
**UNITED STATES PATENT AND TRADEMARK OFFICE
BEFORE THE PATENT TRIAL AND APPEAL BOARD**

In Re: U.S. Patent 10,722,253 : Attorney Docket No. 088594.0119

Inventors: Derek Dee Deville
Matthew A. Palmer
William T. Bales, Jr.
M. Sean McBrayer
Eric Petersen
Richard Cartledge :

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Assignee: RapidPulse, Inc.

Title: Aspiration Thrombectomy System and Methods for Thrombus Removal
with Aspiration Catheter

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P.O. Box 1450
Alexandria, Virginia 22313-1450

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**DECLARATION OF BRIAN BROWN IN SUPPORT OF
PETITION FOR INTER PARTES REVIEW OF U.S. PATENT NO.
10,722,253**

RapidPulse, Inc.
Exhibit 2008
Penumbra v. RapidPulse
IPR2024-01261
Ex. 2008-001

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List of Exhibits

1001	U.S. Patent No. 10,722,253 (“the ’253 Patent”)
1002	U.S. Provisional Application No. 62/701,086
1003	U.S. Provisional Application No. 62/750,011
1004	Prosecution File History of the ’253 Patent
1005	Expert Declaration of Brian Brown
1006	CV of Brian Brown
1007	U.S. Patent No. 11,197,683 (“Teigen”)
1008	U.S. Provisional Application No. 62/702,804 (the “’804 Provisional”)
1009	U.S. Provisional Application No. 62/778,708 (the “’708 Provisional”)
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	06/10/2021 Response to Office Action during prosecution of U.S. Patent No. 11,096,712 (“Teigen ’712”)
1029	06/23/2021 Notice of Allowance during prosecution of U.S. Patent No. 11,096,712 (“Teigen ’712”)
1030	U.S. Patent No. 11,096,712 (“Teigen ’712”)
1031	PCT International Application No. PCT/US2019/043095
1032	U.S. Patent No. 10,531,883 (“the ’883 Patent”)
1033	Prosecution File History of the ’883 Patent

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 hypothetical person of ordinary skill in the art (“POSA”) would understand the scope of the claims and whether certain claims of U.S. Patent No. 10,722,253 (“the ’253 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.

I. 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.

A. 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.

B. 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.

C. 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.

D. 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.

II. 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.

A. 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.

B. 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 plain meaning or 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 '253 Patent to the prior art, I have carefully considered the '253 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.”

III. 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 ’253 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 ’253 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 '253 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 '253 Patent.

IV. Technology Background

49. The '253 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.

A. 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.

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.

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.

B. 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 '253 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 '253 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. 1010 at 2:16-20, 7:10-12; Ex. 1023 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. 1007 at 1:35-45; Ex. 1008 at [003]; Ex. 1009 at [004]. 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. 1010 at 2:16-20, 7:10-12; Ex. 1023 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 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, ex. 1017, to an inner diameter of approximately 0.120” of a 9Fr sheath for

the treatment of peripheral occlusions, ex. 1018. 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 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 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 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* Ex. 1007 at 14:45-62; Ex. 1008 at [0088]; Ex. 1009 at [0076]. 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; Ex. 1020. 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 ("Blanck"). Ex. 1021.

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 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 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. 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. *Id.* 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. *Id.* In a related 2014 patent application by the Virginia Commonwealth University (WO 2014/151209 A1, “Grey”), cyclic frequencies higher than 50 Hz were disclosed. Ex. 1010 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 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. 1007 at 15:44-64 (allowing a minimal volume of fluid to increase the relative pressure); Ex. 1010 at 13:7-11 ("providing a non-zero suction force in the catheter at all times").

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 ("Matteo"). Ex. 1013 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 '253 Patent, including the treatment of ischemic strokes.

V. The '253 Patent

A. Priority Date

66. The '253 Patent was filed on November 12, 2019, as a continuation¹ 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 (the "'086 Provisional") and U.S. Provisional Application No. 62/750,011 filed on October 24, 2018 (the "'011 Provisional"). Ex. 1001 at 1-2; *see also* Ex. 1002 ('086 Provisional); Ex. 1003 ('011 Provisional). I understand that because the patent application that later issued as the '253 patent was filed after 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 '253 Patent, are entitled to the effective filing date of its provisional application.

¹ Notably, the '253 Patent appears to have more than 20 new paragraphs added to the disclosure that were not present in the '883 Patent. Ex. 1001 at 9:26-11:14.

Instead, I understand that Patent Owner bears the burden to establish that the Challenged Claims of the '253 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. It is my opinion that none of the claims of the '253 Patent are entitled to a priority date earlier than July 18, 2019, at least because none of the provisional applications describe or enable the claim limitation of “substantially prevent forward flow of liquid at a distal end of the liquid column” as required by each of the Challenged Claims².

B. Summary of the '253 Patent

67. The '253 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. *See* Ex. 1001 at 1:40-3:19. In particular, the '253 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

² To the extent that Patent Owner produces evidence to support that the '253 Patent is entitled to an earlier priority date, I reserve the right to submit rebuttal opinions not limited to the specific claim limitation identified above.

confirmed.” *Id.* at 2:1-5. 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.” *Id.* at 2:13-35,3:3-19.

68. Notably, the ’253 Patent builds on and explicitly incorporates the disclosures from both of its provisional applications. The ’086 Provisional application discloses a one-handed controller with a compressor-actuator design, which, when actuated, occludes all flow through an aspiration catheter and shifts the fluid column within the aspiration catheter distally, moving the thrombus clogging the distal end of the aspiration catheter distally out of the aspiration catheter and back into the patient’s blood vessel. Ex. 1002 at [0072], claim 1, FIGS. 1-15; *see also* Ex. 1001 at 17:29-30:10, FIGS. 1-15; Ex. 1002 at ¶[0016] (“When the controller is actuated, a positive amount of exit flow is created. . . .”). The ’011 Provisional application, filed after the ’086 provisional, discloses a rotation cam system with pinch valves that includes a vent line to allow “fluid to move through a distal portion of the catheter and create a small distal movement of the clot that is stuck in the distal opening at the end of the catheter.” Ex. 1003 at [00126], FIGS. 25-40; Ex. 1001 at 30:11-37:18, FIGS. 25-40. In contrast, the ’253 patent introduces

embodiments without forward flow, which were neither disclosed nor contemplated by the provisional applications. Ex. 1001 at 37:19-22; *see also id.* at 3:3-17, 3:43-4:19, 5:20-9:25, 35:52-61, 37:19-56:37, FIGS. 47-72 (subject matter not covered in the '086 and '011 Provisionals). Indeed, the '253 patent inserts new language into the embodiment disclosed in the '011 Provisional, stating “[t]he flow of fluid forward in this exemplary embodiment is intentional, which is in contrast to other exemplary embodiments herein where substantially no forward flow occurs.” Ex. 1001 at 32:58-60.

C. Summary of the Alleged Invention

69. To solve these well-known problems, the '253 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.” *Id.* at 3:32-35. The purported invention claimed by the '253 Patent is the use of known vacuum aspiration thrombectomy systems and known aspiration catheters with known methods for “removing all forward flow [or] eliminating positive pressure at the distal end of the catheter” and “significantly increas[ing] the efficacy of such catheter and pump systems.” *Id.* at 2:38-3:19, 3:23-47. The '253 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 '253 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 '253 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.” *Id.* at 2:33-35.

70. For example, the inventors of the '253 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, pushes the thrombus distally out of the lumen, and then re-applies vacuum” to accelerate the vacuum force within the catheter. *Id.* at 3:23-31, 4:30-40. The use of applying vacuum suction during aspiration was well known in the art prior to the date of the '253 Patent. The '253 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 '253 Patent was filed. *See id.* at 5:44-6:3.

71. Moreover, the '253 Patent merely utilizes existing vacuum aspiration system components, including a vacuum valve, a venting 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. *Id.* at 5:20-7:16, 30:62-31:18, 34:43-35:2. Further, the system components that perform the '253 Patent methods may be generic vacuum pumps, liquid reservoirs, and aspiration catheters, which the inventors did not invent. *Id.* at 5:20-7:16, 28:11-40, 32:16-24, 36:38-50.

D. Summary of the Claimed Subject Matter

72. The '253 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,” “catheter,” and “controller.”

73. The two independent claims are repetitive. For example, both Claims 1 and 21 generally recite the same clot removal system to “change a level of vacuum at the distal end” of the catheter and “substantially prevent forward flow” via a “controller configured to carry out a pre-determined pattern of opening and closing the vent and vacuum valves.” Claim 21 replaces “pre-determined pattern” with a “pre-determined cycle.”

74. These systems 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. As an illustration, the '253 Patent explains that “most treatments involve” prior art thrombectomy systems, yet “significant problems occur in practice” that allegedly

limit those systems utility. *Id.* at 1:40-52. 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. *Id.* at 1:40-3:19. The '253 Patent claims nothing more than an obvious combination of generic components and steps known in the art, relying solely on the alleged "preventing of forward flow" for its novelty.

E. '253 Patent File History

75. The '253 Patent had a short prosecution history with no official office action issued. *See* Ex. 1004. It was a continuation of the '883 Patent, which was filed on July 18, 2019, which was a continuation of PCT International Application No. PCT/US2019/043095, filed 23 Jul. 2019, claiming priority to two provisional applications.

76. The parent '883 Patent also had a relatively short prosecution history of its 20 claims under TrackOne with no official office action issued. Ex. 1033. Although the Applicant submitted an 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. *Id.* at 71 (Examiner-initiated Interview Summary, Dated 9-30-2019.) During that interview, Applicant agreed to the Examiner's amendment to

cancel Claims 19 and 20 and put the application in condition for allowance. *Id.* In her 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. 1033 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.” *Id.* at 22 (Notice of Allowance, Dated 11-21-2019, p. 2).

77. The application of the '253 Patent was filed on November 12, 2019, as a continuation of the '883 Patent. Ex. 1004 at 638. The as-filed application contained 21 claims. The Applicant filed an information disclosure statement (“IDS”) on December 20, 2019, disclosing 180 prior art references. *Id.* at 113. The Examiner issued a first Notice of Allowance on March 4, 2020, allowing Claims 1-21. *Id.* at 28 (Notice of Allowance, Dated 3-4-2020). 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." *Id.* 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. *Id.* at 16 (Applicant-Initiated Interview Summary, Dated 5-11-2020).

F. '253 Patent Claims

78. The '253 Patent has 21 claims. Claims 1 and 21 are independent. Claim 1 is illustrative and is set forth below (with each limitation):

(i) Claim 1

[Pre] A clot removal system, comprising:

[A] a catheter having a proximal end and a distal end and defining a lumen configured to be filled with a liquid column having a proximal portion;

[B] a vacuum pump configured to supply vacuum;

[C] a vent container holding a vent liquid;

[D] a vent valve configured to fluidically communicate:
with the vent liquid in the vent container; and
with the proximal portion of the liquid column at the proximal end of the catheter;

[E] a vacuum valve configured to fluidically communicate:
with the vacuum from the vacuum pump; and
with the proximal portion of the liquid column at the proximal end of the catheter; and

- [F] a controller configured to carry out a pre-determined pattern of opening and closing the vent and vacuum valves to change a level of vacuum at the distal end and,
- [G] while changing the level of vacuum at the distal end, to substantially prevent forward flow of liquid at a distal end of the liquid column.

VI. The Challenged Claims

79. The '253 Patent has 21 claims. I understand that Petitioner is challenging the validity of Claims 1-21 of the '253 Patent in the Petition for *Inter Partes* Review. I have considered patent validity with respect to Claims 1-21.

VII. Claim Construction

80. 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.

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

- A. “the change in the level of vacuum at the distal end is one of: greater than approximately [15, 20, or 25] inHg and occurs in no greater than approximately [50, 30, or 20] ms”**

82. The phrase “the change in the level of vacuum at the distal end is one of: greater than approximately [15, 20, or 25] inHg and occurs in no greater than approximately [50, 30, or 20] ms” appears in Claim 14 with each of the three sets of different numerical values and is addressed together here as a grouped set of terms.

83. The plain language of this claim limitation appears ambiguous. The specification of the '253 Patent describes this limitation as:

To accomplish the ROAR effect, the change in the level of vacuum at the distal end is at least approximately 15 inHg, further, at least approximately 20 inHg, and, in particular, at least approximately 25 inHg. A time for the change in the level of vacuum from low to high or from high to low at the distal end is no greater than approximately 50 ms, further, no greater than approximately 30 ms, and, in particular, no greater than approximately 20 ms. This change can be referred to as a maximum pressure delta. Various combinations of these variables include a change in the level of vacuum of approximately 15 inHg and a time for that of no greater than 50 ms, or the change in the level of vacuum of approximately 20 inHg and a time for that change of no greater than 30 ms, or the change in the level of vacuum of approximately 25 inHg and a time for that change of no greater than 20 ms.

Ex. 1001 at 40:57-41:5. Given the specification description above, a POSA would have understood that the patentee intended to characterize two aspects of the “change in the level of vacuum at the distal end.” The first recited numeric value [15, 20, or 25] followed by a pressure unit, inHg, defines “the change in the level of vacuum from low to high or from high to low,” referred to as “a maximum pressure delta,” which a POSA would also have understood as a pulse amplitude. *Id.* The second recited numeric value followed by a unit of time, ms (millisecond), defines the “time for the change in the level of vacuum from low to high or from high to low at the distal end,” which is related to the rate of change of the vacuum level for a given pressure pulse. *Id.*

84. Accordingly, a POSA would have understood the term “the change in the level of vacuum at the distal end is one of: greater than approximately [15, 20, or 25] inHg and occurs in no greater than approximately [50, 30, or 20] ms” to mean the change in the level of vacuum from low to high or from high to low at the distal end is greater than approximately [15, 20, or 25] inHg and the time for that change is no greater than approximately [50, 30, or 20] ms.

VIII. Summary of the Prior Art

85. There are many patents and publications which constitute prior art to the '253 Patent. I have reviewed and considered the following prior art patents and printed publications, which I believe were all publicly available prior to July 18, 2019, the filing date of the '253 Patent. A description of these references follows. None of these references were considered by the USPTO during prosecution. *See* Ex. 1001 at (56) (References Cited). 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.

A. Teigen

86. U.S. Patent No. 11,197,683 (“Teigen”) was issued on December 14, 2021, from U.S. Patent Application No. 17/391,874 filed on August 2, 2021. Teigen is a continuation of U.S. Patent No. 11,096,712 (“Teigen ’712,” Ex. 1030), which

claims priority to U.S. Provisional Application No. 62/702,804 (the “’804 Provisional”) filed on July 24, 2018 and U.S. Provisional Application No. 62/778,708 (the “’708 Provisional”) filed on December 12, 2018. Ex. 1007 (Teigen) at 1; *see also* Ex. 1008 (’804 Provisional); Ex. 1009 (’708 Provisional). Although Teigen was filed after the filing date of the ’253 Patent and the filing date of the ’883 Patent, Teigen qualifies as prior art at least because it claims priority to and is entitled to the benefit of the two U.S. provisional applications that were filed prior to the effective filing date of the ’253 Patent.

87. I understand that if Teigen is entitled to rely upon either the ’804 Provisional or the ’708 Provisional to establish its priority date, then Teigen is prior art to the ’253 Patent. I also understand that under 35 U.S.C. § 102(d)(2), Teigen is entitled to rely on the priority date of its provisional applications if the provisional applications describe the subject matter of the Teigen patent publication. In my opinion, both the ’804 Provisional and the ’708 Provisional adequately describe and fully support the relevant subject matter relied upon in Teigen for this petition, as demonstrated in the parallel citations herein and the representative Claim 1 below that is further demonstrated as being described and enabled by the earlier ’804 Provisional. It is thus my opinion that Teigen is prior art under 35 U.S.C. § 102(a)(2) to the ’253 Patent which has an effective U.S. Application filing date of July 18,

2019, the filing date of the '883 Patent.³ A detailed analysis establishing Teigen's priority back to the '804 provisional is included below. I further reserve the right to provide additional analysis and opinions to establish Teigen's priority to the later filed '708 provisional, if necessitated by patent owner's arguments.

(i) Teigen is Prior Art to the '253 Patent

88. It is my opinion that Teigen is supported by the '804 Provisional application and the '708 Provisional application, therefore Teigen is entitled to the earlier July 24, 2018 filing date of the '804 Provisional application because both provisional applications describe the subject matter of Teigen and at least independent claim 1 is fully supported and enabled by the '804 Provisional disclosures. Teigen and its Provisionals are directed to systems for controlled, pulsed vacuum aspiration thrombectomy using cycles of vacuum aspiration and venting

³ As discussed above, I also note that the issued claims of the '253 Patent are limited to this filing date because neither of the provisional applications that the '253 Patent cites to for priority disclose all of the limitations of any of the issued claims, as discussed above in Section V. I understand that the Patent Owner has the burden to prove otherwise on this issue. I reserve the right to provide rebuttal opinions to the extent that the Patent Owner argues that the '253 Patent is entitled to the benefit of the priority date of any of its provisional applications.

with a source of pressure to create dynamic suction forces on blood clots to be aspirated out of a blood vessel. Ex. 1007 at 1:19-23, 6:24-44; Ex. 1008 at [001], [0063]; Ex. 1009 at [002], [0065]. Teigen and its Provisionals disclose a system with multiple functions to accomplish safer and more effective controlled clot aspiration as compared to prior art systems, comprising an aspiration catheter, vacuum console, and a vacuum aspiration control system. Ex. 1007 at 2:56-67, 3:15-35, 3:52-4:20, FIGS 7A, 7B, 9, 14; Ex. 1008 at [007], [009], [0011], [0012], FIGS 7A, 7B, 9, 13; Ex. 1009 at [009], [0011], [0013], [0014], FIGS 7A, 7B, 9, 13; *see also* Ex. 1007 at 1:59-2:26, 2:49-55; Ex. 1008 at [005]-[007]; Ex. 1009 at [006]-[009]. Teigen and its Provisionals further disclose that its vacuum aspiration system comprises “a connecting tube, an on-off valve, a sensing unit,” a controller, a fluid introduction unit, three-point junction, and a fluid injection valve to control the flow of fluid into the clot flow path to aid in aspiration. Ex. 1007 at 3:63-4:20, 14:63-18:25; Ex. 1008 at [0012], [0063]-[0065]; Ex. 1009 at [0014], [0065]-[0067]. Teigen and its Provisionals explain that its controller is connected to receive signals representative of blood flow from pressure sensors in the system and opens and closes the vacuum and fluid injection valves to alter flow through the connecting tube as necessary to aspirate the clot. Ex. 1007 at 3:63-4:20, 14:63-18:25; Ex. 1008 at [0012], [0063], [0065]; Ex. 1009 at [0014], [0065], [0067]. Teigen and its Provisionals all explain that the pressure pulse can create a force impulse that

momentarily disrupts static friction, allowing a lower dynamic friction to ingest thrombus more efficiently than would otherwise be possible with static vacuum aspiration. Ex. 1007 at 14:63-15:12; Ex. 1008 at [0064], [0065]; Ex. 1009 at [0066], [0067].

a) The Teigen Provisionals Fully Support and Enable at Least Claim 1 of Teigen

(1) Teigen claim 1 preamble: “An aspiration thrombectomy system, comprising:”

89. The Teigen Provisionals disclose an aspiration thrombectomy system. For example, under the sub-heading of “Field of the Invention,” the Teigen Provisionals state that “the invention described herein relates to devices and methods for controlling clot removed from a patient’s vasculature by aspiration thrombectomy,” which a POSA would have understood as an aspiration thrombectomy system. Ex. 1008 at [001]; Ex. 1009 at [002].

(2) Teigen claim limitation [1a]: “a vacuum source comprising a controllable vacuum valve”

90. The Teigen Provisionals disclose that the clot removal system includes “a vacuum aspiration control system for use with a vacuum source and an aspiration catheter.” *See, e.g.*, Ex. 1008 at [0012]; Ex. 1009 at [0014]. The Teigen Provisionals further disclose that an “on-off valve sits between the juncture 292 [and] the vacuum console to cut off vacuum pressure when necessary,” and that “the system will close the on-off valve to the pump” and “reopen the on-off valve.” A POSA would have

readily recognized this as a vacuum source (vacuum console) comprising a controllable vacuum valve (on-off valve for the vacuum console). Ex. 1008 at [0012], [0063]-[0065]; Ex. 1009 at [0014], [0065-0067].

(3) Teigen claim limitation [1b]: “a pressure source comprising a controllable pressure valve”

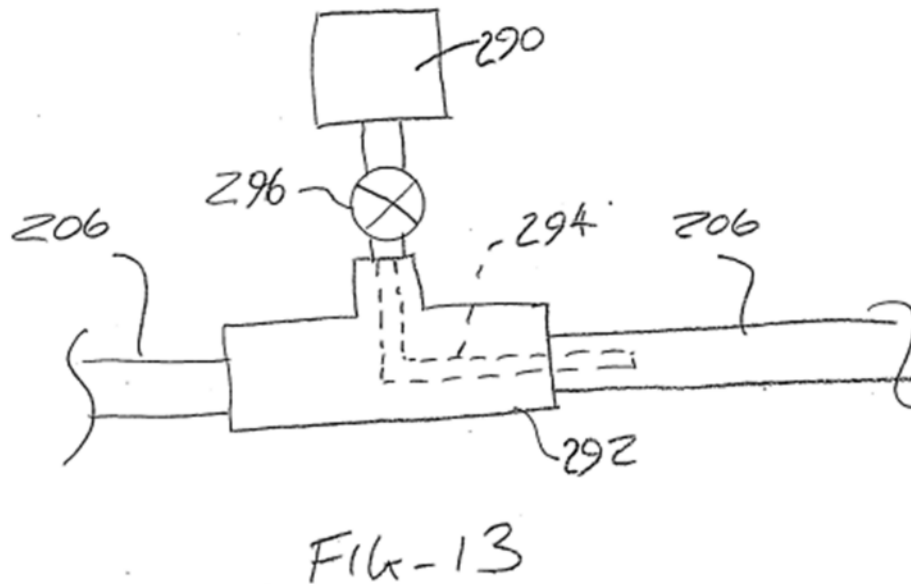
91. The Teigen Provisionals disclose that the clot removal system includes a “saline injection unit 290” and a “saline injection valve 296” to “control[] the flow of saline,” and that “the system will close [an] on-off valve to the pump and open the valve 296 to the saline injection unit 290 [to] partially relieve the vacuum” and “close valve 296 and reopen the on-off valve to reestablish the aspiration vacuum.” *See, e.g.*, Ex. 1008 at [0063]-[0065]; Ex. 1009 at [0065]-[0067]. A POSA would have readily recognized this as a pressure source (saline injection unit 290) comprising a controllable vent/pressure valve (saline injection valve 296).

(4) Teigen claim limitation [1c]: “an aspiration catheter having a proximal end and a distal end, wherein the proximal end of the aspiration catheter comprises connection tubing having a lumen configured to accommodate fluid, and wherein the connection tubing acts as a common conduit for fluid communication between the aspiration catheter and the vacuum and pressure sources via the vacuum and pressure valves, respectively”

92. The Teigen Provisionals disclose that “the present invention provides a vacuum aspiration control system for use with a vacuum source and an aspiration catheter” and a “connecting tube [] configured to connect the vacuum source to an

aspiration lumen in the aspiration catheter.” Ex. 1008 at [0012]; Ex. 1009 at [0014]. The Teigen Provisionals further disclose “engaging a distal end of an aspiration catheter against an occlusion in the blood vessel.” Ex. 1008 at [0012]; Ex. 1009 at [0014]. A POSA would have understood this to be an aspiration catheter having a proximal end and a distal end, and would have readily recognized that the “aspiration lumen in the aspiration catheter” would be configured to accommodate fluid, as recited in claim limitation [1c].

93. The Teigen Provisionals disclose that “[t]he system comprises a connecting tube, an on-off valve, a sensing unit, and a controller. The connecting tube is configured to connect the vacuum source to an aspiration lumen in the aspiration catheter.” Ex. 1008 at [0012]; Ex. 1009 at [0014]. The Teigen Provisionals further disclose a system configuration that “pulsate[s] the aspiration pressure to reduce clogging and promote flow of the clot and thrombus through the aspiration catheter and connecting tubing,” as shown in the Provisionals’ Fig. 13 below. Ex. 1008 at [0063]; Ex. 1009 at [0065].



Ex. 1008 at Fig. 13; Ex. 1009 at Fig. 13. Here, the connection tubing 206 “connects a saline injection unit 290 to the aspiration catheter and the vacuum console.” Ex. 1008 at [0063]; *see also* Ex. 1009 at [0065]. Accordingly, the Teigen Provisionals disclose “wherein the connection tubing acts as a common conduit for fluid communication between the aspiration catheter and the vacuum and pressure sources via the vacuum and pressure valves, respectively,” as recited in claim limitation [1c].

(5) Teigen claim limitation [1d]: “a controller configured to open and close the vacuum and vent valves in a predetermined cycle to change a level of vacuum at the distal end of the aspiration catheter and control flow in and out from the distal end of the catheter”

94. The Teigen Provisionals disclose this claim limitation. For example, the Provisionals state that “the present invention provides a vacuum aspiration

control system for use with a vacuum source and an aspiration catheter.” Ex. 1008 at [0012], [0045]-[0047] (disclosing a microprocessor controller 74 as an embodiment of the controller), [0057]-[0058] (disclosing controller 220 as another embodiment); Ex. 1009 at [0014], [0047]-[0049], [0059]-[0060]. “A vacuum is applied through an aspiration lumen of the aspiration catheter using a vacuum source coupled to a proximal end of the aspiration lumen by a connecting tube.” Ex. 1008 at [0020]; Ex. 1009 at [0022]. “The controller is connected to receive the signal representative of flow through the connecting tube and to open and close the on-off valve in response to the signal.” Ex. 1008 at [0012]; Ex. 1009 at [0014]. The Provisionals disclose that during dynamic/pulsed aspiration, the on-off valve for the vacuum source valve and the saline injection valve for the saline injection unit are modulated by the controller by alternating between opening and closing the valves to generate pressure differentials within the lumen of the aspiration catheter. Ex. 1008 at [0063]-[0065]; Ex. 1009 at [0065]-[0067]. The Provisionals explains that the controller can operate the valves to cycle between various states including, for example, a “full vacuum” state, a “reduc[ed] vacuum” state, and a “positive pressure” state. Ex. 1008 at [0063]-[0065] (“While aspiration is cycled off, saline injection is cycled on”), [0069]; Ex. 1009 at [0065]-[0067] (“an influx of pressure will create a positive pressure”), [0078]. As such, by opening and closing the valves to generate varying pressure differentials, the controller is able to control the

direction and measure of forces experienced by substances at the distal end of the catheter. Ex. 1008 at [0063]-[0065], [0069]; Ex. 1009 at [0065]-[0067], [0078]. The Provisionals additionally note that the pulsed aspiration cycles may be “set by the physician, pre-determined by the algorithm, or any combination thereof.” Ex. 1008 at [0069]; Ex. 1009 at [0078]. Accordingly, a POSA would have understood that the disclosed controller is configured to open and close the vacuum and vent valves in a predetermined cycle to change a level of vacuum at the distal end of the aspiration catheter and control flow in and out from the distal end of the catheter, as recited in claim limitation [1d].

95. Given the well-known components and detailed descriptions provided in the Teigen Provisionals, a POSA would have understood that the inventors are in possession of the invention claimed in claim 1 of Teigen and it requires no undue experimentation to practice the claim. Therefore, it is my opinion that the Teigen Provisionals provide adequate written description and enablement support for claim 1 of Teigen. I further believe that the challenged claims are not entitled to any earlier priority date than the filing date of the '253 Patent. It is my opinion that Teigen is prior art to the '253 Patent. To the extent that the patent owner argues that the challenged claims are entitled to the earlier filing date of a provisional application, I reserve the right to provide rebuttal opinions on the priority issue.

B. Grey

96. International Publication No. WO 2014/151209 A1 (“Grey”) was filed on March 13, 2014, published on September 25, 2014, and claims priority to U.S. Provisional Application No. 61/802,908 filed on March 18, 2013. Ex. 1010 (Grey) at 1. Grey qualifies as prior art at least because it was published prior to the filing date of the ’253 Patent.

97. Grey is directed to “an aspiration system” and method for clot removal by creating “a dynamic suction force at the distal end of the catheter” of the aspiration system. Ex. 1010 at 5:1-4. Grey teaches that its system comprises “a catheter insertable into a body, an aspiration source providing negative pressure in the catheter, and a device which repetitively changes the negative pressure to produce a dynamic suction force at a distal end of the catheter.” *Id.* Grey explains that “negative pressure and negative pressure oscillations are delivered by a fluid medium which may be, for example, one or more liquids, gases, or a combination thereof.” *Id.* at 3:22-24. Grey discloses that “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.” *Id.* at 13:7-11; *see also id.* at 7:10-12, 11:16-20.

C. Rubenstein

98. 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 filing date of the ’253 Patent.

99. 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 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. *Id.* 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.” *Id.* at 2:1-8, 3:21-50, 4:2-7, 4:17-35.

D. Yang

100. 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 ’253 Patent.

101. Yang is directed to a telescoping catheter with a movable jaw for “distal neurovascular aspiration or access” that has a control for advancing the distal section

into the patient's vasculature. Ex. 1012 at Abs., FIGS. 1, 3A, 3B. The catheter is operable to connect to "a controller for applying intermittent vacuum to the lumen" using combinations of vacuum pulses and "spaces of neutral pressure," higher negative pressure or lower negative pressure. *Id.* at [0014], FIG. 14, 25A-C. Yang discloses that the inner diameter of the distal section of the catheter:

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.

Id. at [0068].

E. Matteo

102. U.S. Patent Publication No. 2012/0138833 A1 ("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 filing date of the '253 Patent.

103. 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 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.” *Id.* 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.” *Id.* 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.” *Id.* at [0047].

IX. Ground 1: Claims 1-14, 17-19, and 21 are Rendered Obvious Over Teigen in view of Grey and the Knowledge of a POSA

A. Motivation to Combine

104. A person of ordinary skill in the art at the time the purported invention of the '253 Patent was made would have been motivated to combine Teigen's cyclical aspiration thrombectomy system with Grey's teachings of: (1) providing a non-zero suction force to prevent the migration of distal thrombi; (2) monitoring the level of vacuum pressure change at the distal end of the aspiration catheter; and (3) optimization of aspiration cycle frequencies including the duration vent valve opening and closure to relieve vacuum pressure.

105. A POSA would have been motivated to combine Teigen and Grey 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 venting system to temporarily relieve the negative pressure within the system so as to create an accelerated suction force 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 issues with clogged catheters and the limitations of static aspiration technologies for controlled clot aspiration. Ex. 1007 at 1:59-2:26, 2:49-55, 3:15-35, 14:63-15:36; Ex. 1008 at [005], [009], [0063]-[0065]; Ex. 1009 at [006], [008], [0011], [0065]-[0067]; Ex. 1010 at 1:7-9, 1:15-2:3.

106. The references describe similar approaches to solving these and other issues, including creating a dynamic aspiration force to more effectively clear clots from a clogged catheter. Ex. 1007 at 2:27-67, 3:15-51, 14:63-18:25; Ex. 1008 at [006]-[008], [0009], [0010], [0063]-[0065]; Ex. 1009 at [007]-[009], [0011], [0012], [0065]-[0067]; Ex. 1010 at 2:24-3:24. Both systems utilize an aspiration thrombectomy system with an added venting mechanism to at least partially relieve vacuum pressure within the system to create an acceleration force on the clot for optimal clot aspiration. Ex. 1007 at 14:63-18:25, 19:52-20:43; Ex. 1008 at [0063]-[0066]; Ex. 1009 at [0065]-[0069], [0074], [0075]; Ex. 1010 at 5:1-4, 7:21-30, 8:1-19, 11:16-20, 13:7-11, FIG. 2A.

107. A POSA would understand that Teigen and Grey 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. Accordingly, combining the teachings of Teigen and Grey 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.

108. A POSA would find it obvious to implement Grey's disclosures of cyclic aspiration frequency profiles that optimize the introduction of positive pressures into the vacuum system to modify Teigen's system, which already includes a computer-based controller to operate vacuum and vent valves, to provide for efficient and effective cyclical aspiration of blood clots. Ex. 1007 at 14:63-18:25, 19:52-20:43; Ex. 1009 at [0063]-[0066]; Ex. 1009 at [0065]-[0069]; Ex. 1010 at 5:1-4, 7:21-30, 8:1-19, 11:16-20, 13:7-11, FIG. 2A. The aspiration cycle frequencies described by Grey are consistent with and improve on the aspiration cycles that Teigen discloses to provide effective cyclical aspiration thrombectomy. Ex. 1007 at 14:63-18:25; Ex. 1008 at [0063]-[0066]; Ex. 1009 at [0065]-[0069]; Ex. 1010 at 9:13-25, 10:28-11:3. Using the pressure pulse profiles and constant non-zero suction force provided by Grey on Teigen's patients would help to reduce the risk of complications from aspiration thrombectomy, including clogged catheters and

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

109. Grey's methods to relieve negative pressure within the aspiration system are similar to, if not the same as, the fluid injection unit described by Teigen. 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 to Teigen's system for modulating the pressures contained within the aspiration system, in accordance with the preferable pressure profiles as taught in Grey. Because Teigen'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 Teigen's controller to implement Grey's teachings, if necessary, or incorporate known mechanical components, if needed.

110. 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 Grey within Teigen's aspiration thrombectomy system. Like Grey, Teigen discloses monitoring the level of pressure within the catheter and the aspiration thrombectomy system. *See* Ex. 1007 at 4:29-44, 5:54-6:7, 11:28-12:11; Ex. 1008 at [0014], [0015], [0019], [0058]-[0060]; Ex. 1009 at [0016], [0017], [0021], [0060]-[0062]; *see also* Ex. 1010 at 13:4-6. 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 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. Teigen discloses that a set of pressure sensors can be placed within the connecting tubing to monitor the pressure in the system. Ex. 1007 at 4:29-44, 5:54-6:7, 11:28-12:11; Ex. 1008 at [0014], [0015], [0019], [0058]-[0060]; Ex. 1009 at [0016], [0017], [0021], [0060]-[0062]. Grey builds on the concept of using pressure sensors by disclosing monitoring the vacuum pressure at or near the distal end of the catheter. Ex. 1010 at 13:4-6. 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 Grey, in the context of Teigen, and it would have been trivial to implement these within Teigen's aspiration thrombectomy system.

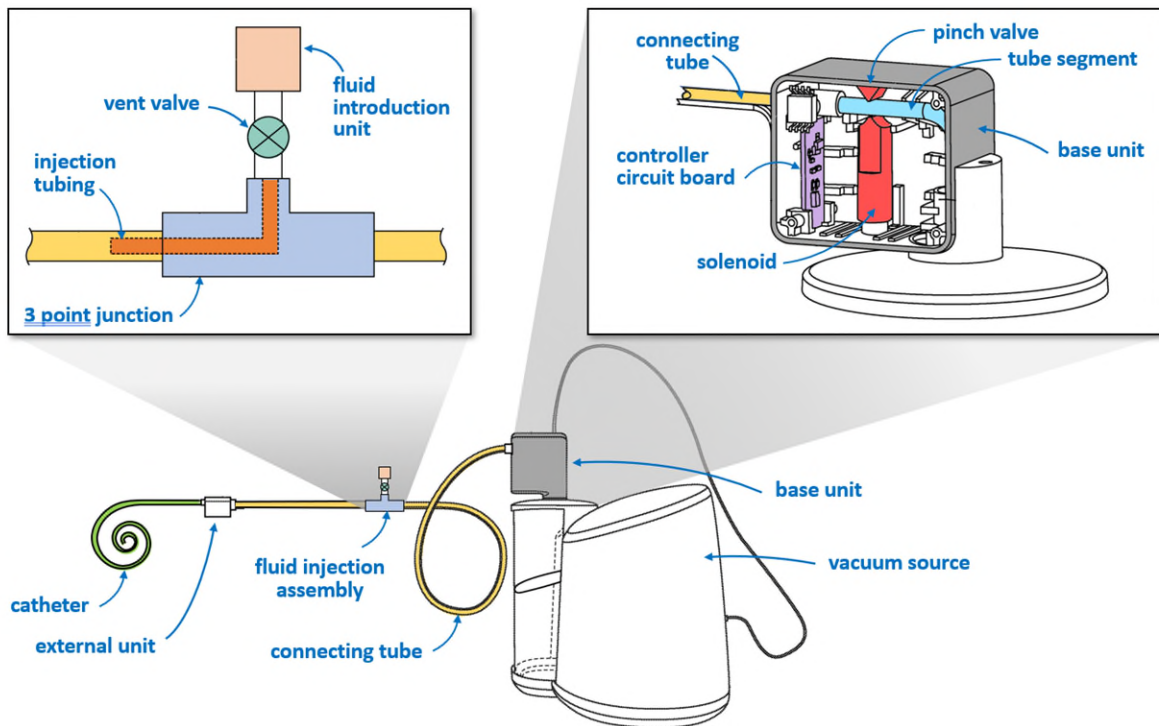
111. For at least these reasons, it would have been obvious to combine Teigen and Grey.

B. Teigen in View of Grey and the Knowledge of a POSA Renders Claim 1 Obvious

(i) 1[Pre] A clot removal system, comprising:

112. To the extent the preamble is limiting, Teigen discloses it.

113. Teigen discloses a clot removal system. Ex. 1007 at Claim 1 (“A clot removal system”); Ex. 1008 at [001]; Ex. 1009 at [002]. As shown in the figures below, which are annotated versions of Teigen’s Figure numbers 7A, 9, and 14 that have in some cases been modified for clarity to add additional elements that are described in the Teigen specification but that are not shown in the original figures or have been transposed to maintain a consistent geometric relationship between the components of the system, Teigen further discloses an “apparatus for controlling the aspiration of thrombus and clot using aspiration catheters in combination with pumping consoles” that allows for “complete removal occlusive material” during “clot extraction.” Ex. 1007 at 2:56-67, 3:15-35, 3:52-62, FIGS 7A, 7B, 9, 14; Ex. 1008 at [007], [009], [0011], FIGS 7A, 7B, 9, 13; Ex. 1009 at [009], [0011], [0013], FIGS 7A, 7B, 9, 13; *see also* Ex. 1007 at 1:59-2:55; Ex. 1008 at [005]-[007]; Ex. 1009 at [006]-[008].



114. Teigen's clot extraction system comprises a vacuum source/collection device, base unit, external unit, and an aspiration catheter. Ex. 1007 at 3:63-4:20; Ex. 1008 at [0012]; Ex. 1009 at [0014]. Teigen further discloses a fluid injection assembly for "pulsed aspiration," including a fluid introduction unit, a three-point junction, and a fluid injection (vent) valve to control the flow of fluid into the clot flow path to aid in aspiration. Ex. 1007 at Abs., 15:47-17:10; Ex. 1008 at [0063], [0065]; Ex. 1009 at [0065], [0067]. Teigen explains that its controller is connected to receive signals representative of blood flow from pressure sensors, which can be in both the base unit (at the proximal end of the connecting tube) and the external unit (located at the distal end of the connecting tube), and opens and closes the

vacuum and fluid injection valves to alter flow through the connecting tube and the catheter, to which it is connected. Ex. 1007 at 3:63-4:20, 4:29-44, 5:54-6:7, 14:63-18:25; Ex. 1008 at [0012], [0014], [0015], [0019], [0063], [0065]; Ex. 1009 at [0014], [0016], [0017], [0021], [0065], [0067].

115. Therefore, it is my opinion that Teigen discloses a “clot removal system” as recited by Claim 1.

(ii) 1[A] a catheter having a proximal end and a distal end and defining a lumen configured to be filled with a liquid column having a proximal portion;

116. Teigen discloses a catheter having a proximal end and a distal end and defining a lumen configured to be filled with a liquid column having a proximal portion. Ex. 1007 at Claim 1 (“an aspiration catheter having a proximal end and a distal end, wherein the proximal end of the aspiration catheter comprises connection tubing having a lumen configured to accommodate fluid”). Teigen further discloses “engaging a distal end of an aspiration catheter against an occlusion in the blood vessel” during vacuum aspiration. Ex. 1007 at 6:8-23; Ex. 1008 at [0020]; Ex. 1009 at [0022]. Teigen further discloses that a “vacuum is applied through an aspiration lumen of the aspiration catheter using a vacuum source coupled to a proximal end of the aspiration lumen by a connecting tube.” Ex. 1007 at 6:8-23; Ex. 1008 at [0020]; Ex. 1009 at [0022].

117. Teigen also inherently discloses that the catheter lumen is “filled with a liquid column having a proximal portion,” because a POSA would have recognized that all catheters used in aspiration thrombectomy define a lumen filled with a liquid column contained within the proximal and distal ends of the catheter, or that it would have been obvious to use the catheter in a manner such that it includes a lumen having opposing distal and proximal ends filled with a liquid column, because the purpose of Teigen’s catheter is to act as a conduit to collect liquid, including blood and clot material from a patient’s blood vessel. Indeed, Teigen contemplates that the catheter lumen’s purpose is to be filled with flowing liquid, such as “blood and clot,” as that material is withdrawn from the patient’s body during “any thrombectomy, embolectomy, atherectomy.” Ex. 1007 at 3:36-62; Ex. 1008 at [0010], [0011]; Ex. 1009 at [0012], [0013]. Had the lumen of the catheter not been filled with a liquid column but instead, for example, included a gas bubble, the gas bubble would anyway have been evacuated by the vacuum unit during a standard operation of the device.

118. Moreover, Teigen explicitly discloses a “distal end” of the catheter. Ex. 1007 at Claim 1. A POSA would have understood that any object with a distal end would also have a proximal end on the opposite end of that object. Because the catheter lumen in Teigen expressly and inherently includes a liquid column, and/or that it would have been obvious to employ the catheter lumen in a manner such that

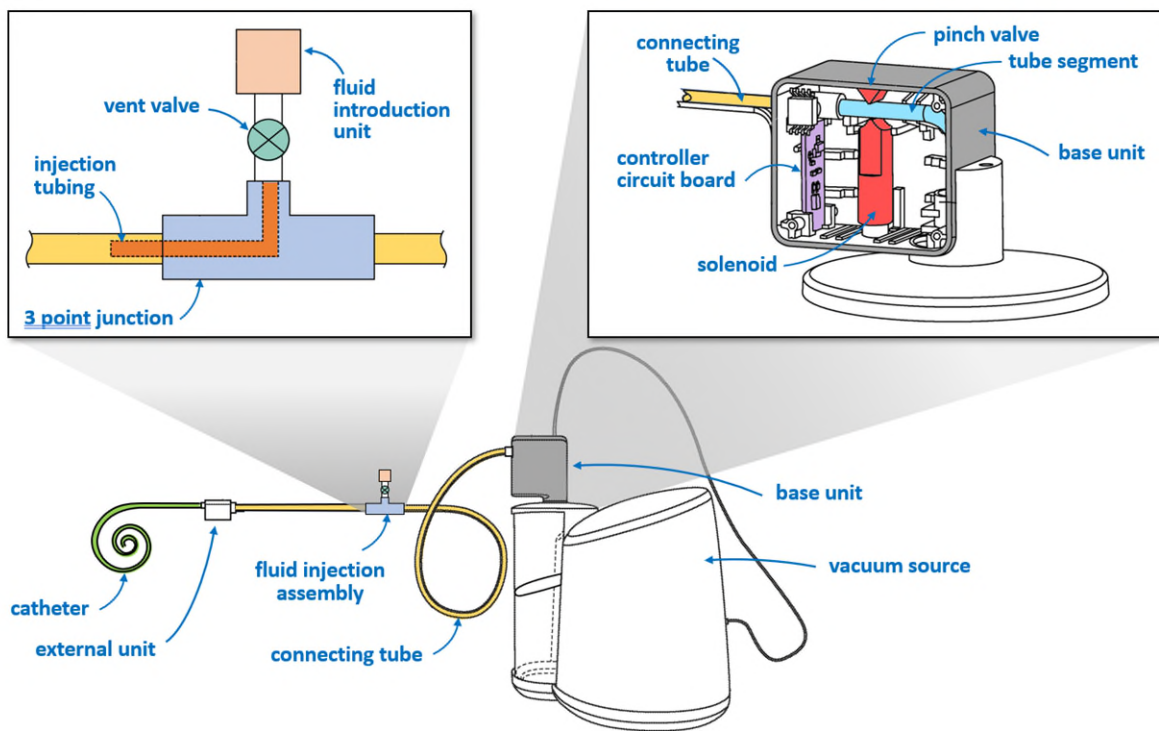
it includes a liquid column, a POSA would also have understood that such a liquid column within the catheter lumen would have a proximal portion within the bounds of the proximal and distal ends of the aspiration lumen disclosed in Teigen.

119. Therefore, it is my opinion that Teigen discloses “a catheter having a proximal end and a distal end and defining a lumen configured to be filled with a liquid column having a proximal portion,” as recited by Claim 1.

(iii) 1[B] a vacuum pump configured to supply vacuum;

120. Teigen discloses a vacuum pump configured to supply vacuum. Ex. 1007 at Claim 1 (“a vacuum source comprising a controllable vacuum valve”); *see also*, Ex. 1007 at 3:63-4:20, 5:40-6:23, 11:3-27, 12:25-39, FIGS. 9, 11; Ex. 1008 at [0012], [0018]-[0020], [0057], [0061], [0063], FIGS. 9, 11; Ex. 1009 at [0014], [0021], [0022], [0059], [0063], [0065], FIGS. 9, 11. As illustrated in the modified, annotated, and transposed version of Teigen’s figures 7A, 9, and 14 below, Teigen also discloses that its “vacuum aspiration control system” comprises a vacuum source, an aspiration catheter, a connecting tube, an on-off valve, and a controller. Ex. 1007 at 3:62-4:20; Ex. 1008 at [0012]; Ex. 1009 at [0014]; *see also* Ex. 1007 at 6:8-23; Ex. 1008 at [0020]; Ex. 1009 at [0022]. A POSA would have understood that a vacuum source includes a vacuum pump, although the terms are often used interchangeably in the context of aspiration thrombectomy, as in this case. *See* Ex. 1007 at 2:8-11 (“As illustrated in FIG. 1, the Pump MAX™ aspiration pump 10

includes a base unit 12 which encloses a vacuum pump (not shown) which operates offline voltage”), FIGS. 1, 3C; Ex. 1008 at [005], [0045]-[0047], FIGS. 1, 3C; Ex. 1009 at [006], [0047]-[0049], FIGS. 1, 3C. Teigen further discloses that “[t]he connecting tube is... configured to connect the vacuum source to an aspiration lumen in the aspiration catheter” and the “on-off valve is configured to be operatively connected to the connecting tube.” Ex. 1007 at 3:62-4:20; Ex. 1008 at [0012]; Ex.



1009 at [0014].

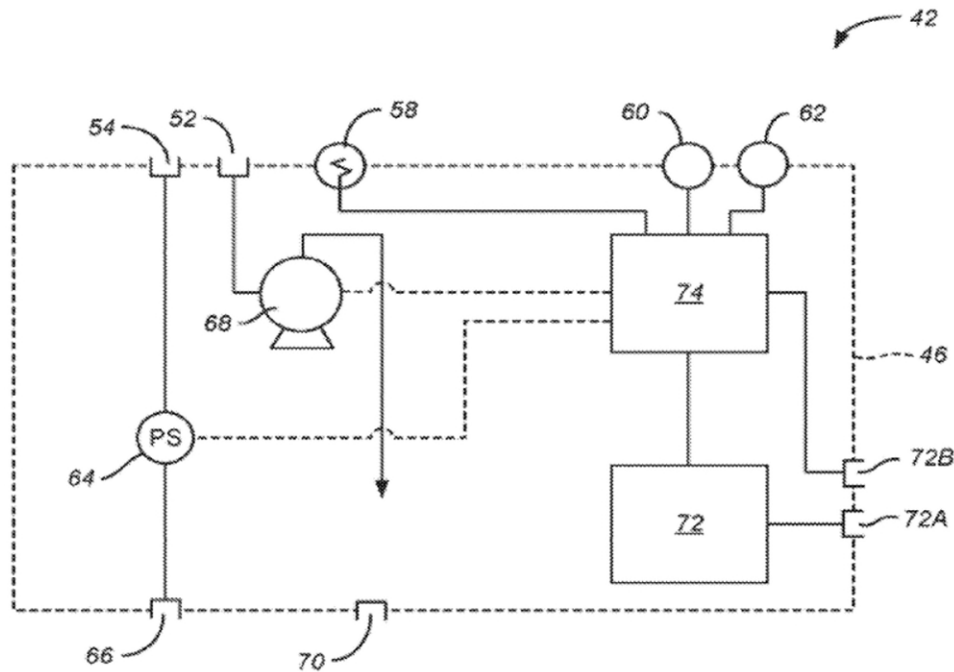


FIG. 3C

121. Teigen explains that “[a] vacuum is applied through an aspiration lumen of the aspiration catheter using a vacuum source coupled to a proximal end of the aspiration lumen by a connecting tube.” Ex. 1007 at 6:8-23; Ex. 1008 at [0020]; Ex. 1009 at [0022]. Because the controllable on-off valve also sits along the connecting tube between the vacuum source and the aspiration catheter “to open to permit aspiration and close to block aspiration,” a POSA would recognize that Teigen’s system is disclosing “a vacuum pump configured to supply vacuum,” as those terms are understood in the art. *See* Ex. 1007 at 3:62-4:20, 5:40-53, 6:8-23, 11:3-27, 12:25-39; Ex. 1008 at [0012], [0018], [0057], [0061], [0063]; Ex. 1009 at [0014], [0022], [0059], [0063], [0065], FIGS. 9, 11.

122. Therefore, it is my opinion that Teigen discloses “a vacuum pump configured to supply vacuum,” as recited by Claim 1.

(iv) 1[C] a vent container holding a vent liquid;

123. Teigen discloses a vent container holding a vent liquid. Ex. 1007 at Claim 1 (“a pressure source comprising a controllable pressure valve”). As illustrated in figure 14 and the modified, annotated, and transposed version of figure 14 below, Teigen discloses a fluid introduction unit. Ex. 1007 at Abs., 6:24-44, 15:13-36, 16:1-16:24, 17:11-19, FIG. 14; Ex. 1008 at [0063]-[0065], FIG. 13; Ex. 1009 at [0065]-[0067], FIG. 13. In particular, Teigen discloses a fluid introduction unit 290 that introduces fluid into the catheter via the fluid injection valve 296 and three-point junction 292. Ex. 1007 at 15:37-46, 16:1-16:24; Ex. 1008 at [0063], [0065], FIG. 13; Ex. 1009 [0065], [0067], FIG. 13. The fluid injection valve 296 “controls the flow of fluid” when the control algorithm opens and closes the fluid injection valve 296 to the fluid reservoir 290. Ex. 1007 at 16:1-16:24; Ex. 1008 at [0063], [0065], FIG. 13; Ex. 1009 at [0065], [0067], FIG. 13. A POSA would have recognized that when the fluid injection valve 296 is closed, the fluid introduction unit 290 would be “holding the vent liquid” until the valve is reopened to allow the fluid to flow into the three-point junction 292 and the vacuum aspiration system connection tubing 206 and into the aspiration catheter. *See* Ex. 1007 at 15:37-46,

16:1-16:24, FIG. 14; Ex. 1008 at [0063], [0067], FIG. 13; Ex. 1009 at [0065], [0067],
FIG. 13.

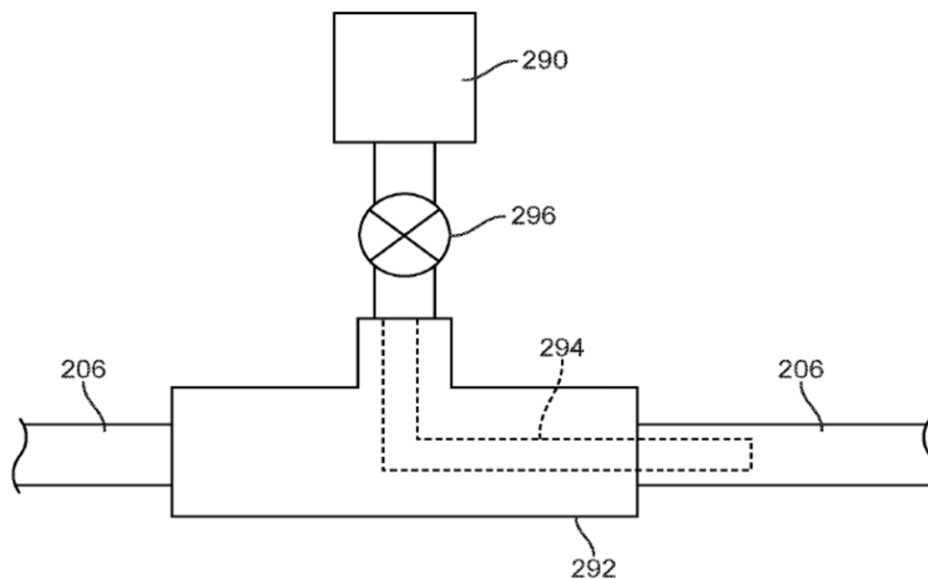
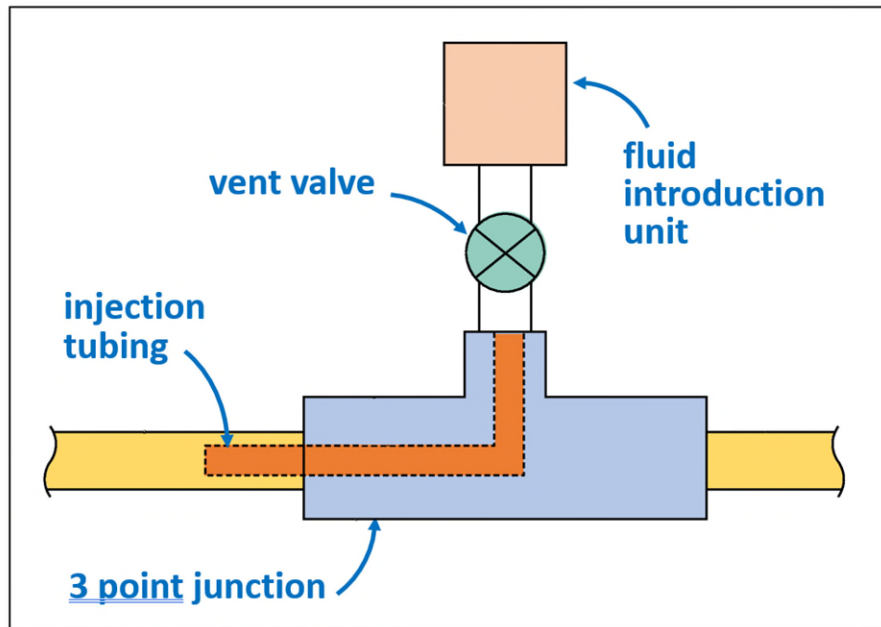
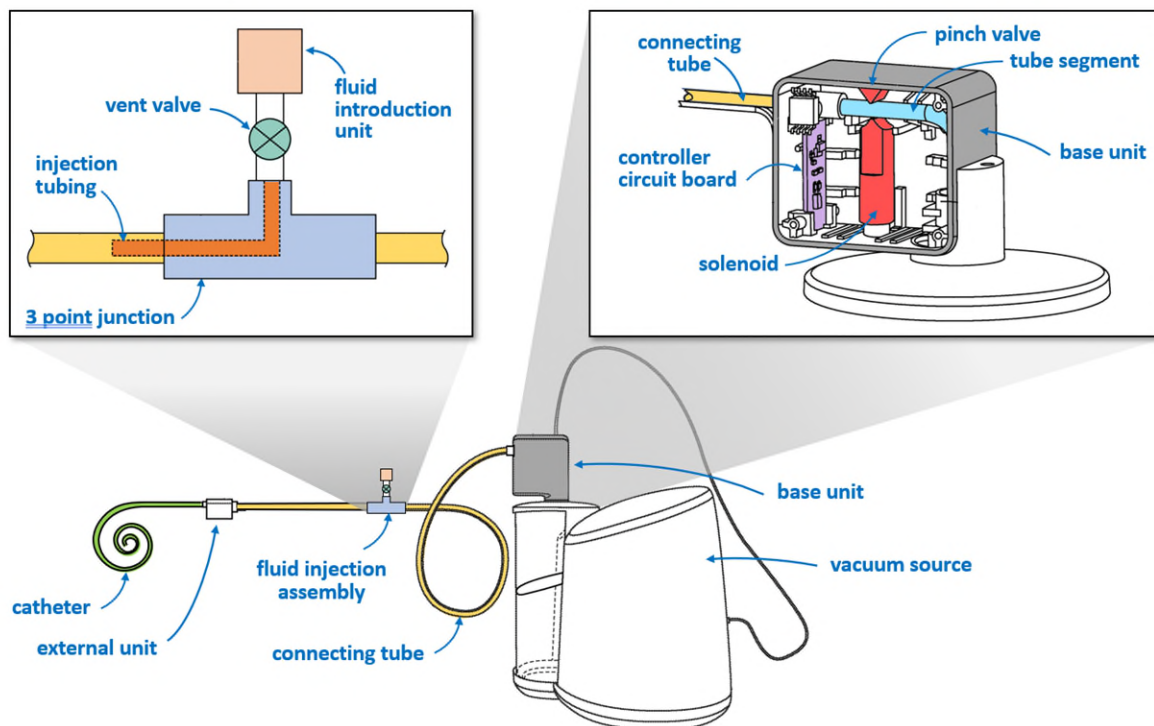


FIG. 14

124. Therefore, it is my opinion that Teigen discloses “a vent container holding a vent liquid” as recited by Claim 1.

- (v) **1[D] a vent valve configured to fluidically communicate: with the vent liquid in the vent container; and with the proximal portion of the liquid column at the proximal end of the catheter;**

125. Teigen discloses a vent valve configured to fluidically communicate with the vent liquid in the vent container and with the proximal portion of the liquid column at the proximal end of the catheter. Ex. 1007 at Claim 1 (“a pressure source comprising a controllable pressure valve” “wherein the connection tubing acts as a common conduit for fluid communication between the aspiration catheter and the vacuum and pressure sources via the vacuum and pressure valves, respectively”). As illustrated in the modified, annotated and transposed version of Teigen’s figures 7A, 9, and 14 below, Teigen discloses a technique for “pulsed aspiration” comprising a fluid injection valve 296 operable to “control[] the flow of fluid” from the fluid introduction unit 290 and “inject pulses of pressure into the clot flow path that may facilitate the extraction of clot or other occlusive substances” to “create a positive pressure or partially relieve the vacuum.” Ex. 1007 at Abs., 6:24-44, 16:1-16:24, FIG. 14; Ex. 1008 at [0063], [0065], FIG. 13; Ex. 1009 at [0065], [0067], FIG. 13.



126. Teigen further discloses that the pulsed aspiration occurs when the system “selectively open[s] and close[s] both the aspiration valve [] and [fluid injection valve] to create pressure differentials within the catheter and/or aspiration tubing.” Ex. 1007 at 17:11-19; Ex. 1008 at [0063]-[0065]; Ex. 1009 at [0065]-[0067]. Teigen further discloses that a controller initiates “an extraction cycle [that] alternates between providing vacuum aspiration and relative positive pressure” via the fluid injection unit or other pressure source. Ex. 1007 at 15:13-36; Ex. 1008 at [0063]; Ex. 1009 at [0065]. A POSA would have understood the fluid injection valve disclosed by Teigen to be a “vent valve” as that term is used in the ’253 Patent because its function is to relieve vacuum pressure by creating a pressure differential

and then reestablish vacuum pressure within the vacuum aspiration system to create a “pressure differential as a negative pressure pulse that negatively impacts the structural integrity of any occlusions to a degree that a static force could only achieve with a greater supply of energy.” *See* Ex. 1007 at 15:13-36; Ex. 1008 at [0064]; Ex. 1009 at [0066]. Teigen discloses “pressure is generated by introducing fluid into the catheter” using “a fluid injection on-off valve 296 [to] control[] the flow of fluid...to inject pulses of pressure into the clot flow path that may facilitate the extraction of clot or other occlusive substances.” *See* Ex. 1007 at 15:37-46, 16:1-16:24; Ex. 1008 at [0063]; Ex. 1009 at [0065].

127. A POSA would have further understood the term “fluidically communicate” to mean that fluid would be able to flow from one component of the system to another, and Teigen discloses a vacuum valve and vent valve fluidically connected (i.e., fluidically communicating), respectively, to a vacuum pump and a vent container holding a vent liquid. *See* Ex. 1007 at 3:63-4:28, 5:6-24, 6:8-23, 11:3-27, 12:25-41:11, 14:63-18:25; Ex. 1008 at [0010]-[0012], [0013], [0017], [0020], [0057], [0061]-[0065]; Ex. 1009 at [0012]-[0014], [0015], [0019], [0022], [0059], [0063]-[0069], FIGS. 9, 11. Teigen further discloses that the connecting tube has a proximal end configured to connect the vacuum source and a distal end configured to connect to an aspiration lumen in the aspiration catheter. Ex. 1007 at 3:62-4:20, 5:54-6:7; Ex. 1008 at [0012], [0019]; Ex. 1009 at [0014], [0021]. As discussed

above for 1[A], a POSA would have recognized that because the purpose of the aspiration catheter lumen is to serve as a conduit between the blood vessel and the vacuum aspiration system, Teigen discloses, expressly and inherently, a liquid column within the catheter lumen with a proximal and distal end. *See* Section IX.B.ii; *see also* Ex. 1007 at 3:36-4:20; Ex. 1008 at [0010], [0011]; Ex. 1009 at [0012], [0013]. Thus, a POSA would have understood that the three-point junction and connecting tubing disclosed in Teigen fluidically connects the fluid column within the lumen of the catheter to the vacuum pump and vent container through their respective valves. Here, because Teigen also discloses that the fluid injection valve 296 is operable to open and close “inject pulses of pressure into the clot flow path” and “introduce[s] fluid into the catheter” from the fluid reservoir 290, a POSA would understand the fluid injection valve 296 to “fluidically communicate,” as that term is used in the art, with both the reservoir 290 and the proximal end of the catheter. *See* Ex. 1007 at 15:37-46, 16:1-16:24; Ex. 1008 at [0063], [0065]; Ex. 1009 at [0065], [0067].

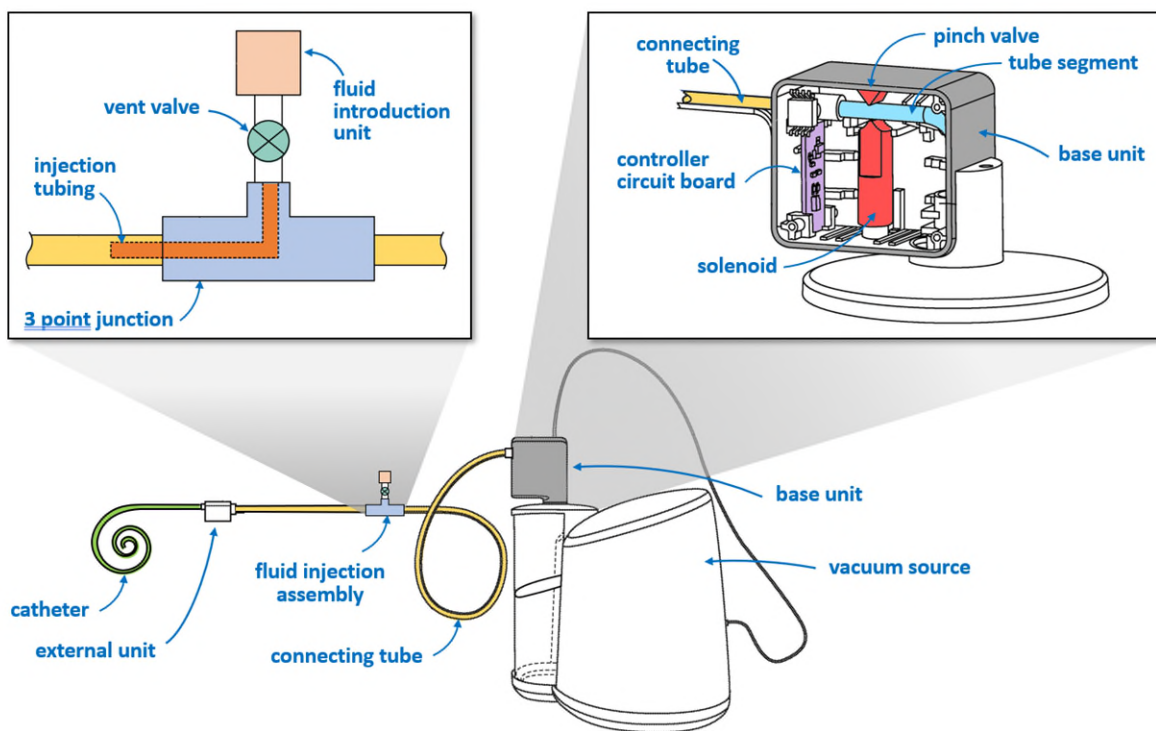
128. Therefore, it is my opinion that Teigen discloses “a vent valve configured to fluidically communicate: with the vent liquid in the vent container; and with the proximal portion of the liquid column at the proximal end of the catheter” as recited by Claim 1.

- (vi) **1[E] a vacuum valve configured to fluidically communicate: with the vacuum from the vacuum pump; and with the**

proximal portion of the liquid column at the proximal end of the catheter; and

129. Teigen discloses a vacuum valve configured to fluidically communicate with the vacuum from the vacuum pump and with the proximal portion of the liquid column at the proximal end of the catheter. Ex. 1007 at Claim 1 (“a vacuum source comprising a controllable vacuum valve” “wherein the connection tubing acts as a common conduit for fluid communication between the aspiration catheter and the vacuum and pressure sources via the vacuum and pressure valves, respectively”). As illustrated in the modified, annotated, and transposed version of Teigen’s figures 7A, 9, and 14 below, Teigen discloses that its vacuum aspiration system comprises “a base unit [illustrated in gray in the figure below] which incorporates at least one on-off valve and the controller.” Ex. 1007 at 5:54-6:7; Ex. 1008 at [0019]; Ex. 1009 at [0021]. Teigen discloses an “on-off valve” coupled to a controller that can cause the valve “to open to permit aspiration and close to block aspiration.” Ex. 1007 at 3:63-4:20, 5:40-53, 6:8-23, 12:25-41; Ex. 1008 at [0012], [0018], [0020], [0061], [0063]; Ex. 1009 at [0014], [0022], [0063], [0065]; *see also* Ex. 1007 at 11:3-27; Ex. 1008 at [0057]; Ex. 1009 at [0059]. Teigen further discloses that the “on-off valve is configured to be operatively connected to the connecting tube” of the vacuum aspiration control system. Ex. 1007 at 3:63-4:20; Ex. 1008 at [0012]; Ex. 1009 at [0014]. The “connecting tube... is configured to connect the

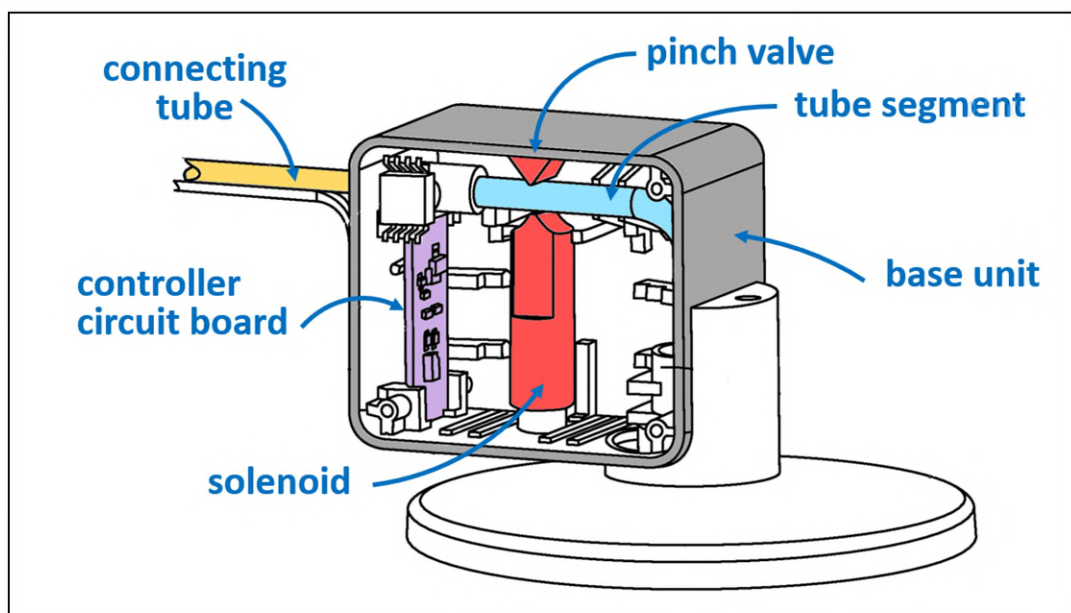
vacuum source to an aspiration lumen in the aspiration catheter.” Ex. 1007 at 3:63-4:20; Ex. 1008 at [0012]; Ex. 1009 [0014].



130. Teigen explains, “[t]he base unit will typically be configured to be mounted directly on or near a vacuum pump or console.” Ex. 1007 at 5:54-6:7; Ex. 1008 at [0019]; Ex. 1009 at [0021]. “The connecting tube typically has a proximal end configured to connect the vacuum source and distal end configured to connect to the aspiration catheter.” Ex. 1007 at 5:54-6:7; Ex. 1008 at [0019]; Ex. 1009 at [0021]. Teigen further discloses “[a] vacuum is applied through an aspiration lumen of the aspiration catheter using a vacuum source coupled to a proximal end of the aspiration lumen by a connecting tube. In this way, portions of clot and other occlusive material may be drawn into the aspiration lumen, through the connecting tube, and into a collection receptacle by the vacuum source.” Ex. 1007 at 6:8-23;

Ex. 1008 at [0020]; Ex. 1009 at [0022]. A POSA would have understood these disclosures to mean that the vacuum source is generated within the vacuum console of the aspiration system, traverses the collection receptacle, and moves through the tube segment within the base unit into the connection tubing and to the aspiration catheter lumen when the on-off pinch valve illustrated in the above figure is in its “on” position.

131. As illustrated in the modified, annotated, and transposed of Teigen’s figure 9 below, Teigen discloses that a collapsible tube segment 232 within a base unit open interior cavity 218 is “positioned in a pinch valve 228 which is driven by a solenoid 230.” Ex. 1007 at 11:3-27, FIG. 9; Ex. 1008 at [0057], FIG. 9; Ex. 1009 at [0059], FIG. 9. Teigen further discloses a controller 220 mounted within the cavity 218 “configured to open and close the pinch valve 228 to allow and prevent,



respectively, the flow of clot and blood through the tubing segment 232 from the aspiration catheter into the collection canister.” Ex. 1007 at 11:3-27, FIG. 9; Ex. 1008 at [0057], FIG. 9; Ex. 1009 at [0059], FIG. 9.

132. Alternatively, an angle valve may be employed instead of the pinch valve in Fig. 9, for the same purpose: to “open [the valve] to permit aspiration and close [the valve] to block aspiration.” Ex. 1007 at 12:25-32, FIG. 11; Ex. 1008 at [0061], FIG. 11; Ex. 1009 at [0063], FIG. 11.

133. As discussed above for 1[D], a POSA would have understood the term “fluidically connected” to mean that fluid would be able to flow from one component of the system to another, and Teigen discloses a vacuum valve and vent valve fluidically connected (i.e., “fluidically communicating”, respectively, to a vacuum pump and a vent container holding a vent liquid. *See* Ex. 1007 at 3:63-4:28, 5:6-24, 6:8-23, 11:3-27, 12:25-41, 14:63-18:25; Ex. 1008 at [0010]-[0012], [0013], [0017], [0020], [0057], [0061]-[0065]; Ex. 1009 at [0012]-[0014], [0015], [0019], [0022], [0059], [0063]-[0069], FIGS. 9, 11. Teigen further discloses that the connecting tube has a proximal end configured to connect the vacuum source and a distal end configured to connect to an aspiration lumen in the aspiration catheter. Ex. 1007 at 3:63-4:20, 5:54-6:7; Ex. 1008 at [0012], [0019]; Ex. 1009 at [0014], [0021]. As discussed above for 1[A], a POSA would have recognized that because the purpose of the aspiration catheter lumen is to serve as a conduit between the blood vessel and

the vacuum aspiration system, Teigen discloses, expressly and inherently, a liquid column within the catheter lumen with a proximal and distal end. *See* Section IX.B.ii; *see also* Ex. 1007 at 3:36-4:20; Ex. 1008 at [0010], [0011]; Ex. 1009 at [0012], [0013]. Thus, a POSA would have understood that the three-point junction and connecting tubing disclosed in Teigen fluidically connects the fluid column within the lumen of the catheter to the vacuum pump and vent container through their respective valves. Here, because Teigen also discloses a vacuum source and an on-off valve that are both connected to the system by the connecting tube that pulls in blood and clot material from the patient through the aspiration catheter, a POSA would understand the on-off valve to “fluidically communicate,” as that term is used in the art, with both the vacuum pump and the proximal end of the catheter. Ex. 1007 at 3:36-4:20; Ex. 1008 at [0010]-[0012]; Ex. 1009 at [0012]-[0014].

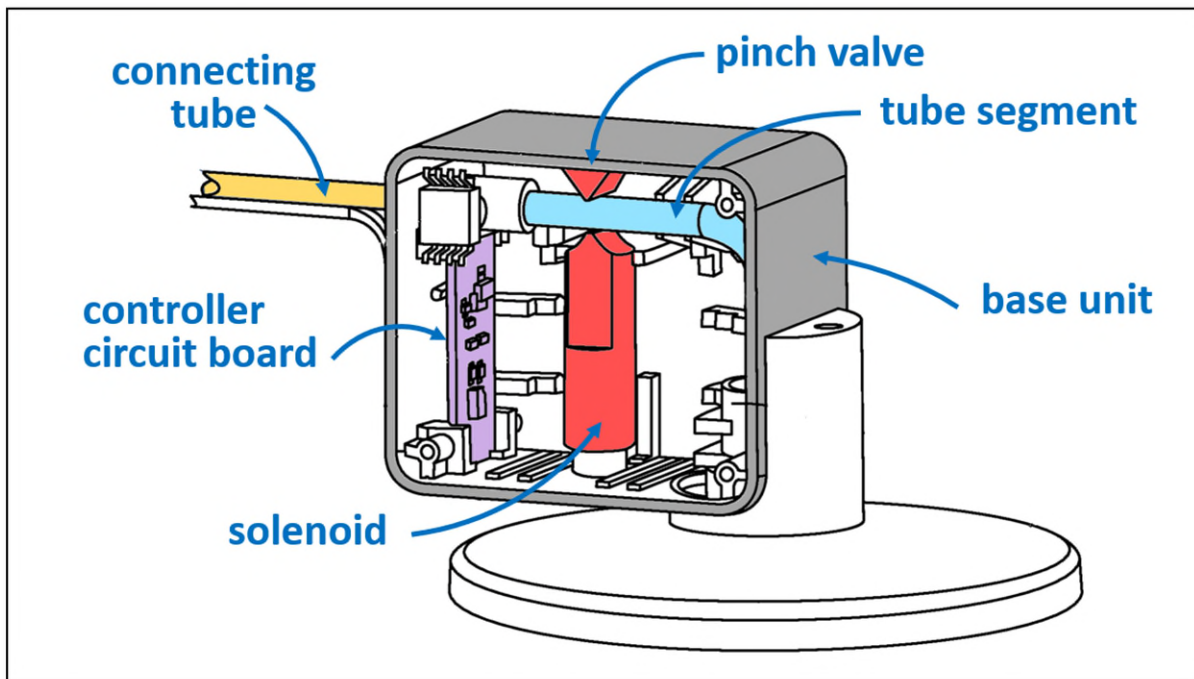
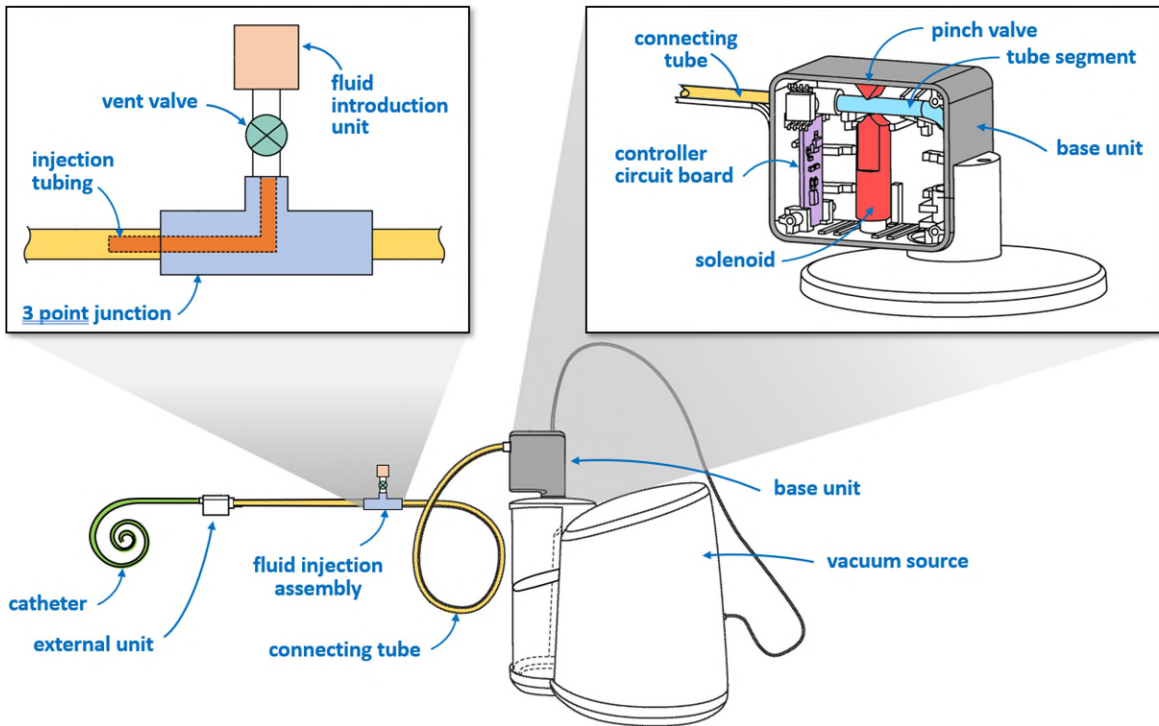
134. Therefore, it is my opinion that Teigen discloses “a vacuum valve configured to fluidically communicate: with the vacuum from the vacuum pump; and with the proximal portion of the liquid column at the proximal end of the catheter” as recited by Claim 1.

(vii) 1[F] a controller configured to carry out a pre-determined pattern of opening and closing the vent and vacuum valves to change a level of vacuum at the distal end and,

135. Teigen discloses a controller configured to carry out a pre-determined pattern of opening and closing the vent and vacuum valves to change a level of

vacuum at the distal end. Ex. 1007 at Claim 1 (“a controller configured to open and close the vacuum and vent valves in a predetermined cycle to change a level of vacuum at the distal end of the aspiration catheter”). Teigen discloses a controller configured to open and close both a vacuum valve and a fluid injection valve to engage “pulsed aspiration” when necessary to supply a “dynamic aspiration force” that creates a pressure differential to “facilitate thrombus ingestion into the aspiration catheter.” Ex. 1007 at 11:3-27, 12:25-41, 14:63-18:25; Ex. 1008 at [0057], [0061]-[0065]; Ex. 1009 at [0059], [0063]-[0069]; *see also* Ex. 1007 at 3:60-4:26, 5:4-22, 6:6-21; Ex. 1008 at [0012], [0013], [0017], [0020]; Ex. 1009 at [0014], [0015], [0019], [0022]. Teigen explains how, in an embodiment, a pressure differential is generated “by introducing fluid into the catheter.” Ex. 1007 at 15:37-46; Ex. 1008 at [0063]-[0066]; Ex. 1009 at [0065]-[0069]. As Teigen explains, “the controller may modulate a vacuum valve and a pressure valve.” Ex. 1007 at 17:20-18:10 (reference numerals omitted); Ex. 1008 at [0061], [0063], [0066]; Ex. 1009 at [0063], [0065], [0069].

136. The controller is illustrated in the modified, annotated, and transposed versions of Teigen’s Figure numbers 7A, 9, and 14 below.



137. As discussed above, Teigen discloses a controller configured to open and close the vacuum on-off valve and the fluid injection valve when the algorithm indicates to do so based on the conditions within the system to more effectively digest blood clots at the distal end of the aspiration catheter. Ex. 1007 at 11:3-27, 14:63-18:25; Ex. 1008 at [0057], [0061]-[0065]; Ex. 1009 [0059], [0063]-[0067]; *see also* Ex. 1007 at 3:60-4:26, 5:4-22, 6:6-21; Ex. 1008 at [0012], [0013], [0017], [0020]; Ex. 1009 at [0014], [0015], [0019], [0022]. Teigen further discloses that the pulsation protocols employed by the controller to initiate pulsed aspiration extraction cycles with the vacuum valve and fluid injection valve may be repeated several times until clot aspiration is accomplished. Ex. 1007 at 14:63-15:36, 20:12-43; Ex. 1008 at [0063]-[0065]; Ex. 1009 at [0065]-[0067]. Teigen teaches that “[t]he frequency with which the on-off valve opens and closes may be predetermined.” Ex. 1007 at 15:30-32; Ex. 1008 at [0068]-[0069]; Ex. 1009 at [0015], [0077].

138. Teigen also discloses that its algorithm can “alternate[] between providing vacuum aspiration and relative positive pressure” to complete an extraction cycle and remove a clot from the patient. Ex. 1007 at 14:63-15:36, 16:1-16:24; Ex. 1008 at [0066], [0067]; Ex. 1009 at [0068], [0069]. Teigen explains that its algorithm initiates an extraction cycle that employs “pulsation protocols” where “vacuum aspiration may be used to reduce pressure within the catheter and the removal of vacuum suction and/or the introduction of fluid may be used to increase

pressure within the catheter.” Ex. 1007 at 19:52-20:43; Ex. 1008 at [0066], [0067]; Ex. 1009 at [0068], [0069].

139. A POSA would have recognized that both Teigen’s disclosures of repeating the steps to open and close the valves and employing “extraction cycles” of varying pressure pulses are disclosures of carrying out a pre-determined pattern of opening and closing the vent and vacuum valves. Ex. 1007 at 14:63-15:36, 16:1-16:24, 19:52-20:43; Ex. 1008 at [0063]-[0067]; Ex. 1009 at [0065]-[0067], [0069].

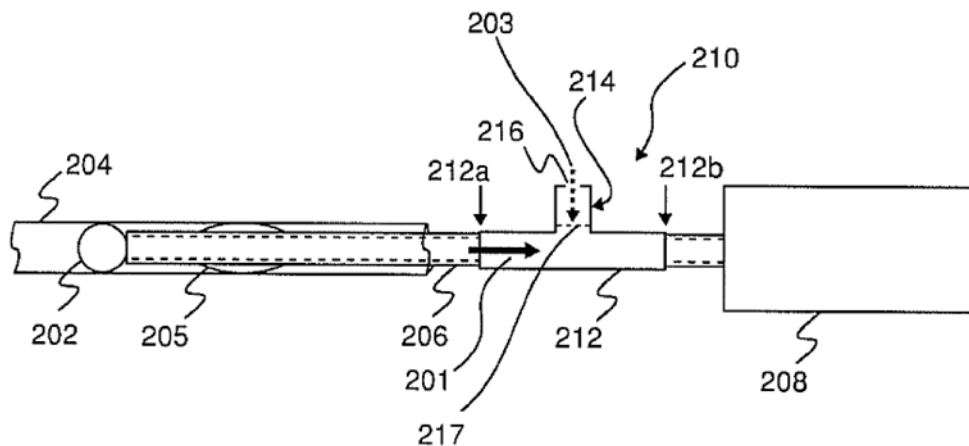
140. Teigen discloses that “an extraction cycle is typically initiated when an aspiration catheter is already under full vacuum” and when “the vacuum on-off valve between the catheter and the aspiration source is closed...the pressure in the aspiration catheter is increased, which may cause a positive pressure pulse.” Ex. 1007 at 14:63-15:36; Ex. 1008 at [0065]; Ex. 1009 at [0066]. Teigen further explains that positive pressure pulses can be introduced via the fluid introduction unit. Ex. 1007 at 16:1-16:24; Ex. 1008 at [0065]; Ex. 1009 at [0067]. Teigen further discloses that pulsed aspiration allows the clot to “experience the pressure differential as a negative pressure pulse that negatively impacts the structural integrity of any occlusions to a degree that a static force could only achieve with a greater supply of energy.” Ex. 1007 at 15:13-36; Ex. 1008 at [0065]; Ex. 1009 at [0067]. A POSA would have understood that because the distal end of the aspiration catheter in Teigen is engaged against the blood vessel occlusion during vacuum aspiration, as

discussed above in 1[A], 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 the Teigen system for the reason that the clot is located at the distal end of the catheter. Ex. 1007 at 6:8-23, 14:63-15:36, 16:1-16:24; Ex. 1008 at [0020], [0064], [0065]; Ex. 1009 at [0022], [0066], [0067].

141. Therefore, it is my opinion that Teigen discloses “a controller configured to carry out a pre-determined pattern of opening and closing the vent and vacuum valves to change a level of vacuum at the distal end,” as recited by Claim 1.

142. Alternatively, Grey also discloses causing a change in the level of vacuum at the distal end of an aspiration catheter, and it would be obvious to a POSA to do so with the Teigen aspiration system in view of Grey.

143. Grey teaches “an aspiration system,” shown in FIG. 2A below, comprising “a catheter insertable into a body, an aspiration source providing negative pressure in the catheter, and a device which repetitively changes the negative pressure to produce a dynamic suction force at a distal end of the catheter” for blood clot removal. Ex. 1010 at 5:1-4; *see also id.* at 7:13-20 (“repetitively to produce a dynamic suction force at the distal end of the catheter”); *id.* at 11:16-20 (“increase the rate of change of suction force at the distal end of the catheter.”). Grey explains that producing a “dynamic suction force at the distal end of the catheter...provides repetitive loading to induce material fatigue in the embolus” to aid its removal via vacuum aspiration. *Id.* at 4:25-30.



Ex. 1010, Figure 2A

144. To the extent that Teigen does not explicitly discuss a change in the level of vacuum at the distal end of the catheter, a POSA would alternatively have

found it obvious to change the level of vacuum at the distal end of Teigen's catheter using the cyclical open and closed state of its valves in view of Grey's disclosures of dynamic suction forces at the distal end of its catheter because Grey explains that such level changes induce material fatigue in the embolus and improves the efficacy of the thrombectomy device. Indeed, a POSA would have been motivated to do so because Teigen discloses the intent of its invention is to "provide systems and methods which optimize system performance, and procedures for removal of occlusive material." Ex. 1007 at 2:56-67; Ex. 1008 at [007]; Ex. 1009 at [009].

145. Thus, it is my opinion that Teigen in view of Grey discloses and renders obvious "a controller configured to carry out a pre-determined pattern of opening and closing the vent and vacuum valves to change a level of vacuum at the distal end" as recited by Claim 1.

(viii) 1[G] while changing the level of vacuum at the distal end, to substantially prevent forward flow of liquid at a distal end of the liquid column.

146. Teigen and the combination of Teigen in view of Grey and the knowledge of a POSA renders this claim limitation obvious.

147. Teigen discloses "a controller configured to... change a level of vacuum at the distal end of the aspiration catheter and control flow in and out from the distal end of the catheter." Ex. 1007 at Claim 1; *see also* Claim 13 ("wherein the controller is configured to substantially control flow in and out from the distal end

of the catheter”). As discussed above for 1[F], Teigen discloses a controller configured to carry out a pre-determined pattern of opening and closing the vent and vacuum valves to change a level of vacuum at the distal end. Ex. 1007 at 11:3-27, 14:63-18:25; Ex. 1008 at [0057], [0061]-[0065]; Ex. 1009 [0059], [0063]-[0069]; *see also* Ex. 1007 at 3:63-4:28, 5:6-24, 6:8-23; Ex. 1008 at [0012], [0013], [0017], [0020]; Ex. 1009 at [0014], [0015], [0019], [0022]. Teigen also discloses: “an extraction cycle may be automatically initiated when an algorithm of the controller 220 detects a clogged catheter, an occluded catheter, or a catheter positioned in clot.” Ex. 1007 at 15:47-67; Ex. 1008 at [0065]; Ex. 1009 at [0067]. Teigen explains that during the pulsed aspiration cycle:

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

Ex. 1007 at 15:47-67, 17:20-18:10; Ex. 1008 at [0065]; Ex. 1009 at [0067]. By only providing a minimal volume of fluid into the catheter to increase the relative pressure at the distal end, the suction force in the catheter is maintained, reducing the risk of occlusive material breaking free of a clot and traveling distally in the vessel. A POSA would have understood Teigen’s disclosure of “control[ling] flow of the distal portion in and out from the distal end during each cycle” to include substantially preventing forward flow, and would have further understood that the purpose of both

Teigen's techniques and those described in the '253 Patent are to prevent positive pressure (i.e., a pressure greater than physiological pressure), or maintain a suction force, at the distal end of the catheter to reduce the risk of distal emboli. Ex. 1007 at Claim 1. To the extent that Teigen does not expressly disclose "to substantially prevent forward flow of liquid at a distal end of the liquid column," Grey does.

148. As discussed above for 1[F], Grey teaches "an aspiration system" comprising "a catheter insertable into a body, an aspiration source providing negative pressure in the catheter, and a device which repetitively changes the negative pressure to produce a dynamic suction force at a distal end of the catheter" for blood clot removal. Ex. 1010 at 5:1-4. Grey further discloses that a "second aspiration fluid may be provided at a positive pressure" for the dynamic aspiration. Ex. 1010 at 8:24-25.

149. Grey explains that "negative pressure and negative pressure oscillations are delivered by a fluid medium which may be, for example, one or more liquids, gases, or a combination thereof." *Id.* at 3:22-24. Grey discloses that "the magnitude of the baseline pressure is preferably maintained above zero (i.e., a vacuum is maintained)." *Id.* at 13:7-11. Grey further discloses that "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." *Id.*; *see also id.* at 7:10-12 ("one very serious risk is the escape and travel of occlusive material from the

initial site of occlusion to a distal portion of the lumen or to another lumen branching therefrom.”); *id.* at 11:16-20 (“increase the rate of change of suction force at the distal end of the catheter.”).

150. A POSA would have recognized that Grey’s disclosure of providing a non-zero suction force to reduce the risk of occlusive clot material traveling distally in the vessel, away from the catheter, constitutes substantial prevention of forward flow of liquid at the distal end of the liquid column in the catheter as described in the ’253 Patent. Indeed, the ’253 Patent explains forward flow in these same terms:

When positive pressure exists at the distal end of the lumen, liquid from inside the lumen exits out from the distal end of the catheter in a distal direction. This is referred to as forward flow.... Forward flow, therefore, can and does remove thrombi off of the distal end and risk sending thrombi further distally in the vasculature.

Ex. 1001 at 3:6-17. Thus, although Grey does not expressly refer to “forward flow,” a POSA would understand that Grey’s disclosure of preventing “material breaking free of a clot and traveling distally in the vessel” is the same as substantially preventing forward flow, and would understand that the purpose of both Grey’s techniques and those described in ’253 Patent are to prevent positive pressure, or maintain a non-zero suction force, at the distal end of the catheter to reduce the risk of distal emboli. A POSA would also have found it obvious, in view of the teachings of Grey, to operate the system disclosed in Teigen in such a way as to substantially prevent forward flow, as that would be the most obvious way to achieve Grey’s

stated goal of reducing “the risk of occlusive material breaking free of a clot and traveling distally.”

151. Considering the well-known fluid dynamic principles that govern the pressure and flow direction in an aspiration catheter, a POSA would have a reasonable expectation of success of doing so. Indeed, Grey discloses “a plurality of parameters” that “control/influence the pressure realized in a catheter and to which an occlusion is subjected.” Ex. 1010 at 10:22-31. A POSA would have been able to follow the explicit directions provided in Grey to “optimize[] treatment efficacy” including substantially preventing forward flow through no more than routine experimentation. *Id.*

152. Therefore, it is my opinion that Teigen in view of Grey and the knowledge of a POSA discloses “while changing the level of vacuum at the distal end, to substantially prevent forward flow of liquid at a distal end of the liquid column” as recited by Claim 1.

C. Teigen in View of Grey, and the Knowledge of a POSA Renders Claim 2 Obvious

- (i) 2[A] The system according to claim 1, wherein the liquid at the distal end of the liquid column is one or more of albumin, d5W water, normal saline, half-normal saline, lactated Ringer’s solution, and blood, and mixtures thereof.**

153. As discussed above for Claim 1[A], Teigen discloses a catheter defining a lumen configured to be filled with a liquid column and that the purpose of Teigen’s

catheter is to act as a conduit to collect liquid, including blood and clot material from a patient's blood vessel. *See* Section IX.B.ii; *see also* Ex. 1007 at 1:56-59, 2:14-26 (“blood and clot are drawn into the collection canister”), Claim 2 (“wherein the fluid is one or more of saline or blood”); Ex. 1008 at [005], [0020], [0057]; Ex. 1009 at [006], [0022], [0059]. Given the nature of aspiration thrombectomy, a POSA would have recognized that the liquid at the distal end of liquid column would include blood, as the device extracts the clot along with blood from the vascular system.

154. Teigen further discloses that “a catheter may be filled with *saline* fluid to remove all the air from the lumen of the catheter” because “[b]efore an aspiration catheter can be used to remove clot and other occlusive material it must be primed with an incompressible fluid.” Ex. 1007, 1:59-2:26, 3:15-4:20, 22:55-67; Ex. 1008 at [0068]; Ex. 1009 at [0077]. Indeed, (normal) saline is a common liquid for medical use that can be safely introduced into human blood stream without causing detrimental effects.

155. Similarly, Grey discloses that “[g]enerally, catheter 206, conduit 212, chamber 214, and any connecting tubules are primed with aspiration medium,” and that “[t]he aspiration mediums may be compressible fluids, such as air, or incompressible fluids such as water or *saline*.” Ex. 1010, 8:20-9:5.

156. Therefore, it is my opinion that both Teigen and Grey disclose “wherein the liquid at the distal end of the liquid column is one or more of albumin, d5W

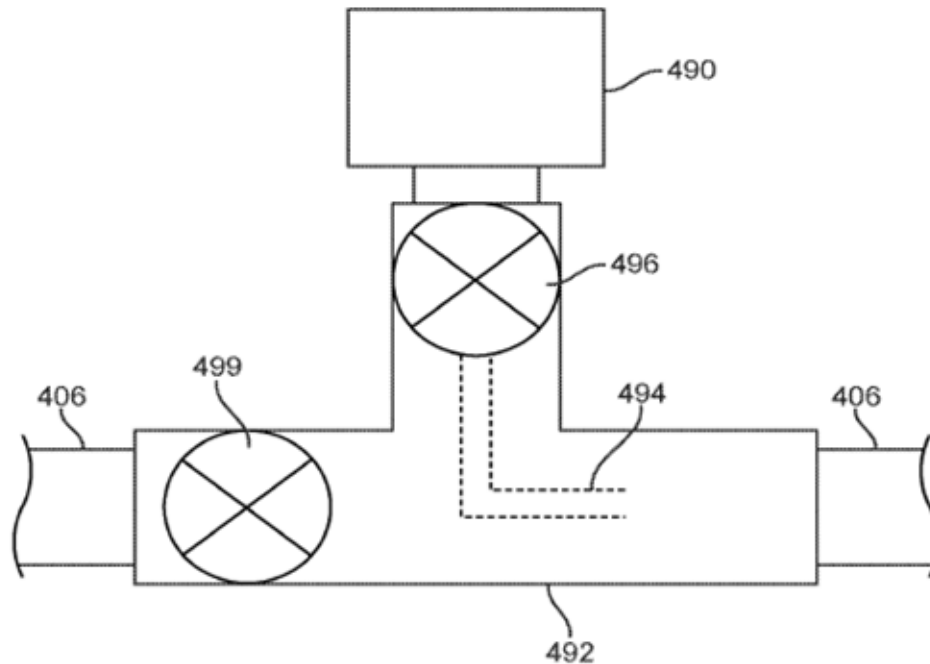
water, normal saline, half-normal saline, lactated Ringer's solution, and blood, and mixtures thereof,” as recited by Claim 2.

D. Teigen in View of Grey, and the Knowledge of a POSA Renders Claim 3 Obvious

- (i) 3[A] The system according to claim 1, further comprising: a manifold comprising the vent valve, the vacuum valve, and an output; and**

157. Teigen discloses a manifold comprising the vent valve, the vacuum valve, and an output. Ex. 1007 at Claim 1 (“a three-way joint comprising the pressure valve, the vacuum valve, and at least a portion of the connection tubing in fluid communication with the aspiration catheter”). As discussed in Claim 1[A]-1[E], Teigen discloses a vent valve in fluidic communication with a vent container to control the introduction of fluid into the catheter, a vacuum valve in fluidic communication with a vacuum pump to permit aspiration through the catheter, and a three-point junction and connection tubing to fluidically connect the liquid column within the catheter to the vacuum pump and vent container. *See* Sections IX.B.iii-vi; *See also* Ex. 1007 at 3:36-4:28, 5:6-24, 5:54-6:23, 11:3-27, 12:25-41, 14:63-18:25; Ex. 1008 at [0010]-[0012], [0013], [0017], [0019], [0020], [0057], [0061]-[0065]; Ex. 1009 at [0012]-[0014], [0015], [0019], [0021], [0022], [0059], [0063]-[0069], FIGS. 9, 11. Teigen explains how, in an embodiment, “the three-point junction 492 has valves to control both vacuum forces and positive pressure pulses. This allows the three-point junction 492 to alternate between applying vacuum aspiration and

pulses of pressure.” Ex. 1007 at 16:54-17:10, FIG. 16; Ex. 1008 at [0063], [0065], FIG. 13; Ex. 1009 [0065], [0067], FIG. 13.



Ex. 1007, Figure 16

A POSA would have recognized Teigen’s disclosure of a three-point junction 492 containing the vent and vacuum valves, which fluidically connects the aspiration catheter, vacuum pump, and vent container, as shown in figure 16 above, to be a “manifold” as that term is used in the art because a POSA would understand the term “manifold” to be a generic word for a component that brings multiple branches of a gas/fluid system together or distributes them apart. A POSA would further understand Teigen’s “manifold” to necessarily comprise an “output” to the

fluidically connected aspiration catheter, as shown on the right-side of Figure 16 above.

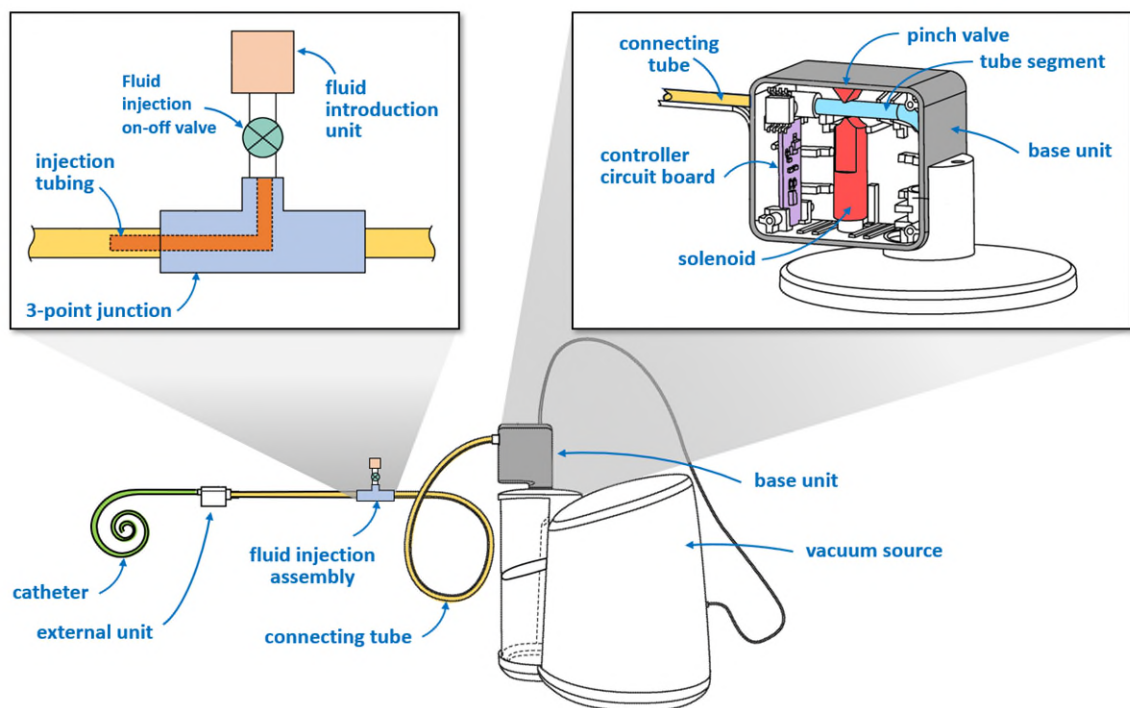
158. Therefore, it is my opinion that Teigen discloses “a manifold comprising the vent valve, the vacuum valve, and an output” as recited by Claim 3.

(ii) 3[B] an extension line fluidically connecting the proximal end of the catheter to the output of the manifold.

159. Teigen discloses this limitation. Ex. 1007 at Claim 3 (“an external unit in fluid communication with the aspiration catheter and the three-way joint, wherein the external unit is in fluid communication with the aspiration catheter and the vacuum source”). As discussed above in 3[A], Teigen discloses a manifold comprising the vent valve, the vacuum valve, and an output.

160. As illustrated in the modified, annotated, and transposed versions of Teigen’s Figure numbers 7A, 9, and 14 below, Teigen further discloses a “connecting tube 206” (shown in yellow) connecting the base unit (gray box) with the external unit (white box). Ex. 1007 at 10:38-11:55, Figs. 7-10; Ex. 1008 at [0019], [0053]-[0059], Figs. 7-10; Ex. 1009 at [0021], [0055]-[0061], Figs. 7-10. Teigen explains that the three-point junction (manifold) “may be positioned between the base unit 210 and the external unit” along that connecting tube, “or may be positioned distal to both the base unit 210 and the external unit 204—i.e. in close proximity to an attached aspiration catheter.” Ex. 1007 at 16:1-24; Ex. 1008 at [0063], Fig. 13; Ex. 1009 at [0065], Fig. 13. The “external unit 204,” in turn, “may

be configured to connect directly to a proximal end of an aspiration catheter.” Ex. 1007 at 10:38-51; Ex. 1008 at [0053], Figs. 7-8; Ex. 1009 at [0055], Figs. 7-8. As illustrated in Teigen’s Figure 10 below, the “external unit 204 includes an external unit enclosure 240 having a flow fitting 242 in an interior cavity” which permits the fluid column to flow from the catheter side to the base unit side of the external unit. Ex. 1007 at 11:28-33, 11:46-53, FIG.10; Ex. 1008 at [0058], Fig. 10; Ex. 1009 at [0060], Fig. 10. The flow fitting 242 “may be connected to portions 206a and 206b of the connecting tubing 206,” as illustrated in Teigen’s Figure 8B below. Ex. 1007 at 11:28-33, 11:48-55, FIG.8B; Ex. 1008 at [0058], Fig. 10; Ex. 1009 at [0060], Fig. 10.



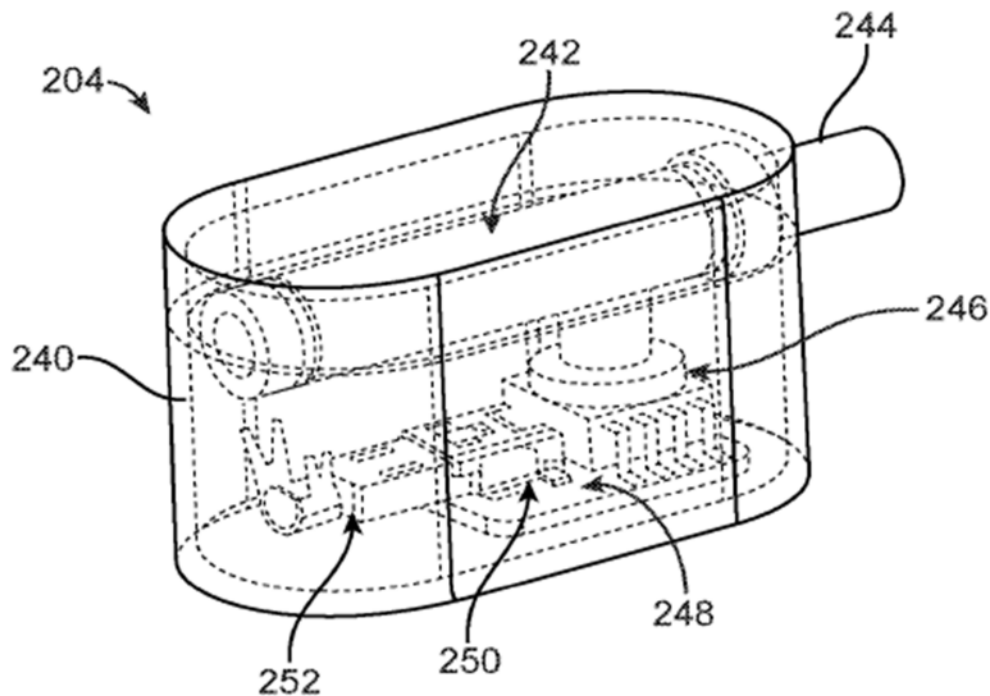


FIG. 10

161. As discussed above for 1[D] and 1[E], a POSA would have understood the term “fluidically connected” to mean that fluid would be able to flow from one component of the system to another. *See* Sections IX.B.v and IX.B.vi. As discussed above for 3[A], Teigen discloses the three-point junction (part of the manifold) having an output in order to fluidically connect the aspiration catheter with the vacuum aspiration system. *See* Section IX.D.i. Because Teigen discloses that the external unit may be positioned between the three-point junction and the aspiration catheter, a POSA would have understood Teigen’s external unit and connecting tubing portions to extend the fluidic connection between the aspiration catheter to

the output of the manifold. Ex. 1007 at 16:5-9; Ex. 1008 at [0063]; Ex. 1009 at [0065].

162. Therefore, it is my opinion that Teigen's connecting tube portion from the three-point junction to the external unit, either alone or together with the portion extending through the external unit, constitutes an extension line fluidically connecting the proximal end of the catheter to the output of the manifold, as recited in Claim 3.

E. Teigen in View of Grey, and the Knowledge of a POSA Renders Claim 4 Obvious

- (i) 4[A] The system according to claim 1, wherein a portion of the pre-determined pattern includes a time period where both the vent and vacuum valves are closed.**

163. Teigen discloses this limitation. Teigen discloses "the pre-determined cycle includes one or more time periods of a double-closed state in which both the pressure and vacuum valves are closed" (i.e., a "double-closed state"). Ex. 1007 at Claim 4. Teigen also teaches sequences of opening and closing the vacuum and vent valves including where "both valves are closed for at least short periods of time." Ex. 1007 at 16:54-18:10; Ex. 1008 at [0063], [0065]; Ex. 1009 at [0065], [0067], [0070].

164. To the extent that Teigen and Grey do not explicitly disclose a double-closed state in which the vacuum valve and vent valve are both closed, a double-closed state would have been obvious in a typical operation of the vacuum valve and

vent valve sequence disclosed in Teigen. As discussed above, Teigen discloses dynamic aspiration by opening and closing vacuum and vent valves to generate pressure pulses to improve clot removal efficiency. An aspiration cycle involves closing the vacuum valve and opening the vent valve to introduce a fluid, e.g. saline, to generate a positive pulse (increase in pressure), and then closing the vent valve and reopening the vacuum valve to generate a negative pulse (decrease in pressure). Ex. 1007 at 15:13-36, 17:20-18:110; Ex. 1008 at [0063]-[0065]; Ex. 1009 at [0065]-[0067].

165. A POSA would have found it obvious and typical 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. In this way, after the vacuum valve has been closed, the positive pressure injected with the fluid would not be evacuated away, efficiently building up a positive pulse. By contrast, opening the vent valve first and then followed by closing the vacuum valve will lead to unnecessary loss of the fluid being directly evacuated through the vacuum, thus less efficient. Because of the nature of serial operation, there is necessarily a finite delay (e.g. 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 that both the vacuum valve and the vent valve are closed, i.e. the double-closed state. Similarly, closing the vent valve first and then reopening the vacuum would be the logical

approach to efficiently generate a negative pulse. Closing the vent valve cuts off the positive pressure source and opening the vacuum valve then allows the full force of the vacuum to be exerted on the clot. For the same reasons, a second double-closed state thus exists here due to the nature of the serial operation. A POSA would have understood and it would have been most logical to conduct the valve operation in serial to yield effective negative pulsing, e.g. closing the vent valve first and then opening the vacuum valve to generate the full vacuum acceleration force. In this way, after the vent valve has been closed and the vacuum valve opened, the applied vacuum would not be minimized by venting, efficiently building up a full negative pulse. Teigen further discloses that pulsed aspiration allows the clot to “experience the pressure differential as a negative pressure pulse that negatively impacts the structural integrity of any occlusions to a degree that a static force could only achieve with a greater supply of energy.” Ex. 1007 at 15:13-36; Ex. 1008 at [0065]; Ex. 1009 at [0067]. Teigen clearly discloses the opening and closing of the vacuum valve and the vent valve are done in serial, not in parallel.

166. Therefore, it is my opinion that Teigen in view of Grey, and the knowledge of a POSA discloses and renders obvious “a portion of the predetermined pattern includes a time period where both the vent and vacuum valves are closed,” as recited in Claim 4.

F. Teigen in View of Grey, and the Knowledge of a POSA Renders Claim 5 Obvious

- (i) 5[A] The system according to Claim 4, wherein the controller is configured to open and close the vent and vacuum valves in a repeated cycle**

167. As discussed above, Teigen in view of Grey renders obvious Claim 1. The combination further discloses “a controller configured to open and close the vacuum and vent valves in a predetermined cycle” for at least the reasons discussed above in the context of claim limitation 1[F]. *See* Section IX.B.vii. *See also*, Ex. 1007 at Claim 8 (“wherein the controller is configured to repeatedly and periodically open and close the vacuum and pressure valves in the predetermined cycle”).

- (ii) 5[B] comprising a double-closed state in which both the vent and vacuum valves are closed.**

168. For the reasons discussed above in the context of Claim 4, Teigen in view of Grey discloses or renders obvious a double-closed state in which both the vent and vacuum valves are closed. *See* Section IX.E; *See also* Ex. 1007 at Claim 4 (“wherein the pre-determined cycle includes one or more time periods of a double-closed state in which both the pressure and vacuum valves are closed”).

G. Teigen in View of Grey, and the Knowledge of a POSA Renders Claim 6 Obvious

- (i) 6[A] The system according to claim 5, wherein a time of the double-closed state is no greater than 30 ms.**

169. As discussed above, Teigen in view of Grey, and the knowledge of a POSA renders obvious Claims 4 and 5, which recite a double-closed state. Teigen

in view of Grey, and the knowledge of a POSA further renders obvious “a time of the double-closed state is no greater than 30 ms.” *See* Ex. 1007 at Claim 5 (“wherein each of the one or more time periods of the double-closed state is no greater than 30 ms”).

170. As discussed above, a POSA would have understood and it would have been most logical to conduct the valve operation in serial to yield effective pulsing, and there is necessarily a delay between the valve operation that leads to a double-closed state. A POSA would have further understood that it would be beneficial and obvious to minimize the delay for efficient pulsing. The strength of the vacuum inside a catheter that is clogged would decrease after the vacuum valve is closed because blood would flow around or seep through the clot, and, accordingly, the pressure differential between the fluid inside the catheter and the vent fluid decreases overtime, leading to less efficient pulsing. Thus, it would have been obvious for a POSA to operate the aspiration system disclosed in Teigen in a way to minimize delay, i.e. a time of the double-closed state. Such adjustment in the delay time requires no more than routine optimization, e.g. adjusting the setting of the controller disclosed in Teigen.

171. Moreover, to the extent that Teigen does not expressly disclose adjusting the delay time, combination with Grey further renders obvious “a time of the double-closed state is no greater than 30 ms.” As discussed above, Grey

discloses an “aspiration profile at the distal end of the catheter” that “chang[es] the negative pressure repetitively . . . to produce a dynamic suction at the distal end of the catheter.” Ex. 1010 at 4:25-30, 7:18-20. Grey teaches that the aspiration profile “supplies repetitive and variable loading to induce material fatigue in an embolus” and “cause[s] fracture and break-up” of the embolus, *id.* at 9:30-10:1, 10:17-19, and “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,” *id.* at 13:7-11.

172. Grey teaches that “[d]ifferent frequencies of cyclic aspiration may be used to improve clot clearance” and “for some embodiments higher frequencies are more effective, particularly frequencies above 1 Hz.” Ex. 1010 at 10:28-30, 10:30-31 (“In some embodiments, frequencies may be at least 10 Hz and, for still some other embodiments, frequencies may be at least 50 Hz.”). A POSA would have understood the well-known inverse relationship between frequency and period. A cyclic aspiration frequency of “at least 50 Hz” corresponds to an aspiration period of “no greater than 20 ms” ($1/(50 \text{ Hz}) = 0.02 \text{ second} = 20 \text{ millisecond}$). Because the double-close state can only last for a time shorter than the full aspiration period for a cyclic aspiration, a POSA would have understood that a cyclic aspiration frequency of “at least 50 Hz” inherently discloses a time of the double-closed state of no greater than 20 ms. *See* Ex. 1010 at 9:13-25, 10:28-11:3.

173. Moreover, Grey invites experimentation to achieve optimal efficacy:

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

Ex. 1010 at 10:22-27. A POSA would have understood that the purpose of altering the parameters of the dynamic aspiration profile of the aspiration cycle, as disclosed in Grey, is to optimize the dynamic suction forces on the thrombus to create efficiencies and reduce risks in the aspiration process. Indeed, Teigen and Grey both teach providing a dynamic aspiration force that will “establish pressure differentials...to facilitate thrombus ingestion” because the experienced pressure differential “negatively impacts the structural integrity of any occlusions to a degree that a static force could only achieve with a greater supply of energy.” Ex. 1007 at 14:63-15:36; Ex. 1008 at [0064], [0065]; Ex. 1009 at [0066], [0067]; *see also* Ex. 1010 at 2:24-3:24.

174. 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. *In re Peterson*, 315 F.3d 1325, 1329 (Fed. Cir. 2003); *E.I DuPont De NeMours & Co. v. Synvina C.V.*, 904 F.3d

996, 1006 (Fed. Cir. 2018) (citing *In re Aller*, 220 F.2d 454, 456 (CCPA 1955)). 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. *E.I DuPont De NeMours & Co.*, 904 F.3d at 1006 (citations omitted). None applies in this situation. Here, the ’253 Patent’s claimed double-closed state for “no greater than 30 ms” is a result-effective and obvious result from the routine experimentation invited by Grey. The alleged inventive concept of the ’253 Patent is to prevent forward flow out of the distal end of the catheter while achieving efficient vacuum aspiration of clots, which are both risks and rewards that Grey warns of. Moreover, as discussed above, Grey teaches a cyclic aspiration frequency of “at least 50 Hz” and a POSA would have understood that disclosure inherently discloses a time of the double-closed state of no greater than 20 ms. *See* Ex. 1010 at 9:13-25, 10:28-11:3. The ’253 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 Teigen or Grey teaches away from a double-closed state of no more than 30 ms, and Grey explicitly invites the reader to optimize the parameters of the cycle frequency profiles disclosed to

achieve “optimized treatment efficacy.” It is my opinion, then, that the claimed double-closed state time of “no greater than 30 ms” is the result of routine optimization and is thus obvious.

175. Accordingly, a POSA would have been motivated to experiment with the dynamic aspiration system disclosed in Teigen, using different delay time between closing the vacuum valve and the vent valve, in view of the preferred aspiration frequencies taught by Grey.

176. Moreover, a POSA would be aware of the inherent risks of forward flow in aspiration thrombectomy, and would recognize that monitoring and controlling the length of time that the valves are actuated, including when they are both in an unactuated or closed state, 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 at ¶19. Thus, a POSA would be able to preserve the overall negative pressure contained in the vacuum aspiration system and increase the efficiency with which the clot is digested by the system by optimizing the amount of time that both the vacuum and vent valve are closed occurs. A POSA would recognize that by adjusting the timing of a double-closed state within 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 forward flow. Thus, a POSA would have been motivated by the teachings in Teigen and Grey to experiment with the duration and amount of time that the valves are closed to optimize the efficiency of aspiration while limiting the risks of forward flow out of the distal end of the catheter.

177. It is my opinion that the '253 Patent's claimed duration of the double closed state is a result-effective and obvious result from the routine experimentation invited by Teigen and Grey. Neither Teigen or Grey teaches away from a double closed state for any time duration, including, no more than 30 ms, and Grey explicitly invites the reader to optimize the parameters of the cycle frequency profiles disclosed to achieve "optimized treatment efficacy." Moreover, as discussed above, Grey teaches a double closed state of no greater than 20 ms, which falls squarely within the claimed range of "no greater than 30 ms."

178. Therefore, it is my opinion that Teigen in view of Grey and the knowledge of a POSA renders obvious Claim 6.

H. Teigen in View of Grey and the Knowledge of a POSA Renders Claim 7 Obvious

(i) 7[A] The system according to claim 1, wherein the controller is configured to open and close the vent and vacuum valves in a repeated cycle

179. For the reasons discussed above for 1[F], Teigen discloses a controller configured to carry out a pre-determined pattern of opening and closing the vent and

vacuum valves. *See* Section IX.B.vii; *See also*, Ex. 1007 at Claim 8 (“wherein the controller is configured to repeatedly and periodically open and close the vacuum and pressure valves in the predetermined cycle”).

(ii) 7[B] comprising a vent-only state in which the vacuum valve is closed and the vent valve is open, and

180. The combination of Teigen and Grey discloses or renders obvious this limitation. Ex. 1007 at Claim 6 (“wherein the pre-determined cycle includes one or more time periods of a pressure-only state in which the vacuum valve is closed and the pressure valve is open”). Further, as discussed for Claim 1[E], Teigen discloses a vacuum on-off valve in the form of a pinch valve or an angle valve that can be caused by the controller “to open to permit aspiration and close to block aspiration.” *See* Ex. 1007 at 3:36-4:20, 5:40-6:23, 11:3-27, 12:25-39, FIGS. 9, 11; Ex. 1008 at [0010]-[0012], [0018]-[0020], [0057], [0061], [0063], FIGS. 9, 11; Ex. 1009 at [0012]-[0014], [0020]-[0022], [0059], [0063], [0065], FIGS. 9, 11. As discussed above for Claim 1[F], Teigen discloses employing pulsed aspiration extraction cycles that alternate between full aspiration and various pressure pulse cycles. Ex. 1007 at 19:52-20:43; Ex. 1008 at [0063]-[0066]; Ex. 1009 at [0067]-[0069].

181. Teigen further discloses applying a vacuum, followed by an increase in pressure with fluid or mechanical pressure relief, and then reapplying full vacuum during the extraction cycle. Ex. 1007 at 15:13-36; Ex. 1008 at [0064]; Ex. 1009 [0066]. Teigen explains:

an extraction cycle alternates between providing vacuum aspiration and relative positive pressure. An extraction cycle is typically initiated when an aspiration catheter is already under full vacuum. When an extraction cycle is initiated, the vacuum on-off valve between the catheter and aspiration source is closed and the pressure in the aspiration catheter is increased [by fluid injection or other mechanism], which may cause a positive pressure pulse and establish a pressure differential between the vacuum source and the catheter. When the on-off valve is then opened, the contents and the distal tip of the aspiration catheter experience the pressure differential as a negative pressure pulse that negatively impacts the structural integrity of any occlusions....

Ex. 1007 at 15:13-36; Ex. 1008 at [0065]; Ex. 1009 [0067]. A POSA would understand that closing the valve to the vacuum source and then increasing the pressure in the aspiration catheter is a disclosure of a state where the vacuum valve is closed and the fluid injection valve is open because Teigen discloses that by doing so, the fluid will create a positive pressure or relieve vacuum within the aspiration system. Moreover, at the end of the process, Teigen explains that vacuum must be reopened, indicating to a POSA that the vacuum is not fully engaged while the fluid injection valve is open.

182. Teigen also discloses that the vacuum/aspiration valve and the fluid/pressure valve “may be opened alternatively,” which a POSA would recognize includes the situation where the vent valve is open and the vacuum valve closed, such that only the vent fluid and not the vacuum is coupled to the catheter. Ex. 1007 at 16:54-17:10; Ex. 1008 at [0065], [0067]; Ex. 1009 at [0067], [0069]. Teigen further discloses that “a fluid injection on-off valve 296 controls the flow of fluid

(either liquid or gas) to inject pulses of pressure into the clot flow path.” Ex. 1007 at 15:47-67; Ex. 1008 at [0065]; Ex. 1009 at [0067].

183. To the extent that Teigen does not explicitly disclose a “vent-only state,” a POSA would have found it obvious to fully close the vacuum valve, at least for a time, to provide more positive pressure influx into the system than would occur if the vacuum valve was only partially closed, or remained open when the vent valve opened. A POSA would also be motivated to do so to prevent additional blood loss and conserve the injection fluid from being vacuumed into the canister. *See* Ex. 1007 at 2:27-48; Ex. 1008 at [005]; Ex. 1009 at [007].

184. Therefore, it is my opinion that Teigen in view of Grey discloses and renders obvious “comprising a vent-only state in which the vacuum valve is closed and the vent valve is open” as recited by Claim 7.

(iii) 7[C] a time of the vent-only state is no greater than 50 ms.

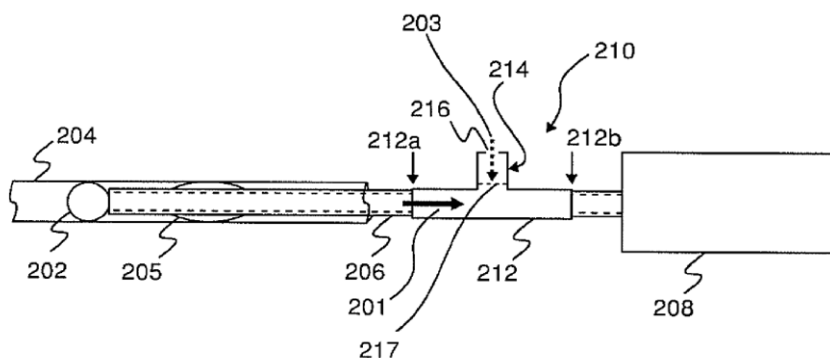
185. Teigen in view of Grey and the knowledge of a POSA renders this claim limitation obvious.

186. As discussed above for Claim 7[B], Teigen discloses a vent-only state as part of a repeated aspiration cycle. Teigen further discloses predetermined time periods for the extraction cycle. *See* Ex. 1007 at Claim 7 (“wherein each of the one or more time periods of the pressure-only state is no greater than 50 ms”). Teigen further discloses applying a vacuum, followed by an increase in pressure with fluid

or mechanical pressure relief, and then reapplying full vacuum during the extraction cycle. Ex. 1007 at 15:13-36; Ex. 1008 at [0064]; Ex. 1009 [0066].

187. To the extent that Teigen does not provide the specifically claimed time period during which the fluid injection valve remains open, Grey discloses that “one very serious risk is the escape and travel of occlusive material from the initial site of occlusion to a distal portion of the lumen or to another lumen branching therefrom.” Ex. 1010 at 7:10-12. Grey further discloses that “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.” *Id.*, 13:7-11. A POSA would have readily recognized that a prolonged vent-only state will lead to a positive pressure in the catheter and increase the risk distal migration of thrombi. Accordingly, a POSA would optimize the time of vent-only state in view of Grey. *Id.*

188. As discussed above for Claim 1[H], Grey discloses a vacuum aspiration system with an appliance 210 to deliver fluid to the catheter to create a dynamic



Ex. 1010, Figure 2A

suction force at the distal end of the catheter. Ex. 1010 at 5:1-4, 11:16-20, 13:7-11, FIG. 2A. Grey further discloses that the appliance 210 includes a conduit 212 and a chamber 214 “connected to and in fluid communication with the conduit 212.” *Id.* at 7:21-28. Grey further discloses that “chamber 214 has one or more openings 216 which permit” “aspiration medium” comprising any “compressible fluids, such as air, or incompressible fluids such as water or saline” “of a second pressure to be mixed with” the negative pressure supplied by the vacuum aspiration source. *Id.* at 7:29-20, 8:20-25. The “opening 216 may be selectively opened and closed” “to achieve a particular dynamic aspiration profile” using any suitable valve. *Id.* at 8:1-8, 8:15-19. Grey teaches that “cyclic aspiration” is characterized by frequency profiles, such as those illustrated in Figures 3A-3C, and “different frequencies of cyclic aspiration may be used to improve clot clearance,” including frequencies of “at least 50 Hz.” *Id.* at 9:13-25, 10:28-11:3.

189. A POSA would have understood the well-known inverse relationship between frequency and period. A cyclic aspiration frequency of “at least 50 Hz” corresponds to an aspiration period of “no greater than 20 ms” ($1/(50 \text{ Hz}) = 0.02 \text{ second} = 20 \text{ millisecond}$). Because the vent-only state can only last for a time shorter than the full aspiration period for a cyclic aspiration, a POSA would have understood that a cyclic aspiration frequency of “at least 50 Hz” inherently discloses a time of the vent-only state of no greater than 20 ms. *See* Ex. 1010 at 9:13-25, 10:28-11:3.

190. Moreover, Grey invites experimentation to achieve optimal efficacy:

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

Ex. 1010 at 10:22-31. A POSA would have understood that the purpose of altering the parameters of the dynamic aspiration profile of the aspiration cycle, as disclosed in Grey, is to optimize the dynamic suction forces on the thrombus to create efficiencies and reduce risks in the aspiration process. Indeed, Teigen and Grey both teach providing a dynamic aspiration force that will “establish pressure differentials...to facilitate thrombus ingestion” because the experienced pressure differential “negatively impacts the structural integrity of any occlusions to a degree that a static force could only achieve with a greater supply of energy.” Ex. 1007 at 14:63-15:36; Ex. 1008 at [0064], [0065]; Ex. 1009 at [0066], [0067]; *see also* Ex. 1010 at 2:24-3:24.

191. Moreover, as discussed above for Claim 1[G], a POSA would have been aware of the inherent risks of forward flow in aspiration thrombectomy, and would recognize that the introduction of a pressure relieving vent would serve to exacerbate these risks if the pressure in the catheter exceeded a threshold based on well-known theories of fluid mechanics. Ex. 1023 at ¶19. Thus, a POSA would

have been able to preserve the overall negative pressure contained in the vacuum aspiration system by limiting the amount of time that the vacuum valve was closed and the vent valve was open. A POSA would have recognized that by adjusting the timing of the opening and closing of the vacuum and vent valves, a POSA would be able to achieve a vent-only state while ensuring that the momentum of fluid at the distal end of the catheter does not change direction sufficiently to create any forward flow. Ex. 1023 at ¶20. Thus, a POSA would have been motivated by the teachings in Teigen and Grey to experiment with the duration of the vent-only state in order to optimize the efficiency of aspiration while limiting the risks of forward flow out of the distal end of the catheter. A POSA would have recognized that a period of vent-only in excess of a given time could cause the positive pressure from the vent source to eclipse the negative pressure provided by the vacuum source and may lead to undesirable forward flow. Ex. 1023 at ¶20. Accordingly, “a time of vent-only state” is a result effective parameter that a POSA would have recognized to optimize through routine experimentation.

192. As discussed above for claim 6, 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. *In re Peterson*, 315 F.3d at 1329; *E.I DuPont De NeMours & Co.*, 904 F.3d at 1006 (citations omitted). 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. *E.I DuPont De NeMours & Co.*, 904 F.3d at 1006 (citations omitted). None applies in this situation. Here, the ’253 Patent’s claimed vent-only state for “no greater than 50 ms” is a result-effective and obvious result from the routine experimentation invited by Grey. The alleged inventive concept of the ’253 Patent is to prevent forward flow out of the distal end of the catheter while achieving efficient vacuum aspiration of clots, which are both risks and rewards that Grey warns of. Moreover, as discussed above, Grey teaches a vent-only state of no greater than 20 ms, which falls squarely within the claimed range of “no greater than 50 ms.” The ’253 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 Teigen or Grey teaches away from a vent-only state of no more than 50 ms, and Grey explicitly invites the reader to optimize the parameters of the cycle frequency profiles disclosed to achieve “optimized treatment efficacy.” It is my opinion, then, that the claimed vent-only time of “no greater than 50 ms” is the result of routine optimization and is thus obvious.

193. Therefore, it is my opinion that Teigen in view of Grey and the knowledge of a POSA renders obvious “a time of the vent-only state is no greater than 50 ms,” as recited by Claim 7.

I. Teigen in View of Grey and the Knowledge of a POSA Renders Claim 8 Obvious

- (i) 8[A] The system according to claim 1, wherein the controller is configured to repeatedly and periodically carry out the pre-determined pattern.**

194. For the reasons discussed above for 1[F], Teigen discloses a controller configured to repeatedly and periodically carry out the pre-determined pattern. *See* Section IX.B.vii; *See also*, Ex. 1007 at Claim 8 (“wherein the controller is configured to repeatedly and periodically open and close the vacuum and pressure valves in the predetermined cycle”).

J. Teigen in View of Grey and the Knowledge of a POSA Renders Claim 9 Obvious

- (i) 9[A] The system according to claim 1, wherein the controller is configured to selectively open and close the vent and vacuum valves in a repeated cycle comprising:**

195. For the reasons discussed above in Claim 1[F], Teigen discloses a controller configured to selectively open and close a vacuum and vent valve in a repeated cycle. *See* Section IX.B.vii; *See also*, Ex. 1007 at Claim 9 (“wherein the controller is configured to selectively open and close the pressure and vacuum valves in a repeated cycle”).

- (ii) 9[B] a vacuum-only state in which the vacuum valve is open**

and the vent valve is closed;

196. Teigen discloses this claim limitation. Ex. 1007 at Claim 9 (“a vacuum-only state in which the vacuum valve is open and the pressure valve is closed”). As discussed above in the context of claim limitation 1[E], Teigen discloses a vacuum valve operable to open and close to establish aspiration or cut off aspiration from the vacuum source when necessary. As discussed above in the context of claim limitation 1[D], Teigen discloses a vent valve operable to open and close to inject fluid into the clot path when necessary. A POSA would recognize that during aspiration thrombectomy, “a vacuum-only state in which the vacuum valve is open and the vent valve is closed” is the default and conventional aspiration mode, the injection of positive pressure fluids into the system is not always necessary, and a constant negative pressure is desirable until the system reaches a point where dynamic aspiration should occur. Teigen further teaches that “an extraction cycle is typically initiated when the aspiration catheter is already under full vacuum” and “an extraction cycle alternates between providing vacuum aspiration and relative positive pressure.” Ex. 1007 at 15:13-36; Ex. 1008 at [0064], [0065]; Ex. 1009 [0066], [0067]. A POSA would have understood that in order to achieve efficient clot extraction with the aspiration system disclosed in Teigen, the system must be able to create vacuum suction without leaving the vent valve open, which would reduce the strength of the vacuum suction. Therefore, Teigen in view of Grey and

the knowledge of a POSA discloses and renders obvious “a vacuum-only state in which the vacuum valve is open and the vent valve is closed,” as recited in Claim 9.

(iii) 9[C] a first double-closed state in which the vacuum valve is closed and the vent valve is closed;

197. As discussed above in the context of claim limitation 4, Teigen in view of Grey and the knowledge of a POSA discloses or renders obvious “a first double-closed state in which the vacuum valve is closed and the vent valve is closed,” as the aspiration transitions from vacuum only to vent only state to create a positive pressure pulse. *See* Ex. 1007 at Claim 9 (“a first double-closed state in which the vacuum valve is closed and the pressure valve is closed”). Accordingly, Teigen in view of Grey and the knowledge of a POSA discloses and renders obvious “a first double-closed state in which the vacuum valve is closed and the vent valve is closed,” as recited in Claim 9.

(iv) 9[D] a vent-only state in which the vacuum valve is closed and the vent valve is open; and

198. For the reasons discussed above in the context of claim limitation 7, Teigen in view of Grey discloses or renders obvious a vent-only state in which the vacuum valve is closed and the vent valve is open. *See* Section IX.H.ii; *See also* Ex. 1007 at Claim 9 (“a pressure-only state in which the vacuum valve is closed and the pressure valve is open”).

(v) 9[E] a second double-closed state in which the vacuum valve is closed and the vent valve is closed.

199. As discussed above in the context of claim limitation 4, Teigen in view of Grey and the knowledge of a POSA discloses or renders obvious “a second double-closed state in which the vacuum valve is closed and the vent valve is closed,” as the aspiration transitions from vent only to vacuum only state to create a negative pressure pulse.

200. Accordingly, Teigen in view of Grey and the knowledge of a POSA discloses and renders obvious Claim 9. *See also* Ex. 1007 Claim 9 (“a second double-closed state in which the vacuum valve is closed and the pressure valve is closed”).

K. Teigen in View of Grey and the Knowledge of a POSA Renders Claim 10 Obvious

- (i) 10[A-E] The system according to claim 1, wherein the controller is configured to selectively open and close the vent and vacuum valves in a repeated cycle comprising a vacuum-only state in which the vacuum valve is open and the vent valve is closed, followed by a first double-closed state in which the vacuum valve is closed and the vent valve is closed and a time of the first double-closed state is no greater than 30 ms, followed by a vent-only state in which the vacuum valve is closed and the vent valve is open, followed by a second double-closed state in which the vacuum valve is closed and the vent valve is closed.**

201. As discussed above, Teigen in view of Grey renders Claims 1 and 9 obvious. For the reasons discussed above in the context of claim 9, Teigen in view of Grey and the knowledge of a POSA renders each of these claim limitations obvious, both individually and in combination. *See* Section IX.J; *See also* Ex. 1007 at Claim 11 (“wherein the controller is configured to selectively open and close the

pressure and vacuum valves in a repeated cycle comprising: a vacuum-only state in which the vacuum valve is open and the pressure valve is closed; followed by a first double-closed state in which the vacuum valve is closed and the pressure valve is closed; followed by a pressure-only state in which the vacuum valve is closed and the pressure valve is open; and followed by a second double-closed state in which the vacuum valve is closed and the pressure valve is closed”), Claim 12 (“wherein a time period of the first double-closed state is no greater than 30 ms”). A POSA would have found it obvious to perform the limitations of Claim 9 in a sequential order as recited in Claim 10, not only because it is the exact order in which the limitations appear in Claim 9, but also because it would be obvious to a POSA to begin an aspiration thrombectomy sequence with a vacuum-only state because it is the default and conventional aspiration mode, as discussed above in Claim 9[B]. *See* Section IX.J.ii; *See also* Ex. 1007 at 15:13-36 (“an extraction cycle is typically initiated when the aspiration catheter is already under full vacuum”); Ex. 1008 at [0064], [0065]; Ex. 1009 [0066], [0067]. As discussed above for Claim 4, a POSA would also find it obvious to implement a double-closed state after the vacuum-only state before proceeding to a vent-only state to avoid an inefficient and unnecessary loss of vent fluid being directly evacuated through the vacuum if the vent valve were opened before the vacuum valve was closed. *See* Section IX.E. As also discussed above for Claim 4, a POSA would find it similarly obvious to follow the vent-only

state with a double-closed state before proceeding to a vacuum-only state to generate the full vacuum acceleration force when the vacuum valve is opened. *See* Section IX.E.

202. Therefore, it is my opinion that Teigen in view of Grey, and the knowledge of a POSA discloses and renders obvious the sequential order of the disclosed elements as recited in Claim 10.

L. Teigen in View of Grey and the Knowledge of a POSA Renders Claim 11 Obvious

- (i) 11[A] The system according to claim 9, wherein a time between an opening of the vent valve and a closing of the vent valve is between approximately 10 ms and approximately 50 ms.**

203. As discussed above, Teigen in view of Grey renders Claim 9 obvious. Teigen in view of Grey and the knowledge of a POSA further renders this claim limitation obvious. *See* Ex. 1007 at Claim 10 (“wherein a time between an opening of the pressure valve and a closing of the pressure valve is between approximately 10 ms and approximately 50 ms”).

204. As discussed above for Claim 1[F], Teigen discloses a controller connected to a fluid injection valve (i.e. a vent valve) that can be opened and closed to inject fluid into the clot flow path when necessary. *See* Section IX.B.vii.

205. As discussed above for Claims 1[F] and 4, Teigen discloses applying a vacuum, followed by an increase in pressure with fluid or mechanical pressure relief,

and then reapplying full vacuum during the extraction cycle. Ex. 1007 at 15:13-36; Ex. 1008 at [0064]; Ex. 1009 at [0066]. See Section IX.B.vii and IX.E. While Teigen does not provide specific times or frequencies during which the fluid injection valve remains open, Grey does for its system.

206. As discussed above in the context of Claims 6 and 7, Grey discloses cyclical aspiration conducted at preferred frequencies of “at least 10 Hz” and “at least 50 Hz” that can create a dynamic suction force at the distal end of the catheter. Ex. 1010 at 10:28-11:3. A POSA would have understood the well-known inverse relationship between frequency and period. A cyclic aspiration frequency of “at least 50 Hz” corresponds to an aspiration period of “no greater than 20 ms” ($1/(50 \text{ Hz}) = 0.02 \text{ second} = 20 \text{ millisecond}$). A cyclic aspiration frequency of “at least 10 Hz” corresponds to an aspiration period of “no greater than 100 ms” ($1/(10 \text{ Hz}) = 0.1 \text{ second} = 100 \text{ millisecond}$). Because the vent state, i.e. between an opening of the vent valve and a closing of the vent valve, can only last for a time shorter than the full aspiration period for a cyclic aspiration, a POSA would have understood that a cyclic aspiration frequency of “at least 50 Hz” inherently discloses a time of the vent state (*i.e.* the time between opening and closing the vent valve) of no greater than 20 ms, or that a cyclic aspiration frequency of “at least 10 Hz” inherently discloses a time of the vent-only state of no greater than 100 ms. See Ex. 1010 at 9:13-25, 10:28-11:3. A POSA would have reasonably operated Teigen with the

preferred frequencies taught by Grey in order to achieve the efficient and safe aspiration motivated both Teigen and Grey. Accordingly, Teigen in view of Grey discloses a time length of the vent-only state that overlaps with the claimed range in Claim 11 and thus render it obvious.

207. Moreover, as discussed above in Claims 6 and 7, Grey invites experimentation to achieve optimal efficacy and a POSA would have understood that the purpose of altering the parameters of the dynamic aspiration profile of the aspiration cycle, as disclosed in Grey, is to optimize the dynamic suction forces and pressure differentials experienced on the surface of the thrombus to create efficiencies and reduce risks in the aspiration process. *See* Ex. 1010 at 10:22-31, 2:24-3:24; *see also* Ex. 1007 at 2:56-67, 14:63-15:46; Ex. 1008 at [007], [0064], [0067]; Ex. 1009 at [009], [0066], [0067]. It would have been obvious for a POSA to experiment with the aspiration frequencies disclosed in Grey and apply that methods to Teigen to arrive at the claimed “time between an opening of the vent valve and a closing of the vent valve” through routine optimization.

208. As discussed above for Claims 1[F], 4, 6, and 7, a POSA would be aware of the inherent risks of forward flow in aspiration thrombectomy and would recognize that monitoring the introduction of a pressure relieving vent would serve to exacerbate these risks if the pressure in the catheter exceeded a threshold based on well-known theories of fluid mechanics. Thus, a POSA would be able to preserve

the overall negative pressure contained in the vacuum aspiration system and increase the efficiency with which the clot is digested by the system by limiting the amount of time that the vacuum valve was closed and the vent valve was open. A POSA would recognize that by adjusting the timing of the opening and closing of the vacuum and vent valves, a POSA would be able to achieve a vent-only state while ensuring that the momentum of fluid at the distal end of the catheter does not change direction sufficiently to create any forward flow. Ex. 1023 at ¶20. A POSA would recognize that too short of a duration where the system is in vent would not allow the clot to experience a sufficient degree of accelerated forces to break it up in accordance with Teigen's invention, but a period of vent in excess of a given time would risk that the positive pressure from the vent source would eclipse the negative pressure provided by the vacuum source and may lead to undesirable forward flow. Thus, a POSA would have been motivated by the teachings in Teigen and Grey to experiment with the duration of the vent-only state in order to optimize the efficiency of aspiration while limiting the risks of forward flow out of the distal end of the catheter.

209. Accordingly, Teigen in view of Grey and the knowledge of a POSA renders obvious Claim 11.

M. Teigen in View of Grey and the Knowledge of a POSA Renders Claim 12 Obvious

(i) 12[A] The system according to claim 9, wherein a frequency

of the cycle is between approximately 6 Hz and approximately 16 Hz

210. As discussed above for Claim 1[F], Teigen discloses cyclical aspiration that operates for extraction cycles. Ex. 1007 at 6:8-23, 14:63-18:25, 20:12-57; Ex. 1008 at [0020], [0063]-[0065]; Ex. 1009 at [0022], [0065]-[0067], [0069]. Teigen further discloses “wherein a period of the cycle is based on a predetermined frequency.” Ex. 1007 at Claim 1; *See also*, Ex. 1007 at 15:13-36, 15:47-67; Ex. 1008 at [0064], [0069]; Ex. 1009 at [0066], [0068], [0078]. To the extent that Teigen does not disclose specific ranges of cycle frequencies for vacuum aspiration, those ranges are obvious in view of Grey.

211. As discussed above for Claims 6 and 7, Grey discloses cyclical aspiration frequencies “above 1 Hz,” “at least 10 Hz,” and “at least 50 Hz.” Ex. 1010 at 9:13-25, 10:28-11:3. A POSA would easily recognize that the disclosed frequency ranges in Grey encompass or overlap with the recited range of 6 to 16 Hz of Claim 12. Moreover, Grey discloses a specific embodiment at “a frequency of approximately 6.3 Hz,” that falls within the claimed range. Ex. 1010 at 11:29-31.

212. To the extent that Patent Owner argues that the claimed range of cycle frequencies is novel or non-obvious, a POSA would understand those ranges to be the result of routine optimization and obvious to try in view of Grey’s disclosure of cycle frequencies, for the reasons discussed for Claims 6 and 7. *In re Peterson*, 315 F.3d 1325, 1329 (Fed. Cir. 2003); *E.I DuPont De NeMours & Co. v. Synvina C.V.*,

904 F.3d 996, 1006 (Fed. Cir. 2018) (citing *In re Aller*, 220 F.2d 454, 456 (CCPA 1955)).

213. Indeed, Grey invites experimentation:

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

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

Ex. 1010 at 9:29-11:15; see also *id.* at 24:6-16 (discussing results at different frequencies). Moreover, the '253 Patent does not describe the claimed range as critical or having any unexpected results. Therefore, it is my opinion that Teigen in view of Grey and the knowledge of a POSA renders Claim 12 obvious.

N. Teigen in View of Grey and the Knowledge of a POSA Renders Claim 13 Obvious

- (i) 13[A] The system according to claim 9, wherein a frequency of the cycle is between approximately 8 Hz and 12 Hz**

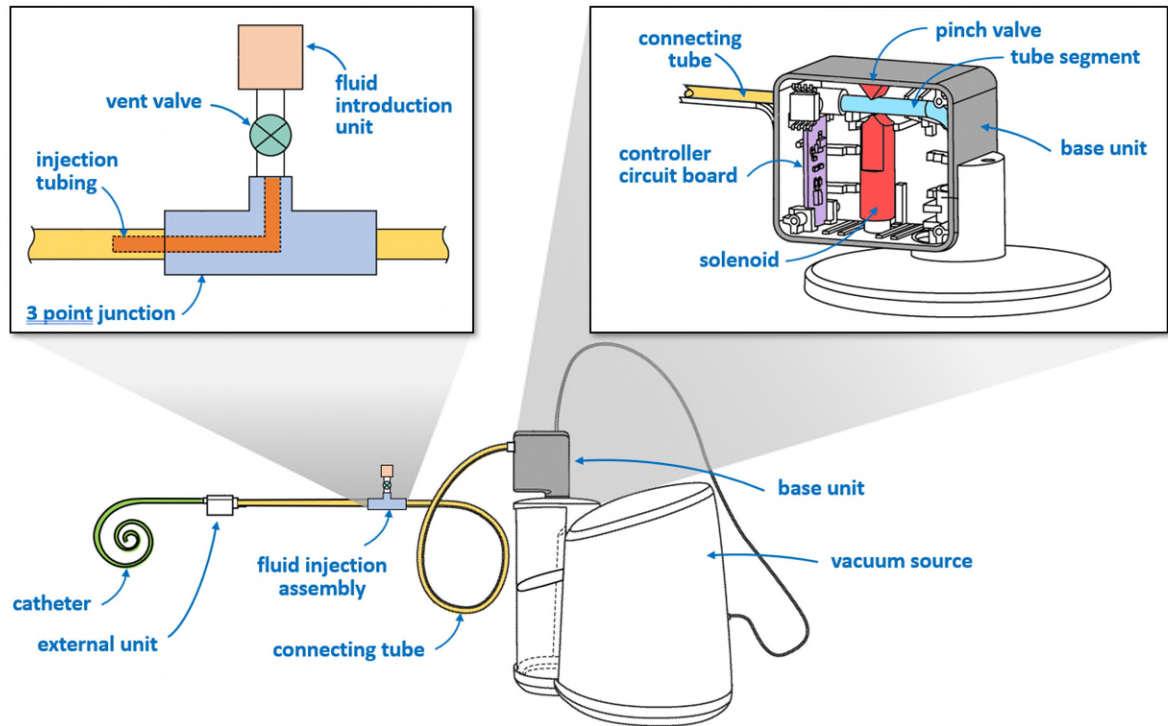
214. As discussed for Claim 12 above, Teigen in View of Grey and the knowledge of a POSA renders obvious a cycle period between approximately 6 Hz and 16 Hz. Claim 13 recites a slightly different numerical range, “wherein a period of the cycle is between approximately 8 Hz and approximately 12 Hz,” which is neither critical nor having any unexpected results. For at least the same reasons stated above, Teigen in view of Grey and the knowledge of a POSA also renders Claim 9 obvious.

O. Teigen in View of Grey and the Knowledge of a POSA Renders Claim 14 Obvious

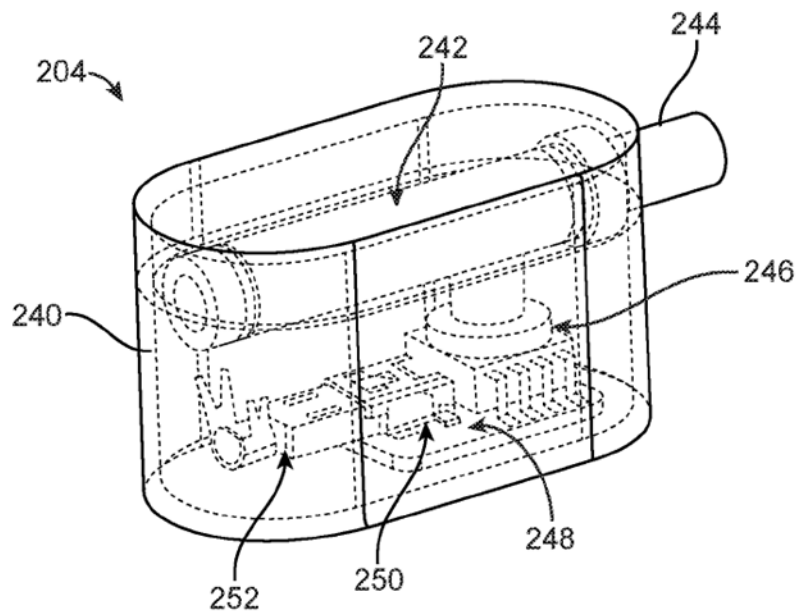
- (i) 14[A] The system according to claim 1, wherein the change in the level of vacuum at the distal end is one of: greater than approximately 15 inHg and occurs in no greater than approximately 50 ms; greater than approximately 20 inHg and occurs in no greater than approximately 30 ms; and greater than approximately 25 inHg and occurs in no greater than approximately 20 ms.**

215. As discussed for Claim 1[F], Teigen discloses a change in the level of vacuum at the distal end of the catheter. *See* Ex. 1007 at 6:8-23, 14:63-36, 16:1-16:24; Ex. [1008] at [0020], [0064], [0065]; Ex. 1009 at [0022], [0066], [0067]. Teigen further discloses employing a first and second “spaced-apart” pressure sensor within the system to monitor the pressure differential in the base unit and the

connecting tubing to calculate the “material flow rate through the connecting tube.” *See* Ex. 1007 at 11:3-12:11; Ex. 1008 at [0057]-[0060]; Ex. 1009 at [0059]-[0062]. To the extent that Teigen does not explicitly disclose measuring pressure changes and length of any pressure changes at the distal end of the catheter itself, it would have been obvious to a POSA to situate the one or more of the pressure sensors disclosed in Teigen, as discussed for Claim 1[F], close enough to the distal end of the catheter to monitor the change in the level of vacuum at the distal end for a given time. *See* Ex. 1007 at 4:39-44, 10:38-12:11; Ex. 1008 at [0061]-[0064], Ex. 1009 at [0059]-[0062]. Teigen teaches that its second pressure sensor, housed in the external unit shown in the modified, annotated, and transposed figures 7A, 9, and 14 from Teigen below, is “located on or adjacent the connecting tube between the vacuum source and the aspiration catheter.” *See* Ex. 1007 at 5:54-6:7, 7:15-19; Ex. 1008 at [0019], [0022]; Ex. 1009 at [0021], [0024].



216. Teigen further discloses that the external unit “may be configured to connect directly to a hub or other proximal end of an aspiration catheter.” Ex. 1007 10:38-51; Ex. 1008 at [0053]; Ex. 1009 at [0055]. Teigen explains that the external unit 204, shown in Figure 10 below, has a pressure sensor 246 that is mounted on circuit board 248 and “the output of the pressure sensor may be delivered to the controller 220 via a connective cable (not shown).” Ex. 1007 at 11:28-47, FIG. 10; Ex. 1008 at [0058], FIG. 10; Ex. 1009 at [0060], FIG. 10.



Ex. 1007, Figure 10

Ex. 1007 at FIG. 10. A POSA would understand Teigen to teach a pressure sensor mounted on or near the proximal end of the aspiration catheter that sends detected pressure signals to the controller within the base unit.

217. A POSA would have understood that while the change in the level of vacuum near the distal end of the catheter may be different than the change in the level of vacuum near the proximal end of the catheter, such a difference would be slight and predictable using well-established principles of fluid dynamics. Regardless, a POSA would have understood that the changes to the level of vacuum anywhere in the catheter would be a good indicator of the change of level of vacuum at the distal end. A POSA would have understood that Teigen's proximal pressure sensor disclosures inherently teach determining the change in a level of vacuum at

the distal end of the catheter. *See* Ex. 1007 at 5:54-6:7, 7:15-19, 10:38-51, 11:28-47, FIG. 10; Ex. 1008 at [0019], [0022], [0053], [0058]; Ex. 1009 at [0021], [0024], [0055], [0060], FIG. 10. Indeed, the '253 Patent is consistent with this general principle in its Figure 50 that an approximate change of 15 psi in the proximal pressure translates to an approximate change of 11 psi (22 inHg) in distal pressure. Ex. 1001, FIG. 50.

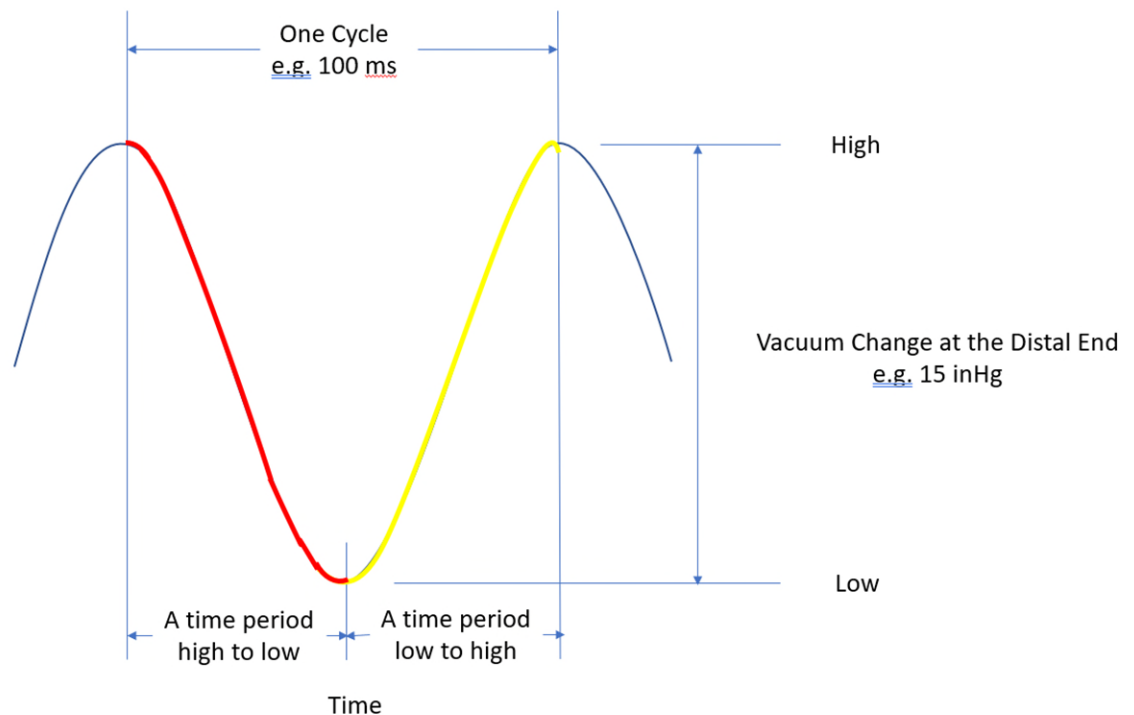
218. Moreover, further to the discussion above in the context of claim limitations 1[F] and 1[G], Grey discloses an “aspiration profile at the distal end of the catheter” that “chang[es] the negative pressure repetitively . . . to produce a dynamic suction at the distal end of the catheter.” Ex. 1010 at 4:25-30, 7:18-20. Grey teaches that the aspiration profile “supplies repetitive and variable loading to induce material fatigue in an embolus” and “cause[s] fracture and break-up” of the embolus, *id.* at 9:30-10:1, 10:17-19, and “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,” *id.* at 13:7-11. For these stated purposes, Grey identifies, and a POSA would have well understood, that “a plurality of parameters” to “control/influence the pressure realized in a catheter” include “static baseline aspiration pressure, frequency, aspiration medium, and pressure waveform.” *Id.* at 10:22-27.

219. With respect to the pressure waveform, Grey discloses that “the realized pressure differential (i.e. the magnitude of the difference between the maximum and minimum pressure achieved at the catheter tip) may be between 0 and -100 inHg”, or “in some embodiments . . . between -5 and -20 inHg.” Ex. 1010 at 13:4-11. A POSA would have recognized that the pressure differential is a result effect variable for safe and efficient thrombus extraction. For example, a POSA would have understood that a high-pressure differential generally speeds up the material fatigue taught in Grey. The disclosed pressure differential range in Grey overlaps with the claimed range of “greater than approximately [15, 20, or 25] inHg” of “the change in the level of vacuum at the distal end” in claim 10 of the ’253 Patent. The ’253 does not describe any particular effect of the claimed range, let alone any criticality or unexpectedness related to the claimed range. Therefore, it is my opinion that Teigen in view of Grey and the knowledge of a POSA discloses and renders obvious “a change in the level of vacuum at the distal end is greater than approximately [15, 20, or 25] inHg.”

220. With respect to frequency, Grey discloses that “[d]ifferent frequencies of cyclic aspiration may be used to improve clot clearance” and “for some embodiments higher frequencies are more effective, particularly frequencies above 1 Hz.” Ex. 1010 at 10:28-30, 10:30-31 (“In some embodiments, frequencies may be at least 10 Hz and, for still some other embodiments, frequencies may be at least 50

Hz.”). Moreover, Grey discloses in connection with a given frequency that “the rate of change of suction/vacuum pressure in the catheter and thus the total change of suction/vacuum pressure in the catheter can be selectively varied,” which allows “control [of] both the frequency and amplitude of aspiration individually.” Ex. 1010 at 11:16-12:13. A POSA would have recognized that the rate of change of vacuum pressure can be expressed in terms of “the time for the change in the level of vacuum from low to high or from high to low” and Grey teaches that the rate of change and pulse amplitude can be adjusted independently. *See id.* A POSA would have further understood that rate of change, i.e. “the time for the change in the level of vacuum from low to high or from high to low,” is another result effect variable for safe and efficient thrombus extraction. A higher cycle frequency would necessarily require a higher rate of change. For example, a frequency of at least 10 Hz corresponds to a period of less than 100 ms; a frequency of at least 50 Hz corresponds to a period of less than 20 ms. Accordingly, a POSA would have understood that the aspiration frequency imposes an inherent limitation to the rate of change. In other words, “the time for the change in the level of vacuum from low to high or from high to low” must be shorter than the aspiration period.

221. As illustrated below, each aspiration cycle includes at least a time period during which the level of vacuum increases from low to high and a time period during which the level of vacuum decreases from high to low.



In the example profile above, the aspiration period is taken to be 100 ms. *See* Ex. 1010 at 10:30-31 (disclosing a preferred aspiration frequency of “at least 10 Hz”). The example profile also represents a scenario that is the least demanding on the rate of change, where the vacuum level does not reach a steady state in an aspiration cycle, and each cycle only includes an upward pressure ramp and a downward pressure ramp. Assuming that the upward and downward pressure ramps require a similar amount of time, *see, e.g.* Ex. 1010 at FIGURE 3C, the rate of change defined as “the time for the change in the level of vacuum from low to high or from high to low” should be at least less than about 50 ms (a half of the cycle) in order to maintain

an aspiration frequency of “at least 10 Hz.”⁴ Accordingly, Grey inherently discloses a time for the change in the level of vacuum from low to high or from high to low of no greater than [50, 30, or 20] ms. Similarly, for the preferred aspiration frequency of “at least 50 Hz,” Ex. 1010 at 10:30-31, Grey inherently discloses a time for the change in the level of vacuum from low to high or from high to low of no greater than 10 ms (the half cycle of 50 Hz). Accordingly, the disclosed frequency ranges in Grey either overlap or fall within the claimed range of “no greater than approximately [50, 30, or 20] ms,” as recited in claim 14 of the ’253 Patent. As discussed above, Grey discloses the rate of change, e.g. the time for the change in the level of vacuum from low to high or from high to low, as result effective variable. The ’253 Patent does not describe any particular effect of the claimed range, let alone any criticality or unexpectedness related to the recited range, alone or in combination with other claim limitations. Therefore, it is my opinion that Teigen in view of Grey and the knowledge of a POSA discloses and renders obvious “a change in the level of vacuum at the distal end is one of: greater than approximately [15, 20, or 25] inHg

⁴ In situations where the upward and downward pressure ramps are not of the same time length, at least one of them would still satisfy the limitation of “no greater than approximately [50, 30, or 20] ms.”

and occur in no greater than approximately [50, 30, or 20] ms.” *See also* Section VII above.

222. Moreover, as discussed above in Claims 6 and 7, Grey invites experimentation to achieve optimal efficacy and a POSA would understand that the purpose of altering the parameters of the dynamic aspiration profile of the aspiration cycle, as disclosed in Grey, is to optimize the dynamic suction forces and pressure differentials experienced on the thrombus to improve efficiency and reduce risks in the aspiration process. *See* Ex. 1010 at 10:22-31, 2:24-3:24; *see also* Ex. 1007 at 2:56-67, 15:13-36, 15:47-67; Ex. 1008 at [007], [0064], [0065], [0069]; Ex. 1009 at [009], [0066]-[0068], [0078]. Accordingly, a POSA would be motivated to experiment with different “change in the level of vacuum at the distal end” in both magnitude and rate of change to arrive at the claimed ranges through routine optimization.

223. Therefore, it is my opinion that Teigen in view of Grey and the knowledge of a POSA renders obvious Claim 14.

P. Teigen in View of Grey and the Knowledge of a POSA Renders Claim 17 Obvious

- (i) 17[A] The system according to claim 1, wherein the controller is configured to open and close the vent and vacuum valves in a repeated cycle of the pre-determined pattern and**

224. Teigen discloses this limitation for the reasons discussed above for Claim 1[F] and 4. *See* Sections IX.B.vii and IX.E; *See also*, Ex. 1007, at Claim 8 (“wherein the controller is configured to repeatedly and periodically open and close the vacuum and pressure valves in the predetermined cycle”).

(ii) 17[B] prevent forward flow of the liquid column out from the distal end during each cycle by regulating timing of the vent valve.

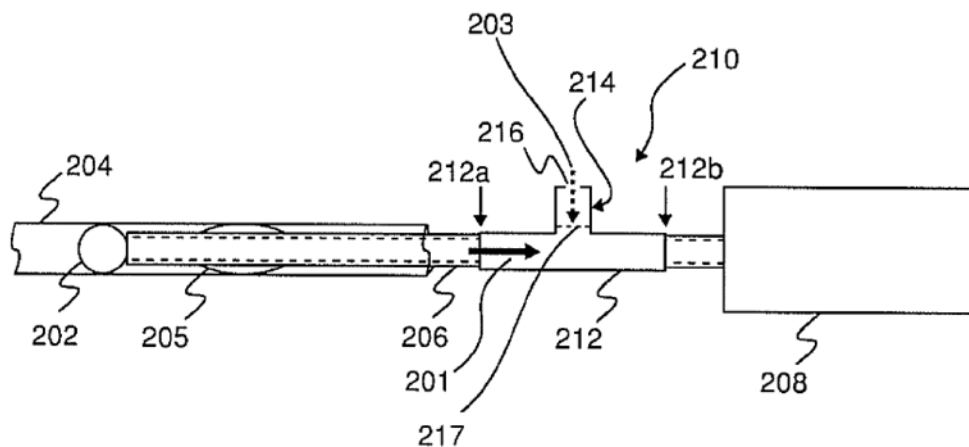
225. As discussed above for Claim 1[G], Teigen in view of Grey and the knowledge of a POSA discloses and renders obvious “substantially prevent forward flow at a distal end of the liquid column.” *See* Section IX.B.viii. Teigen also specifically recites configuring the controller to regulate the valve timings to prevent forward flow. *See* Ex. 1007 at Claim 13 (“wherein the controller is configured to substantially control flow in and out from the distal end of the catheter by regulating a timing of the pressure valve”).

226. Teigen discloses regulating the timing of the vent valve and that regulating the timing of the vent valve at least in part contributes to the prevention of forward flow of the distal portion out from the distal during each cycle. As discussed for Claim 1[G], Teigen discloses that each extraction cycle employs one or more pulsation protocols that incorporate combinations of pressures. Ex. 1007 at 6:8-23, 14:63-15:36, 19:52-20:43; Ex. 1008 at [0020], [0063]-[0067]; Ex. 1009 at [0022], [0065]-[0067]. Teigen further discloses that the pressure pulses may be

generated by a variety of methods, including injecting fluid into the aspiration tubing from the fluid injection unit or opening and closing of a valve alone. Ex. 1007 at 14:63-15:36, 16:1-16:24; Ex. 1008 at [0066], [0067]; Ex. 1009 at [0065], [0068], [0069]. Because the magnitude of the pressure pulses are created by opening and closing a valve or injecting fluid into the system via the fluid injection unit for specific durations, a POSA would recognize the Teigen system to be capable of regulating the timing of its fluid injection valve and the accompanying fluid injections. As discussed in Claim 1[C] and 1[D], the fluid injection valve operates as a vent valve to relieve pressure within the system via fluid injections. Therefore, a POSA would understand Teigen to disclose regulating timing of the vent valve.

227. To the extent that Teigen does not expressly disclose that its pulsation protocols substantially prevent forward flow, a POSA would find it obvious to adjust the pulsation protocols employed in Teigen to adopt Grey's maintenance of a non-zero suction force at the distal end of the catheter to reduce the risk of distal emboli and thus prevent forward flow, as discussed in Claim 1[G]. This would be obvious to a POSA to do because the risks of distal emboli and damage that forward flow can cause were well known in the art at the time of the Teigen invention, and a POSA would be motivated to reduce that risk by regulating the timing of the venting valves to maintain that non-zero suction force. *See* Ex. 1023 at ¶20.

228. Alternatively, Grey also teaches regulating timing of its vent valve, and that regulating the timing of the vent valve at least in part contributes to the prevention of forward flow of the distal portion out from the distal during each cycle. As discussed above for Claims 1[F] and 7, Grey discloses a vacuum aspiration system with an appliance 210, including a conduit 212 and a chamber 214, to deliver fluid to the catheter to create a dynamic suction force at the distal end of the catheter. Ex. 1010 at 5:1-4, 11:16-20, 13:7-11, FIG. 2A. Grey further discloses that “chamber



Ex. 1010, Figure 2A

214 has one or more openings 216 which permit” “aspiration medium” comprising any “compressible fluids, such as air, or incompressible fluids such as water or saline” “of a second pressure to be mixed with” the negative pressure supplied by the vacuum aspiration source. *Id.* at 7:29-30, 8:20-25. The “opening 216 may be selectively opened and closed” “to achieve a particular dynamic aspiration profile” using any suitable valve. *Id.* at 8:1-8, 8:15-19. Grey teaches that “cyclic aspiration”

is characterized by frequency profiles, such as those shown in Figures 3A-3C, and “different frequencies of cyclic aspiration may be used to improve clot clearance,” including frequencies of “at least 10 Hz” and “at least 50 Hz.” *Id.* at 9:13-25, 10:28-11:3. A POSA would understand that selectively opening and closing a valve to deliver fluid into the catheter based on specifically defined dynamic aspiration profiles is a disclosure of regulating the timing of that vent valve.

229. To the extent that Grey does not explicitly discuss regulating the timing of the vent valve to prevent forward flow, Grey does disclose that “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.” *Id.* at 13:7-11. Alternatively, a POSA would have found it obvious to regulate the timing of the vent valve to prevent forward flow in view of Grey’s disclosures of achieving the optimal dynamic suction forces at the distal end of its catheter because Grey explains that such level changes induce material fatigue in the embolus and improves the efficacy of the thrombectomy device and can prevent forward flow. Ex. 1023 at ¶20. Moreover, a POSA would have at least recognized when the timing of the vent valve is not regulated, there will be a significant risk in the forward flow of the distal portion out from the distal end.

230. Therefore, it is my opinion that Teigen in view of Grey and the knowledge of a POSA discloses and renders obvious “prevent forward flow of the

distal portion out from the distal end during each cycle by regulating timing of the vent valve,” as recited by Claim 17.

Q. Teigen in View of Grey and the Knowledge of a POSA Renders Claim 18 Obvious

- (i) 18[A] The system according to claim 1, wherein the controller is configured to open and close the vacuum valve and the vent valve in a repeated cycle of the pre-determined pattern to**

231. Teigen discloses this limitation for the reasons discussed above for Claim 1[F]. *See* Section IX.B.vii.

- (ii) 18[B] retain a level of pressure at the distal end at less than physiological pressure.**

232. Teigen in view of Grey and the knowledge of a POSA renders this claim limitation obvious.

233. As discussed above for 1[F], Teigen discloses a controller configured to cyclically open and close its vacuum and fluid injection valves to change a level of vacuum at the distal end of the catheter during each extraction cycle. *See* Section IX.B.vii. Teigen teaches that the fluid supplied by the fluid injection unit may be “at ambient pressure, between ambient pressure and systolic [i.e. physiological] pressure, at systolic pressure, or above systolic pressure.” Ex. 1007 at 6:24-44, 15:37-46; Ex. 1008 at [0063], [0067]; Ex. 1009 at [0065], [0069]. To the extent Patent Owner argues that Teigen does not expressly disclose “retain a level of pressure at the distal end at less than physiological pressure,” Grey does.

234. As discussed above for 1[G], Grey teaches that there is a risk of distal thrombi migration as a result of thrombectomy procedures, but that “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.” *See* Section IX.B.viii. *See also*, Ex. 1010 at 13:7-11.; *see also id.* at 7:10-12 (“one very serious risk is the escape and travel of occlusive material from the initial site of occlusion to a distal portion of the lumen or to another lumen branching therefrom”). Grey also discloses that it is preferable to maintain a magnitude of a baseline pressure above zero, in other words that a “vacuum is maintained” throughout aspiration. *Id.* at 13:7-11.

235. A POSA would have understood the teachings in Grey to mean that the pressure at the distal end of the catheter remains less than physiological pressure because if the pressure were to cross from a negative baseline pressure to one that exceeds the physiological pressure at the distal end, a non-zero suction force no longer exists and flow direction changes. A POSA would have recognized that the pressure difference between the physiological pressure and the pressure inside the distal end of the catheter drives the movement direction of emboli. Thus, although Grey is not referring to “physiological pressure” explicitly, a POSA would understand that the purposes of Grey include “[p]roviding a non-zero suction force” at the distal end of the catheter, i.e. retaining a level of pressure at the distal end at

less than physiological pressure,” to reduce the risk of distal emboli. Ex. 1010 at 13:4-11.

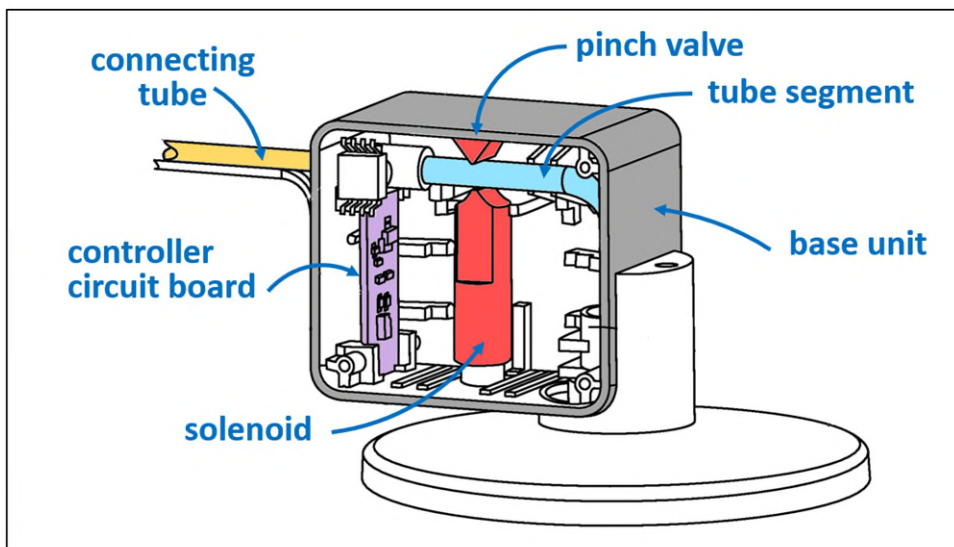
236. Moreover, while Teigen does not expressly state that its pulsation protocols retain a level of pressure at the distal end at less than physiological pressure, a POSA would find it obvious to adjust the pulsation protocols employed in the Teigen to adopt Grey’s maintenance of a non-zero suction force at the distal end of the catheter to reduce the risk of distal emboli and maintain a distal pressure less than that of the pressure in the blood vessel. This would be obvious to a POSA to do because the risks of distal emboli and damage that forward flow can cause were well known in the art at the time of the Teigen invention and a POSA would have been motivated to reduce that risk by regulating the timing of the venting valves to maintain that non-zero suction force. Ex. 1023 at ¶20.

R. Teigen in View of Grey and the Knowledge of a POSA Renders Claim 19 Obvious

- (i) 19[A] The system according to claim 1, wherein the controller is one of a mechanical valve controller and an electronic valve controller.**

237. As discussed above for 1[F], Teigen discloses a controller configured to open and close the vacuum valve and the vent valve. *See* Section IX.B.vii; Ex. 1007 at Claim 15 (“wherein the controller is an electronic controller”). Teigen specifically discloses that the controller “typically includ[es] a microprocessor on a printed circuit board,” and is “configured to open and close the pinch valve.” Ex.

1007 at 11:3-27; Ex. 1008 at [0057]; Ex. 1009 at [0059]. In my opinion, a POSA would have understood the controller to be an electronic valve controller.



238. Therefore, Teigen discloses “wherein the controller is one of a mechanical valve controller and an electronic valve controller,” as recited by Claim 19.

S. Teigen in View of Grey and the Knowledge of a POSA Renders Claim 21 Obvious

(i) 21[Pre] A clot removal system, comprising:

239. For the reasons discussed above for Claim 1[Pre], Teigen discloses a clot removal system. *See* Section IX.B.i.

(ii) 21[A] a catheter having a proximal end and a distal end and defining a lumen configured to be filled with a liquid column having a proximal portion;

240. For the reasons discussed above for Claim 1[A], Teigen discloses this limitation. *See* Section IX.B.ii.

(iii) 21[B] a vacuum pump configured to supply vacuum;

241. For the reasons discussed above for Claim 1[B], Teigen discloses this limitation. *See* Section IX.B.iii.

(iv) 21[C] a vent liquid container holding a vent liquid;

242. For the reasons discussed above for Claim 1[C], Teigen discloses this limitation. *See* Section IX.B.iv.

(v) 21[D] a vent valve configured to fluidically communicate: with the vent liquid in the liquid container; and with the proximal portion of the liquid column at the proximal end of the catheter;

243. For the reasons discussed above for Claim 1[D], Teigen discloses this limitation. *See* Section IX.B.v.

(vi) 21[E] a vacuum valve configured to fluidically communicate: with the vacuum from the vacuum pump; and with the proximal portion of the liquid column at the proximal end of the catheter; and

244. For the reasons discussed above for Claim 1[E], Teigen discloses a controllable vacuum valve. *See* Section IX.B.vi.

(vii) 21[F] a controller configured to carry out a pre-determined cycle of opening and closing the vent and vacuum valves to change a level of vacuum at the distal end during each cycle and,

245. For the reasons discussed above for Claim 1[F], Teigen discloses this claim limitation. *See* Section IX.B.vii. A POSA would have understood a “pre-determined pattern” to be substantially equivalent to a “pre-determined cycle.”

(viii) 21[G] during each cycle, to substantially prevent forward flow of liquid at the distal end of the liquid column.

246. For the reasons discussed above for Claims 1[F], 1[G], and 21[F], Teigen in view of Grey and the knowledge of a POSA discloses and renders obvious “during each cycle, to substantially prevent forward flow the distal end of the liquid column.” *See* Sections IX.B.vii, IX.B.viii, and IX.S.vii.

247. Accordingly, Teigen in view of Grey and the knowledge of a POSA discloses and renders obvious Claim 21.

X. Ground 2: Claims 4-6 and 9-13 Are Rendered Obvious Over Teigen in View of Grey, Rubenstein, and the Knowledge of a POSA

A. Motivation to Combine

248. A person of ordinary skill in the art at the time the purported invention of the '253 Patent was made would have been motivated to combine Teigen and Grey's 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 venting state when necessary using a time-controlled valve. The motivation to combine Teigen and Grey is discussed above at Claim 1, Section IX.A.

249. A POSA would have been motivated to combine Teigen, Grey, 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 venting system 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 clogged catheters and the limitations of static aspiration technologies for controlled clot aspiration. Ex. 1007 at 1:19-2:55; Ex. 1008 at [001]-[007]; Ex. 1009 at [002]-[008]; Ex. 1010 at 1:7-9, 1:15-2:3; Ex. 1011 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 at 2:27-67, 3:15-51, 14:63-18:25; Ex. 1008 at [006]-[008], [0009], [0010], [0063]-[0065]; Ex. 1009 at [007]-[009], [0011], [0012], [0065]-[0067]; Ex. 1010 at 2:24-3:24; Ex. 1011 at Abs., 1:7-14, 1:64-68, 2:1-12.

250. A POSA would have understood that Teigen, Grey, 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. Accordingly, combining the teachings of Teigen, Grey, 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.

251. For at least these reasons, it would have been obvious to combine Teigen, Grey, and Rubenstein.

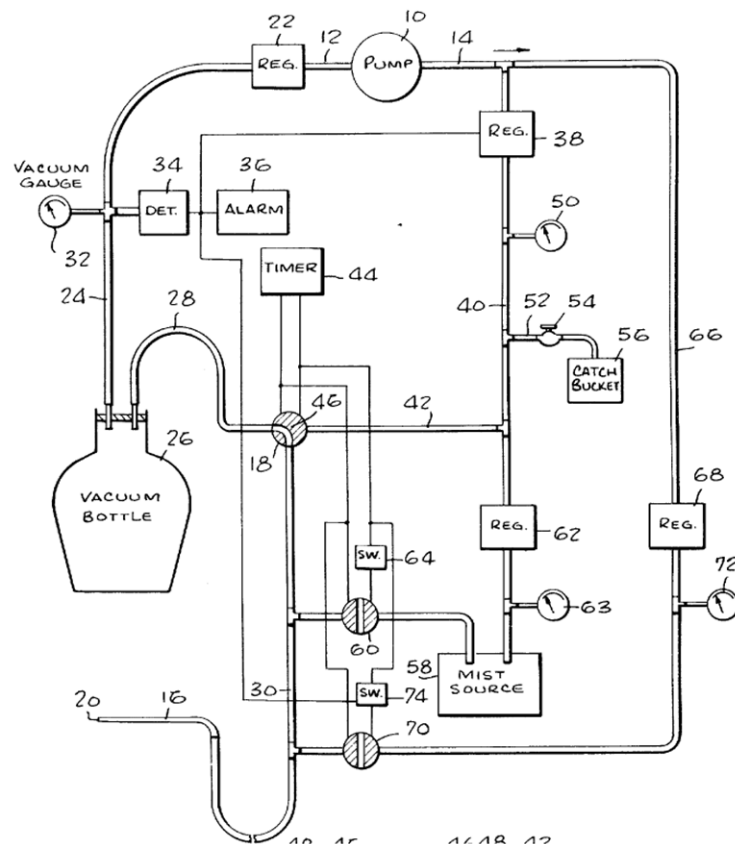
B. Teigen in View of Grey, Rubenstein, and the Knowledge of a POSA Renders Claim 4 Obvious

- (i) 4[A] The system according to Claim 1, wherein a portion of the pre-determined pattern includes a time period where both the vent and vacuum valves are closed.**

252. Teigen in view of Grey, Rubenstein, and the knowledge of a POSA renders Claim 1 obvious. Disclosures in Rubenstein strengthen the obviousness analysis based on Teigen and Grey. As discuss in Ground 1 above, Teigen discloses “wherein the controller is configured to open and close the vent and vacuum valves in a repeated cycle” for at least the reasons discussed above in the context of claim limitation 1[F]. *See, e.g.*, Sections IX.B.vii and IX.E. As also discussed in Ground 1 above, Teigen and Teigen in view of Grey teaches a double-closed state in which both the vent and vacuum valves are closed. *See* Section IX.E. As discussed below, Rubenstein further discloses and renders this claim limitation obvious.

253. 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 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

254. As shown in figures 1 and 2 below, 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



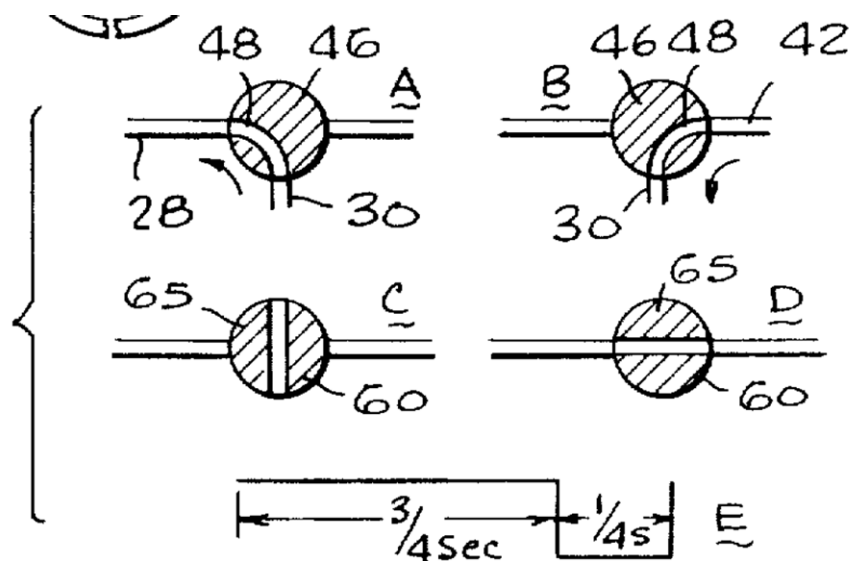
143

source of mist is connected to allow controlled injection of detergent or enzymatic fluid through the catheter.” *Id.*

255. 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.” *Id.* 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.” *Id.* 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.

256. 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.” *Id.* at 4:2-8. As shown in Fig. 2, below, “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 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 at 4:17-23.



257. 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.” 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 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.

258. 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 at 3:41-50.

259. A POSA would have understood that the time it would take to rotate the movable plug within valve 46 and valve 60 would not be instantaneous during the one second cycle disclosed in Rubenstein. Therefore, a POSA would realize there is a period when both valves are closed due to a lack of full connection of both the valve 46 and valve 60 at least part of the time as the system transitions from its suction to blowing modes. A POSA would also find it obvious to employ this time-controlled valve opening and closing system and method within its own system 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 Teigen system. *See* Ex. 1011 at 3:41-50.

260. As discussed above in Section IX.E, 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 discloses such serial operations of vacuum and vent valves that a POSA would readily and easily adopt for dynamic aspiration taught by Teigen and Grey. *See* Ex. 1011 at 4:17-35. Alternatively, a POSA could also adopt the valves disclosed in Rubenstein to accomplish the dynamic aspiration taught by Teigen and Grey including “a time period where both the vent and vacuum valves are closed.”

261. Therefore, it is my opinion that Teigen in view of Grey, Rubenstein, and the knowledge of a POSA renders Claim 4 obvious.

C. Teigen in View of Grey, Rubenstein, and the Knowledge of a POSA Renders Claim 5 Obvious

(i) 5[A] The system according to Claim 4, wherein the controller is configured to open and close the vent and vacuum valves in a repeated cycle

262. As discussed above, Teigen discloses a controller configured to carry out a pre-determined pattern of opening and closing the vent and vacuum valves. For the same reasons discussed in Sections IX.B and X.B, Teigen in view of Grey, Rubenstein, and the knowledge of a POSA further renders obvious “wherein the

controller is configured to open and close the vent and vacuum valves in a repeated cycle.”

- (ii) 5[B] comprising a double-closed state in which both the vent and vacuum valves are closed.**

263. As discussed above, Teigen in view of Grey, Rubenstein, and the knowledge of a POSA renders obvious Claim 4, which recites a time period where both the vent and vacuum valves are closed (i.e., a double-closed state). For the same reasons discussed in Sections IX.E and X.B, Teigen in view of Grey, Rubenstein, and the knowledge of a POSA further renders obvious “a double-closed state in which both the vent and vacuum valves are closed.”

D. Teigen in View of Grey, Rubenstein, and the Knowledge of a POSA Renders Claim 6 Obvious

- (i) 6[A] The system according to claim 5, wherein a time of the double-closed state is no greater than 30 ms.**

264. As discussed above, Teigen in view of Grey, Rubenstein, and the knowledge of a POSA renders obvious Claims 4 and 5, which recites a double-closed state. For the same reasons discussed in Sections IX.E, X.B, and X.C, Teigen in view of Grey, Rubenstein, and the knowledge of a POSA further renders obvious “a time of the double-closed state is no greater than 30 ms.”

E. Teigen in View of Grey, Rubenstein, and the Knowledge of a POSA Renders Claim 9 Obvious

- (i) 9[A] The system according to claim 1, wherein the controller is configured to selectively open and close the vent and vacuum valves in a repeated cycle comprising:**

265. For the same reasons discussed in Sections IX.J.i and X.B, Teigen in view of Grey, Rubenstein, and the knowledge of a POSA renders obvious this claim limitation.

(ii) **9[B] a vacuum-only state in which the vacuum valve is open and the vent valve is closed;**

266. For the same reasons discussed in Sections IX.J.ii and X.B, Teigen in view of Grey, Rubenstein, and the knowledge of a POSA renders obvious this claim limitation.

(iii) **9[C] a first double-closed state in which the vacuum valve is closed and the vent valve is closed;**

267. For the same reasons discussed in Sections IX.J.iii and X.B, Teigen in view of Grey, Rubenstein, and the knowledge of a POSA renders obvious this claim limitation. *See also, e.g.,* Ex. 1011 at 1:7-14, 1:10-14, 1:51-68, 2:1-8, 3:21-36, 3:41-50, 4:2-7, 4:17-35, FIGS. 1, 2.

(iv) **9[D] a vent-only state in which the vacuum valve is closed and the vent valve is open; and**

268. For the same reasons discussed in Section IX.J.iv, Teigen in view of Grey, Rubenstein, and the knowledge of a POSA renders obvious this claim limitation.

(v) **9[E] a second double-closed state in which the vacuum valve is closed and the vent valve is closed.**

269. For the same reasons discussed in Sections IX.J.v and X.B, Teigen in view of Grey, Rubenstein, and the knowledge of a POSA renders obvious this claim

limitation. *See also, e.g.*, Ex. 1011 at 1:7-14, 1:10-14, 1:51-68, 2:1-8, 3:21-36, 3:41-50, 4:2-7, 4:17-35, FIGS. 1, 2.

F. Teigen in View of Grey, Rubenstein, and the Knowledge of a POSA Renders Claim 10 Obvious

- (i) **10[A-E] The system according to claim 1, wherein the controller is configured to selectively open and close the vent and vacuum valves in a repeated cycle comprising a vacuum-only state in which the vacuum valve is open and the vent valve is closed, followed by a first double-closed state in which the vacuum valve is closed and the vent valve is closed and a time of the first double-closed state is no greater than 30 ms, followed by a vent-only state in which the vacuum valve is closed and the vent valve is open, followed by a second double-closed state in which the vacuum valve is closed and the vent valve is closed.**

270. For the same reasons discussed in Sections IX.K and X.B, Teigen in view of Grey, Rubenstein, and the knowledge of a POSA renders Claim 10 obvious.

G. Teigen in View of Grey, Rubenstein, and the Knowledge of a POSA Renders Claim 11 Obvious

- (i) **11[A] The system according to claim 9, wherein a time between an opening of the vent valve and a closing of the vent valve is between approximately 10 ms and approximately 50 ms.**

271. For the same reasons discussed in Sections IX.L and X.B, Teigen in view of Grey, Rubenstein, and the knowledge of a POSA renders Claim 11 obvious.

H. Teigen in View of Grey, Rubenstein, and the Knowledge of a POSA Renders Claim 12 Obvious

- (i) **12[A] The system according to claim 9, wherein a period of the cycle is between approximately 6 Hz and approximately 16 Hz**

272. For the same reasons discussed in Sections IX.M and X.B, Teigen in view of Grey, Rubenstein, and the knowledge of a POSA renders Claim 12 obvious.

I. Teigen in View of Grey, Rubenstein, and the Knowledge of a POSA Renders Claim 13 Obvious

(i) 13[A] The system according to claim 9, wherein a period of the cycle is between approximately 8 Hz and 12 Hz

273. For the same reasons discussed in Sections IX.M, IX.N, and X.B, Teigen in view of Grey, Rubenstein, and the knowledge of a POSA renders Claim 13 obvious

XI. Ground 3: Claims 15 and 16 are Rendered Obvious Over Teigen in view of Grey, Yang and the Knowledge of a POSA

A. Motivation to Combine

274. A person of ordinary skill in the art at the time the purported invention of the '253 Patent was made would have been motivated to combine Teigen's cyclical aspiration thrombectomy system with at least Grey's optimization of aspiration cycle frequencies to provide a non-zero suction force to prevent the migration of distal thrombi and monitoring the level of vacuum pressure change at the distal end of the aspiration catheter with Yang's disclosed aspiration thrombectomy catheter and its internal diameter ranges. The motivation to combine Teigen and Grey is discussed above at Claim 1, Section IX.A.

275. A POSA would have been motivated to combine Teigen, Grey, and Yang because (1) all three references address similar problems related to

conventional methods of aspiration thrombectomy for the treatment of ischemic stroke, including clogged catheters and achieving optimal clot aspiration, and (2) all three references teach similar solutions involving using aspiration thrombectomy devices and catheters to provide for safer, more complete removal of thrombus from the blood vessel. Both Grey and Yang comment on the limitations and risks associated with traditional methods to treat ischemic strokes. As an example, both references describe issues with complete aspiration of thrombus that are stuck to the walls of the blood vessel, and the limitations of static aspiration technologies for controlled clot aspiration in this context. Ex. 1010 at 1:30-2:3; Ex. 1012 at [0006]-[0009]. Both systems utilize an aspiration thrombectomy system with an added mechanism to be used in combination with conventional static vacuum pressure within the system to more completely remove thrombi from blood vessels. Ex. 1010 at 5:1-4, 7:21-30, 8:1-19, 11:16-20, 13:7-11, FIG. 2A; Ex. 1012 at Abs., [0011], [0013].

276. A POSA would have understood that Teigen, Grey, and Yang are each directed to an improved aspiration thrombectomy system and related methods using a source of negative pressure and an additional pressure to subject a blood clot to additional forces and more efficiently aspirate blood clots. Accordingly, combining the teachings of Teigen, Grey, and Yang would have been well within the skill of a POSA, because it is nothing more than combining known thrombectomy

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

277. A POSA would have found it obvious to implement Yang's disclosures of catheter internal diameters with the combination of Teigen and Grey's teachings of cyclical catheter aspiration because the conventional French catheter system, upon which Teigen and Grey relies, is well-known in the art and a standardized method for determining outer diameter catheter sizes around the world. Ex. 1023 at ¶13-14. However, there are no standardized internal diameters for aspiration catheters, so a POSA would have known that internal catheter diameters can be optimized for particular applications, as is taught in Yang. Ex. 1012 at [0067], [0068]. A POSA would have been motivated, in view of the desire to use the combined system in the manner disclosed in Yang, to implement the system in a manner such that it would be used with catheters having internal lumen diameters in accordance with the ranges claimed.

278. Indeed, Teigen discusses prior art systems that use an 8 French size catheter (outer diameter=0.105 inches), which a POSA would have understood falls within the internal diameter catheter sizes disclosed by Yang. Ex. 1007 at 2:27-48; Ex. 1008 at [006], Ex. 1009 at [007]; Ex. 1012 at [0068]. Because the range of catheter diameters that would fit within the human blood vessels is limited in practice by human physiology, a POSA would have found it obvious to consider the

application for treatment and the internal diameter of the blood vessel to be aspirated when selecting a catheter for use in well-known methods of thrombectomy via aspiration catheters. Ex. 1023 at ¶13-14.

279. For at least these reasons, it would have been obvious to combine Teigen, Grey, and Yang.

B. Teigen in View of Grey, Yang, and the Knowledge of a POSA Renders Claim 15 Obvious

- (i) 15[A] The system according to claim 1, wherein: the lumen has a diameter of between approximately 0.038” and approximately 0.106”; and**

280. As discussed above for Claim 1[A], Teigen discloses a catheter with an internal lumen. *See* Section IX.B above. *See also* Ex. 1007 at 3:36-3:62, 6:8-23; Ex. 1008 at [0010], [0011], [0020]; Ex. 1009 at [0012], [0013], [0022]. Moreover, Teigen discloses both “determin[ing] the diameter of the attached catheter” and “switching between catheters of different diameters,” thus inviting routine optimization for the ideal catheter sizes based on the specific patient case. *See* Ex. 1007 at 12:33-41, 14:17-29; Ex. 1008 at [0067]; Ex. 1009 at [0076], [0084]. To the extent that Teigen does not explicitly disclose the diameter ranges of 0.038”-0.106”, Yang does.

281. Yang is directed to a telescoping catheter with a movable jaw for “distal neurovascular aspiration or access” that has a control for advancing the distal section into the patient’s vasculature. Ex. 1012 at Abs., FIGS. 1, 3A, 3B. The catheter is

operable to connect to “a controller for applying intermittent vacuum to the lumen” using combinations of vacuum pulses and “spaces of neutral pressure,” higher negative pressure or lower negative pressure. *Id.* at [0014], FIGS. 14, 25A-C. Yang discloses that the inner diameter of the distal section of the catheter:

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.

Id. at [0068] (emphasis added).

282. Therefore, it is my opinion that the combination of Teigen, Grey, Yang, and the knowledge of a POSA renders “the lumen has a diameter of between approximately 0.038” and approximately 0.106” obvious.

(ii) **15[B] the controller is configured to repeatedly and periodically carry out the pre-determined pattern of opening and closing the vent and vacuum valves at a frequency of between 2 and 16 Hz.**

283. For the same reasons discussed above for Claims 1[F] and 12, Teigen in view of Grey discloses and renders obvious “the controller is configured to cyclically open and close the vacuum valve and the vent valve at a frequency of between 2 and 16 Hz.” *See* Sections IX.B and IX.M above. *See also* Ex. 1007 at 3:63-4:28, 5:6-24, 6:8-23, 11:3-27, 14:63-18:25; Ex. 1008 at [0012], [0013], [0021],

[0024], [0057], [0061]-[0065]; Ex. 1009 at [0014], [0015], [0019], [0022], [0059], [0063]-[0067]; Ex. 1010 at 9:13-25, 10:28-11:3.

284. Because disclosures in Yang do not detract from but instead strengthen the obviousness analysis based on Teigen and Grey, it is my opinion that Teigen in view of Grey, Yang, and the knowledge of a POSA discloses and renders obvious, “the controller is configured to repeatedly and periodically carry out the pre-determined pattern of opening and closing the vent and vacuum valves at a frequency of between 2 Hz and 16 Hz,” as recited by Claim 15.

C. Teigen in View of Grey, Yang, and the Knowledge of a POSA Renders Claim 16 Obvious

(i) 16[A] The system according to claim 1, wherein: the lumen has an internal diameter of between approximately 0.068” and approximately 0.088”; and

285. For the reasons discussed above for Claim 15[A], Teigen in view of Grey, Yang, and the knowledge of a POSA discloses and renders obvious catheter lumen internal diameters between 0.030 inches and 0.112 inches. *See* Section XI.B. Ex. 1007 at 3:36-3:62, 6:8-23, 12:33-41, 14:17-29; Ex. 1008 at [0010], [0011], [0020], [0067]; Ex. 1009 at [0012], [0013], [0022], [0076], [0084]; Ex. 1012 at [0068].

286. Because the range of approximately 0.068” and approximately 0.088” required by Claim 16 falls within the range of internal diameters required by Claim 15, a POSA would understand the ranges claimed within Claim 16 to be covered by

the ranges of Claim 15. Moreover, to the extent that Patent Owner argues that the narrowed inner diameter range in Claim 16 is novel or non-obvious, a POSA would realize that the claimed catheter lumen internal diameter ranges are well known in the art and cover the entire range of catheters suitable to fit within human blood vessels. Moreover, a POSA would recognize that narrowing a range of inner catheter diameters to meet the needs of a given thrombectomy would be the result of obvious, routine optimization. *See* Ex. 1023 at ¶13-14.

287. Therefore, it is my opinion that Teigen in view of Grey, Yang, and the knowledge of a POSA discloses and renders obvious, “the lumen has an internal diameter of between approximately 0.068” and approximately 0.088”.”

(ii) 16[B] the controller is configured to repeatedly and periodically carry out the pre-determined pattern of opening and closing the vent and vacuum valves at a frequency of between 6 and 12 Hz.

288. For the reasons discussed above for Claims 1[F], 12, and 15[B], Teigen in view of Grey, Yang, and the knowledge of a POSA discloses and renders obvious, “the controller is configured to repeatedly and periodically carry out the pre-determined pattern of opening and closing the vent and vacuum valve at a frequency of between 6 Hz and 12 Hz.” *See* Sections IX.B, IX.M, and XI.B. *See also* Ex. 1007 at 3:63-4:28, 5:6-24, 6:8-23, 11:3-27, 14:63-18:25; Ex. 1008 at [0012], [0013], [0021], [0024], [0057], [0061]-[0065]; Ex. 1009 at [0014], [0015], [0019], [0022], [0059], [0063]-[0067]; Ex. 1010 at 9:13-25, 10:28-11:3.

XII. Ground 4: Claim 20 is Rendered Obvious Over Teigen in view of Grey, Matteo, and the Knowledge of a POSA

A. Motivation to Combine

289. A person of ordinary skill in the art at the time the purported invention of the '253 Patent was made would have been motivated to combine Teigen's cyclical aspiration thrombectomy system and Grey's teachings of providing a non-zero suction force to prevent the migration of distal thrombi and optimization of aspiration cycle frequencies including the duration vent valve opening and closure to relieve vacuum pressure with Matteo's cam system for valve control. The motivation for combining Teigen and Grey is discussed above at Claim 1, Section IX.A.

290. A POSA would have been motivated to combine Teigen, Grey, 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 pinch valves to separate and combine the fluids to achieve desired results. Both Teigen and Matteo describe similar approaches to solving these and other issues, including using a controller to control valves that can be switched between varying states of open and closed positions. Ex. 1007 at 3:63-4:20, 14:63-18:25, FIG. 9; Ex. 1008 at [0012], [0063]-[0066], FIG. 9; Ex. 1009 at [0014], [0065]-[0069], FIG. 9; Ex. 1013 at FIGS. 10A-C.

291. 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 Teigen, Grey, 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 Teigen and Grey with known controlled valve systems described in Matteo to perform their intended functions with described benefits and predictable results.

292. A POSA would find it obvious to implement Matteo's disclosures of cam-driven valves that optimize the introduction of fluid into chambers with Teigen's teachings of a controller to operate vacuum and vent valves and Grey's cyclical aspiration profiles to provide for more efficient and effective cyclical aspiration of blood clots, because a POSA would recognize that Matteo's valves were a well-understood and effective technique to implement a valve having the necessary timing precision to implement the techniques taught in Teigen and Grey, while also providing benefits of reduced complexity and space-savings as disclosed in Matteo. Ex. 1007 at 14:63-18:25; Ex. 1008 at [0063]-[0066]; Ex. 1009 at [0065]-[0069]; Ex. 1010 at 5:1-4, 7:21-30, 8:1-19, 11:16-20, 13:7-11, FIG. 2A; Ex. 1013 at [0010], [0011], [0012]. For example, Grey teaches the use of any "commercially

suitable valve”: “[a]ppliance 210 may include a customized or commercially available valve for regulating the opening/closing or enlarging/narrowing of an opening 216” and those “may include but are not limited to motor actuated valves and solenoid valves....Other suitable valves and actuation mechanisms will occur to skilled persons in the art in view of the teachings herein.” Ex. 1010 at 8:15-16; 19:28-31. Teigen also discloses that “the valve itself may take a variety of forms, including a pinch valve, an angle valve, or any one of a variety of other valves of the type found in medical aspiration equipment.” Ex. 1007 at 4:64-5:5; Ex. 1008 at [0016]; Ex. 1009 at [0018]. Thus, it would have been well within the skill of a POSA to utilize any number of valves as vacuum and vent valves in Teigen’s aspiration thrombectomy system, including cam-driven valves.

293. Additionally, Matteo itself explains that the improved fluid flow control techniques described therein are applicable to a variety of chemical, biological, and biomedical applications, including “medical and scientific instrumentation,” which a POSA would understand includes the aspiration thrombectomy medical devices taught in Teigen and Grey. Ex. 1013 at Abs., [0006], [0012], [0029], FIGS. 11, 12.

294. A POSA would have a reasonable expectation of success in implementing this combination, because it would simply add additional control over the fluids contained within the aspiration systems of Teigen and Grey, using a widely known shaft and cam actuator technology to control valves, as disclosed in Matteo.

A POSA would recognize that Grey's system could include a motor driven valve, as taught in Matteo, because Grey teaches that "[s]uitable commercially available valves may include but are not limited to motor actuated valves and solenoid valves....Other suitable valves and actuation mechanisms will occur to skilled persons in the art in view of the teachings herein." Ex. 1010 at 19:28-31. Moreover, a POSA would recognize that Teigen's system could be modified to allow the vacuum and vent valves to be controlled via a single shaft, as taught in Matteo. For instance, Teigen does not require that the fluid injection unit, and its associated vent valve be located remotely from the vacuum valve. The only limitation described in Teigen is that the vacuum valve be located between the three-point junction (where the fluid injection unit is located) and the vacuum source. Ex. 1007 at 16:1-16:24; Ex. 1008 at [0063]; Ex. 1009 at [0065]. Indeed, in one embodiment, Teigen shows both valves co-located on the three-point junction. Ex. 1007 at 16:51-17:7, FIG. 16.

295. For at least these reasons, it would have been obvious to combine Teigen, Grey, and Matteo.

B. Teigen in View of Grey, Matteo, and the Knowledge of a POSA Renders Claim 20 Obvious

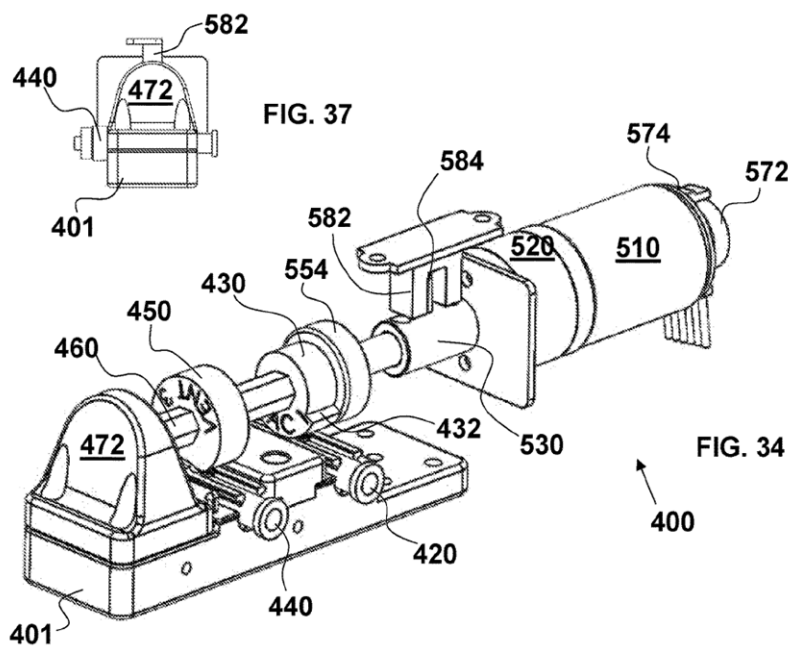
- (i) 20[A] The system according to claim 1, which further comprises a shaft and the vent and vacuum valves are cam-driven valves with respective cams mounted together on the shaft.**

296. Teigen in view of Grey, Matteo, and the Knowledge of a POSA renders this claim obvious. As discussed above for 1[D] and 1[E], Teigen discloses a vacuum valve and vent valve as components of the same aspiration thrombectomy system. Teigen further discloses the vacuum and vent valves being cam-driven valves. Ex. 1007 at Claim 16 (“wherein the vacuum and pressure valves are driven by cam follower actuators”).

297. To the extent that Teigen does not explicitly disclose the vent and vacuum valves being cam-driven valves with respective cams and a shaft having the vacuum and vent valves mounted together, the combination of Teigen, Grey, and Matteo renders it obvious.

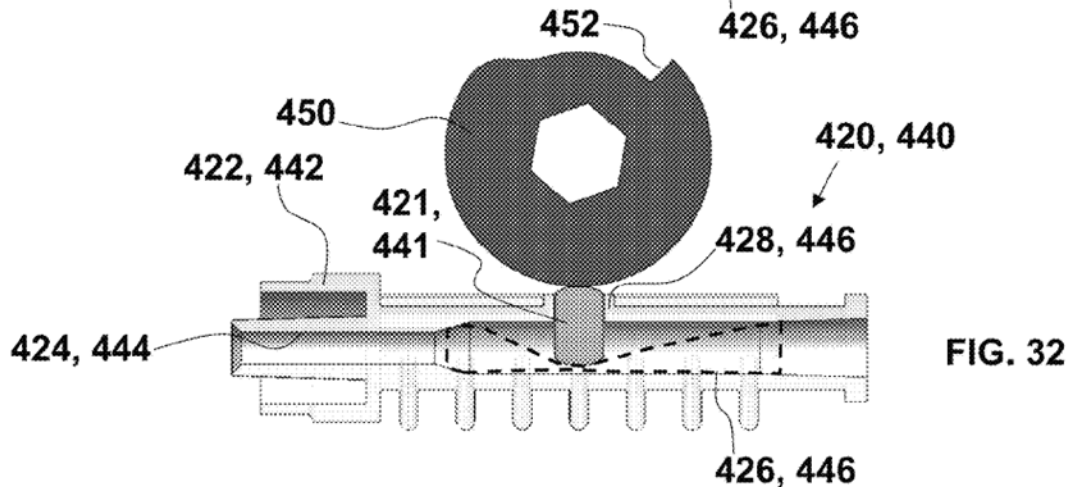
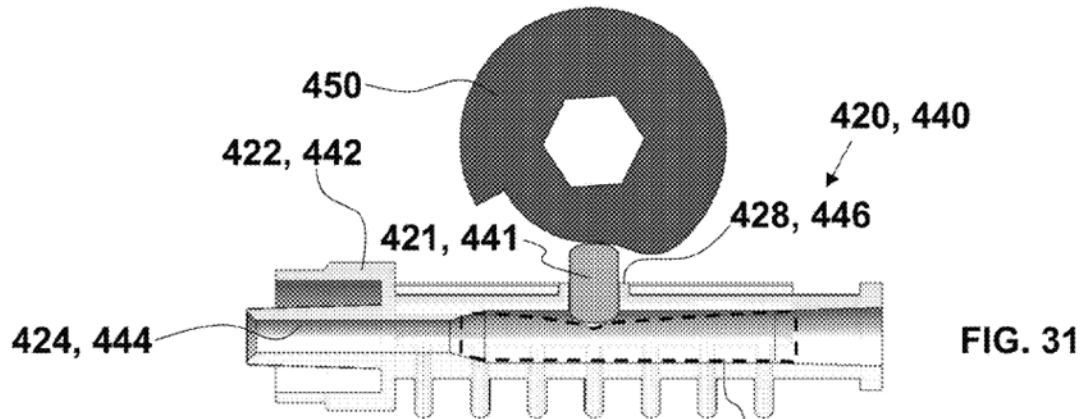
298. One embodiment of the '253 Patent describes cam-actuated vacuum and vent valves that share a cam shaft to operate “an automatic, rapid, and repeated onset of pressure change.” Ex. 1001 at 30:11-40; FIGS. 25-41. A pair of pinch valves, 420 and 440, as shown in Fig. 34 below, respectively control the vacuum

flow and vent flow through the aspiration system. *Id.* at 30:11-31. The '253 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.” *Id.* at 30:41-52. The '253 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. *Id.* The '253 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. *Id.* at 30:57-61. The '253 Patent further explains, “the vacuum and vent cams 430, 450 are fixed rotationally to the cam shaft 460” and



Ex. 1001, Figure 34

“these cams 430, 450 have various cam profiles to operate the valves 420, 440.” *Id.* at 31:19-21.



Ex. 1001, FIGS. 31, 32

299. 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. *Id.* at 32:18-22.

300. 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 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. *Id.* 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.” *Id.* at [0010].

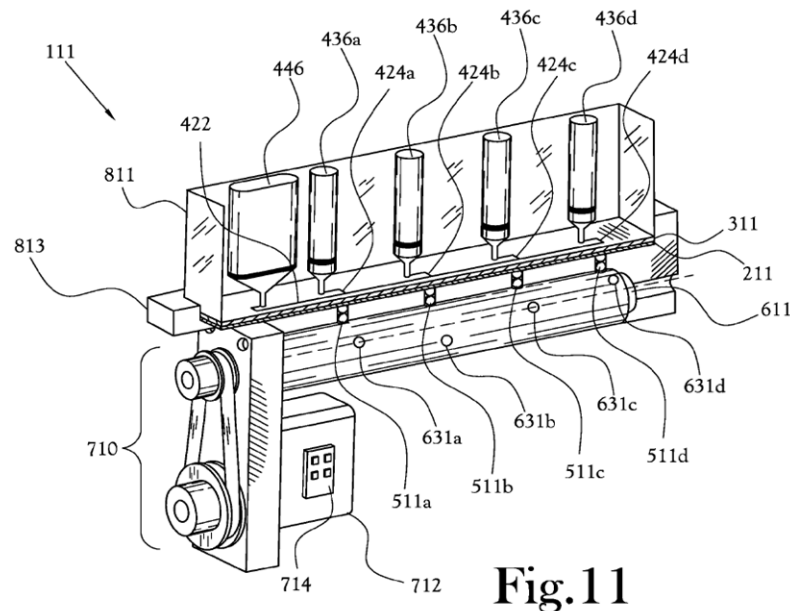
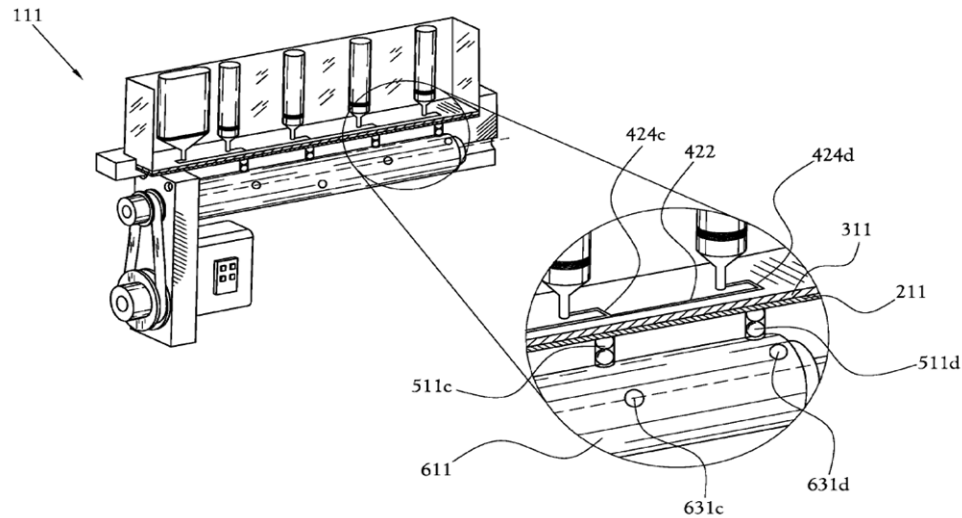


Fig. 11

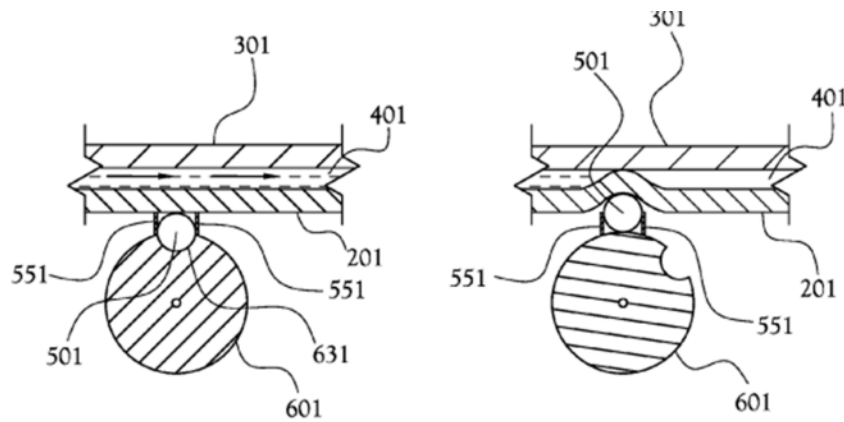
Ex. 1013, Figure 11



Ex. 1013, Figure 12

301. 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.” *Id.* 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.” *Id.* 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. *Id.* at [0045]. 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.” *Id.* at [0045], FIGS. 3, 11, 12. Matteo explains “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.” *Id.* at [0045], FIGS 3, 6A, 6B. Matteo teaches that, in embodiments that include multiple microvalves, “a single cam, controlled by a single position-control mechanism, is able to control multiple microvalves.” *Id.* at Abs., [0010], [0011], FIGS. 11 and 12. As shown in FIGS. 11 and 12, “the [cam] cylinder’s axis of rotation [runs] approximately parallel to the plane of the elastomeric first layer.” *Id.* at [0057]. A POSA would understand that because the elastomeric layers line the channel and form microvalves when the first layer is in contact with the valves respective cam-actuators and the cam cylinder runs parallel to that first layer, all of the microvalves are along the same plane. *See id.* at FIGS. 6A, 6B, 11, 12.



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

302. A POSA would have known that the term “shaft,” as used in the ’253 patent and in the art at the time of its invention, is a generic engineering term commonly referring to a cylindrical rotating machine element used to transmit power or movement to another part of the same machine. A POSA would therefore

recognize the disclosures of the “single cam, controlled by a single-position control mechanism” in Matteo to be a shaft with mounted valves because the cam disclosed in Matteo is used to move the cam actuators in and out of position to open and close their respective valves that all lie in the same plane. It would have been obvious for a POSA and required no undue experimentation to implement the valve operations and controls taught by Teigen and Grey with the cam-driven valves disclosed in Matteo to achieve the desired dynamic aspiration.

303. Therefore, it is my opinion that Teigen in view of Grey, Matteo, and the Knowledge of a POSA renders claim 20 obvious.

XIV. Reservation of Rights

304. 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 '253 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 '253 Patent and to consider new information that becomes available to me.

XV. Declaration

305. 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 February 2, 2022.

Brian Brown