

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

MIM SOFTWARE INC.,
Petitioner,

v.

EXINI DIAGNOSTICS AB,
Patent Owner.

IPR2025-00827
U.S. Patent No. 11,941,817

DECLARATION OF MILAN SONKA, PH.D.

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PATENT OWNER'S EXHIBIT LIST

EXHIBIT	DESCRIPTION
EX2001	Defendant's Memorandum of Law in Support of its Motion to Stay Pending <i>Inter Partes</i> Review, <i>Progenics Pharmaceuticals v. MIM Software Inc.</i> , Civil Action No. 1:24-cv-10437-PBS, Dkt. 89, Apr. 8, 2025.
EX2002	MIM's Invalidity and Noninfringement Contentions, Civil Action No. 1:24-cv-10437-PBS.
EX2003	PACER Docket, <i>Progenics Pharmaceuticals v. MIM Software Inc.</i> , Civil Action No. 1:24-cv-10437-PBS (as of June 30, 2025).
EX2004	Defendant's Motion to Dismiss the Second Amended Complaint, <i>Progenics Pharmaceuticals v. MIM Software Inc.</i> , Civil Action No. 1:24-cv-10437-PBS, Dkt. 43, June 17, 2024.
EX2005	Motion to Dismiss Hearing Transcript (excerpted pp. 1, 4-6), <i>Progenics Pharmaceuticals v. MIM Software Inc.</i> , Civil Action No. 1:24-cv-10437-PBS, Oct. 8, 2024.
EX2006	Order Granting in Part and Denying in Part Defendant's Motion to Dismiss the Second Amended Complaint, <i>Progenics Pharmaceuticals v. MIM Software Inc.</i> , Civil Action No. 1:24-cv-10437-PBS, Dkt. 72, Jan. 14, 2025.
EX2007	Motion to Stay Hearing Transcript (excerpted pp. 1, 5-6), <i>Progenics Pharmaceuticals v. MIM Software Inc.</i> , Civil Action No. 1:24-cv-10437-PBS, May 12, 2025.
EX2008	Order Granting in Part and Denying in Part Defendant's Motion to Stay Pending <i>Inter Partes</i> Review, <i>Progenics Pharmaceuticals v. MIM Software Inc.</i> , Civil Action No. 1:24-cv-10437-PBS, Dkt. 102, May 13, 2025.
EX2009	Scheduling Order, <i>Progenics Pharmaceuticals v. MIM Software Inc.</i> , Civil Action No. 1:24-cv-10437-PBS, Dkt. 85, Mar. 5, 2025.
EX2010	U.S. District Courts, Judicial Caseload Profile 2024 (D. Mass. excerpted).
EX2011	<i>Cancer Control Month, 2025 – The White House</i> (Apr. 3, 2025).
EX2012	<i>NIH Strategic Plan for Data Science FY 2025-2030</i> , Nat'l Institutes of Health.

EXHIBIT	DESCRIPTION
EX2013	Rowe, S.P. et al., <i>PET Imaging of Prostate-Specific Membrane Antigen in Prostate Cancer: Current State of the Art and Future Challenges</i> , Prostate Cancer & Prostatic Diseases (2016).
EX2014	Declaration of Dr. Milan Sonka.
EX2015	Curriculum Vitae of Dr. Milan Sonka.
EX2016	RESERVED
EX2017	Crisan, et al., <i>Radiopharmaceuticals for PET and SPECT Imaging: A Literature Review over the Last Decade</i> , International Journal of Molecular Sciences 23(9):5023 (2022).
EX2018	<i>PET Scans</i> , CancerQuest, Emory Winship Cancer Institute (2025).
EX2019	Rowe, S.P., et al., <i>PSMA-Based [¹⁸F]DCFPyL PET/CT Is Superior to Conventional Imaging for Lesion Detection in Patients with Metastatic Prostate Cancer</i> , Molecular Imaging and Biology 18(3):411-419 (2016).
EX2020	<i>FDA Approves First PSMA-Targeted PET Imaging Drug for Prostate Cancer</i> , Oncology Practice Management (2020).
EX2021	<i>FDA Approves Second PSMA-Targeted PET Imaging Drug for Men with Prostate Cancer</i> , Food and Drug Administration (2021).
EX2022	<i>Atlas-Based vs. AI Auto-Contouring in Clinical Practice</i> , MIM Software Inc. (2023).
EX2023	Brown, <i>Machine Learning, Explained</i> , MIT Sloan (Apr. 21, 2021).
EX2024	RESERVED
EX2025	Krizhevsky, et al., <i>ImageNet Classification with Deep Convolutional Neural Networks</i> , Advances in Neural Information Processing Systems 25 (2012).
EX2026	Deng, et al., <i>ImageNet: A large-scale hierarchical image database</i> , IEEE Conference on Computer Vision and Pattern Recognition (2009).
EX2027	Bushberg, J.T., et al., <i>The Essential Physics of Medical Imaging</i> (2012), Ch. 1, Sec. 1.1, pp. 3-15.
EX2028	Bushberg, J.T., et al., <i>The Essential Physics of Medical Imaging</i> (2012), Ch. 3, Sec. 3.1, pp. 33-38.

EXHIBIT	DESCRIPTION
EX2029	Kelleher, <i>Deep Learning</i> (2019), Ch. 1, “What Is Machine Learning?,” pp. 9-17.
EX2030	Kelleher, <i>Deep Learning</i> (2019), Ch. 1, “The Key Ingredients of Machine Learning,” pp. 22-30.
EX2031	Kelleher, <i>Deep Learning</i> (2019), Ch. 3, “Neural Networks: The Building Blocks of Deep Learning,” pp. 65-67.
EX2032	Kelleher, <i>Deep Learning</i> (2019), Ch. 4, “The Era of Deep Learning,” pp. 143-145.
EX2033	Kelleher, <i>Deep Learning</i> (2019), Ch. 4, “Layer-Wise Pretraining Using Autoencoders,” pp. 145-148.
EX2034	Kelleher, <i>Deep Learning</i> (2019), Ch. 4, “Weight Initialization and ReLU Activation Functions,” pp. 148-153.
EX2035	Kelleher, <i>Deep Learning</i> (2019), Ch. 4, “The Virtuous Cycle: Better Algorithms, Faster Hardware, Bigger Data,” pp. 153-156.

I, Milan Sonka, hereby declare as follows:

I. INTRODUCTION

1. I have been retained by Progenics Pharmaceuticals, Inc. (“Progenics”) to provide expert opinions in this *Inter Partes* Review (IPR). I am being compensated for my time at my customary rate of \$715 per hour for my work on this matter. I am being paid for my time regardless of the outcome of this IPR. Beyond the compensation I received for my time in this matter, I will not be affected in any way, positively or negatively, by the outcome of this case.

II. QUALIFICATIONS

2. I am Professor of Electrical and Computer Engineering in the College of Engineering at the University of Iowa. I also hold the Lowell C. Battershell Chair in Biomedical Imaging, am the co-director of the Iowa Institute for Biomedical Imaging, and am the Director of the Iowa Initiative for Artificial Intelligence. I also hold secondary appointments at the University of Iowa in the Applied Mathematical and Computational Sciences, Ophthalmology and Visual Sciences, Radiation Oncology, and Biomedical Engineering departments.

3. I earned my Ph.D. in Technical Cybernetics-Digital Image Analysis from the Czech Technical University of Prague in 1983.

4. I was an Assistant Professor at the Czech Technical University of Prague from 1984-1990, before moving to the University of Iowa, where I have been a professor since 1990.

5. For the past 35 years, as the head of a research group at the University of Iowa, I have researched and developed techniques for semi-automated and automated analysis of medical images, including foundational research in quantitative medical image analysis and medical image segmentation, and development of artificial intelligence (AI) and machine learning (ML) techniques for prediction of disease outcomes and image analysis.

6. I was elected as a Fellow of the Institute of Electrical and Electronics Engineers (IEEE) in 2002 for my contributions to medical image analysis and computer vision. I am also a Fellow of the American Institute for Medical and Biomedical Engineering, a Fellow of the Medical Image Computing and Computer-Aided Intervention Society, and a Fellow of the National Academy of Inventors.

7. My curriculum vitae is provided herewith as EX2015.

III. MATERIALS CONSIDERED

8. In forming my opinions, I have read U.S. Patent No. 11,941,817 (the “817 Patent”) (EX1001) and reviewed relevant parts of its prosecution history. I have also reviewed the Petitioner’s Petition for *Inter Partes* Review (IPR) dated April 4, 2025 (the “Petition”) along with the accompanying Declaration of Dr. Rosen

(EX1002). I have also reviewed the following references, which the Petitioner cited in their Petition against the '817 Patent:

- U.S. Patent Application Publication No. 2012/0123253 (“Renisch”) (EX1005);
- U.S. Patent Application Publication No. 2011/0007954 (“Suehling”) (EX1006);
- U.S. Patent No. 10,140,544 (“Zhao”) (EX1007);
- U.S. Patent Application Publication No. 2018/0144828 (“Baker”) (EX1008);
- Eiber, “Prostate Cancer Molecular Imaging Standardized Evaluation (PROMISE): Proposed miTNM Classification for the Interpretation of PSMA-Ligand PET/CT,” The Journal of Nuclear Medicine 59(3):469-478 (March 2018) (“Eiber”) (EX1009).

9. I have also reviewed other references that illuminate the state of the art as of January 7, 2019, which I have been instructed to use as the “priority date” of the '817 Patent. I have also called upon my extensive knowledge and experience in the field of medical imaging, medical image analysis, and artificial intelligence and machine learning.

10. I reserve the ability to review documents, deposition transcripts, or other information provided to me after the date of this Declaration and to supplement my opinions based upon such review.

IV. LEGAL PRINCIPLES

11. I have been informed of the following legal standards by Patent Owner's attorneys. I am not an attorney, but I have applied these understandings in my analysis herein.

A. Priority Date

12. I have been instructed to assume for purposes of my analysis that January 7, 2019, is the "priority date" for assessing the state of the art and for determining what is "prior art" when considering whether the claims of the '817 Patent would have been obvious.

B. A Person of Ordinary Skill in the Art

13. I have been asked to develop and offer opinions related to how a person of ordinary skill in the art ("POSA") would have understood the '817 Patent and the relevant references cited herein as of the priority date (January 7, 2019).

14. I have been informed and understand that certain factors may be considered in determining the level of ordinary skill in the art, for example, (1) the types of problems encountered in the art, (2) the prior art solutions to these problems, (3) the rapidity with which innovations are made, (4) the sophistication of the technology, and (5) the educational level of active workers in the field.

15. It is my opinion that a POSA for purposes of the '817 Patent 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.

16. I consider myself to be at least a POSA and to have been at least a POSA as of the priority date, January 7, 2019.

C. Claim Construction

17. I have been informed and understand that, in an IPR proceeding, the claims of a patent are to “be construed using the same claim construction standard that would be used to construe the claim in a civil action under 35 U.S.C. § 282(b), including construing the claim in accordance with the ordinary and customary meaning of such claim as understood by one of ordinary skill in the art and the prosecution history pertaining to the patent.” 37 C.F.R. § 42.100(b).

18. Specifically, I have been informed and understand that under the standard set forth in *Phillips v. AWH Corp.*, 415 F.3d 1303 (Fed. Cir. 2005) (*en banc*), the claims of a patent are given their ordinary and customary meaning as would be understood by a POSA at the time of the invention. I have been informed that a *Phillips* construction of a claim is based on the entire record, including both intrinsic evidence (*i.e.*, the claims, specification, and prosecution history) as well as extrinsic evidence (*e.g.*, dictionary definitions and expert testimony). I have applied this standard in formulating my opinions in this matter.

19. I reserve the right to supplement my opinions in view of any additional information regarding the interpretation of the claims of the '817 Patent that becomes available to me and any matters raised by the parties, the Board, and/or other experts in this matter.

D. Novelty and Non-Obviousness

20. I have been informed that to be valid patent claims must be novel and nonobvious. 35 U.S.C. §§ 102 and 103.

21. I have been informed that a patent claim is not novel if it is anticipated by a prior art reference. I have been informed that in order for a prior art reference to anticipate a claim, that prior art reference must disclose each and every limitation as set forth in the claim.

22. I have been informed and understand that a patent claim is obvious if the differences between what is set forth in the claims and what is disclosed in the prior art are such that what is claimed would have been obvious to a POSA as of the patent's priority date (January 7, 2019 in the case of the '817 Patent). I have been informed and understand that a POSA is presumed to have knowledge of all of the relevant art as of the priority date. I have further been informed and understand that as part of the analysis of whether a patent claim is obvious, I should consider: (a) the scope and content of the prior art; (b) the level of ordinary skill in the art; (c) the

differences between what is claimed and the prior art; and (d) any secondary considerations that may indicate that the claim is not obvious.

23. I have been informed and understand that obviousness can be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so; and that a reasonable expectation of success in achieving the subject matter of the claim at issue must also be shown. Further, I have been informed and understand that the teaching, suggestion, or motivation test is flexible and that an explicit suggestion to combine the prior art is not necessary – the motivation to combine may be implicit and may be found in the knowledge of one of ordinary skill in the art, from the nature of the problem to be solved, market demand, or common sense. In undertaking an obviousness analysis, I have been informed and understand that I may take into account the inferences and creative steps that a person of ordinary skill would have employed in reviewing the prior art at the time of the invention. If the claimed invention combines elements known in the prior art and the combination yields results that would have been predictable to a person of ordinary skill at the time of the invention, then this evidence would make it more likely that the claim was obvious.

24. I have been informed and understand that an obviousness analysis must also take into account any “secondary considerations” or, as they are sometimes

called, objective indicia of non-obviousness. These secondary considerations can include: (i) a long-felt but unsolved need for the solution provided by the patent claim; (ii) unexpected results that arise from what is provided in the patent claim; (iii) unsuccessful attempts by others to find the solution provided by the patent claim; (iv) industry skepticism regarding what is provided in the patent claim; (v) praise from others in the field; (vi) commercial success of a product due to the merits of what is provided in the patent claim; and (vii) copying by others of what is claimed in the patent. I further understand that a “nexus” must exist between the claimed invention and the evidence proffered on secondary considerations. Such secondary considerations, when present, offer objective information as to the state of the art at the time of the invention and provide a check to hindsight analysis.

V. TECHNOLOGY BACKGROUND

25. The '817 Patent is generally directed to computer-implemented methods and systems for analyzing medical images that facilitate decision making in the context of cancer diagnosis, monitoring, and treatment. As such, in order to frame my analysis and provide the proper context for my opinions, I provide the following overview of relevant technology at issue in this Petition.

A. Medical Imaging Techniques

26. Medical imaging (e.g., image acquisition) technologies provide a valuable way to detect and monitor disease in a non-invasive fashion. There are many

different medical imaging techniques (or “modalities”), each relying on different physical mechanisms to create images and having different benefits and shortcomings. EX2027, 3. Often images produced by different types of medical imaging modalities convey different information. Accordingly, multiple different types of images may be acquired and relied on, for example by physicians, to make decisions about patient diagnosis, treatment, and prognosis.

27. For example, anatomical imaging modalities are a class of imaging techniques that produce images showing detailed anatomical structures, like organs and bones, within a patient. More specifically, intensity variations (e.g., light and dark regions) within anatomical images typically reflect the differences in physical properties of various tissue regions within a patient’s body, which, in turn, impact the way tissue absorbs, reflects, or otherwise interacts with electromagnetic radiation (e.g., x-rays), magnetic fields, or pressure waves. Examples of anatomical imaging techniques are computed tomography (CT), magnetic resonance imaging (MRI), and ultrasound (US).

28. Functional imaging techniques, on the other hand, reflect physiological properties and activity in a subject. They are often acquired using molecular probes administered to the subject and have intensity variations that reflect a spatial distribution of a probe within an imaged portion of the subject.

29. Nuclear medicine images are a type of functional image. EX2027, 11. Examples of nuclear medicine images include positron emission tomography (PET) images and single photon emission tomography (SPECT) images. EX2027, 14. PET and SPECT images are three-dimensional images.

30. Each of these nuclear medicine images is obtained by administering a specific type of probe – namely, a radiolabeled imaging agent, referred to as a radiopharmaceutical, containing a radioactive isotope, referred to as a radionuclide – to a patient. EX2027, 11. The radiopharmaceutical distributes throughout the patient’s body and, as explained further below, often selectively concentrating in regions associated with or exhibiting a particular molecular behavior, which, in turn, may be indicative of disease. Images are formed by detecting radiation emitted by the radionuclide as it decays, from within the patient. Accordingly, rather than conveying information that directly reflects the physical structures and properties of tissue within a patient, nuclear medicine images map the spatial distribution of radiopharmaceutical within the patient and thus relay information about tissue molecular properties or function.

31. The composition of a given radiopharmaceutical dictates (i) the type of nuclear medicine imaging modality with which it is compatible and (ii) the manner in which the radiopharmaceutical distributes throughout a patient’s body and, thus, the particular types and stages of disease for which it serves as a useful probe.

32. In particular, the radioactive decay properties of the radionuclide component of a radiopharmaceutical determine the specific imaging modality with which it can be used. PET imaging detects radioactive decay that results in positron emission,¹ and thus relies on radionuclides that are short half-life positron-emitting isotopes, such as carbon-11 (¹¹C) and fluorine-18 (¹⁸F), as well as gallium-68 (⁶⁸Ga). EX2017, 2, 11. SPECT imaging, on the other hand, detects the direct emission of gamma radiation and use gamma-emitting radionuclides, such as ^{99m}Tc, ¹²³I, ¹³¹I, ¹¹¹In, ⁶⁷Ga, ²⁰¹Tl, ^{81m}Kr, ¹³³Xe. *Id.*, 4.

33. The manner in which an administered radiopharmaceutical is distributed throughout a patient depends upon the particular radiopharmaceutical and the patient's physiological status. For example, the radiopharmaceutical fluorodeoxyglucose (FDG) is an ¹⁸F-labeled form of glucose and thus concentrates most heavily in tissue with high metabolic activity. EX2018, 3. Since cancer cells

¹ In a PET scanner, positron emission is detected by observing/measuring a characteristic byproduct of positron emission – specifically, simultaneously emitted and oppositely directed pairs of photons (gamma rays) that result from the annihilation of a positron-electron pair – as opposed to the positrons themselves. *See, e.g.*, EX2028, 37.

are typically characterized by higher metabolic activity than surrounding normal cells, PET images acquired with FDG can be used to detect cancer lesions, which typically appear as “hot spots” within images. *Id.*, 4. FDG, however, is not specific to cancer, and may also be absorbed by other cells with high metabolic activity, including areas of inflammation and infection. *Id.* FDG is also limited in its ability to detect slower growing cancers, which absorb less glucose. *Id.* Other radiopharmaceuticals, like F-18 sodium fluoride (^{18}F -NaF) and $^{99\text{m}}\text{Tc}$ -methyl diphosphonate ($^{99\text{m}}\text{Tc}$ -MDP) tend to accumulate within new bone and were used to detect bone metastases. Like FDG, however, these tracers target cancer cells indirectly, via the propensity of cancer cells to divide rapidly, and thus are also limited in their sensitivity and specificity.

34. Around the time of the '817 Patent's priority date (2019), new imaging agents were being researched and developed. EX2019, 412, 419. Among these new imaging agents, PSMA targeting radiopharmaceuticals were being assessed for their clinical utility to detect and stage prostate cancer. PSMA binding agents are different from the aforementioned agents, like FDG, in that they expressly target, and bind to molecular targets – proteins – that are overexpressed on certain cancer cells. They thus provide improved sensitivity and specificity. The first small-molecule PSMA

inhibitors² would ultimately obtain approval from the Food and Drug Administration (FDA) for PET imaging only in late 2020 and mid-2021 (after the priority date of the '817 Patent). EX2013, 1; EX2020, 1; EX2021, 1.

B. Image Analysis

35. While radiologists and physicians have various medical imaging modalities and techniques at their disposal, the selection of exactly which types of images to obtain, and exactly how to interpret one or more of these images is not straightforward. 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 often subjective, varying from physician to physician. In efforts to facilitate and standardize medical image analysis, researchers in the image

² The first molecular imaging agent targeting PSMA was an indium-111-labeled monoclonal antibody (ProstaScint®), which could be used for SPECT (not PET) imaging, but suffered from a number of intrinsic limitations that made it an ultimately unsuccessful agent. EX2013, 1. The two small-molecule PSMA inhibitors that have ultimately obtained FDA approval for PET – ⁶⁸Ga-PSMA-11 and [¹⁸F]DCFPyL – only obtained FDA approval in 2020 and 2021, respectively. EX2020, 1; EX2021, 1.

processing and computer vision fields have sought to develop computer algorithms that automate various tasks associated with medical image analysis.

36. Conventional image analysis techniques aim to craft a detailed series of step-by-step instructions for computers to follow in order to, for example, classify whether an image contains a particular object, like a lesion – referred to as “classification” or “object detection,” or to delineate complex boundaries of certain structures of interest within an image – referred to as “segmentation.”

37. For example, a simple conventional image segmentation technique is thresholding, whereby regions of an image are identified as part of one object or another based on whether their intensity values are above or below a particular threshold value or lie within a given range. EX1016, 7. This simple approach is best suited to segmenting objects that have uniquely high or low intensity values in an image, such as bones which tend to appear brighter in CT images than soft-tissue, and, even so, selection of proper threshold values may be challenging, and performance may be impacted by image variability and presence of artifacts. EX1016, 7.

38. Another common conventional image segmentation technique is atlas-based segmentation. Atlas image segmentation relies on one or more templates, referred to as atlas images, in which various structures of interest, like organs or bones, have been manually delineated. When a new image of a patient is received,

one of the atlas images is registered with the new patient image, and the manually delineated contours from the atlas image are transferred to the new patient image. Atlas-based segmentation continues to be used in medical image analysis products today, even as newer techniques have been developed. *See* EX2022, 1.

C. Deep Learning and Convolutional Neural Networks

39. Machine learning techniques are different from conventional computer programs. Machine learning generally refers to the development and use of algorithms that allow computers to extract, or “learn,” desired functionality from datasets in an automated fashion. EX2023, 1; EX2029, 11. Thus, machine learning algorithms do not require a human programmer to explicitly create a detailed series of instructions for the computer to follow to perform a specific task. *Id.* Instead, machine learning algorithms involve a two-step process comprising a training phase and an inference phase. EX2029, 12. During training, examples from a training dataset are repeatedly provided to a computational model, the parameters of which are refined to optimize performance on a specified task (and on examples from the training dataset) according to desired behavior or output (like labeling an image as depicting a dog, cat, etc.). *Id.* During inference, once trained, the (trained) computational model can be provided with new data not previously included in the training dataset and generate output reflecting the trained model’s predictions based on information derived from the new input data. *Id.*, 14.

40. Machine learning algorithms can be trained (e.g., can “learn”). Supervised machine learning algorithms are trained using labeled datasets. EX2023, 4; EX2030, 26. In labeled datasets, each example is labeled with the desired output (e.g., “ground truth”) that the machine learning algorithm is intended to reproduce. EX2030, 26.

41. There are also different computational models that can be used in connection with, and optimized via, machine learning techniques. These include simpler statistical models, like models based on Bayes’ theorem (e.g., Naïve Bayes’ classifiers), and more complex models, like neural networks.

42. While the term “neural network,” is, today, closely associated with machine learning, machine learning and neural networks are distinct terms and convey different ideas. That is, as explained above, machine learning refers to the development and use of algorithms that allow computers to extract, or “learn,” functions from datasets in an automated fashion.

43. A neural network, however, is a particular computational model inspired by the structure of a human brain. EX2031, 65. In this model, the weights of each neuron’s excitations in a neural network can be used as adjustable parameters. While the weights can be determined using machine learning, the term “neural network” is distinct from the term “machine learning.” A neural network is a type of

model, whereas machine learning refers to algorithms that allow computers to extract, or “learn,” functions from datasets in an automated fashion. EX2023, 1.

44. Conventional artificial neural networks are shallow – they do not have many hidden layers. Before the confluence of multiple breakthroughs in the 2010’s, this was generally viewed as a requirement for any practical application, because multiple hidden layers were challenging and impractical to train. *See* EX2032, 143.

45. An important implication of the restriction to shallow neural networks is that conventional neural networks are not able to operate efficiently directly on raw, low-level data, like image pixels. EX2030, 23; EX1018, 1. Instead, they operated on limited and predefined sets of “handcrafted” features that could be extracted from raw low-level data. EX2030, 23-24; EX1018, 1. For example, a shallow neural network tasked with classifying an image would not operate directly on the image itself, but, instead, would require a pre-processing routine to extract features (things like a maximum intensity, variance in image intensity, a relative weight of different colors, etc.) from the image that, in turn, would be fed as input to the neural network. The task of designing sets of handcrafted features that would allow neural networks to effectively perform various desired tasks was a challenging, labor intensive, and highly subjective process that relied on human expertise. EX2030, 23, 30. As a result, ultimately, traditional shallow neural networks failed to lead to commercially viable levels of performance and practical accuracy.

46. Deep-learning techniques (i) use neural networks with many hidden layers (hence, deep) and (ii) train them to learn complex patterns from data, including raw or low-level data (like image pixels or voxels). In doing so, deep-learning methods overcome key challenges that made conventional neural networks impractical.

47. Before 2012, deep learning algorithms were not considered viable for certain imaging applications. Limitations in learning algorithms, computational power, computer hardware, and the availability of sufficiently large datasets made training neural networks with multiple hidden layers impractical. EX2032, 143. Only in 2012, the confluence of (i) new algorithmic approaches, (ii) hardware improvements, and (iii) the creation of and access to large, labeled datasets that could be used paved the way for a breakthrough. In particular, on the algorithm side, new techniques like Glorot initialization, rectified linear units (ReLU's), and dropout techniques, greatly improved the ability to train deep neural networks. EX2034, 152. In terms of hardware, training was also dramatically improved via the discovery that graphical processing units (GPUs) could be used to train neural networks much more efficiently than conventional computer processing units (CPUs), which was made widely accessible via NVIDIA's release of its CUDA programming language in 2007. EX2035, 153-154. Finally, the ImageNet database, created via a massive crowdsourcing effort, provided a huge hierarchical repository of millions of labeled

images that could be used to train supervised image classifiers. EX2025, 1; EX2026, Abstract. By taking advantage of new algorithms, improved hardware capabilities, and the large ImageNet database, a convolutional neural network (CNN), referred to as AlexNet was able to achieve record performance on the ImageNet Large Scale Visual Recognition Challenge (ILSVRC). EX2025, Abstract, 7-8. This December 2012 report is now considered a watershed moment that led to the use of deep learning for certain image analysis tasks such as basic image classification (also called automated image labeling). EX1018, 2.

48. While the performance of the AlexNet CNN spurred interest in deep learning techniques, the AlexNet report demonstrated performance of a CNN on an image classification task. EX2025, Abstract, 7. That is, given an example image, the AlexNet CNN was tasked with outputting a label for the image – i.e., “mite,” “container ship,” etc. (as shown in Fig. 1, below). EX2025, Figure 4. It would take several more years for deep learning techniques like CNNs to be developed for performance on the more challenging task of image segmentation – which requires delineating complex boundaries of objects within an image. EX1018, 5-6. Namely, neural network architectures that could adequately avoid degradations in resolution when performing segmentation would not appear until around 2015, when the U-net architecture was proposed. EX1018, 5-6.

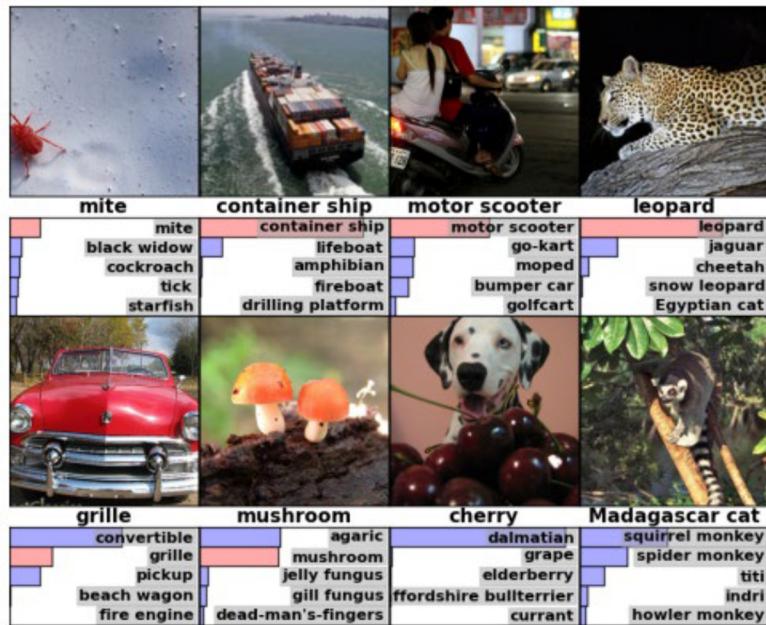


Fig. 1 Example test images and the five most probable labels for each predicted by the AlexNet CNN. EX2025, Figure 4.

49. Around 2016 and thereafter, deep learning approaches like CNNs started to be used for practical applications as their utility began to be better understood for image segmentation.

VI. THE PRIOR ART

A. Renisch

50. Renisch discloses “diagnostic imaging systems and methods” for analyzing PET/CT images on a dedicated computer workstation. EX1005, [0001], [0020]. To the extent Renisch describes image segmentation, the disclosure focuses on conventional atlas-based image segmentation. EX1005, [0028] (“The segmentation unit 76 can also employ an atlas of normal anatomical structures which is mapped to the actual anatomical image.”).

B. Zhao

51. Zhao discloses a method for analyzing digital images using a processing circuitry and a predictive model with loss functions. EX1007, 1:32-62. Zhao's method is directed to segmenting individual 2D images. EX1007, 7:56-64, 8:63-9:3 ("For example, a 100-pixel by 100-pixel input, after convolution with a 5-pixel by 5-pixel feature sliding through the input with a stride of 1, the resulting feature map may be of 96 pixel by 96 pixel").

C. Baker

52. Baker discloses a network-based (e.g., cloud-based) platform and supported graphical user interface (GUI) decision-making tool for use by medical practitioners and/or their patients, for example, to aid in the process of making decisions about a course of cancer treatment and/or to track treatment and/or the progress of a disease. EX1008, [0011].

D. Eiber

53. Eiber describes a standardized reporting framework for PET/CT and PET/MRI called the molecular imaging TNM system (miTNM). EX1009, 469. Eiber's framework is designed to work with manual approaches for determining reference values for grading lesions. EX1009, 471 ("The liver SUV can be measured by placing a 3-cm-diameter circular region of interest in the normal inferior right liver lobe in the axial plane; the blood pool, by centering a 2-cm-diameter circular region of interest in the aortic arch in the axial plane; the parotid gland, by centering a 1.5-

cm-diameter circular region of interest in the right parotid gland in the axial plane; and a tumor lesion, by centering a 1-cm-diameter circular region of interest over the voxel with maximum uptake in the axial plane.”).

E. Suehling

54. Suehling discloses a method and system for detecting lesions in a 3D medical image with region-specific lesion detectors. EX1006, [0030]-[0031]. Suehling partitions a patient’s body into search regions based on detected landmarks, organs and bone structures, and detects lesions in each search region using a region-specific lesion detector. *Id.*

VII. THE ’817 PATENT AND ITS PROSECUTION HISTORY

A. The ’817 Patent

55. The ’817 Patent is directed to machine learning-based techniques for analyzing three-dimensional (3D) medical images to facilitate identification, assessment, and tracking of cancer. EX1001, 3:1-48. Among other things, the ’817 Patent describes, in detail, convolutional neural network (CNN)-based 3D image segmentation methods that can be used to identify a variety of specific target tissue volumes of interest (VOIs) within 3D anatomical images. EX1001, 31:60-32:21, 34:41-37:10, 42:5-48:41.

56. The ability to perform accurate and robust machine-learning-based 3D image segmentation as described in ’817 Patent provides advantages over previous image analysis techniques. EX1001, 3:1-48. Moreover, the CNN-based image

analysis tools described in the '817 Patent provide for full body segmentation and automated image-based analysis of cancerous lesions throughout various relevant target tissue regions throughout a subject's body. EX1001, 4:66-5:11. The machine learning-based systems and methods described in the '817 Patent thus allow for analysis of cancer at a variety of stages. *Id.* The techniques can be used to identify and stage localized disease in relevant tissue regions such as the prostate, for example for early-stage screening and monitoring, as well as to monitor regions such as bone and lymph nodes for metastasis as disease progresses. *Id.* As such, the technologies described in the '817 Patent provide a complete set of tools for automated image-based detection of cancer, and tracking disease evolution, progression, and response to treatment. *Id.*

57. One advance of the '817 Patent is the creation of a 3D segmentation map using CNN-based image segmentation of 3D anatomical images. EX1001, 31:64-32:21. The 3D segmentation map, as described in the '817 Patent, is a specific element that is created and used to represent multiple volumes of interest (VOIs) that are identified via the CNN-based segmentation techniques described therein. EX1001, 34:27-39.

58. Among other things, creation of a 3D segmentation map is significant in the context of the '817 Patent, which describes performing detailed whole-body segmentation via multiple CNN-modules that are tasked with segmenting subsets of

organs and bones in various anatomical sub-regions (e.g., as described in the '817 Patent, the specific anatomical subregion is a group of related tissue, such as a pelvic region, a chest region, a head and/or neck region, a spine region, an upper body region, a lower body region, etc.). EX1001, 6:40-42, 42:66-46:51, 34:27-29. Results of these different CNN modules can then be combined, for example, stitched together, to form a 3D segmentation map. EX1001, 49:7-10, 50:20-21; *see also, id.*, 5:37-48, 31:67-32:21, 34:27-29. This allows the complex problem of whole-body segmentation to be broken down into manageable portions that can be efficiently and accurately segmented via a collection of CNN modules, and the overall whole-body segmentation results combined in a unified fashion, via a single element. EX1001, 35:10-26, 49:7-10, 50:20-21; *see also id.*, 5:37-48, 31:67-32:21, 34:27-29. This process is illustrated, for example, in FIGs. 6A and 6B of the '817 Patent (reproduced below).

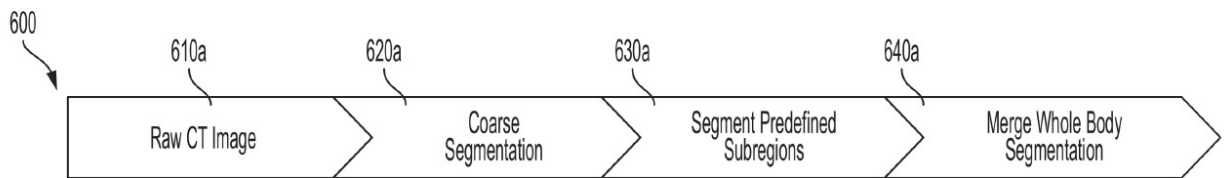


FIG. 6A

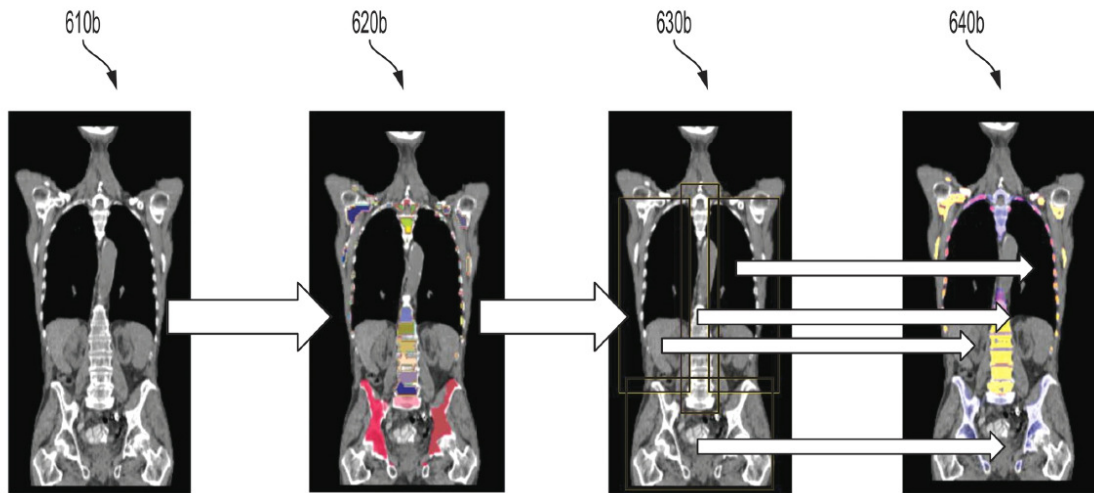


FIG. 6B

FIGs. 6A and 6B of the '817 Patent

59. As illustrated, for example in FIG. 8 of the '817 Patent (reproduced below), the 3D segmentation map provides detailed 3D information about anatomical geometry of various organs and bones within a subject. EX1001, 31:67-32:21.

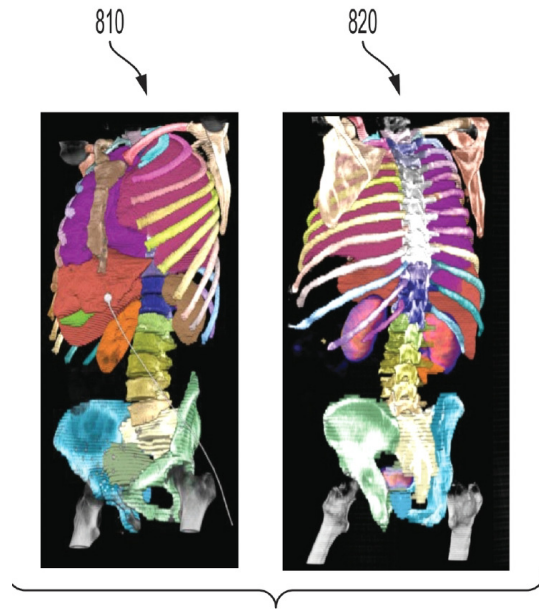


FIG. 8

FIG. 8 from the '817 Patent.

60. As described in the '817 Patent, the resultant 3D segmentation map can be used as a foundational element on which to build a variety of image analysis techniques. EX1001, 32:65-33:40. In particular, the '817 Patent describes techniques for combining the 3D segmentation map, derived from 3D anatomical images, with 3D functional images, like full PET or SPECT images, which may be acquired with a variety of different radiopharmaceuticals. EX1001, 32:65-33:40. This approach is illustrated schematically, for example, in FIG. 3 of the '817 Patent (reproduced below). *See also* EX1001, 33:65-34:3.

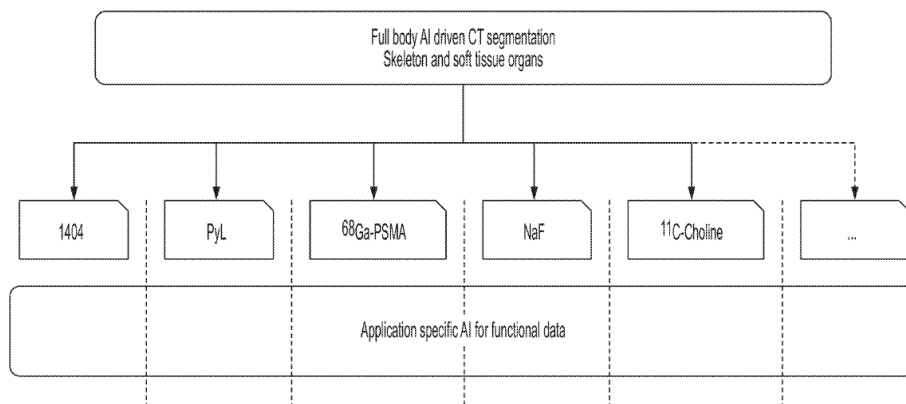


FIG. 3

FIG. 3 of the '817 Patent.

61. For example, the 3D segmentation map can be accessed and used to provide anatomical context to functional images, where it is often difficult to obtain. EX1001, 33:9-34:39. As described in the '817 Patent, the CNN-created 3D segmentation map encompasses organs and skeletal regions throughout a patient's body and is sufficiently robust and accurate to serve a variety of applications, using different tracers, in a platform agnostic fashion. EX1001, 33:9-34:39.

62. Moreover, the '817 Patent describes a variety of example uses whereby the 3D segmentation map can be used to isolate specific regions for the search for cancerous lesions, classify lesions (e.g., as primary tumor, skeletal or lymph metastases), correct for physiological uptake in regions such as the bladder and kidneys, and quantify lesion severity in an improved fashion by virtue of the 3D nature of the segmented volumes. EX1001, 3:49-5:11.

63. As such, the claimed methods provide numerous advantages over prior art methods.

B. Prosecution History of the '817 Patent

64. I have reviewed relevant parts of the publicly available prosecution history of the '817 Patent. The Application for the '817 Patent was filed on March 29, 2023 as a divisional application, claiming earliest priority to U.S. Provisional Application 62/789,155 filed on January 7, 2019. EX1004, 224. The '817 Patent issued on March 26, 2024. EX1004, 464.

65. It appears that, during prosecution, the Examiner considered the Renisch, Baker, and Eiber references that the Petition asserts against the independent claims and allowed the claims in their current form.

66. For example, during prosecution, the Patent Owner cited three of the Petition's references, Renisch, Baker, and Eiber, in an IDS submitted to the Office on June 26, 2023. *See* EX1004, 246, 251. On October 4, 2023, the Examiner signed the IDS, noting at the bottom that "ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /J.M.S./." The Examiner did not line through the Renisch, Baker, or Eiber references. EX1004, 280, 285.

67. On October 13, 2023, the Examiner allowed the application after considering all the references and stated, in the Notice of Allowance, that "[t]he closest prior art is **Hamadeh et al. (US 8,855,387)**." EX1004, 323 (emphasis in

original). On October 30, 2023, the Applicant filed a Request for Continued Examination with an IDS citing additional references and an amendment to the specification addressing informalities identified in a Notice to File Corrected Application Papers issued by the Office. EX1004, 327-351. The Examiner then issued a second Notice of Allowance on November 21, 2023, presenting the same reason for allowance. EX1004, 421-431.

68. It thus appears, in my opinion, that the references that Petition relies on for its challenges against the claims are identical to the Renisch, Baker, and Eiber references that were cited and considered during prosecution of the '817 Patent.

VIII. ANALYSES OF THE PETITION GROUNDS

A. Ground A: Renisch does not anticipate claims 1-5, 7, 10-14, 16, 19, and 26.

69. It is my opinion that the Petition does not establish that Renisch anticipates claims 1-5, 7, 10-14, 16, 19, and 26.

1. Claim 1

a. Renisch does not disclose “automatically identifying, . . . , using one or more machine learning modules, for each of a plurality of target tissue regions, a corresponding target volume of interest (VOI) within the 3D anatomical image” as recited in claim 1.

70. Limitation (b) of claim 1 states “automatically identifying, . . . , using one or more machine learning modules, for each of a plurality of target tissue regions, a corresponding target volume of interest (VOI) within the 3D anatomical image.”

Pet., 22; EX1001, 79:14-18. The Petition alleges that Renisch discloses this element. Respectfully, I disagree.

71. The Petition argues that Renisch discloses machine learning algorithms, referencing what appears to be an isolated and off-hand mention of the terms “neural network” and “clustering” in paragraph [0027] of Renisch, which states “It is to be appreciated, however, that other segmentation methods such as clustering, edge detection, region growing, principle components [sic] analysis, neural network, and the like are also contemplated.”. Pet., 22-23. Referring to paragraph [0027] of Renisch, the Petition states “Both clustering and artificial neural networks are machine learning algorithms used for medical image segmentation tasks.” Pet., 23.

72. Here, however, without providing any proposed construction of the term “machine learning module,” the Petition attempts to take two isolated terms in Renisch – “neural network” and “clustering” – and allege that they disclose a machine learning module as it is used in the ’817 Patent. I disagree that Renisch discloses a machine learning module as the term is used in the ’817 Patent.

73. First, the term “neural network” in isolation, as mentioned in Renisch, does not disclose a machine learning module as a POSA would understand it from reading the ’817 Patent. A neural network is a specific computational model that uses variable weights and interconnected neurons to capture a wide variety of behavior. As discussed above, a neural network is not the same thing as, and does

not necessitate the use of, a machine learning module. A neural network on its own (as it appears in Renisch) does not include any learning algorithm and thus is incapable of “learning.” Second, the term “clustering” in isolation is also insufficient to disclose a “machine learning module” as recited in claim 1. Clustering refers to a general class of statistical methods for grouping similar objects into different groups, or more precisely, for partitioning a data set into subsets (e.g., according to some defined distance measure in the (multi-dimensional) space of features (descriptors)). Clustering methods do not necessitate the use of machine learning.

74. Third, the two techniques – neural network and clustering – which the Petition tries to read on the claim element, are different algorithms or classes of algorithms that work in different ways. Each would imply a unique interpretation of the term, “machine learning module,” inconsistent with each other and at odds with the way machine learning is described in the ’817 Patent. The Petition, however, fails to provide an explicit construction for the term “machine learning module,” as it is used in the ’817 Patent and in the context of the understanding of a POSA at the time the ’817 Patent was filed.

75. The ’817 Patent provides extensive detail and examples of CNN techniques for performing detailed anatomical segmentation and describes approaches for efficient whole-body 3D image segmentation with CNN modules. *See, e.g.,* EX1001, 31:60-32:21, 34:41-37:10, 42:5-48:41. As explained above in

Section V.C, machine learning techniques evolved significantly, especially after 2010, with breakthroughs leading to new understandings about the viability of deep-learning CNNs. Thus, the understanding of what terms like machine learning, neural network, deep neural network, and associated learning algorithms meant was in flux and, at the time of the priority date (January 7, 2019), the use of the term machine learning in connection with specific algorithms, like CNNs, as appears in the '817 Patent would mean something very different from Renisch's off-hand mention of "neural network" (in 2009, when deep-learning CNN techniques were not used) or clustering (a family of general algorithms for sorting data).

76. Accordingly, the Petition does not set out any explicit construction for the term "machine learning algorithm," as it is used in the claims of the '817 Patent, and any interpretation implied from the Petition's arguments relies on different and inconsistent constructions. Moreover, any such implied interpretation is also at odds with the way one would understand the term "machine learning algorithm" as recited in the claims of the '817 Patent.

77. In my opinion, given the failure of the Petitioner to propose a claim construction for this key term, the offhand mention of "clustering" and "neural network" in Renisch, without more, is insufficient to disclose use of a "machine learning module," as recited in claim 1. Thus, it is my opinion that the Petition fails

to establish a reasonable likelihood that limitation (b) of in claim 1 is taught by Renisch.

- b. Renisch does not disclose “determining . . . a 3D segmentation map representing a plurality of 3D segmentation masks, each 3D segmentation mask representing a particular identified target VOI” as recited in claim 1.**

78. Limitation (c) of claim 1 states “determining, by the processor, a 3D segmentation map representing a plurality of 3D segmentation masks, each 3D segmentation mask representing a particular identified target VOI.” Pet., 23; EX1001, 79:19-22.

79. To begin with, the Petition alleges that “Renisch discloses [1(c)] to a POSITA even though Renisch does not use the same terminology.” Pet., 24. However, in my opinion, the distinctions between Renisch and claim 1 go beyond terminology.

80. In particular, as described in the '817 Patent, the “3D segmentation map” element represents multiple 3D volumes corresponding to target tissue regions such as organs and skeletal regions (e.g., bones) that are identified via machine learning-based image segmentation methods – namely, supervised deep-learning techniques like CNNs. For instance, the '817 Patent describes identifying multiple target volumes via CNN-based image segmentation techniques and stitching the target volumes together to form a segmentation map. EX1001, 34:27-39. In contrast,

Renisch does not describe any particular processing or format of representation like a 3D segmentation map as recited in claim 1.

81. As described in the '817 Patent, the resultant 3D segmentation map can be used as a basis for providing anatomical context to 3D functional images acquired with a variety of tracers and for various applications. EX1001, 32:65-33:38, 37:12-25, FIG. 8. As shown in FIGs. 6A and 6B, and 8, below, the 3D segmentation map, as recited in claim 1, is a specific element that provides a detailed 3D anatomical map representing multiple volumes identified, specifically, via one or more machine learning modules. It is my opinion that Renisch does not describe creation of a detailed 3D segmentation map in this way, as recited in claim 1 of the '817 Patent.

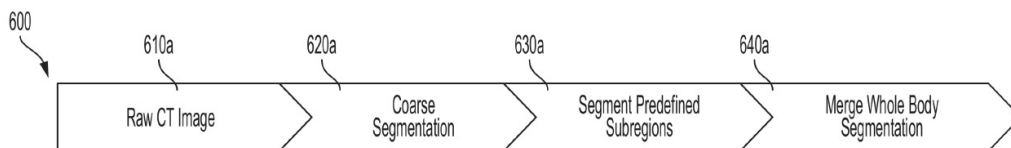


FIG. 6A

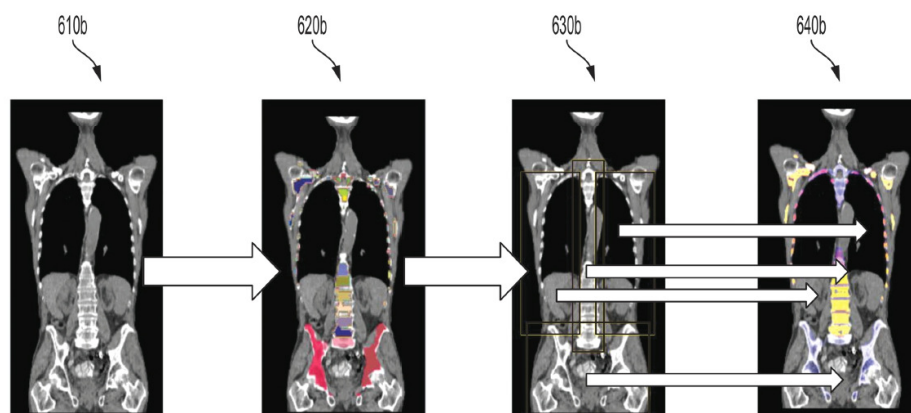


FIG. 6B

FIGs. 6A and 6B of the '817 Patent (above)

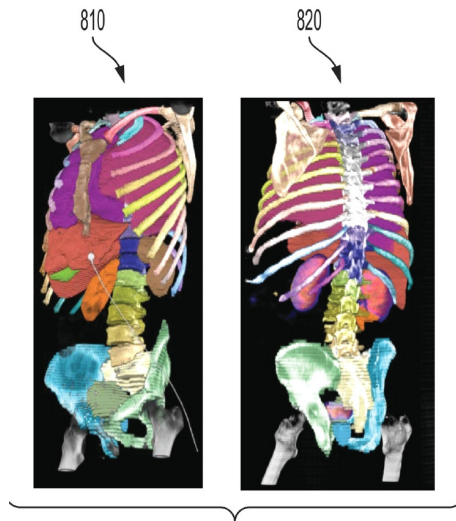


FIG. 8

FIG. 8 from the '817 Patent.

82. Moreover, the Petition does not, in my opinion, point to a specific step in Renisch whereby, once multiple VOIs are identified within a 3D anatomical image through one or more machine learning modules, a 3D segmentation map representing those multiple VOIs is expressly created. Nor does the Petition identify a specific element in Renisch and argue that that element is another term for a “3D segmentation map” as recited in claim 1. Instead, the Petition points to portions of Renisch that describe suppressing certain regions of high intensity (which, as explained below, Renisch describes as regions of *high-metabolic activity* identified in a functional image representation and thus not VOIs that are identified as representing specific organs), and attempts to infer that, as a result, Renisch discloses 3D segmentation masks (which, still, do not necessarily require a 3D segmentation map). Pet., 24. The Petition then makes a jump to conclude – without further evidence or explanation –

that, because Renisch discloses the functionality to suppress intensities from certain regions, it must also disclose 3D segmentation masks, and thus a 3D segmentation map. Pet., 24-25.

83. Thus, at the outset, the distinctions between Renisch and Patent Owner's claims are more than differences in terminology. Claim 1 recites an entire step and a particular way of representing image segmentation results that is absent from Renisch. As a result, the Petition's arguments rest on Petitioner's attempts to infer the presence of unstated elements and steps where Renisch is, in fact, silent.

84. In my opinion, the Petition's arguments are insufficient to show that Renisch specifically determines, as Patent Owner does, a 3D segmentation map representing a plurality of 3D segmentation masks as recited in claim 1. It is my opinion that the Petition fails to show that the missing element of a "3D segmentation map" element, created to represent multiple machine-learning module-identified VOIs, as recited in claim 1 is *necessarily* present in Renisch. As explained above, the creation and use of a 3D segmentation map was a particular way that Patent Owner chose to represent results of 3D CNN-based image analysis that was driven by and tailored to Patent Owner's technique of performing detailed whole-body segmentation via multiple CNN-modules. As explained above and in the '817 Patent, the 3D segmentation map, as recited in claim 1, allows for the results of multiple CNN modules that are tasked with segmenting subsets of organs and bones in various

anatomical sub-regions to be combined into a single unified element. EX1001, 49:7-10, 50:20-21; *see also id.*, 5:37-48, 32:1-21, 34:27-29. Among other things, this approach provides flexibility and facilitates use of the machine-learning-based 3D image segmentation techniques for a variety of downstream image applications.

85. While Petition makes conclusory statements, such as, “[e]ach segmented VOI is represented by its own segmentation mask,” it does not explain further why this must *necessarily* be the case in Renisch. Pet., 24. Instead, the Petition fills in gaps in the cited reference, Renisch, with the claim elements. The Petition’s arguments thus fail to appreciate that Patent Owner’s choice was not the only possibility, and, instead, a specific selection driven Patent Owner’s specific needs and insight into how multiple machine-learning modules, like multiple CNNs, could be used to effectively perform whole-body segmentation. Renisch does not include this insight, and, in my opinion, there are other ways that Renisch could have chosen to represent his segmentation results. For example, given that Renisch focuses primarily on “model-based segmentation,” based on already stored or pre-defined structural models that are registered to an image, it might be most natural to store a registration field or values such as scaling factors, center positions, rotations, warping function parameters, as the result of his segmentation unit.

86. Further, having reviewed Renisch, it is my opinion that the cited paragraphs of Renisch in the Petition do not describe what the Petition purports they do.

87. For example, the Petition argues, in reference to Renisch “Each segmented VOI is represented by its own segmentation mask because, as explained below, each can be used separately to selectively suppress (or mask) uptake within corresponding volumes of a 3D functional image. Ex1005, [0030]-[0031].” Pet., 24. However, the word “mask” does not appear in those passages of Renisch. Moreover, there is no specific element in those passages that the Petition points to as allegedly equivalent to a 3D segmentation mask, let alone a 3D segmentation map as recited in claim 1. Finally, the regions that Renisch describes as being suppressed are *not* volumes that correspond to VOIs that are segmented, via machine learning, in a 3D anatomical image. Instead, they are “regions of high intensity...in the functional second image representation.” EX1005, [0031] (“[a] suppression unit, processor, or algorithm 102 uses the results of the classification unit to **suppress the regions of high intensity 92 in the functional second image representation 74.**” (emphasis added)); *see also* EX1005, [0006], [0029]. As Renisch explains, these regions of high intensity 92 are not segmented anatomical structures, but rather, are “regions in the functional second image representation that indicate high metabolic activity” (e.g., which might be tumors or might be organs with high metabolic activity such as

the heart, bladder, liver, kidney, and brain). EX1005, [0029]. Renisch states that these high intensity regions are detected by a classical watershed algorithm. *Id.* A watershed algorithm is not a machine learning module. Thus, it is my opinion that the suppressed regions in Renisch are not volumes segmented within a 3D anatomical image via machine learning.

88. The Petition also references paragraphs [0030] and [0031] of Renisch and argues “[a]fter segmented organs are carried over from the anatomical image to the functional image, Renisch analyzes the uptake in each segmented organ . . . Thus, some segmented organs might be suppressed while others are kept for further analyses,” Pet., 24. However, neither of these passages of Renisch (paragraphs [0030] and [0031]) state that segmented organs are carried over from the anatomical image to the functional image. Instead, in paragraph [0030], Renisch describes “correlat[ing] metabolic activity”. EX1005, [0030]. It is, however, not clear from Renisch how this correlation step is performed. Moreover, as explained above, what Renisch “suppresses” are certain “regions of high intensity.”

89. Renisch even makes clear that identifying functional image regions of high intensity as corresponding to various anatomical structures does not require creation of a 3D segmentation map from regions identified in a 3D anatomical image. Renisch states that his “identification unit . . . uses anatomical information, such as size, shape, location, or the like, from [an] anatomical database 84 to identify the

regions with high tracer uptake, for example as a salivary gland.” *Id.* This procedure does not involve creation of a 3D segmentation map to represent multiple volumes identified via machine-learning-based segmentation of a 3D anatomical image. Instead, here, Renisch appears to rely on accessing pre-defined anatomical structural models. EX1005, [0027] (“A library of three-dimensional anatomical structure models explaining the shape, geometrical location, size, and variations thereof are defined in an anatomical database 84 . . .”).

90. Thus, in my opinion, the Petition’s arguments repeatedly deviate from the actual disclosure of Renisch. Renisch is silent on the 3D segmentation map element, yet the Petition continuously contends that this silence can be treated as a placeholder that can be filled in with the alleged anticipated elements. In my opinion, Renisch fails to explicitly disclose “determining . . . a 3D segmentation map representing a plurality of 3D segmentation masks, each 3D segmentation mask representing a particular identified target VOI,” as recited in claim 1.

c. Conclusion

91. Based at least on the above-explained reasons, it is my opinion that Renisch does not anticipate independent claim 1.

2. Claim 10

92. Claim 10 is the second independent claim in the ’817 Patent and is similar to claim 1.

93. Since the same limitations above (in Section VIII.A.1) appear in independent claim 10, in my opinion, Renisch does not anticipate independent claim 10.

3. Claims 2-5, 7, 11-14, 16, 19, and 26.

94. Claims 2-5, 7, and 19 are dependent claims, each depending from claim 1. Similarly, claims 11-14, 16, and 26 are dependent claims, each depending from claim 10. As I understand it, each of these claims necessarily includes the limitations of claim 1 or claim 10, from which each depends. Therefore, at least because, as explained above, Renisch does not anticipate claims 1 and 10, Renisch does not anticipate any of these dependent claims.

B. Ground B: Renisch in view of Zhao do not render obvious claims 1-5, 7, 10-14, 16, 19, and 26.

95. It is my opinion that the Petition does not establish that Renisch in view of Zhao renders claims 1-5, 7, 10-14, 16, 19, and 26 obvious.

1. Claim 1

a. Zhao does not disclose “determining . . . a 3D segmentation map representing a plurality of 3D segmentation masks” as recited in claim 1.

96. Limitation (c) of claim 1 states “determining, by the processor, a 3D segmentation map representing a plurality of 3D segmentation masks, each 3D segmentation mask representing a particular identified target VOI.” Pet., 23; EX1001, 79:19-22.

97. The Petition contends that Zhao discloses a 3D segmentation map because Zhao mentions “[a] multi-value mask . . . may be decomposed into a combination [sic] the more fundamental binary masks each for one type of ROI.” Pet., 26 (quoting EX1007, 5:30-42). Respectfully, I disagree.

98. In my opinion, Zhao does not disclose three-dimensional segmentation masks, let alone a 3D segmentation map representing a plurality of 3D segmentation masks. It is my opinion that Zhao does not describe three-dimensional image processing, nor does Zhao mention three-dimensional segmentation. Instead, Zhao repeatedly limits his description explicitly to two-dimensional images throughout. For instance, throughout the specification, Zhao repeatedly uses the terms “pixel” as opposed to “voxel.” EX1007, 7:56-64. Zhao describes a “100-pixel by 100-pixel input” – i.e., a two-dimensional image. *Id.* When describing image processing techniques, such as pooling and down-sampling, Zhao refers to “two spatial dimensions.” EX1007, 7:65-8:7. In fact, Zhao always and only discusses two-dimensional image processing. *See, e.g.*, EX1007, 8:60-9:7; 10:29-34 (designating spatial locations as “(i,j)” – i.e., in two dimensions).

99. In my opinion, Zhao’s description, repeatedly referencing and describing *two-dimensional* image processing, is in sharp contrast with the ’817 Patent. The claims of the ’817 Patent expressly refer to three-dimensional images. *See, e.g.*, EX1001, 79:5-32. The description of the ’817 Patent emphasizes the

importance and advantages of applying accurate machine-learning-based segmentation to handle *three-dimensional* images as input and to identify *volumes* therein. EX1001, 3:21-29; *see also id.*, 55:63-56:9. For example, the specification of the '817 Patent states, “[t]he capability of the approaches described herein to handle 3D images is an important advantage over certain other image analysis that only identify 2D regions in 2D images.” EX1001, 3:21-29; *see also id.*, 55:63-56:9 (“Notably, a significant advantage of the approach described in this example . . . In contrast to such small 2D regions, the 3D volume that are identified via the approaches used herein capture intensities throughout entire organs, and thereby offer increased accuracy and repeatability.”). The specification further states:

For example, for a 6x3x3 array, a given 3x3x3 subpatch refers to a given 3x3x3 set of adjacent values (e.g., a neighborhood) of the array, such that there are five distinct 3x3x3 subpatches in the 6x3x3 array (each patch shifted one position over along the first dimension).

EX1001, 29:66-30:4; *see also id.*, 30:55-56 (“For example, an $N \times M \times L \times K_0$ size input array, has three spatial dimensions and K_0 output channels.”), Tables 1, 5, and 8 (listing explicitly three-dimensional inputs for the described CNN networks).

100. The Petition does not address this deficiency in Zhao. Instead, at best, the Petition appears to equate Zhao’s mention of a CT image with a “3D medical image.” Pet., 25. However, it is my opinion that the Petition ignores the fact that Zhao repeatedly characterizes his analysis and his masks as two-dimensional, as I

explained above. To the extent Zhao refers to CT images, he is, therefore, referring to analysis of entirely two-dimensional CT images or single CT image slices at best.

101. Thus, it is my opinion that Zhao is silent with regard to a 3D segmentation mask, let alone a 3D segmentation map, as recited in claim 1. The Petition fails to acknowledge the 2D nature of Zhao and is silent as to how Zhao could be implemented in 3D.

b. Renisch in view of Zhao do not render obvious limitation (c), as recited in claim 1.

102. Limitation (c) of claim 1 states “determining, by the processor, **a 3D segmentation map representing a plurality of 3D segmentation masks, each 3D segmentation mask representing a particular identified target VOI.**” Pet., 23; EX1001, 79:19-22 (emphasis added). Thus, as explained above, the method of claim 1 determines a 3D segmentation map that represents multiple target VOIs which, as recited at step (b), are identified via machine-learning based segmentation of a 3D anatomical image. EX1001, 79:14-18 (“(b) automatically identifying, by the processor, using one or more machine learning modules, for each of a plurality of target tissue regions, a corresponding target volume of interest (VOI) within the 3D anatomical image.”).

103. As discussed above, as described in the '817 Patent, the “3D segmentation map” element represents multiple 3D volumes corresponding to target tissue regions such as organs and skeletal regions (e.g., bones) that are identified via

machine learning-based image segmentation methods – namely, supervised deep-learning techniques like CNNs. For instance, the '817 Patent describes identifying multiple target volumes via CNN-based image segmentation techniques and stitching the target volumes together to form a segmentation map. EX1001, 34:27-39.

104. Accordingly, claim 1 of the '817 Patent recites more than an arbitrary 3D segmentation map. Reading the claim as a whole, the recited “3D segmentation map” is, specifically, created from and used to represent multiple target VOIs that are identified by segmenting a 3D anatomical image with one or more machine learning modules. This specific step reflects the particular way that the '817 Patent performs detailed whole-body 3D image segmentation using deep-learning techniques like CNNs.

105. Neither Renisch nor Zhao contemplate the particular challenges associated with performing detailed 3D image segmentation with deep learning-techniques, as described in the '817 Patent, let alone the particular techniques that the '817 Patent describes for addressing them, which include stitching together the results of multiple machine learning modules (e.g., each performing segmentation in a dedicated anatomical subregion) to create 3D segmentation map.

106. For example, unlike the '817 Patent, to the extent Renisch describes segmentation of anatomical images, Renisch focuses primarily on a conventional model-based segmentation approach, apart from the offhand listing (in a single

sentence) of “neural network” and “clustering” in a list of what appears to be arbitrary segmentation techniques. Renisch does not contemplate the kind of deep-learning-based 3D image segmentation that the approach of claim 1, including the creation of a 3D segmentation map from the results of machine-learning model-based segmentation, is designed for. Unlike the ’817 Patent, Zhao is directed solely to 2D images. Zhao does not perform 3D image segmentation, nor does Zhao contemplate the need for anatomical context in functional images. Zhao also does not mention 3D functional images, let alone the particular shortcomings and advantages that benefit from the accurate 3D segmentation performed by the ’817 Patent. Therefore, in my opinion, it would not be obvious to combine both Renisch and Zhao in a way that would yield Patent Owner’s claimed subject matter.

107. It is my opinion that the Petition’s reasons to combine the two references are insufficient. For example, the Petition states, as a rationale to combine Zhao and Renisch, that these two references “are directed to segmentation of 3D medical images, such as CT images, using neural networks.” Pet., 26. However, as explained above. Renisch mentions a “neural network” once, in passing, and does not discuss or contemplate any practical approach by which neural network-based segmentation could be implemented. Moreover, Renisch does not contemplate the kind of deep-learning-based 3D image segmentation that Patent Owner’s approach – including step (c) of claim 1 – allows to be performed in efficient fashion across a

whole-body of a patient. Further, as I discussed above, Zhao is not directed to 3D segmentation. Zhao only describes 2D segmentation, and, like Renisch, fails to contemplate the particular challenges that the technologies described in the '817 Patent and reflected in the claim are designed to address.

108. Elsewhere, the Petition argues that “improving Renisch with the teachings of Zhao would merely have amounted to applying a known technique (segmentation masks) to a known device (Renisch) ready for improvement to yield predictable results.” Pet., 27. But, as discussed above, Zhao’s segmentation masks involved exclusively 2D images. Furthermore, Renisch’s disclosure of suppressing high-intensity regions is not akin to the step of creating a 3D segmentation map representing multiple VOIs identified via machine-learning based segmentation of a 3D anatomical image. This is because Renisch’s high-intensity regions are regions of high-metabolic activity identified in a functional image representation—not VOIs that are identified, within a 3D anatomical image, as representing specific organs via one or more machine-learning modules.

109. Thus, the Petition fails to show that a POSA would have been motivated to combine Renisch and Zhao to achieve the claimed limitation with a reasonable expectation of success. It is my opinion that the Petition thus fails to show that Renisch and Zhao render this limitation obvious.

c. Conclusion

110. Based at least on the foregoing reasons, it is my opinion that Renisch in view of Zhao fail to render claim 1 obvious.

2. Claim 10

111. Claim 10 is the second independent claim in the '817 Patent and is similar to claim 1. Since the same limitations above (in Section VIII.B.1) appear in independent claim 10, in my opinion, the Petition also fails to show that a POSA would have had a motivation to combine Renisch and Zhao to achieve these same limitations in independent claim 10. The Petition thus also fails to carry its burden for claim 10.

3. Claims 2-5, 7, 11-14, 16, 19, and 26.

112. Claims 2-5, 7, and 19 are dependent claims, each depending from claim 1. Similarly, claims 11-14, 16, and 26 are dependent claims, each depending from claim 10. As I understand it, each of these claims necessarily includes the limitations of claim 1 or claim 10, from which each depends. Therefore, at least because, as explained above, Renisch in view of Zhao fails to render claims 1 and 10 obvious, Renisch in view of Zhao also fails to render any of these dependent claims obvious.

C. Ground C: Renisch, or Renisch-Zhao, each in view of Baker, do not render obvious claims 8-9, 17-18, 22-25, and 29-32.

113. The Petition challenges claims 8-9, 17-18, 22-25, and 29-32 as allegedly obvious based on Renisch, or Renisch-Zhao, each in view of Baker. Each

of these claims depends from claim 1 or claim 10. As I understand it, each of these claims necessarily includes the limitations of claim 1 or claim 10, from which each depends.

114. As I explained above in Grounds A and B, respectively, Renisch fails to anticipate claims 1 and 10, and Renisch in view of Zhao fails to render claims 1 and 10 obvious. Accordingly, for at least the reasons above, Renisch, or Renisch-Zhao, each in view of Baker, fails to render dependent claims 8-9, 17-18, 22-25, and 29-32 obvious.

D. Ground D: Renisch, or Renisch-Zhao, each in view of Eiber, do not render obvious claims 8-9, 17-18, 22, 24-25, 29, and 31-32.

115. The Petition challenges claims 8-9, 17-18, 22, 24-25, 29, and 31-32 as allegedly obvious based on Renisch, or Renisch-Zhao, each in view of Eiber. Each of these claims depends from claim 1 or claim 10. As I understand it, each of these claims necessarily includes the limitations of claim 1 or claim 10, from which each depends.

116. As I explained above in Grounds A and B, respectively, Renisch fails to anticipate claims 1 and 10, and Renisch in view of Zhao fails to render claims 1 and 10 obvious. Accordingly, for at least the reasons above, Renisch, or Renisch-Zhao, each in view of Eiber, fails to render dependent claims 8-9, 17-18, 22, 24-25, 29, and 31-32 obvious.

E. Ground E: Baker in view of Zhao do not render obvious claims 1-2, 7-11, 16-18, 22-25, and 29-32.

1. Claim 1

117. Limitation (c) of claim 1 states “determining, by the processor, a 3D segmentation map representing a plurality of 3D segmentation masks, each 3D segmentation mask representing a particular identified target VOI.” Pet., 49; EX1001, 79:19-22. The Petition argues that Baker in view of Zhao renders this limitation obvious because “a POSITA would have been motivated to combine the references to arrive at the limitation.” Pet., 50. The Petition further states that “Baker does not use the term ‘segmentation masks,’ but Zhao teaches and suggests the use of segmentation masks to implement 3D medical image segmentation like that discussed in Baker.” *Id.*

118. However, as I explained above in Section VIII.B.1.a, Zhao fails to disclose, or even suggest, “a 3D segmentation mask,” let alone “a 3D segmentation map representing a plurality of 3D segmentation masks,” as recited in claim 1. Accordingly, for at least the reasons above, Baker in view of Zhao fails to render claim 1 obvious.

2. Claim 10

119. Since limitation 1(c) above also appears in independent claim 10, in my opinion, the Petition also fails to show that a POSA would have been motivated to

combine Baker and Zhao to achieve this limitation in independent claim 10. The Petition thus also fails to carry its burden for claim 10.

3. Claims 2, 7-9, 11, 16-18, 22-25, and 29-32

120. Claims 2, 7-9, 11, 16-18, 22-25, and 29-32 are dependent claims, each depending from claim 1 or claim 10. As I understand it, each of these claims necessarily includes the limitations of claim 1 or claim 10, from which each depends. Therefore, at least because, as explained above, Baker in view of Zhao fails to render claims 1 and 10 obvious, Baker in view of Zhao also fails to render any of these dependent claims obvious.

F. Ground F: Baker-Zhao in view of Eiber do not render obvious claims 3-5 and 12-14.

121. The Petition challenges claims 3-5 and 12-14 as allegedly obvious based on Baker-Zhao in view of Eiber. Each of these claims depends from claim 1 or claim 10. As I understand it, each of these claims necessarily includes the limitations of claim 1 or claim 10, from which each depends. For at least the reasons above in Ground E, Baker-Zhao in view of Eiber fail to render claims 3-5 and 12-14 obvious.

G. Ground G: Baker-Zhao in view of Suehling do not render obvious claims 19, 26, and 28.

122. The Petition challenges claims 19, 26, and 28 as allegedly obvious based on Baker-Zhao in view of Suehling. Each of these claims depends from claim 1 or claim 10. As I understand it, each of these claims necessarily includes the

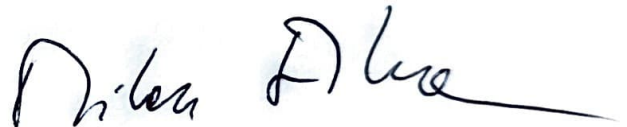
limitations of claim 1 or claim 10, from which each depends. For at least the reasons above in Ground E, Baker-Zhao in view of Suehling fail to render claims 19, 26, and 28 obvious.

IX. CONCLUSION

123. For the reasons stated herein, it is my view that claims 1-5, 7-14, 16-19, 22-26, and 28-32 of the '817 Patent are novel and nonobvious over the cited art. I reserve the right to expand or modify my opinions as my analysis continues, and to supplement my opinions in response to any additional information that becomes available to me and any matters raised by the parties, the Board, and/or the opinions provided by other experts.

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

Date: 8/3/2025

By: 
Milan Sonka