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BEFORE THE PATENT TRIAL AND APPEAL BOARD

Ex parte JOHN C. DOCHERTY, MARK HEWKO,
GURPREET MANGAT, ROBERT W. FLOWER, and
SESHADRI M. CHARI

Appeal 2018-008729
Application 14/543,429
Technology Center 3700

Before STEFAN STAICOVICI, JAMES P. CALVE, and
MICHAEL J. FITZPATRICK, *Administrative Patent Judges*.

STAICOVICI, *Administrative Patent Judge*.

DECISION ON APPEAL

STATEMENT OF THE CASE

Appellant¹ appeals under 35 U.S.C. § 134(a) from the Examiner's decision in the Non-Final Office Action (dated Oct. 26, 2017) rejecting claims 1, 2, 5–8, 11–13, 15, 16, 22, 23, 25–28, and 33–35. We have jurisdiction over this appeal under 35 U.S.C. § 6(b).

¹ We use the word “Appellant” to refer to “applicant” as defined in 37 C.F.R. § 1.42. Novadaq Technologies ULC is identified as the real party in interest in Appellant's Appeal Brief (filed May 25, 2018). Appeal Br. 2.

SUMMARY OF DECISION

We AFFIRM.

INVENTION

Appellant's invention is directed to a method for determining the extent of perfusion in a portion of animal tissue. Spec. para. 2.²

Claims 1, 8, and 25 are independent. Claim 1 is illustrative of the claimed invention and reads as follows:

1. A method for determining the extent of perfusion in a portion of tissue of an animal, the method comprising:
 - administering indocyanine green to the bloodstream of the animal such that the indocyanine green enters the portion of tissue;
 - exciting the indocyanine green within the portion of tissue with a source of illumination such that the indocyanine green emits radiation;
 - detecting through a skin surface, with an imaging system, the radiation emitted by the indocyanine green moving through the portion of tissue at a depth of at least 0.5 cm from the skin surface while the animal's heart is beating, the radiation emitted by the indocyanine green moving through the portion of tissue representing perfusion in the portion of tissue, wherein the imaging system comprises a camera and an image processor;
 - obtaining a series of images of the radiation emitted by the indocyanine green moving through the portion of tissue at a depth of at least 0.5 cm from the skin surface in real time at an image acquisition rate of at least 15 frames per second for determining the extent of perfusion in the portion of tissue; and
 - outputting the series of images to a display.

² Substitute Specification, filed Jan. 7, 2015.

REJECTIONS

- I. The Examiner rejects claims 1, 2, 5–8, 11–13, 15, 16, 22, 23, 25–28, and 33–35 under 35 U.S.C. § 103(a) as being unpatentable over Flower³ in view of Svetliza⁴ or Achilefu⁵ alone or further in view of Kijima.⁶
- II. The Examiner rejects claims 1, 2, 5–8, 11–13, 15, 16, 22, 23, 25–28, and 33–35 on the ground of nonstatutory double patenting as being unpatentable over claims 1–40 and 50–83 of U.S. Patent No. 6,351,663 B1⁷ in view of Svetliza or Achilefu alone or further in view of Kijima.

ANALYSIS

Rejection I

Appellant does not present arguments for the patentability of claims 2, 5–8, 11–13, 15, 16, 22, 23, 25–28, and 33–35 apart from claim 1. *See* Appeal Br. 18, 20–21. Therefore, in accordance with 37 C.F.R. § 41.37(c)(1)(iv), we select claim 1 as the representative claim to decide the appeal of the rejection of these claims, with claims 2, 5–8, 11–13, 15, 16, 22, 23, 25–28, and 33–35 standing or falling with claim 1.

The Examiner finds that Flower discloses a method including, *inter alia*, “administering ICG^[8] to the bloodstream of the animal, exciting the

³ Flower et al., US 6,351,663 B1, issued Feb. 26, 2002.

⁴ Svetliza, US 6,178,340 B1, issued Jan. 23, 2001.

⁵ Achilefu et al., US 6,217,848 B1, issued Apr. 17, 2001.

⁶ Kijima et al., US 6,882,366 B1, issued Apr. 19, 2005.

⁷ *See* footnote 3.

⁸ “ICG” refers to indocyanine green, which is a fluorescent dye. *See* Spec. para. 40.

ICG with a source of illumination, detecting with an imaging system the radiation emitted by the ICG, obtaining a series of images of the emitted radiation and outputting the series of images to a display.” Non-Final Act. 4–5 (citing Flower, col. 2, ll. 18–25, col. 3, ll. 1–17, col. 5, ll. 41–55, col. 7, ll. 36–54, col. 8, ll. 6–35). The Examiner further finds that Flower does not “disclose determining the extent of perfusion in a portion of tissue.” *Id.* at 5. Nonetheless, the Examiner finds that “Svetliza discloses using ICG to visualize both blood flow through vessels as well as perfusion at a location deep below the skin surface” and “Achilefu . . . disclose[s] imaging perfusion below the skin surface using ICG and a CCD camera.” *Id.* (citing Svetliza, col. 5, ll. 64–67, col. 6, ll. 1–12; Achilefu, col. 10, ll. 62–67, col. 11, ll. 1–14). Thus, the Examiner concludes that “[i]t would have been obvious to one skilled in the art to have modified Flower . . . such that the method is applied on any vasculature in the body to observe either blood flow through a vessel or perfusion in view of Svetliza or Achilefu.” *Id.*

The Examiner further determines that because “it is a well-known expedient to time the capture of images to a time when the dye has reached a desired location,” it would have been obvious to a person of ordinary skill in the art to acquire “a series of images based on such timing . . . [in order] to yield predictable and optimal results and would include the images as set forth.” *Id.* Alternatively, the Examiner determines that because Flower discloses a CCD camera to capture images and Kijima discloses an imaging system with a CCD camera having a frame rate of at least 15 frames per second (hereinafter “fps”), it would have been obvious to a skilled artisan to modify Flower, according to Kijima, “such that the imaging system used includes a CCD camera that images in real time and has a frame rate of at least 15 frames per second in order to image all details of blood flow more

efficiently.” *Id.* According to the Examiner, the “modification merely involves the substitution of one known type of imaging system used to image fluid/blood flow for another and such modification amounts to substituting known equivalents to yield predictable results, which has previously been held as unpatentable.” *Id.* (citing *KSR Int’l Co. v. Teleflex Inc.*, 550 U.S. 398, 416 (2007)).

Appellant argues that neither Flower, nor Svetliza, nor Achilefu discloses imaging tissue perfusion. *See* Appeal Br. 7–18. Rather, according to Appellant, Flower discloses imaging blood flow in individual vessels, which is “not the same as imaging tissue perfusion.” *Id.* at 7–9 (citing paragraphs 6–10 of the Declaration filed under 37 CFR § 1.132 by Dr. Michael Robert Zenn on October 2, 2017 (hereinafter “Zenn Decl.” or “Zenn Declaration)). Appellant further contends that even though Svetliza makes a *singular* mention to perfusion, as Svetliza’s disclosure as a *whole* is concerned with imaging blood vessels deep below the skin to facilitate accurate subcutaneous puncture during insertion of a hypodermic needle, a skilled artisan “would not have had any reason to image tissue perfusion,” and, thus, Appellant asserts that “Svetliza [likewise] does not disclose imaging tissue perfusion.” *Id.* at 10–12 (citing Svetliza, col. 5, l. 63–col. 6, l. 12); *see also* Reply Br. 6–7.⁹ In regards to Achilefu, Appellant asserts that although Achilefu discloses imaging of perfusion of ICG agent into a tumor “to evaluate the structural or anatomic boundaries of the tumor over extended imaging sessions,” this type of perfusion “is not the tissue perfusion required by the claims,” namely, “the movement of blood through

⁹ Appellant’s Reply Brief, filed Aug. 31, 2018.

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the tissue” in real time. *Id.* at 15–16 (citing Achilefu, col. 10, l. 62–col. 11, l. 14); Reply Br. 8.

We are not persuaded by Appellant’s arguments because the combination of familiar elements according to known methods is likely to be obvious when it does no more than yield predictable results. *KSR*, 550 U.S. at 415–16. Here, we appreciate that “imaging blood flow in individual vessels is not [the same as] imaging tissue perfusion,” as argued by Appellant and thoroughly explained in the Zenn Declaration. *See* Appeal Br. 9, Zenn Decl. paras. 6–10. Nonetheless, as the Examiner correctly finds, Flower does disclose an imaging process similar to that of claim 1, in which the fluorescent emission of a fluorescent dye composition, such as ICG, administered into the bloodstream of an animal, is detected and visualized using a CCD camera. *See* Flower, col. 3, ll. 1–15, col. 4, ll. 16–18, 39–41, col. 7, ll. 50–54, col. 10, ll. 3–4. Furthermore, the Examiner employs Svetliza to show that visualizing the fluorescent emission of ICG, such as in the imaging process of Flowers, can be used for imaging *both* “the human arterio-venous circulation *and* perfusion of tissue.” Svetliza, col. 5, l. 66–col. 6, l. 12 (emphasis added). The Examiner further employs Achilefu to emphasize the well-known process of fluorescence imaging of ICG perfusion into a tumor (i.e., tissue). *See* Achilefu, col. 1, ll. 52–59, col. 4, ll. 56–58, col. 10, l. 66–col. 11, l. 4. Moreover, even though we appreciate Appellant’s position that the purpose of “perfusion” in Achilefu is not to “imag[e] the flow of blood through the tissue in *real time*,” nonetheless, Achilefu does disclose imaging perfusion of ICG agent into a tumor (tissue) after a predetermined period of time. *See* Appeal Br. 16 (emphasis added); *see also* Reply Br. 8. The Examiner is correct that Achilefu’s imaging of ICG perfusion into a tumor (tissue) is similar to Appellant’s description of

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tissue perfusion as assessing “[t]he extent of blood flow within a particular tissue.” *See* Ans. 7–8;¹⁰ Spec. para. 9.

As such, because both Svetliza and Achilefu disclose fluorescence imaging of ICG tissue perfusion, we agree with the Examiner’s determination that it would have been obvious for a skilled artisan to employ Flower’s fluorescent emission of ICG to image tissue perfusion in *addition* to imaging blood in individual vessels. *See* Non-Final Act. 5. More specifically, as Svetliza *explicitly* discloses visualizing the fluorescent emission of ICG for *both* “the human arterio-venous circulation and perfusion of tissue,” the Examiner’s modification to employ Flower’s method to image tissue perfusion in *addition* to imaging blood in individual vessels is merely a predictable use of prior art elements according to their established functions. *KSR*, 550 U.S. at 417.

Moreover, we are not persuaded by Appellant’s argument regarding Svetliza’s *singular* mention of tissue perfusion because “a prior art reference is relevant for all that it teaches to those of ordinary skill in the art.” *See In re Fritch*, 972 F.2d 1260, 1264 (Fed. Cir. 1992). We do not agree with Appellant that the Examiner has taken the phrase “perfusion of tissue” out of context, because the paragraph bridging columns 5 and 6 of Svetliza, upon which the Examiner relies, discloses a novel imaging system for visualizing the fluorescent emission of ICG capable of studying *both* human arterial and venous circulation *and* tissue perfusion. *See* Reply Br. 6.

Appellant further argues that the Examiner’s conclusion that it would have been obvious to a skilled artisan to image tissue perfusion in the process of Flower, as modified by Svetliza or Achilefu, using a CCD camera

¹⁰ Examiner’s Answer, dated July 3, 2018.

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having a frame rate of at least 15 fps, “can only be the result of improper hindsight.” Appeal Br. 19. Appellant asserts that: (1) “Flower provides no reason to select the frame rate recited in the claims for tissue perfusion imaging”; (2) “Svetliza and Achilefu are also silent with respect to image acquisition rates”; and (3) “Kijima has nothing at all to do with fluorescent imaging.” *Id.*; *see also* Reply Br. 9.

We are not persuaded by Appellant’s arguments because the lack of an express disclosure of a particular claim element in the Examiner’s combination of Flower, as modified by Svetliza and Achilefu, does not defeat a rejection under 35 U.S.C. § 103(a), and such a requirement would essentially defeat the purpose of 35 U.S.C. § 103(a). We must attribute skill to the hypothetical person described in 35 U.S.C. § 103(a). *In re Sovish*, 769 F.2d 738, 742 (Fed. Cir. 1985). In this case, the Examiner is correct that a person of ordinary skill in the art would know “to time the capture of images to a time when the dye has reached a desired location” when trying to image blood flow in the fluorescent emission process of Flower, as modified by Svetliza or Achilefu. *See* Non-Final Act. 5; Ans. 8. Furthermore, a skilled artisan in the art of dynamic image processing would readily understand that in order to accurately capture *movement* of an object, which in this case is the fluorescent dye, an adequate frame rate is required.

Accordingly, the fact that some judgment and skill may be required to merely select a camera having the claimed frame rate of at least 15 fps to image tissue perfusion in the fluorescent emission process of Flower, as modified by Svetliza or Achilefu, does not mean that such combination constitutes a nonobvious invention. *Graham v. John Deere Co.*, 383 U.S. 1, 10–12 (1966) (discussing *Hotchkiss v. Greenwood*, 52 U.S. 248 (1851)). Here, Flower already discloses the use of a CCD camera, and, thus, selecting

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a particular CCD camera with a frame rate of at least 15 fps from readily available known CCD cameras might not be the product of innovation but something that occurs in the ordinary course of using a known device such as a CCD camera. *See* Appeal Br. 20 (“Appellant does not pretend to have invented imaging at 15 frames per second.”). Stated differently, selecting a particular CCD camera with a specific frame rate of at least 15 fps from readily available known CCD cameras amounts to choosing from a finite number of identified, predictable solutions, with a reasonable expectation of success. *See, e.g., In re Kubin*, 561 F.3d 1351, 1358–60 (discussing “obvious to try” situations in light of *In re O’Farrell*, 853 F.2d 894, 903 (Fed. Cir. 1988) and *KSR*, 550 U.S. at 421).

In addition, we are not persuaded by Appellant’s arguments that the Examiner’s determination of obviousness is based on impermissible hindsight reconstruction because the proposed modification is an improvement to the imaging process of Flower, as modified by Svetliza or Achilefu, in the same way as taught by Kijima, to lead to a predictable result, and the modification is well within the skill of a person having ordinary skill in this art. *KSR*, 550 U.S. at 417 (“[I]f a technique has been used to improve one device, and a person of ordinary skill in the art would recognize that it would improve similar devices in the same way, using the technique is obvious unless its actual application is beyond his or her skill.”). Here, Kijima specifically discloses that *dynamic imaging* requires an increased frame rate, that is, a frame rate higher than 15 fps (“at least 15 frames per second”). *See* Kijima, col. 1, ll. 9–10, 19–23, col. 3, ll. 16–18, 22–24, 40–43. In other words, Kijima specifically discloses that a frame rate of less than 15 fps is not sufficient for adequate *dynamic imaging*. *See* Reply Br. 9 (“Why 15 frames per second as opposed to 10 frames per second

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or 5 frames per second?”). Furthermore, a person of ordinary skill in the art would understand that blood *flow* in an individual vessel or through tissue (tissue perfusion) constitutes a *dynamic* process. *See In re Jacoby*, 309 F.2d 513, 516 (CCPA 1962) (An artisan must be presumed to know something about the art apart from what the references disclose.).

Accordingly, we agree with the Examiner that it would have been obvious to a skilled artisan to employ Kijima’s CCD camera with a frame rate of at least 15 fps, in the dynamic imaging process of Flower, as modified by Svetliza or Achilefu, in order to obtain “images in real time and . . . to image all details of blood flow more efficiently.” Ans. 8. Appellant does not persuasively argue that the Examiner’s findings and reasoning are in error.

Appellant further argues that (1) Flower’s fundus camera or endoscope is not suitable for imaging tissue perfusion (*see* Appeal Br. 9); (2) Svetliza’s system is unsuitable for imaging tissue perfusion (*see id.* at 13–15); (3) Achilefu does not image blood flow through tissue in real time, teaches away from using ICG, and its system is not suitable for tissue perfusion imaging (*see id.* at 15–18); and (4) “Kijima has nothing at all to do with fluorescent imaging” (*see id.* at 19; *see also* Reply Br. 9).

We are not persuaded by Appellant’s arguments because such arguments represent an individual attack on the respective teachings of Flower, Svetliza, Achilefu, and Kijima, whereas the Examiner’s rejection is based on a combination of these references. It is well settled that “[n]on-obviousness cannot be established by attacking references individually where the rejection is based upon the teachings of a combination of references. [Each reference] must be read, not in isolation, but for what it

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fairly teaches in combination with the prior art as a whole.” *See In re Merck & Co.*, 800 F.2d 1091, 1097 (Fed. Cir. 1986) (citation omitted).

In this case, the Examiner does not employ the system of any of Flower, Svetliza, or Achilefu to visualize movement of the fluorescent dye in real time in the process of Flower, as modified by Svetliza or Achilefu, but rather uses Kijima’s CCD camera with a frame rate of at least 15 fps. *See Non-Final Act. 5*. As blood flow is a *dynamic* process and Kijima’s CCD camera with a frame rate of at least 15 fps is required for *dynamic imaging*, it is not clear from Appellant’s arguments why a skilled artisan would not employ Kijima’s camera to visualize movement of the fluorescent dye in the process of Flower, as modified by Svetliza or Achilefu.

Lastly, we do not agree with Appellant that Achilefu teaches away from fluorescence imaging of ICG perfusion into a tumor because Achilefu discloses that “novel bioconjugate contrast agents are far *superior* to ICG for tumor imaging.” Appeal Br. 17 (citing Achilefu, col. 10, l. 63–col. 11, l. 31) (emphasis added). Teaching away requires a reference to actually criticize, discredit, or otherwise discourage the claimed solution. *See In re Fulton*, 391 F.3d 1195, 1201 (Fed. Cir. 2004) (prior art does not teach away from claimed subject matter merely by disclosing a different solution to a similar problem unless the prior art also criticizes, discredits, or otherwise discourages the solution claimed). Here, in the portion cited by Appellant, Achilefu does not disclose that ICG is *always* inferior to Cytate 1 and Cytate 2, as Appellant appears to assert. Rather, out of three tumor lines tested, only in one tumor line, i.e., CA 20948, does Achilefu disclose ICG is inferior to its novel contrast agents (Cytate 1 and Cytate 2). *See Achilefu*, col. 11, ll. 4–23. The other two tumor lines “indicated slow perfusion of the agent [ICG] over time into the tumor and reasonable images were obtained

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for each.” *Id.* at col. 11, ll. 1–4. As such, Achilefu’s disclosure would not have led a person of ordinary skill away from the proposed modification; rather, such disclosure would have been instructive. *See W.L. Gore & Assocs., Inc. v. Garlock, Inc.*, 721 F.2d 1540, 1550 (Fed. Cir. 1983) (A prior art reference must be considered in its entirety, i.e., as a whole, including portions that would lead away from the claimed invention.).

In conclusion, for the foregoing reasons, we sustain the rejection of independent claim 1 under 35 U.S.C. § 103(a) as unpatentable over Flower in view of Svetliza or Achilefu alone or further in view of Kijima. Claims 2, 5–8, 11–13, 15, 16, 22, 23, 25–28, and 33–35 fall with claim 1.

Rejection II

Appellant relies on the same arguments discussed *supra*. *See* Appeal Br. 21. Therefore, for the same reasons discussed above, we also sustain the rejection of claims 1, 2, 5–8, 11–13, 15, 16, 22, 23, 25–28, and 33–35 on the ground of nonstatutory double patenting as being unpatentable over claims 1–40 and 50–83 of U.S. Patent No. 6,351,663 B1 in view of Svetliza or Achilefu alone or further in view of Kijima.

CONCLUSION

| Claim(s) rejected | 35 U.S.C. § | Basis | Affirmed | Reversed |
|--|--------------------|------------------------------------|--|-----------------|
| 1, 2, 5–8, 11–13, 15, 16, 22, 23, 25–28, 33–35 | 103(a) | Flower, Svetliza, Achilefu, Kijima | 1, 2, 5–8, 11–13, 15, 16, 22, 23, 25–28, 33–35 | |
| 1, 2, 5–8, 11–13, 15, 16, 22, 23, 25–28, 33–35 | | Obviousness-type Double Patenting | 1, 2, 5–8, 11–13, 15, 16, 22, 23, 25–28, 33–35 | |
| Overall outcome | | | 1, 2, 5–8, 11–13, 15, 16, 22, 23, 25–28, 33–35 | |

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

AFFIRMED