UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

MIM SOFTWARE INC.,
Petitioner,

v.

PROGENICS PHARMACEUTICALS, INC.,
Patent Owner.

IPR2025-00726
U.S. Patent No. 11,894,141

PATENT OWNER'S PRELIMINARY RESPONSE

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EX2008	MIM's Invalidity and Noninfringement Contentions, Civil Action No. 1:24-cv-10437-PBS.
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EX2011	*Cancer Control Month, 2025 – The White House* (Apr. 3, 2025).
EX2012	*NIH Strategic Plan for Data Science FY 2025-2030*, Nat'l Institutes of Health.
EX2013	Rowe, S.P. et al., *PET Imaging of Prostate-Specific Membrane Antigen in Prostate Cancer: Current State of the Art and Future Challenges*, Prostate Cancer & Prostatic Diseases (2016).
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EX2019	Rowe, S.P., et al., *PSMA-Based [^{18}F]DCFPyL PET/CT Is Superior to Conventional Imaging for Lesion Detection in Patients with Metastatic Prostate Cancer*, Molecular Imaging and Biology 18(3):411-419 (2016).
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I. INTRODUCTION

U.S. Patent No. 11,894,141 (the "'141 Patent") discloses a novel and inventive solution to serious challenges that doctors faced when analyzing medical images to diagnose, monitor and treat cancer. More specifically, the '141 Patent claims an inventive process for taking anatomical and functional images, automatically segmenting organs, identifying regions of cancer within relevant organs, and then using the organ segmentation (with the functional image information and/or identified cancer regions) to determine values of risk indices that indicate (e.g., quantify) cancer state or progression.

Among other things, key advances of the '141 Patent include systems and methods that incorporate specific machine learning-based techniques that are tailored to, and provide innovative solutions for, the analysis of specific types of medical images, and a network-based system approach that is particularly valuable in the context of cancer diagnosis and treatment.

For example, the '141 Patent recognized that machine learning (ML) algorithms could be used to geographically identify 3D boundaries of particular tissue regions in a more accurate and robust manner than had been possible previously. Moreover, the '141 Patent applied this approach specifically to identifying organs from a CT scan using ML-based segmentation, and then creating a composite of the segmented CT scan overlaid with a nuclear medicine image, such as a 3D PET or SPECT image. This is especially inventive and valuable because, as described in the ’141 Patent, nuclear medicine images are often best suited to identify cancer. *See* EX1001, 15:41-62. However, they are limited in their ability to capture features of anatomy and structure of organs and/or tissues, for example, at sufficiently high resolution. EX2014, ¶¶27-30, 57; *see also* EX1001, 28:6-30. In this way, one can more accurately identify 3D boundaries of organs, thereby adding valuable anatomical context to the nuclear medicine image. As a result, one can use the combination of (i) highly sensitive functional image information provided by 3D PET or SPECT images and (ii) accurate and reliable tissue region boundaries created via ML-based segmentation of CT images to compute risk index values that provide improved indications of cancer state or progression in a patient.

The ’141 Patent’s inventions did not end there. The ’141 Patent also recognized that it would be especially valuable for cloud-based systems of cancer diagnosis/treatment if one could take advantage of remote networking by uploading medical images to, and accessing them from, databases via network-based systems. The ’141 Patent also leverages particular radiopharmaceuticals – PSMA binding agents – that, around the time of filing, were in the early stages of study for their potential use in prostate cancer diagnosis. EX2014, ¶89; *see also id.*, ¶34.

None of the references that Petitioner relies on teaches or suggests this unique combination of features, which are recited in the claims of the ’141 Patent. Instead, for its main grounds against the independent claims, the Petition relies on a combination of three references that are directed to fundamentally distinct and incompatible techniques. Petitioner fails to adequately explain why a POSA would have been motivated to combine such fundamentally different asserted references with any reasonable expectation of success.

Therefore, Patent Owner requests that the Board deny institution of the Petition.

II. TECHNOLOGY BACKGROUND

One major challenge in treating and managing cancer, as well as other serious diseases, has long been the difficulty of accurately and consistently interpreting the diagnostic images produced by medical imaging tools. *See* EX2014, ¶¶35, 55. Both anatomical scans (such as X-rays or CT scans) and functional scans (like PET or single-photon emission computed tomography (SPECT)) are valuable tools. EX2014, ¶¶26-28. However, before the inventions described in the ’141 Patent, physicians faced significant obstacles in using these scans to form a complete and reliable picture of a patient’s condition.

One difficulty was that each type of scan could only capture part of the relevant picture for any given patient. Simply put, anatomical scans show the anatomy or structure of organs and tissues within the body (but not the function); functional scans show the activity and function of those organs or tissues (but not the anatomy/structure). *See* EX2014, ¶¶27-28. As applied to cancer, an anatomical scan thus cannot reliably detect the activity of a tumor, whereas a functional scan can struggle to differentiate between the organs and tissue surrounding a tumor. *See id*. As a result, physicians were left to parse two different types of scans to try to piece together the full picture, which often led to inaccurate or inconsistent diagnoses or treatments.

While radiologists and physicians have various medical imaging modalities and techniques at their disposal, the selection of which types of images to obtain, and how to interpret these images is not straightforward. EX2014, ¶35. To the contrary, the task of determining, for example, whether a particular patient has cancer, how severe it is, and what course of action to take is laborious, error prone, and highly subjective, often varying from physician to physician. *Id.* Without effective automated integration, mapping, and assessment of those scan results, a physician might miss a critical diagnostic insight.

III. CITED REFERENCES

a. Maier

Maier is directed to a "computer implemented method for assessing and communicating a patient's health status and risk." EX1005, [0007]. EX2014, ¶50. Maier is concerned primarily with smoking-related diseases like "myocardial infarction, Chronic Obstructive Pulmonary Disease (COPD), emphysema, lung cancer, decreased lung function, COPD exacerbations, coronary artery disease, and stroke." EX1005, [0007]; EX2014, ¶50. Maier's approach for assessing patient risk involves extracting values of image features such as numbers or percentages of voxels with certain intensities, mean image intensities, complex texture features, etc. and using them as, what he calls, "imaging biomarkers," presumably by way of analogy to conventional, e.g., genetic or molecular biomarkers. EX1005, [0007]-[0008]; EX2014, ¶50. Maier correlates values of imaging biomarkers determined for a given patient with values from historical patient populations having known clinical outcomes – similar to how, for example, the BRCA1 and BRCA2 genes are genetic biomarkers for breast cancer risk and cholesterol levels are biomarkers for risk of heart disease. EX1005, [0007]-[0008]; EX2014, ¶50.

b. Huang

Huang discloses a method for analyzing digitized images for body landmark modeling and detection. EX1006, [0002], [0014]. Huang's method is directed to applications related to CAD tools for fluorine-18 deoxyglucose (FDG) uptake imaging. EX1006, [0003], [0006], [0051], [0098], [0108]; EX2014, ¶51.

c. Armor

Armor discloses Tc-99m labeled PSMA targeting agents (a gamma-emitting transition metal complex conjugated to a targeting moiety), suitable for SPECT imaging. EX1007, [0008]; EX2014, ¶52. Armor also describes a method of evaluating a human subject suspected of harboring a prostate tumor that uses his SPECT imaging compounds, but otherwise appears to involve conventional SPECT/CT imaging techniques and analysis. EX1007, [0096] (requiring a user to manually place "[c]ircular regions of interest with a diameter of approximately 20 pixels" on regions adjacent to the prostate gland and recording counts in that region as background). EX2014, ¶52.

d. Neumaier, Cardinale, Giesel, and Weineisen

Neumaier (EX1008), Cardinale (EX1009), Giesel (EX1010), and Weineisen (EX1011) each describes specific methods for synthesizing particular radiopharmaceutical compounds or analyses of their characteristics, via otherwise conventional imaging techniques. EX1008, Abstract, 1:1-13; EX1009, 2:64-67; EX1010, 1929; EX1010, 1929; EX1011, 1169, 1171; EX2014 ¶53.

IV. THE '141 PATENT

a. The Invention

As of the priority date (October 27, 2016), there remained a critical need for innovative solutions to increase the accuracy, reliability, and consistency of medical imaging analysis, especially for (but not limited to) cancer diagnosis and treatment. EX2014, ¶55. The '141 Patent addresses this need through an inventive process for taking anatomical and functional images, automatically segmenting organs within them, identifying regions of cancer within relevant organs, and then determining values of risk indices that indicate cancer state or progression in a patient. EX2014, ¶¶54-56.

The ’141 Patent thus reflects multiple key innovations and leverages insight into how they could be combined in a synergistic fashion to provide a valuable tool for tracking and aiding physicians over the course of a patient’s prostate cancer progression and treatment. EX2014, ¶¶54-56.

One of those innovations was to leverage machine learning (“ML”) techniques, including, but not limited to, convolutional neural networks (“CNNs”) to perform organ segmentation in 3D images (e.g., 3D CT scans). EX2014, ¶57; *see also id.*, ¶¶44-49. The ’141 Patent recognized that ML could be used to geographically identify 3D boundaries of particular tissue regions in a more accurate and robust manner with desirable scan-to-scan reproducibility than had been possible previously. EX2014, ¶57; *see also id.*, ¶¶44-49.

The ’141 Patent leveraged this ML-based organ segmentation for analysis of composite images comprising a CT scan overlaid with a nuclear medicine image acquired using a PSMA binding agent. EX2014, ¶57. The claims of the ’141 Patent describe analyzing these composite images by first, using the composite image to identify 3D boundaries of imaged tissue within the nuclear medicine image. EX2014, ¶57. For example, as described in the ’141 Patent, ML-based segmentation of the CT scan can be performed to create accurate and reliable 3D boundaries of tissue regions, which (since the CT scan is overlaid with the nuclear medicine image), in turn, can be transferred to the overlaid nuclear medicine image (e.g., 3D PET or SPECT images). EX2014, ¶57.

This is especially significant because, although cancer is often best detected via nuclear medicine imaging approaches (like 3D PET or 3D SPECT), nuclear medicine imaging techniques do not capture features of anatomy and structure of organs and/or tissues at sufficiently high resolution and thus cannot always reliably distinguish between different organs or tissue regions. EX2014, ¶57; *see also id.*, ¶¶28-30. The '141 Patent's approach thus adds valuable anatomical context to nuclear medicine images where it is often impossible to obtain, inaccurate, or subjective. EX2014, ¶57. As a result, the combination of (i) highly sensitive functional image information provided by 3D PET or SPECT images and (ii) accurate and reliable tissue region boundaries created via ML-based segmentation of CT images can be used to compute risk index values that provide improved indications of cancer state or progression in a patient. *Id.*

Another key innovation of the '141 Patent was combining the insight about ML techniques with the insight that taking advantage of remote networking by uploading medical images to, and accessing them from, databases via network-based systems would be especially valuable in the context of cancer diagnosis in treatment. EX2014, ¶58.

Finally, the ’141 Patent leverages particular radiopharmaceuticals – PSMA binding agents – that, around the time of filing, were in early stages of being studied for their potential for prostate cancer diagnosis. EX2014, ¶59; *see also id.*, ¶34.

The ’141 Patent thus combines insight into the promise of those imaging agents, together with the above-described image analysis techniques and network-based platform delivery platform, to provide a comprehensive solution tailored for assisting physicians and patients from prostate cancer diagnosis, to monitoring, and through treatment. EX2014, ¶59.

As such, the claimed methods provide numerous advantages over prior art methods. EX2014, ¶60.

b. Prosecution History

The Application for the ’141 Patent was filed on July 12, 2022, claiming priority to U.S. Provisional Application 62/413,936 filed on October 27, 2016. EX1004, 113; EX2014, ¶61. The ’141 Patent issued on February 06, 2024. EX1004, 307; EX2014, ¶61. During prosecution, the Examiner identified six references on his “Notice of References Cited,” including Huang and Maier. EX1004, 224; EX2014, ¶¶62-63. The ’141 Patent also cited the Petition’s third main reference, Armor, in an IDS submitted to the Office on January 10, 2023. *See* EX1004, 179; EX2014, ¶63. On September 19, 2023, the Examiner also signed the IDS, noting at the bottom that “ALL REFERENCES CONSIDERED EXCEPT WHERE LINED

THROUGH. /S.H.A./." The Examiner did not line through the Armor reference. EX1004, 242; *see also* EX2014, ¶63.

On September 18, 2023, per the Examiner's interview summary, the Examiner conducted "a telephone interview, which was initiated by the examiner with applicant's representative," and "Examiner suggested ways to clarify the independent claim or amend the claim that may overcome **the prior art of record** and requested a Terminal Disclaimer, and agreement was reached." EX1004, 223 (emphasis added); *see also* EX2014, ¶64. In granting the claim, the Examiner stated: "Based on telephone on September 18, 2023, with respect to cancellation of claims 3-10, 15, 17-18, 22-39, 43-44, 46-49, 52, and amended claims 1, 19, 40, 45, 55, 59, 67 and new claims 68-71, also **review of prior art of record**, all have been fully considered and are persuasive." EX1004, 286 (emphasis added); *see also* EX2014, ¶64.

The Examiner thus allowed the claims after considering Maier, Huang, and Armor, and requesting amendments to the independent claims to overcome the art. In the Notice of Allowance, the Examiner listed the following key features:

> automatically analyze the one or more medical images using a machine learning algorithm; and generate a radiologist report for the particular patient, wherein the one or more medical images comprise a composite image of the particular patient, comprising a CT scan "overlaid" with a nuclear medicine image obtained at a same time as the CT scan and following administration to the patient of an imaging agent comprising a Prostate Specific Membrane Antigen (PSMA) binding agent comprising a radionuclide, wherein the instructions cause the processor

> to automatically analyze the composite image by: using the "composite image" to geographically identify a "3D boundary" for each of one or more regions of imaged tissue within the nuclear medicine image; and computing, using the nuclear medicine image with the identified 3D boundary of the one or more region, a value of each of one or more risk indices, each risk "index value" indicative of cancer state or progression in the patient, and wherein the system is a cloud-based system".

EX1004, 297-298.

V. PERSON OF ORDINARY SKILL

Petitioner argues that a POSA "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." Pet., 8-9; EX2014, ¶15.

For purposes of this preliminary response, Patent Owner does not dispute Petitioner's definition of a POSA. EX2014, ¶¶13-16.

VI. CLAIM CONSTRUCTION

Under 37 C.F.R. § 42.104(b), the Petitioner bears the burden to set forth "how the challenged claim is to be construed" and "how the construed claim is unpatentable." Therefore, when a petition relies on an incorrect claim construction (either expressly or impliedly), and fails to offer any evidence of unpatentability under the proper claim construction, institution should be denied. *See, e.g.*, *Amazon Web Servs., Inc. v. Saint Regis Mohawk Tribe*, No. IPR2019-00103, Paper 22, 14–

15, 17, 19–20 (P.T.A.B. May 10, 2019) (denying institution); *Jiawei Tech. Ltd. v. Richmond*, No. IPR2014-00937, Paper 22, 7-8 (P.T.A.B. Dec. 16, 2014) (denying institution where petition did not provide express construction for term and did not adequately explain how term read on cited prior art).

Patent Owner submits that the terms "network-based system," and "database," should be construed as stated below. The Petition does not offer any construction for these terms, however, at various times appears to take them for granted as contemplated by inapposite disclosures of the cited art.

Based on claim construction alone, institution should thus be denied. Patent Owner addresses each relevant claim term below.

a. The Petition relies on an incorrect implied construction of "network-based…system."

The term "network-based system" appears in claims 1, 32, and 33 of the '141 Patent. For example, in its preamble, claim 1 recites, "A **network-based** decision support **system** comprising . . .." EX1001, 37:8 (emphasis added).

The correct construction of the term "a network-based system" is "a system involving interaction across multiple interconnected and physically dispersed computing devices." This construction comports with both the claim language and the specification. EX2014, ¶69.

First, the claim language expressly uses the term "[a] network-based . . . system" (as opposed to "A system"), and, accordingly, the words "network-based" would be afforded meaning by a POSA. EX2014, ¶¶70-71. Second, the specification affirms that "a network-based system" means a system involving interaction across multiple interconnected and physically dispersed computing devices. EX2014, ¶72. The specification repeatedly describes the '141 Patent's claimed technology as a part of a distributed platform, rather than a standalone machine like a simple computer workstation connected to an imaging device. EX2014, ¶¶72-79. Numerous figures in the '141 Patent convey interactions between distinct computing devices, such as serve and client devices and members of a cloud-based service, and they are repeatedly described as providing platform-based functionality that allows interaction across multiple interconnected and physically dispersed computing devices. EX1001, FIG. 1 (showing mobile app providing access to three cloud-based services), FIG. 2 (showing a schematic showing the relationship between a platform and a computing device), FIG. 7 (a block diagram of an exemplary cloud computing environment), FIG. 9 (a block diagram of an example architecture for implementing the cloud based platform); EX2014, ¶¶74-77.

Furthermore, the specification of the '141 Patent repeatedly emphasizes the ability of the network-based platform to provide access to multiple users and to obtain, store, and analyze medical images that are obtained over the course of multiple visits to one or more doctors and/or clinical specialists. EX1001, 30:13-34;

EX2014, ¶78. Altogether, then, a POSA would understand these various and repeated disclosures to require that "a network-based system" involves multiple physically distinct machines whose interaction occurs across a network. EX2014, ¶79.

In light of both the claim language and the specification, a POSA would understand that "a network-based system" thus refers to a system involving interaction across multiple interconnected and physically dispersed computing devices. *Id*.

b. The Petition relies on an incorrect implied construction of "database."

The term "database" appears in independent claims 1, 24, 27, and 31-35 of the '141 Patent. For example, steps (i) and (ii) of claim 1 recite "receiv[ing] and storing, by the processor, a plurality of medical images in a **database**," and "access[ing] one or more medical images associated with a particular patient from the **database**…," respectively. EX1001, 37:13-14; 37:16-17 (emphasis added); EX2014, ¶80. Claims 1, 24, and 32-35 include similar language. Claims 27 and 31 also recite, *inter alia*, "repeatedly receiving and storing in a **database**, over time… a plurality of medical images for each of the one or more patient(s) to obtain, for each of the one or more patient(s), a series of medical images taken over time." EX1001, 39:57-62; 40:60-63 (emphasis added).

The correct construction of the term "database" is "a large structured set of data that contains multiple records that contain multiple fields." EX2014, ¶81. This construction comports with both the claim language and the specification. EX2014, ¶81. Moreover, a POSA reading the claims and specification of the '141 Patent would understand that the term "database" is not synonymous with the term "memory."

First, the claim language makes clear that a "database" is a persistent, structured repository that is distinct from a processor or memory. EX2014, ¶82. For example, step (ii) of Claim 1 teaches "access[ing] one or more medical images associated with a particular patient from the database..." EX2014, ¶82. A "database" is thus a data set from which the recorded "medical images" can be "access[ed]." *Id.* Second, the specification repeatedly affirms that "database" means a large structured set of data that contains multiple records that contain multiple fields. EX2014, ¶83. For example, when describing the cloud diagram in FIG. 7, the specification identifies "application servers and/or databases with storage and retrieval capabilities" as discrete network resources, separate from compute nodes. EX1001, 32:31-33; EX2014, ¶83. That language mirrors Plaintiffs' proposed definition of a database: a store built for structured retrieval.

The specification also describes how the systems and methods of the '141 Patent "allow[s] multiple users to store, access, analyze, and/or provide feedback regarding a given set of image data for the patient." EX1001, 3:5-7; EX2014, ¶¶83-84. Moreover, the specification describes how the claimed invention causes the processor to "repeatedly receive and store in a database over time, a plurality of medical images for each of the one or more patient(s) to obtain, a series of medical images taken over time (e.g., over the course of multiple visits to one or more doctor. . . . thereby tracking determined values of the one or more risk indices over a course of prostate cancer progression and treatment for the patient[.]" EX1001, 11:50-65; EX2014, ¶85. This language further affirms that "database" means a structured, multi-record repository that carries multiple records (patients, series, images, etc.) and multiple fields (timestamps, modality, dose, metadata, etc.). *See id.*, ¶¶84-85.

In light of both the claim language and the specification, a POSA would understand that a "database" thus refers to a large structured set of data that contains multiple records that contain multiple fields. EX2014, ¶87.

A POSA would also understand, reading the claims in the context of the specification, that "database" is different than "memory." The claims and specification of the '141 Patent use the term "database" differently than "memory." For example, claim 1 begins: "A network-based decision support system comprising: a **processor**; and a **memory** having instructions stored thereon, wherein the instructions, when executed by the processor, cause the processor to: (i) receive and store a plurality of medical images in a **database**…," and "access one or more of the medical images associated with a particular patient from the database." EX1001, 37:8-17 (emphasis added); EX2014, ¶82. Other claims make the same distinctions. EX1001, 39:10-13; 39:15-17 (claim 24). Reading "database" to mean a simple memory would thus collapse the two expressly different claim terms. *Supra*, 14.

The specification differentiates between the two terms as well. The specification describes "memory" as a hardware element within the computing device, whereas "database" means a structured store of data. *See, e.g.*, EX1001, 33:41-46 ("The memory 804 stores information within the computing device 800. In some implementations, the memory 804 is a volatile memory unit or units. In some implementations, the memory 804 is a non-volatile memory unit or units. The memory 804 may also be another form of computer-readable medium, such as a magnetic or optical disk."); 35:19-27 ("The memory may include, for example, flash memory and/or NVRAM memory . . . The instructions can also be stored by one or more storage devices, such as one or more computer- or machine-readable mediums (for example, the memory 864 . . .").

VII. THE PETITION DOES NOT ESTABLISH A "REASONABLE LIKELIHOOD" OF UNPATENTABILITY

Under 35 U.S.C. § 314(a), the Board may not institute inter partes review unless the Petition demonstrates "that there is a reasonable likelihood that the petition would prevail with respect to at least 1 of the claims challenged in the petition." This is a threshold requirement that the Petition must satisfy. *Harmonic Inc. v. Avid Tech., Inc.*, 815 F.3d 1356, 1363 (Fed. Cir. 2016) ("the petitioner has the burden from the onset to show with particularity why the patent it challenges is unpatentable"). Here, the Petition fails to establish a "reasonable likelihood" of unpatentability as to any challenged claim. Institution should thus be denied. Patent Owner addresses each ground below.

a. Ground A: Maier in view of Huang and Armor does not render obvious claims 1, 24, and 32-35.

The Petition fails to establish a reasonable likelihood that Maier in view of Huang and Armor renders claims 1-3, 6-9, 13-26, 32-35 obvious. Patent Owner addresses claims 1, 24, 32-35 since those are the only independent claims.

Independent claim 1 is directed to using a "machine learning algorithm" to analyze medical images and compute values of risk indices that are indicative of cancer state or progression in the patient. As briefly previewed above, the claimed invention includes several key advances for helping physicians track a patient's prostate cancer progression and treatment. EX2014, ¶88. For example, the '141 Patent recognized that machine learning (ML) could be used to geographically identify 3D boundaries of particular tissue regions in a more accurate and robust manner than was previously possible. EX2014, ¶89. Further, the claimed invention presented a new way of leveraging ML techniques in the context of a particular type of image – a composite image comprising a CT scan overlaid with a nuclear medicine image obtained via use of a PSMA binding agent. *Id*. At the time the '141 Patent was effectively filed, imaging with PSMA binding agents was just beginning to show promise for sensitive diagnosis of prostate cancer. *Id*.

In particular, the Patent teaches how to analyze a composite image that comprises a CT scan overlaid with a nuclear medicine image acquired using a PSMA binding agent. EX2014, ¶90. The claims describe analyzing these composite images by first using the composite image to identify 3D boundaries of imaged tissue within the nuclear medicine image, and then using the nuclear medicine image with the identified 3D boundaries to compute the risk indices. *Id*. This approach is described in detail in the specification of the '141 Patent, for example at Section A.iv ("Positron Emission Tomography (PET) Scans"). *Id*. It leverages the fact that complementary anatomical and functional information are provided by the CT scan and nuclear medicine image, respectively, and that this information can be combined by virtue of the overlay between the two images in a composite image, such as a PET/CT or SPECT/CT. *Id*.

The claims of the '141 Patent combine this insight about ML and new imaging approaches with the insight that taking advantage of remote networking by uploading medical images to, and accessing them from, databases via network-based systems would be especially valuable in the context of, for instance, cloud-based systems for cancer diagnosis and treatment. EX2014, ¶91.

As explained in further detail below, the Petition acknowledges that the primary reference, Maier, does not disclose key features of the ’141 Patent’s claimed subject matter that are recited in the claims. EX2014, ¶92. Maier does not disclose the particular type of medical image that is recited in claim 1. *See id.* Maier also does not disclose any radiopharmaceutical, let alone the particular radiopharmaceutical that is used and recited in claim 1. *See id.* And Maier does not disclose the particular way of analyzing those images that is recited in claim 1. *See id.*

The Petition thus includes two additional references – Huang and Armor – to attempt to cure these deficiencies in Maier. *See id*. As explained in further detail below, they do not fill Maier’s glaring gaps. *See id*. Maier, Huang, and Armor all relate to fundamentally distinct and incompatible approaches for obtaining and analyzing images and have different goals. *See id*. The Petition attempts to skirt this issue by providing element-wise obviousness arguments that gloss over significant incompatibilities between the cited references, and ultimately fail to show that a POSA would be motivated to, or even could, combine them to arrive at the claimed subject matter of the ’141 Patent. *Id*.

i. Maier and Huang do not render obvious the element "wherein the one or more medical images comprise a composite image comprising a CT scan overlaid with a nuclear medicine image" as recited in claims 1, 24, and 32-35.

Limitation (f)[1] of claim 1 is directed to "generat[ing] a radiologist report for the particular patient according to the one or more medical images for the patient, **wherein the one or more medical comprise a composite image comprising a CT scan overlaid with a nuclear medicine image** . . .." Pet., 23 (emphasis added). Similar language appears in claims 24 and 32-35. Pet., 53, 55-56; EX1001, 41:38-40, 42:14-16, 42:56-58, 43:28-30. The Petition acknowledges that Maier fails to disclose this, but alleges that Huang discloses this element, and that the combination of Maier and Huang thus render this claim element obvious. Pet., 23.

The Petition fails to demonstrate a reasonable likelihood of unpatentability because it fails to show that a POSA would have been motivated to combine Maier and Huang with a reasonable expectation of success. This is true for at least three reasons.

First, the Petition fails to carry its burden to show motivation to combine because the Petition improperly focuses on individual limitation (f), rather than the

[1] For the sake of convenience, Patent Owner references claim limitations using the Petition's labeling scheme.

claim as a whole. *See KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398, 418 (2007) ("[A] patent composed of several elements is **not proved obvious** merely by demonstrating that each of its elements was, **independently**, known in the prior art.") (emphasis added); *Envtl. Designs, Inc. v. Union Oil Co.*, 713 F.2d 693, 698 (Fed. Cir. 1983) ("Virtually all inventions are combinations and virtually all are combinations of old elements. A court must consider what the prior art **as a whole** would have suggested to one skilled in the art[.]") (emphasis added). Here, however, the Petition argues only that a POSA would have had a motivation to combine Maier and Huang to perform *limitation (f)*, rather than claim 1 as a whole. Pet., 23 ("Maier in view of Huang renders obvious this limitation."). The Petition makes a similar mistake for several other limitations. Pet., 27 (limitation 1(g)), 31 (limitation 1(h)), 35 (limitation 1(i)), 39 (limitation 1(j)). Apart from the conclusory statement at the end of Section B.1 of the Petition ("Therefore, Maier in view of Huang and Armor renders obvious claim 1"), the Petition never presents a sustained and detailed argument for why Maier, Huang, and Armor render any of the entirety of the challenged claims obvious, as is required under 35 U.S.C. § 103. Pet., 40. Instead, the Petition's motivation to combine argument fails because it improperly proceeds on a limitation-by-limitation basis without sufficiently explaining why a POSA would have been motivated to combine the asserted references to achieve the claim as a whole with a reasonable expectation of success.

Second, the Petition's limitation-by-limitation approach is especially confounding because, for each individual limitation, the Petition presents multiple distinct and individualized (e.g., with respect to the particular limitation) arguments about whether a POSA would have a motivation to combine the cited references. For example, for limitation 1(f), the Petition argues two different options for motivations to combine: (i) "Teaching, suggestion, motivation," apparently for the specific reason of "Improved physician decision-making" or (ii) "Combination according to known methods to yield predicable results." Pet. 25-26. Next, for limitation 1(g), the Petition presents another two potential motivations to combine, individualized for this particular limitation: (i) "Teaching, suggestion, motivation," apparently for the specific reasons to (a) "Improve cancer diagnosis and monitoring," or (b) "Compatibility with Maier and Huang's multi-modal imaging," or (ii) "Simple substitution of one known element for another to obtain predicable results." Pet., 29-30. For limitation 1(h), the Petition offers up another mix of individualized motivations to combine. The Petition argues (i) "Teaching, suggestion, motivation," now on (a) "Improved, organ-specific identification," or (b) "Compatibility with machine-learning algorithms" or (ii) "Combining prior art elements according to known methods to yield predicable results," (iii) "Known technique to improve similar devices in the same way," or (iv) "Reasonable expectation of success." Pet., 32-34. Finally, at limitation 1(i), the Petition's motivation to combine cross-references its arguments made in regard to limitations 1(g) and 1(h) (though apparently not those in regard to limitation 1(f)), arguing that those reasons apply to limitation 1(i) based on nothing more than the cryptic and conclusory statement, "[s]ince the resultant risk indices were merely applications of known mathematical calculations to PSMA-binding agent-measured uptake within an identified 3D boundary, e.g., the prostate or, specifically, a prostate tumor. Ex1002, ¶¶185-190." Pet., 39.

If anything, the Petition's multiple, distinct, limitation-specific arguments that the Petition provides reflect the non-obviousness of the claimed invention. At no point does the Petition step back to consider both the claims and the art as a whole, as is required under 35 U.S.C. § 103. The Petition thus fails to present a coherent and particularized argument as to why a POSA would have the required motivation to combine three distinct references to arrive at the '141 Patent's claimed subject matter.

Third, even to the extent one can follow the Petition's scattered treatment, the Petition fails to show on the merits a reasonable likelihood that a POSA would have been motivated to combine Maier and Huang to perform limitation (f) of claim 1. The Petition contends that "a POSITA would have found it obvious, with a reasonable expectation of success, to incorporate Huang's fused PET/CT imaging into the system and method of Maier. Pet., 25. Not so. Maier and Huang are simply too different for a POSA to have been motivated to combine them with a reasonable expectation of success. EX2014, ¶93; *see also id.*, ¶94.

The differences are striking. Maier focuses primarily on analysis of CT (or MRI) images to determine "imaging biomarkers" that correlate with various smoking-related diseases, like "myocardial infarction, Chronic Obstructive Pulmonary Disease (COPD), emphysema, lung cancer, decreased lung function, COPD exacerbations, coronary artery disease, and stroke." EX1005, [0007]; EX2014, ¶95. Maier repeatedly explains that imaging biomarkers are characteristic patterns in images that are correlated with disease (again, focusing on smoking related diseases):

> By way of example, but not limitation, these imaging biomarkers may be: characteristic patterns of intensity values (e.g., percentage or volume of voxels below or above a threshold value, mean image intensity below or above a threshold value, skew of a histogram of image voxel intensities, value for a certain percentile of the image voxel intensity histogram, etc.), image textures (e.g., reticular pattern, honeycomb pattern, ground glass opacities, etc. on CT lung images) …

EX1005, [0031]; EX2014, ¶95. Huang, in contrast, focuses on CAD tools for segmenting hotspots in FDG PET-CT images. EX1006, [0003], [0006], [0051], [0098], [0108]; EX2014, ¶96. Whereas Maier analyzes single CT images to detect characteristic patterns that might correlate with lung disease, Huang's analysis centers around the fact that tumors appear as bright spots in FDG-PET images. EX2014, ¶96. It is not even clear how Maier could be applied to a PET/CT image, or how Maier's approach of using machine learning to assign risk to imaging biomarkers would yield predictable results for a PET/CT image. EX2014, ¶96; *see also id.*, ¶¶97-99. Accordingly, Maier's complicated correlations and various flavors of imaging biomarkers would be irrelevant in Huang. EX2014, ¶96; *see also id.*, ¶¶97-99. It is not clear how, if at all, Huang's FDG-PET imaging approach would even allow for assessing risk of all varieties of lung disease, including emphysema, etc. EX2014, ¶96; *see also id.*, ¶¶97-99. The Petition never attempts to address these key distinctions and incompatibilities between Maier and Huang. EX2014, ¶98; *see also id.*, ¶¶97-99.

Ultimately, then, the Petition's motivation to combine arguments fails because it ignores the fundamental incompatibilities between Maier and Huang. EX2014, ¶98. The Petition cannot satisfy its burden by simply noting that both Maier and Huang are directed to diagnostics and that Huang says PET/CT imaging is useful. *Supra*, 25; EX2014, ¶98. Institution should thus be denied. *See* EX2014, ¶100.

Since this same limitation appears in independent claims 24 and 32-35, the Petition also fails to carry its burden to show that a POSA would have had a motivation to combine Maier and Huang to achieve this same limitation in claims 24 and 32-35. EX2014, ¶101. The Petition thus also fails to carry its burden for claims 24 and 32-35. *Id.*

ii. Maier, Huang, and Armor do not render obvious the use of a "PSMA binding agent," as recited in claims 1, 24, and 32-35.

Limitation (g) of claim 1 is directed to "generat[ing] a radiologist report for the particular patient according to the one or more medical images for the patient, wherein the one or more medical images comprise a composite image comprising a CT scan overlaid with a nuclear medicine image obtained at a substantially same time as the CT scan and following administration to the patient of an imaging agent **comprising a Prostate Specific Membrane Agent (PSMA) binding agent** . . ." Pet., 27 (emphasis added); EX2014, ¶102; claims 24, 32-35 (similar).

Institution should be denied because the Petition fails to show that Maier and Huang render obvious the claimed use of a "PSMA binding agent." EX2014, ¶¶103-104. The Petition conclusorily argues that "Maier and Huang disclose administering a radiolabeled imaging agent to the patient," citing in footnotes to "fluorine-18 deoxyglucose ("FDG")" and "an imaging biomarker such as a functional imaging agent." Pet., 27 (citing EX1005, [0003]-[0005]). The Petition's argument fails for at least two reasons.

First, Maier does not disclose *any* radiolabeled imaging agent suitable for use in nuclear medicine imaging, let alone an agent specifically directed to prostate cancer (like PSMA binding agent). EX2014, ¶105. The cited passage in Maier does not even reference a "functional imaging agent," as the Petition's quoted footnote contends. *Id.* Instead, the cited passage describes an imaging biomarker as some kind of pattern or feature that one can calculate from an image. EX1005, [0031] ("By way of example, but not limitation, these imaging biomarkers may be: characteristic patterns of intensity values . . ., image textures . . ., dimensions or amount of an anatomical feature . . ., other measurable characteristics of anatomical features . . . , or physiological metrics derived from functional imaging exams . . ."). EX2014, ¶105. The only mention of an "agent" in this laundry list of "imaging biomarkers" in Maier is "metrics related to contrast agent uptake in MR or CT in tumors, or other vascularized tissues, etc." *See id.* A metric related to a contrast agent is not a radiolabeled imaging agent. Moreover, MR and CT images are not nuclear medicine images, and therefore do not use radiolabeled imaging agents. *See id.* Thus, Maier does not even disclose the use of a radiolabeled imaging agent. *See id.*

Second, Huang does not even mention the prostate or prostate cancer, let alone the idea of radiolabeled agents like PSMA that target specific types of cancer. EX2014, ¶106. Huang describes FDG, which is a generic imaging agent specific to PET imaging. EX1006, [0003]. *Id.* Huang describes FDG as a glucose analogue that is absorbed preferentially by tissue with high metabolic activity, and which is not specific to any cancer type. *See* EX1006, [0098]; EX2014, ¶106. In contrast, PSMA binding agents expressly bind to prostate-specific membrane antigen, a protein that is overexpressed in prostate cancer. EX2014, ¶106. FDG thus operates in a fundamentally different way than a PSMA binding agent: FDG is non-specific, whereas PSMA expressly targets prostate cancer. EX2014, ¶107; *see also* EX1006, [0098] (noting that "normal physiology, such as heart, kidney, or bladder, and pathology such as tumor or inflammations, produce hot-spots"). Therefore, Huang is inapposite.

Third, although Armor describes the use of a PSMA binding agent, Armor is necessarily incompatible with Maier-Huang. EX2014, ¶108. The Petition argues that Armor supplies the reference to a PSMA binding agent that is missing from Maier-Huang. Pet., 30 ("A POSITA could have predictably substituted Armor's PSMA-binding agents into the Maier-Huang combination to predictably arrive at this claim limitation."). The Petition's argument fails, though, because (as discussed above) Armor and Maier-Huang relate to fundamentally different imaging methods. EX2014, ¶108; *see also id.*, ¶¶32-35. Huang, as discussed above, involves the use of FDG, which is specific to PET imaging. *Id.,* ¶108. Armor's PSMA binding agent, on the other hand, only works for SPECT imaging. *Id.* PET and SPECT detect different kinds of radiation, and thus require different types of radionuclides. *Id.* Therefore, a POSA would know that they could not simply substitute Armor's SPECT-specific compounds for FDG, since that would result in a non-functioning system. EX2014, ¶¶108-109.

Fourth, apart from disclosing PSMA binding agents, Armor is otherwise directed to a wholly conventional imaging technique, and it is not clear from the Petition why a POSA would seek to combine Armor with Huang. EX2014, ¶110. Armor describes image analysis that relies on users (e.g., physicians) to manually mark circular regions of interest. *See* EX1007, [0096]; EX2014, ¶110. Armor does not contemplate the shortcomings of a manual image analysis approach, let alone the particular shortcomings in situations where images are repeatedly obtained and analyzed over the course of multiple visits (which is where the '141 Patent's insights into combining automated machine learning-based analysis with cloud-based systems are especially powerful). EX2014, ¶110. Neither Maier nor Huang appear to appreciate this point. EX2014, ¶110. Thus, Maier, Huang, and Armor fail to render limitation (g) of claim 1 obvious. EX2014, ¶111. The Petition appears to take for granted that Armor would be combined in such a network-based system as recited in claim 1 and described in the '141 Patent. The Petition thus glosses over the fact that Armor appears directed to conventional workstations, in contrast with the '141 Patent's network-based approach which includes databases of patient image data to facilitate monitoring patient's cancer. As explained above, these terms (e.g., "network-based system" and "database") have particular constructions and, among other things, combine with other elements that work together to provide a comprehensive solution for physicians to diagnose, monitor, and evaluate treatment efficacy for cancer patients. *Supra*, Section IV.

Since this same limitation appears in independent claims 24 and 32-35, the Petition also fails to carry its burden to show that a POSA would have had a motivation to combine Maier, Huang, and Armor to achieve this same limitation in claims 24 and 32-35. EX2014, ¶112. The Petition thus also fails to carry its burden for claims 24 and 32-35.

iii. Maier and Huang do not disclose or render obvious "using the composite image to geographically identify…" as recited in claims 1, 24, and 32-35.

Limitation (h) of claim 1 is directed to "**using the composite image to geographically identify** a 3D boundary for each of one or more regions of imaged tissue within the nuclear medicine image[.]" Pet., 31-32 (emphasis added); EX2014, ¶113; claims 24, 32-35 (similar). The Petition argues that Maier and Huang render this limitation obvious because "Maier teaches that its processor analyzes medical images," and "while Maier does not teach automatic analysis of a composite image, Huang teaches this, and a POSITA would have found it obvious to combine these references to arrive at this claim limitation." Pet., 31. However, for at least three reasons, the Petition fails to establish that a POSA would have been motivated to combine Maier and Huang with a reasonable expectation of success. EX2014, ¶113.

First, contrary to the Petition's contention, Huang does not disclose this limitation. The Petition claims that "Huang trains 'discriminative classifiers and detectors' to analyze [CT, PET, and composite PET/CT] images, including creating '3D bounding boxes' of organs." Pet., 31-32. But Huang's "discriminative classifiers" do not segment organs and do not identify a 3D boundary for tissue regions. EX2014, ¶114; *see also id.*, ¶36. Instead, Huang's classifiers are binary – they take an entire image (which may be a rectangular patch of a larger image) as input and classify the input image as either (i) a positive example of the landmark (essentially any anatomical point or structure of interest) (i.e., the landmark is in the image) or (ii) a negative example of the landmark (i.e., the landmark is not in the image). EX2014, ¶114; *see also* EX1006, [0065], [0066], [0069], [0071], and [0072]. Huang's "bounding boxes" are thus just the boundaries of a rectangular patch that was classified as containing a given landmark. EX2014, ¶114. That is not segmentation, and Huang's "bounding box" is not a 3D boundary of a tissue region. EX2014, ¶114; *see also id.*, ¶36. Segmentation requires determining a 3D boundary – i.e., a complex outline – of a given organ or bone. EX2014, ¶114; *see also id.*, ¶36. Thus, contrary to the Petition's contention, Huang does not even disclose this limitation of claim 1.

Second, as discussed above, Huang and Maier disclose fundamentally different solutions to fundamentally different types of imaging. *Supra*, 24-25;

EX2014, ¶115. The Petition argues that Huang provides "[i]mproved, organ-specific identification," but fails to explain why a POSA would be motivated to combine Huang with Maier notwithstanding that Huang focuses entirely on FDG imaging, unlike Maier. Pet., 32; EX2014, ¶115. The Petition notes that both Huang and Maier use machine learning algorithms, but the Petition cannot carry its burden to show motivation to combine by simply noting that both Maier and Huang sometimes use machine learning. *See* Pet., 33; EX2014, ¶115.

Third, the Petition does not explain why a POSA would have a reasonable expectation of success in combining Huang and Maier. EX2014, ¶116. The Petition argues that a POSA would have reasonably expected success because "Huang teaches that its system which automatically identifies hotspots is 'fast (real time), robust and accurate, and can be used as a practical application on a regular basis for hot-spot detection, segmentation, and change quantification' in fused PET/CT or SPECT/CT images." Pet., 34; EX2014, ¶116. This conclusory assertion—unsupported by any other argument—is insufficient. The question is whether a POSA would have had a reasonable expectation of success in combining the two very different references—not whether Huang considered its own invention to be fast and accurate. EX2014, ¶116. The Petition thus fails to establish a motivation to combine Huang and Maier to perform limitation (h). *Id.*

Since this same limitation appears in independent claims 24 and 32-35, the Petition also fails to carry its burden to show that a POSA would have had a motivation to combine Maier and Huang to achieve this same limitation in those claims. EX2014, ¶117. The Petition thus also fails to carry its burden for claims 24 and 32-35.

iv. Maier, Huang, and Armor do not disclose or render obvious "computing, using the nuclear medicine image with the identified 3D boundary(ies) of the one or more region(s), a value of each of one or more risk indices, each risk index value indicative of cancer state or progression in the patient," as recited in claims 1, 24, and 32-35.

Limitation (i) of claim 1 recites "computing, using the nuclear medicine image with the identified 3D boundary(ies) of the one or more region(s), a value of each of one or more risk indices, each risk index value indicative of cancer state or progression in the patient." Pet., 35; EX2014, ¶118; claims 24, 32-35 (similar). The Petition argues that "[w]hile Maier does not teach computation using a composite image, Huang teaches this," and a POSA would have found it obvious to combine Maier and Huang. Pet., 37; *see also* EX2014, ¶¶118-120.

The Petition's argument is incorrect for at least three reasons. EX2014, ¶¶118-120.

First, Huang does not fill the gap left by Maier. EX2014, ¶¶120-121. The Petition argues that Huang discloses computing risk indices using a composite image because "Huang teaches that joint-imaging modalities like PET/CT 'enable[] the computer to understand on which organs or tissue regions each hot-spot is located . . . to separate normal hotspots from pathological ones . . ..'" Pet., 38 ("A POSITA would recognize this as computing a risk index, fully as claimed."); EX2014, ¶¶120-121. Not so. Calculating a risk index involves calculating some kind of value that indicates cancer state and/or progression in a patient (as the Petition admits in its construction of "risk index" to mean "**value(s)** indicative of cancer state and/or progression…" , Pet., 11-12). EX2014, ¶¶120-121. The Petition's referenced to Huang does not describe calculation of any value (let alone one indicative of cancer state and/or progression) and the Petition does not even argue that Huang does. EX2014, ¶¶120-121. Thus, the Petition fails to show that Huang discloses this limitation.

Second, Armor does not fill the gap left by Maier and Huang because Armor does not compute risk indices "using the nuclear medicine image with the identified 3D boundary(ies)," as claimed. EX2014, ¶¶122-123. The Petition argues that "Armor discloses that uptake levels of its compounds directly correspond with a risk index, e.g., a Gleason score for tumors in the prostate," and "[a] POSITA would recognize this as computing a risk index, fully as claimed." Pet., 38; EX2014, ¶122. Again, not so. Armor never discloses how to calculate a risk index *using the nuclear medicine image with the identified 3D boundaries*. EX2014, ¶122. The paragraphs in Armor that the Petition cites disclose a "ratio of tumor uptake to background" and a "Gleason score," but do not disclose how these are being computed, and do not explain how Armor uses the nuclear medicine image with the identified 3D boundaries in that computation.[2] EX2014, ¶122.

Third, the Petition fails to explain how or why a POSA would combine the three very different references: (i) Maier, which analyzes CT images to detect emphysema, (ii) Huang, which creates CAD tools for FDG-PET images to detect tumors (but does not mention any specific cancer type and does not even mention the prostate), and (iii) Armor, which is directed to PSMA binding agents for SPECT-CT imaging (which are incompatible with PET). EX2014, ¶124. The Petition claims that "the resultant risk indices were merely applications of known mathematical calculations to PSMA-binding agent-measured uptake within an identified 3D boundary, e.g., the prostate or, specifically, a prostate tumor." Pet., 39; EX2014, ¶125. But the Petition does not explain why a POSA would have been motivated to combine the three very different references with a reasonable expectation of success. EX2014, ¶125.

Since this same limitation appears in independent claims 24 and 32-35, the Petition also fails to carry its burden to show that a POSA would have had a

[2] Gleason scores are calculated via histology, by a pathologist looking at a sample, and not by analyzing a CT or PET image directly. *See* EX2036, 2.

motivation to combine Maier, Huang, and Armor to achieve this same limitation in those claims. EX2014, ¶126. The Petition thus also fails to carry its burden for claims 24 and 32-35.

For the foregoing reasons, Maier in view of Huang and Armor does not render claims 1, 24, and 32-35 obvious. EX2014, ¶127.

b. Ground B: Maier in view of Huang and Armor, further in view of Neumaier, does not render obvious claims 6-11.

For Ground B, the Petition only alleges that Neumaier discloses "PSMA-specific PET tracers such as [^{18}F]DCFPyL," but otherwise relies on Maier, Huang, and Armor for every other element of claims 6-11. Pet., 56-60. EX2014, ¶128. The Petition does not contend that Neumaier discloses any other limitations of those claims. *Id.* Accordingly, for at least the reasons above, Maier, Huang, Armor, and Neumaier fail to render claims 6-11 obvious. *See id.*

c. Ground C: Maier in view of Huang and Armor, further in view of Cardinale and/or Giesel, does not render obvious claims 6 and 12.

For Ground C, the Petition only alleges that Cardinale and Giesel "are both directed to the radiotracer ^{18}F-PSMA-1007," but otherwise relies on Maier, Huang, and Armor for every other element of claims 6 and 12. Pet., 60-63; EX2014, ¶129. The Petition does not contend that Cardinale or Giesel disclose any other limitations of those claims. EX2014, ¶129. Accordingly, for at least the reasons above, Maier, Huang, Armor, and Neumaier fail to render claims 6 and 12 obvious. *See id.*

d. Ground D: Huang in view of Armor and Maier does not render obvious claims 27 and 31.

Huang in view of Armor and Maier fails to render claims 27 and 31 obvious for several reasons. Patent Owner addresses each reason in turn.

i. Huang and Armor do not disclose or render obvious tracking risk indices that are indicative of "prostate cancer state or progression" "over a course [of] prostate cancer progression and treatment," as recited in claims 27 and 31.

Limitations (b)(2) and (c) of claim 27 recite "tracking determined values of the one or more risk indices over a course [of] **prostate cancer progression and treatment for the patient**," and "for each of the one or more patient(s), storing, by the processor, the determined values of the one or more risk indices, each indicative of **prostate cancer state or progression** . . .." Pet., 66-67 (emphasis added); EX2014, ¶130; claim 31 (similar). The Petition argues that Huang alone, or with Armor, discloses this limitation. The Petition relies on cross-references to its arguments for limitation 1(i) and dependent claim 2, "addressed in Sections VIII.B.1.j) and VIII.B.2." Pet., 66-67.

The Petition's argument fails for two reasons. First, dependent claim 2 does not recite a risk index indicative of prostate cancer state or progression, nor does dependent claim 2 recite tracking determined values of risk indices ***over a course of prostate cancer progression and treatment for the patient*** as recited in these claims. EX2014, ¶130. With regard to claim 2, the Petition only states: "While Maier does not teach tracking using a composite image, Huang and Armor teach this, and a POSITA would have found it obvious to combine these references to arrive at this claim limitation." Pet., 40; EX2014, ¶130. There is no mention of, for example, tracking ***over a course of prostate cancer progression and treatment for the patient.*** EX2014, ¶130. Second, Huang alone does not disclose this limitation because Huang fails to disclose prostate cancer or prostate generally. *See id.* Therefore, the Petition fails to carry its burden to establish a reasonable likelihood that Huang and Armor render this limitation obvious. *See id.*

ii. Maier, Huang, and Armor do not render obvious a "Prostate Specific Membrane Antigen (PSMA) binding agent…" as recited in claims 27 and 31.

Limitation (e) of claim 27 recites medical images comprising "a CT scan overlaid with a nuclear medicine image acquired at a substantially same time as the CT scan and following administration to the patient of an **imaging agent comprising a Prostate Specific Membrane Antigen (PSMA) binding agent comprising a radionuclide** . . .." Pet., 68 (emphasis added); EX2014, ¶131; claim 31 (similar). The Petition cross-references its arguments for this limitation from limitation (g) to claim 1. Pet., 68; EX2014, ¶131. For the reasons explained in Section VII.a.ii, the cited references fail to render this limitation obvious. *Supra*, 26-30; EX2014, ¶131.

iii. Huang does not disclose or render obvious "using the composite image to geographically identify a 3D boundary . . . " as recited in claims 27 and 31.

Limitation (f) of claim 27 recites "using the composite image to geographically identify a 3D boundary for each of one or more region of imaged tissue within the nuclear medicine image." Pet., 68-69; EX2014, ¶132; Claim 31 (similar). The Petition argues Huang discloses this limitation and that it is "substantively identical" to the similar limitation (h) in claim 1. Pet., 69; EX2014, ¶132. Accordingly, for the reasons explained in Section VII.a.iii, Huang does not disclose this limitation. *Supra*, 30-33; EX2014, ¶132.

iv. Huang, Armor, and Maier do not disclose or render obvious "computing the value of each of the one or more risk indices using the nuclear medicine image with the identified 3D boundary(ies) of the one or more region(s)," as recited in claims 27 and 31.

Limitation (g) of claim 27 recites "computing the value of each of the one or more risk indices using the nuclear medicine image with the identified 3D boundary(ies) of the one or more region(s)." Pet., 69; EX2014, ¶133; Claim 31 (similar). The Petition alleges Huang discloses this claim limitation, and Huang in view of Armor and Maier renders it obvious because it is "substantively identical" to the similar limitation (i) in claim 1. Pet., 69; EX2014, ¶133. Accordingly, for the reasons explained in Section VII.a.iv, the cited references fail to render this limitation obvious. *Supra*, 33-36; EX2014, ¶133.

e. Ground E: Huang in view of Armor and Maier, further in view of Giesel and Weineisen, does not render obvious claims 28-30.

For Ground E, the Petition only alleges that Giesel and Weineisen teach elements specific to dependent claims 28-30, but otherwise relies on Huang, Armor, and Maier for every other element of independent claim 27 (from which claims 28-30 depend). Pet., 70-74; EX2014, ¶135. The Petition does not contend that Giesel or Weineisen disclose any other limitations of those claims. EX2014, ¶135. Accordingly, for at least the reasons above, Huang, Armor, Maier, Giesel, and Weineisen fail to render claims 28-30 obvious. EX2014, ¶135.

VIII. CONCLUSION

For all the foregoing reasons, the Board should deny institution of the Petition.

Respectfully submitted,

Date: July 14, 2025

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

I hereby certify that the foregoing complies with the type-volume limitation of 37 C.F.R. § 42.24 and contains 9,255 words based on the word count indicated by the word-processing system used to prepare the paper, excluding the table of contents, table of authorities, mandatory notices under 37 C.F.R. § 42.8, certificate of service, certificate of word count, appendix of exhibits, and claim listing.

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<u>CERTIFICATE OF SERVICE</u>

The undersigned hereby certifies that the foregoing **PATENT OWNER'S PRELIMINARY RESPONSE** was served electronically in its entirety on July 14, 2025 via electronic mail to the following attorneys of record:

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