Abstract: A wearable treatment device for a patient may include at least one electrode coupled to a garment configured to be worn by the patient, at least one electrode being configured to be placed in contact with the patient's tissue and measure electrical impedance of the patient; and at least one actuator operatively coupled to the garment, the at least one actuator being configured to deliver a treatment to the patient in response to the measured electrical impedance.
ELECTRICAL IMPEDANCE MYOGRAPHY BASED MONITORING AND
CONDITIONING OF TISSUE

Cross-Reference to Related Applications

[0001] This application claims priority to U.S. Provisional Application No. 62/155,645, filed May 1, 2015, the entirety of which is incorporated by reference herein.

Technical Field

[0002] Embodiments of the present disclosure relate generally to systems and methods for monitoring and/or conditioning of body tissue using electrical impedance myography (EIM). Some embodiments of the present disclosure relate to sensors and/or devices to detect electrical impedance of tissue and devices and/or methods to apply treatment based on the detected impedance. Some embodiments of the disclosure relate to methods for evaluating the health of tissue (e.g., human tissue) and measurement schemes to improve the sensitivity to change in health over time.

Background

[0003] Electrical impedance myography (EIM) is a non-invasive, painless approach to tissue assessment based upon the application and measurement of high-frequency, low-intensity electrical current. In contrast to conventional needle electromyography (EMG) and most standard neurophysiological techniques, EIM does not focus on measuring the inherent electrical activity of the tissues. Rather, similar to diagnostic ultrasound, measurements are made over a small area of interest, with energy being applied to the body and the resultant surface patterns being analyzed. Unlike ultrasound, however, in which energy is in the form of sound waves and the main interest is image reconstruction, in the case of EIM, electrical current is used and the output is a set of quantitative parameters describing the state of the tissue.
Summary

[0004] Examples of the present disclosure relate to, among other things, devices, systems, and methods for electrical impedance myography based monitoring and conditioning of tissue. Each of the examples disclosed herein may include one or more of the features described in connection with any of the other disclosed examples.

[0005] In one example, a wearable treatment device for a patient may include at least one electrode coupled to a garment configured to be worn by the patient, the at least one electrode being configured to be placed in contact with the patient's tissue and measure electrical impedance of the patient; and at least one actuator operatively coupled to the garment, the at least one actuator being configured to deliver a treatment to the patient in response to the measured electrical impedance.

[0006] The treatment device may additionally or alternatively include one or more of the following features: the measured electrical impedance may indicate a change in a muscle characteristic; the at least one actuator may include a plurality of inflatable cuffs configured to apply pressure to a portion of the patient; the at least one actuator may include a heater; the at least one actuator may be configured to deliver electrical stimulation to the patient; the at least one actuator may be configured to vibrate; the at least one electrode may include a first pair of spaced apart current electrodes and a second pair of spaced apart voltage electrodes, and the device may be configured to direct a current into the patient's tissue through the first pair of current electrodes and measure a voltage across the second pair of voltage electrodes; and the at least one electrode may include multiple pairs of current electrodes and multiple pairs of voltage electrodes.

[0007] In another example, a method for treating a patient may include positioning a garment around a portion of the patient, wherein the garment is coupled to at least one electrode positioned in contact with the patient's tissue; measuring electrical impedance of the patient
using the at least one electrode; and in response to the measured electrical impedance, using
at least one actuator operatively coupled to the garment to deliver a treatment to the patient.

[0008] The method may additionally or alternatively include one or more of the following
features or steps: the measured electrical impedance may indicate a change in a muscle
characteristic; the at least one actuator may include a plurality of inflatable cuffs, and the
method may further include inflating the plurality of cuffs in sequence; the method may
further include using the actuator to apply heat to the patient; the method may further include
using the actuator to deliver electrical stimulation to the patient; and the at least one electrode
may include a first pair of spaced apart current electrodes and a second pair of spaced apart
voltage electrodes, and the method may further include directing a current into the patient's
tissue through the first pair of current electrodes and measuring a voltage across the second
pair of voltage electrodes.

[0009] In yet another example, a system for treating a patient may include a garment; a
plurality of electrodes coupled to the garment, wherein the plurality of electrodes are
configured to obtain electrical impedance data relating to one or more muscles of the patient;
a computational device configured to detect an anomaly in the electrical impedance data; and
a plurality of actuators coupled to the garment and configured to deliver a treatment to the
patient in response to the anomaly in the electrical impedance data.

[0010] The system may additionally or alternatively include one or more of the following
features: the anomaly may be a measured impedance signal that exceeds a threshold value;
the garment may include a shirt, and the shirt may include a plurality of electrodes configured
to be positioned adjacent an abdomen, a plurality of electrodes configured to be positioned
adjacent a bicep, a plurality of electrodes configured to be positioned adjacent an atricep, and a
plurality of electrodes configured to be positioned adjacent a back; the plurality of electrodes
may include a first pair of spaced apart current electrodes and a second pair of spaced apart
voltage electrodes, and the system may be configured to direct a current into the patient's tissue through the first pair of current electrodes and measure a voltage across the second pair of voltage electrodes; the at least one actuator may be configured to at least one of deliver heat, electrical stimulation, or vibrations to the patient; and the at least one actuator may be inflatable.

[0011] It may be understood that both the foregoing general description and the following detailed description are exemplary and explanatory only and are not restrictive of the invention, as claimed. As used herein, the terms "comprises," "comprising," or any other variation thereof, are intended to cover a non-exclusive inclusion, such that a process, method, article, or apparatus that comprises a list of elements does not include only those elements, but may include other elements not expressly listed or inherent to such process, method, article, or apparatus. The term "exemplary" is used in the sense of "example," rather than "ideal."

**Brief Description of the Drawings**

[0012] The accompanying drawings, which are incorporated in and constitute a part of this specification, illustrate examples of the present disclosure and together with the description, serve to explain the principles of the disclosure.

[0013] FIG. 1A illustrates a system for treating a patient, according to an exemplary embodiment.

[0014] FIG. 1B illustrates a sensor having a pattern of electrodes, according to an exemplary embodiment.

[0015] FIG. 2A illustrates the progression of a disease over time, according to an exemplary embodiment.
FIG. 2B illustrates the progression of a disease over time using more frequent EIM measurements than the progression shown in FIG. 2A, according to an exemplary embodiment.

FIG. 3 illustrates an exemplary method of characterizing disease progression using frequent EIM measurements, according to an exemplary embodiment.

**Detailed Description**

In some embodiments of the current disclosure, EIM sensors may be used to detect physiological parameters of a subject. Although not a requirement, in some embodiments, these EIM sensors may be wearable sensors. Based on the detected signals, muscle condition and/or health of the subject may be determined. In general, these sensors may be attached to the subject by any means (e.g., adhesive, etc.). Sensors may include electrodes, devices, etc. that are adapted to produce a signal in response to a bioelectric signal of the subject. In some embodiments, the sensors may be embedded in a garment that may be worn by the subject. The garment may be worn over any part of the body (e.g., legs, arms, trunk, neck, head, etc.). The same garment, or more than one garment, may be used to target different muscle groups, such as the biceps, triceps, abdomen, back, chest, and calves. The term "garment" is intended to refer to any type of clothing or accessory worn by, draped on, or placed on the subject. In some embodiments, the garment may include: a patch that is placed over muscle and held in place by bands (e.g., Velcro straps, etc.) or adhesive materials; a cuff that is wrapped around the limb or portion of a limb (similar to a blood pressure cuff) and secured with Velcro strips, bands, or adhesives; snug-fitting or close fitting clothing, including shirts, pants, gloves, socks, hats, etc.; belts; straps; a neck wrap; trunk wrap (e.g. corset); etc. Although the sensors are described as being embedded in the garment, in some embodiments, some or all of the sensors may be attached (using adhesives, sewn, etc.) to the garment. Other variations are also contemplated. For instance, in some embodiments, some or all of the sensors may be
separate from the garment, and in some embodiments, some or all of the sensors may be implanted in the subject.

[0019] It is also contemplated that, in some embodiments, the sensors may be incorporated in a portable device that the user may periodically press against the user’s skin to take measurements. Although the sensors are described as being incorporated in a garment in the description below, it should be recognized that the description is also applicable when the sensors are incorporated in a portable device.

[0020] Electronic components or devices associated with (e.g., operatively coupled to) the garment or portable device may receive the EIM signals measured by the sensors and determine muscle condition and health of the subject based on the signals. The signals measured by the sensors may include electrical impedance measurements. In one embodiment, the measured electrical impedance may indicate a muscle characteristic (e.g., structure, composition) of the subject, and changes in the electrical impedance may indicate changes in the muscle characteristic. The sensors embedded in the garment (device, etc.) may be operationally coupled to the associated electronic components by any means. In some embodiments, the sensors may have a direct hardwire connection (e.g., wire) to these components. In some embodiments, the sensors may be wirelessly connected to the electronic components (e.g., Bluetooth, etc.). The sensors and/or their associated electronic components also may include circuitry and/or components configured to enhance the accuracy (e.g., filters, etc.) and extend the range of capability (amplifiers, etc.) of the measured impedance-related data. The sensors and the associated electronic components may use impedance techniques to determine the status and/or health of the subject. In this disclosure, the phrase health of the subject is used to broadly refer to any parameter that is indicative of the health or well-being of a particular muscle/region of the subject or a parameter indicative of overall health of the subject. For example, as used herein, health of
the subject may include parameters such as muscle percentage, fat percentage, muscle quality (MQ), etc. These and other parameters that may constitute the health of the subject are described in U.S. Patent Application No. 14/950,821 filed November 24, 2015 (the ’821 application), which is incorporated by reference herein in its entirety.

[0021] The sensors and/or the associated electronic components may be configured to determine the health of the subject by any known method/technique. The methods/techniques may include, among others, 4-electrode impedance measurements, whole body bioimpedance analysis, impedance phlebography, impedance cardiography, impedance pulmonography, hydration status, surface electromyography, skin temperature measurement, electrocardiography, pulse oximetry, muscle tonometry measurements (to assess strength of contraction), diagnostic ultrasound, etc. In some embodiments, the sensors may include accelerometers for measurement of movement and sensors to measure blood pressure or any other biological parameter, etc. The sensors may also detect additional electrical impedance data, such as, for example, for assessment of hydration, cardiac output, localized blood flow, breathing rate and vital capacity; electromyographic signal data including individual motor unit potential data, recruitment and interference partem data; temperature at one or multiple locations along the garment, including measurement of temperature differentials between sensors; electrocardiogram data, including, pulse rate, heart-rate variability; blood pressure at specific areas where sensors are located, including blood pressure differentials; blood oxygenation levels; movement of body or specific limbs/muscles, including specific number of muscle or length of muscle contractions; strength and duration of muscle-specific contractions; ultrasound data on underlying muscle and subcutaneous fat.

[0022] Hydration sensors, if any, included in the garment may have different forms. These sensors may include the use of electrodes embedded in the garment (pants, shirt, etc.) to measure the trans-lower-extremity or trans-upper-extremity impedances versus thoracic or
localized impedances to provide data on the overall hydration status of the body. In some embodiments, this sensor also may be a cuff around a limb that may be used to provide electrical impedance data of both the large veins and arteries (the measures of hydration status) versus more superficial muscle regions.

[0023] The garment also may include sensors configured for location detection (GPS sensors), altimeter/barometric pressure detection, external temperature, etc. The data collected by the sensors may include, but is not restricted to, the following: electrical impedance data obtained from muscle, fat, and skin as part of electrical impedance myography methods using electrode arrangements and methods described in co-assigned U.S. Patent No. 8,892,198, issued November 18, 2014 (the ’198 patent), co-assigned U.S. Patent No. 9,113,808, issued August 25, 2015 (the ’808 patent), and the ’821 application, each of which is incorporated by reference in its entirety herein.

[0024] In some embodiments, in addition to sensing, the disclosed technique also may apply a treatment or other conditioning to the subject. The treatment may be administered in response to a health condition detected by the sensors coupled to the subject. For example, in an embodiment where EIM signals from the sensors indicate a deteriorating muscle condition (e.g., MQ below a threshold value) of the subject, the treatment may include a treatment to improve the muscle performance or condition. In other examples, treatment may be administered to improve muscle condition even when a deteriorating muscle condition is not detected. In general, any type of treatment may be administered to the subject. In some embodiments, the treatment may include one or more of the following: application of heat or cooling to specific regions of muscle (e.g., relative to the patient’s body temperature); electrical stimulation of muscle or nerves; compression and/or relaxation, including massage (e.g., through peristalsis-like motion of a wrapped fabric); vibration at varying frequencies; application of induced magnetic fields; application of therapeutic ultrasound; iontophoresis of
therapeutic small molecules; activating flow a drug or a medicine into the subject (e.g., from a vial implanted or fluidly coupled to the subject); activating an interventional device (e.g., implanted in the patient); etc.

In some embodiments, the treatments may be administered by one or more actuators associated with the sensors. The term "actuator" is intended to include any device or mechanism that may cause an effect on the subject. In some cases, the treatment may be administered using the same sensors used to sense EIM signals or other information related to the patient (e.g., if the treatment is electrical stimulation). Accordingly, the sensors may act as actuators. In some embodiments, some or all of these actuators may be embedded in the garment or within the subject. Thus, in addition to sensing, in some embodiments, the garment may assist in treatment of a health condition detected by the sensors, or may assist in improving the muscle characteristics of the patient. Some or all of these actuators may be interfaced directly with the impedance or other measuring systems as well as with separate, stand-alone devices such as a smart phone, tablet or desktop computer. They also may be directly connected to Wi-Fi or wireless networks as deemed appropriate.

Each of the measurements may be used in conjunction with each other such that detailed data on the body and specific muscles can be obtained. For example, one technology could be used to specifically improve the accuracy and interpretation of the data obtained with a second modality. Or together, multiple modalities may be used to infer a more accurate status of the body's or muscle's condition. These technologies may include (but are not limited to): using electrical impedance data to improve/filter an EMG signal; adjusting electrical impedance data based on a recorded temperature; evaluating pulse oximetry data in conjunction with movement data to evaluate level of fatigue and onset of muscle injury; using tonometry data and EMG data to assess the level of contraction to assess changes in
impedance data; combining movement, oximetry, EMG, tonometry, and impedance data to provide measure of muscle status and onset of fatigue.

[0027] The individual modalities also may be used separately. These individual measurements may provide information to: help/inform onset of muscle injury and identify appropriate treatments; avoid overtraining; measure effort level and at what point a maximum is reached; reduce the development of muscle atrophy and weakness in hospitalized patients; measure long term changes in muscle quality, muscle endurance (body composition, muscle quality, muscle endurance, muscle recovery capability, etc.); measure short term changes (fatigue, exertion levels, form, heart rate and HRV, temperature, etc.); use in spaceflight or underwater to monitor muscle atrophy; measure the impact of disease on normal muscle function; and measure whole body and localized region hydration status so as to better understand the impact on muscle condition.

[0028] In an exemplary application, the disclosed system and method may be used by a user performing exercise. The user may wear one or more garments that include the sensors (e.g., cuffs with sensors worn over different muscles) and one or more garments that include actuators (e.g., wraps that include treatment modalities (heaters, air cuff to apply compression, etc.) incorporated therein). When the user exercises (e.g., runs), the sensors may measure muscle characteristics (e.g., bicep MQ, tricep MQ, etc.) through EIM measurements. In some embodiments, based on the measured values or trends of the characteristics of a muscle (e.g., bicep MQ < a threshold value), one or more actuators (e.g., positioned on the bicep) may be activated to apply a treatment to the muscle and rejuvenate the muscle.

[0029] In some embodiments, the disclosed measurement systems may be used in conjunction with environmental measures to assess the physiologic adaption to environmental alterations, including changes in altitude, temperature or barometric parametric. In addition
to these systems being used simultaneously to provide an accurate measurement of the
muscle/physical condition, these measurements can be used in combination to ensure
appropriate and accurate application of the actuators.

[0030] Specific use of the actuators may include but would not be limited to the following:
treatment and prevention of impending fatigue with massage or compression; treatment of
muscle injury with cooling, heating or magnetic fields; application of muscle heating to
improve performance metrics; use of vibration to treat muscle discomfort (as indicated by
increased heart rate at rest, for example); electrical stimulation to treat muscle discomfort or
increase blood oxygentation; compression to increase blood flow to active limbs or to
account for elevated altitude; iontophoresis of drugs and other therapies to mitigate pain and
improve performance; improve function in weak muscles/limbs; and prevention and
treatment of low back or neck discomfort, indicated by electromyographic, tonographic, and
impedance-based, via use of compression, vibration, ultrasonography, or iontophoretic
therapy. Furthermore, any of the treatments referenced herein may be used to improve
muscle condition for fitness, aesthetic, or other reasons, even absent underlying fatigue,
injury, discomfort, pain, or decrease in function.

[0031] In some embodiments of the current disclosure, a sensor array in a shirt or similar
garment may obtain data on the truncal muscles, including abdominal and back muscles to
provide real time assessment of position/condition of these muscles and apply a treatment as
a remedy to a detected muscle condition (e.g., to help prevent and alleviate back pain). FIG.
1A illustrates an exemplary embodiment of a system used to detect and apply treatment to the
abdominal muscles of a subject. The system of FIG. 1A includes a garment 30 worn by a
subject 100. Garment 30 includes a wrap positioned around the subject's trunk. Garment 30
may include a plurality of actuators in the form of inflatable cuffs 20A, 20B, 20C (similar to
blood pressure monitoring cuffs) that may be selectively or collectively inflated by a
compressed fluid (air, liquid, etc.). In some embodiments, the fluid for inflation may be provided in a canister (not shown) included in the garment 30. In some embodiments, the canister may be provided on the person of subject 100. It is also contemplated that, in some embodiments, a remotely positioned canister may be fluidly coupled to the garment 30 for the purposes of inflation and deflation.

[0032] Garment 30 also includes a plurality of sensors 10 embedded therein (or attached thereto). The sensors 10 may be configured to detect EIM signals associated with the muscles in the subject's back. The measured electrical impedance may be indicative of the health condition of the back muscles. The sensors 10 may direct (e.g., transmit wirelessly or transfer through a wired connection) the measured EIM signals to a computational device 50 positioned remote from the subject 100. The collected data may be continuously or periodically transmitted to the device 50. The frequency of the periodic transmission may be selected by a user. Alternatively or additionally, in some embodiments, the garment 30 may be associated with a memory to store the collected EIM data. This memory may be incorporated into the garment 30 or otherwise coupled to the garment 30. In such embodiments, the collected EIM data may be stored in the memory and downloaded to device 50 when desired (e.g., during a visit to a doctor).

[0033] Sensors 10 may include a pattern of electrodes 18a-18i (referred to collectively as electrodes 18), as shown in FIG. 1B. FIG. 1B illustrates an exemplary partem of electrodes 18 that may be included on an interior of garment 30. Electrodes 18 may include any electrically conductive material (e.g., copper, aluminum, silver, gold, etc.). In some embodiments, the electrodes 18 may be coated with (or treated with) another material to impart desirable properties to the electrodes 18 (e.g., oxidation, wear, and/or corrosion resistance, decreased interfacial contact resistance, etc.). In some embodiments, the electrodes 18 may protrude from the surface of the garment 30 on which they are positioned.
In some embodiments, the electrodes 18 may be flush with, or recessed relative to, the surface. The electrodes 18 may include a first pair of spaced apart current electrodes and a second pair of spaced apart voltage electrodes, wherein the device is configured to direct a current into the patient's tissue through the first pair of current electrodes and measure a voltage across the second pair of voltage electrodes. In some embodiments, twelve electrodes 18a-18l may be arranged in a partem to allow different configurations to be used in a measurement. In general, the electrodes 18 may be arranged in any desired pattern. In some embodiments, the electrodes 18 may be arranged in a partem about a central axis 22 of the device 10 that extends perpendicular to the surface on which the electrodes 18 are positioned. In some embodiments, electrodes 18 may include a plurality of electrodes 18g, 18i, 18k, and 18h spaced apart and arranged parallel to a first axis 24 and a plurality of electrodes 18a, 18b, 18c, 18j, 18i, 18d, 18e, and 18f spaced apart and arranged parallel to a second axis 26 perpendicular to the first axis 24.

[0034] Device 50 may be configured to analyze (e.g., using software) the received signals to determine the health of the muscles. The analysis may detect an anomaly associated with the muscles (e.g., a sprain, etc.). In some embodiments, the analysis may include computations using the collected EIM data. In some embodiments, the analysis may include a review of the collected EIM data. If an anomaly is detected (e.g., a computed parameter or the measured signal exceeds a threshold value, a signal pattern resembles a pattern associated with an anomaly, etc.), device 50 may activate the cuffs 20A, 20B, 20C embedded in the garment 30 to administer a treatment to the back muscles. Upon activation, fluid from the canister (not shown) may inflate the cuffs 20A, 20B, 20C to compress (or massage) the muscles. In some embodiments, the device 50 may selectively activate the cuffs 20A, 20B, 20C in response to detection of an anomaly. For example, cuffs 20A, 20B, and 20C may be inflated in sequence to administer a peristalsis-like massage treatment to the muscles.
[0035] In some embodiments, heaters and/or other actuators also may be incorporated into the garment 30 to apply additional (or alternate) treatment to the muscles. For example, for some identified anomalies, device 50 may activate the cuffs 20A, 20B, 20C, and for other anomalies the device 50 may, additionally or alternatively, activate the heaters to apply heat as treatment. The treatment may be stopped by any method. In some embodiments, the subject may press a button (e.g., associated with garment 30) to stop the treatment. In some embodiments, the treatment may be stopped after a pre-programmed time. It is also contemplated that, in some embodiments, the treatment may be stopped when the sensors 10 indicate that the health of the muscles have improved.

[0036] Although the computational device 50 is illustrated as a computer positioned close to subject 100, this is not a requirement. In general, device 50 may be any electronic component (server, iPad, tablet, etc.) with software adapted to analyze the signals from the sensors 10. Device 50 may be placed at any location. In some embodiments, device 50 may be portable and may be carried by (or be attached to) the subject. In some embodiments, the device 50 may be positioned at a remote site (e.g., a remote health monitoring facility or a doctor's office). In some embodiments, an auxiliary device 40 (e.g., a phone, watch, etc.) carried by (or attached to) the patient may receive the signals from the sensors 10 and transmit (e.g., using a cellular network) the signals to the remotely positioned device 50.

[0037] Rather than being attached to sensors in or on the garment itself, it is also contemplated that the actuators may be separate from, but operationally coupled with (e.g., synced to), the sensors in the garment. For example, the actuators may be incorporated into automated chairs, beds, or recliners, such that the position of lumbar support of the furniture may be modified to actuate and reduce the identified discomfort of the subject. For example, when the EIM signals from the sensors 10 indicate that the subject is experiencing back pain,
the device 50 may activate a reclining bed that the patient is lying on to a more comfortable position.

[0038] In some embodiments, an actuator may be used to apply cooling to a limb by a wrap after identifying alterations in the muscle impedance data during an activity (e.g., exercise). Impedance changes during an activity may indicate excessive muscle injury after heavy exertion and a wrap around a limb may provide cooling therapy. A compression actuator (e.g., cuffs 20A, 20B, 20C) also may increase pressure if there is evidence of fatigue in the muscle.

[0039] In addition to these short-term measurement techniques, some embodiments of the current disclosure may include longer-term measurement and therapy. The ability to track nerve and muscle disease progression and its response to drug therapy remains challenging for a variety of reasons. These reasons include the general slowness of disease progression (often only detectable over the course of several months or even a year or longer), the absence of effective outcome measures or biomarkers of disease progression (since functional measures are often challenging to employ and imaging modalities are limited), and considerable variability in disease progression across individuals and their response to therapy. A similar situation exists, although changes are somewhat faster, for other conditions that involve muscle, including disuse atrophy or muscle injury from overuse.

[0040] In addition to evaluating gradual changes in muscle status, evaluating changes in body composition and fat content may be similarly slow. For example, it may be difficult to observe the effects of decreasing fat % in the body during a low calorie diet or during an exercise program. These changes could be used to help modify risk factors for diseases such as, for example, Type 2 diabetes (i.e., increased muscle mass and reduced fat content reduce the likelihood of developing Type 2 diabetes). Frequent measurements of EIM signals may assist in identifying the impact of drug treatments that affect the deposition of fat. For
example, corticosteroid use is known to increase fat % in specific body regions, including the face, upper back and abdomen, with relatively less impact on the extremities.

[0041] Frequent EIM measurements also may be used to evaluate neuromuscular disease progression, including in amyotrophic lateral sclerosis, muscular dystrophy, spinal muscular atrophy, disuse atrophy, and even polyneuropathy. Standard clinical trial research approaches for employing EIM envision it being applied at several-month intervals along with standard measures of disease progression (e.g., questionnaires, strength testing, functional tests and imaging (e.g., MRI)). Whereas ordinary modalities of testing can only be reasonably applied on an intermittent basis by trained individuals or are insensitive to change over very short intervals, EIM measures and associated improvements as noted above in this application can be performed frequently at home by patients or their family members/caretakers. These frequent EIM measurements also may be used to monitor alterations in fat content.

[0042] The term "frequent" in this disclosure is used to indicate an inter-measurement time that is significantly less than (or a measurement frequency that is significantly more than) the several-month intervals between typical EIM measurements. Although, in general, the frequency of a frequent measurement of the current disclosure may depend upon the disease being monitored, in all embodiments, the frequency of measurement is greater than or equal to one measurement per month. In some embodiments, the term frequent measurement refers to multiple measurements per month (e.g., one measurement every two weeks, one measurement every week, etc.) In some embodiments, it refers to multiple measurements per week (e.g., one measurement every few days, one measurement every day, etc.). In some embodiments, the term frequent measurement refers to multiple measurements per day (e.g., one measurement every few hours, one measurement per hour, multiple measurements per hour, etc.).
In some examples, a user may carry out frequent measurements at home, without the assistance of a medical professional. All or a portion of the frequent measurements may be conducted using the same sensor (e.g., a sensor 10 shown in FIGs. 1 and 1A). In some cases, the sensor 10 may remain in contact with the user's skin between the frequent measurements. In one example, the sensor 10 may remain in contact with the patient's skin for a plurality of the frequent measurements (e.g., the measurements during the course of a day), although the user may remove the sensor 10 at certain times (e.g., to shower). The sensor 10 may be a part of garment 30 or may be any other sensor 10 secured to the patient's skin and/or used during the frequent measurements. As explained previously, in some embodiments, the EIM measurements may be taken by a user periodically pressing electrodes/sensors incorporated in a portable device against the user's skin.

FIGS. 2A and 2B show the basic concepts underlying the ability to obtain frequent measurements over longer periods of time and the improved ability to detect change. FIG. 2A illustrates a typical case where data of a patient with a progressive disease is measured once every 100 days. Curve 55 is a plot of disease progression, assuming a linear decline over time (a standard assumption in most neuromuscular disease clinical trials). The dashed lines 60 in FIG. 2A represent the 95% confidence intervals for the slope of decline over time. As can be seen in FIG. 2A, when the measurement is infrequent, the confidence interval is fairly wide leading to large uncertainty. FIG. 2B illustrates the results of an exemplary frequent measurement technique in which data of the patient is measured frequently. As can be seen in FIG. 2B (the frequent measurement approach), the 95% confidence intervals are narrow relative to the intervals in FIG. 2A and remain relatively constant over time. This implies that curve 55 of FIG. 2B is a much more accurate measure of disease progression than curve 55 of FIG. 2A. Therefore, by obtaining data at frequent intervals, response to therapy can be obtained for each individual participating in a clinical trial. This achievement
means that for the same clinical trial, considerably fewer subjects may be needed in order to
detect the effect of a treatment. Using such a frequent measurement approach, the effect of
treatment also may be identified much more quickly (i.e., over 6-8 weeks instead of over 6
months or a year).

[0045] In an exemplary application of the disclosed frequent measurement technique, we
performed a sample size determination (i.e., determination of the number of subjects needed
for a clinical trial) using standard methods for two-level mixed-effects model analysis
assuming a clinical trial in which we were seeking to identify a treatment effect after 6
months. In this model, we assumed a linear progression of the disease with alpha = 0.05, a
two-tailed Wald test, with equal randomization between drug and placebo, with between-
subject variability being four times greater than within-subject variability and an intra-class
correlation coefficient for the measurements of 0.80, seeking a treatment effect of 0.5 SD in a
given parameter. In the standard approach, a child is assessed at baseline, and then every 2
months for a total of 4 assessments. With this method, we would need a total of 91 subjects
per group. However, if we performed weekly measurements, the number of subjects needed
would decrease to 24 subjects per group. And with daily measurement (162 during the 6
month period) the number of subjects needed would decrease to just 4 subjects per group.
While this last value may not be realistic or statistically valid for some diseases (since it may
not represent the population of affected individuals), this dramatic reduction in the number of
subjects demonstrates the potential power of the disclosed frequent measurement strategy.

[0046] Embodiments of the disclosed frequent measurement approach may be used in ALS
clinical trials, muscular dystrophy clinical trials, or any other disorder characterized by a
progressive change in the condition of muscle, whether a deterioration or an improvement in
the condition of muscle is being identified (e.g., the graphs in FIG. 2B could show an
improving trend over time and it would therefore be easier to identify improvement rather
than just a slowing of deterioration). One example of this may be in the treatment of sarcopenia where over the time of a clinical trial no appreciable change in the character of the muscle will be observed in a placebo group. If a patient were placed on a medication to improve muscle condition or an exercise therapy program or both in combination, the frequent measurements may mean that a treatment effect could be identified much more readily, with fewer people, over shorter periods of time, and at lower cost.

FIG. 3 illustrates an exemplary method 200 of characterizing disease progression using frequent EIM measurements. The EIM measurements may be made at frequent intervals (1/day, 1/2 days, 1/week, etc.) using an EIM measurement device (step 210). Any EIM measurement device may be used for these measurements. In some embodiments, a measurement device disclosed in the ’198 patent and the ’808 patent (which are incorporated by reference herein) may be used for frequent EIM measurements. In some embodiments, garment 30 of FIG. 1A may be used as the EIM measurement device. The EIM data may be measured by the patient or a caregiver using the EIM measurement device.

The collected EIM data may be uploaded or transferred to a cloud server, a remote database, or a remote computational device (such as device 50 of FIG. 1A) for analysis (step 220). The collected data may be uploaded to the remote database at any frequency (e.g., continuously, periodically, etc.). In some embodiments, the collected data may be uploaded based on a request from the remote database. In some embodiments, instead of uploading, the data may be stored in the EIM measurement device. The stored data then may be transferred to a remote database as desired (e.g., using a disk, memory device, etc.). It also is contemplated that, in some embodiments, the collected data may not be transferred to the remote database. Instead, analysis on the stored data may be performed on the EIM measurement device.
The central database may perform analysis on the received data to determine a health parameter of the patient (step 230). The health parameter may be an indicator of the disease or other change being monitored by the EIM measurement device. In one example, the health parameter may be a muscle characteristic indicative of a change (e.g., deterioration or improvement) of one or more muscles in response to a lack of or an increase in exercise. The '198 patent, the '808 patent, and the '821 application describe some of the analysis that may be performed by the database. In general, the type of analysis performed by the database may depend upon the disease being monitored. Since analysis techniques and algorithms to detect diseases monitored using the EIM measurement device (discussed previously) are known in the art, these techniques are not discussed herein. In some embodiments, the collected EIM data may itself indicate the health of the patient and the progression of the disease. In such embodiments, the analysis may only include a review of the collected data. The determined health parameter may be plotted over time to indicate the progression of the monitored disease or health parameter over time (step 240). In some embodiments, the data may be plotted on a display device (screen) associated with the remote database. In some examples, health care providers, personal trainers, or other professionals may have access to the determined health parameter information and the plot of the determined health parameter as a function of time in order to inform clinical decisions and/or training programs.

In some embodiments, an application (e.g., a software application or an app) associated with the EIM measurement device may capture a variety of other information including movement data, heart rate, and other readily obtainable data sets with a smartphone (e.g., auxiliary device 40) or the EIM measurement device itself. The EIM measurement device may include circuits and features (e.g., impedance measuring fidelity, circuitry for measuring multiple frequencies, additional configurations, enhanced memory, extended ranges, etc.) adapted to measure abnormal EIM data. Additionally, the device may be
configured to be handled by a weak individual (i.e., portable device having reduced weight, size, etc.). The device may have (or be associated with) a display or a screen that is configured to display information to the patient (e.g., to inform the patient that a data upload was successfully completed, etc.). For example, in the embodiment of FIG. 1A, the screen of the auxiliary device 40 associated with the garment 30 may be used to convey information/messages to the patient. In some embodiments, the screen may be adapted to display information in a simple and easily understandable manner. For example, in some embodiments, only a colored (e.g., green) symbol (e.g., check mark) may be shown to indicate that good data was obtained and/or uploaded.

[0051] In some embodiments, the EIM measurement device may be programmed to automatically acquire EIM signals from the patient at the desired frequency (e.g., on a preprogrammed schedule). For example, the garment 30 of FIG. 1A may be programmed to measure EIM signals every hour, etc. In some embodiments, the remote database (or device 50 of FIG. 1A) may send an instruction signal (e.g., on a periodic basis) to the garment 30 to take EIM measurements. In some embodiments, the application associated with the EIM measurement device (such as, an EIM measurement device of the '198 patent or the '808 patent) may include an alarm to remind the patient or the caregiver to obtain their daily measurements. In some embodiments, the application may share an application program interface (API) with devices or sensors that collect other physiological data of the patient (movement data, heart rate, blood pressure, etc.). This physiological data may be collected, uploaded, and analyzed along with the EIM data collected by the EIM measurement device.

[0052] In some embodiments, EIM measurement device and/or the application may be configured to collect, store, and/or transmit input and/or oral communications from the patient and/or family. For example, in some embodiments, by pressing a button associated with the EIM measurement device (e.g., on the garment 30 of FIG. 1A), the patient may
report what the patient is experiencing at a certain time (nausea, dizziness, etc.). This communication from the patient may also be uploaded along with the collected EIM data to the remote database. The data communicated by the patient may help in better analyzing and/or understanding the collected EIM data. In some embodiments, input related to surveys and/or questionnaires (e.g. ALS -Functional rating scale revised, etc.) may also be included in the data communicated by the patient. In some embodiments, the application may also provide dietary and exercise commentary to assist the patient in monitoring EIM data and/or the health more effectively.

[0053] The frequent EIM data of method 200 may be used to reduce the number of subjects needed to be recruited into a clinical trial in neuromuscular disease, greatly reduce the duration of the trial, and/or greatly increase the sensitivity to a treatment effect (or any combination of these three effects). Other tangible benefits of the disclosed technique may include (a) the ability to perform studies in very rare diseases, (b) the ability to enroll and monitor subjects in remote areas, (c) the ability to perform N = 1 (single subject) studies in a meaningful way (e.g., the power to detect drug effect in N = 1 studies would be greatly increased), (d) outside of clinical trials, the ability to follow individual patients during a course of treatment, to help ensure that the therapy is working, (e) to assist in drug dosing (either in a clinical trial or in individual patient care). Specifically, by tracking data closely, it will be clear whether a patient is responding as expected to a medication or whether they would benefit from a higher dose of the medication. Alternatively, the patient's status could be tracked from one dose to a higher dose. If there is no specific change in the monitored health parameters at the higher dose, and a higher potential for greater side effects and/or cost at the higher dose, the drug dose may be reduced to a lower dose.

[0054] A similar approach can be used in studies of body composition and reduction in fat content or monitoring of body-region specific deposition of fat. Thus, the disclosed frequent-
measurement approach may have similar effects as described above, except that it may also impact other conditions and diseases beyond the realm of neuromuscular disease, including recovery and treatment for muscle injury, therapies focused on reducing body fat content and increasing muscle (such as for the prevention or treatment of type 2 diabetes), and for the evaluation of potential medication side effects impacting body composition, such as the use of corticosteroids.

[0055] The EIM measurement device and the disclosed frequent measurement technique may also be used to assist in the initial diagnosis of a neuromuscular condition. For example, patients with progressive disease may find alterations in their condition by performing daily measurements, even when less frequent measurements would not have revealed the alterations. Accordingly, frequent measurements may allow a practitioner to more quickly determine whether a disease requires treatment or not. Such frequent measurements may more clearly help in establishing efficacy effects, and therefore, may assist in the removal of bad data points.

[0056] An exemplary application of the disclosed frequent measurement approach may include a placebo-controlled, double-blind clinical trial in neuromuscular or other disease (e.g. diet therapy to reduce obesity). In such a trial, some patients may receive the actual drug and others may receive a placebo. Each patient may be provided an EIM measurement device to take home. They may be instructed to take daily measurements (i.e., frequently collect EIM data) on a set of muscles and regularly sync the device to the internet (either through phone or directly depending on the type of connection) to upload the collected data to a remote database. The patients may continue to take the drug/placebo for the length of the study. At the end of the study, all the data points would be analyzed and the trajectories of change could be utilized to help identify the rate of change in drug versus placebo (either deterioration or improvement, depending on the disease). The frequent measurements may
help ensure that the most accurate data had been gathered. A determination may then be made as to whether the drug was effective and whether further studies or FDA approval could be sought.

[0057] In another embodiment, an individual patient may be provided the EIM measurement device and placed on an FDA-approved therapy and the patient asked to perform measurements daily and upload the measured EIM data to the web. The doctor may then be able to evaluate the data as needed and make adjustments to the medication dosing or perhaps switch medications entirely.

[0058] In another embodiment, a physical therapist may provide the EIM measurement system to a patient while the patient is undergoing physical therapy. The patient may be instructed to collect EIM data of the muscles being treated daily. The collected data may be stored in the device or may be periodically uploaded to a database at the physical therapist's office. Based on a review of daily EIM data, the physical therapist thus might alter the treatment.

[0059] In another embodiment, a specialist treating a patient with botulinum toxin for a variety of conditions (e.g., dystonia or headache) may perform EIM measurements on a regular basis (daily, weekly, etc.). The frequently collected data (or a health parameter computed using the EIM data) may indicate when it is time to again treat the patient with botulinum toxin. This would reduce delays in therapy and help ensure a patient's treatments are being accurately timed.

[0060] In another embodiment, the disclosed frequent measurement technique may be used to assist with initial diagnosis of a patient. A patient may complain of weakness that is progressive or other neuromuscular symptoms that are difficult to quantify. The patient may be provided with an EIM measurement device and instructed to perform daily measurements over a period of several weeks or months. The collected data may be stored in the EIM
measurement device. The patient may then return for follow up visit and the data analyzed. The collected data may then be used to determine whether there is evidence of disease progression or not during that time period, or whether there are fluctuations in muscle status. This information may then be used for diagnostic purposes.

[0061] In another embodiment, the EIM measurement device may be supplied to a patient to ensure that they are actively participating in a therapy or drug routine. In this embodiment, the device may also provide feedback data (potentially in real time) to help provide continuing encouragement to the patient.

[0062] In another embodiment an automatic feedback loop may be created whereby the patients self-adjust medication dosing based on continuous feedback from the EIM measurement device over a period of weeks or months. The entire operation can become automated such that the device (or a remote database that analyzes the collected data) informs the patient of the appropriate dose based on the results of the frequent measurement data without the input (or with minimal input) of a physician or other medical professional. In some embodiments, a device implanted in the patient may release an appropriate dose of the drug based on input from the remote database.

[0063] It should be understood from the foregoing that, while particular implementations have been illustrated and described, various modifications can be made thereto and are contemplated herein. It is also not intended that the invention be limited by the specific examples provided within the specification. While the invention has been described with reference to the aforementioned specification, the descriptions and illustrations of the embodiments herein are not meant to be construed in a limiting sense. Furthermore, it shall be understood that all aspects of the invention are not limited to the specific depictions, configurations or relative proportions set forth herein which depend upon a variety of conditions and variables. Various modifications in form and detail of the embodiments of the
invention will be apparent to a person skilled in the art. It is therefore contemplated that the invention shall also cover any such modifications, variations and equivalents.
CLAIMS

We claim:

1. A wearable treatment device for a patient, comprising:
   at least one electrode coupled to a garment configured to be worn by the patient, the at least one electrode being configured to be placed in contact with the patient's tissue and measure electrical impedance of the patient; and
   at least one actuator operatively coupled to the garment, the at least one actuator being configured to deliver a treatment to the patient in response to the measured electrical impedance.

2. The device of claim 1, wherein the measured electrical impedance indicates a change in a muscle characteristic.

3. The device of claim 1, wherein the at least one actuator includes a plurality of inflatable cuffs configured to apply pressure to a portion of the patient.

4. The device of claim 1, wherein the at least one actuator includes a heater.

5. The device of claim 1, wherein the at least one actuator is configured to deliver electrical stimulation to the patient.

6. The device of claim 1, wherein the at least one actuator is configured to vibrate.

7. The device of claim 1, wherein the at least one electrode includes a first pair of spaced apart current electrodes and a second pair of spaced apart voltage electrodes, wherein
the device is configured to direct a current into the patient's tissue through the first pair of current electrodes and measure a voltage across the second pair of voltage electrodes.

8. The device of claim 7, wherein the at least one electrode includes multiple pairs of current electrodes and multiple pairs of voltage electrodes.

9. A method for treating a patient, comprising:
   positioning a garment around a portion of the patient, wherein the garment is coupled to at least one electrode positioned in contact with the patient's tissue;
   measuring electrical impedance of the patient using the at least one electrode; and
   in response to the measured electrical impedance, using at least one actuator operatively coupled to the garment to deliver a treatment to the patient.

10. The method of claim 9, wherein the measured electrical impedance indicates a change in a muscle characteristic.

11. The method of claim 9, wherein the at least one actuator includes a plurality of inflatable cuffs, and the method further comprises inflating the plurality of cuffs in sequence.

12. The method of claim 9, further comprising using the actuator to apply heat to the patient.

13. The method of claim 9, further comprising using the actuator to deliver electrical stimulation to the patient.

14. The method of claim 9, wherein the at least one electrode includes a first pair of spaced apart current electrodes and a second pair of spaced apart voltage electrodes, wherein the method further includes directing a current into the patient's tissue through the
first pair of current electrodes and measuring a voltage across the second pair of voltage electrodes.

15. A system for treating a patient, comprising:

a garment;

a plurality of electrodes coupled to the garment, wherein the plurality of electrodes are configured to obtain electrical impedance data relating to one or more muscles of the patient;

a computational device configured to detect an anomaly in the electrical impedance data; and

a plurality of actuators coupled to the garment and configured to deliver a treatment to the patient in response to the anomaly in the electrical impedance data.

16. The system of claim 15, wherein the anomaly is a measured impedance signal that exceeds a threshold value.

17. The system of claim 15, wherein the garment includes a shirt, and the shirt includes a plurality of electrodes configured to be positioned adjacent an abdomen, a plurality of electrodes configured to be positioned adjacent a bicep, a plurality of electrodes configured to be positioned adjacent a tricep, and a plurality of electrodes configured to be positioned adjacent a back.

18. The system of claim 15, wherein the plurality of electrodes includes a first pair of spaced apart current electrodes and a second pair of spaced apart voltage electrodes, wherein the system is configured to direct a current into the patient's tissue through the first pair of current electrodes and measure a voltage across the second pair of voltage electrodes.
19. The system of claim 15, wherein the at least one actuator is configured to at least one of deliver heat, electrical stimulation, or vibrations to the patient.

20. The system of claim 15, wherein the at least one actuator is inflatable.
FIG. 3

200

Measure EIM Signals From A Patient At Frequent Intervals

210

Upload The EIM Data To A Central Database

220

Perform Analysis On The EIM Data To Determine The Health Of The Patient

230

Plot The Determined Health As A Function Of Time

240
INTERNATIONAL SEARCH REPORT

A. CLASSIFICATION OF SUBJECT MATTER

IPC(8) - A61B 5/00; A61B 5/04; A61B 5/05; A61B 5/053; A61N 1/04; A61N 1/08; A61N 1/36 (2016.01)
CPC - A61B 5/0006; A61B 5/0408; A61B 5/8704; A61N 1/0452; A61N 1/0456; A61N 1/0484 (2016.05)

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

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC - A61B 5/00; A61B 5/04; A61B 5/05; A61B 5/053; A61N 1/04; A61N 1/08; A61N 1/36
CPC - A61B 5/0006; A61B 5/0006; A61B 5/0006; A61B 5/8704; A61N 1/0452; A61N 1/0456; A61N 1/0484

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

USPC - 600/300, 382, 386, 393, 509, 547, 607/2, 6 (keyword delimited)

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

Orbit, Google Patents, Google, Google Scholar, YouTube

Search terms used: wearable, treatment, electrode, garment, tissue, actuator, impedance, muscle, deliver treatment, electrical stimulation, voltage, current, anomaly, threshold

C. DOCUMENTS CONSIDERED TO BE RELEVANT

<table>
<thead>
<tr>
<th>Category</th>
<th>Citation of document, with indication, where appropriate, of the relevant passages</th>
<th>Relevant to claim No.</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>US 8,644,925 B2 (VOLPE et al) 04 February 2014 (04.02.2014) entire document</td>
<td>1-20</td>
</tr>
</tbody>
</table>

* Special categories of cited documents:
  "A" document defining the general state of the art which is not considered to be of particular relevance
  "E" earlier application or patent but published on or after the international filing date
  "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
  "O" document referring to an oral disclosure, use, exhibition or other means
  "P" document published prior to the international filing date but later than the priority date claimed
  "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
  "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
  "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
  "Z" document member of the same patent family

Further documents are listed in the continuation of Box C. [See patent family annex.]

Date of the actual completion of the international search: 30 June 2016
Date of mailing of the international search report: 28 JUL 2016

Name and mailing address of the ISA/Authorized officer
Mail Stop PCT, Attn: ISA/US, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450
Facsimile No. 571-273-8300

Blaine R. Copenhaver
PCT Helpdesk: 571-272-4300
PCT OSP 571-272-7774

Form PCT/ISA/2 10 (second sheet) (January 2015)