UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

Palette Life Sciences, Inc.,
Petitioner,

v.

Incept, LLC,
Patent Owner.

Case IPR2020-00005
Patent No. 7,744,913

PETITION FOR *INTER PARTES* REVIEW

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1009	U.S. Provisional Application No.: 60/444,143, W.R. Noyes (filed: January 31, 2003)
1010	U.S. Patent No.: 6,624,245, D.G. Wallace et al., Issued: September 23, 2003
1011	PCT Publication No.: WO 94/25080, L. Griffith-Cima et al. (published: November 10, 1994)
1012	A.B.S. Ball et al., "Silicone implant to prevent visceral damage during adjuvant radiotherapy for retroperitoneal sarcoma," *British Journal of Radiology* 63:346-348 (May 1990)
1013	U.S. Patent No.: 6,375,634, R.G. Carroll, Issued: April 23, 2002
1014	A. Jemal et al, "Cancer statistics, 2002," *CA: A Cancer Journal for*

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1056	U.S. Patent No.: 5,922,025, W.G. Hubbard, Issued: July 13, 1999
1057	U.S. Patent No.: 4,674,488, A.S. Nashef and T.D. Campbell, Issued: June 23, 1987
1058	U.S. Patent No.: 4,706,652, B.S. Horowitz, Issued: November 17, 1987
1059	U.S. Patent No.: 6,635,267, T. Miyoshi et al., Issued: October 21, 2003
1060	U.S. Patent No.: 6,723,709, D. Pressato et al., Issued: April 20, 2004
1061	U.S. Patent No.: 6,129,761, J.A. Hubbell, Issued: October 10, 2000
1062	B.E. Waddell et al., "Prevention of chronic radiation enteritis," *Journal of the American College of Surgeons* 189:611-624 (1999) ("Waddell II")

I. INTRODUCTION

Petitioner Palette Life Sciences, Inc. ("Palette") seeks *inter partes* review of claims 1-25 of U.S. Patent No. 7,744,913 ("the '913 patent," EX1001). 37 U.S.C. ch. 31. This petition shows a reasonable likelihood that the challenged claims are unpatentable.

II. MANDATORY NOTICES

A. Real Parties-In-Interest

The real parties-in-interest are Palette Life Sciences, Inc. and Pharmanest AB. Moreover, in an acquisition that closed on October 2, 2019, Nestlé S.A. sold Galderma S.A., Galderma Laboratories, Inc., Galderma Laboratories LP, Galderma Research & Development SNC, Nestlé Skin Health, Inc. (now SHDS, Inc.), and Nestlé Skin Health S.A. to an investment consortium of EQT Partners AB, Public Sector Pension Investment Board (PSP Investments), and Luxinva, a wholly owned subsidiary of Abu Dhabi Investment Authority. Galderma S.A., Galderma Laboratories, Inc., Galderma Laboratories LP, Galderma Research & Development SNC, Nestlé Skin Health, Inc., Nestlé Skin Health S.A., Nestlé S.A., EQT Partners AB, Public Sector Pension Investment Board (PSP Investments), Luxinva, and Abu Dhabi Investment Authority are identified as possible real-parties-in-interest.

B. Related Matters

A second petition for *inter partes* review of the ’913 patent is concurrently being filed, IPR2020-00004. In addition, two petitions for *inter partes* review, IPR2020-00002 and IPR2020-00003, are being filed concurrently against a related patent, U.S. Patent No. 8,257,723 (“the ’723 patent,” EX1002). The ’723 patent is a continuation of the ’913 patent.

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III. CERTIFICATIONS

Palette certifies the '913 patent is available for IPR, and that it is not barred or estopped from requesting IPR on these grounds.

IV. IDENTIFICATION OF CHALLENGE; STATEMENT OF PRECISE RELIEF REQUESTED

Palette seeks cancellation of the challenged claims for the reasons stated below, supported with exhibits, including the Declaration of Dr. Adam Dicker (EX1003). The claims are unpatentable under pre-AIA 35 U.S.C. §103 on these grounds:

Ground	Claims	Basis
1	1-9, 12, 14-19, 23	Obvious under §103(a) over the combination of U.S. Patent No. 6,206,930 ("Burg," EX1041) and U.S. Patent No. 6,066,856 ("Fishman," EX1055)
2	10-11, 13, 20-22, 24	Obvious under §103(a) over the combination of Burg, Fishman, and U.S. Patent No. 6,375,634 ("Carroll," EX1013)
3	25	Obvious under §103(a) over the combination of Burg, Fishman, and International Patent Application Publication No. WO94/25080 ("Griffith-Cima," EX1011)

V. STATEMENT OF REASONS FOR RELIEF REQUESTED

A. Summary of Argument

The '913 patent broadly claims a method for delivering a therapeutic dose of radiation to a patient. At its core, the claimed invention aims to protect healthy tissues and organs from unsafe levels of exposure to radiation—a fundamental tenet that has been recognized by those in the art since the inception of radiation therapy. The '913 patent claims a means for accomplishing this aim through the injection of a biocompatible, biodegradable gel into a patient. The gel acts as a "filler," filling a space within the patient such that an organ (specifically, the rectum) is displaced from a nearby tissue intended to be irradiated (specifically, the

prostate gland), allowing the organ to receive less of a radiation dose than what would have been received absent the gel. The gel is then left in place, and removed from the body through biodegradation.

Prior to the claimed invention, the use of filler devices to displace organs prior to subjecting a patient to radiation therapy had been well known in the art. Moreover, the use of biocompatible, biodegradable gel materials for various medical treatments was common, and the benefits of using gels removed by biodegradation within the body was thoroughly appreciated. Indeed, the art had already recognized that such gels would be an appropriate and successful tool for organ displacement during radiation therapy. As this petition demonstrates, the claimed invention is nothing more than a predictable use of common, well-established materials for an already-recognized, beneficial purpose.

B. The '913 Patent

1.Background

The '913 patent is entitled "Fillers and Methods for Displacing Tissues to Improve Radiological Outcomes." EX1001, title. The patent aims "to provide a protocol to decrease the radiation dose to the rectum during radiotherapy for prostate cancer," while also "decreas[ing] radiation treatment-induced side effects on sensitive organs resulting from other therapies and applications directed to a target organ." *Id.*, 1:46-50. The patent discloses the use of a "filler" that is placed

between the radiation target tissue and other tissues to increase the distance between the tissues "so that the other tissues receive less radiation." *Id.*, 2:28-31. The filler may take many forms. It may be "a degradable material that is installed once prior to the course of radiation treatment." *Id.*, 2:32-35. It may also be an "inflatable device[] that [is] introduced" into the patient's body. *Id.*, 2:37-42. The '913 patent further discloses that many known materials may form the filler, which may, when introduced into the patient, form a gel. *See, e.g.*, *id.*, 6:25-32, 7:49-53. The '913 patent specifically describes the injection of human collagen into the space (*i.e.*, Denonvilliers' space) between the rectum and the prostate, such that the rectum is displaced during radiation treatment of the prostate. *See id.*, 11:35-40.

2.Challenged Claims

The '913 patent includes 25 claims. Claims 1 and 17 are independent, and claims 2-16 and 18-25 depend from claim 1. Claim 1 reads (formatting added):

> 1. A method of delivering a therapeutic dose of radiation to a patient comprising
>
> introducing a biocompatible, biodegradable filler device between a first tissue location and a second tissue location to increase a distance between the first tissue location and the second tissue location, and
>
> treating the second tissue location with the therapeutic dose of radiation so that the presence of the filler device causes the first tissue location to receive less of the dose of radioactivity compared to the

amount of the dose of radioactivity the first tissue location would receive in the absence of the filler device,

wherein the filler device is introduced an injectable material and is a gel in the patient that is removed by biodegradation of the filler device in the patient

wherein the first tissue location is associated with the rectum and the second tissue location is associated with the prostate gland.

Claims 2-16 and 18-25 are directed to well-known materials that may form part of the filler device, well-known agents that may be included within the filler device, and well-known properties that the filler device may take. EX1003, ¶51.

3.Prosecution History

The '913 patent issued from U.S. Patent Application No. 10/602,526 ("the '526 application"), which was filed on June 24, 2003. EX1001, cover.

During prosecution, the pending claims were subject to an obviousness rejection. EX1005, 122-125.[1] In response, Applicant amended the independent claims to recite that a biocompatible, biodegradable "filler device" is introduced into the patient's body. *Id.*, 135. Applicant argued that the applied reference did not teach the introduction of a "filler device" that was biodegradable. Instead,

[1] Citations to the prosecution history of Exhibit 1005 refer to the page numbering added by Petitioner.

according to Applicant, the reference described a device that included a non-degradable, outer "hollow member 24 and a covering 33," and, regardless whether degradable materials were captured within the outer covering, the described "filler device" was not biodegradable as recited by the claims. *Id.*, 146. The examiner withdrew the rejection. *Id.*, 193.

The examiner then made an enablement rejection with regard to the claims' recitation that the filler device incorporated the use of various "biocompatible, biodegradable" materials as part of the claimed method. The examiner stated that "Applicant ha[d] only established ample support in the specification for the use of 'collagen' as a suitable filler material." EX1005, 193. Applicant ultimately overcame the rejection by submitting an expert declaration of Dr. Amarpreet Sawhney and several supporting references. *See id.*, 263-381. Based on this evidence, Applicant contended that the materials claimed were well-known and well-understood such that Applicant's specifically-disclosed use of collagen enabled the POSA to successfully use those materials for the purpose of displacing tissues during radiation therapy without undue experimentation. *See id.*, 251-252, 270-271.

C. Relevant Timeframe

The '913 patent claims priority to three provisional applications: Nos. 60/391,027, filed June 24, 2002 ("the '027 provisional"; EX1007), 60/427,662,

filed November 19, 2002 ("the '662 provisional"; EX1008), and 60/444,143, filed January 31, 2003 ("the '143 provisional"; EX1009). *Id.* Claims 1-16 and 18-25, however, lack written description support under §112 in the '027 and the '662 provisionals, and thus are not entitled to a priority date earlier than the filing date of the '143 provisional: January 31, 2003. *See* pre-AIA §§119 and 120; *In re Gosteli*, 872 F.2d 1008 (Fed. Cir. 1989).

Specifically, both the '027 and '662 provisionals are limited to using collagen between the prostate and the rectum in order to reduce the radiation dose to the rectum. EX1007, 2[2]; EX1008, 2. Although both the '027 and '662 provisionals suggest using the method with any target organ and a critically-sensitive body organ, neither provisional describes the use of a filler material other than collagen. *See, e.g.*, *id.* It is not until the filing of the '143 provisional that other fillers, such as polysaccharides, alginates, polyethylene glycol, etc., were added. EX1009, 3. Thus, the earliest effective filing date to which the '913 patent

[2] Unless otherwise noted, the citation to a page number is to the original page number in the reference, and not the page number added by Petitioner.

is entitled is January 31, 2003, making this date the relevant timeframe for the '913 patent.[3]

D. Level of Ordinary Skill

At the time of invention, a person of ordinary skill in the art ("POSA") would have held an M.D. with practical, academic, or industrial experience in radiation oncology. EX1003, ¶30. The POSA would further have knowledge of the side effects of radiation treatment, including, for example, tissue necrosis and formations of fibrotic plaques, and methods of counteracting the adverse side effects of radiation therapy. *Id*. The POSA would have experience in performing radiation treatments known at the time, as well as methods of shielding normal tissue or organs from the harmful effects of such treatments. *Id*. This experience is consistent with the ongoing teaching that normal tissue and organs should be protected when delivering a therapeutic amount of radiation to a patient. *Id*. Such a teaching was especially important during the relative timeframe, where the development of improved radiation oncology treatments was occurring at a rapid

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[3] Nevertheless, the analysis provided in this petition applies equally even if the relevant timeframe were June 24, 2002, the filing date of the earliest-filed provisional.

pace, especially the use of increased and sustained radiation energy (*e.g.*, high-dose radiation therapies). *Id*., ¶31.

E. Claim Construction

Claims should be given their ordinary and customary meaning, consistent with the specification, as a POSA understood them. 37 C.F.R. §42.100(b) (as amended Nov. 13, 2018); *Phillips v. AWH Corp.*, 415 F.3d 1303, 1312-13 (Fed. Cir. 2005) (en banc). Except as discussed below, for purposes of this IPR, the claim terms should be given their plain and ordinary meaning.[4]

1. "Filler device" and "filler"

The independent claims of the '913 patent recite a "filler device," while the dependent claims simply claim a "filler." Thus, "filler device" and "filler" as used in

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[4] Without taking a position here on whether the claims are sufficiently definite, even when the metes and bounds of a claim are indefinite, the Board nevertheless can determine whether embodiments plainly within the scope of the claim would have been obvious. *Ex parte Tanksley*, 26 U.S.P.Q.2d 1384, 1387 (B.P.A.I. 1991) (embodiment within scope despite indefiniteness); *Ex parte Sussman*, 8 U.S.P.Q.2d 1443, 1445 n.* (B.P.A.I. 1988) (affirming obviousness despite indefinite claim format).

the claims of the ’913 patent should be construed consistently with one another.

Although the term “filler device” does not appear in the specification of the ’913 patent, the term “filler” is defined as:

> [A] substance that occupies a volume after its introduction into a body. Examples of fillers include but are not limited to polymers, gels, sols, hydrogels, sponges, bulking agents, and balloons.

EX1001, 4:34-37. Thus, as defined by the specification, a “filler” or “filler device” should be construed as “a substance that occupies a volume after its introduction into a body.” *See also* EX1005, 9 (reiterating that a “filler is a substance that occupies a volume after its introduction into a body”). Neither the claim language nor the prosecution history excludes the use of multiple fillers, as long as the fillers are biocompatible and biodegradable. Thus, given the use of the transition term “comprises,” the claims encompass the use of multiple fillers, so long as one of the fillers is “introduced [as] an injectable material and is a gel in the patient.”

Moreover, claim 1 requires that the “filler device” be introduced as an “injectable material” that “is a gel in the patient.” EX1001, 16:43-57. However, for those embodiments that include a balloon or some other type of outer sheath that may be filled with an aqueous solution or gel, the ’913 patent does not describe *balloons* or other outer sheaths that are themselves introduced as an “injectable material” that “is a gel in the patient.” *See, e.g.*, EX1001, 10:17-21 (noting a balloon as an embodiment of a filler, wherein the balloon may be recovered after treatment), 10:51-57 (noting

that a filler may be introduced while folded, de-swelled, or rolled). Thus, to the extent that the term "filler device" may be construed to mean the *entire* device (*e.g.*, a balloon *and* the material filling the balloon) that is introduced into a patient's body, the claim does not exclude embodiments when the device comprises a biocompatible, biodegradable balloon that is itself not an injectable, gel material, but is instead filled with an "injectable material" that "is a gel in the patient."

2. "Consists essentially of collagen"

Claim 8 states that the "biocompatible, biodegradable material consists essentially of collagen." The transition phrase "consists essentially of" "limits the scope of a claim to the specified ingredients and those that do not *materially affect the basic* and *novel* characteristic(s) of a composition." *In re Herz*, 537 F.2d 549, 551-52 (C.C.P.A. 1976) (emphasis added) (citation omitted); *see also PPG Indus., Inc. v. Guardian Indus. Corp.*, 156 F.3d 1351, 1354 (Fed. Cir. 1998). The basic and novel characteristics of the collagen of claim 8 are its use as a filler that is biocompatible and bioabsorbable. Thus, "consists essentially of" as used in claim 8 allows components other than collagen to be present so long as they do not prevent collagen from being used as a biocompatible, bioabsorbable filler.

F. State of the Art

Cancer is one of the leading causes of death, and is also a difficult and costly disease to treat. EX1003, ¶53. At the time of invention, the POSA would have

understood that there were a wide variety of options for the treatment of cancer. *Id.*, ¶¶54-58. The choice of one or more treatments would depend on the type of cancer, as well as the relative susceptibility of the cancer tissue to a given treatment. *Id.*, ¶58. Examples of treatments at the relevant time period typically included chemotherapy, surgical resection, radiotherapy, and cryotherapy. *See, e.g.*, EX1017, 197; EX1003, ¶58. In particular, radiotherapy could be applied preoperatively to reduce the size of a tumor prior to removal, as a standalone treatment for locally reducing or eliminating tumor tissue, or postoperatively to reduce local recurrence of excised cancer tissue. *See, e.g.*, EX1016, Abstract, 7-8; EX1003, ¶58.

Radiation was administered in one of two ways: internally or externally. EX1003, ¶¶58-64. External radiation treatments included both 3D-conformational radiation therapy and intensity-modulated radiation therapy ("IMRT"). *Id.*, ¶60. In 3D-conformational radiotherapy, a tumor is mapped through imaging, and then beams of radiation are directed towards the tumor. EX1003, ¶61. IMRT allowed the radiologist to more accurately deliver radiation to the tumor, which helped preserve the healthy tissue around the tumor. *Id.* In internal radiation therapy, or brachytherapy, an implant comprising a radioactive source is placed in or near a tumor. *Id.*, ¶¶62-64.

One of the basic tenets of radiotherapy, whether external or internal, is to minimize the radiation's effect on nearby healthy tissue. EX1003, ¶¶52, 65-70. A POSA would have understood that the effect of radiation on the surrounding tissue decreases with distance from the source of radiation, with radiation exposure being inversely related to distance. EX1003, ¶¶82-83. For example, with brachytherapy the radiation at a distance from the source follows the relationship of $1/d^2$, wherein "d" is the distance from the source. EX1003, ¶82. As a result, even small increases in distance between the tumor to be irradiated and the healthy tissue can minimize damage to the healthy tissue. *Id.*, ¶83. Thus, a POSA at the relevant time period would have understood the need to increase the space between the tumor and the surrounding healthy tissue in order to decrease the impact of the radiation on the healthy tissue. *Id.*, ¶¶82-83.

For instance, treatment of abdominal or pelvic cancers with radiation can result in severe toxicity to abdominal organs due to incidental irradiation. EX1020, 51; EX1003, ¶¶84-85. Thus, at the time of invention, various techniques to protect the surrounding tissue were being employed, including advances in radiation field size and intensity (EX1053, Abstract), administration of antioxidants (EX1052, Abstract), and surgical insertion of a prosthesis capable of shielding the bowel from radiation damage (EX1039, 1212). EX1003, ¶¶85-93.

Of particular interest in the ’913 patent is the use of radiation for the treatment of prostate cancer. EX1003, ¶¶39-52. Prostate cancer is the most commonly diagnosed cancer in men in the United States. *Id.*, ¶54. The prostate contacts the rectum posteriorly through the Denonvilliers’ fascia. *Id.*, ¶55. Both external beam radiation and brachytherapy have been used for the treatment of prostate cancer. *Id.*, ¶56. Although high doses of radiation can lead to increased control of the cancer, there are often also increased significant complications to the rectum, including rectal bleeding and pain. *Id.*, ¶¶72-73, 77-81. Thus, at the time of invention, various materials and methods had been used to increase the distance between the prostate gland and the rectum during radiation treatment of prostate cancer. *Id.*, ¶¶94-100. Ein-Gal, for example, injected water in the area of Denonvilliers’ fascia to reflect the rectal wall from the prostate in order to reduce the effect of radiation on the rectum. EX1049, 1:31-36; EX1003, ¶102.

Moreover, the POSA would have understood at the relevant time that biocompatible and bioabsorbable polymers had been used and were being used as a means for protecting healthy tissue. EX1003, ¶¶101-106. For example, in the 1980s, absorbable polyglycolic acid mesh slings were developed, which could be surgically sewn above the pelvis site specifically to minimize radiation toxicity in the pelvic cavity. EX1039, 1216; EX1003, ¶94. Polyglycolic acid is a non-toxic material known to biodegrade in the body, and is often used in the production of

biocompatible sutures. EX1054, Abstract; EX1003, ¶94. As such, the biocompatible mesh sling would be left in the body after surgery, thereby minimizing additional complications from surgical removal of the sling. EX1003, ¶94. In addition, biocompatible, bioabsorbable implants were used to displace cancer tissue from healthy tissue during radiation therapy. EX1055, 2:61-3:11; EX1003, ¶¶101-106. The use of biocompatible, bioabsorbable tissue expanders for displacing healthy tissue from the radiation field was also known, in which the tissue expander may be filled with a biocompatible liquid or gel. EX1041, 2:62-3:6, 3:56-58; EX1003, ¶104. Moreover, the use of biocompatible, bioabsorbable gels to encapsulate a tumor to allow more aggressive therapy of the tumor was known. EX1013, 3:55-65.

Additionally, a POSA would have known that surgical prosthetics had been used to exclude healthy abdominal tissue from radiation-induced toxicity through insertion into the pelvic cavity to separate the tumor from the healthy tissue. EX1003, ¶¶95-100. For example, silicone prostheses typically used for breast implants were found to afford protection from radiation toxicity when secured in the pelvic cavity prior to post-operative radiation. EX1012, 346; EX1003, ¶¶96-99. However, the static nature of the implant within the body after surgery could result in perforation of the bowel due to the additional space occupied by the silicone implant. EX1012, 348; EX1003, ¶99. Another approach involved the use

of saline-filled tissue expanders. EX1020, Abstract; EX1003, ¶97. However, such devices are not bioabsorbable and require eventual removal, thus increasing surgically-related complications, such as infection. EX1003, ¶¶96-99. A POSA would have understood that use of a biodegradable implant would ameliorate both risks due to the gradual degradation of the prosthesis, which would limit the mass-effect risk associated with silicone implants, and would also eliminate the need for additional surgery to remove the prosthesis. EX1012, 348; EX1003, ¶¶101-106. For example, Fishman disclosed the use of a bioimplantable, biodegradable device that may be used to shield the rectum from radiation directed at the prostate. EX1055, 2:61-3:11, 5:35-5:52; EX1003, ¶104. As taught by Fishman, the device is left in place during radiation treatment, which may extend over several days and weeks, and if biodegradable, it is left in place to biodegrade over time. EX1055, 5:48-5:52; EX1003, ¶104.

At the time of invention, a POSA would have been aware of a wide variety of biocompatible, bioabsorbable materials. EX1003, ¶102. As discussed above, materials such as a polyglycolic acid were already employed as biodegradable sutures that could be absorbed in the body without production of toxic byproducts. EX1054, Abstract; EX1003, ¶94. Other naturally-occurring polymers, such as gelatin, hyaluronic acid ("HA"), and collagen, were additionally in use in surgical and medical applications prior to June 2002. EX1003, ¶¶101-106.

For example, a POSA would have understood collagen to be a widely-used biocompatible material. EX1003, ¶105. Collagen was commonly used as a soft tissue implant, for example, in plastic surgery, and to prevent surgical adhesions. EX1056, 1:18-24; EX1057, 2:37-55. Collagen had also been used as an absorbable delivery system for brachytherapy. EX1058, 3:35-42, 4:3-6; EX1003, ¶105. As collagen is a naturally-occurring polymer present in animal tissue, a POSA would have understood collagen to have low immunogenicity and toxicity when placed in the body. Thus, a POSA would have recognized collagen as a viable space-filler for separating tumor tissue from surrounding healthy tissue. *See, e.g.*, EX1013, 7:45-50; EX1003, ¶105.

Another known natural polymer, HA, is present in connective tissues in mammals, and is a biocompatible polymer capable of being formulated as an injectable sol-gel solution. EX1059, Abstract, 1:18-20; EX1003, ¶105. For instance, HA was developed as an injectable treatment for arthritis by placing high molecular weight HA into the synovial space. EX1059, 1:38-57. HA had also been used as a biodegradable carrier to deliver drugs. EX1013, 8:38-59, 14:64-15:9. Further, HA viscous gels had been used to protect against surgical adhesions post-surgery by acting as a space-filler between adjacent healing tissue. EX1060, 1:46-50. To prevent surgical adhesions, injective formulations of HA were injected into the abdomen to cover injured areas, which allowed the injected

material to conform to the surface of the tissue and act as a barrier to prevent adhesion of injurious tissue before eventually degrading. EX1060, 43:30-39. A POSA would thus understand HA to have low immunogenicity and toxicity when placed in the body. Moreover, a POSA at the relevant time would have also recognized that HA gels may be used as a viable space-filler for separating tumor tissue from the healthy tissue surrounding it. EX1013, 2:18-22; EX1003, ¶105.

Accordingly, prior to June 2002, compositions containing biocompatible, biodegradable polymers, which are capable of forming gels *in vivo*, such as HA and collagen, had been proposed for use in preventing radiation-induced toxicity in abdominal tissue. EX1003, ¶¶101-106. For example, Wallace taught that these compositions could be used as a "large space-filling device" when injected into a body cavity to, for example, displace and "protect the intestines during a planned course of radiation to the pelvis" during surgery and radiation procedures. EX1010, 33:64-67; EX1003, ¶105. Thus, at the time of invention, a POSA would have understood that biocompatible compositions, such as collagen and HA, may be used as a superior replacement for non-biodegradable devices, such as saline-filled devices, which require removal. EX1003, ¶105.

The prior art applied to the claims challenged in this petition is described briefly below.

1. Burg

Burg discloses bioabsorbable tissue expanders that are useful for various medical procedures, including the displacement of organs, such as the intestines during radiation therapy.[5] EX1041, 2:62-3:6, 9:17-46; EX1003, ¶¶117-120. The tissue expander includes an envelope, which is formed of a biocompatible, bioabsorbable material. EX1041, Abstract; EX1003, ¶118. The envelope includes a chamber that is filled with a biocompatible, bioabsorbable liquid or gel to displace tissue during a medical treatment. EX1041, Abstract; EX1003, ¶118. Such a configuration allows the expander to be left in place, as it slowly degrades within the patient's body over time. EX1041, 3:2-6, 9:37-41; EX1003, ¶119.

2. Fishman

Fishman discloses the use of "a bioimplantable device for adjusting the position of and/or shielding selected tissues of a human body during radiation therapy."[6] EX1055, Abstract; EX1003, ¶¶129-131. The device comprises a

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[5] Burg published March 27, 2001, making it prior art under §102(b). Burg was not before the examiner during prosecution of the '526 application.

[6] Fishman published May 23, 2000, making it prior art under §102(b). Fishman was not before the examiner during prosecution of the '526 application

hollow structure, formed from a biocompatible material, which may be selectively inflated to displace tissues from the site of applied radiation. EX1055, Abstract, 2:1-8; EX1003, ¶130. In one example, Fishman expressly teaches the use of its inflatable device to displace the rectum relative to the prostate gland during radiation therapy. EX1055, 5:10-52, FIGS. 7-8; EX1003, ¶130. Like Burg, Fishman also teaches that the device may be "constructed of bioabsorbable material, left in place to degrade over time." EX1055, 5:50-52.

3. Carroll

Carroll discloses biocompatible hydrogel compositions that may be used to encapsulate tissue, thereby providing a protective barrier for surrounding healthy tissue during medical procedures, such as radiation therapy.[7] EX1013, Abstract;

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[7] Carroll was filed on April 6, 1999, making it prior art under §102(e). Carroll was not before the examiner during prosecution of the '526 application. To swear behind Carroll, Incept must prove conception of the claimed invention before Carroll's filing date and diligence in reducing the invention to practice after that date. *Apator Miitors APS v. Kamstrup A/S*, 887 F.3d 1293, 1295 (Fed. Cir. 2018) (citing *Perfect Surgical Techniques, Inc. v. Olympus Am., Inc.*, 841 F.3d 1004, 1007 (Fed. Cir. 2016)). Thus, Incept must show diligence over a time period of

EX1003, ¶¶126-128. The compositions may be formed from a variety of known, biocompatible materials that may be configured to degrade within the patient's body over a predetermined amount of time. EX1013, 5:2-6, 7:62-8:59, 14:64-15:4; EX1003, ¶¶127-128. Thus, Carroll evidences that the use of biocompatible, biodegradable polymers to separate tissues from surrounding healthy tissue was known. EX1003, ¶¶127-128.

4. Griffith-Cima

Similar to Carroll, Griffith-Cima discloses a variety of biocompatible, polysaccharide hydrogels useful for medical treatments within the body.[8] *See, e.g.*, EX1011, Abstract, 9:32-10:18, 15:27-34; EX1003, ¶¶121-123. Applicant relied on Griffith-Cima during prosecution of the '526 application to establish that

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nearly thirty-nine months for the '913 patent's collagen-specific claims and nearly forty-six months for all other claims. Moreover, with respect to the latter, Incept's failure to suggest the use of filler materials other than collagen in the '027 and '662 provisionals is evidence of lack of diligence on Incept's part. *See supra*, section V.C.

[8] Griffith-Cima published November 10, 1994, making it prior art under §102(b).

polysaccharide hydrogels for human use was well-known and well-understood at the time of invention. EX1005, 199, 254.

G. Ground 1: Claims 1-9, 12, 14-19, and 23 Are Obvious over the combination of Burg and Fishman

As described more below, Burg teaches each and every element of independent claims 1 and 17. Moreover, to the extent Burg does not explicitly disclose the use of a gel that is both biocompatible and biodegradable, Burg renders use of such a gel obvious. Burg does not expressly disclose that the relative tissue locations displaced are the rectum and the prostate gland. Fishman, however, expressly teaches the use of a biocompatible, bioabsorbable device to displace the rectum relative to the prostate gland. As discussed below, a POSA would have considered it obvious to introduce a biocompatible, biodegradable tissue expander having a gel composition, like that taught by Burg, to displace the rectum relative to the prostate gland during radiation therapy in order to protect the rectum from the radiation's harmful effects, as taught generally by Burg and specifically by Fishman. Claims 1-9, 12, 14-19, and 23 are thus rendered obvious over the prior art.

1. Independent Claim 1

a. [1.Preamble] A method of delivering a therapeutic dose of radiation to a patient comprising

Burg teaches "an absorbable implantable tissue expander device that can be used in surgeries as a gradually diminishing space filler." EX1041, Abstract; EX1003, ¶185. Burg further discloses that the expander "may be used in positioning a particular organ or tissue inside the body." EX1041, 9:21-22; EX1003, ¶185. By positioning the tissue using the filler, Burg further discloses that a dose of radiation may be applied to tissue intended to be treated without adversely affecting the displaced normal tissue. *See* EX1041, 9:25-37; EX1003, ¶185. Thus, to the extent the preamble is limiting, the combination of Burg and Fishman teaches it. EX1003, ¶¶185-186.

b. [1.1] introducing a biocompatible, biodegradable filler device between a first tissue location and a second tissue location to increase a distance between the first tissue location and the second tissue location, and

Burg teaches a "filler device" in the form of a tissue expander that includes an envelope made from biocompatible and biodegradable materials. EX1041, 3:45-50; EX1003, ¶¶187-189. Burg further teaches that the envelope itself is filled with an injectable composition, which may be a gel that is biocompatible. *See, e.g.*, EX1041, 2:54-3:6, 6:37-41, 9:25-41; EX1003, ¶188. Burg teaches that, as the envelope degrades within the patient's body, the gel is "gradually released" into

the patient's body. EX1041, 4:29-31, 6:37-41, 9:25-41 (disclosing that the expander "will gradually degrade and eventually be absorbed by the surrounding tissue"); EX1003, ¶188. A POSA would have understood this to mean that, like the envelope, the gel may also be made from a material that is biodegradable. EX1003, ¶188. When the envelope is filled with the gel composition, a distance between a first tissue location and a second tissue may be increased. EX1041, 2:54-3:6, 9:25-41; EX1003, ¶189.

Moreover, to the extent Burg does not explicitly disclose the use of a gel that is both biocompatible and biodegradable, Burg suggests the use of such a gel. *See* EX1003, ¶¶187-189. Specifically, Burg generally discloses the use of a gel filler that is injected into an envelope to increase the distance between an organ and surrounding tissue. *See* EX1041, 2:54-3:6; 9:25-41; EX1003, ¶¶187-189. Burg also discloses that the gel filler is biocompatible, and may be "gradually released" into the patient's body as the outer envelope degrades, such that the gel is "eventually … absorbed by the surrounding tissue." *See* EX1041, 4:29-31, 6:37-41, 9:25-41; EX1003, ¶188. Burg further provides a number of materials that may form the absorbable tissue expander device and were known to be biodegradable. *See, e.g.*, EX1041, 4:58-5:10; EX1003, ¶¶187-189. Thus, to the extent Burg does not explicitly disclose that the gel itself may comprise these biodegradable materials, a POSA would have understood that such materials would be

appropriate to form a gel that would biodegrade within the patient's body so that it would be "eventually … absorbed by the surrounding tissue" after completion of radiation therapy. EX1003, ¶¶187-189.

In addition, as noted above in section V.B.3, during prosecution of the '526 application, Applicant amended the claims to recite that a biocompatible, biodegradable filler "device" is introduced into the patient to distinguish the claims from the applied prior art, which taught introducing a non-biodegradable balloon having biodegradable fillers injected therein. *See* EX1005, 135,146. As further noted above in section V.E.1, the terms "filler device" and "filler," as used in the claims, should be construed consistently as "a substance that occupies a volume after its introduction into a body." As such, the claim does not preclude embodiments where a filler, in the form of a balloon or envelope, contains a second filler, in the form of a liquid or gel. Thus, Burg's disclosure of a method for treating a patient with radiation therapy using two types of fillers in conjunction (an envelope injected with a gel) that are both biocompatible and biodegradable falls within the scope of the claim. *Supra*, section V.E.1.

To the extent that the word "device" adds anything to the claims, it would mean that all filler components that make up the introduced "filler device," including a balloon or outer sheath (if present), are biocompatible and biodegradable, so long as it is filled with an "injectable material" that "is a gel in the patient." As explained

above, Burg teaches such a "filler device" in the form of a tissue expander having a biocompatible, biodegradable envelope that is filled with a biodegradable, biocompatible gel such that it "occupies a volume after its introduction into the body."

Accordingly, the combination of Burg and Fishman teaches this element.

c. [1.2] treating the second tissue location with the therapeutic dose of radiation so that the presence of the filler device causes the first tissue location to receive less of the dose of radioactivity[9] compared to the amount of the dose of radioactivity the first tissue location would receive in the absence of the filler device,

As explained above, Burg teaches introducing a tissue-expanding filler device having a biodegradable, biocompatible envelope that may contain a biodegradable, biocompatible gel filler into a patient to displace organs during radiation therapy. *See, e.g.*, EX1041, 2:54-3:6, 9:25-41; EX1003, ¶¶190-192. At

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[9] The '913 patent uses "dose of radioactivity" here rather than "dose of radiation." The claim, however, uses "dose of radioactivity" as describing the result of the active step of "treating the second tissue location with the therapeutic dose of radiation," thus providing the antecedent for "dose of radioactivity. The POSA would thus understand that the claim is thus using the terms "dose of radiation" and "dose of radioactivity" interchangeably. EX1003, ¶¶41-42.

the time of invention, it was well-understood that the strength of an applied radiative field decreases as a function of distance, and a tissue spaced a given distance relative to the field's maximum strength would receive a dose of radiation that is less than the field's maximum strength. EX1003, ¶191; *see also supra*, section V.F. As such, the POSA would have understood Burg as disclosing that, when the second tissue location was subjected to a therapeutic dose of radiation, the first tissue location (*e.g.*, the bowel) would receive a lesser dose of radiation compared to the amount that would have been received absent the space-filling device. EX1003, ¶191. Accordingly, the combination of Burg and Fishman teaches this element.

d. [1.3] wherein the filler device is introduced as an injectable material and

As explained above in section V.E, the term "filler device" should be consistently construed with the term "filler" as described and defined in the specification of the '913 patent. Moreover, the term "filler device" does not exclude devices where a balloon, although itself not an "injectable material" that "is a gel in the patient," is filled with an "injectable material" that "is a gel in the patient."

Burg teaches a "biocompatible, biodegradable filler device" in the form of a biocompatible, biodegradable envelope, which may be filled with a biocompatible, biodegradable gel to displace tissue. Burg teaches that the gels are introduced into

a patient's body through injection into the envelope, and are thus "introduced as an injectable material." *See, e.g.*, EX1041, 2:27-34, 6:9-15, 6:50-52, 9:7-10; EX1003, ¶192. Accordingly, the combination of Burg and Fishman teaches this element.

e. [1.4] [the filler device] is a gel in the patient that is removed by biodegradation of the filler device in the patient

As explained above, Burg teaches a filler device that includes a biocompatible, biodegradable envelope that is injected with a gel material that is also biocompatible and biodegradable. Thus, Burg teaches that the filler device is "removed by biodegradation." *See, e.g.*, EX1041, 4:29-31, 6:37-41, 9:25-41; EX1003, ¶193. Accordingly, the combination of Burg and Fishman teaches this element.

f. [1.5] wherein the first tissue location is associated with the rectum and the second tissue location is associated with the prostate gland.

As explained above, Burg generally teaches the use of a biodegradable, biocompatible tissue expander to displace tissue during radiation therapy, but does not specifically disclose that the tissue may be the rectum or the prostate gland. *See* EX1003, ¶194. Similar to Burg, Fishman specifically teaches the use of a biocompatible, biodegradable tissue expander to displace the rectum away from the prostate gland during a planned course of radiation therapy. EX1055, 5:13-52; EX1003, ¶194. As explained below in section V.G.1.g, a POSA would have

considered it obvious to introduce a biocompatible, biodegradable tissue expander, like those taught by Burg and Fishman, into a patient to displace the rectum away from the prostate gland during radiation therapy.

g. Rationale to combine and Reasonable expectation of success

Based on the teachings of Burg and Fishman, a POSA would have had reason to displace the rectum relative to the prostate gland during radiation therapy using the biocompatible, bioabsorbable tissue expanders of Burg and Fishman, and would have had a reasonable expectation of success in doing so. *See* EX1003, ¶¶194-197.

Both Burg and Fishman recognize and appreciate the benefit of displacing tissue away from a site intended to be irradiated, as doing so would protect the tissue from the harmful effects of radiation. EX1041, Abstract; EX1055, Abstract; EX1003, ¶195. Fishman particularly teaches that by displacing the rectum away from the prostate gland during radiation therapy, the harmful side effects that may result from irradiation of healthy rectal tissue may be avoided. EX1055, 5:13-18; EX1003, ¶195.

Burg expressly teaches a biocompatible, biodegradable envelope that may be filled with a biocompatible, biodegradable gel composition in order to displace tissue for this purpose. EX1003, ¶196. Fishman similarly teaches the use of a biocompatible, biodegradable tissue expander to displace tissue, and recognizes the

benefits of such a device as it may be left in place after treatment has completed. EX1055, 5:50-52; EX1003, ¶196. Thus, understanding the benefits of displacing the rectum relative to the prostate gland during radiation therapy using materials that can biodegrade, the POSA would have had reason to use a biocompatible, biodegradable tissue expander, like those taught by both Burg and Fishman, to displace the rectum away from the prostate gland. A POSA would also have a reasonable expectation of success that such a device would successfully displace the rectum relative to the prostate gland, thus protecting the rectum from the harmful effects of the radiation. EX1003, ¶¶196-197. Accordingly, the combination of Burg and Fishman render claim 1 obvious.

2. Independent claim 17

For those elements of claim 17 that are substantially identical to an element of claim 1, reference is made to the analysis detailed above with regard to claim 1, with the understanding that the corresponding analysis equally applies.

a. [17.Preamble]: A method of delivering a therapeutic dose of radiation to a patient comprising:

See analysis for element [1.Preamble] above. *Supra*, section V.G.1.a.

b. [17.1]: (i) injecting anesthesia and

Burg and Fishman do not explicitly disclose injecting anesthesia during the course of radiation treatment disclosed. EX1003, ¶200. A POSA, however, would have understood that anesthesia should be administered prior to introducing a

tissue expander, like those taught by Burg and Fishman, into the patient's body, and its use was well-known and routine to the POSA to reduce the amount of pain felt by the patient. EX1003, ¶¶200, 202.

c. [17.2]: (ii) injecting saline to expand the space between the first and second tissue location,

Burg and Fishman do not explicitly disclose injecting saline into the space between the tissue locations. EX1003, ¶201. A POSA, however, would have recognized that, for tissues in close proximity, a space may be created prior to introduction of the gel composition to aid in displacing the tissues. *See, e.g.*, EX1049, 1:31-36 (teaching the introduction of water into the area of Denonvilliers' fascia to reflect the rectal wall away from the prostate gland to create a space therebetween); EX1003, ¶201. At the time of the invention, the injection of saline to create a needed space between tissue locations was considered a common, effective, and safe method. EX1003, ¶201. Thus, a POSA would have found it obvious to, prior to injection of the tissue expander, to inject saline to create an initial space between the first and second tissue locations. EX1003, ¶¶201-202.

d. [17.3]: wherein the first tissue location is associated with the rectum and the second tissue location is associated with the prostate gland and

As explained above with regard to claim 1, Burg generally teaches the use of its biocompatible, biodegradable filler device to displace tissue locations for radiation therapy, while Fishman specifically teaches the use of a biocompatible,

biodegradable filler device to displace the rectum relative to the prostate gland prior to radiation treatment. *See supra*, sections V.G.1.f-g. For the same reasons discussed above, a POSA would have found it obvious to displace the rectum relative to the prostate gland based on the combined teachings of Burg and Fishman. *See supra*, sections V.G.1.f-g.

e. [17.4]: introducing a biocompatible, biodegradable filler device between the first tissue location and the second tissue location to increase a distance between the first tissue location and the second tissue,

See analysis for element [1.1] above. *Supra*, section V.G.1.b.

f. [17.5]: said biocompatible, biodegradable filler being collagen and

Burg teaches that the tissue expander may include collagen. *See, e.g.*, EX1041, 5:5-7; EX1003, ¶203.

g. [17.6]: introducing collagen into Denovillier's space and

As explained above, a POSA would have readily appreciated introducing the filler device of Burg between the rectum and the prostate gland to displace the rectum prior to radiation therapy as taught by Fishman. *See supra*, sections V.G.1.f-g. A POSA would have also understood that, anatomically, the space between the rectum and the prostate gland is known as Denonvilliers' space. EX1003, ¶204. Thus, the POSA would have understood that, to effectively

displace the rectum relative to the prostate gland, the filler device should be introduced into this space. EX1003, ¶204.

> ***h. [17.7]: treating the second tissue location with a therapeutic dose of radiation, said therapeutic dose of radiation being 70 to 100 Gy, so that the presence of the filler device causes the first tissue location to receive less than 50% of the dose of radioactivity[10] compared to the amount of the dose of radioactivity the first tissue location would have received in the absence of the filler device,***

As noted above, it was well-known that the strength of an applied radiative field decreases as a function of distance, and tissues spaced apart from the maximum strength of the field received less of the applied dose of radiation. *See supra*, sections V.F, V.G.1.c; EX1003, ¶205. The POSA also would have understood the amount of dose of radiation that would be acceptably safe for a given tissue. EX1003, ¶205. The POSA would have further understood that, by displacing a tissue location away from a treated tissue location, a higher dose of radiation, such as 70 to 100 Gy, could be applied, with the displaced tissue receiving less of that dose, thus making the radiation treatment more effective. *Id.,* ¶¶205-206. A POSA also would have readily appreciated the distance the tissue

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[10] As discussed above as to claim 1, the terms "dose of radiation" and "dose of radioactivity" are being used interchangeably in the claim.

should be displaced to receive less than 50% of that dose such that the tissue received an acceptably-safe dose. EX1003, ¶¶206-207.

i. [17.8]: wherein the filler device is removed by biodegradation of the filler device in the patient.

See analysis for element [1.4] above. *Supra*, section V.G.1.e.

3. Dependent Claims

a. Claims 3, 7-9, 15, 18-19, and 23

Claims 3, 7-9, 15, 18-19, and 23 recite specific materials that may form the filler. In that regard, as to the state of the art at the time of invention, the specification of the '913 patent specifically states that "[t]he successful use of collagen as a filler shows that other materials may also be used." EX1001, 3:46-47.

Claim 3 recites that the "filler comprises a member of the group consisting of alginate, gelatin, fibrin, fibrinogen, albumin, polyethylene glycol, thixotropic polymers, thermoreversible polymers, and mixtures thereof." EX1001, 16:60-63. Burg discloses that the tissue expanders may include those materials. *See* EX1041, 4:58-5:10 (teaching, *e.g.*, the use of alginate, polyethylene glycols); EX1003, ¶209, 211.

Claim 7 recites that "the filler comprises an extracellular matrix molecule." EX1001, 17:5-6. Burg generally teaches that the compositions may include proteins such as collagen. *See, e.g.*, EX1041, 5:5-7; EX1003, ¶210-211. A POSA

would have understood that proteins, such as those disclosed by Burg, are extracellular matrix molecules. EX1003, ¶210.

Claims 9, 15, 19, and 23 recite that the filler comprises at least one polysaccharide, a synthetic polymer, alginate, and polyethylene glycol, respectively. EX1001, 17:9-10, 26-27, 18:19-20, 27-28. Burg discloses that the tissue expanders may include those materials. *See* EX1041, 4:58-5:10 (teaching, *e.g.*, the use of alginate); EX1003, ¶209, 211.

Claim 8 recites that the "filler consists essentially of collagen." EX1001, 17:7-8. Burg discloses that the tissue expanders may include collagen. *See* EX1041, 5:5-7; EX1003, ¶210-211. A POSA would have understood that this would include expanders having gel fillers that "consisted essentially of" collagen. EX1003, ¶210; *cf.* EX1001 (providing no lower bound limit to the term "essentially of"). Moreover, as discussed above, the transition phrase "consisting essentially of" allows components other than collagen to be present so long as they do not prevent the collagen from being used as a biocompatible, biodegradable filler. *See supra*, section V.E.2. Burg teaches that the tissue expanders, such as those including collagen, may be used as a filler device during radiation therapy.

Claim 18 recites that the "filler comprises a member of the group consisting of polylactide, polyglycolide, polycaprolactone, and poly(alpha-hydroxy acid)." EX1001, 18:16-18. Burg expressly teaches that the tissue expanders can include

polylactide, polyglycolide, and polycaprolactone. EX1041, 4:58-62; EX1003, ¶209, 211.

b. Claims 4-5, 12, and 14

Claims 4-5, 12, and 14 recite additional agents that may be added to the filler.

Claims 4-5 recite that the filler includes at least one therapeutic agent, which may be "a member of the group consisting of an anti-inflammatory drug, an antibiotic, an antimycotics, a hemostat, a steroid, and an analgesic." EX1001, 16:64-17:2. Burg discloses that the gel may include therapeutic materials, such as antibiotics and growth factors. *See, e.g.*, EX1041, 3:7-10, 4:29-34, 7:21-36, 8:23-44, 9:41-46; EX1003, ¶213.

Claims 12 and 14 recite that the filler includes a pH buffering agent. EX1001, 17:18-19, 24-25. Burg does not expressly disclose the use of pH buffering agents in the tissue expanders. Nevertheless, a POSA would have understood that buffering agents were a common, well-understood, and predictable material that would prevent rapid changes in the pH of the filler materials during use, thereby maintaining the filler material's stability. EX1003, ¶214. A POSA thus would have readily understood the benefit of incorporating buffering agents into filler devices like those taught by Burg, and would have had a reasonable expectation of success in doing so. *Id*.

c. Claims 2, 6, and 16

Claim 2 recites that the "filler is introduced into Denovillier's space." EX1001, 16:58-59. As explained above with regard to claim 17 (17.6), a POSA would have understood that, to displace the rectum relative to the prostate gland, the tissue expander should be introduced into the space between the prostate and the rectum, known as Denonvilliers' space. *See supra*, section V.F.2; EX1049, 1:31-36 (teaching the introduction of water into the area of Denonvilliers' fascia to reflect the rectal wall away from the prostate gland to create a space therebetween) EX1003, ¶216.

Claim 6 recites that "the filler is biodegradable in vivo in less than approximately 90 days." EX1001, 17:3-4. Burg discloses that the speed of absorption of the tissue expanders can be chosen to suit different needs. EX1041, 5:52-63; EX1003, ¶217. As an example, Burg further discloses that the period of degradation of the tissue expander may occur "from about 1 month to about 2 years, more preferably from about 3 months to about 1 year after the device is implanted." EX1041, 4:35-39; EX1003, ¶217. A POSA would have understood that such degradation time would encompass the degradation time of a biocompatible, biodegradable gel filler that has been injected into the outer envelope. EX1003, ¶217. Thus, a POSA would have known and readily

understood how to configure the gel filler to biodegrade within a predetermined time, including less than approximately 90 days, to suit the given need. *Id*.

Claim 16 recites that "the filler occupies a volume in the range of about 10 to about 200 cubic centimeters in the patient." EX1001, 17:28-30. Burg discloses that the tissue expander may occupy a volume that "depend[s] on the defect area," including, for example, "from about 1 cm^3 to about 1000 cm^3." EX1041, 5:32-35; EX1003, ¶218; *see also* EX1001, 10:39-41 (noting that "[f]iller volumes for separating tissues are dependent on the configuration of the tissues to be treated and the tissues to be separated from each other.").

H. Ground 2: Claims 10-11, 13, 20-22, and 24 Are Obvious over Burg, Fishman, and Carroll

Claims 10-11, 13, 20-22, and 24 recite specific materials that may form or be included with the filler device. In that regard, as to the state of the art at the time of invention, the specification of the '913 patent specifically states that "[t]he successful use of collagen as a filler shows that other materials may also be used." EX1001, 3:46-47.

Claim 10 recites that the filler comprises hyaluronic acid, and claim 24 recites that the filler comprises a thixotropic polymer. EX1001, 17:11-12, 18:29-30. Burg generally discloses the use of polysaccharides, a material that was known

to include polymers that could be configured to be thixotropic. EX1041, 4:63-66; EX1003, ¶220; EX1061, 8:35-39[11]; *cf.* EX1005, 200, 211, 216-218. Carroll similarly discloses the use of polysaccharides as a polymer appropriate for forming biocompatible, biodegradable hydrogel compositions, including hyaluronic acid, which a POSA would have understood to be a polysaccharide that is thixotropic. *See* EX1013, 8:52-62; EX1003, ¶220. A POSA would have understood that thixotropic polymers, such as hyaluronic acid, would be materials appropriate for successfully forming the gel fillers taught by Burg, and thus would have found it obvious to include such materials in the gel fillers taught by Burg. EX1003, ¶220.

Claim 11 and 13 recites that the filler includes "a member of the group consisting of . . . a radio opaque marker [.]" EX1001, 17:13-17, 20-23. Carroll teaches the use of markers so that the gel fillers can be readily evaluated by imaging techniques, including x-ray. EX1013, 10:28-34; EX1003, ¶221. A POSA would have understood that, for x-ray imaging techniques, radio opaque markers should be utilized. EX1003, ¶221. A POSA also would have readily appreciated

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[11] Note that this teaching by Hubbell was added by amendment to the specification of the '913 patent during prosecution. EX1005, 211, 216-218.

the benefit of incorporating such markers into the gel fillers taught by Burg in order to better visualize placement of the filler within the patient's body. *Id*.

Claims 20-22 recite that the filler comprises gelatin, fibrin or fibrinogen, and albumin, respectively. EX1001, 18:21-28. Burg does not explicitly disclose that the gel filler may include these materials, but Burg does disclose that the tissue expander may be formed from protein materials. *See* EX1041, 5:5-7; EX1003, ¶222. Carroll discloses biocompatible, biodegradable hydrogel compositions that may be inserted into a patient's body and used for medical treatment, such as radiation therapy. EX1013, Abstract; EX1003, ¶222. Carroll similarly discloses that proteins, such as gelatin, fibrin or fibrinogen, and albumin, may be used as part of the hydrogel compositions. EX1013, 8:46, 7:47, 25:67; EX1003, ¶222. A POSA would have understood that proteins, such as gelatin, fibrin or fibrinogen, and albumin, would be materials appropriate for successfully forming the gel fillers taught by Burg, and thus would have found it obvious to include such materials in the gel fillers taught by Burg. EX1003, ¶223.

I. Ground 3: Claim 25 Is Obvious over Burg, Fishman, and Griffith-Cima

Claim 25 recites that the filler includes a thermoreversible polymer. EX1001, 18:31-32.

Burg generally teaches the use of gel fillers that can be injected into an envelope within a patient's body to displace organs. EX1041, 2:37-38, 2:54-61,

3:2-6, 4:18-32; EX1003, ¶224. Burg expressly contemplates that the tissue expanders may be formed of a variety of polymer materials. EX1041, 4:58-5:10; EX1003, ¶224.

Thermoreversible polymer compositions were well-known and well-understood prior to the filing date of the '913 patent. EX1003, ¶225 . For instance, as noted above, Dr. Sawhney cited Pluronics™ as an example of a well-known thermoreversible polymer that can form a gel. *See* EX1005, 256, 273. Griffith-Cima similarly teaches the use of Pluronics™ to form a biocompatible hydrogel that may be crosslinked by temperature. *See, e.g.*, EX1011, 15:20-34. Thus, a POSA would have found the use of thermoreversible polymers in the gel fillers of Burg to be well-known, well-understood, and predictable. EX1003, ¶¶224-227.

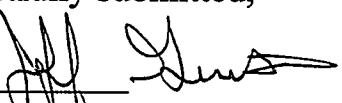
VI. SECONDARY CONSIDERATIONS

Palette is unaware of any objective evidence of nonobviousness that would outweigh a conclusion of obviousness of the claims.

VII. CONCLUSION

The challenged claims are unpatentable. Palette respectfully requests that IPR be instituted.

Respectfully submitted,



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CERTIFICATION UNDER 37 C.F.R. §42.24(d)

I certify that the word count for this Petition for Inter Partes Review totals 8,942, which is less than the 14,000 allowed under 37 C.F.R. 42.24(a)(i). In accordance with 37 C.F.R. 42.24(a), this word count does not include table of contents, table of authorities, mandatory notices under §42.8, certificate of service or word count, or appendix of exhibits or claim listing.

Dated: 14 October 2019

Jeff Guise, Reg. No. 34,613

CERTIFICATE OF SERVICE

I certify that today I caused to be served a true and correct copy of the foregoing **PETITION FOR *INTER PARTES* REVIEW OF U.S. PATENT NO. 7,744,913 and Exhibits 1001-1062** by *Federal Express Next Business Day Delivery* to the Patent Owner's correspondence address of record:

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