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Canadian Intellectual Property Office

CA 3042101 C 2024/04/09

(11)(21) 3 042 101

(12) BREVET CANADIEN
CANADIAN PATENT

(13) C

(86) Date de dépôt PCT/PCT Filing Date: 2018/02/02
(87) Date publication PCT/PCT Publication Date: 2018/08/09
(45) Date de délivrance/Issue Date: 2024/04/09
(85) Entrée phase nationale/National Entry: 2019/04/26
(86) N° demande PCT/PCT Application No.: US 2018/016738
(87) N° publication PCT/PCT Publication No.: 2018/144943
(30) Priorités/Priorities: 2017/02/03 (US62/454,467); 2017/06/19 (US62/521,890)

(51) Cl.Int./Int.Cl. *A61B 5/00* (2006.01), *A61B 5/0537* (2021.01), *G16H 50/20* (2018.01)

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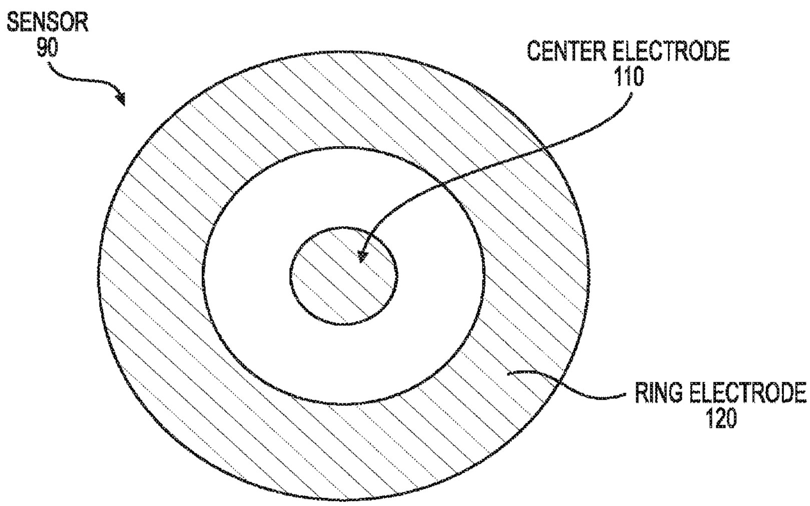
(54) Titre : MESURE D'UN OEDEME
(54) Title: MEASUREMENT OF EDEMA



(57) Abrégé/Abstract:
The present disclosure provides apparatuses and methods for measuring sub-epidermal moisture to provide clinicians with information related to physical conditions and ailments associated with accumulation or depletion of extracellular fluid.

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
09 August 2018 (09.08.2018)

WIPO | PCT

(10) International Publication Number
WO 2018/144943 A1

(51) International Patent Classification:
A61B 5/00 (2006.01) *A61B 5/053* (2006.01)

(21) International Application Number:
PCT/US2018/016738

(22) International Filing Date:
02 February 2018 (02.02.2018)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
62/454,467 03 February 2017 (03.02.2017) US
62/521,890 19 June 2017 (19.06.2017) US

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(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DJ, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JO, JP, KE, KG, KH, KN, KP, KR, KW, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(84) Designated States *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG).

(54) **Title:** MEASUREMENT OF EDEMA

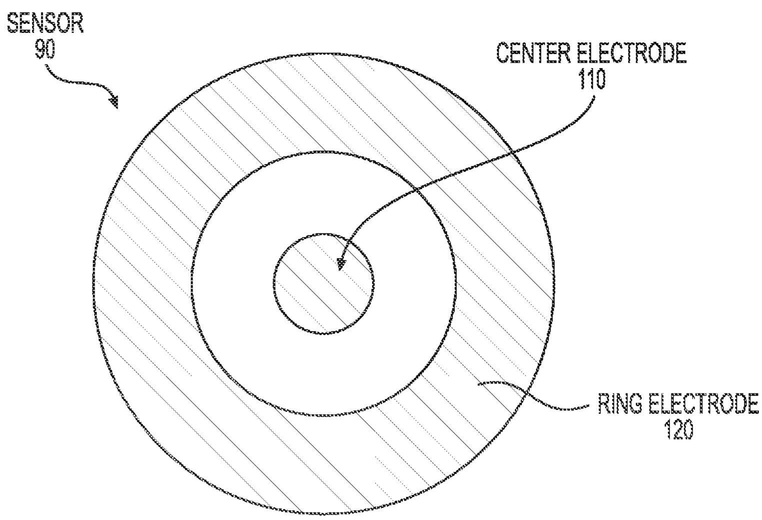

FIG. 1A

(57) **Abstract:** The present disclosure provides apparatuses and methods for measuring sub-epidermal moisture to provide clinicians with information related to physical conditions and ailments associated with accumulation or depletion of extracellular fluid.

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[Continued on next page]

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Published:
— *with international search report (Art. 21(3))*

MEASUREMENT OF EDEMA

FIELD

[0001] The present disclosure provides apparatus and methods for measuring sub-epidermal moisture (SEM) in patients as an indication of tissue damage associated with elevated or diminished levels of moisture in the tissue.

DESCRIPTION OF THE RELATED ART

[0002] Many physical conditions and diseases cause the tissue structure of a patient to degrade, allowing fluid to leak into the interstitial spaces between cells, causing swelling known as "edema." Other conditions reduce the amount of extracellular fluid (ECF) in certain tissues.

[0003] Preeclampsia is a potentially life-threatening condition that affects about 5 percent of pregnant women. It ranges in impact from mild to severe, in which case it can cause serious or even life-threatening problems. One effect of preeclampsia is for blood vessels to constrict thereby causing high blood cause changes in capillaries that allow fluid to "leak" into the surrounding tissue, thereby causing edema. This swelling may happen in the face, hands, or feet or ankles.

[0004] Dehydration may cause a reduced level of moisture in the body, which may result in low blood volume that reduces the amount oxygen delivered to tissue. Local dehydration at the surface of a wound, which may be caused by general dehydration of a patient or by local damage, may slow cellular migration and delay the healing process.

[0005] Another condition associated with edema is "compartment syndrome." Groups of organs or muscles are organized into areas called "compartments." Strong webs of connective tissue called "fascia" form the walls of these compartments. After an injury, blood or fluid may accumulate in the compartment. The fascia cannot easily expand and therefore the pressure in the compartment increases, preventing adequate blood flow to tissues inside the compartment that may result in tissue damage. When this condition occurs in a limb, such as a lower leg, the increase in pressure may cause swelling of the affected limb.

SUMMARY

[0006] In an aspect, the present disclosure provides for, and includes, an apparatus for assessing preeclampsia, the apparatus comprising: a sensor comprising at least one first electrode and at

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least one second electrode, where the sensor is configured to be placed against a patient's skin; a circuit electronically coupled to the first and second electrodes and configured to measure an electrical property between the first and second electrodes and provide information regarding the electrical property; a processor electronically coupled to the circuit; and a non-transitory computer-readable medium electronically coupled to the processor and comprising instructions stored thereon that, when executed on the processor, perform the steps of: receiving the information from the circuit, converting the information into a first sub-epidermal moisture (SEM) value, and determining a difference between the first SEM value and a reference value, where the magnitude of the difference exceeding the reference value is indicative of preeclampsia.

[0007] An aspect of the present disclosure provides for, and includes, an apparatus for assessing hypovolemia, the apparatus comprising: a sensor comprising at least one first electrode and at least one second electrode, where the sensor is configured to be placed against a patient's skin; a circuit electronically coupled to the first and second electrodes and configured to measure an electrical property between the first and second electrodes and provide information regarding the electrical property; a processor electronically coupled to the circuit, and a non-transitory computer-readable medium electronically coupled to the processor and comprising instructions stored thereon that, when executed on the processor, perform the steps of: receiving the information from the circuit, converting the information into a first SEM value, and determining a difference between the first SEM value and a reference value, where the magnitude of the difference lesser than the reference value is indicative of hypovolemia.

[0008] In one aspect, the present disclosure provides for, and includes, a method for detecting preeclampsia at a first location of a patient's skin, the method comprising: obtaining a sub-epidermal moisture (SEM) value at the first location; and determining that the SEM value is greater than a reference value to indicate preeclampsia.

[0009] In an aspect, the present disclosure provides for, and includes, a method for detecting hypovolemia at a first location of a patient's skin, the method comprising: obtaining a sub-epidermal moisture (SEM) value at the first location; and determining that the SEM value is lesser than a reference value to indicate hypovolemia.

[0010] An aspect of the present disclosure provides for, and includes, an apparatus for assessing compartment syndrome, the apparatus comprising: a sensor comprising at least one first electrode and at least one second electrode, where the sensor is configured to be placed against a

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patient's skin, a circuit electronically coupled to the first and second electrodes and configured to measure an electrical property between the first and second electrodes and provide information regarding the electrical property, a processor electronically coupled to the circuit, and a non-transitory computer-readable medium electronically coupled to the processor and comprising instructions stored thereon that, when executed on the processor, perform the steps of: receiving information from the circuit, converting the information into a first sub-epidermal moisture (SEM) value, and determining a difference between the first SEM value and a reference value, where the magnitude of the difference exceeding a predetermined amount is indicative of compartment syndrome.

[0011] In an aspect, the present disclosure provides for, and includes, a method for detecting compartment syndrome at a first location of a patient's skin, the method comprising: obtaining a first sub-epidermal moisture (SEM) value at the first location; obtaining a second SEM value at a second location of the patient's skin; and determining whether the difference between the first SEM value and the second SEM value exceeds a predetermined amount indicative of compartment syndrome.

BRIEF DESCRIPTION OF THE DRAWINGS

[0012] Aspects of the disclosure are herein described, by way of example only, with reference to the accompanying drawings. With specific reference now to the drawings in detail, it is stressed that the particulars shown are by way of example and are for purposes of illustrative discussion of aspects of the disclosure. In this regard, the description and the drawings, considered alone and together, make apparent to those skilled in the art how aspects of the disclosure may be practiced.

[0013] Figure 1A discloses a toroidal bioimpedance sensor.

[0014] Figure 1B discloses a SEM scanner that comprises the sensor of Figure 1A.

[0015] Figure 2 is a first exemplary array of electrodes.

[0016] Figure 3 is an exemplary array of electrodes according to the present disclosure.

[0017] Figure 4A illustrates a first example of how the array of electrodes disclosed in Figure 3 is configured to form a bioimpedance sensor according to the present disclosure.

[0018] Figure 4B illustrates a second example of how the array of electrodes disclosed in Figure 3 is configured to form a bioimpedance sensor according to the present disclosure.

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[0019] Figure 5A illustrates exemplary measurement locations for assessment of edema related to preeclampsia on a hand according to the present disclosure.

[0020] Figure 5B illustrates exemplary measurement locations for assessment of edema related to preeclampsia at the upper ankle region according to the present disclosure.

[0021] Figure 5C illustrates exemplary measurement locations for assessment of edema related to preeclampsia on the face according to the present disclosure.

[0022] Figure 6 discloses an exemplary measurement location for assessment of dehydration on the back of a hand according to the present disclosure.

[0023] Figure 7A illustrates an exemplary measurement location for assessment of compartment syndrome in the forearm area according to the present disclosure.

[0024] Figure 7B illustrates an exemplary measurement location for assessment of compartment syndrome in the calf area according to the present disclosure.

DETAILED DESCRIPTION

[0025] The present disclosure describes applications of the measurement of various electrical characteristics and derivation of SEM values to physical conditions and ailments associated with accumulation or depletion of extracellular fluid (ECF), also referred to as intercellular fluid. Examples provide application to particular conditions, including preeclampsia, dehydration, compartment syndrome, and burns and other open wounds. These examples are not limiting and the demonstrated principles may be applied to a larger scope of injuries and conditions than the specific example. For example, apparatus and methods disclosed in relation to a 3rd-degree burn may be used with equal efficacy to an open cut, gangrene, an ulcer, or other similar injury.

[0026] Women are susceptible to preeclampsia during pregnancy, with one of the symptoms being swelling in areas such as the face, hands, feet, or ankles. Providing a quantitative assessment of the degree of swelling would be beneficial compared to the subjective assessment methods current in use to assess the possibility of a patient having preeclampsia.

[0027] Patients who lose a significant amount of ECF are often considered to be dehydrated while, in fact, depletion of ECF is caused by hypovolemia, which is a decrease in volume of blood plasma. As intravascular volume is controlled by sodium regulation while the total body water content is not, it is important to differentiate between the two conditions so as to select the proper treatment.

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[0028] Compartment syndrome occurs when excessive pressure builds up inside an enclosed muscle space in the body. Compartment syndrome may result from internal bleeding or swelling after an injury. The dangerously high pressure in compartment syndrome impedes the flow of blood to and from the affected tissues, which leads to tissue death if the blood flow is impeded for a sufficient amount of time. It can be an emergency, requiring surgery to prevent permanent injury and a quick and accurate assessment of this condition is vital to determining when to intervene.

[0029] This description is not intended to be a detailed catalog of all the different ways in which the disclosure may be implemented, or all the features that may be added to the instant disclosure. For example, features illustrated with respect to one embodiment may be incorporated into other embodiments, and features illustrated with respect to a particular embodiment may be deleted from that embodiment. Thus, the disclosure contemplates that in some embodiments of the disclosure, any feature or combination of features set forth herein can be excluded or omitted. In addition, numerous variations and additions to the various embodiments suggested herein will be apparent to those skilled in the art in light of the instant disclosure, which do not depart from the instant disclosure. In other instances, well-known structures, interfaces, and processes have not been shown in detail in order not to unnecessarily obscure the invention. It is intended that no part of this specification be construed to effect a disavowal of any part of the full scope of the invention. Hence, the following descriptions are intended to illustrate some particular embodiments of the disclosure, and not to exhaustively specify all permutations, combinations and variations thereof.

[0030] Unless otherwise defined, all technical and scientific terms used herein have the same meaning as commonly understood by one of ordinary skill in the art to which this disclosure belongs. The terminology used in the description of the disclosure herein is for the purpose of describing particular aspects or embodiments only and is not intended to be limiting of the disclosure.

[0031] All publications, patent applications, patents and other references cited herein are referred to for the teachings relevant to the sentence and/or paragraph in which the reference is presented. References to techniques employed herein are intended to refer to the techniques as commonly understood in the art, including variations on those techniques or substitutions of equivalent techniques that would be apparent to one of skill in the art.

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[0032] U.S. Patent Application Serial No. 14/827,375 discloses an apparatus that uses radio frequency (RF) energy to measure the sub-epidermal capacitance that corresponds to the moisture content of the target region of skin of a patient. The '375 application also discloses an array of these bipolar sensors of various sizes.

[0033] U.S. Patent Application Serial No. 15/134,110 discloses an apparatus for measuring sub-epidermal moisture (SEM) using an RF signal at a frequency of 32 kHz to generate a bioimpedance signal, then converting this signal to a SEM value.

[0034] Unless the context indicates otherwise, it is specifically intended that the various features of the disclosure described herein can be used in any combination. Moreover, the present disclosure also contemplates that in some aspects of the disclosure, any feature or combination of features set forth herein can be excluded or omitted.

[0035] The methods disclosed herein include and comprise one or more steps or actions for achieving the described method. The method steps and/or actions may be interchanged with one another without departing from the scope of the present invention. In other words, unless a specific order of steps or actions is required for proper operation of the embodiment, the order and/or use of specific steps and/or actions may be modified without departing from the scope of the present invention.

[0036] As used in the description of the disclosure and the appended claims, the singular forms "a," "an" and "the" are intended to include the plural forms as well, unless the context clearly indicates otherwise.

[0037] As used herein, "and/or" refers to and encompasses any and all possible combinations of one or more of the associated listed items, as well as the lack of combinations when interpreted in the alternative ("or").

[0038] The terms "about" and "approximately" as used herein when referring to a measurable value such as a length, a frequency, or a SEM value and the like, is meant to encompass variations of ± 20%, ± 10%, ± 5%, ± 1%, ± 0.5%, or even ± 0.1% of the specified amount.

[0039] As used herein, phrases such as "between X and Y" and "between about X and Y" should be interpreted to include X and Y. As used herein, phrases such as "between about X and Y" mean "between about X and about Y" and phrases such as "from about X to Y" mean "from about X to about Y."

[0040] As used herein, the term "sub-epidermal moisture" or "SEM" refers to the increase in tissue fluid and local edema caused by vascular leakiness and other changes that modify the

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underlying structure of the damaged tissue in the presence of continued pressure on tissue, apoptosis, necrosis, and the inflammatory process.

[0041] As used herein, a "system" may be a collection of devices in wired or wireless communication with each other.

[0042] As used herein, "interrogate" refers to the use of radiofrequency energy to penetrate into a patient's skin.

[0043] As used herein, a "patient" may be a human or animal subject.

[0044] As used herein, "total body water" or "TBW" refers to the total water content in a subject's body including intravascular fluid and extracellular fluid.

[0045] As used herein, "intravascular volume" refers to fluid contained within cells.

[0046] As used herein, "extracellular fluid" or "ECF" refers to bodily fluid contained outside of cells, including plasma, interstitial fluid, and transcellular fluid.

[0047] As used herein, "interstitial fluid" refers to fluid that surrounds tissue cells of a multicellular subject.

[0048] As used herein, "skin tent" refers to the slow return of the skin to its normal position after being pinched.

[0049] Figure 1A discloses a toroidal bioimpedance sensor 90. In an aspect, a center electrode 110 is surrounded by a ring electrode 120. Without being limited to a particular theory, the gap between the two electrodes affects the depth of field penetration into the substrate below sensor 90. In one aspect, a ground plane (not visible in Figure 1A, is parallel to and separate from the plane of the electrodes and, in an aspect, extends beyond the outer diameter of ring electrode 120. Without being limited to a particular theory, a ground plane may limit the field between electrodes 110 and 120 to a single side of the plane of the electrodes that is on the opposite side of the plane of the electrodes from the ground plane.

[0050] Figure 1B provides top and bottom views of a SEM scanner 170 that comprise electronics that drive sensor 174, which is similar to sensor 90 of Figure 1, and measure a capacitance between electrodes 110 and 120. This capacitance is converted to a SEM value that is displayed on display 176.

[0051] Aspects of sensor 90 and SEM scanner 170 are disclosed in International Publication No. WO 2016/172263, from which the U.S. Patent Application 15/134,110 was filed as a national phase entry.

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[0052] Figure 2 depicts an exemplary electrode array 290, according to the present disclosure. Array 290 is composed of individual electrodes 300 disposed, in this example, in a regular pattern over a substrate 292. In an aspect, each electrode 300 is separately coupled (through conductive elements not shown in Figures 6 through 8B) to a circuit, such as described with respect to Figure 4A, that is configured to measure an electrical parameter. In one aspect, a "virtual sensor" is created by selective connection of predetermined subsets of electrodes 300 to a common element of a circuit. In this example, a particular electrode 310 is connected as a center electrode, similar to electrode 110 of Figure 1A, and six electrodes 320A-320F are connected together as a "virtual ring" electrode, similar to electrode 120 of Figure 1A. In an aspect, two individual electrodes are individually connected to a circuit to form a virtual sensor, for example electrodes 310 and 320A are respectively connected as two electrodes of a sensor. In one aspect, one or more electrodes 300 are connected together to form one or the other of the electrodes of a two-electrode sensor.

[0053] Any pair of electrodes, whether composed of single electrodes or a set of electrodes coupled together to form virtual electrodes, is coupled to electronics that are configured to measure an electrical property or parameter that comprises one or more of electrical characteristics selected from the group consisting of a resistance, a capacitance, an inductance, an impedance, a reluctance, or other electrical characteristic with one or more of sensors 90, 174, 290, 430, 440, or other two-electrode sensor.

[0054] Figure 3 depicts another exemplary array 400 of electrodes 410, according to the present disclosure. In this example, each of electrodes 410 is an approximate hexagon that is separated from each of the surrounding electrodes 410 by a gap 420. In an aspect, electrodes 410 are one of circles, squares, pentagons, or other regular or irregular shapes. In one aspect, gap 420 is uniform between all electrodes 410. In an aspect, gap 420 varies between various electrodes. In one aspect, gap 420 has a width that is narrower than the cross-section of each of electrodes 410. Electrodes 410 may be interconnected to form virtual sensors as described below with respect to Figures 8A and 8B.

[0055] Figure 4A depicts an array 400 of electrodes 410 that are configured, e.g. connected to a measurement circuit, to form an exemplary sensor 430, according to the present disclosure. A single hexagonal electrode 410 that is labeled with a "1" forms a center electrode and a ring of electrodes 410 that are marked with a "2" are interconnected to form a ring electrode. In one aspect, electrodes 410 between the center and ring electrode are electrically "floating." In an

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aspect, electrodes 410 between the center and ring electrode are grounded or connected to a floating ground. In one aspect, electrodes 410 that are outside the ring electrode are electrically "floating." In an aspect, electrodes 410 that are outside the virtual ring electrode are grounded or connected to a floating ground.

[0056] Figure 4B depicts an alternate aspect where array 400 of electrodes 410 has been configured to form a virtual sensor 440, according to the present disclosure. In an aspect, multiple electrodes 410, indicated by a "1," are interconnected to form a center electrode while a double-wide ring of electrodes, indicated by a "2," are interconnected to form a ring electrode. In one aspect, various numbers and positions of electrodes 410 are interconnected to form virtual electrodes of a variety of sizes and shapes.

[0057] Figure 5A discloses exemplary measurement locations 510 and 520 on a hand 500 for assessment of edema related to preeclampsia, according to the present disclosure. Location 510 is generally located on the thenar of a left hand, while location 520 is generally located on the hypothenar eminence of a left hand. Similar locations exist in the same areas of a right hand. Other locations where edema related to preeclampsia is observable are known to those in the field. In an aspect, a measured SEM value may be compared to a predetermined reference value, where the measured SEM value being above or below a threshold is indicative of edema. In one aspect, multiple measurements taken at multiple locations are averaged or compared to an average, where a difference between a reading and the average is indicative of edema at the respective location. In an aspect, a maximum and a minimum SEM value are identified within a set of measurements, where a characteristic of the comparison such as the difference between the maximum and minimum is compared to a predetermined threshold. In one aspect, a SEM value measured at a first predetermined location is compared to a SEM value measured at a second predetermined location, where a characteristic of the comparison such as a difference greater than a threshold is indicative of edema at one of the locations.

[0058] Figure 5B disclose exemplary measurement locations 552 and 562 for assessment of edema in upper ankle region 550 and foot 560 that are related to preeclampsia, according to the present disclosure. In an aspect, SEM values derived from measurements made at one of more locations 552 and 562 are compared to each other, a parameter calculated from one of more of the measurements, e.g. an average SEM value, or to predetermined thresholds.

[0059] In one aspect, a SEM sensor as described herein, for example sensor 90 or sensor 400, is embedded in a band 554 that can be wrapped around a calf as shown in Figure 5B. In one

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aspect, band 554 comprises sensors configured to measure one or more of oxygenation of the tissue, which may comprise measurement of one or both of oxyhemoglobin and deoxyhemoglobin, temperature of one or more points on the skin, pulse rate, and blood pressure in a patient. In an aspect, the combination of measurements made by band 554 provides information regarding blood flow and edema in the lower leg of a patient.

[0060] Figure 5C discloses exemplary measurement locations 572, 574, 576 for assessment of edema on face 570 that is related to preeclampsia, according to the present disclosure. Swelling may occur in one or more of location 572 near the eyes, location 574 on the infraorbital triangle, location 574 over the cheek bone, or other locations between and around locations in a patient as identified in Figure 5C. SEM values derived from measurements at one of more of these locations may be assessed as discussed in relation to Figures 5A and 5B.

[0061] In general, edema caused by preeclampsia is a system condition and would be expected to be present at the same level in equivalent locations on a patient's body. For example, swelling of a left hand would be expected to be roughly the same as the corresponding right hand, and vice versa. In one aspect, a SEM scanner comprises two electrodes, a circuit electronically coupled to the electrodes and configured to measure an electrical property between the electrodes and provide information regarding the electrical property to a processor that is configured to convert the information into a SEM value. In an aspect, multiple electrical property measurements are used to generate an average SEM value. A processor of a SEM scanner then compares SEM values derived from measurements at similar locations and calculated one or more of an average, a difference, a percentage difference, or other computational characteristic of the set of SEM values. In an aspect, a determination that the SEM values in two corresponding locations are both above a predetermined threshold and are also within a predetermined range of each other is indicative of preeclampsia. In one aspect, a single SEM value exceeding a reference value, which may be predetermined or derived from other SEM measurements, is indicative of preeclampsia.

[0062] In an aspect, a predetermined reference value for preeclampsia may range from 0.1 to 8.0, such as from 0.1 to 1.0, from 1.1 to 2.0, from 2.1 to 3.0, from 3.1 to 4.0, from 4.1 to 5.0, from 5.1 to 6.0, from 6.1 to 7.0, from 7.1 to 8.0, from 0.1 to 7.5, from 0.5 to 8.0, from 1.0 to 7.0, from 1.5 to 6.5, from 2.0 to 6.0, from 3.0 to 5.5, from 3.5 to 5.0, or from 4.0 to 4.5. In an aspect, a predetermined reference value for preeclampsia may range from 0.1 to 4.0, such as from 0.5 to 4.0, from 0.1 to 3.5, from 1.0 to 3.5, from 1.5 to 4.0, from 1.5 to 3.5, from 2.0 to 4.0, from 2.5 to

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3.5, from 2.0 to 3.0, from 2.0 to 2.5, or from 2.5 to 3.0. In one aspect, a predetermined reference value for preeclampsia may range from 4.1 to 8.0, such as from 4.5 to 8.0, from 4.1 to 7.5, from 5.0 to 7.5, from 5.5 to 7.0, from 5.5 to 7.5, from 6.0 to 8.0, from 6.5 to 7.5, from 6.0 to 7.0, from 6.0 to 6.5, or from 6.5 to 7.0. In one aspect, a predetermined reference value for preeclampsia may be about 0.3, 0.35, 0.4, 0.45, 0.5, 0.55, 0.6, 0.65, 0.7, 0.75, 0.8, 0.85, 0.9, 0.95, 1.0, 1.1, 1.2, 1.3, 1.4, 1.5, 1.6, 1.7, 1.8, 1.9, 2.0, 2.1, 2.2, 2.3, 2.4, 2.5, 2.6, 2.7, 2.8, 2.9, 3.0, 3.1, 3.2, 3.3, 3.4, 3.5, 3.6, 3.7, 3.8, 3.9, 4.0, 4.1, 4.2, 4.3, 4.4, 4.5, 4.6, 4.7, 4.8, 4.9, 5.0, 5.1, 5.2, 5.3, 5.4, 5.5, 5.6, 5.7, 5.8, 5.9, 6.0, 6.1, 6.2, 6.3, 6.4, 6.5, 6.6, 6.7, 6.8, 6.9, 7.0, 7.1, 7.2, 7.3, 7.4, or 7.5. In an aspect, a predetermined reference value for preeclampsia can be scaled by a factor or a multiple based on the values provided herein.

[0063] One or more regions may be defined on a body. In an aspect, measurements made within a region are considered comparable to each other. A region may be defined as an area on the skin of the body wherein measurements may be taken at any point within the area. In an aspect, a region corresponds to an anatomical region (e.g., heel, ankle, lower back). In an aspect, a region may be defined as a set of two or more specific points relative to anatomical features wherein measurements are taken only at the specific points. In an aspect, a region may comprise a plurality of non-contiguous areas on the body. In an aspect, the set of specific locations may include points in multiple non-contiguous areas.

[0064] In an aspect, a region is defined by surface area. In an aspect, a region may be, for example, between 5 and 200 cm^2, between 5 and 100 cm^2, between 5 and 50 cm^2, or between 10 and 50 cm^2, between 10 and 25 cm^2, or between 5 and 25 cm^2.

[0065] In an aspect, measurements may be made in a specific pattern or portion thereof. In an aspect, the pattern of readings is made in a pattern with the target area of concern in the center. In an aspect, measurements are made in one or more circular patterns of increasing or decreasing size, T-shaped patterns, a set of specific locations, or randomly across a tissue or region. In an aspect, a pattern may be located on the body by defining a first measurement location of the pattern with respect to an anatomical feature with the remaining measurement locations of the pattern defined as offsets from the first measurement position.

[0066] In an aspect, a plurality of measurements are taken across a tissue or region and the difference between the lowest measurement value and the highest measurement value of the plurality of measurements is recorded as a delta value of that plurality of measurements. In an

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aspect, 3 or more, 4 or more, 5 or more, 6 or more, 7 or more, 8 or more, 9 or more, or 10 or more measurements are taken across a tissue or region.

[0067] In an aspect, a threshold may be established for at least one region. In an aspect, a threshold of 0.2, 0.3, 0.4, 0.5, 0.6, 0.7, 0.8, 0.9, or other value may be established for the at least one region. In an aspect, a delta value is identified as significant when the delta value of a plurality of measurements taken within a region meets or exceeds a threshold associated with that region. In an aspect, each of a plurality of regions has a different threshold. In an aspect, two or more regions may have a common threshold.

[0068] In an aspect, a threshold has both a delta value component and a chronological component, wherein a delta value is identified as significant when the delta value is greater than a predetermined numerical value for a predetermined portion of a time interval. In an aspect, the predetermined portion of a time interval is defined as a minimum of X days wherein a plurality of measurements taken that day produces a delta value greater than or equal to the predetermined numerical value within a total of Y contiguous days of measurement. In an aspect, the predetermined portion of a time interval may be defined as 1, 2, 3, 4, or 5 consecutive days on which a plurality of measurements taken that day produces a delta value that is greater than or equal to the predetermined numerical value. In an aspect, the predetermined portion of a time interval may be defined as some portion of a different specific time period (weeks, month, hours etc.).

[0069] In an aspect, a threshold has a trending aspect wherein changes in the delta values of consecutive pluralities of measurements are compared to each other. In an aspect, a trending threshold is defined as a predetermined change in delta value over a predetermined length of time, wherein a determination that the threshold has been met or exceeded is significant. In an aspect, a determination of significance will cause an alert to be issued. In an aspect, a trend line may be computed from a portion of the individual measurements of the consecutive pluralities of measurements. In an aspect, a trend line may be computed from a portion of the delta values of the consecutive pluralities of measurements.

[0070] In an aspect, the number of measurements taken within a single region may be less than the number of measurement locations defined in a pattern. In an aspect, a delta value will be calculated after a predetermined initial number of readings, which is less than the number of measurement locations defined in a pattern, have been taken in a region and after each additional

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reading in the same region, wherein additional readings are not taken once the delta value meets or exceeds the threshold associated with that region.

[0071] In an aspect, the number of measurements taken within a single region may exceed the number of measurement locations defined in a pattern. In an aspect, a delta value will be calculated after each additional reading.

[0072] In an aspect, a quality metric may be generated for each plurality of measurements. In an aspect, this quality metric is chosen to assess the repeatability of the measurements. In an aspect, this quality metric is chosen to assess the skill of the clinician that took the measurements. In an aspect, the quality metric may include one or more statistical parameters, for example an average, a mean, or a standard deviation. In an aspect, the quality metric may include one or more of a comparison of individual measurements to a predefined range. In an aspect, the quality metric may include comparison of the individual measurements to a pattern of values, for example comparison of the measurement values at predefined locations to ranges associated with each predefined location. In an aspect, the quality metric may include determination of which measurements are made over healthy tissue and one or more evaluations of consistency within this subset of “healthy” measurements, for example a range, a standard deviation, or other parameter.

[0073] In one aspect, a measurement, for example, a threshold value, is determined by SEM Scanner Model 200 (Bruin Biometrics, LLC, Los Angeles, CA). In another aspect, a measurement is determined by another SEM scanner.

[0074] In an aspect, a measurement value is based on a capacitance measurement by reference to a reference device. In an aspect, a capacitance measurement can depend on the location and other aspects of any electrode in a device. Such variations can be compared to a reference SEM device such as an SEM Scanner Model 200 (Bruin Biometrics, LLC, Los Angeles, CA). A person of ordinary skill in the art understands that the measurements set forth herein can be adjusted to accommodate a difference capacitance range by reference to a reference device.

[0075] Figure 6 discloses an exemplary measurement location for assessment of dehydration, according to the present disclosure. Dehydration is often used to describe either true dehydration, which is a reduction in the total body water, or as a proxy for hypovolemia, which is a decrease in volume of blood plasma. Total body water is not controlled via sodium regulation while intravascular volume is controlled by sodium regulation, so this distinction is important to guide therapy. Patients who lose a significant amount of ECF are often considered

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to be dehydrated while, in fact, depletion of ECF is caused by hypovolemia. Providing accurate guidance as to the amount of interstitial, or extracellular, fluid is therefore important guidance to a clinician treating the patient.

[0076] A current method of assessing hydration is to pull up a skin tent 610 in an area of loose skin and assess how skin tent 610 relaxes, where a slow return or failure to completely return is considered indicative of dehydration.

[0077] Measuring capacitance, or other electrical characteristic of the local tissue of a patient, using sensors such as sensor 90 or 440, will detect a reduction in the amount of ECF. An exemplary location for assessment of dehydration is location 620 over the junction of the second and third compartment of a hand. Comparison of SEM values derived from such measurements with predetermined thresholds will provide a quantitative indication of whether a patient is suffering from hypovolemia. In an aspect, use of a SEM measurement to assess the amount of ECF in conjunction with a measurement that is responsive to the total water content of a tissue, which includes both the ECF and the fluid within cells, and comparison of the two measurements with thresholds or with each other will provide an indication of true dehydration. In an aspect, multiple electrical property measurements are used to generate an average SEM value to assess the amount of ECF. In an aspect, a single SEM value being less than a reference value, which may be predetermined or derived from other SEM measurements, is indicative of hypovolemia.

[0078] In an aspect, a predetermined reference value for hypovolemia may range from 0.1 to 8.0, such as from 0.1 to 1.0, from 1.1 to 2.0, from 2.1 to 3.0, from 3.1 to 4.0, from 4.1 to 5.0, from 5.1 to 6.0, from 6.1 to 7.0, from 7.1 to 8.0, from 0.1 to 7.5, from 0.5 to 8.0, from 1.0 to 7.0, from 1.5 to 6.5, from 2.0 to 6.0, from 3.0 to 5.5, from 3.5 to 5.0, or from 4.0 to 4.5. In an aspect, a predetermined reference value for hypovolemia may range from 0.1 to 4.0, such as from 0.5 to 4.0, from 0.1 to 3.5, from 1.0 to 3.5, from 1.5 to 4.0, from 1.5 to 3.5, from 2.0 to 4.0, from 2.5 to 3.5, from 2.0 to 3.0, from 2.0 to 2.5, or from 2.5 to 3.0. In one aspect, a predetermined reference value for hypovolemia may range from 4.1 to 8.0, such as from 4.5 to 8.0, from 4.1 to 7.5, from 5.0 to 7.5, from 5.5 to 7.0, from 5.5 to 7.5, from 6.0 to 8.0, from 6.5 to 7.5, from 6.0 to 7.0, from 6.0 to 6.5, or from 6.5 to 7.0. In one aspect, a predetermined reference value for hypovolemia may be about 0.3, 0.35, 0.4, 0.45, 0.5, 0.55, 0.6, 0.65, 0.7, 0.75, 0.8, 0.85, 0.9, 0.95, 1.0, 1.1, 1.2, 1.3, 1.4, 1.5, 1.6, 1.7, 1.8, 1.9, 2.0, 2.1, 2.2, 2.3, 2.4, 2.5, 2.6, 2.7, 2.8, 2.9, 3.0, 3.1, 3.2, 3.3, 3.4, 3.5, 3.6, 3.7, 3.8, 3.9, 4.0, 4.1, 4.2, 4.3, 4.4, 4.5, 4.6, 4.7, 4.8, 4.9, 5.0, 5.1, 5.2, 5.3, 5.4, 5.5, 5.6, 5.7, 5.8, 5.9, 6.0, 6.1, 6.2, 6.3, 6.4, 6.5, 6.6, 6.7, 6.8, 6.9, 7.0, 7.1, 7.2, 7.3, 7.4, or 7.5. In an

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aspect, a predetermined reference value for hypovolemia can be scaled by a factor or a multiple based on the values provided herein.

[0079] Figures 7A and 7B disclose exemplary measurement locations for assessment of compartment syndrome, according to the present disclosure. Compartment syndrome is defined as a symptom complex resulting from increased tissue pressure within a limited space that compromises the circulation and function of the contents of that space. This occurs when intramuscular pressure is elevated to a level and for a period of time sufficient to reduce capillary perfusion. Muscles and nerves can tolerate ischemia up to 4 hours and irreversible damage occurs at 8 hours. There are numerous compartments in a human body, including three forearm compartments and ten separate osteofascial compartments in the hand. Symptoms of compartment syndrome include pain in the affected region, passive stretching of the involved muscles, localized swelling, paresthesia (e.g. tingling) in the involved nerve distribution, and muscle paresis (e.g. weakness). Current practice for quantification of the degree of compartment syndrome for a limb is to measure the circumference of the limb at sequential times. This method is slow and dependent upon the time period between the injury and the initial measurement. A new method to quantify edema within a compartment and to track changes in the degree of edema on a time scale of minutes would provide important information to a clinician.

[0080] The swelling of compartment syndrome is thought to be driven primarily by ECF. Measurement of the capacitance of tissue in a compartment will respond to the increase in ECF. As compartment syndrome typically affects only one region of the body, for example a single leg, SEM values can be derived from capacitance measurements on corresponding locations on both the affected leg and the other leg and compared, with a difference greater than a predetermined threshold being indicative of compartment syndrome. In one aspect, the magnitude of the difference between measurements of an affected and an unaffected body part is indicative of the severity of compartment syndrome and the associated urgency of the condition.

[0081] In an aspect, a predetermined threshold indicative of compartment syndrome may range from 0.1 to 8.0, such as from 0.1 to 1.0, from 1.1 to 2.0, from 2.1 to 3.0, from 3.1 to 4.0, from 4.1 to 5.0, from 5.1 to 6.0, from 6.1 to 7.0, from 7.1 to 8.0, from 0.1 to 7.5, from 0.5 to 8.0, from 1.0 to 7.0, from 1.5 to 6.5, from 2.0 to 6.0, from 3.0 to 5.5, from 3.5 to 5.0, or from 4.0 to 4.5. In an aspect, a predetermined threshold indicative of compartment syndrome may range from 0.1 to 4.0, such as from 0.5 to 4.0, from 0.1 to 3.5, from 1.0 to 3.5, from 1.5 to 4.0, from 1.5 to 3.5,

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from 2.0 to 4.0, from 2.5 to 3.5, from 2.0 to 3.0, from 2.0 to 2.5, or from 2.5 to 3.0. In one aspect, a predetermined threshold indicative of compartment syndrome may range from 4.1 to 8.0, such as from 4.5 to 8.0, from 4.1 to 7.5, from 5.0 to 7.5, from 5.5 to 7.0, from 5.5 to 7.5, from 6.0 to 8.0, from 6.5 to 7.5, from 6.0 to 7.0, from 6.0 to 6.5, or from 6.5 to 7.0. In one aspect, a predetermined threshold indicative of compartment syndrome may be about 0.3, 0.35, 0.4, 0.45, 0.5, 0.55, 0.6, 0.65, 0.7, 0.75, 0.8, 0.85, 0.9, 0.95, 1.0, 1.1, 1.2, 1.3, 1.4, 1.5, 1.6, 1.7, 1.8, 1.9, 2.0, 2.1, 2.2, 2.3, 2.4, 2.5, 2.6, 2.7, 2.8, 2.9, 3.0, 3.1, 3.2, 3.3, 3.4, 3.5, 3.6, 3.7, 3.8, 3.9, 4.0, 4.1, 4.2, 4.3, 4.4, 4.5, 4.6, 4.7, 4.8, 4.9, 5.0, 5.1, 5.2, 5.3, 5.4, 5.5, 5.6, 5.7, 5.8, 5.9, 6.0, 6.1, 6.2, 6.3, 6.4, 6.5, 6.6, 6.7, 6.8, 6.9, 7.0, 7.1, 7.2, 7.3, 7.4, or 7.5. In an aspect, a predetermined threshold indicative of compartment syndrome can be scaled by a factor or a multiple based on the values provided herein.

[0082] In Figure 7A, forearm 642 of arm 640 is swelling as schematically indicated by dashed line envelope 642A. A measurement in a location 644 that is selected to be directly coupled to one of the compartments in forearm 642 will provide a SEM value that is related to the degree of edema in that compartment. Comparison of this SEM value with a second SEM value derived from a measurement in an equivalent location (not shown in Figure 7A) on the other arm will provide information on the degree of edema and the severity of the condition. In an aspect, s SEM value is associated with a pressure in the measured compartment.

[0083] Figure 7B depicts a situation for a right leg 650R that is similar to the situation of Figure 7A. Lower leg 660 is swelling as indicated by dashed line envelope 660A. An SEM value derived from a capacitance measurement at location 670, which has been selected to be coupled to one of the compartments in lower leg 650R, will provide an indication of the edema in that compartment. As in Figure 7A, an SEM value from a corresponding location (not shown in Figure 7B) on left lower leg 650L provides a baseline, where a comparison of the two readings provides an indication of the degree of edema and urgency of the compartment syndrome.

[0084] From the foregoing, it will be appreciated that the present invention can be embodied in various ways, which include but are not limited to the following:

[0085] Embodiment 1. An apparatus for assessing preeclampsia, the apparatus comprising: a sensor comprising at least one first electrode and at least one second electrode, where the sensor is configured to be placed against a patient's skin, a circuit electronically coupled to the first and second electrodes and configured to measure an electrical property between the first and second electrodes and provide information regarding the electrical property, a processor electronically

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coupled to the circuit, and a non-transitory computer-readable medium electronically coupled to the processor and comprising instructions stored thereon that, when executed on the processor, perform the steps of: receiving information from the circuit, converting the information into a first sub-epidermal moisture (SEM) value, and determining a difference between the first SEM value and a reference value, where the magnitude of the difference exceeding the reference value is indicative of preeclampsia.

[0086] Embodiment 2. The apparatus of embodiment 1, where the reference value is predetermined.

[0087] Embodiment 3. An apparatus for assessing hypovolemia, the apparatus comprising: a sensor comprising at least one first electrode and at least one second electrode, where the sensor is configured to be placed against a patient's skin, a circuit electronically coupled to the first and second electrodes and configured to measure an electrical property between the first and second electrodes and provide information regarding the electrical property, a processor electronically coupled to the circuit, and a non-transitory computer-readable medium electronically coupled to the processor and comprising instructions stored thereon that, when executed on the processor, perform the steps of: receiving information from the circuit, converting the information into a first sub-epidermal moisture (SEM) value, and determining a difference between the first SEM value and a reference value, where the magnitude of the difference lesser than the reference value is indicative of hypovolemia.

[0088] Embodiment 4. The apparatus of embodiment 3, where the reference value is predetermined.

[0089] Embodiment 5. A method for detecting preeclampsia at a first location of a patient's skin, the method comprising: obtaining a sub-epidermal moisture (SEM) value at the first location; and determining that the SEM value is greater than a reference value to indicate preeclampsia.

[0090] Embodiment 6. The method of embodiment 5, where the reference value is predetermined.

[0091] Embodiment 7. A method for detecting hypovolemia at a first location of a patient's skin, the method comprising: obtaining a sub-epidermal moisture (SEM) value at the first location; and determining that the SEM value is lesser than a reference value to indicate hypovolemia.

[0092] Embodiment 8. The method of embodiment 7, where the reference value is predetermined.

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[0093] Embodiment 9. An apparatus for assessing compartment syndrome, the apparatus comprising: a sensor comprising at least one first electrode and at least one second electrode, where the sensor is configured to be placed against a patient's skin, a circuit electronically coupled to the first and second electrodes and configured to measure an electrical property between the first and second electrodes and provide information regarding the electrical property, a processor electronically coupled to the circuit, and a non-transitory computer-readable medium electronically coupled to the processor and comprising instructions stored thereon that, when executed on the processor, perform the steps of: receiving information from the circuit, converting the information into a first sub-epidermal moisture (SEM) value, and determining a difference between the first SEM value and a reference value, where the magnitude of the difference exceeding a predetermined amount is indicative of compartment syndrome.

[0094] Embodiment 10. The apparatus of embodiment 9, where: the first SEM value is derived from a measurement taken at a first location of the patient's skin; the reference value is a second SEM value derived from a measurement taken at a second location of the patient's skin.

[0095] Embodiment 11. The apparatus of embodiment 10, where the first and second locations are symmetric with respect to a centerline of the patient's body.

[0096] Embodiment 12. The apparatus of embodiment 10, where the first SEM value exceeding the second SEM value by the predetermined amount is indicative of compartment syndrome at the first location.

[0097] Embodiment 13. The apparatus of embodiment 10, where the second SEM value exceeding the first SEM value by the predetermined amount is indicative of compartment syndrome at the second location.

[0098] Embodiment 14. A method for detecting compartment syndrome at a first location of a patient's skin, the method comprising: obtaining a first sub-epidermal moisture (SEM) value at the first location; obtaining a second SEM value at a second location of the patient's skin; and determining whether the difference between the first SEM value and the second SEM value exceeds a predetermined amount indicative of compartment syndrome.

[0099] Embodiment 15. The method of embodiment 14, where the first and second locations are symmetric with respect to a centerline of the patient's body.

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[0100] Embodiment 16. The method of embodiment 14, where the first SEM value exceeding the second SEM value by the predetermined amount is indicative of compartment syndrome at the first location.

[0101] Embodiment 17. The method of embodiment 14, where the second SEM value exceeding the first SEM value by the predetermined amount is indicative of compartment syndrome at the second location.

While the invention has been described with reference to particular aspects, it will be understood by those skilled in the art that various changes may be made and equivalents may be substituted for elements thereof without departing from the scope of the invention. In addition, many modifications may be made to a particular situation or material to the teachings of the invention without departing from the scope of the invention. Therefore, it is intended that the invention not be limited to the particular aspects disclosed but that the invention will include all aspects falling within the scope and spirit of the appended claims.

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The embodiments of the present invention for which an exclusive property or privilege is claimed are defined as follows:

1. An apparatus for assessing preeclampsia, said apparatus comprising:
   a sensor comprising at least one first electrode and at least one second electrode, wherein said sensor is configured to be placed against a patient's skin sequentially at a first location and a second location, wherein the locations are corresponding locations on a patient's body,
   a circuit electronically coupled to said first and second electrodes and configured to measure a first electrical property and a second electrical property at said first and said second locations respectively and provide information regarding said first and said second electrical properties, wherein each electrical property is measured between said first and second electrodes,
   a processor electronically coupled to said circuit and configured to receive said information, and
   a non-transitory computer-readable medium electronically coupled to said processor and comprising instructions stored thereon that, when executed on said processor, perform the steps of:
      converting said information regarding said first and said second electrical properties into a first sub-epidermal moisture (SEM) value and a second SEM value respectively, and
      comparing said first SEM value and said second SEM value to a predetermined threshold, wherein a determination that said first SEM value and said second SEM value are both above the predetermined threshold and are also within a predetermined range of each other indicates preeclampsia in said patient.

2. An apparatus for assessing hypovolemia, said apparatus comprising:
   a sensor comprising at least one first electrode and at least one second electrode, wherein said sensor is configured to be placed against a patient's skin,
   a circuit electronically coupled to said first and second electrodes and configured to measure an electrical property between said first and second electrodes and provide information regarding said electrical property,

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a processor electronically coupled to said circuit and configured to receive said information, and

a non-transitory computer-readable medium electronically coupled to said processor and comprising instructions stored thereon that, when executed on said processor, perform the steps of:

converting said information into a sub-epidermal moisture (SEM) value,

receiving a measurement of total water content of the patient,

comparing said SEM value with a first threshold, and

comparing said measurement of total water content with a second threshold and a third threshold, wherein said second threshold is higher than said third threshold,

wherein said SEM value less than said first threshold and said measurement of total water content less than said second threshold and greater than said third threshold indicates hypovolemia in said patient.

3. The apparatus of claim 2, wherein said first threshold, said second threshold, and said third threshold are predetermined.

4. A method for detecting preeclampsia in a patient, said method comprising:

obtaining a first sub-epidermal moisture (SEM) value at a first location;

obtaining a second SEM value at a second location, wherein said first location and said second location are corresponding locations on a patient's body; and

determining that said patient has preeclampsia when said first SEM value and said second SEM value are both above a predetermined threshold and are also within a predetermined range of each other.

5. A method for detecting hypovolemia at a first location of a patient's skin, the method comprising:

obtaining a sub-epidermal moisture (SEM) value at said first location;

obtaining a measurement of total water content of the patient;

comparing said first SEM value with a first threshold;

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comparing said measurement of total water content with a second threshold and a third threshold, wherein said second threshold is higher than said third threshold; and

determining that said patient has hypovolemia when said SEM value is less than said first threshold and said measurement of total water content is less than said second threshold and greater than said third threshold.

6. The method of claim 5, wherein said first threshold, said second threshold, and said third threshold are predetermined.

7. An apparatus for assessing compartment syndrome, said apparatus comprising:

a sensor comprising at least one first electrode and at least one second electrode, wherein said sensor is configured to be placed against a patient's skin,

a circuit electronically coupled to said first and second electrodes and configured to measure an electrical property between said first and second electrodes and provide information regarding said electrical property,

a processor electronically coupled to said circuit and configured to receive said information, and

a non-transitory computer-readable medium electronically coupled to said processor and comprising instructions stored thereon that, when executed on said processor, perform the steps of:

converting said information into a first sub-epidermal moisture (SEM) value, and

determining a difference between said first SEM value and a reference value,

wherein said first SEM value is derived from a measurement taken at a first location of the patient's skin,

wherein said reference value is a second SEM value derived from a measurement taken at a second location of the patient's skin,

wherein said first location is located in a first compartment of the patient's body and said second location is located in a second compartment of the patient's body, and

wherein said difference exceeding a predetermined amount is indicative of compartment syndrome in said patient.

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8. The apparatus of claim 7, wherein said first SEM value exceeding said second SEM value by said predetermined amount is indicative of compartment syndrome at said first location.

9. The apparatus of claim 7, wherein said second SEM value exceeding said first SEM value by said predetermined amount is indicative of compartment syndrome at said second location.

10. A method for detecting compartment syndrome at a first location of a patient's skin, the method comprising:

obtaining a first sub-epidermal moisture (SEM) value at said first location;

obtaining a second SEM value at a second location of the patient's skin, wherein said first and second locations are symmetric with respect to a centerline of the patient's body; and

determining whether a difference between said first SEM value and said second SEM value is greater than a predetermined amount to indicate compartment syndrome in said patient.

11. The method of claim 10, wherein said first SEM value exceeding said second SEM value by said predetermined amount indicates compartment syndrome at said first location.

12. The method of claim 10, wherein said second SEM value exceeding said first SEM value by said predetermined amount indicates compartment syndrome at said second location.

13. The apparatus of claim 7, wherein said first and second locations are symmetric with respect to a centerline of the patient's body.

14. The apparatus of claim 7, wherein the first compartment is a forearm compartment in one arm and the second compartment is the corresponding forearm compartment in the other arm.

15. The apparatus of claim 7, wherein the first compartment is a calf compartment in one leg and the second compartment is the corresponding calf compartment in the other leg.

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16. The apparatus of claim 7, wherein the first compartment is an osteofascial compartment in one hand and the second compartment is the corresponding osteofascial compartment in the other hand.

17. The apparatus of claim 7, wherein the electrical property is biocapacitance.

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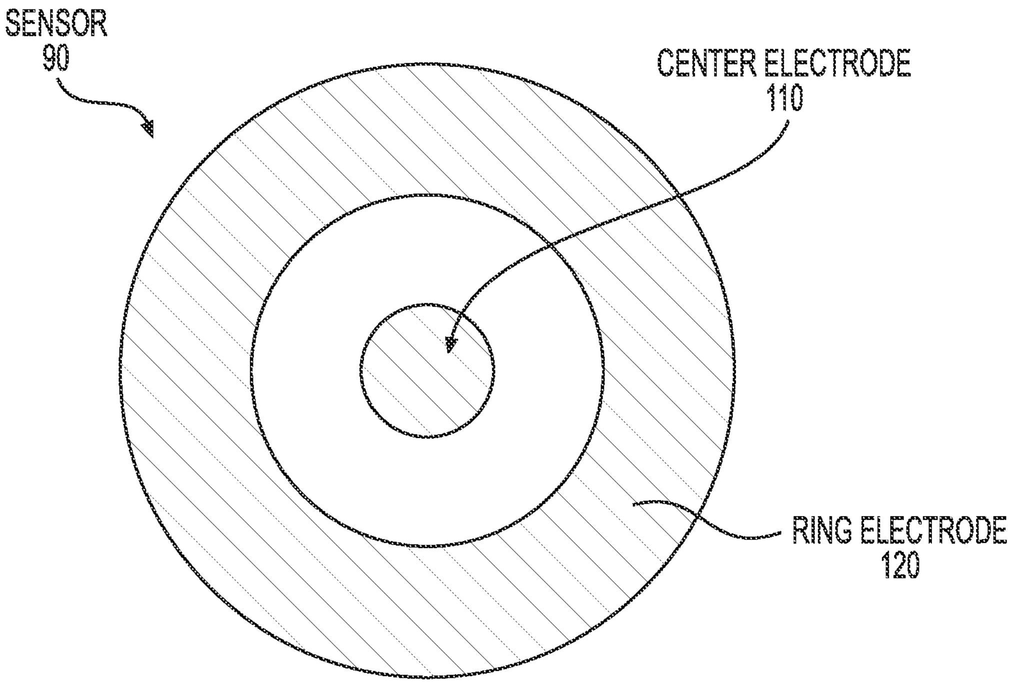


FIG. 1A

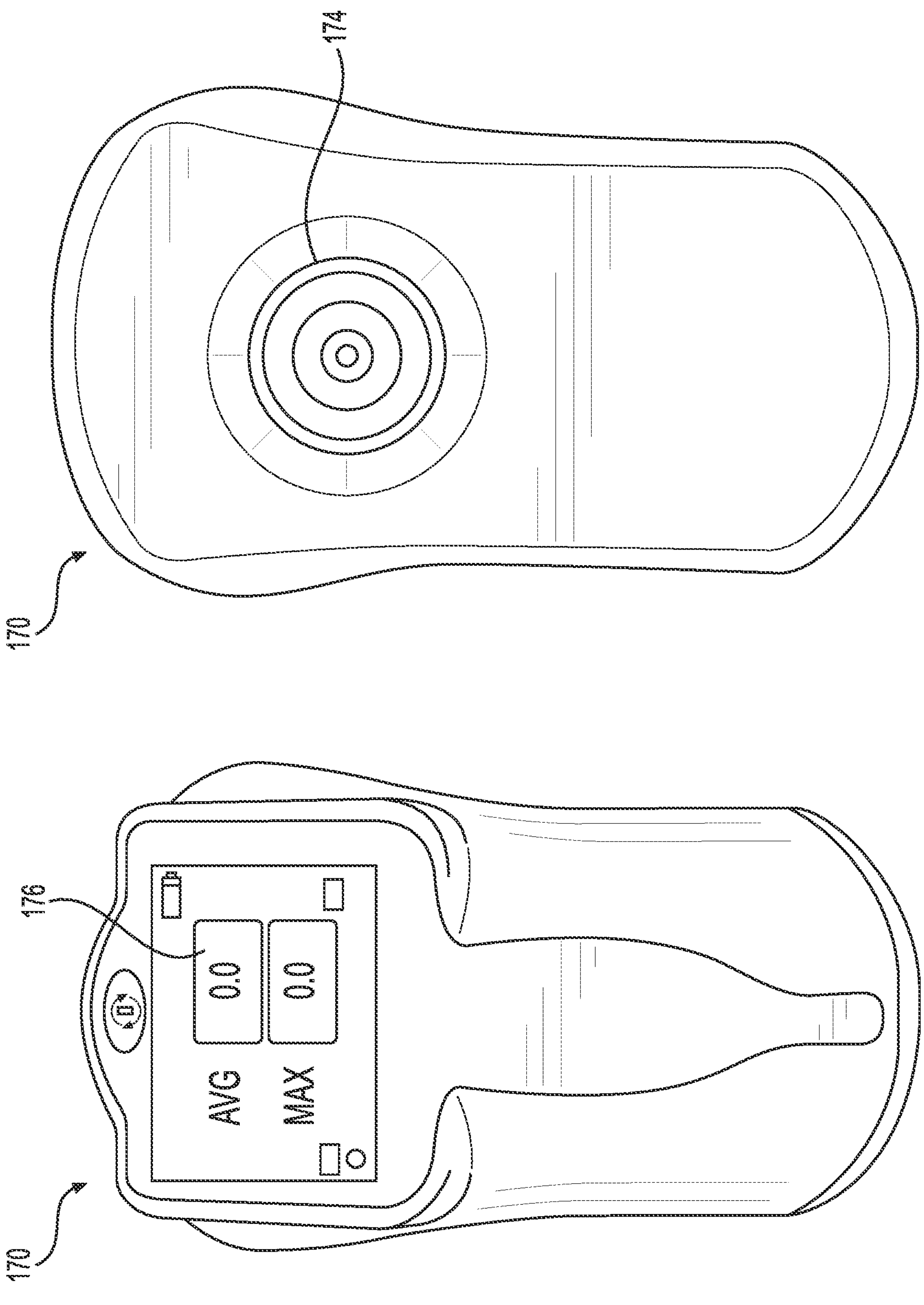
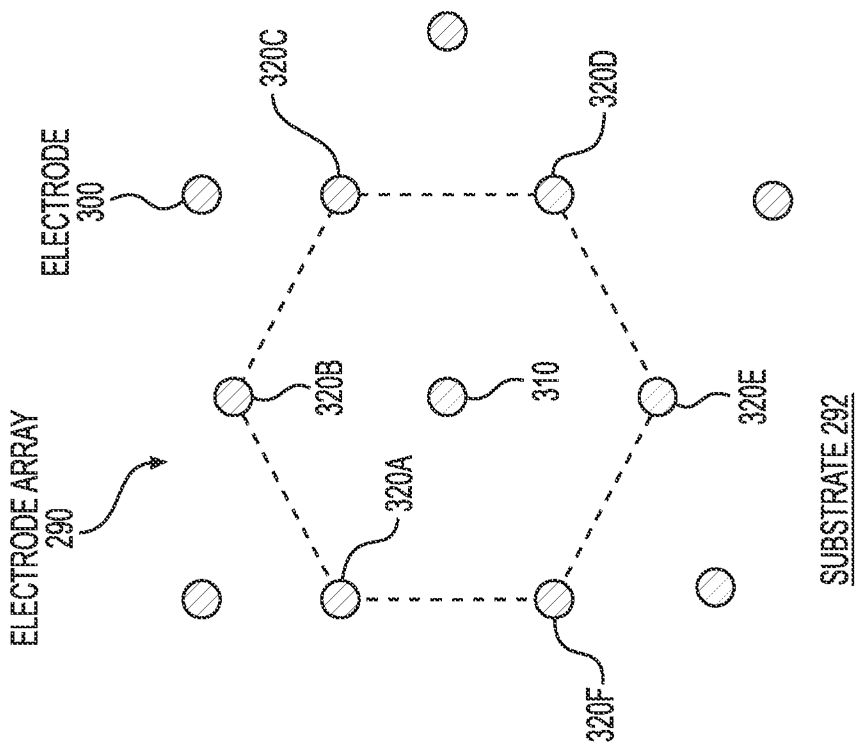


FIG. 1B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ELECTRODE 300
310
320A
320B
320C
320D
320E
320F
SUBSTRATE 292

FIG. 2

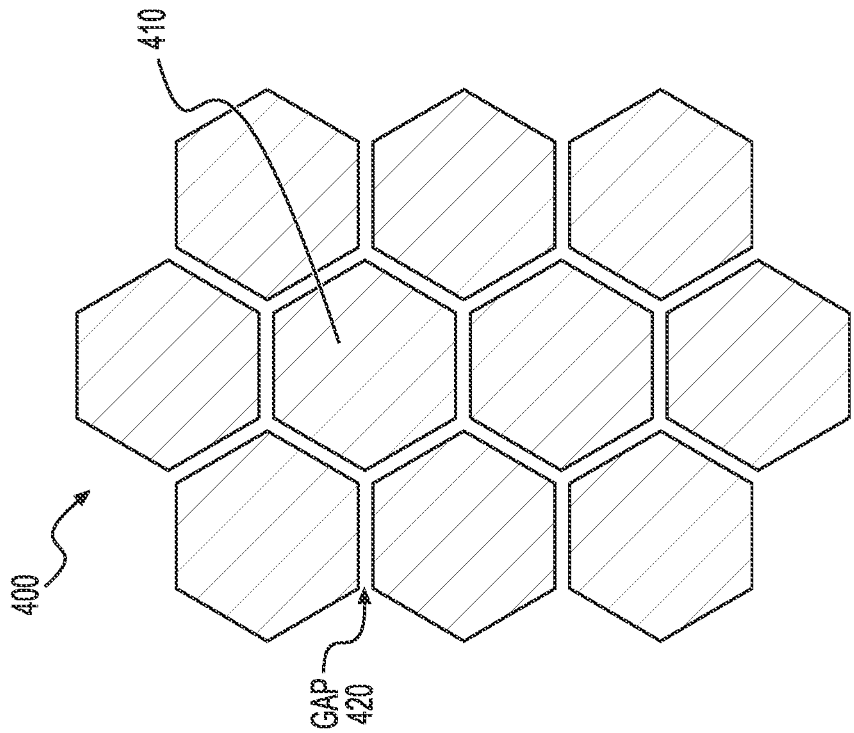
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FIG. 3

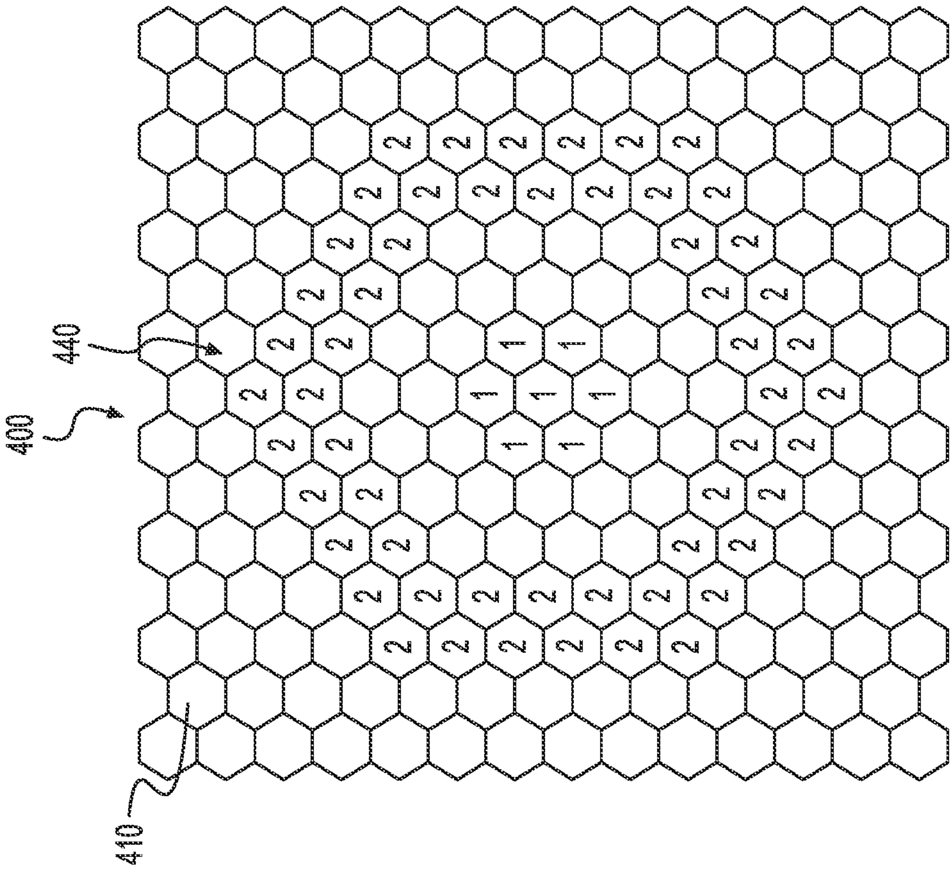


FIG. 4B

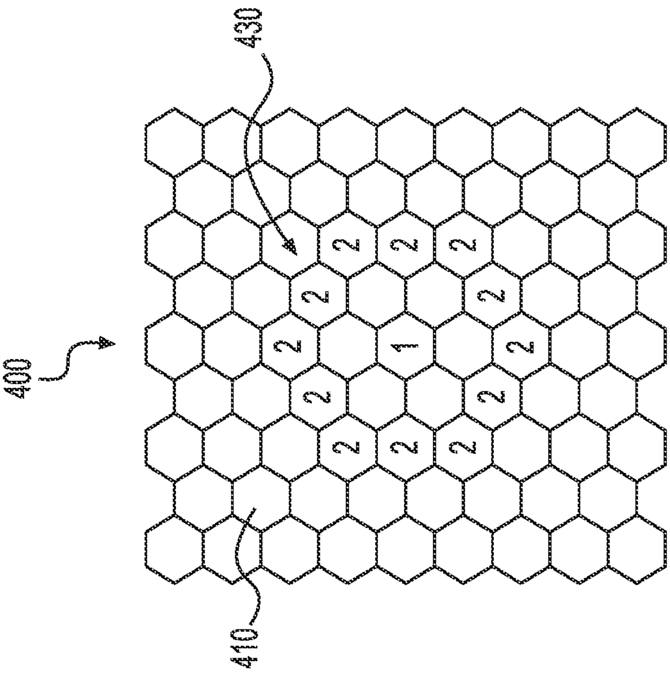


FIG. 4A

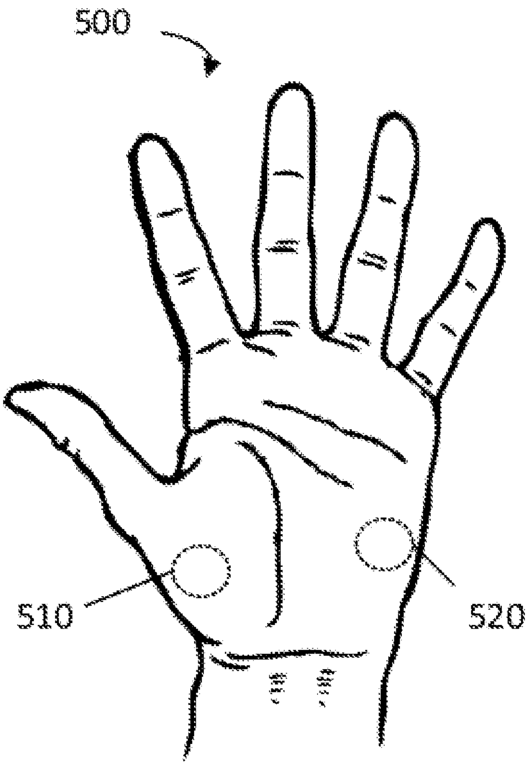


FIG. 5A

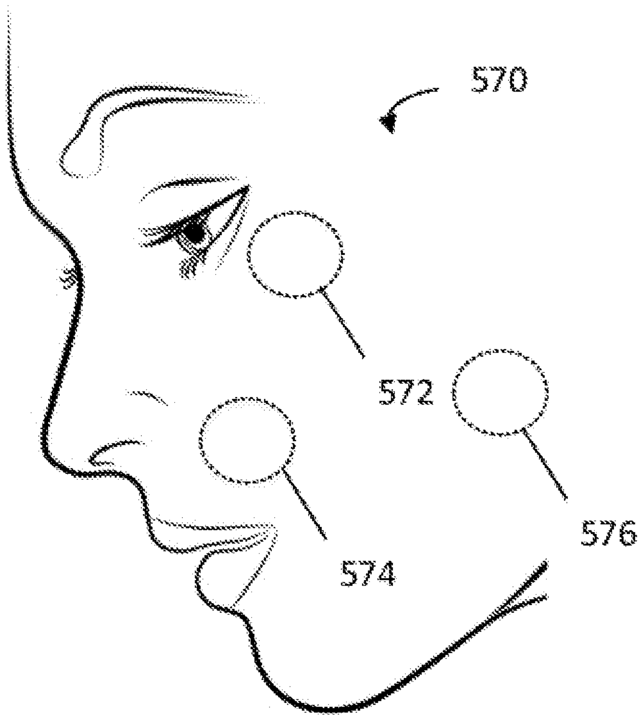


FIG. 5C

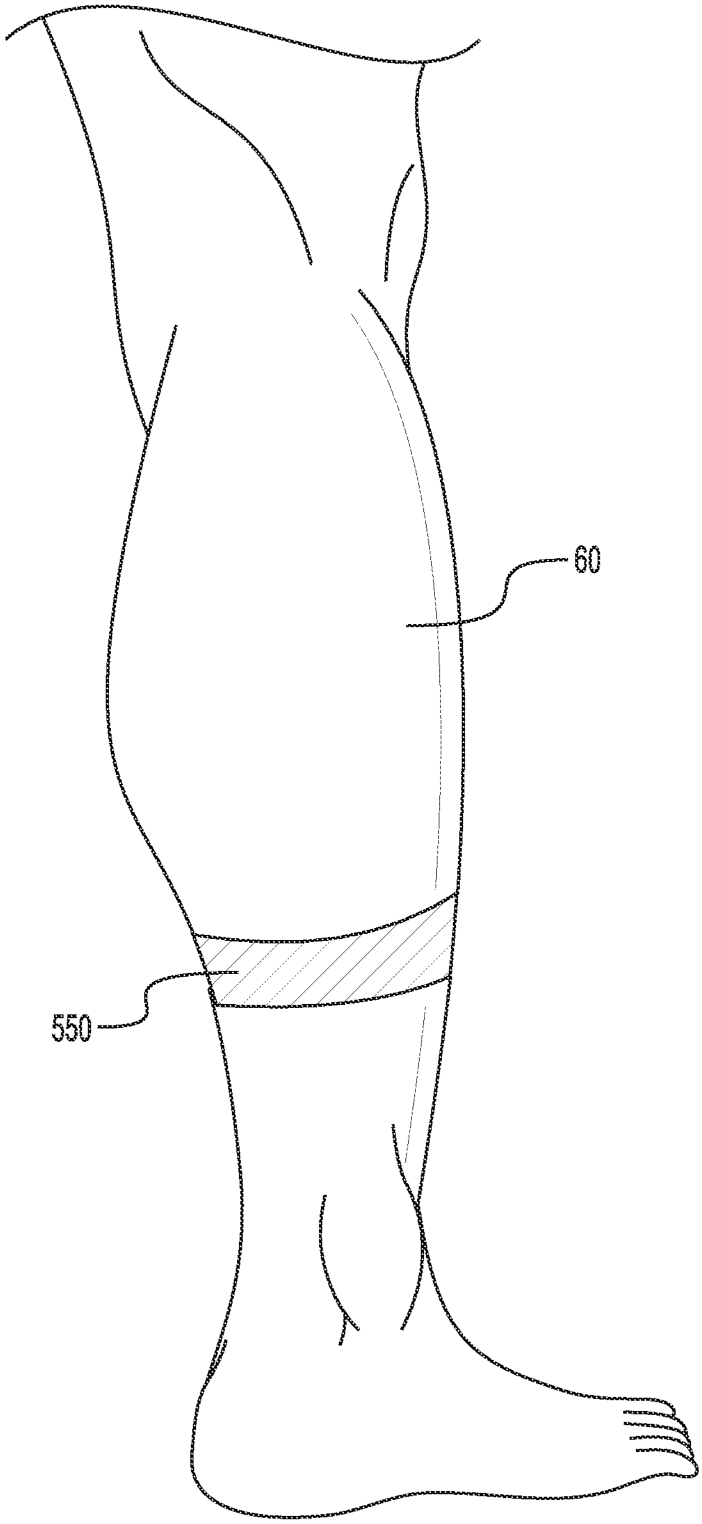


FIG. 5B

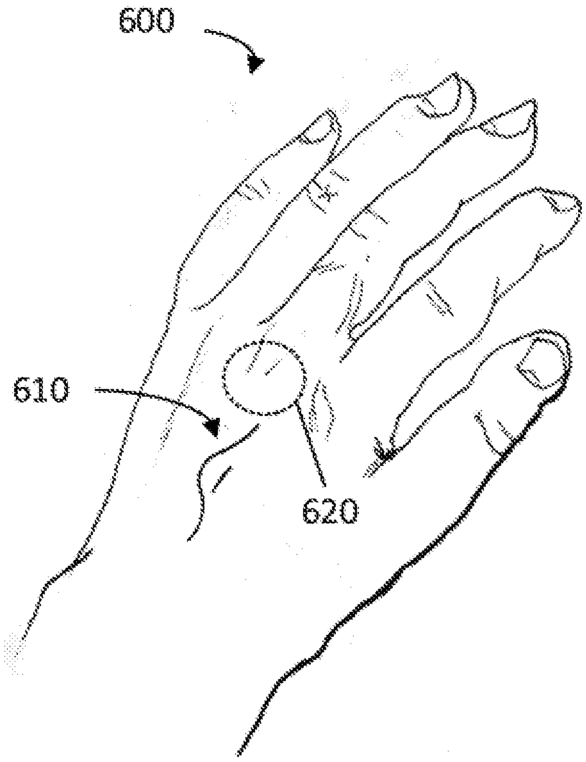


FIG. 6

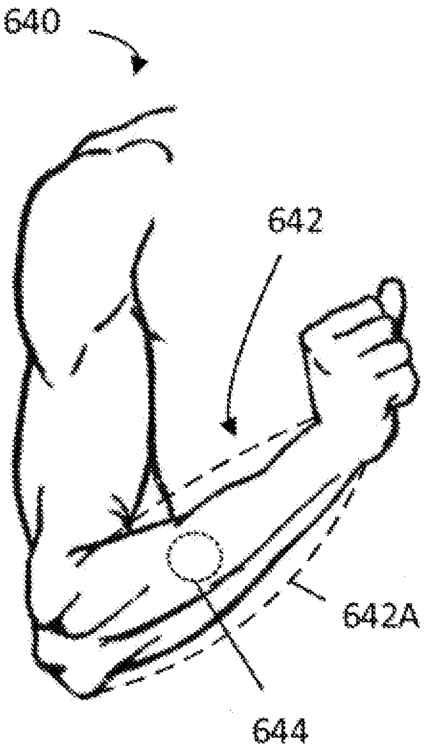


FIG. 7A

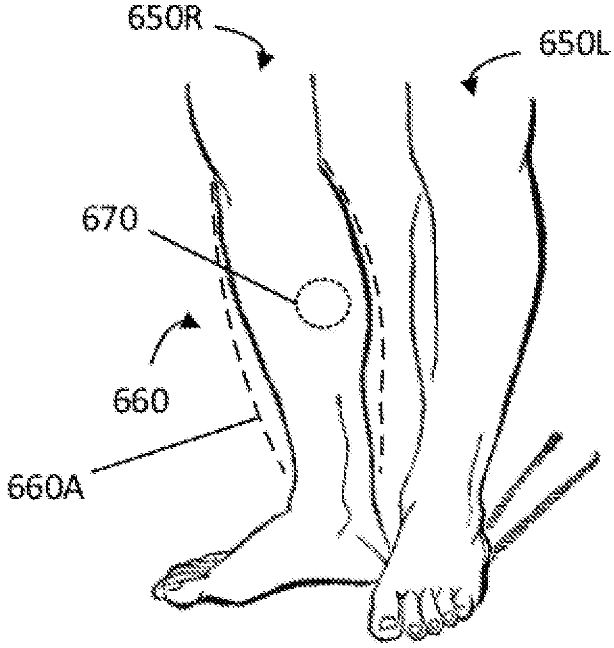
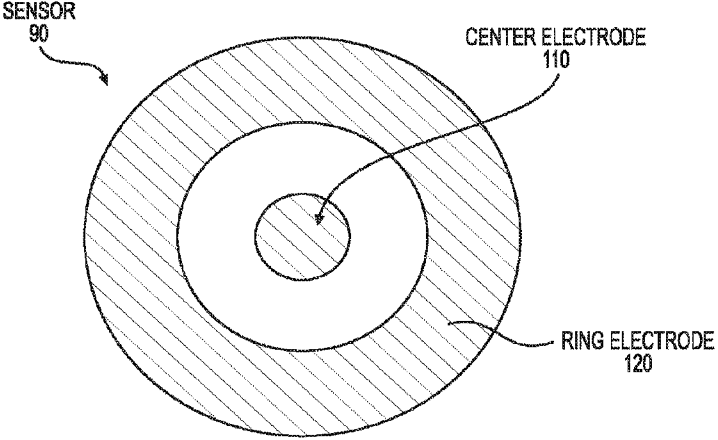


FIG. 7B


SENSOR
90
CENTER ELECTRODE
110
RING ELECTRODE
120