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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

Ex parte VASILIS NTZIACHRISTOS and RALPH WEISSLEDER

Appeal 2018-005627
Application 13/481,568¹
Technology Center 3700

Before MURRIEL E. CRAWFORD, BRUCE T. WIEDER, and
KENNETH G. SCHOPFER, *Administrative Patent Judges*.

WIEDER, *Administrative Patent Judge*.

DECISION ON APPEAL

This is a decision on appeal under 35 U.S.C. § 134 from the Examiner's rejection of claims 30–44. We have jurisdiction under 35 U.S.C. § 6(b).

We AFFIRM.

¹ According to Appellants, the real parties in interest are “the General Hospital Corporation, and the licensee, VisEn Medical Inc., which is a subsidiary of PerkinElmer, Inc.” (Appeal Br. 3.)

CLAIMED SUBJECT MATTER

Appellants' "invention relates to extracting quantitative, three-dimensional molecular information from living mammals and patients using fluorochromes" and tomographic imaging. (Spec. 1, ll. 9–11.)

Claims 30 and 40 are the independent claims on appeal. Claim 30 is illustrative. It recites:

30. A method of obtaining a three-dimensional, quantitative tomographic image of a target region within a patient or animal body, the method comprising:

administering a near-infrared fluorescent probe to the patient or animal body, wherein the probe selectively accumulates within a target region in the patient or animal body;

directing near-infrared excitation light into the patient or animal body at multiple locations, thereby transilluminating the patient or animal body;

detecting at multiple points excitation light transmitted through the patient or animal body;

detecting fluorescent light emitted from the patient or animal body; and

processing a measure of the detected excitation light and a measure of the detected fluorescent light using a forward model of (i) an excitation field from the near-infrared excitation light source to the probe within the patient or animal body and (ii) an emission field from the probe within the patient or animal body to a detector to provide a three-dimensional tomographic image that corresponds to the three-dimensional target region within the patient or animal body and to the quantity of the probe accumulated in the target region.

REJECTIONS²

Claims 30–34, 36, and 37 are rejected under 35 U.S.C. § 103(a) as unpatentable in view of Benaron (US 6,167,297, iss. Dec. 26, 2000), Alfano (US 6,208,886 B1, iss. Mar. 27, 2001) (hereinafter “Alfano ’886”), Yokoi (US 6,396,053 B1, iss. May 28, 2002), and Alfano (US 6,205,353 B1, iss. Mar. 20, 2001) (hereinafter “Alfano ’353”).

Claim 35 is rejected under 35 U.S.C. § 103(a) as unpatentable in view of Benaron, Alfano ’886, Yokoi, Alfano ’353, and Klaveness (US 2003/0170173 A1, pub. Sept. 11, 2003).

Claim 38 is rejected under 35 U.S.C. § 103(a) as unpatentable in view of Benaron, Alfano ’886, Yokoi, Alfano ’353, and Rohler (US 6,130,958, iss. Oct. 10, 2000).

Claim 39 is rejected under 35 U.S.C. § 103(a) as unpatentable in view of Benaron, Alfano ’886, Yokoi, Alfano ’353, and Hochman (US 6,671,540 B1, iss. Dec. 30, 2003).

Claims 40–44 are rejected under 35 U.S.C. § 103(a) as unpatentable in view of Benaron, Alfano ’886, Yokoi, Rohler, and Alfano ’353.

ANALYSIS

Claim 30

Obviousness is a legal conclusion involving a determination of four underlying facts.

Under § 103, the scope and content of the prior art are to be determined; differences between the prior art and the claims at issue are to be ascertained; and the level of ordinary skill in the

² The rejection of claims 30–44 under 35 U.S.C. § 112, first paragraph, was withdrawn. (See Answer 14–15.)

pertinent art resolved. Against this background, the obviousness or nonobviousness of the subject matter is determined. Such secondary considerations as commercial success, long felt but unsolved needs, failure of others, etc., might be utilized to give light to the circumstances surrounding the origin of the subject matter sought to be patented.

KSR Int'l Co. v. Teleflex Inc., 550 U.S. 398, 406 (2007) (quoting *Graham v. John Deere Co. of Kansas City*, 383 U.S. 1, 17–18 (1966)).

With regard to the scope and content of the prior art, the Examiner finds that Benaron teaches “detecting at multiple points excitation light transmitted through the patient or animal body (Col. 9 lines 36-47 multiple light detectors)” and “detecting fluorescent light emitted from the patient or animal body (Col. 10 lines 35-47).” (Non-Final Action 4.)

Appellants argue that “Benaron does not, at any point, teach or suggest processing a measure of both excitation light that is transmitted through the body of a patient or animal and fluorescent light emitted from the body.” (Appeal Br. 14–15.)

The Examiner answers, and we agree,

that in optical imaging system[s such] as Benaron, [when] transmitting light through [an] object (which is labeled with fluorescent probe), [the] output light that transmitted through the object will have fluorescent [light] emitted as well as light transmitted that did not go through the portion of [the] fluorescent probe within the object (which is excitation light in [the] claimed invention). Unless, one specifically filters solely for fluorescent emitted light, light collected will contain both fluorescent and excitation light.

(Answer 16.)

Benaron discloses

[a] system for detecting, localizing and targeting a medical instrument toward a target tissue within the body using an optical

contrast agent in which a light source is optically coupled to the tissue to be diagnosed, a light detector is optically coupled to the tissue to detect a portion of the light which passes through the tissue, and either one or both of the light source and light detector are coupled to a medical instrument used in a medical procedure.

(Benaron, Abstract (reference numbers omitted).) Specifically, Benaron discloses that a light “emitter may consist of a single or multiple light emitting elements,” (*id.* at col. 9, ll. 34–35) and that a light detector or light collector is

[a] collector or light [sic] that generates a signal in response to the collected light. As above, it may be single or multiple, simple or complex. The detection may be performed in reflectance or in transmission. The collected light may be light that has been influenced by transmission, absorbance, scattering, fluorescence, phosphorescence, or other optical interactions of the contrast moiety with the illuminating radiation. Detection may include time-, frequency, or spatially-resolved measures.

(*Id.* at col. 9, ll. 36–45; *see also* Answer 16–17.) Benaron also discloses the use of a blue contrast agent, such as isosulfan blue (Benaron, col. 19, l. 16) or “a fluorescent contrast could be substituted, and the fluorescence imaged” (*id.* at col. 20, ll. 32–33).

In other words, Benaron discloses detecting light that passes through the body, i.e., excitation light, and detecting fluorescent light emitted from the body in the presence of a fluorescent contrast agent. Appellants have not persuaded us that the Examiner erred in finding that Benaron discloses detecting and processing both excitation and fluorescent light.

Appellants also argue that Benaron fails to teach or suggest use of a forward model. (Appeal Br. 16.) The Examiner agrees and explains that “Examiner did not use Benaron for disclosing a forward model, rather [the Examiner] incorporated Alfano[, i.e., Alfano ’353] for teaching a forward

model.” (Answer 17.) Therefore, we do not find Appellants’ argument persuasive of error.

Appellants also argue that “Alfano ’886 expressly filters out the excitation light, so that it is *not detected*.” (Appeal Br. 17.) “[B]ecause Alfano ’886 describes filtering out the excitation light, this reference fails to teach or even suggest detecting both excitation and fluorescent light, or any processing of measures of the detected excitation and emission light.” (*Id.*)

The Examiner answers, and we agree, that Alfano ’886 need not disclose detecting both excitation and fluorescent light as Benaron already discloses this. (*See* Answer 17.) Specifically, we note that “one cannot show non-obviousness by attacking references individually where, as here, the rejections are based on combinations of references.” *In re Keller*, 642 F.2d 413, 426 (CCPA 1981). A reference “must be read, not in isolation, but for what it fairly teaches in combination with the prior art as a whole.” *In re Merck & Co.*, 800 F.2d 1091, 1097 (Fed. Cir. 1986).

Appellants further argue that Alfano ’886 “fails to teach or suggest using a forward model of (i) an excitation field from the near-infrared excitation light source to the probe within the patient or animal body and (ii) an emission field from the probe within the patient or animal body to a detector.” (Appeal Br. 17.) Specifically, Appellants argue that Alfano ’886 “does not mention or suggest using a forward model for reconstruction and . . . , the point scanning approach described in Alfano ’886 is distinct from the tomographic reconstruction and processing in applicant’s claimed subject matter.” (*Id.*)

The Examiner answers that Alfano ’886 is not relied upon for teaching a forward model. Rather, Alfano ’886 is relied upon “for teaching

optical tomography of in vivo biological tissues where tissues are illuminated and detected lights by one or more detectors are used to construct a three dimensional tomographic map (Col. 2 lines 28-55 and Col. 8 lines 63-Col. 9 lines 3).” (Answer 18 (emphasis omitted).) Therefore, we do not find Appellants’ argument persuasive of error.

Appellants also argue that Yokoi does not teach “detecting both excitation light that is transmitted through the body . . . and fluorescent light emitted from the body, or processing a measure of both excitation light that is transmitted through the body . . . and fluorescent light emitted from the body.” (Appeal Br. 18.) Specifically, Appellants argue that “Yokoi explicitly states that the excitation light is reflected light, which is not transmitted through a patient or animal (see, e.g., page 18, column 9, lines 41-56; and page 19, column 11, lines 1-3).” (*Id.*)

We do not find this argument persuasive of error. The Examiner does not rely on Yokoi for teaching excitation light that is transmitted through a body. Rather, the Examiner relies on Yokoi for teaching “that having both excitation light [regardless of whether it is transmitted through or reflected from a body] and fluorescent light (Col. 9 lines 13-26 and Col. 9 lines 40-60) [has the] advantage of obtaining an image with [a high] signal-to-noise ratio.” (Answer 19.)

Appellants also argue that Yokoi does not teach “use of a forward model as recited in claim 30.” (Appeal Br. 19.)

We do not find this argument persuasive of error as the Examiner did not rely on Yokoi as disclosing a forward model. (*See Non-Final Action 6; see also Answer 19.*)

Appellants also argue that “Alfano ’353 does not mention fluorescence, and accordingly, therefore cannot disclose detecting or processing both excitation and fluorescence light.” (Appeal Br. 20.)

We do not find this argument persuasive of error. The Examiner relies on Alfano ’353 for teaching that “a forward model . . . is widely and routinely used [as a] mathematical model in processing data to construct optical images.” (Answer 20.) Specifically, the Examiner finds that Alfano ’353 teaches “a mathematical formula to represent [a f]orward model in 3D optical tomography (Col. 8 lines 21-65).” (Non-Final Action 6.)

Appellants also argue that “although Alfano ’353 uses the term ‘forward model,’ it does not disclose a forward model as recited in independent claim 30 (or claim 40).” (Appeal Br. 21.) Specifically, Appellants argue that

claim 30 does not recite just any forward model, but rather a specific forward model that models both (i) an excitation field from the near-infrared excitation light source to the probe within the patient or animal body and (ii) an emission field from the probe within the patient or animal body to a detector to provide a three-dimensional tomographic image that corresponds to the three-dimensional target region within the patient or animal body and to the quantity of the probe accumulated in the target region.

(*Id.* at 21.) In particular, Appellants argue that “Alfano ’353 does not relate to fluorescence imaging . . . and, thus does not disclose a fluorescent probe or a forward model of excitation light to the probe and emission field from such a probe to a detector.” (*Id.* at 21–22.) Moreover, Appellants argue,

each of Benaron, Alfano ’886, and Yokoi are directed to a point scanning approach that is fundamentally distinct from Applicant’s tomographic reconstruction approach. That is, the point scanning approaches disclosed in Benaron, Alfano ’886, and Yokoi form images in a fashion that is not based on use of a

forward model to generate predictions of measured data, and does not contemplate such an approach. As a result, one of skill in the art would not have been motivated to process data obtained via the approaches of any of Benaron, Alfano '886, and Yokoi using a forward model of any kind to provide a three-dimensional tomographic image.

(*Id.*)

The Examiner answers:

Although, Benaron and Yokoi do not specify that one is constructing a tomographic image[], examiner incorporated Alfano 886 for optical tomography of in vivo biological tissues where tissues are illuminated and detected lights by one or more detectors are used to construct a three dimensional tomographic map (Col. 2 lines 28-55 and Col. 8 lines 63-Col. 9 lines 3).

(Answer 21.) Additionally, the Examiner has included Alfano '353 “which discloses a mathematical formula to represent [a f]orward model in 3D optical tomography.” (*Id.*) Moreover, the Examiner determines that it

would have been obvious to one of ordinary skill in the art, having the teachings of Benaron, Alfano, Yokoi and Alfano 353 before him at the time the invention was made, to modify the method and apparatus taught by Benaron, Alfano and Yokoi to include the teachings of Alfano 353, as using a forward model are [sic] well known in the art and suitable for use in the method and apparatus of optical imaging system. One of ordinary skill in the art would have been motivated to make such a combination as it provides more accurate image with increased resolution (Col. 5 lines 5-15).

(Non-Final Action 6–7.)

As noted above, a reference “must be read, not in isolation, but for what it fairly teaches in combination with the prior art as a whole.” *In re Merck & Co.*, 800 F.2d at 1097. In other words, obviousness is more than what is specifically disclosed in the cited references. “If a person of

ordinary skill can implement a predictable variation, § 103 likely bars its patentability.” *KSR Int’l Co. v. Teleflex Inc.*, 550 U.S. 398, 417 (2007). Moreover, “[u]nder the correct analysis, any need or problem known in the field of endeavor at the time of invention and addressed by the patent can provide a reason for combining the elements in the manner claimed.” *Id.* at 420.

As discussed above, the Examiner finds that, e.g., Benaron teaches “detecting at multiple points excitation light transmitted through the patient” and “detecting fluorescent light emitted from the patient.” (Non-Final Action 4.) Even if we were to agree with Appellants that “the point scanning approaches disclosed in Benaron, Alfano ’886, and Yokoi form images in a fashion that is not based on use of a forward model” (Appeal Br. 22), Appellants do not persuasively argue *why* the Examiner erred in determining that “it is well known in the art of optical imaging system[s] and method[s] to construct a forward model as part of image reconstruction.” (Non-Final Action 6.) Nor do Appellants persuasively argue *why* the Examiner erred in determining that it would have been obvious “to modify the method and apparatus taught by [*the combination of*] Benaron, Alfano and Yokoi to include the teachings of Alfano 353, as using a forward model [was] well known in the art.” (*See id.*)

Therefore, we are not persuaded that the Examiner erred in rejecting independent claim 30. Dependent claims 31–34, 36, and 37 are not separately argued and fall with claim 30. *See* 37 C.F.R. § 41.37(c)(1)(iv).

In arguing the patentability of dependent claims 35 and 38–44, Appellants rely on the same arguments presented with regard to claim 30.

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For the reasons discussed, we do not find these arguments persuasive of error.

DECISION

The Examiner's rejection of claim 30–44 under 35 U.S.C. § 103(a) is affirmed.

No time period for taking any subsequent action in connection with this appeal may be extended under 37 C.F.R. § 1.136(a). *See* 37 C.F.R. § 1.136(a)(1)(iv).

AFFIRMED