

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

MIM SOFTWARE INC.
Petitioner

v.

PROGENICS PHARMACEUTICALS, INC.
Patent Owner

U.S. PATENT NO. 10,665,346
Filing Date: December 18, 2019
Issue Date: May 26, 2020
Title: NETWORK FOR MEDICAL IMAGE ANALYSIS, DESIGN SUPPORT
SYSTEM, AND RELATED GRAPHICAL USER INTERFACE (GUI)
APPLICATIONS

Inter Partes Review No.: IPR2025-00630

**PETITION FOR *INTER PARTES* REVIEW OF
U.S. PATENT NO. 10,665,346**

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EXHIBIT LIST

No.	Description
Ex1001	U.S. Patent No. 10,665,346 (“the Patent”)
Ex1002	Declaration of Dr. Rosen
Ex1003	Dr. Rosen Curriculum Vitae
Ex1004	Prosecution History File of the Patent (Application No. 16/718,839)
Ex1005	U.S. Patent Application Publication No. 2012/0123253 (“Renisch”)
Ex1006	U.S. Patent Application Publication No. 2015/0063667 (“Sprenicz”)
Ex1007	U.S. Patent Application Publication No. 2011/0007954 (“Suehling”)
Ex1008	U.S. Patent Application Publication No. 2016/0203263 (“Maier”)
Ex1009	U.S. Patent Application Publication No. 2016/0335395 (“Wu”)
Ex1010	U.S. Patent No. 9,028,800 (“D’Souza”)
Ex1011	RESERVED
Ex1012	U.S. Patent Application Publication No. 2016/0180042 (“Menon”)
Ex1013	Second Amended Complaint, <i>Progenics Pharmaceuticals, Inc. v. MIM Software Inc.</i> , Case No. 1:24-cv-10437-PBS, Dkt. 25, April 5, 2024.
Ex1014	RESERVED
Ex1015	Kaur, “Various Image Segmentation Techniques: A Review,” <i>International Journal of Computer Science and Mobile Computing</i> 3(5):809-814 (May 5, 2014) (“Kaur”)
Ex1016	Sharma, “Automated medical image segmentation techniques,” <i>Journal of Medical Physics</i> 35(1):3-14 (2010) (“Sharma”)
Ex1017	Greenspan, “Deep Learning in Medical Imaging: Overview and Future Promise of an Exciting New Technique,” <i>IEEE Transactions on Medical Imaging</i> , 35(5):1153-1159 (May 2016) (“Greenspan”)
Ex1018	Litjens, “A Survey on Deep Learning in Medical Image Analysis,” <i>Medical Image Analysis</i> 42:60-88 (Dec. 2017) (“Litjens”)
Ex1019	Shen, “Deep Learning in Medical Image Analysis,” <i>Annual Review of Biomedical Engineering</i> 19:221-248 (2017) (“Shen”)
Ex1020	Seifert, Suehling, et al., “Hierarchical Parsing and Semantic Navigation of CT Data,” <i>Medical Imaging 2009: Image Processing</i> , Proceedings of SPIE Vol. 7259, pp. 725902-1 to

	725902-8 (2009) (“Seifert”)
Ex1021	RESERVED
Ex1022	Gandaglia, “Distribution of metastatic sites in patients with prostate cancer: A population-based analysis,” <i>The Prostate</i> 74(2):210-216 (2014) (“Gandaglia”)
Ex1023	Guntur, “Bone as an endocrine organ.” <i>Endocrine Practice</i> . 18(5):758-762 (2012) (“Guntur”)
Ex1024	U.S. Patent Application Publication No. 2010/0032575 (“Iagaru”)
Ex1025	U.S. Patent Application Publication No. 2010/0080434 (“Seifert”)
Ex1026	Electronic Order, <i>Progenics Pharmaceuticals, Inc. v. MIM Software Inc.</i> , Case No. 1:24-cv-10437-PBS, Dkt. 69, October 8, 2024.
Ex1027	Amended Joint Statement, <i>Progenics Pharmaceuticals, Inc. v. MIM Software Inc.</i> , Case No. 1:24-cv-10437-PBS, Dkt. 75, January 31, 2025.

CLAIM LISTING

Claim 1: A network-based system for generating a disease risk map for use as a decision-making support for evaluating risk of cancer or risk of recurrence of cancer, the system comprising:

[1(a)] a processor; and a memory having instructions stored thereon, wherein the instructions, when executed by the processor, cause the processor to:

[1(b)] (i) access one or more medical images associated with a particular patient from a database;

[1(c)] (ii) perform an analysis of the one or more medical images associated with the particular patient using a machine learning algorithm, to generate the risk map, wherein the risk map comprises a visual representation of tissue overlaid with graphical denotations marking one or more regions of risk of cancer or risk of recurrence of cancer; and

[1(d)] (iii) cause display of the risk map via a graphical user interface (GUI) for presentation or review of the risk map by a user,

[1(e)] wherein the analysis of the one or more medical images comprises creation of a 3D image of the one or more regions of risk of cancer or risk of recurrence of cancer overlaid on the one or more medical images, and wherein the 3D image comprises geographic identification of one or more specific tissue region(s) overlaid on the one or more medical images.

Claim 2: The system of claim 1, wherein the one or more medical images comprise one or more magnetic resonance images (MRIs).

Claim 3: The system of claim 1, wherein the one or more medical images comprise (i) one or more PET/CT image(s) or (ii) one or more SPECT/CT image(s).

Claim 4: The system of claim 1, wherein the visual representation of tissue is at least a portion of one of the one or more medical images of the particular patient.

Claim 5: The system of claim 1, wherein the cancer is prostate cancer.

Claim 6: The system of claim 1, wherein the visual representation of tissue comprises a visual representation of bone.

Claim 7: The system of claim 1, wherein the one or more specific tissue region(s) comprise one or more members selected from the group consisting of organs, organ structures, sub-organs, and organ regions.

Claim 8: The system of claim 1, wherein the one or more specific tissue region(s) comprise one or more particular bones.

Claim 9: The system of claim 1, wherein the instructions cause the processor to generate a radiologist report for the particular patient based at least in part on the analysis of the one or more medical images.

Claim 10: The system of claim 9, wherein the radiologist report comprises the one or more medical images and the risk map.

Claim 11: The system of claim 9, wherein the radiologist report comprises one or more reference images or reference risk maps.

Claim 12: The system of claim 1, wherein the instructions cause the processor to apply a machine learning algorithm to update a process for automatically analyzing the one or more medical images using accumulated image data in the database.

Claim 13: A method for generating a disease risk map for use as a decision-making support for evaluating risk of cancer or risk of recurrence of cancer, the method comprising:

(i) accessing, by a processor, one or more medical images associated with a particular patient from a database;

(ii) automatically analyzing, by the processor, using a machine learning algorithm, the one or more medical images to generate the risk map, wherein the risk map comprises a visual representation of tissue overlaid with graphical denotations marking one or more regions of risk of cancer or risk of recurrence of cancer; and

(iii) causing, by the processor, display of the risk map via a graphical user interface (GUI) for presentation or review of the risk map by a user,

[(iv)] wherein step (ii) comprises creation of a 3D image of the one or more regions of risk of cancer or risk of recurrence of cancer overlaid on the one or more medical images, and wherein the 3D image comprises geographic identification of one or more specific tissue region(s) overlaid on the one or more medical images.

I. MANDATORY NOTICES

A. Real Party-in-Interest (37 C.F.R. §42.8(b)(1))

The real parties-in-interest are Petitioner MIM Software Inc.; Petitioner's parent company, GE HealthCare Technologies Inc.; and Petitioner's insurer, AIG Specialty Insurance Company.

B. Related Matters (37 C.F.R. §42.8(b)(2))

Progenics Pharmaceuticals, Inc. ("Progenics") has asserted U.S. Patent No. 10,665,346 ("the Patent") against Petitioner MIM in *Progenics Pharmaceuticals, Inc. et al v. MIM Software Inc.*, 1:24-cv-10437-PBS (D. Mass.) ("MA litigation"). Ex1013. The earliest date of service is February 23, 2024.

C. Lead and Back-up Counsel and Service Information (37 C.F.R. § 42.8(b)(3)-(4))

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II. INTRODUCTION AND RELIEF REQUESTED

Petitioner requests *inter partes* review and a finding that all claims of U.S. Patent No. 10,665,346 (“the Patent”) are not patentable.

The Patent is generally directed to a system for automatically analyzing one or more medical images of a patient using “a machine learning algorithm” to generate “a disease risk map for use as a decision-making support for evaluating risk of cancer.” *See, e.g.*, Ex1001, claim 1. The Patent does not describe the machine learning algorithm except in general terms as “e.g., artificial neural networks (ANNs); e.g., convolutional neural networks (CNNs).” Ex1001, 25:32-35.

The claims of the Patent, as they were presented for examination, recited only generic features such as: (i) “access one or more medical images”; (ii) “perform an analysis of the one or more medical images ... using a machine learning algorithm, to generate the risk map”; and (iii) “cause display of the risk map via a graphical user interface.” Ex1004, p.124 (preliminary amendment). Likewise, the claimed “risk map” was only described generically as just “a visual representation of tissue overlaid with graphical denotations marking one or more regions of risk of cancer.” *Id.*

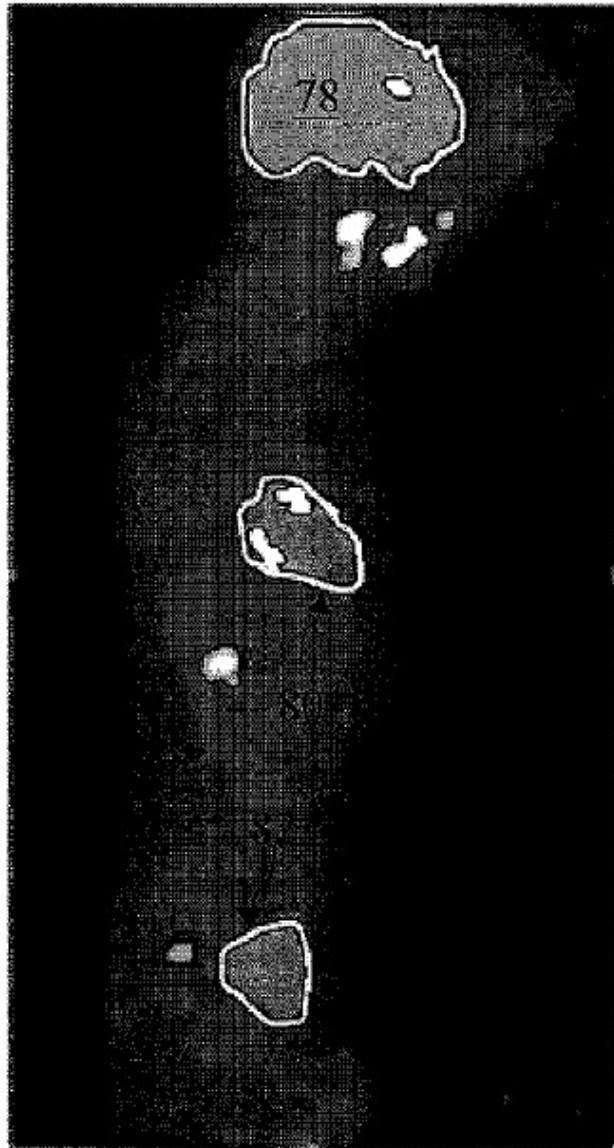
The Examiner was not satisfied and added – by Examiner’s amendment – more detail regarding the “analysis” that produces the risk map. Ex1004, pp.164-

167. For example, the Examiner amended claim 1 to add:

wherein the analysis of the one or more medical images comprises creation of a 3D image of the one or more regions of risk of cancer or risk of recurrence of cancer overlaid on the one or more medical images, and wherein the 3D image comprises geographic identification of one or more specific tissue region(s) overlaid on the one or more medical images.

Ex1004, p.165 (emphasis added). With this change, the Examiner allowed the claims, *emphasizing* in his Reasons for Allowance that the closest prior art he was aware of did not show a 3D image of one or more regions of risk of cancer “overlaid” on the medical images or identification of one or more “specific tissue” region(s) overlaid on the one or more medical images. Ex1004, p.167.

Importantly, the Examiner did not consider any of the three primary references before the PTAB in this Petition. For example, the Examiner did not consider U.S. Published Application 2012/0123253 (“Renisch”) (EX1005), which automatically analyzes 3D medical images using machine learning algorithms to produce images like the one shown below, having graphical denotations of 3D segmented lesions (i.e., regions of risk of cancer) and 3D segmented organs (i.e., specific tissue regions) overlaid on a medical image.



As detailed in this Petition and supporting Declaration from Dr. Rosen (Ex1002), claims 1-13 of the Patent are unpatentable as anticipated by and/or obvious in view of the prior art.

III. GROUNDS FOR STANDING AND FEES

Petitioner certifies that the Patent is available for *inter partes* review and Petitioner is not barred or estopped from requesting review.

The undersigned authorizes the charge of any required fees to Deposit Account No. 20-0809.

IV. THE PATENT AND PROSECUTION HISTORY

The Patent was filed on December 18, 2019, claiming priority to provisional application no. 62/413,936, filed Oct. 27, 2016. Ex1001. After approximately 2 months, the Patent received Notice of Allowance following an Examiner's Amendment on February 21, 2020. Ex1004, pp.159-168. The Patent issued with two independent claims (system and method) that are nearly identical. Both independent claims were amended in substantially the same way by the Examiner prior to allowance. Ex1004, pp.165-167.

The Patent describes generation of “a 3D risk image corresponding to a patient organ (and/or other tissue) for comparison with reference images.” Ex1001, 3:15-20 (emphasis added). “For example, a patient for whom a risk of cancer is detected can display a map indicating areas and/or degrees of risk and can compare this risk map with those of others for whom a given course of treatment is recommended.” Ex1001, 3:26-30 (emphasis added). An example risk map comprises “a visual representation (e.g., 3D representation) of tissue (e.g., an organ or other part of the body) with graphical denotations (e.g., texture- or color-coding) marking regions of risk of current disease ..., e.g., cancer.” Ex1001, 4:3-7.

To produce the risk map, the Patent uses nuclear medicine images

(PET/SPECT) to identify the regions of risk of cancer and anatomical images (CT/MR) to identify specific tissue regions such as organs and bones. To identify the regions of risk of cancer, the Patent explains that “hotspots” are “localized regions of high intensity in nuclear medicine images” (Ex1001, 15:52-53) that can be “classified as corresponding to cancerous lesions” (Ex1001, 25:41-42). To identify specific tissue regions, the Patent explains:

3D boundaries of specific regions of imaged tissue can be accurately identified by analysis of CT scans. For example, automated segmentation of CT scans can be performed to identify 3D boundaries of specific organs (e.g., a prostate, lymph nodes, a lung or lungs), sub-organs, organ regions, as well as other regions of imaged tissue, such as particular bones and an overall skeletal region of the patient.

Ex1001, 26:40-50 (emphasis added).

The Patent also explains that “overlaying one image (e.g., a CT scan) with another (e.g., a PET scan) refers to establishing a mapping between coordinates and/or pixels or voxels of the two images that that [sic] represent the same physical locations (e.g., within the patient).” Ex1001, 26:36-40. Accordingly, “[o]nce the 3D boundaries of various regions are identified within a CT scan ... the identified 3D boundaries can be transferred to [a] PET image” such that “regions of the PET image falling within and/or outside of the identified 3D boundaries can be accurately identified.” Ex1001, 26:61-66. Thus, “intensity values of the PET scan in relation to (e.g., within and/or outside of) the 3D boundaries of the identified

regions can be used to determine levels of cancerous tissue with the identified regions, e.g., based on features of detected hotspots.” Ex1001, 27:15-20.

Figure 4 of the Patent, below, depicts “full body gamma camera images showing hotspots automatically identified by the system” and includes graphical overlays delineating skeletal areas. Ex1001, 13:53-56, 29:7-9.

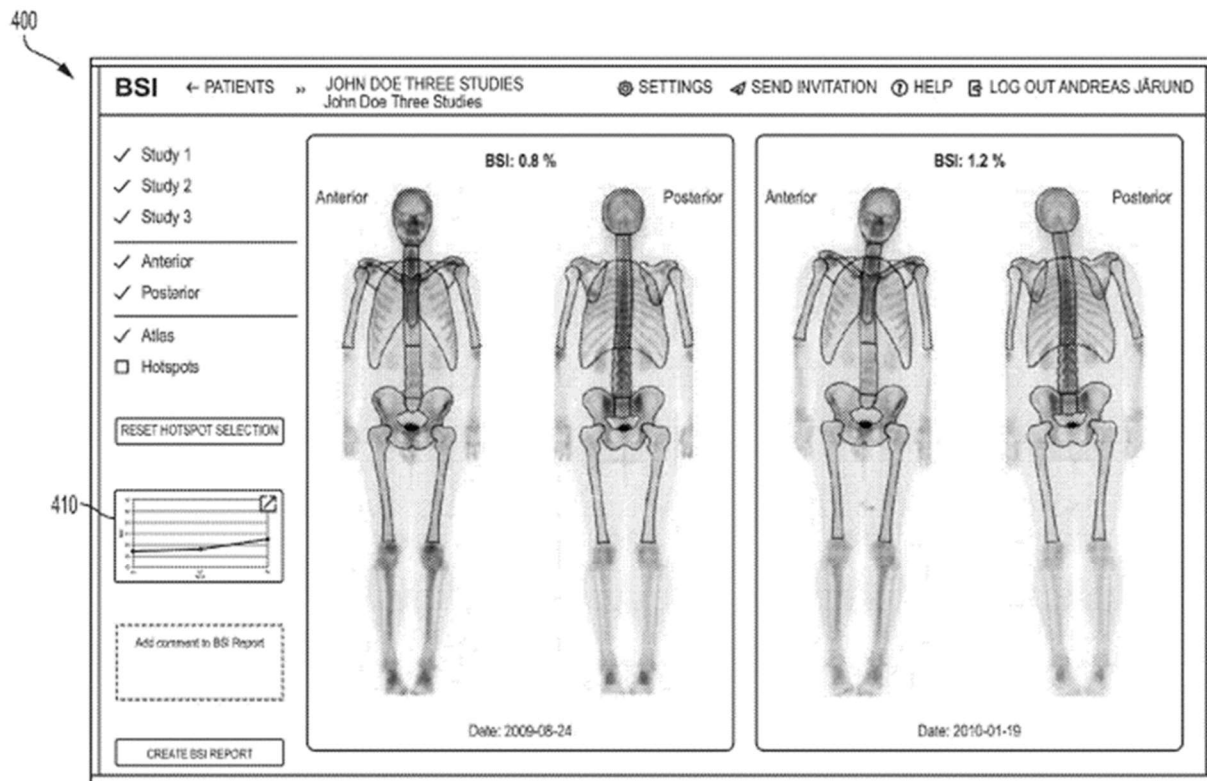


FIG. 4

As for the use of machine learning algorithms, the Patent states, *but only generally*, that machine learning algorithms, including artificial neural networks, can perform tasks such as: (i) segmentation of tissue regions in CT scans (Ex1001, 26:50-55); (ii) classification of hotspots as cancerous lesions (Ex1001, 25:41-45); and/or (iii) updating the process by which images are analyzed “(e.g., updating

segmentation and/or classification routines based on [the] growing image database)” (Ex1001, 3:7-10, Fig. 6 (V)).

V. IDENTIFICATION OF CHALLENGE

Petitioner requests review of claims 1-13 of the Patent on the following grounds:

Ground	Prior Art	Basis	Claims Challenged
A	Renisch	§102(a)(1)/(2)	1-7, 9-10, 13
B	Renisch in view of Wu	§103	1-7, 9-10
C	Renisch, or Renisch in view of Wu, each in view of the Applicant’s Admitted Prior Art (“AAPA”) or D’Souza	§103	5
D	Renisch, or Renisch in view of Wu, each in view of Sprencz	§103	8
E	Renisch, or Renisch in view of Wu, each in view of Maier	§103	9-11
F	Renisch, or Renisch in view of Wu, each in view of Menon	§103	12
G	Sprencz	§102(a)(1)/(2)	1-10, 13
H	Sprencz in view of AAPA or D’Souza	§103	5
I	Sprencz in view of Maier	§103	11
J	Suehling	§102(a)(1)/(2)	1-10, 13
K	Suehling in view of Maier	§103	11
L	Suehling in view of Menon	§103	12

VI. LEVEL OF SKILL IN THE ART

A person of ordinary skill in the art (“POSITA”) would include a person with a medical (MD) degree and/or an advanced degree in Computer Engineering,

Computer Science, Physics, or other field related to computer imaging, and at least 3 years of field experience with medical imaging devices, such as PET/CT or SPECT/CT systems. Ex1002, ¶39.

VII. CLAIM CONSTRUCTION (37 C.F.R. § 42.100(b))

Except for the term “risk map,” the claim terms of the Patent do not require an express construction.

A. “Risk Map” (claims 1, 10, 11, and 13)

The term “risk map” does not have a well-established ordinary and customary meaning. Therefore, Petitioner looks to the intrinsic evidence to determine the meaning within the Patent.

The claims themselves internally define a risk map, stating “wherein the risk map comprises a visual representation of tissue overlaid with graphical denotations marking one or more regions of risk of cancer or risk of recurrence of cancer.” Ex1001, 35:59-62, 36:50-54. This description is consistent with the Patent specification, which similarly describes a risk map as an image corresponding to a patient organ or other tissue that indicates areas and/or degrees of cancer risk with graphical denotations such as texture or color. *See* Ex1001, 3:17-18 (“risk image corresponding to a patient organ (and/or other tissue)”), 3:28-29 (“a map indicating areas and/or degrees of risk ... [i.e.,] risk map”); 4:3-10 (“a risk map, e.g., a visual representation ... of tissue (e.g., an organ or other part of the body) with graphical

denotations (e.g., texture- or color-coding) marking regions of risk of current disease ..., e.g., cancer”).

As a matter of extrinsic evidence, the Patent Owner has asserted that Petitioner infringes claim 1 of the Patent (Ex1013, ¶¶62-66) and that Petitioner’s accused product satisfies the third element of claim 1 (i.e., “cause display of the risk map via a graphical user interface (GUI) ...”) because it “displays the risk map (i.e., tumor segmentation) via a graphical user interface (GUI).” Ex1013, ¶66 (emphasis added). Based on this allegation, Patent Owner’s position appears to be that displaying segmented tumors (i.e., segmented lesions) overlaid on a visual representation of tissue (e.g., medical image) constitutes display of a “risk map.” *See Toshiba Corp. v. Gold Charm Ltd.*, IPR2016-00462, Paper 29, pp.14-16 (accepting, as persuasive, the patent owner’s prior statements and allegations regarding claim scope).

Accordingly, for the purpose of this Petition, the term “risk map” may be construed according to any of the following:

- (1) “an image corresponding to a patient organ or other tissue that indicates areas and/or degrees of cancer risk with graphical denotations such as texture or color,” consistent with the Patent specification;
- (2) “a visual representation of tissue overlaid with graphical denotations marking one or more regions of cancer or risk of recurrence of cancer,”

consistent with the definition in the Patent claims; and

(3) “a visual representation of tissue overlaid with segmented lesions,” consistent with Patent Owner’s allegations in litigation against Petitioner.

These constructions differ, if at all, only in the degree to which they expressly recite particular details.

VIII. DETAILED EXPLANATION OF GROUNDS FOR INVALIDITY

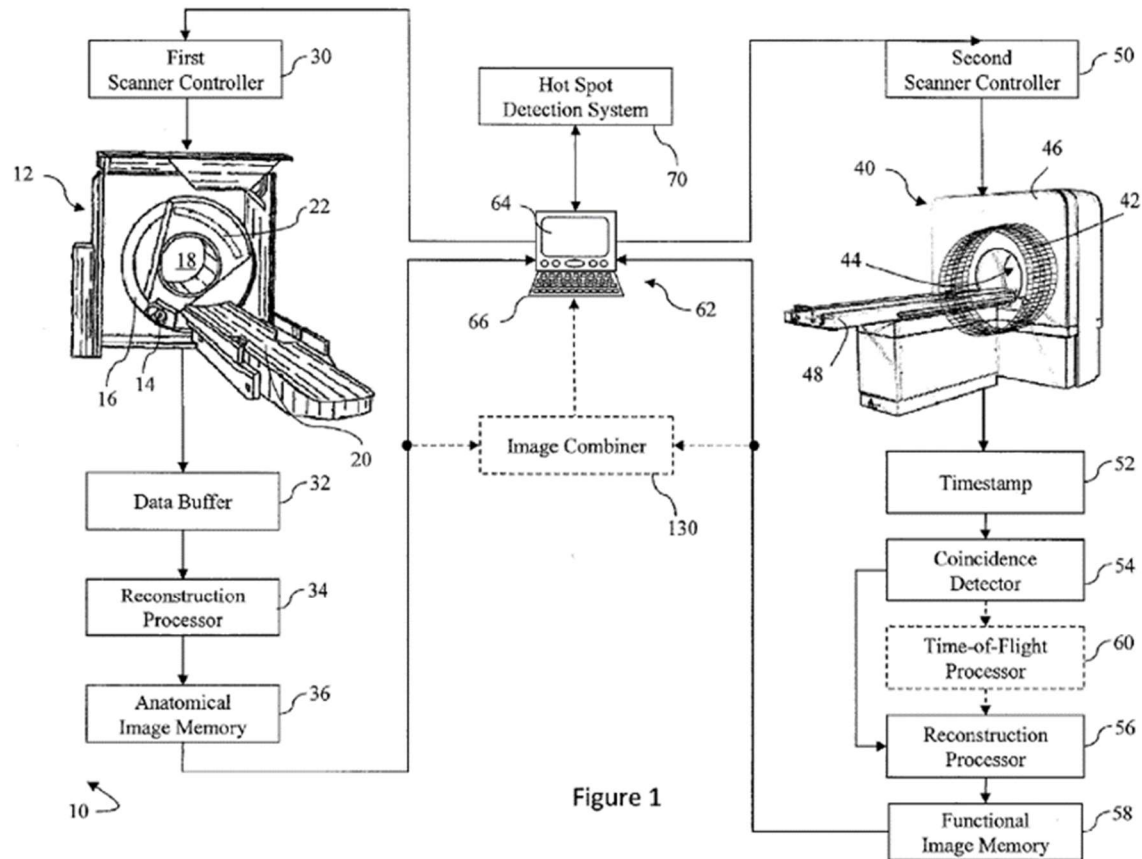
A. Summary of the Prior Art

1. US2012/0123253 (“Renisch”)

Renisch is a United States patent application that published on May 17, 2012. Ex1005. It is prior art under 35 U.S.C. §102(a)(1) and (a)(2).

Renisch discloses a diagnostic system 10 that includes: (i) a first imaging scanner 12 for obtaining 3D anatomical diagnostic images (e.g., CT/MRI); (ii) a second imaging scanner 40 for obtaining 3D functional images (e.g., PET/SPECT); (iii) a workstation/GUI 62 for displaying image data; and (iv) a hotspot detection system 70 for automatically detecting and quantifying cancerous lesions based on anatomical and functional images. Ex1005, Fig. 1, [0020]-[0022], [0025]. The hotspot detection system 70 includes: (i) a segmentation unit that segments anatomical images into regions corresponding to anatomical structures, e.g., brain, heart, liver, and kidneys (Ex1005, [0025]); and (ii) a hotspot detection unit that sorts voxels in functional images into regions of high intensity referred to as “hot spots ... , which can potentially be caused by tumor growth or by other malignant

processes.” (Ex1005, [0029]). To differentiate between possible cancer and regions of high intensity that correspond to normally functioning organs, Renisch



teaches that “[t]he anatomical regions identified in the anatomical ... image ... can be carried over to the functional ... image ... to delineate anatomical structures in the [functional] image,” (Ex1005, [0034]) which “can ... be helpful for accurately determining a location of the hot spots relative to the patient’s anatomy” (Ex1005, [0025]).

Referring to Figs. 3A-3C below, Renisch produces images in which 3D

segmented hotspots are identified by a “color overlay” 92 on a functional image (Fig. 3A), images in which 3D segmented organs (e.g., brain 78, heart 80, bladder 82) are identified by graphical overlays in the same image with 3D segmented hotspots (Fig. 3B), and images in which hotspots located within normal functioning organs are suppressed, leaving only hotspots that are suspected to be cancerous lesions. (Fig. 3C). Ex1005, [0015]-[0017], [0025], [0029], [0031].



Figure 3A

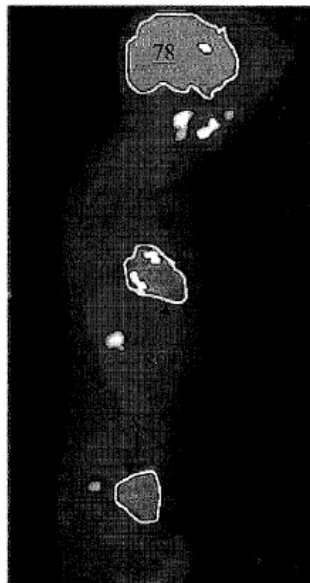


Figure 3B

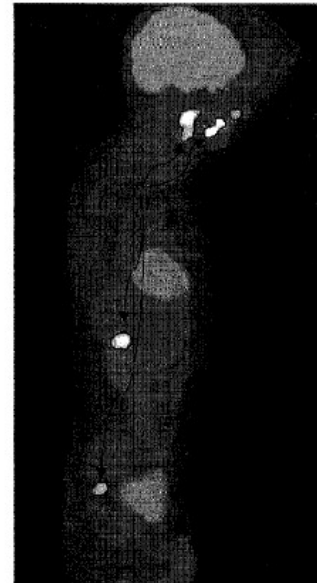


Figure 3C

Renisch expressly states that its segmented anatomical and functional images can be combined for concurrent display on a GUI: “For example, the images can be superimposed in different colors, the outline of the functional second image

representation hotspots can be superimposed on the first image representation, the outline of the segmented anatomical structures of the anatomical first image representation can be superimposed on the functional second image representation, ... or the like.” Ex1005, [0036]-[0037] (emphasis added). Likewise, Renisch states that “[t]he segmented and unsegmented anatomical images, the function[al] images, the functional image with high uptake organs suppressed, in image or map of quantified hot spots, and superimposed combinations thereof” can be stored in the memory of GUI 62 for display. Ex1005, [0036] (emphasis added).

2. US2015/0063667 (“Sprencz”)

Sprencz is a U.S. patent application published on March 5, 2015. Ex1006. It is prior art under 35 U.S.C. §102(a)(1) and (a)(2).

Sprencz discloses a system for automatically segmenting, displaying, and quantifying lesions throughout the body (bone and non-bone) using multi-modality 3D imaging data. Ex1006, Abstract, [0011], [0041]-[0044], [0048]-[0050], [0055]-[0056]. A CPU 12 controls the system, which may be connected via a network to one or more remotely located imaging system 20, workstation 28, and image database 18. Ex1006, [0023]-[0027].

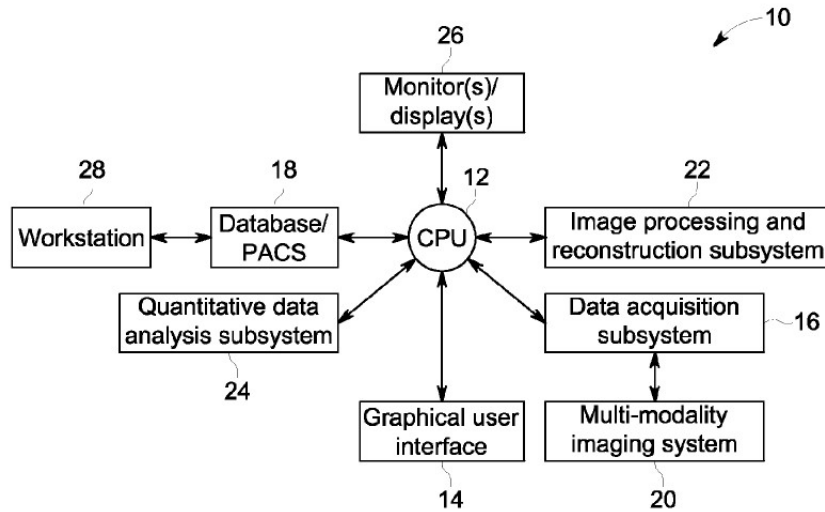
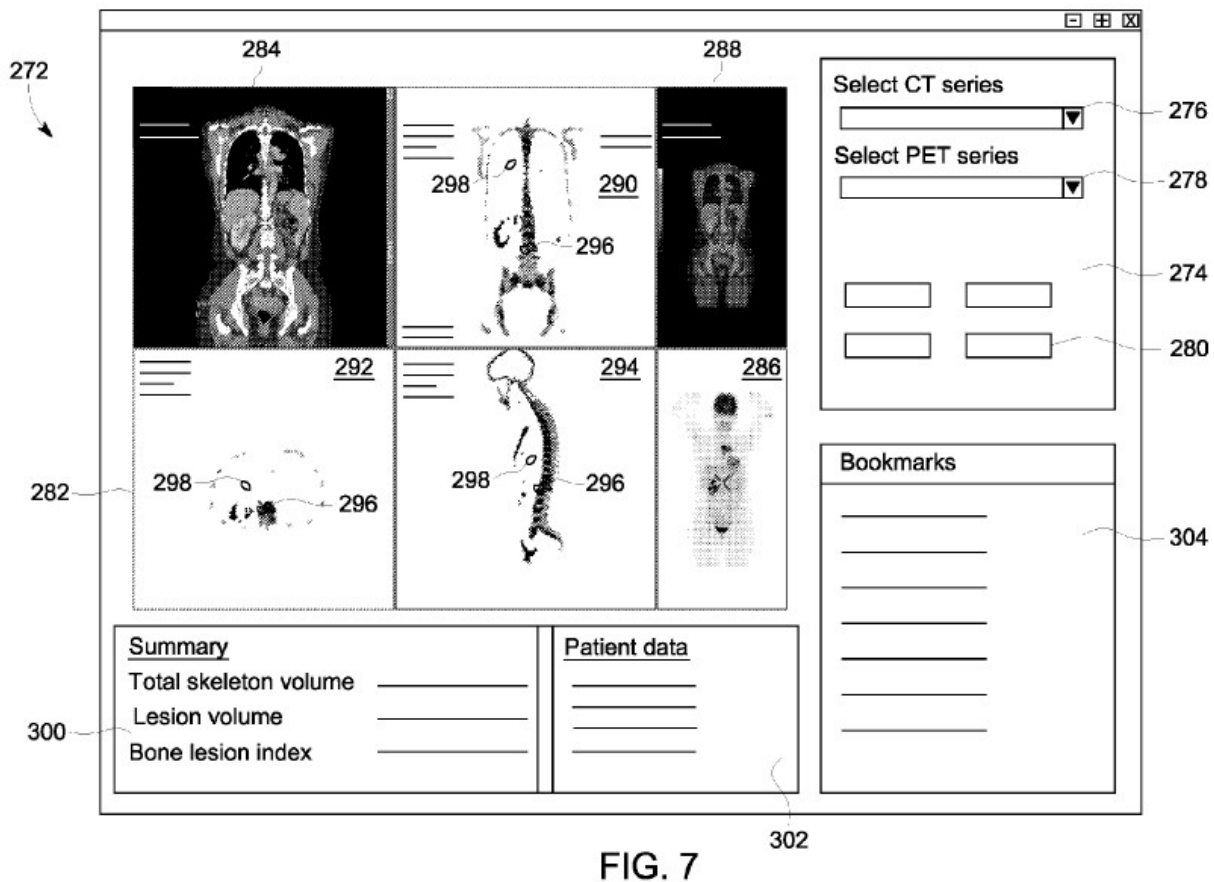


FIG. 1

Sprenetz accesses at least one 3D anatomical image and at least one 3D functional image for a patient. Ex1006, [0041]; Fig. 4. Sprenetz then registers the images to accurately overly the anatomical data and the functional image data. Ex1006, [0042]. The anatomical image is automatically segmented to identify the patient's 3D bone volume using simple thresholding or machine learning algorithms such as "clustering." Ex1006, [0043]-[0046], Fig. 5. The functional image is likewise segmented to identify lesions, and the lesions are classified as either bone lesions or non-bone lesions by comparing the location of each lesion with the location of the segmented skeletal volume. Ex1006, [0048]-[0049], [0052].

Referring to Fig. 7 below, Sprenetz displays "the segmented skeletal volume ... overlaid with contours of lesion candidates 296, 298." Ex1006, [0056]

(emphasis added). In another embodiment, “the segmented skeletal structure from a CT image series is projected into a PET image that includes the lesion candidates.” Ex1006, [0050] (emphasis added).



3. US2011/0007954 (“Suehling”)

Suehling is a U.S. patent application published on January 13, 2011. Ex1007. It is prior art under 35 U.S.C. §102(a)(1) and (a)(2).

Suehling discloses a system for automatically segmenting, displaying, and quantifying lesions in a 3D medical image such as a CT image or hybrid PET/CT

image. Ex1007, Abstract, Fig. 1, [0006], [0022], [0025]. The system detects lesions throughout the body and automatically labels them by location so that results can be navigated on a region-by-region basis (e.g., displaying only liver lesions). Ex1007, [0042]-[0043].

Suehling receives a 3D medical image and automatically segments the image into search regions corresponding to particular organs and bones such as the brain, liver, lungs, spine, pelvis, femur, etc. Ex1007, [0026]-[0031]. Suehling then detects lesions in each of the search regions using trained region-specific lesion detectors. Ex1007, [0032]-[0033].

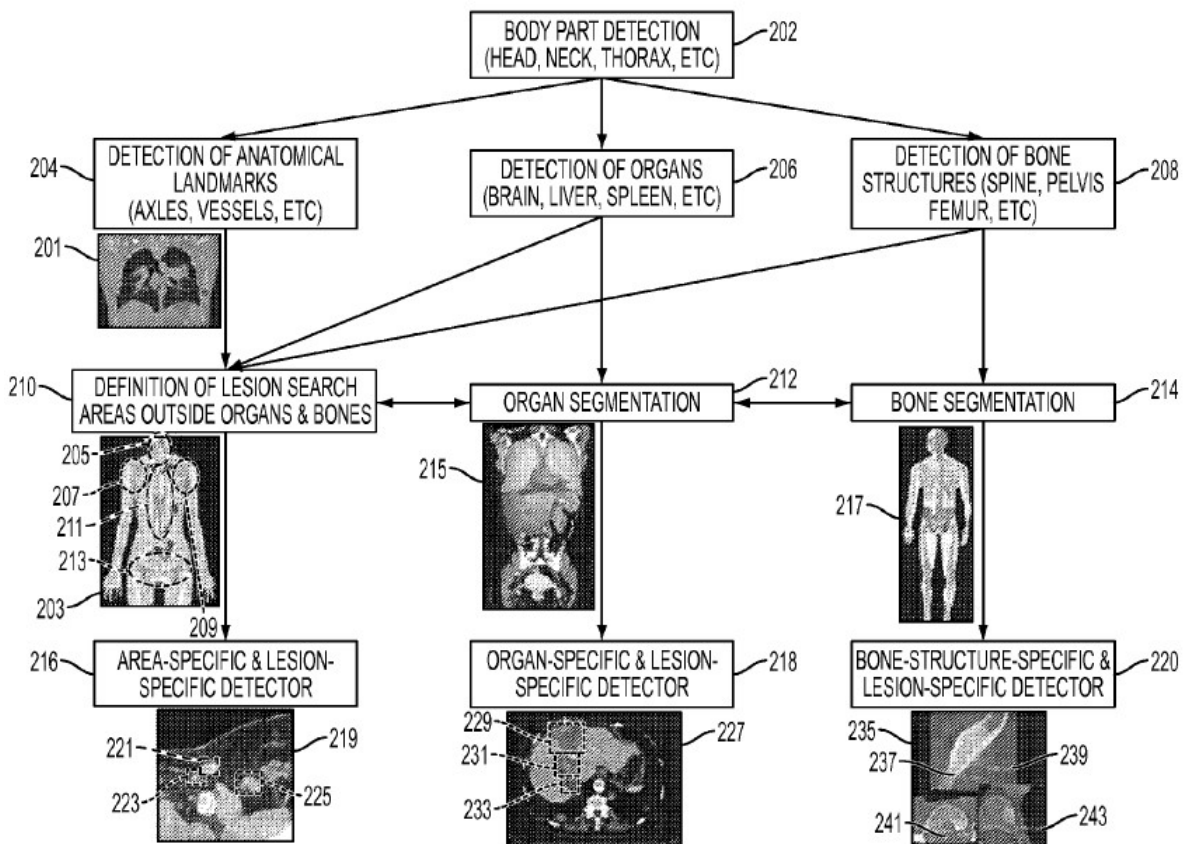


FIG. 2

Referring to Fig. 2 above, Suehling states: “Image 215 of FIG. 2 shows exemplary organ segmentation results” (Ex1007, [0030] (emphasis added)) and “[i]mage 227 shows lesions 229, 231, and 233 detected in an exemplary segmented organ” (Ex1007, [0033] (emphasis added)). Likewise, Suehling states: “Image 217 of FIG. 2 shows exemplary bone segmentation results” (Ex1007, [0031] (emphasis added)) and “[i]mage 235 shows lesions 237, 239, 241, and 243 detected in exemplary segmented bone structures” (Ex1007, [0033] (emphasis added)).

4. US2016/0203263 (“Maier”)

Maier is a U.S. patent application published on July 14, 2016. Ex1008. It is prior art under 35 U.S.C. §102(a)(1) and (a)(2).

Maier discloses a computer implemented method for communicating a patient’s health status and risk by automatically generating a report tailored for the intended user. Ex1008, [0014]. Maier receives one or more medical images from a medical imaging system or database and compares the medical image(s) to reference images from other patients having known clinical outcomes. Ex1008, [0027], Fig. 1. Based on the comparison, Maier calculates quantitative metrics related to the patient’s risk of future health outcomes and automatically generates a report that includes the patient’s medical images and reference images of others for comparison. Ex1008, [0026], [0041], Fig. 3.

5. US2016/0335395 (“Wu”)

Wu is a U.S. patent application, filed on July 28, 2016, and published on November 17, 2016. Ex1009. It is prior art under 35 U.S.C. §102(a)(2).

Wu discloses a cloud-based server for providing medical image processing services over the Internet, including “bone removal, ... registration, ... [and] segmentation of structures.” Ex1009, [0027], [0029]-[0033], [0043], Figs. 1A and 1B.

6. U.S. Patent No. 9,028,800 (“D’Souza”)

D’Souza is a U.S. Patent issued on May 12, 2015. Ex1010. It is prior art under 35 U.S.C. §102(a)(1) and (a)(2).

D’Souza discloses compositions of ^{18}F -labeled molecules and describes their uses in PET and SPECT nuclear medicine imaging, including ^{18}F -labeled PSMA for use in imaging prostate cancer. Ex1010, Abstract, 12:19-26, 49, 35:42-49, 36:17-24, 37.

7. US2016/0180042 (“Menon”)

Menon is a U.S. patent application published on June 23, 2016. Ex1012. It is prior art under 35 U.S.C. §102(a)(1) and (a)(2).

Menon describes an automated triaging decision support tool 22 that utilizes machine learning to continuously refine (i.e., update) the tool. Ex1012, [0010], [0032], [0055], [0078], [0103]-[0104], [0180], [0189], [0195]. For example, Menon states: “The tool 22 may continue to refine the model ... using machine

learning and improve its predictive accuracy using new information that will be available when the product is being tested real time and when the product is in clinical use.” Ex1012, [0195].

8. Applicant’s Admitted Prior Art (“AAPA”)

The Patent admits that “a number of radiopharmaceuticals [are] available for imaging particular kinds of cancer” including prostate cancer. Ex1001, 1:49-61.

The Patent states:

For example, the small molecule diagnostic 1404 targets the extracellular domain of prostate specific membrane antigen (PSMA), a protein amplified on the surface of >95% of prostate cancer cells and a validated target for the detection of primary and metastatic prostate cancer. 1404 is labeled with technetium-99m, a gamma-emitter isotope that is widely available, relatively inexpensive, facilitates efficient preparation, and has spectrum characteristics attractive for nuclear medicine imaging applications.

Ex1001, 1:52-61. Additionally, the Patent admits:

Another example radiopharmaceutical is PyLTM (also known as [18F]DCFPyL), which is a clinical-stage, fluorinated PSMA-targeted PET imaging agent for prostate cancer. A proof-of-concept study published in the April 2015 issue of the Journal of Molecular Imaging and Biology demonstrated that PET imaging with PyLTM showed high levels of PyLTM uptake in sites of putative metastatic disease and primary tumors, suggesting the potential for high sensitivity and specificity in detecting prostate cancer.

Ex1001, 1:62-2:3.

B. Grounds A-F, Renisch-based Anticipation and Obviousness

1. Independent Claim 1 (System Claim)

Claim 1 is anticipated by Renisch or, in the alternative, obvious over Renisch in view of Wu. Renisch discloses every limitation of claim 1. But, if Renisch does not disclose a “network-based system,” then Renisch in combination with Wu teaches every limitation of claim 1.

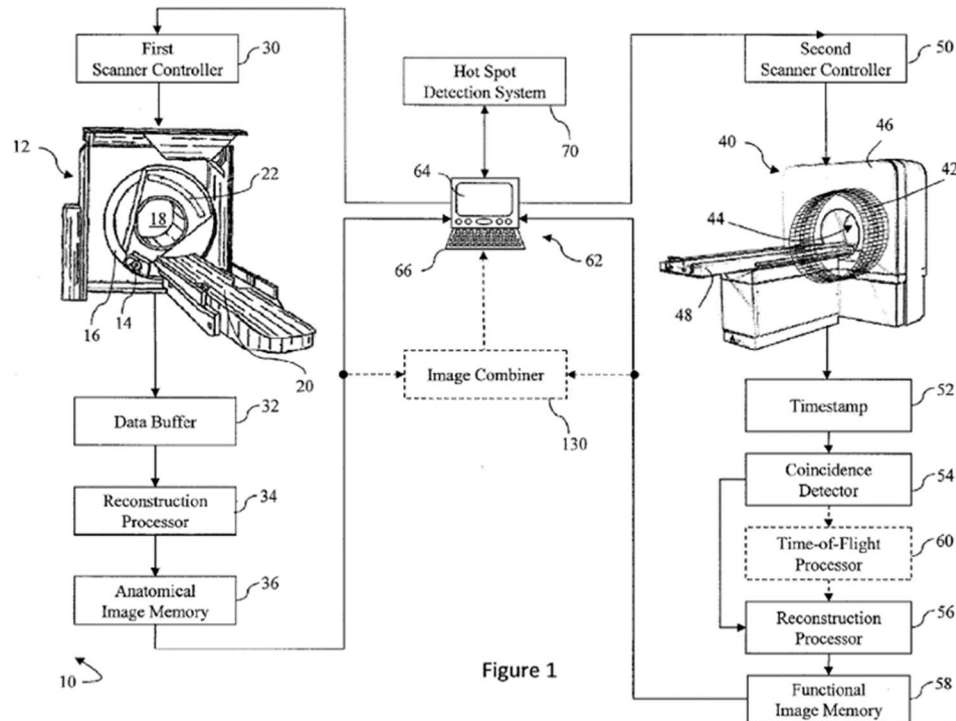
a) Preamble: A Network-based System

Claim 1 recites: “A network-based system for generating a disease risk map for use as a decision-making support for evaluating risk of cancer or risk of recurrence of cancer, the system comprising”

(1) Anticipation by Renisch

Renisch discloses the limitations of the preamble. Ex1005, [0006], [0008], [0020]-[0023], [0025], [0029], [0031]-[00033], [0036]-[0037]; Ex1002, ¶¶144-148. With reference to Fig. 1 below, Renisch is a network-based system because the automatic hotspot detection system 70 is interconnected for sharing data and resources with a workstation/GUI 62 as well as an anatomical imaging system 12 and a functional imaging system 40. Ex1002, ¶148. Additionally, Renisch generates a disease risk map for evaluating risk of cancer because it generates 3D medical images with color overlays that indicate the location of suspected cancerous lesions. Ex1005, Figs. 3A-3C, [0006] (“identifies unsuppressed regions

of high uptake as one of potential lesion and non-potential lesion.”), [0029] (“color overlay”), [0036] (“map of quantified hot spots”), [0037] (“the outline of the ... hotspots can be superimposed on the [anatomical] image representation”); Ex1002, ¶147.



(2) Obviousness over Renisch with Wu

If Renisch does not disclose a network-based system, then Wu discloses this limitation, and a POSITA would have been motivated to operate the hotspot detection system of Renisch on a network server based on Wu’s express teachings. Ex1002, ¶¶149-154.

Wu discloses a cloud-based server that provides medical image processing

services over a network, such as the Internet. Ex1009, [0027], [0029]-[0033], [0035], [0094], Figs. 1A, 1B, and 2. Examples of image processing services provided by Wu include services like those described in Renisch, including “registration” of anatomical and functional images and “segmentation of structures” such as organs. Ex1009, [0043], [0118]. Additionally, Wu supplies the express motivation to provide medical image processing services via a network server rather than workstation-based systems because a network server can provide services to multiple workstations, simultaneously and remotely. Ex1009, [0007], [0008], [0027], [0035].

A POSITA would have been motivated, based on the express teachings in Wu, to implement Renisch over a network so the user did not need to physically go to a single workstation and so more than one user could simultaneously and remotely use the hotspot detection system. Ex1002, ¶150. Alternatively, combining Renisch and Wu, which are in the same field, would have merely amounted to combining existing prior art elements (automated medical image processing systems and cloud servers) according to known methods (computer networking) to yield predictable results (remote image processing). Ex1002, ¶152. Moreover, a POSITA would have had a reasonable expectation of success implementing Renisch on a network server using the methods described in Wu. Ex1002, ¶¶152-154.

b) 1(a): Processor and Memory

Limitation 1(a) recites “a processor; and a memory having instructions stored thereon, wherein the instructions, when executed by the processor, cause the processor to” Renisch discloses this limitation, which is a generic recitation of structures present in any computer implemented system like Renisch. Ex1002, ¶¶156-157. For example, Renisch’s hotspot detection system comprises various functional units that Renisch alternatively describes as “processors” or “algorithms”. Ex1005, Fig. 2, [0014], [0030] (“uptake unit, processor, or algorithm”), [0031] (“classification unit, processor, or algorithm”), [0032], [0034]. Algorithms are stored instructions carried out by one or more processors to perform the respective described functions. Ex1002, ¶¶156.

c) 1(b): Access from a Database

Limitation 1(b) recites: “(i) access one or more medical images associated with a particular patient from a database.” Renisch discloses this limitation. Ex1005, [0025], Fig. 1 (36, 58), Fig. 2 (72, 74); Ex1002, ¶¶158-159. The automatic hotspot detection system 70 of Renisch accesses medical images from an anatomical image memory 36 of a first scanner 12 and a functional image memory 58 of a second scanner 40. Ex1005, [0025]. The images, which could also be obtained from a combined hybrid imaging system, are both associated with a particular patient. Ex1005, [0024].

d) 1(c): Analyze Using a Machine Learning Algorithm

Limitation 1(c) recites: “(ii) perform an analysis of the one or more medical images associated with the particular patient using a machine learning algorithm, to generate the risk map, wherein the risk map comprises a visual representation of tissue overlaid with graphical denotations marking one or more regions of risk of cancer or risk of recurrence of cancer.” Renisch discloses these limitations. Ex1005, [0025], [0027], [0029], [0033], [0036]-[0037], Fig. 3A-3C; Ex1002, ¶¶160-163.

Renisch discloses “a hot spot detection system 70 for automatic detection of a region of interest (ROI) pertaining to a lesion ... based on anatomical images 72 from the anatomical image memory 36 and functional images 74 from the functional image memory 58.” Ex1005, [0025]. “A segmentation unit 76 segments the anatomical first image representation 72 into regions which correspond to anatomical structures.” *Id.* “The segmentation unit 76 is capable of employing different types of segmentation methods” including machine learning algorithms such as a “neural network” (Ex1005, [0027]) as taught in the Patent (Ex1001, 26:50-54).

Renisch also discloses that “a hot spot detection unit 90 detects from the functional image representation 74 regions of high intensity” that “potentially can be caused by tumor growth.” Ex1005, [0029]. Regions of high intensity above a

certain threshold are “highlighted ... with a cover overlay” and further evaluated based on their location relative to segmented organs to determine if they are lesions or just normal physiological uptake. Ex1005, [0029]-[0032]. Renisch then generates a risk map from the results of its analysis, stating: “the outline of the functional second image representation hotspots can be superimposed on the [anatomical] first image representation, the outline of the segmented anatomical structures of the anatomical first image representation can be superimposed on the functional second image representation, ... or the like.” Ex1005, [0037] (emphasis added). Additionally, “[t]he segmented and unsegmented anatomical images, ... map of quantified hot spots, and superimposed combinations thereof” are generated for storage and display. Ex1005, [0036]. Thus, Renisch automatically analyzes one or more medical images of a patient using a machine learning algorithm to generate a visual representation of tissue overlaid with graphical denotations marking one or more regions of risk of cancer. Ex1002, ¶¶160,162.

e) 1(d): Display Via GUI

Limitation 1(d) recites: “(iii) cause display of the risk map via a graphical user interface (GUI) for presentation or review of the risk map by a user.” Renisch discloses this limitation. Ex1002, ¶¶164-165.

Renisch discloses “[a] workstation or graphic user interface 62” that “includes a display device 64 ... which a clinician can use to ... display image

data, and the like.” Ex1005, [0023]. Renisch also states that the results of its image analysis “are visualized on the display device 64” and “[t]he user is asked to confirm or edit the selected hot spots, i.e. high uptake regions ... before a summary report is generated.” Ex1005, [0033], [0037].

f) 1(e): 3D Identification of Specific Tissue Region(s)

Limitation 1(e) recites: “wherein the analysis of the one or more medical images comprises creation of a 3D image of the one or more regions of risk of cancer or risk of recurrence of cancer overlaid on the one or more medical images, and wherein the 3D image comprises geographic identification of one or more specific tissue region(s) overlaid on the one or more medical images.” Renisch discloses these limitations. Ex1005, [0006], [0008], [0021] (“3D image”), [0022] (“three-dimensional imaging data”), [0025], [0029] (“color overlay”), [0036]-[0037], Fig. 3B; Ex1002, ¶¶166-169.

Renisch describes segmenting 3D anatomical images into specific tissue regions, such as specific organ volumes (Ex1005, [0025]), and transferring those segmented anatomical regions to a 3D functional image (Ex1005, [0008], [0034]) so the location of segmented hotspots can be compared to the organ locations to determine if the hotspots are cancerous lesions or just normal physiological uptake (Ex1005, [0006], [0025], [0031]). Renisch also describes displaying the organ and lesion segmentation results in a multitude of combinations. For example, “the

outline of the functional second image representation hotspots can be superimposed on the first image representation, the outline of the segmented anatomical structures of the anatomical first image representation can be superimposed on the functional second image representation, ... or the like.” Ex1005, [0037]. Additionally, “[t]he segmented and unsegmented [3D] anatomical images, the [3D] function[al] images, the functional image with high uptake organs suppressed, in image or map of quantified hot spots, and superimposed combinations thereof” are generated and stored for display. Ex1005, [0036] (emphasis added). For example, Renisch shows in Fig. 3B below a risk

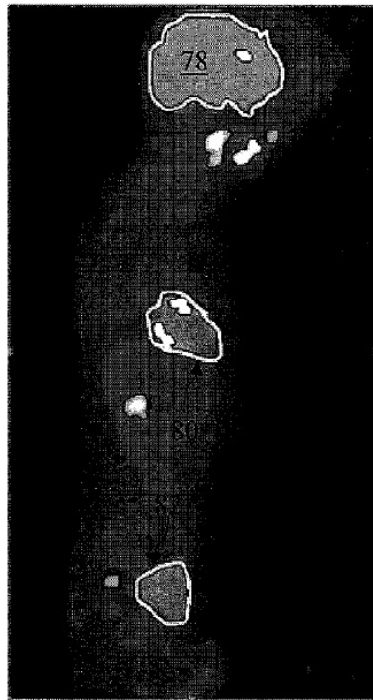


Figure 3B

map comprising a 3D medical image overlaid with the outlines of segmented organs and containing color overlays of identified lesions. Ex1005, [0016], [0025] (referring to Fig. 3B as depicting the segmented brain, heart, and bladder) [0029]. Thus, Renisch discloses the creation of a 3D image of one or more regions of risk of cancer “wherein the 3D image comprises geographic identification of one or more specific tissue region(s) overlaid on the one or more medical images.” Ex1002, ¶¶167-168.

2. Dependent Claim 2

Claim 2 depends from claim 1 and further recites: “wherein the one or more medical images comprise one or more magnetic resonance images (MRIs).”

Renisch discloses this limitation, thus rendering this claim anticipated by Renisch or obvious over Renisch in view of Wu. Ex1002, ¶¶171-173; Section VIII.B.1 *supra*. Renisch states: “With reference to FIG. 1, a diagnostic system 10 includes ... a diagnostic imaging scanner 12 such as ... an MRI scanner ... for obtaining anatomical diagnostic images.” Ex1005, [0020] (emphasis added), [0026] (stating that the anatomical image 72 and functional image 74 can both be “MR” images).

3. Dependent Claim 3

Claim 3 depends from claim 1 and further recites: “wherein the one or more medical images comprise (i) one or more PET/CT image(s) or (ii) one or more

SPECT/CT image(s).”

Renisch discloses these limitations, thus rendering this claim anticipated by Renisch or obvious over Renisch with Wu. Ex1002, ¶174-177; Section VIII.B.1. Renisch discloses a diagnostic system that includes a first anatomical imaging system, which could be a CT scanner, and a second functional imaging system, which could be a PET or SPECT scanner. Ex1005, [0020], [0022], [0025]. An “image combiner 130 combines the anatomical first image representation and the functional second image representation into a combined image.” Ex1005, [0037]. Renisch also states “[a]lthough the anatomical and functional scanners are illustrated separate, it is to be appreciated that they can be combined” such as “combined PET/CT [or] SPECT/CT.” Ex1005, [0024].

4. Dependent Claim 4

Claim 4 depends from claim 1 and further recites: “wherein the visual representation of tissue is at least a portion of one of the one or more medical images of the particular patient.”

For reasons already explained in Section VIII.B.1.d) above, Renisch discloses this limitation, rendering this claim anticipated by Renisch and obvious over Renisch with Wu. Ex1002, ¶¶178-180; Section VIII.B.1. The risk map generated by Renisch includes the outline of segmented lesions overlaid on a medical image. Ex1005, [0036], [0037].

5. Dependent Claim 5

Claim 5 depends from claim 1 and further recites: “wherein the cancer is prostate cancer.”

a) Anticipation by Renisch or Obviousness Over Renisch with Wu

Renisch inherently discloses this limitation, rendering this claim anticipated by Renisch and obvious over Renisch with Wu. Ex1002, ¶¶181-187; Section VIII.B.1. Renisch discloses the detection of cancerous lesions – generally – and is not limited to any particular cancer type. Ex1002, ¶182. In fact, Renisch depicts the detection and quantification of lesions throughout the body and describes the calculation of “total tumor burden,” which would account for metastatic cancer that has spread throughout the body. Ex1005, Figs. 3A-3C, [0032], [0034]. Imaging cancer throughout the body, including the pelvic region where the prostate is located, would necessarily include imaging prostate cancer if it is present. Ex1002, ¶¶182-186.

b) Obviousness Over Renisch or Renisch with Wu, Each in view of AAPA or D’Souza

In the alternative, claim 5 is obvious over Renisch (or Renisch with Wu) in view of the Applicant’s admitted prior art (“AAPA”) or D’Souza. Ex1002, ¶¶210-220. Renisch images cancer throughout the body and the Patent admits that “[t]here are ... a number of radiopharmaceuticals available for imaging particular kinds of cancer” including prostate cancer. Ex1001, 1:51-2:3. Accordingly, a

POSITA would have been motivated to use Renisch to image prostate cancer and would have had a reasonable expectation of success in doing so based on the knowledge of a POSITA and the prostate-cancer-specific radiopharmaceuticals described in the AAPA. Ex1002, ¶¶211-213.

Alternatively, both Renisch and D’Souza teach the use of ^{18}F -labeled fluorodeoxyglucose (FDG) to image cancer generally (Ex1005, [0003], [0023]; Ex1010, 2:15-21), and D’Souza further teaches alternative ^{18}F -labeled peptides, proteins and/or antibodies for imaging prostate cancer specifically (Ex1010, 36:22-37 (“prostate cancer”), 12:19-49 (“PSMA”). A POSITA would have been motivated to use Renisch to image prostate cancer based on the express teachings in D’Souza. Ex1002, ¶¶215-217. Alternatively, combining Renisch and D’Souza would have merely amounted to combining existing prior art elements (automated lesion detection systems and prostate-cancer-specific radiotracers) according to known methods (selecting a suitable delivery molecule for targeting a particular disease) to yield predictable results (better imaging of prostate cancer). Ex1002, ¶¶218-219. Moreover, a POSITA would have had a reasonable expectation of success in combining Renisch and D’Souza. Ex1002, ¶220. Renisch already teaches the use of an ^{18}F -labeled molecule to image cancer using a PET scanner (Ex1005, [0023]) and nothing in the disclosure of Renisch would discourage the use of a different ^{18}F -labeled molecule for the same purpose. Ex1002, ¶220.

D'Souza expressly teaches that any of its disclosed disease-specific targeting molecules could be used with any known PET imaging technique (like Renisch). Ex1010 at 35:42-36:21. Therefore, the ^{18}F -labeled molecules of D'Souza would be readily applicable to, and easily implemented with, Renisch's hotspot detection system.

6. Dependent Claim 6

Claim 6 depends from claim 1 and further recites: "wherein the visual representation of tissue comprises a visual representation of bone."

Renisch discloses this limitation, rendering claim 6 anticipated by Renisch and obvious over Renisch with Wu. Ex1002, ¶¶188-190; Section VIII.B.1. As already explained in Sections VIII.B.1 and VIII.B.5 above, Renisch images cancer throughout the body and produces risk maps comprising, e.g., an anatomical CT image overlaid with outlined lesions and outlined organ contours. Ex1005, [0036]-[0037], Fig. 3B. A full-body CT image (or even a head or chest image) provides a visual representation of bones, which are located throughout the body.

7. Dependent Claim 7

Claim 7 depends from claim 1 and further recites: "wherein the one or more specific tissue region(s) comprise one or more members selected from the group consisting of organs, organ structures, sub-organs, and organ regions."

Renisch discloses the limitations of claim 7, rendering this claim anticipated

by Renisch and obvious over Renisch in view of Wu. Ex1002, ¶¶191-193; Section VIII.B.1. Renisch automatically segments anatomical structures in anatomical images, including specific organs such as the brain and liver. Ex1005, [0025]. Renisch also states that “the outline of the segmented anatomical structures of the anatomical first image representation can be superimposed on the functional second image representation.” Ex1005, [0037]. For example, Fig. 3B of Renisch (*supra*, p.30) depicts a functional image in which lesions are identified by a “color overlay” and segmented organs are identified by overlaid graphical “outline[s]”. Ex1005, [0025], [0029], [0037], [0015]-[0016]. Thus, Renisch discloses the geographic identification of organs overlaid on one or more medical images.

8. Dependent Claim 8

Claim 8 depends from claim 1 and further recites: “wherein the one or more specific tissue region(s) comprise one or more particular bones.”

As explained in Section VIII.B.7 above, Renisch describes geographic identification of one or more specific organs. Renisch does not, however, expressly include “particular bones” among the organs that are identified. Sprencz discloses this limitation, rendering claim 8 obvious over Renisch (or Renisch with Wu) in view of Sprencz. Ex1002, ¶¶221-228; Section VIII.B.1.

Sprencz, like Renisch, discloses a system for automatically segmenting, displaying, and quantifying lesions using multi-modality 3D imaging data.

Ex1006, [0011], [0041]-[0044], [0048]-[0050], [0055]-[0056]. Sprencz automatically segments an anatomical image (e.g., CT image) to identify the patient's 3D bone volume (Ex1006, [0043]-[0046], Fig. 5) and classifies detected lesions as either bone lesions or non-bone lesions by comparing the location of each lesion with the location of the skeletal volume (Ex1006, [0048]-[0049], [0052]). Sprencz states: "Images of the lesion candidates are generated ... and displayed as an overlay on the patient skeletal image generated from the segmented skeletal structure." Ex1006, [0050] (emphasis added). Alternatively, "the segmented skeletal structure from a CT image series is projected into a PET image that includes the lesion candidates." *Id.* (emphasis added). Thus, Sprencz discloses the limitations of claim 8.

A POSITA would have been motivated to modify Renisch, which already calculates quantitative metrics, to also segment bones based on Sprencz's express teaching that "[q]uantification of bone lesions using medical images is an important aspect of clinical diagnostics and therapy." Ex1006, [0004]; Ex1002, ¶225. Additionally, combining Renisch (or Renisch with Wu) with Sprencz would have merely amounted to combining existing prior art elements (automatic lesion detection and bone segmentation) according to known methods (machine learning segmentation of anatomical structures) to yield predictable results (detection of bone lesions). Ex1002, ¶226. Renisch and Sprencz teach segmentation of

anatomical structures using overlapping methods, including thresholding, clustering, and region growing. Ex1005 at [0027]-[0028]; Ex1006 at [0045]. A POSITA would have had a reasonable expectation of success improving Renisch, as proposed, by applying the same or additional segmentation techniques to segment additional structures, such as bones. Ex1002, ¶¶226-227.

9. Dependent Claim 9

Claim 9 depends from claim 1 and further recites: “wherein the instructions cause the processor to generate a radiologist report for the particular patient based at least in part on the analysis of the one or more medical images.”

a) Anticipation by Renisch or Obviousness Over Renisch with Wu

Renisch discloses this limitation, rendering this claim anticipated by Renisch or obvious over Renisch with Wu. Ex1002, ¶¶194-196; Section VIII.B.1. Renisch discloses “[a]n identification unit ... configured to calculate metrics” including “total tumor burden, glycolytic volume, ... maximum activity, ... homogeneity, and the like.” Ex1005, [0032]. Renisch states that “the results of the identification unit 106 are visualized on the display device 64” and “[t]he user is asked to confirm or edit the selected hot spots, i.e. high uptake regions, using the input device 66 before a summary report is generated.” Ex1005, [0033] (emphasis added). Thus, Renisch generates a report with quantitative metrics based on analysis of a nuclear medicine image and final confirmation by the user (i.e.,

radiologist) of lesion candidates.

b) Obviousness Over Renisch or Renisch with Wu, Each in view of Maier

Alternatively, claim 9 is obvious over Renisch (or Renisch with Wu) in view of Maier. Ex1002, ¶¶229-236. Maier discloses a system for assessing medical images and automatically generating a report of the patient's health status tailored for the intended user, including a "radiologist." Ex1008, [0014], [0015]-[0016], [0026], [0027], [0041]. As depicted in Fig. 3 below, the report includes the

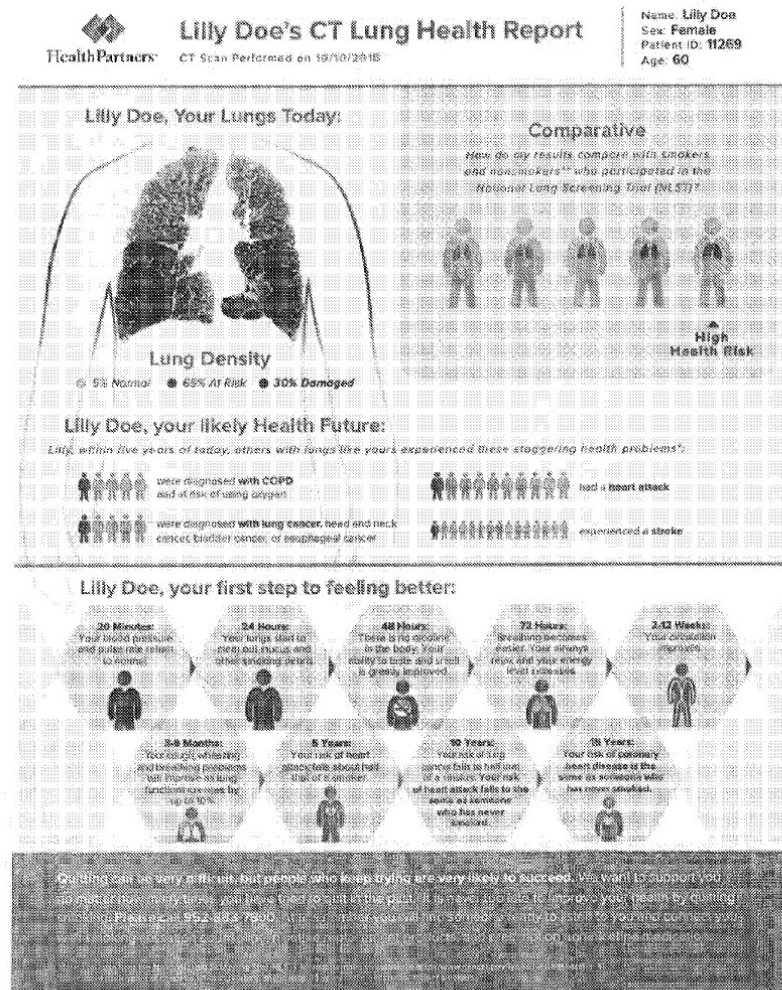


FIG. 3

patient's own medical images and reference images of others for comparison. Ex1008, [0026], [0041]. In some embodiments, a software application “converts the speech of a radiologist to text and then combines the text with the contents of [a] data file to create a user-readable report for review by a user.” Ex1008, [0036] (emphasis added).

Maier provides the express motivation and teaching to combine its radiologist report generating system with other diagnostic systems like Renisch. Ex1002, ¶233. For example, Maier states that it “may be implemented as a software application running in a hospital enterprise data center,” and “may receive [] medical images directly ... from a medical imaging system, or ... a separate device ..., or via a manual push by a user.” Ex1008, [0043]. Alternatively, combining Renisch (or Renisch with Wu) with Maier, would merely have amounted to combining prior art elements (medical diagnostic system and medical report generating system) according to known methods (network data sharing) to yield predictable results (automated radiologist report). Ex1002, ¶234. Renisch and Maier are in the same field and combining them to automatically generate a radiologist report from images generated by Renisch would not require any alteration or modification of Renisch or Maier. Ex1002, ¶234. Accordingly, a POSITA would have had a reasonable expectation of success because the combination would merely have amounted to transferring image data produced by

Renisch to Maier using standard data transfer methods and formats. Ex1002, ¶235.

10. Dependent Claim 10

Claim 10 depends from claim 9 and further recites: “wherein the radiologist report comprises the one or more medical images and the risk map.”

a) Anticipation by Renisch or Obviousness Over Renisch with Wu

Renisch discloses these limitations, rendering this claim anticipated by Renisch or obvious over Renisch in view of Wu. Ex1002, ¶¶197-202; Section VIII.B.1, VIII.B.9.a).

As previously explained in Sections VIII.B.1.d) and VIII.B.1.f), Renisch produces risk maps comprising graphical denotations of segmented lesions and organs overlaid on medical images. The risk maps produced by Renisch, therefore satisfy both the “risk map” and the “one or more medical images” limitations of claim 10 because the risk maps produced by Renisch include one or more of the patient’s medical images. Alternatively, Renisch explains that its generated risk maps and medical images can be displayed concurrently side-by-side. Ex1005, [0036]-[0037]. Thus, whether the summary report generated by Renisch displays a single risk map comprising segmented lesions over a medical image or a risk map side-by-side with a medical image, the summary report generated by Renisch discloses all the limitations of claim 10.

b) Obviousness Over Renisch, or Renisch with Wu, Each in view of Maier

Alternatively, claim 10 is obvious over Renisch (or Renisch with Wu) in view of Maier. Ex1002, ¶237. Maier discloses the additional limitations of claim 10 because it discloses that the radiologist report it generates “may include a CT image with transparent color overlay indicating areas of [disease]” and “may also include a complete new set of images generated by the computer-implemented algorithm with transparent color overlays on the original gray-scale CT images to indicate the areas of likely [disease].” Ex1008, [0026]. Accordingly, Renisch, or Renisch in view of Wu, each in view of Maier, also renders claim 10 obvious under the same rationales set forth in Section VIII.B.9.b) above.

11. Dependent Claim 11

Claim 11 depends from claim 9 and further recites: “wherein the radiologist report comprises one or more reference images or reference risk maps.”

As explained in Section VIII.B.9.b) above, Renisch (or Renisch with Wu) in view of Maier renders claim 9 obvious. As also explained in that Section, Maier also discloses the additional limitations of claim 11. The report automatically generated by Maier includes not only the patient’s medical images, but also comparative reference images from others with known medical outcomes. Ex1008 at [0041]. Thus, Renisch (or Renisch with Wu) in view of Maier renders claim 11 obvious based on the same rationales set out in Section VIII.B.9.b). Ex1002,

¶¶238-240.

12. Dependent Claim 12

Dependent claim 12 depends from claim 1 and further recites: “wherein the instructions cause the processor to apply a machine learning algorithm to update a process for automatically analyzing the one or more medical images using accumulated image data in the database.”

As explained in Section VIII.B.1 above, claim 1 is anticipated by Renisch or obvious over Renisch with Wu. Menon discloses the additional limitations in claim 12 and a POSITA would have been motivated to improve Renisch (or Renisch with Wu) using Menon based on the express teachings and suggestions in Renisch and Menon. Ex1002, ¶¶241-246.

Menon discloses an automated triaging decision support tool that utilizes machine learning to continuously refine the tool. Ex1012 at [0010], [0032], [0055], [0078], [0103]-[0104], [0180], [0189], [0195]. The tool takes, as input, various data, including the patient’s medical images (Ex1012, [0104], [0110]), and outputs risk analysis and treatment recommendations (Ex1012, [0104]-[0109], [0189]). The tool also uses this output and accumulated imaging data to continuously refine the tool. Ex1012, [0180], [0189]. For example, Menon states that the tool may “continue to refine the model ... using machine learning and improve its predictive accuracy using new information that will be available when the product is being

tested real time and when the product is in clinical use.” Ex1012, [0195]. Accordingly, Menon discloses the limitations recited in claim 12.

Renisch explains that accurate image segmentation is important for the identification of normal physiological uptake unrelated to potential cancer. Ex1005, [0004], [0025], [0031]. Common sense dictates that improved segmentation, if possible, would be desirable. Improving Renisch (or Renisch with Wu) with the teachings in Menon would merely have amounted to using a known technique (i.e., machine learning) to improve similar devices in the same way. Ex1002, ¶¶244-245. Renisch and Menon are both automated medical image analysis systems. It would have been obvious to apply the same technique described in Menon to a similar medical image analysis system (Renisch) for the same purpose, which is to continually improve the analysis technique. Ex1002, ¶245. Furthermore, a POSITA would have had a reasonable expectation of success in doing so since the techniques for training machine learning algorithms using new data are well-established. Ex1002, ¶244.

13. Independent Claim 13 (Method Claim)

Independent claim 13 is nearly identical to independent claim 1 except claim 1 is directed to a “system for generating a disease risk map” whereas claim 13 is directed to a “method for generating a disease risk map.” Ex1001, claims 1 and 13. Whereas claim 1 recites a “processor and memory” having stored instructions for

performing a series of steps, claim 13 recites essentially the same steps performed “by a processor.” Accordingly, for the avoidance of repetition, the chart below indicates the limitations of claim 1 that correspond to the limitations of claim 13, as well as the locations in this Petition where the limitations of claim 13 have already been addressed. Unlike claim 1, claim 13 does not include a “network-based” limitation. Accordingly, claim 13 is anticipated by Renisch for the same reasons explained in Section VIII.B.1 and Wu is not needed as an alternative ground. Ex1002, ¶¶203-209.

<u>Claim 13 Limitation</u>	<u>Claim 1 Limitation(s)</u>	<u>Section(s)</u>
Preamble	Preamble	VIII.B.1.a)
13(i): Accessing, by a Processor, from a Database	1(a): Processor and Memory 1(b): Access from a Database	VIII.B.1.b) VIII.B.1.c)
13(ii): Analyze, by the Processor, Using a Machine Learning Algorithm	1(a): Processor and Memory 1(c): Analyze Using a Machine Learning Algorithm	VIII.B.1.b) VIII.B.1.d)
13(iii): Causing, by the Processor, Display via GUI	1(a): Processor and Memory 1(d): Display via GUI	VIII.B.1.b) VIII.B.1.e)
13(iv): Wherein Step (ii) Comprises	1(e): Wherein the Analysis Comprises	VIII.B.1.f)

C. Grounds G-I, Sprencz-based Anticipation and Obviousness

1. Independent Claim 1

Claim 1 is anticipated by Sprencz.

a) Preamble: A Network-based System

Sprencz discloses the preamble of claim 1. Ex1006 at Abstract, [0011],

[0041]-[0044], [0048]-[0050], [0055]-[0056], Figs. 1, 4, 6, 7; Ex1002, ¶¶247-252.

Sprenzc discloses a system that automatically detects, segments, and displays cancerous lesions using graphical denotations that delineate the location of the lesions relative to a patient's skeletal structure. Ex1006, Abstract, [0011], [0023]-[0027], [0041]-[0044], [0048]-[0050], [0055]-[0056]. For example, Sprenzc states that the disclosed "medical diagnostic tool ... includes a graphical user interface (GUI) constructed to display an image generated from overlaying a first image corresponding to ... skeletal data on a second image corresponding to ... bone lesion data." Ex1006, [0011]. Sprenzc also states that "[i]mages of the lesion candidates are generated ... and displayed as an overlay on the patient skeletal image" (*id.*) where Sprenzc is "configured to display bone lesions and non-bone lesions in different colors or with different shading to visually distinguish detected bone lesions from non-bone lesions" (Ex1006, [0056]). Accordingly, Sprenzc discloses a system for generating a disease risk map as claimed.

Additionally, the system disclosed by Sprenzc is network-based. Referring to Fig. 1, which is reproduced below, Sprenzc discloses a distributed system 10 controlled by a CPU 12 and including one or more remotely located imaging system 20, workstation 28, and image database 18. Ex1006, [0023]-[0027].

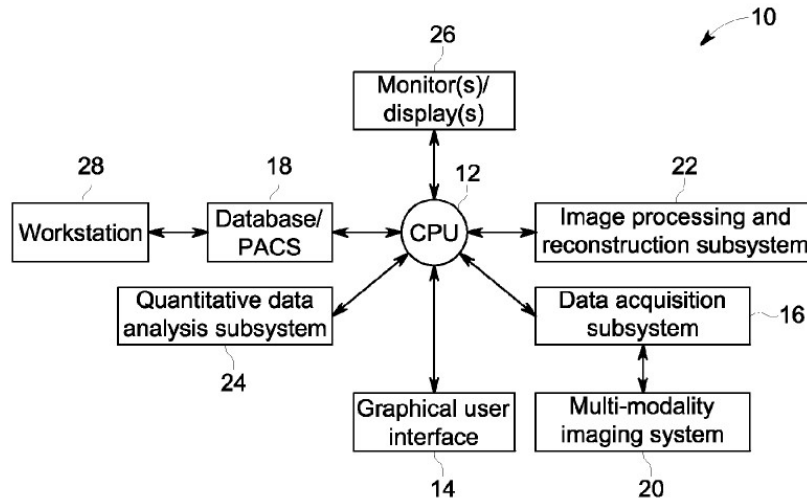


FIG. 1

Sprenzc states: “it is contemplated that a dedicated workstation 28 having a computer, monitor(s), and operably connected to the one or more databases may be used such that a physician may analyze the image and quantitative data remote from the scanner.” Ex1006, [0026], [0024] (“database 18 may be ... remotely located from the site of data acquisition.”). Thus, Sprenzc’s system for obtaining, analyzing, and displaying images is carried out on a network of remotely located components.

b) Limitation 1(a): Processor and Memory

Sprenzc discloses this limitation. Ex1006, [0009], [0023], [0041], [0061], Fig. 1; Ex1002, ¶¶253-254. Sprenzc states that “the system 10 includes a central processor (CPU) 12 that controls the system 10.” Ex1006, [0023], [0041]. Additionally, Sprenzc explains: “embodiments of the invention may be interfaced

to and controlled by a computer readable storage medium having stored thereon a computer program” wherein the “computer readable storage media ... generally stores instructions such as software, firmware and/or assembly language for performing one or more portions of one or more implementations or embodiments.” Ex1006, [0061].

c) Limitation 1(b): Access from a Database

Sprenzc discloses this limitation. Ex1006, [0041], [0023] (“data acquisition subsystem 16 may *access previously acquired data stored in database 18*”) (emphasis added), Fig. 1 (18), Fig. 4 (202), [0009] (“instructions that when executed by the computer causes the computer to access ...”), [0010]-[0011] (“The computer processor is programmed to access the first and second image datasets.”); Ex1002, ¶¶255-256. For example, with reference to Fig. 4, Sprenzc states: “Technique 200 begins with step 202, by selecting and loading one or more exams to be processed by the computer system corresponding to one or more imaging sessions during which multi-modality image data was acquired from a patient of interest.” Ex1006 at [0041].

d) Limitation 1(c): Analyze Using a Machine Learning Algorithm

Sprenzc discloses this limitation. Ex1006, [0041]-[0050], [0055]-[0056], [0011], Figs. 4-7; Ex1002, ¶¶257-263. As explained in Section VIII.C.1.a) above, Sprenzc generates a risk map comprising a visual representation of tissue (e.g., the

patient's skeleton) overlaid with graphical denotations marking one or more regions of risk of cancer (e.g., segmented lesions). Ex1006, [0050]. Additionally, Sprencz generates the risk map by analyzing one or more medical images using a machine learning algorithm.

With reference to Fig. 4, which is reproduced below, Sprencz states: “FIG. 4 sets forth a technique 200 for quantifying bone lesions in a patient using multi-modality three dimensional image data.” Ex1006, [0041].

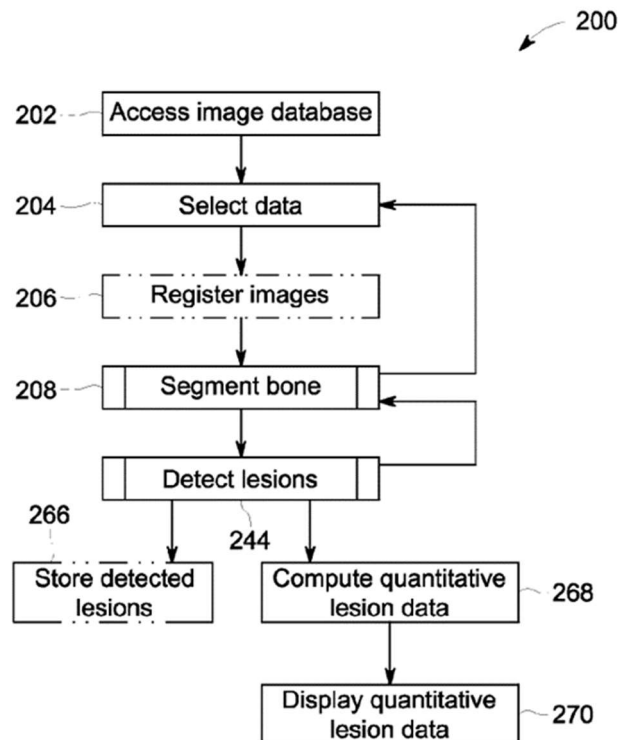


FIG. 4

“During step 208 an automatic bone segmentation is performed on the anatomical image data (e.g., data corresponding to the CT volume) using a bone segmentation

subroutine.” Ex1006, [0043]. Although bone segmentation can be accomplished by something as simple as thresholding, Sprencz also states that “one having skill in the art will recognize that embodiments of the invention may segment different anatomical region bone structures using alternative techniques, such as, for example, clustering.” Ex1006, [0045] (emphasis added). Clustering is a machine learning technique for image segmentation. Ex1002, ¶259; Ex1016, pp. 10-11.

With continuing reference to Fig. 4 above, Sprencz states that “after the bone segmentation subroutine 210 of step 208 is complete, technique 200 continues to step 244 wherein technique 200 uses the segmented anatomical image data output from bone segmentation subroutine 210 and the functional image data selected at step 204 to detect bone lesions.” Ex1006, [0048]. Accordingly, Sprencz describes using a machine learning algorithm to segment an anatomical image and using the segmented anatomical image and a functional image to generate a risk map as claimed. Ex1006, [0050].

e) Limitation 1(d): Display Via GUI

Sprencz discloses this limitation. Ex1006, Fig. 1 (14), Fig. 7 (272), [0055]-[0056]; Ex1002, ¶¶264-264. Sprencz discloses a “GUI” that “includes an image display region” that is “configured as an interactive workspace to permit a user to interact with the images to perform various tasks including, for example, manually identify lesion candidates, delete an automatically identified lesion, and/or change

the classification of an automatically detected lesion.” Ex1006, [0056]. Examples of displayed images include “various views of the segmented skeletal volume ... overlaid with contours of lesion candidates.” *Id.*

f) Limitation 1(e): Identification of Specific Tissue Region(s)

Sprenzc discloses this limitation. Ex1006, [0041], [0050], [0052], [0054], [0056], Fig. 7; Ex1002, ¶¶266-268.

Sprenzc describes a technique for quantifying bone lesions in a patient using “multi-modality three dimensional image data” including “three-dimensional CT and PET data.” Ex1006, [0041]. Sprenzc segments an anatomical image to produce “a patient skeletal image representing the skeleton of the patient.” Ex1006, [0043], [0046]. Sprenzc identifies lesion candidates by thresholding a functional image to segment voxels above a set standardized uptake value (SUV). Ex1006, [0049]. Quantification is performed by calculating a “total skeletal volume” and a “total bone lesion volume.” Ex1006, [0054] (emphasis added).

Images of lesion candidates can be displayed as an overlay on the segmented skeletal structure. Ex1006, [0050], [0056]. Additionally, “[i]n one embodiment, the segmented skeletal structure from a CT image series is projected into a PET image that includes the lesion candidates.” Ex1006, [0050] (emphasis added). This discloses Limitation 1(e) because the generated image includes segmented lesions and specific tissue regions overlaid on a 3D medical image. Ex1002, ¶267.

2. Dependent Claim 2: MRIs

Sprenzc also discloses the limitations of claim 2, rendering claim 2 anticipated by Sprenzc. Ex1006, [0022]-[0023], [0027], [0031], [0041]-[0042]; Ex1002, ¶¶270-272. For example, Sprenzc states its multi-modality imaging system may include “a positron emission tomography (PET) imaging system and one of an magnetic resonance (MR) imaging system and a ... computed tomography (CT) imaging system.” Ex1006, [0022] (emphasis added), [0041] (“anatomical image data ... such as CT or MR”).

3. Dependent Claim 3: PET/CT or SPECT/CT

Sprenzc also discloses the limitations of claim 3, rendering claim 3 anticipated by Sprenzc. Ex1006, [0022]-[0023], [0033]-[0034], [0041]-[0042]; Ex1002, ¶¶273-275. Sprenzc states that its multi-modality imaging system “may be ... a combined PET/CT system (as shown in FIG. 3) ... or a combined SPECT/CT system, as non-limiting examples.” Ex1006, [0023]. Sprenzc further explains that it may operate by registering separate three-dimensional CT and PET series or “where the multi-modality image data is acquired from a combined PET/CT ..., the acquired multi-modality image data may be automatically registered.” Ex1006, [0042].

4. Dependent Claim 4: Medical Images of the Patient

Sprenzc discloses the limitations of claim 4 for the same reasons explained in Sections VIII.C.1.a) and VIII.C.1.e) above, rendering claim 4 anticipated.

Ex1002, ¶¶276-278. For example, Sprencz states that “[i]mages of the lesion candidates are generated ... and displayed as an overlay on the patient skeletal image.” Ex1006, [0050]. And, “[i]n one embodiment, the segmented skeletal structure from a CT image series is projected into a PET image that includes the lesion candidates.” *Id.*

5. Dependent Claim 5: Prostate Cancer

a) Anticipation by Sprencz

Sprencz inherently discloses the additional limitation of claim 5, rendering claim 5 anticipated. Ex1002, ¶¶279-281.

Sprencz discloses the detection of cancerous lesions throughout the body and is not limited to any type of cancer. Ex1006 at [0056] (“display bone lesions and non-bone lesions in different colors or with different shading to visually distinguish detected bone lesions from non-bone lesions”). Accordingly, Sprencz would necessarily detect prostate cancer – using standard radiotracers like ¹⁸F-FDG – if prostate cancer was present. Ex1002, ¶280 (citing Ex1024).

b) Obviousness Over Sprencz in view of AAPA or D’Souza

Alternatively, claim 5 is obvious over Sprencz in view of the AAPA or D’Souza. Ex1002, ¶¶308-316.

A POSITA would have been motivated to use Sprencz for imaging prostate cancer based on the knowledge of a POSITA, as evidenced by the AAPA. Ex1002,

¶310. As explained in Section VIII.C.5.a) above, Sprencz teaches the quantification of lesions throughout the body, including bone lesions, which would have broad application to a wide variety of metastatic cancers. Additionally, Sprencz does not identify any particular radiopharmaceutical, suggesting any known target molecule can be used.

The AAPA establishes that a POSITA would have known that many radiopharmaceuticals were available for imaging particular kinds of cancer including prostate cancer. *See* Section VIII.B.5.b). A POSITA would have known, therefore, that Sprencz could be used to image prostate cancer, and would have had a reasonable expectation of success doing so. Ex1002, ¶310. Additionally, the motivation to use Sprencz to image prostate cancer is supplied by the knowledge of POSITA, who would know that prostate cancer, including prostate cancer that has metastasized to the patient's bones, is one of the most common and deadly forms of cancer. *Id.*

Alternatively, the combined teachings of Sprencz and D'Souza render claim 5 obvious. Ex1002, ¶¶311-316. D'Souza discloses a wide range of ¹⁸F-labeled molecules that are usable to image different diseases, including prostate cancer. Ex1010, 3:57-58, 4:51-64, 36:22-37. Moreover, D'Souza teaches that its disclosed ¹⁸F-labeled molecules can be used with any known method of imaging using labeled molecules. Ex1010, 35:42-36:21, 4:60-64 ("Any known TAA[(tumor-

associated antigen)]-binding antibody or fragment may be labeled with ^{18}F by the described methods and used for imaging and/or detection of tumors, for example by PET scanning or other known techniques.”).

A POSITA would have been motivated to use prostate cancer specific targeting molecules, as taught by D’Souza, with Sprencz, for the purpose of more accurately imaging metastatic prostate cancer that has spread to bones. Ex1002, ¶315. Moreover, combining Sprencz and D’Souza would have merely amounted to combining existing prior art elements (i.e., nuclear medicine imaging systems and prostate-cancer-specific radiotracers) according to known methods (i.e., selecting a suitable delivery molecule for targeting a particular disease) to yield predictable results. Ex1002, ¶314. Additionally, a POSITA would have had a reasonable expectation of success in combining Sprencz and D’Souza since Sprencz teaches the identification of cancerous lesions using a PET scanner (Ex1006 at [0022]-[0023], [0033], [0041]) and D’Souza expressly teaches that any of its disclosed disease-specific targeting molecules could be used with any known PET imaging technique (Ex1010 at 4:57-64, 35:42-36:21). Ex1002, ¶316.

6. Dependent Claim 6: Visual Representation of Bone

Sprencz also discloses the limitation of claim 6, rendering claim 6 anticipated. Ex1006, [0011], [0050], [0056], Fig. 7; Ex1002, ¶¶282-284.

For example, Sprencz states that “[i]mages of the lesion candidates are

generated ... and displayed as an overlay on the patient skeletal image.” Ex1006, [0050]. Additionally, with reference to Fig. 7, Sprencz states that “windows 290, 292, 294 include various views of the segmented skeletal volume obtained from the CT image ... overlaid with contours of lesion candidates.” Ex1006, [0056].

7. Dependent Claim 7: Specific Tissue Regions Comprise Organs

Sprencz also discloses the limitation of claim 7, rendering claim 7 anticipated. Ex1002, ¶¶285-288.

As explained in Section VIII.C.1.f) above, Sprencz generates and displays risk maps that geographically identify a specific tissue region, i.e., the patient’s skeletal structure, overlaid on one or more 3D medical images. Ex1006, [0050] (“In one embodiment, the segmented skeletal structure from a CT image series is projected into a PET image that includes the lesion candidates.”), [0056], Fig. 7. The skeleton is an organ. Ex1002, ¶287 (citing Ex1023). Thus, Sprencz discloses the limitations of claim 7.

8. Dependent Claim 8: Specific Tissue Regions Comprise Bones

For the same reasons explained in Sections VIII.C.1 and VIII.C.7 above, Sprencz discloses the limitations of claim 8, rendering claim 8 anticipated by Sprencz. Ex1002, ¶¶289-291.

9. Dependent Claim 9: Radiologist Report

Sprencz also discloses the limitations of claim 9, rendering claim 9

anticipated by Sprencz. Ex1006 at [0055]-[0057], Fig. 7 (282, 300, 302); Ex1002, ¶¶292-297.

The Patent characterizes a “radiologist report” as “a technical evaluation of the PET or SPECT images” which “includes, for example, the type of study performed, the clinical history, ... the technique used to perform the study, [and] the radiologist’s observations and findings.” Ex1001 at 2:11-19. The Patent also shows, in Fig. 5, an example of a radiologist report 510 displayed on a graphical user interface 400. Ex1001, 29:14-16. The report 510 contains, for example, the patient’s name, the patient’s medical images, the quantitatively calculated “BSI” (bone scan index), i.e., the ratio of bone lesion volume to total bone volume, and information regarding the study performed, including the date of the study.

Sprencz likewise produces a radiologist report, stating that “portions of the selected anatomical and functional image series, visual representations of the lesion candidates, and the quantitative information calculated by technique 200 [including the ratio of total bone lesion volume to total bone volume] may be displayed on a graphical user interface (GUI) 272 as illustrated in FIG. 7.” Ex1006, [0055]. With continuing reference to Fig. 7 (below), Sprencz also states: “An information display region 302 is also located within in GUI 272 to provide the user with patient and scan information including, for example, name, age, the date of scans, and/or various parameters associated with the scans.” Ex1006, [0057].

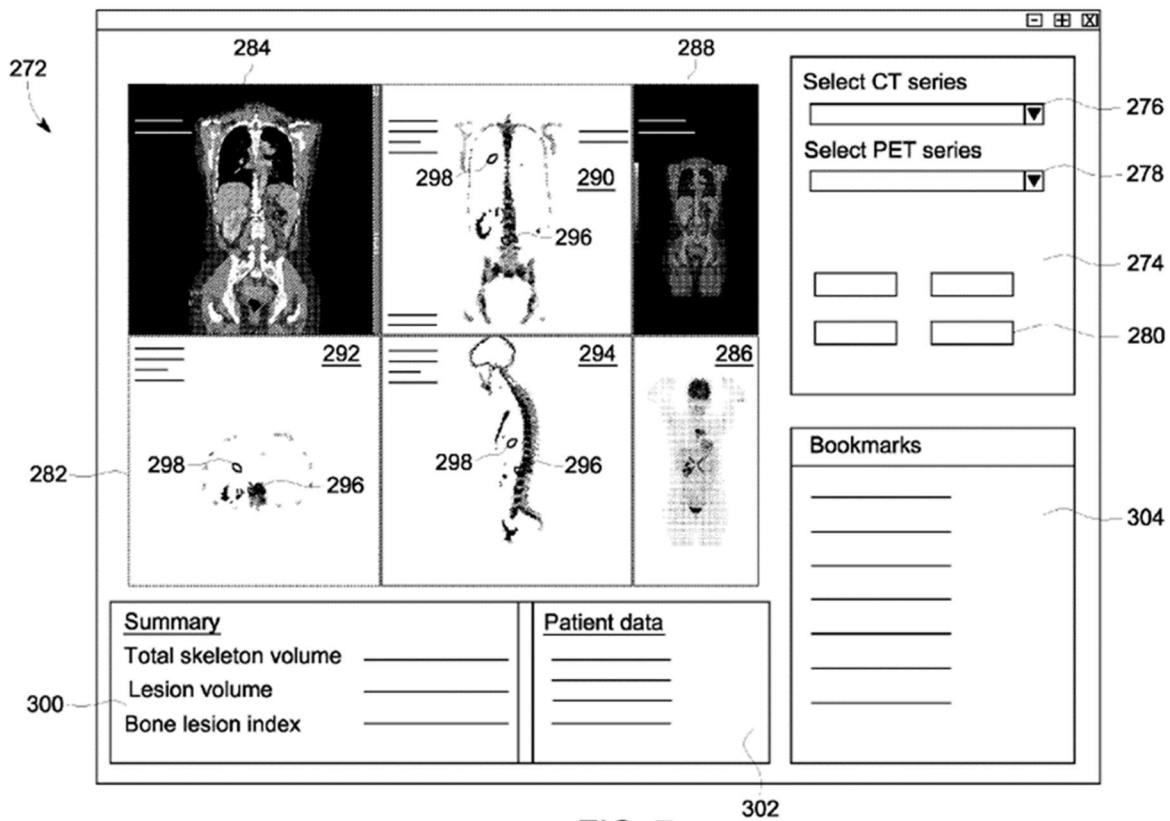


FIG. 7

Accordingly, Sprenzc discloses the limitations of claim 9, including an automatically generated radiologist report based on analysis of the patient's medical images.

10. Dependent Claim 10: Radiologist Report Includes Medical Image and Risk Map

Sprenzc also discloses the limitations of claim 10, rendering claim 10 anticipated by Sprenzc. Ex1002, ¶¶298-301.

As explained in Section VIII.C.9 above, Sprenzc produces a radiologist

report, which is displayed on a GUI 272 as depicted in Fig. 7 above. Sprencz explains that “a first window 284 ... displays a CT image, a second window 286 ... displays a corresponding PET image,” and “[f]ourth, fifth, and sixth windows 290, 292, 294 include various views of the segmented skeletal volume ... overlaid with contours of lesion candidates.” Ex1006, [0056]. Thus, Sprencz discloses that its radiologist report contains both the original medical images and the claimed risk map comprising visual representations of tissue overlaid with graphical denotations of regions of risk of cancer (i.e., segmented lesions).

11. Dependent Claim 11: Radiologist Report Includes Reference Image or Reference Risk Map

Claim 11 depends from claim 9 and is obvious over Sprencz in view of Maier. Sprencz discloses all the limitations of claim 9. *See* Section VIII.C.9. Maier discloses the additional limitations of claim 11, and it would have been obvious to improve the report generated by Sprencz to include reference images for comparison, as taught by Maier. Ex1002, ¶¶317-328.

As explained in Section VIII.C.9 above, Sprencz automatically generates and displays a radiologist report that includes the patient’s medical images, the patient’s risk map, and calculated lesion metrics, including total lesion volume. Ex1006, at Fig. 7, [0056]-[0057]. Maier discloses assessing a patient’s health status and risk by comparing the patient’s medical images to one or more comparison images from one or more individuals for whom the corresponding

health status and/or outcomes are known. Ex1008, [0014], Fig. 3 (showing a report that includes the patient's images and comparative reference images), [0041]. It would have been obvious to improve the report generated by Sprencz by including one or more reference images based on the express teachings and motivations supplied in Sprencz and Maier, respectively. Ex1002, ¶¶322-324.

Sprencz states: "Quantification of bone lesions using medical images is an important aspect of clinical diagnostics and therapy." Ex1006, [0004]. Maier states: "[t]he quantitative status and/or risk metrics for the patient may ... be calculated based on the known health status and/or outcomes for the corresponding cohort." Ex1008, [0022]. Accordingly, Sprencz and Maier supply express motivation to combine their teachings. Sprencz teaches clinical diagnosis through quantification of bone lesions. Maier teaches calculation of quantitative status and/or risk based on comparison to reference images with known outcomes. Therefore, a POSITA would have been motivated to improve diagnosis and quantification of bone lesions, as addressed in Sprencz, by comparing the patient's images to reference images of cohorts with known medical results, as taught by Maier. Ex1002, ¶324.

Additionally, improving the report generated by Sprencz based on the teachings of Maier would merely have amounted to applying a known technique to a known device, method, or product ready for improvement to yield predictable

results. The practice of diagnosing and/or staging disease progression by comparing a patient's medical images to the images of others with known medical outcomes is as old as medical imaging itself. Although Sprencz may not expressly describe the use of reference images in its generated report, it would have been obvious based on standard medical practice and the teachings in Maier to include a reference image for the purpose of improving diagnosis and/or staging. Ex1002, ¶326. Moreover, a POSITA would have had a reasonable expectation of success in combining Maier with Sprencz in this manner because the combination would merely have amounted to adding one or more additional images to those already displayed on Sprencz's GUI. Ex1002, ¶327.

12. Independent Claim 13

As explained in Section VIII.B.13 above, independent claim 13 is essentially identical to independent claim 1 except that claim 13 is directed to a method, whereas claim 1 is directed to a system. Accordingly, for the avoidance of repetition, claim 13 is anticipated by Sprencz for the same reasons provided in Section VIII.C.1 above as indicated in the chart below. Ex1002, ¶¶302-307.

<u>Claim 13 Limitation</u>	<u>Claim 1 Limitation(s)</u>	<u>Section(s)</u>
Preamble	Preamble	VIII.C.1.a)
13(i): Accessing, by a Processor, from a Database	1(a): Processor and Memory 1(b): Access from a Database	VIII.C.1.b) VIII.C.1.c)
13(ii): Analyze, by the Processor, Using a Machine Learning Algorithm	1(a): Processor and Memory 1(c): Analyze Using a Machine Learning Algorithm	VIII.C.1.b) VIII.C.1.d)

13(iii): Causing, by the Processor, Display via GUI	1(a): Processor and Memory 1(d): Display via GUI	VIII.C.1.b) VIII.C.1.e)
13(iv): Wherein Step (ii) Comprises	1(e): Wherein the Analysis Comprises	VIII.C.1.f)

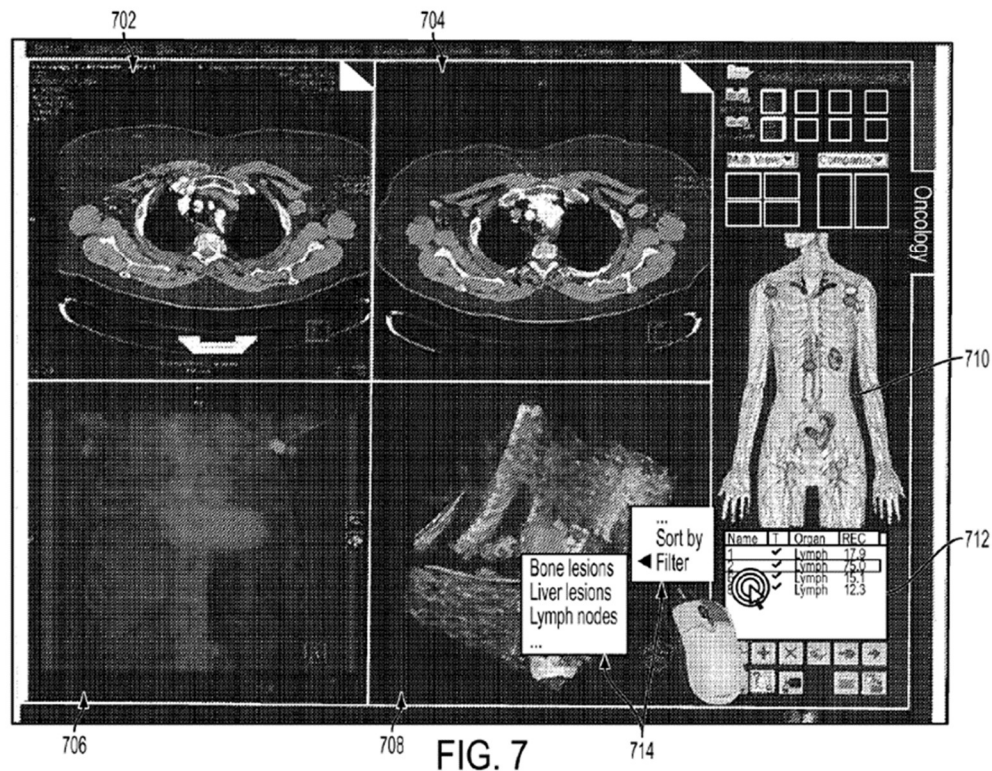
D. Grounds J-L, Suehling-based Anticipation and Obviousness

1. Independent Claim 1

Suehling anticipates claim 1.

a) Preamble: A Network-based System

Suehling discloses the limitations of the preamble. Ex1002, ¶¶329-334. Suehling discloses “a method and system for automatic detection of lesions in 3D medical images” (Ex1007, [0006]) where “the detected and segmented lesions can be displayed in combination with the received 3D image data” (Ex1007, [0034]). For example, referring to Fig. 7 below, Suehling states “the interactive display 700 displays detected lesions in various slices 702 and 704 of the medical image data, a 3D rendering 706 of the image data, ... and in corresponding locations in a 3D model of a body 710.” Ex1007, [0041]. Thus, Suehling displays areas of risk of cancer (i.e., segmented lesions) overlaid on a visual representation of tissue.



Additionally, Suehling is network-based. For example, Suehling states: “Upon arrival of new image data at the workstation/server 506, the fully automatic lesion detection pre-processing of the image data is triggered on the workstation/server 506.” Ex1007, [0038] (emphasis added). Additionally, Suehling states: “The above-described methods for automatic lesion detection ... and visualizing lesion detection results may be implemented on a computer” where “[t]he computer 902 ... includes one or more network interfaces 906 for communicating with other devices via a network.” Ex1007, [0046].

b) Limitation 1(a): Processor and Memory

Suehling discloses Limitation 1(a). Ex1002, ¶¶335-336. For example,

referring to Fig. 9, Suehling states: “Computer 902 contains a processor 904 which controls the overall operation of the computer 902 by executing computer program instructions” and “the steps of the methods of FIGS. 1, 2, 4, and 6 may be defined by the computer program instructions stored in the memory 910 and/or storage 912 and controlled by the processor 904 executing the computer program instructions.” Ex1007, [0046].

c) Limitation 1(b): Access from a Database

Suehling discloses Limitation 1(b). Ex1007, Fig. 1 (102), Fig. 4 (402), Fig. 5 (508, 502), [0024]-[0025], [0037]; Ex1002, ¶¶337-338. For example, Suehling states that a 3D medical image “representing anatomy of a patient” (Ex1007, [0024]) can be received directly from an image acquisition device or “can be received by loading a medical image that was previously stored, for example on a memory or storage of a computer system or a computer readable medium” (Ex1007, [0025]).

d) Limitation 1(c): Analyze Using a Machine Learning Algorithm

Suehling discloses Limitation 1(c). Ex1002, ¶¶339-342. As already explained in Section VIII.D.1.a) above, Suehling generates a risk map, as claimed, comprising a visual representation of tissue overlaid with graphical denotations marking one or more regions of risk of cancer. Ex1007, [0041], Fig. 7, [0045], Fig. 8. Suehling generates the risk map by analyzing one or more medical images

using a machine learning algorithm.

Suehling receives a 3D medical image and automatically segments the image into search regions corresponding to particular organs and bones such as the brain, liver, spine, etc. Ex1007, [0026]-[0031], Fig. 1. Anatomical segmentation of the 3D anatomical image is accomplished using “well known organ segmentation techniques” including trained machine learning algorithms such as “Marginal Space Learning.” Ex1007, [0030]. Suehling then detects lesions in each of the search regions using a region-specific machine learning algorithm such as clustered marginal space learning. Ex1007, [0032]-[0033]. A POSITA would know that marginal space learning (MSL) is a supervised machine learning technique used for classification and segmentation tasks. *See generally* EX1020.

e) Limitation 1(d): Display Via GUI

Suehling discloses this limitation. Ex1007 at [0034], [0041], Fig. 5 (510), Fig. 7; Ex1002, ¶¶343-344. For example, Suehling states that “the detected and segmented lesions can be displayed in combination with the received 3D image data” on “an interactive display” (Ex1007, [0034]) where “[t]he interactive display ... can ... provide the user with an option to accept, refine, or reject detected lesions” (Ex1007, [0043]). Additionally, Suehling states that “lesion detection results can be displayed on an interactive pictogram, ... within a 3D rendering of the image data, and/or as a graphical overlay of the original image data.” Ex1007,

[0041].

f) Limitation 1(e): Identification of Specific Tissue Region(s)

Suehling discloses this limitation. Ex1007, [0033], [0036], [0041]-[0043], [0045], Fig. 2, Fig. 7 (706, 710) (showing graphical overlay of segmented lesions on segmented anatomical structures, e.g., sortable by bone lesions, liver lesions, etc.); Ex1002, ¶345-349.

Suehling analyzes medical images to produce a 3D risk map by: (i) segmenting a 3D medical image into search regions corresponding to particular organs and bones (Ex1007, [0026]-[0031]); (ii) detecting lesions in each of the search regions (Ex1007, [0032]-[0033]); and (iii) displaying the lesion detection results “within a 3D rendering of the image data and/or as a graphical overlay of the original image data” (Ex1007, [0041], [0034] (“segmented lesions can be displayed in combination with the received 3D image data”)). This constitutes “creation of a 3D image of the one or more regions of risk of cancer or risk of recurrence of cancer overlaid on the one or more medical images,” as claimed. Ex1002, ¶345.

Referring to Fig. 2, which is reproduced below, Suehling states: “Image 215 of FIG. 2 shows exemplary organ segmentation results” (Ex1007, [0030] (emphasis added)) and “[i]mage 217 of FIG. 2 shows exemplary bone segmentation results” (Ex1007, [0031] (emphasis added)). Both images include

graphics showing segmented tissue regions overlaid on the medical image.

Ex1002, ¶346.

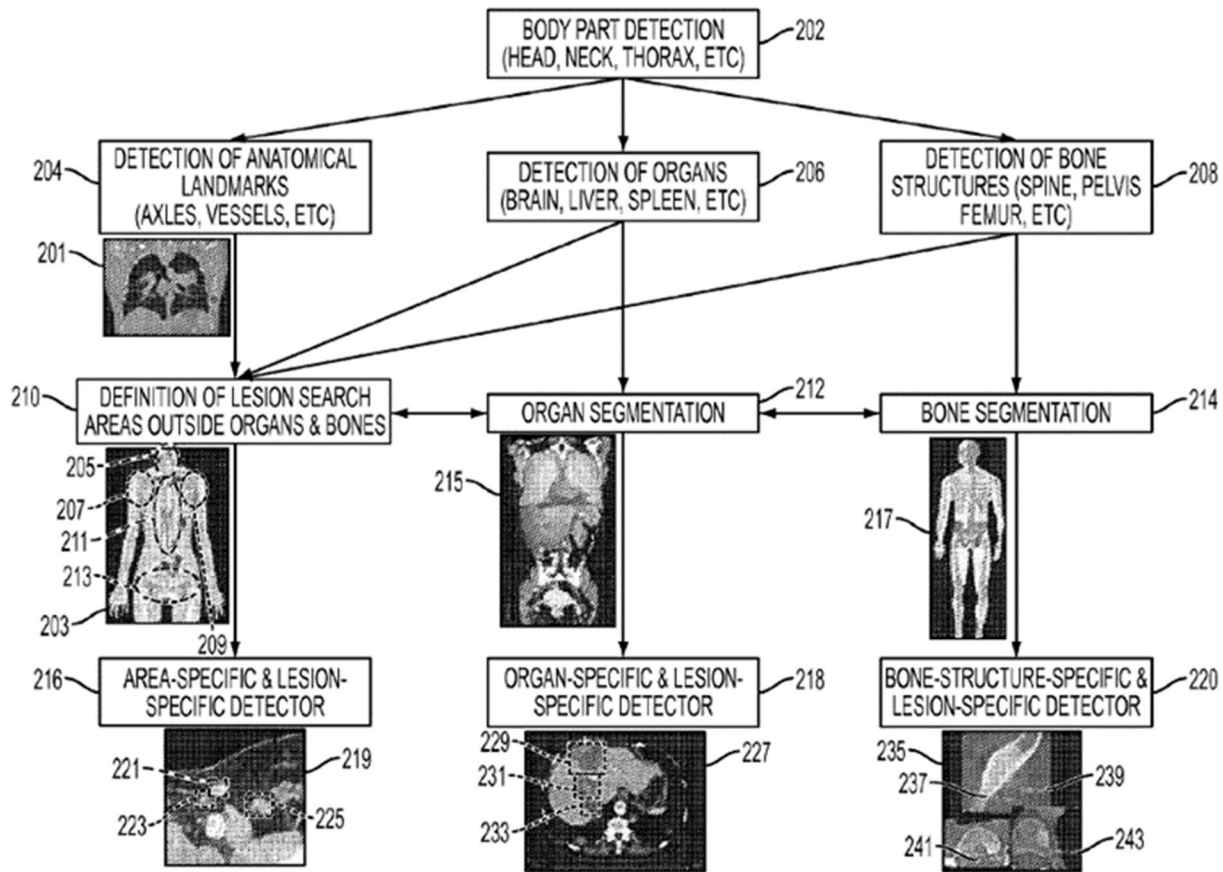


FIG. 2

Suehling also states that “[i]mage 227 shows lesions 229, 231, and 233 detected in an exemplary segmented organ” (Ex1007, [0033] (emphasis added)) and “[i]mage 235 shows lesions 237, 239, 241, and 243 detected in exemplary segmented bone structures” (Ex1007, [0033] (emphasis added)). Thus, Suehling analyzes the patient’s medical images, as claimed, to produce a 3D image of the regions of risk of cancer (i.e., segmented lesions) wherein the 3D image also comprises

geographic identification of one or more specific tissue region(s) overlaid on the one or more medical images. Ex1002, ¶347.

2. Dependent Claim 2: MRIs

Suehling also discloses the limitations of claim 2, rendering claim 2 anticipated by Suehling. Ex1002, ¶¶351-352. For example, Suehling states that “[t]he present invention is directed to a method and system for automatic detection of lesions in 3D medical images, such as a computed tomography (CT) and magnetic resonance (MR) images.” Ex1007, [0020], [0025].

3. Dependent Claim 3: PET/CT or SPECT/CT

Suehling discloses the limitations of claim 3, rendering claim 3 anticipated by Suehling. Ex1002, ¶¶353-354. For example, Suehling states: “The medical images can also be a 3D medical image generated using a hybrid imaging modality, such as PET/CT.” Ex1007, [0025], [0036].

4. Dependent Claim 4: Medical Images of the Patient

Suehling also discloses the limitations of claim 4, rendering claim 4 anticipated by Suehling. Ex1007, Fig. 2, Fig. 7, Fig. 8, [0034], [0041], [0045]; Ex1002, ¶¶355-357.

Suehling discloses that the visual representation of tissue over which segmented lesions are overlaid is the patient’s medical image. For example, Suehling states that “lesion detection results can be displayed ... within a 3D

rendering of the image data and/or as a graphical overlay of the original image data.” Ex1007, [0041]. Additionally, or alternatively, with reference to Fig. 8, Suehling discloses that a “probability map” of each voxel belonging to a lesion candidate can be displayed “in a fused mode, overlaid on morphological image data.” Ex1007, [0045].

5. Dependent Claim 5: Prostate Cancer

Suehling inherently discloses the limitation of claim 5, rendering claim 5 anticipated by Suehling. Ex1002, ¶¶358-360.

Suehling discloses the detection of cancerous lesions throughout the body and is not limited to any particular cancer type. Ex1007, Figs. 2, 3, 7. Accordingly, the regions of risk of cancer detected by Suehling would necessarily include regions of risk of prostate cancer, including metastatic cancer. Ex1002, ¶359. Additionally, Suehling incorporates by reference U.S. Published Patent Application 2010/0080434 (“Seifert”) (Ex1025) to describe the segmentation of organs for creating search regions for cancer. Ex1007, [0028]. Although Suehling does not expressly list the prostate among the various organs that can be detected (Ex1007, [0027] (“including but not limited to”), Seifert expressly discloses segmentation of the prostate. Ex1025, [0031], [0047], Fig. 7. Accordingly, because Suehling images the region of the prostate, as well as regions of metastatic prostate cancer, including the lymph nodes and bones, Suehling discloses the

limitations of claim 5. Ex1002, ¶360.

6. Dependent Claim 6: Visual Representation of Bone

Suehling discloses the limitations of claim 6, rendering it anticipated by Suehling. Ex1007, [0041]-[0043], Fig. 2 (235), Fig. 7; Ex1002, ¶¶361-362. As already explained in Section VIII.D.1.f) above, Suehling displays lesion detection results overlaid on segmented bone structures.

7. Dependent Claim 7: Specific Tissue Regions Comprise Organs

For the same reasons explained in Section VIII.D.1.f) above, Suehling discloses the limitations of claim 7, rendering claim 7 anticipated by Suehling. Ex1002, ¶¶363-365. Suehling displays segmented lesions and 3D segmented organs overlaid on a medical image. For example, Suehling states that “[i]mage 215 of FIG. 2 shows exemplary organ segmentation results” (Ex1007, [0030]) and “[i]mage 227 shows lesions 229, 231, and 233 detected in an exemplary segmented organ” (Ex1007, [0033] (emphasis added)). As explained in Section VIII.D.1.f), the segmented organs (e.g., lungs) appear as a graphical overlay on the 3D anatomical image and/or are overlaid on a functional image (e.g., PET) in embodiments that utilize hybrid images (e.g., PET/CT). Ex1002, ¶364.

8. Dependent Claim 8: Specific Tissue Regions Comprise Bones

For the same reasons explained in Section VIII.D.1f) above, Suehling discloses the limitations of claim 8, rendering claim 8 anticipated by Suehling. Ex1002, ¶¶366-368. Suehling states that “[i]mage 217 of FIG. 2 shows exemplary bone segmentation results” (Ex1007, [0031]) and “[i]mage 235 shows lesions 237, 239, 241, and 243 detected in exemplary segmented bone structures” (Ex1007, [0033] (emphasis added)). As explained in Section VIII.D.1.f), the segmented bones appear as a graphical overlay on the anatomical image and/or are overlaid on a functional image (e.g., PET) in embodiments that utilize hybrid images (e.g., PET/CT).

9. Dependent Claim 9: Radiologist Report

Suehling also discloses the limitations of claim 9, rendering claim 9 anticipated by Suehling. Ex1007, [0009], [0022], [0035]-[0037], [0041], [0043], [0044], Fig. 7; Ex1002, ¶¶369-374.

Suehling discloses a “fully automatic lesion detection method ... integrated into a clinical workflow as a fully automatic pre-processing step that is executed before a users [sic] starts reads [sic] a scanned medical image.” Ex1007, [0037]. Detected lesions are automatically labeled according to their location, and the user is provided with “an option to accept, refine, or rejected detected lesions.” Ex1007, [0042]-[0043]. Additionally, “lesion detection results can be compared to

previous lesion detection results for the same patient in order to detect whether the detected lesions have changed” Ex1007, [0035], [0044] (comparing tumor burden). Thus, Suehling automatically produces a technical evaluation of, e.g., hybrid PET/CT images that includes, e.g., comparison between images and quantitatively calculated metrics such as total tumor burden. Ex1007, [0035]-[0037], [0022]. The results of the automatic evaluation can be accepted or refined by a user on an interactive display (Ex1007, [0043]) and saved (Ex1007, [0038]), thus producing a radiologist report. Ex1002, ¶373.

10. Dependent Claim 10: Radiologist Report Includes Medical Image and Risk Map

Suehling also discloses the limitations of claim 10, rendering claim 10 anticipated by Suehling. Ex1002, ¶¶375-376. As already explained in Section VIII.D.9, Suehling automatically produces a radiologist report that includes a technical evaluation of medical images, including identification of lesions and quantitatively calculated metrics such as total tumor burden. Additionally, the radiologist report may include one or more medical images and/or risk maps in which lesions that have changed are highlighted and/or color coded to indicate degree of growth or shrinkage. Ex1007, [0044].

11. Dependent Claim 11: Radiologist Report Includes Reference Image or Reference Risk Map

Claim 11 depends from claim 9, which is anticipated by Suehling as

explained in Section VIII.D.9 . Claim 11 further requires that “the radiologist report comprises one or more reference images or reference risk maps” which is disclosed by Maier. It would have been obvious to improve Suehling’s report by including reference images for comparison, as taught by Maier, thus rendering claim unpatentable over Suehling in view of Maier. Ex1002, ¶¶383-388.

As explained in Section VIII.D.9 above, Suehling automatically evaluates a patient’s medical images and displays the results on an interactive graphical user interface, including the patient’s medical images, the patient’s risk map, and calculated metrics, such as total tumor burden. Ex1007, [0022], [0041], [0044]. Additionally, Suehling explains that the “interactive display may also be used in a follow-up scenario in which the current tumor burden is compared to one or more prior exams” and “lesions that changed (e.g., grew or shrank) may be highlighted” for example with “different color schemes.” Ex1007, [0044]. Suehling does not, however, clearly describe comparing the patient’s images to reference images or risk maps *of others*.

Maier discloses computer implemented systems and methods for assessing medical images and communicating a patient’s health status and risk by automatically generating a report. Ex1008, [0014], [0015]-[0016], [0026], [0041]. Like Suehling, Maier discloses assessing a patient’s health status and risk by comparing the patient’s medical images to the patient’s own prior images and

calculating values related to the change in the patient's own images. Ex1008, [0024]. Maier also discloses assessing a patient's health status and risk by comparing the patient's medical images to one or more comparison images from one more individuals for whom the corresponding health status and/or outcomes are known. Ex1008, [0014], Fig. 3, [0041].

It would have been obvious and straightforward to improve Suehling's report simply by including one or more reference images and/or risk maps based on the express teachings and motivations supplied in Maier. Ex1002, ¶387. Specifically, Maier teaches that comparison to a "corresponding cohort" permits quantitative calculation of "risk metrics" (Ex1008 at [0022]) that "may be used for screening disease, prognosis or diagnosis of diseases, base-line assessments, treatment planning, treatment follow-up, or other user education regarding tissue state" (Ex1008, [0018]). Additionally, Maier explains that its teachings are applicable to any type of tissue and/or disease. Ex1008, [0016]-[0018]. Therefore, Maier supplies motivation to a POSITA to also include a reference image for comparison in the report generated by Suehling. Furthermore, in view of the teachings in Maier, a POSITA would have had a reasonable expectation of success in doing so since Maier and Suehling are in the same field, both already disclose comparison to a patient's own prior images, and the improvement would only have amounted to including an additional image. Ex1002, ¶¶387-388.

12. Dependent Claim 12: Apply Machine Learning Algorithm to Update Process

Claim 12 depends from claim 1, which is anticipated by Suehling as explained in Section VIII.D.1. Menon discloses the additional limitations of Claim 12 as explained in Section VIII.B.12 above. It would have been obvious to combine the teachings of Suehling and Menon, rendering claim 12 obvious over Suehling in view of Menon. Ex1002, ¶¶389-394.

Suehling and Menon are in the same field of automated medical image analysis systems. A POSITA would have looked to Menon, and have been motivated to improve Suehling as described in Menon, based on Menon's express teaching that the application of machine learning to accumulated data (i.e., validated output) results in continuous refinement of the automatic image analysis system. Ex1012 at [0189] ("refine the system model continuously"); Ex1002, ¶392. Alternatively, improving Suehling with the teachings in Menon would merely have amounted to using a known technique (i.e., machine learning) to improve similar devices in the same way. Ex1002, ¶393. Moreover, a POSITA would have had a reasonable expectation of success in making such an improvement. Ex1002, ¶392.

13. Independent Claim 13

As explained in Section VIII.B.13 above, independent claim 13 is essentially identical to independent claim 1 except that claim 13 is directed to a method, whereas claim 1 is directed to a system. Accordingly, for the avoidance of

repetition, claim 13 is anticipated by Suehling for the same reasons provided in Section VIII.D.1 above as indicated in the chart below. Ex1002, ¶¶377-382.

<u>Claim 13 Limitation</u>	<u>Claim 1 Limitation(s)</u>	<u>Section(s)</u>
Preamble	Preamble	VIII.D.1.a)
13(i): Accessing, by a Processor, from a Database	1(a): Processor and Memory 1(b): Access from a Database	VIII.D.1.b) VIII.D.1.c)
13(ii): Analyze, by the Processor, Using a Machine Learning Algorithm	1(a): Processor and Memory 1(c): Analyze Using a Machine Learning Algorithm	VIII.D.1.b) VIII.D.1.d)
13(iii): Causing, by the Processor, Display via GUI	1(a): Processor and Memory 1(d): Display via GUI	VIII.D.1.b) VIII.D.1.e)
13(iv): Wherein Step (ii) Comprises	1(e): Wherein the Analysis Comprises	VIII.D.1.f)

IX. *FINTIV* FACTORS FAVOR INSTITUTION

Institution should not be denied under 35 U.S.C. § 314(a) based on analysis of the *Fintiv* factors,¹ which are relevant here because the Patent is also the subject of the pending MA litigation.

The first factor is “whether the court granted a stay or evidence exists that one may be granted if a proceeding is instituted.” *Fintiv*, Paper 11, p.6. Petitioner MIM has not yet requested a stay. Petitioner will be filing additional petitions for

¹ *Apple Inc. v. Fintiv Inc.*, IPR2020-00019, Paper 11 at 5–6 (PTAB March 20, 2020).

IPR directed to other patents that are being asserted in the MA litigation, and Petitioner plans to move to stay the MA litigation if the petitions are granted. The court already stayed all discovery and refused to adopt a case schedule, during the recent pendency of MIM's motion to dismiss. Ex1026. As such, the court is likely to grant a forthcoming motion to stay pending IPRs, and this factor weighs against denying institution.

The second factor is the "proximity of the court's trial date to the Board's projected statutory deadline for a final written decision." *Fintiv*, Paper 11, p.6. The court has still not adopted a case schedule in the MA litigation and, as such, has not set a trial date or any other deadlines. As a result, this factor also weighs against denying institution.

The third factor is "investment in the parallel proceeding by the court and the parties." *Fintiv*, Paper 11, p.6. The MA litigation is still in its infancy. Petitioner MIM answered the complaint less than two weeks ago, and the parties have not taken any discovery. Even if the court adopts the parties' proposed case schedule, the only impending deadline will be for the exchange of initial disclosures on February 28. Ex1027, pp.8-11. As such, this factor, too, weighs against denying institution.

The fourth factor is "overlap between issues raised in the petition and in the parallel proceeding." *Fintiv*, Paper 11, p.6. This factor only further serves to

highlight the lack of progress in the MA litigation. Because the Patent Owner has not served infringement contentions and Petitioner has not served invalidity contentions, it is unknown to what extent the issues raised in this petition will overlap with those in the MA litigation. As such, this factor should be, at worst, neutral.

The fifth factor is “whether the petitioner and the defendant in the parallel proceeding are the same party.” *Fintiv*, Paper 11, p.6. “Although this factor may, standing alone, be neutral, under these circumstances in which the trial date is not set and may occur after [the panel’s] Final Written Decision date . . . the fifth *Fintiv* factor weighs against discretionary denial of institution.” *Fusion Orthopedics, LLC v. Extremity Medical, LLC*, IPR2023-00894, Paper 15, p.32 (Nov. 17, 2023).

The sixth factor is “other circumstances that impact the Board’s exercise of discretion, including the merits.” *Fintiv*, Paper 11, p.6. In view of Director Vidal’s Review of *CommScope Technologies LLC v. Dali Wireless, Inc.*, IPR2022-01242, the Board need only analyze the sixth *Fintiv* factor if factors one through five favor denial. Such analysis is moot in view of the above.

The Board should not deny institution under § 314(a) based on the *Fintiv* factors.

X. CONCLUSION

For the foregoing reasons, claims 1-13 are unpatentable.

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

Pursuant to 37 C.F.R. §42.24(a)(1)(i), I certify that this paper includes 13,986 words. In accordance with 37 C.F.R. §42.24(a)(1), this word count does not include a count of the words in a table of contents, a table of authorities, mandatory notices under §42.8, a certificate of service or word count, or appendix of exhibits or claim listing. Furthermore, in accordance with 37 C.F.R. §42.24(d), this word count is the word count of the word-processing system used to prepare the paper.

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CERTIFICATE OF SERVICE

Pursuant to 37 C.F.R. §§ 42.6 and 42.105, the undersigned hereby certifies that a true and correct copy of the Petition for *Inter Partes* Review in connection with U.S. Patent No. 10,665,346 and supporting evidence was served on February 21, 2025, upon agreement of the parties, via electronic mail on the following counsel of record for Patent Owner, Progenics:

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