 30, 2018) https://jnls.bmj.com/content/11/2/190
1033	Richard E. Klabunde, <i>Viscosity of Blood</i> , CARDIOVASCULAR PHYSIOLOGY CONCEPTS (revised Dec. 27, 2022) https://cvphysiology.com/hemodynamics/h011
1034	U.S. Patent No. 9,820,761 (“Garrison”)

II. INTRODUCTION

I, Brian Brown, declare as follows:

1. My name is Brian Brown. I am an engineering consultant in the area of medical device design, development, manufacturing and intellectual property. I have prepared this declaration as an expert witness retained by Penumbra, Inc. Herein I give my opinions as to how a person of ordinary skill in the art (“POSA”) would understand the scope of the claims and whether certain claims of U.S. Patent No. 11,406,402 (“the ’402 Patent”) are invalid. I provide technical bases for these opinions as appropriate.

2. This declaration contains statements of my opinions formed to date and the bases and reasons for those opinions. I may offer additional opinions based on further review of materials in this case, including opinions and/or testimony of other expert witnesses. I make this declaration based upon my own personal knowledge and, if called upon to testify, would testify competently to the matters contained herein. For my efforts in connection with the preparation of this declaration I have been compensated at my standard rate for this type of consulting activity. My compensation is in no way contingent on the results of these or any other proceedings relating to the above-captioned patent.

III. BACKGROUND AND QUALIFICATIONS

3. In formulating my opinions, I have relied upon my training, knowledge, and experience in the relevant art. I have summarized in this section my educational background, career history, publications, and other relevant qualifications. My full curriculum vitae is attached as Exhibit 1006 to this report.

Educational Background

4. I received a Bachelor of Science in Mechanical Engineering from North Dakota State University, with an emphasis on electro-mechanical automation. As part of my studies, I took classes covering many different engineering areas including chemistry, physics, advanced mathematics, statistics, software engineering and architecture, statics, dynamics, thermodynamics, robotics, technical writing, material science, fluid dynamics and engineering design.

Career History

5. I have over 30 years of research and development experience working in the cardiovascular and medical device industries across a wide variety of application areas including development of neurovascular and aspiration thrombectomy devices.

6. For 24 years, I served in various roles at SciMED Life Systems and Boston Scientific, including multiple research and development engineering positions in various application areas including catheters, stents, guidewires,

thrombectomy systems, and cardiovascular implants. For my final 10 years at Boston Scientific, I served as the global vice president of R&D Interventional Cardiology, where I was tasked to direct worldwide cardiovascular research and development activities for accelerated launches of implantable stents, drug delivery technologies, structural heart devices, disposable catheters, and adjunctive products.

7. I also held various leadership roles at medical device and diagnostics companies, including Chief Technology Officer at OvaGene Oncology and Vice President of R&D and Operations at both Cogentix Medical, Inc. and Sunshine Heart, Inc, focused on advancing the medical device and diagnostics industries.

8. For the past 4 years, I have served as a technical consultant for various early-stage medical device companies in product design and intellectual property development as the founder and President of Brown-Tech, LLC, including QXMedical, Peytant Solutions, and CardioMech. I am also one of the founding partners for Northern Nitinol, LLC, specializing in Nitinol design and prototyping for medical device components.

9. I was the two-time recipient of the BSC Patent of the Year award, recognized as one of Minnesota's leading inventors by Twin City Business Magazine in 2013, elected to College of Fellows, American Institute for Medical and Biological Engineering, and serve as an Advisor to the University of Minnesota

Office of Technology Commercialization. I also currently serve as a mentor to students enrolled in the University of Minnesota Design of Medical Device program.

Patents

10. I am a named inventor on approximately forty issued U.S. medical device patents covering a wide variety of technologies, including two aspiration thrombectomy patents and several others on stent geometries, nitinol, balloon catheters, infusion catheters, and ePTFE processing.

11. My curriculum vitae contains further details on my education, experience, and other qualifications to render an expert opinion. Ex. 1006. My work on this case is being billed at my standard litigation consulting rate, with reimbursement for actual expenses. My compensation is not contingent upon the outcome of this *Inter Partes* Review proceeding.

Materials and Other Information Considered

12. I have considered information from various sources in forming my opinions. I have reviewed and considered each of the exhibits listed above in the Table of Exhibits in forming my opinions.

IV. UNDERSTANDING OF THE LAW

13. I have applied the following legal principles provided to me by counsel in arriving at the opinions set forth in this report.

Legal Standard for Obviousness

14. I understand that a patent is invalid if the differences between the claimed subject matter and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person of ordinary skill in the pertinent art.

15. I understand that a person of ordinary skill in the art provides a reference point from which the prior art and claimed invention should be viewed. This reference point prevents a person from using one's insight or hindsight in deciding whether a claim is obvious.

16. I also understand that an obviousness determination includes the consideration of various factors such as (1) the scope and content of the prior art, (2) the differences between the prior art and the challenged claims, (3) the level of ordinary skill in the pertinent art, and (4) the existence of secondary considerations, also referred to as objective considerations, of non-obviousness.

17. I am informed that objective considerations of non-obviousness may include (1) a long felt but unmet need in the prior art that was satisfied by the invention of the patent; (2) failure of others where the invention succeeds; (3) commercial success or lack of commercial success of processes covered by the patent; (4) unexpected results achieved by the invention; (5) praise of the invention by others skilled in the art; (6) taking of licenses under the patent by others; and

(7) deliberate copying of the invention. I also understand that there must be a relationship or nexus between any such objective considerations and the claimed invention. I am aware of no such evidence relevant to this case. If any such evidence is introduced by the Patent Owner, I reserve the right to consider that evidence at such time. I further understand that contemporaneous and independent invention by others is an objective consideration supporting an obviousness determination.

18. I understand that an obviousness evaluation can be based on a combination of multiple prior art references. I understand that the prior art references themselves may provide a suggestion, motivation, or reason to combine, but other times the nexus linking two or more prior art references may be the background knowledge of one of ordinary skill or simple common sense. I further understand that an obviousness analysis recognizes that market demand, rather than scientific literature, often drives innovation, and that a motivation to combine references may be supplied by the direction of the marketplace.

19. I understand that if a technique has been used to improve one device, and a person of ordinary skill in the art would recognize that it would improve similar devices in the same way, using the technique is obvious unless its actual application is beyond his or her skill.

20. I also understand that practical and common-sense considerations should guide a proper obviousness analysis, because familiar items may have obvious uses beyond their primary purposes. I further understand that a person of ordinary skill in the art looking to overcome a problem will often be able to fit the teachings of multiple publications together like pieces of a puzzle, although the prior art need not be like two puzzle pieces that must fit perfectly together. I understand that obviousness analysis therefore considers the inferences and creative steps that a person of ordinary skill in the art would employ under the circumstances.

21. I understand that a particular combination may be proven obvious by showing that it was obvious to try the combination. For example, when there is a design need or market pressure to solve a problem and there are a finite number of identified, predictable solutions, a person of ordinary skill has good reason to pursue the known options within his or her technical grasp because the result is likely the product not of innovation but of ordinary skill and common sense.

22. I understand that the combination of familiar elements according to known methods may be proven obvious when it does no more than yield predictable results. When a work is available in one field of endeavor, design incentives and other market forces can prompt variations of it, either in the same field or a different

one. If a person of ordinary skill can implement a predictable variation, obviousness likely bars its patentability.

23. It is also my understanding that there are additional considerations that may be used as further guidance as to when a claim is obvious, including the following:

- the claimed invention is a simple substitution of one known element for another to obtain predictable results;
- the claimed invention uses known techniques to improve similar devices or methods in the same way;
- the claimed invention applies a known technique to a known device or method that is ready for improvement to yield predictable results; and
- there existed at the time of invention a known problem for which there was an obvious solution encompassed by the patent's claims.

24. It is further my understanding that a proper obviousness analysis focuses on what was known or obvious to a person of ordinary skill in the art, not just the patentee. Accordingly, I understand that any need or problem known in the field of endeavor at the time of invention and addressed by the patent can provide a reason for combining the elements in the manner claimed.

25. I understand that a claim can be obvious in light of a single reference, without the need to combine references, if the limitations of the claim that are not found explicitly or inherently in the reference can be supplied by the common sense of one of skill in the art.

26. I understand that a person of ordinary skill could have combined two pieces of prior art or substituted one prior art element for another if the substitution can be made with predictable results, even if the swapped-in element is different from the swapped-out element. In other words, the prior art need not be like two puzzle pieces that must fit together perfectly. The relevant question is whether prior art techniques are interoperable with respect to one another, such that that a person of skill would view them as a design choice, or whether a person of skill could apply prior art techniques into a new combined system.

27. In sum, my understanding is that prior art teachings are properly combined where a person of ordinary skill in the art having the understanding and knowledge reflected in the prior art and motivated by the general problem facing the inventor, would have been led to make the combination of limitations recited in the claims. Under this analysis, the prior art references themselves, or any need or problem known in the field of endeavor at the time of the invention, can provide a

reason for combining the limitations of multiple prior art references in the claimed manner.

28. I have been informed and understand that the obviousness analysis requires a comparison of the properly construed claim language to the prior art on a limitation-by-limitation basis.

29. I understand that in an *Inter Partes* Review obviousness must be shown by a preponderance of the evidence.

Legal Standard for Claim Construction

30. I understand that a patent may include two types of claims, independent claims and dependent claims. An independent claim stands alone and includes only the limitations it recites. A dependent claim can depend from an independent claim or another dependent claim. I understand that a dependent claim includes all the limitations that it recites in addition to all of the limitations recited in the claim or claims from which it depends.

31. I understand that the purpose of claim construction is to understand how one skilled in the art would have understood the claim terms at the time the claimed invention was made. I also understand that claim construction is a matter of law for the Patent Trial and Appeal Board to decide.

32. I understand that a claim construction analysis begins with the ordinary and customary meaning of the claim term in the context of the patent in which the term is used. The ordinary and customary meaning is the meaning that the term would have to a person of ordinary skill in the relevant art at the time of the invention in light of what the patent teaches. I understand that in this proceeding, I am supposed to apply what is known as the *Phillips* standard for claim construction, described in the *Phillips v. AWH Corp.* decision.

33. In comparing the claims of the '402 Patent to the prior art, I have carefully considered the '402 Patent and its file history in light of the understanding of a person of skill at the time of the alleged invention.

34. I understand that to determine how a person of ordinary skill would understand a claim term, one should look to those sources available that show what a person of skill in the art would have understood disputed claim language to mean. The available sources may include both evidence intrinsic and extrinsic to the patent. Intrinsic evidence includes the words of the claims themselves, the remainder of the patent's specification, including materials incorporated by reference, and the prosecution history of the patent, including materials cited and statements made during the prosecution history. Extrinsic evidence, which is evidence external to the

patent and the prosecution history, may include materials concerning relevant scientific principles, the meaning of technical terms, and the state of the art.

35. I understand that, in construing a claim term, one looks first to the intrinsic patent evidence. The extrinsic evidence may also be useful in interpreting the claim term when the intrinsic evidence alone is insufficient to correctly resolve the meaning.

36. I understand that words or terms, which may include phrases, should be given their ordinary and accepted meaning unless it appears that the inventors were using them to mean something else. In making this determination, the claims, the patent specification, and the prosecution history are of paramount importance. Additionally, the specification and prosecution history must be consulted to confirm whether the patentee has acted as its own lexicographer (i.e., provided its own special meaning to any disputed terms), or intentionally disclaimed, disavowed, or surrendered any claim scope.

37. I understand that the claims of a patent define the scope of the rights conferred by the patent. Patentees are required to particularly point out and distinctly claim the subject matter which they regard as their invention. Because patentees are required to define precisely what they claim their inventions are, it is improper to construe claims in a manner different from the plain import of the terms used

consistent with a patent's specification. Accordingly, a claim construction analysis must begin with, and remain centered on, the claim language itself. Additionally, the context in which a term is used in the challenged claim can be highly instructive. Likewise, other claims of the patent in question, both challenged and non-challenged, can inform the meaning of a claim term. For example, because claim terms are normally used consistently throughout the patent, the usage of a term in one claim can often illuminate the meaning of the same term in other claims. Differences among claims can also be a useful guide in understanding the meaning of particular claim terms.

38. I understand that a person of ordinary skill in the art is deemed to read a claim term not only in the context of the particular claim in which the disputed term appears, but in the context of the entire patent, including the specification. For this reason, the words of the claim must be interpreted in view of the entire specification. The specification is the primary basis for construing the claims and provides a safeguard such that correct constructions are closely aligned with the specification. Ultimately, the interpretation to be given a term can only be determined and confirmed with a full understanding of what the inventors actually invented and intended to envelop with the claim as set forth in the patent itself.

39. I understand that it is improper to place too much emphasis on the plain or ordinary meaning of a claim term without adequate grounding of that term within the context of the specification of the challenged patent. Hence, claim terms should not be broadly construed to encompass subject matter that is not supported when the claims are read in light of the invention described in the specification.

40. I understand that the role of the specification is to describe and enable the invention. In turn, the claims cannot be of broader scope than the invention that is set forth in the specification. Care must be taken lest word-by-word definition, removed from the context of the patent, leads to an overall result that departs significantly from the patented invention.

41. I understand that claim terms must be construed in a manner consistent with the context of the intrinsic record. In addition to consulting the specification, one should also consider the patent's prosecution history. The prosecution file history provides evidence of how both the Patent Office and the patentee understood the terms of the patent, particularly in light of what was known in the prior art. Further, where the specification describes a claim term broadly, arguments and amendments made during prosecution may require a narrower interpretation.

42. I understand that while intrinsic evidence is of primary importance, extrinsic evidence, including expert and inventor testimony, dictionaries, and

learned treatises, can also be considered. For example, technical dictionaries may help one better understand the underlying technology and the way in which one of skill in the art would understand the claim terms. Extrinsic evidence should not be considered, however, divorced from the context of the intrinsic evidence. Evidence beyond the patent specification, prosecution history, and other claims in the patent should not be relied upon unless the claim language is ambiguous in light of these intrinsic sources. Furthermore, while extrinsic evidence can shed useful light on the relevant art, it is less significant than the intrinsic record in determining the legally operative meaning of claim language.

43. I understand that in general, a term or phrase found in the introductory words of the claim, referred to as the preamble of the claim, should be construed as a limitation if it recites essential structure or steps, or is necessary to give life, meaning, and vitality to the claim. Conversely, a preamble term or phrase is not limiting where a patentee defines a structurally complete invention in the claim body and uses the preamble only to state a purpose or intended use for the invention. In making this distinction, one should review the entire patent to gain an understanding of what the inventors claim they actually invented and intended to encompass by the claims.

44. I understand that language in the preamble may limit claim scope (i) if dependence on a preamble phrase for antecedent basis indicates a reliance on both the preamble and claim body to define the claimed invention; (ii) if reference to the preamble is necessary to understand limitations or terms in the claim body; (iii) if the preamble recites additional structure or steps that the specification identifies as important; or (iv) if the patentee relied on the preamble during prosecution to distinguish the prior art.

45. I understand that claim limitations may be stated in means-plus-function format in which a term is defined by functional language without a defined structure. In particular, I understand that a means-plus-function limitation should be interpreted to cover the recited function, and only the corresponding structure described in the specification, and equivalents thereof. I also understand that a limitation will be presumed to be a means-plus-function limitation if (a) the claim limitation uses the phrase “means for”; (b) the “means for” is modified by functional language; and (c) the phrase “means for” is not modified by sufficient structure for achieving the specified function.

46. I understand that a structure will be considered structurally equivalent to the corresponding structure identified in the specification only if the differences between them are insubstantial. For example, a structure may be deemed to be a

structural equivalent to the corresponding structure where the structure performs the same function in substantially the same way to achieve substantially the same result. I further understand that a structural equivalent must have been available at the time of the issuance of the claim.

47. I understand that an indefinite article “a” or “an” in patent parlance carries the meaning of “one or more” in open-ended claims containing the transitional phrase “comprising.” I understand that, unless the claim is specific as to the number of limitations, the article “a” receives a singular interpretation only in rare circumstances when the patentee evinces a clear intent to so limit the article, and thus, under this conventional rule, the claim limitation “a,” without more, requires “at least one.”

V. LEVEL OF SKILL OF ONE OF ORDINARY SKILL IN THE ART

48. In determining the characteristics of a hypothetical person of ordinary skill in the art (“POSA”) of the ’402 Patent at the time of the claimed invention, I considered several things, including various prior art techniques relating to aspiration embolectomy and thrombectomy, the type of problems that such techniques gave rise to, and the rapidity with which innovations were made. I also considered the sophistication of the technologies involved, and the educational background and experience of those actively working in the field. I also considered

the level of education that would be necessary to understand the '402 Patent. I also considered the prior art references discussed below that may indicate the level of skill in the relevant art. Finally, I placed myself back in the relevant period of time, and considered the academics, engineers, medical professionals, and graduate students that I had worked with in the field of aspiration embolectomy and thrombectomy. I came to the conclusion that the characteristics of a person of ordinary skill in the field of art of the '402 Patent would have been either (1) a person with a Bachelor of Science degree in engineering or an equivalent field, with two to four years of academic or industry experience in the aspiration embolectomy and thrombectomy industry or comparable industry experience who would, where necessary or desired, work or consult with others including a physician to develop embolectomy or thrombectomy devices; or (2) an interventional neurosurgeon with at least three years of experience developing and/or using medical devices in embolectomy or thrombectomy procedures, and who would, where necessary, work or consult with others including an engineer to develop such a medical device. A person with less education but more relevant practical experience, or more relevant education but less practical experience, may also meet this standard. According to this standard, I was at least a person of ordinary skill in the art at the time of the alleged invention of the '402 Patent.

VI. TECHNOLOGY BACKGROUND

49. The '402 Patent relates to systems, apparatuses, and methods that lie in the field of thrombus removal. The patent relates to an aspiration thrombectomy system and the methods for thrombus removal with an aspiration catheter.

Thrombectomy Procedures

50. Thrombectomy refers to physical removal of soft, fresh thrombus, or clotted blood. The idea of doing this with a small, percutaneously inserted device is that it atraumatically “vacuums” the thrombus out of the vessel. Such a device offers the speed of surgical intervention with the advantage of minimally invasive therapy—a concept that is not new to the field of medicine or thrombectomy procedures. The Fogarty balloon, a device developed in 1961, is a standard tool for rapid thrombus debulking and requires a surgical incision. Ex. 1014 (“Thorpe”).

51. Catheter-based thrombectomy systems are routinely used to remove blood clots from vessels inside the body, often as an adjunct therapy to systemic pharmaceutical thrombolytics. These systems are used in veins, as in the case of deep vein thrombosis (DVT), and in arteries, in the case of pulmonary embolism (PE), ST-elevated myocardial infarction (STEMI) and ischemic stroke. The systems can also quickly clear dialysis arteriovenous grafts, which are prone to thrombus formation. Ex. 1015 (“Fornell”).

52. Traditionally DVT and intervacular clot-based conditions have been treated with drugs (lytics) to break down the clot over hours or days, or by the physical extraction of the thrombus through a catheter.

53. There are three types of catheter thrombectomy devices — aspiration catheters to vacuum the clot out of the vessel, lytic delivery catheters to infuse the clot with targeted thrombolytic drug treatment, and mechanical thrombectomy systems that break up the clot. Systems routinely combine one or more of these attributes in their designs. Ex. 1015 (Fornell).

Aspiration Thrombectomy

54. Aspiration and mechanical thrombectomy devices offer many benefits in short-term therapy for patients that were well-known in the art prior to the '402 Patent. Faster thrombus removal, smaller doses of thrombolytic agents, and shorter treatment times that translate into improved symptom relief, decreased complications, and more efficient patient care.

55. One of the major limitations of thrombus aspiration devices is embolization of thrombus debris downstream in the circulation. This risk can be remarkable with large and organized thrombi. This phenomenon, referred to as “forward flow” in the '402 patent, has been well-documented in the field as a risk of thrombectomy in the literature and prior art, with several devices focused on

reducing that risk. Ex. 1008 (“Mullins”) at 25:43-50, 26:12-16; Ex. 1010 (“Grey”) at 2:16-20, 7:10-12; Ex. 1023 (“Ross Decl.”) at ¶17.

56. Thromboembolism occurs when part or all of a thrombus breaks away from the blood vessel wall. This clot (now called an embolus) is then carried in the direction of blood flow. An ischemic stroke may result if the clot lodges in the cerebral vasculature. Ex. 1012 (“Yang”) at [0003]. A pulmonary embolism may result if the clot originates in the venous system or in the right side of the heart and lodges in a pulmonary artery or branch thereof.

57. A clot is essentially a living polymer, comprising a matrix of intertwined and cross-linked fibrin strands within which are situated red and white blood cells, platelets and numerous other proteins and components. The mechanical properties of a clot are influenced by the relative percentages of fibrin and red blood cells, and clots with a high (and highly organized) fibrin content and low red blood cell content tend to be firmer and more cohesive than clots of a higher red cell content. Such clots have also been found to have a higher coefficient of friction, or in other words tend to be “stickier.” These firm and sticky clots can be challenging to remove from a vessel. Clots with a low fibrin content and high red cell content have been found to be less cohesive, more friable and to have a lower coefficient of friction than the more organized fibrin rich clots previously described. These

properties mean that such clots may be easier to dislodge from the site of occlusion, but may tend to fragment during the retrieval process, with the consequent risk of loss of clot fragments into distal or new vascular territories, as described in Grey. Ex. 1008 (Mullins) at 25:43-50, 26:12-16; Ex. 1010 (Grey) at 2:16-20, 7:10-12; Ex. 1023 (Ross Decl.) at ¶17.

58. Typical clot aspiration involves inserting a catheter into the patient's vasculature and advancing the catheter up to the occlusive clot. A syringe or vacuum pump is then attached to the proximal end of the catheter and a vacuum applied to attempt to suck the clot into the catheter tip and out through the catheter. The level of the vacuum applied can be controlled by the force applied to the syringe or by the pump setting, and typically a fairly constant pressure drop (static loading) of 500mmHg (19.7 inHg) to 760mmHg (29.9 inHg) (or "full" vacuum) is applied. The difference in pressure between the blood vessel in which the clot is situated and the interior of the catheter creates a pressure gradient (which may exceed 760mmHg (29.9 inHg) as the patient's blood pressure is higher than atmospheric pressure) which urges the clot into the catheter mouth. Ex. 1016 ("Brady") at 3:9-18.

59. In order to aspirate clots into a catheter, the clot often needs be deformed to fit into the catheter lumen, and the energy required to deform such clots is not easily attained by aspiration alone. The diameter of a clot can be greater than

the inner diameter of the catheter. Therefore, for such a clot to be aspirated into a catheter, the clot may deform and elongate to fit into the catheter tip. The inner diameter of the catheter can range from 0.038” for the treatment of smaller cerebral vessels (*see, e.g.*, Ex. 1017 (“Rioufol”)), to an inner diameter of approximately 0.120” of a 9Fr sheath for the treatment of peripheral occlusions, (*see, e.g.*, Ex. 1018 (“Haude”)). These catheter diameters are variable, but inherently limited by the size of human physiology and the inner diameter of the vessels that the catheters are designed to treat. Ex. 1023 (Ross Decl.) at ¶¶13-14.

60. The energy to deform the clot to fit into the catheter is effectively an extrusion energy as the catheter tip acts as a form of extrusion die for the clot. This extrusion energy is related to the fibrin content of the clot with higher fibrin clots requiring increased extrusion energy to aspirate the clot into the catheter. Ex. 1016 (Brady) at 3:21-25. A classic technique to aspirate the clot involves applying a steady state vacuum to the tip of the catheter; however, in many cases this does not provide sufficient energy to aspirate the clot fully into the catheter, as discussed in the prior art. Ex. 1010 (Grey) at 1:25-2:1. Subsequent retrieval of the catheter while maintaining a vacuum either does not dislodge the clot or dislodges the partially retrieved clot and creates the risk of losing the partially exposed clot into a side branch or new vessel.

61. One of the well-known problems of using vacuum to remove mucus or other heavy matter (thrombus) from the body is the clogging of catheters or tubing. *See generally* Ex. 1008 (“Ofek”); *see also* Ex. 1009 (Mullins) at 3:39-4:11, 25:1-26:16. Such clogging prevents the flow of fluids from the patient, through the catheter, to remove the matter. As early as the late 1950s and early 1960s, physicians were using Intermittent Suction Units (ISU’s) to automatically alleviate the clogging problem. Such devices stop the vacuum on a predetermined cycle and open the tubing leading to the patient to atmospheric pressure. In this way, the flow of fluid from the patient is temporarily stopped and some of the fluid is allowed to run backward toward the patient. Examples of typical ISU’s are shown and described in U.S. Pat. No. 3,086,528 (“Eichelman”), U.S. Pat. No. 3,659,605 (“Sielaff”) and others. Ex. 1019 (Eichelman); Ex. 1020 (Sielaff). A further improvement to dislodge clogging material has been to force a fluid backward toward the patient under a positive pressure, with particular emphasis on the introduction of a liquid, such as a saline solution into the patient tubing. An example of such a positive backflow system is described in U.S. Pat. No. 3,042,042. Ex. 1021 (“Blanck”).

62. When the steady state vacuum normally applied at the tip of the catheter is modified to a pulsatile or wave configuration so that the pressure differential between the catheter tip and the blood vessel plotted against time resembles a sine

wave, as disclosed in Grey, the application of the aspiration force to the clot in a wave or pulsatile configuration applies an ‘impact load’ to the clot which can deform the clot and overcome the resistance or extrusion energy required to get the clot into the catheter more quickly and effectively than applying a continuous or steady aspiration force. Ex. 1010 (Grey) at 2:24-3:24. The application of a pulsatile force to the clot can cause the clot to vibrate or move slightly proximally and distally, so that the interaction between the clot and the internal surface of the catheter changes from static friction to a dynamic friction interaction. Dynamic friction is known to be lower than static friction, and therefore the total force to remove the clot is reduced when using cyclic aspiration. Ex. 1016 (Brady) at 4:15-20.

63. In 2013, researchers from the Pennsylvania State University, Hershey, Pennsylvania and the Virginia Commonwealth University, Richmond, Virginia published their findings that cyclic aspiration outperformed static aspiration in overall clot removal and removal speed. Ex. 1022 (“Simon”). Within cyclic aspiration, higher frequencies (~6.3 Hz) cleared clots faster than 1 Hz and 2 Hz. Loading cycle dynamics (specific pressure waveforms) affected speed and overall clearance. The researchers explained that the introduction of cyclic aspiration forces in suction thrombectomy would generate clot fatigue, and that the increased aspiration frequencies would lead to increased treatment efficacy. Ex. 1022 (Simon).

The additional dimensions of frequency and amplitude modulation may be added to this technique in which their values are temporally adjusted to increase treatment efficacy. They also observed that “[t]his technique can [] be optimized to provide uninterrupted net reverse flow to prevent distal migration,” i.e., the net flow of liquid at the distal end of the catheter remains positive in the proximal direction, and substantially no flow out of the distal end of the catheter occurs during a thrombus retrieval procedure. Ex. 1022 (Simon). In a related 2014 patent application by the Virginia Commonwealth University (Ex. 1010, (Grey)), cyclic frequencies higher than 50 Hz were disclosed. Ex. 1010, (Grey) at 9:13-25, 10:28-11:3. The researchers at Virginia Commonwealth University made salient observations about the impact that distal migration of flow would have on a patient, observing that when the positive pressure exceeds a certain amount, the risk of occlusions breaking off of the clot and traveling distally into the patient’s vessel increases. Ex. 1010 (Grey) at 7:10-12, 13:7-11. A POSA would have necessarily considered the balance between efficient clot removal and the risk of distal migration of thrombi as part of the design choice. See Ex. 1010 (Grey) at 13:7-11 (“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”).

64. The cycling between applying vacuum aspiration and pulses of pressure, wherein the pressure is above that of the vacuum source can be achieved via a number of different fluid valve combinations that are ascertainable by a person of skill in the art via routine optimization. The use of a vacuum valve fluidly connected to a vacuum source, and a vent valve fluidly connected to a vent source is a common and simple configuration. The timing and the actuation of the valves can be synchronized by an electronic controller or mechanical actuator. A common and inexpensive mechanical actuator to control one or more valves is one or more eccentric cams on a common drive shaft. An example of one or more valves mounted together on a single cam shaft is shown and described in U.S. Patent Publication Application 2012/0138833. Ex. 1013 (“Matteo”) at Abs., [0006], [0012], [0029], FIGS. 11, 12.

65. Thus, the use of many of the above capabilities was well-known in a variety of medical applications prior to the ’402 Patent, including the treatment of ischemic strokes.

VII. THE ’402 PATENT

A. Priority Date

66. The ’402 Patent was filed on February 11, 2022, as a continuation of U.S. Patent App. No. 16/899,514, which was filed June 11, 2020, which is a

continuation of U.S. Patent No. 10,722,253 (“the ’253 Patent”), which was filed November 12, 2019, which is a continuation of U.S. Patent No. 10,531,883 (“the ’883 Patent”), which was filed July 18, 2019, and claims priority to two provisional applications, U.S. Provisional Application No. 62/701,086 filed on July 20, 2018 (“Deville-Prov1”) and U.S. Provisional Application No. 62/750,011 filed on October 24, 2018 (“Deville-Prov2”). Ex. 1001 (’402 Patent) at 1-2; *see also* Ex. 1002 (Deville-Prov1); Ex. 1003 (Deville-Prov2). I understand that because the patent application that later issued as the ’402 patent does not claim priority to any application filed before March 16, 2013, patentability is governed by the Leahy-Smith America Invents Act (“AIA”) version of 35 U.S.C. §§ 102 and 103. I also understand that even if a patent claims priority to prior provisional applications, the Patent Owner is not entitled to a presumption that claims of its patent, including the ’402 Patent, are entitled to the effective filing date of its provisional application. Instead, I understand that Patent Owner bears the burden to establish that the Challenged Claims of the ’402 Patent are entitled to the benefit of priority to the provisional applications by demonstrating that the provisional applications provide the full support required by 35 U.S.C § 112(a) for each claim. Given that Patent Owner bears that burden, in this declaration, I have not analyzed whether the ’402

Patent claims are entitled to a priority date earlier than July 18, 2019.¹ In the event that Patent Owner carries their burden and produces evidence to establish that the Challenged Claims are entitled to the benefit of priority to the provisional applications, I reserve the right to submit rebuttal opinions to respond to any arguments raised by Patent Owner, including any arguments regarding the priority date of the '402 Patent in relation to any prior art reference. However, it is my opinion that the references relied upon herein are prior art even if the '402 Patent receives the benefit of the provisional applications.

¹ I also note that this patent family appears to have added, for at least one or more of its continuing applications (including the '402 Patent), increasing amounts of additional content into the disclosure of the continuations that were not present in the '883 Patent. *See, e.g.*, Ex. 1001 at 9:29-15:26. I understand that disclosure added in a continuing application can be considered new matter, and that any claims that may rely on new matter may not necessarily be entitled to a priority date earlier than the date when the new matter was added. Should Patent Owner make arguments reliant on any new matter, I reserve the right to supplement my opinion to address such arguments.

B. Prosecution History

67. The '402 Patent had a short prosecution history under Track One with no official office action issued. *See* Ex. 1004 (Prosecution File History of the '402 Patent). Various earlier applications with similar claims in the patent family line of continuity of the '402 Patent (e.g., U.S. Patent No. 10,531,883 (“the '883 Patent”); U.S. Patent No. 10,722,253 (“the '253 Patent”)) had several notable prosecution history events. *See* Ex. 1028 ('883 Patent); Ex. 1029 ('883 Patent Prosecution File History); Ex. 1030 ('253 Patent); Ex. 1031 ('253 Patent Prosecution File History). For example, in the IPR proceedings invalidating two of the parent patents to the '402 Patent (*see* IPR2021-01466; IPR2022-00608), I discussed certain of those prosecution history events in my declarations, as recounted below.

68. The '883 Patent, the original non-provisional application in the '402 Patent family, also had a relatively short prosecution history of its 20 claims under Track One with no official office action issued. Ex. 1028 ('883 Patent); Ex. 1029 ('883 Patent Prosecution File History). Although the Applicant submitted an information disclosure statement (“IDS”) listing over 150 references, the Examiner initiated an interview to discuss 112 issues and a single reference pertaining only to Claims 19 and 20. Ex. 1029 ('883 Patent Prosecution File History) at 71 (Examiner-initiated Interview Summary, Dated Sept. 30, 2019.) During that interview,

Applicant agreed to the Examiner's amendment to cancel Claims 19 and 20 and put the application in condition for allowance. Ex. 1029 ('883 Patent Prosecution File History) In the Notice of Allowance, the Examiner stated with regard to Claims 1-17:

The prior art fails to disclose or suggest, in combination with other limitations recited in the claims, 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, and 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 response [sic] to opening the vacuum and vent 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.

Ex. 1029 ('883 Patent Prosecution File History) at 67 (Notice of Allowance, Dated 9-26-2019, p. 2). In a second Notice of Allowance dated November 21, 2019, the Examiner allowed Claims 1-18 while amending the language in Claim 10: "is greater than approximately 15 inHg [[in]] and no greater than approximately 50 ms." Ex. 1029 ('883 Patent Prosecution File History) at 22 (Notice of Allowance, Dated 11-21-2019, p. 2).

69. The '253 Patent was the first continuation application in the '402 Patent family, and had a short prosecution history with no official office action issued. *See* Ex. 1030 ('253 Patent); Ex. 1031 ('253 Patent Prosecution File History). The

application of the '253 Patent was filed on November 12, 2019, as a continuation of the '883 Patent. Ex. 1031 ('253 Patent Prosecution File History) at 638. The as-filed application of the '253 Patent contained 21 claims. The Applicant filed an IDS on December 20, 2019, disclosing 180 prior art references. Ex. 1031 ('253 Patent Prosecution File History) at 113. The Examiner issued a first Notice of Allowance on March 4, 2020, allowing Claims 1-21. Ex. 1031 ('253 Patent Prosecution File History) at 28 (Notice of Allowance, Dated March 4, 2020). The Examiner stated that the application added new disclosure, directed Applicant to comply with requirements for a continuation-in-part application, and rejected Applicant's claim of priority to the '883 patent and its provisional applications because they lacked supporting disclosure for both "a pre-determined cycle changing the level of vacuum at the distal end" and "substantially preventing the forward flow of liquid at the distal end of the liquid column." Ex. 1031 ('253 Patent Prosecution File History) at 33. The Examiner issued a second Notice of Allowance on May 11, 2020, attaching an Applicant-Initiated Interview Summary stating only that "pre-determined pattern" was supported by the parent application. Ex. 1031 ('253 Patent Prosecution File History) at 16 (Applicant-Initiated Interview Summary, Dated May 11, 2020).

C. Subject Matter

70. The '402 Patent is directed to addressing well-known problems and risks inherent in the use of aspiration thrombectomy systems in the treatment of ischemic strokes, including catheters becoming clogged with blood clots and risks of distal migration of thrombi. Ex. 1001 ('402 Patent) at 1:43-3:22. In particular, the '402 Patent recognizes that conventional aspiration thrombectomy systems “rarely” “aspirate[] the clot entirely out of the neurovasculature and to the proximal end of the aspiration catheter so that extraction and re-establishment of blood flow [can] be confirmed.” Ex. 1001 ('402 Patent) at 2:4-8. Instead, the clot, or thrombus, can become “lodged completely within, partially within, or at the distal opening of the aspiration catheter,” preventing clearance of the clot through conventional aspiration and creating a risk that the clot may be “forcibly and uncontrollably eject[ed]” from the catheter by a positive pressure, or forward flow, and caused “to move further distally within the vessel in which it was originally lodged.” Ex. 1001 ('402 Patent) at 2:16-37, 3:5-22.

71. To solve these well-known problems, the '402 Patent alleges that its disclosures of aspiration thrombectomy “completely vacuum[] up the clot so that clots are no longer dragged out of vasculature while half hanging out of a catheter tip.” Ex. 1001 ('402 Patent) at 3:35-38. The purported invention claimed by the '402

Patent is the use of known vacuum aspiration thrombectomy systems and known aspiration catheters with known methods to “change a level of vacuum at the distal end of the catheter” and “control fluid flow in and out from the distal end of the catheter.” Ex. 1001 (’402 Patent) at Claim 1. The ’402 Patent does not describe any innovative system components for achieving the outcomes described or for performing any of the processes included in its aspiration thrombectomy methods. Instead, the ’402 Patent merely applies well known and routine methods for treating ischemic stroke via periodic cycling of vacuum aspiration using well-known vacuum aspiration thrombectomy solutions. The ’402 Patent admits that “Those of skill in the art know that these situations [of clogged catheters and forward flow] are to be avoided because of the serious potential risks to the patient.” Ex. 1001 (’402 Patent) at 2:35-37.

72. For example, the inventors of the ’402 Patent did not invent a novel clot extraction method. The specification explains that a clogged catheter is unclogged by a system that “temporarily halts vacuum at the distal end of the aspiration catheter,” and “then re-applies vacuum” to accelerate the vacuum force within the catheter. Ex. 1001 (’402 Patent) at 3:26-34, 4:33-43. The use of applying vacuum suction during aspiration was well known in the art prior to the date of the ’402 Patent. The ’402 Patent specification further relies on a vent valve to introduce a

pressure pulse into the vacuum aspiration system, which was a well-known method to relieve vacuum pressure at the time that the '402 Patent was filed. See Ex. 1001 ('402 Patent) at 5:47-6:6.

73. Moreover, the '402 Patent merely utilizes existing vacuum aspiration system components, including a vacuum valve, a vent valve, an aspiration catheter, and a blood collection apparatus, using a generic controller and data analysis algorithms to operate the system. The system relies on a generic controller to open and close the vacuum and vent valves in the system using well-known frequencies and durations with predictable outcomes. Ex. 1001 ('402 Patent) at 5:23-7:19, 35:3-26, 38:55-39:14. Further, the system components that perform the '402 Patent methods may be generic vacuum pumps, liquid reservoirs, and aspiration catheters, which the inventors did not invent. Ex. 1001 ('402 Patent) at 5:23-7:19, 36:25-33, 40:50-62.

D. Challenged Claims

74. The '402 Patent has 20 claims. I understand that Petitioner is challenging the validity of Claims 1-20 of the '402 Patent in the Petition for *Inter Partes* Review. I have considered patent validity with respect to Claims 1-20.

Limitation	Claim Language from '402 Patent
[1-Pre]	An aspiration thrombectomy system, comprising:

[1-A]	an aspiration catheter having a proximal portion, a distal end and a lumen extending through the catheter;
[1-B]	a vacuum source fluidically coupled to the catheter;
[1-C]	a vacuum valve connected between the vacuum source and the proximal portion of the catheter to control a vacuum flow in the catheter lumen;
[1-D]	a vent valve fluidically coupled to the proximal portion of the catheter, the vent valve being configured to control a flow of a vent fluid in the catheter lumen; and
[1-E]	a controller configured to open and close the vacuum valve and the vent valve in a predetermined cycle
[1-F]	to change a level of vacuum at the distal end of the catheter
[1-G]	and to control fluid flow in and out from the distal end of the catheter.
Limitation	Claim Language from '402 Patent
[2-A]	The system of claim 1, further comprising a vent fluid source, and wherein:
[2-B]	the vent fluid source is configured to provide vent fluid at a pressure greater than atmospheric pressure; and
[2-C]	the controller is configured to cyclically open and close the vacuum valve and the vent valve
[2-D]	to change a level of negative pressure and positive pressure at the distal end of the catheter during each cycle.
Limitation	Claim Language from '402 Patent
[3-A]	The system of claim 2 wherein the controller is configured to cyclically open and close the vacuum valve and the vent valve
[3-B]	such that movement of the fluid column at the distal end of the catheter is limited to a positive amount of exit flow... before fluid is drawn back into the catheter lumen.
[3-C]	limited to a positive amount of exit flow from approximately 0.001 ml to approximately 1.0 ml
Limitation	Claim Language from '402 Patent

[4-A]	The system of claim 2 wherein the controller is configured to cyclically open and close the vacuum valve and the vent valve
[4-B]	such that movement of the fluid column at the distal end of the catheter is limited to a positive amount of exit flow... before fluid is drawn back into the catheter lumen.
[4-C]	limited to a positive amount of exit flow of approximately 0.1 ml to approximately 0.5 ml
Limitation	Claim Language from '402 Patent
[5-A]	The system of claim 1 wherein the controller is configured to cyclically open and close the vacuum valve and the vent valve in a repeated cycle
[5-B]	comprising an off-off state in which the vacuum valve is closed while the vent valve is closed.
Limitation	Claim Language from '402 Patent
[6-A]	The system of claim 1 wherein: the controller is configured to cyclically open and close the vacuum valve and the vent valve in a cycle comprising
[6-B]	(a) a first off-off state in which the vacuum valve is closed while the vent valve is closed, (b) a vacuum-only state following the first off-off state in which the vacuum valve is open while the vent valve is closed, (c) a second off-off state following the vacuum-only state in which the vacuum valve is closed while the vent valve is closed, and (d) a vent-only state following the second off-off state in which the vacuum valve is closed while the vent valve is open; and the cycle is repeated.
Limitation	Claim Language from '402 Patent
[7]	The system of claim 6 wherein the cycle is repeated at a frequency of 2 Hz to 12 Hz.
Limitation	Claim Language from '402 Patent
[8]	The system of claim 1 wherein the vacuum valve and the vent valve are solenoid pinch valves.
Limitation	Claim Language from '402 Patent

[9]	The system of claim 1 wherein the vacuum valve and the vent valve are cammed pinch valves.
Limitation	Claim Language from '402 Patent
[10-A]	The system of claim 1 wherein the controller is configured to cyclically open and close the vacuum valve and the vent valve
[10-B]	such that an amount of momentum transfer from the fluid column in the catheter lumen is sufficient to unstick thromboembolic material at the distal end of the catheter.
Limitation	Claim Language from '402 Patent
[11-Pre]	A method for removing thromboembolic material, comprising: aspirating thromboembolic material from a person using the system of claim 1 by—
[11-A]	(a) positioning the distal end of the catheter at least proximate to thromboembolic material in a blood vessel of the person;
[11-B]	(b) applying a vacuum through the lumen of the catheter such that a vacuum flow draws at least a portion of the thromboembolic material into the catheter lumen; and
[11-C]	(c) controlling the vacuum valve fluidically coupled to the vacuum source and the catheter and the vent valve fluidically coupled to a vent fluid source and the catheter
[11-D]	such that a level of vacuum at the distal end of the catheter changes
[11-E]	and thereby controls flow in and out from the distal end of the catheter.
Limitation	Claim Language from '402 Patent
[12-A]	The method of claim 11 wherein: the vent fluid source is configured to provide the vent fluid at a pressure greater than atmospheric pressure; and
[12-B]	controlling the vacuum valve and the vent valve comprises cyclically opening and closing the vacuum valve and the vent valve
[12-C]	to change a level of negative pressure and positive pressure at the distal end of the catheter during each cycle.

Limitation	Claim Language from '402 Patent
[13-A]	The method of claim 12 wherein controlling the vacuum valve and the vent valve comprises limiting movement of a fluid column in the catheter lumen at the distal end of the catheter to a positive amount of exit flow
[13-B]	limiting... to a positive amount of exit flow within a range of a length of the fluid column that exits the distal end of the catheter.
Limitation	Claim Language from '402 Patent
[14-A]	The method of claim 13 wherein limiting movement of the fluid column at the distal end of the catheter comprises stopping a distal flow through the catheter lumen and reapplying the vacuum through the catheter lumen... before fluid is drawn back into the catheter lumen.
[14-B]	such that the positive amount of exit flow is approximately 0.5 mm to approximately 30 mm of the fluid column
Limitation	Claim Language from '402 Patent
[15-A]	The method of claim 12 wherein controlling the vacuum valve and the vent valve comprises limiting movement of a fluid column in the catheter lumen at the distal end of the catheter to a positive amount of exit flow
[15-B]	limiting... to a positive amount of exit flow within a range of volume of fluid that exits the distal end of the catheter.
Limitation	Claim Language from '402 Patent
[16-A]	The method of claim 15 wherein limiting movement of the fluid column at the distal end of the catheter comprises stopping a distal flow through the catheter lumen and reapplying the vacuum through the catheter lumen... before fluid is drawn back into the catheter lumen.
[16-B]	such that the positive amount of exit flow is approximately 0.001 ml to approximately 1.0 ml
Limitation	Claim Language from '402 Patent

[17-A]	The method of claim 15 wherein limiting movement of the fluid column at the distal end of the catheter comprises stopping a distal flow through the catheter lumen and reapplying the vacuum through the catheter lumen... before fluid is drawn back into the catheter lumen.
[17-B]	such that the positive amount of exit flow is approximately 0.1 ml to approximately 0.5 ml
Limitation	Claim Language from '402 Patent
[18-A]	The method of claim 11, further comprising cyclically opening and closing the vacuum valve and the vent valve in a repeated cycle
[18-B]	including an off-off state in which the vacuum valve is closed while the vent valve is closed.
Limitation	Claim Language from '402 Patent
[19-A]	The method of claim 11, further comprising: cyclically opening and closing the vacuum valve and the vent valve in a cycle including
[19-B]	(a) a first off-off state in which the vacuum valve is closed while the vent valve is closed, (b) a vacuum-only state following the first off-off state in which the vacuum valve is open while the vent valve is closed, (c) a second off-off state following the vacuum-only state in which the vacuum valve is closed while the vent valve is closed, and (d) a vent-only state following the second off-off state in which the vacuum valve is closed while the vent valve is open; and repeating the cycle.
Limitation	Claim Language from '402 Patent
[20]	The method of claim 19 wherein the cycle is repeated at a frequency of 2 Hz to 12 Hz.

75. The '402 Patent claims conventional arrangements of commonplace technologies well-known to provide known and predictable outcomes of vacuum

aspiration thrombectomy methods. The claims do not recite any specific type of system or device, relying on only generic system components, such as “vacuum valve,” “vent valve,” “aspiration catheter,” and “controller.”

76. The only independent claim, Claim 1, generally recites a thrombectomy system to “change a level of vacuum at the distal end” of the catheter and “control fluid flow in and out from the distal end of the catheter” via a “controller configured to open and close the vacuum valve and vent valve in a predetermined cycle.” Claim 11 is a method claim reciting “a person using the system of claim 1,” along with similar functional limitations as in Claim 1.

77. These systems and methods and any alleged benefits provided are not new and would have been obvious to, and well understood by a POSA prior to July 18, 2019, the filing date of the first non-provisional application (the '883 Patent), as well as, to the extent it is relevant, prior to July 20, 2018, and October 24, 2018, the filing dates of the provisional applications (Deville-Prov1 and Deville-Prov2). As an illustration, the '402 Patent explains that “most treatments involve” prior art thrombectomy systems, yet “significant problems occur in practice” that allegedly limit those systems utility. Ex. 1001 ('402 Patent) at 1:48-55. The purported invention claims the use of known vacuum aspiration technologies to extract a blood clot from a patient’s blood vessel without the need to remove the catheter during the

procedure and reduce the risk of forward flow of the material within the aspiration catheter into the patient's blood vessel. Ex. 1001 ('402 Patent) at 1:40-3:19. The '402 Patent claims nothing more than an obvious combination of generic components and steps known in the art, with no apparent novelty in the claimed functionality, including the generic, well-known, and basic steps of causing an aspiration catheter to "change a level of vacuum" and "control fluid flow in and out" at the "distal end of the catheter."

VIII. CLAIM CONSTRUCTION

78. For purposes of this *Inter Partes* Review, I have considered the claim language, specification, and relevant portions of the prosecution history, to determine the meaning of the claim language as it would have been understood by a person of ordinary skill in the art at the time of the invention.

79. I have afforded all claim terms not identified below their ordinary and customary meaning as understood by a POSA at the time of the invention.

A. Claim Term: "limited to a positive amount of exit flow" / "limiting... to a positive amount of exit flow"

80. The phrase "[limited / limiting] to a positive amount of exit flow" appears in Claims 3, 4, 13, and 15. Claims 3, 4, 13, 16, and 17 additionally recite particular values for the maximum amount of exit flow permitted by the claims.

81. The plain language of this claim limitation appears ambiguous. The specification of the '402 Patent only uses the term “exit flow” a single time (in contrast to “forward flow”), but does not describe, with particularity, what exactly “limiting” the amounts of “exit flow” entails:

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.

Ex. 1001 ('402 Patent) at 4:50-54. In the context of the '402 Patent specification (including the excerpt above), the claim language, the intended purpose of the alleged invention, and the inherent and well-known risks of distal clot migration, a POSA would have understood that the patentee intended to characterize the “limiting” of “positive amount of exit flow” as the threshold value, or range of threshold values, for which the amount of exit flow could not be permitted to exceed.

Ex. 1001 ('402 Patent) at 4:50-54, 24:36-25:26.

82. Accordingly, a POSA would have understood the term “[limited / limiting] to a positive amount of exit flow” to mean the maximum permitted amount of positive exit flow in the distal direction and would include no exit flow.

IX. SUMMARY OF THE PRIOR ART

83. There are many patents and publications which constitute prior art to the '402 Patent. I have reviewed and considered the following prior art patents and

printed publications, which I believe were all either publicly available prior to, or have a priority date earlier than, July 18, 2019, the effective filing date of the '402 Patent (as well as the filing dates of the provisional applications discussed above). A description of these references follows. The file history does not reveal any attempt by the examiner to apply the cited references to the claims, nor is there any explanation or reasoning from the examiner as to why the claims were allowable over the cited references. *See* Ex. 1003. In particular, although the Yang reference appears on the cover of the '402 Patent in "References Cited," the Examiner did not appear to have substantively evaluated Yang in the context of the allowed claims, nor is there any discussion or mention of why the claims were allowable over Yang. *See* Ex. 1003.

E. Yang

84. U.S. Patent Publication No. 2017/0238953 A1 ("Yang") was filed on February 27, 2017, and published on August 24, 2017. Ex. 1012 (Yang) at 1. Yang qualifies as prior art at least because it was published prior to the filing date of the '402 Patent.

85. Yang is directed to an "aspiration catheter" that has "an elongate tubular body 16 extending between a proximal end 12 and a distal functional end 14." Ex. 1012 (Yang) at ¶ [0065]. The catheter has a "[d]istal 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.” Ex. 1012 (Yang) at ¶ [0067].

86. Yang explains that “catheters of the present invention can be readily modified to incorporate additional structures.” Ex. 1012 (Yang) at ¶¶ [0063]. In particular, Yang discloses that the “aspiration catheter” can be implemented with an “aspiration catheter system configured to apply pulsatile negative pressure through the aspiration catheter.” Ex. 1012 (Yang) at ¶¶ [0029], [0029], [0063]. Yang states that “a pulsatile vacuum pressure aspirator may be used in order to improve effectiveness of aspiration for vascular thrombectomy.” Ex. 1012 (Yang) at ¶ [0123]. Yang further teaches that a “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.” Ex. 1012 (Yang) at ¶ [0123]. In describing aspiration of a clot, Yang explains that “[p]ulsatile 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.” Ex. 1012 (Yang) at ¶ [0102]. This creates a “water hammer effect, which can further facilitate both transluminal navigation as well as dislodging or breaking up the obstruction.” Ex. 1012 (Yang) at ¶ [0108].

F. Ofek

87. U.S. Patent No. 10,322,230 (“Ofek”) was filed on June 9, 2017, and was issued on June 18, 2019. Ex. 1007 (Ofek) at 1. Ofek qualifies as prior art at least because it issued before the effective filing date of the ’402 Patent and because it has an effective filing date earlier than that of the ’402 Patent.

88. Ofek is directed to medical devices for catheter assemblies. Ex. 1007 (Ofek) at Abs. Ofek teaches a system and method which “preserves patency of one or more lumens” by providing “impulses of positive pressure” which includes “negative pressure” to “aspirate the occlusion.” Ex. 1007 (Ofek) at Abstract. The system may be used to “impinge on an occlusion (such as a clot []) or other obstruction that has formed in the lumen 14, typically at or proximate the distal end 12B of the catheter tube 12.” Ex. 1007 (Ofek) at 4:21-44. The system contains a vacuum (negative pressure) and fluid (positive pressure) source in fluidic communication with a catheter, valves for both sources, and a controller responsible for adjusting the positive or negative pressure. Ex. 1007 (Ofek) at 3:43-60, 4:45-5:7.

89. Ofek teaches using the controller to provided cyclic positive pressure impulses, which changes the pressure at the distal tip, to aid in clot removal. Ex. 1007 (Ofek) at 2:56-3:2, 4:21-44, 4:62-5:7, 6:20-45, FIG. 2. Ofek further discloses utilizing the controller to adapt the negative pressure as well. Ex. 1007 (Ofek) at 6:9-

19. Ofek teaches these positive pressure impulses combined with negative pressure to aid in the removal of clots. Ex. 1007 (Ofek) at 2:56-3:2, 4:21-44, 4:62-5:7, 6:20-45, FIG. 2.

G. Mullins

90. U.S. Patent No. 11,197,977 (“Mullins”) was filed March 13, 2020, and was issued on December 14, 2021. Ex. 1008 (Mullins) at 1. It is a continuation of International Application No. PCT/EP2018/085064 filed on December 14, 2018, which claims priority to U.S. Provisional Application 62/599,560 (“Mullins-Prov1”), filed December 15, 2017, U.S. Provisional Application 62/599,573 (“Mullins-Prov2”), filed December 15, 2017, and U.S. Provisional Application 62/616,188 (“Mullins-Prov3”), filed January 11, 2018. Ex. 1009.1 (Mullins-Prov1); Ex. 1009.2 (Mullins-Prov2); Ex. 1009.3 (Mullins-Prov3). Mullins qualifies as prior art at least because it claims priority to Mullins-Prov1, Mullins-Prov2, and Mullins-Prov3, each of which were filed prior to the earliest effective filing date of the ’402 patent, and because everything disclosed in Mullins that is relied upon herein is fully supported by the Mullins provisional applications, as evidenced by the corresponding citations to the Mullins provisional applications throughout the invalidity grounds below.

91. Mullins and its provisional applications are directed to a catheter and accompanying aspiration system to help insure effective aspiration of a clot of thrombus. Ex. 1008 (Mullins) at Abstract, 3:29-38; Ex. 1009.1 (Mullins-Prov1) at ¶¶ [0001]-[0023], FIGs. 1-7; Ex. 1009.2 (Mullins-Prov2) at pg. 1-11, FIGs. 1-10; Ex. 1009.3 (Mullins-Prov3) at pg. 1-4. Mullins and its provisional applications teach the aspiration system having a pump, a fluid reservoir, and tubing connected to a catheter, the system being capable of creating both positive and negative pressure, and being programmed using a controller to cycle through both negative and positive pressures to aid in thrombus removal. Ex. 1008 (Mullins) at 3:29-38, 3:46-4:11, 26:17-27:67, FIGs. 46-49; Ex. 1009.2 (Mullins-Prov2) at pg. 4-9. Mullins and its provisional applications disclose the aspiration system being configured to monitor both pressure and flow/fluid displacement for the catheter and aspiration system. Ex. 1008 (Mullins) at 3:29-38, 26:31-37; Ex. 1009.2 (Mullins-Prov2) at pg. 4-7. Mullins and its provisional applications further disclose a technique for macerating a thrombus to aid in aspiration, including by changing pressures at the distal end of the catheter, which can aid in macerating the clot, thereby allowing for easier clot aspiration. Ex. 1008 (Mullins) at 27:18-26, FIGs. 47(a)-(n); Ex. 1009.2 (Mullins-Prov2) at pg. 3-9. In particular, Mullins and its provisional applications disclose drawing in a portion of a clot to the catheter, via negative pressure, subsequently

pushing at least a portion of the clot out from the distal end of the catheter, and then using aspiration to draw the clot further into the catheter and aspiration system. Ex. 1008 (Mullins) at 26:65-27:39, FIGs. 47(a)-(n); Ex. 1009.2 (Mullins-Prov2) at pg. 4-9. Mullins and its provisionals also disclose utilizing a similar technique for keeping the interior of the catheter unclogged during the aspiration process. Ex. 1008 (Mullins) at 27:54-65; Ex. 1009.2 (Mullins-Prov2) at pg. 3-9.

H. Rubenstein

92. U.S. Patent No. 3,955,574 (“Rubenstein”) was filed on December 9, 1974, and issued on May 11, 1976. Ex. 1011 (Rubenstein) at 1. Rubenstein qualifies as prior art at least because it was issued prior to the earliest effective filing date of the ’402 Patent.

93. Rubenstein is directed to an “improved pumping system for use with catheter suction units” “for drawing fluids and other viscous materials from a body” during medical procedures. Ex. 1011 (Rubenstein) at Abs., 1:7-14. Rubenstein discloses applying cyclical reversals of positive and negative pressure to create a “self-cleaning” catheter that can clear clogs at the catheter tip. Ex. 1011 (Rubenstein) at 1:10-14, 1:64-68. Rubenstein further discloses the use of “time[-]controlled valve[s] which [are] operated at predetermined time intervals to have suction through the catheter interrupted by a predetermined period of positive pressure to

cause a reversal of fluid flow therethrough.” Ex. 1011 (Rubenstein) at 2:1-8, 3:21-50, 4:2-7, 4:17-35.

I. Matteo

94. U.S. Patent Publication No. 2012/0138833 (“Matteo”) was filed on December 2, 2010, and published on June 7, 2012. Ex. 1013 (Matteo) at 1. Matteo qualifies as prior art at least because it was published prior to the earliest effective filing date of the ’402 Patent.

95. Matteo is directed to a microfluidics system with “one cylindrical cam controlling several actuator balls and several microvalves” for use in a variety of chemical, biological, and biomedical applications, including “medical and scientific instrumentation.” Ex. 1013 (Matteo) at Abs., ¶¶ [0006], [0012], [0029], FIGS. 11, 12. Matteo discloses that “[c]am-driven pinch-style microvalves are useful for serving as on/off valve devices for a microfluidic system.” Ex. 1013 (Matteo) at ¶ [0010]. Matteo further discloses that “a cam-driven actuator activates a microvalve by pressing on the elastomeric layer, deforming the elastomeric layer so that it meets a second layer at a location within the channel thereby either partially or completely obstructing the flow of liquid through the channel at that location, i.e. ‘pinching’ the channel.” Ex. 1013 (Matteo) at Abs., ¶¶ [0009], [0045], [0047]. Conversely, “when

the microvalve 101 is in the open state,” as shown in Fig. 6A, “fluid flows through the channel 401.” Ex. 1013 (Matteo) at ¶ [0047].

X. ASSERTED GROUNDS OF INVALIDITY

A. Ground 1: Claims 1-8 and 10-20 are Rendered Obvious Over Yang in view of Mullins and the Knowledge of a POSA

Motivation to Combine

96. A person of ordinary skill in the art at the time the purported invention of the '402 Patent was made would have been motivated to combine Yang's cyclical aspiration thrombectomy system consisting of a catheter with Mullins's teachings of: (1) explicit discussion of utilizing different cycles of negative and positive pressure to change pressure and control loading and unloading of a clot at the distal end of the catheter; and (2) further optimization of momentum and unsticking of a thrombus, including, for example, the optimization of cycle frequencies.

97. A POSA would have been motivated to combine Yang and Mullins because (1) both references address similar problems related to conventional methods of aspiration thrombectomy, including clogged catheters and achieving optimal vacuum pressures, and (2) both references teach similar solutions involving using a positive pressure state to provide for cyclical changes in pressure to more efficiently remove blood clots from the patient's blood vessel. Both references comment on the limitations and risks associated with traditional methods to treat

ischemic strokes. As an example, both references describe the limitations of static aspiration technologies for controlled clot aspiration, as well as related issues, for example, with clogged catheters. Ex. 1012 (Yang) at ¶¶ [0008]-[0009], [0014], [0085], [0148], [0166]; Ex. 1008 (Mullins) at 25:22-26:16; 28:27-37; Ex. 1009.2 (Mullins-Prov2) at pg. 2-9.

98. The references describe similar approaches to solving these and other issues, including creating a dynamic aspiration force to more effectively break up and clear clots in blood vessel. Ex. 1012 (Yang) at ¶¶ [0014], [0067], [0091], [0123]-[0128], [0131], [0135]-[0136], [0168]-[0170]; Ex. 1008 (Mullins) at 1:53-2:2, 3:29-4:11, 26:17-28:64, FIGs. 46-49; Ex. 1009.2 (Mullins-Prov2) at pg. 3-10. Both systems utilize an aspiration thrombectomy system designed with a controller to vary fluid flow and pressure to at least partially relieve vacuum pressure within the system to create an acceleration force on the clot for optimal aspiration. Ex. 1012 (Yang) at ¶¶ [0123]-[0128], [0131], [0135], [0168]-[0170]; Ex. 1008 (Mullins) at 3:29-4:11, 26:17-28:64; Ex. 1009.2 (Mullins-Prov2) at pg. 2-10.

99. A POSA would understand that Yang and Mullins are each directed to a cyclical aspiration thrombectomy system and related methods using a source of both positive and negative pressure to subject a blood clot to dynamic suction forces and more efficiently aspirate blood clots. Ex. 1012 (Yang) at ¶¶ [0102], [0108],

[0123]-[0128], [0131], [0135], [0168], [0170], Figs. 13-18; Ex. 1008 (Mullins) at 3:29-4:11, 26:17-28:64; Ex. 1009.2 (Mullins-Prov2) at pg. 2-10. Accordingly, combining the teachings of Yang and Mullins would have been well known within the skill of a POSA, because it is nothing more than combining known vacuum aspiration technologies described in these references to perform their intended functions with described benefits and predictable results.

100. A POSA would find it obvious to implement Mullins' disclosures of forward flow and improvements in unsticking clots to modify Yang's system, which includes a catheter aspiration system that is ready for improvement by Mullins's techniques for efficient and effective cyclical aspiration of blood clots. Ex. 1012 (Yang) at ¶¶ [0131], [0168]-[0170]; Ex. 1008 (Mullins) at 3:29-4:11, 26:17-28:64. The methods of cyclical pressure changes described by Mullins are consistent with and improve on the aspiration cycles that Yang discloses to provide effective cyclical aspiration thrombectomy. Ex. 1012 (Yang) at ¶¶ [0103], [0123], [0131], [0168]-[0170]; Ex. 1008 (Mullins) at 3:294:11, 26:17-28:64; Ex. 1009.2 (Mullins-Prov2) at pg. 2-10. Additionally, using the pressure sensor provided by Mullins on Yang's device would help implement the most efficient pressure changes to the catheter to reduce the risk of complications from aspiration thrombectomy, including clogged

catheters and excessive forward flow of material out of the distal end of the catheter into the patient's blood stream, as explicitly taught by Mullins.

101. Mullins' methods to change a level of vacuum at the distal end of the catheter are similar to, if not the same as, the pulsatile application of vacuum oscillating between various pressures described by Yang. A POSA would have had a reasonable expectation of success in implementing this combination, because any modification, if necessary, would simply add additional control logic from Mullins' system for modulating the pressures contained within the aspiration system, in accordance with the preferable pressure cycles as taught in Yang. Because Yang's system is already computer-controlled via various disclosed algorithms to be selected by the system implementer, it would have been well within the level of skill in the art to modify the logic of Yang's controller to implement Mullins's teachings, if necessary, or incorporate known mechanical components, if needed.

102. A POSA would also find it obvious to implement monitoring the level of vacuum pressure change at the distal end of the aspiration catheter contemplated by Mullins within Yang's aspiration thrombectomy system. Monitoring pressure inside the aspiration catheter and vacuum system was a known concept that was used to improve the knowledge available to clinicians about the ongoing aspiration procedure and allow for more effective aspiration techniques, including

repositioning the catheter or utilizing procedures to remove a clog, based on the pressure inside the system. Mullins discloses that a lumen pressure sensor and a controller can be used to monitor the pressure in the system, and builds on the concept of altering vacuum pressure levels by utilizing a pressure sensor. Ex. 1008 (Mullins) at 3:29-59, 6:34-36, 26:31-37; Ex. 1009.2 (Mullins-Prov2) at pg. 3. A POSA would have recognized the benefit of monitoring the vacuum pressure levels at various points throughout the aspiration system, including the distal tip of the catheter, as disclosed in Mullins, in the context of Yang, and it would have been trivial to implement these within Yang's aspiration thrombectomy system.

103. For at least these reasons, it would have been obvious to combine Yang and Mullins.

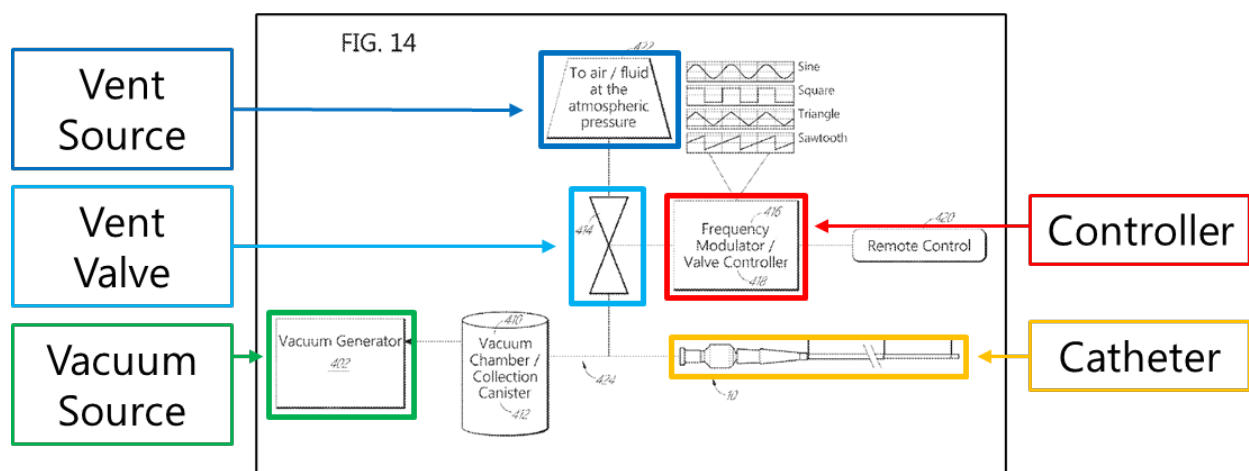
Claim 1

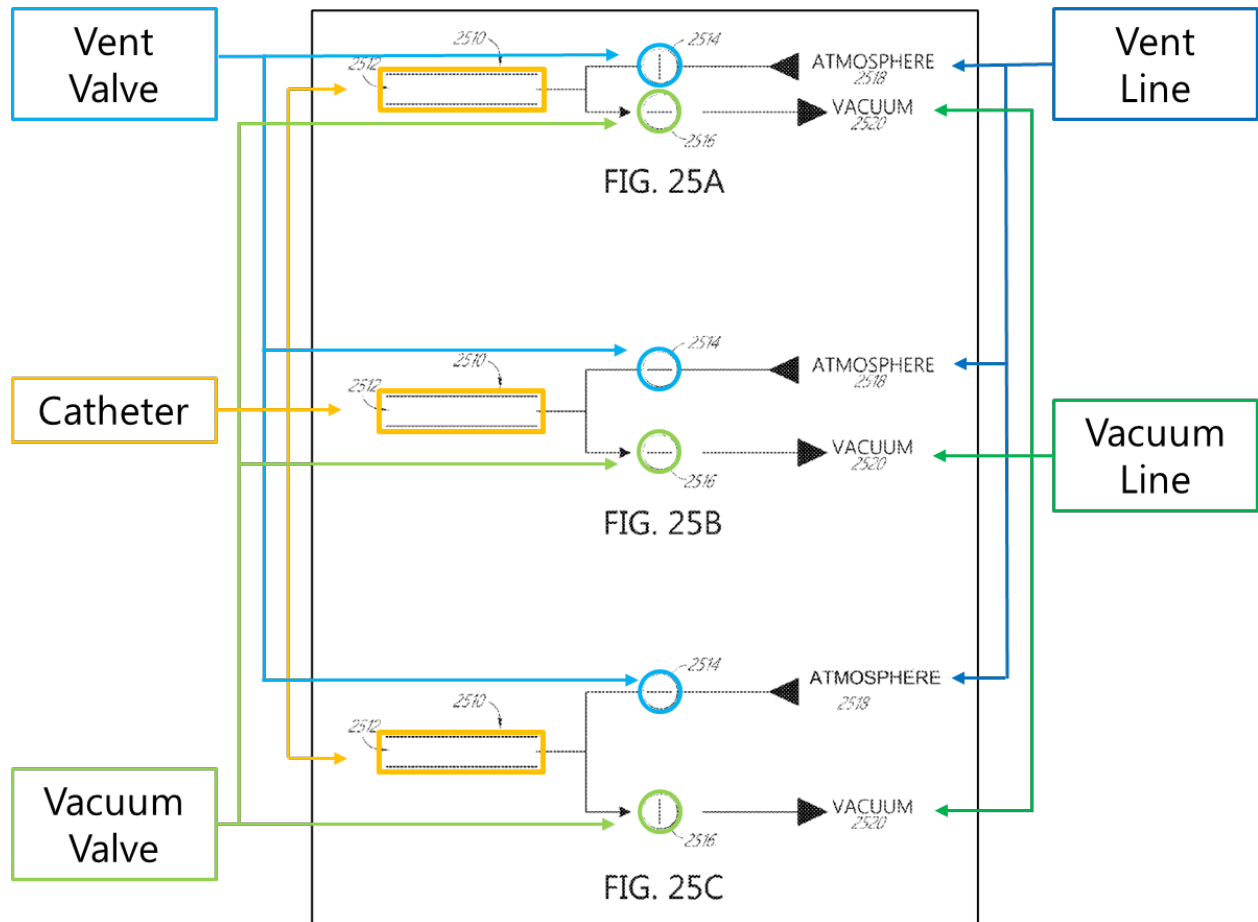
[1-Pre]: An aspiration thrombectomy system, comprising:

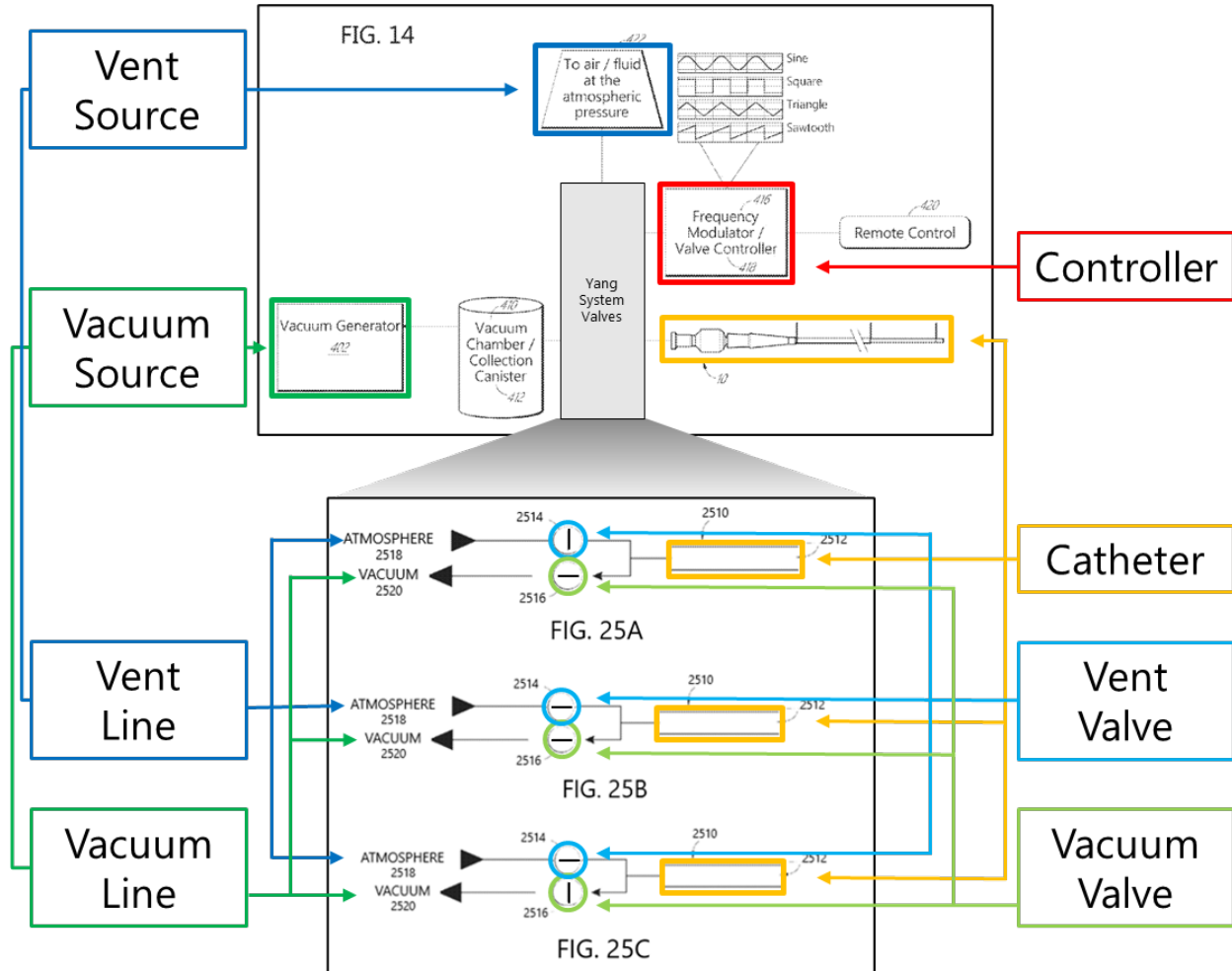
104. To the extent the preamble is limiting, Yang discloses this limitation.

105. Yang discloses an aspiration thrombectomy system. Ex. 1012 (Yang) at Figs. 13-18 (illustrating aspiration systems); *see also* ¶ [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.”). For example, as shown below in Figures 14 and 25, Yang discloses aspiration systems which “apply pulsatile negative pressure through the aspiration catheter” and “a pulsed aspiration cycle.” Ex. 1012 (Yang) at ¶¶ [0028]-[0029], [0040], *see also* ¶ [0123] (“A pulsatile vacuum pressure aspirator may be used in order to improve effectiveness of aspiration for vascular thrombectomy”). This system is used to remove “obstructive material from remote vasculature in the brain.” Ex. 1012 (Yang) at ¶ [0063]. Yang’s Figures 14 and 25 are reproduced and annotated below, shown first separately and then shown combined (reoriented and overlaid for clarity to illustrate the interrelationship between the figures). Ex. 1012 (Yang) at FIG. 14 (annotated), FIG. 25 (annotated), and FIG. 14 and 25 (combined, reoriented, overlaid, annotated).







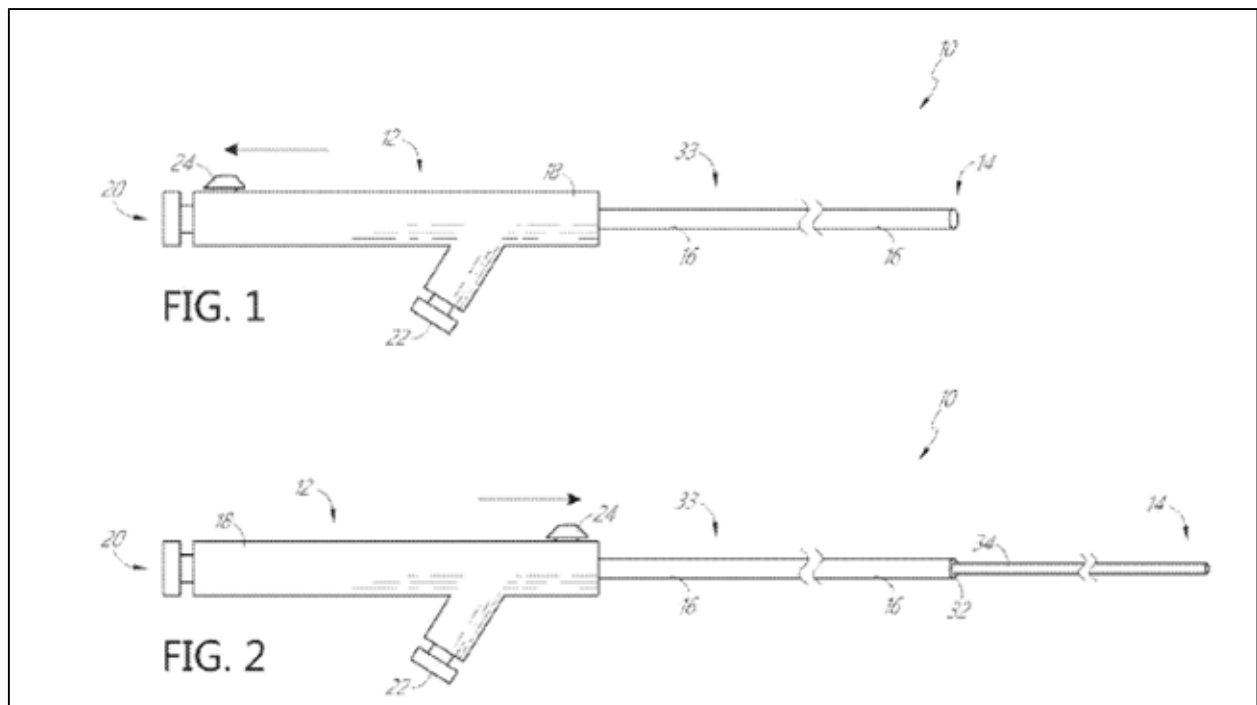
106. Therefore, it is my opinion that Yang discloses an “aspiration thrombectomy system” as recited by Claim 1.

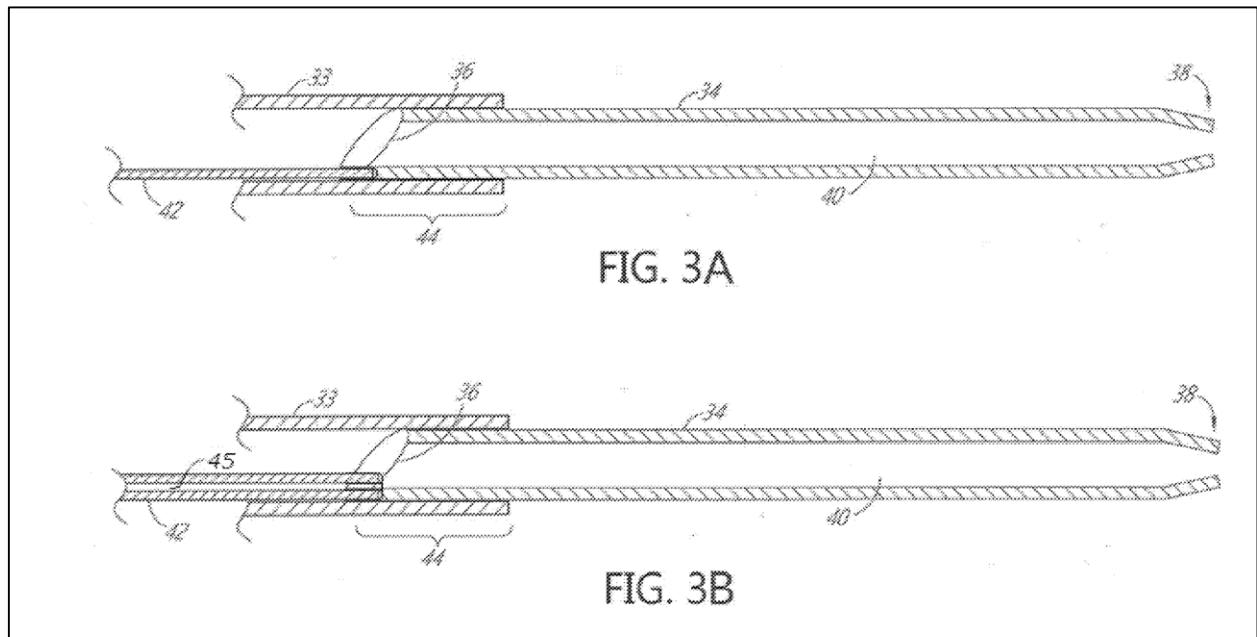
[1-A]: an aspiration catheter having a proximal portion, a distal end and a lumen extending through the catheter;

107. Yang discloses this limitation.

108. Yang explicitly describes a catheter, and describes it having two ends, referred to as a proximal end and a distal end, and a lumen within the catheter. Ex. 1012 (Yang) at ¶¶ [0065] (“The catheter 10 generally comprises an elongate tubular

body 16 extending between a proximal end 12 and a distal functional end 14.”), [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”). A POSA would have understood this description of a proximal end to also include a proximal portion. The lumen within the catheter is illustrated in Yang’s figures (e.g., Figures 1-3 below) and described in Yang’s specification. Ex. 1012 (Yang) at Figs. 1-3, *see also* FIGs. 4, 13, 14, 25, ¶¶ [0063]-[0067], [0168]-[0170].





109. Yang describes the catheter as being implemented in an aspiration system to perform aspiration on a clot. Ex. 1012 (Yang) at Abs. (“A telescoping catheter is provided such as for distal neurovascular aspiration”), ¶¶ [0101] (“Aspiration may be applied via lumen 40”), [0102] (“to provide a net aspiration through the lumen 40”), [0108] (“A pressure surge or wave is generated inside the lumen 40 of the aspiration catheter 10”), [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”), [0170] (“vacuum is applied to the catheter 2510 to aspirate the clot”), [0237] (“the aspirating thrombus step comprises

applying alternating negative and positive pressure to the first elongate tubular body”), *see also* ¶¶ [0063]-[0071], [0123]-[0128], [0131], [0168]-[0170].

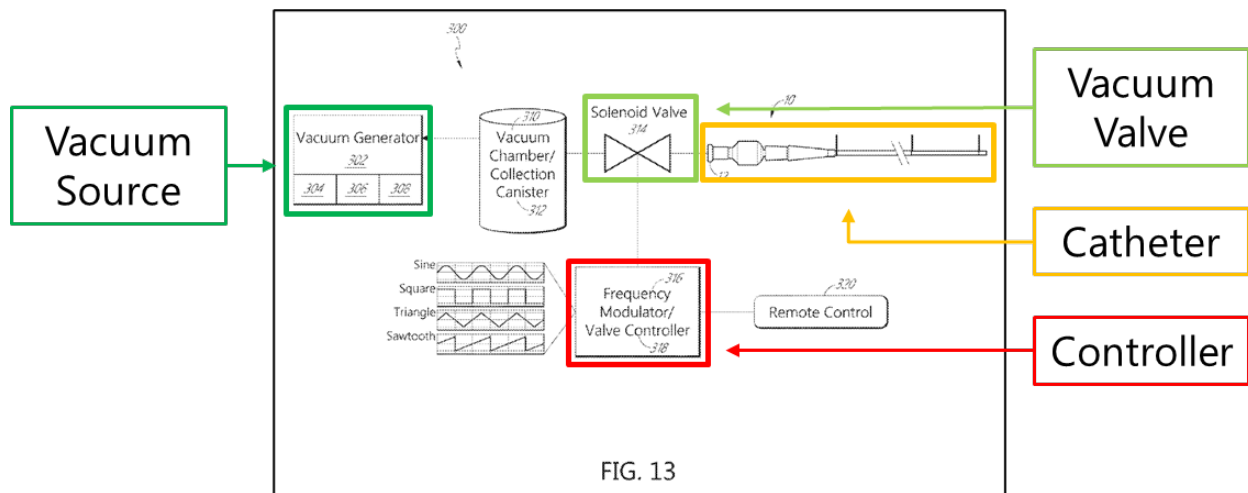
110. Therefore, it is my opinion that Yang discloses “an aspiration catheter having a proximal portion, a distal end and a lumen extending through the catheter,” as recited by Claim 1.

[1-B]: a vacuum source fluidically coupled to the catheter;

111. Yang discloses this limitation.

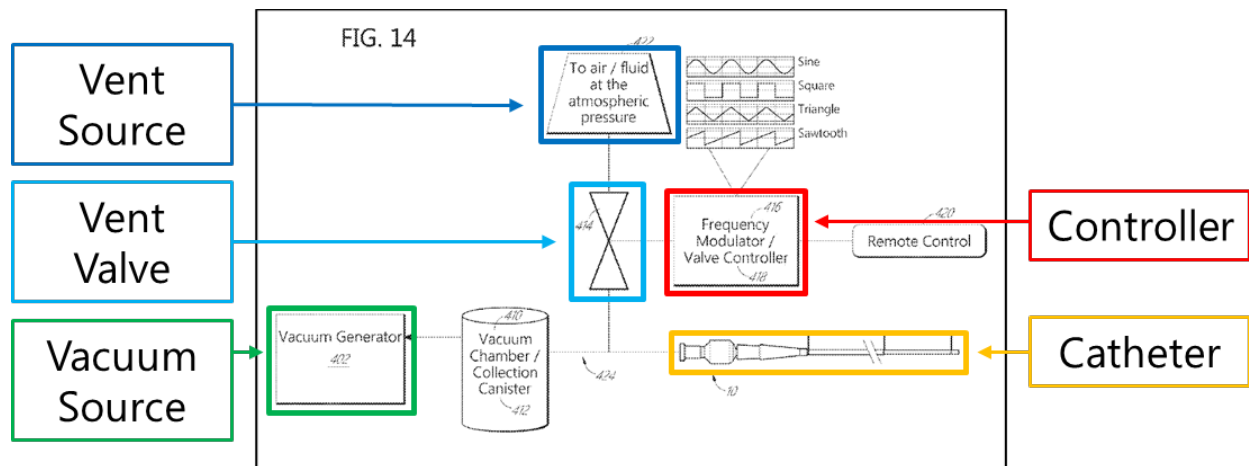
112. Yang discloses, in relation to Figure 13, a vacuum source fluidically coupled to the catheter. Ex. 1012 (Yang) at FIG. 13, ¶¶ [0123] (“A pulsatile vacuum pressure aspirator may be used [] for vascular thrombectomy... FIG. 13 shows an embodiment of a pulsatile vacuum pressure aspirator 300 that applies intermittent or pulsatile vacuum to lumen 40... 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”), [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.”), [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.”); *see also*, ¶ [0114]

(“A vacuum pressure is then applied at the proximal end of the aspiration catheter 1128 to aspirate the clot 1102 through the central lumen of the aspiration catheter 1128.”). A POSA would understand Yang’s “vacuum generator” to be a vacuum source, and that the vacuum source would be connected to the catheter.

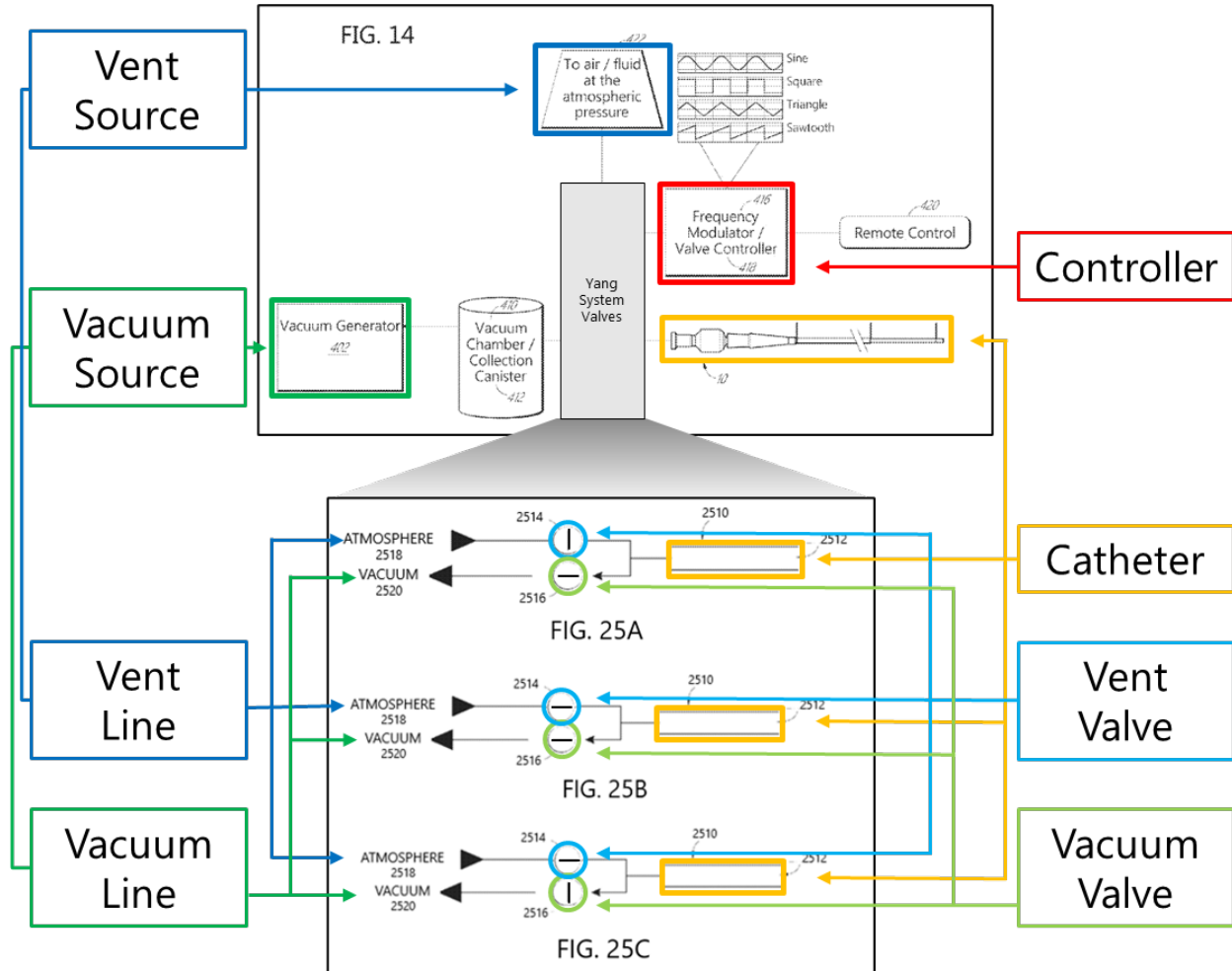


113. Yang further discloses, in relation to Fig. 14, “In another embodiment, shown in FIG. 14, an alternative aspiration system may comprises [sic] a vacuum generator 402... Unlike the first embodiment in FIG. 13, this system modulates pressure in the catheter 10 by allowing pressure to vary from vacuum 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.” Ex. 1012 (Yang) at ¶ [0131]², FIG. 14. A POSA would understand vacuum generator 402 to be a vacuum source configured similarly to vacuum generator 302 in Figure 13.



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.”)



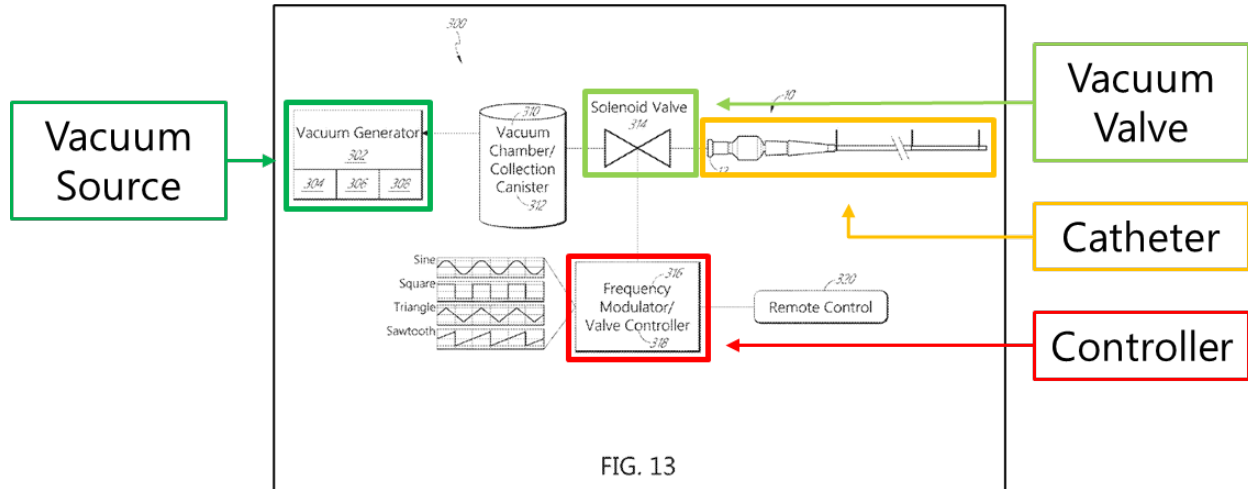
115. Therefore, it is my opinion that Yang discloses “a vacuum source fluidically coupled to the catheter,” as recited by Claim 1.

[1-C]: a vacuum valve connected between the vacuum source and the proximal portion of the catheter to control a vacuum flow in the catheter lumen;

116. Yang discloses this limitation.

117. Yang discloses, in relation to Fig. 13, a vacuum valve connected between the vacuum source and the proximal portion of the catheter. Ex. 1012

(Yang) at FIG. 13, ¶ [0123] (“A pulsatile vacuum pressure aspirator may be used [] for vascular thrombectomy... FIG. 13 shows an embodiment of a pulsatile vacuum pressure aspirator 300 that applies intermittent or pulsatile vacuum to lumen 40... 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”). Vacuum valve 314 controls a vacuum flow in the catheter lumen. Ex. 1012 (Yang) at ¶¶ [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.”), [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.”). A POSA would understand valve 314 as a vacuum valve connected between the vacuum source and the proximal portion of the catheter.



118. Yang further discloses, in relation to Figure 25, how the disclosed vacuum valve may operate in the disclosed configuration including both the vacuum valve and a vent valve. Ex. 1012 (Yang) at ¶¶ [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.”). A POSA would have understood vacuum valve 2516 as a vacuum valve connected to the proximal end of the catheter, and would further understand it to be connected to the disclosed vacuum source in order to apply the vacuum to the catheter from vacuum line 2520.

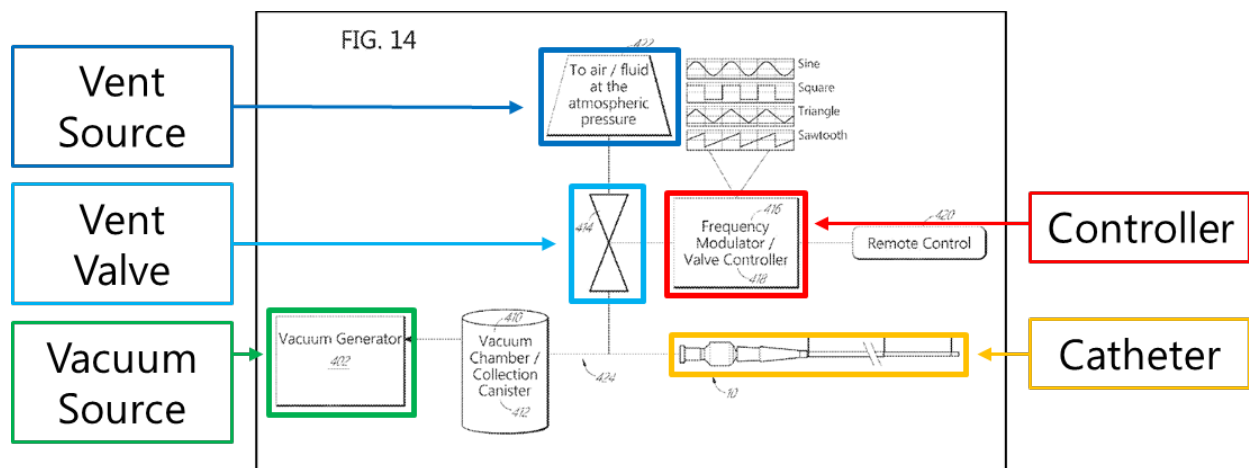
119. Therefore, it is my opinion that Yang discloses “a vacuum valve connected between the vacuum source and the proximal portion of the catheter to control a vacuum flow in the catheter lumen” as recited by Claim 1.

[1-D]: a vent valve fluidically coupled to the proximal portion of the catheter, the vent valve being configured to control a flow of a vent fluid in the catheter lumen; and

120. Yang discloses this limitation.

121. Yang discloses, in relation to Fig. 14, a vent valve fluidically coupled to the proximal portion of the catheter. Ex. 1012 (Yang) at FIG. 14, ¶ [0131] (“In

another embodiment, shown in FIG. 14, an alternative aspiration system may comprises [sic] 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.”). A POSA would understand valve 414 as a vent valve coupled to the proximal portion of the catheter and configured to control flow of a vent fluid in the catheter lumen.



122. Yang further discloses, in relation to Figure 25, how the disclosed vent valve may operate in the disclosed configuration including both the vacuum valve and a vent valve. Ex. 1012 (Yang) at ¶¶ [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.”). A POSA would have understood release valve 2514 as a vent valve coupled to the proximal portion of the catheter and configured to control flow of a vent fluid in the catheter lumen from release line 2518.

123. A POSA would further have understood Yang’s description of “pulsed aspiration” to demonstrate that a mechanism of Yang, such as a vent valve, is configured to control a flow of vent fluid in the catheter lumen. Ex. 1012 (Yang) at ¶¶ [0040], [0102], [0168]-[0170]. A POSA would have understood this pulsed aspiration to include changes to the pressure in the catheter using different mechanisms such as valves.

124. Therefore, it is my opinion that Yang discloses “a vent valve fluidically coupled to the proximal portion of the catheter, the vent valve being configured to control a flow of a vent fluid in the catheter lumen,” as recited by Claim 1.

[1-E]: a controller configured to open and close the vacuum valve and the vent valve in a predetermined cycle

125. Yang alone or in view of Mullins discloses or renders obvious this limitation.

126. Yang discloses, in relation to Fig. 13, a controller configured to open and close the vacuum valve. Ex. 1012 (Yang) at ¶¶ [0123] (“A pulsatile vacuum pressure aspirator may be used [] for vascular thrombectomy... FIG. 13 shows an

embodiment of a pulsatile vacuum pressure aspirator 300 that applies intermittent or pulsatile vacuum to lumen 40... the pulsatile vacuum pressure aspirator 300 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”); [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...”).

127. Yang further discloses, in relation to Fig. 14, the controller being configured to open and close the vent valve. Ex. 1012 (Yang) at FIG. 14, ¶ [0131], (“In another embodiment, shown in FIG. 14, an alternative aspiration system may comprises [sic] 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.”).

128. Yang further discloses, in relation to Figure 25, how the disclosed controller may open and close the vacuum valve and the vent valve in a predetermined cycle. Ex. 1012 (Yang) at Yang explains that this opening and closing is done in a predetermined cycle. Ex. 1012 (Yang) at ¶¶ [0168] (“Referring to FIGS. 25A-25C... 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... The release line 2518... has a release valve 2514 configured to open or close... The vacuum line 2520... has a vacuum valve 2516 configured to open or close...”), [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.”). A POSA would have understood the controller opening and closing the valves in repeated cycles as a predetermined cycle.

129. Yang further discusses its predetermined cycles and alternating between levels of pressure throughout its disclosure. Ex. 1012 (Yang) at ¶¶ [0014] (“alternate between applying pulses of higher negative pressure and lower negative pressure”), [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.”), [0040] (“pulsed aspiration cycle”), [0127] (“duty cycles”), [0130] (“duty cycle”), [0168]-[0170] (“vacuum and release cycle”), [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

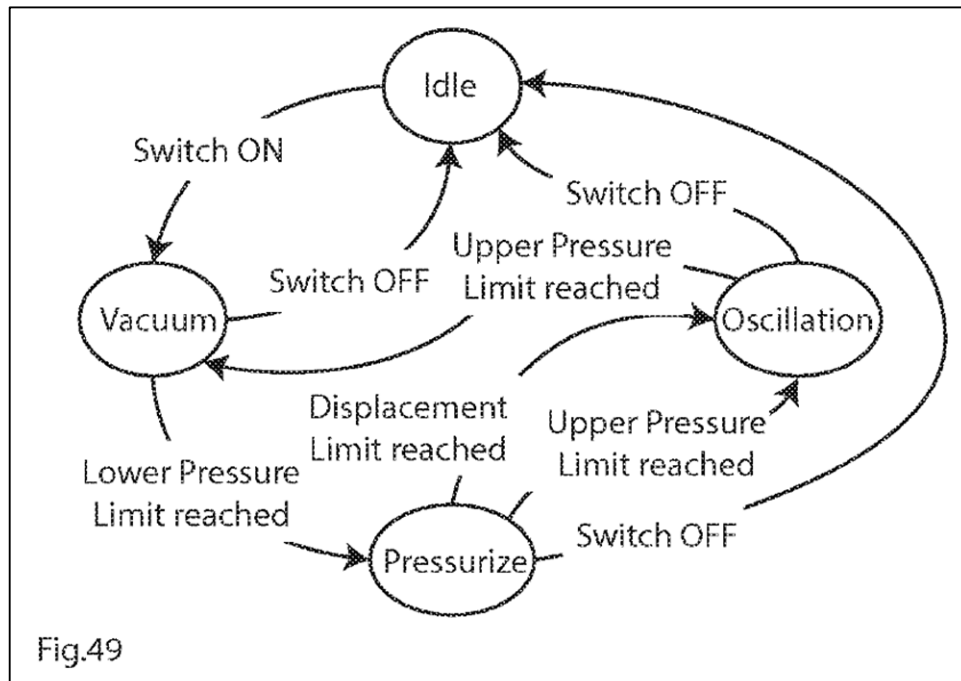
body.”), Claim 12 (“wherein the controller is configured to alternate between applying pulses of higher negative pressure and lower negative pressure”).

130. In addition to Yang’s disclosure of a controller configured to open and close the vacuum valve and the vent valve in a predetermined cycle, the combination of Yang and Mullins renders it obvious.

131. Mullins discloses a cycling controller that “varies aspiration pressure according to sensed pressure within the catheter lumen.” Ex. 1008 (Mullins) at 3:46-59; Ex. 1009.2 (Mullins-Prov2) at pg. 3-9. Mullins further explains that “[t]here 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.” Ex. 1008 (Mullins) at 3:48-59; *see also*, 4:5-11 (“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.”); Ex. 1009.2 (Mullins-Prov2) at pg. 3-9.

132. Mullins discloses this change in pressure being done in a predetermined cycle. Ex. 1008 (Mullins) at 3:60-4:4 (“The controller... may cause the catheter to cyclically ingest and if required expel, at least some of a clot”), 26:43-49 (“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.”), 27:40-28:10 (“A novel aspect of this pump system is the incorporation of feedback into the pump algorithm in order to produce more effective pressure cycling... 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)... Another aspect is the incorporation of rate based cycling of a negative and positive pressure signal. The addition of this oscillation is shown in the form of the state diagram in FIG. 49. In one embodiment the shake signal may be initiated for a predefined number of cycles.”); Ex. 1009.2 (Mullins-Prov2) at pg. 3-9.



133. Mullins describes in detail the process of changing pressures to enable ingestion of a clot and the resulting changes in efficiency. Ex. 1008 (Mullins) at 26:65-27:39 (“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... 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...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)."); Ex. 1009.2 (Mullins-Prov2) at pg. 4-7.

134. In particular, Mullins discloses implementing its "pulse cycling" in "infuse-to-aspirate" cycles to alternate between infuse and aspirate phases of each cycle at particular frequencies. Ex. 1008 (Mullins) at 28:59-64 ("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."); Ex. 1009.2 (Mullins-Prov2) at pg. 4-7. A POSA would

recognize Mullins' "pulse cycling" and "infuse-to-aspirate cycles" as predetermined cycles.

135. Therefore, it is my opinion that Yang alone or in view of Mullins and the knowledge of a POSA discloses and renders obvious "a controller configured to open and close the vacuum valve and the vent valve in a predetermined cycle" as recited by Claim 1.

[1-F]: to change a level of vacuum at the distal end of the catheter

136. Yang alone or in view of Mullins discloses or renders obvious this limitation.

137. Yang discloses the controller applying vacuum to the catheter. Ex. 1012 (Yang) at ¶¶ [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."), [0028]-[0029] ("aspiration system configured to apply pulsatile negative pressure through the aspiration catheter"), [0101]-[0102] ("Aspiration may be applied via lumen 40, either in a constant mode, or in a pulsatile

mode... “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.”).

138. Yang specifically discloses the controller causing a water hammer effect at the distal tip of the catheter. Ex. 1012 (Yang) at ¶ [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 [a] water hammer effect, which can further facilitate... 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.”). A POSA would understand a water hammer effect to be

caused by changes in the levels of vacuum because it represents a pressure surge caused by a sudden change in momentum of a fluid. A POSA would further understand that Yang's disclosure of the water hammer effect causing "the pressure wave [to] propagate[] in the catheter" would affect the level of vacuum at the distal end of the catheter.

139. Yang additionally explains how the water hammer effect can be further manipulated with shock waves propagated to the distal end of the catheter. Ex. 1012 (Yang) at ¶ [0135] ("In addition or as an alternative to the water hammer construction discussed above,... shock waves may be propagated to or generated at the distal end of the catheter using... electric solenoids,... or any of a variety of other impulse generating sources well understood for example in the lithotripsy arts."). A POSA would recognize this as further disclosure of Yang changing the level of vacuum at the distal end of the catheter.

140. Yang further explains, in relation to Figure 25, how the disclosed controller may operate the valves in a progression of steps within each cycle, and how each step in the cycle changes a level of vacuum at the distal tip of the catheter in order to ultimately dislodge a clot. Ex. 1012 (Yang) at ¶¶ [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.”), [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.”).

141. A POSA would have understood, and as disclosed and illustrated in Yang, that because the distal end of the aspiration catheter in Yang is engaged against the blood vessel occlusion during vacuum aspiration, the pressure differential and acceleration force created on the clot by the repeated opening and closing of the vacuum on-off valve and the fluid injection valve would occur at the distal end of the catheter lumen in Yang’s system, which is also common sense given that the clot is located at the distal end of the catheter when the catheter engages with

the clot. As such, a POSA would understand that Yang discloses the controller changing a level of vacuum at the distal tip of the catheter to dislodge the clot.

142. In addition to Yang's disclosure of the controller changing the level of vacuum at the distal end of the catheter, the combination of Yang and Mullins renders it obvious.

143. Mullins discloses a "pulse cycling," which a POSA would have understood would include changes in pressure at the distal end of the catheter. Ex. 1008 (Mullins) at 27:54-57 ("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)."); Ex. 1009.2 (Mullins-Prov2) at pg. 8-10.

144. Mullins further discloses changes in vacuum pressure used to ingest a clot. Ex. 1008 (Mullins) at 26:65-27:26 ("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... 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.”); Ex. 1009.2 (Mullins-Prov2) at pg. 4-7.

145. Mullins further describes cycling of these pressure changes, and particularly describes “infuse-to-aspirate cycles” to alternate between infuse and aspirate phases of each cycle. Ex. 1008 (Mullins) at 27:31-39 (“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).”), 28:59-64 (“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.”); Ex. 1009.2 (Mullins-Prov2) at pg. 4-7.

146. A POSA would find it obvious to change the level of vacuum at the distal end of Yang’s catheter using the cyclical open and closed state of its valves in view of Mullins’s disclosures of using pulse cycling and infuse-to-aspirate cycles to implement dynamic pressure forces at the distal end of its catheter. *See, e.g.*, Ex. 1008 (Mullins) at 26:23-26 (“The invention utilizes 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...”), 27:18-26 (“allowing some or all of the clot to be pushed distally towards the catheter tip”); Ex. 1009.2 (Mullins-Prov2) at pg. 3-7.

147. Thus, it is my opinion that Yang alone or in view of Mullins and the knowledge of a POSA discloses and renders obvious “to change a level of vacuum at the distal end of the catheter” as recited by Claim 1.

[1-G]: and to control fluid flow in and out from the distal end of the catheter.

148. Yang alone or in view of Mullins discloses or renders obvious this limitation.

149. Yang discloses various mechanisms of controlling fluid flow in and out from the distal end of the catheter. Ex. 1012 (Yang) at ¶ [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”). A POSA would have understood that at least a portion of this fluid flow may be in and out from the distal end of the catheter. As the pressure within the catheter changes, so does the volume and/or direction of fluid flow. This change in direction directs fluid towards a clot so it may break up said clot.

150. Yang further provides additional disclosure indicating that the controller controls flow at the distal end of the catheter. For example, Yang describes generating vibrations and shock waves. Ex. 1012 (Yang) at ¶ [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.”).

151. Yang additionally describes applying alternating negative and positive pressure in vacuum and release cycles to manipulate the shape and position of the clot and fluid engaged at the distal tip of the catheter. Ex. 1012 (Yang) at ¶ [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 [] the vacuum and allowing the clot to relax before reapplying a vacuum is found to aspirate the corked clot most efficiently.”). A POSA would understand these disclosed implementations as the controller controlling fluid flow in and out from the distal end of the catheter.

152. To the extent that Yang does not explicitly disclose controlling fluid flow in and out of the distal end of the catheter, the combination of Yang and Mullins renders it obvious.

153. Mullins describes measuring the pressure in the catheter with a pressure sensor in order to “utilise[] 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: ... maceration and deformation of the clot to enable it to travel through the lumen.” Ex. 1008 (Mullins) at 26:23-37 (“The pump incorporates a sensor which measures the pressure in the catheter lumen.”), 26:55-64 (“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”), 29:10-12 (“The pressure sensor is connected to the tube-lumen, which is connected to the catheter, thereby enabling pressure measurement within the catheter.”); Ex. 1009.2 (Mullins-Prov2) at pg. 3-9.

154. Mullins discloses controlling fluid at the distal end of a catheter using changes in pressure based on the measured pressure levels and predetermined cycles. Ex. 1008 (Mullins) at 3:46-4:11 (“We also describe methods of use of an aspiration

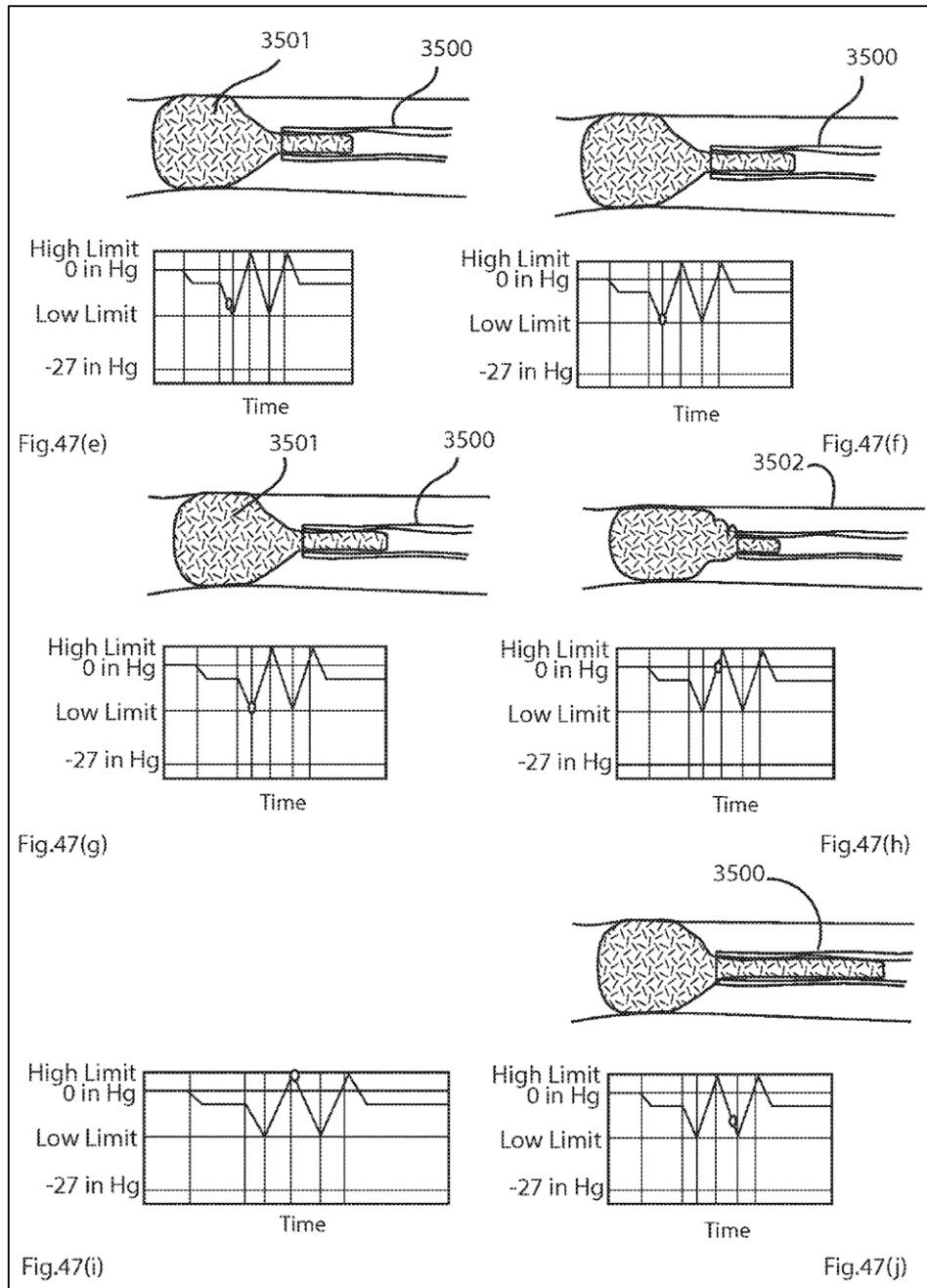
system of any embodiment, in which the controller varies aspiration pressure during aspiration of a clot. There may be a lumen fluid flow sensor, and the controller varies aspiration pressure according to sensed fluid displacement in the lumen... Preferably, the controller improves efficiency of aspiration 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 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.”); Ex. 1009.2 (Mullins-Prov2) at pg. 2-10.

155. Mullins further discusses the controller utilizing pressure and fluid displacement at the catheter tip to aspirate clots based on the measured pressure

levels. Ex. 1008 (Mullins) at 26:38-49 (“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. 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.”) Ex. 1009.2 (Mullins-Prov2) at pg. 2-10.

156. Mullins additionally illustrates how the controller uses positive and negative pressure to control the flow of clot and fluid in and out at the distal tip of the catheter. Ex. 1008 (Mullins) at FIGs. 47(a)-(n), 26:65-27:26 (“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 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).”); Ex. 1009.2 (Mullins-Prov2) at pg. 2-10.



157. A POSA would understand, as also illustrated and explained by Mullins as discussed above, that the cyclical application of positive and negative pressure to the catheter would control fluid flow in and out from the distal end of the catheter.

158. Therefore, it is my opinion that Yang alone or in view of Mullins and the knowledge of a POSA discloses or renders obvious “to control fluid flow in and out from the distal end of the catheter,” as recited by Claim 1.

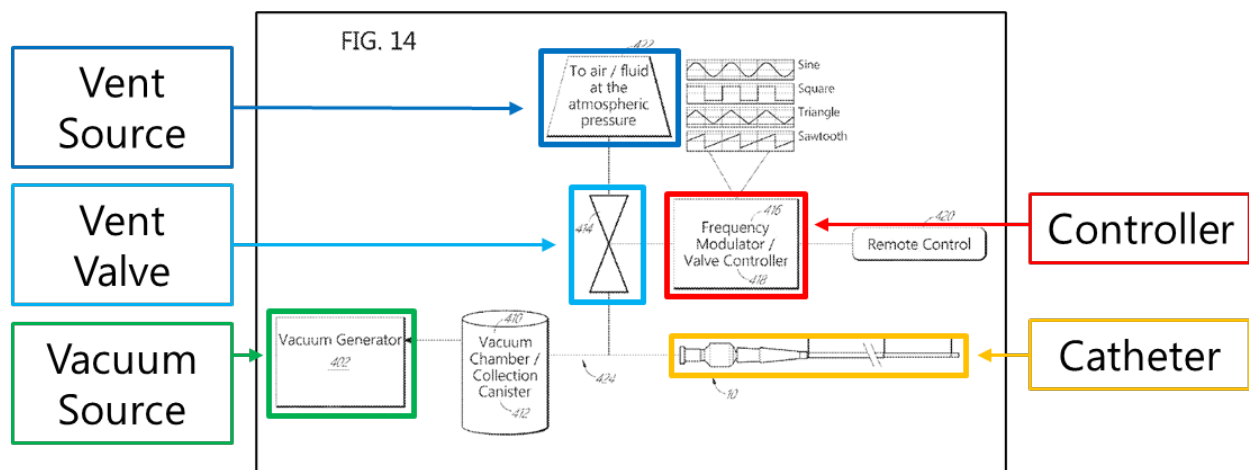
Claim 2

[2-A]: The system of claim 1, further comprising a vent fluid source, and wherein:

159. Yang discloses this limitation.

160. Yang discloses, in relation to Fig. 14, a vent fluid source. Ex. 1012 (Yang) at FIG. 14, ¶ [0131] (“In another embodiment, shown in FIG. 14, an alternative aspiration system may comprises [sic] 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.”). A POSA would understand air/fluid reservoir 422 as a vent fluid source (e.g., a reservoir to hold fluid which could be fluidically communicated to the catheter for pulsated aspiration).



161. Therefore, it is my opinion that Yang discloses “a vent fluid source,” as recited by Claim 2.

[2-B]: the vent fluid source is configured to provide vent fluid at a pressure greater than atmospheric pressure; and

162. Yang alone or in view of Mullins renders obvious this limitation.

163. Yang discloses, in relation to Figure 14, the vent fluid source being configured to provide vent fluid at atmospheric pressure. Ex. 1012 (Yang) at ¶ [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.”).

164. Yang similarly discloses, in relation to Figure 25, the vent fluid source being configured to vent at atmospheric pressure. Ex. 1012 (Yang) at ¶ [0168] (“venting to atmospheric pressure”), [0169] (“The release line 2518 is in communication with atmospheric pressure”).

165. However, Yang also discloses operating its system using varying or unspecified levels of positive and negative pressure. Ex. 1012 (Yang) at ¶¶ [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

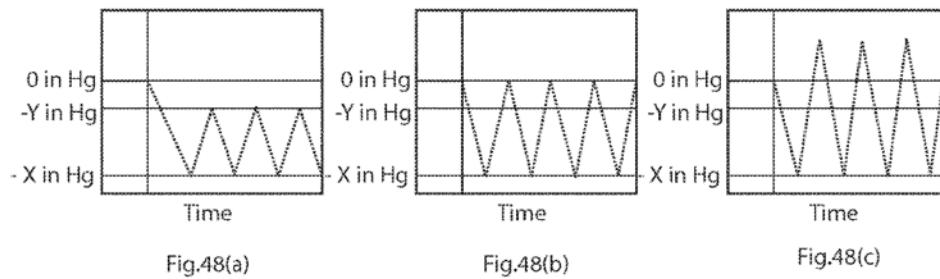
lumen.”), [0102] (“Pulsatile application of a vacuum may oscillate between positive vacuum and zero vacuum, or between a first lower negative pressure and a second higher negative pressure. Alternatively, a slight positive pressure may be alternated with a negative pressure, with the application of negative pressure dominating to provide a net aspiration through the lumen 40”), [0237] (“In another aspect of the present disclosure, the aspirating thrombus step comprises applying alternating negative and positive pressure to the first elongate tubular body.”).

166. A POSA would have understood these disclosures as indicating that Yang contemplated using various level of positive pressure when implementing the disclosed pulsated aspiration by applying alternating negative and positive pressure to the catheter. For example, Yang discloses that the positive pressure could be based on “atmospheric pressure” or alternatively, an undefined “slight positive pressure.” As such, Yang’s disclosure invites a POSA to experiment with different levels of positive pressure to find an optimal level of positive pressure that would most efficiently aspirate a given clot. Given that Yang already discloses that one example of positive pressure is atmospheric pressure, it would be obvious to a POSA to experiment with positive pressure values in the vicinity of atmospheric pressure, including positive pressure values both above and below atmospheric pressure.

Thus, a POSA would find it obvious that the vent fluid could be greater than atmospheric pressure.

167. Like Yang, Mullins similarly invites a POSA to experiment with levels of positive pressure.

168. For example, Mullins discloses increasing positive pressure until a “High Limit is reached.” Ex. 1008 at 27:18-30 (“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.”), 27:36-39 (“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).”); Ex. 1009.2 (Mullins-Prov2) at pg. 4-9.



169. Mullins also explicitly invites a POSA to determine “Real numbers” for the range of pressure values through experimentation. Ex. 1008 (Mullins) at 28:27-37 (“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 ingestion. Real numbers will be added in the future based on experiment.”); Ex. 1009.2 (Mullins-Prov2) at pg. 4-9.

170. Thus, both Yang and Mullins disclose using various levels of positive pressure, and both invite a POSA to determine what those positive pressure values should be. Given that a POSA would find atmospheric pressure to be an obvious starting point for experimentation, at least because Yang explicitly discloses

“venting to atmospheric pressure,” a POSA would find it obvious to experiment with positive pressure values similar to atmospheric pressure, including values both above and below atmospheric pressure.

171. Therefore, it is my opinion that Yang alone or in view of Mullins renders obvious “the vent fluid source is configured to provide vent fluid at a pressure greater than atmospheric pressure,” as recited by Claim 2.

[2-C]: the controller is configured to cyclically open and close the vacuum valve and the vent valve

172. For the reasons discussed above for Ground 1, Claim [1-E], this limitation is met by Yang alone or in view of Mullins.

[2-D]: to change a level of negative pressure and positive pressure at the distal end of the catheter during each cycle.

173. Yang alone or in view of Mullins discloses or renders obvious this limitation.

174. As discussed above for Ground 1, Claim [1-F], Yang alone or in view of Mullins discloses or renders obvious the controller changing a level of vacuum at the distal end of the catheter.

175. A POSA would recognize that both Yang and Mullins may change the level of vacuum at the distal end of the catheter by changing a level of negative pressure and positive pressure at the distal end of the catheter during each cycle.

176. For example, as discussed above, Yang explicitly discloses changing a level of negative pressure and positive pressure at the distal end of the catheter during each cycle. Ex. 1012 (Yang) at ¶¶ [0014] (“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.”), [0102] (“Pulsatile application of a vacuum may... 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.”), [0237] (“In another aspect of present disclosure, the aspirating thrombus step comprises applying alternating negative and positive pressure to the first elongate tubular body.”).

177. Yang further discloses these changes in pressure being done at the distal end of the catheter. Ex. 1012 (Yang) at ¶ [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 [a] water hammer effect”). A POSA would understand Yang’s description of adjusting the pulsatile vacuum intensity to represent changing pressure levels, and would further understand the disclosure of the adjusted intensity causing the distal tip to experience a water hammer effect to mean that the change

in pressure levels is taking place at the distal end of the catheter. A POSA would likewise understand these changes in negative and positive pressures at the distal end of the catheter to occur during each cycle, in part because of descriptions of a hammer effect, oscillation, and “pulse cycling.”

178. Like Yang, Mullins also discloses the controller being configured to change a level of negative pressure and positive pressure at the distal end of the catheter during each cycle.

179. Mullins discloses changing a level of negative pressure and positive pressure. Ex. 1008 (Mullins) at 3:46-4:11 (“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... 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 increase a vacuum to ingest more of a clot and reverse at a low limit of pressure”), 26:31-37 (“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.”) Ex. 1009.2 (Mullins-Prov2) at pg. 4-7.

180. Mullins further describes the high limit being any of a negative, 0, or high pressure. Ex. 1008 (Mullins) at 26:65-27:39 (“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).”) Ex. 1009.2 (Mullins-Prov2) at pg. 7. A POSA would thus understand that the cycling can involve changes to both negative pressure and/or positive pressure.

181. Mullins further describes an oscillation or “shake” signal, which cycles between two pressure limits. Specifically, Mullins explicitly describes “the incorporation of rate based cycling of a negative and positive pressure signal.” Ex. 1008 (Mullins) at 27:54-65 (“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 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.”); Ex. 1009.2 (Mullins-Prov2) at pg. 8-10. A POSA would have

understood this cycling of positive and negative pressures to occur at the distal end of the catheter, at least in part to allow the clot to travel through the lumen, as is the purpose of its disclosure.

182. Mullins specifically recites the invention implementing the “Variations in pressure and/or fluid displacement at the catheter tip.” Ex. 1008 (Mullins) at 26:23-30. Ex. 1009.2 (Mullins-Prov2) at pg. 3-7. A POSA would have understood this catheter tip to refer to “the distal end of the catheter” in the context of the disclosure.

183. Therefore, it is my opinion that Yang alone or in view of Mullins and the knowledge of a POSA discloses or renders obvious “to change a level of negative pressure and positive pressure at the distal end of the catheter during each cycle,” as recited by Claim 2.

Claim 3

[3-A]: The system of claim 2 wherein the controller is configured to cyclically open and close the vacuum valve and the vent valve

184. For the reasons discussed above for Ground 1, Claim [1-E], this limitation is met by Yang alone or in view of Mullins.

[3-B]: such that movement of the fluid column at the distal end of the catheter is limited to a positive amount of exit flow ... before fluid is drawn back into the catheter lumen.

185. Yang alone or in view of Mullins discloses or renders obvious this limitation.

186. Yang discloses that the clot must be completely loosened through releasing and reapplying vacuum. Ex. 1012 (Yang) at ¶ [0168] (“Merely stopping the vacuum is not sufficient to loosen the clot. Completely releasing [] the vacuum and allowing the clot to relax before reapplying a vacuum is found to aspirate the coked clot most efficiently.”).

187. Yang further discloses various mechanisms of controlling fluid flow in and out from the distal end of the catheter. Ex. 1012 (Yang) at ¶ [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”).

188. Yang also provides additional disclosure indicating that the controller controls movement of the fluid at the distal end of the catheter. For example, Yang describes generating vibrations and shock waves. Ex. 1012 (Yang) at ¶ [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.”).

189. Yang additionally describes applying alternating negative and positive pressure in vacuum and release cycles to manipulate the shape and position of the clot and fluid engaged at the distal tip of the catheter. Ex. 1012 (Yang) at ¶ [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 [] the vacuum and allowing the clot to relax before reapplying a vacuum is found to aspirate the corked clot most efficiently.”).

190. As a preliminary matter, a POSA would understand that at least some positive amount of exit flow would occur at the distal end of the catheter when implementing and utilizing pulsated/cyclical aspiration on a clot engaged at the distal end of the catheter. A POSA would also understand, from these disclosed implementations, that Yang’s controller controls the movement of fluid and limits the exit flow out of the distal end of the catheter. For example, a POSA would understand Yang’s disclosure of a water hammer effect at the distal end of the catheter to suggest that at least a portion of this fluid flow may be in and out from the distal end of the catheter, i.e., a positive amount of exit flow may occur before fluid is drawn back into the catheter lumen. Additionally, a POSA would understand, consistent with the disclosure of Yang, that subsequent to any exit flow that may occur at the distal end of the catheter, the fluid column would be drawn back into the catheter lumen, at least because the purpose of pulsated aspiration is to draw the clot back into the lumen and away from the vessel.

191. To the extent that Yang does not explicitly disclose the movement of the fluid column being limited to a positive amount of exit flow, the combination of Yang and Mullins renders it obvious.

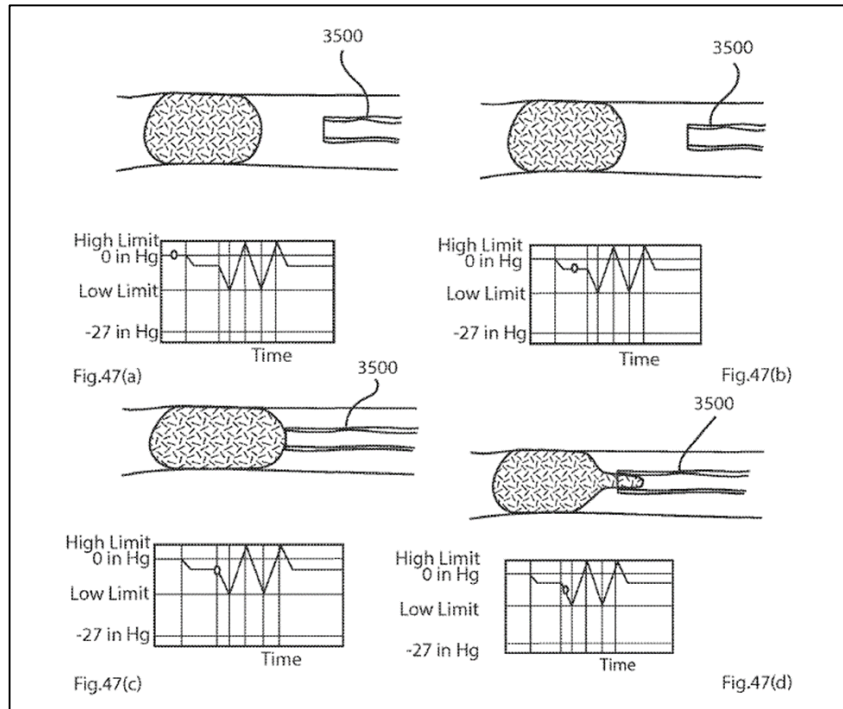
192. Mullins discloses controlling fluid at the distal end of a catheter using changes in pressure. Ex. 1008 (Mullins) at 3:46-4:11 (“We also describe methods of use of an aspiration system of any embodiment, in which the controller varies aspiration pressure during aspiration of a clot. There may be a lumen 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 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

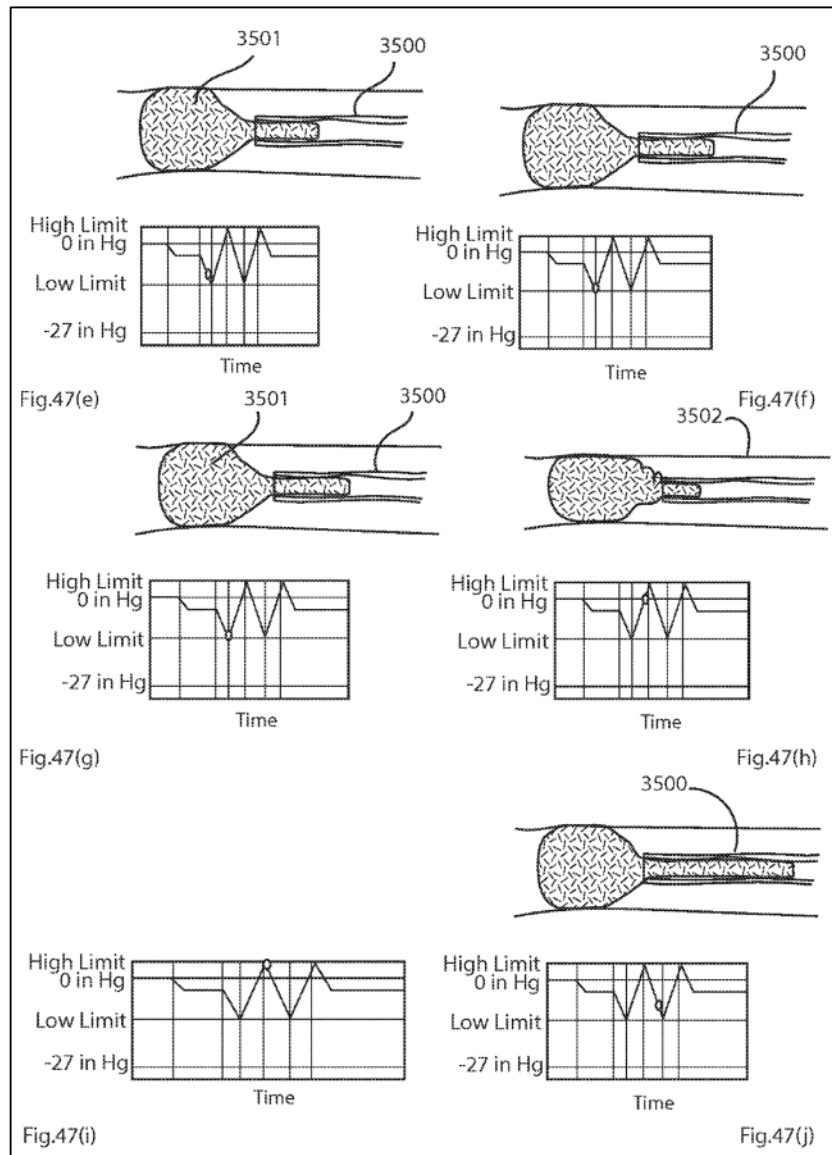
ingestion of too large a clot that could clog the catheter.”); Ex. 1009.2 (Mullins-Prov2) at pg. 2-10.

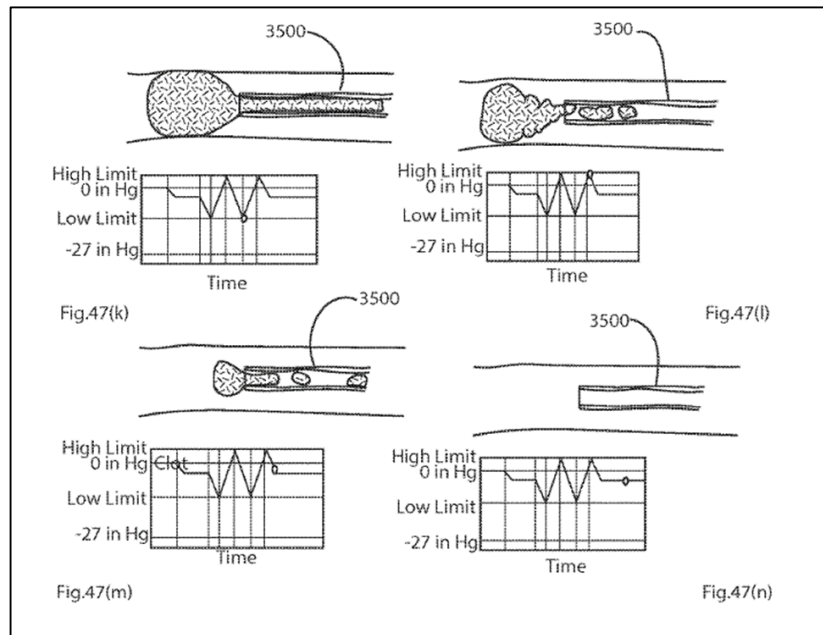
193. Mullins further discusses the controller utilizing pressure and fluid displacement at the catheter tip to aspirate clots. Ex. 1008 (Mullins) at 26:23-49 (“The invention utilises control and/or, variation of the vacuum pressure and/or, fluid displacement during aspiration to improve the efficiency 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 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... Based on the measured pressure, the pump may change direction hence altering the pressure and fluid displacement. 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.”) Ex. 1009.2 (Mullins-Prov2) at pg. 2-10, FIGs. 4(a)-4(n).

194. Mullins additionally illustrates how the controller uses positive and negative pressure to control the flow of clot and fluid in and out (i.e., positive exit flow) at the distal tip of the catheter. Ex. 1008 (Mullins) at FIGs. 47(a)-(n), 26:65-27:26 (“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 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).”); Ex. 1009.2 (Mullins-Prov2) at pg. 2-10.

195. Mullins also illustrates in Figs. 47(a)-(n) the movement of the clot at the distal end of the catheter, which visually demonstrates how the controller limits the positive exit flow. Ex. 1008 at 27:27-30 (“The pressure [being] 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.”); Ex. 1009.2 (Mullins-Prov2) at pg. 4-7.







196. Mullins further explains how it implements predetermined pulse cycles (referred to as “shake” signals) which utilize upper and lower pressure limits to control amounts of fluid displacement in the catheter. Ex. 1008 (Mullins) at FIG. 49, 28:1-64 (“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 addition of this oscillation is shown in the form of the state diagram in FIG. 49... 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 another embodiment, the pump may use positive and negative fluid displacement to

alternately infuse and aspirate the catheter.”); Ex. 1009.2 (Mullins-Prov2) at pg. 2-10.

197. A POSA would recognize, based at least on Mullins’ discussion of using reverse flow and fluid displacement to cyclically ingest and expel part of a clot, allowing the clot to be pushed distally, and using upper and lower pressure limits to control how measured amounts of flow displacement, that Mullins’ controller not only controls the movement of fluid at the distal end of the catheter, but also limits the amount of exit flow before drawing the fluid back into the catheter. A POSA would understand that Mullins limits the positive exit flow to ensure that the clot is not entirely expelled from the catheter and therefore avoids risking any distal migration of the clot.

198. Therefore, it is my opinion that Yang alone or in view of Mullins discloses or renders obvious “movement of the fluid column at the distal end of the catheter is limited to a positive amount of exit flow...before fluid is drawn back into the catheter lumen,” as recited in Claim 3.

[3-C]: ...limited to a positive amount of exit flow from approximately 0.001 ml to approximately 1.0 ml...

199. Yang in view of Mullins and the knowledge of a POSA renders obvious this limitation.

200. As discussed above for Ground 1, Claim [3-B], Yang alone or in view of Mullins discloses or renders obvious controlling fluid at the distal end of the catheter to limit to a positive amount of exit flow before drawing the fluid back into the catheter.

201. As a preliminary matter, Although Yang/Mullins doesn't specify a particular value of acceptable exit flow, a POSA would understand the values of approximately 0.001 ml to approximately 1.0 ml to be reasonable values for implementing a limited amount of exit flow, at least because a POSA would be motivated to limit the amount of positive exit flow, and because a POSA would have a reasonable expectation that at least some values would not result in an unacceptable level of risk of distal migration. In particular, as discussed in greater detail below for this claim limitation in regard to both my particular analysis and calculations below, and with regard to routine optimization, a POSA would recognize that limiting to a small amount of positive exit flow, such as the claimed values here, would minimize the risk of distal clot migration and ensure that the clot remains retrievable by the catheter.

202. Further, as discussed above, Mullins discloses controlled and measured changes in fluid displacement at the catheter tip during aspiration. Ex. 1008 (Mullins) at 26:23-30 ("The invention utilizes 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...”), 3:56-59 (“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”); Ex. 1009.2 (Mullins-Prov2) at pg. 3-7.

203. As also discussed above, Mullins explains how it implements predetermined pulse cycles (referred to as “shake” signals) which utilize upper and lower pressure limits to control amounts of fluid displacement in the catheter and limit exit flow at the distal tip of the catheter, and that a flow displacement meter could be used to measure the flow displacement and use that to define the upper and lower pressure limits. Ex. 1008 (Mullins) at 28:53-56 (“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).”); Ex. 1009.2 (Mullins-Prov2) at pg. 3-7.

204. Furthermore, Mullins demonstrates that it contemplated experimenting with particular values and ranges in implementing its fluid displacement and aspiration techniques. Ex. 1008 (Mullins) at 28:59-64 (“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 between 0.1 and 0.9, or more preferably between 0.4 and 0.9.”); Ex. 1009.2 (Mullins-Prov2) at pg. 10.

205. A POSA would have found it obvious, in implementing the techniques taught by Mullins, to experiment, using routine optimization, with particular values of measured flow displacement to achieve the desired goal of aspirating the clot while still limiting the likelihood of distal migration of the clot. In particular, a POSA would reasonably experiment, based on routine optimization, with the claimed values of approximately 0.001 ml to approximately 1.0 ml, because a POSA would expect that such values may sufficiently limit the risk of the clot, or portions of the clot, from distally migrating farther into the patient’s vasculature, while still being able to aspirate the clot, in order to ensure the safety of the patient.

206. I understand that routine optimization to discover the optimum ranges of conditions for an invention’s operation is obvious where the prior art discloses general conditions of claimed features or ranges. I further understand that there are four ways for a patent owner to overcome obviousness based on routine optimization: (1) producing a new or unexpected result which is different in kind and not merely in degree from the results of the prior art; (2) if the prior art teaches away from the claimed ranges; (3) if the parameter was not recognized as result-effective; and (4) if the prior art discloses very broad ranges that do not invite routine

optimization. None of these paths to overcoming obviousness apply in this situation. Here, the claimed range of exit flow values are simply a limit to the permitted amount of positive exit flow.

207. Further, a POSA would understand that to function as an aspiration catheter, the net negative fluid displacement to aspirate the catheter should be greater than the net positive fluid displacement to infuse the catheter. A POSA would recognize that, if reversed, the catheter would be an infusion catheter rather than an aspiration catheter. As defined in Claim [3-C], the positive amount of exit flow is limited to approximately 0.001 ml to approximately 1.0 ml. Therefore, the negative amount of exit flow (aspiration) must be greater than the positive amount of exit flow from approximately 0.001 ml to approximately 1.0 ml to function as an aspiration catheter.

208. Furthermore, a POSA would have found it obvious to calculate and estimate particular values for the extent to which exit flow should be limited, as invited to do by Yang and Mullins. A POSA would also find it obvious to perform such calculations using known catheter/physiological data including laboratory measured flow rates for the types of catheters disclosed and utilized by the combination of Yang and Mullins.

209. I have performed the below analysis based on such known datapoints. In particular, the below calculations are based on the values disclosed in the research literature published in the Journal of Neurointerventional Surgery, by Long, et al., titled “Novel aspiration catheter design for acute stroke thrombectomy,” but I note that a POSA would recognize that similar values could be obtained by any suitable source. Ex. 1032 (Long) at pg. 190-195.

210. Long measured exact flow rates for various catheters diameters and lengths under a constant pressure of 600 mmHg. Ex. 1032 (Long) at pg. 191, Table 2. The measurements were taken using water at room temperature, which has a dynamic viscosity of 1 cP. Ex. 1032 (Long) at pg. 191. One of the catheter rates measured had a distal internal diameter of 0.061” (“the 0.061” catheter”), which is selected both for simplicity and because it corresponds with the catheter size ranges found in Yang. Ex. 1032 (Long) at Table 1; Ex. 1012 (Yang) at ¶ [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.”). Referencing the table in Long, a POSA would see that the flow rate for the 0.061” catheter was measured to be 4.01 mL/s.

211. In order to approximate the corresponding flow rate for blood for the same sized catheter and conditions, because blood has a higher dynamic viscosity than water, a POSA would recognize that the flow rate for blood could be converted from the flow rate of water based on the dynamic viscosity difference utilizing the Hagen-Poiseuille law ($Q = \Delta P \pi r^4 / 8 \mu L$). Ex. 1032 (Long) at pg. 191; Ex. 1033 (Klabunde) at pg. 1. Given that a reasonable estimate of the dynamic viscosity of blood is 4 cP, and that water at room temperature has a dynamic viscosity of 1 cP, a POSA would recognize that dynamic viscosity is a linear term in the denominator of Hagen-Poiseuille’s law, and therefore a reasonable calculation for the flow rate of blood would be 1.0 mL/s in the same 0.061” catheter with a measured flow rate of 4.0 mL/s of water. Ex. 1032 (Long) at pg. 191; Ex. 1033 (Klabunde) at pg. 1.

212. Equipped with a numeric flow rate of blood for a given catheter size contemplated by the combination of Yang and Mullins, the disclosures in Yang and Mullins for particular values regarding the frequency of each predetermined cycle (as disclosed in Yang) and the percentages of each predetermined cycle corresponding to application of positive pressure versus negative pressure (as

disclosed in Mullins) can then be used to calculate possible values of exit flow that a POSA would be motivated to experiment with in implementing the teachings of Yang and Mullins.

213. Regarding cycle frequency, Yang discloses a variety of potential times to complete the infuse-to-aspirate cycle. Ex. 1012 (Yang) at ¶ [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.”). Each of these values are accounted for in my calculations in the tables shown below.³

³ For the sake of simplicity and convenience, the tables shown below account for cycle frequencies disclosed by both Yang (for Ground 1), and for Ofek (for Ground 4). For the relevant Claims in Ground 4, I will reference back to this discussion to avoid unnecessary repetition.

214. Regarding cycle percentages for application of positive pressure versus negative pressure, Mullins discloses “infuse-to-aspiration cycles” for varying ratios of displacement in which the system will alternately infuse and aspirate the catheter. Ex. 1008 (Mullins) at 28:59-64 (“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.”); Ex. 1009.2 (Mullins-Prov2) at pg. 10.

215. In view of the above, the table below reflects the amount of exit flow that a POSA might experiment with in implementing Yang and Mullins for a .061” catheter at cycle frequencies of 0.100 Hz to 10 Hz.

Distal Lumen Flow Volume Catheter Internal Diameter: 0.061 inches Flow Rate (Blood): 1.0 mL/sec Distal Flow Volume (mL) = Blood Flow Rate (mL/sec) * Cycle Percentage (%) * Cycle Duration (sec)							
Fluid Displacement Ratios "Infuse-to-aspirate cycle": [Mullins (Ex. 1008) at 28:59-64]		"between 0.01 and 0.99"		"between 0.1 and 0.9"		"between 0.4 and 0.9"	
Normalized percentage of time per cycle:		Infuse %	Aspirate %	Infuse %	Aspirate %	Infuse %	Aspirate %
		1%	99%	10%	90%	31%	69%
Cycle frequency (Hz)	Cycle duration (sec)	Exit-flow (mL)	In-flow (mL)	Exit-flow (mL)	In-flow (mL)	Exit-flow (mL)	In-flow (mL)
0.100	10.000	0.100000	9.900000	1.000000	9.000000	3.100000	6.900000
0.111	9.000	0.090000	8.910000	0.900000	8.100000	2.790000	6.210000
0.125	8.000	0.080000	7.920000	0.800000	7.200000	2.480000	5.520000
0.143	7.000	0.070000	6.930000	0.700000	6.300000	2.170000	4.830000
0.167	6.000	0.060000	5.940000	0.600000	5.400000	1.860000	4.140000
0.200	5.000	0.050000	4.950000	0.500000	4.500000	1.550000	3.450000
0.250	4.000	0.040000	3.960000	0.400000	3.600000	1.240000	2.760000
0.333	3.000	0.030000	2.970000	0.300000	2.700000	0.930000	2.070000
0.500	2.000	0.020000	1.980000	0.200000	1.800000	0.620000	1.380000
1.000	1.000	0.010000	0.990000	0.100000	0.900000	0.310000	0.690000
2.000	0.500	0.005000	0.495000	0.050000	0.450000	0.155000	0.345000
3.000	0.333	0.003333	0.330000	0.033333	0.300000	0.103333	0.230000
4.000	0.250	0.002500	0.247500	0.025000	0.225000	0.077500	0.172500
5.000	0.200	0.002000	0.198000	0.020000	0.180000	0.062000	0.138000
6.000	0.167	0.001667	0.165000	0.016667	0.150000	0.051667	0.115000
7.000	0.143	0.001429	0.141429	0.014286	0.128571	0.044286	0.098571
8.000	0.125	0.001250	0.123750	0.012500	0.112500	0.038750	0.086250
9.000	0.111	0.001111	0.110000	0.011111	0.100000	0.034444	0.076667
10.000	0.100	0.001000	0.099000	0.010000	0.090000	0.031000	0.069000
20.000	0.050	0.000500	0.049500	0.005000	0.045000	0.015500	0.034500
50.000	0.020	0.000200	0.019800	0.002000	0.018000	0.006200	0.013800
100.000	0.010	0.000100	0.009900	0.001000	0.009000	0.003100	0.006900
150.000	0.007	0.000067	0.006600	0.000667	0.006000	0.002067	0.004600

216. As is evident from the above calculations, the claimed exit flow values of 0.001 mL and 1.0 mL are well within the specific exit flow values that would have been obvious to a POSA based on known flow rates and catheter sizes, along with the cycle values disclosed by Yang and Mullins. Additionally, as will be referenced for the relevant claims, additional exit flow values such as 0.1 mL and 0.5 mL would be similarly obvious to a POSA.

217. A POSA would also recognize that known flow rates for a particular catheter diameter could be converted to reflect a flow rate in another catheter having

a different inner diameter using the Hagen-Poiseuille law. This can be accomplished by calculating the radius of the different sized catheter, taking that to the fourth power (consistent with the Hagen-Poiseuille law), and then divide that value by the corresponding factor of the starting catheter in order to determine a scaling factor to apply to the starting flow rate.

218. For example, Mullins discloses using a catheter having an internal diameter of 0.088". Ex. 1008 (Mullins) at 14:16-19 ("Consider the example of an 0.088 in ID"). Utilizing the Hagen-Poiseuille law as described above, a POSA would calculate the scaling factor for going from a .061" diameter to a .088" diameter to result in a multiplier of 4x the flow rate, or a blood flow rate of 4.0 mL/s for the .088" diameter catheter.

219. In view of the above, the table below reflects the amount of exit flow that a POSA might experiment with in implementing Yang and Mullins for a .088" catheter.

Distal Lumen Flow Volume Catheter Internal Diameter: 0.088 inches Flow Rate (Blood): 4.0 mL/sec Distal Flow Volume (mL) = Blood Flow Rate (mL/sec) * Cycle Percentage (%) * Cycle Duration (sec)							
Fluid Displacement Ratios "Infuse-to-aspirate cycle": [Mullins (Ex. 1008) at 28:59-64]		"between 0.01 and 0.99"		"between 0.1 and 0.9"		"between 0.4 and 0.9"	
Normalized percentage of time per cycle:		Infuse %	Aspirate %	Infuse %	Aspirate %	Infuse %	Aspirate %
		1%	99%	10%	90%	31%	69%
Cycle frequency (Hz)	Cycle duration (sec)	Exit-flow (mL)	In-flow (mL)	Exit-flow (mL)	In-flow (mL)	Exit-flow (mL)	In-flow (mL)
0.100	10.000	0.400000	39.600000	4.000000	36.000000	12.400000	27.600000
0.111	9.000	0.360000	35.640000	3.600000	32.400000	11.160000	24.840000
0.125	8.000	0.320000	31.680000	3.200000	28.800000	9.920000	22.080000
0.143	7.000	0.280000	27.720000	2.800000	25.200000	8.680000	19.320000
0.167	6.000	0.240000	23.760000	2.400000	21.600000	7.440000	16.560000
0.200	5.000	0.200000	19.800000	2.000000	18.000000	6.200000	13.800000
0.250	4.000	0.160000	15.840000	1.600000	14.400000	4.960000	11.040000
0.333	3.000	0.120000	11.880000	1.200000	10.800000	3.720000	8.280000
0.500	2.000	0.080000	7.920000	0.800000	7.200000	2.480000	5.520000
1.000	1.000	0.040000	3.960000	0.400000	3.600000	1.240000	2.760000
2.000	0.500	0.020000	1.980000	0.200000	1.800000	0.620000	1.380000
3.000	0.333	0.013333	1.320000	0.133333	1.200000	0.413333	0.920000
4.000	0.250	0.010000	0.990000	0.100000	0.900000	0.310000	0.690000
5.000	0.200	0.008000	0.792000	0.080000	0.720000	0.248000	0.552000
6.000	0.167	0.006667	0.660000	0.066667	0.600000	0.206667	0.460000
7.000	0.143	0.005714	0.565714	0.057143	0.514286	0.177143	0.394286
8.000	0.125	0.005000	0.495000	0.050000	0.450000	0.155000	0.345000
9.000	0.111	0.004444	0.440000	0.044444	0.400000	0.137778	0.306667
10.000	0.100	0.004000	0.396000	0.040000	0.360000	0.124000	0.276000
20.000	0.050	0.002000	0.198000	0.020000	0.180000	0.062000	0.138000
50.000	0.020	0.000800	0.079200	0.008000	0.072000	0.024800	0.055200
100.000	0.010	0.000400	0.039600	0.004000	0.036000	0.012400	0.027600
150.000	0.007	0.000267	0.026400	0.002667	0.024000	0.008267	0.018400

220. I note that a POSA would recognize that flow rates will vary based on various factors for various different catheters and aspiration systems, and that flow rate values utilized above are theoretical. However, a POSA would also understand that these theoretical values are realistic starting points for tuning an aspiration thrombectomy system, and therefore provide a realistic basis for demonstrating why the claimed exit flow values are obvious.

221. Therefore, it is my opinion that Yang in view of Mullins and the knowledge of a POSA discloses and renders obvious "limited to a positive amount

of exit flow from approximately 0.001 ml to approximately 1.0 ml,” as recited in Claim 3.

Claim 4

[4-A]: The system of claim 2 wherein the controller is configured to cyclically open and close the vacuum valve and the vent valve

222. For the reasons discussed above for Ground 1, Claim [1-E], this limitation is met by Yang alone or in view of Mullins.

[4-B]: such that movement of the fluid column at the distal end of the catheter is limited to a positive amount of exit flow ... before fluid is drawn back into the catheter lumen.

223. For the reasons discussed above for Ground 1, Claim [3-B], this limitation is met by Yang alone or in view of Mullins.

[4-C]: ...limited to a positive amount of exit flow of approximately 0.1 ml to approximately 0.5 ml...

224. For the reasons discussed above for Ground 1, Claim [3-C], this limitation is met by Yang in view of Mullins and the knowledge of a POSA.

Claim 5

[5-A]: The system of claim 1 wherein the controller is configured to cyclically open and close the vacuum valve and the vent valve in a repeated cycle

225. For the reasons discussed above for Ground 1, Claim [1-E], this limitation is met by Yang alone or in view of Mullins.

[5-B]: comprising an off-off state in which the vacuum valve is closed while the vent valve is closed.

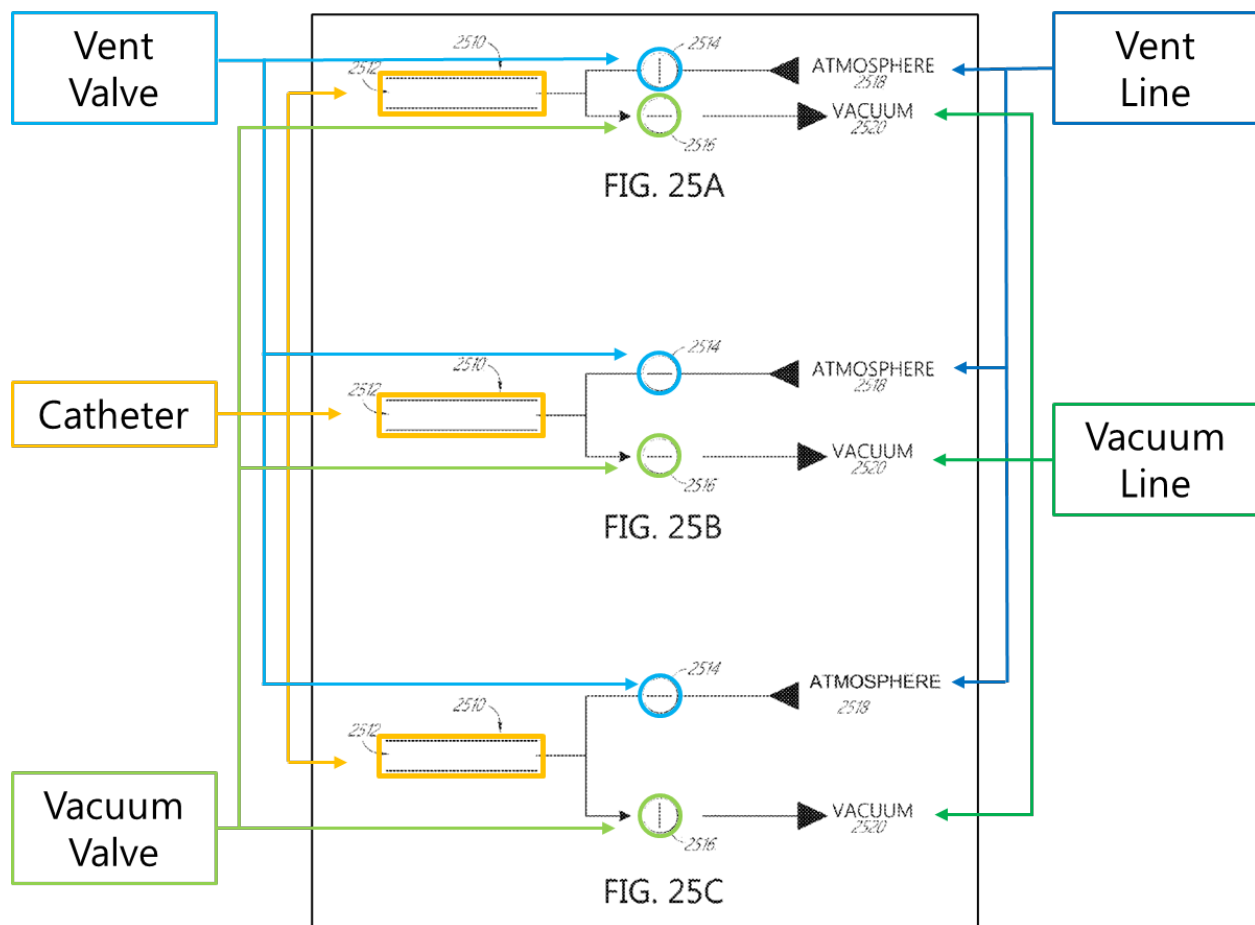
226. Yang and the knowledge of a POSA renders obvious this limitation.

227. As discussed above for Ground 1, Claim [1-E], Yang alone or in view of Mullins discloses or renders obvious cyclically opening and closing the vacuum valve and the vent valve in a repeated cycle.

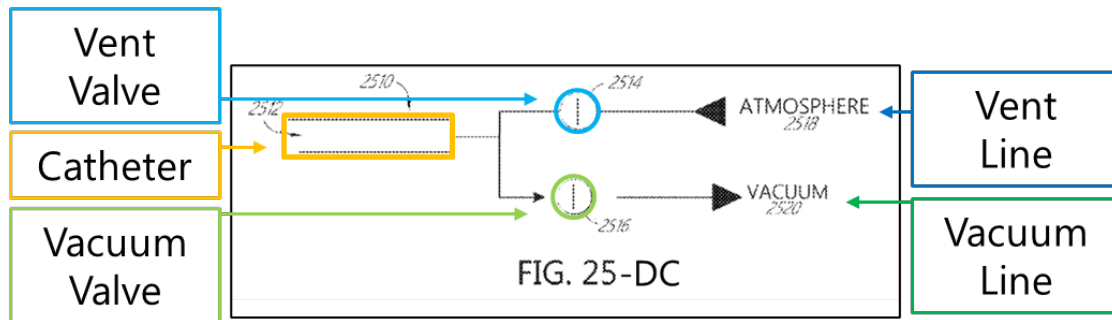
228. Yang expressly discloses serial operation of the vacuum and vent valves. Ex. 1012 (Yang) at ¶ [0170] (“In the first step as shown in FIG. 25A, the release valve 2514 is closed, and the vacuum valve 2516 is open such that the vacuum is applied to the catheter 2510 to aspirate the clot. Then, as shown 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.”)

229. Yang also explicitly illustrates this serial operation of the vacuum and vent valves in the multiple different valve states shown in Figures 25A-25C. Figure

25A illustrates a state in the aspiration cycle where the vent valve is closed while the vacuum valve is open (i.e., a 'vacuum-only state'). Ex. 1012 (Yang) at FIG. 25A. Figure 25B illustrates a state in the aspiration cycle where the vent valve is open and the vacuum valve is open (i.e., a 'double-open state' or 'on-on state'). Ex. 1012 (Yang) at FIG. 25B. Figure 25C illustrates a state in the aspiration cycle where the vent valve is open and the vacuum valve is closed, (i.e., a 'vent-only state'). Ex. 1012 (Yang) at FIG. 25C.



230. Although not illustrated in Figure 25, Yang specifically explains that after the ‘vent-only state’ of Figure 25C, “another cycle from FIG. 25A to FIG. 25C begins by closing the release valve 2514 and opening the vacuum valve 2516.” Ex. 1012 (Yang) at ¶ [0170]. A POSA would understand, in the context of Figures 25A-25C and the other valve states disclosed in [0170], that Yang is describing an additional valve state that enables Yang to transition from the vent-only state in Figure 25C to the vacuum-only state in Figure 25A. This disclosure in Yang teaches that the transition state is achieved from Figure 25C by “closing the release valve 2514,” which a POSA would understand results in a state in the aspiration cycle where the vent valve is closed while the vacuum valve is still closed (as it was in the vent-only state of Figure 25C). Thus, this transition state disclosed by Yang is a ‘double-closed state’ (or ‘off-off state’) where the vent valve is closed and the vacuum valve is closed. A modified illustration of Yang’s double-closed state consistent with the other valve states shown in Figures 25A-C is shown below (‘FIG. 25-DC’). Yang then completes the loop and begins another cycle by “opening the vacuum valve 2516,” thereby resulting in the vacuum-only state of Figure 25A. Ex. 1012 (Yang) at ¶ [0170].



231. A POSA would recognize that Yang would transition from the vent-only state to the vacuum-only state via a double-closed state at least in part because it would be consistent with the operation and transition of each of the other disclosed vacuum states, in which each successive state is reached by serially opening or closing one of the valves while maintaining the other valve in the same open/closed state as it was in the previous state. Thus, a POSA would find it obvious that there is a transition state that completes the cycle of Figure 25 by having a double-closed state to transition from Figure 25C back to Figure 25A.

232. The double-closed state in Yang's aspiration cycle is also consistent with other disclosures in Yang. For example, Yang discloses various possible levels of vacuum (e.g., positive vacuum, zero vacuum, negative pressure, slight positive pressure, etc.) during the pulsed aspiration cycles, which is consistent with, and in some cases corresponds to, the various valve states with respect to Figure 25 and the discussion above (e.g., vacuum-only state, double-closed state, vent-only state). Ex. 1012 (Yang) at ¶¶ [0040] ("FIGS. 25A-25C depict a pulsed aspiration cycle

according to an embodiment.”), [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.”), [0169] (“FIGS. 25A-25C show a logical progression of the vacuum and release cycle as applied to the catheter 2510.”). A POSA would have understood the sequences of opening and closing the vacuum and vent valves to include periods where both valves are closed for at least short periods of time, e.g., before the start of each new cycle illustrated in Fig. 25.

233. Further, to the extent that Yang does not explicitly disclose a double-closed state in which the vacuum and vent valve are both closed, a POSA would have found a double-closed state an obvious manner of implementing the dynamic aspiration sequence disclosed by Yang. As discussed above, Yang discloses operating in serial (as shown in Fig. 25) to achieve the pulsatile vacuum pressure (e.g., as discussed in Figures 13 and 14). Closing the vent valve first before reopening the vacuum would be the logical approach to efficiently generate a pulse, allowing the full force of the vacuum to be exerted on the clot. Closing the vent valve

first cuts off the positive pressure source and then opening the vacuum valve then allows the full force of the vacuum to be exerted on the clot. In this way, after the vent valve has been closed and the vacuum valve opened, the applied vacuum would not be minimized by the positive pressure of an open vent valve, thereby efficiently building up a full negative pulse. Ex. 1012 (Yang) at ¶ [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 [] 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.”).

234. As an additional point, a POSA would have further found it obvious to implement a double-closed state in Yang because there are only a finite number of ways to order the opening and closing of valves, and one such way is by including a phase where both valves are closed. Given that there is a limited number of combinations and states in which two valves can individually be opened or closed, in implementing and optimizing the system of Yang, a POSA would find it obvious

to experiment with each such combination. In particular, a POSA would be motivated to experiment with a double-closed state because if both valves are closed, there would not be any resulting flow within the catheter, and therefore would not risk any distal clot migration.

235. As a final point, a POSA would have also found it obvious to implement a double-closed state in Yang because it is far more typical, predictable, and reliable to conduct serial operations in medical devices. For example, an automated valve typically includes position sensors to tell whether the valve is in an open or closed state. It is far more reliable for a controller to initiate a valve operation and verify the completion of the valve operation before proceeding with the other valve operation. A POSA would also understand that parallel operations tend to compound operation errors of the parallel steps, reducing system reliability.

236. Therefore, it is my opinion that Yang and the knowledge of a POSA renders obvious “an off-off state in which the vacuum valve is closed while the vent valve is closed,” as recited by Claim 5.

Claim 6

[6-A]: The system of claim 1 wherein: the controller is configured to cyclically open and close the vacuum valve and the vent valve in a cycle comprising

237. For the reasons discussed above for Ground 1, Claim [1-E], this limitation is met by Yang alone or in view of Mullins .

[6-B]: (a) a first off-off state in which the vacuum valve is closed while the vent valve is closed, (b) a vacuum-only state following the first off-off state in which the vacuum valve is open while the vent valve is closed, (c) a second off-off state following the vacuum-only state in which the vacuum valve is closed while the vent valve is closed, and (d) a vent-only state following the second off-off state in which the vacuum valve is closed while the vent valve is open; and the cycle is repeated.

238. Yang and the knowledge of a POSA renders obvious this limitation.

239. As discussed above for Ground 1, Claim [1-E], Yang alone or in view of Mullins discloses or renders obvious cyclically opening and closing the vacuum valve and the vent valve in a repeated cycle. As also discussed above for Ground 1, Claim [5-B], Yang and the knowledge of a POSA renders obvious an off-off state in which the vacuum valve is closed while the vent valve is closed.

240. As further discussed above for Ground 1, Claim [5-B], the aspiration cycle disclosed or rendered obvious in Yang takes place in the following sequence of valve states: (1) double-closed state, (2) vacuum-only state, (3) double-open state, and (4) vent-only state.

241. As a preliminary matter, Yang explains that “another cycle from FIG. 25A to FIG. 25C begins by closing the release valve 2514 and opening the vacuum valve 2516.” Ex. 1012 (Yang) at ¶ [0170]. A POSA would therefore understand that the beginning of this cycle would be in a double-closed state, satisfying the first step of this claim element.

242. Yang describes the following step being “the release valve 2514 is closed, and the vacuum valve 2516 is open,” thus describing a vacuum-only state. Ex. 1012 (Yang) at ¶ [0170]. It next describes a double-open state when it states that “the release valve 2514 is opened while the vacuum valve 2516 stays open.” Ex. 1012 (Yang) at ¶ [0170]. A POSA would find it obvious to change this double-open state to a double-closed state because, in progressing to the vent-only state (see Fig. 25C), the vacuum valve would already need to be turned off. A POSA would understand that the intermediate step could involve either a double-open or a double-closed state.

243. A POSA would be further motivated to choose a second double-closed state instead of a double-open state at least in order to prevent additional blood loss and conserve the injection fluid from being vacuumed into the canister. A POSA would also be motivated to choose a second double-closed state instead of a double-open state at least because the stated reasoning in Yang for using a double-open state

for the third (3) phase is “dropping vacuum applied to the catheter.” However, it would be obvious to a POSA that if the intended goal of the double-open state is to reduce the vacuum applied to the catheter, it would be simpler, cheaper, and more efficient to do so by implementing a double-closed state rather than a double-open state. For example, not only is a first and second double-closed state the manner in which the ’402 Patent chose to approach such a situation, but other POSAs in the relevant time period also understood that opting for a double-closed state over a double-open state was well-known to be a better solution for the desired goal of dropping vacuum applied to the catheter. *See, e.g.*, Ex. 1007 (Ofek) at 5:49-62 (“During each impulse when the N.O valve 140 [vacuum valve] is opened, the N.O. valve 150 [vent valve] is shut so as to prevent impulse fluid from entering the N.O. valve [vacuum valve] and diverting to the syringe pump 162 instead of entering the catheter tube lumen 14 as desired.”). Relatedly, a corollary to the reason why a POSA would find it obvious to use a double-closed state rather than a double-open state when aiming to reduce a level of vacuum is that both Yang and Mullins, along with their embodiments that I discuss throughout, are specifically focused on pulsated aspiration, as opposed to, for example, alternative purposes/use cases. In particular, both Yang and Mullins are expressly focused on pulsated aspiration systems which use “pulsed aspiration cycle[s]” that “alternate between applying

pulses of higher negative pressure and lower negative pressure.” Ex. 1012 (Yang) at ¶¶ [0014], [0040]; *see also* Ex. 1008 (Mullins) at 27:54-65 (“the applied pressure signal incorporates... the application of pulse cycling between two pressure limits... [that] provides acute aspiration of the clot”). For all of the reasons discussed above, a POSA would recognize the value of using a double-closed instead of a double-open state in Yang’s sequence of valve states, which Yang specifically teaches for the purpose/use case of pulsated aspiration. This would be especially apparent to a POSA when considered in contrast to the well-known and practical purpose to implementing a double-open state. Specifically, a POSA would understand that an aspect of a double-open state is that it allows for retention of vacuum pressure in the aspiration catheter while concurrently utilizing the vent source. A POSA would also recognize that it was well-known to implement distinct flushing functionalities within aspiration systems separate from the functionality of pulsated aspiration. *See generally* Ex. 1034 (Garrison) (teaching that aspiration systems may implement specific functionality to perform flushing within the aspiration system in addition to the separate functionality of performing pulsated aspiration). As such, a POSA would find it obvious that a double-open state would be useful for the purpose of implementing a flushing functionality within the aspiration system while also retaining the vacuum in the catheter. *See, e.g.*, Ex. 1001 (’402 Patent) at 41:23-31

(“It is noted that one desirable goal to achieve with the system 400 is to fully ingest a clot and bring it back a standard aspiration canister (in a typical thrombectomy end reservoir) or into the thrombus trap 200. When using a standard aspiration canister and the thrombus trap 200, the system 400 *can use the vent liquid to flush* the thrombus trap 200 through the intake bleed valve 214 instead of using air. This allows retention of vacuum pressure in the aspiration canister.”). Moreover, a POSA would recognize that using a double-closed state (rather than a double-open state) would generate the strongest water hammer effect possible to macerate the clot, and/or to produce the greatest change in momentum possible to macerate the clot, both of which are done by starting, stopping, and reversing fluid flow very abruptly. In contrast, a double-open state would not allow for abrupt changes in pressure or flow direction. Put differently, a POSA would find it obvious that implementing a double-closed state would result in sharp pressure spikes that would result in an ideal water hammer effect, whereas implementing a double-open state would not result in such sharp pressure spikes, and thereby reduce the efficacy of the pulsated aspiration.

244. Therefore, it is my opinion that Yang and the knowledge of a POSA renders obvious “(a) a first off-off state in which the vacuum valve is closed while the vent valve is closed, (b) a vacuum-only state following the first off-off state in

which the vacuum valve is open while the vent valve is closed, (c) a second off-off state following the vacuum-only state in which the vacuum valve is closed while the vent valve is closed, and (d) a vent-only state following the second off-off state in which the vacuum valve is closed while the vent valve is open; and the cycle is repeated,” as recited by Claim 6.

Claim 7

[7]: The system of claim 6 wherein the cycle is repeated at a frequency of 2 Hz to 12 Hz.

245. Yang and the knowledge of a POSA renders obvious this limitation.

246. As discussed above for Ground 1, Claim [1-E], Yang alone or in view of Mullins discloses or renders obvious a controller configured to open and close the vacuum valve and the vent valve in a predetermined cycle. As also discussed above for Ground 1, Claim [6-A] and [6-B], Yang and the knowledge of a POSA renders obvious the sequence of valve states recited by Claim 6.

247. Yang discloses a variety of periods for each vacuum and release cycle, including frequencies of 2 Hz (i.e., 0.5 seconds/cycle) to 10 Hz (i.e., 0.1 seconds/cycle). Ex. 1012 (Yang) at ¶ [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 [] the vacuum and allowing the clot to relax before reapplying a vacuum is found to aspirate the clogged 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.”). A POSA would therefore recognize that Yang discloses nearly an identical range (i.e., 2 Hz to 10 Hz) of cycle frequencies as is required by this claim (2 Hz to 12 Hz).

248. Yang also discloses a wide variety of certain other frequencies for various purposes. *See, e.g.*, Ex. 1012 (Yang) at ¶¶ [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.”), [0129]-[0130] (“Remote control 320 enables physicians to control the frequency modulator 316 and/or the valve controller 318 for various purposes, such as turning

the valve on/off, selecting different wave frequencies, and selecting different wave forms, while manipulating the catheter 10 at the patient side. Remote control 320 may be in wired or wireless communication with aspirator 300. By tuning frequency, duty cycle, and wave form, one skilled in the art may match or approximate the resonating frequency to the natural frequency of the catheter. This may further enhance the efficacy of aspiration. The natural frequency of the catheter is typically less than about 260 Hz.”). A POSA would therefore recognize that Yang’s disclosures of various ranges for various types of frequencies, including cycle frequency, invite the POSA to experiment and optimize such frequencies in implementing the teachings of Yang.

249. I understand that routine optimization to discover the optimum ranges of conditions for an invention’s operation is obvious where the prior art discloses general conditions of claimed features or ranges. I further understand that there are four ways for a patent owner to overcome obviousness based on routine optimization: (1) producing a new or unexpected result which is different in kind and not merely in degree from the results of the prior art; (2) if the prior art teaches away from the claimed ranges; (3) if the parameter was not recognized as result-effective; and (4) if the prior art discloses very broad ranges that do not invite routine optimization. None of these paths to overcoming obviousness apply in this situation.

Here, the '402 Patent's claimed "cycle [] repeated at a frequency of 2 Hz to 12 Hz" is nothing more than a result-effective and obvious result from the routine experimentation invited by Yang. The '402 does not describe nor demonstrate any particular effect of the claimed range, let alone any criticality or unexpectedness related to the claimed range. Finally, neither Yang nor Mullins teaches away from the cycle being "repeated at a frequency of 2 Hz to 12 Hz," and Yang explicitly invites the reader to tune "frequency, duty cycle, and wave form" to "further enhance the efficiency of aspiration." Ex. 1012 (Yang) at ¶ [0130]. Therefore, it is my opinion that the claimed "cycle [] repeated at a frequency of 2 Hz to 12 Hz" is the result of routine optimization and is thus obvious.

250. Moreover, a POSA would be aware of the inherent risks of positive exit flow and distal migration of clot in aspiration thrombectomy, and would recognize that monitoring and controlling the frequencies of the cycles would be necessary to minimize the risks of forward flow because these risks would be exacerbated if the pressure within the catheter exceeded a threshold based on well-known theories of fluid mechanics because the vacuum valve cuts off the negative pressure source within the system. Ex. 1023 (Ross Declaration) at ¶ 19. Thus, a POSA would find it obvious to implement the techniques disclosed in Yang in a manner that avoids those inherent risks, including, for example, by adjusting the frequency of the extraction

cycle expressly disclosed by Yang. A POSA would recognize that by adjusting the frequency of the extraction cycle, a POSA would be able to achieve maximum clot digestion while ensuring that the momentum of fluid at the distal end of the catheter does not change direction sufficiently to create too much forward flow. Thus, a POSA would have been motivated by the teachings in Yang to experiment with the cycle frequency to optimize the efficiency of aspiration while limiting the risks of excessive exit flow at the distal end of the catheter.

251. Therefore, it is my opinion that Yang and the knowledge of a POSA renders obvious “wherein the cycle is repeated at a frequency of 2 Hz to 12 Hz,” as recited in Claim 7.

Claim 8

[8]: The system of claim 1 wherein the vacuum valve and the vent valve are solenoid pinch valves.

252. Yang discloses this limitation.

253. Yang expressly discloses using solenoid valves. Ex. 1012 at ¶¶ [0126] (“The solenoid valve 314 controls the fluid flow from the catheter 10 to the vacuum chamber 310/collection canister 312.”), [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.”). A POSA would have understood

that this solenoid valve disclosed in Yang is a more general term that could include a solenoid pinch valve and/or from which implementation using known solenoid pinch valves would be obvious.

254. Therefore, it is my opinion that Yang discloses or renders obvious “wherein the vacuum valve and the vent valve are solenoid pinch valves,” as recited in Claim 8.

Claim 10

[10-A]: The system of claim 1 wherein the controller is configured to cyclically open and close the vacuum valve and the vent valve

255. For the reasons discussed above for Ground 1, Claim [1-E], this limitation is met by Yang alone or in view of Mullins.

[10-B]: such that an amount of momentum transfer from the fluid column in the catheter lumen is sufficient to unstick thromboembolic material at the distal end of the catheter.

256. Yang alone or in view of Mullins discloses or renders obvious this limitation.

257. Yang discloses methods to loosen and aspirate a clot, and teaches that unsticking the clot may be done at the distal end of the catheter. Ex. 1012 (Yang) at ¶¶ [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”), [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 [] the vacuum and allowing the clot to relax before reapplying a vacuum is found to aspirate the corked clot most efficiently.”).

258. To the extent that Yang does not explicitly disclose an amount of momentum transfer sufficient to unstick thromboembolic material at the distal end of the catheter, the combination of Yang and Mullins renders it obvious.

259. Mullins discloses reversing the direction of fluid displacement and allowing some or all of the clot to be pushed to cause the clot to become more “free” with respect to the catheter. Ex. 1008 (Mullins) at 27:18-26 (“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.”); Ex. 1009.2 (Mullins-Prov2) at pg. 3-7. A POSA would understand and find it obvious that causing the clot to become more “free” may take place at the distal end of the catheter, at least because the nature of thrombus removal involves the distal end of the catheter being engaged with the thrombus.

260. Therefore, it is my opinion that Yang alone or in view of Mullins and the knowledge of a POSA discloses and renders obvious “such that an amount of momentum transfer from the fluid column in the catheter lumen is sufficient to

unstick thromboembolic material at the distal end of the catheter,” as recited by Claim 10.

Claim 11

[11-Pre]: A method for removing thromboembolic material, comprising: aspirating thromboembolic material from a person using the system of claim 1 by—

261. For the reasons discussed above for Ground 1, Claim [1-Pre], this limitation is met by Yang.

[11-A]: (a) positioning the distal end of the catheter at least proximate to thromboembolic material in a blood vessel of the person;

262. Yang alone or in view of Mullins discloses this limitation.

263. Yang discloses placing the catheter in a blood vessel, with the distal end proximate to the material sought to be removed. Ex. 1012 (Yang) at ¶¶ [0101] (“Application of aspiration may be accompanied by distal advance of the distal tip 38 into the thrombotic material.”), [0177] (“The method of retrieving a clot may comprise providing the aspiration catheter,... placing the catheter adjacent to the clot; attempting to aspirate clot...”).

264. Like Yang, Mullins also discloses positioning the distal end of the catheter at least proximate to thromboembolic material in a blood vessel of the person.

265. Mullins discloses placing the catheter tip adjacent to the clot. Ex. 1008 (Mullins) at 3:6-9 (“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,... applying a vacuum to the catheter so that the clot is aspirated into the distal portion.”), 3:60-4:4 (“once the catheter is advanced and engaged with the clot, an increase in the vacuum is observed”), 29:26-35 (“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 physic again moves the catheter tip distally to engage the next piece of clot.”); Ex. 1009.2 (Mullins-Prov2) at pg. 3-7, 11.

266. Therefore, it is my opinion that Yang alone or in view of Mullins discloses “positioning the distal end of the catheter at least proximate to thromboembolic material in a blood vessel of the person,” as recited by Claim 11.

[11-B]: (b) applying a vacuum through the lumen of the catheter such that a vacuum flow draws at least a portion of the thromboembolic material into the catheter lumen; and

267. Yang alone or in view of Mullins discloses or renders obvious this limitation.

268. Yang discloses using vacuum to cause at least a portion of a clot to be drawn into a catheter lumen. Ex. 1012 (Yang) at ¶¶ [0101] (“Aspiration may be applied via lumen 40”), [0120] (“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.”).

269. Like Yang, Mullins also discloses applying a vacuum through the lumen of the catheter such that a vacuum flow draws at least a portion of the thromboembolic material into the catheter lumen.

270. Mullins discloses using vacuum to cause at least a portion of the clot to be aspirated and ingested by the catheter. Ex. 1008 (Mullins) at 4:5-11 (“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”), 26:65-66 (“the pump appl[ying] a vacuum enabling the catheter to ingest some of the clot, Fig. 47 (d).”); See Ex. 1009.2 (Mullins-Prov2) at pg. 3-7, 11.

271. Therefore, it is my opinion that Yang alone or in view of Mullins discloses “applying a vacuum through the lumen of the catheter such that a vacuum flow draws at least a portion of the thromboembolic material into the catheter lumen” as recited by Claim 11.

[11-C]: (c) controlling the vacuum valve fluidically coupled to the vacuum source and the catheter and the vent valve fluidically coupled to a vent fluid source and the catheter

272. For the reasons discussed above for Ground 1, Claims [1-B], [1-E], and [2-A], this limitation is met by Yang alone or in view of Mullins.

273. Additionally, Yang discloses that the vent valve is fluidically coupled to the vent fluid source. Ex. 1012 (Yang) at FIGs. 25A-25C, ¶ [0169] (“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.”).

274. Therefore, it is my opinion that Yang alone or in view of Mullins discloses “controlling the vacuum valve fluidically coupled to the vacuum source and the catheter and the vent valve fluidically coupled to a vent fluid source and the catheter,” as recited by Claim 11.

[11-D]: such that a level of vacuum at the distal end of the catheter changes

275. For the reasons discussed above for Ground 1, Claim [1-F], this limitation is met by Yang alone or in view of Mullins.

[11-E]: and thereby controls flow in and out from the distal end of the catheter.

276. For the reasons discussed above for Ground 1, Claim [1-G], this limitation is met by Yang alone or in view of Mullins.

Claim 12

[12-A]: The method of claim 11 wherein: the vent fluid source is configured to provide the vent fluid at a pressure greater than atmospheric pressure; and

277. For the reasons discussed above for Ground 1, Claim [2-B], this limitation is met by Yang alone or in view of Mullins.

[12-B]: controlling the vacuum valve and the vent valve comprising cyclically opening and closing the vacuum valve and the vent valve

278. For the reasons discussed above for Ground 1, Claim [1-E], this limitation is met by Yang alone or in view of Mullins.

[12-C]: to change a level of negative pressure and positive pressure at the distal end of the catheter during each cycle.

279. For the reasons discussed above for Ground 1, Claim [2-D], this limitation is met by Yang alone or in view of Mullins.

Claim 13

[13-A]: The method of claim 12 wherein controlling the vacuum valve and the vent valve comprises limiting movement of a fluid column in the catheter lumen at the distal end of the catheter to a positive amount of exit flow

280. For the reasons discussed above for Ground 1, Claim [3-B], this limitation is met by Yang alone or in view of Mullins.

[13-B]: limiting... to a positive amount of exit flow within a range of a length of the fluid column that exits the distal end of the catheter.

281. As discussed above for Ground 1, Claim [3-C], Yang alone or in view of Mullins discloses or renders obvious limiting a positive amount of exit flow at the distal end of the catheter before fluid is drawn back into the catheter.

282. A POSA would further recognize the equivalence between measuring exit flow could be based on length rather than volume. Given that volume is a function of length, a teaching of one teaches of the other. For a catheter, which may have a largely equivalent diameter along its full length, this conversion would be simple. A POSA would further understand that having a steady diameter along the length of the catheter would allow for a clot to be aspirated. A POSA would recognize that controlling the exit flow fluid column length rather than the exit flow volume would more directly correspond to the distance a clogged clot travels away from the distal end of the catheter before the pressure within the catheter is reversed to draw fluid and clot back into the catheter lumen. In comparison, when the volume of exit flow is controlled, the distance a clogged clot is allowed to travel away from the distal end of the catheter varies with each catheter lumen diameter. For a fixed exit flow volume, the smaller the catheter lumen diameter, the longer the length of the exit flow fluid column.

283. Therefore, it is my opinion that Yang alone or in view of Mullins and the knowledge of a POSA renders obvious “limiting... to a positive amount of exit flow within a range of a length of the fluid column that exits the distal end of the catheter,” as recited by Claim 13.

Claim 14

[14-A]: The method of claim 13 wherein limiting movement of the fluid column at the distal end of the catheter comprises stopping a distal flow through the catheter lumen and reapplying the vacuum through the catheter lumen ... before fluid is drawn back into the catheter lumen.

284. Yang alone or in view of Mullins discloses or renders this claim limitation obvious.

285. As discussed above for Ground 1, Claim [3-B], Yang alone or in view of Mullins discloses or renders obvious limiting an amount of positive exit flow and subsequently drawing fluid back into the catheter.

286. Yang further discloses stopping distal flow and reapplying vacuum in a cyclical pattern. Ex. 1012 (Yang) at ¶¶ [0168] (“Merely stopping the vacuum is not sufficient to loosen the clot. Completely releasing [] the vacuum and allowing the clot to relax before reapplying a vacuum is found to aspirate the corked clot most efficiently.”), [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”). A POSA would have understood this starting and stopping to result in fluid being drawn back into the catheter lumen as this is part of the thrombectomy process, thus removing the thrombus.

287. To the extent that Yang does not explicitly disclose limiting movement of the fluid column at the distal end by stopping a distal flow through the catheter lumen and reapplying the vacuum through the catheter lumen before fluid is drawn

back into the catheter lumen, the combination of Yang and Mullins renders it obvious.

288. In Mullins, figures 47(g)-(h) illustrate this start and stop of fluid flow and vacuum within the lumen. Ex. 1008 (Mullins) at Figs. 47(g)-(h); Ex. 1009.2 (Mullins-Prov2) at pg. 4-7. Furthermore, Mullins describes a sensor used to determine fluid displacement and vary pressure, such as by reapplying vacuum. Ex. 1008 (Mullins) at 3:35-38 (“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.”); Ex. 1009.2 (Mullins-Prov2) at pg. 3. Mullins further explicitly discloses the controller providing vacuum for this task. Ex. 1008 (Mullins) at 3:56-59 (“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.”); Ex. 1009.2 (Mullins-Prov2) at pg. 4-10.

289. Therefore, it is my opinion that Yang alone or in view of Mullins discloses or renders obvious “wherein limiting movement of the fluid column at the distal end of the catheter comprises stopping a distal flow through the catheter comprises stopping a distal flow through the catheter lumen and reapplying the vacuum through the catheter lumen... before fluid is drawn back into the catheter lumen,” as recited by Claim 14.

[14-B]: ...such that the positive amount of exit flow is approximately 0.5 mm to approximately 30 mm of the fluid column...

290. Yang in view of Mullins and the knowledge of a POSA renders this claim limitation obvious.

291. As discussed above for Ground 1, Claim [13-B], Yang alone or in view of Mullins and the knowledge of a POSA discloses or renders obvious limiting to a positive amount of exit flow within a range of length.

292. As a preliminary matter, a POSA would understand the values of approximately 0.5 mm to approximately 30 mm of fluid column to be reasonable values for implementing a limited amount of exit flow, at least because a POSA would be motivated to limit the amount of positive exit flow, and because a POSA would have a reasonable expectation that those values would not result in an unacceptable level of risk of distal migration.

293. A POSA would recognize the clinical safety concerns of positive exit flow pushing the clot material away from the distal end of the catheter to a distance that the reversed catheter pressure (vacuum) can no longer draw the clot back to the catheter. If the vacuum is unable to draw the clot back to the catheter, the clot becomes embolic material along with its associated clinical risks and hazards. A POSA would recognize that an exit flow range of approximately 0.5 mm to

approximately 30 mm of fluid column is a reasonable distance that would not preclude the catheter vacuum from drawing the clot back into the catheter.

294. Additionally, a POSA would understand how to convert the exit flow volumes described in Ground 1, [3-C] to respective values of exit flow length.

295. In view of the above, consistent with my analysis for Ground 1, [3-C], the table below reflects the amount of exit flow (in millimeters) that a POSA might experiment with in implementing Yang in view of Mullins for a .061” inner diameter catheter and a .088” inner diameter catheter.

Distal Lumen Flow Length Catheter Internal Diameter: 0.061 inches Catheter Internal Cross-Section Area: 1.885 mm ² Flow Rate (Blood): 1.0 mL/sec Distal Flow Volume (mL) = Blood Flow Rate (mL/sec) * Cycle Percentage (%) * Cycle Duration (sec) Distal Flow Length (mm) = 1000 (mm ³ /mL) * Distal Flow Volume (mL) / Lumen Cross-Section Area (mm ²)							
Fluid Displacement Ratios "Infuse-to-aspirate cycle": [Mullins (Ex. 1008) at 28:59-64]		"between 0.01 and 0.99"		"between 0.1 and 0.9"		"between 0.4 and 0.9"	
Normalized percentage of time per cycle:		Infuse %	Aspirate %	Infuse %	Aspirate %	Infuse %	Aspirate %
		1%	99%	10%	90%	31%	69%
Cycle frequency (Hz)	Cycle duration (sec)	Exit-flow (mm)	In-flow (mm)	Exit-flow (mm)	In-flow (mm)	Exit-flow (mm)	In-flow (mm)
0.100	10.000	53.050398	5251.989390	530.503979	4774.535809	1644.562334	3660.477454
0.111	9.000	47.745358	4726.790451	477.453581	4297.082228	1480.106101	3294.429708
0.125	8.000	42.440318	4201.591512	424.403183	3819.628647	1315.649867	2928.381963
0.143	7.000	37.135279	3676.392573	371.352785	3342.175066	1151.193634	2562.334218
0.167	6.000	31.830239	3151.193634	318.302387	2864.721485	986.737401	2196.286472
0.200	5.000	26.525199	2625.994695	265.251989	2387.267905	822.281167	1830.238727
0.250	4.000	21.220159	2100.795756	212.201592	1909.814324	657.824934	1464.190981
0.333	3.000	15.915119	1575.596817	159.151194	1432.360743	493.368700	1098.143236
0.500	2.000	10.610080	1050.397878	106.100796	954.907162	328.912467	732.095491
1.000	1.000	5.305040	525.198939	53.050398	477.453581	164.456233	366.047745
2.000	0.500	2.652520	262.599469	26.525199	238.726790	82.228117	183.023873
3.000	0.333	1.768347	175.066313	17.683466	159.151194	54.818744	122.015915
4.000	0.250	1.326260	131.299735	13.262599	119.363395	41.114058	91.511936
5.000	0.200	1.061008	105.039788	10.610080	95.490716	32.891247	73.209549
6.000	0.167	0.884173	87.533156	8.841733	79.575597	27.409372	61.007958
7.000	0.143	0.757863	75.028420	7.578628	68.207654	23.493748	52.292535
8.000	0.125	0.663130	65.649867	6.631300	59.681698	20.557029	45.755968
9.000	0.111	0.589449	58.355438	5.894489	53.050398	18.272915	40.671972
10.000	0.100	0.530504	52.519894	5.305040	47.745358	16.445623	36.604775
20.000	0.050	0.265252	26.259947	2.652520	23.872679	8.222812	18.302387
50.000	0.020	0.106101	10.503979	1.061008	9.549072	3.289125	7.320955
100.000	0.010	0.053050	5.251989	0.530504	4.774536	1.644562	3.660477
150.000	0.007	0.035367	3.501326	0.353669	3.183024	1.096375	2.440318

Distal Lumen Flow Volume Catheter Internal Diameter: 0.088 inches Catheter Internal Cross-Section Area: 3.923 mm ² Flow Rate (Blood): 4.0 mL/sec Distal Flow Volume (mL) = Blood Flow Rate (mL/sec) * Cycle Percentage (%) * Cycle Duration (sec) Distal Flow Length (mm) = 1000 (mm ³ /mL) * Distal Flow Volume (mL) / Lumen Cross-Section Area (mm ²)							
Fluid Displacement Ratios "Infuse-to-aspirate cycle": [Mullins (Ex. 1008) at 28:59-64]		"between 0.01 and 0.99"		"between 0.1 and 0.9"		"between 0.4 and 0.9"	
Normalized percentage of time per cycle:		Infuse %	Aspirate %	Infuse %	Aspirate %	Infuse %	Aspirate %
		1%	99%	10%	90%	31%	69%
Cycle frequency (Hz)	Cycle duration (sec)	Exit-flow (mm)	In-flow (mm)	Exit-flow (mm)	In-flow (mm)	Exit-flow (mm)	In-flow (mm)
0.100	10.000	101.962784	10094.315575	1019.627836	9176.650523	3160.846291	7035.432067
0.111	9.000	91.766505	9084.884017	917.665052	8258.985470	2844.761662	6331.888861
0.125	8.000	81.570227	8075.452460	815.702269	7341.320418	2528.677033	5628.345654
0.143	7.000	71.373949	7066.020902	713.739485	6423.655366	2212.592404	4924.802447
0.167	6.000	61.177670	6056.589345	611.776702	5505.990314	1896.507775	4221.259240
0.200	5.000	50.981392	5047.157787	509.813918	4588.325261	1580.423146	3517.716034
0.250	4.000	40.785113	4037.726230	407.851134	3670.660209	1264.338516	2814.172827
0.333	3.000	30.588835	3028.294672	305.888351	2752.995157	948.253887	2110.629620
0.500	2.000	20.392557	2018.863115	203.925567	1835.330105	632.169258	1407.086413
1.000	1.000	10.196278	1009.431557	101.962784	917.665052	316.084629	703.543207
2.000	0.500	5.098139	504.715779	50.981392	458.832526	158.042315	351.771603
3.000	0.333	3.398759	336.477186	33.987595	305.888351	105.361543	234.514402
4.000	0.250	2.549070	252.357889	25.490696	229.416263	79.021157	175.885802
5.000	0.200	2.039256	201.886311	20.392557	183.533010	63.216926	140.708641
6.000	0.167	1.699380	168.238593	16.993797	152.944175	52.680772	117.257201
7.000	0.143	1.456611	144.204508	14.566112	131.095007	45.154947	100.506172
8.000	0.125	1.274535	126.178945	12.745348	114.708132	39.510579	87.942901
9.000	0.111	1.132920	112.159062	11.329198	101.962784	35.120514	78.171467
10.000	0.100	1.019628	100.943156	10.196278	91.766505	31.608463	70.354321
20.000	0.050	0.509814	50.471578	5.098139	45.883253	15.804231	35.177160
50.000	0.020	0.203926	20.188631	2.039256	18.353301	6.321693	14.070864
100.000	0.010	0.101963	10.094316	1.019628	9.176651	3.160846	7.035432
150.000	0.007	0.067975	6.729544	0.679752	6.117767	2.107231	4.690288

296. Therefore, it is my opinion that Yang alone or in view of Mullins and the knowledge of a POSA renders obvious “the positive among of exit flow is approximately 0.5 mm to approximately 30 mm of the fluid column,” as recited by Claim 14.

Claim 15

[15-A]: The method of claim 12 wherein controlling the vacuum valve and the vent valve comprises limiting movement of a fluid column in the catheter lumen at the distal end of the catheter to a positive amount of exit flow

297. For the reasons discussed above for Ground 1, Claim [3-B], this limitation is met by Yang alone or in view of Mullins.

[15-B]: limiting...to a positive amount of exit flow within a range of volume of fluid that exits the distal end of the catheter.

298. For the reasons discussed above for Ground 1, Claims [3-B] and [3-C], this limitation is met by Yang in view of Mullins and the knowledge of a POSA.

Claim 16

[16-A]: The method of claim 15 wherein limiting movement of the fluid column at the distal end of the catheter comprises stopping a distal flow through the catheter lumen and reapplying the vacuum through the catheter lumen ... before fluid is drawn back into the catheter lumen.

299. For the reasons discussed above for Ground 1, Claims [3-B] and [14-A], this limitation is met by Yang alone or in view of Mullins.

[16-B]: ...such that the positive amount of exit flow is approximately 0.001 ml to approximately 1.0 ml...

300. For the reasons discussed above for Ground 1, Claim [3-C], this limitation is met by Yang in view of Mullins and the knowledge of a POSA.

Claim 17

[17-A]: The method of claim 15 wherein limiting movement of the fluid column at the distal end of the catheter comprises stopping a distal flow through the catheter lumen and reapplying the vacuum through the catheter lumen ... before fluid is drawn back into the catheter lumen.

301. For the reasons discussed above for Ground 1, Claims [3-B] and [14-A], this limitation is met by Yang alone or in view of Mullins.

[17-B]: ...such that the positive amount of exit flow is approximately 0.1 ml to approximately 0.5 ml...

302. For the reasons discussed above for Ground 1, Claims [3-C] and [4-C], this limitation is met by Yang in view of Mullins and the knowledge of a POSA.

Claim 18

[18-A]: The method of claim 11, further comprising cyclically opening and closing the vacuum valve and the vent valve in a repeated cycle

303. For the reasons discussed above for Ground 1, Claims [1-E], this limitation is met by Yang alone or in view of Mullins.

[18-B]: including an off-off state in which the vacuum valve is closed while the vent valve is closed.

304. For the reasons discussed above for Ground 1, Claim [5-B], this limitation is met by Yang and the knowledge of a POSA.

Claim 19

[19-A]: The method of claim 11, further comprising: cyclically opening and closing the vacuum valve and the vent valve in a cycle including

305. For the reasons discussed above for Ground 1, Claims [1-E], this limitation is met by Yang alone or in view of Mullins.

[19-B]: (a) a first off-off state in which the vacuum valve is closed while the vent valve is closed, (b) a vacuum-only state following the first off-off state in which the vacuum valve is open while the vent valve is closed, (c) a second off-off state following the vacuum-only state in which the vacuum valve is closed while the vent valve is closed, and (d) a vent-only state following the second off-off state in which the vacuum valve is closed while the vent valve is open; and repeating the cycle.

306. For the reasons discussed above for Ground 1, Claim [6-B], this limitation is met by Yang and the knowledge of a POSA.

Claim 20

[20]: The method of claim 19 wherein the cycle is repeated at a frequency of 2 Hz to 12 Hz.

307. For the reasons discussed above for Ground 1, Claim [7], this limitation is met by Yang and the knowledge of a POSA.

B. Ground 2: Claims 5, 6, 18, and 19 Are Rendered Obvious Over Yang in View of Mullins, Rubenstein, and the Knowledge of a POSA

Motivation to Combine

308. A person of ordinary skill in the art at the time the purported invention of the '402 Patent was made would have been motivated to combine Yang and

Mullins' cyclical aspiration thrombectomy system with Rubenstein's teachings of: (1) a pumping system to eliminate clogs within the catheter; (2) applying cyclical reversals of positive and negative pressure in the catheter; and (3) transitioning between a vacuum suction state and a blowing, or positive pressure state when necessary using a time-controlled valve. The motivation to combine Yang and Mullins is discussed above at Ground 1 (Yang in view of Mullins and the knowledge of a POSA).

309. A POSA would have been motivated to combine Yang, Mullins, and Rubenstein because (1) all three references address similar problems related to conventional methods of medical aspiration procedures, including clogged catheters, and (2) all three references teach similar solutions involving using a positive pressure state to temporarily relieve the negative pressure within the system so as to more efficiently remove blood clots from the clogged catheter and ultimately the patient. As an example, all three references describe issues with catheter systems, such as clogged catheters and the limitations of static aspiration technologies for controlled clot aspiration. Ex. 1012 (Yang) at ¶¶ [0008]-[0009], [0085], [0148], [0166]; Ex. 1008 (Mullins) at 4:5-11, 25:22-26:16, 28:27-37; Ex. 1009.2 (Mullins-Prov2) at pg. 2-9; Ex. 1011 (Rubenstein) at 1:24-31, 2:1-12. The references describe similar approaches to solving these and other issues, including creating a dynamic force

within the catheter using a combination of vacuum and vent/pressure sources connected to a catheter via controllable valves. Ex. 1012 (Yang) at ¶¶ [0014], [0067], [0123]-[0128], [0131], [0135]-[0136], [0168]-[0170]; Ex. 1008 (Mullins) at 1:53-2:2, 3:29-4:11, 26:17-28:64; Ex. 1009.2 (Mullins-Prov2) at pg. 3-10; Ex. 1011 (Rubenstein) at Abstract, 1:7-14, 1:64-2:12.

310. A POSA would have understood that Yang, Mullins, and Rubenstein are each directed to medical aspiration systems and related methods using a source of both positive and negative pressure to clear clogged catheters via dynamic suction forces to more efficiently reinstate vacuum in a catheter after a clog. Ex. 1012 (Yang) at ¶¶ [0102], [0108], [0123]-[0128], [0131], [0135], [0168], [0170], Figs. 13-18; Ex. 1008 (Mullins) at 3:29-4:11, 26:17-28:64; Ex. 1009.2 (Mullins-Prov2) at pg. 2-10; Ex. 1011 (Rubenstein) at 1:7-14, 1:64-2:12. Accordingly, combining the teachings of Yang, Mullins, and Rubenstein would have been well within the skill of a POSA, because it is nothing more than combining known vacuum aspiration technologies described in these references to perform their intended functions with described benefits and predictable results. As discussed below in Ground 2, Claim [5-B], Rubenstein also shows it was typical to implement controllable valves in a vacuum/vent system such that there is a double-closed state where the catheter is temporarily isolated from both the vacuum and vent valves.

311. For at least these reasons, it would have been obvious to combine Yang, Mullins, and Rubenstein.

Claim 5

[5-A]: The system of claim 1 wherein the controller is configured to cyclically open and close the vacuum valve and the vent valve in a repeated cycle

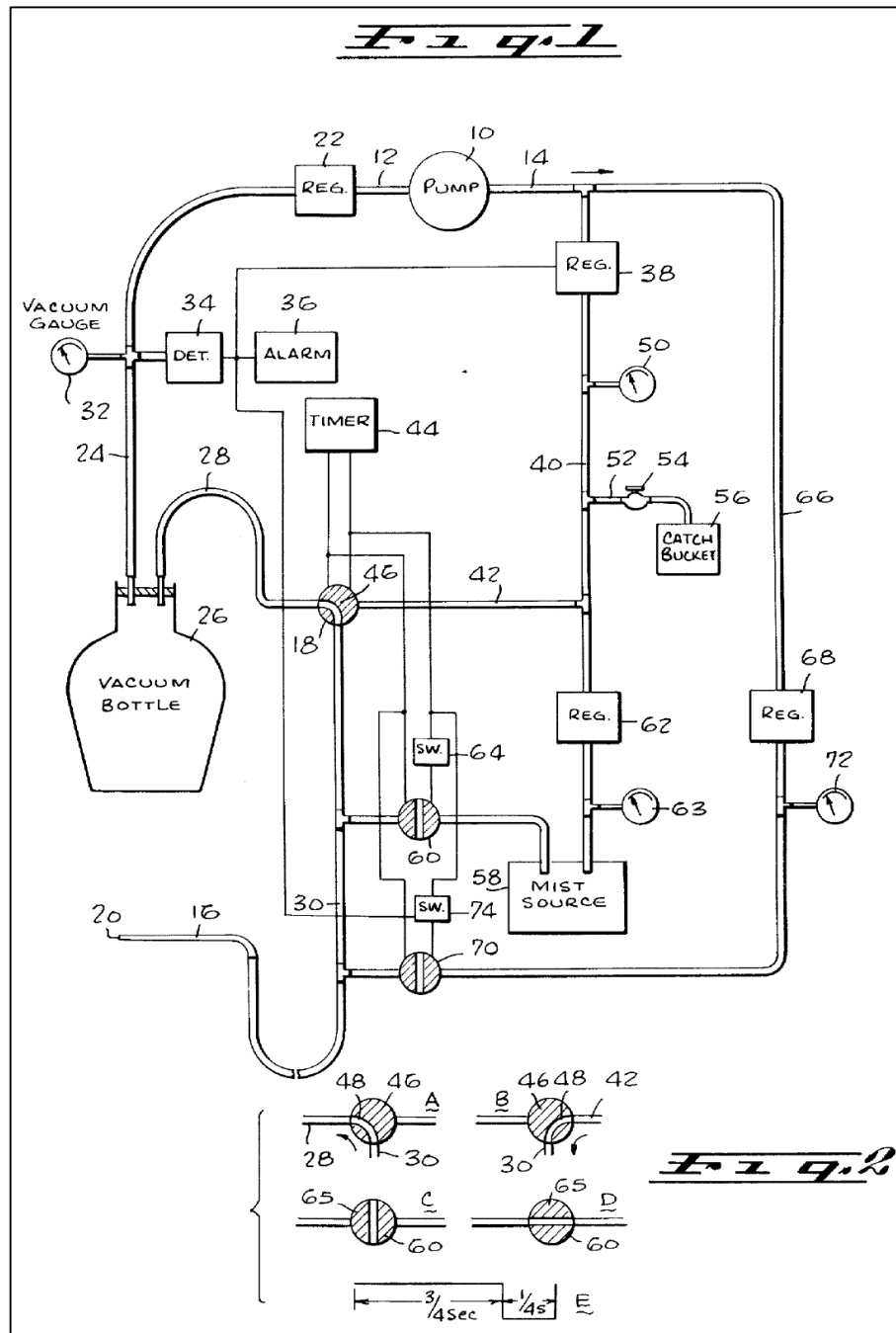
312. For the reasons discussed above for Ground 1, Claim 1 is disclosed or rendered obvious by Yang in view of Mullins, and therefore also met by Yang in view of Mullins and Rubenstein. In particular, for the reasons discussed above for Ground 1, Claim [1-E], this limitation is met by Yang in view of Mullins, and therefore also met by Yang in view of Mullins and Rubenstein.

[5-B]: comprising an off-off state in which the vacuum valve is closed while the vent valve is closed.

313. Yang in view of Mullins, Rubenstein, and the knowledge of a POSA renders obvious this limitation.

314. As discussed above for Ground 1, Claim [1-E], Yang alone or in view of Mullins discloses or renders obvious cyclically opening and closing the vacuum valve and the vent valve in a repeated cycle. As also discussed above for Ground 1, Claim [5-B], Yang and the knowledge of a POSA renders obvious an off-off state in which the vacuum valve is closed while the vent valve is closed. As discussed below, Rubenstein further renders this limitation obvious.

315. Rubenstein discloses a pumping system “used with catheters for drawing fluids and other viscous materials from a body, such as may be required for certain medical procedures.” Ex. 1011 (Rubenstein) at 1:7-14. Rubenstein further discloses that its invention provides “a pumping system wherein cyclical reversals of pumping pressure are applied to the catheter connected thereto to have negative and positive pressure cyclically alternated” to “have the flow of fluid through a catheter cyclically reversed and thereby self-cleaning.” Ex. 1011 (Rubenstein) at 1:10-14, 1:64-68.



316. As shown in figures 1 and 2, Rubenstein discloses “a suction system which allows a mist of detergent, enzymatic fluid, or other fluids to be controllably ejected through the catheter to dissolve viscous materials such as phlegm to facilitate

the suction thereof.” Ex. 1011 (Rubenstein) at 1:51-61. Rubenstein further discloses “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 fluid flow therethrough,” and “[a] source of mist is connected to allow controlled injection of detergent or enzymatic fluid through the catheter.” Ex. 1011 (Rubenstein) at 2:1-8.

317. Rubenstein further discloses that “[t]he 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.” Ex. 1011 (Rubenstein) at 2:28-31. When a catheter becomes clogged, Rubenstein discloses that “[p]ositive 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. Position control or switching of the valve 18 may be readily accomplished by use of a timer 44 having any conventional design.” Ex. 1011 (Rubenstein) at 2:56-64. A POSA would have understood the use of valve 18 to deliver both the negative and positive pressure to be a disclosure of a single valve.

318. In another embodiment, Rubenstein discloses the use of separate vacuum and vent valves. Rubenstein explains that “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.” Ex. 1011 (Rubenstein) at 4:2-8. As shown in 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.” Ex. 1011 (Rubenstein) at 3:21-36. Rubenstein further discloses that “diagram C illustrates a movable plug 65 as being positioned to prohibit fluid flow through valve 60. By comparison, diagram D illustrates the movable plug 65 as being positioned to allow fluid flow through the valve 60.” Ex. 1011 (Rubenstein) at 4:17-23.

319. Rubenstein further discloses that both of the valves are “connected to be controlled by the timer 44 when electrically connected thereto via a switch 64.” Ex. 1011 (Rubenstein) at 4:24-26. Referring to the vent valve, Rubenstein explains: “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 timer 44 must be adjusted to vary the ratio of times during which negative and positive pressures are applied from the pump 10 such that the net outflow rather than inflow, i.e., suction, occurs through the catheter 16.” Ex. 1011 (Rubenstein) at 4:24-35. A POSA would have understood the mist source valve and the suction valve to be a vent valve and vacuum valve respectively. Rubenstein further explains that “suction periods of three-fourths of a second interrupted by blowing periods of one-fourth of a second as illustrated by waveform E of FIG. 2, is highly effective to have net suction accomplished by the suction unit using a vacuum of approximately twenty inches of mercury and a positive pressure of five pounds per square inch.” Ex. 1011 (Rubenstein) at 3:41-50.

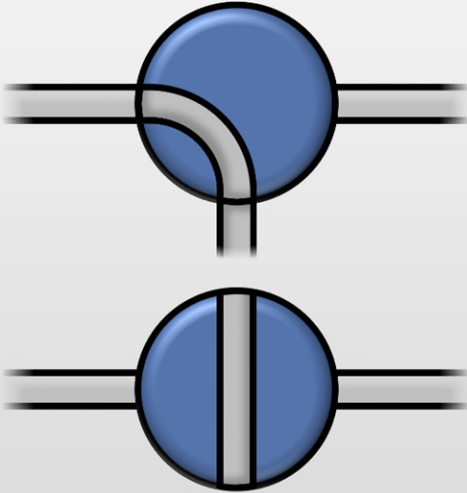
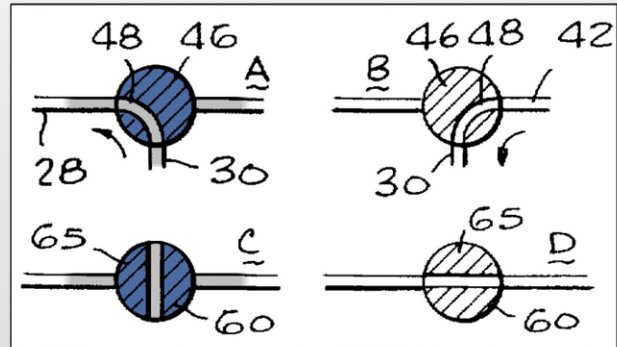
320. A POSA would find it obvious that Rubenstein discloses a double-closed state. In Rubenstein’s system, “cyclical reversals of pumping pressure are applied to the catheter connected thereto to have negative and positive pressure cyclically alternated.” Ex. 1011 at 1:10-14. As explained below, Rubenstein discloses a rotary valve 46/18 which may be rotated between a first position (FIG. 2A) in which the catheter is fluidically connected with a vacuum line to provide a negative pressure in the catheter, to a second position (FIG. 2B), in which the

vacuum line is disconnected from the catheter. Ex. 1011 (Rubenstein) at FIGs. 1, 2. Similarly, Rubenstein discloses a rotary valve 60 which may be rotated between a first position (FIG. 2C) in which a fluid line is disconnected from the catheter, to a second position (FIG. 2D) in which the catheter is fluidically connected with the fluid line to reduce the negative pressure in the catheter. Ex. 1011 (Rubenstein) at FIGs. 1, 2.

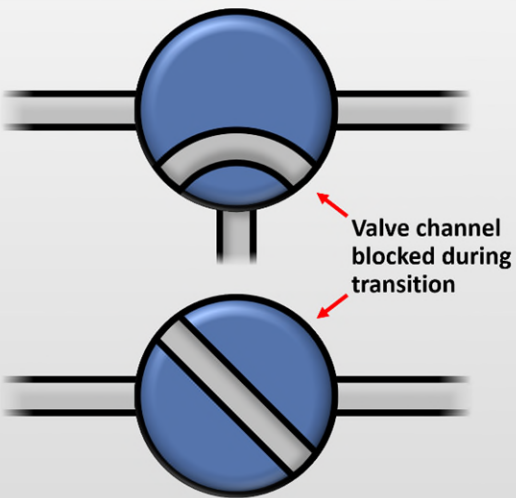
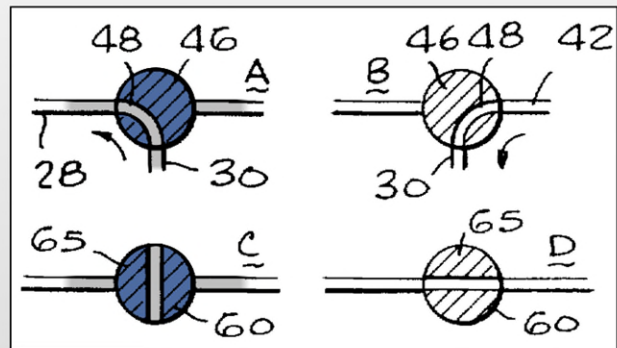
321. Rubenstein explicitly describes the operation and rotational transition of these valves: “The valve 18 simply may involve a movable plug 46 having a connecting channel 48 and which is **alternately rotated** under the control of the timer 44 to have the channel 48 connect the tubing 30 to either the tubing 28 or the tubing 42... 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.” Ex. 1011 (Rubenstein) at 3:21-36.

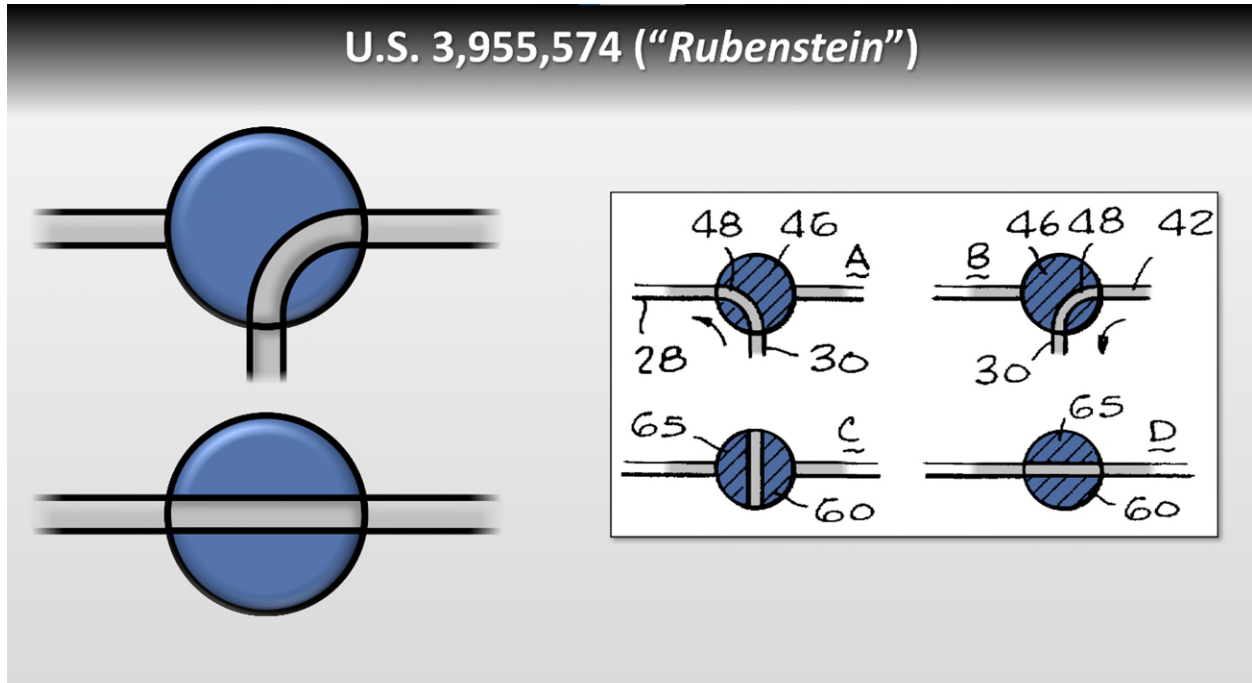
322. Rubenstein also explains: “The valve 60 **may be of the same type** as the valve 46.... Referring to FIG. 2, diagram C illustrates a movable plug 65 as being positioned to prohibit fluid flow through the valve 60. By comparison, diagram D illustrates the movable plug 65 as being positioned to allow fluid flow through the valve 60.” Ex. 1011 (Rubenstein) at 3:21-36.

U.S. 3,955,574 ("Rubenstein")



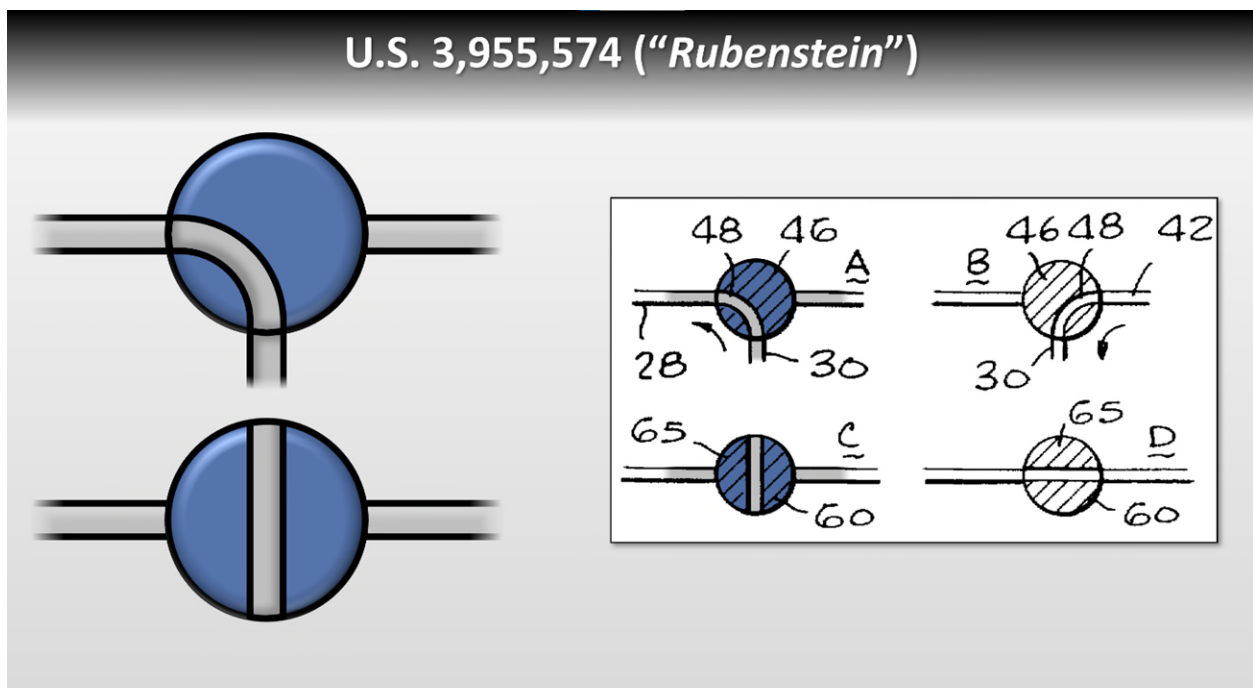
U.S. 3,955,574 ("Rubenstein")



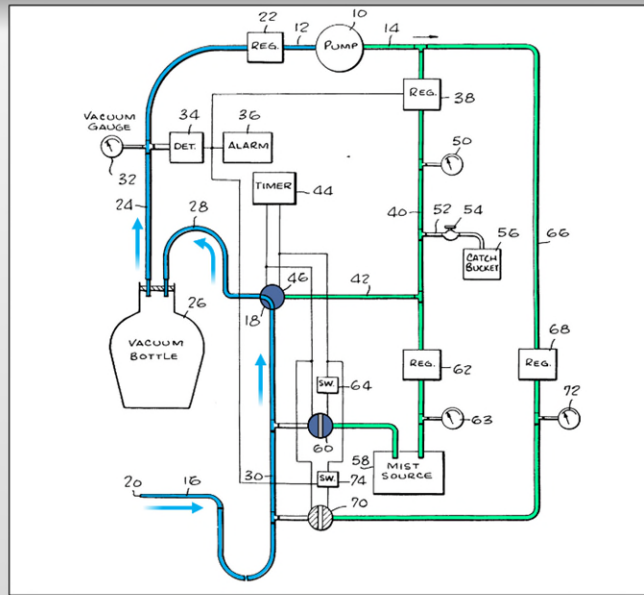


323. A POSA would find it obvious that Rubenstein's **rotary valves** must actually **rotate** between their different positions, and that it would be impossible for rotary valves to make an instantaneous transition that does not include any delay time, otherwise it would be contrary to basic physics and common sense. It is well-known, and explained in Rubenstein, that a rotary valve functions by rotating a connecting channel to different locations in order to connect and/or disconnect channels attached to the valve. Ex. 1011 (Rubenstein) at 3:21-26. Given the finite distance between the different positions, it requires a finite time period for the valve to rotate between different positions, which therefore, by definition, not instantaneous.

324. Rubenstein's rotary valves are in a double-closed state when they are rotating between the positions where the connecting channels are aligned to fluid and vacuum channels, as illustrated in the annotated diagrams of Rubenstein's system provided herein. Consistent with the disclosure of Rubenstein discussed above, the rotary valves begin in a first position "A" and "C," respectively, in which the catheter is connected through a connecting channel 48 of valve 46/18⁴ to the vacuum, but disconnected from the fluid line, which is closed off by valve 60:



⁴ Figure 2 of Rubenstein does not identify the valve numbering 18, but instead illustrates components of valve 18 including "a movable plug 46 having a connecting channel 48." Ex. 1011 at 3:21-26.

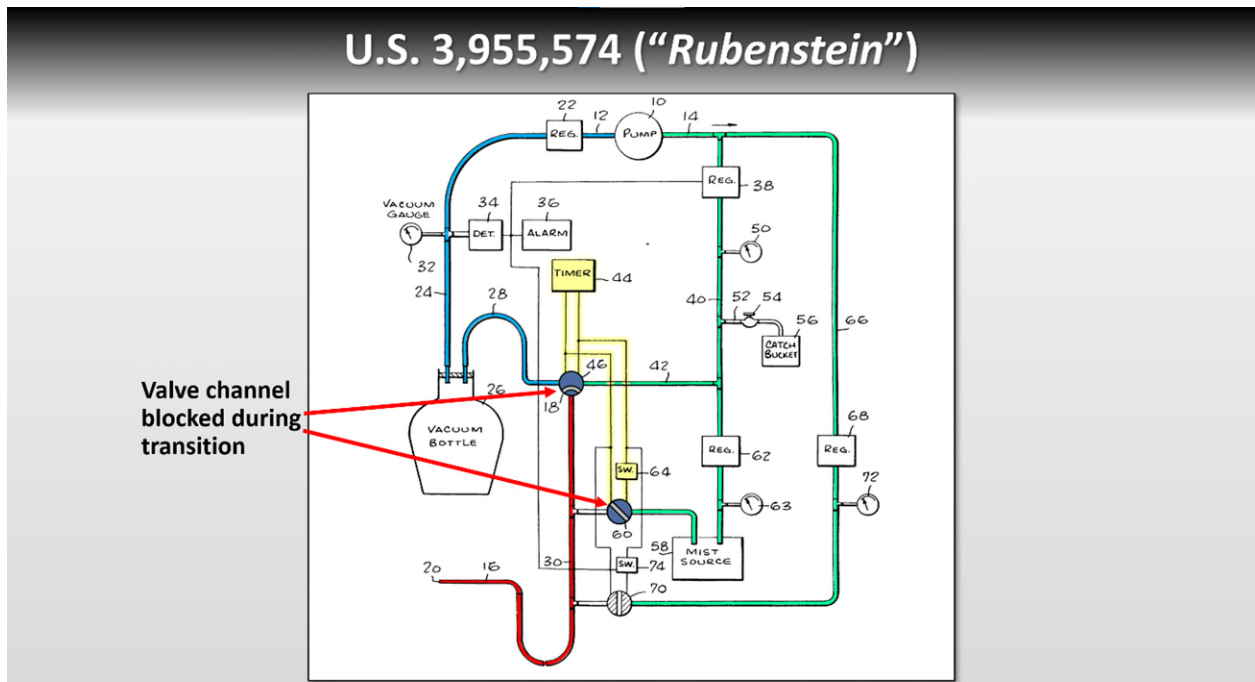


325. The Rubenstein system then rotates connecting channels in valves 46/18 and 60 from their first position towards a second position. A POSA would understand that during this transition, the connecting channels are not aligned with either the vacuum or fluid line, and are therefore in a double-closed state, as illustrated below.

U.S. 3,955,574 ("Rubenstein")

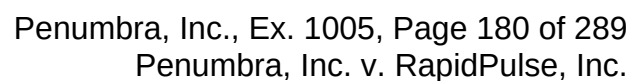
The diagram illustrates a valve mechanism in two states. The top state shows a blue spherical valve with a grey channel. A red arrow points to the channel with the text "Valve channel blocked during transition". The bottom state shows the same valve with a diagonal grey line across it, indicating a different configuration or transition.

Four cross-sectional views of a valve mechanism are shown, labeled A, B, C, and D. Each view shows a blue spherical valve with a grey channel. The views are labeled with numbers: 48, 46, 28, 30, 65, 60, 42, and 30. View A shows the valve in a closed position. View B shows the valve in an open position. View C shows the valve in a closed position. View D shows the valve in an open position.



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U.S. 3,955,574 (“Rubenstein”)



327. Therefore, a POSA would understand that Rubenstein discloses and/or renders obvious a “double-closed state” while the rotary valves are rotating between their first and second positions.

328. Further, a POSA would find it obvious to modify the system in Yang to adopt the valves disclosed in Rubenstein, which would result in a double-closed state during serial or parallel operation of the incorporated valves. A POSA would also find it obvious to employ Rubenstein’s time-controlled valve opening and closing because Rubenstein notes that “any cycle and ratio of negative and positive pressure can be used to satisfy a particular need” which would invite a POSA to optimize the positive and negative pressure system in Rubenstein to achieve optimal clot aspiration within the Yang system. Ex. 1011 (Rubenstein) at 3:41-50; *see also id.* at 2:64-68 (disclosing certain example rotary valves that can be automated).

329. Thus, consistent with the serial operation of Yang’s valve states, a POSA would have understood, and it would be most logical and obvious to conduct the valve operation in serial to yield effective pulsing, e.g., closing the vacuum valve first and then opening the vent valve to generate the positive pulse. Rubenstein similarly discloses such serial operations of vacuum and vent valves that a POSA would readily and easily adopt for dynamic aspiration taught by Yang and Mullins. Ex. 1012 (Yang) at ¶¶ [0102], [0108], [0168], [0170], FIGs. 13, 14, 25(a)-(c); Ex.

1008 (Mullins) at 3:48-59, 4:5-11, 27:54-57, 26:65-27:39, 27:54-65, FIGs. 46, 47(a)-47(n), 49; Ex. 1009.2 (Mullins-Prov2) at pg. 3-10, FIGs. 3-8; Ex. 1011 (Rubenstein) at 1:10-14, 1:64-68. Alternatively, a POSA could also adopt the valves disclosed in Rubenstein to accomplish the dynamic aspiration taught by Yang and Mullins including an off-off state in which the vacuum valve is closed while the vent valve is closed.

330. I also understand that to be used in a prior art combination, a reference may need to be regarded based on certain factors including: (1) whether it can be considered to be in the same field of endeavor as the challenged patent, and (2) whether it can be considered to be reasonably pertinent to the problem faced by the inventors of the challenged patent. It is my opinion that Rubinstein is in the same field of endeavor as the '402 Patent at least because the '402 Patent expressly discloses that its catheter system “can be coupled with conventional aspiration catheters to significantly increase the efficacy of such catheter and pump systems,” and because Rubenstein specifically “relates to pumping systems that are used with catheters for drawing fluids and other viscous materials from a body,” which “is a conventional medical procedure.” Ex. 1001 at 3:46-50; Ex. 1011 (Rubenstein) at 1:6-18.

331. It is further my opinion that Rubenstein is reasonably pertinent to the problem faced by the inventors of the '402 Patent, at least because the '402 Patent's stated goal is "to overcome the problems with the prior art systems, designs, and processes as discussed above," including: "During conventional aspirations, it is common... at the distal opening of the aspiration catheter, a condition that can be referred to as clogged or clogging." Ex. 1001 at 2:12-19, 3:21-22. Rubenstein similarly addresses "[t]he problem of clogging and traumatic injury... to be solved by the design and use of catheters," explaining that "[p]rior art suction units presently in use essentially involve a catheter to which is connected a suction pump for applying negative pressure thereto... As may be expected, the tip of the catheter frequently becomes clogged." Ex. 1011 (Rubenstein) at 1:19-38.

332. Thus, it is my opinion that Rubenstein is in the same field of endeavor as the '402 Patent, and is at least reasonably pertinent to the particular problem with which the inventor faced because it describes issues with clogged catheters and using alternative cycling of negative and positive pressure to overcome these problems. Ex. 1011 (Rubenstein) at 1:10-14, 1:26-27, 1:64-68.

333. Therefore, it is my opinion that Yang in view of Mullins and Rubenstein renders obvious "an off-off state in which the vacuum valve is closed while the vent valve is closed," as recited by Claim 5.

Claim 6

[6-A]: The system of claim 1 wherein: the controller is configured to cyclically open and close the vacuum valve and the vent valve in a cycle comprising

334. For the reasons discussed above for Ground 1, Claim [1-E], this limitation is met by Yang in view of Mullins, and therefore also met by Yang in view of Mullins and Rubenstein.

[6-B]: (a) a first off-off state in which the vacuum valve is closed while the vent valve is closed, (b) a vacuum-only state following the first off-off state in which the vacuum valve is open while the vent valve is closed, (c) a second off-off state following the vacuum-only state in which the vacuum valve is closed while the vent valve is closed, and (d) a vent-only state following the second off-off state in which the vacuum valve is closed while the vent valve is open; and the cycle is repeated.

335. For the reasons discussed above for Ground 1, Claims [5-B] and [6-B], this limitation is met by Yang and the knowledge of a POSA, and therefore also met by Yang in view of Mullins and Rubenstein and the knowledge of a POSA. Additionally, in view of the reasons discussed above for Ground 2, Claim [5-B], with regard to the double-closed state that is further rendered obvious by Rubenstein, this limitation is also further rendered obvious by Rubenstein.

Claim 18

[18-A]: The method of claim 11, further comprising cyclically opening and closing the vacuum valve and the vent valve in a repeated cycle

336. For the reasons discussed above for Ground 1, Claim [1-E], this limitation is met by Yang in view of Mullins, and therefore also met by Yang in view of Mullins and Rubenstein.

[18-B]: including an off-off state in which the vacuum valve is closed while the vent valve is closed.

337. For the reasons discussed above for Ground 1, Claim [5-B], this limitation is met by Yang in view of Mullins, and therefore also met by Yang in view of Mullins and Rubenstein. Additionally, in view of the reasons discussed above for Ground 2, Claim [5-B], with regard to the double-closed state that is further rendered obvious by Rubenstein, this limitation is also further rendered obvious by Rubenstein.

Claim 19

[19-A]: The method of claim 11, further comprising: cyclically opening and closing the vacuum valve and the vent valve in a cycle including

338. For the reasons discussed above for Ground 1, Claim [1-E], this limitation is met by Yang in view of Mullins, and therefore also met by Yang in view of Mullins and Rubenstein.

[19-B]: (a) a first off-off state in which the vacuum valve is closed while the vent valve is closed, (b) a vacuum-only state following the first off-off state in which the vacuum valve is open while the vent valve is closed, (c) a second off-off state following the vacuum-only state in which the vacuum valve is closed while the vent valve is closed, and (d) a vent-only state following the second off-off state in which the vacuum valve is closed while the vent valve is open; and repeating the cycle.

339. For the reasons discussed above for Ground 1, Claims [5-B] and [6-B], this limitation is met by Yang and the knowledge of a POSA, and therefore also met by Yang in view of Mullins and Rubenstein and the knowledge of a POSA. Additionally, in view of the reasons discussed above for Ground 2, Claims [5-B] and [6-B], with regard to the double-closed state that is further rendered obvious by Rubenstein, this limitation is also further rendered obvious by Rubenstein.

C. Ground 3: Claim 9 Is Rendered Obvious Over Yang in View of Mullins, Matteo, and the Knowledge of a POSA

Motivation to Combine

340. A person of ordinary skill in the art at the time the purported invention of the '402 Patent was made would have been motivated to combine Yang's and Mullins's cyclical aspiration thrombectomy system with Matteo's cam system for valve control. The motivation to combine Yang and Mullins is discussed above at Ground 1 (Yang in view of Mullins and the knowledge of a POSA).

341. A POSA would have been motivated to combine Yang, Mullins, and Matteo because (1) all three references address similar problems related to the precise combination of multiple fluids at precise times in scientific and medical applications, and (2) all three references teach similar solutions involving using multiple flow control mechanisms (e.g., valves or pumps) to separate and combine the fluids to achieve desired results. Ex. 1012 (Yang) at ¶¶ [0102], [0108], [0170], FIGs. 13, 14, 25(a)-(c); Ex. 1008 (Mullins) at 26:31-37, 26:65-27:39; Ex. 1009.2 (Mullins-Prov2) at pg. 3-10; Ex. 1013 (Matteo) at ¶ [0059], FIGS. 10A-C. As an example, all three references describe similar approaches to solving these and other issues, including using a controller to control flow control mechanisms (e.g., valves or pumps) that can be switched between varying states of open and closed positions. Ex. 1012 (Yang) at ¶ [0170], FIGs. 13, 14, 25(a)-(c); *See* Ex. 1008 (Mullins) at 26:65-27:39; Ex. 1009.2 (Mullins-Prov2) at pg. 3-10; Ex. 1013 (Matteo) at FIGS.10A-C.

342. A POSA would have understood that all three references are each directed to systems and related methods that rely on precise timing and pressures of fluid to enter the system via open valves, using controlled valves to introduce fluid into the system that provide energy efficiencies and control over fluid introductions. Accordingly, combining the teachings of Yang, Mullins, and Matteo would have

been well within the skill of a POSA, because it is nothing more than combining known vacuum aspiration technologies described in Yang and Mullins with known controlled valve systems described in Matteo to perform their intended functions with described benefits and predictable results.

343. A POSA would find it obvious to implement Matteo's disclosures of cam-driven pinch valves that optimize the introduction of fluid when implementing the combination of Yang and Mullins, because a POSA would recognize that Matteo's cam-driven pinch valves were a well-understood and effective technique to implement a valve having the necessary timing precision to implement the techniques taught in Yang and Mullins, while also providing benefits of reduced complexity and space-savings, as disclosed in Matteo. Ex. 1013 (Matteo) at Abstract. It would have been well within the skill of a POSA to utilize any type of suitable valves as vacuum and vent valves in the systems of Yang and Mullins, including cam-driven pinch valves, as disclosed in Matteo. Additionally, Matteo explains that "Cam-driven pinch-style microvalves are useful for controlling multi-channel microfluidic systems with an energy-efficient and space-efficient apparatus. Thus, these microvalves have uses in a number of diverse fields and applications, including medical and scientific instrumentation," which a POSA would understand

includes the medical systems taught in Yang and Mullins Ex. 1013 (Matteo) at ¶ [0012].

344. A POSA would have recognized that the aspiration systems of Yang and Mullins could be modified such that the vacuum and vent valves could be cam-driven pinch valves, and would have a reasonable expectation of success in implementing this combination, because it would simply be using widely known shaft and cam actuator technology to control valves, as disclosed in Matteo, within the aspiration systems of Yang and Mullins. Ex. 1013 (Matteo) at Claim 1.

345. For at least these reasons, it would have been obvious to combine Yang, Mullins, and Matteo.

Claim 9

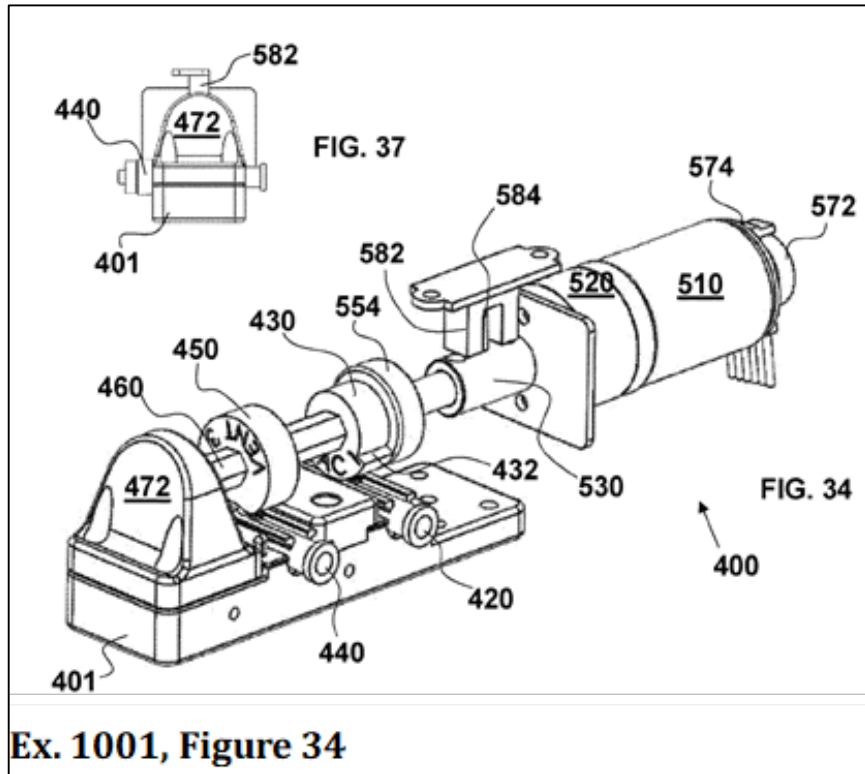
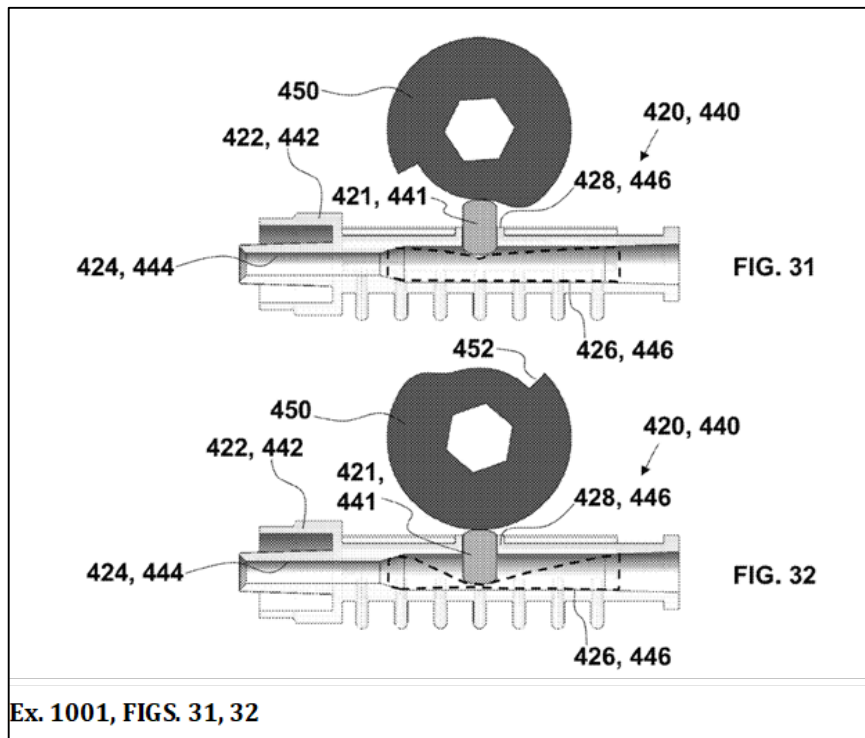
[9]: The system of claim 1 wherein the vacuum valve and the vent valve are cammed pinch valves.

346. Yang in view of Mullins and Matteo renders obvious this limitation.

347. For the reasons discussed above for Ground 1, Claim 1 is disclosed or rendered obvious by Yang in view of Mullins, and therefore also met by Yang in view of Mullins and Matteo.

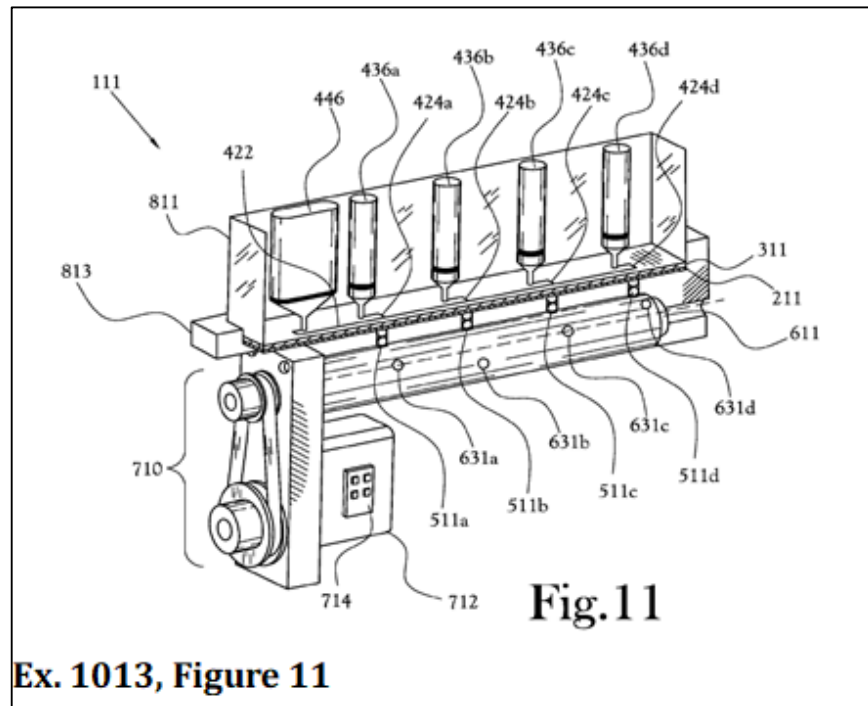
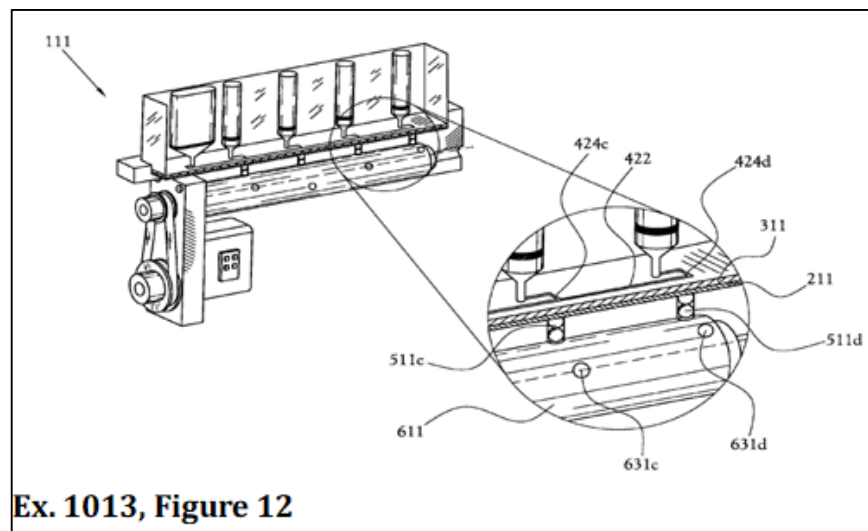
348. To the extent that Yang and Mullins do not explicitly disclose the vacuum and vent valves being cammed pinch valves, the combination of Yang, Mullins, and Matteo renders this claim limitation obvious.

349. In the '402 Patent, one embodiment describes cam-actuated vacuum and vent valves that share a cam shaft to operate “an automatic, rapid, and repeated onset of pressure change.” Ex. 1001 ('402 Patent) at 34:19-25. A pair of pinch valves, 420 and 440, as shown in Fig. 34 below, respectively control the vacuum flow and vent flow through the aspiration system. Ex. 1001 ('402 Patent) at 34:25-29. The '402 Patent discloses that the valves are mounted onto a base 401 and are “operatively associated with” respective cams, “a vacuum cam 430 and a vent cam 450,” which are “connected to a cam shaft 460.” Ex. 1001 ('402 Patent) at 34:49-57. The '402 Patent further discloses that the cam shaft is connected to a “drive shaft assembly 500” comprising “a motor 510, a transmission or gear box 520, a shaft coupler 530, and a motor controller assembly 550.” Ex. 1001 ('402 Patent) at 24:56-60. The '402 Patent explains that the “rotation of the motor 510 corresponds to a rotation...of the cam shaft 460 with a corresponding rotation of the vacuum and vent cams 430, 450.” Ex. 1001 ('402 Patent) at 34:65-35:2. The '402 Patent further explains, “the vacuum and vent cams 430, 450 are fixed rotationally to the cam shaft 460” and “these cams 430, 450 have various cam profiles to operate the valves 420, 440.” Ex. 1001 ('402 Patent) at 35:27-29.



350. In the '402 Patent, as shown in Figs. 31 and 32 above, “[i]n operation, the vacuum cam 430 and vent the cam 450 push down on the respective cam followers 421, [441,] which pinch down on the short sections of tubing 426, 446 [contained within the respective valve bodies], each respectively fluidically connected to the vacuum line 402 and the vent line 404,” to close the respective vacuum and vent valves and thereby control the flow through those valves. Ex. 1001 ('402 Patent) at 36:27-37:2.

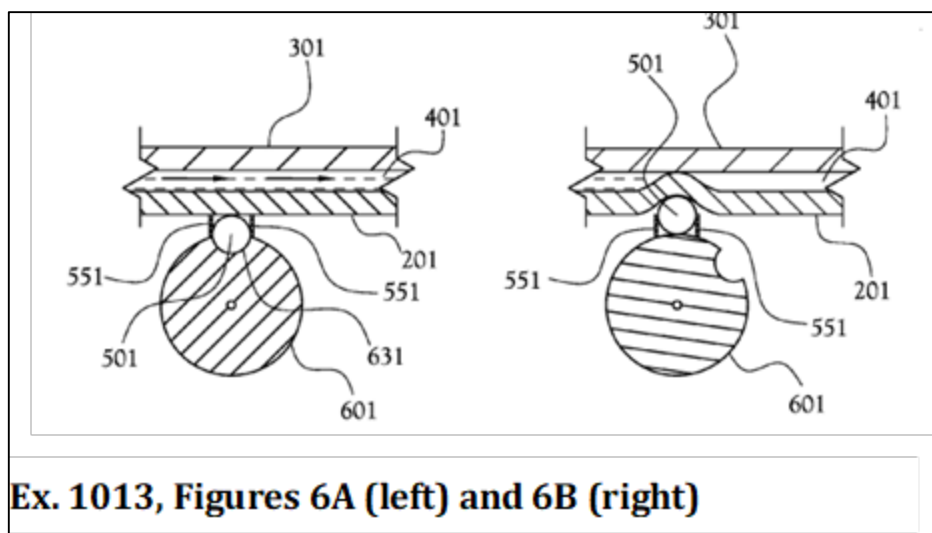
351. Matteo discloses a microfluidics system “to control multiple microvalves” for use in a variety of chemical, biological, and biomedical applications, including “medical and scientific instrumentation.” Ex. 1013 (Matteo) at Abs., ¶¶ [0006], [0012]. An exemplary embodiment of the system with “one cylindrical cam controlling several actuator balls and several microvalves” is shown below in Figures 11 and 12. Ex. 1013 (Matteo) at ¶ [0029], FIGS. 11, 12. Matteo further discloses that “[c]am driven pinch-style microvalves are useful for serving as on/off valves for devices for a microfluidic system.” Ex. 1013 (Matteo) at ¶ [0010].



352. Matteo discloses that “a cam-driven actuator [501] activates a microvalve by pressing on the elastomeric layer [201], deforming the elastomeric layer so that it meets a second layer [301] at a location within the channel [401] thereby either partially or completely obstructing the flow of liquid through the

channel [401] at that location, i.e. ‘pinching’ the channel.” Ex. 1013 (Matteo) at Abs., [0009], [0045], [0047]. Conversely, “when the microvalve 101 is in the open state,” as shown in Fig. 6A, “fluid flows through the channel 401.” Ex. 1013 (Matteo) at ¶ [0047]. Matteo illustrates this in Figs. 6A, and 6B below, where 6A illustrates the microvalve in an open state, and 6B illustrates the microvalve in a closed state. Ex. 1013 (Matteo) at ¶ [0045].

353. Matteo further discloses that the “position-control mechanism (PCM) 701 controls the cam 601 by turning the axle 651, thereby turning the cylindrical cam 601.” Ex. 1013 (Matteo) at ¶ [0045], FIGS. 3, 11, 12. Matteo explains that “cam 601...is a cylindrical cam; rotation of the cylinder moves a detent 631 on the cylinder into and out of position under the actuator ball 501.” Ex. 1013 (Matteo) at ¶ [0045], FIGS 3, 6A, 6B.



Ex. 1013, Figures 6A (left) and 6B (right)

354. Therefore, it is my opinion that Yang in view of Mullins and Matteo renders claim 9 obvious.

D. Ground 4: Claims 1-8 and 10-20 are Rendered Obvious Over Ofek in view of Mullins and the Knowledge of a POSA

Motivation to Combine

355. A POSA at the time the purported invention of the '402 Patent was made would have been motivated to combine Ofek's aspiration thrombectomy system with Mullin's teachings of: (1) explicit discussion of utilizing different cycles of negative and positive pressure to change pressure and control loading and unloading of a clot at the distal end of the catheter; and (2) further optimization of momentum and unsticking of a thrombus, including, for example, the optimization of cycle frequencies.

356. A POSA would have been motivated to combine Ofek and Mullins because (1) both references address similar problems related to conventional methods of aspiration thrombectomy, and share the common objective of improving the efficiency of removing blood clots, particularly around clogged catheters and (2) both references teach similar solutions involving utilizing both positive and negative pressure, in a cyclic fashion, to aid in the aspiration of a clot. Ex. 1007 (Ofek) at 3:43-60, 4:21-5:7, 5:63-6:8, 6:20-45, 7:18-26; Ex. 1008 (Mullins) at 3:29-4:11, 26:17-27:67; Ex. 1009.2 (Mullins-Prov2) at pg. 3-10. As an example, both

references describe utilizing positive pressure impulse coupled with additional periods of negative pressure to aid in the aspiration of a clot of thrombus by ensuring the aspiration lumen does not get clogged. Ex. 1007 (Ofek) at 2:56-3:2, 3:30-42, 4:21-44, 5:63-6:45, 8:38-49. FIGs. 2, 3; Ex. 1008 (Mullins) at 3:29-4:11, 26:17-27:67, FIGs. 46-49; Ex. 1009.2 (Mullins-Prov2) at pg. 3-10.

357. The references describe similar approaches to solving these and other issues, such as utilizing a cycle of negative and positive pressure to aid in clot aspiration and prevent catheter obstruction by the thrombus. Ex. 1007 (Ofek) at 2:56-3:2, 3:30-42, 4:21-5:7, 5:63-6:8, 6:20-45, 8:38-49. FIGs. 2, 3; Ex. 1008 (Mullins) at 1:53-2:2, 3:29-4:11, 26:17-28:64, FIGs. 46-49. Ex. 1009.2 (Mullins-Prov2) at pg. 3-10.

358. A POSA would understand that Ofek and Mullins are each directed to a cyclical aspiration thrombectomy system and related methods using a source of both positive and negative pressure to subject a blood clot to dynamic suction forces and more efficiently aspirate blood clots. Ex. 1007 (Ofek) at 2:56-3:2, 3:30-42, 4:21-44, 5:63-6:8, 6:20-45, 8:38-49. FIGs. 2, 3; Ex. 1008 (Mullins) at 3:29-4:11, 26:17-28:64, FIGs. 46-49; Ex. 1009.2 (Mullins-Prov2) at pg. 3-10. Accordingly, combining the teachings of Ofek and Mullins would have been well known within the skill of a POSA, because it is nothing more than combining known aspiration

technologies described in these references to perform their intended functions with described benefits and predictable results.

359. A POSA would find it obvious to implement Mullins' disclosures of forward flow and improvements in unsticking clots to modify Ofek's system, which includes a catheter aspiration system that is ready for improvement by Mullins's techniques for efficient and effective cyclical aspiration of blood clots. Ex. 1007 (Ofek) at 4:45-5:7, 7:18-26, FIGs. 3, 5; Ex. 1008 (Mullins) at 3:29-4:11, 26:17-28:64, FIGs. 46-49; Ex. 1009.2 (Mullins-Prov2) at pg. 3-10. The methods of cyclical pressure changes described by Mullins are consistent with and improve on the aspiration cycles that Ofek discloses to provide effective cyclical aspiration thrombectomy, including, for example, Ofek's short-duration high pressure impulses used to clear the lumen. Ex. 1007 (Ofek) at 2:56-3:2, 3:30-4:6, 6:9-19; Ex. 1008 (Mullins) at 3:29-4:11, 26:17-28:64; Ex. 1009.2 (Mullins-Prov2) at pg. 2-10.

360. Mullins' methods to change a level of vacuum at the distal end of the catheter are similar to, if not the same as, the pressure profiles alternating between positive pressure impulses and negative pressures described by Ofek. A POSA would have had a reasonable expectation of success in implementing this combination, because any modification, if necessary, would simply add additional control logic from Mullins' system for modulating the pressures contained within

the aspiration system, in accordance with the pressure profiles and functionality as taught in Ofek. Because Ofek's system is already computer-controlled via the controller that operates the system and valves in Ofek, and that Ofek's controller expressly "enables customization of the characteristics of the impulses, rest periods, baseline pressure, etc. by the user," it would have been well within the level of skill in the art to modify the logic of Ofek's controller to implement Mullins's teachings, if necessary, or incorporate known mechanical components, if needed. Ex. 1007 (Ofek) at 6:59-63.

361. A POSA would also find it obvious to implement monitoring the level of vacuum pressure change at the distal end of the aspiration catheter contemplated by Mullins within Ofek's aspiration system. Consistent with Ofek's use of a pressure transducer to measure pressure of the catheter, monitoring pressure inside the aspiration catheter and vacuum system was a known concept that was used to improve the knowledge available to clinicians about the ongoing aspiration procedure and allow for more effective aspiration techniques, including repositioning the catheter or utilizing procedures to remove an obstruction, based on the pressure inside the system. Mullins discloses that a lumen pressure sensor and a controller can be used to monitor the pressure in the system, and builds on the concept of altering vacuum pressure levels by utilizing a pressure sensor. Ex. 1008

(Mullins) at 3:29-59, 6:34-36, 26:31-37; Ex. 1009.2 (Mullins-Prov2) at pg. 2-10. A POSA would have recognized the benefit of controlling the vacuum pressure levels and fluid flow at the distal tip of the catheter, as disclosed in Mullins, in the context of Ofek, which also includes a pressure transducer, and it would have been trivial to implement these within Ofek's aspiration thrombectomy system.

362. For at least these reasons, it would have been obvious to combine Ofek and Mullins.

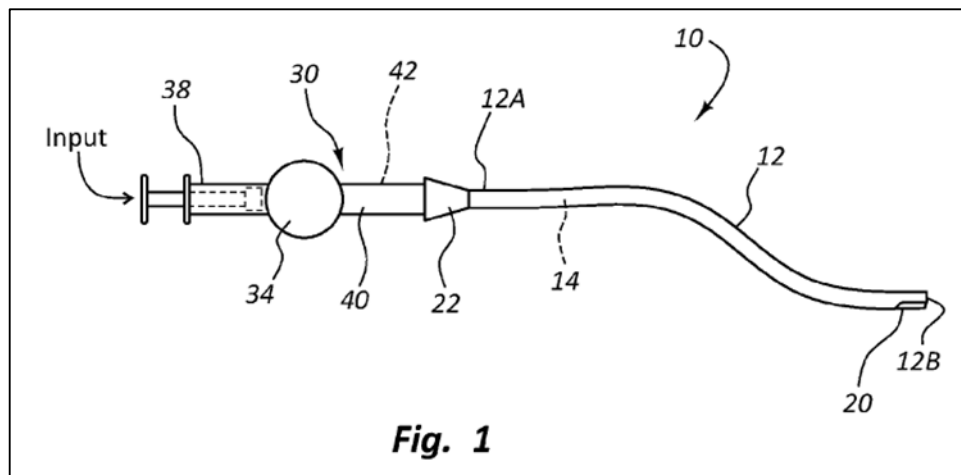
Claim 1

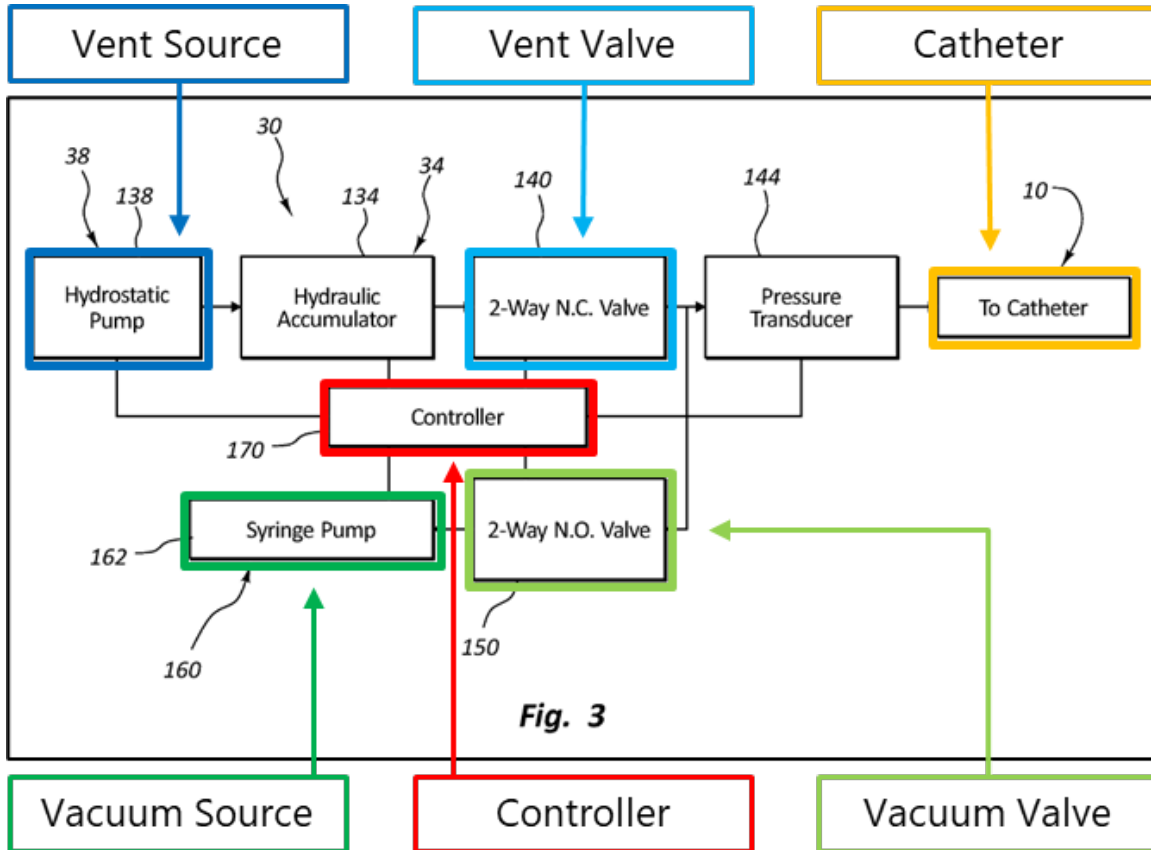
[1-Pre]: An aspiration thrombectomy system, comprising:

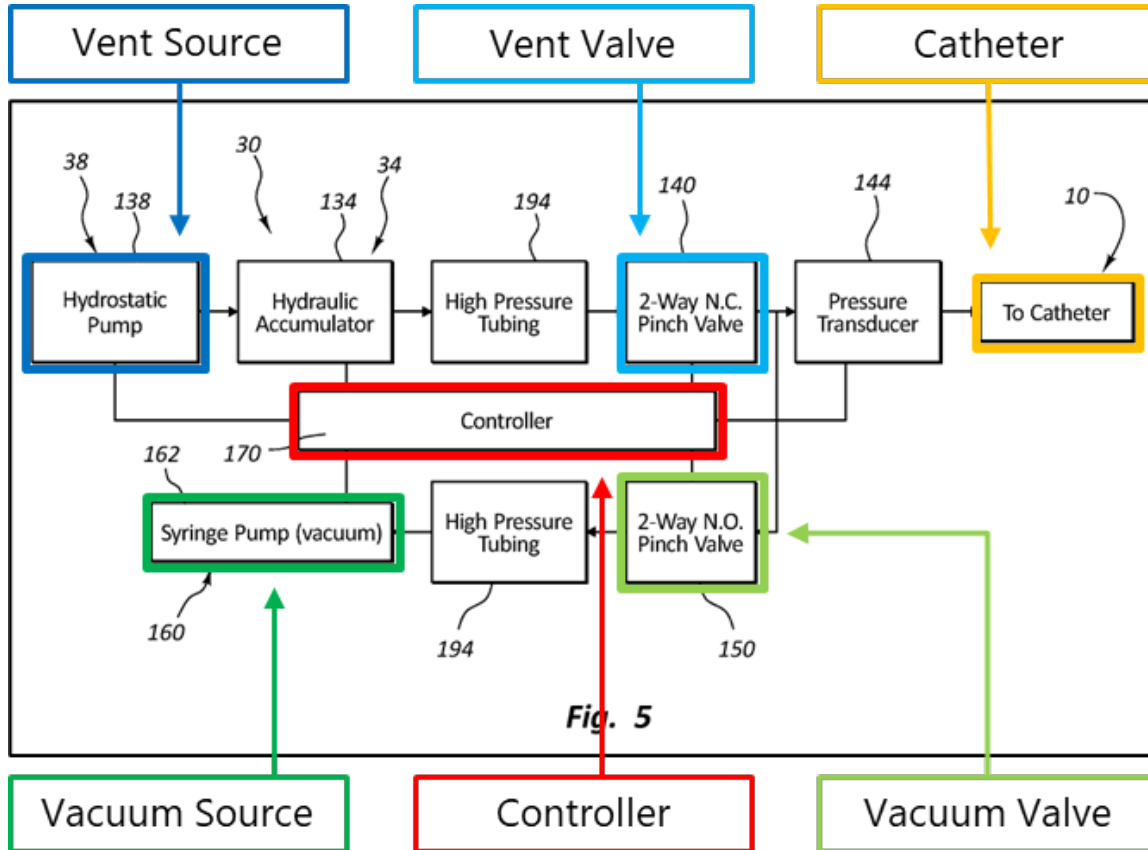
363. To the extent the preamble is limiting, Ofek alone or in view of Mullins discloses or renders obvious this limitation.

364. Ofek discloses a patency device for catheter assemblies that can aspirate occlusions and remove the occlusions from the catheter assembly. Ex. 1007 (Ofek) at 1:16-33 ("embodiments of the present invention are directed to a patency device for catheter assemblies... used for establishing access to an interior body portion of a patient. The patency device establishes [] 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 (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.”), FIGs. 1 (annotated), 3 (annotated), 5 (annotated).



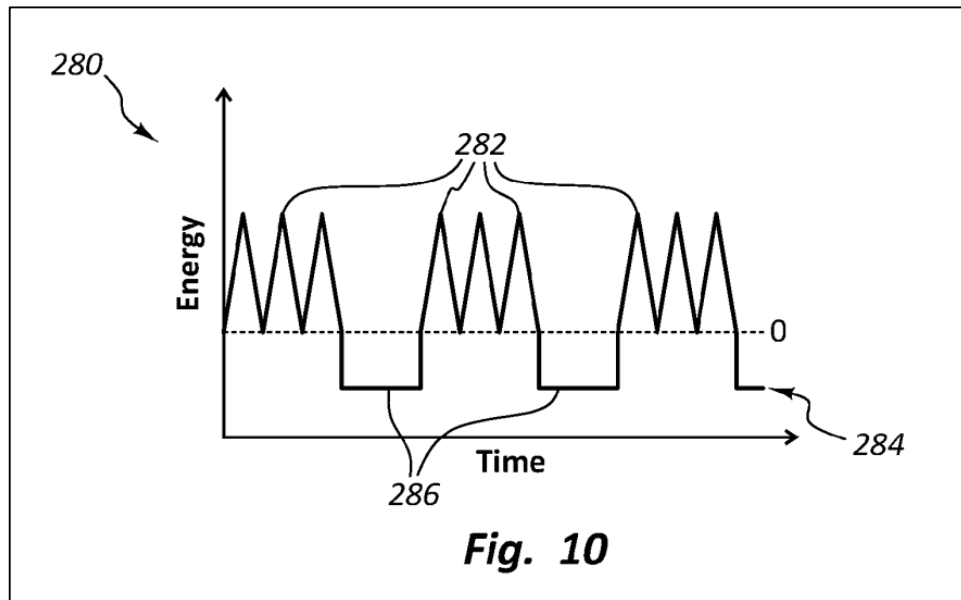




365. Ofek explains that the patency device can be used for both (1) aspirating occlusions (including thrombus) at the distal end of the catheter and (2) to provide patency within the catheter lumen. Ex. 1007 (Ofek) at 2:56-3:2 (“FIG. 1 further shows details regarding a patency device 30 configured to operably connect on a temporary basis with the catheter 10 and provide patency to the catheter tube lumen 14. 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.”).

366. Ofek discloses aspiration techniques that alternate between using periodic impulses and periods of negative pressure in order to aspirate occlusions via the catheter. Ex. 1007 (Ofek) at 8:38-49 (“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.”), FIG. 10.



367. Ofek additionally discloses that the disclosed system can be implemented with arterial catheters and components designed to perform pulsated aspiration. Ex. 1007 (Ofek) at 2:38-55 (“FIG. 1 [] generally depicts various details of a catheter assembly (“catheter”), generally designated at 10, and a patency device... 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.”), 6:46-58 (“The patency device 30 can further include ports to enable fluids or other substances to be infused into or aspired from the catheter tube lumen(s) 14”).

368. As evident from the above disclosures, and as discussed throughout the invalidity grounds below, a POSA would recognize that the system disclosed by Ofek is both explicitly, and also obviously, designed and configured for both (1)

establishing patency (i.e., a state of being unobstructed) within the catheter, and also (2) performing pulsated aspiration of clots engaged at the distal tip of the catheter. Ex. 1007 (Ofek) at 4:21-44 (“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”). Thus, a POSA would understand that Ofek discloses an aspiration thrombectomy system.

369. Like Ofek, Mullins also discloses an aspiration thrombectomy system.

370. Mullins discloses an aspiration system configured to aspiration a clot. Ex. 1008 (Mullins) at 25:22 (“Aspiration System with Pressure-Controlling Pump”), 3:29-38 (“We [] 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.”), 3:46-59 (“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.”), 3:60-4:4 (“The controller may have defined upper and lower limits of pressure or displacement to

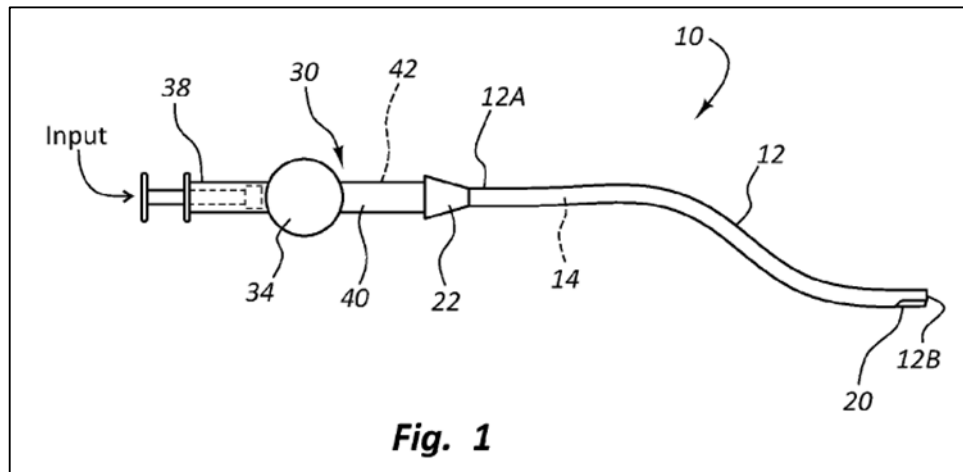
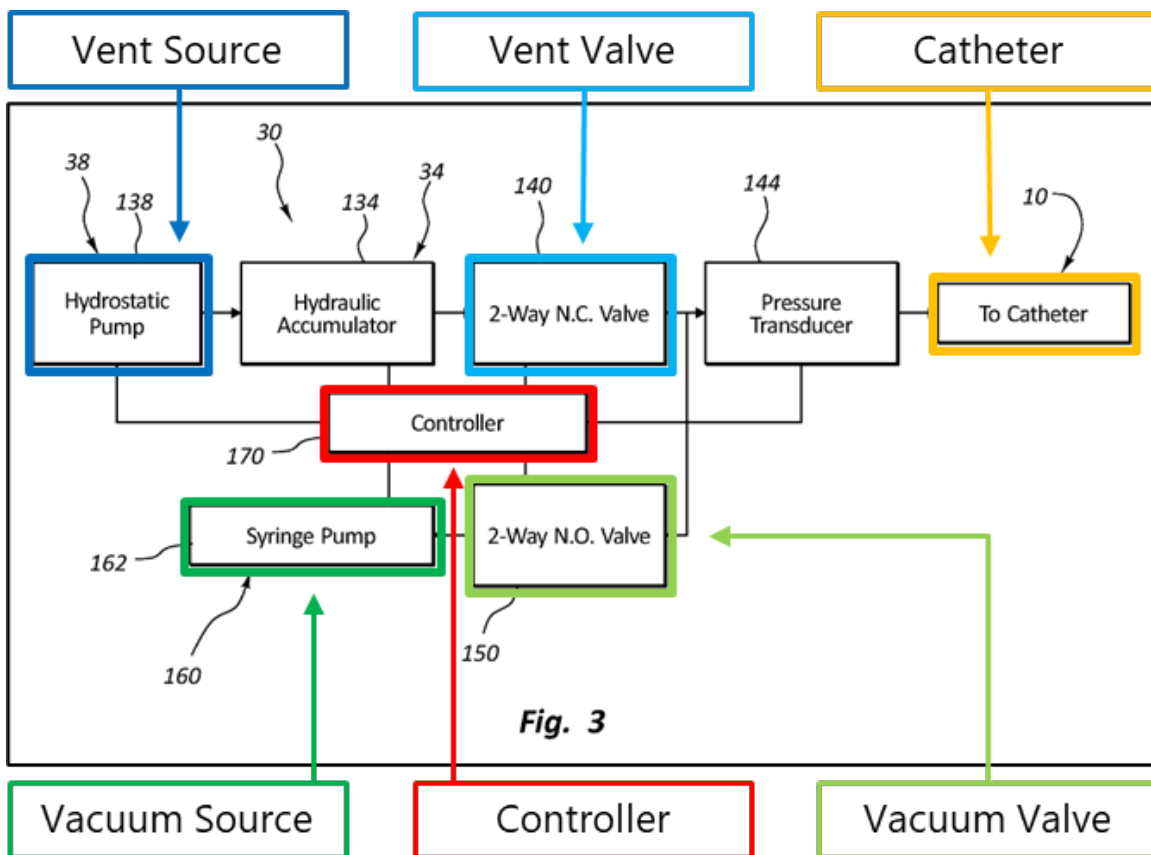
decide whether to apply a vacuum or pressurize, and/or it may cause the catheter to cyclically ingest and if required expel, at least some of a clot, whereby there is deformation of the clot to improve efficiency of aspiration”); Ex. 1009.2 (Mullins-Prov2) at pg. 2-3.

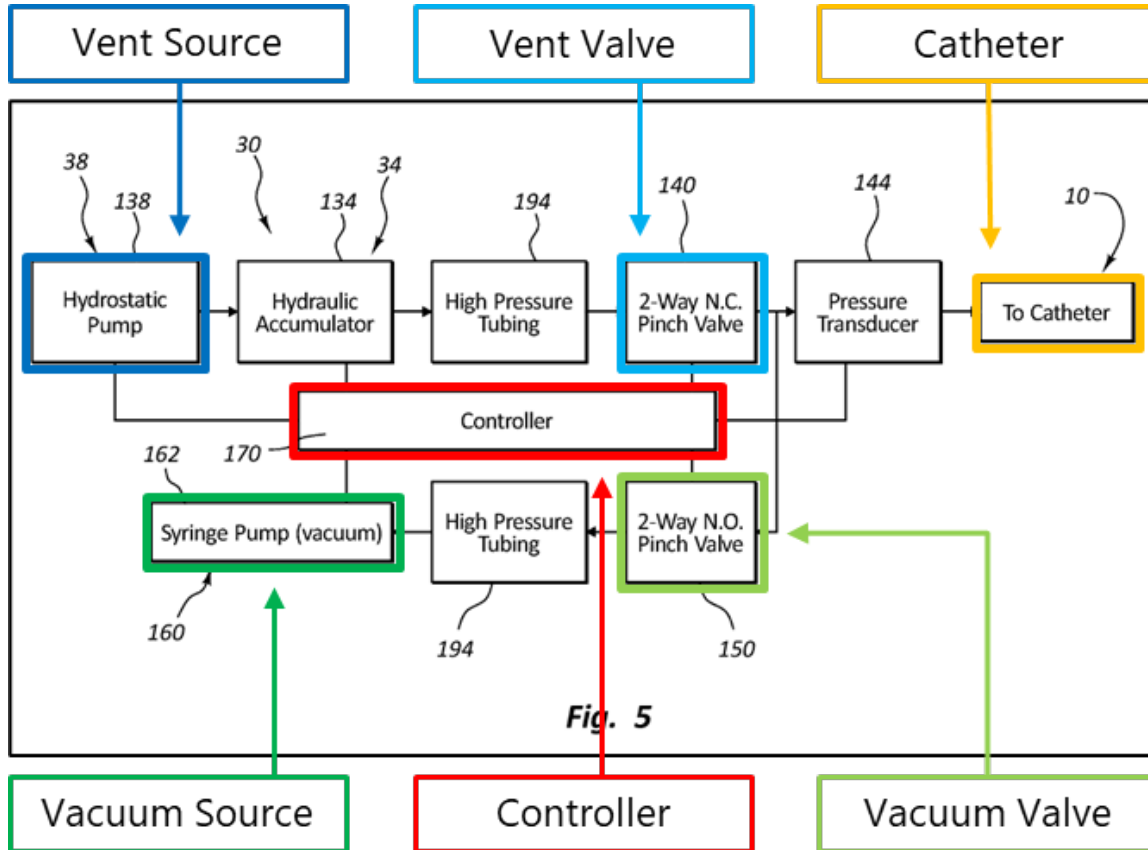
371. Therefore, it is my opinion that Ofek alone or in view of Mullins discloses or renders obvious an “aspiration thrombectomy system,” as recited by Claim 1.

[1-A]: an aspiration catheter having a proximal portion, a distal end and a lumen extending through the catheter;

372. Ofek alone or in view of Mullins discloses or renders obvious this limitation.

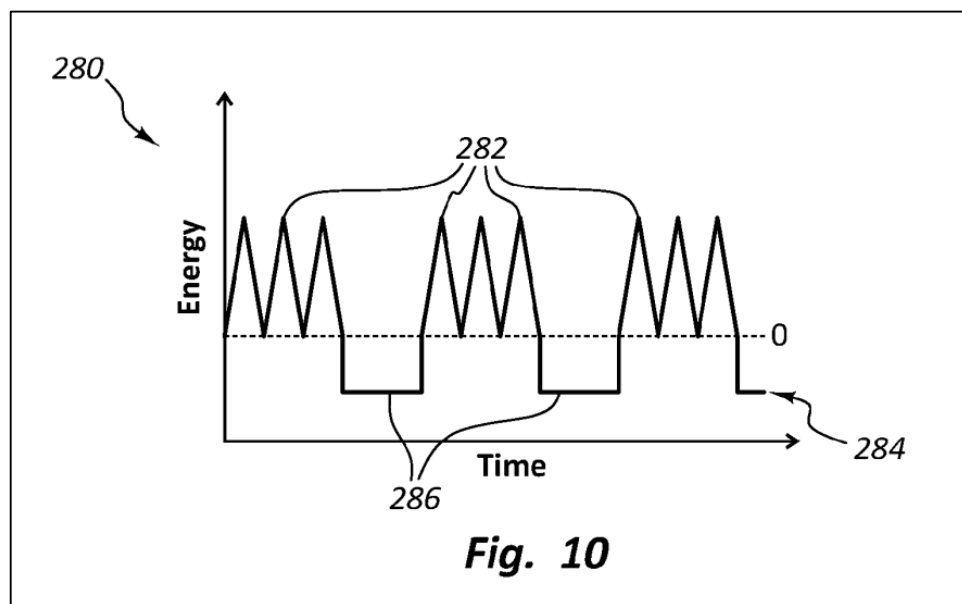
373. Ofek explicitly describes a catheter, and describes it having a proximal end, a distal end, and a lumen extending within the catheter between the proximal and distal ends. Ex. 1007 (Ofek) at 2:38-49 (“Reference is first made to FIG. 1, which generally depicts various details of a catheter assembly (“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.”), FIGs. 1, 3, 5.





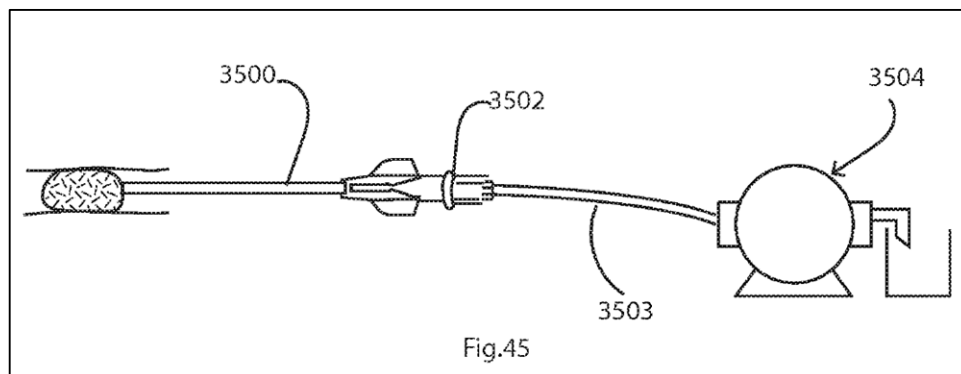
374. Ofek explains that the disclosed device and catheter can be used for aspirating occlusions (including thrombus) at the distal end of the catheter. Ex. 1007 (Ofek) at 2:56-3:2 (“FIG. 1 further shows details regarding a patency device 30 configured to operably connect on a temporary basis with the catheter 10 and... is configured [] 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.”).

375. Ofek discloses using the disclosed device and catheter to alternate between using periodic impulses and periods of negative pressure in order to aspirate occlusions via the catheter. Ex. 1007 (Ofek) at 8:38-49 (“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.”), FIG. 10.



376. Like Ofek, Mullins also discloses an aspiration catheter having a proximal portion, a distal end and a lumen within the catheter.

377. Mullins discloses a catheter and a lumen within the catheter, a proximal portion of the catheter, and a distal tip (also referred to as “catheter tip”). Ex. 1008 (Mullins) at 3:29-42 “(We []) 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 controller may be configured to improve the efficiency of aspiration... and/or to promote maceration and deformation of a clot to enable it to travel through the lumen”), 27:54-65 (“distal tip of the catheter”), 29:26-35 (“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 physic [sic] again moves the catheter tip distally to engage the next piece of clot.”), FIG. 45.



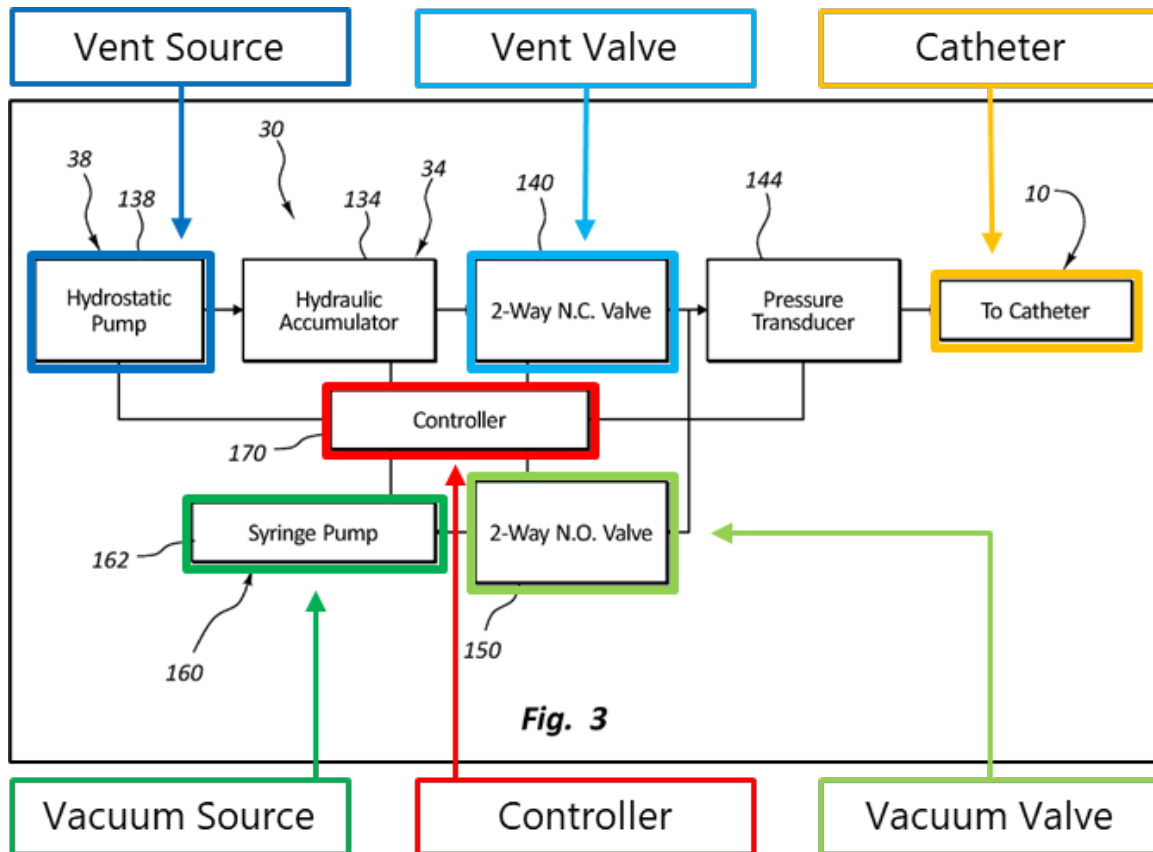
378. Therefore, it is my opinion that Ofek alone or in view of Mullins discloses or renders obvious “an aspiration catheter having a proximal portion, a distal end and a lumen extending through the catheter,” as recited by Claim 1.

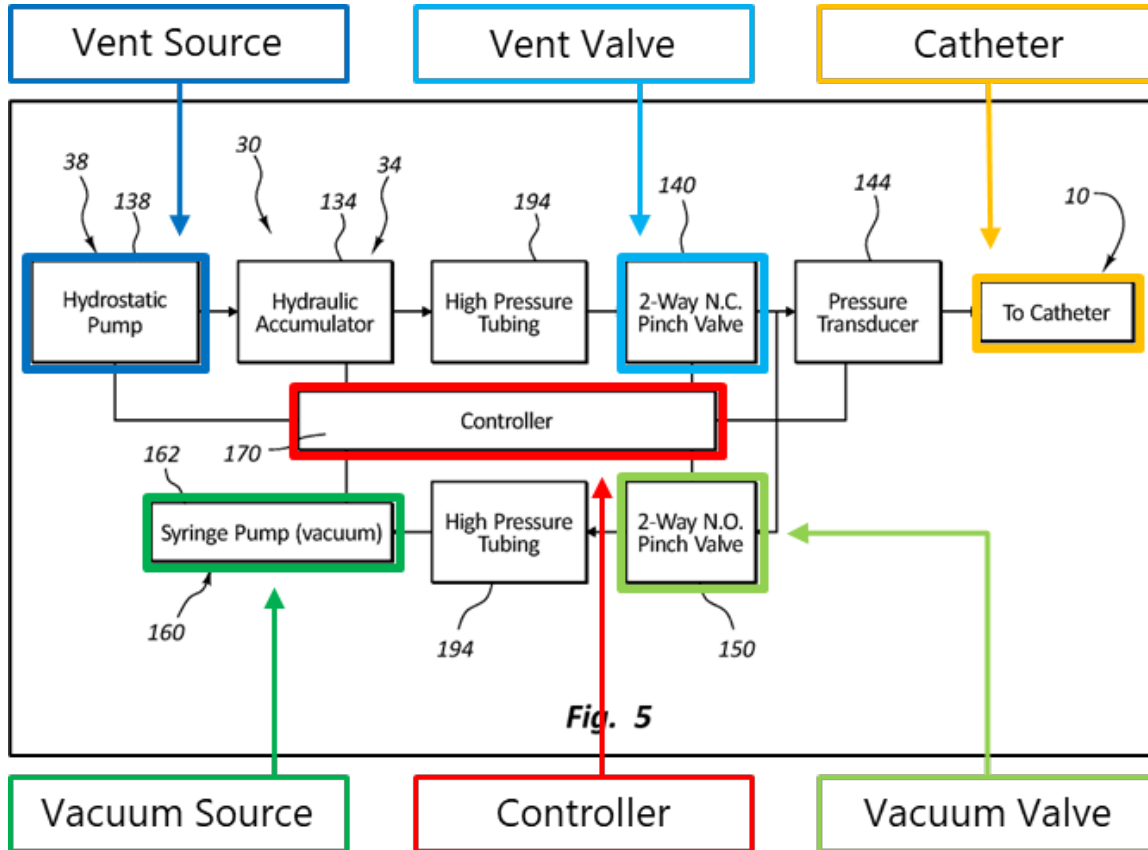
[1-B]: a vacuum source fluidically coupled to the catheter;

379. Ofek discloses this limitation.

380. Ofek discloses, in relation to Figures 3 and 5, a vacuum pump and a vacuum input portion that supplies negative pressure to the lumen of the catheter. Ex. 1007 (Ofek) at 4:62-5:7 (“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.”), Claim 4 (“wherein the temporary negative pressure is provided by a vacuum input portion”), Claim 5 (“wherein the vacuum input portion includes at least one of a syringe pump and a vacuum pump”), 8:50-67 (“A vacuum input portion 160 is provided to supply negative baseline pressure/negative pressure impulses to fluid in the lumen 14”), FIGs. 3, 5. A POSA would understand Ofek’s vacuum pump and vacuum input portion to be a vacuum source, and that the vacuum

source is fluidically coupled to the catheter in order to supply negative pressure to the catheter lumen.





381. Therefore, it is my opinion that Ofek discloses “a vacuum source fluidically coupled to the catheter,” as recited by Claim 1.

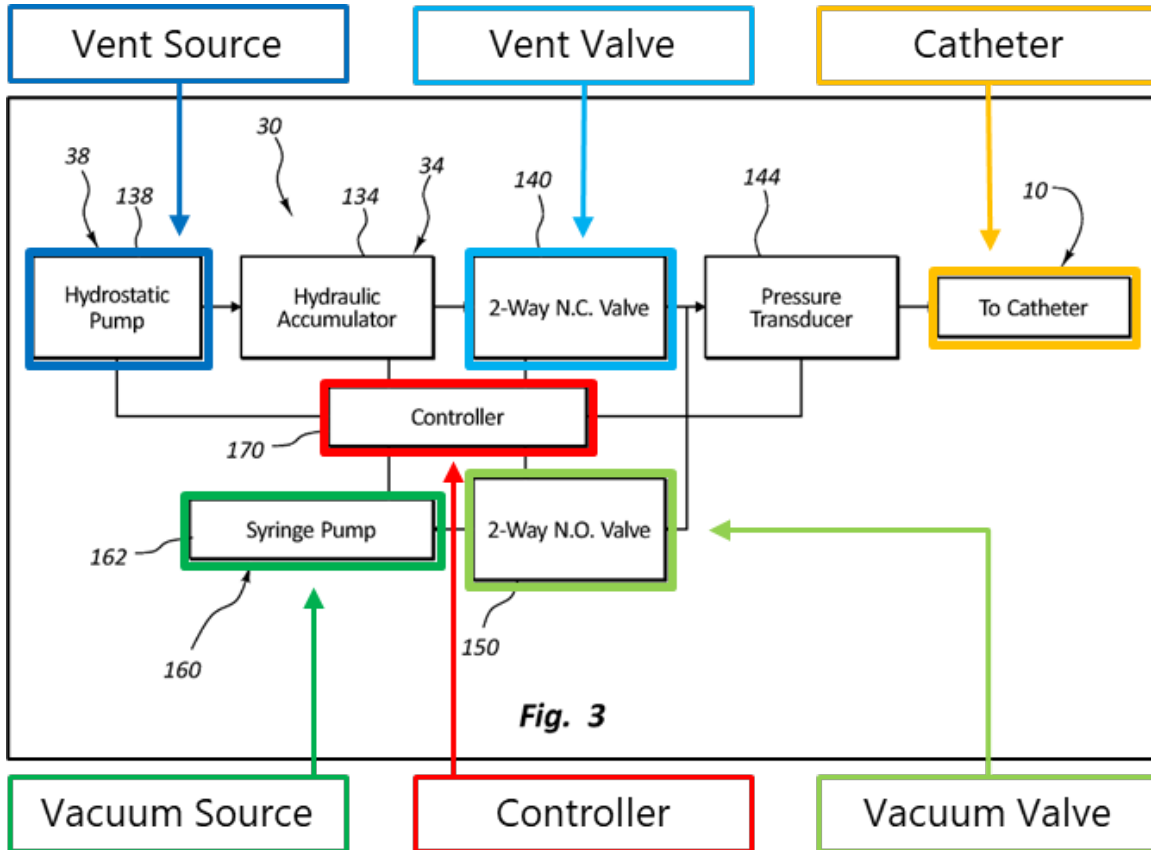
[1-C]: a vacuum valve connected between the vacuum source and the proximal portion of the catheter to control a vacuum flow in the catheter lumen;

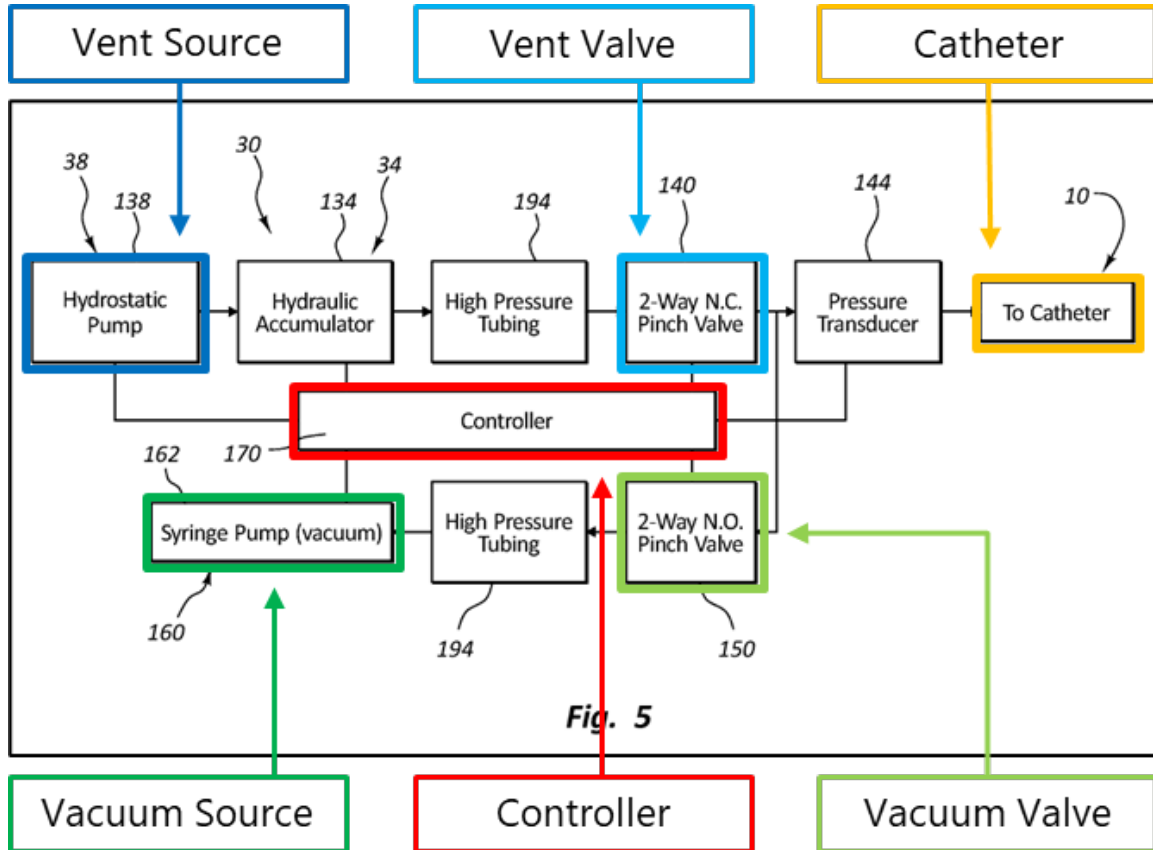
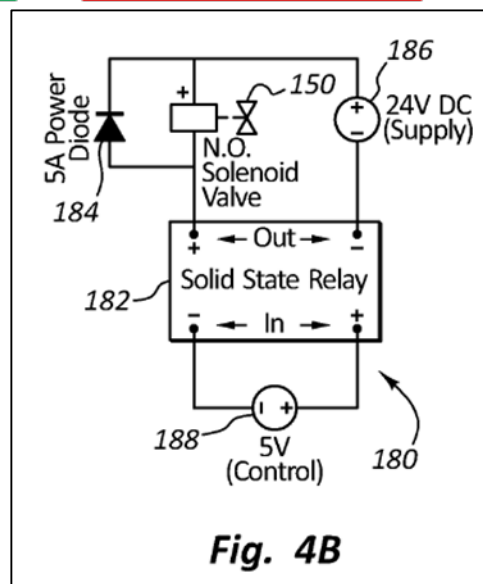
382. Ofek discloses this limitation.

383. Ofek discloses two-way, normally open (“N.O.”) valve fluidically connected between the vacuum pump/vacuum input portion and the catheter to control negative pressure in the catheter lumen. Ex. 1007 (Ofek) at 4:62-67 (“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.”), 5:8-33 (“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.”), 5:34-48 (“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.”), 5:63-6:8 (“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.”), 7:18-26 (“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.”), 4:45-61 (“Note that the fluid lines between the various components discussed herein can include tubing or other suitable modes for fluid transport.”), FIGs. 3, 4B, 5. A POSA would understand two-way, normally open (“N.O.”) valve as a vacuum valve fluidically connected between the vacuum source and the proximal portion of the catheter to control flow of vacuum in the catheter.





384. Therefore, it is my opinion that Ofek discloses “a vacuum valve connected between the vacuum source and the proximal portion of the catheter to control a vacuum flow in the catheter lumen,” as recited by Claim 1.

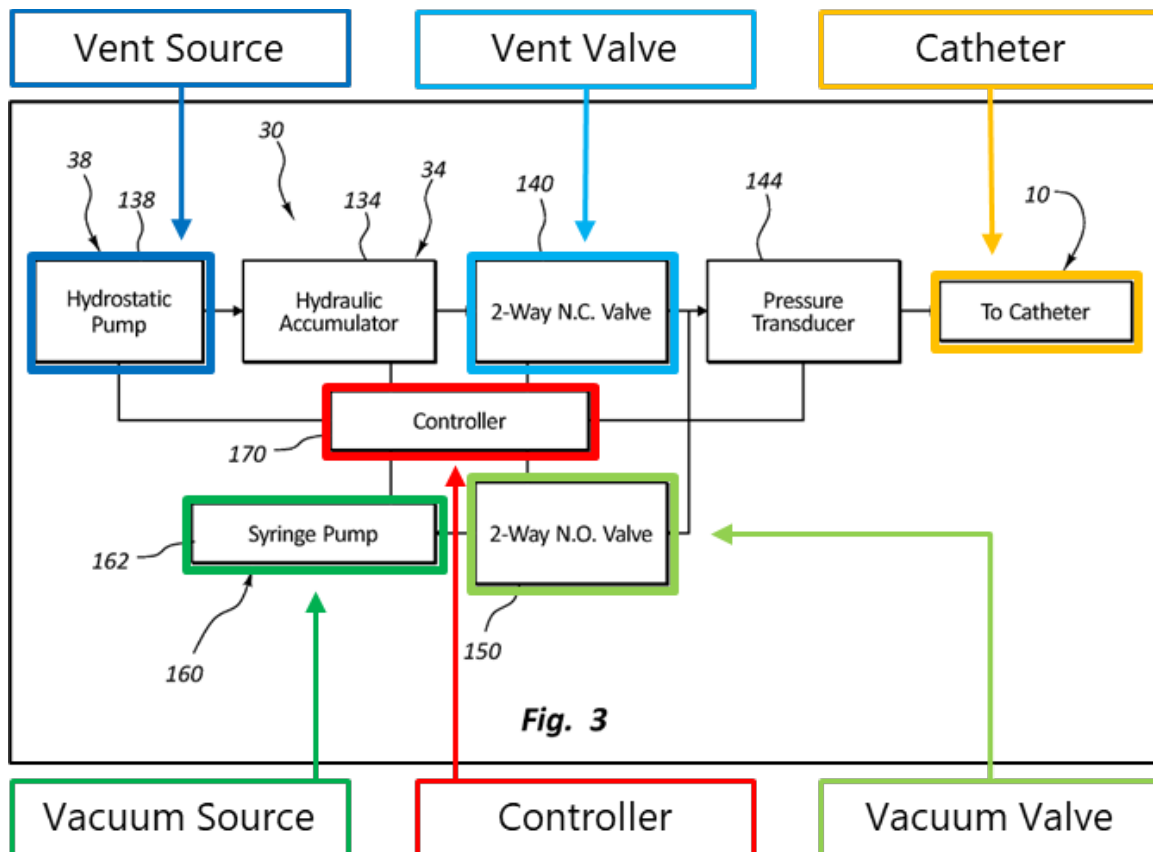
[1-D]: a vent valve fluidically coupled to the proximal portion of the catheter, the vent valve being configured to control a flow of a vent fluid in the catheter lumen; and

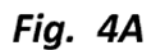
385. Ofek discloses this limitation.

386. Ofek discloses two-way, normally closed (“N.C.”) valve fluidically connected between the vacuum pump/vacuum input portion and the catheter to control positive pressure in the catheter lumen. Ex. 1007 (Ofek) at 4:45-61 (“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.”), 5:8-33 (“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... 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.”), 5:34-48 (“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.”), 5:49-62 (“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”), 7:18-26 (“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.”), 4:45-61 (“Note that the fluid lines between the various components discussed herein can include tubing or other suitable modes for fluid transport.”),

FIGs. 3, 4A, 5. A POSA would understand the two-way, normally closed (“N.C.”) valve as a vent valve fluidically connected between the vacuum source and the proximal portion of the catheter to control flow of vent fluid in the catheter.



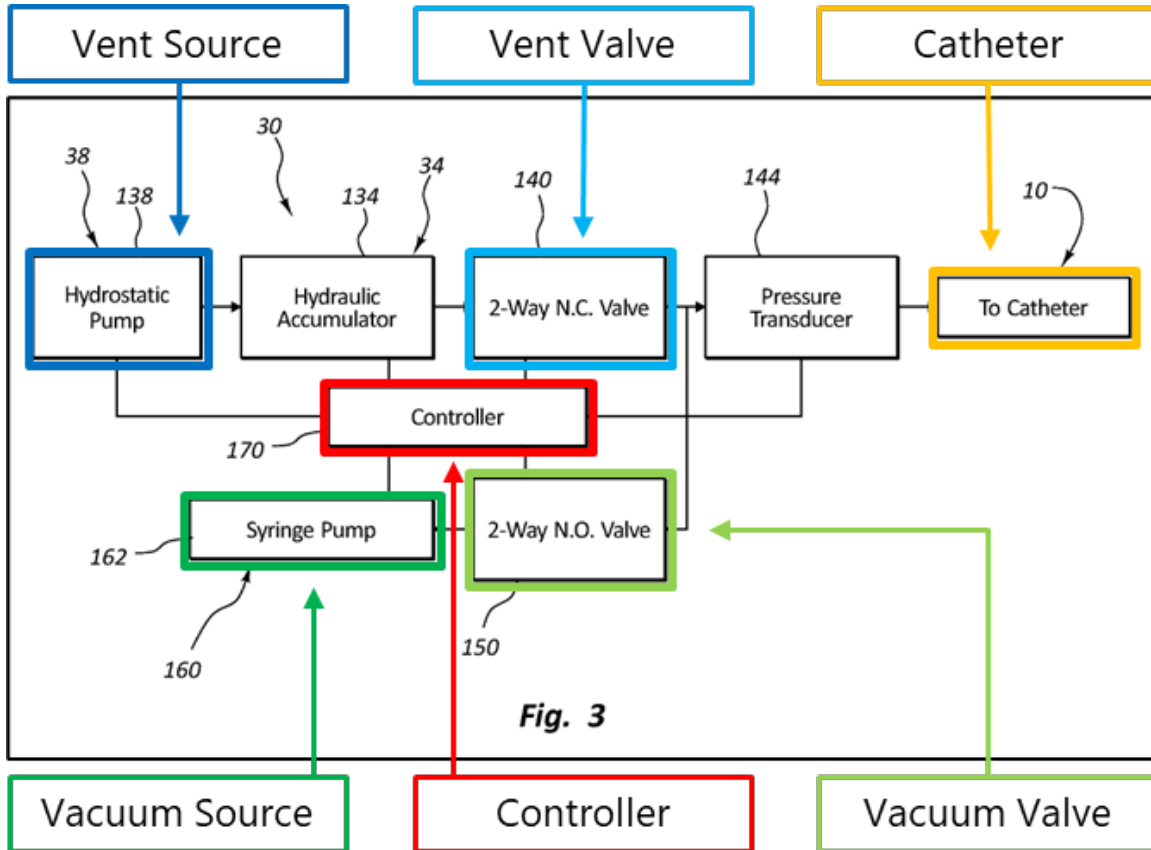


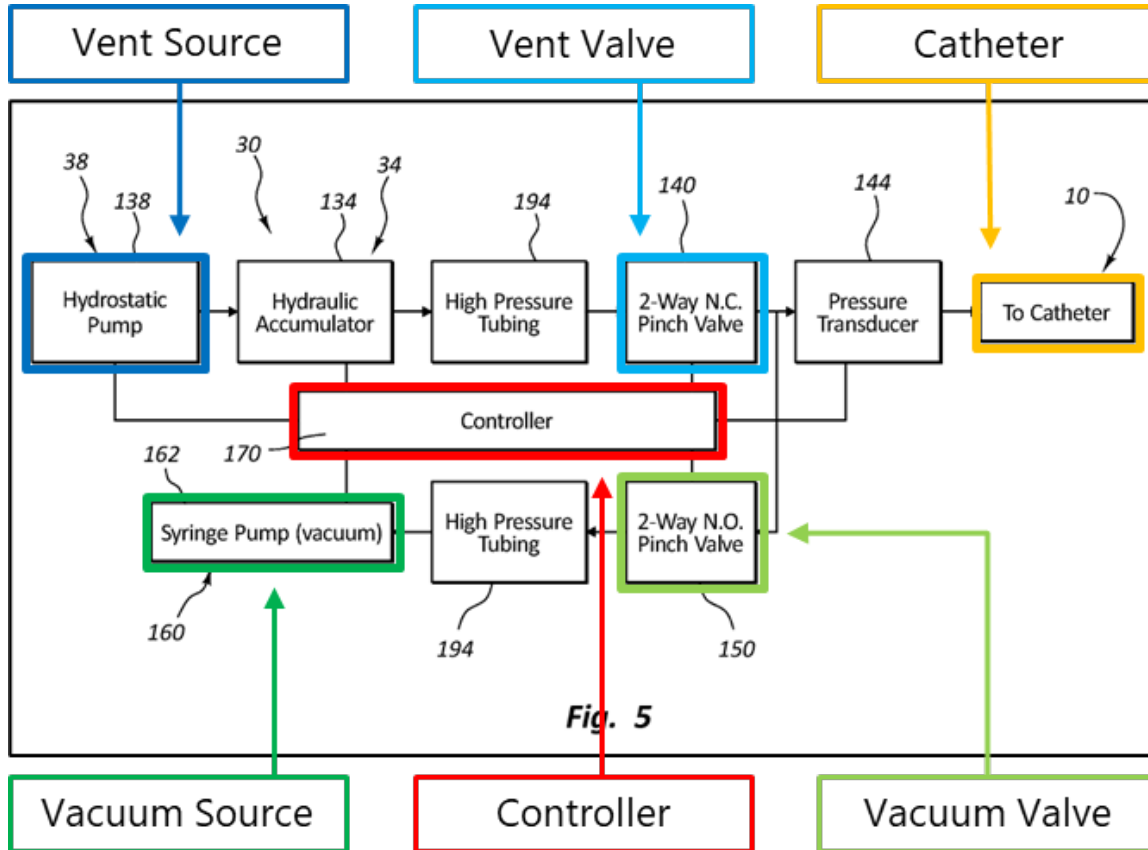
387. Therefore, it is my opinion that Ofek discloses “a vent valve fluidically coupled to the proximal portion of the catheter, the vent valve being configured to control a flow of a vent fluid in the catheter lumen,” as recited by Claim 1.

[1-E]: a controller configured to open and close the vacuum valve and the vent valve in a predetermined cycle

388. Ofek discloses this limitation.

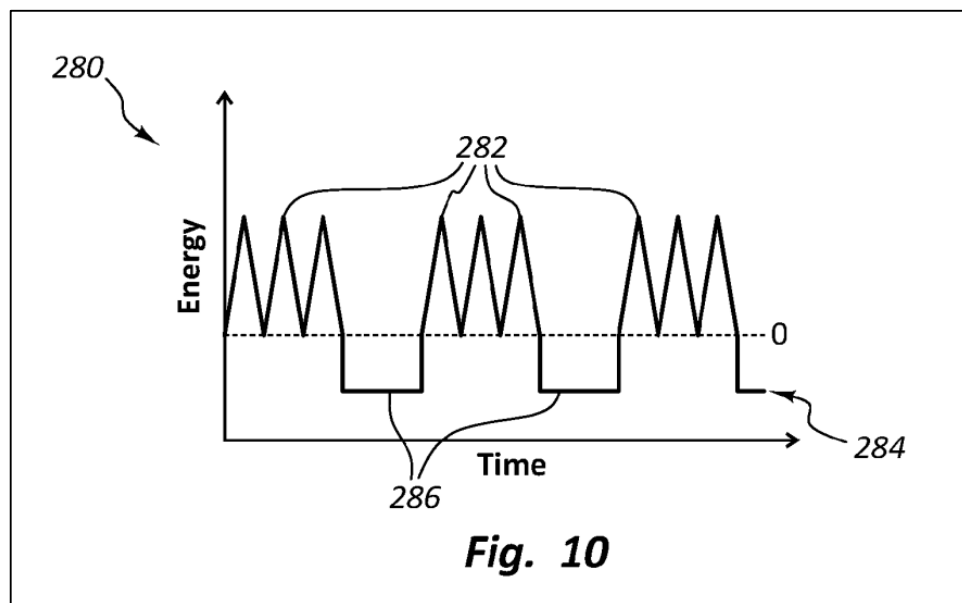
389. Ofek discloses a controller configured to open and close the vacuum valve and the vent valve. Ex. 1007 (Ofek) at 4:62-5:7 (“A controller 170 is operably connected to the aforementioned components of the patency device 30 to govern their operation. The controller 170 in one embodiment includes a power source, a printed circuit board including a processor, etc.”), 5:34-48 (“The controller 170 or other suitable component can control valve opening/closing.”), 5:49-62 (“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.”), 5:63-6:8 (“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.”), FIGs. 3, 5.





390. Ofek discloses that the controller is configured to open and close the valves in a predetermined cycle. Ex. 1007 (Ofek) at 6:20-45 (“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”), 6:59-63 (“Note further that in one embodiment that the controller 170 can enable customization of the characteristics of the impulses, rest periods, baseline pressure, etc.”), 7:11-17 (“a method for... 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.”), 8:23-32 (“FIGS. 8-10 depict various operation cycles for the positive pressure

impulses produced by the present patency device”), 8:38-49 (“In FIG. 10, a series of groups of impulses is shown... note that the number of impulses in each group can vary according to [] a pre-set predetermined pattern, as can the pressure, frequency, etc.”), FIG. 10.



391. Therefore, it is my opinion that Ofek discloses “a controller configured to open and close the vacuum valve and the vent valve in a predetermined cycle,” as recited by Claim 1.

[1-F]: to change a level of vacuum at the distal end of the catheter

392. Ofek alone or in view of Mullins discloses or renders obvious this limitation.

393. As discussed above for Ground 4, Claim [1-Pre], Ofek discloses an aspiration thrombectomy system. As also discussed above for Ground 4, Claim [1-E], Ofek discloses a controller configured to open and close the vacuum valve and the vent valve in a predetermined cycle.

394. Ofek further discloses that the controller's opening and closing of the vacuum valve and vent valve according to various operation cycles and pressure profiles that change the level of vacuum in the catheter. Ex. 1007 (Ofek) at 3:43-60 ("FIG. 2 depicts a graph of a pressure profile 80 (including fluid pressure vs. time) produced [] during operation... 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."), 5:49-62 ("The controller 170 determines the [] impulses to be delivered [] to the catheter tube lumen(s) 14... The impulses are propagated distally down the lumen 14, which is fluid-filled... to provide a propagation medium for the impulses"), 5:63-6:8 ("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").

395. Thus, a POSA would recognize that Ofek's controller opening and closing the vacuum valve and vent valve in the disclosed system manipulates the pressure within the catheter and lumen (i.e., changes a level of vacuum in the catheter).

396. Ofek also expressly discloses that the manipulation of the level of vacuum is specifically intended to affect the level of vacuum at the distal tip of the catheter. Ex. 1007 (Ofek) at 2:56-3:2 ("Generally, the patency device 30 [] is configured [] to provide one or more relatively short-duration impulses... 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."), 3:43-60 ("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."), 4:21-44 ("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.”).

397. Thus, Ofek states, and a POSA would recognize, that the positive and negative pressure impulses are used to change the level of vacuum at the distal end of the catheter. A POSA would understand that the positive and negative pressure impulses would propagate through the fluid in the catheter, and thus would affect the level of vacuum at the distal end of the catheter to achieve the stated goal of “prevent[ing] the formation of thrombus or other occlusion in the lumen 14, especially at the distal end.” Ex. 1007 (Ofek) at 2:66-67.

398. To the extent that Ofek does not explicitly disclose the controller changing the level of vacuum at the distal end of the catheter, the combination of Ofek and Mullins renders it obvious.

399. For the reasons discussed above (in greater detail) regarding Mullins in Ground 1, Claim [1-F], Mullins discloses “pulse cycling” including changes in vacuum pressure at the distal end of the catheter to ingest a clot. A POSA would have found it obvious to change the level of vacuum at the distal end of Ofek’s catheter using the cyclical open and closed state of its valves in view of Mullins’s disclosures of using pulse cycling and infuse-to-aspirate cycles to implement

dynamic forces at the distal end of its catheter. *See, e.g.*, Ex. 1008 (Mullins) at 26:23-26 (“The invention utilizes 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...”), 27:18-26 (“allowing some or all of the clot to be pushed distally towards the catheter tip”); Ex. 1009.2 (Mullins-Prov2) at pg. 3-7.

400. Thus, it is my opinion that Ofek alone or in view of Mullins discloses and renders obvious “to change a level of vacuum at the distal end of the catheter,” as recited by Claim 1.

[1-G]: and to control fluid flow in and out from the distal end of the catheter.

401. Ofek alone or in view of Mullins discloses or renders obvious this limitation.

402. As discussed above for Ground 4, Claim [1-F], Ofek alone or in view of Mullins discloses or renders obvious opening and closing the vacuum valve and vent valve to change a level of vacuum at the distal end of the catheter.

403. Ofek’s disclosures demonstrate that it changes the level of vacuum at the distal end in order to control fluid flow at the distal end. Ex. 1007 (Ofek) at 2:56-3:2 (“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.”), 3:43-60 (“The negative baseline pressure present between impulses... prevent[s] the dislodged occlusion from entering the bloodstream from the distal end 12B of the catheter tube 12.”), 4:21-44 (“As noted above, the high-pressure fluid impulses impinge on an occlusion (such as a clot[])... 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.”).

404. A POSA would find it obvious that Ofek’s use of impulses and vacuum control over occlusions at the distal end of the catheter necessarily mean that it is controlling the flow of material and fluid at the distal end, at least because Ofek utilizes negative pressure in conjunction with the impulses to prevent clots from escaping the distal end and entering the bloodstream. Therefore, in my opinion, Ofek discloses or renders obvious controlling the fluid flow at the distal end of the catheter.

405. Moreover, Ofek extensively discusses how the operation cycles and pressure profiles can be customized by the controller in various different ways (e.g., number of impulses, level of pressure, frequency, etc.), and further includes

examples of the pressure impulses being high-pressure impulses that in some cases can be configured to have substantially high pressure peaks. Ex. 1007 (Ofek) at 3:43-60 (“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... thus preventing the dislodged occlusion from entering the bloodstream from the distal end 12B of the catheter tube 12. Note that the rest periods... can include a reduction to a neutral pressure or lower (but still positive) pressure or to varying pressures over time as may be desired.”), 3:61-4:6 (“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.”), 4:7-11 (“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.”), 4:12-20 (“In the present embodiment, the maximum pressure achieved by the impulses is about 400 psi, though this can vary according to desired application”).

406. A POSA would recognize that pressure levels as high as the disclosed 400 psi, (depending on the number, duration, and frequency, which Ofek explicitly describes as being configurable to the desired application) would place sufficient amounts of positive pressure on the fluid in the catheter to not only incur distal pressure impulses in the fluid within the catheter, but could also cause at least some amount of controlled flow of fluid and occlusive material out from the distal end of the catheter. In such a case, a POSA would also find it obvious, consistent with the teachings and stated purpose of Ofek, that negative pressure characteristics could similarly be configured in the operation cycles and pressure profiles to prevent the clot from escaping into the bloodstream even if some portion of it had shifted out from the distal end of the catheter due to the positive pressure impulses.

407. To the extent that Ofek does not explicitly disclose controlling fluid flow in and out from the distal end of the catheter, the combination of Ofek and Mullins renders it obvious.

408. For the reasons discussed above (in greater detail) regarding Mullins in Ground 1, Claim [1-G], Mullins discloses controlling fluid at the distal end of a

catheter using changes in pressure, utilizing pressure and fluid displacement at the catheter tip to aspirate clots, and shows how the controller uses positive and negative pressure to control the flow of clot and fluid in and out at the distal tip of the catheter. As also discussed, a POSA would understand that the cyclical application of positive and negative pressure to the catheter would control fluid flow in and out from the distal end of the catheter.

409. Therefore, it is my opinion that Ofek alone or in view of Mullins discloses or renders obvious “to control fluid flow in and out from the distal end of the catheter,” as recited by Claim 1.

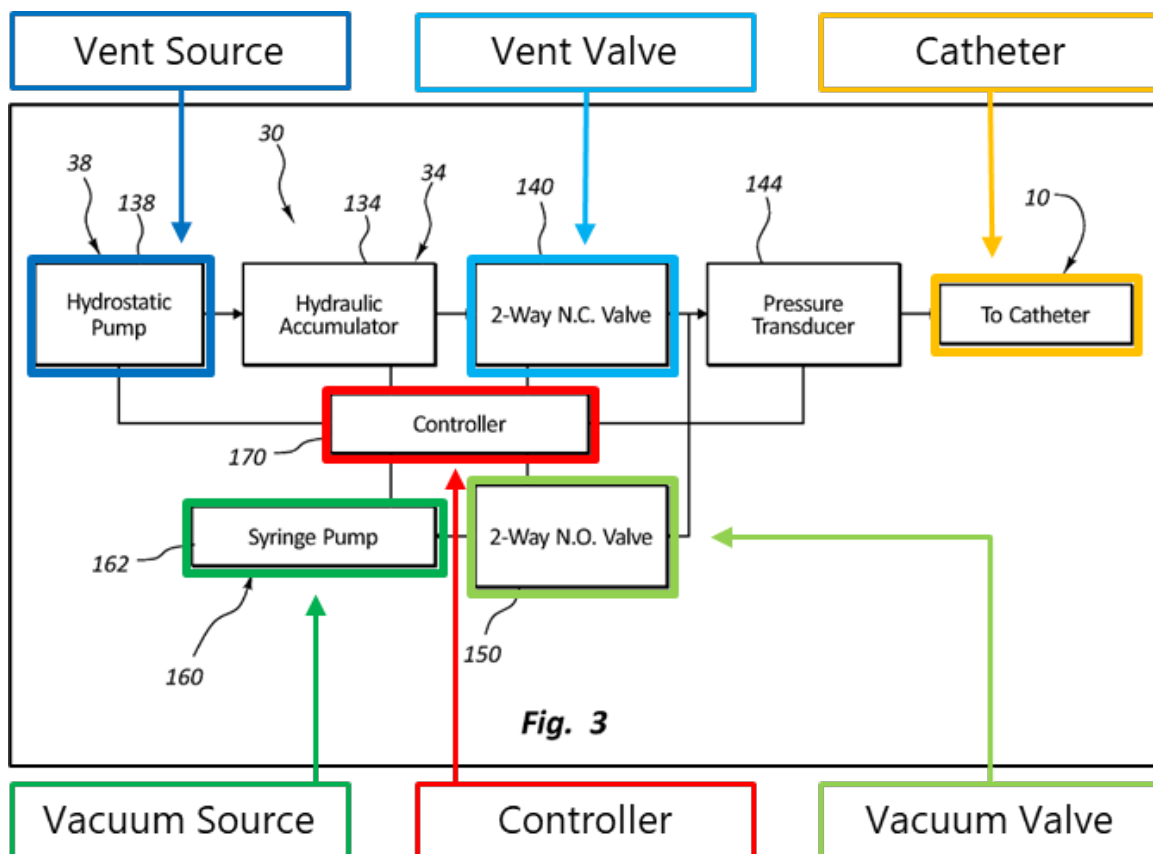
Claim 2

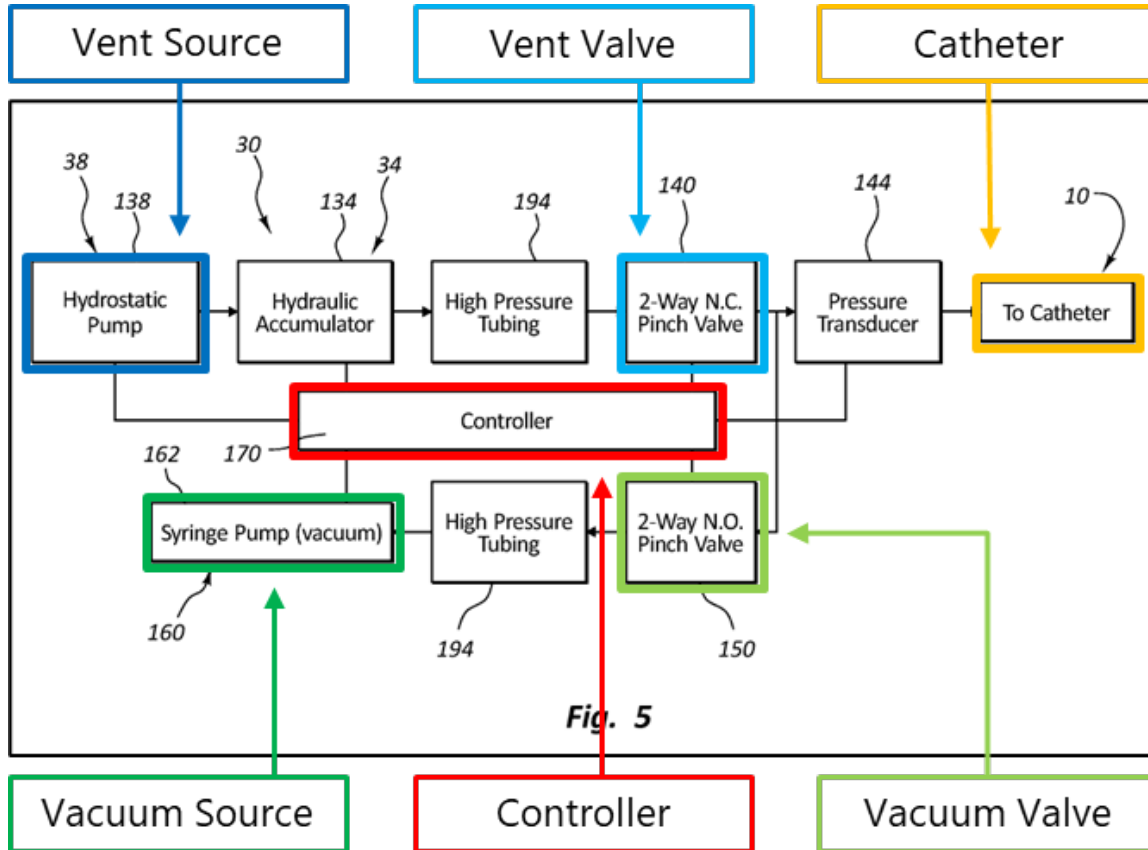
[2-A]: The system of claim 1, further comprising a vent fluid source, and wherein:

410. Ofek discloses this limitation.

411. Ofek discloses, in relation to Figures 3 and 5, a hydrostatic pump that serves as pressure input and a hydraulic accumulator that serves as a fluid reservoir. Ex. 1007 (Ofek) at 4:21-44 (“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.”), 4:45-61 (“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.”), 5:34-48 (“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.”), FIGs. 3, 5.





412. Therefore, it is my opinion that Ofek discloses “a vent fluid source,” as recited by Claim 2.

[2-B]: the vent fluid source is configured to provide vent fluid at a pressure greater than atmospheric pressure; and

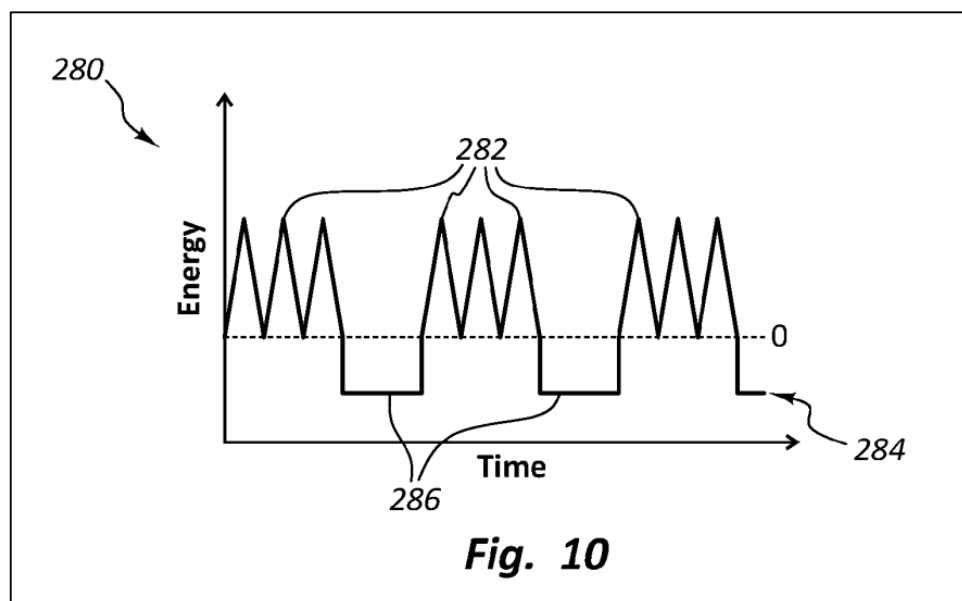
413. Ofek discloses this limitation.

414. Ofek discloses the providing high-pressure fluid impulses.

415. As discussed above for Ground 4, Claim [1-G], Ofek extensively discusses particular examples of the pressure impulses being high-pressure impulses that in some cases can be configured to have substantially high pressure peaks, along

with other variable characteristics. *See, e.g.*, Ex. 1007 (Ofek) at 4:7-11 (“In the present embodiment, the maximum pressure achieved by the impulses is about 400 psi, though this can vary according to desired application”).

416. Similarly, Ofek discloses utilizing various types of vent fluids, and further being able to configure altering impulse characteristics based on the type of vent fluid used. Ex. 1007 (Ofek) at 4:21-44 (“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.”), FIG. 10.



417. From all of these examples, a POSA would recognize that the vent fluid could be provided at a pressure (e.g., 400 psi) greater than atmospheric pressure (e.g., 14.7 psi).

418. Therefore, it is my opinion that Ofek discloses “the vent fluid source is configured to provide vent fluid at a pressure greater than atmospheric pressure” as recited by Claim 2.

[2-C]: the controller is configured to cyclically open and close the vacuum valve and the vent valve

419. For the reasons discussed above for Ground 4, Claim [1-E], this limitation is met by Ofek.

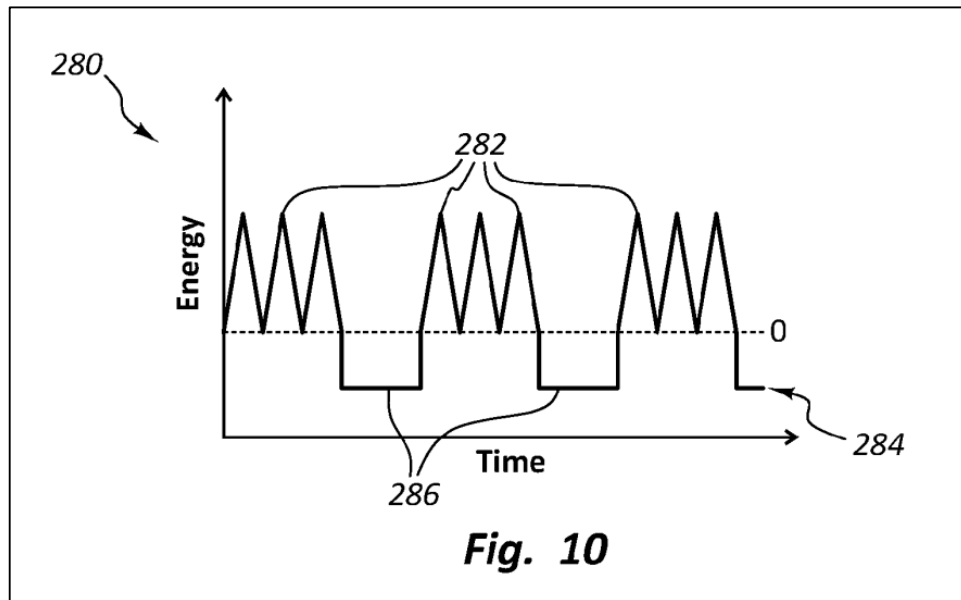
[2-D]: to change a level of negative pressure and positive pressure at the distal end of the catheter during each cycle.

420. Ofek alone or in view of Mullins discloses or renders obvious this limitation.

421. As discussed above for Ground 4, Claim [1-F], Ofek in view of Mullins discloses or renders obvious changing a level of vacuum at the distal end of the catheter.

422. A POSA would recognize that both Ofek and Mullins may change the level of vacuum at the distal end of the catheter by changing a level of negative pressure and positive pressure at the distal end of the catheter during each cycle.

423. For example, as discussed above, Ofek discloses that positive and negative pressure impulses are used to change the level of vacuum at the distal end of the catheter. Ex. 1007 (Ofek) at 2:56-3:2 (“Such impulses, when performed periodically, are configured to prevent the formation of thrombus... in the lumen 14, especially at the distal end.”), 3:43-60 (“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.”), 4:21-44 (“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.”), 5:63-6:8 (“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”), FIG. 10.



424. In addition to Ofek's disclosure of the controller changing the level of negative pressure and positive pressure at the distal end of the catheter, the combination of Ofek and Mullins renders it obvious.

425. For the reasons discussed above (in greater detail) regarding Mullins in Ground 1, Claim [2-D], Mullins discloses cycling of positive and negative pressures at the distal end of the catheter.

426. Therefore, it is my opinion that Ofek alone or in view of Mullins discloses and renders obvious a controller configured "to change a level of negative pressure and positive pressure at the distal end of the catheter during each cycle," as recited by Claim 2.

Claim 3

[3-A]: The system of claim 2 wherein the controller is configured to cyclically open and close the vacuum valve and the vent valve

427. For the reasons discussed above for Ground 4, Claim [1-E], this limitation is met by Ofek.

[3-B]: such that movement of the fluid column at the distal end of the catheter is limited to a positive amount of exit flow ... before fluid is drawn back into the catheter lumen.

428. Ofek alone or in view of Mullins renders obvious this limitation.

429. As discussed above for Ground 4, Claim [1-G], Ofek discloses or renders obvious controlling the fluid flow at the distal end of the catheter.

430. Additionally, as also discussed above, Ofek extensively discusses how the operation cycles and pressure profiles can be customized by the controller in various different ways (e.g., number of impulses, level of pressure, frequency, etc.), and further includes examples of the pressure impulses being high-pressure impulses that in some cases can be configured to have substantially high pressure peaks. Ex. 1007 (Ofek) at 3:43-60 (“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... thus preventing the dislodged occlusion from entering the bloodstream from the distal end 12B of the catheter tube 12. Note that

the rest periods... can include a reduction to a neutral pressure or lower (but still positive) pressure or to varying pressures over time as may be desired. ”), 3:61-4:6 (“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.”), 4:7-11 (“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.”), 4:12-20 (“In the present embodiment, the maximum pressure achieved by the impulses is about 400 psi, though this can vary according to desired application”).

431. A POSA would recognize that pressure levels as high as the disclosed 400 psi, (depending on the number, duration, and frequency, which Ofek explicitly describes as being configurable to the desired application) would place sufficient amounts of positive pressure on the fluid in the catheter to not only incur distal

pressure impulses in the fluid within the catheter, but could also cause at least some amount of controlled flow of fluid and occlusive material out from the distal end of the catheter. In such a case, a POSA would also find it obvious, consistent with the teachings and stated purpose of Ofek, that negative pressure characteristics could similarly be configured in the operation cycles and pressure profiles to prevent the clot from escaping into the bloodstream even if some portion of it had shifted out from the distal end of the catheter due to the positive pressure impulses. Thus, a POSA would find it obvious to configure Ofek (which Ofek invites a POSA to do) to limit movement of fluid at the distal end of the catheter to a positive amount of exit flow before fluid is drawn back into the catheter lumen.

432. To the extent that Ofek does not explicitly disclose that movement of the fluid column at the distal end of the catheter is limited to a positive amount of exit flow before fluid is drawn back into the catheter lumen, the combination of Ofek and Mullins renders it obvious.

433. For the reasons discussed above (in greater detail) regarding Mullins in Ground 1, Claim [3-B], Mullins discloses controlling fluid at the distal end of a catheter using changes in pressure, utilizing pressure and fluid displacement at the catheter tip to aspirate clots, using positive and negative pressure to control the flow of clot and fluid in and out (i.e., positive exit flow) at the distal tip of the catheter,

and illustrates the movement of the clot at the distal end of the catheter, which demonstrates how the controller limits the positive exit flow. As also discussed, A POSA would recognize, based at least on Mullins' discussion of using reverse flow and fluid displacement to cyclically ingest and expel part of a clot, allowing the clot to be pushed distally, and using upper and lower pressure limits to control how measured amounts of flow displacement, that Mullins' controller not only controls the movement of fluid at the distal end of the catheter, but also limits the amount of exit flow before drawing the fluid back into the catheter. A POSA would understand that Mullins limits the positive exit flow to ensure that the clot is not entirely expelled from the catheter and therefore avoid risking any distal migration of the clot (*see, e.g.,* displacement ratios disclosed in Mullins, discussed further below for Claim [3-C]).

434. A POSA would be motivated to implement Mullins' technique of cycling from negative to positive pressure to unload and reload the clot at the distal tip of the catheter within Ofek's system because Mullins and Ofek both have the same aim of successfully aspirating a clot.

435. Therefore, it is my opinion that Ofek alone or in view of Mullins renders obvious "movement of the fluid column at the distal end of the catheter is

limited to a positive amount of exit flow...before fluid is drawn back into the catheter lumen,” as recited in Claim 3.

[3-C]: ...limited to a positive amount of exit flow from approximately 0.001 ml to approximately 1.0 ml...

436. Ofek in view of Mullins and the knowledge of a POSA renders obvious this limitation.

437. As discussed above for Ground 4, Claim [3-B], Ofek alone or in view of Mullins renders obvious controlling fluid at the distal end of the catheter to limit to a positive amount of exit flow before drawing the fluid back into the catheter.

438. As also discussed above (in greater detail) regarding exit flow values as a preliminary matter in Ground 1, Claim [3-C], a POSA would understand the values of approximately 0.001 ml to approximately 1.0 ml to be reasonable values for implementing a limited amount of exit flow. As also discussed above (in greater detail) regarding Mullins in Ground 1, Claim [3-C], a POSA would have found it obvious, in implementing the techniques taught by Mullins, to experiment, using routine optimization, with particular values of measured flow displacement to achieve the desired goal of aspirating the clot while still limiting the likelihood of distal migration of the clot. In particular, a POSA would reasonably experiment, based on routine optimization, with the claimed values of approximately 0.001 ml to approximately 1.0 ml, because a POSA would expect that such values may

sufficiently limit the risk of the clot, or portions of the clot, from distally migrating farther into the patient's vasculature, while still being able to aspirate the clot, in order to ensure the safety of the patient.

439. As also discussed above (in greater detail) regarding experimenting with exit flow limitations in Ground 1, Claim [3-C], the same reasoning is equally applicable to the combination of Ofek and Mullins. Regarding cycle frequency, Ofek discloses specific timing constraints for a positive and negative pressure cycle. Ex. 1007 (Ofek) at 6:20-45 ("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.")

440. In view of the above frequencies in Ofek, and all of the analysis in Ground 1, Claim [3-C], the same tables are reproduced below, which reflects the amounts of exit flow that a POSA might experiment with in implementing Ofek and Mullins with a .061" inner diameter catheter or a .088" inner diameter catheter.

Distal Lumen Flow Volume Catheter Internal Diameter: 0.061 inches Flow Rate (Blood): 1.0 mL/sec Distal Flow Volume (mL) = Blood Flow Rate (mL/sec) * Cycle Percentage (%) * Cycle Duration (sec)							
Fluid Displacement Ratios "Infuse-to-aspirate cycle": [Mullins (Ex. 1008) at 28:59-64]		"between 0.01 and 0.99"		"between 0.1 and 0.9"		"between 0.4 and 0.9"	
Normalized percentage of time per cycle:		Infuse %	Aspirate %	Infuse %	Aspirate %	Infuse %	Aspirate %
		1%	99%	10%	90%	31%	69%
Cycle frequency (Hz)	Cycle duration (sec)	Exit-flow (mL)	In-flow (mL)	Exit-flow (mL)	In-flow (mL)	Exit-flow (mL)	In-flow (mL)
0.100	10.000	0.100000	9.900000	1.000000	9.000000	3.100000	6.900000
0.111	9.000	0.090000	8.910000	0.900000	8.100000	2.790000	6.210000
0.125	8.000	0.080000	7.920000	0.800000	7.200000	2.480000	5.520000
0.143	7.000	0.070000	6.930000	0.700000	6.300000	2.170000	4.830000
0.167	6.000	0.060000	5.940000	0.600000	5.400000	1.860000	4.140000
0.200	5.000	0.050000	4.950000	0.500000	4.500000	1.550000	3.450000
0.250	4.000	0.040000	3.960000	0.400000	3.600000	1.240000	2.760000
0.333	3.000	0.030000	2.970000	0.300000	2.700000	0.930000	2.070000
0.500	2.000	0.020000	1.980000	0.200000	1.800000	0.620000	1.380000
1.000	1.000	0.010000	0.990000	0.100000	0.900000	0.310000	0.690000
2.000	0.500	0.005000	0.495000	0.050000	0.450000	0.155000	0.345000
3.000	0.333	0.003333	0.330000	0.033333	0.300000	0.103333	0.230000
4.000	0.250	0.002500	0.247500	0.025000	0.225000	0.077500	0.172500
5.000	0.200	0.002000	0.198000	0.020000	0.180000	0.062000	0.138000
6.000	0.167	0.001667	0.165000	0.016667	0.150000	0.051667	0.115000
7.000	0.143	0.001429	0.141429	0.014286	0.128571	0.044286	0.098571
8.000	0.125	0.001250	0.123750	0.012500	0.112500	0.038750	0.086250
9.000	0.111	0.001111	0.110000	0.011111	0.100000	0.034444	0.076667
10.000	0.100	0.001000	0.099000	0.010000	0.090000	0.031000	0.069000
20.000	0.050	0.000500	0.049500	0.005000	0.045000	0.015500	0.034500
50.000	0.020	0.000200	0.019800	0.002000	0.018000	0.006200	0.013800
100.000	0.010	0.000100	0.009900	0.001000	0.009000	0.003100	0.006900
150.000	0.007	0.000067	0.006600	0.000667	0.006000	0.002067	0.004600

Distal Lumen Flow Volume Catheter Internal Diameter: 0.088 inches Flow Rate (Blood): 4.0 mL/sec Distal Flow Volume (mL) = Blood Flow Rate (mL/sec) * Cycle Percentage (%) * Cycle Duration (sec)							
Fluid Displacement Ratios "Infuse-to-aspirate cycle": [Mullins (Ex. 1008) at 28:59-64]		"between 0.01 and 0.99"		"between 0.1 and 0.9"		"between 0.4 and 0.9"	
Normalized percentage of time per cycle:		Infuse %	Aspirate %	Infuse %	Aspirate %	Infuse %	Aspirate %
		1%	99%	10%	90%	31%	69%
Cycle frequency (Hz)	Cycle duration (sec)	Exit-flow (mL)	In-flow (mL)	Exit-flow (mL)	In-flow (mL)	Exit-flow (mL)	In-flow (mL)
0.100	10.000	0.400000	39.600000	4.000000	36.000000	12.400000	27.600000
0.111	9.000	0.360000	35.640000	3.600000	32.400000	11.160000	24.840000
0.125	8.000	0.320000	31.680000	3.200000	28.800000	9.920000	22.080000
0.143	7.000	0.280000	27.720000	2.800000	25.200000	8.680000	19.320000
0.167	6.000	0.240000	23.760000	2.400000	21.600000	7.440000	16.560000
0.200	5.000	0.200000	19.800000	2.000000	18.000000	6.200000	13.800000
0.250	4.000	0.160000	15.840000	1.600000	14.400000	4.960000	11.040000
0.333	3.000	0.120000	11.880000	1.200000	10.800000	3.720000	8.280000
0.500	2.000	0.080000	7.920000	0.800000	7.200000	2.480000	5.520000
1.000	1.000	0.040000	3.960000	0.400000	3.600000	1.240000	2.760000
2.000	0.500	0.020000	1.980000	0.200000	1.800000	0.620000	1.380000
3.000	0.333	0.013333	1.320000	0.133333	1.200000	0.413333	0.920000
4.000	0.250	0.010000	0.990000	0.100000	0.900000	0.310000	0.690000
5.000	0.200	0.008000	0.792000	0.080000	0.720000	0.248000	0.552000
6.000	0.167	0.006667	0.660000	0.066667	0.600000	0.206667	0.460000
7.000	0.143	0.005714	0.565714	0.057143	0.514286	0.177143	0.394286
8.000	0.125	0.005000	0.495000	0.050000	0.450000	0.155000	0.345000
9.000	0.111	0.004444	0.440000	0.044444	0.400000	0.137778	0.306667
10.000	0.100	0.004000	0.396000	0.040000	0.360000	0.124000	0.276000
20.000	0.050	0.002000	0.198000	0.020000	0.180000	0.062000	0.138000
50.000	0.020	0.000800	0.079200	0.008000	0.072000	0.024800	0.055200
100.000	0.010	0.000400	0.039600	0.004000	0.036000	0.012400	0.027600
150.000	0.007	0.000267	0.026400	0.002667	0.024000	0.008267	0.018400

441. As discussed before, it is evident from the above calculations that the claimed exit flow values of 0.001 mL and 1.0 mL are well within the specific exit flow values that would have been obvious to a POSA based on known flow rates and catheter sizes, along with the cycle values disclosed by Ofek and Mullins. Additionally, as will be referenced for the relevant claims, additional exit flow values such as 0.1 mL and 0.5 mL would be similarly obvious to a POSA.

442. Therefore, it is my opinion that Ofek in view of Mullins and the knowledge of a POSA renders obvious “limited to a positive amount of exit flow from approximately 0.001 ml to approximately 1.0 ml,” as recited in Claim 3.

Claim 4

[4-A]: The system of claim 2 wherein the controller is configured to cyclically open and close the vacuum valve and the vent valve

443. For the reasons discussed above for Ground 4, Claim [1-E], this limitation is met by Ofek.

[4-B]: such that movement of the fluid column at the distal end of the catheter is limited to a positive amount of exit flow ... before fluid is drawn back into the catheter lumen.

444. For the reasons discussed above for Ground 4, Claim [3-B], this limitation is met by Ofek alone or in view of Mullins.

[4-C]: ...limited to a positive amount of exit flow of approximately 0.1 ml to approximately 0.5 ml...

445. For the reasons discussed above for Ground 4, Claim [3-C], this limitation is met by Ofek in view of Mullins and the knowledge of a POSA.

Claim 5

[5-A]: The system of claim 1 wherein the controller is configured to cyclically open and close the vacuum valve and the vent valve in a repeated cycle

446. For the reasons discussed above for Ground 4, Claim [1-E], this limitation is met by Ofek.

[5-B]: comprising an off-off state in which the vacuum valve is closed while the vent valve is closed.

447. Ofek and the knowledge of a POSA renders obvious this limitation.

448. As discussed above for Ground 4, Claim [1-E], Ofek discloses cyclically opening and closing the vacuum valve and the vent valve in a repeated cycle.

449. Ofek further discloses “Between each impulse and after the series of impulses has ended, the N.C. valve 140 closes and the N.O. valve 150 opens” and “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” Ex. 1007 (Ofek) at 5:63-6:8, Claim 8.

450. Ofek’s “normally open” valve is valve 150 in Fig. 3, which is connected to the vacuum pressure, and the “normally closed” valve is valve 140 in Fig. 3. Ex. 1007 (Ofek) at 4:62-67. A POSA would have found it obvious to execute the transition between the negative and positive pressure serially to generate the positive pulse. Because of the nature of serial operation, it would be obvious to have a finite delay (e.g., for confirming the state of the valve) between the closing of the vacuum valve and the opening of the vent valve, which leads to at least a brief period where

both valves are closed, i.e., a double-closed, or off-off state. This would lead to more reliable and predictable operation of the system. Similarly, closing the vent first and then reopening the vacuum would be a logical and obvious method of efficiently generating a negative pulse. Thus, it would be obvious for a second double-closed state to occur in the course of generating a negative pulse during an aspiration cycle.

451. Ofek further discloses “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.” Ex. 1007 (Ofek) at 5:26-31.

452. In a situation where a three-way valve comprises both the vent valve and the vacuum valve, as described here, a POSA would find it obvious that while the three-way valve is transitioning from one state to another state (e.g., from a vent state to a vacuum state), there would be an intermediary “off-off” state during the transition because neither of the respective channels would be connected through the three-way valve. Put differently, for example, if the three-way valve were a rotary three-way valve, it would result in an off-off state when the three-way valve is rotating between the positions where the connecting channels are aligned to fluid

and vacuum channels. A similar example was discussed in Ground 2, Claim [5-B], with regard to the three-way valve 46 in Rubenstein. As was illustrated in the associated visual representations in that ground, the channels of the three-way valve would necessarily be disconnected from both the vent and vacuum channels while it is in transition. A POSA would recognize that the same result would occur here if the vent and vacuum valves are combined into a three-way valve.

453. Therefore, it is my opinion that Ofek and the knowledge of a POSA renders obvious “an off-off state in which the vacuum valve is closed while the vent valve is closed,” as recited by Claim 5.

Claim 6

[6-A]: The system of claim 1 wherein: the controller is configured to cyclically open and close the vacuum valve and the vent valve in a cycle comprising

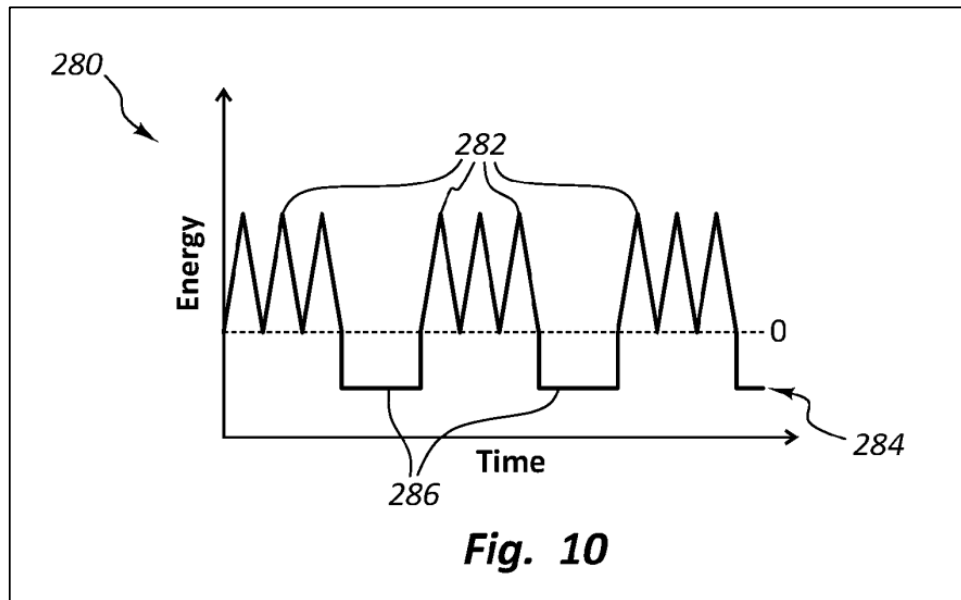
454. For the reasons discussed above for Ground 4, Claim [1-E], this limitation is met by Ofek.

[6-B]: (a) a first off-off state in which the vacuum valve is closed while the vent valve is closed, (b) a vacuum-only state following the first off-off state in which the vacuum valve is open while the vent valve is closed, (c) a second off-off state following the vacuum-only state in which the vacuum valve is closed while the vent valve is closed, and (d) a vent-only state following the second off-off state in which the vacuum valve is closed while the vent valve is open; and the cycle is repeated.

455. Ofek and the knowledge of a POSA renders obvious this limitation.

456. As discussed above for Ground 4, Claim [1-E], Ofek discloses cyclically opening and closing the vacuum valve and the vent valve in a repeated cycle. As also discussed above for Ground 4, Claim [5-B], Ofek and the knowledge of a POSA renders obvious an off-off state in which the vacuum valve is closed while the vent valve is closed.

457. In addition to the discussion above for Ground 4, Claim [5-B], the example operation cycle disclosed in relation to Figure 10 in Ofek is the following sequence: (1) no vacuum and no pressure impulse (starting point (time = 0)), (2) group of positive pressure impulses 282, (3) no vacuum and no pressure impulse (transition point between impulses 282 and negative pressure 286), (4) negative pressure 286. Put in terms of the valve states, the sequence would be as follows: (1) off-off state, (2) multiple vent-only states alternating with off-off state, (3) off-off state, (4) vacuum-only state.



458. As discussed above for Ground 4, Claim [1-G], Ofek extensively discusses how the operation cycles and pressure profiles can be customized by the controller in various different ways (e.g., number of impulses, level of pressure, frequency, etc.). A POSA would recognize that one such customization could be customizing the number of impulses in a given impulse period 282 to just a single positive pressure impulse. In such a configuration, the sequence with respect to Figure 10 would then be the following: (1) no vacuum and no pressure impulse (starting point (time = 0)), (2) single positive pressure impulse during 282 period, (3) no vacuum and no pressure impulse (transition point between impulse 282 and negative pressure 286), (4) negative pressure 286. Put in terms of the valve states, the sequence would then be as follows: (1) off-off state, (2) vent-only state, (3) off-off state, (4) vacuum-only state.

459. Therefore, it is my opinion that Ofek and the knowledge of a POSA renders obvious “(a) a first off-off state in which the vacuum valve is closed while the vent valve is closed, (b) a vacuum-only state following the first off-off state in which the vacuum valve is open while the vent valve is closed, (c) a second off-off state following the vacuum-only state in which the vacuum valve is closed while the vent valve is closed, and (d) a vent-only state following the second off-off state in which the vacuum valve is closed while the vent valve is open; and the cycle is repeated,” as recited by Claim 6.

Claim 7

[7]: The system of claim 6 wherein the cycle is repeated at a frequency of 2 Hz to 12 Hz.

460. Ofek and the knowledge of a POSA renders obvious this limitation.

461. As discussed above for Ground 4, Claim [1-E], Ofek alone or in view of Mullins renders obvious a controller configured to open and close the vacuum valve and the vent valve in a predetermined cycle. As also discussed above for Ground 4, Claim [6-A] and [6-B], Ofek alone or in view of Mullins and the knowledge of a POSA discloses or renders obvious the sequence of valve states recited by Claim 6.

462. As discussed above for Ground 4, Claim [1-G], Ofek extensively discusses how the operation cycles and pressure profiles can be customized by the

controller in various different ways (e.g., number of impulses, level of pressure, frequency, etc.), and invites a POSA to configure these variables with flexibility as may be desired or varied according to the desired application. Ex. 1007 (Ofek) at 3:30-42 (“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.”), 6:20-45 (“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.”).

463. I understand that routine optimization to discover the optimum ranges of conditions for an invention’s operation is obvious where the prior art discloses general conditions of claimed features or ranges. I further understand that there are

four ways for a patent owner to overcome obviousness based on routine optimization: (1) producing a new or unexpected result which is different in kind and not merely in degree from the results of the prior art; (2) if the prior art teaches away from the claimed ranges; (3) if the parameter was not recognized as result-effective; and (4) if the prior art discloses very broad ranges that do not invite routine optimization. None of these paths to overcoming obviousness apply in this situation. Here, the '402 Patent's claimed "cycle [] repeated at a frequency of 2 Hz to 12 Hz" is nothing more than a result-effective and obvious result from the routine experimentation invited by Ofek. The '402 does not describe nor demonstrate any particular effect of the claimed range, let alone any criticality or unexpectedness related to the claimed range. Finally, neither Ofek nor Mullins teaches away from the cycle being "repeated at a frequency of 2 Hz to 12 Hz," and Ofek explicitly invites the reader to customize the operating cycles, including cycle frequency, to the desired application. Notably, the claimed frequencies are within a range of frequencies (1 to 150 Hz) expressly disclosed by Ofek. Therefore, it is my opinion that the claimed "cycle [] repeated at a frequency of 2 Hz to 12 Hz" is the result of routine optimization and is thus obvious.

464. Therefore, it is my opinion that Ofek and the knowledge of a POSA renders obvious the "wherein the cycle is repeated at a frequency of 2 Hz to 12 Hz."

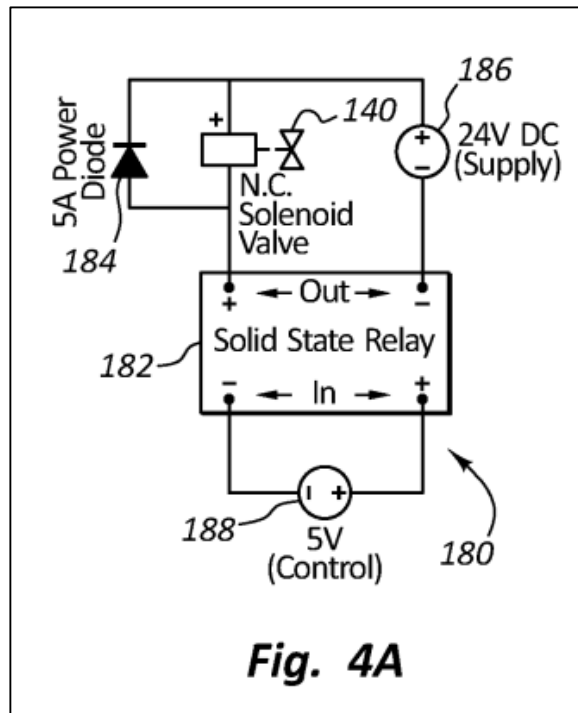
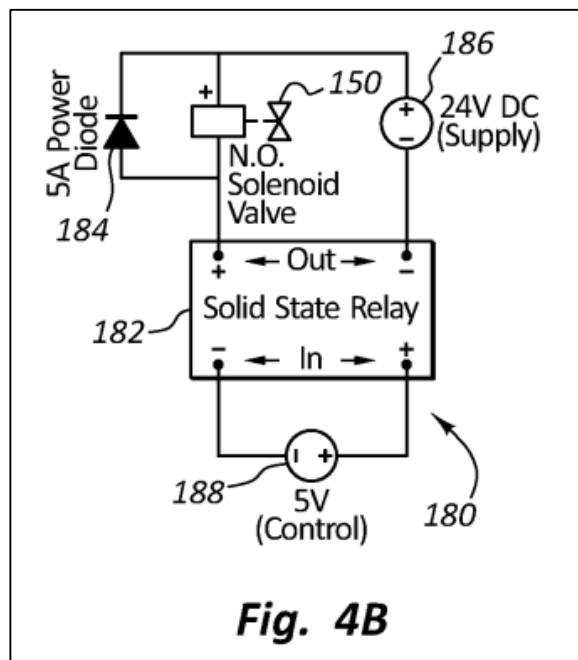
Claim 8

[8]: The system of claim 1 wherein the vacuum valve and the vent valve are solenoid pinch valves.

465. Ofek discloses this limitation.

466. Ofek discloses the vacuum valve and vent valve being solenoid pinch valves. Ex. 1007 (Ofek) at 7:18-26 (“The patency device of FIG. 5 replaces the gate valve-type of valves with tubing pinch valves for the N.O 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.”), FIGs. 4A, 4B.

467. The vacuum and vent valves in Ofek’s system are solenoid valves (valves 140 and 150) as depicted in figures 4(a) and 4(b) below. Ex. 1007 (Ofek) at FIGs. 4(a), 4(b).



468. Therefore, it is my opinion that Ofek discloses “the vacuum valve and the vent valve are solenoid pinch valves,” as recited by Claim 8.

Claim 10

[10-A]: The system of claim 1 wherein the controller is configured to cyclically open and close the vacuum valve and the vent valve

469. For the reasons discussed above for Ground 4, Claim [1-E], this limitation is met by Ofek.

[10-B]: such that an amount of momentum transfer from the fluid column in the catheter lumen is sufficient to unstick thromboembolic material at the distal end of the catheter.

470. Ofek alone or in view of Mullins discloses or renders obvious this limitation.

471. As discussed above for Ground 4, Claims [1-G] and [2-D], Ofek alone or in view of Mullins discloses or renders obvious changing a level of vacuum at the distal end of the catheter.

472. Ofek places significant focus on utilizing negative and positive pressure to dislodge occlusive material. Ex. 1007 (Ofek) at 2:56-3:2 (“are configured to prevent the formation of thrombus or other occlusion in the lumen 14, especially at the distal end thereof.”), 4:21-44 (“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.”), 6:9-19 (“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.”), 8:16-22 (“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”).

473. Further, a POSA would recognize that by utilizing negative and positive pressure to dislodge the thrombus that there must be a changing in the direction of flow within the catheter fluid column, which requires a changing in the direction of flow within the catheter fluid column. This, in turn, requires changing the momentum within the fluid column. This momentum of fluid, as a result of pressure changes, is a law of physics. That is because fluid will move from higher pressure areas to lower pressure areas. Because momentum is a function of velocity, any changes in direction or speed of the fluid will change the momentum. Therefore, by using negative and positive pressure, there are momentum changes in the fluid column, and the momentum of the fluid causes the occlusion to be dislodged.

474. To the extent that Ofek does not explicitly disclose an amount of momentum transfer sufficient to unstick thromboembolic material at the distal end of the catheter, the combination of Ofek and Mullins renders it obvious.

475. For the reasons discussed above (in greater detail) regarding Mullins in Ground 1, Claim [10-B], Mullins discloses reversing the direction of fluid displacement and allowing some or all of the clot to be pushed to cause the clot to become more “free” with respect to the catheter, and a POSA would understand and find it obvious that causing the clot to become more “free” may take place at the distal end of the catheter, at least because the nature of thrombus removal involves the distal end of the catheter being engaged with the thrombus.

476. Therefore, it is my opinion that Ofek alone or in view of Mullins discloses or renders obvious “such that an amount of momentum transfer from the fluid column in the catheter lumen is sufficient to unstick thromboembolic material at the distal end of the catheter,” as recited by Claim 10.

Claim 11

[11-Pre]: A method for removing thromboembolic material, comprising: aspirating thromboembolic material from a person using the system of claim 1 by—

477. For the reasons discussed above for Ground 4, Claim [1-Pre], this limitation is met by Ofek.

[11-A]: (a) positioning the distal end of the catheter at least proximate to thromboembolic material in a blood vessel of the person;

478. Ofek alone or in view of Mullins discloses or renders obvious this limitation.

479. As discussed above for Ground 4, Claim [1-Pre], [1-A], and regarding the motivation to combine Ofek and Mullins, Ofek discloses an aspiration thrombectomy system. A POSA would know that a central aspect of performing a thrombectomy procedure is positioning the distal end of the catheter next to the thrombus. A POSA would know that navigating the distal portion of the thrombectomy device to the clot in the vasculature is equivalent to positioning the distal end of the catheter proximate to the thrombus.

480. To the extent that Ofek does not explicitly disclose positioning the distal end of the catheter at least proximate to thromboembolic material in a blood vessel of the person, the combination of Ofek and Mullins renders it obvious.

481. For the reasons discussed above (in greater detail) regarding Mullins in Ground 1, Claim [11-A], Mullins discloses positioning the catheter tip adjacent to the clot.

482. Therefore, it is my opinion that Ofek alone or in view of Mullins discloses or renders obvious “positioning the distal end of the catheter at least

proximate to thromboembolic material in a blood vessel of the person,” as recited by Claim 11.

[11-B]: (b) applying a vacuum through the lumen of the catheter such that a vacuum flow draws at least a portion of the thromboembolic material into the catheter lumen; and

483. Ofek alone or in view of Mullins discloses this limitation.

484. As discussed above for Ground 4, Claim [1-Pre] and regarding the motivation to combine Ofek and Mullins, Ofek discloses an aspiration thrombectomy system.

485. Ofek discloses using negative pressure to draw an occlusion into the catheter lumen. Ex. 1007 (Ofek) at Abs. (“A negative pressure can then be provided to the lumen to aspirate the occlusion and remove it from the catheter assembly”), 3:43-60 (“The negative baseline pressure present between impulses enables any occlusion dislodged by the impulses to be sucked proximally up the catheter tube lumen 14”), 4:21-44 (“In addition, a suction process can be performed by the patency device 30 to withdraw the clot proximally”).

486. Like Ofek, Mullins also discloses applying a vacuum through the lumen of the catheter such that a vacuum flow draws at least a portion of the thromboembolic material into the catheter lumen.

487. For the reasons discussed above (in greater detail) regarding Mullins in Ground 1, Claim [11-B], Mullins discloses using vacuum to cause at least a portion of the clot to be aspirated and ingested by the catheter.

488. Therefore, it is my opinion that Ofek or in view of Mullins discloses “applying a vacuum through the lumen of the catheter such that a vacuum flow draws at least a portion of the thromboembolic material into the catheter lumen” as recited by Claim 11.

[11-C]: (c) controlling the vacuum valve fluidically coupled to the vacuum source and the catheter and the vent valve fluidically coupled to a vent fluid source and the catheter

489. For the reasons discussed above for Ground 4, Claims [1-B], [1-E], and [2-A], this limitation is met by Ofek.

490. Additionally, Ofek discloses that the vent valve is fluidically coupled to the vent fluid source. Ex. 1007 (Ofek) at 4:45-61 (“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.”), 7:18-26 (“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.”), 4:45-61 (“Note that the fluid lines between the various components discussed herein can include tubing or other suitable modes for fluid transport.”), FIGs. 3, 4A, 5.

491. Therefore, it is my opinion that Ofek discloses “controlling the vacuum valve fluidically coupled to the vacuum source and the catheter and the vent valve fluidically coupled to a vent fluid source and the catheter,” as recited by Claim 11.

[11-D]: such that a level of vacuum at the distal end of the catheter changes.

492. For the reasons discussed above for Ground 4, Claim [1-F], this limitation is met by Ofek in view of Mullins.

[11-E]: and thereby controls flow in and out from the distal end of the catheter.

493. For the reasons discussed above for Ground 4, Claim [1-G], this limitation is met by Ofek in view of Mullins.

Claim 12

[12-A]: The method of claim 11 wherein: the vent fluid source is configured to provide the vent fluid at a pressure greater than atmospheric pressure; and

494. For the reasons discussed above for Ground 4, Claim [2-B], this limitation is met by Ofek.

[12-B]: controlling the vacuum valve and the vent valve comprises cyclically opening and closing the vacuum valve and the vent valve

495. For the reasons discussed above for Ground 4, Claim [1-E], this limitation is met by Ofek.

[12-C]: to change a level of negative pressure and positive pressure at the distal end of the catheter during each cycle.

496. For the reasons discussed above for Ground 4, Claim [2-D], this limitation is met by Ofek in view of Mullins.

Claim 13

[13-A]: The method of claim 12 wherein controlling the vacuum valve and the vent valve comprises limiting movement of a fluid column in the catheter lumen at the distal end of the catheter to a positive amount of exit flow

497. For the reasons discussed above for Ground 4, Claim [3-B], this limitation is met by Ofek in view of Mullins.

[13-B] limiting... to a positive amount of exit flow within a range of a length of the fluid column that exits the distal end of the catheter.

498. As discussed above for Ground 4, Claim [3-C], the limitation of ranges of volumes of positive exit flow is met by Ofek in view of Mullins.

499. A POSA would further recognize that the equivalence between measurement of exit flow could be based on length rather than volume. Given that volume is a function of length, a teaching of one teaches of the other. For a catheter,

which may have a largely equivalent diameter along its full length, this conversion would be simple. A POSA would further understand that having a steady diameter along the length of the catheter would allow for a clot to be aspirated. A POSA would recognize that controlling the exit flow fluid column length rather than the exit flow volume would consistently limit the distance a coked clot travels away from the distal end of the catheter before the pressure within the catheter is reversed to draw fluid and clot back into the catheter lumen. In comparison, when the volume of exit flow is controlled, the distance a coked clot is allowed to travel away from the distal end of the catheter varies with each catheter lumen diameter. For a fixed exit flow volume, the smaller the catheter lumen diameter, the longer the length of the exit flow fluid column.

500. Therefore, it is my opinion that Ofek alone or in view of Mullins discloses and renders obvious “limiting... to a positive amount of exit flow within a range of a length of the fluid column that exits the distal end of the catheter,” as recited by Claim 13.

Claim 14

[14-A]: The method of claim 13 wherein limiting movement of the fluid column at the distal end of the catheter comprises stopping a distal flow through the catheter lumen and reapplying the vacuum through the catheter lumen ... before fluid is drawn back into the catheter lumen.

501. Ofek alone or in view of Mullins and the knowledge of a POSA renders this claim limitation obvious.

502. As discussed above for Ground 4, Claim [3-B], Ofek alone or in view of Mullins discloses or renders obvious limiting an amount of positive exit flow and subsequently drawing fluid back into the catheter.

503. Ofek further discloses stopping distal impulses and reapplying vacuum in a predetermined pattern. Ex. 1007 (Ofek) at 5:63-6:8 (“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”), 7:11-17 (“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.”), 8:38-49 (“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.

504. To the extent that Ofek does not explicitly disclose limiting movement of the fluid column at the distal end by stopping a distal flow through the catheter lumen and reapplying the vacuum through the catheter lumen before fluid is drawn back into the catheter lumen, the combination of Ofek and Mullins renders it obvious.

505. In Mullins, figures 47(g)-(h) illustrate this start and stop of fluid flow and vacuum within the lumen. Ex. 1008 (Mullins) at Figs. 47(g)-(h); Ex. 1009.2 (Mullins-Prov2) at pg.4-9. Furthermore, Mullins describes a sensor used to determine fluid displacement and vary pressure, such as by reapplying vacuum. Ex. 1008 (Mullins) at 3:35-38 (“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.”); Ex. 1009.2 (Mullins-Prov2) at pg. 3-9. Mullins further explicitly discloses the controller providing vacuum for this task. Ex. 1008 (Mullins) at 3:56-59 (“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.”); Ex. 1009.2 (Mullins-Prov2) at pg. 4-10.

506. Therefore, it is my opinion that Ofek alone or in view of Mullins discloses and renders obvious “limiting movement of the fluid column at the distal end of the catheter comprises stopping a distal flow through the catheter lumen and reapplying the vacuum through the catheter lumen ... before fluid is drawn back into the catheter lumen,” as recited by Claim 14.

[14-B]: ...such that the positive amount of exit flow is approximately 0.5 mm to approximately 30 mm of the fluid column...

507. Ofek alone or in view of Mullins and the knowledge of a POSA renders this claim limitation obvious.

508. As discussed above for Ground 4, Claim [13-B], Ofek alone or in view of Mullins and the knowledge of a POSA discloses or renders obvious limiting to a positive amount of exit flow within a range of length.

509. As also discussed above (in greater detail) regarding exit flow values as a preliminary matter in Ground 1, Claim [3-C], a POSA would understand the values of approximately 0.5 mm to approximately 30 mm of fluid column to be reasonable values for implementing a limited amount of exit flow, at least because a POSA would be motivated to limit the amount of positive exit flow, and because a POSA would have a reasonable expectation that those values would not result in an unacceptable level of risk of distal migration.

510. A POSA would recognize the clinical safety concerns of positive exit flow pushing the clot material away from the distal end of the catheter to a distance that the reversed catheter pressure (vacuum) can no longer draw the clot back to the catheter. If the vacuum is unable to draw the clot back to the catheter, the clot becomes embolic material along with its associated clinical risks and hazards. A POSA would recognize that an exit flow range of approximately 0.5 mm to approximately 30 mm of fluid column is a reasonable distance that would not preclude the catheter vacuum from drawing the clot back into the catheter.

511. Additionally, a POSA would understand how to convert the exit flow volumes describe in Ground 1, [3-C] to respective values of exit flow length.

512. In view of the above, consistent with my analysis for Ground 1, [3-C], the table below reflects the amount of exit flow (in millimeters) that a POSA might experiment with in implementing Ofek in view of Mullins for a .061” inner diameter catheter and a .088” inner diameter catheter.

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U.S. Patent 11,406,402
Declaration of Brian Brown

Distal Lumen Flow Length Catheter Internal Diameter: 0.061 inches Catheter Internal Cross-Section Area: 1.885 mm ² Flow Rate (Blood): 1.0 mL/sec Distal Flow Volume (mL) = Blood Flow Rate (mL/sec) * Cycle Percentage (%) * Cycle Duration (sec) Distal Flow Length (mm) = 1000 (mm ³ /mL) * Distal Flow Volume (mL) / Lumen Cross-Section Area (mm ²)							
Fluid Displacement Ratios "Infuse-to-aspirate cycle": [Mullins (Ex. 1008) at 28:59-64]		"between 0.01 and 0.99"		"between 0.1 and 0.9"		"between 0.4 and 0.9"	
Normalized percentage of time per cycle:		Infuse %	Aspirate %	Infuse %	Aspirate %	Infuse %	Aspirate %
		1%	99%	10%	90%	31%	69%
Cycle frequency (Hz)	Cycle duration (sec)	Exit-flow (mm)	In-flow (mm)	Exit-flow (mm)	In-flow (mm)	Exit-flow (mm)	In-flow (mm)
0.100	10.000	53.050398	5251.989390	530.503979	4774.535809	1644.562334	3660.477454
0.111	9.000	47.745358	4726.790451	477.453581	4297.082228	1480.106101	3294.429708
0.125	8.000	42.440318	4201.591512	424.403183	3819.628647	1315.649867	2928.381963
0.143	7.000	37.135279	3676.392573	371.352785	3342.175066	1151.193634	2562.334218
0.167	6.000	31.830239	3151.193634	318.302387	2864.721485	986.737401	2196.286472
0.200	5.000	26.525199	2625.994695	265.251989	2387.267905	822.281167	1830.238727
0.250	4.000	21.220159	2100.795756	212.201592	1909.814324	657.824934	1464.190981
0.333	3.000	15.915119	1575.596817	159.151194	1432.360743	493.368700	1098.143236
0.500	2.000	10.610080	1050.397878	106.100796	954.907162	328.912467	732.095491
1.000	1.000	5.305040	525.198939	53.050398	477.453581	164.456233	366.047745
2.000	0.500	2.652520	262.599469	26.525199	238.726790	82.228117	183.023873
3.000	0.333	1.768347	175.066313	17.683466	159.151194	54.818744	122.015915
4.000	0.250	1.326260	131.299735	13.262599	119.363395	41.114058	91.511936
5.000	0.200	1.061008	105.039788	10.610080	95.490716	32.891247	73.209549
6.000	0.167	0.884173	87.533156	8.841733	79.575597	27.409372	61.007958
7.000	0.143	0.757863	75.028420	7.578628	68.207654	23.493748	52.292535
8.000	0.125	0.663130	65.649867	6.631300	59.681698	20.557029	45.755968
9.000	0.111	0.589449	58.355438	5.894489	53.050398	18.272915	40.671972
10.000	0.100	0.530504	52.519894	5.305040	47.745358	16.445623	36.604775
20.000	0.050	0.265252	26.259947	2.652520	23.872679	8.222812	18.302387
50.000	0.020	0.106101	10.503979	1.061008	9.549072	3.289125	7.320955
100.000	0.010	0.053050	5.251989	0.530504	4.774536	1.644562	3.660477
150.000	0.007	0.035367	3.501326	0.353669	3.183024	1.096375	2.440318

Distal Lumen Flow Volume Catheter Internal Diameter: 0.088 inches Catheter Internal Cross-Section Area: 3.923 mm ² Flow Rate (Blood): 4.0 mL/sec Distal Flow Volume (mL) = Blood Flow Rate (mL/sec) * Cycle Percentage (%) * Cycle Duration (sec) Distal Flow Length (mm) = 1000 (mm ³ /mL) * Distal Flow Volume (mL) / Lumen Cross-Section Area (mm ²)							
Fluid Displacement Ratios "Infuse-to-aspirate cycle": [Mullins (Ex. 1008) at 28:59-64]		"between 0.01 and 0.99"		"between 0.1 and 0.9"		"between 0.4 and 0.9"	
Normalized percentage of time per cycle:		Infuse %	Aspirate %	Infuse %	Aspirate %	Infuse %	Aspirate %
		1%	99%	10%	90%	31%	69%
Cycle frequency (Hz)	Cycle duration (sec)	Exit-flow (mm)	In-flow (mm)	Exit-flow (mm)	In-flow (mm)	Exit-flow (mm)	In-flow (mm)
0.100	10.000	101.962784	10094.315575	1019.627836	9176.650523	3160.846291	7035.432067
0.111	9.000	91.766505	9084.884017	917.665052	8258.985470	2844.761662	6331.888861
0.125	8.000	81.570227	8075.452460	815.702269	7341.320418	2528.677033	5628.345654
0.143	7.000	71.373949	7066.020902	713.739485	6423.655366	2212.592404	4924.802447
0.167	6.000	61.177670	6056.589345	611.776702	5505.990314	1896.507775	4221.259240
0.200	5.000	50.981392	5047.157787	509.813918	4588.325261	1580.423146	3517.716034
0.250	4.000	40.785113	4037.726230	407.851134	3670.660209	1264.338516	2814.172827
0.333	3.000	30.588835	3028.294672	305.888351	2752.995157	948.253887	2110.629620
0.500	2.000	20.392557	2018.863115	203.925567	1835.330105	632.169258	1407.086413
1.000	1.000	10.196278	1009.431557	101.962784	917.665052	316.084629	703.543207
2.000	0.500	5.098139	504.715779	50.981392	458.832526	158.042315	351.771603
3.000	0.333	3.398759	336.477186	33.987595	305.888351	105.361543	234.514402
4.000	0.250	2.549070	252.357889	25.490696	229.416263	79.021157	175.885802
5.000	0.200	2.039256	201.886311	20.392557	183.533010	63.216926	140.708641
6.000	0.167	1.699380	168.238593	16.993797	152.944175	52.680772	117.257201
7.000	0.143	1.456611	144.204508	14.566112	131.095007	45.154947	100.506172
8.000	0.125	1.274535	126.178945	12.745348	114.708132	39.510579	87.942901
9.000	0.111	1.132920	112.159062	11.329198	101.962784	35.120514	78.171467
10.000	0.100	1.019628	100.943156	10.196278	91.766505	31.608463	70.354321
20.000	0.050	0.509814	50.471578	5.098139	45.883253	15.804231	35.177160
50.000	0.020	0.203926	20.188631	2.039256	18.353301	6.321693	14.070864
100.000	0.010	0.101963	10.094316	1.019628	9.176651	3.160846	7.035432
150.000	0.007	0.067975	6.729544	0.679752	6.117767	2.107231	4.690288

513. Therefore, it is my opinion that Ofek alone or in view of Mullins discloses and renders obvious “the positive amount of exit flow is approximately 0.5 mm to approximately 30 mm of the fluid column,” as recited by Claim 14.

Claim 15

[15-A]: The method of claim 12 wherein controlling the vacuum valve and the vent valve comprises limiting movement of a fluid column in the catheter lumen at the distal end of the catheter to a positive amount of exit flow

514. For the reasons discussed above for Ground 4, Claim [3-B], this limitation is met by Ofek in view of Mullins.

[15-B]: limiting ... to a positive amount of exit flow within a range of volume of fluid that exits the distal end of the catheter.

515. For the reasons discussed above for Ground 4, Claims [3-B] and [3-C], this limitation is met by Ofek in view of Mullins and the knowledge of a POSA.

Claim 16

[16-A]: The method of claim 15 wherein limiting movement of the fluid column at the distal end of the catheter comprises stopping a distal flow through the catheter lumen and reapplying the vacuum through the catheter lumen... before fluid is drawn back into the catheter lumen.

516. For the reasons discussed above for Ground 4, Claims [3-B] and [14-A], this limitation is met by Ofek in view of Mullins.

[16-B]: ...such that the positive amount of exit flow is approximately 0.001 ml to approximately 1.0 ml...

517. For the reasons discussed above for Ground 4, Claim [3-C], this limitation is met by Ofek in view of Mullins and the knowledge of a POSA.

Claim 17

[17-A]: The method of claim 15 wherein limiting movement of the fluid column at the distal end of the catheter comprises stopping a distal flow through the catheter lumen and reapplying the vacuum through the catheter lumen ... before fluid is drawn back into the catheter lumen.

518. For the reasons discussed above for Ground 4, Claims [3-B] and [14-A], this limitation is met by Ofek in view of Mullins.

[17-B]: ...such that the positive amount of exit flow is approximately 0.1 ml to approximately 0.5 ml...

519. For the reasons discussed above for Ground 4, Claims [3-C] and [4-C], this limitation is met by Ofek in view of Mullins and the knowledge of a POSA.

Claim 18

[18-A]: The method of claim 11, further comprising cyclically opening and closing the vacuum valve and the vent valve in a repeated cycle

520. For the reasons discussed above for Ground 4, Claim [1-E], this limitation is met by Ofek.

[18-B]: including an off-off state in which the vacuum valve is closed while the vent valve is closed.

521. For the reasons discussed above for Ground 4, Claim [5-B], this limitation is met by Ofek and the knowledge of a POSA.

Claim 19

[19-A]: The method of claim 11, further comprising: cyclically opening and closing the vacuum valve and the vent valve in a cycle including

522. For the reasons discussed above for Ground 4, Claim [1-E] , this limitation is met by Ofek.

[19-B]: (a) a first off-off state in which the vacuum valve is closed while the vent valve is closed, (b) a vacuum-only state following the first off-off state in which the vacuum valve is open while the vent valve is closed, (c) a second off-off state following the vacuum-only state in which the vacuum valve is closed while the vent valve is closed, and (d) a vent-only state following the second off-off state in which the vacuum valve is closed while the vent valve is open; and repeating the cycle.

523. For the reasons discussed above for Ground 4, Claim [6-B], this limitation is met by Ofek and the knowledge of a POSA.

Claim 20

[20]: The method of claim 19 wherein the cycle is repeated at a frequency of 2 Hz to 12 Hz.

524. For the reasons discussed above for Ground 4, Claim [7], this limitation is met by Ofek.

E. Ground 5: Claims 5, 6, 18, and 19 Are Rendered Obvious Over Ofek in View of Mullins, Rubenstein, and the Knowledge of a POSA

Motivation to Combine

525. A person of ordinary skill in the art at the time the purported invention of the '402 Patent was made would have been motivated to combine Ofek and

Mullins' cyclical aspiration thrombectomy system with Rubenstein's teachings of: (1) a pumping system to eliminate clogs within the catheter; (2) applying cyclical reversals of positive and negative pressure in the catheter; and (3) transitioning between a vacuum suction state and a blowing, or positive pressure state when necessary using a time-controlled valve. The motivation to combine Ofek and Mullin is discussed above at Ground 4 (Ofek in view of Mullins and the knowledge of a POSA).

526. A POSA would have been motivated to combine Ofek, Mullins, and Rubenstein because (1) all three references address similar problems related to conventional methods of medical aspiration procedures, including clogged catheters, and (2) all three references teach similar solutions involving using a positive pressure state to temporarily relieve the negative pressure within the system so as to more efficiently remove blood clots from the clogged catheter and ultimately the patient. As an example, all three references describe issues with catheter systems, such as clogged catheters and the limitations of static aspiration technologies for controlled clot aspiration. Ex. 1007 (Ofek) at Abstract, 1:16-33, 2:28-37; Ex. 1008 (Mullins) at 4:5-11, 25:22-26:16, 28:27-37; Ex. 1009.2 (Mullins-Prov2) at pg. 2-11; Ex. 1011 (Rubenstein) at 1:24-31, 2:1-12. The references describe similar approaches to solving these and other issues, including creating a dynamic force within the catheter

using a combination of vacuum and vent sources connected to a catheter via controllable valves. Ex. 1007 (Ofek) at 4:45-5:7, 7:18-26; Ex. 1008 (Mullins) at 1:53-2:2, 3:29-4:11, 26:17-28:64; Ex. 1009.2 (Mullins-Prov2) at pg. 3-10; Ex. 1011 (Rubenstein) at Abstract, 1:7-14, 1:64-68, 2:1-12.

527. A POSA would have understood that Ofek, Mullins, and Rubenstein are each directed to medical aspiration systems and related methods using a source of both positive and negative pressure to clear clogged catheters via dynamic suction forces to more efficiently reinstate vacuum in a catheter after a clog. Ex. 1007 (Ofek) at 3:45-53, 4:19-5:7, 6:5-8, 6:20-23; Ex. 1008 (Mullins) at 3:29-4:11, 26:17-28:64; Ex. 1009.2 (Mullins-Prov2) at pg. 2-10. Ex. 1011 (Rubenstein) at 1:7-14, 1:64-68. Accordingly, combining the teachings of Ofek, Mullins, and Rubenstein would have been well within the skill of a POSA, because it is nothing more than combining known vacuum aspiration technologies described in these references to perform their intended functions with described benefits and predictable results. As discussed above and below in Grounds 2, Claim [5-B], and Ground 5, Claim [5-B], Rubenstein also shows it was typical to implement controllable valves in a vacuum/vent system such that there is a double-closed state where the catheter is temporarily isolated from both the vacuum and vent valves.

528. For at least these reasons, it would have been obvious to combine Ofek, Mullins, and Rubenstein.

Claim 5

[5-A]: The system of claim 1 wherein the controller is configured to cyclically open and close the vacuum valve and the vent valve in a repeated cycle

529. For the reasons discussed above for Ground 4, Claim 1 is disclosed or rendered obvious by Ofek in view of Mullins, and therefore also met by Ofek in view of Mullins and Matteo. In particular, for the reasons discussed above for Ground 4, Claim [1-E], this limitation is met by Ofek, and therefore also met by Ofek in view of Mullins and Rubenstein.

[5-B]: comprising an off-off state in which the vacuum valve is closed while the vent valve is closed.

530. Ofek in view of Mullins, Rubenstein, and the knowledge of a POSA renders obvious this limitation.

531. As discussed above for Ground 4, Claim [1-E], Ofek discloses cyclically opening and closing the vacuum valve and the vent valve in a repeated cycle. As also discussed above for Ground 4, Claim [5-B], Ofek and the knowledge of a POSA discloses or renders obvious an off-off state in which the vacuum valve is closed while the vent valve is closed.

532. To the extent that Ofek in view of Mullins does not explicitly disclose an off-off state in which the vacuum valve is closed while the vent valve is closed, the combination of Ofek, Mullins, and Rubenstein renders it obvious.

533. For the reasons discussed above (in greater detail) regarding Rubenstein in Ground 2, Claim [5-B], Rubenstein discloses an off-off state in which the vacuum valve is closed while the vent valve is closed.

534. A POSA would find it obvious to modify the system in Ofek to adopt the valves disclosed in Rubenstein, which would result in a double-closed state during serial or parallel operation of the incorporated valves. A person of skill in the art would also find it obvious to employ Rubenstein's time-controlled valve opening and closing because Rubenstein notes that "any cycle and ratio of negative and positive pressure can be used to satisfy a particular need" which would invite a POSA to optimize the positive and negative pressure system in Rubenstein to achieve optimal clot aspiration within the Ofek system. Ex. 1011 (Rubenstein) at 3:41-50; *see also id.* at 2:64-68 (disclosing certain example rotary valves that can be automated).

535. Thus, consistent with the serial operation of Ofek's valve states, a POSA would have understood, and it would be most logical and obvious to conduct the valve operation in serial to yield effective pulsing, e.g., closing the vacuum valve

first and then opening the vent valve to generate the positive pulse. Rubenstein similarly discloses such serial operations of vacuum and vent valves that a POSA would readily and easily adopt for dynamic aspiration taught by Ofek and Mullins. Ex. 1011 (Rubenstein) at 1:10-14, 1:64-68. Alternatively, a POSA could also adopt the valves disclosed in Rubenstein to accomplish the dynamic aspiration taught by the combination of Mullins and Ofek, including an off-off state in which the vacuum valve is closed while the vent valve is closed.

536. Therefore, it is my opinion that Ofek in view of Mullins and Rubenstein further renders obvious “an off-off state in which the vacuum valve is closed while the vent valve is closed,” as recited by Claim [5-B].

Claim 6

[6-A]: The system of claim 1 wherein: the controller is configured to cyclically open and close the vacuum valve and the vent valve in a cycle comprising

537. For the reasons discussed above for Ground 4, Claims [1-E], this limitation is met by Ofek, and therefore also met by Ofek in view of Mullins and Rubenstein.

[6-B]: (a) a first off-off state in which the vacuum valve is closed while the vent valve is closed, (b) a vacuum-only state following the first off-off state in which the vacuum valve is open while the vent valve is closed, (c) a second off-off state following the vacuum-only state in which the vacuum valve is closed while the vent valve is closed, and (d) a vent-only state following the second off-off state in which the vacuum valve is closed while the vent valve is open; and the cycle is repeated.

538. For the reasons discussed above for Ground 4, Claims [5-B] and [6-B], this limitation is met by Ofek and the knowledge of a POSA, and therefore also met by Ofek in view of Mullins and Rubenstein and the knowledge of a POSA. Additionally, in view of the reasons discussed above for Ground 2, Claim [5-B], with regard to the double-closed state that is further rendered obvious by Rubenstein, this limitation is also further rendered obvious by Rubenstein.

Claim 18

[18-A]: The method of claim 11, further comprising cyclically opening and closing the vacuum valve and the vent valve in a repeated cycle

539. For the reasons discussed above for Ground 4, Claim [1-E], this limitation is met by Ofek, and therefore also met by Ofek in view of Mullins and Rubenstein.

[18-B]: including an off-off state in which the vacuum valve is closed while the vent valve is closed.

540. For the reasons discussed above for Ground 4, Claim [5-B], this limitation is met by Ofek in view of Mullins, and therefore also met by Ofek in view of Mullins and Rubenstein. Additionally, in view of the reasons discussed above for Ground 2, Claim [5-B], with regard to the double-closed state that is further rendered obvious by Rubenstein, this limitation is also further rendered obvious by Rubenstein.

Claim 19

[19-A]: The method of claim 11, further comprising: cyclically opening and closing the vacuum valve and the vent valve in a cycle including

541. For the reasons discussed above for Ground 4, Claim [1-E], this limitation is met by Ofek, and therefore also met by Ofek in view of Mullins and Rubenstein.

[19-B]: (a) a first off-off state in which the vacuum valve is closed while the vent valve is closed, (b) a vacuum-only state following the first off-off state in which the vacuum valve is open while the vent valve is closed, (c) a second off-off state following the vacuum-only state in which the vacuum valve is closed while the vent valve is closed, and (d) a vent-only state following the second off-off state in which the vacuum valve is closed while the vent valve is open; and repeating the cycle.

542. For the reasons discussed above for Ground 4, Claims [5-B] and [6-B], this limitation is met by Ofek and the knowledge of a POSA, and therefore also met by Ofek in view of Mullins and Rubenstein and the knowledge of a POSA. Additionally, in view of the reasons discussed above for Ground 2, Claim [5-B], with regard to the double-closed state that is further rendered obvious by Rubenstein, this limitation is also further rendered obvious by Rubenstein.

F. Ground 6: Claim 9 is Rendered Obvious Over Ofek in view of Mullins, Matteo, and the Knowledge of a POSA

Motivation to Combine

543. A person of ordinary skill in the art at the time of the purported invention of the '402 Patent was made would have been motivated to combine Ofek's and Mullins's cyclical aspiration thrombectomy systems with Matteo's cam system for valve control. The motivation to combine Ofek and Mullins is discussed above at Ground 4 (Ofek in view of Mullins and the knowledge of a POSA).

544. A POSA would have been motivated to combine Ofek, Mullins, and Matteo because (1) all three references address similar problems related to the precise combination of multiple fluids at precise times in scientific and medical applications, and (2) all three references teach similar solutions involving using multiple flow control mechanisms (e.g., valves or pumps) to separate and combine the fluids to achieve desired results. Ex. 1007 (Ofek) at 4:21-6:8, 6:20-45, 6:59-7:26; Ex. 1008 (Mullins) at 26:31-37, 26:65-27:39; Ex. 1009.2 (Mullins-Prov2) at pg. 4-10; Ex. 1013 (Matteo) at ¶ [0059], FIGS. 10A-C. As an example, all three references describe similar approaches to solving these and other issues, including using a controller to control flow control mechanisms (e.g., valves or pumps) that can be switched between varying states of open and closed positions. Ex. 1007 (Ofek) at 4:21-6:8, 6:20-45, 6:59-7:26; Ex. 1008 (Mullins) at 26:65-27:39; Ex. 1009.2 (Mullins-Prov2) at pg. 4-7; Ex. 1013 (Matteo) at FIGS.10A-C.

545. A POSA would have understood that all three references are each directed to systems and related methods that rely on precise timing and pressures of fluid to enter the system via open valves, using controlled valves to introduce fluid into the system that provide energy efficiencies and control over fluid introductions. Accordingly, combining the teachings of Ofek, Mullins, and Matteo would have been well within the skill of a POSA, because it is nothing more than combining

known vacuum aspiration technologies described in Ofek and Mullins with known controlled valve systems described in Matteo to perform their intended functions with described benefits and predictable results.

546. A POSA would find it obvious to implement Matteo's disclosures of cam-driven pinch valves that optimize the introduction of fluid when implementing the combination of Ofek and Mullins, because a POSA would recognize that Matteo's cam-driven pinch valves were a well-understood and effective technique to implement a valve having the necessary timing precision to implement the techniques taught in Ofek and Mullins, while also providing benefits of reduced complexity and space-savings as disclosed in Matteo. Ex. 1013 (Matteo) at Abstract. It would have been well within the skill of a POSA to utilize any type of suitable valves as vacuum and vent valves in the systems of Ofek and Mullins, including cam-driven pinch valves as disclosed in Matteo. Additionally, Matteo explains that "Cam-driven pinch-style microvalves are useful for controlling multi-channel microfluidic systems with an energy-efficient and space-efficient apparatus. Thus, these microvalves have uses in a number of diverse fields and applications, including medical and scientific instrumentation," which a POSA would understand includes the medical systems taught in Ofek and Mullins Ex. 1013 (Matteo) at ¶ [0012].

547. A POSA would have recognized that the aspiration systems of Ofek and Mullins could be modified such that the vacuum and vent valves could be cam-driven pinch valves, and would have a reasonable expectation of success in implementing this combination, because it would simply be using widely known shaft and cam actuator technology to control valves, as disclosed in Matteo, within the aspiration systems of Ofek and Mullins. Ex. 1013 (Matteo) at Claim 1.

548. For at least these reasons, it would have been obvious to combine Ofek, Mullins, and Matteo.

Claim 9

[9]: The system of claim 1 wherein the vacuum valve and the vent valve are cammed pinch valves.

549. For the reasons discussed above for Ground 4, Claim 1 is disclosed or rendered obvious by Ofek in view of Mullins, and therefore also met by Ofek in view of Mullins and Matteo. Further, Ofek already discloses pinch valves. Ex. 1007 (Ofek) at FIGs. 4A, 4B.

550. To the extent that Ofek and Mullins do not explicitly disclose the vacuum and vent valves being cammed pinch valves, the combination of Ofek, Mullins, and Matteo renders it obvious.

551. For the reasons discussed above (in greater detail) regarding Matteo in Ground 3, Claim [9], Matteo discloses the vacuum valve and the vent valve being cammed pinch valves.

552. Therefore, it is my opinion that Ofek in view of Mullins and Matteo renders claim 9 obvious.

XIV. RESERVATION OF RIGHTS

553. My opinions are based upon the information that I have considered to date. I am unaware of any evidence of objective indicia with respect to the '402 Patent that would render any of the challenged claims non-obvious. I reserve the right, however, to supplement my opinions in the future to respond to any arguments raised by the owner of the '402 Patent and to consider new information that becomes available to me.

XI. DECLARATION

554. I hereby declare that all statements made herein of my own knowledge are true and all statements made on information and belief are believed to be true. I further understand that willful false statements and the like are punishable by fine or imprisonment, or both under Section 1001 of Title 18 of the United States Code. I declare under penalty of perjury that the foregoing is true and correct.



Executed on July 31, 2024.

Brian Brown