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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

Ex parte CHRISTOPHER B. ARENA, RAFAEL V. DAVALOS, and MICHAEL B. SANO

Appeal 2018-001806
Application 13/332,133
Technology Center 3700

Before LISA M. GUIJT, LEE L. STEPINA, and BRENT M. DOUGAL, *Administrative Patent Judges*.

GUIJT, *Administrative Patent Judge*.

DECISION ON APPEAL

Appellants[1] appeals under 35 U.S.C. § 134(a) from the Examiner's rejection[2] of claims 44–64 and 81–102. We have jurisdiction under 35 U.S.C. § 6(b).

We AFFIRM.

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[1] Appellants identify the real party in interest as Virginia Tech Intellectual Properties, Inc. Br. 3.

[2] Appeal is taken from the Final Office Action dated March 15, 2017.

STATEMENT OF THE CASE

Claims 44, 62, 91, and 94 are the independent claims on appeal. Claim 44, reproduced below with disputed limitations italicized for emphasis, is exemplary of the subject matter on appeal.

> 1. A medical device for ablating tissue cells by non-thermal irreversible electroporation comprising:
>
> one or more electrodes adapted to be positioned near a target area containing target tissue cells to be ablated;
>
> a power supply adapted to generate and deliver electrical pulses to the electrodes; and
>
> a controller in operable connection with and programmable to control the power supply to output one or more bursts of the electrical pulses, wherein said pulses have predetermined pulse parameters with *each burst containing multiple electrical pulses at a frequency rate of 50 kHz or higher* and being sufficient to subject that target tissue cells to non-thermal irreversible electroporation, each electrical pulse having a pulse width of 10 microseconds or less so as to ablate the target tissue cells by non-thermal irreversible electroporation;
>
> wherein the controller is programmable to allow for independent selection of width and amplitude of positive and negative pulses within one or more of the bursts and to allow for a delay between each burst of pulses; and
>
> wherein the controller is programmable to control the power supply to output the negative pulses with an amplitude of between 500-4,000 V/cm.

THE REJECTIONS

I. Claims 44–64, 81–83, and 94–102 stand rejected under 35 U.S.C. § 103(a) as unpatentable over Deem '672 (US 2005/0261672 A1; published Nov. 24, 2005), Francischelli (US 2010/0023004 A1; published Jan. 28, 2010), and Chang (US 4,822,470; issued Apr. 18, 1989).

II. Claims 84–88 stand rejected under 35 U.S.C. § 103(a) as unpatentable over Deem '672, Francischelli, Chang, Nanda (US 6,150,148; issued Nov. 21, 2000), Zhang (US 6,972,013 B1; issued Dec. 6, 2005), Dzekunov (US 2003/0059945 A1; published Mar. 27, 2003), and Herbst (US 6,029,090; issued Feb. 22, 2000).

III. Claim 91 stands rejected under 35 U.S.C. § 103(a) as unpatentable over Deem '672, Francischelli, Chang, Nanda, and Zhang.

IV. Claims 89 and 90 stand rejected under 35 U.S.C. § 103(a) as unpatentable over Deem '672, Francischelli, Chang, and Demarais (US 2007/0129760 A1; published June 7, 2007).

V. Claims 92 and 93 stand rejected under 35 U.S.C. § 103(a) as unpatentable over Deem '672, Francischelli, Chang, Nanda, Zhang, and Deem '989 (US 2007/0060989 A1; published Mar. 15, 2007).

ANALYSIS

Rejection I

Appellants argue claims 44–64, 81–83, and 94–102 as a group. We select independent claim 44 as representative, with claims 45–64, 81–83, and 94–102 standing or falling with claim 44. *See* 37 C.F.R. § 41.37(c)(1)(iv).

Regarding independent claim 44, the Examiner finds that Deem '672 discloses a medical device for ablating tissue cells by irreversible electroporation (IRE) including one or more electrodes 126, 127, a power supply, and a controller to output electrical pulses. Final Act. 2 (citing Deem '672 ¶¶ 58, 64, 69, Fig. 8). The Examiner determines that Deem '672 does not disclose, *inter alia*, bursts containing multiple electrical pulses at a

frequency rate of 50 kHz or higher, although the Examiner finds that Deem '672 teaches that "the disclosed device could be modified to include the ability to output any pulse parameters that are known to produce electroporation." *Id.* at 4.

The Examiner relies on Chang for disclosing "an electroporation device capable of ablating via electroporation." Final Act 5 (citing Chang 7:7–10 ("[t]he cell normally remains viable after such reversible breakdown," however, "if the induced potential is much higher than V_c, the membrane breakdown is irreversible"). The Examiner finds that Chang discloses using "pulsed [radiofrequency (RF)] energy on the order of 50 kHz to 500 MHz" for electroporation. *Id.* (citing Chang 3:30–39). The Examiner reasons that it would have been obvious "to allow the system of [Deem '672, as modified by Francischelli] to produce RF pulses as taught by Chang to produce the predictable result of allowing an operator to program a generator/controller to interact with tissue in a desired manner." *Id.*

Appellants argue that Chang discloses "a *thermal* ablation technique" and "teaches away from[] *non-thermal* IRE." Br. 5; *see also id.* 10 ("RF energy is a thermal ablation technique, which teaches away from [Appellants'] *non-thermal* IRE technique"). Appellants submit that "[i]t is well known in the medical device arts that RF energy produces thermal effects, including radiant thermal heating in target and non-target tissue." *Id.* at 12 (citing Francischelli ¶¶ 7, 27). Appellants refer to dictionary definitions of the term "radiofrequency ablation," for example, "'[a] procedure that uses radio waves to heat and destroy abnormal cells'" and "'[a] technique for removing a tumor by heating it with a radiofrequency current.'" *Id.* at 12. Appellants argue that "reliance on the quantitative

pulse parameter of *Chang* cannot be divorced from the type of energy resulting from those parameters, RF energy, a thermal ablation technique." *Id.* 10–11.

The Examiner responds that the Specification discloses that "it is tissue ablation that is non-thermal, not the IRE process itself" (Ans. 5 (citing Spec. ¶¶ 15, 80, 85, 113)). The Examiner further finds that "the non-thermal benefit is associated with minimizing Joule heating, not the utter absence of any temperature increase." *Id.* at 5–6. The Examiner also determines that neither Deem '672 nor Chang discloses, with respect to the IRE process, that "thermal ablation is contemplated or required, or that Joule heating is the primary mechanism of ablation." *Id.* at 6.

Appellants' argument does not provide sufficient explanation or evidence for concluding that using a pulsed RF field across the electrodes to porate the cells (as taught in Chang) is inherently a *thermal* IRE process. *See* Chang, Abstract ("The power function generator can apply . . . a pulsed radiofrequency electric field across the electrodes," wherein "[t]he pulsed radiofrequency electrical field porates . . . the cells."). Appellants argue that cited prior art is limited to the use of heat in a conventional RF ablation procedure, wherein radio waves heat and destroy cells. However, as discussed *infra*, the prior art distinguishes between these two types of RF procedures.

As determined by the Examiner, the Specification does not provide a precise meaning for the claim term "non-thermal irreversible electroporation," for example, as compared to "thermal irreversible electroporation." *See, e.g.*, Ans. 5–6; Spec. ¶ 34 (distinguishing non-thermal IRE by disclosing that "[m]ethods according to the invention can be

modified to provide for administering non-thermal IRE, IRE, and/or reversible electroporation"). The Specification discloses that "[t]o maintain its non-thermal benefits, the pulse parameters for IRE procedures are restricted to those that minimize any associated Joule heating" (*id.* ¶ 86) and that "[h]igh-frequency electroporation . . . reduces the potential for thermal damage in low passive conductivity tissue" (*id.* ¶ 101). The Specification also discloses that, with respect to "high frequency IRE" (Example 7), "[p]ulse parameters were chosen based on the results from the analytical and numerical models to ensure the greatest potential for non-thermal tissue ablation." Spec. ¶¶ 129, 132. Thus, on the record before us, we determine that "non-thermal irreversible electroporation" means irreversible electroporation (IRE) ablation performed without causing Joule heating in the treated tissue that results in thermal damage, for example, by the appropriate selection of pulse parameters. Non-thermal IRE, as determined by the Examiner *supra*, does not use Joule heating as the mechanism to destroy or ablate the treated tissue, and further, involves the selection of pulse parameters to prevent thermal damage to the treated tissue.

Deem '672 discloses using "RF energy" to "ablate the site," wherein "[e]lectrodes **44**, **52** employ energy (e.g., RF energy) for stimulating, targeting, and/or ablating target tissue," which "may also be accomplished using microwaves, cryothermia probes/balloons, alcohol injection, laser light, magnetic stimulation, and/or ultrasound energy." Deem '672 ¶ 44. Deem '672 *alternatively* discloses that "it may be desirable . . . [to use] pulsed electric fields and/or electroporation," and describes, in relevant part, "electroporation" as "encompass[ing] the use of pulsed electric fields," and "'ablation' [as encompassing] the mechanism of electroporation leading to

denervation whether it be . . . reversible or irreversible . . . *without necessitating the presence of a thermal effect*." *Id.* ¶ 55 (emphasis added). Deem '672 further teaches that "[v]arious waveforms or shapes of pulses may be applied to achieve electroporation, including sinusoidal AC pulses, DC pulses, square wave pulses, exponentially decaying waveforms or other pulse shapes such as combined AC/DC pulses, or DC shifted RF signals." *Id.* ¶ 60. Therefore, Deem '672 recognizes a distinction between the (conventional) use of RF energy to ablate tissue by heating the tissue with an RF current (a definition relied on by Appellants *supra*), as compared to the use of pulsed electric fields for electroporation, including the use of RF signals. Deem '760 further discloses that "[w]hen utilizing an electric field to achieve desired neuromodulation [(by performing IRE)], parameters [include] voltage, field strength, pulse width, pulse duration, the shape of the pulse, the number of pulses (e.g., duty cycle), power, etc.," wherein "[s]uitable shapes of the waveform include . . . RF waveforms[3]." Deem '760 ¶ 25.

Chang discloses "an apparatus and a method for the poration . . . of cells using radiofreqency electrical pulses, . . . wherein [t]he power generator can apply a continuous AC electric field and/or a pulsed radiofrequency electrical field across the electrodes." Chang, Abstract. Appellants' argument does not provide sufficient evidence that the use of a pulsed RF electric field for electroporation, when selected as a parameter for use in the

[3] An ordinary definition of "wave form" is "the profile or shape of a wave, especially the graphical representation of one of its characteristics, e.g., frequency or amplitude, relative to time." *Waveform-Definition*-Microsoft® Encarta® College Dictionary, 1625 (2001).

device of Deem '672 as modified by Francischelli, as proposed by the Examiner *supra*, necessarily causes Joule heating in the treated tissue which results in tissue damage. Instead, Appellants' argument appears to address the conventional use of thermally-induced ablation that uses RF energy to destroy tissue by using heat. *See* Ans. 5 ("Chang is not [a conventional] ablation device.").[4] As set forth *supra*, the Examiner relies on electrodes 126, 127 used for electroproration as disclosed in Deem '672 (not conventional RF ablating electrodes 44, 52) in the rejection of the claims. *See, e.g.*, Deem '672 ("[e]lectroproration element **125** includes first electrode **126** and second electrode **127** operatively coupled to pulse generator **121** for delivering a desired number, duration, amplitude and frequency of pulses to targeted cardiac tissue" which "parameters can be modified . . . whether a reversible or irreversible cell poration is desired"). *Id.* at ¶ 63.

Additionally, Appellants have not presented sufficient argument or evidence that Chang teaches away from *non-thermal* IRE. Rather, Chang recognizes that "[e]xcessive current is harmful to the cell because of the resulting thermal effects." Chang 11:1–2. As set forth *supra* Deem '672 describes electroporation ablation as a procedure *without necessitating the presence of a thermal effect.*[5]

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[4] The Examiner also responds that if the mere use of an electric field having a radio frequency (i.e., "50 kHz or higher") results in *thermal* IRE, then the medical device recited in claim 44 "would also necessarily produce a thermal response." Ans. 5. Appellants neither address nor demonstrate error in this finding by the Examiner.

[5] Francischelli ¶ 39 (disclosing that "optimization of the electroporation pulsed energy is, at least in part, a function of thickness and composition of a tissue to be ablated [wherein] optimal energy parameters (e.g., voltage,

Accordingly, we sustain the Examiner's rejection of independent claim 44, and claims 45–64, 81–83, and 94–102 fall therewith.

Rejections II, III, and V

Regarding claims 84–88 and 91–93, the Examiner determines that "[t]he claimed generator elements are commonly used in the electroporation art." Final Act. 7, 9 (citing Nanda 11:23–29 (for disclosing "a capacitor bank"); Zhang 40:67 (for disclosing "a polarity switch"); Dzekunov ¶ 153 (for disclosing "current limiting resistors"); Herbst 6:54 (for disclosing "an arbitrary function generator") and 3:42–45 (for teaching that "the generator can produce a wave of any arbitrary shape and allows individual adjustment of electrical parameters")). The Examiner reasons that "the art discloses that known elements (the various circuit components) can be combined according to known methods (the methods that allow any of the prior art references to be functional) to produce predictible results (electroporation)." *Id.* 7–8, 9 (citing *KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398, 416 (2007) ("[t]he combination of familiar elements according to known methods is likely to be obvious when it does no more than yield predictable results.")). The Examiner also determines that, with respect to the spacing of the electrodes, "considering the device is used in the body, a distance on the order of mm or cm would be expected and it is well within the purview of one of ordinary skill in the art to select an electrode gap that would produce a desired result." Final Act. 11 (citing Deem '672, Fig. 6).

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pulse duration, etc.) are characterized as those resulting in a narrow, transmural lesion, with minimal damage to surrounding tissue and not generating excessive heat").

Appellants argue that the Examiner has failed to show *how* the prior art "teaches or suggest any of the specific claimed circuits." Br. 13. In support, Appellants submit that "[t]he fact that known circuit components such as resistors and capacitors exist does not render every circuit configuration incorporating these components obvious," and that "[h]ere, there are not a finite number of possibilities for the different components of the claimed systems, nor a finite number of ways those components could be arranged." *Id.* at 14. Appellants conclude that the Examiner "has not shown that it would have been *obvious to choose* the particular components claimed, let alone the particular arrangement of components claimed." *Id.* at 15 (emphasis added) (citing, for example, *Bayer Schering Pharma AG v. Barr Lab., Inc.*, 575 F.3d 1341, 1347 (Fed. Cir. 2009) ("[A]n invention is not *obvious to try* where vague prior art does not guide an inventor toward a particular solution") (emphasis added).

Claims 85–88 and 91–93 recite, in relevant part, a polarity switch wherein an input of the polarity switch is in direct operable connection with an output of [a] capacitor bank"; "current limiting resistors . . . in direct operable connection with an output of the power supply; "an input of the current limiting resistors is in direct operable connection with an output of the power supply"; "an arbitrary function generator, wherein an output of the arbitrary function generator is in direct operable connection with an input of the polarity switch"; "a positive and negative polarity switch in communication with the power supply and a capacitor bank disposed between the power supply and the positive and negative polarity switches"; and "wherein the electrodes are spaced at least 1 mm apart" or "up to 3 cm apart or less." Br. 22–23 (Claims App.). The Specification discloses that

"[t]he system relies upon both commercially available components and circuits built by the inventors," which "allows for a flexible treatment program that may be tailored to meet a patient's individual needs." Spec. ¶ 118. The Specification also acknowledges that "[o]ther systems are available in the literature for generating bipolar pulses, and the invention should not be limited to the system described [in Paragraph 118]." *Id.* ¶ 119.

Appellants' argument that the Examiner has failed to demonstrate that the claimed combinations of electrical components are *obvious to try* does not address the Examiner's articulated reasoning that the claimed combinations of electrical components constitute a combination of familiar elements according to known methods. Thus, Appellants' argument does not apprise us of error in the Examiner's findings or reasoning.

Accordingly, we sustain that Examiner's rejection of claims 84–88 and 91–93.

Rejection IV

Appellants chose not to present separate arguments for the patentability of claims 89 and 90, which depend from independent claim 44. Therefore, for essentially the same reasons set forth *supra*, we also sustain the Examiner's rejection of claims 89 and 90.

DECISION

The Examiner's decisions rejecting claims 44–64 and 81–102 are 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