

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

PCT

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43bis.1)

To: Daryl Richardson
1801 N. Griffin Dallas
Dallas, Texas
United States of America

Date of mailing
(day/month/year)

26 AUG 2019

Applicant's or agent's file reference
PCTP2019-000005

FOR FURTHER ACTION

See paragraph 2 below

International application No.

PCT/IB19/51007

International filing date (day/month/year)

07 February 2019 (07.02.2019)

Priority date (day/month/year)

07 February 2018 (07.02.2018)

International Patent Classification (IPC) or both national classification and IPC

IPC - A61N 1/04, 1/32, 1/36 (2019)

CPC - A61N 1/04, 1/323, 1/36014

Applicant

PANACEA QUANTUM LEAP TECHNOLOGY LLC

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis. I(a)(i) with regard to novelty, inventive step and industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

Name and mailing address of the ISA/US
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Date of completion of this opinion

30 July 2019 (30.07.2019)

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**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.

PCT/IB19/51007

Box No. I Basis of this opinion

1. With regard to the **language**, this opinion has been established on the basis of:
 - ☒ the international application in the language in which it was filed.
 - ☐ a translation of the international application into _____ which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1(b)).
2. ☐ This opinion has been established taking into account the **rectification of an obvious mistake** authorized by or notified to this Authority under Rule 91 (Rule 43*bis*.1(b)).
3. ☐ With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, this opinion has been established on the basis of a sequence listing:
 - a. ☐ forming part of the international application as filed:
 - ☐ in the form of an Annex C/ST.25 text file.
 - ☐ on paper or in the form of an image file.
 - b. ☐ furnished together with the international application under PCT Rule 13*ter*.1(a) for the purposes of international search only in the form of an Annex C/ST.25 text file.
 - c. ☐ furnished subsequent to the international filing date for the purposes of international search only:
 - ☐ in the form of an Annex C/ST.25 text file (Rule 13*ter*.1(a)).
 - ☐ on paper or in the form of an image file (Rule 13*ter*.1(b) and Administrative Instructions, Section 713).
4. ☐ In addition, in the case that more than one version or copy of a sequence listing has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that forming part of the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
5. Additional comments:

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.

PCT/IB19/51007

Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step and industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	1-44, 46-56	YES
	Claims	45	NO
Inventive step (IS)	Claims	1-44, 46-56	YES
	Claims	45	NO
Industrial applicability (IA)	Claims	1-56	YES
	Claims	NONE	NO

2. Citations and explanations:

Claim 45 lacks novelty under PCT Article 33(2) as being anticipated by US 2016/0106976 A1 to Theodore R. Kucklick (hereinafter 'Kucklick').

As for claim 45, Kucklick discloses a method for stimulating a tissue with electric fields and magnetic fields (an electro-stimulation device for patients in the form of a TENS unit; figures 1 and 2; paragraphs [0009]), the method comprising: a*) applying an electric field and a magnetic field stimulus to a tissue through an arrangement of electromagnetic transducers that receive an activation signal, the parameters of which varies in time (an electro-stimulation device for patients in the form of a TENS unit applies stimulation via electrode pads 8 to the tissue; figures 1-4; paragraphs [0009, 0015]); b*) measuring the tissue impedance response to the stimulus of stage (a*) through the arrangement of electromagnetic transducers and storing said measure in a memory register of a computing unit (the device monitors the impedance of the tissue and shuts off the current if the tissue impedance becomes too high due to the tissue becoming too dry, the device including a programmable microcontroller with tolerance set by the physician; figures 1-4; paragraphs [0010, 0012, 0016]); c*) changing the parameters of the activation signal according to the tissue impedance response measured in stage (b*) through the computing unit and returning to stage (a*) (the device, via the programmable microcontroller, monitors the impedance of the tissue and shuts off the current if the tissue impedance becomes too high due to the tissue becoming too dry; figures 1-4; paragraphs [0010, 0012, 0016]); wherein the parameters of the activation signal are, modulation, phase, frequency, amplitude, duration, duty cycle and shape (the device monitors the impedance of the tissue and shuts off the current if the tissue becomes too high due to the tissue becoming too dry, the parameters including those of the waveform including pulse power, frequency, session length, amplitude, duration, and charge are all terminated in response to the impedance exceeding the limit; figures 1-4; paragraphs [0010, 0012, 0016]).

Claims 1 and 46 meet the criteria set out in PCT Article 33(2)-(3), because the prior art does not teach or fairly suggest that a device for stimulating a tissue with electromagnetic fields, the device comprising: - a computing unit; - an external power source connected to the computing unit; - a decoupling circuit connected to the external power source and to the computing unit; and - an arrangement of electromagnetic transducers connected to the computing unit and to the decoupling circuit, the arrangement is functionally disposed over the tissue; wherein the computing unit implements a method for stimulating a tissue with electromagnetic fields, the method comprising the stages of: a) applying an electric field stimulus to a tissue through an arrangement of electromagnetic transducers that receives an activation signal, the frequency of which varies from an initial tissue stimulation frequency (f_{ie}) to a final tissue stimulation frequency (f_{fe}) with increments or decrements in steps of a frequency delta (Δf_e) during a time delta (Δt_e); b) measuring the tissue impedance response to the stimulus of stage (a); c) establishing a reference level with the tissue impedance response measured in stage (b); d) establishing a tolerance (NT) to the reference level established in stage (c); e) determining lower tissue stimulation frequencies (f_{bx}) as the point where the tissue impedance response falls below the tolerance (NT) established in stage (d); f) determining upper tissue stimulation frequencies (f_{rx}) as the point where the tissue impedance response returns to the tolerance (NT) established in stage (d); wherein the upper tissue stimulation frequencies (f_{rx}) are greater than the lower tissue stimulation frequencies (f_{bx}) and "x" is a natural number greater than or equal to 1.

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**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.

PCT/IB19/51007

Supplemental Box

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In the first prior art, US 2005/0278001 A1 to Qin, L. et al. (hereinafter 'Qin') discloses a device for stimulating a tissue with electromagnetic fields (stimulator 10 is an electrostimulation device for providing therapy; figures 1-3; paragraphs [0003, 0063, 0105]), the device comprising: - a computing unit (stimulator 10 includes a microcontroller unit 42; figure 4A; paragraph [0070]); - an external power source connected to the computing unit (the stimulator 10 has power to the microcontroller unit 42 via a rechargeable battery 64 which can be charged via a charger 72; figure 4A; paragraphs [0070, 0071]); - a decoupling circuit connected to the external power source and to the computing unit (power management circuitry 62 controls the power for the battery 64 and controller 42; figure 4A; paragraphs [0070, 0071]); and - an arrangement of electromagnetic transducers connected to the computing unit and to the decoupling circuit (stimulator 10 apply electrical stimulation to a patient via applicator electrodes 34 and can use IF, NMES or PDC treatment via signals sent to the electrodes; figures 3 and 4A; paragraphs [0069, 0070, 0080, 0085, 0105]), the arrangement is functionally disposed over the tissue (stimulator 10 is an electrostimulation device for providing therapy to tissue; figures 1-3; paragraphs [0003, 0063, 0105]); wherein the computing unit implements a method for stimulating a tissue with electromagnetic fields (stimulator 10 is an electrostimulation device for providing therapy; figures 1-3; paragraphs [0003, 0063, 0105]), the method comprising: a) applying an electric field stimulus to a tissue through an arrangement of electromagnetic transducers that receives an activation signal (stimulator 10 apply electrical stimulation to a patient via applicator electrodes 34 and can use IF, NMES or PDC treatment via signals sent to the electrodes; figure 3; paragraphs [0069, 0080, 0085, 0105]), the frequency of which varies from an initial tissue stimulation frequency (fie) to a final tissue stimulation frequency (fre) with increments or decrements in steps of a frequency delta (Δfe) during a time delta (Δte) (stimulator 10 may be configured to use preset programs with the frequency varying over a sweep range of frequencies from a bottom range to a top range over a preset time period; figures 1-3; paragraphs [0087-0092]); b) measuring the tissue impedance response to the stimulus of stage (a) (stimulator 10 can be programmed to perform an initial impedance measurement to determine the impedance tolerance of the patient, then before each treatment remeasure impedance to verify the impedance is within the patient's tolerance range; figures 1-3; paragraph [0125]); c) establishing a reference level with the tissue impedance response measured in stage (b) (stimulator 10 can be programmed to perform an initial impedance measurement to determine the impedance tolerance of the patient, then before each treatment remeasure impedance to verify the impedance is within the patient's tolerance range; figures 1-3; paragraph [0125]); d) establishing a tolerance (NT) to the reference level established in stage (c) (stimulator 10 can be programmed to perform an initial impedance measurement to determine the impedance tolerance of the patient, then before each treatment remeasure impedance to verify the impedance is within the patient's tolerance range; figures 1-3; paragraph [0125]).

In the second closest prior art, Kucklick discloses device for stimulating a tissue with electromagnetic fields (an electro-stimulation device for patients in the form of a TENS unit; figures 1 and 2; paragraphs [0009]), the device comprising: - a computing unit (the device including a programmable microcontroller with tolerance set by the physician; figures 1-4; paragraphs [0010, 0012, 0016]); - an external power source connected to the computing unit (the device including the microcontroller 6, may be battery powered, rechargeable, or powered from a cord; figures 1-4; paragraphs [0009, 0015]); - a decoupling circuit connected to the external power source and to the computing unit (the device including the microcontroller 6, may be battery powered, rechargeable, or powered from a cord, with a rechargeable battery including decoupling circuits from the charger; figures 1-4; paragraphs [0009, 0015]); and - an arrangement of electromagnetic transducers connected to the computing unit and to the decoupling circuit (electrodes pad areas 4 part of the device and receiving power from a rechargeable battery and instructions from the microcontroller; figures 1-4; paragraphs [0009, 0015]), the arrangement is functionally disposed over the tissue (the device may be built into a mouth guard to accept the users teeth; figures 1-4; paragraphs [0009]); wherein the computing unit implements a method for stimulating a tissue with electromagnetic fields (an electro-stimulation device for patients in the form of a TENS unit; figures 1 and 2; paragraphs [0009]), the method comprising: a) applying an electric field stimulus to a tissue through an arrangement of electromagnetic transducers that receives an activation signal (an electro-stimulation device for patients in the form of a TENS unit applies stimulation via electrode pads 8 to the tissue; figures 1-4; paragraphs [0009, 0015]), the frequency of which varies from an initial tissue stimulation frequency (fie) to a final tissue stimulation frequency (fre) with increments or decrements in steps of a frequency delta (Δfe) during a time delta (Δte) (the range of the effective frequencies as well as pulse duration are adjusted to match the user's confirm level; figures 1-4; paragraphs [0010, 0012, 0014]); b) measuring the tissue impedance response to the stimulus of stage (a) (the device monitors the impedance of the tissue and shuts off the current if the tissue becomes too high due to the tissue becoming too dry; figures 1-4; paragraphs [0010, 0012, 0016]); c) establishing a reference level with the tissue impedance response measured in stage (b) (the device monitors the impedance of the tissue and shuts off the current if the tissue becomes too high due to the tissue becoming too dry; figures 1-4; paragraphs [0010, 0012, 0016]).

In the third closest prior art, US 2014/0330345 A1 to John, M (hereinafter "John") discloses a device for stimulating a tissue with electromagnetic fields (a stimulator 10 using electrical generating stimulators 10 a or 10b to provide stimulation to a patient; figures 1A, 1B; paragraphs [0031]), the device comprising: - a computing unit (a control subsystem 20 with memory and computational abilities; figures 1A; paragraphs [0033, 0034, 0045]); - an external power source connected to the computing unit (power source 26 provides power to control subsystem 22 may be a rechargeable battery; figures 1A; paragraphs [0045, 0047]); - a decoupling circuit connected to the external power source and to the computing unit (power source 26 provides power to control subsystem 22 may be a rechargeable battery; figure 1A; paragraphs [0045, 0047]); and - an arrangement of electromagnetic transducers connected to the computing unit and to the decoupling circuit (stimulation electrodes or external magnetic stimulator coils; figures 1A; paragraphs [0049]), the arrangement is functionally disposed over the tissue (the stimulator can be located partially or completely outside of the patient; paragraph [0031]); wherein the computing unit implements a method for stimulating a tissue with electromagnetic fields (a stimulator 10 using electrical generating stimulators 10 a or 10b to provide stimulation to a patient; figures 1A, 1B; paragraph [0031]), the method comprising: a) applying an electric field stimulus to a tissue through an arrangement of electromagnetic transducers that receives an activation signal (a stimulation signal 50 provides signals to the contacts 54 to generate electrical fields for tissue stimulation; figure 2B; paragraph [0052]), the frequency of which varies from an initial tissue stimulation frequency (fie) to a final tissue stimulation frequency (fre) with increments or decrements in steps of a frequency delta (Δfe) during a time delta (Δte) (the frequency may have a first partial signal roving from 20-25 hz and a second roves from 26 to 27 to cause the modulation of the beat to rove from 6 to 2 hz; figure 4; paragraphs [0055]);

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**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.

PCT/IB19/51007

Supplemental Box

In case the space in any of the preceding boxes is not sufficient.
Continuation of:

---Continued from Box V: Citations and Explanations---

b) measuring the tissue impedance response to the stimulus of stage (a) (the stimulation subsystem 22 can include impedance sensing and the actual signals within the target tissue may vary in impedance, so a calibration signal may stimulate a set of contacts i and a signal may be used to sense and adjust the stimulation in response to the sensed data; figures 1A, 2B; paragraphs [0045, 0052]); c) establishing a reference level with the tissue response measured in stage (b) (the stimulation subsystem 22 can include impedance sensing and the actual signals within the target tissue may vary in impedance, and an intended summation will be set with corresponding signals (reference level); figures 1A, 2B; paragraphs [0045, 0052]); d) establishing a tolerance (NT) to the reference level established in stage (c) (an iterative adjustment of the signals may be calculated until the sense signal is within a tolerance level with the intended signal; figures 1A, 2B; paragraphs [0045, 0052]).

In the fourth closest prior art, WO 2017/142948 A1 to Nalu Medical, Inc. (hereinafter "Nalu") discloses a device for stimulating a tissue with electromagnetic fields (an electro-dermal patch device 110 is used for stimulating nerves in body tissues; figure 1A; paragraphs [0567, 0694]), the device comprising: - a computing unit (an external programmable 550 may be a computer; figure 1; paragraph [0202, 204]); - an external power source connected to the computing unit (power supply 570 is connected via the transmitter 530 to the external programmable 550; figure 1; paragraphs [0202-0204]); - a decoupling circuit connected to the external power source and to the computing unit (power supply 570 is connected via the transmitter 530 to the external programmable 550, and the power supply may be a rechargeable battery and an ac power supply to allow decoupling; figure 1; paragraphs [0202-0204]); and - an arrangement of electromagnetic transducers connected to the computing unit and to the decoupling circuit (power supply 570 is connected via the transmitter 530 to the external programmable 550, and the power supply may be a rechargeable battery and an ac power supply to allow decoupling and connected to functional elements 560 and 260 which may be electrodes or transducers able to generate electrical or magnetic fields; figure 1; paragraphs [0186, 0202-0204]), the arrangement is functionally disposed over the tissue (the external device 500 is on the skin; figure 1; paragraphs [0186]); wherein the computing unit implements a method for stimulating a tissue with electromagnetic fields (a medical apparatus 10 for stimulating tissue of a patient using an electromagnetic field energy; figure 1; paragraphs [0168, 0169, 0175, 0189]), the method comprising: a) applying an electric field stimulus to a tissue through an arrangement of electromagnetic transducers that receives an activation signal (a medical apparatus 10 for stimulating tissue of a patient using an electromagnetic field energy via one or more functional elements 260 which deliver energy to the tissue in response to a stimulation signal; figure 1; paragraphs [0169, 0175, 0179, 0189]), the frequency of which varies from an initial tissue stimulation frequency (fie) to a final tissue stimulation frequency (fre) with increments or decrements in steps of a frequency delta (Δf_e) during a time delta (Δt_e) (the apparatus 10 may perform a frequency sweep; figure 1; paragraphs [0285]); b) measuring the tissue impedance response to the stimulus of stage (a) (the apparatus 10 may include function elements 260 or 560 measuring impedance in the tissue and may be used such as during a frequency sweep and measure periodically; figures 1; paragraphs [0179, 0214-0216, 0285, 0390]).

In the fifth closest prior art, US 2018/0000347 A1 to Elira, Inc. (hereinafter "Elira") discloses a device for stimulating a tissue with electromagnetic fields (an electro-dermal patch device 110 is used for stimulating nerves in body tissues; figure 1A; paragraphs [0567, 0694]), the device comprising: - a computing unit (microcontroller 112; figure 1A; paragraphs [0567, 0568]); - an external power source connected to the computing unit (power management module 120 providing power to the microcontroller 112 may be a rechargeable battery such as a lithium ion battery and may include receptor slots for additional batteries (external power source) to be added and removed; figure 1A; paragraphs [0567, 0568]); - a decoupling circuit connected to the external power source and to the computing unit (power management module 120 providing power to the microcontroller 112 may be a rechargeable battery such as a lithium ion battery and may include receptor slots for additional batteries (external power source) to be added and removed (decoupled); figure 1A; paragraphs [0567, 0568]); and - an arrangement of electromagnetic transducers connected to the computing unit and to the decoupling circuit (one or more electrodes 118; figures 1A; paragraphs [0567, 0568]), the arrangement is functionally disposed over the tissue (the device is an electro-dermal patch device 110 is used for stimulating nerves in body tissues by being placed over skin; figure 1A; paragraphs [0567, 0694]); wherein the computing unit implements a method for stimulating a tissue with electromagnetic fields (an electro-dermal patch device 110 is used for stimulating nerves in body tissues; figure 1A; paragraphs [0567, 0694]), the method comprising: a) applying an electric field stimulus to a tissue through an arrangement of electromagnetic transducers that receives an activation signal (the electro-dermal patch device 110 has a pulse generator to apply pulses through one or more electrodes to provide stimulation therapy into the patients epidermal layer by providing electrical stimulation; figures 1A; paragraphs [0568, 0592]), the frequency of which varies from an initial tissue stimulation frequency (fie) to a final tissue stimulation frequency (fre) with increments or decrements in steps of a frequency delta (Δf_e) during a time delta (Δt_e) (in order to avoid habituation the stimulation intensity may gradually increase with the frequency decreased arithmetically with time; figures 1A; paragraphs [0313, 0972-0974, 01126]); b) measuring the tissue impedance response to the stimulus of stage (a) (the impedance electrode monitors skin contact impedance and may determine at the start of a session whether or not a user is wearing the EDP device; figures 1A; paragraphs [0722, 1022]); c) establishing a reference level with the tissue impedance response measured in stage (b) (a base line to biomarkers may be established with skin impedance values using impedance sensors in the edp; figure 1A; paragraph [0936]); d) establishing a tolerance (NT) to the reference level established in stage (c) (a maximum tolerable stimulation reaction threshold is measured at step 2744, and habituation may be measured; figures 27B, 59A and 59B; paragraphs [0852, 0982-0986, 1076]).

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**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.

PCT/IB19/51007

Supplemental Box

In case the space in any of the preceding boxes is not sufficient.
Continuation of:

---Continued from Box V: Citations and Explanations---

Qin, Kucklick, John, Nalu, and Elira provide close references as they are directed to electromagnetic tissue stimulators able to measure impedance and alter the frequency over time. However, Qin uses the impedance measurements to determine use and lacks any relationship between the impedance, the tolerance and frequencies. Kucklick provides the use of impedance to stop the process, but lacks any relationship between the frequencies and tolerance. John may alter the frequency to remain in tolerance, but lacks an established link to teach, suggest or motivate the impedance setting the tolerance, nor changes in the impedance to set limits on the frequency based on the tolerance, as John is using tolerance to refer to a limit in the sensors, not patient tolerance. Elira provides a relationship between frequency and impedance, and uses it frequency to control habitation, but Elira does not establish a reference level of tolerance and use it to set the frequency limits based on impedance, as Elira Nalu measures impedance over a frequency sweep, but lacks establishing a reference level to the impedance or to the tolerance. None of the references clearly establishes that the impedance measurements may determine a reference level of tolerance which may determine lower tissue stimulation frequencies (fbx) as the point where the tissue impedance response falls below the tolerance (NT), and may determine upper tissue stimulation frequencies (ftx) as the point where the tissue impedance response returns to the tolerance (NT) wherein the upper tissue stimulation frequencies (frx) are greater than the lower tissue stimulation frequencies (fbx) and "x" is a natural number greater than or equal to 1. As none of the above references discloses, teach, or suggest, the nexus between tolerance, impedance, and frequency it would not be obvious to modify them to include such a relationship.

Claims 2-22 and 47-52 meet the criteria set out in PCT Article 33(2)-(3), because of their dependency on claim 1 and 46.

Claim 23 and 53 meets the criteria set out in PCT Article 33(2)-(3), because the prior art does not teach or fairly suggest that a device for stimulating a tissue with electromagnetic fields, the device comprising: - a computing unit; - an external power source connected to the computing unit; - a decoupling circuit connected to the external power source and to the computing unit; and - an arrangement of electromagnetic transducers connected to the computing unit and to the decoupling circuit, the arrangement is functionally disposed over the tissue; wherein the computing unit implements a method for stimulating a tissue with magnetic fields, the method comprising the stages of: a') applying a magnetic field stimulus to a tissue through an arrangement of electromagnetic transducers that receive an activation signal, the frequency of which varies from an initial tissue stimulation frequency (fim) to a final tissue stimulation frequency (frm) with increments or decrements in steps of a frequency delta (Δfm) during a time delta (Δtm); b') measuring the tissue impedance response to the magnetic field stimulus through the electrical field transducers of the arrangement of electromagnetic transducers; c') establishing a reference level with the tissue impedance response measured in stage (b'); d') establishing a tolerance (NT) to the reference level established in stage (c'); e') determining lower tissue stimulation frequencies (fbx) as the point where the tissue impedance response falls below the tolerance (NT) established in stage (d'); f') determining upper tissue stimulation frequencies (ftx) as the point where the tissue impedance response returns to the tolerance (NT) established in stage (d'); wherein the upper tissue stimulation frequencies (ftx) are greater than the lower tissue stimulation frequencies (fbx) and "x" is a natural number greater than or equal to 1.

In the first prior art, Qin discloses a device for stimulating a tissue with electromagnetic fields (stimulator 10 is an electrostimulation device for providing therapy; figures 1-3; paragraphs [0003, 0063, 0105]), the device comprising: - a computing unit (stimulator 10 includes a microcontroller unit 42; figure 4A; paragraph [0070]); - an external power source connected to the computing unit (the stimulator 10 has power to the microcontroller unit 42 via a rechargeable battery 64 which can be charged via a charger 72; figure 4A; paragraphs [0070, 0071]); - a decoupling circuit connected to the external power source and to the computing unit (power management circuitry 62 controls the power for the battery 64 and controller 42; figure 4A; paragraphs [0070, 0071]); and - an arrangement of electromagnetic transducers connected to the computing unit and to the decoupling circuit (stimulator 10 apply electrical stimulation to a patient via applicator electrodes 34 and can use IF, NMES or PDC treatment via signals sent to the electrodes; figures 3 and 4A; paragraphs [0069, 0070, 0080, 0085, 0105]), the arrangement is functionally disposed over the tissue (stimulator 10 is an electrostimulation device for providing therapy to tissue; figures 1-3; paragraphs [0003, 0063, 0105]); wherein the computing unit implements a method for stimulating a tissue with applying a magnetic field stimulus to a tissue through an arrangement of electromagnetic transducers that receive an activation signal fields (stimulator 10 is an electrostimulation device for providing therapy; figures 1-3; paragraphs [0003, 0063, 0105]), the method comprising: a') applying a magnetic field stimulus to a tissue through an arrangement of electromagnetic transducers that receive an activation signal (stimulator 10 apply electrical stimulation to a patient via applicator electrodes 34 and can use IF, NMES or PDC treatment via signals sent to the electrodes; figure 3; paragraphs [0069, 0080, 0085, 0105]), the frequency of which varies from an initial tissue stimulation frequency (fim) to a final tissue stimulation frequency (frm) with increments or decrements in steps of a frequency delta (Δfm) during a time delta (Δtm) (stimulator 10 may be configured to use preset programs with the frequency varying over a sweep range of frequencies from a bottom range to a top range over a preset time period; figures 1-3; paragraphs [0087-0092]); b) measuring the tissue impedance response to the magnetic field stimulus through the electrical field transducers of the arrangement of electromagnetic transducers (stimulator 10 can be programed to perform an initial impedance measurement to determine the impedance tolerance of the patient, then before each treatment remeasure impedance to verify the impedance is within the patient's tolerance range; figures 1-3; paragraphs [0125]); c) establishing a reference level with the tissue impedance response measured in stage (b) (stimulator 10 can be programed to perform an initial impedance measurement to determine the impedance tolerance of the patient, then before each treatment remeasure impedance to verify the impedance is within the patient's tolerance range; figures 1-3; paragraphs [0125]); d) establishing a tolerance (NT) to the reference level established in stage (c) (stimulator 10 can be programed to perform an initial impedance measurement to determine the impedance tolerance of the patient, then before each treatment remeasure impedance to verify the impedance is within the patient's tolerance range; figures 1-3; paragraphs [0125]).

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**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.

PCT/IB19/51007

Supplemental Box

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In the second closest prior art, Kucklick discloses device for stimulating a tissue with electromagnetic fields (an electro-stimulation device for patients in the form of a TENS unit; figures 1 and 2; paragraphs [0009]), the device comprising: - a computing unit (the device including a programable microcontroller with tolerance set by the physician; figures 1-4 paragraphs [0010, 0012, 0016]); - an external power source connected to the computing unit (the device including the microcontroller 6, may be battery powered, rechargeable, or powered from a cord; figures 1-4; paragraphs [0009, 0015]); - a decoupling circuit connected to the external power source and to the computing unit (the device including the microcontroller 6, may be battery powered, rechargeable, or powered from a cord, with a rechargeable battery including decoupling circuits form the charger; figures 1-4; paragraphs [0009, 0015]); and - an arrangement of electromagnetic transducers connected to the computing unit and to the decoupling circuit (electrodes pad areas 4 part of the device and receiving power from a rechargeable battery and instructions from the microcontroller; figures 1-4; paragraphs [0009, 0015]), the arrangement is functionally disposed over the tissue (the device may be built into a mouth guard to accept the users teeth; figures 1-4; paragraphs [0009]); wherein the computing unit implements a method for stimulating a tissue with applying a magnetic field stimulus to a tissue through an arrangement of electromagnetic transducers that receive an activation signal fields (an electro-stimulation device for patients in the form of a TENS unit; figures 1 and 2; paragraphs [0009]), the method comprising: a a') applying a magnetic field stimulus to a tissue through an arrangement of electromagnetic transducers that receive an activation signal (an electro-stimulation device for patients in the form of a TENS unit applies stimulation via electrode pads 8 to the tissue; figures 1 -4; paragraphs [0009, 0015]), the frequency of which varies from an initial tissue stimulation frequency (fim) to a final tissue stimulation frequency (frm) with increments or decrements in steps of a frequency delta (Δfm) during a time delta (Δtm) (the range of the effective frequencies as well as pulse duration are adjusted to match the user's confirm level; figures 1-4; paragraphs [0010, 0012, 0014]); b) measuring the tissue impedance response to the magnetic field stimulus through the electrical field transducers of the arrangement of electromagnetic transducers (the device monitors the impedance of the tissue and shuts off the current if the tissue becomes too high due to the tissue becoming too dry; figures 1-4 paragraphs [0010, 0012, 0016]); c) establishing a reference level with the tissue impedance response measured in stage (b) (the device monitors the impedance of the tissue and shuts off the current if the tissue becomes too high due to the tissue becoming too dry; figures 1-4 paragraphs [0010, 0012, 0016]).

In the third closest prior art, John discloses a device for stimulating a tissue with electromagnetic fields (a stimulator 10 using electrical generating stimulators 10 a or 10b to provide stimulation to a patient; figures 1A, 1B; paragraphs [0031]), the device comprising: - a computing unit (a control subsystem 20 with memory and computational abilities; figures 1A; paragraphs [0033, 0034, 0045]); - an external power source connected to the computing unit (power source 26 provides power to control subsystem 22 may be a rechargeable battery; figures 1A; paragraphs [0045, 0047]); - a decoupling circuit connected to the external power source and to the computing unit (power source 26 provides power to control subsystem 22 may be a rechargeable battery; figures 1A; paragraphs [0045, 0047]); and - an arrangement of electromagnetic transducers connected to the computing unit and to the decoupling circuit (stimulation electrodes or external magnetic stimulator coils; figures 1A; paragraphs [0049]), the arrangement is functionally disposed over the tissue (the stimulator can be located partially or completely outside of the patient; paragraph [0031]); wherein the computing unit implements a method for stimulating a tissue with magnetic fields (a stimulator 10 using electrical generating stimulators 10 a or 10b to provide stimulation to a patient; figures 1A, 1B; paragraphs [0031]), the method comprising: a') applying a magnetic field stimulus to a tissue through an arrangement of electromagnetic transducers that receive an activation signal (a stimulation signal 50 provides signals to the contacts 54 to generate electrical fields for tissue stimulation; figures 2B; paragraphs [0052]), the frequency of which varies from an initial tissue stimulation frequency (fim) to a final tissue stimulation frequency (frm) with increments or decrements in steps of a frequency delta (Δfm) during a time delta (Δtm) (the frequency may have a first partial signal roving from 20-25 hz and a second roves form 26 to 27 to cause the modulation of the beat to rove from 6 to 2 hz; figures 4; paragraphs [0055]); b) measuring the tissue impedance response to the magnetic field stimulus through the electrical field transducers of the arrangement of electromagnetic transducers (the stimulation subsystem 22 can include impedance sensing and the actual signals within the target tissue may vary in impedance, so a calibration signal may stimulate a set of contacts i and a signal may be used to sense and adjust the stimulation in response to the sensed data; figures 1A, 2B; paragraphs [0045, 0052]); c) establishing a reference level with the tissue response measured in stage (b) (the stimulation subsystem 22 can include impedance sensing and the actual signals within the target tissue may vary in impedance, and an intended summation will be set with corresponding signals (reference level); figures 1A, 2B; paragraphs [0045, 0052]); d) establishing a tolerance (NT) to the reference level established in stage (c) (an iterative adjustment of the signals may be calculated until the sense signal is within a tolerance level with the intended signal; figures 1A, 2B; paragraphs [0045, 0052]).

In the fourth closest prior art, Nalu discloses a device for stimulating a tissue with electromagnetic fields (an electro-dermal patch device 110 is used for stimulating nerves in body tissues; figure 1A; paragraphs [0567, 0694]), the device comprising: - a computing unit (an external programable 550 may be a computer; figure 1; paragraph [0202, 0204]); - an external power source connected to the computing unit (power supply 570 is connected via the transmitter 530 to the external programable 550; figure 1; paragraphs [0202-0204]); - a decoupling circuit connected to the external power source and to the computing unit (power supply 570 is connected via the transmitter 530 to the external programable 550, and the power supply may be a rechargeable battery and an ac power supply to allow decoupling; figure 1; paragraphs [0202-0204]); and - an arrangement of electromagnetic transducers connected to the computing unit and to the decoupling circuit (power supply 570 is connected via the transmitter 530 to the external programable 550, and the power supply may be a rechargeable battery and an ac power supply to allow decoupling and connected to functional elements 560 and 260 which may be electrodes or transducers able to generate electrical or magnetic fields; figure 1; paragraphs [0186, 0202-0204]), the arrangement is functionally disposed over the tissue (the external device 500 is on the skin; figure 1; paragraphs [0186]); wherein the computing unit implements a method for stimulating a tissue with applying a magnetic field stimulus to a tissue through an arrangement of electromagnetic transducers that receive an activation signal fields (a medical apparatus 10 for stimulating tissue of a patient using an electromagnetic field energy; figure 1; paragraphs [0168, 0169, 0175, 0189]), the method comprising: a) applying a magnetic field stimulus to a tissue through an arrangement of electromagnetic transducers that receive an activation signal (a medical apparatus 10 for stimulating tissue of a patient using an electromagnetic field energy via one or more functional elements 260 which deliver energy to the tissue in response to a stimulation signal; figure 1; paragraphs [0169, 0175, 0179, 0189]).

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**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.

PCT/IB19/51007

Supplemental Box

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Continuation of:

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the frequency of which varies from an initial tissue stimulation frequency (fim) to a final tissue stimulation frequency (frm) with increments or decrements in steps of a frequency delta (Δfm) during a time delta (Δtm); (the apparatus 10 may perform a frequency sweep; figure 1; paragraphs [0285]); b) measuring the tissue impedance response to the magnetic field stimulus through the electrical field transducers of the arrangement of electromagnetic transducers (the apparatus 10 may include function elements 260 or 560 measuring impedance in the tissue and may be used such as during a frequency sweep and measure periodically; figures 1; paragraphs [0179, 0214-0216, 0285, 0390]).

In the fifth closest prior art, Elira discloses a device for stimulating a tissue with electromagnetic fields (an electro-dermal patch device 110 is used for stimulating nerves in body tissues; figure 1A; paragraphs [0567, 0694]), the device comprising: - a computing unit (microcontroller 112; figure 1A; paragraphs [0567, 0568]); - an external power source connected to the computing unit (power management module 120 providing power to the microcontroller 112 may be a rechargeable battery such as a lithium ion battery and may include receptor slots for additional batteries (external power source) to be added and removed; figure 1A; paragraphs [0567, 0568]); - a decoupling circuit connected to the external power source and to the computing unit (power management module 120 providing power to the microcontroller 112 may be a rechargeable battery such as a lithium ion battery and may include receptor slots for additional batteries (external power source) to be added and removed; figure 1A; paragraphs [0567, 0568]); and - an arrangement of electromagnetic transducers connected to the computing unit and to the decoupling circuit (one or more electrodes 118; figures 1A; paragraphs [0567, 0568]), the arrangement is functionally disposed over the tissue (the device is an electro-dermal patch device 110 is used for stimulating nerves in body tissues by being placed over skin; figure 1A; paragraphs [0567, 0694]); wherein the computing unit implements a method for stimulating a tissue with applying a magnetic field stimulus to a tissue through an arrangement of electromagnetic transducers that receive an activation signal fields (an electro-dermal patch device 110 is used for stimulating nerves in body tissues; figure 1A; paragraphs [0567, 0694]), the method comprising: a) applying a magnetic field stimulus to a tissue through an arrangement of electromagnetic transducers that receive an activation signal (the electro-dermal patch device 110 has a pulse generator to apply pulses through one or more electrodes to provide stimulation therapy into the patients epidermal layer by providing electrical stimulation; figures 1A; paragraphs [0568, 0592]), the frequency of which varies from an initial tissue stimulation frequency (fim) to a final tissue stimulation frequency (frm) with increments or decrements in steps of a frequency delta (Δfm) during a time delta (Δtm) (in order to avoid habituation the stimulation intensity may gradually increase with the frequency decreased arithmetically with time; figures 1A; paragraphs [0313, 0972-0974, 01126]); b) measuring the tissue impedance response to the magnetic field stimulus through the electrical field transducers of the arrangement of electromagnetic transducers (the impedance electrode monitors skin contact impedance and may determine at the start of a session whether or not a user is wearing the EDP device; figures 1A; paragraphs [0722, 1022]); c) establishing a reference level with the tissue impedance response measured in stage (b) (a base line to biomarkers may be established with skin impedance values using impedance sensors in the edp; figure 1A; paragraph [0936]); d) establishing a tolerance (NT) to the reference level established in stage (c) (a maximum tolerable stimulation reaction threshold is measured at step 2744, and habituation may be measured; figures 27B, 59A and 59B; paragraphs [0852, 0982-0986, 1076]).

Qin, Kucklick, John, Nalu, and Elira provide close references as they are directed to electromagnetic tissue stimulators able to measure impedance and alter the frequency over time. However, Qin uses the impedance measurements to determine use and lacks any relationship between the impedance, the tolerance and frequencies. Kucklick provides the use of impedance to stop the process, but lacks any relationship between the frequencies and tolerance. John may alter the frequency to remain in tolerance, but lacks an established link to teach, suggest or motivate the impedance setting the tolerance, nor changes in the impedance to set limits on the frequency based on the tolerance, as John is using tolerance to refer to a limit in the sensors, not patient tolerance. Elira provides a relationship between frequency and impedance, and uses it frequency to control habituation, but Elira does not establish a reference level of tolerance and use it to set the frequency limits based on impedance, as Elira Nalu measures impedance over a frequency sweep, but lacks establishing a reference level to the impedance or to the tolerance. None of the references clearly establishes that the impedance measurements may determine a reference level of tolerance which may determine lower tissue stimulation frequencies (fbx) as the point where the tissue impedance response falls below the tolerance (NT), and may determine upper tissue stimulation frequencies (frx) as the point where the tissue impedance response returns to the tolerance (NT) wherein the upper tissue stimulation frequencies (frx) are greater than the lower tissue stimulation frequencies (fbx) and "x" is a natural number greater than or equal to 1. As none of the above references discloses, teach, or suggest, the nexus between tolerance, impedance, and frequency it would not be obvious to modify them to include such a relationship.

Claims 24-44 and 54-56 meet the criteria set out in PCT Article 33(2)-(3), because of their dependency on claim 23 and 53.

Claims 1-56 have industrial applicability as defined by PCT Article 33(4) because the subject matter can be made or used in industry.