

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

PENUMBRA, INC.
Petitioner

v.

RAPIDPULSE, INC.
Patent Owner

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

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

DECLARATION OF DR. IAN ROSS

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List of Materials Considered

1001	U.S. Patent No. 11,406,402 (“the ’402 Patent”)
1007	U.S. Patent No. 10,322,230 (“Ofek”)
1008	U.S. Patent No. 11,197,977 (“Mullins”)
1010	International Application No. WO 2014/151209 A1 (“Grey”)
1011	U.S. Patent No. 3,955,574 (“Rubenstein”)
1012	U.S. Patent Publication No. 2017/0238953 A1 (“Yang”)
1015	Dave Fornell, <i>Catheter-Based Clot Busting Therapies</i> , DIAGNOSTIC AND INTERVENTIONAL CARDIOLOGY (Feb. 4, 2013), https://www.dicardiology.com/article/catheter-based-clot-busting-therapies
1016	International Application No. WO 2018/019829 A1 (“Brady”)
1017	Gilles Rioufol et al., <i>Large Tube Section Is the Key to Successful Coronary Thrombus Aspiration: Findings of a Standardized Bench Test</i> , 67 CATHETERIZATION & CARDIOVASCULAR INTERVENTIONS 254-257 (Dec. 5, 2005), https://onlinelibrary.wiley.com/doi/10.1002/ccd.20471
1018	Michael Haude, <i>Mechanical Thrombectomy Catheter Systems</i> , 2 INTERVENTIONAL CARDIOLOGY 58-60 (2007), https://www.icrjournal.com/articles/thrombectomy-catheter-systems
1022	Scott Simon, et al., <i>Exploring the Efficacy of Cyclic vs. Static Aspiration in a Cerebral Thrombectomy Model: An Initial Proof of Concept Study</i> , 6 J. NEUROINTERVENT. SURG. 677 (Dec. 14, 2014)
1023	Expert Declaration of Ian Ross, MD
1024	CV of Ian Ross, MD
1025	U.S. Patent Publication No. 2010/0204672 A1 (“Lockhart”)

1026	U.S. Patent No. 4,634,435 (“Ingraham”)
1027	Stephan A Munich, et al., <i>Overview of Mechanical Thrombectomy Techniques</i> , 85 NEUROSURGERY S60-S67 (June 14, 2019), https://academic.oup.com/neurosurgery/article/85/suppl_1/S60/5512732

I, Ian Ross, declare as follows:

1. My name is Ian Ross. I am a neurosurgeon specializing in the treatment of cerebrovascular diseases, including stroke interventions using thrombectomy devices. I have prepared this declaration as an expert witness retained by Penumbra, Inc. Herein I provide an overview of the medical community’s understanding of mechanical thrombectomy prior to July 18, 2019, and in particular, the potential side effects caused by mechanical thrombectomy, including distal embolus/thrombus migration and pressure build up in an aspiration catheter during a thrombectomy procedure that can cause fluid to exit the distal end of the aspiration catheter and push the thrombus and other material distally into the patient’s blood vessel. I understand that this concept is commonly known, and sometimes referred to as forward flow in the art, and it was well known prior to July 18, 2019 to consider the potential of forward flow when considering treatments and patient outcomes for ischemic strokes.

2. I make this declaration based upon my own personal knowledge and, if called upon to testify, would testify competently to the matters contained herein. For

my efforts in connection with the preparation of this declaration I have been compensated at my standard rate for this type of consulting activity. My compensation is in no way contingent on the results of these or any other proceedings relating to the above-captioned patent.

I. Background and Qualifications

3. In formulating my opinions, I have relied upon my training, knowledge, and experience in the relevant art. I have summarized in this section my educational background, career history, publications, and other relevant qualifications. My full curriculum vitae is attached as Exhibit 1024 to this IPR.

A. Educational Background

4. My scientific background includes an undergraduate degree in chemistry from McGill University, Montreal, Canada. I was awarded a Natural Sciences and Engineering Research Council of Canada (NSERC) Graduate Scholarship to pursue a PhD but decided to study medicine instead. I obtained my Doctor of Medicine from Queen's University in Kingston and also a Master of Science in Experimental Medicine from the University of Toronto, where my thesis research included the study of the vascular aspects of spinal cord injury. My clinical surgical training was at McGill University, where I specialized in neurosurgery. I took a sabbatical, in 1998-1999 and trained in interventional neuroradiology at the Fondation Rothschild in Paris, France.

B. Career History

5. I have practiced neurosurgery for over 31 years. I currently am in private practice in neurosurgery in Southern California, where my practice includes interventional neuroradiology (which I have practiced since my return from France in 1999). My major affiliate hospital, Huntington Memorial Hospital, is a primary stroke center. I share on-call duties with one other individual, an interventional neuroradiologist, splitting the stroke cases equally with him. We, combined, do about 70 stroke interventions per year using methods and devices for mechanical thrombectomy, in addition to other interventional neuroradiology procedures.

6. Prior to entering private practice, I held multiple academic appointments. I began my academic career as an Assistant Professor of Neurosurgery at University of Manitoba. After becoming an associate professor at University of Mississippi in 2000, I was promoted to Professor of Neurosurgery at in 2005 and was a Visiting Associate in Biology at the California Institute of Technology from 2008-2018. I have also held 15 hospital appointments over the last 31 years, including the Chair of Neurosurgery at Huntington Memorial Hospital.

7. I have published over 80 peer-reviewed abstracts and publications in my specialty of neurosurgery, many of which cover the field of interventional neuroradiology and stroke treatment.

8. My clinical practice of stroke intervention has applied, and continues to apply, principles of flow reversal, clot aspiration and mechanical retrieval of clots and other emboli. In the past I have worked as a consultant for medical device companies on various neurosurgical applications.

9. My curriculum vitae contains further details on my education, experience, publications, and other qualifications to render an expert opinion. Ex. 1024.

II. Overview of Thrombectomies

10. I understand that analyzing the state of thrombectomy technologies for stroke, with respect to aspiration systems, during the period prior to the possible priority date of the '402 Patent can provide valuable insight into what people of ordinary skill in the art were aware of at the time, and in what direction the industry was heading.

11. Stroke may be caused by a blood clot that blocks a cerebral artery (ischemic stroke) or by a ruptured cerebral artery (hemorrhagic stroke). These blood clots are also known as thrombi or emboli, and the phenomenon is often referred to as thromboembolism. Ischemic stroke is commonly caused by a piece of blood clot that has become dislodged from somewhere in a patient's vasculature and traveled downstream and occluded a distal cerebral artery. Ex. 1012 ("Yang") at ¶ [0003]. Clots can "embolize" to other parts of a patient's vasculature, causing pathologies

such as pulmonary embolism and acute limb ischemia. A patient suffering from an ischemic stroke experiences a medical emergency and may become severely disabled or die. This is because the disruption of normal blood flow to the brain deprives it of nutrients such as oxygen and glucose, and interferes with waste exchange, to the point where part of the brain may suffer irreversible injury. Ex. 1012 (“Yang”) at ¶ [0003]; Ex. 1010 (“Grey”) at 1:15-20.

12. Treatment for ischemic stroke in the acute setting aims to restore blood flow as fast as possible, by removing the obstruction, before irreversible injury has occurred. These treatments include mechanical thrombectomy, which is most often accomplished with a stent retriever or aspiration thrombectomy device. Experience with these tools is widespread. These are considered mature technologies, with well-known risks and benefits. See Ex. 1015 (“Fornell”) at 1-2. There is indeed some overlap. For instance, stent retrievers can be used in conjunction with aspiration catheters to aid in clot removal and increase protection from distal embolus migration. Ex. 1027 (“Munich”) at S61-65.

III. Aspiration Thrombectomy

13. The concepts described in the ’402 Patent were recognized and described for use in aspiration thrombectomy in 2014, WO 2014/151209 (Ex. 1010, “Grey”), as well as various other references prior to 2019, including U.S. Patent No. 10,322,230 (Ex. 1007, “Ofek,”) and U.S. Patent Publication No. 2017/0238953 (Ex.

1012, “Yang”). Aspiration thrombectomy is conducted with a catheter with an internal lumen and a vacuum source proximally connected to the catheter lumen. Ex. 1012 (“Yang”) at ¶¶ [0009], [0014], [0063]; Ex. 1008 (“Mullins”) at 1:53-2:2, 3:29-42; 25:22, 26:17-42. When the vacuum source is turned on, the pressure in the catheter is under vacuum and a suction effect is created that allows any liquid or particles at the distal end of the catheter to move proximally through the catheter lumen and into a collection canister at or near the vacuum source. The inner diameters of aspiration catheters vary, but typically range from approximately 0.038” for the treatment of narrow cerebral vessels to approximately 0.120” for the treatment of peripheral occlusions. Ex. 1012 (“Yang”) at [0068]; *see also* Ex. 1017 (“Rioufol”); Ex. 1018 (“Haude”). For the treatment of ischemic stroke, these sizes are limited by the size of the blood vessels leading up to and inside the head. I personally, at the time of the 2019 initial Application filing for the ’402 Patent family, had used catheters as large as outer diameter (OD) 0.106” inner diameter (ID) 0.075” (Cello 8F, Medtronic) and as small as OD 0.050” ID 0.035” (3 MAX, Penumbra) to aspirate clots. At the time of the ’402 Patent family, Medtronic marketed catheters with OD 0.114” ID 0.085” (Cello 9F, Medtronic). There have been no surprising developments in the medical literature regarding the selection of catheter sizes to market for the purpose of mechanical thrombectomy.

14. The French catheter system is a standardized and conventional way to determine the OD of a catheter for specific applications, but there is no standardized system for describing the ID of such catheters. Catheters with specific ODs and IDs are selected depending on the patient's anatomy. The OD of an aspiration catheter cannot be greater than the ID of the patient's blood vessel that it is intended for. To aspirate clots via a catheter lumen, a clot that has a diameter larger than the ID of the catheter may need to be deformed and elongated to fit into the catheter lumen, and the energy required to deform such clots is not easily attained by static aspiration alone. Ex. 1008 ("Mullins") at 25:22-26:11; Ex. 1012 ("Yang") at ¶ [0168].

15. Dynamically changing suction pressure over time, which provides a therapeutic effect by induction of fatigue stress within an embolic clot, was embodied in an invention to improve aspiration of embolic clots for the treatment of ischemic stroke and other thromboembolic events by at least 2014. Ex. 1010 ("Grey"); *see also* Ex. 1008 ("Mullins") at 1:53-2:2. Indeed, this concept of intermittently varying suction to within a catheter was patented in 1976 by Rubenstein, U.S. Patent No. 3,955,574. *See* Ex. 1011 ("Rubenstein"). The concept of inducing forward flow (of dubious benefit and safety in the setting of aspiration thrombectomy for the treatment of acute thromboembolic stroke) to unclog a blocked catheter, through pre-determined periods of positive pressure was also described in Rubenstein. Ex. 1011 ("Rubenstein").

16. The concept of venting a body cavity catheter to atmospheric pressure, for clinical use, dates to the 1960s, when the Salem Sump stomach tube (no identifiable patent), a dual lumen catheter allowing air at atmospheric pressure to be drawn into the stomach to prevent clogging of the catheter against the gastric mucosa, first came into use. I personally learned of this type of catheter as a senior medical student circa 1984, when it was in widespread use. It is used to this day. The feature of a dual lumen catheter was described in U.S. Patent No. 4,634,435, “Nasogastric tube.” Ex. 1026 (“Ingraham”).

IV. Forward Flow

17. One of the major limitations of aspiration thrombectomy devices is the potential for embolization of clot debris downstream in the circulation of the patient’s vasculature. This risk can be remarkable with large and organized clots, especially those that are challenging to fully remove due to their physical consistency and fibrin-content. These clots may be easier to dislodge from the site of occlusion, but may fragment during the retrieval process, with the consequent risk of loss of clot fragments into distal vascular territories, as described in Mullins and Grey. Ex. 1008 (“Mullins”) at 25:43-50, 26:12-16; Ex. 1010 (“Grey”) at 2:16-20, 7:10-12; *see also* Ex. 1016 (“Brady”) at 2:5-10. If a clot fragment breaks loose and travels distally, there is a subsequent risk that embolic clots will make their way distally in the patient’s vasculature, causing obstructions that are more difficult to

remove and cause irreversible brain ischemia. The phenomenon, referred to as “forward flow” in the ’402 patent, has been well-documented as a risk of thrombectomy in the literature and prior art, with several devices focused on reducing that risk. Ex. 1008 (“Mullins”) at 25:43-50, 26:12-16; Ex. 1010 (“Grey”) at 2:16-20, 7:10-12. As such, there is a balance between efficient clot removal and the risk of distal migration of thrombi as part of the design choice of thrombectomy devices and treatment plans for each patient.

18. As taught by Grey, Ofek, Yang, and Mullins, aspiration thrombectomy systems that maintain controlled levels of suction force at the distal end of the catheter can help protect the patient from distal embolus migration and thus prevent forward flow. Ex. 1010 (“Grey”) at 13:7-11; Ex. 1007 (“Ofek”) at 4:21-44; Ex. 1008 (“Mullins”) at FIGs. 47-50, 26:65-28:64; Ex. 1012 (“Yang”) at ¶¶ [0102], [0168], [0178]. The risks of distal emboli and damage that forward flow can cause, and ways to mitigate or protect the patient from distal embolus migration were well known and thoroughly documented in the medical community prior to the filing of the ’402 Patent family. *See* Ex. 1025 (“Lockhart”) at ¶¶ [007], [008]. With preventing distal embolus migration in mind, Grey, Ofek, Yang, Mullins, and others, including International Patent Publication No. 2018/019829 (“Brady”), developed methods of dynamic aspiration to optimize the efficiency of aspiration thrombectomy systems by introducing a pressure relieving pulse into the catheter to affect vacuum changes

in order to induce material fatigue in the embolus and improving the efficacy of the thrombectomy device. *See* Ex. 1010 (“Grey”) at abstract; *see also* Ex. 1016 (“Brady”) at abstract; Ex. 1007 (“Ofek”) at abstract; Ex. 1008 (“Mullins”) at 3:29-4:11, 28:22-64; Ex. 1012 (“Yang”) at ¶¶ [0168]-[0170].

19. It is common for doctors conducting aspiration thrombectomies to consider how best to protect the patient from fragmentation of the clot and any resulting distal migration of clot fragments (emboli). One way to accomplish this is to maintain a distal pressure less than that of the pressure in the blood vessel, or the patient’s blood pressure (i.e. physiological pressure). The risk of distal migration of emboli and forward flow may be heightened in connection with dynamic aspiration thrombectomy, if a positive pressure source is used to temporarily relieve the vacuum level within the catheter. The introduction of a pressure relieving vent to effectuate the dynamic aspiration could potentially exacerbate these risks. Too 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. If the pressure at the distal end of the catheter eclipses the amount of negative pressure in the catheter provided by the vacuum source, it is well known that the risk of forward flow out from the distal end of the catheter will be exacerbated. Ex. 1010 (“Grey”) at 7:10-12, 13:7-11; *see also* Ex. 1008 (“Mullins”) at 25:22-28:64. Therefore, 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 and protect the patient from distal embolus migration was known and understood prior to 2019.

20. An aspiration thrombectomy device that is capable of dynamic aspiration using a combination of venting and vacuuming may be capable of a state where the vent valve is open, introducing positive pressure into the system. Ex. 1012 (“Yang”) at ¶¶ [0131], [0168]-[0170], Ex. 1007 (“Ofek”) at 4:45-61, 5:49-62. If the vent valve is open while the vacuum valve is closed or partially closed, there may be a point in time where the positive pressure from the vent source will eclipse the negative pressure provided by the vacuum source and lead to some amount of forward flow, and in some cases, undesirable amounts of forward flow. Ex. 1010 (“Grey”) at 7:10-12, 13:7-11; Ex. 1008 (“Mullins”) at FIGs. 47-50, 26:65-28:64 (“The pressure [being] further increased until a High Limit is reached. In one embodiment this High Limit is defined such that the ingested clot may not be completely expelled from the catheter.”); Ex. 1012 (“Yang”) at ¶¶ [0135], [0168]; Ex. 1022 (“Simon”) at 680. Thus, to reduce the risk of forward flow, the aspiration thrombectomy system and/or persons of skill in the art 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. 1010 (“Grey”) at 7:10-12, 13:7-11; Ex. 1007 (“Ofek”) at 4:21-44; Ex. 1008 (“Mullins”) at FIGs. 47-50, 26:65-28:64; Ex. 1012 (“Yang”) at ¶¶ [0102], [0178]; Ex. 1022 (“Simon”) at 680. By controlling sufficient levels of vacuum in the catheter (i.e., generally keeping the overall pressures exerted on the fluid within the catheter below blood pressure), the risk of creating forward flow of material out of the distal end of the catheter is reduced. One known way to control sufficient levels of vacuum in the catheter is to carefully control the duration and amount of change in the level of vacuum pressure at the distal end by limiting the amount of time that the vacuum valve is closed and the vent valve is open. Too short of a duration and amount of pressure change at the distal end of the catheter will not allow the clot to experience a sufficient degree of accelerated forces to break it up, however, too long a period of significant pressure change will eclipse the negative pressure provided by the vacuum source and may lead to undesirable forward flow. *See, e.g.*, Ex. 1007 (“Ofek”) at 4:21-44, 6:46-58; Ex. 1008 (“Mullins”) at 27:54-28:64. So, by manipulating 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, the clinician is able to maximize efficiency of the clot digestion via dynamic aspiration while ensuring that the momentum of fluid at the distal end of the catheter does not change direction sufficiently to create any forward flow.

XIV. Reservation of Rights

21. My declaration is based upon the information that I have considered to date. I reserve the right to supplement my declaration in the future to respond to any arguments raised by the owner of the '402 Patent and to consider new information that becomes available to me.

XV. Declaration

I hereby declare that all statements made herein of my own knowledge are true and all statements made on information and belief are believed to be true. I further understand that willful false statements and the like are punishable by fine or imprisonment, or both under Section 1001 of Title 18 of the United States Code. I declare under penalty of perjury that the foregoing is true and correct.

Executed on August 1, 2024.

A handwritten signature in dark ink, appearing to be 'IR', is written on a light yellow rectangular background.

Ian Ross, MD