

Filed on behalf of: RapidPulse, Inc.

Entered: May 30, 2025

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

PENUMBRA, INC.,
Petitioner,

v.

RAPIDPULSE, INC.,
Patent Owner.

Case IPR2024-01261
Patent 11,406,402

PATENT OWNER RESPONSE

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Exhibit List

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2001	Declaration of Brad Culbert in Support of Patent Owner's Preliminary Response (Nov. 22, 2024) ("Culbert Decl.")
2002	<i>Curriculum Vitae</i> of Brad Culbert
2003	Declaration of Brian Brown in Support of Petition for Inter Partes Review of U.S. Patent No. 10,531,883, <i>Penumbra, Inc. v. RapidPulse, Inc.</i> , IPR2021-01466, Ex. 1005 (P.T.A.B. Aug. 30, 2021) ("883 Brown Decl.")
2004	Declaration of Ian Ross, MD in Support of Petition for Inter Partes Review of U.S. Patent No. 10,531,883, <i>Penumbra, Inc. v. RapidPulse, Inc.</i> , IPR2021-01466, Ex. 1023 (P.T.A.B. Aug. 30, 2021) ("883 Ross Decl.")
2005	Supplemental Declaration of Brian Brown for Inter Partes Review of U.S. Patent No. 10,531,883, <i>Penumbra, Inc. v. RapidPulse, Inc.</i> , IPR2021-01466, Ex. 1030 (P.T.A.B. Oct. 3, 2022) ("883 Brown Suppl. Decl.")
2006	Transcript of the Remote Videoconferenced Deposition of Ian Beaudoin Ross, MD, taken June 24, 2022, <i>Penumbra, Inc. v. RapidPulse, Inc.</i> , IPR2021-01466, Ex. 2016 (P.T.A.B. July 11, 2022) ("883 Ross Dep. Tr.")
2007	Judgment: Final Written Decision, <i>Penumbra, Inc. v. RapidPulse, Inc.</i> , IPR2021-01466, Paper 34 (P.T.A.B. Mar. 10, 2023) ("883 FWD")
2008	Declaration of Brian Brown in Support of Petition for Inter Partes Review of U.S. Patent No. 10,722,253, <i>Penumbra, Inc. v. RapidPulse, Inc.</i> , IPR2022-00608, Ex. 1005 (P.T.A.B. Feb. 15, 2022) ("253 Brown Decl.")

Exhibit	Description
2009	Declaration of Ian Ross, MD in Support of Petition for <i>Inter Partes</i> Review of U.S. Patent No. 10,722,253, <i>Penumbra, Inc. v. RapidPulse, Inc.</i> , IPR2022-00608, Ex. 1023 (P.T.A.B. Feb. 15, 2022) (“‘253 Ross Decl.”)
2010	Transcript of the Remote Videoconference Deposition of Brian Brown, Vol. 2, taken May 22, 2023, <i>Penumbra, Inc. v. RapidPulse, Inc.</i> , IPR2022-00608, Ex. 2018 (P.T.A.B. May 26, 2023) (“‘253 Brown Dep. Tr.”)
2011	Judgment: Final Written Decision, <i>Penumbra, Inc. v. RapidPulse, Inc.</i> , IPR2022-00608, Paper 34 (P.T.A.B. Sept. 6, 2023) (“‘253 FWD”)
2012	Sudheer Gorla et al., <i>The Role of Interventional Cardiology in the Management of Thrombotic Conditions in the Pediatric Population</i> in CARDIOVASCULAR THROMBUS: FROM PATHOLOGY & CLINICAL PRESENTATIONS TO IMAGING, PHARMACOTHERAPY & INTERVENTIONS 565–575 (2018)
2013	<i>Patency</i> , MERRIAM-WEBSTER DICTIONARY, https://www.merriam-webster.com/dictionary/patency (last visited Nov. 22, 2024)
2014	Declaration of Brad Culbert in Support of Patent Owner’s Response (May 30, 2025) (“Culbert POR-Decl.”)
2015	U.S. Patent Application Publication No. US 2016/0220741 A1 (“Garrison”)
2016	Transcript of the Remote Videoconference Deposition of Brian Brown (Vol. 1), taken December 9, 2022, <i>Penumbra, Inc. v. RapidPulse, Inc.</i> , IPR2022-00608, Ex. 2016 (P.T.A.B. Jan. 6, 2023) (“IPR2022-00608, Ex. 2016”)
2017	Transcript of the Remote Videoconference Deposition of Ian Ross, MD, No. IPR2024-01261, <i>Penumbra, Inc. v. RapidPulse, Inc.</i> , taken May 16, 2025 (“Ross Dep.”)

Exhibit	Description
2018	Transcript of the Remote Videoconference Deposition of Brian J. Brown, No. IPR2024-01261, <i>Penumbra, Inc. v. RapidPulse, Inc.</i> , taken May 9, 2025 (“Brown Dep.”)
2019	Errata and signed Acknowledgment from Transcript of the Remote Videoconference Deposition of Brian J. Brown, No. IPR2024-01261, <i>Penumbra, Inc. v. RapidPulse, Inc.</i> , taken May 9, 2025
2020	NEW OXFORD AMERICAN DICTIONARY (3rd ed. 2010) (EXCERPT)
2021	Patrick A. Brouwer, MD et al., <i>Clot Pathophysiology: Why is It Clinically Important?</i> , 28 NEUROIMAGING CLINICAL N. AM. 611-623 (2018) (“Brouwer 2018”)
2022	Decision Granting Institution of <i>Inter Partes</i> Review, No. IPR2021-01466, <i>Penumbra, Inc. v. RapidPulse, Inc.</i> , dated March 14, 2022
2023	Decision Granting Institution of <i>Inter Partes</i> Review, No. IPR2022-00608, <i>Penumbra, Inc. v. RapidPulse, Inc.</i> , dated September 9, 2022
2024	Transcript of the Remote Videoconference Deposition of Brian Brown, taken June 15, 2022 <i>Penumbra, Inc. v. RapidPulse, Inc.</i> , No. IPR2021-1466, Ex. 2013 (P.T.A.B. July 11, 2022) (“IPR2021-01466, Ex. 2013”)
2025	Osama O. Zaidat, MD et al., <i>First Pass Effect – A New Measure for Stroke Thrombectomy Devices</i> , 49 STROKE 660-666 (2018) (“First Pass Effect”)
2026	Gyula Gal et al., <i>Improved LVO First-Pass Effect With Precise Cyclic Aspiration: Early Experience with the RapidPulse™ System</i> , 14 (Suppl.) J. NEUROINTERVENTIONAL SURGERY A40-A41 (2022)

Exhibit	Description
2027	Arsida Bajrami et al., <i>RapidPulse™ Cyclic Aspiration System for Acute Ischemic Stroke Due to Large Vessel Occlusions</i> , 22 INTERVENTIONAL NEURORADIOLOGY (2024)
2028	Raul Nogueira, MD et al., <i>Data Presented at SVIN 2024</i> , RapidPulse™ (2024)
2029	RESERVED
2030	RESERVED
2031	<i>Duplex Fuel Selectors</i> , ANDAIR PRODUCTS, https://www.andair.co.uk/category/duplex-fuel-selectors/ (last visited May 28, 2025)
2032	<i>Solenoid Valves</i> , CANNON WATER TECHNOLOGY INC., https://cannonwater.com/pipe-valves-and-fittings/solenoid-valves/?srsltid=AfmBOoqfhXocs7qr7O-snnaGmL5GabfvVdzYEE8shLCAPXabAn6YSf (last visited May 28, 2025)
2033	Brian Booth, <i>V-Port Ball Valves vs. Globe</i> , VALVE WORLD AMERICAS (2018)

I. Introduction

The challenged claims of U.S. Patent No. 11,406,402 (“’402 Patent”) should be found patentable over the grounds raised in Petitioner Penumbra, Inc.’s petition for *inter partes* review (“IPR”).

First, Petitioner’s combinations of Yang and Ofek, respectively, with Mullins incorporate cycling based on feedback from Mullins’s pressure sensor, but as the examiner found in allowing the claims, a sensor feedback system does *not* render the claimed predetermined cycle obvious.

Second, Petitioner fails to show that its combinations render obvious aspirating clots using a predetermined cycle by controlling flow in and out, as dependent claim 11 requires. Petitioner fails to offer any evidence that a person of ordinary skill in the art (“POSA”) would have a reasonable expectation of success of aspirating clots with controlled flow in and out using a predetermined cycle—without Mullins’s sensor. Indeed, due to the size and density variations of clots and the complexity of the aspiration catheter system, a POSA would not have had a reasonable expectation of success.

Third, Petitioner fails to show that claims 3-4, 14, and 16-17, reciting specific amounts of exit flow, are rendered obvious. Petitioner admits that its references do not disclose the claimed amounts of exit flow. Instead, Petitioner relies on hindsight and its expert’s testimony to argue that a POSA would find the claimed amounts of

exit flow obvious. But Petitioner's expert's calculations rely on flawed assumptions and fail to demonstrate obviousness. On the contrary, those calculations confirm that the claimed amounts of exit flow are *nonobvious*.

Fourth, Petitioner has not shown obviousness of claims 5-7 and 18-20, the off-off state claims. In trying to argue otherwise, Petitioner goes to extreme lengths—conjuring up non-existent figures from the prior art, contradicting the prior art's disclosures, and relying on disclosures that the Board previously found did *not* render the off-off state obvious. Petitioner's unsupported arguments are entitled to no weight. A POSA would not have found the claimed off-off state obvious.

Finally, Patent Owner's inventive approach met a long-felt need for improved aspiration thrombectomy, as evidenced by its greater efficacy.

Accordingly, Patent Owner RapidPulse respectfully requests that the Board confirm the patentability of the challenged claims.

II. Factual Background

A. The '402 Patent (Ex.1001)

The '402 Patent's inventions relate to an aspiration thrombectomy system for removing thrombi/clots from blood vessels. Ex.1001, 1:36-39.¹ As the '402 Patent explains, “[t]he basic configuration for an aspiration catheter includes a length of

¹ Citations omitted, emphases added, and annotations added unless otherwise noted.

hollow catheter ... connected to a vacuum or suction pump [where] [o]peration of the suction pump causes fluid and particulates at the distal end of the catheter to enter the distal opening of the hollow lumen.” *Id.*, 1:55-61.

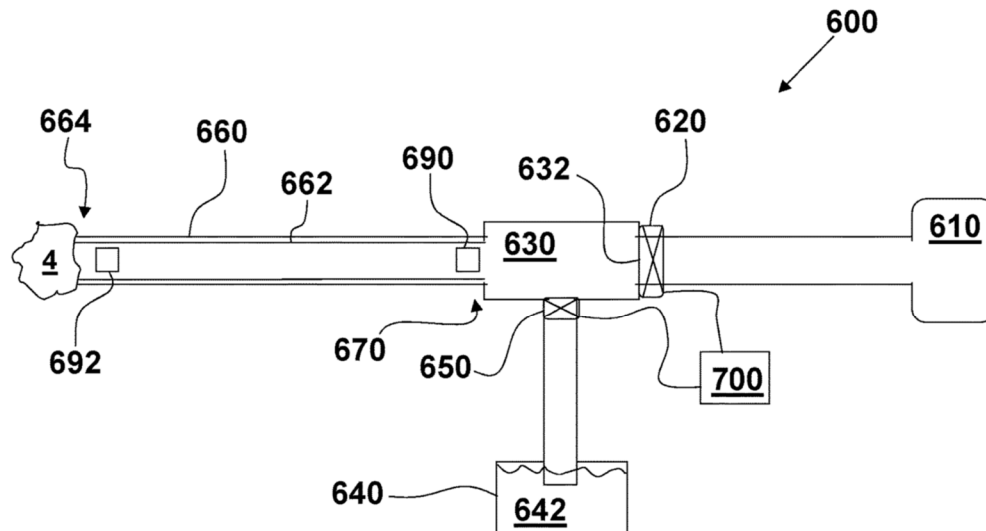


FIG. 47

Ex.1001, FIG. 47

The '402 Patent explains some disadvantages of conventional aspiration systems and discloses features that address them, including using “a predetermined cycle” to aspirate clots by controlling “fluid flow in and out,” limiting the amounts of exit flow, and utilizing off-off states. Ex.1001, cls. 1, 3-7, 11, 14, and 16-20. For example, the '402 Patent discusses that, “[d]uring conventional aspirations, it is common for applied vacuum to partially draw a thrombus into the distal opening of the aspiration catheter’s lumen, thereby deforming some of the thrombus to the

catheter's inner diameter.” *Id.*, 2:12-16. However, “[a]t this point, the thrombus becomes lodged completely within, partially within, or at the distal opening of the aspiration catheter.” *Id.*, 2:16-18. It is not viable to “revers[e] the suction to pressurize the clot and eject it forcibly and uncontrollably out of the distal opening of the aspiration catheter” because this “may cause the clot to move further distally within the vessel,” and can “permanently lodge the clot into that vessel, making it impossible to remove, or it could burst the vessel,” which poses “serious potential risks to the patient.” *Id.*, 2:23-37.

The '402 Patent explains that the claimed “predetermined cycle” with controlled “flow in and out” achieves clot aspiration and addresses this problem. The “predetermined cycle” is set for the specific catheter to perform effective aspiration. Ex.1001, 12:52-60; Culbert POR-Decl. (Ex.2014) ¶34. Further, the inventive aspiration system addresses the situation where the catheter's distal end is clogged by a clot by having the controller be “actuated to cause the fluid column to shift distally to the shift distance,” which “imparts a controlled reversal of flow to the fluid column within the vacuum channel ... that slightly translates the thrombus ... distally relative to the distal opening of the vacuum channel.” Ex.1001, 26:17-23. In other words, the '402 Patent discloses a precisely controlled flow out that temporarily pushes the thrombus out of the distal end of the catheter. *Id.*, 27:18-20. Then, “the controller 10 re-applies vacuum,” “and the thrombus ... accelerates back

into the vacuum channel” *Id.*, 27:20-23. “With one or just a few applications to displace the thrombus ..., the vacuum channel ... becomes unclogged.” *Id.*, 27:24-27.

To ensure that the flow out is controlled, the ’402 Patent teaches specific amounts of exit flow and explains that, “[w]hen the controller is actuated, a positive amount of exit flow is created without possibility of overshooting”² and its movement “is limited to a specific volume and/or pressure and is automatically and precisely controlled.” Ex.1001, 4:50-54. To further control flow in and out, the ’402 Patent teaches the off-off state—where both the vacuum and vent valves are closed—to optimize the cycle based on “the dynamics or the resonance of a particular catheter.” *Id.*, 49:48-64; Culbert POR-Decl. ¶¶37-38.

² Overshooting could cause the thrombus to be released uncontrollably into the vasculature, leading to extreme adverse effects. Ex.2018 (Brown Dep.), 99:1-14; Culbert POR-Decl. ¶36.

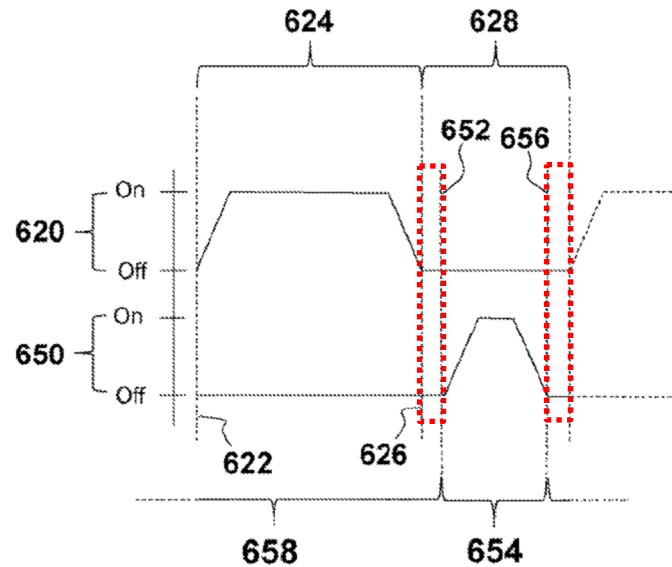


FIG. 52

Ex.1001, FIG. 52 (annotated to show off-off states)

B. The Examiner Found The “Predetermined Cycle” Limitation Overcame Prior Art During Prosecution

As-filed claim 1 recited controlling “fluid flow in and out” and “a predetermined cycle.” Ex.1004 (’402 FH), 336. After a preliminary amendment, claim 1 also recited “an aspiration catheter” and “a controller configured to open and close the vacuum valve and the vent valve in a predetermined cycle ... and to control fluid flow in and out from the distal end of the catheter.” *Id.*, 228.

As Petitioner acknowledges, the claims of the ’402 Patent were not rejected during prosecution. Pet. 10. The examiner gave the following statement of reasons for allowance:

[T]he prior art does not teach or suggest, ..., a controller configured to open and close the vacuum valve and the vent valve in a ***predetermined cycle*** to change the level of vacuum applied to the catheter. Garrison (US 20160220741) discloses a similar device, but the controller disclosed in [0113] ***changed the cycle of opening and closing the valves based on feedback from sensors and is not a pre-determined pattern.***

Ex.1004, 86. The examiner thus recognized that “a predetermined cycle” differs from a “cycle of opening and closing valves based on feedback from sensors.” *Id.*; *see also Arendi S.A.R.L. v. Google, LLC*, 882 F.3d 1132, 1136 (Fed. Cir. 2018) (examiner’s statements in Reasons for Allowance should be considered in interpreting claims).

A POSA reviewing the ’402 Patent would have come to the same conclusion as the examiner: a “predetermined cycle” as the claims recite, and as explained throughout the specification (as a “pre-determined pattern of opening and closing the vent and vacuum valves” (Ex.1001, 9:29-45), or “pre-determined cycle of opening and closing the vent and vacuum valves” (*id.*, 9:46-61)), is unlike a cycle where the timing of opening and closing valves is continually modified based on, for example, feedback from a sensor (e.g., Garrison’s “flow sensor,” Garrison (Ex.2015), [0113]). Culbert POR-Decl. ¶39. Despite the Examiner’s clear statements differentiating sensor-based cycles from predetermined cycles,

Petitioner's arguments attempt to retread this old ground, and the Board should reject those arguments.

C. Person Of Ordinary Skill In The Art

For purposes of this response, Patent Owner accepts Petitioner's description of a POSA. Pet. 11; Culbert POR-Decl. ¶44.³

D. Summary Of Prior Art References

1. Yang (Ex.1012)

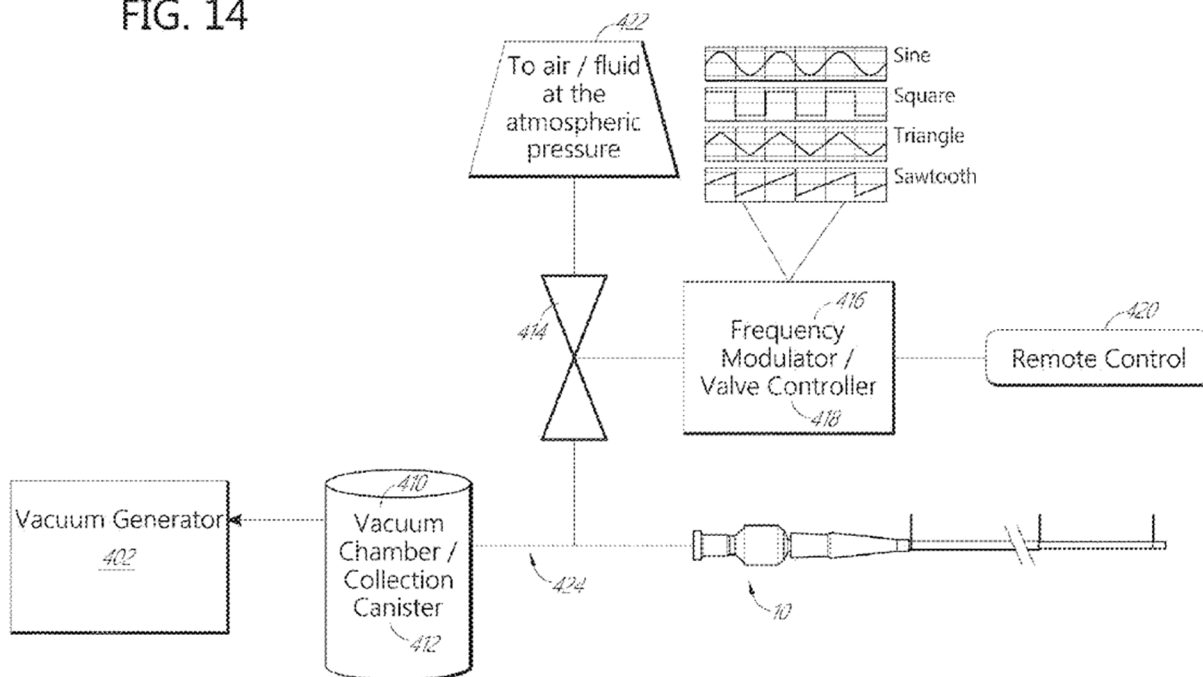
Yang is a published patent application titled "Telescoping Neurovascular Catheter With Active Distal Tip." Ex.1012. The "telescoping catheter" is intended for applications such as "distal neurovascular aspiration." *Id.*, Abstract. Yang discloses a controller "for applying intermittent vacuum to the lumen" of the catheter. *Id.*, [0014]. Specifically, an obstruction can be drawn into the lumen to be removed from the body "upon application of constant or pulsatile negative pressure." *Id.*, [0100]. "The intensity of intermittent or pulsatile vacuum applied to lumen 40 may be adjusted to cause the distal tip 38 of the catheter 10 to experience an axial reciprocation or water hammer effect, which can further facilitate both transluminal

³ Patent Owner's expert, Brad Culbert, is a medical device engineer with substantial experience designing and developing thrombectomy systems and devices for removing blood clots from vessels. Culbert POR-Decl. ¶4.

navigation as well as dislodging or breaking up the obstruction.” *Id.*, [0108]. Yang explains that water hammer “is a pressure surge or wave caused when a fluid in motion is forced to stop or change direction suddenly, creating a momentum change,” which can be caused, e.g., when a vacuum valve “closes suddenly at the end of a pipeline system.” *Id.* However, Yang does not disclose flow out or the control of flow out of the catheter. Ex.2016 (IPR2022-00608, Ex.2016), 93:13-25; Institution Decision (“ID”) 19; Culbert POR-Decl. ¶46.

Petitioner’s analysis centers on Yang’s Figure 14 embodiment (depicted below) where a “solenoid valve 414” connects an “air/fluid reservoir 422 at the atmospheric pressure and the aspiration line 424 connecting the catheter 10 to the vacuum chamber 410/collection canister 412.” Ex.1012, [0131].

FIG. 14



“[T]his system modulates pressure in the catheter 10 by allowing pressure to vary from vacuum to atmospheric pressure.” *Id.*

Yang further discloses that, when “a corked clot” is “stuck at the distal end,” “[c]ompletely releasing (venting to atmospheric pressure) the vacuum and allowing the clot to relax before reapplying a vacuum is found to aspirate the corked clot most efficiently.” Ex.1012, [0168]. This “vacuum and release cycle” is illustrated in Figures 25A-25C (reproduced below). In Figure 25A, the vacuum valve 2516 is open (horizontal line) and the release valve 2514 to atmosphere is closed (vertical line), then the release valve 2514 to atmosphere is opened in Figure 25B while the vacuum valve 2516 remains open, and finally the vacuum valve 2516 is closed in Figure 25C before being opened again when the cycle restarts. *Id.*, [0169]-[0170]. Yang thus discloses having both valves open at the same time during each cycle, rather than having any state where both valves are closed. *Id.*

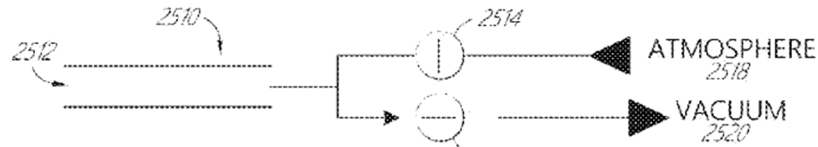


FIG. 25A

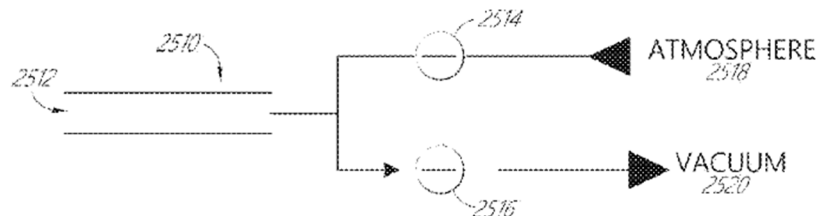


FIG. 25B

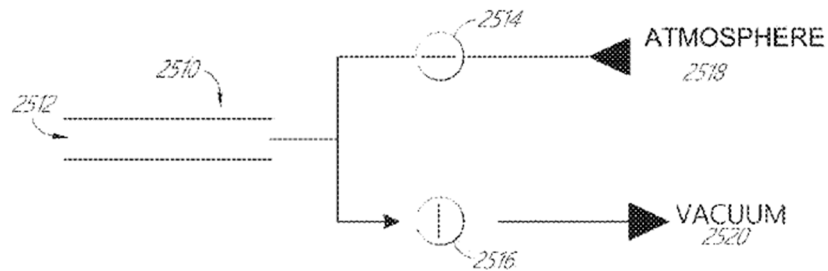


FIG. 25C

2. Mullins (Ex.1008)

Mullins discloses an aspiration system that uses the catheter “with a pump which dynamically applies negative or positive pressure to optimally aspirate a clot.” Ex.1008, Abstract. Mullins’s system includes a “pressure sensor” or “fluid flow sensor” and “var[ies] aspiration pressure according to the sensed pressure” or “fluid

displacement” within the catheter lumen. *Id.*, 3:29-38, 3:46-59. The sensor is incorporated into the pump located at the catheter’s proximal end. Ex.1008, 26:35-37; Culbert POR-Decl. ¶50. The controller and pressure/fluid flow sensor in Mullins’s system use “defined upper and lower limits of pressure or displacement to decide whether to apply a vacuum or pressurize,” “to improve efficiency of aspiration.” Ex.1008, 3:60-65, 25:43-49.

Mullins’s “pump 3504” shown in Figure 45 (depicted below) can “provide a negative fluid displacement thereby decreasing pressure (enabling a vacuum) or positive displacement, thereby increasing pressure.” *Id.*, 26:31-37. The pump can have “a peristaltic pump mechanism.” *Id.*, 29:4-5. Further, “[t]he pump will continuously measure the pressure within the catheter lumen during the procedure.” *Id.*, 26:55-56.

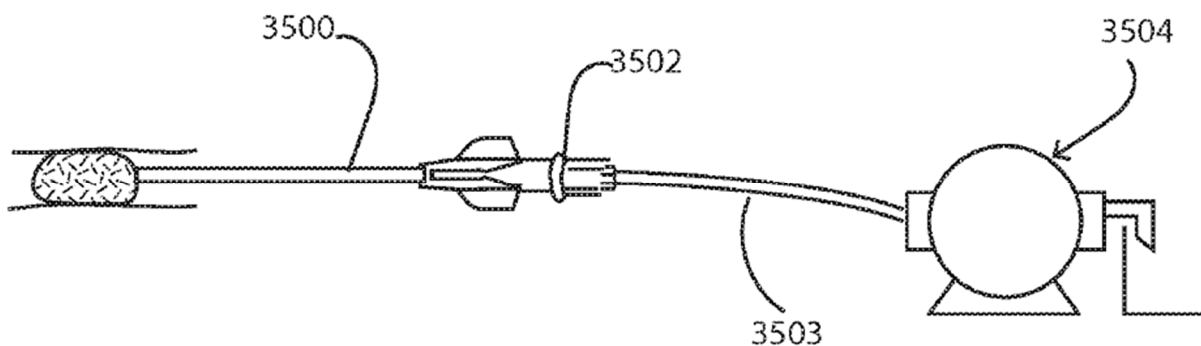


Fig.45

The pump initially “applies a vacuum” and, when measured pressure reaches a “Low Limit,” “defined such that during vacuum, a portion of the clot has been aspirated

but not so much that the clot has become irreversibly clogged,” the “direction of fluid displacement of the pump is now reversed,” “thereby increasing the pressure.” *Id.*, 26:25-27:20. This allows “some or all of the clot to be pushed distally towards the catheter tip,” making the clot “more ‘free’ within the catheter.” *Id.*, 27:21-26. “The pressure is further increased until a High Limit is reached,” and “this High Limit is defined such that the ingested clot may not be completely expelled from the catheter.” *Id.*, 27:27-30. This pressure-dependent cycle, illustrated in Figure 47 (reproduced below), is repeated to “complete ingestion of the clot.”⁴ *Id.*, 27:31-35.

⁴ The drawing of the catheter and clot is missing in Figure 47(i).

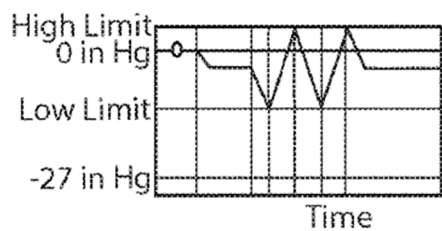
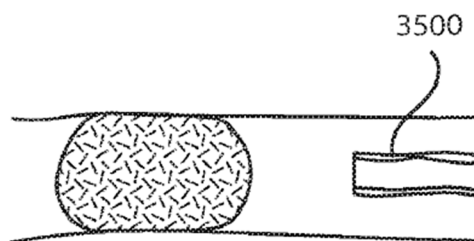
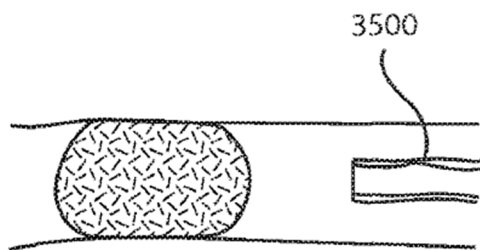


Fig.47(a)

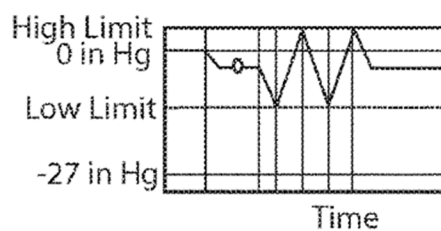


Fig.47(b)

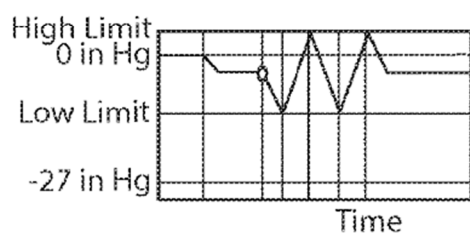
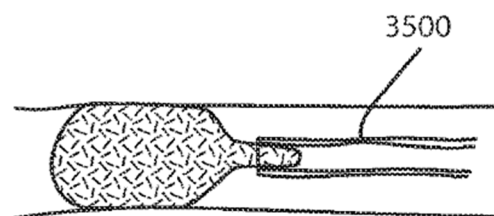
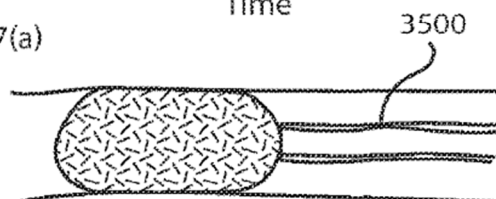


Fig.47(c)

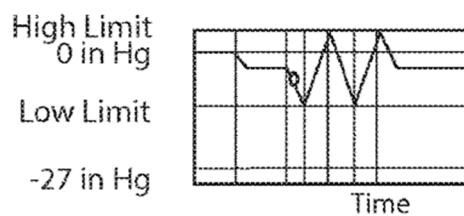
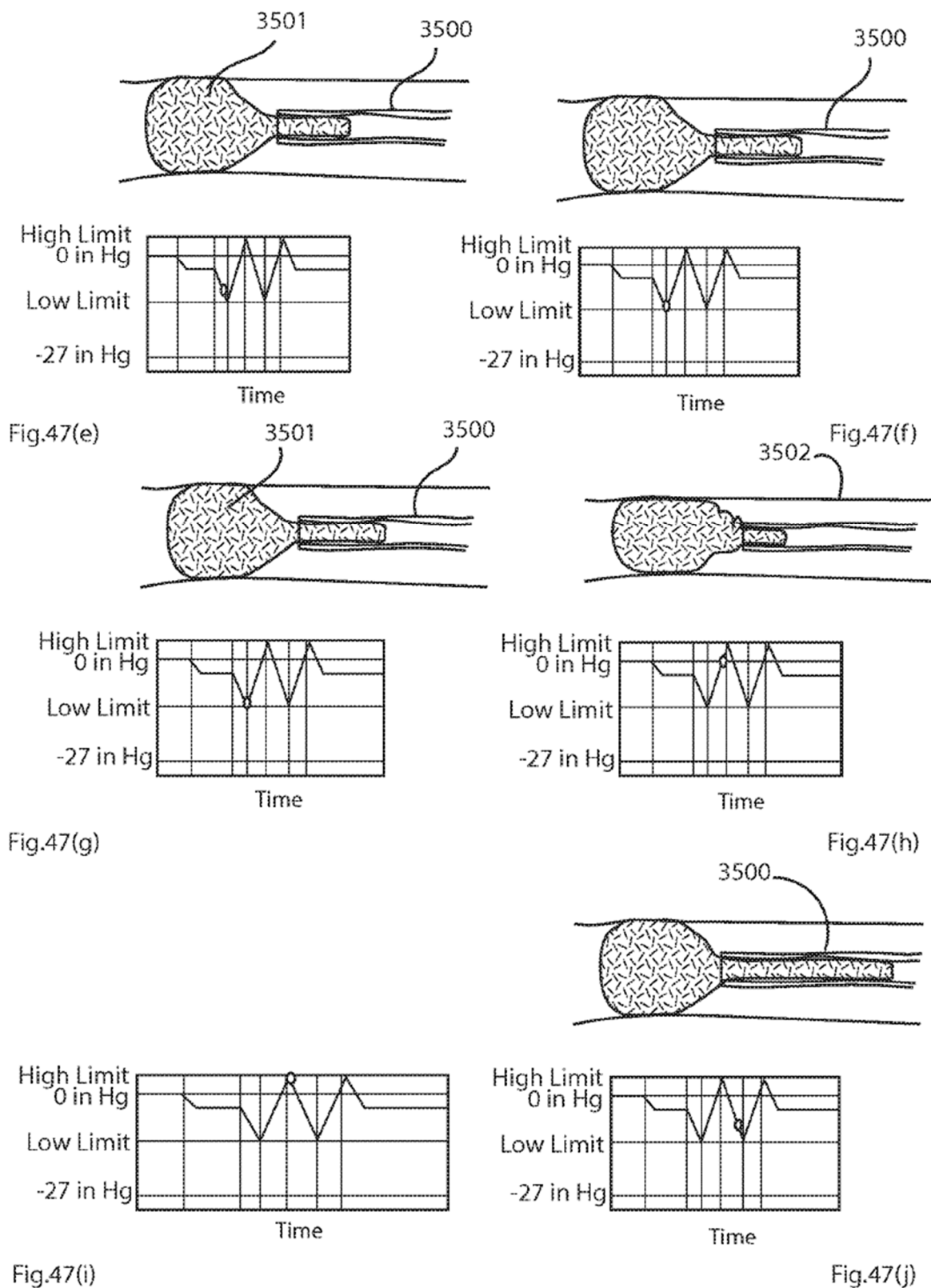
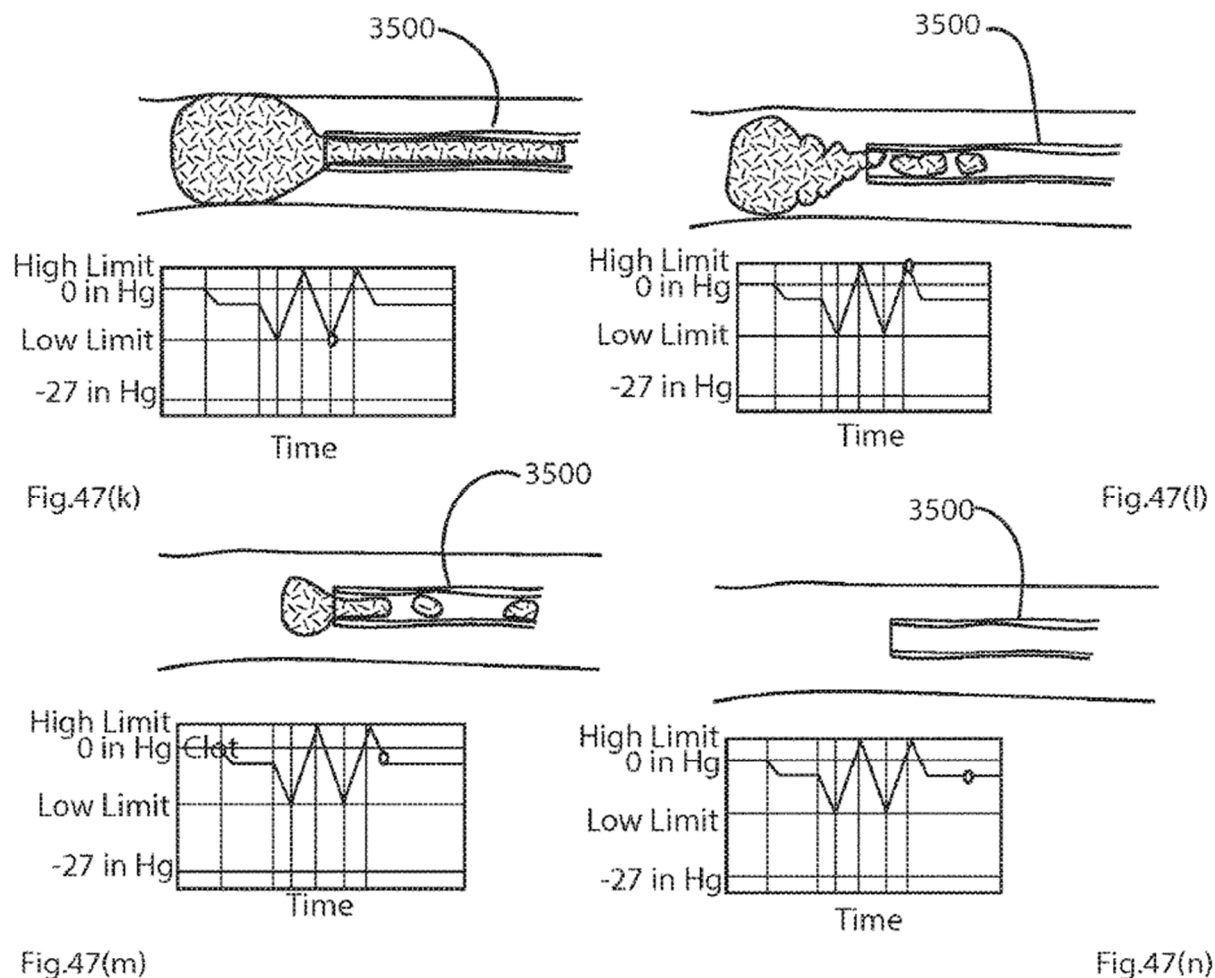


Fig.47(d)





Mullins touts the “feedback” that this approach provides, namely “the ability of the pump to measure the condition in the pump (e.g. pressure or fluid displacement), and continue or alter its behaviour.” Ex.1008, 27:48-53.

3. Ofek (Ex.1007)

Ofek is titled “Systems And Methods For Correcting And Preventing Occlusion In A Catheter” and discloses “[a] patency device for catheter assemblies and other elongate tubular devices used for establishing access to an interior body portion of a patient.” Ex.1007, Abstract. This device preserves patency in the

catheter by “providing impulses of positive pressure to fluid disposed in the lumen of the catheter assembly.” *Id.*, 1:19-23; *see also* Ex.2017 (Ross Dep.), 25:3-13. “The impulses are configured to dislodge occlusions that may have formed in the lumen.” Ex.1007, 1:29-31.

Figure 1 below depicts Ofek’s catheter assembly 10 and patency device 30. Ex.1007, 2:35-41.

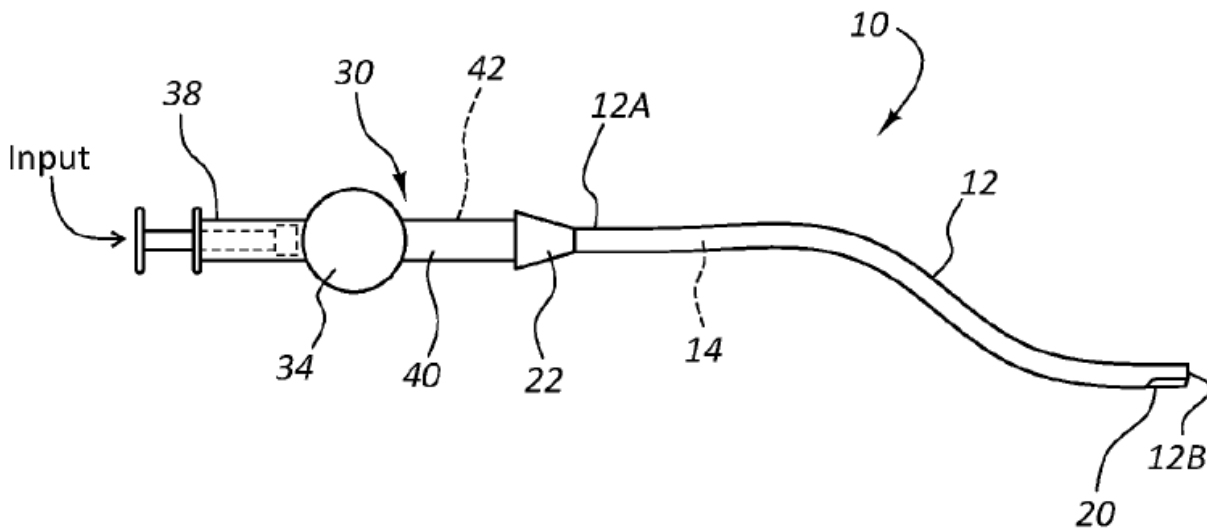


Fig. 1

“[T]he catheter 10 includes an elongate catheter tube 12 that defines a lumen 14 extending between a proximal end 12A and a distal end 12B of the catheter tube.” *Id.*, 2:41-44.

Ofek’s patency device 30 is “configured to operably connect on a temporary basis with the catheter 10 and provide patency to the catheter tube lumen 14” by providing impulses “to prevent the formation of thrombus or other occlusion in the

lumen 14, especially at the distal end thereof.” Ex.1007, 2:56-67. These “high pressure pulses can also be used to clear the lumen after occlusions have formed therein.” *Id.*, 2:67-3:2. By focusing on a “patency device” for “temporary” use, and “correcting and preventing occlusion,” Ofek’s disclosure would be understood to be directed to addressing a thrombus formed within a catheter tube, rather than aspirating a thrombus in the vasculature (as in the claimed inventions). Culbert POR-Decl. ¶55.

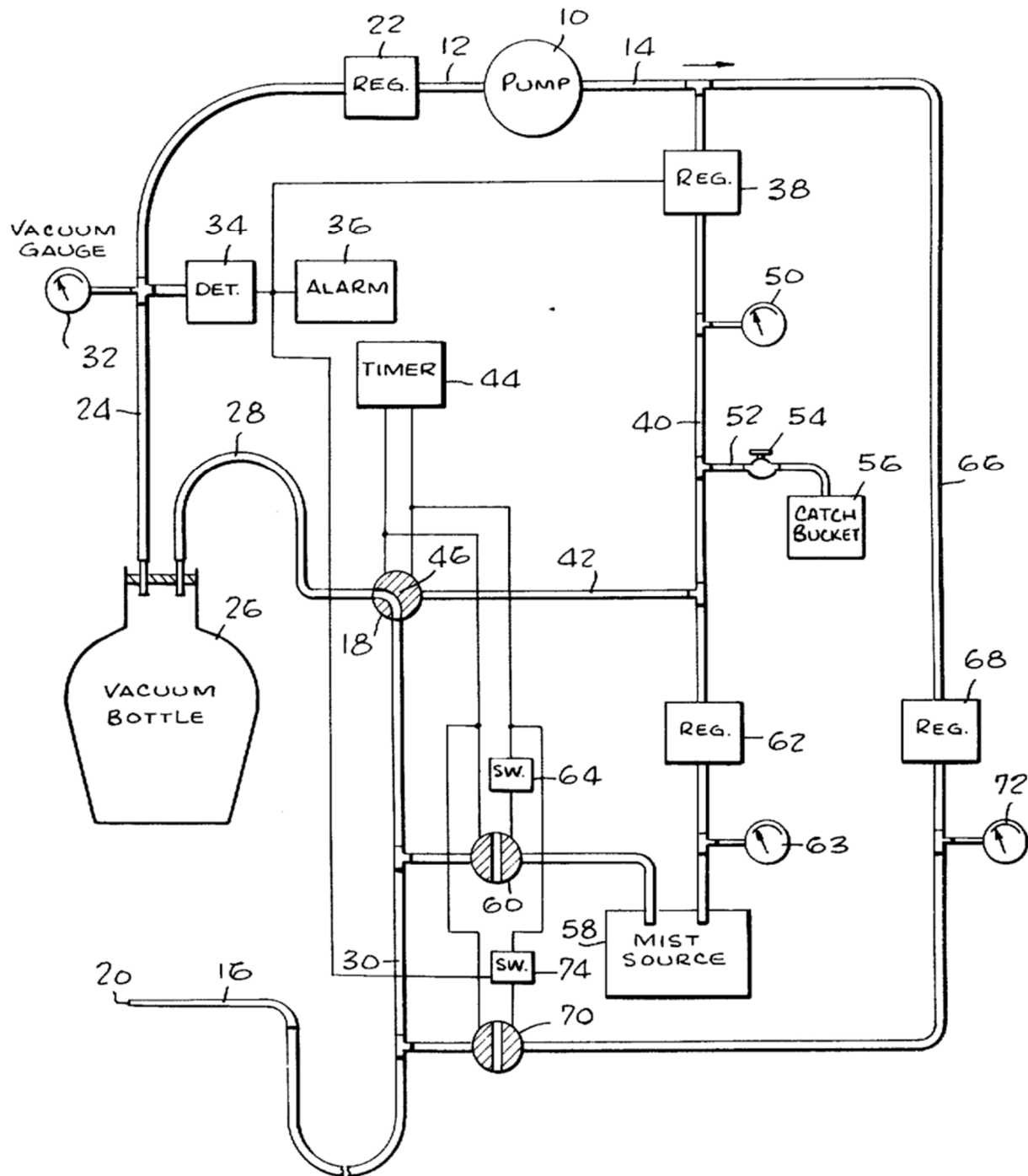
Ofek explains that the high pressure pulses are “interspersed by relatively longer rest periods 84 of negative baseline pressure,” which enable “any occlusion dislodged by the impulses to be sucked proximally up the catheter tube lumen 14 and removed therefrom,” “thus preventing the dislodged occlusion from entering the bloodstream from the distal end 12B of the catheter tube 12.” Ex.1007, 3:47-57. “The occlusion is dislodged by the high-pressure impulses, which are strong enough to dislodge the occlusion but are not of sufficient duration to push it out the distal end 12B of the catheter tube 12.” *Id.*, 4:33-37. “The subsequent negative pressure rest period following each impulse can act to prevent escape of the clot from the catheter tube 12,” such that “any clot or occlusion present in the catheter 10 can be acceptably removed.” *Id.*, 4:37-44.

Ofek notes that “periodic use of the patency devices” “can also serve to prevent the formation of an occlusion by preventing initial adherence and growth of

the occlusion in the first place.” Ex.1007, 6:64-67. Thus, Ofek’s patency devices “can be employed to provide fluid impulses for the dislodgement of occlusive material within the lumen of a catheter and/or to maintain the patency of the lumen, free from occlusions.” *Id.*, 8:16-22.

4. Rubenstein (Ex.1011)

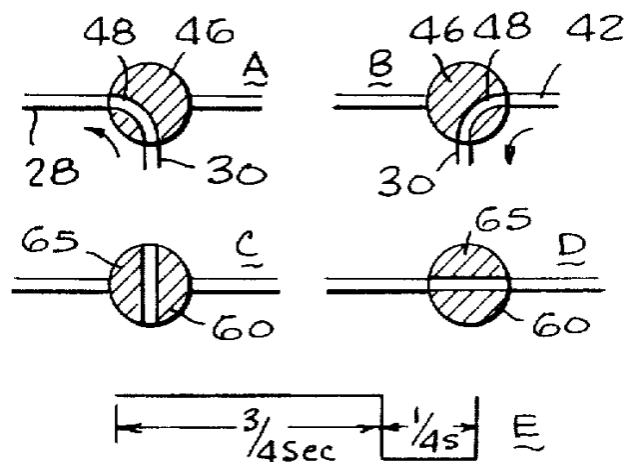
Rubenstein describes a pumping system for the removal of “[m]ucous membranes and viscous materials such as phlegm.” Ex.1011, 1:24-26. Rubenstein’s system provides aspiration in larger cavities with durable walls, e.g., throat, intestines, ears. Culbert POR-Decl. ¶57. Rubenstein’s Figure 1 is reproduced below:



When catheter 20 is blocked by phlegm, Rubenstein discloses that “[a]ny mucous membrane or other material just entering the tip 20 of the catheter will be blown free when positive pressure is applied to the catheter 16.” Ex.1011, 3:17-20. However,

as relevant to the '402 Patent, a POSA would understand blowing material free by applying positive pressure is not a safe technique for use in brain vessels. Ex.2006, 65:3-15; Culbert POR-Decl. ¶57.

Rubenstein's Figure 2 (reproduced below) illustrates the two positions of the valves. In diagram A, valve 18/46 is in a first open state "to have the channel 48 permit fluid flow between the tubing 28 and the tubing 30 such that negative pressure is applied" to the catheter. Ex.1011, 3:26-31. Alternatively, in diagram B, valve 18/46 is in a second open state to permit positive pressure to be applied to the catheter. *Id.*, 3:31-36. In other words, valve 18/46 is either applying positive or negative pressure to the catheter at all times.



Rubenstein's valve 60 connects a "mist source 58" to catheter 16 so "detergent or other enzymatic fluid" can be "ejected through the catheter." Ex.1011, 4:2-8. Rubenstein also discloses that "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.” *Id.*, 4:26-31. Diagram C of Figure 2 illustrates valve 60 “being positioned to prohibit fluid flow through valve 60” and diagram D illustrates valve 60 alternatively “being positioned to allow fluid flow through the valve 60.” *Id.*, 4:17-23.

III. Claim Construction

Petitioner seeks to construe the claim term “limited/limiting ... to a positive amount of exit flow” in claims 3-4, 13, and 15 as “the maximum permitted amount of positive exit flow in the distal direction, **including no exit flow.**” Pet. 15-16; *see also* Ex.2018 (Brown Dep.), 14:4-15:3. Petitioner’s proposed construction is plainly wrong and should be rejected. By its plain language, “a *positive* amount” is greater than zero—***not*** “no exit flow,” as Petitioner proposes. *Id.*; Ex.2020 (NEW OXFORD AMERICAN DICTIONARY) (“positive” means “(of a quantity) greater than zero.”); Culbert POR-Decl. ¶42. Petitioner provides no basis to depart from the plain meaning of the word “positive.” Furthermore, consistent with this plain meaning, claims 3 and 4 require specific amounts of non-zero exit flow. Ex.1001, cl. 3 (“a positive amount of exit flow from approximately 0.001 ml to approximately 1.0 ml”), cl. 4 (“a positive amount of exit flow of approximately 0.1 ml to approximately 0.5 ml”).

At institution, the Board invited the parties to address the proper construction of “flow ... out from the distal end.” ID 10. The Board also noted that, in earlier

IPRs, it construed the term “forward flow” in the claim phrases “prevent forward flow out from the distal end” and “substantially prevent forward flow of liquid at a distal end” to mean “an amount of liquid in the lumen that exits the distal end in the distal direction that is greater than 6 microliters of fluid” based on a definition of “forward flow” in the specification. ID 10; Ex.2007, 6, 15; Ex.2011, 6, 13-14. To begin with, the Board’s previous construction of “forward flow” is inapplicable to the claims here, which do not use the term “forward flow.” In addition, dependent claims confirm that the Board’s previous construction is inapplicable because the claims recite that the claimed “exit flow” can be less than 6 microliters and more than 6 microliters. *E.g.*, Ex.1001, cl. 3 (reciting “exit flow from approximately 0.001 ml [1 microliter] to approximately 1.0 ml [1,000 microliters]”).

Petitioner has not proposed a construction of “flow ... out from the distal end,” and Patent Owner agrees that it needs no construction. By its plain language, “flow ... out from the distal end” is the opposite of “flow in.” The specification refers to this flow out from the distal end consistent with its plain meaning as flow out from, *i.e.*, that exits, the distal end of the catheter. *See, e.g.*, Ex.1001, 36:42-45 (“This [pressure] change also draws out a small volume of liquid from within the lumen of the catheter 410. In an exemplary embodiment, the volume is approximately 0.2 ml.”); 43:31-35 (“In other words, a ‘pressure pulse’ or ‘pressure wave’ is momentum

within a column of fluid that can act to move a distal portion of the fluid column in the catheter lumen distally out from a distal end of the catheter.”).

IV. Petitioner Fails To Show That Yang/Mullins Or Ofek/Mullins Includes “A Predetermined Cycle” To “Control Fluid Flow In And Out” (All Claims)

Neither Petitioner’s Yang/Mullins (Ground 1) nor Ofek/Mullins (Ground 4) combination has “a controller configured to open and close the vacuum valve and the vent valve in a *predetermined cycle* to change a level of vacuum at the distal end of the catheter and to control fluid flow in and out from the distal end of the catheter as claim 1 requires. Ex.1001, cl. 1.

Yang alone does not disclose fluid flow in and out from the distal end of the catheter. ID 19. The Board acknowledged that, “on the current record, we agree with Patent Owner that Yang may not explicitly disclose flow out from the distal end of the catheter.” ID 19. Petitioner’s expert, Mr. Brown, conceded that “[Yang] does not describe [] flow out and whether [Yang’s] system controls flow out.” Ex.2016 (IPR2022-00608, Ex.2016), 93:13-25. Rather, at institution, the Board only found a reasonable likelihood of success based on Petitioner’s combining Mullins with Yang. ID 19 (“Whether Yang alone renders [the fluid flow in and out] limitation obvious may be explored further on a full trial record; however, because this limitation appears to be taught by Mullins ... we are sufficiently persuaded that Petitioner has met its burden to show a reasonable likelihood that this limitation is

rendered obvious by the combined disclosures of Yang and Mullins.”). Similarly, the Board acknowledged that Ofek alone may not disclose controlling flow in and out and that only “the combined disclosures of Ofek and Mullins” may render obvious control of flow in and out. ID 34 (“Further, even if Ofek does not explicitly disclose controlling flow out of the distal end of the catheter, this limitation appears to be taught by Mullins.”).

Each combination needs to be considered as a whole as opposed to individually. *W.L. Gore & Assocs., Inc. v. Garlock, Inc.*, 721 F.2d 1540, 1550 (Fed. Cir. 1983) (district court erred by “considering the references in less than their entirety, i.e., in disregarding disclosures in the references that diverge from and teach away from the invention at hand”). Consideration of Yang/Mullins and Ofek/Mullins, however, reveals a critical flaw in Petitioner’s analysis. Because Petitioner’s contentions rely on incorporating Mullins’s pressure sensor feedback in both combinations, both lack “a controller configured to open and close the vacuum valve and the vent valve in a predetermined cycle.” Ex.1001, cl. 1.

As the examiner acknowledged in allowing the ’402 Patent, a controller that “changed the cycle of opening and closing the valves based on feedback from sensors” does not disclose “a pre-determined pattern” or a “pre-determined cycle” as claimed. Ex.1004, 86. Relying on this distinction, the examiner allowed the ’402 Patent over Garrison, where the timing of the opening and closing of valves is

adjusted based on feedback from pressure sensors. *Id.*; Garrison, [0113] (“[A]spiration source 600 further includes a flow sensor 275 that senses flow in the aspiration line 230, coupled to a controller that controls the level of aspiration. The aspiration source 600 can increase in aspiration level when the flow rate is slow and decrease when the flow rate is increased.”). For similar reasons, Petitioner’s combinations likewise fail to render obvious the claimed “predetermined cycle.”

A. Yang/Mullins Combination

Petitioner concedes repeatedly that its Yang/Mullins combination uses Mullins’s sensor, which means that the combination does *not* have a “predetermined cycle.” For instance, in alleging a motivation to combine Yang and Mullins to meet claim 1, Petitioner unequivocally states: “[a] POSA would recognize Yang could be configured to achieve the benefits, as taught by Mullins, of cyclical pressure changes, *including the use of a pressure sensor.*” Pet. 17-18, *see also, e.g., id.*, 34. Likewise, in addressing claim 14, which depends on claim 1 and recites additional limitations on the “positive amount of exit flow,” Petitioner argues “*Mullins’s sensor would be used* in Yang/Mullins to determine fluid displacement as part of the vacuum application cycle.” Pet. 51.

Petitioner’s repeated arguments relying on inclusion of Mullins’s pressure sensor in the Yang/Mullins combination confirms that there would be no “predetermined cycle” because the controller would vary the applied pressure based

on the pressure sensed by the sensor. Indeed, Petitioner admits that Mullins’s “cycling controller ... ‘*varies* aspiration pressure according to sensed pressure within the catheter lumen.’” Pet. 30 (quoting Ex.1008, 3:36-59). This is precisely the type of system that the examiner distinguished as not having “a predetermined cycle.” Ex.1004, 86 (“the cycle of opening and closing the valves based on feedback from sensors [] is not a pre-determined pattern”).

Petitioner does not propose any Yang/Mullins combination that does not include Mullins’s pressure sensor. At institution, the Board recognized that Mullins uses “a sensor” to measure the pressure and, “[b]ased on the measured pressure, the pump may change direction hence altering the pressure and fluid displacement.” ID 13-14 (quoting Ex.1008, 26:35-37, 26:40-42). The Board cited Yang’s disclosure of a valve controller in finding that, at the institution phase, Yang “discloses a valve controller to control the vacuum and vent valves in a ‘predetermined cycle’ as required by the language of the claims.” ID 22. But implementing Mullins’s pressure-sensing based teaching (which would destroy opening/closing valves in a predetermined cycle) is precisely how Petitioner proposes to modify Yang to address Yang’s lack of disclosure of flow out from the catheter’s distal end. Petitioner’s expert, Mr. Brown, specifically argues for improving Yang’s system by “using the pressure sensor provided by Mullins on Yang’s device”:

A POSA would find it obvious to implement Mullins' disclosures ... to modify Yang's system, which includes a catheter aspiration system that is ready for improvement by Mullins's techniques The methods of cyclical pressure changes described by Mullins are consistent with and improve on the aspiration cycles that Yang discloses Additionally, *using the pressure sensor provided by Mullins on Yang's device would help implement the most efficient pressure changes* to the catheter to reduce the risk of complications from aspiration thrombectomy, including clogged into the patient's blood stream, as *explicitly taught by Mullins*.

Ex.1005 ¶100.

Mr. Brown could not have been clearer that he proposes altering pressure based on monitoring pressure using a pressure sensor in the Yang/Mullins combination:

A POSA would also find it obvious to implement monitoring the level of vacuum pressure change at the distal end of the aspiration catheter contemplated by Mullins within Yang's aspiration thrombectomy system. ... Mullins discloses that a lumen pressure sensor and *a controller can be used to monitor the pressure* in the system, *and builds on the concept of altering vacuum pressure levels by utilizing a pressure sensor. A POSA would have recognized the benefit of monitoring the vacuum pressure levels* at various points throughout the aspiration system, ... as disclosed in Mullins, in the context of Yang, *and it would have been trivial to implement these within Yang's aspiration thrombectomy system*.

Ex.1005 ¶102.

Mr. Brown reaffirms that Petitioner’s Yang/Mullins combination involves using Mullins’s pressure-sensing approach in addressing the claim limitation requiring the controller “to control fluid flow in and out from the distal end of the catheter.” He points out that “Mullins describes measuring the pressure in the catheter with a pressure sensor” and “discusses the controller utilizing pressure and fluid displacement at the catheter tip to aspirate clots based on the measured pressure levels.” Ex.1005 ¶¶153, 155. Mr. Brown then refers to this explanation in contending that Yang/Mullins render obvious controlling fluid flow in and out from the distal end of the catheter. *Id.* ¶157; *see also id.* ¶¶196-97 (relying on Mullins’s “using upper and lower pressure limits to control how measured amounts of flow displacement” to contend that Yang/Mullins renders obvious a limited “positive amount of exit flow” in claim 3), ¶¶288-89 (relying on Mullins’s “sensor used to determine fluid displacement and vary pressure” to contend that Yang/Mullins renders obvious “limiting movement of the fluid column at the distal end of the catheter” in claim 14).

Neither Petitioner nor Mr. Brown propose a Yang/Mullins combination that does not include Mullins’s pressure-sensing approach to controlling fluid flow. To the contrary, in addressing the “predetermined cycle” limitation, Mr. Brown contends (incorrectly) that Mullins’s “cycling controller that ‘varies aspiration

pressure according to sensed pressure within the catheter lumen” “discloses this change in pressure being done in a predetermined cycle.” Ex.1005 ¶¶131-32 (citing, e.g., Ex.1008, 27:40-28:20 (“[a] novel aspect of this pump system is the incorporation of feedback into the pump algorithm in order to produce more effective pressure cycling”)).

In sum, Petitioner’s proposed Yang/Mullins combination controls fluid flow by varying pressure based on pressure sensed by a pressure sensor, and thus lacks the “predetermined cycle” that the claims require.

B. Ofek/Mullins Combination

Petitioner’s Ofek/Mullins combination similarly lacks the claimed “predetermined cycle” because, as in Petitioner’s Yang/Mullins combination, Petitioner relies on Mullins’s pressure-based feedback approach for control of fluid flow. Petitioner cites paragraphs 355-362 of Mr. Brown’s declaration to contend that “[a] POSA would have been motivated to combine the teachings of Ofek and Mullins.” Pet. 67. In paragraph 361, Mr. Brown contends that a POSA would have controlled pressure levels in the Ofek/Mullins combination by altering pressure levels based on monitoring pressure using a pressure sensor:

A POSA would also find it obvious to implement monitoring the level of vacuum pressure change at the distal end of the aspiration catheter contemplated by Mullins within Ofek’s aspiration system. Consistent with Ofek’s use of a pressure transducer to measure pressure of the

catheter, monitoring pressure inside the aspiration catheter and vacuum system was a known concept that was used to improve the knowledge available to clinicians about the ongoing aspiration procedure and allow for more effective aspiration techniques, ... *Mullins discloses that a lumen pressure sensor and a controller can be used to monitor the pressure in the system, and builds on the concept of altering vacuum pressure levels by utilizing a pressure sensor. A POSA would have recognized the benefit of controlling the vacuum pressure levels and fluid flow* at the distal tip of the catheter, *as disclosed in Mullins*, in the context of Ofek, which also includes a pressure transducer, and it would have been trivial to implement these within Ofek's aspiration thrombectomy system.

Ex.1005 ¶361. Indeed, in its arguments applying the Ofek/Mullins combination to claim 14, Petitioner relies on Mullins's disclosure of "a sensor used to determine fluid displacement and vary pressure." Pet. 101. Petitioner does not describe any Ofek/Mullins combination that does not alter pressure levels based on feedback from a pressure sensor.

Thus, like the Yang/Mullins combination, the Ofek/Mullins combination does not use "a predetermined cycle" to control fluid flow, as the claims require.

V. Petitioner's Grounds Fail To Render Obvious Dependent Claim 11 (Claims 11-20)

Claim 11, and its dependent claims (claims 12-20), are patentable over the two grounds Petitioner raises against it—Ground 1 (Yang/Mullins) and Ground 4 (Ofek/Mullins)—for additional reasons. Claim 11 recites "[a] method for removing

thromboembolic material” comprising “aspirating thromboembolic material from a person using the system of claim 1 by,” among other limitations, “positioning the distal end of the catheter at least proximate to thromboembolic material in a blood vessel of the person.” Claim 1, from which claim 11 depends, in turn recites “[a]n aspiration thrombectomy system” using “a controller configured to open and close the vacuum valve and the vent valve in a predetermined cycle” “to control fluid flow in and out from the distal end of the catheter.” Simply put, claim 11 recites a method to achieve clot aspiration using controlled fluid flow in and out of the catheter’s distal end in a predetermined cycle, where the catheter’s distal end is placed next to the clot in the blood vessel. Neither of Petitioner’s grounds render this method obvious.

First, even if Petitioner had argued for combining Mullins with Yang or Ofek without using Mullins’s pressure sensor-based feedback approach, Petitioner fails to offer any evidence that a POSA would have a reasonable expectation of success in achieving clot aspiration using fluid flow in and out of the catheter tip in a predetermined cycle—without Mullins’s sensor.

Second, given the complexities of aspirating clots, a POSA would not have had a reasonable expectation of success in achieving clot aspiration using fluid flow in and out in a predetermined cycle.

Third, Petitioner’s Ofek/Mullins combination fails because it involves removing clots from within a catheter rather than “positioning the distal end of the catheter at least proximate to thromboembolic material in a blood vessel of the person,” as claim 11 requires.

A. Petitioner Fails To Offer Any Evidence That A POSA Would Have A Reasonable Expectation Of Success In “Aspirating Thromboembolic Material From A Person” By “Control[ling] Fluid Flow In And Out” “In A Predetermined Cycle”

Even if Petitioner had proposed combining Yang or Ofek with Mullins without using Mullins’s pressure sensor-based feedback approach (i.e., using a predetermined cycle), Petitioner’s argument would still fail because Petitioner offers no evidence that a POSA would have a reasonable expectation of success in achieving clot aspiration using fluid flow in and out of the distal end of the catheter without incorporating Mullins’s pressure sensor.

Petitioner had to show a POSA would have had a reasonable expectation of success in arriving at a proposed combination that meets the claim requirements, which include “aspirating thromboembolic material from a person” using a “predetermined cycle” to control “fluid flow in and out.” Ex.1001, cls. 1, 11; *see Intelligent Bio-Systems v. Illumina Cambridge*, 821 F.3d 1359, 1367 (Fed. Cir. 2016) (“one must have a motivation to combine accompanied by a reasonable expectation of achieving **what is claimed in the patent-at-issue**”); *KEYnetik, Inc. v. Samsung Elecs. Co.*, 841 F. App’x 219, 227 (Fed. Cir. 2021) (“Where a party argues a skilled

artisan would have been motivated to combine references, it must show the artisan ‘would have had a reasonable expectation of success from doing so.’”). Petitioner cannot meet its burden by arguing that a combination is well-known or simple. *Juniper Networks, Inc. v. Correct Transmission, LLC*, No. 2023-1046, 2024 WL 3517862, at *5 n.3 (Fed. Cir. July 24, 2024) (“While [Petitioner’s expert] testified that synchronizing forwarding tables was ‘very well known’... that testimony alone does not demonstrate a reasonable expectation of success in combining these particular prior art references.”); *id.* at *6 (“[Petitioner] presented no theory other than that the combination was simple.”).

Here, as in *Juniper Networks*, Petitioner only offers expert testimony that pressure sensors were well-known and that combining Mullins’s pressure sensors with Yang’s or Ofek’s system would have been simple to do. While Petitioner asserts that a POSA would have been able to implement this combination, Petitioner provides no evidence that a POSA would have had a reasonable expectation of success in “aspirating thromboembolic material from a person,” as claimed, without using Mullins’s pressure sensor.

For the Yang/Mullins combination, Mr. Brown only addresses “a reasonable expectation of success” in stating, “[a] POSA would have had a reasonable expectation of success *in implementing this combination*, because any modification, if necessary, *would simply add additional control logic from Mullins’ system for*

modulating the pressures contained within the aspiration system, in accordance with the preferable pressure cycles as taught in Yang.” Ex.1005 ¶101; Culbert POR-Decl. ¶89. Mr. Brown makes an almost verbatim statement for the Ofek/Mullins combination. Ex.1005 ¶360. Thus, Mr. Brown only argues, at best, that Yang and Ofek are technically compatible with Mullins—not that they would have been combined to meet the claims’ limitations. Indeed, rather than address why a POSA would have a reasonable expectation of success in aspirating clots without using Mullins’s pressure sensor, Petitioner entirely glosses over claim 11’s step of “aspirating thromboembolic material from a person using the system of claim 1.” Petitioner incorrectly posits that this step is part of the preamble—even though it follows “comprising:”—and simply refers to its earlier arguments without addressing this step in claim 11. Pet. 5, 49, 98.⁵ Mr. Brown does the same. Ex.1005 ¶¶261, 477.

In sum, Petitioner failed to offer evidence that a POSA would have had a reasonable expectation of successfully aspirating clots by controlling fluid flow in and out in a predetermined cycle, as claim 11 requires, for either its Yang/Mullins

⁵ Even assuming “aspirating thromboembolic material from a person” is part of claim 11’s preamble, which is not the case, Petitioner makes no argument that the claim 11’s preamble is not limiting—nor would such an argument be correct.

or Ofek/Mullins combination. Even viewing Petitioner’s evidence in the most charitable light, Petitioner has offered only a single, conclusory sentence to try to support a reasonable expectation of success when using Mullins’s “control logic ... for modulating the pressures” (i.e., reversing pressure when sensed pressure reaches a limit), which is not a “predetermined cycle.” Ex.1005 ¶¶101, 360.

B. A POSA Would Not Have A Reasonable Expectation Of Success In Achieving “Aspirati[on] [Of] Thromboembolic Material From A Person” By “Control[ling] Fluid Flow In And Out” “In A Predetermined Cycle”

Beyond the deficiency in Petitioner’s contentions addressed above, a POSA would *not* have had a reasonable expectation of success in combining Yang or Ofek with Mullins—without using Mullins’s sensor feedback-based approach—to achieve clot aspiration using a predetermined cycle of fluid flow in and out from the catheter’s distal end.

At institution, the Board cited Mr. Brown’s testimony that Yang “invites a POSA to experiment with different levels of positive pressure to find an optimal amount of positive pressure that would most efficiently aspirate a given clot,” and noted that “this issue can be further explored on a full trial record.” ID 23 (quoting Ex.1005 ¶166); *see also id.*, 36-37 (similar for Ofek/Mullins combination). Mr. Brown’s testimony provides insight into why a POSA would not have had a reasonable expectation of success in using a predetermined cycle of fluid flow in and

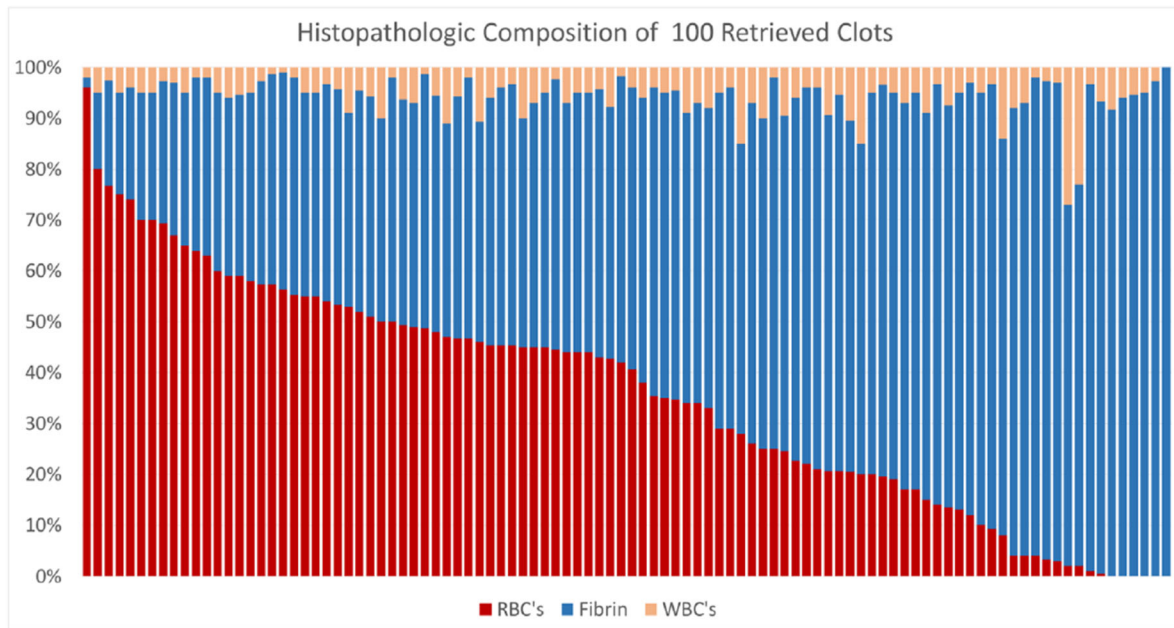
out from the catheter's distal end to achieve clot aspiration in either Yang/Mullins or Ofek/Mullins.

First, Mr. Brown admits that a POSA would experiment to try to find the “optimal amount of positive pressure that would most efficiently aspirate **a given clot**,” i.e., a POSA's experimentation would focus on optimizing efficiency for a particular clot. Ex.1005 ¶166. Mr. Brown's proposal to use pressure optimized to a particular clot is the opposite of pursuing a predetermined cycle to aspirate a clot. Culbert POR-Decl. ¶92. A predetermined cycle is, by definition, *independent* of the conditions in the catheter, such as the properties of the clot in the person (which are typically unknown before aspirating the clot), and must be designed to achieve clot aspiration regardless of the clot's properties. Ex.2006, 67:2-15 (Dr. Ross explaining that he “can't see the clot” and “do[es]n't know what it looks like” until “when it comes out and [he] can look at it”); Culbert POR-Decl. ¶92.

Mr. Brown admits that the clots' “mechanical properties”—one of the variables that affects conditions in the catheter during aspiration—can vary tremendously, depending on “the relative percentages of fibrin and red blood cells.” Ex.1005 ¶57; *see also* Ex.2018 (Brown Dep.), 95:1-7. There are “firm and sticky clots” that “can be challenging to remove from a vessel.” Ex.1005 ¶57; *see also* Ex.2018, 95:8-96:1. Other clots are “more friable” (i.e., more easily broken up) and “have a lower coefficient of friction,” such that they “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.” Ex.1005 ¶57; *see also* Ex.2018, 96:3-18. POSAs agree that clots vary substantially in size, density, and coefficient of friction (or “stickiness”) to the vessel walls. Ex.2018, 95:1-7, 96:20-97:3; Culbert POR-Decl. ¶93.

Published literature corroborates that, at the time of the invention in 2018, “[o]ne of the most important obstacles” in developing a device to remove clots was “the fact that clots tend to differ in consistency and removability,” such that one clot could be removed easily while the next may be “too resilient to be removed.” Ex.2021 (Brouwer 2018), 1-2. This literature confirms the “high variability” and “unpredictable nature of the clots” that POSAs “face on a daily basis.” *Id.*, 2. The figure below shows the “striking” “spread” in composition across “different clots.” *Id.*, 3.

**FIGURE 5.**

Histopathologic clot composition

Composition distribution of Red Blood Cells (RBC) Fibrin and White Blood Cells (WBC) in 100 clots retrieved from cerebral ischemic stroke patients. (Courtesy of M. Mirza MD, Neuravi/Cerenovus, Galway, Ireland)

Id., 17.

A POSA would not have had a reasonable expectation of success in implementing a predetermined cycle of flow in and out to aspirate a clot from a person in view of the tremendous variability in catheter conditions, including clot property variations. Culbert POR-Decl. ¶¶95-96. In a predetermined cycle, the parameters are, by definition, set in advance so there is no feedback based on conditions present in the catheter to adjust the applied pressure (as in Mullins). *Id.* ¶96. Mr. Brown effectively acknowledges that a POSA would not pursue—let alone have a reasonable expectation of success in implementing—such a one size-fits-all

approach. Instead, as he admits, a POSA would “experiment with different levels of positive pressure to find an optimal level of positive pressure that would most efficiently aspirate a given clot.” Ex.1005 ¶166; *see also* Ex.1023 ¶20 (Dr. Ross testifying that the operator of an aspiration thrombectomy system would “monitor, control, and regulate the timing of the vent and vacuum valves”). But the “optimal level of positive pressure” to “efficiently aspirate” one clot may be vastly different than that to aspirate another clot due to the substantial variation in clot properties and other conditions of the catheter. Culbert POR-Decl. ¶96. A predetermined cycle, however, affords no opportunity to adjust the applied pressure to optimize it based on feedback from a sensor that depends on the conditions of the catheter. *Id.* ¶97.

A POSA would not have a reasonable expectation of success in using a predetermined cycle having flow in and out to aspirate clots because a POSA would not have reasonably expected the cycle to work without varying it to apply appropriate pressure given the state of the system, which depends on conditions in the catheter, such as the clot’s properties. Culbert POR-Decl. ¶97. Mr. Brown recognizes that 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.” Ex.1005 ¶63. If a POSA conservatively chooses a predetermined cycle that applies relatively low positive pressure to minimize the “risk of distal

migration,” then a POSA would expect this pressure to be insufficient to remove the “firm and sticky clots” that “can be challenging to remove.” *Id.* ¶57; Culbert POR-Decl. ¶98. On the other hand, if a POSA more aggressively chooses a predetermined cycle that applies relatively high pressure to remove such clots, “the risk of occlusions breaking off of the clot and traveling distally into the patient’s vessel increases.” Ex.1005 ¶63; Culbert POR-Decl. ¶98. Indeed, Mr. Brown acknowledges “the clinical safety concerns of positive exit flow pushing the clot material away from the distal end of the catheter to a distance that the reversed catheter pressure (vacuum) can no longer draw the clot back to the catheter.” Ex.1005 ¶¶293, 510 (same); *see also* Ex.2018, 98:13-99:14. Petitioner’s other expert, Dr. Ross—a neurosurgeon with over 30 years of experience (Ex.1023 ¶¶1, 5),—similarly recognizes, “[t]oo high a positive pressure increases the risk of fluid exiting the distal end of the catheter and of occlusive material breaking free of a clot and traveling distally in the vessel” (*id.* ¶19). He emphasizes the “**high importance** during aspiration thrombectomy procedures to **monitor and control** the level of vacuum at the distal end of the catheter to minimize the risks of forward flow.” *Id.*

Mullins’s approach of monitoring and controlling the pressure is intended to allow for removal of “harder, larger diameter, and longer clots,” without applying too much positive pressure to clots that break up more easily. Ex.1008, 25:22-28. Mr. Brown notes that “[a] POSA would understand that Mullins limits the positive

exit flow to ensure that the clot is not entirely expelled from the catheter and therefore avoids risking any distal migration of the clot.” Ex.1005 ¶197; *see also id.* ¶433 (same). That is only possible when, as Mr. Brown admits, Mullins “us[es] upper and lower pressure limits to control ... measured amounts of flow displacement.” *Id.* ¶197; *see also id.* ¶433 (same). By contrast, a POSA would not have had a reasonable expectation of success in implementing a *predetermined cycle* of flow in and out to aspirate clots from persons because using it does not involve measuring pressure to sense whether it has reached a limit and adjusting the cycle accordingly. Culbert POR-Decl. ¶¶96-99.

Second, and relatedly, a POSA would not have had a reasonable expectation of success in implementing a predetermined cycle because, in a predetermined cycle, the timing is (by definition) fixed—not adjusted based on sensing whether, and to what degree, the catheter is clogged. Culbert POR-Decl. ¶99. In other words, the timing of the vent and vacuum valves opening and closing is applied without regard for whether the catheter is entirely open or clogged (either partially or fully) at a particular point in the cycle. *Id.* A POSA would not have had a reasonable expectation that this would successfully aspirate clots using flow in and out. *Id.* On the contrary, a POSA reasonably would have expected that this approach would have posed serious safety concerns. *Id.*

Depending on “whether there is free flow through the catheter versus a clogged catheter,” the pressure within the catheter and the amount of pressure differential (and as a result, the duration that each pressure is applied) can vary substantially. Ex.2018, 85:1-4, 85:16-86:1; Culbert POR-Decl. ¶100. Indeed, Mullins relies on this pressure variation to control timing of the cycle, ensuring that vacuum is applied when the catheter is in a free-flow condition and positive pressure is only applied when the catheter is sufficiently clogged. *Id.* ¶¶100-101. Mullins senses that the magnitude of negative pressure is significantly greater when a clot clogs the catheter compared to when there is “free-flow,” triggering reversal of flow when the measured negative pressure reaches the “Low Limit.” Ex.1008, 26:55-27:19, *see also* Ex.2018, 87:20-88:4. Similarly, Mullins relies on the fact that the pressure builds in the opposite direction, until the “High Limit” is reached, before reversing to apply vacuum. Ex.1008, 27:27-30, *see also* Ex.2018, 90:7-91:5.

A POSA would recognize that, using a predetermined cycle, there is no way to ensure that only the vacuum phase is used during free flow and only the vent phase is used when the catheter is clogged. Culbert POR-Decl. ¶101. Because the cycle timing is predetermined, the vent phase can be applied when the clot has already been unclogged and there is free flow of fluid through the catheter. *Id.* A POSA reasonably would have expected that this would risk excessive flow out, presenting

“the inherent and well-known risks of distal clot migration.” Ex.1005 ¶81; *see also id.* ¶250; Ex.2018, 98:13-99:14; Culbert POR-Decl. ¶101.

Indeed, Petitioner’s expert Dr. Ross explains that at the time of the invention, a POSA would have understood that monitoring and controlling the timing of the vent and vacuum valves—the exact opposite of implementing a predetermined cycle—is necessary to provide safety. He testified that, to reduce the risk of excessive flow out, POSAs “understood, well before 2019, that the operator of the system ***should monitor, control, and regulate the timing*** of the vent and vacuum valves to maintain the levels of suction force, as described in Mullins, Yang, Ofek, and Grey, thereby preserving sufficient levels of pressure contained in the vacuum aspiration system.” Ex.1023 ¶20.

Dr. Ross further explains why a POSA would not have had a reasonable expectation of success in using fixed timing, i.e., a predetermined cycle, to aspirate clots using flow in and out. If the vent phase applying positive pressure has “[t]oo short of a duration,” then this “will not allow the clot to experience a sufficient degree of accelerated forces to break it up[;] however,” if the vent phase is applied for “too long,” then this “may lead to undesirable forward flow.” Ex.1023 ¶20. As discussed, a POSA would reasonably expect what is “too short” or “too long” a vent phase to depend on, among other things, the properties of the particular clot being aspirated. *Supra* at 40-41. Accordingly, Dr. Ross admits that a POSA would

“manipulat[e] the timing of the opening and closing of the vacuum and vent valves *to adjust the timing* of the pressure change at the distal end of the catheter,” “to maximize efficiency of the clot digestion” while maintaining safety. *Id.* In other words, a trained neurosurgeon who regularly applies, in a clinical setting, “principles of flow reversal” and “clot aspiration” (*id.* ¶8), would **not** use a predetermined cycle. Mr. Brown agrees that a POSA “would recognize that *monitoring and controlling the frequencies of the cycles would be necessary to minimize the risks*” of flow out from the catheter’s distal end. Ex.1005 ¶250. Both Petitioner’s experts independently reached these consistent conclusions without speaking to each other. Ex.2018, 7:1-2; Ex.2017, 7:17-20.

Thus, as Petitioner’s own expert testimony confirms, a POSA would not have reasonably expected to succeed in aspirating clots from persons using a predetermined cycle of flow in and out from the catheter’s distal end, as claim 11 requires. Culbert POR-Decl. ¶¶103-105. Instead, as Mullins teaches and advocated by Petitioner’s experts, a POSA would have monitored pressure and adjusted the cycle based on the measured pressure—the opposite of using a predetermined cycle—to address the variation in catheter conditions, including those caused by variations in clot properties, while maintaining safety. Accordingly, Petitioner’s proposed Yang/Mullins and Ofek/Mullins combinations fail to render claim 11 obvious.

C. Ofek/Mullins Does Not Render Obvious Positioning The Distal End Of The Catheter As Claimed

Petitioner's Ofek/Mullins combination fails for the additional reason that Ofek does not disclose or suggest "positioning the distal end of the catheter at least proximate to thromboembolic material in a blood vessel of the person," as claim 11 requires. Petitioner erroneously argues that "Ofek discloses an aspiration thrombectomy system, for which a central aspect is positioning the distal end of the catheter next to the thrombus and applying Mullins's technique to Ofek would entail placing the catheter tip adjacent to the clot." Pet. 98. Petitioner cites nothing from Ofek to support this statement—nothing does. Ofek does not disclose placing the catheter tip adjacent to a clot in a blood vessel of a person. Culbert POR-Decl. ¶107. Ofek is a "patency device [that] establishes and/or preserves patency of one or more lumens defined by the catheter assembly"—i.e., a device for keeping the catheter lumen unobstructed—not for removing a clot in a blood vessel of a person. Ex.1007, 1:16-23 (quoted at ID 27); Culbert POR-Decl. ¶107. As the Board recognized at institution, Ofek "describe[s] catheters *that may have a thrombus in the lumen*"—not removing a thrombus "in the blood vessel of a person" as claim 11 requires. ID 33.

At institution, the Board stated, "Ofek explains that the catheter can be used for aspirating a thrombus at the distal end of the catheter." ID 33 (citing Ex.1007, 2:56-3:2; Ex.1005 ¶374). But the cited passage only teaches "prevent[ing] the

formation of thrombus or other occlusion *in the lumen 14*, especially at the distal end thereof,” and that “high pressure pulses can also be used to clear the lumen after *occlusions have formed therein*.”⁶ Ex.1007, 2:56-3:2. Ofek does not teach removing a thrombus outside the catheter lumen, “in a blood vessel of [a] person” by “positioning the distal end of the catheter at least proximate” to it. Ex.1001, cl. 11; Culbert POR-Decl. ¶107.

Petitioner’s proposal to “apply[] Mullins’s technique to Ofek” does not help Petitioner. Pet. 98. Applying Mullins’s technique of using feedback from a pressure sensor to adjust Ofek’s cycle would simply modify how Ofek prevents the formation of, or clears, occlusions in the catheter lumen. Culbert POR-Decl. ¶108. That still would not involve “positioning the distal end of the catheter at least proximate to thromboembolic material in a blood vessel of the person,” as claim 11 requires. Petitioner does not argue that Ofek would be modified in any respect to meet the “positioning” requirement or provide a motivation to do so.

Thus, Petitioner’s argument for claim 11 based on its Ofek/Mullins combination fails because it does not “position[] the distal end of the catheter at least

⁶ The cited paragraph of Mr. Brown’s declaration (Ex.1005 ¶374) just reiterates the Board’s statement, citing the same disclosure.

proximate to thromboembolic material in a blood vessel of the person.” Culbert POR-Decl. ¶108.

VI. Petitioner Fails To Demonstrate That The “Amount Of Exit Flow” Claims—Claims 3-4, 14, And 16-17—Are Rendered Obvious By Yang/Mullins Or Ofek/Mullins

Claims 3-4, 14, and 16-17 require specific amounts of exit flow. Each claim requires limiting the “positive amount of exit flow” to specific amounts “before fluid is drawn back into the catheter lumen” by applying vacuum. In claims 3 and 16, the amount is “approximately 0.001 ml to approximately 1.0 ml” and in claims 4 and 17 is “approximately 0.1 ml to approximately 0.5 ml.” Claim 14 recites the amount is “approximately 0.5 mm to approximately 30 mm of the fluid column.” Neither Yang/Mullins (Ground 1) nor Ofek/Mullins (Ground 4) renders these claims obvious.

None of Yang, Ofek, or Mullins disclose any particular amount of acceptable exit flow. Petitioner admits that “Yang/Mullins doesn’t specify a particular value of acceptable exit flow.” Pet. 42. Ofek does not disclose any amount of exit flow either. Culbert POR-Decl. ¶110. Dr. Ross further explains that forward flow, or exit flow, is “something that we seek to avoid and generally doesn’t happen.” Ex.2006, 18:24-19:11. But still, Petitioner argues that “a POSA would understand approximately 0.001 ml to approximately 1.0 ml to be reasonable values for implementation and/or would perform routine optimization resulting in that range,”

and relies on this reasoning for both combinations for claims 3-4 and 16-17. Pet. 42 (cl. 3, Yang/Mullins); *see also id.*, 91 (similar, cl. 3, Ofek/Mullins); *id.*, 43, 92 (cl. 4); *id.*, 52-53, 102 (cls. 16-17). As to claim 14, Petitioner contends that “[a] POSA would understand the values of approximately 0.5 mm to approximately 30 mm of fluid column to be a reasonable distance” and “would understand how to convert the exit flow volumes described [for claim 3] to respective values of exit flow length.” *Id.*, 51-52 (Yang/Mullins), 101 (similar for Ofek/Mullins).

Petitioner’s obviousness arguments for claims 3-4 and 16-17 fail. Petitioner’s assertion, in hindsight, that the claimed amounts are “reasonable” is based on nothing more than *ipse dixit* expert testimony entitled to no weight. 37 C.F.R. § 42.65(a) (“Expert testimony that does not disclose the underlying facts or data on which the opinion is based is entitled to little or no weight.”); *see also Xerox Corp. v. Bytemark, Inc.*, IPR2022-00624, Paper 9 at 15-17 (P.T.A.B. Aug. 24, 2022) (precedential) (according “little weight” to an expert’s verbatim restatement of a petition’s conclusory assertions without additional supporting evidence or reasoning, also noting it is “particularly problematic in cases where expert testimony is offered not simply to provide a motivation to combine prior-art teachings, but rather to supply a limitation missing from the prior art”). Mr. Brown simply parrots Petitioner’s assertions. Ex.1005 ¶¶201, 438 (“a POSA would understand the values of approximately 0.001 ml to approximately 1.0 ml to be reasonable values”); *id.*

¶¶292, 509 (“POSA would understand the values of approximately 0.5 mm to approximately 30 mm of fluid column to be reasonable values”). Neither Petitioner nor Mr. Brown cite *any* evidence to support the “reasonable” nature of these values. They instead appear to work backwards from the ’402 Patent’s claims and specification to support their assertion of reasonableness, impermissibly using hindsight. *Sensonics, Inc. v. Aerosonic Corp.*, 81 F.3d 1566, 1570 (Fed. Cir. 1996) (“To draw on hindsight knowledge of the patented invention, when the prior art does not contain or suggest that knowledge, is to use the invention as a template for its own reconstruction — an illogical and inappropriate process by which to determine patentability.”). Regardless, declaring claimed quantities “reasonable” does not render them obvious. *Elbit Sys. of Am., LLC v. Thales Visionix, Inc.*, 881 F.3d 1354, 1359 (Fed. Cir. 2018) (“attorney argument is not evidence”).

Moreover, Petitioner’s attempt to show that a POSA would arrive at the claimed amounts through “routine optimization” actually proves the opposite. Pet. 42, 91. As explained below, Mr. Brown’s calculations purporting to show that a POSA would arrive at the claimed amounts are premised on flawed assumptions. His calculations reinforce that, without the benefit of hindsight, a POSA would not have found the claimed amounts of exit flow obvious.

Mr. Brown contends that “a POSA would have found it obvious to calculate and estimate particular values for the extent to which exit flow should be limited, as

invited to do by Yang and Mullins.” Ex.1005 ¶208. He proceeds to calculate values based on certain inputs and assumptions. Mr. Brown performs calculations for two catheter internal diameters—0.061" and 0.088". *Id.* ¶¶210, 218. Mr. Brown calculates “the flow rate of blood would be 1.0 mL/s” and “4.0 mL/s” for the 0.061" and 0.088" catheters, respectively. *Id.* ¶¶211, 218. To determine the amount of time the catheter would experience flow in versus flow out, Mr. Brown relies on Mullins’s disclosure of ratios of “infuse-to-aspirate cycles,” i.e., “cycle percentages for application of positive pressure versus negative pressure”: “0.01 and 0.99,” “0.1 and 0.9,” and “0.4 and 0.9.” *Id.* ¶214 (citing Ex.1008, 28:59-64). Although “0.4 and 0.9” (*id.*), appears to be a typographical error in Mullins because those values do not sum to 1, Mr. Brown computes the percentages of the total (1.3), that the 0.4 and 0.9 represent (31% and 69%, respectively), and uses those in his calculations. *Id.* ¶¶215, 219.

Mr. Brown presents tables of his calculations. *Id.* For example, he reports an exit flow of 3.1 mL for a cycle frequency of 0.100 Hz (i.e., 10 seconds) and infusion 31% of the time. Ex.1005 ¶215. To illustrate how his calculations work, he arrives at 3.1 mL by multiplying the blood flow rate (1.0 mL/second) by the cycle duration (10 seconds) and the percentage of that cycle when positive pressure is applied (31%). *Id.*

Mr. Brown's calculations rely on several flawed assumptions. *First*, he assumes that there is always free flow of blood through the catheter, so that blood flows at the same rate during both the positive pressure (infusion) and negative pressure (aspiration) portions of the cycle. Culbert POR-Decl. ¶115. That is wrong. Mr. Brown ignores that the entire point of applying positive pressure is to address a condition where the catheter is becoming partially or entirely clogged by a clot, requiring controlled fluid flow to try to dislodge and break up the clot, as he acknowledges elsewhere in his declaration. Ex.1005 ¶61; Culbert POR-Decl. ¶116. Mr. Brown has assumed away the entire reason to have any positive flow because his calculations "assume free flow of blood through the catheter" at all times. Ex.2018, 105:11-19; Culbert POR-Decl. ¶116. His calculations are thus incorrect and inapplicable because there will not be free flow of fluid either into or out of the catheter when it is at least partially clogged. Ex.2018, 93:21-94:17; Culbert POR-Decl. ¶116.

Second, Mr. Brown's assumption that flow rates in and out of the catheter are the same (in a free flow condition) indicates that he incorrectly assumes that the pressure level in the catheter is always the same magnitude (but opposite in direction) for the infusion and aspiration portions of the cycle. Ex.2018, 105:20-106:12, 107:3-10; Culbert POR-Decl. ¶117. Indeed, his flow rates were based on a study using "constant pressure of 600 mmHg." Ex.1005 ¶210. Again, Mr. Brown

assumes away the entire reason for applying positive pressure in the first place—to dislodge and break up a clot clogging the catheter. *Id.* ¶61; Culbert POR-Decl. ¶118. When a clot clogs the catheter, the pressure in the catheter varies substantially. Ex.2018, 85:16-86:1; Culbert POR-Decl. ¶118. At first, the vacuum pressure increases during the aspiration phase as the clot prevents fluid from entering the catheter, so the vacuum pressure increases. *Id.* ¶118; Ex.1008, 28:40-44 (“as the catheter becomes clogged, there is generally a rapid increase in the vacuum pressure”). Indeed, Mullins discloses detecting this increase in vacuum pressure and reversing pressure at a “Lower Limit” that indicates a clot is clogging the catheter. Ex.1008, 27:4-17. During the infusion phase, vacuum pressure inside the catheter is relieved and may reach a positive pressure. Culbert POR-Decl. ¶118. Mullins similarly relies on detecting a high pressure limit to determine when to resume aspiration, as the extent that the catheter is clogged is “one of the variables that will dictate the time it takes to hit the high limit.” Ex.2018, 90:16-91:5; Ex.1008, 27:27-53.

Mr. Brown’s assumption of instantaneous reversal from constant aspiration pressure to equal and opposite infusion pressure is also flawed. He assumes that constant exit flow will start the instant that infusion begins. Ex.1005 ¶215; Culbert POR-Decl. ¶119. But there will be no exit flow until sufficient fluid enters the catheter to relieve the built-up vacuum pressure due to the clog. Ex.2018, 93:21-

94:17; Culbert POR-Decl. ¶119. Thus, there would be no exit flow at all for many of the cycles Mr. Brown calculates. *Id.* He does not take into account that it takes time from when the pump begins to apply positive pressure until exit flow would occur. *Id.* Further, as the experts agree, to have flow out of the catheter’s distal end when it is in a patient, the pressure not only needs to be positive but further needs to exceed mean arterial pressure. *Id.*; Ex.2010, 126:15-21; *see also* ID 19. And even if the pressure is above mean arterial pressure, there may not be flow out if a clot is corking the catheter’s distal end, as Mr. Brown admitted. Ex.2010, 126:23-127:5; Ex.2018, 93:21-94:17. Thus, for many other cycles Mr. Brown calculates, there may be no exit flow until pressure builds up sufficiently to unclog the clot, and at that point there may be a release of substantial exit flow that would risk distal migration of the clot—which he admits is contrary to Mullins’s teachings. Ex.1005, ¶197 (“A POSA would understand that Mullins limits the positive exit flow to ensure that the clot is not entirely expelled from the catheter and therefore avoids risking any distal migration of the clot.”); Culbert POR-Decl. ¶¶119-20.

Third, Mr. Brown’s calculations are inapt because he fails to account for the physical characteristics of an aspiration thrombectomy system. His calculations do not account for the fact that an aspiration catheter is “an elongate, flexible tubular body.” Ex.1012, [0011]; Culbert POR-Decl. ¶121. Mr. Brown’s assumption that pressure instantaneously reverses from a constant aspiration pressure to an equal and

opposite infusion pressure effectively assumes an entirely rigid system. *Id.* That is wrong and is another reason his calculations are flawed. Because the catheter is flexible and has length, it takes time for vent fluid to relieve compression of the catheter during the aspiration phase and reach the catheter's distal end, which the '402 Patent explains is a "critical" factor. Ex.1001, 48:39-44; Ex.2018, 18:12-19:6; Culbert POR-Decl. ¶121.

As the '402 Patent explains, there are two sources of pressure waves that travel through the catheter in a real-world aspiration thrombectomy system having the vent valve that the claims require. When the catheter is partially or entirely clogged, it compresses due to the increase in vacuum pressure because it is compliant—not rigid. Ex.1001, 8:53-64, 43:4-12; Ex.2018, 20:2-10; Culbert POR-Decl. ¶122. This causes the catheter to store "potential energy" and act "like a spring," such that "a pressure pulse or pressure wave" is created that contributes significantly to exit flow when infusion relieves the built-up vacuum pressure. Ex.1001, 42:62-43:35; Ex.2018, 20:21-21:4; Culbert POR-Decl. ¶122. Mr. Brown disregards this effect (which would be present in Yang, just as in the '402 Patent). *Id.* In addition, he ignores that use of valves introduces a "water hammer effect"—"a pressure surge or wave caused ... when a valve closes suddenly," as both Yang and the '402 Patent recognize. Ex.1012, [0108]; *see also* Ex.1001, 43:48-57. As the '402 Patent states and Mr. Brown admits, this effect also can contribute significantly to exit flow.

Ex.1001, 42:62-65; Ex.2018, 22:19-23:15; Culbert POR-Decl. ¶123. It is remarkable that Mr. Brown assumes away the water hammer effect in his calculations, which depend only on the time infusion or aspiration pressure is applied, because Petitioner’s obviousness arguments against claims 1 and 3 *rely* on Yang’s disclosure of the water hammer effect. Pet. 31, 33, 39. But Mr. Brown disregards the pressure waves resulting from the catheter’s compliance and the water hammer effect—and the time that they take to traverse the length of the catheter—in his simplistic calculations that have no applicability to a real-world aspiration thrombectomy system. Culbert POR-Decl. ¶123.

Accordingly, Mr. Brown’s calculations reflect a complete failure to account for multiple critical aspects of the system that make his calculations insufficient to demonstrate obviousness. Culbert POR-Decl. ¶124. That Mr. Brown’s purported “routine optimization” fails to provide a reasoned basis for a POSA to arrive at the amounts of exit flow in claims 3-4, 14, and 16-17 only reinforces their non-obviousness. His calculations are nothing more than an attempt to justify the claimed amounts through spurious hindsight reasoning. *Univ. of Strathclyde v. Clear-Vu Lighting LLC*, 17 F.4th 155, 162 (Fed. Cir. 2021) (rejecting the Board’s obviousness finding relying on hindsight reasoning).

VII. Petitioner Fails To Show That The “Off-Off State” Claims (Claims 5-7 And 18-20) Are Rendered Obvious By Yang/Mullins Or Ofek/Mullins, With Or Without Rubenstein

Claims 5-7 and 18-20 recite an “off-off state” in which both the vacuum and vent valves are closed. Claims 5 and 18 require one such state, while claims 6-7 and 19-20 require two such states in each cycle. Petitioner fails to show that these claims are rendered obvious by Yang/Mullins (Ground 1), Ofek/Mullins (Ground 4), or in further combination with Rubenstein (Grounds 2 and 5).

A. The Off-Off State In Claims 5-7 And 18-20 Is A Purposeful State

The claimed “off-off *state*” is a purposeful *state*, not a mere incidental, momentary overlap as valves transition between open and closed states. Culbert POR-Decl. ¶130. The ’402 Patent explains that the off-off state is implemented to address practical considerations, such as the catheter’s length and compliance. Ex.1001, 48:39-51. For example, a properly tuned off-off state maximizes efficacy by being long enough for pressure pulses to traverse the catheter, while maintaining safety by being short enough to limit exit flow. *Id.*, 48:37-39. Specifically, the timing of the off-off state, as well as the vacuum and vent states, are optimized for “the dynamics/resonance/compliance/length of the particular catheter 660 and extension set.” *Id.*, 50:49-51.

B. Claims 5-7 And 18-20 Are Not Rendered Obvious By Yang/Mullins

Petitioner’s arguments that the off-off state claims are rendered obvious by Yang/Mullins fail. Yang does not disclose any off-off state. To the contrary, Yang

only discloses a state where both vacuum and vent valves are open—an “on-on state.” Culbert POR-Decl. ¶131.

Petitioner incorrectly argues that Yang discloses an off-off state based on Yang’s Figure 25, reproduced below.

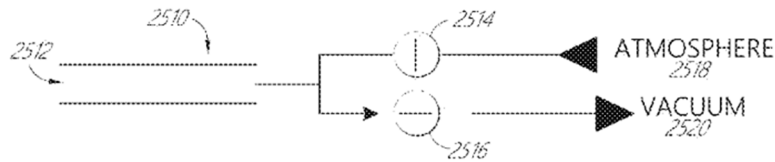


FIG. 25A

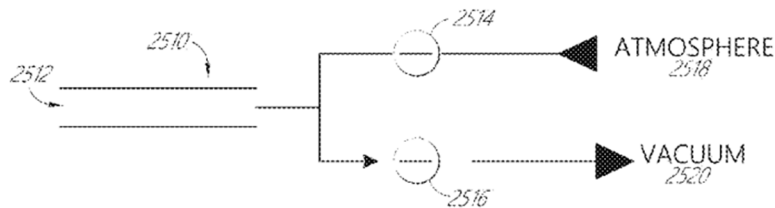


FIG. 25B

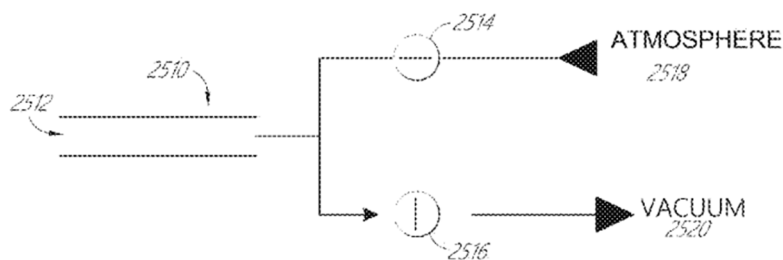
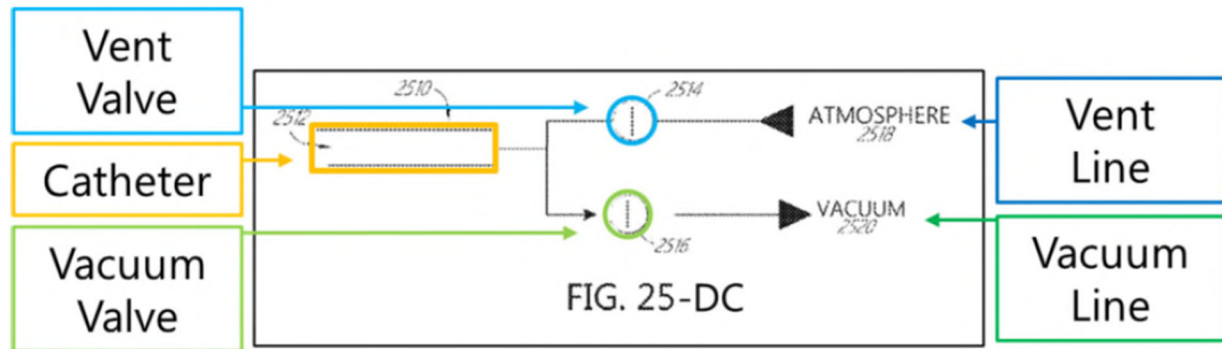


FIG. 25C

Ex.1012, Fig. 25. At least one valve is open in Figures 25A-25C, and both valves are open in Figure 25B. *Id.*, [0170]. There is an “on-on state” but no “off-off state.”

Petitioner argues that *after* Figure 25C, there would be an off-off state between Figures 25C and 25A when the cycle repeats and creates a new “FIG. 25-DC” (reproduced below), to illustrate it. Pet. 44-46.



Id., 45 (annotations in original). Relying on this created figure, Petitioner argues that Yang includes an “additional valve state” where both valves are closed. *Id.*, 44-45. But Yang’s Figure 25 does not include an off-off state, and Petitioner’s manufactured “FIG. 25-DC” has no basis in Yang. Ex.2018, 44:11-12; Culbert POR-Decl. ¶¶133-34. Yang only discloses the opposite—a state where both valves are open, shown in Figure 25B. Ex.1012, [0170]; Culbert POR-Decl. ¶134.

Petitioner relies on Yang’s disclosure that “another cycle from FIG. 25A to FIG. 25C begins by closing the release valve 2514 and opening the vacuum valve 2516.” Ex.1012, [0170] (cited at Pet. 44). But this does not support Petitioner’s argument. That paragraph merely states that one valve is closed, “and” another is opened. *Id.*; Culbert POR-Decl. ¶135. There is no disclosure of closing the release

valve before opening the vacuum valve, or that doing so would serve any purpose. Culbert POR-Decl. ¶¶133-37.

Petitioner’s argument that a POSA would have implemented the off-off state Petitioner manufactured lacks merit. Culbert POR-Decl. ¶¶138-40. Mr. Brown relies on Yang paragraph 168 to argue that “the logical approach” for “allowing the full force of the vacuum to be exerted on the clot” is to have an off-off state. Pet. 45; Ex.1005 ¶233 (citing Ex.1012, [0168]). But Yang paragraph 168 discusses how “[m]erely stopping the vacuum is not sufficient to loosen the clot,” and thus “[c]ompletely releasing (venting to atmospheric pressure) the vacuum and allowing the clot to relax before reapplying a vacuum is found to aspirate the corked clot most efficiently.” Ex.1012, [0168]. Yang thus teaches not only closing the vacuum valve but also opening the vent valve. *Id.* But rather than teach closing the vacuum valve *before* opening the vent valve (as Petitioner proposes), Yang teaches exactly the opposite—closing the vacuum valve *after* opening the vent valve. Ex.1012, [0170], Fig. 25B; Culbert POR-Decl. ¶134. And instead of operating the valves in serial as Petitioner suggests, a POSA would only find it obvious to operate both valves simultaneously, resulting in no off-off state. *Id.* ¶¶135-39. Furthermore, a POSA would not find any reason to implement Petitioner’s “FIG. 25-DC” because it does not result in any water hammer effect. *Id.* ¶¶133, 139.

Petitioner also argues that claims 6 and 19, which require a second “off-off” state in each cycle, are rendered obvious by Yang because “a POSA would find [it] obvious to modify [Figure 25B] to become a[n off-off] state because, in progressing to the vent-only state (*see* Fig. 25C), the vacuum valve would already need to be turned off.” Pet. 46-47. Again, Petitioner’s argument directly contradicts Yang’s express teaching to have an on-on state, as shown in Figure 25B, rather than the claimed off-off state. Ex.1012, [0170]; Culbert POR-Decl. ¶141. Neither Petitioner nor its expert identifies any reference disclosing an off-off state or teaching in the prior art to implement one. The only reference Mr. Brown cites as purportedly providing such a teaching, Ofek, merely discloses that when one valve “is opened” the other “is shut”—not having both valves shut. Ex.1005 ¶243 (citing Ex.1007 at 5:49-62). Petitioner is improperly arguing, in hindsight, to reconstruct the claimed invention by modifying Yang to operate *opposite* to its disclosed operation. Culbert POR-Decl. ¶141; *Sensonics*, 81 F.3d at 1570.

C. Claims 5-7 And 18-20 Are Not Rendered Obvious By Ofek/Mullins

Ofek/Mullins likewise fails to render the off-off state claims obvious. Petitioner argues that serial valve operation will lead to finite delays between closing one valve and opening another, resulting in off-off states, relying on Ofek’s disclosure that, “[d]uring each impulse when the [N.C.] valve [i.e., vent valve] 140 is opened, the N.O. valve [i.e., vacuum valve] 150 is shut ... Between each impulse

and after the series of impulses has ended, the N.C. valve 140 closes and the N.O. valve 150 opens.” Ex.1007, 5:55-65, Pet. 92. Petitioner relies on Ofek’s Figure 10, reproduced below, to argue that when the “Energy” is at the baseline “0,” the cycle would have off-off states. Pet. 94.

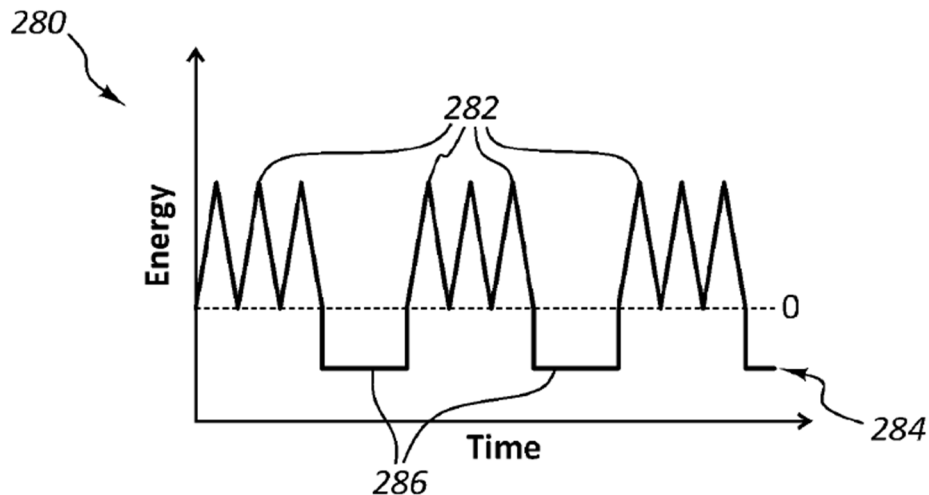


Fig. 10

Ex.1007, Fig. 10. But there is no period (i.e., flat section) at baseline “0,” nor is there any period at the peak “Energy,” only sharp transitions from closing one valve to opening another, indicating that the valves are operated simultaneously. Culbert POR-Decl. ¶143. Nowhere does Ofek disclose that the valves are operated serially. Similar to Yang, Ofek only discloses closing the vent valve *and* opening the vacuum valve—“the [vent] valve 140 closes *and* the [vacuum] valve 150 opens”—not that one valve closes before the other opens. Ex.1007, 5:63-6:2. Petitioner’s arguments fail.

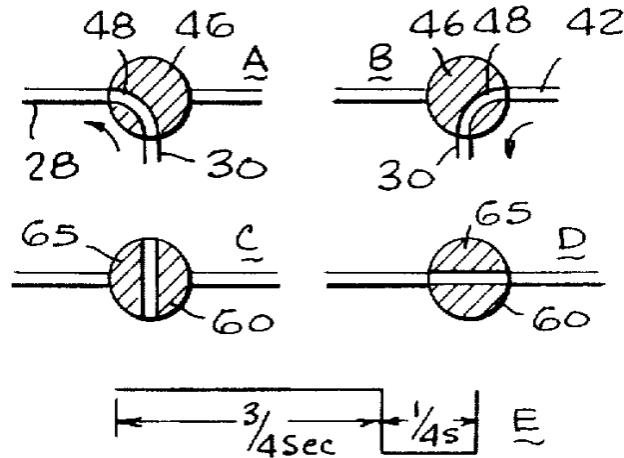
Petitioner further argues that Ofek would disclose an off-off state if it employed a rotary three-way valve because there would be an off-off state when that valve transitions from one state to another. Pet. 93. But Ofek does not mention a “rotary” three-way valve, and other three-way valves, e.g., linear three-way valves, would not necessarily have such an off-off state. Culbert POR-Decl. ¶144; *see also* Ex.2018, 58:5-7. Additionally, Ofek does not disclose or even suggest Petitioner’s hypothetical “transition” period between the vent and vacuum positions. Culbert POR-Decl. ¶145. And as discussed above, the claims require an “off-off state”—not merely a momentary transition between open and closed states. *Id.* ¶130. Furthermore, as discussed below, the Board has already recognized that rotary valves do not render obvious an off-off state.

Thus, Petitioner fails to show that Ofek/Mullins renders the off-off state claims obvious.

D. Claims 5-7 And 18-20 Are Not Rendered Obvious By Rubenstein

Petitioner argues that the off-off state is rendered obvious by Rubenstein’s additional teachings. Petitioner relies on Rubenstein’s rotary valves, arguing that because “Rubenstein’s rotary valves *rotate* between their different positions rather than making an instantaneous transition,” Rubenstein would have an off-off state during the valve transition. Pet. 57-63 (emphasis in original).

Petitioner's argument was considered by the Board twice and found unpersuasive. Petitioner previously argued that Rubenstein's rotary valves are not instantaneous and that both valves are closed during rotation. Ex.2022 (IPR2021-01466, Paper 7), 38; Ex.2023 (IPR2022-00608, Paper 7), 44. The Board disagreed, explaining "that Rubenstein does not appear to disclose a[n off-off] state" because even when Rubenstein's vent valve is closed, the vent source is still connected to the catheter, and thus, positive pressure fluid still flows to the catheter. Ex.2022, 39-40; Ex.2023, 45-46. This is because Rubenstein discloses a valve 18/46 that has two different open states—one open to vacuuming, and the other open to venting. As shown in Rubenstein's Figure 2 (reproduced below), valve 18/46 switches between a first open state (on the left below) "to have the channel 47 permit fluid flow between the tubing 28 and the tubing 30 such that negative pressure is applied" and a second open state (on the right below) "to permit fluid flow between the tubing 42 and the tube 30 such that positive pressure is applied." Ex.1011, 3:32-36. Rubenstein does not disclose any state where both valves are closed. Culbert POR-Decl. ¶148.



Petitioner manufactures a transition period of valve 18/46 to argue that it renders obvious an off-off state, but that argument should be rejected. Pet. 57-63. Petitioner's new figures depicting a transition period are not shown or described in Rubenstein. *Id.*, 58 (bottom), 61; Ex.2018, 119:13-120:6. Instead, waveform E in Rubenstein's Figure 2 above, which depicts "operation of the subject invention," shows a step pressure change when valve 18/46 switches between suction (the first 3/4 second) and blowing (the last 1/4 second). Ex.1011, Fig. 2. Thus, the more reasonable interpretation of Rubenstein is that channel 48 and plug of Rubenstein's three-way valve 18/46 are sized, and the rotation is timed, so that there is no delay time between switching from tubing 28 (first open state) to tubing 42 (second open state). Culbert POR-Decl. ¶149. And regardless, Petitioner's hypothesized momentary transition is not the "off-off state" that the claims require. *Id.* ¶149.

E. A POSA Would Not Find The Off-Off State Claims Obvious

In addition to the failings of the prior art identified above, a POSA would not have found it obvious to implement an off-off state in Yang/Mullins or Ofek/Mullins, alone or with Rubenstein. Petitioner entirely misses the reasons for implementing an off-off state, which highlights its non-obviousness. As the '402 Patent explains, implementing a defined time duration of an off-off state allows sufficient time for the pressure pulse created by opening a valve to traverse the length of the catheter to reach the clot, but ensures the off-off state is not too long so that the vacuum valve is opened quickly enough to avoid too much flow out of the distal end. Ex.1001, 47:28-48:21; Culbert POR-Decl. ¶¶151-52. Thus, a properly tuned off-off state maximizes efficacy by being long enough for the pressure pulses to traverse the catheter, while maintaining safety by being short enough to limit flow out. Ex.1001, 48:37-39, Culbert POR-Decl. ¶¶152-55.

The implementation and timing of the off-off state would not have been obvious to a POSA because of the multiple purposes and complexity of the off-off state—none of which is identified by Petitioner's prior art references or Petitioner's expert. Culbert POR-Decl. ¶¶152-55. Thus, Petitioner fails to show that the off-off state claims in claims 5-7 and 18-20 are rendered obvious.

VIII. Objective Indicia Of Non-Obviousness

Objective evidence of non-obviousness—such as long-felt but unmet need and failure of others—“may often be the most probative and cogent evidence in the record” and “must be considered in *every* case.” *WBIP, LLC v. Kohler Co.*, 829 F.3d 1317, 1328-37 (Fed. Cir. 2016) (emphasis in original); *see also Polaris Indus. Inc. v. Arctic Cat, Inc.*, 882 F.3d 1056, 1071-72 (Fed. Cir. 2018). Such evidence serves “to ‘guard against slipping into use of hindsight’ ... and to resist the temptation to read into the prior art and teachings of the invention.” *Graham v. John Deere Co. of Kan. City*, 383 U.S. 1, 36 (1966).

A. The Claimed Invention Satisfied A Long-Felt But Unmet Need

At the time of the claimed invention in July 2018, aspiration thrombectomy faced many challenges. Culbert POR-Decl. ¶158. The commonly used techniques were thrombectomy systems such as a stent retriever, which as Petitioner’s expert Dr. Ross explained, “was proven to be safe” and “effective.” Ex.2006, 38:2-39:2. As he explained, “the biggest concern [of aspiration thrombectomy] is it’s not going to work,” because “[i]t’s just very dangerous” and “[y]ou could push clots.” *Id.*, 39:14-40:20. As Petitioner’s other expert, Mr. Brown explained, there was a long-felt but unmet need in the field of aspiration thrombectomy “for a thrombectomy device that does not cause thrombus to break free and embolize,” because that “would have clinical complications associated with it,” such as “a stroke.” Ex.2024,

62:12-63:18. The '402 Patent confirms that when positive pressure at the distal end leads to significant flow out, it “can and does remove thrombi off of the distal end and risk sending thrombi further distally in the vasculature.” Ex.1001, 3:10-20; Culbert POR-Decl. ¶158.

Mr. Brown explained that the “other need in the area of thrombectomy is also a device that’s able to break up the clot,” “[b]ecause the clot would stick in the end of the catheter and would not be aspirated.” Ex.2024, 64:9-65:19. A failure to aspirate would mean that the thrombus is not removed, and as a result, the patient’s risk of ischemic stroke would remain. Culbert POR-Decl. ¶158. Because of these long-felt but unmet needs, Dr. Ross “evolved to using stent retriever technology more than aspiration thrombectomy technology.” Ex.2006, 39:10-12.

The long-felt but unmet needs for better thrombectomy devices was quantified in February 2018, prior to the claimed invention, when a published study introduced a “novel measure for newer generation devices.” Ex.2025 (First Pass Effect), 1; Culbert POR-Decl. ¶159. The study introduced the metric of “first pass effect (FPE),” “defined as achieving a complete recanalization with a single thrombectomy device pass.” Ex.2025, 1. In other words, the FPE rate is the rate at which the thrombus was removed in applying a thrombectomy device the first time. Culbert POR-Decl. ¶159. The FPE rate was quickly recognized as a key metric because it is

associated with patient outcomes. *Id.* Dr. Ross agreed that it is better “to achieve your goal in one pass.” Ex.2006, 33:2-6; *see also* Ex.2017, 56:1-21.

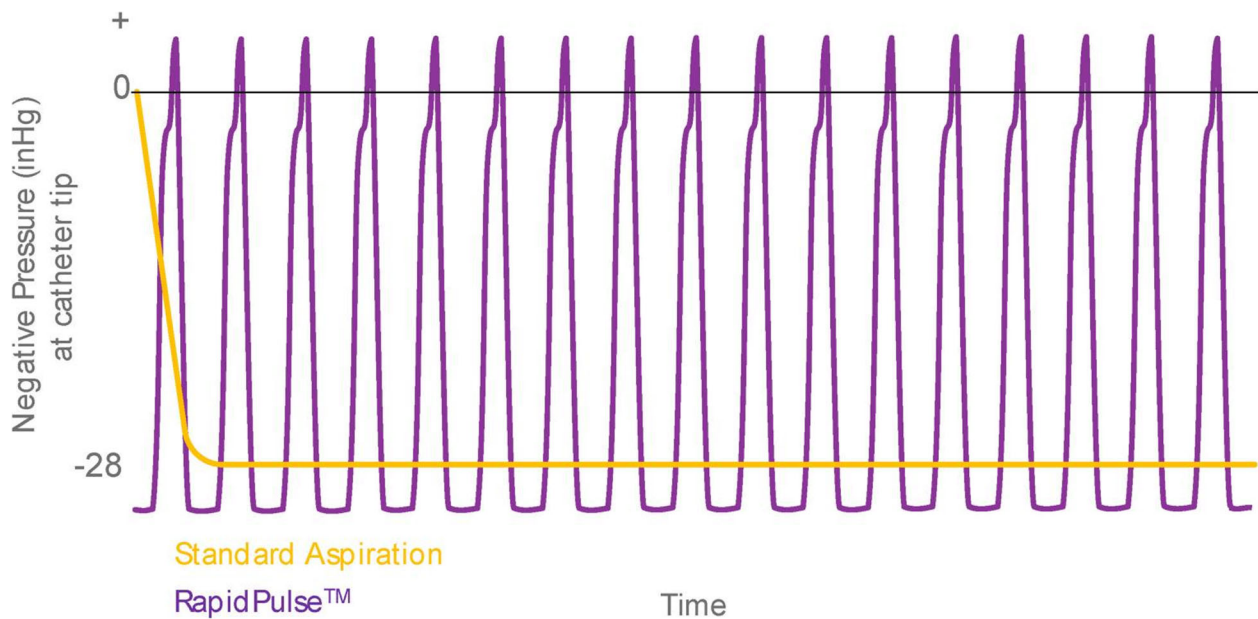
The February 2018 study showed that, in “[a] total of 354 acute ischemic stroke patients [who] underwent thrombectomy,” FPE was achieved in only “89 out of 354 (25.1%)” patients. Ex.2025, 1. Dr. Ross confirmed the low FPE rate, explaining that “it would be a low percentage of time that I get all the clot out because there’s just -- I use it when there’s just tons and tons of clot and I know that I’m going to have to go up many times.” Ex.2006, 34:7-21.

The unmet need for improved aspiration thrombectomy devices was met by Patent Owner’s invention through extensive research and development. Compared to other thrombectomy devices at the time that only achieved FPE rates of lower than 50%, the RapidPulse™ Cyclic Aspiration System (hereinafter “the Aspiration System”) achieves FPE rates of at least 60%. Culbert POR-Decl. ¶161; Ex.2026, 2; Ex.2027, 2; Ex.2028, 1. The significantly increased FPE addressed both the unmet need for “a thrombectomy device that does not cause thrombus to break free and embolize” and “a device that’s able to break up the clot.” Culbert POR-Decl. ¶161; Ex.2024, 62:12-63:18, 64:9-65:19. And as Dr. Ross explains, the claimed invention is still relatively new as he has not yet used any device that performs dynamic aspiration in an automated way in his practice. Ex.2017, 56:1-21.

B. A Strong Nexus Exists Between The Objective Evidence And The Claimed Invention

There is a strong nexus between the unmet needs of the thrombectomy devices and the claimed invention. Absent a presumption of nexus, “the patent owner is still afforded an opportunity to prove nexus by showing that the evidence of secondary considerations is the ‘direct result of the unique characteristics of the claimed invention.’” *Volvo Penta of the Ams., LLC v. Brunswick Corp.*, 81 F.4th 1202, 1210 (Fed. Cir. 2023).

Here, a presumption of nexus applies and, regardless, the evidence shows that the improved FPE is due to Patent Owner’s Aspiration System claimed in the Challenged Claims. Culbert POR-Decl. ¶162. The Aspiration System used a “commercially available ... thrombectomy catheter and thrombectomy pump,” showing that the catheter and the pump were not the causes for the device’s success. *See, e.g.*, Ex.2027, 3. Rather, the difference in the Aspiration System is that it used “a controllable valve system that intermittently cycles and vacuum pressure” by “alternately open[ing] and clos[ing] the vacuum line and a saline-filled vent line.” *Id.* As shown below, the Aspiration System operated in accordance with the ’402 Patent claims, using a predetermined cycle that produces positive pressure at the distal end (causing exit flow when unclogged).



Ex.2027, Fig. 1; Culbert POR-Decl. ¶162. The timing and method of the valve system is based on the claimed off-off state in claims 5-7 and 18-20, the claimed method of removing thromboembolic material in claim 11, and the amounts of exit flow in claims 3-4, 14, and 16-17. *Id.* Thus, the claimed invention was the driving factor resulting in improved FPE. *Id.*

IX. Conclusion

For the reasons set forth above, Petitioner fails to establish by a preponderance of the evidence that the challenged claims are unpatentable. Accordingly, the claims should be confirmed under 35 U.S.C. § 316.

Respectfully submitted,

Dated: May 30, 2025

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CERTIFICATE OF COMPLIANCE WITH 37 C.F.R. § 42.24

I hereby certify that this Patent Owner Response complies with the word count limitation of 37 C.F.R. § 42.24(b)(2) because the Patent Owner Response contains 13,816 words using Microsoft Word's counting feature, excluding the cover page, signature block, and the parts of the Patent Owner Response exempted by 37 C.F.R. § 42.24(b)(2).

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CERTIFICATE OF SERVICE

Pursuant to 37 C.F.R. § 42.6(e), I certify that on this 30th day of May, 2025, a true and correct copy of the foregoing **Patent Owner Response and all Exhibits** were served by electronic mail on Petitioner's lead and backup counsel at the following email addresses:

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