UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

ABIOMED, INC.,
Petitioner,

v.

WHITE SWELL MEDICAL LTD.,
Patent Owner

PGR2021-00107
U.S. Patent No. 10,926,069

DECLARATION OF BORIS LESCHINSKY

WhiteSwell Exhibit 2006
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I. Introduction

1. My name is Boris Leschinsky, and I have been retained as a technical expert by Patent Owner White Swell Medical Ltd. ("WhiteSwell") to address certain issues relating to U.S. Patent No. 10,926,069 ("the '069 patent") in post-grant review ("PRG") proceeding PGR2021-00107, which was initiated pursuant to a petition filed by Petitioner Abiomed, Inc. ("Petitioner").

2. I am being compensated at my usual consulting rate of $400.00 per hour for my time spent working on issues in this matter. My compensation does not depend on the outcome of this matter or the opinions I express.

3. If called as a witness, I could and would testify completely and truthfully with regard to the matters set forth herein.

II. Qualifications

4. I am an engineer and inventor with over 30 years of experience in the development of medical devices. I have extensive experience in cardiovascular and endovascular devices, with a focus on percutaneous catheters, balloons, heart assist devices, vascular closure products, and delivery systems. I have a comprehensive understanding of surgical and interventional treatments of various heart diseases and deep knowledge of cardiovascular anatomy, physiology, and pathophysiology. I have designed a variety of indwelling catheters with access ports for infusing and sampling fluids. I have also designed vascular closure devices that rely on

palpating blood vessels through the skin during deployment procedures. I have invented a number of long-term implantable devices, such as vascular grafts. I also designed intra-aortic balloon catheters and stent grafts with radiopaque markers to identify their location using x-ray after implantation through a skin puncture.

5. I earned a master's degree in Mechanical Engineering from Moscow State Technical University in 1987. I was recruited out of college by the Russian Scientific Institute for Transplantology and Artificial Organs in Moscow, where I became a lead engineer in their artificial heart laboratory. While at the Russian Scientific Institute, I developed new concepts for centrifugal blood pumps, worked on protypes for several artificial heart devices in large animals, and worked on the clinical trials of the first Russian artificial heart.

6. From 1990 through 2009, I worked in various positions with Datascope Corp., a diversified medical device company based in Montvale, NJ with major product lines in intra-aortic balloon pumping, patient monitoring, vascular sealing, and vascular grafts. I began my tenure with Datascope as an Engineer and was eventually promoted to Scientific Director and then Vice President, Technology. As Scientific Director, I was responsible for advanced development of new generations of products primarily in the fields of counterpulsation, vascular closure, and endovascular aneurysm treatment devices. As Vice President, Technology, I was responsible for directing the research and

development activities of all four of the company's divisions. At Datascope, among many other technologies that I developed, I invented a key concept for a new catheter-based heart assist device combining low-profile insertion with full-flow assist capability. This project was bought by Abbott in 2016.

7. From 2009 to 2013, I worked as the Chief Technology Officer of Cerus Endovascular Inc., where I was responsible for leading a start-up team in developing proprietary, non-invasive devices for treating brain aneurysms.

8. In 2009, in addition to working at Cerus Endovascular, I co-founded LifeCuff Technologies Inc. I have served as LifeCuff's Chief Technology Officer on a part-time basis from its founding through the present. At LifeCuff, I developed (and am named as an inventor on several patents relating to) technologies relating to automated devices for remote ischemic conditioning, which is a similar treatment to the post-conditioning treatments disclosed in several of the prior art references at issue in this PGR. The LifeCuff devices were developed for the treatment of ischemia in patients suffering from heart attacks, strokes, or trauma by providing a series of interruptions of blood flow prior to the restoration of normal perfusion of the target ischemic organ. This type of treatment is known as "ischemic preconditioning." (In the prior art references at issue in the PGR, a series of interruptions of blood flow to previously ischemic tissue is provided ***after*** normal perfusion has been restored, which is why the treatments

disclosed in those references are known as ***post***-conditioning treatments.) Rather than directly target blood flow to the affected organ by using a balloon catheter that is used inside a blood vessel, as is done in the prior art references at issue in the PGR, the LifeCuff device works "remotely" and noninvasively by using an external cuff that cycles through periods of blocking and restoring blood flow and which monitors and uses the patient's systolic blood pressure during the treatment to ensure its efficacy. The theories and principles according to which both the remote preconditioning LifeCuff device and the invasive post-conditioning devices of the prior art references at issue in this PGR treat ischemia and reduce the extent of injuries from reperfusion of previously ischemic tissue are similar.

9. Since 2013, I have worked as the Vice President of Product Development for Corinnova Inc., which is a medical device start-up company. At Corinnova, I am responsible for leading the engineering team in developing a minimally invasive, non-blood contacting cardiac assist device for acute heart failure treatment. The device is designed to conform to the external surface of the heart and increase cardiac output through the use of a pneumatic driver that gently squeezes the heart by using minimal air pressure. The device has a control system that complies with FDA and CE regulations and guidelines and uses sensors to detect the heart's EKG signal, which enables monitoring of the heart's

performance, and which controls the inflation and deflation of the device in synchrony with the heart's beating.

10. I am an inventor on 58 U.S. patents and numerous international patents and patent applications, including the ones listed in the below table.

Patent	Title
U.S. Patent No. 5,817,001	Method and apparatus for driving an intra-aortic balloon pump
U.S. Patent No. 6,179,825	Oval vascular catheter
U.S. Patent No. 6,191,111	Method and device for enhancing biobypass by increasing the coronary blood flow
U.S. Patent No. 6,346,092	Intra-aortic balloon catheter and insertion sheath
U.S. Patent No. 8,038,623	Calibration of in vivo blood pressure sensors
U.S. Patent No. 8,114,026	Methods and devices for remote ischemic preconditioning and near-continuous blood pressure monitoring
U.S. Patent No. 8,795,323	Dual mode remote ischemic preconditioning devices and methods
U.S. Patent No. 9,801,780	Methods and devices for remote ischemic conditioning via partial limb occlusion
U.S. Patent No. 10,624,649	Multi-mode inflatable limb occlusion devices and methods
U.S. Patent No. 11,123,256	Systems and methods for delivery of repeated remote ischemic conditioning and monitoring compliance

Patent	Title
U.S. Patent Publication No. 2012/0226340	Temporary perfusion channel percutaneous delivery of balloon-expandable stents

11. A true and correct copy of my curriculum vitae, which includes a list of cases in which I have provided expert declarations/reports and/or testimony, is attached hereto as Exhibit A.

III. Basis of Opinions

12. I have been retained by WhiteSwell to provide various analyses and opinions, including to address the technology claimed in the '069 patent and to evaluate whether proposed claim 22 of the '069 patent ("the Substitute Claim"), which is set out in WhiteSwell's Non-Contingent Motion to Amend, is not unpatentable in view of the arguments raised by Petitioner in its Opposition to Patent Owner's Non-Contingent Motion to Amend.

13. All of the opinions I express in this Declaration have been made from the standpoint of a person of ordinary skill in the relevant art ("POSA") at the time of the invention of the '069 patent, which I am informed is, for purposes of this matter, the '069 patent's earliest claimed priority date of June 1, 2014 (the filing date of U.S. Provisional Patent Application No. 62/006,206). My opinions would not change if the priority date were taken to be February 19, 2015 (the filing date

the earliest non-provisional application — U.S. Patent Application No. 14/625,930 — to which the '069 patent claims priority). *See* § V.B below.

14. My opinions are based on my experience and knowledge and the information I have reviewed as of the date of this Declaration. In connection with my analysis, I have reviewed the exhibits and other documents cited herein, including the following papers and exhibits.

Paper	Description	Date
1	Petition for Post-Grant Review of U.S. Patent No. 10,926,069	Aug. 2, 2021
9	Patent Owner's Preliminary Response	Nov. 8, 2021
12	Petitioner's Reply Pursuant to Board Order	Dec. 23, 2021
13	Patent Owner's Preliminary Sur-Reply	Jan. 4, 2022
14	Decision[:] Granting Institution of Post-Grant Review	Jan. 27, 2022
17	Patent Owner's Non-Contingent Motion to Amend	Apr. 21, 2022
18	Petitioner's Opposition to Patent Owner's Non-Contingent Motion to Amend	July 14, 2022
20	Preliminary Guidance[:] Patent Owner's Non-Contingent Motion to Amend	Aug. 4, 2022

Exhibit	Description
1001	'069 Patent
1002	Declaration of Steven W. Day in Support of Petition for Post-Grant Review of Patent No. 10,926,069 ("Day Pet. Decl.")

Exhibit	Description
1003	Curriculum Vitae of Steven W. Day
1004	European Patent Application No. 2 353 503 A1 (“Gille503”)
1005	European Patent Application No. 2 353 501 A1 (“Gille501”)
1006	U.S. Patent Application Publication No. 2001/095302 A1 (“Mohl” or “Mohl302”)
1007	File History for the ’069 Patent
1008	File History for U.S. Provisional Patent Application No. 60/006,206 (filed June 1, 2014, to which the ’069 patent claims priority)
1009	excerpt from American Heritage College Dictionary (3d ed. 1993) (definition of “retract”)
1014	Declaration of Steven W. Day in Opposition to Patent Owner’s Non-Contingent Motion to Amend (“Day Opp. Decl.”)
1015	U.S. Patent Application Publication No. 2006/0100639 (“Levin”)
1016	U.S. Patent No. 4,934,996 (“Mohl”)
1017	International Patent Application Publication No. 2008/042347 A2 (“Mashimo”)
1018	U.S. Patent No. 9,008,769 B2 (“Mika”)
1019	*Introduction to Homeostasis*
1020	IEC 60601-1-10 (ed. 1.0 Nov. 2007)
1021	Center for Devices and Radiological Health, *Technical Considerations for Medical Devices with Physiologic Closed-Loop Control Technology: Draft Guidance for Industry and Food and Drug Administration Staff* (Dec. 23, 2021)

Exhibit	Description
1022	Lucy Norcliffe-Kaufmann *et al.*, *Pain and Autonomic Dysfunction*, Encyclopedia of Neurological Sciences (2d ed.)
1023	excerpt from Richard C. Dorf *et al.*, Modern Control Systems (12th ed. 2011)
1024	Werner Mohl *et al*, *Effects of Pressure-Controlled Intermittent Coronary Sinus Occlusion on Regional Ischemic Myocardial Fucntion*, 5 J. Am. College of Cardiology 939–947 (1985)
1025	Updated Curriculum Vitae of Steven W. Day
1026	Errata Sheet for the Transcript of the Mar. 30, 2022 Deposition of Steven W. Day
2001	Statutory Disclaimer Under 37 C.F.R. § 1.321(a) (Nov. 4, 2021)
2002	Transcript of the Mar. 30, 2022 Deposition of Steven W. Day
2003	U.S. Patent Application No. 14/625,930 (filed Feb. 19, 2015, to which the ’069 patent claims priority)
2004	U.S. Patent Application No. 15/471,842 (filed Mar. 28, 2017, to which the ’069 patent claims priority)
2005	U.S. Patent Application No. 16/225,453 (filed Dec. 19, 2018, to which the ’069 patent claims priority)

IV. Legal Standards

15. For the purposes of this Declaration, counsel for WhiteSwell have informed me of the following legal standards.

A. Level of Ordinary Skill in the Art

16. I understand that my analysis herein must be from the perspective of a POSA as of the date of the invention.

17. I understand that the POSA is a hypothetical person who is presumed to have known the relevant art at the time of the invention. By "relevant," I understand that is relevant to the claims of the '069 patent.

18. I understand that factual indicators of the level of ordinary skill in the art include the various prior art approaches employed, the types of problems encountered in the art, the rapidity with which innovations are made, the sophistication of the technology involved, and the educational background of those actively working in the field. Thus, in assessing the level of skill of a POSA, I consider the type of problems encountered in the art, the prior solutions to those problems found in the prior art references, the rapidity with which innovations are made, the sophistication of the technology, the level of education of active workers in the field, and my own experience working with those of skill in the art at the time of the invention.

B. Claim Construction

19. I understand that patent claims are to be interpreted in light of a patent's specification and prosecution history. I am informed that claim

construction starts with the plain language of the claims as understood by a POSA at the time the patent was filed.

C. Anticipation

20. I understand that a patent claim is unpatentable as anticipated if a single prior art reference discloses each and every limitation of the claimed invention, either expressly or inherently.

21. I understand that a prior art reference inherently discloses a claim limitation only when that reference necessarily includes the limitation that is not expressly disclosed.

22. I understand that a prior art reference can only anticipate a claimed invention if it describes the claimed invention in sufficient detail to enable a POSA to carry out the claimed invention.

D. Obviousness

23. I understand that a patent claim is unpatentable if the claimed invention would have been obvious to a POSA at the time of the purported invention.

24. I understand that an obviousness analysis involves comparing a claim to the prior art to determine whether the claimed invention would have been obvious to a POSA at the time of the invention in view of the prior art and in light of the general knowledge in the art at that time, as a whole. I also understand that

obviousness is ultimately a legal conclusion based on underlying facts of four general types, all of which must be considered: (1) the scope and content of the prior art; (2) the level of ordinary skill in the art; (3) the differences between the claimed invention and the prior art; and (4) any objective indicia of non-obviousness, including any praise of the invention.

25. I also understand that obviousness may be established under certain circumstances by combining or modifying the teachings of the prior art. Specific teachings, suggestions, or motivations to combine any first prior art reference with a second prior art reference can be explicit or implicit, but must have existed before the date of purported invention. I understand that prior art references themselves may be one source of a specific teaching or suggestion to combine features of the prior art, but that such suggestions or motivations to combine art may come from the knowledge that a POSA would have had.

26. I understand that a reference may be relied upon for all that it teaches, including uses beyond its primary purpose, but also including teachings that lead away from the invention. I understand that a reference may be said to teach away from a particular development path when a POSA, upon reading the reference, would be discouraged from following the path set out in the reference, although the mere disclosure of alternative designs does not teach away.

27. I understand that in order to rely on inherency to establish the existence of a claim limitation in the prior art in an obviousness analysis, the limitation at issue necessarily must be present, or the natural result of the combination of elements explicitly disclosed by the prior art.

28. I further understand that whether there is a reasonable expectation of success in combining references in a particular way is also relevant to the analysis.

29. I understand that it is improper to use hindsight — namely, using the claims as a guide — to combine references or elements of references to reconstruct the invention.

30. I understand that to render a claim obvious, the prior art, taken as a whole, must enable a POSA to make and use the claimed invention. I understand that in the absence of other supporting evidence to enable a POSA to make the claimed invention, a standalone prior art reference must enable the portions of its disclosure being relied upon.

31. I am not offering any legal opinions in this declaration. I only consider such legal standards in framing my opinions and conclusions. Additionally, from a subject matter perspective, I understand that the petitioner always has the burden of persuasion regarding a challenge of patentability of an invention under an PGR.

V. The ’069 Patent

32. The invention of the ’069 patent relates to an inventive treatment that helps avoid the “risk of developing acute heart failure or compromised renal function” in certain patients such as those experiencing edema. ’069 patent at Abstract, 7:54–56. The ’069 patent teaches that in patients at risk of developing acute heart failure, “the capillary hydrostatic pressure and the venous pulmonary pressure can become elevated and fluid flows excessively out of the blood vessels and into the interstitial and alveolar spaces,” which is known as edema. ’069 patent at 1:30–34. When this happens, “[t]he pressure gradient between the initial lymphatics and at the outflow of the thoracic duct and the lymphatic duct is reduced and the lymphatic system cannot clear the additional fluid which accumulates in the air spaces of the lungs,” which “is a life threatening condition as gas exchange is impaired to the extent that it may lead to respiratory failure. ’069 patent at 1:34–40. Accordingly, the ’069 patent provides treatments “for reducing edema conditions, such as pulmonary edema, in a patient by lowering the outflow pressure in a region around the thoracic/lymphatic duct outflow,” the result of which is “enabling the lymphatic vessel flow to be at or near normal levels.” ’069 patent at 6:41–47.

33. In particular, the invention of the ’069 patent includes a catheter designed to be “implanted within a vein of a patient,” ’069 patent at 7:10, and “can

also include pressure sensors and one or more selectively deployable restrictions," '069 patent at 7:27–29. The '069 patent teaches that the sensors can "be used for sensing [blood] pressure at various locations along the vein in which the catheter is implanted," '069 patent at 9:9–11, and that a control module can "be configured to process the data received from the various sensors to alter the … restriction volume," '069 patent at 15:21–23. The '069 patent teaches that "the control module [] can include multiple feedback loops to adjust performance of the system [] to create and maintain a low pressure zone while the lymphatic fluid is cleared." '069 patent at 15:25–28.

34. For example, the '069 patent describes that the "catheter's sensors can be used to attain a baseline pressure measurement in the internal jugular, SVC, and the junction of the jugular and subclavian veins." '069 patent at 18:60–62. Subsequently, "[t]he first and second restrictions 24, 26 can be adjusted to alter the innominate vein and the SVC pressures from the baseline," '069 patent at 19:6–8, thereby creating the "localized low pressure zone" that allows lymphatic fluid to be cleared, as described above. In doing this, a POSA would understand that the baseline pressure measurements are compared to current pressure measurements in order to detect the creation of the desired localized low pressure zone, *i.e.*, a change in pressure, and that the system alters the volume of the restrictions in

response to that detected change in order to obtain and maintain the low pressure zone.

A. The Substitute Claim

35. The text of the Substitute Claim is set out below:

> 22. A device comprising:
>
> **[a]** a catheter;
>
> **[b]** a first restrictor operably associated with the catheter, **[c]** wherein the first restrictor comprises a retracted and deployed configuration and in the deployed configuration, the first restrictor comprises a diameter of a vein;
>
> **[d]** one or more sensors positioned on the catheter and **[e]** in operable communication with the first restrictor, the one or more sensors operable to provide data that is used to alter the diameter of the first restrictor inside the vein, **[f]** wherein the one or more sensors comprise pressure sensors; and
>
> **[g]** a control module for processing the data provided by the sensors, **[h]** wherein the control module compares a blood pressure measurement provided by the sensors to a baseline blood pressure measurement to detect a change in blood pressure and **[i]** directly adjusts a volume of the first restrictor in response to the detected change in blood pressure.

B. Level of Ordinary Skill in the Art

36. I understand that Petitioner has asserted that a POSA would be a person with "(i) an M.D. or a Bachelor's or Master's degree in mechanical engineering, biomedical engineering or a similar field, as well as two or more years of work experience with catheters or similar medical devices or (ii) a Ph.D. in mechanical or biomedical engineering, or in a similar field." Petition at 15.

37. Based on my experience, including in the development of medical devices and treatments using such devices, I generally accept and agree with Petitioner's proposed definition of a POSA for the purposes of this PGR.

38. I believe I satisfy the definition of a POSA. In particular, I have a Master's degree in mechanical engineering and over 2 years of work experience with catheters and similar medical devices and therefore qualify as a POSA under Petitioner's proposed definition.

C. Claim Construction

39. I understand that WhiteSwell, Petitioner, and the Board all agree that the construction of any terms of the Substitute Claim is not relevant to the issues in dispute. *See* Institution Decision at 11; Motion to Amend at 5; Opposition at 7. For each term of the Substitute Claim, I have therefore applied their plain and ordinary meanings as would be understood by a POSA in at the time of the invention.

VI. Analysis

A. Gille503 Does Not Anticipate the Substitute Claim

40. In my opinion, Gille503 does not anticipate Substitute Claim 22 because it does not disclose at least limitation c — "wherein the first restrictor comprises a retracted and deployed configuration and *in the deployed configuration, the first restrictor comprises a diameter of a* ***vein***" (*see* § VI.A.3 below) — and limitation h — "wherein the control module compares a blood pressure measurement provided by the sensors *to* ***a baseline blood pressure measurement*** *to detect a change in blood pressure*" (*see* § VI.A.2below).

1. Background

41. Gille503 describes "a catheter adapted for use in post conditioning treatment." Gille503 at ¶ 1; *see also* Gille503 at ¶ 4 ("It is an objective of the present invention to provide an improved catheter for post conditioning treatment."). As described by Gille503 and as a POSA would be aware, post-conditioning treatment is a procedure that is performed after a vessel that was previously occluded (such as due to a myocardial infarction ("MI")) is reopened in order to reduce what is known as reperfusion injury (better known as ischemia reperfusion injury). *See* Gille503 at ¶ 3. Reperfusion refers to the restoration of blood flow to previously ischemic tissue (*i.e.*, tissue whose blood supply has been restricted or interrupted and is therefore deprived of adequate oxygen). As

Gille503 teaches, "the process of restoring the blood flow to the ischemic tissue … can also induce injury … termed reperfusion injury, [that] can paradoxically reduce the beneficial effects of the reperfusion." Gille503 at ¶ 3. Post-conditioning treatment helps to reduce the extent of this injury by "sequentially and alternately … complete[ly] dilati[ng] and complete[ly] deflati[ng] [a] balloon in the affected body lumen." Gille503 at ¶ 3. According to Gille503, "common dilation balloons are not suitable for controlling the reperfusion flow and regulating the desirable flow restriction" and "with the manually controlled inflation and deflation of the dilation balloon it is almost impossible to control the flow rate of the blood and to prevent or reduce reperfusion injury." Gille503 at ¶ 3.

42. Accordingly, Gille503 describes "a catheter adapted for use in post-conditioning treatment," Gille503 at ¶ 5, that includes, among other things, "the inventive provision of a sensor integrally on the catheter … to allow a reduced and low blood flow through the vessel during post conditioning treatment which is found to be beneficial in comparison to a series of full inflation and deflation of the balloon and the resulting on/off behaviour of the normal blood flow to in the vessel," Gille503 at ¶6.

2. Gille503 Does Not Disclose a Comparison of a Blood Pressure Measurement Provided by Sensors to a Baseline Blood Pressure Measurement to Detect a Change in Blood Pressure

43. In my opinion, Gille503 does not disclose that its control module "compares a blood pressure measurement provided by the sensors *to* ***a baseline blood pressure measurement*** *to detect a change in blood pressure*" as required by limitation h of the Substitute Claim.

44. In my opinion, a POSA would recognize that Gille503 does not disclose that its system makes use of comparing a sensed blood pressure to a target (regardless of whether the target is a baseline blood pressure measurement or a predetermined blood pressure value) in order to detect a change in blood pressure. Gille503 describes that "a target low blood pressure during the post conditioning treatment avoiding a full sealing of the vessel can be achieved with an adjustment of the inflation extent of the balloon depending on the sensed data." Gille503 at ¶ 19. However, as discussed below, a POSA reading Gille503 would understand that achieving the target pressure without fully sealing the vessel would only be feasible where the inflation of the balloon is being controlled manually by a medical practitioner based on the sensed data, rather than automatically by a control module.

45. In particular, a POSA would understand that the vessels within which the balloon of Gille503 would be expanded are very narrow (on the order of about

2mm in diameter) and that expanding a balloon to partially occlude such a vessel (*i.e.*, "avoiding a full sealing of the vessel") would require a very high degree of precision in terms of the amount of fluid that would need to be introduced into the balloon in order to expand it to such a level. This is especially true because the fluid used to inflate the balloon must travel a relatively long distance (about 1 meter or more) from where the catheter is inserted into the body to where the balloon is used within a coronary artery. A POSA would understand the distance the fluid must travel to reach the balloon can result in differences between the amount of fluid introduced into the catheter and the amount of fluid added to the balloon itself.

46. In addition, a POSA would understand that measurements of blood pressure downstream of the balloon would provide only indirect feedback regarding the degree of expansion of the balloon within the vessel because until the vessel is almost completely occluded any impact on the blood pressure downstream of the balloon would be very slight (if there is an impact at all) and then once the vessel is almost completely occluded (on the order of 95% or more), the blood pressure downstream of the balloon would decrease in a manner that is not linearly or proportionally correlated to the degree of occlusion. A POSA would therefore understand that using a low blood pressure to target a balloon to be inflated to almost, but not quite completely seal a blood vessel during a post-

conditioning treatment would require a greater degree of precision — both in terms of the blood pressure measurements and the control over the amount of fluid introduced into the balloon to control its volume — than could typically be expected of an automated system (as is required by the Substitute Claim's requirement that "the control module … directly adjusts a volume of the first restrictor in response to the detected change in blood pressure").

47. A POSA would understand that because using blood pressure as a target to attempt to not quite fully seal a vessel during a post-conditioning treatment is only compatible with manual control, Gille503 teaches that "when there is an automated system it might be more feasible to sense the pressure of the balloon itself in order to avoid any unwanted overexpansion and to monitor the behavior of the balloon during inflation depending on the condition of the vessel during treatment." Gille503 at ¶ 19. A POSA would understand that by using a pressure sensor to sense the pressure of the balloon itself, rather than the pressure of the blood in the vessel downstream of the balloon), the automated system would be able to obtain more accurate information relating to the expansion of the balloon and would be able to more precisely control the balloon inflation to "avoid a full sealing of the vessel." Indeed, it is this arrangement that is described in the drawings and specific description of Gille503. *See* Gille503 at ¶¶ 23–24.

48. Moreover, even to the extent that one were to consider using a "target low blood pressure" in controlling the inflation of a balloon during a post-conditioning treatment according to the teachings of Gille503 (which, as described above, is not supported by Gille503), in my opinion, a POSA would recognize that any measurements of blood pressure provided by the sensors of Gille503 would be compared only to pre-programmed targets, not "to a baseline blood pressure measurement" as required by the Substitute Claim.

49. In particular, Gille503 describes that "***optimal*** blood flow and blood pressure in the targeted area in risk of reperfusion injury can be achieved by adjusting ***pre-programmed*** inflation and deflation series of the balloon in accordance with the actual measurements of the sensor." Gille503 at ¶ 14 (emphasis added). In reading this, a POSA would recognize and understand that the "***optimal*** … blood pressure in the targeted area in risk of reperfusion injury" that Gille503 teaches "can be achieved" would necessarily be a predetermined value and not a baseline blood pressure measurement from the patient being treated. This is because in post-conditioning treatment, the blood flow through the area being treated is repeatedly reduced and restored. During the period when the blood flow is reduced, the pressure downstream would be decreased. A POSA would recognize that whether the change in blood pressure is "optimal" could not be determined by simply comparing a current sensed blood pressure to a baseline

blood pressure measurement, which would simply provide information that some change has occurred but would not provide sufficient information to determine if the change was sufficient to be "optimal" for the purposes of the post-conditioning treatment. A POSA would recognize that only by comparing the sensed blood pressure to a predetermined target could it be determined that the alteration in blood pressure due to the inflation or deflation of the balloon is sufficient for effective post-conditioning.

50. This would be further emphasized for a POSA by Gille503's teaching that the adjustments to the inflation and deflation of the balloon are made based on a "***pre-programmed*** inflation and deflation series … in accordance with the actual measurements of the sensor." A POSA would understand this to mean that the balloon is held at inflation and deflation levels that permit the "actual measurements of the sensor" to match the predetermined "optimal … blood pressure" levels for "pre-programmed" durations.

51. Neither Petitioner nor its expert, Dr. Day, cite to any description in Gille503 of a comparison of a sensed blood pressure to a baseline blood pressure measurement to detect a change in blood pressure (because no such descriptions exist in Gille503).

52. For example, Petitioner cites to Gille503 at 4:58–5:7 (in ¶ 19) as describing that "a target low blood pressure during the post conditioning treatment

avoiding a full sealing of the vessel can be achieved with an adjustment of the inflation extent of the balloon depending on the sensed data." *See* Opposition at 11. But Gille503 never describes the "target low blood pressure" as being a "baseline blood pressure measurement" as required by the Substitute Claim. Instead, as described above, in my opinion a POSA would understand that the "target low blood pressure" would need to be a predetermined value in order to be useful to determine whether the pressure has been reduced to a level sufficient for effective post-conditioning without fully sealing the vessel. As explained above, a POSA would understand that a baseline blood pressure measurement from the patient would not work for such a target.

53. That the "target low blood pressure" would be a predetermined value and not a baseline blood pressure measured is further confirmed by Paragraph 18 of Gille503, which describes that "different pre-programmed series of sequential inflation and deflation of the balloon ***in a targeted extent resulting in full sealing or reduced low pressure blood flow*** at a time ***can be stored in the control unit*** and thus be ***chosen by the medical person*** to fit the needs of the patient" (emphasis added). A POSA would understand that this describes that the "pre-programmed series of sequential inflation and deflation of the balloon" includes the target low pressure for "resulting in full sealing or reduced low pressure blood flow." A POSA would also understand that the targeted low blood pressure must be

predetermined in order to be "stored in the control unit" and "chosen by the medical person to fit the needs of the patient."

54. Rather than rely on any description in Gille503 of a comparison of a sensed blood pressure to a baseline blood pressure measurement to detect a change in blood pressure — which does not exist — I understand that Petitioner and Dr. Day instead rely on the ***absence*** of an explicit statement in Gille503 that it does not make use of a comparison of a sensed blood pressure to a baseline blood pressure measurement to detect a change in blood pressure. *See* Opposition at 12–13; Day Opp. Decl. at ¶ 116. I disagree with Petitioner and Dr. Day that a POSA would understand the absence of such an explicit statement in Gille503 to somehow mean that Gille503 discloses the use of such a comparison.

55. First, as explained above, a POSA would understand based on the teachings of Gille503 that any comparison of a sensed blood pressure to a target value according to its invention would make use of a predetermined target value as described in Gille503, not a baseline blood pressure measurement which would not be useful in the context of a catheter for use in post-conditioning treatments. Indeed, neither Petitioner nor Dr. Day even attempt to explain how a baseline blood pressure measurement could be useful as a target blood pressure in the context of post-conditioning treatment, as Gille503 discloses its invention is used

for.[1] As explained above, a POSA would understand that it would not be useful in that context.

56. Second, I understand that Petitioner's reasoning is insufficient under the legal standard for anticipation, as it has been explained to me. *See* IV.C above. In particular, I understand that in order to anticipate a patent claim, "a single prior art reference [must] disclose[] each and every limitation of the claimed invention, ether expressly or inherently." As described above, Gille503 clearly does not

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[1] Petitioner asserts that "Gille503 also teaches controlled reperfusion or angioplasty." Opposition at 13; *see also* Day Opp. Decl. at ¶ 118. This is misleading. Gille503's teachings relate only to providing post-conditioning treatment. Gille503 references reperfusion (*i.e.*, restoring blood flow and therefore oxygen to previously ischemic tissue) and angioplasty (*i.e.*, using a balloon to reopen a previously occluded vessel) because the post-conditioning treatment of Gille503 is performed after ("post") these procedures in order to reduce the reperfusion injury that would otherwise result from these procedures. Gille503 does not include any teachings relating performing reperfusion and/or angioplasty procedures on their own, nor to using blood pressure measurements (or any other measurements) to control the inflation and/or deflation of a catheter balloon as part of the angioplasty and/or reperfusion treatments.

explicitly disclose a comparison of a sensed blood pressure to a baseline blood pressure measurement to detect a change in blood pressure. Similarly, Gille503 does not inherently disclose this limitation because Gille503 does not ***necessarily*** include a comparison between of a sensed blood pressure to a baseline blood pressure measurement to detect a change in blood pressure. Instead, as Petitioner and Dr. Day concede, Gille503 includes, at a minimum, a comparison to a predetermined target value.

57. Moreover, contrary to Petitioner and Dr. Day, "the only general possibilities" for a target value are not a predetermined blood pressure value or a baseline blood pressure measurement. *See* Opposition at 12; Day Opp. Decl. at ¶ 116. Indeed, Petitioner's framing of this as simply a choice between "a Measured Value or [a] Predetermined Value" represents an improper and misleading narrowing of the options that a POSA would consider in constructing a catheter for use in a post-conditioning treatment according to the teachings of Gille503. It appears that Petitioner improperly relies on hindsight from the Substitute Claim itself in framing the choice to be made as being between the potential sources for target blood pressures against which sensed blood pressures should be compared. In doing so, Petitioner ignores that Gille503 teaches that there are several other ways that sensed values can be used to control the inflation and deflation of its balloon in performing a post-conditioning treatment, only some of which even

involve blood pressures at all and none of which involve a comparison to a baseline blood pressure measurement. Petitioner also ignores the reason why a comparison of a sensed value to a target is being made in Gille503.

58. For example, rather than rely on sensing blood pressure at all, Gille503 describes that a sensor for measuring blood ***flow*** may be used. *See, e.g.*, Gille503 at ¶ 14 ("According to an aspect of the invention the flow sensor is positioned distal from the balloon. Like that, the blood flow in the treated vessel behind the balloon can be controlled during the whole treatment.").

59. Gille503 also describes that rather than sensing ***blood*** pressure, "a pressure sensor for measuring the ***balloon inflation*** pressure" may be used. Gille503 at ¶ 15 (emphasis added). Such a sensor could be "directly placed inside the balloon or on its surface" and provides "a possibility to control and adjust the inflation and/or deflation of the balloon specifically according to the need of the patient." Gille503 at ¶ 15. Indeed, Petitioner cites to Gille503's description at 4:33–46 (in ¶ 18) of "controlling the inflation or deflation of the balloon in relation to the sensed flow of a fluid and/or in relation to ***the sensed pressure***" (emphasis added). *See* Opposition at 11. In this context, it is clear that "the sensed pressure" being referred to is "the inflation pressure applied to the regulating balloon" as stated in the very next sentence, which describes that "[t]his allows for an even more exact regulation of a fluid flow."

60. Finally, rather than compare a sensed blood pressure to a target value, Gille503 describes that two simultaneous sensed blood pressures (from sensors located on opposite sides of the balloon) can be compared to each other to determine "the pressure difference in the blood vessel obtained by the inflation or deflation of the balloon." Gille503 at ¶ 16.

61. Thus, a POSA would understand that Gille503 presents several options for using sensed data to control the inflation and deflation of a catheter balloon during a post-conditioning treatment and that, therefore, a POSA would not simply be presented with a choice between using a predetermined blood pressure value or a baseline blood pressure measurement.

62. I understand that Petitioner also relies on IEC standard 60601-1-10 in asserting that "a POSA would know Gille50[3] could use either [a Measured Value of a Predetermined Value] as a target." Opposition at 12. I disagree that IEC 60601-1-10 provides any support for this argument.

63. First, in my opinion, a POSA would not understand IEC 60601-1-10 to be relevant to the interpretation of Gille503. Gille503 does not reference or incorporate the standard and in my opinion a POSA would consider the standard to be too generic to provide any practical insight into how a control algorithm should be implemented for the purposes of a specific procedure. For example, while the standard might describe that certain types of targets could be used in implementing

closed-loop controllers for medical devices generally, a POSA would not understand that to mean that every example in the standard is suitable for use by controllers designed for specific procedures. Instead, a POSA would understand that appropriate targets need to be selected based on the particulars of each procedure.

64. Second, Petitioner and Dr. Day misleadingly state the standard "places no restrictions on the source of 'target' values in a feedback loop." Opposition at 12; *see also* Day Opp. Decl. at ¶ 42. But the only examples given in the standard of targets[2] are predetermined targets. In particular, the standard provides four examples of COMMAND VARIABLEs being set and/or manipulated, all of which a POSA would understand as relating to the use of predetermined target values.

65. In the first example, the standard describes that "***[t]he OPERATOR sets*** the target end-tidal CO_2 to ***30 mmHg*** and the allowable range of peak airway

[2] Under the standard, the "target" or "desired value or state" is the "COMMAND VARIABLE." IEC 60601-1-10 at § 3.4, Definition 3.4; *see also* Day Opp. Decl. at ¶ 42. The "REFERENCE VARIABLE" is a variable that is calculated using the COMMAND VARIABLE. IEC 60601-1-10 at §§ 3.4, 3.22, Definition 3.3, 3.22; *see also* Day Opp. Decl. ¶¶ 42–43.

pressures ***from 15 cmH$_2$O to 35 cmH$_2$O***." IEC 60601-1-10 at Definition 3.4 (emphasis added). Similarly, in the second example, the standard describes that "***the OPERATOR sets*** the target end-tidal CO2 to increase linearly ***from 25 mmHg to 45 mmHg*** over a 30 min period." IEC 60601-1-10 at Definition 3.4 (emphasis added). Because the standard describes the COMMAND VARIABLE as being "set" by the OPERATOR as particular values (*i.e.*, 30 mmHg, 15 cmH$_2$O to 35 cmH$_2$O, and 25 mmHg to 45 mmHg), a POSA would understand these examples as relating to the use of predetermined values as targets, not measured baselines.

66. In the third example, the standard describes that "***the OPERATOR will gradually decrease*** the COMMAND VARIABLE to wean the PATIENT from the medication …." IEC 60601-1-10 at Definition 3.4 (emphasis added). Again, this describes the COMMAND VARIABLE being set through action by the OPERATOR, not based on any baseline measurement being taken.

67. And finally, in the fourth example, in discussing the REFERENCE VARAIBLE, the standard describes that "[t]he ***OPERATOR enters*** a new fixed COMMAND VARIABLE" and that "[u]nder this circumstance, the COMMAND TRANFSER ELEMENT converts the fixed value into a time-varying REFERENCE VARIABLE that slowly increases to the ***desired value set by the OPERATOR*** as the COMMAND VARIABLE." IEC 60601-1-10 at Definition

3.22 (emphasis added). Again, since the COMMAND VARIABLE is "set" by the OPERATOR and the REFERENCE VARIABLE is based on that, a POSA would understand that the target is predetermined (or calculated based on a predetermined value) and is not based on any baseline measurement being taken.

68. Accordingly, as IEC 60601-1-10 does not provide any examples of baseline measurements being used as targets, in my opinion a POSA would not understand from it that Gille503, which also does not provide any examples of baseline measurements being used as targets, includes within the scope of its disclosure a comparison of a sensed blood pressure to a baseline blood pressure measurement to detect a change in blood pressure.

69. Finally, I understand that the Board in its Preliminary Guidance found that "[e]ven if Gille503's target value was *initially* predetermined, because Gille503 discloses 'continuous measurement' and adjustment 'depending on the sensed data,' a first measurement to determine whether the blood pressure is at the target value could be considered a baseline and then any second or subsequent measurement is used to determine whether the balloon needs to be inflated or deflated based on the difference between the two measurements." Preliminary Guidance at 6. I disagree that this reasoning satisfies the requirement of the Substitute Claim that "the control module ***compares*** a blood pressure measurement provided by the sensors *to* ***a baseline blood pressure measurement*** to detect a

change in blood pressure." It is not sufficient under the claim merely for the blood pressure to have changed between the time when a first measurement was taken and the time when a second or subsequent measurement was taken. Rather, under requirements of the claim, the control module must specifically perform a comparison between a baseline measurement and another measurement. Not only would a POSA understand that a measurement taken after the procedure has begun (*e.g.*, the "first measurement" described by the Board) is not a "baseline" measurement, but, even if it could be considered as such, Gille503 does not describe that any such comparison between a first measurement taken during the treatment and a second measurement is ever performed. Rather, a POSA would understand from Gille503 that each of the successive sensor measurements are compared ***to the original target value***. Indeed, Petitioner's expert, Dr. Day, in the portion of his declaration quoted by the Board in its Preliminary Guidance, states exactly this — that the "feedback loop successively compares sensor-provided readings of current pressure ***against the specified target pressure***." Day Opp. Decl. at ¶ 114 (emphasis added). Because Gille503 does not describe that the target value is ever updated to equal any measured value, in my opinion the fact that Gille503 performs successive comparisons is insufficient to meet this limitation even under the reasoning presented in the Preliminary Guidance. Indeed, updating the target value based on one of the successive measurements would defeat the purpose of

the use of the target value in Gille503: to set an "optimal" value for the blood pressure to reach through operation of the inflation or deflation of the balloon. If the target against which the successive sensor measurements were compared were updated to one of the measurements, then there would be no way for the system to determine if the blood pressure had reached the desired "optimal" value because, by definition, at the time of the earlier measurements that the Board asserts would become the target, the pressure would not yet have reached the "optimal" level.

3. Gille503 Does Not Disclose Altering the Diameter of the First Restrictor Inside a *Vein*

70. In my opinion, Gille503 does not disclose that "in the deployed configuration, the first restrictor comprises a diameter of a ***vein***" as required by limitation c of the Substitute Claim.

71. I understand that in its Institution Decision, the Board found that "although Gille503 uses the general term 'blood vessel,' [it did] not read the reference as excluding the use of the catheter in veins," including because "considering Dr. Day's [then] unopposed testimony, [it] accept[ed] for the purpose of institution that (1) the ordinary meaning of 'blood vessel' includes both veins and arteries; and (2) one of ordinary skill in the art would understand that the angioplasty, reperfusion, and drug delivery techniques disclosed in Gille503 could be performed in veins." Institution Decision at 29 (citing Day Pet. Decl. at ¶¶ 80, 122–23). However, in my opinion a POSA would not understand Gille503 as

teaching that it can be used for any procedure that would involve its balloon being expanded within a vein. Rather, in my opinion, in the context of Gille503's teaching that its "invention relates to a catheter adapted for use in post conditioning treatment," Gille503 at ¶ 1, a POSA would understand Gille503 as only disclosing the use of a catheter for procedures that involve expanding its balloon within an artery, ***not*** a vein.

72. In particular, in my opinion, a POSA would understand that Gille503 describes a catheter for use in post-conditioning treatment to reduce the extent of reperfusion injury following the reopening of an occluded artery following a heart attack. *See* § VI.A.1 above. Gille503 describes that "[m]yocardial infarction (MI) or acute myocardial infarction (AMI), commonly known as a heart attack is the interruption of blood supply ***to*** part of the heart, commonly due to the occlusion of a coronary artery." Gille503 at ¶ 3 (emphasis added). Since, as Gille503 accurately describes, an MI/AMI involves the interruption of blood being supplied ***to*** the heart and a POSA would know that blood is supplied to the heart via arteries, a POSA would understand that the post-conditioning treatment described by Gille503 following an MI/AMI relates exclusively to treatments provided in connection with the restoration of blood flow in arteries. A POSA would understand that Gille503 accurately describes that the most common arteries involved in such treatments are the coronary arteries. *See* Gille503 at ¶ 3. Gille503 thus describes that the post-

conditioning treatments that its invention is used in the context of are provided in connection with "[p]ercutaneous transluminal angioplasty, particularly coronary angioplasty using balloon catheters … for revascularization of stenotic and occluded body vessels, ***such as coronary arteries***." Gille503 at ¶ 3 (emphasis added).

73. Similarly, Gille503 describes that its invention can be used to "reduce[] or even avoid[]" reperfusion injuries following "organ transplantation." Gille503 at ¶ 10. In this case, the "[i]schemia-reperfusion injuries" that Gille503 seeks to reduce or avoid "occur[] when blood supply ***to*** the transplanted tissues or organs is temporarily interrupted and then reintroduced again (reperfusion)." Gille503 at ¶ 10 (emphasis added). Since blood is supplied to organs via arteries, not veins, a POSA would understand that performing the procedures described by Gille503 in this context also necessarily relates to the control of blood flow through arteries, not veins.

74. Thus, based on the context of the type of procedure being described — *i.e.*, post-conditioning treatments in connection with the restoration of blood flow ***to*** portions of the heart following MIs/AMIs or ***to*** transplanted organs, in my opinion a POSA would understand that Gille503's references to "body vessels" relate only to arteries, not veins.

75. While Dr. Day asserts that "Gille503 lists reperfusion, angioplasty, or drug delivery as therapeutic contexts in which its balloon catheter can be used" and that "[e]ach of these procedures can be performed in a vein," Day Pet. Decl. at ¶ 123, Dr. Day ignores that Gille503 does not describe that its device is suitable for use in connection with any conceivable reperfusion, angioplasty, or drug delivery procedure. Instead, Gille503 only describes reperfusion, angioplasty, and drug delivery in the context of the post-conditioning treatment that is the subject of the invention of Gille503.

76. Gille503 does not describe or relate to performing a reperfusion treatment in a vein. At 2:12–17 (in ¶ 6) (cited by Dr. Day at ¶ 123), Gille503 describes that "[t]he provision of at least one flow sensor and/or pressure sensor integrally on the catheter allows a better control of the reperfusion ***of the treated blood vessel***" (emphasis added). Gille503 goes on from there, describing that, "[f]or example, with the inventive provision of a sensor integrally on the catheter it is possible to allow a reduced and low blood flow through the vessel ***during the post-condition treatment***" (emphasis added). And Gille503 at 3:1–5 (in ¶ 10) (also cited by Dr. Day at ¶ 123) relates to Gille503's description of the reperfusion of blood supply ***to*** transplanted tissues or organs, which, as is also described above, a POSA would understand also relates only to procedures being performed on arteries, not veins. It is therefore clear that the reperfusion being referred to here is

only the reperfusion performed in connection with the post-conditioning treatments described by Gille503, which, as described above, a POSA would understand are arterial treatments and do not involve the expansion of a balloon within a vein.

77. Gille503 also does not describe or relate to performing an angioplasty treatment in a vein. Gille503 at 5:50–52 (in ¶ 22) (also cited by Dr. Day at ¶ 123) describes that "[t]he present invention also relates to the use of a catheter ***according to the invention*** in percutaneous transluminal coronary angioplasty" (emphasis added). Thus, because a POSA would understand that the invention of Gille503 relates to providing post-conditioning treatments, which are arterial treatments, a POSA would not understand that Gille503's catheter could be used in venous treatments such as angioplasty procedures in veins because such treatments would have no connection to the arterial post-conditioning treatments that Gille503's invention relates to.[3] Indeed, Gille503 specifically describes that the referenced "[p]ercutaneous transluminal angioplasty" is used "for revascularization

[3] In addition, a POSA would know that angioplasty procedures are much less frequently performed in veins than in arteries. Therefore, in my opinion, unless it was specifically stated that a reference to angioplasty refers to venous angioplasty, a POSA would understand the reference (as in Gille503) to relate to arterial angioplasty only.

of stenotic and occluded body vessels, such as coronary arteries" following MIs/AMIs, *see* Gille503 at ¶ 3, which is the main context in which the invention of Gille503 is used to provide post-conditioning treatment.

78. Finally, Gille503 does not describe or relate to delivering a drug in a vein. Gille503 at 4:17–23 (in ¶ 16) and 5:44–49 (in ¶ 21) (also cited by Dr. Day at ¶ 123) relates to "the exact ***targeted*** application of a drug ***to the area***" that the post-conditioning treatment is being provided and "***local*** delivery of a drug," respectively (emphasis added). In my opinion, a POSA would understand that each of these passages relates only to drugs being provided in connection with the post-conditioning treatment described by Gille503 and that such drugs would be provided to the same area where the post-conditioning is taking place (*i.e.*, by "target[ing]" the "local" area being treated). Moreover, Gille503 describes that "[i]n this embodiment of the invention [involving the delivery of a drug], the means for a local delivery of a drug comprise ***a separate lumen*** in the tubular body or a coating ***on the balloon*** or a delivery via ***pores in the balloon***." Gille503 at ¶ 21 (emphasis added). A POSA would thus understand from this that either the same balloon that is being used for the post-conditioning treatment (*i.e.*, a balloon being used for an arterial treatment) is the balloon through or via which the drugs are delivered or that a separate lumen is used for the delivery of the drugs, in which

case a balloon that may be expanded to the diameter of the delivery area is not involved.

B. Gille501 Does Not Anticipate the Substitute Claim

79. In my opinion, Gille501 does not anticipate the Substitute Claim because it does not disclose at least limitation c — "wherein the first restrictor comprises a retracted and deployed configuration and *in the deployed configuration, the first restrictor comprises a diameter of a* ***vein***" (*see* § VI.B.3 below) — and limitation h — "wherein the control module compares a blood pressure measurement provided by the sensors *to* ***a baseline blood pressure measurement*** *to detect a change in blood pressure*" (*see* § VI.B.2below).

1. Background

80. Gille501 describes "a computer controlled post conditioning device" Gille501 at ¶ 1; *see also* Gille501 at ¶ 3 ("It is an objective of the present invention to provide an improved medical device especially adapted for use in post conditioning treatment."). Gille501, like Gille503, describes that post-conditioning treatment is a procedure that is performed after a vessel that was previously occluded (such as due to an MI) is reopened in order to reduce ischemia reperfusion injury. *See* Gille501 at ¶ 2. According to Gille501, "common dilation devices are not especially designed for controlling the reperfusion flow and regulating the desirable flow restrictions" and "manually controlled inflation and

deflation of the dilation balloon does not allow an exact control of the flow rate of the blood and therefore represents no exact defined intervention protocol to prevent or reduce reperfusion injury." Gille501 at ¶ 2.

81. Accordingly, Gille501 describes "a medical device adapted for use in post conditioning treatment" that includes, among other things, "a control unit for controlling [a] pump depending on at least one physiological parameter and/or catheter-specific parameter and/or in correspondence to a predefined, time-dependent algorithm according to a pre-established post conditioning perfusion protocol." Gille501 at ¶ 4. According to Gille501, this "allows for an even more exact regulation of a fluid flow dependent on the inflation pressure applied to the balloon and the resulting expansion thereof," thereby reducing or avoiding "the factors or human inconsistency and error in both the dilation phase and post conditioning treatment." Gille501 at ¶ 6.

2. Gille501 Does Not Disclose a Comparison of a Blood Pressure Measurement Provided by Sensors to a Baseline Blood Pressure Measurement to Detect a Change in Blood Pressure

82. In my opinion, Gille501 does not disclose that its control module "compares a blood pressure measurement provided by the sensors *to* ***a baseline blood pressure measurement*** *to detect a change in blood pressure*" as required by limitation h of substitute claim 22.

83. I understand that Petitioner relies on Gille501's disclosure that a "physiological parameter … [that] is selected from the group consisting of systemic blood pressure, blood pressure before the balloon catheter, blood pressure behind the balloon catheter, blood flow before the balloon catheter, blood flow behind the balloon catheter, the heart rate and/or electrocardiogram … can advantageously be used to stay within ***desired physiological limits***" in asserting that Gille501 discloses a comparison of a sensed blood pressure to a baseline blood pressure measurement to detect a change in blood pressure. *See* Opposition at 7–8 (emphasis added) (citing Gille501 at ¶ 15). However, in my opinion, a POSA would understand that regardless of which of these physiological parameters are used, Gille501 does not disclose that a desired physiological limit can be a baseline measurement.

84. Moreover, preliminarily, a POSA would understand that each of the seven different physiological parameters disclosed in the list could not be used in the same manner as limits to control the inflation of a balloon used in providing a post-conditioning treatment. For example, a POSA would understand that how (if at all) a limit relating to the heart rate of a patient could be used to control the inflation of such a balloon would be significantly different than how (if at all) a limit relating to blood flow behind the balloon catheter could be used. Indeed, a POSA would understand that at least one of the entries in this list — systemic

blood pressure — likely would not be useful as a parameter to control balloon inflation because the systemic pressure would likely not be significantly impacted by the inflation of a balloon during a post-conditioning treatment. A POSA would therefore look for specific guidance in Gille501 in order to understand how each of the mentioned parameters could be used and, absent that, would not understand that limits relating to each could actually be used as parameters for controlling the inflation of a balloon used for a post-conditioning treatment. A POSA would also understand that a teaching relating to the use of a limit relating to one of these parameters could not be understood to necessarily apply to the use of a limit relating to another one of these parameters.

85. Moreover, in my opinion a POSA would recognize that the physiological limits disclosed by Gille501 are predetermined limits and are not based on any baseline measurement. Accordingly, Gille501 only discloses that measurements provided by the sensors of Gille501 are compared to pre-programmed limits, not "to a baseline [] measurement" as required by the Substitute Claim.

86. In asserting that Gille501 "affirmatively discloses that the target pressures in its feedback loops can be Measured Values, which it refers to as 'beneficial physiological limits,'" Petitioner relies on Gille501's disclosure that the "repeated inflation and deflation of the balloon can be performed with continuous

or period adjustment and/or *maintenance of beneficial* ***physiological limits*** *or in beneficial* ***predetermined limits***." Opposition at 8 (emphasis added) (quoting Gille501 at ¶ 17, emphasis as added by Petitioner). Petitioner, however, misreads Gille501. In my opinion, a POSA would understand that the difference between "beneficial physiological limits" and "beneficial predetermined limits" is not that one is predetermined and the other is measured. Rather, the difference is that "beneficial physiological limits" refers to limits relating to ***physiological*** parameters such as blood pressure, blood flow, or heart rate, *see* Gille501 at ¶ 15, while "beneficial predetermined limits" refers to limits relating to ***non-physiological*** parameters that are specific to the catheter, such as the inflation pressure of the balloon or the volume of the fluid pumped through the catheter, *see* Gille501 at ¶ 16. A POSA would understand that Gille501 does not teach that the limits can be based on a baseline measurement of either a physiological parameter or a catheter-specific parameter.

87. In particular, Gille501 repeatedly distinguishes between limits that are based on physiological parameters and those that are based on catheter-specific parameters, including the following:

- "[T]he present invention provides a medical device adapted for use in post conditioning treatment comprising: … a control unit for controlling the pump depending on *at least one physiological*

parameter and/or catheter-specific parameter ….” Gille501 at ¶ 4 (emphasis added).

- “With the control unit of the invention the pump can be controlled depending on *at least one physiological parameter and/or catheter-specific parameter* ….” Gille501 at ¶ 7 (emphasis added).
- “In another embodiment of the present invention the medical device comprised at least one pressure transducer for measuring *the physiological parameter and/or catheter-specific parameter* …. According to the submitted signals the balloon inflation may be controlled, based on the systemic blood pressure or on other above mentioned *physiological parameters or catheter specific parameters* ….” Gille501 at ¶ 17 (emphasis added).

88. Indeed, in defining its invention in its claims, Gille501 continues to identify that the distinction between the different types of parameters that may be used for controlling its pump is between ones that are physiological and ones that are catheter specific:

- claim 1: “A medical device adapted for use in post conditioning treatment comprising: … a control unit for controlling the pump depending on *at least one physiological parameter and/or catheter-specific parameter* ….” (emphasis added).

- claim 8: "The medical device according to one of the preceding claims characterized in that the medical device comprises at least one pressure transducer for measuring *the physiological parameter and/or catheter-specific parameter*." (emphasis added).

89. In this context, a POSA would understand Gille501's reference to "beneficial physiological limits or [] beneficial predetermined limits" as referring to the same distinction that Gille501 makes throughout its specification and claims between limits that relate to physiological parameters and limits that relate to catheter-specific parameters. Given Gille501's repeated references to physiological versus catheter-specific parameters, a POSA would not understand Gille501's use of the phrase "beneficial predetermined limits" as introducing a new distinction — not referenced anywhere else in Gille501 — relating not to the type of parameter the limits related to but to how the limits are determined.

90. Indeed, as described above with respect to Gille503, a POSA would understand that using a baseline blood pressure measurement would not be useful in the context of a device for use in post-conditioning treatments, which is what Gille501 describes. This is because in post-conditioning treatment, the blood flow through the area being treated is repeatedly reduced and restored. During the period when the blood flow is reduced, the pressure downstream would be decreased (the pressure upstream, which a POSA would recognize as the patient's

systemic blood pressure, would not be changed). A POSA would recognize that comparing measurements of the blood pressure downstream of the balloon to a predetermined target could assist in determining whether the balloon has been expanded to a size that results in the cutting off of sufficient blood flow to cause a period of ischemia, which is required in order for the post-conditioning treatment to be effective. By contrast, a POSA would recognize that comparing measurements of the blood pressure downstream of the balloon to a baseline blood pressure measurement would not assist in determining whether the balloon has been expanded to a size that results in the cutting off of sufficient blood flow to cause a period of ischemia. Comparing measurements of blood pressure to a baseline blood pressure measurement would only provide information that a change in blood pressure has occurred. It would not provide information that the change results in the cutting off of sufficient blood flow to cause a period of ischemia.

91. That both the beneficial physiological limits and beneficial predetermined limits of Gille503 are necessarily predetermined limits is further emphasized for a POSA by Gille501's teaching that the adjustments to the inflation and deflation of the balloon are made based on a "***pre-programmed*** series of sequential inflation and deflation … in a targeted extent resulting in full sealing or reduced low blood pressure flow," which "can be stored in the control unit and can

thus be chosen by the medical person to fit the needs of the patient." Gille501 at ¶ 8 (emphasis added). A POSA would understand this to mean that the balloon is held at inflation and deflation levels that permit "full sealing or reduced low blood pressure flow" for "pre-programmed" durations, which a POSA would understand could only be achieved by comparing the sensed parameters to pre-programmed limits. Baseline measurements of blood pressure would not provide sufficient information to enable a determination of whether a subsequent sensor measurement is indicative of full sealing or reduced low blood pressure flow.

92. In addition, Petitioner is incorrect that Gille501 "confirms that Measured Values can be used as targets because Gille501 discloses that such values can be stored and used in parameterization files." *See* Opposition at 9 (relying on Gille501 at ¶ 9). While Gille501 describes that "[t]he control unit may advantageously be capable of storing data, for example relevant parameters of the performed procedure" such as "example data of physiological parameters of the treated patient," Gille501 at ¶ 9, a POSA would understand that it does not describe that any measured parameters that are stored can used be as a baseline against which successive measurements can be compared for the purpose of detecting a change.

93. A POSA would instead understand that Gille501 here describes that any parameters for use in "a suitable automated run of the medical device" must be

capable of being "chosen and/or modified" by the medical practitioner, which means that any parameters against which sensed measurements are compared must be known before the procedure begins so they can be chosen or modified. This is consistent with Gille501's disclosure that "[w]ith the control unit 5 … different ***pre-programmed*** series of sequential inflation and deflation of the balloon 2 in a ***targeted*** extent resulting in full sealing or reduced low pressure blood flow at a time can be performed ***and chosen by the medical practitioner*** to fit the needs to the patient," Gille501 at ¶ 25 (emphasis added), which a POSA would understand further demonstrates that the "target" values against which any sensed measurements would be compared in order to have the procedure result in full sealing or reduced low blood pressure must be "pre-programmed" and capable of being "chosen by the medical practitioner."

94. In addition, a POSA would understand that Gille501 here describes that any data from the current procedure are stored only for the purpose of use ***after*** the procedure is over, not for comparison during the procedure. First, Gille501 uses the past tense when discussing procedures that the stored data relates to. In particular, Gille501 describes "storing data" including "relevant parameters of the ***performed*** procedure … for example data of physiological parameters of the ***treated*** patient." This would suggest to a POSA that the data is not being stored for the purpose of being actively used within the same procedure. Second, Gille501

describes that the stored "physiological parameters of the treated patient" are "***example*** data." This too would suggest to a POSA that the data being stored is not for the purpose of selecting a specific, appropriate baseline target. A POSA would instead understand that the storage of "example data" is more appropriate when using the stored data for after-the-fact evaluation of the procedure.

95. That this is the purpose of Gille501's storage of data from a current procedure is confirmed by Gille501's description that

> this embodiment [*i.e.*, including a control unit capable of storing data] … can give additional information about the quality of treatment to the medical practitioner and helps to further improve the post conditioning treatment as a medical method. Standardization and reproduction of optimized performance with the obtained reliable data of the medical treatment are made possible. Even the performance of different medical practitioners can be compared and optimized clinical studies are conceivable.

Gille501 at ¶ 9. A POSA would understand from this that the use of the stored data to "improve the post conditioning treatment ***as a medical method***" relates to after-the-fact analysis and use to refine the method. This is emphasized by the fact that Gille501 teaches that data from multiple procedures performed by multiple practitioners would be analyzed as part of this refinement. For example, a POSA would understand that "standardization and reproduction of optimized

performance" and "compar[ing]" "the performance of different medical practitioners" both require that data from multiple procedures be stored for subsequent analysis, such as might be done as part of an "optimized clinical stud[y]."

96. Even if Gille501 were to be read as disclosing the use of a baseline blood pressure measurement as a target against which a current sensed blood pressure is compared (which, as explained above, it does not), Gille501 does not disclose that any such comparison for the purposes of detecting a change in blood pressure is used to adjust a volume of a restrictor in response to the detected change, as required by the Substitute Claim.

97. Instead, Gille501 in fact only specifically discloses how comparisons of catheter-specific parameters such as the pressure of the balloon itself are used to adjust a volume of the balloon. In particular, the only specific description provided by Gille501 is at its Paragraphs 25 and 26, where it describes that "the pressure measurements can help to determine the exact *pressure* ***of the balloon*** 2, for example to just seal a body vessel from the blood flow without risking injury of the vessel by over-expansion or by applying too much pressure to the vessel." Gille501 at ¶ 25 (emphasis added). Thus, when Gille501 goes on to describe that "[t]he balloon inflation and therefore also the degree of obstruction of the blood flow can be controlled periodically or continuously based on *the pressure signal*," a POSA

would understand that the described "pressure signal" refers to "the pressure of the balloon." Similarly, Gille501 describes that "[t]he software can be parameterized with arbitrary intermediacy patterns and raises or lowers the pressure ***inside the balloon*** in order to decrease or increase the flow of a fluid, especially the reperfusion flow," which also demonstrates that the pressure being controlled is the balloon pressure, not blood pressure. Accordingly, a POSA would understand that Gille501 does not describe how any comparison of blood pressure to a target (whether or not the target is based on a predetermined or measured value) is used to detect a change in pressure for the purposes of adjusting a volume of a restrictor in response to the detected change, as is required by the Substitute Claim.

98. Finally, I understand that the Board in its Preliminary Guidance found that "[e]ven if Gille501's *initial* target pressure was predetermined, because Gille501 discloses 'continuous adjustment' to maintain the 'beneficial physiological limits,' a first measurement to determine whether the blood pressure is within limit (at the target pressure) could be considered a baseline and then any second or subsequent measurement is used to determine whether the balloon needs to be inflated or deflated based on the difference between the two measurements." Preliminary Guidance at 8. I disagree that this reasoning satisfies the requirement of the Substitute Claim that "the control module ***compares*** a blood pressure measurement provided by the sensors *to* ***a baseline blood pressure measurement***

to detect a change in blood pressure." It is not sufficient under the claim merely for the blood pressure to have changed between the time when a first measurement was taken and the time when a second or subsequent measurement was taken. Rather, under requirements of the claim, the control module must specifically perform a comparison between a baseline measurement and another measurement. Not only would a POSA understand that a measurement taken after the procedure has begun (*e.g.*, the "first measurement" described by the Board) is not a "baseline" measurement, but, even if it could be considered as such, Gille501 does not describe that any such comparison between a first measurement taken during the treatment and a second measurement is ever performed. Rather, a POSA would understand from Gille501 that each of the successive sensor measurements are compared ***to the original target value***. Indeed, Petitioner's expert, Dr. Day, in the portion of his declaration quoted by the Board in its Preliminary Guidance, states exactly this — that the "feedback loop … determines whether or not to inflate or deflate the balloon, and that determination is made based on the comparison of a current sensed blood pressure measurement with a target value." Day Opp. Decl. at ¶ 87. Because Gille501 does not describe that the target value is ever updated to equal any measured value (and neither Petitioner nor Dr. Day assert anything to the contrary), in my opinion the fact that Gille501 performs continuous adjustments based on comparisons to the target value is insufficient to meet this limitation even

under the reasoning presented in the Preliminary Guidance. Indeed, updating the target value based on earlier measurements would defeat the purpose of the use of the target value in Gille501: to set a value for the blood pressure to reach through operation of the inflation or deflation of the balloon that results in full sealing or reduced low pressure blood flow for the purposes of a successful post-conditioning treatment. If the target against which the later sensor measurements were compared were updated to one of the earlier measurements, then there would be no way for the system to determine if the blood pressure had reached the desired value because, by definition, at the time of the earlier measurements that the Board asserts would become the target, the pressure would not yet have reached the desired level.

3. Gille501 Does Not Disclose Altering the Diameter of the First Restrictor Inside a *Vein*

99. In my opinion, Gille501 does not disclose that "in the deployed configuration, the first restrictor comprises a diameter of a ***vein***" as required by limitation c of the Substitute Claim.

100. I understand that in its Institution Decision, the Board found that "although Gille503 uses the general term 'blood vessel,' [it did] not read the reference as excluding the use of the catheter in veins" and stated that this finding applied as to Gille501 "[c]onsidering the similarities between Gille503 and Gille501." Institution Decision at 29. I understand that the Board based its finding

on "Dr. Day's [then] unopposed testimony, [which it] accept[ed] for the purpose of institution[,] that (1) the ordinary meaning of 'blood vessel' includes both veins and arteries; and (2) one of ordinary skill in the art would understand that the angioplasty, reperfusion, and drug delivery techniques disclosed in Gille503 could be performed in veins." Institution Decision at 29 (citing Day Pet. Decl. at ¶¶ 80, 122–23); *see also* Day Pet. Decl. at ¶¶ 178–79 (similar with respect to Gille501). However, in my opinion a POSA would not understand Gille501 as teaching that it can be used for any procedure that would involve its balloon being expanded within a vein. Rather, in my opinion, in the context of Gille501's teaching that its "invention relates to a medical device adapted for use in post conditioning treatment," Gille501 at ¶ 1, a POSA would understand Gille501 as only disclosing the use of catheter for procedures that involve expanding its balloon within an artery, ***not*** a vein.

101. In particular, in my opinion, a POSA would understand that Gille501 describes a medical device for use in post-conditioning treatment to reduce the extent of reperfusion injury following the reopening of an occluded artery following a heart attack. *See* § VI.B.1 above. Gille501 describes that "[m]yocardial infarction (MI) or acute myocardial infarction (AMI), commonly known as a heart attack is the interruption of blood supply ***to*** part of the heart, commonly due to the occlusion of a coronary artery." Gille501 at ¶ 2 (emphasis added). Since, as

Gille501 accurately describes, an MI/AMI involves the interruption of blood being supplied ***to*** the heart and a POSA would know that blood is supplied to the heart via arteries, a POSA would understand that the post-conditioning treatment described by Gille501 following an MI/AMI relates exclusively to treatments provided in connection with the restoration of blood flow in arteries. A POSA would understand that Gille501 accurately describes that the most common arteries involved in such treatments are the coronary arteries. *See* Gille501 at ¶ 2. Gille501 thus describes that the post-conditioning treatments that its invention is used in the context of are provided in connection with "[p]ercutaneous transluminal angioplasty, particularly coronary angioplasty using balloon catheters … for revascularization of stenotic and occluded body vessels, ***such as coronary arteries***." Gille501 at ¶ 2 (emphasis added).

102. Similarly, Gille501 describes that its invention "also relates to the use of the medical device of the invention in the treatment of infarctions of organs, for example lung, kidney, liver or splenic infarctions, myocardial infarct or other occlusions of body vessels or body tissues, especially in procedures like angioplasty and/or in therapies based on local drug delivery." Gille501 at ¶ 22. In this case, Gille501 describes that its medical device "can be advantageously used in post conditioning treatment" and that with such use "it is possible to reduce or even prevent reperfusion injury or other complication in connection with

uncontrolled restoring of the blood flow." Since the blood flow that is being restored in such procedures would be the blood flowing to the organs via arteries, a POSA would understand that performing the procedures described by Gille501 in the context of the treatment of infarctions of organs necessarily relates to the control of blood flow through arteries, not veins.

103. Finally, Gille501 describes that is invention can be used to "reduce[] or even prevent[]" reperfusion injuries following "organ transplantation." Gille501 at ¶ 23. In this case, the "[i]schemia-reperfusion injuries" that Gille501 seeks to reduce or prevent "occur[] when blood supply ***to*** the transplanted tissues or organs is temporarily interrupted and then reintroduced again (reperfusion)." Gille501 at ¶ 23 (emphasis added). Since blood is supplied to transplanted organs via arteries, not veins, a POSA would understand that performing the procedures described by Gille501 in the context of the reperfusion of transplanted organs or tissues also necessarily relates to the control of blood flow through arteries, not veins. Thus, based on the context of the type of procedure being described — *i.e.*, post-conditioning treatments in connection with the restoration of blood flow ***to*** portions of the heart following MIs/AMIs, ***to*** organs that have been reperfused following infarctions, or ***to*** transplanted organs, in my opinion a POSA would understand that Gille501's references to "body vessels" relate only to arteries, not veins.

104. While Dr. Day asserts that "Gille501 states that the balloon catheter comprising its invention can be used 'in procedures like angioplasty,'" "for reperfusion," and "for drug delivery," and that "a POSA would know that Gille501's catheter can be used in veins for any of these therapeutic objectives," Day Pet. Decl. at ¶ 179, Dr. Day ignores that Gille501 does not describe that its device is suitable for use in connection with any conceivable reperfusion, angioplasty, or drug delivery procedure. Instead, Gille501 only describes reperfusion, angioplasty, and drug delivery in the context of the post-conditioning treatment that is the subject of the invention of Gille501.

105. Gille501 does not describe or relate to performing a reperfusion treatment in a vein. At 3:46–48 (in ¶ 12) (cited by Dr. Day at ¶ 179), Gille501 describes that "[w]ith the automatically controlled ***inflation/deflation cycles*** especially reperfusion can be performed in a secure and smooth manner" (emphasis added). A POSA would understand that this is describing that the post-conditioning treatment offered by the invention of Gille501, which is characterized by inflation and deflation cycles, is what makes it so that a reperfusion can be performed in a secure and smooth manner (because, as described earlier, without a post-conditioning treatment, reperfusion can lead to ischemia reperfusion injury). It is therefore clear that the reperfusion being referred to here is only the reperfusion performed in connection with the post-conditioning treatments described by

Gille501, which, as described above, a POSA would understand are arterial treatments and do not involve the expansion of a balloon within a vein.

106. Further, Gille501 does not describe or relate to performing an angioplasty treatment in a vein. First, as described above with respect to Gille503, *see* ¶ 77 n. 3, because angioplasty is performed in a vein much less frequently than in arteries, a POSA would understand Gille501's reference to angioplasty to relate to an angioplasty procedure performed in an artery. Second, Gille501 at 5:40–41 (in ¶ 22) (also cited by Dr. Day at ¶ 179) describes that "[t]he present invention also relates to the use of the medical device ***of the invention*** in the treatment of infarction of organs …, especially in procedures like angioplasty." Gille501 at ¶ 22 (emphasis added). Thus, because a POSA would understand that the invention of Gille501 relates to providing post-conditioning treatments, which are arterial treatments, a POSA would not understand that Gille501's medical device could be used in venous treatments such as angioplasty procedures in veins because such treatments would have no connection to the arterial post-conditioning treatments that Gille501's invention relates to. Indeed, Gille501 specifically goes on in the next sentence to state that, "[i]n particular, the medical device of the present invention can be advantageously used in post conditioning treatment." Gille501 at ¶ 22.

107. Finally, Gille501 does not describe or relate to delivering a drug in a vein. Gille501 at 5:26–35 (also cited by Dr. Day at ¶ 179) relates to "the local delivery of a drug" that "can especially be used *to treat the* ***occluded segment of a body vessel***." Gille501 at ¶ 21 (emphasis added). Based on this description, in my opinion, a POSA would understand that this passage relates only to drugs being provided in connection with the post-conditioning treatment described by Gille501 and that such drugs would be provided to the same area where the post-conditioning is taking place (*i.e.*, "the occluded segment of a body vessel). Gille501's description of delivery of drugs does not expand the scope of vessels the balloons of Gille501 may be expanded in, as is confirmed by Gille501's description in the same passage cited by Dr. Day that "the means for the local delivery of a drug according to one aspect of the invention comprise ***a separate lumen*** in the catheter or a coating ***on the balloon*** surface or a delivery via ***pores in the balloon***." Gille501 at ¶ 21 (emphasis added). A POSA would thus understand from this that either the same balloon that is being used for the post-conditioning treatment (*i.e.*, a balloon being used in an artery) is the balloon through or via which the drugs are delivered or that a separate lumen is used for the delivery of the drugs, in which case a balloon that may be expanded to the diameter of the delivery area is not involved.

C. Mohl996 Does Not Anticipate the Substitute Claim

108. In my opinion, Mohl996 does not anticipate the Substitute Claim because it does not disclose at least limitation h — "wherein the control module compares a blood pressure measurement provided by the sensors *to* ***a baseline blood pressure measurement*** *to detect a change in blood pressure*" (*see* § VI.C.2 below).

1. Background

109. Mohl996 describes a device and method for "intermittent periodic occlusion of the coronary sinus in order to accomplish retroperfusion, *i.e.*, repeatedly temporarily blocking the major vein which collects blood from the heart muscle in order to cause venous blood to flow back from the normal contracting myocardium to reach ischemic portions of the heart muscle." Mohl996 at 1:10–16. As described by Mohl996, one "technique for retroperfusion uses an inflatable balloon held on the end of a catheter to intermittently occlude the coronary sinus." Mohl996 at 1:34–36. When using this technique, "[b]lood pressure in the sinus then rises as the heart beats so that blood received in the sinus through the healthy tissue of the heart muscle is forced back into the ischemic tissue." Mohl996 at 1:36–39. The balloon is inflated and deflated, "for example at a rate synchronized with the heart pulse rate, or on the basis of pressure," by controlling a gas or liquid that is supplied to via a pump. Mohl996 at 1:42–46.

110. According to Mohl996, its invention "concerns an improvement [to this technique] that leads to making intermittent occlusion of a coronary sinus a successful and useful technique." Mohl996 at 1:49–51. In particular, Mohl996 describes that its "invention employs … a controller responsive to [a] transducer [for sensing the fluid pressure within the sinus] and arranged to provide trigger signals to [an] occluding means [for occluding the sinus] to trigger an occlusion and to interrupt the occlusion," wherein "the controller is arranged to estimate a plateau level of the fluid pressure during each occlusion and to provide the trigger signals to interrupt each occlusion on the basis of said estimate." Mohl996 at 1:51–62.

2. Mohl996 Does Not Disclose a Comparison of a Blood Pressure Measurement Provided by Sensors to a Baseline Blood Pressure Measurement to Detect a Change in Blood Pressure

111. In my opinion, Mohl996 does not disclose that its control module "compares a blood pressure measurement provided by the sensors *to* ***a baseline blood pressure measurement*** *to detect a change in blood pressure*" as required by limitation h of the Substitute Claim.

112. I understand that Petitioner asserts that "the processor in Mohl996's controller senses coronary sinus pressure in a given patient, compares successive readings to determine the maximum local pressure at each heartbeat, stores those maxima, and then uses them to calculate a target that is 94% of the plateau above

which measured pressure likely cannot rise" and that "[t]he controller then repeatedly compares the sensed maximum pressures to the target." Opposition at 18 (citing Mohl996 at 4:59–65, 5:13–34, Fig. 1A); *see also* Opposition at 25 (asserting "baseline pressure measurement is the 94% value"); Day Opp. Decl. at ¶ 224 (asserting that "[t]he 'baseline blood pressure measurement' is 94% of the maximum heartbeat pressure predicted by analyzing blood pressure measurements in the patient"); Preliminary Guidance at 9 ("On this record, we agree with Petitioner's declarant that in Mohl996, '[t]he "baseline blood pressure measurement" is 94% of the maximum heartbeat pressure'"). However, in my opinion a POSA would recognize that the "94% value" referenced by Petitioner is not a baseline blood pressure measurement and that Mohl996 does not, in fact, disclose that any comparison is performed between a blood pressure measurement provided by the sensors and baseline blood pressure measurement to detect a change in blood pressure.

113. Instead, as referenced by Petitioner and its expert, Mohl996 discloses that blood pressure measurements provided by the sensors are compared to an "***estimated plateau level***." Contrary to Petitioner and Dr. Day, this "estimated plateau level" (or 94% thereof) is not a baseline blood pressure measurement, or even a series of baseline blood pressure measurements. Instead, a POSA would understand that the plateau is an ***estimate*** (not a measurement) of a maximum safe

future pressure that is based on multiple measurements taken during the course of the treatment. *See* Mohl996 at 5:3–8 ("We also realize that a benefit of retroperfusion, the washout of metabolites, is dependent upon attainment of pressure, but not prolongation of pressure, as the ischemic site, while continuing to occlude the sinus once plateau 72 is reached could damage healthy heart tissue."). Indeed, because Mohl996 discloses that occlusion is interrupted before the pressure ever reaches the plateau level, Mohl996 at 5:30–34, the plateau level represents a pressure that in fact never occurs and thus could not possibly be a measured value. Moreover, because the plateau level is repeatedly recalculated on a beat-to-beat basis throughout the treatment, it also does not represent a baseline because it is not determined at the start of the treatment.

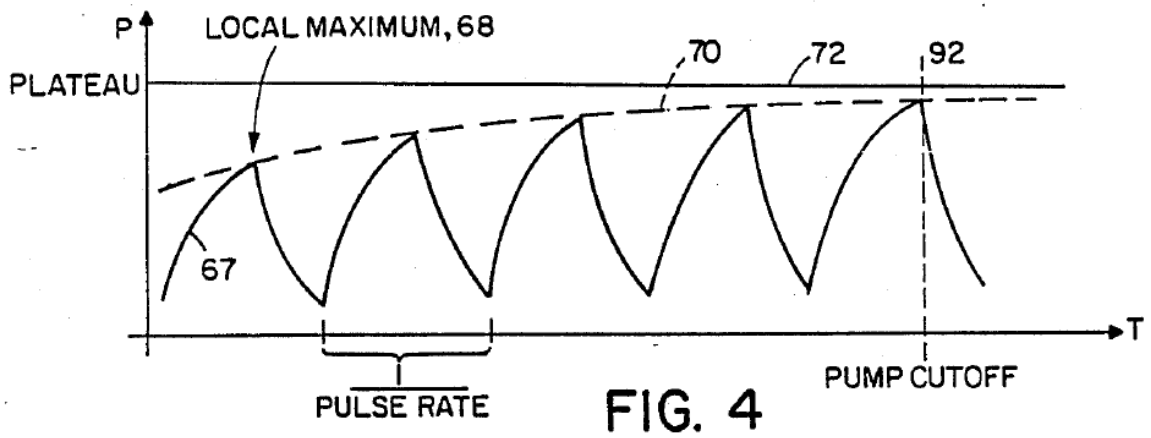
114. Mohl996 repeatedly describes that the plateau level that Petitioner relies on is a calculated estimate (*i.e.*, not a measured baseline). For example, Mohl996 describes that "the plateau level is ***estimated*** *in real time during each period of occlusion* ***based on exponential curve fitting***" and that in order to make this calculation "the controller includes sampling circuitry for sensing the fluid pressure signals, *e.g.*, by storing the sensed signals …, first analysis circuitry for determining and storing a local maximum value of the pressure for each heartbeat from the stored sensed signals [and] second analysis circuiting *for* ***estimating*** *in real time the plateau level from the stored local maximum values*." Mohl996 at

2:3–15; *see also* Mohl996 at 2:15–18 (confirming that it is a "predetermined percentage" of this calculated "estimate plateau level" against which "successive local maximum values" are compared). Mohl996 later specifically describes such "a curve fitting routine" for calculating an estimated plateau level, which further confirms that the estimated plateau level is not a measured baseline. *See* Mohl996 at 5:13–34.

115. In particular, Mohl996 describes that "[p]rocessor 56 … performs ***a curve fitting routine*** (86), *e.g.*, ***by regression analysis,*** *in which the available local maxima are fitted to an exponential function* in the form $P = A - Be^{-ct}$, where P is the pressure as a function of time, A is the plateau pressure, t is time and B is the difference between the plateau and the base-line pressures, and c is the slope constant." Mohl996 at 5:19–26. Mohl996 describes that "[f]rom the resulting function, processor 56 estimates (88) the level that plateau 72 would have and calculates 94% of the plateau (89)." Mohl996 at 5:26–28; *see also* Mohl996 at 5:28–34 (confirming that it is this "94% value" against which "each newly calculated local maximum" is compared).

116. The relationship between the predicted plateau level of Mohl996 and the pressure measurements from its sensors, which shows that the predicted plateau level is not a baseline blood pressure measurement against which the pressure

measurements are compared, is illustrated by its Figure 4, which is reproduced below.



In this figure, the patient's measured systolic pressure is depicted as the wave 67, which rises and falls "cyclically with the heart pulse rate." Mohl996 at 4:59–60. Within "each heartbeat, pressure rises to a local maximum," which is labeled as 68, "and then falls near to a base level, after which the cycle is repeated." Mohl996 at 4:61–63.

117. Based on the teachings discussed above, a POSA would understand that the predicted plateau level (depicted in Figure 4 as line 72) is calculated based on the local maximum values using a "curve fitting routine" (the calculated curve being depicted in Figure 4 as dashed line 70). *See* Mohl996 at 4:63–65. A POSA would further understand that the local maximums are not themselves used as a target or point of comparison, and that the predicted plateau level is not set to and does not equal any of the local maximum values. Instead, the predicted plateau

(depicted as line 72 in Figure 4) is a value that the local maximum values approach "asymptotic[ly]," but never reach. Mohl996 at 4:63–65; *see also* Mohl996 at 5:8–12 ("According to the invention, controller 28 is arranged to terminate the occlusion on the basis of the predicted plateau, more specifically when the sinus reaches a predetermined level (e.g., 94% of the predicted plateau)."), Figure 4 at 92 (showing that the pump is cutoff at the time indicated at dashed line 92, before the pressure reaches the plateau level). Thus, not only is it clear that the plateau level is an estimated maximum future pressure calculated based on past measurements that rise towards the plateau, but it would indeed be impossible for a measured baseline pressure to be used as the plateau level because at no time during the treatment does the measured pressure ever equal the plateau level.

118. Accordingly, in my opinion a POSA would understand that a plateau level that is calculated in the manner taught by Mohl996 based on multiple measurements taken throughout a treatment is not the same as a target that itself is a baseline measurement and that comparing a currented sensed pressure to a calculated plateau level, regardless of what factors were taken as inputs to the calculation, is not the same a comparing a current sensed pressure to a baseline measurement itself.

119. In addition, even if the estimated plateau level (or 94% of it) were considered to be a baseline blood pressure measurement (which, as discussed

above, a POSA would understand it is not), Mohl996 does not teach that "a blood pressure measurement provided by the sensors" is compared to it "to detect a change in blood pressure," as required by the claim. Instead Mohl996 discloses that what is compared to the 94% value is a "***calculated*** local maximum." *See* Mohl996 at 5:28–34 ("Finally, processor 56 compares (90) each newly calculated local maximum with the 94% value, (*e.g.*, at time 92 in FIG. 4) …."). Thus, because what Mohl996 discloses is compared to the 94% value is a "calculated" value, Mohl996 does not disclose that "a blood pressure measurement provided by the sensors" is compared to the 94% value.

D. Levin Does Not Anticipate the Substitute Claim

120. In my opinion, Levin does not anticipate the Substitute Claim because it does not disclose at least limitation h — "wherein the control module compares a blood pressure measurement provided by the sensors *to* ***a baseline blood pressure measurement*** *to detect a change in blood pressure*" (*see* § VI.D.2 below) — and limitation i — "wherein the control module … ***directly adjusts*** *a volume of the first restrictor* ***in response to*** *the detected change* in blood pressure" (*see* § VI.D.3 below).

1. Background

121. Levin describes an invention that "relates to a method for reducing reperfusion injury after therapeutic reperfusion of an infarct of a heart or other

organ" and "percutaneous transluminal coronary angioplasty PTCA catheters" for use during such therapies. Levin at ¶ 2. In particular, Levin describes that "reperfusion of [] ischemic myocardium can be followed by dramatic functional and structural changes that can lead to additional heart dysfunction and even death." Levin at ¶ 4. Levin describes that this "damage that occurs to an organ that is caused by the resumption of blood flow after an episode of ischemia" is known as "[r]eperfusion injury," which "results from several complex and interdependent mechanisms that involve the production of reactive oxygen species, endothelial cell dysfunction, microvascular injury, alterations in intracellular Ca2+ handling, changes in myocardial metabolism, and activation of neutrophils, platelets, and the complement system." Levin at ¶ 5.

122. Levin thus describes that its invention is intended to address "a clear clinical need for a novel treatment that can be applied shortly after [an] MI to reduce the extent of the infarct expansion that is minimally invasive and can be performed in a cathlab as an adjunct to PTCA reperfusion." Levin at ¶ 10. In particular, Levin describes that its "invention may be embodied by modulating blood flow (or oxygen delivery) to the reperfused zones of the heart muscle over a short period of time (*e.g.*, seconds to minutes) immediately following the re-opening of the blood vessel thus altering the abrupt transition of the muscle at risk from extremely low to high blood supply." Levin at ¶ 11. A POSA would

recognize this as treatment as what is known as "post-conditioning treatment." *See* Levin at ¶ 23 ("The procedure characterized by these elements may be called 'balloon post-conditioning'.").

2. Levin Does Not Disclose a Comparison of a Blood Pressure Measurement Provided by Sensors to a Baseline Blood Pressure Measurement to Detect a Change in Blood Pressure

123. In my opinion, Levin does not disclose that its control module "compares a blood pressure measurement provided by the sensors *to* ***a baseline blood pressure measurement*** *to detect a change in blood pressure*" as required by limitation h of the Substitute Claim.

124. I understand that Petitioner relies on Levin's disclosure that its "balloon 502 inflation and consequently the degree of obstruction to blood flow can be controlled continuously based on the CS [coronary sinus] pressure feedback to maintain CS pressure ***within desired physiological limits***" in asserting that Levin discloses this limitation. *See* Opposition at 16–17 (emphasis added) and 25 (citing Levin at ¶ 54); Day Opp. Decl. at ¶¶ 140–43 and ¶ 208 (same); Preliminary Guidance at 10 (relying on Day Opp. Decl. at ¶ 208). However, in my opinion, a POSA would recognize that Levin teaches that its desired physiological limits are predetermined limits. They are not baseline blood pressure measurements and Levin therefore does not disclose this limitation.

125. Petitioner is incorrect that "Levin repeatedly teaches that the 'desired physiologic limits' can be based on ***a patient's*** normal pressure measurements." Opposition at 16 (emphasis added). While Levin does teach "[i]t can be expected that effective C[S] pressures will be in the range higher than ***normal venous pressures*** but lower than ***normal arterial pressure***," Levin at ¶ 54, Levin does not describe that these "normal" pressures are "a patient's." Instead, a POSA would recognize in the context of Levin's disclosure and how post-conditioning treatment works that the referenced "normal" pressures are "normal" in a global, predetermined sense (in the same way that one might say that a "normal" resting heart rate for a person is about 60 bpm or that a "normal" highway driving speed is 65 mph).

126. This is made explicit by Levin's description that "the range higher than normal venous pressure but lower than normal arterial pressure" is, "for example, ***between 10 to 60 mmHg***," Levin at ¶ 54 (emphasis added); *see also* Levin at ¶ 54 ("The CS pressure can be for example gradually reduced from high (***for example 50 mmHg***) to low (***for example 10 mmHg***) over the desired period of time (for example 5 to 30 minutes) immediately after PTCA opening of an infarcted coronary artery." (emphasis added)). A POSA would recognize that Levin is here providing examples of predetermined "normal" pressures to be used as desired physiological limits. The fact that the examples provided by Levin are

round and correspond to values that a POSA would recognize as globally "normal' for higher than normal venous pressure and lower than normal arterial pressure further supports this understanding, as does the fact that the use of a patient's own "normal" blood pressure as a desired physiological limit does not make sense in the context of the post-conditioning treatment described by Levin (as explained below). Levin does not describe that these limits would vary from patient-to-patient nor that they could be determined based on a measurement from the patient being treated as would be necessary for the patient's normal blood pressure to be used as a baseline blood pressure measurement.

127. As referenced above, a POSA would recognize that in the context of post-conditioning treatment, it does not make sense to use a blood pressure measurement from the patient being treated as a baseline to which measurements of the patient's blood pressure during the treatment are compared. This is because the objective of post-conditioning treatment is to create periods of ischemia (reduced blood supply) by deliberately oscillating the amount of blood that is allowed to flow through an area. *See, e.g.*, Levin at ¶ 21 ("The balloon can be rapidly inflated and deflated to interrupt blood flow in the coronary artery supplying the heart muscle at risk of reperfusion injury," which "reduces blood flow to the tissue at risk when the balloon is cyclically inflated by modulating this flow during the period of time at risk for reperfusion injury."). In doing so, a

POSA would recognize the need to set certain predetermined limits that the patient's blood pressure should be kept between in order to have a safe but effective treatment. In particular, on the high end, Levin teaches that "[e]xcessively high CS pressure can lead to angina and ischemia." Levin at ¶ 54. A POSA would therefore understand the need to set a predetermined limit to prevent such adverse consequences. On the low end, Levin teaches that "excessively low CS pressure can result in insufficient post-conditioning." Levin at ¶ 54. A POSA would thus understand that if the CS pressure remains excessively low during the occlusion period of the treatment, the objective of reducing blood flow to the tissue at risk would not be achieved and the post-conditioning treatment would not result in the desired decrease in reperfusion injury. A POSA would understand that a patient's own normal blood pressure would be irrelevant as a baseline in this context, as it would not provide any information about what pressure would be excessively high and therefore lead to risks of angina and ischemia nor any information about what pressure would be excessively low and therefore lead to ineffective treatment. A POSA would recognize that such limits would need to be predetermined by a medical practitioner based on their knowledge and experience.

128. Moreover, a POSA would recognize that it would in fact be impossible in the context of Levin to use a patient's own "normal" blood pressure as the "desired physiologic limit." The desired physiological limits are those within

which the patient's blood pressure should be kept during the treatment. They are thus necessarily different from the patient's normal blood pressure prior to the treatment, when no balloon is being used to periodically occlude the patient's coronary sinus. It would therefore be impossible to use the patient's normal blood pressure as a limit, as the patient's normal blood pressure would not be an excessively high blood pressure that would lead to risks of angina and ischemia and would also not be an excessively low blood pressure that would cause the treatment to be ineffective (and certainly could not be both at the same time).

129. I understand that Petitioner asserts that Levin's disclosure that "[i]implementation of a user requested CS pressure control algorithm could be achieved by applying methods known in the field of control engineering" supports its assertion that Levin discloses a comparison of a sensed blood pressure to a baseline blood pressure measurement because, according to its expert, a POSA would understand "methods known in the field of controls engineering" "to encompass a feedback loop that compares the sensed blood pressure against the baseline measurement." Day Opp. Decl. at ¶ 208 (relying on Levin at ¶ 61); Opposition at 25 (same). In my opinion, Petitioner's reliance on this disclosure is misplaced. Levin describes that the algorithms that it is referring to here "can be used to maintain a physiologic parameter (such as CS pressure or CSvO2) or a calculated index ***at the target level or within the desired range***." Levin at ¶ 61

(emphasis added). A POSA would thus understand that maintaining a physiological parameter or a calculated index "at the target level or within the desired range" is the goal of the mentioned algorithms and that the algorithms therefore relate to how the parameter or index is maintained at that level or within that range, not to what the target or range itself is. Stated differently, Levin in this paragraph describes that different algorithms can be used, for example, to maintain CS pressure within desired physiologic limits, which as described above would necessarily be predetermined limits.

130. The algorithms "known in the field of controls engineering" referenced by Levin in this paragraph could be as simple as comparing current pressure to a predetermined pressure limit and increasing or decreasing the size of the balloon accordingly. Or they could be more complex, such as the referenced PI feedback controller, which produces an output (*e.g.*, a change to the balloon inflation) that is proportional of integral of the error (*i.e.*, the difference between the measured pressure and the desired pressure) with respect to time. In any event, Levin in this paragraph (or anywhere else) does not describe that a baseline blood pressure measurement can be used as the target for a control algorithm for use in a post-conditioning treatment. To the contrary, as described above, a POSA would understand that such a target would not be useful in a controlling a balloon to provide a safe and effective post-conditioning treatment.

131. I understand that Petitioner also asserts that Paragraphs 84 and 85 of Levin, which relate to Figures 9 and 10, respectively, provide "examples using baseline measurements." *See* Opposition at 25. In my opinion, Petitioner is incorrect that these examples show a comparison of a blood pressure measurement provided by sensors to a baseline blood pressure measurement to detect a change in blood pressure in response to which a volume of a restrictor is directly adjusted, as required by the Substitute Claim.

132. With respect to Levin at Paragraph 84 and Figure 9, first, Levin here describes a "method of graded reperfusion" in which the coronary artery is occluded. *See* Levin at ¶ 84 ("Graded … reperfusion is based on the idea of *gradually letting blood flow* ***through the infarct zone*** *after the reopening* ***of the coronary artery***. … The post-conditioning balloon 801 is first inflated to the level of occlusion that corresponds to 25% *of normal* ***coronary artery*** *perfusion pressure or flow 901*." (emphasis added)). Second, Levin here describes that the balloon is inflated to, for example, "the level of occlusion that corresponds to 25% of normal coronary artery perfusion or flow 901." As described above with respect to Paragraph 54 of Levin, a POSA would not understand the "normal" pressure being referred to here to be "the patient's" "normal" pressure, but would instead understand it to be a predetermined limit. And third, even if the "normal coronary artery pressure" referenced here were a measured value, Levin does not describe

that a subsequent measured pressure is compared to it in order to detect a change in pressure and then directly adjust a volume of the restrictor in response to the detected change. Instead, Levin describes that the balloon pressure is adjusted ***until*** the goal pressure (*e.g.*, 25% of normal coronary artery perfusion pressure) is achieved, at which point the pressure of the balloon stops being adjusted and the volume of the balloon "is held at that level for … [a] duration of time." This is the opposite of what is required by the Substitute Claim. Rather than a detected change causing an adjustment to be made to the balloon, as required the claim, the balloon is adjusted until the pressure has changed to equal the goal pressure, at which point the detected change causes the balloon to ***stop*** being adjusted.

133. Levin at Paragraph 85 and Figure 10 describes a method of "post-conditioning by gradual occlusion of the contrary sinus" in which "the pressure ramp or trajectory starts from its highest value 1001 that may correspond [to] the blood pressure in the totally occluded CS or some value just below it," "[t]he balloon 502 … is maximally extended," "the balloon is released somewhat [and] pressure is reduced to the level 1002, then to 1003 and 1005," and "[i]n the end of the ramp 1005 pressure in CS is equal to normal right atrial pressure of that particular patient." First, while Levin does here mention the "normal right arterial

pressure of that particular patient,"[4] it describes that such a pressure is only achieved "[i]n the end of the ramp." Thus, because the patient's normal blood pressure must be known at the beginning of the treatment in order to be used as a measured baseline, it cannot be used as such when it is not known until the end. Second, Levin does not disclose that the pressure ramp levels 1001, 1002, 1003, 1004, and 1005 are targets based on a baseline blood pressure measurement. Instead, a POSA would understand, for example, that the ramp is predetermined. According to Levin's disclosure, a medical practitioner would thus choose the "highest value 1001 that may correspond to the blood pressure in the totally occluded CS or some value just below it" and would then "maximally extend[] the balloon until the pressure in the CS reaches that level, which is how the practitioner would know that that the CS is totally occluded (or just below totally occluded). Similarly, levels 1002, 1003, and 1004 would be predetermined stepping points on the ramp to the balloon being totally deflated. And level 1005 does not represent a target pressure at all, but instead merely represents the

[4] This also indicates that where Levin intended to refer to the "normal" pressure of a particular patient, it understood the need to explicitly clarify that the pressure was of a particular patient, and that Levin's other references to "normal" pressure do not refer to a pressure measured from a particular patient.

pressure achieved when the balloon is "substantially deflated and is not obstructing drainage of venous blood from the heart." Third, as with the example of Paragraph 84 and Figure 9 discussed above, even if pressure ramp levels referenced here were measured values, Levin does not describe that a subsequent measured pressure is compared to them in order to detect a change in pressure and then directly adjust a volume of the restrictor in response to the detected change. Instead, as with the example of Paragraph 84 and Figure 9, a POSA would understand that the balloon pressure is adjusted ***until*** patient's blood pressure equals each of the levels, at which point the pressure of the balloon stops being adjusted for a period of time and the volume of the balloon is held constant until the time for the next step in the ramp. This is the opposite of what is required by the Substitute Claim. Rather than a detected change causing an adjustment to be made to the balloon, as required the claim, the balloon is adjusted until the pressure has changed to equal the desired level, at which point the detected change causes the balloon to ***stop*** being adjusted.

134. Finally, in my opinion, a POSA would understand that the teachings of Paragraphs 84 and 85 of Levin are not likely to work for the purposes of providing an effective post-conditioning treatment and therefore would not rely on them. In particular, both paragraphs teach the targeting of certain blood pressures in the coronary sinus or coronary artery. But a POSA would understand that while

adjusting the blood ***flow*** in the coronary sinus or coronary artery to reach certain percentage targets could be relatively easily accomplished using an occlusion balloon, targeting a specific blood pressure would be much more difficult, if not impossible. This is because the pressure in the coronary sinus or coronary artery would not change in direct response to changes in the amount of occlusion provided. Instead, a POSA would understand that until the vessel is almost completely occluded any impact on the blood pressure downstream of the balloon would be very slight (if there is an impact at all) and then once the vessel is almost completely occluded (at least about 95% or more), the blood pressure downstream of the balloon would decrease in a manner that is not linearly or proportionally correlated to the degree of occlusion. Accordingly, a POSA would understand that it would be very difficult, if not impossible, to reduce the pressure in the coronary artery or views to target levels such as the 25% levels indicated in Paragraphs 84 and 85. This is especially true because the vessels within which the balloon of Levin would be expanded are relatively narrow and the fluid that would need to be introduced in the balloon in order to expand it must travel a relatively long distance from where the catheter is inserted into the body to where the balloon is used, which a POSA would understand can result in the amount of fluid being introduced into the catheter outside of the patient's body not resulting an exactly equal amount or fluid being introduced into the balloon itself. Moreover, a POSA would

understand that reducing flow to a 25% level as is taught by Paragraphs 84 and 85 of Levin would not be effective for a post-conditioning treatment. A POSA would instead understand that tissue receiving 25% of blood flow would not become ischemic and that therefore reducing the flow to such a level would provide no benefit in preventing reperfusion injury.

3. Levin Does Not Disclose That a Volume of a First Restrictor is Directly Adjusted in Response to a Detected Change in Blood Pressure

135. In my opinion, Levin does not disclose that its control module "***directly adjusts*** *a volume of the first restrictor* ***in response to*** *the detected change* in blood pressure" as required by limitation i of the Substitute Claim.

136. I understand that that Petitioner asserts that that Levin discloses this limitation by virtue of its teaching that "[c]ontrol signals can be applied continuously or periodically to adjust the size of the balloon." Levin at ¶ 61; *see also* Levin at ¶ 54 ("The balloon 502 inflation … can be controlled continuously based on the CS pressure feedback to maintain CS pressure within desired physiologic limits."); Day Opp. Decl. at ¶ 209 (relying on Levin at ¶¶ 54 and 61); Opposition at 25 (same). In my opinion, however, this does not show that a volume of a balloon is directly adjusted in response to a detected change in blood pressure, as there are many ways that control signals can be used to control the volume of a balloon based on inputs such as detected changes in pressure. Levin, in fact, only

describes two specific ways of responding to what Petitioner asserts is a detected change in pressure. *See* Opposition at 25 (citing ¶¶ 84 and 85 (relating to Figures 9 and 10, respectively). In particular, as described above, in Paragraph 84 (relating to Figure 9), Levin describes that the balloon pressure is adjusted ***until*** the goal pressure (*e.g.*, 25% of normal coronary artery perfusion pressure) is achieved, at which point the pressure of the balloon stops being adjusted and the volume of the balloon "is held at that level for … [a] duration of time." Similarly, a POSA would understand in Levin at Paragraph 85 (relating to Figure 10) the balloon pressure is adjusted ***until*** patient's blood pressure equals each of the levels, at which point the pressure of the balloon stops being adjusted for a period of time and the volume of the balloon is held constant until the time for the next step in the ramp. Each of these examples is the opposite of what is required by the Substitute Claim. Rather than a detected change causing an adjustment to be made to the balloon, as required the claim, the balloon is adjusted until the pressure has changed to equal the desired level, at which point the detected change causes the balloon to ***stop*** being adjusted.

E. Gille501 and Gille503 Do Not Render the Substitute Claim Obvious

137. In my opinion, the Substitute Claim is not obvious based on Gille501 or Gille503, either on their own or in view of the secondary references cited by Petitioner — Levin, Mohl996, and Mashimo — because, as discussed above in

Sections VI.A and VI.B, they do not disclose at least limitation c — "wherein the first restrictor comprises a retracted and deployed configuration and *in the deployed configuration, the first restrictor comprises a diameter of a* ***vein***" (*see* §§ VI.A.3 and VI.B.3 above) — and limitation h — "wherein the control module compares a blood pressure measurement provided by the sensors *to* ***a baseline blood pressure measurement*** *to detect a change in blood pressure*" (*see* §§ VI.A.2 and VI.B.2 above and § VI.E.1 below) — and because it would not have been obvious to a POSA to modify them to perform such limitations (*see* §§ VI.E.2 and VI.E.3 below).

1. The Secondary References Relied on by Petitioner Do Not Disclose a Comparison of a Blood Pressure Measurement Provided by Sensors to a Baseline Blood Pressure Measurement to Detect a Change in Blood Pressure

138. I understand that Petitioner asserts that three secondary references — Mohl996, Levin, and Mashimo — disclose the use of a baseline blood pressure measurement for comparison to a blood pressure measurement provided by sensors to detect a change in blood pressure. Opposition at 15–19. However, in my opinion, none of Levin, Mohl996, and Mashimo disclose comparing "a blood pressure measurement provided by the sensors *to* ***a baseline blood pressure measurement*** *to detect a change in blood pressure*" as required by limitation h.

139. As discussed in Sections VI.C.2 and VI.D.2 above, Mohl996 and Levin, respectively, do not disclose comparison of a blood pressure measurement

provided by sensors to a baseline blood pressure measurement to detect a change in blood pressure.

140. Mashimo also does not disclose comparison of a blood pressure measurement provided by sensors to a baseline blood pressure measurement to detect a change in blood pressure.

141. Mashimo describes "a catheter for the diagnosis and treatment of a narrowing lumen." Mashimo at 2:14–15; *see also* Mashimo at 2:24–25 ("the invention provides a method for the diagnosis and assessment of a narrowing lumen with a balloon catheter"). A POSA would recognize this could be used for an angioplasty treatment, *see* Mashimo at 1:5–8 ("[A]ngioplasty catheterization typically involves locating an obstruction in a lumen and then inserting a balloon catheter into the lumen at the location of the obstruction. Once the balloon is positioned within the obstruction, it is dilated with a fluid causing the balloon to expand against the obstruction."), or "for the sweeping of ducts," Mashimo at 1:8–10 ("such as the removal of concretions including gallstones and kidney stones"). Mashimo describes that a "common risk … with both procedures is the possibility of improper dilation of the balloon portion of the catheter." Mashimo at 1:10–11. Accordingly, Mashimo describes a "smart balloon catheter [that] includes pressure and diameter sensing features along with a feedback system to control the dilation of the balloon." Mashimo at 5:1–4.

142. I understand that Petitioner asserts that Mashimo discloses this limitation on the basis of its teachings that "computer 14 compares the information from the pressure sensors 34a, 34b, 34c … with known pressure, volume and diameter endpoints" and that "[t]he endpoints can be calculated on theoretical models, or can be based on empirical data." *See* Opposition at 19 (relying on Mashimo at 11:24–26 and 11:28–30); *see also* Day Opp. Decl. at ¶¶ 157–59. However, in my opinion, a POSA would understand that the "known pressure … endpoints" of Mashimo are necessarily predetermined. Mashimo does not disclose that they can be based on baseline blood pressure measurements.

143. In particular, in the same paragraph relied on by Petitioner, Mashimo discloses that "[t]he endpoints *established and* ***programmed*** *prior to a controlled dilation of the membrane 30* and are dependent on etiology of the lumen 62 and the obstruction 64, as well as the type of membrane 30 used." Mashimo at 11:26–28 (emphasis added). In my opinion, a POSA in the art would understand that "programmed" endpoints are different from baseline blood pressure measurements. A POSA would understand that according to the teachings on Mashimo the endpoints would be predetermined values that are included in the programming of the control unit itself and would not be adjustable during a procedure. Indeed, because Mashimo discloses that "the type of membrane 30 used" is one of the considerations on which the endpoint depends, it would be impossible for the

programmed endpoint to be a baseline blood pressure measurement because the membrane 30 would not have any impact on the patient's baseline blood pressure "prior to a controlled dilation of the membrane 30." Mashimo at 11:26–27.

144. Indeed, the block flow diagram of Figure 7 of Mashimo, reproduced below, does not include any step at which an endpoint is determined based on a pressure measurement.

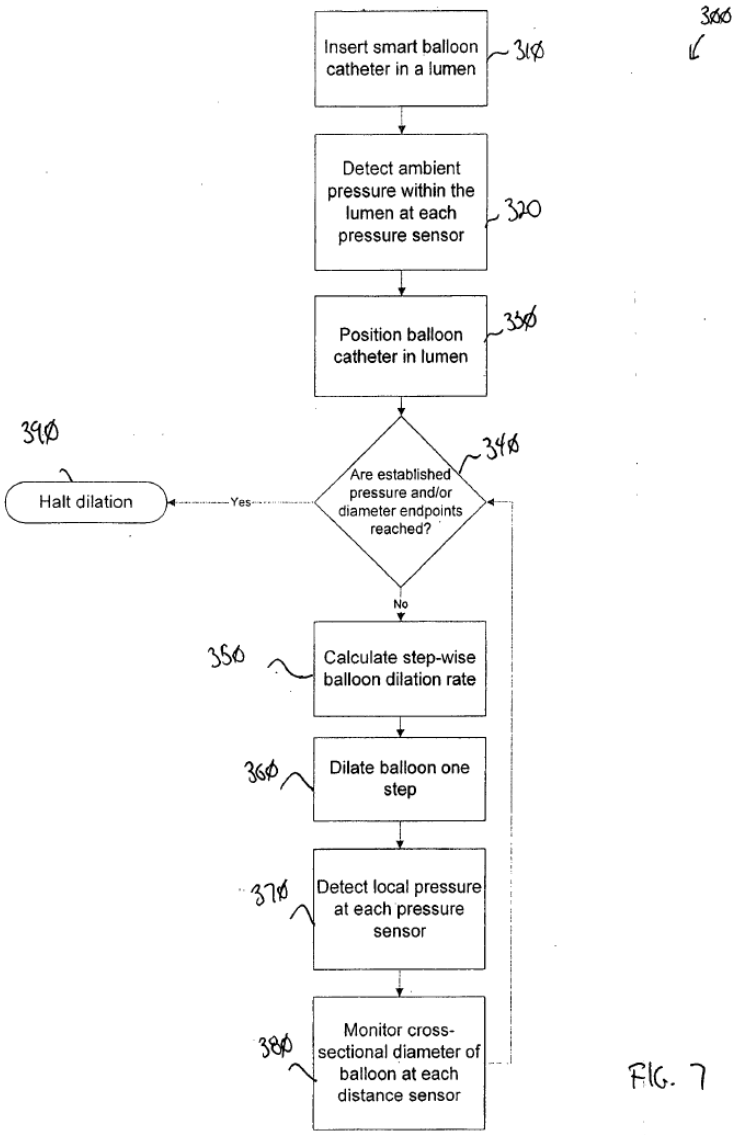


FIG. 7

Instead, it shows the balloon catheter is positioned in the lumen at step 330 and that immediately thereafter the pressure from the pressure sensors on the catheter are compared to "established pressure … endpoints" at step 340. A POSA would understand from this that no step of setting the pressure endpoints based on a baseline blood pressure measurement is disclosed. Indeed, this evidences that it would not make sense in the context of Mashimo to use a baseline blood pressure measurement as the endpoint, because that would result in the measured pressure immediately equally the endpoint and the process being terminated (*i.e.*, the process would immediately go to "end dilation" step 390), without ever reaching steps 350, 360, 370, and 380.

145. While Petitioner and Dr. Day assert that "[a] POSA would know that the reference to 'empirical data' means that the pressure endpoints can comprise or be based on actual measurements," Opposition at 19; Day Opp. Decl. at ¶ 158, in my opinion, a POSA would in fact understand "empirical data" to refer to data that was previously collected, such as from prior procedures on other patients and/or clinical studies. This is true for several reasons.

146. First, a POSA would understand the term "empirical data" to refer to multiple pieces of information collected in a reliable manner from which determinations could be made. A POSA would not refer to a baseline blood pressure measurement, which is a single bit of information, as "empirical data."

147. Second, a POSA would understand in the context of Mashimo's disclosure that "endpoints *can be calculated on* <u>*theoretical models*</u>*, or can be based on* <u>*empirical data*</u>," Mashimo at 11:28–29, that both the theoretical models and empirical data are of a similar nature, *i.e.*, both exist prior to the treatment and can be used to determine the endpoints based on the "etiology of the lumen 62 and the obstruction 64, as well as the type of membrane 30 used." Mashimo at 11:26–28. A POSA would understand the difference between these to be that the "theoretical models" would provide, for example, formulas based on theories regarding what an appropriate endpoint would be based on inputs including information regarding the lumen, obstruction, and type of membrane being used, while empirical data, for example, would provide direct information about the values of endpoints that would be appropriate given a certain lumen, obstruction, and type of membrane. A POSA would understand that based on either "theoretical models" or "empirical data," the control unit could be programmed based on the lumen that the device is to be used in, the obstruction that the device is to treat, and the type of membrane used to determine the appropriate endpoints to use for the treatment.

148. Third, a POSA would understand that it would not make sense, and indeed would be impossible, to use a baseline blood pressure measurement as a "pressure … endpoint" for the type of procedure that Mashimo discloses, and that

Mashimo's reference to "empirical data" therefore could not be understood in such an illogical manner to refer to a baseline blood pressure measurement. The treatment of Mashimo begins with an occluded vessel, and the treatment has a goal of eliminating the occlusion, which would have the effect of changing the pressure within the previously occluded vessel. Thus, the "endpoint" pressure is necessarily different than the baseline blood pressure in the vessel. Indeed, since the "endpoint" pressure is by definition the pressure in the vessel at the ***end*** of the treatment, it is not experienced at any point prior to it being reached (at which point the treatment is terminated) and any measurement taken prior to that point could not be used as the endpoint.

2. A POSA Would Not Modify Gille501 or Gille503 to Compare a Blood Pressure Measurement Provided by Sensors to a Baseline Blood Pressure Measurement to Detect a Change in Blood Pressure

149. As stated above, I understand that Petitioner asserts that "[a] POSA would be motivated to combine either Gille reference with the knowledge reflected in Mohl996, Levin, and Mashimo (or, alternatively with the teachings of any individual reference) to arrive at the alleged invention of the Substitute Claim." Opposition at 20. However, in my opinion, a POSA would not in fact, be motivated, either by Levin, Mohl996, and Mashimo (individually or in combination) or by Gille501 or Gille503 themselves to modify either Gille501 or Gille503 to compare a blood pressure measurement provided by the sensors *to* ***a***

baseline blood pressure measurement *to detect a change in blood pressure*" as required by limitation h. In my opinion, not only does Petitioner not provide any reason why a POSA would have been motivated to alter Gille501 or Gille503 in the manner suggested by Petitioner, but a POSA would understand that the suggested alteration would not in fact even work for the intended purpose of Gille501 and Gille503 and a POSA would have been motivated not to combine teachings relating to different, potentially incompatible catheter devices or to alter Gille501 and Gille503 in a different manner to use "more feasible" ways of controlling the inflation of their balloons.

150. Preliminarily, Petitioner and Dr. Day mischaracterize and oversimplify the invention of the '069 patent in asserting that the invention merely relates to the use of a feedback loop to control the value of a variable based on a target and that the only question is whether it would be obvious to change the target used in the feedback loop from a predetermined to a measured value. *See, e.g.*, Opposition at 2–6, 13–15. But, as discussed in Section V above, a POSA would recognize that the '069 patent discloses and claims the use of a specific method that enables the creation of a low pressure zone in the region around the thoracic/lymphatic duct outflow in order to enable the clearance of lymphatic fluid. A POSA would recognize that the '069 patent does not just rely on the use of known feedback loops in order to adjust the pressure in the region around the

thoracic/lymphatic duct outflow based on any target. Instead, as reflected in the Substitute Claim, the '069 patent describes the use of a specific comparison of a blood pressure measurement provided by the sensors to a baseline blood pressure measurement to detect a change in blood pressure and that a volume of a restrictor is directly adjusted in response to the detected change. A POSA would understand that by directly adjusting a volume of a restrictor in response to a change in blood pressure detected by comparing a blood pressure measurement provided by the sensors to a baseline blood pressure measurement, the invention of the '069 patent is able to create the low pressure zone that causes lymph to drain from the thoracic/lymphatic duct outflow.

151. In addition, in asserting that "the only alternative to a Predetermined Value is a Measured Value," Opposition at 13, it appears that Petitioner has chosen as its starting point the control algorithms of Gille501 and Gille503 that, according to Petitioner, perform comparisons to targets only because of the hindsight offered by the Substitute Claim, which requires that a comparison be used to detect a change in blood pressure. Moreover, even accepting the use of the control algorithms of Gille501 and Gille503 that, according to Petitioner, perform comparisons to targets, Petitioner does not provide any reason why a POSA would seek to use a baseline blood pressure measurement as the target in their algorithms instead of a predetermined value. A POSA could instead decide not the alter the

algorithms of Gille501 and Gille503 since Petitioner has not identified any flaws or downsides to them. Or, a POSA could choose from many potential alternative algorithms for the purposes of the post-conditioning treatments taught by Gille501 and Gille503.

152. A POSA would understand that there are many potential algorithms that could be used for controlling a balloon for use in such a post-conditioning treatment. For example, instead of using blood pressure as a target at all, a control algorithm for a post-conditioning treatment could use the pressure in the balloon itself as the target/variable to be controlled (which Gille503 in fact teaches would be more effective, *see* Gille503 at ¶ 19). Or, instead of comparing a blood pressure measurement to a target, the algorithm could use a number of measurements over time to calculate a prediction of when in the future the pressure will reach a target, which would allow the balloon to be adjusted in anticipation of where it will be. Or, instead of relying on a single target/variable, the algorithm could rely on multiple factors, such as both blood flow ***and*** pressure.

153. Moreover, even if the only choice to be made were between whether a predetermined value or a measured value should be used as the target in a comparison, in my opinion a POSA would not understand that "a self-evident choice in keeping pressure within safe or desired limits during the operation of a medical device is to derive those limits from measurements of pressure in the

patient before or when the device is used," as Petitioner asserts. Opposition at 2. Instead, a POSA would understand that the choice of a target may be limited or dictated by the purpose for which the comparison is being made. For example, a POSA would recognize that measured values could not be used as the basis for comparisons performed as part of certain treatments such as the post-conditioning treatments of Gille501 and Gille503. *See* ¶¶ 48–49, 90 above. And in any event, a POSA would recognize that many medical devices make use of predetermined values as targets in safe manner, as demonstrated by the fact that Gille501 and Gille503 themselves rely on predetermined values as targets.

154. I understand that the Board in its Preliminary Guidance stated that "a measured value is the more likely choice" for a target in the context of the feedback loops used by Gille501 and Gille503. Preliminary Guidance at 11. However, in the context of the post-conditioning treatments taught by Gille501 and Gille503, in my opinion, a POSA would understand that baseline blood pressure measurements would not be viable choices as targets at all and that the evidence demonstrates that the predetermined values are, in fact, "the more likely choice."

155. First, baseline blood pressure measurements are not "the more likely choice" for the target of a comparison used to detect a change in pressure when controlling a balloon catheter for use during a post-conditioning treatment, as is demonstrated by the fact that Gille501, Gille503, and Levin all relate to post-

conditioning treatment but do not use baseline blood pressure measurements as targets. *See* §§ VI.A.2, VI.B.2, and VI.D.2 above.

156. Second, a POSA would understand it does not make sense (and indeed would not be useful) to use measurement from the patient as the "baseline" when performing post-conditioning treatment. In particular, a POSA would recognize that in the context of post-conditioning treatment where the objective is to create periods of ischemia (reduced blood supply) by deliberately oscillating the amount of blood that is allowed to flow through an area, the patient's "baseline" blood pressure is irrelevant. A POSA would understand that sensed blood pressures are compared to targets values in those references in order to ensure that blood flow has been restricted sufficiently by their balloon for the post-conditioning treatment to be effective and/or to ensure that blood flow has not been restricted too much to the point where it could cause its own damage. *See, e.g.*, Levin at ¶ 54. A POSA would understand that the blood pressure values indicative of too much restriction or too little restriction cannot be the baseline blood pressure measurements, but would instead necessarily be predetermined values.

157. Gille503 provides at least two additional reasons why a POSA would not seek to modify its teachings based on other prior art references such as Levin, Mohl996, and Mashimo. First, Gille503 teaches that "there is no standard to the components of a catheter" and that practitioners must therefore "handl[e]

restrictions and incompatibilities especially with exterior devices like displays, control units and the like." Gille503 at ¶ 17. This would suggest to a POSA that due to restrictions and incompatibilities between different catheter devices and components thereof it would be undesirable to mix and match components of different catheter devices (including the algorithms implemented by the control units).

158. Second, while Gille503 mentions that "a target low blood pressure during the post conditioning treatment avoiding a full sealing of the vessel can be achieved with an adjustment of the inflation extent of the balloon depending on the sensed data," it immediately thereafter goes on to state, "[h]owever when there is an automated system it might be more feasible to sense the pressure of the balloon itself in order to avoid any unwanted over-expansion and to monitor the behaviour of the balloon during inflation depending on the condition of the vessel during treatment." Gille503 at ¶ 19. Accordingly, if a POSA were to modify the portion of Gille503 that describes the use of "a target low blood pressure" when implementing an automated system such as that described by the Substitute Claim, they would be motivated by Gille503's teachings not to use a measured blood pressure value as the target, but to instead change to using the pressure of balloon itself as the target.

159. In my opinion, a POSA would similarly be discouraged by this from mixing and matching components of catheter devices taught by different prior art references to modify the device of Gille501, and would similarly be motivated not to modify Gille501 to use a measured blood pressure value as the target, but to instead change to using the pressure of balloon itself as the target.

160. Finally, in my opinion, a POSA would not rely on Mohl996 or Mashimo in seeking to modify Gille501 or Gille503 because Mohl996 and Mashimo relate to an entirely different types of treatment than that taught by Gille501 and Gille503. While Gille501 and Gille503 relate to post-conditioning treatment (which seeks to reduce the extent of reperfusion injury by alternately inflating and deflating a balloon in an affected body lumen in order to create intermittent periods of ischemia), *see* §§ VI.A.1 and VI.B.1 above, Mohl996 relates to retroperfusion therapy (in which oxygenated blood is supplied to ischemic tissue in the heart by raising the pressure in the coronary sinus so that blood flows backwards from the coronary sinus to the affected tissue), *see* § VI.C.1 above, and Mashimo relates to an angioplasty treatment or a sweeping treatment for removing obstructions such as gallstones and kidney stones, *see* ¶ 141. In my opinion, a POSA would not have sought to combine teachings from references relating to such different types of treatments. Moreover, a POSA would understand that the smart balloon catheter of Mashimo requires significant hardware that

would make it too large and therefore unsuitable for use in a post-conditioning treatment as taught by Gille501 and Gille503. For this reason as well, a POSA would not have sought to combine teachings from Mashimo with those of Gille501 or Gille503.

3. A POSA Would Not Modify Gille501 or Gille503 to Alter the Diameter of the First Restrictor Inside a *Vein*

161. Further, in my opinion, it would not have been obvious for a POSA to modify Gille501 or Gille503 to alter the diameter of a first restrictor inside a vein.

162. As discussed in Sections VI.B.3 and VI.A.3 above, Gille501 and Gille503, respectively, do not disclose that "in the deployed configuration, the first restrictor comprises a diameter of a vein." Moreover, because the inventions of Gille501 and Gille503 relate to a medical device and a catheter, respectively, "adapted for use in post conditioning treatment," Gille501 at ¶ 1; Gille503 at ¶ 1, which a POSA would understand is a treatment that works by repeatedly restricting ***arterial*** blood flow in order to induce periods of ischemia and thereby reduce the extent of reperfusion injuries, *see* ¶¶ 41, 80 above, a POSA would recognize that there would be no reason to attempt to modify the invention of Gille501 or the invention of Gille503 for use within a vein. Moreover, Gille501 and Gille503 do not disclose that their inventions can be used for procedures that are not related to the post-conditioning treatment that they provide. *See* ¶¶ 55 n.1, 75–78, 104–107

above. A POSA therefore would not seek to use the inventions of Gille501 and Gille503 to perform a non-post-conditioning related treatment in a vein.

F. Mohl302 Does Not Render the Substitute Claim Obvious

163. In my opinion, the Substitute Claim is not obvious based on Mohl302, including in view of Mohl996 or Levin, because Mohl302 does not disclose or render obvious a control module that "compares a blood pressure measurement provided by the sensors *to* ***a baseline blood pressure measurement*** *to detect a change in blood pressure*" as required by limitation h (*see* § VI.F.2 below) and because Mohl302 does not disclose a control module that "***directly adjusts*** *a volume of the first restrictor* ***in response to*** *the detected change* in blood pressure" as required by limitation i and, in my opinion, a POSA would not have been motivated by Mohl996 and/or Levin to modify Mohl302 to perform such a direct adjustment (*see* § VI.F.3 below).

1. Background

164. Mohl302 describes an invention that relates "to repair[ing] or treat[ing] [] ischemic heart muscle tissues by supplying the ischemic tissue with blood through ***retrograde perfusion***." Mohl302 at ¶ 3 (emphasis added). Consistent with the understanding of a POSA, retrograde perfusion is a treatment to supply blood to ischemic tissue by "temporarily occlud[ing] [the coronary sinus] so that the blood therein counterflows back from the coronary sinus through the

coronary venous system and toward the ischemic muscle tissue that previously did not received blood from the arterial side." Mohl302 at ¶ 3. Mohl302 teaches that its invention enables "ischemic or otherwise damaged heart muscle tissue [to] receive a redistribution of blood flow from the coronary venous system (*e.g.*, due to an instrument that temporarily occludes the coronary sinus) prior to the restoration of normal blood flow from the coronary arterial system," which "can lead to improved muscle tissue recovery after the coronary arterial blockage is treated and arterial blood flow returns to the previously blood-deprived portion of the heart muscle tissue." Mohl302 at ¶ 5.

165. Mohl302 teaches that its "system for treating heart tissue can include a coronary sinus occlusion catheter having an inflatable balloon device and a control system to control the inflation and deflation of the inflatable balloon device" and that "the coronary sinus occlusion catheter can be activated to perform a pressure-controlled intermittent coronary sinus occlusion (PICSO) procedure for at least a portion of the time in which the catheter [] is positioned in the coronary sinus of the heart." Mohl302 at ¶ 6. Mohl302 teaches that "[i]n particular circumstances, the control system can be configured to activate the inflatable balloon device as part of a predetermined patter of occlusion periods and release periods … as part of a pressure-dependent pattern that is at least partially defined by the coronary sinus pressure readings during the procedure." Mohl302 at ¶ 6.

2. Mohl302 Does Not Disclose a Comparison of a Blood Pressure Measurement Provided by Sensors to a Baseline Blood Pressure Measurement to Detect a Change in Blood Pressure

166. In my opinion, Mohl302 does not disclose that its control module "compares a blood pressure measurement provided by the sensors *to* ***a baseline blood pressure measurement*** *to detect a change in blood pressure*" as required by limitation h of the Substitute Claim.

167. I understand that Petitioner asserts that Mohl302 discloses comparing pressure measurements with each other because it discloses that its "software module can be configured to determine a time derivative of the coronary sinus pressure curve over time during PICSO, which can be employed as a parameter in determining the balloon inflate and deflate times." Opposition at 21 (relying on Mohl302 at ¶ 42). While Dr. Day asserts that "generating a time derivative requires storing and comparing blood pressure measurements with each other," Day Opp. Decl. at ¶ 169, a POSA would understand that computing a time derivative of a curve is not the same as performing a comparison between a baseline and a subsequent value.

168. First, it is clear from Mohl302 that in determining a time derivative, it is performing an operation that relates to at least several data points necessary to define a "coronary pressure sinus ***curve***." A POSA would understand that at least several blood pressure sensor measurements (*i.e.*, not just a baseline and a

subsequent data point) would be needed in order to determine a coronary sinus pressure curve because a curve could not be defined by just two data points (which could define, at best, a line). Accordingly, the time derivative calculation of Mohl302 is not a comparison between a blood pressure measurement from a sensor and a baseline blood pressure measurement based on which a volume of a restrictor is directly adjusted, as required by the Substitute Claim. It instead involves the analysis of at least three (and likely more) data points defining a curve, and that there is no comparison of two of such data points that causes the volume of a restrictor to be directly adjusted.

169. Second, even if determining a time derivative did involve comparing between a blood pressure measurement from a sensor and a baseline blood pressure measurement with each other (which a POSA would understand is not true), a POSA would not understand Mohl302 as disclosing that either of the pressure measurements being compared is a "***baseline*** blood pressure measurement." Instead, because Mohl302 is concerned with rate of change, a POSA would understand that the two measured values being compared could occur at any point in time during the treatment and that the rate of change could vary over the course of the treatment. Mohl302 therefore would not be interested in repeatedly comparing each newly measured pressure to a baseline blood pressure measurement, but would instead, for example, compare consecutive measurements

in order to determine the rate of change in blood pressure at a particular, present moment during the procedure.

3. A POSA Would Not Modify Moh302 to Directly Adjust the Volume of a First Restrictor in Response to a Change in Pressure Based on Mohl996 or Levin

170. As admitted by Petitioner and Dr. Day, Mohl302 does not disclose that its control module "***directly adjusts*** *a volume of the first restrictor* ***in response to*** *the detected change* in blood pressure" as required by limitation i of the Substitute Claim. Instead, Mohl302 "uses the sensor measurements to update a ***schedule*** of balloon inflation and deflation." Opposition at 21 (emphasis added); *see also* Day Opp. Decl. at ¶ 178.

171. I understand that Petitioner asserts that a POSA would "know to use the pressure measurements made by Mohl[302]'s sensors … to directly adjust balloon inflation or deflation, as taught, for example, in both Mohl996 and Levin." Opposition at 21; *see also* Preliminary Guidance at 12 ("[W]e have considered this ground as either (1) that Mohl996 or Levin provide the knowledge of one of ordinary skill in the art, or (2) that Mohl996 or Levin provide a rationale for modifying Mohl302."). However, in my opinion, a POSA would not be motivated, including by Mohl996 or Levin, to modify Mohl302 to directly adjust a volume of a restrictor in response to a detected change in blood pressure, as required by limitation i. In my opinion, not only does Petitioner not provide any reason why a

POSA would have been motivated to alter Mohl302 in the manner suggested by Petitioner, but a POSA would understand that the suggested alteration would not in fact even work for the intended purpose of Mohl302.

172. First, as discussed in Section VI.D.3 above, Levin does not disclose directly adjusting a volume of a restrictor in response to a detected change in blood pressure. Accordingly, in my opinion, Levin could not provide the knowledge or motivation necessary to modify Mohl302 to directly adjust a volume of a restrictor in response to a detected change in blood pressure.[5]

173. Second, Petitioner provides no reason why a POSA would be motivated to modify Mohl302 based on either Mohl996 or Levin to perform such direct adjustment. Instead, Petitioner asserts that "it would be readily apparent that Mohl[302]'s balloon catheter is not limited to performing any particular algorithm

[5] Similarly, as discussed in Sections VI.C.2 and VI.D.2 above, neither Mohl996 nor Levin disclose comparing a blood pressure measurement provided by sensors to a baseline blood pressure measurement to detect a change in blood pressure. Accordingly, in my opinion, neither Mohl996 nor Levin could provide the knowledge or motivation necessary to modify Mohl302 to compare a blood pressure measurement provided by sensors to a baseline blood pressure measurement to detect a change in blood pressure.

to occlude the coronary sinus" and that "it could perform other occlusion algorithms, including those of coronary sinus occlusion devices such as Mohl996 or Levin." Opposition at 23; *see also* Preliminary Guidance at 12 ("Given that Mohl302 discloses a 'customized algorithm,' we agree with Petitioner's declarant that an ordinary artisan would have been motivated to use algorithms with measured values and direct adjustment, such as those of Mohl996 or Levin, because 1) 'Mohl302 has all of the components necessary to execute such algorithms,' 2) 'Mohl302's processor could execute such an algorithm simply by being programmed with it,' and 3) they would have a reasonable expectation of success in doing so …. Alternatively, or in addition, the present record supports that one of ordinary skill in the art would have been motivated to modify the algorithm of Mohl302 with that of Mohl996 or Levin as a simple substitution of one known algorithm … for another known algorithm."). But, in my opinion, a POSA would recognize that this reasoning by Petitioner (and the Board) is simply an assertion that it would be possible to make such a modification to Mohl302. It does not provide any reason why a POSA would in fact want to make such a change by, for example, substituting the algorithm of either Mohl996 or Levin for the algorithm of Mohl302, which Mohl302 teaches works for the intended purpose of providing a retrograde perfusion therapy. For example, neither Petitioner nor Mohl996 or Levin describe that using the algorithm of Mohl996 or Levin would

improve the performance of the retrograde perfusion therapy of Mohl302 in any way. Indeed, a POSA would recognize that Levin relates to an entirely different type of therapy — post-conditioning therapy — and that the algorithm of Levin therefore could not be substituted into Mohl302 without entirely altering the purpose that Mohl302 is used for.

174. Moreover, in my opinion a POSA would in fact recognize that modifying Mohl302 to directly adjust a volume of a restrictor in response to a detected change would frustrate Mohl302's goal of providing a mechanism by which data from early cycles of occlusion and non-occlusion can be used to optimize how later cycles are performed, which a POSA would recognize can result in a more effective retroperfusion treatment.

175. A POSA would understand that the objective of Mohl302 is to induce blood to flow backwards from the coronary sinus into areas of the heart that are not receiving arterial blood flow due to an occlusion, Mohl302 at ¶ 5, and that Mohl302 achieves this objective by occluding and un-occluding the coronary sinus for periods of time, *see, e.g.*, Mohl302 at ¶ 6 ("the control system can be configured to activate the inflatable balloon device as part of a ***predetermined pattern of occlusion periods and release periods***" (emphasis added)), ¶ 9 ("the control system, during a second period of operation, may activate the inflatable balloon device of the coronary occlusion catheter to ***intermittently*** occlude the

coronary sinus in a ***pattern***" (emphasis added)), ¶ 25 ("the control system 140 can be configured to activate the occlusion component of the catheter 120 in the coronary sinus 20 as part of a predetermined pattern of occlusion periods and release periods"), ¶ 56 (providing an example of a "predetermined pattern" of occluded and non-occluded states).

176. Mohl302 discloses that "in some embodiments, the balloon inflate and deflate software module … can implement a customized algorithm that calculates and updates the time periods during which the coronary sinus is in an occluded state and a non-occluded state based on the coronary sinus pressure measurements." Mohl302 at ¶ 43. A POSA would understand that this updating the time periods for occlusion and non-occlusion enables a form of self-learning, in which data from earlier cycles of occlusion and non-occlusion inform how later cycles are performed in order to optimize those later cycles. In particular, Mohl302 teaches that "during ***an initial phase*** … the control system 140 can inflate and deflate the balloon device 122 according to [a] predetermined pattern of inflated times and deflated times," "during [which] the coronary sinus pressure measurements are recorded by the control system." Mohl302 at ¶¶ 56–74 (emphasis added).

177. Mohl302 then uses the coronary sinus pressure data gathered during the initial phase to perform "comparisons of the pressure curve at different times

[which] permits the control system 140 to adjust or optimize a cycle length during the next phase." Mohl302 at ¶ 74. Thus, "[a]fter [the] initial phase, the control system 140 can automatically switch the second type of operation in which the time periods for the occluded state and the non-occluded state are a function of the previously recorded coronary sinus pressure measurements." Mohl302 at ¶ 75. A POSA would thus understand that Mohl302 teaches performing an entire cycle of occlusions and non-occlusions during which data is gathered and then using that data to determine new time periods for the next cycle of occlusions and non-occlusions. In this manner, each subsequent cycle of occlusions and non-occlusions is optimized based on data from the previous cycles.

178. A POSA would understand that at no point during this operation is a volume of a restrictor directly adjusted based on a detected change in blood pressure. A POSA would understand that if a volume of a restrictor were to be directly adjusted based upon a detected change in blood pressure, that modification would have the result of altering the cycle of occlusions and non-occlusions being performed (for example, by ending one of the occlusions or non-occlusions early or by prematurely terminating the cycle altogether). A POSA would understand that altering a cycle in this manner while it is being performed would fundamentally alter how Mohl302 performs its retroperfusion therapy, which is based on cycles of occlusions and non-occlusions being performed based on

predetermined patterns (*i.e.*, either a pattern set for the initial cycle or a pattern determined for subsequent cycles based on data form earlier cycles in a form of self-learning and optimization). Moreover, altering a cycle in this manner would make it more difficult or impossible to optimize future cycles based on data from earlier cycles, as how each cycle is performed may no longer be comparable to each other. Accordingly, in my opinion a POSA would not, in fact, be motivated to modify Mohl302 to use an algorithm that directly adjusts the volume of a restrictor in response to a detected change in blood pressure because doing so would fundamentally alter how Mohl302 performs its retroperfusion therapy and would frustrate Mohl302's purpose of providing a self-learning method for optimizing how later cycles are performed based on data from earlier cycles.

179. In addition, in my opinion, a POSA would not be motivated to modify Mohl302 to directly adjust a volume of the first restrictor in response to a detected change in blood pressure because Mohl302 teaches that its "control system can be configured to activate the inflatable balloon device as part of a predetermined pattern of occlusion periods and release periods that is ***independent*** *of the coronary sinus pressure*." Mohl302 at ¶ 6 (emphasis added); *see also* Mohl302 at ¶ 25 ("the control system 140 can be configured to activate the occlusion component of the catheter 120 in the coronary sinus 20 as part of a predetermined pattern of occlusion periods and release periods that is ***independent*** *of the*

coronary sinus pressure ….” (emphasis added)); ¶ 56 (“In particular embodiments, the control system 140 (FIGS. 2–3) can activate and deactivate the balloon device 122 (causing inflation and deflation) according to … a predetermined pattern of intermittent coronary sinus occlusions (time periods are ***independent*** *of coronary sinus pressure measurements*) ….” (emphasis added)). Accordingly, if a POSA were to modify the embodiments of Mohl302 that make use of coronary sinus pressure, in my opinion they would be more likely to do so by switching to the embodiment of Mohl302 that does not rely on coronary sinus pressure measurements than by developing a new system based on combining Mohl302 with other references.

VII. Conclusion

180. In this declaration, I have presented my opinions that Substitute Claim 22 of the ’069 patent is not invalid on the grounds raised by Petitioner in its Opposition to WhiteSwell’s Motion to Amend, including that the Substitute Claim is not anticipated by Gille501, Gille503, Mohl996, or Levin and that the Substitute Claim is not obvious based on Gille501, Gille503, or Mohl302, either on their own or in view of secondary references including Mohl996, Levin, and Mashimo.

181. My opinions are based on the information available to me and are subject to change in view of opinions provided by Petitioner or its expert, or any

additional information that I may receive. I reserve the right to supplement my opinions accordingly.

In signing this declaration, I recognize that it will be filed as evidence in contested cases before the Patent Trial and Appeal Board of the United States Patent and Trademark Office.

I declare under penalty of perjury under the laws of the United States of America that the foregoing is true and correct.

Executed on: September 1, 2022

Boris Leschinsky

Boris Leschinsky

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SENIOR EXECUTIVE / CTO

Senior medical device expert with broad expertise in cardiovascular and endovascular fields with a focus on percutaneous catheters, heart assist devices, perfusion and blood pumps, percutaneous aneurysm treatments, and vascular closure products. Skilled in early recognition of major clinical and market trends. Inventor of a principal concept for a new cardiology product, Percutaneous Heart Pump, aimed at $8+ billion market opportunity.

Key qualifications include:

- Strong blend of business, technical, clinical, and IP knowledge based on 30+ years in the medical device industry
- Successful in directing R&D and M&A activities and for a large publicly-traded medical device company
- Track record of driving projects forward within approved timelines and budgets
- Personal network of contacts with renowned US and EU cardiac surgeons and interventional cardiologists
- Inventor in 55 US and 70+ international patents
- Deep knowledge of cardiovascular anatomy, physiology, and pathophysiology
- Close familiarity with clinical and regulatory aspects of bringing products to market
- Comprehensive understanding of surgical and interventional treatments of various heart diseases
- Strong sense of new product marketability
- Competent hands-on leadership in developing major new products
- Coordinating internal R&D activities with partners in academia to reduce time to market

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PROFESSIONAL EXPERIENCE

CORINNOVA INC. (since 2013) – **Vice President, Product Development**
Medical device start-up, remote position

- Leading a small engineering team and coordinating several external vendors in developing a novel external compression cardiac assist device:
  - Development of thin-film polyurethane multi-segment inflatable subassemblies
  - Development of NiTinol wire frame and hub structures
  - Development of miniaturized pressure monitoring of the passive and active inflatable chambers
  - Development of insertion and delivery methods and devices
  - Development of a pneumatic driver and controller for operating the device
  - Development of bench test methods and devices for fatigue and other tests
- Primary Investigator on animal studies and NIH grant applications

FRESH CONCEPT DESIGN CORP. (since 1995) – **President**
Sole principal – R&D and patent consulting services. Involved with a broad range of medical devices, including nebulizers, subcutaneous ports, dialysis machines, perfusion and infusion pumps, ultrasound and other imaging devices, patient monitors, etc. Prepared and filed over 350 patent applications

CERUS ENDOVASCULAR INC. (2009 to 2013) – **CTO**
Leading a start-up team in developing proprietary non-invasive devices for treating brain aneurysms

LIFECUFF TECHNOLOGIES INC. (since 2009) – **Founder**
Part-time position with a medical device company developing automated devices for remote ischemic conditioning based on 10 issued US patents.

DATASCOPE CORP., Montvale, NJ (1990 to 2009)

Diversified medical device company with $400 million total sales volume and major product lines in intra-aortic balloon pumping, patient monitoring, vascular sealing, and vascular grafts

Vice President, Technology (Aug 2005 to Feb 2009)
Responsible for directing R&D activities of all four divisions of the company with a total budget of $30+ million, regular market introductions of new products, identifying organic growth opportunities as well as technical and IP assessment for new business development and technology acquisitions

- Invented a key concept for a new revolutionary catheter-based heart assist device combining a low-profile insertion with full-flow assist capability – Percutaneous Heart Pump (PHP)
- Led internal and external technical teams with a combined yearly budget of $2 million in developing this concept through feasibility and achieving major performance goals
- Project acquired for $8.5 million by a major medical device company – Thoratec – now in clinical trials
- Acquired by Abbott for **$450 million** in 2016 after obtaining CE Mark
- Completed detailed technical and patent due diligence assessments on 100+ acquisition targets

Scientific Director (Oct 1998 to Aug 2005)
Responsible for advanced development of new generations of company products, primarily in the fields of counterpulsation, vascular closure and endovascular aneurysm treatment devices

Early Positions: **Engineer** (1990 to 1994), **Sr. Research Engineer** (1994 to 1995), **Principal Engineer** and **Sr. Principal Engineer** (1995 to 1998)

SCIENTIFIC INSTITUTE FOR TRANSPLANTOLOGY AND ARTIFICIAL ORGANS,
Moscow, Russia (1987 to 1990)

Lead Engineer – artificial heart laboratory (1988 to 1990)

- Controlled performance of the first Russian artificial heart in limited clinical use on 10 patients
- Implanted and evaluated outputs of several artificial heart prototypes in large animals
- Invented and patented 5 new concepts for centrifugal blood pumps

Engineer (1987 to 1988)

EDUCATION

Masters in Mechanical Engineering – Moscow State Technical University, Russia, 1987

Advanced Ph.D. courses in biomedical sciences – Moscow, Russia, 1990

OTHER QUALIFICATIONS

Registered Patent Agent with US Patent and Trademark Office

Inventions

- Named inventor in 55 US and 70+ international patent filings (published patents list here)
- Sole inventor or co-inventor in 40% of all patent filings by Datascope between 1990 and 2009
- 2009 "Inventor of the Year" nominee for a lifetime of innovation achievements

Professional Societies Membership

- ASAIO - American Society for Artificial Internal Organs
- ESAO – European Society for Artificial Organs
- ISRBP - International Society for Rotary Blood Pumps
- AUTM - Association of University Technology Managers

Other

- Authored 6 peer-reviewed articles as well as 4 abstracts and oral presentations at scientific conferences
- Invited speaker at 2008 Medical Device and Manufacturing Conference
- Invited moderator for 2007 ASAIO conference
- Listed Reviewer for ASAIO Journal

- Adviser for a Ph.D. thesis at PennState University

PUBLICATIONS

- Letsou GV, Bolch CM, Hord EC, Altman WC, Youngblood BL, **Leschinsky B**, Criscione JC. Mechanical Cardiac Support With an Implantable Direct Cardiac Compression Device: Proof of Concept. Ann Thorac Surg (in press) 2022.
- Letsou GV, Bolch CM, Hord EC, Altman WC, **Leschinsky B**, Criscione JC. The CorInnova Implantable Cardiac Assist System for Direct Cardiac Compression. Rev. Cardiovasc. Med. 23(6), 211, 2022.
- Letsou GV, **Leschinsky B**, Hord E, Bolch C, Criscione J. Effective Diastolic Mechanical Support Using a New Implantable Cardiac Compression Device. The Journal of Heart and Lung Transplantation. 40: S103–S104, 2021.
- Letsou GV, **Leschinsky B**, Hord E, Bolch C, Criscione J. Mechanical cardiac support using a new implantable cardiac compression device. 101st AATS annual meeting, Oral presentation, 2021.
- Letsou GV, Bolch C, Hord E, **Leschinsky B**, Criscione J. Extracardiac Mechanical Support Device Placement by a Minimally Invasive Approach is Safe and Effective. The Journal of Heart and Lung Transplantation. 39: S189–S190, 2020.
- Hord EC, Bolch CM, Tuzun E, Cohn WE, **Leschinsky B**, Criscione JC. Evaluation of the CorInnova Heart Assist Device in an Acute Heart Failure Model. J Cardiovasc Transl Res 12(2):155-163, 2019.
- Garratt KN, **Leschinsky B**. Remote Ischemic Conditioning: The Commercial Market: LifeCuff Perspective. J Cardiovasc Pharmacol Ther. Sep;22(5):408-413, 2017.
- Ohley WJ, Antonelli L, **Leschinsky B**. Influence of catheter and arterial diameter on flow distal to an intra-aortic balloon insertion site: a theoretic examination and in vitro assessment. ASAIO J. Nov-Dec;44(6):786-93, 1998.
- **Leschinsky B**, Itkin GP, Zimin NK. Centrifugal blood pumps--a brief analysis: development of new designs. Perfusion.6(2):115-21, 1991.

SERVICE

NIH Reviewer for grant applications

EXPERT WITNESS

- *Abiomed, Inc. v. Maquet Cardiovascular, LLC*, No. 1:16-cv-10914 (D. Mass.) (provided expert report; testified at deposition)
- *Atrium Medical Corporation v. Bard Peripheral Vascular, Inc.*, IPR2021-01197 (PTAB) (provided expert declaration)
- *Atrium Medical Corporation v. Bard Peripheral Vascular, Inc.*, IPR2021-01199 (PTAB) (provided expert declaration)
- *Atrium Medical Corporation v. Bard Peripheral Vascular, Inc.*, IPR2021-01200 (PTAB) (provided expert declaration)