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(54) **UNIVERSAL CLOSED-LOOP ELECTRICAL STIMULATION SYSTEM**

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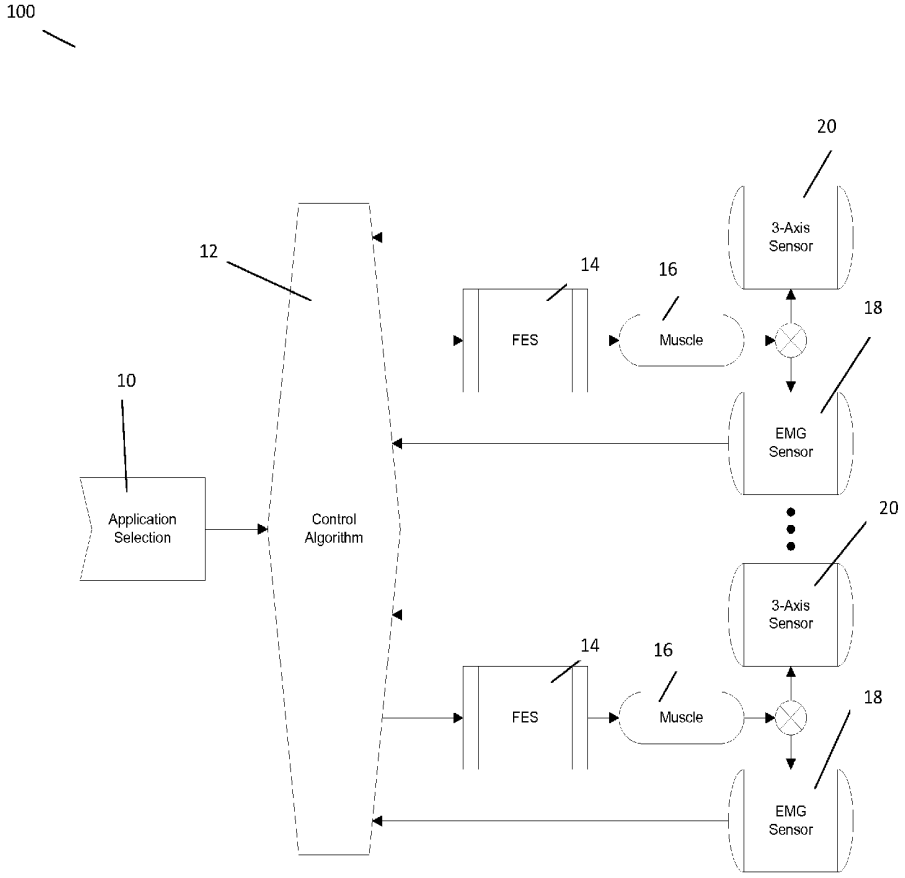
(57) **ABSTRACT**

A universal closed-loop functional electrical stimulation system comprising at least one electrode assembly adapted to deliver an electrical stimulation signal to the central nervous system, peripheral nervous system, or muscles of a user, a sensor system adapted to detect a mechanical response to a muscle stimulation signal of at least one muscle associated with a muscle group stimulated through the nervous system or proximate to the electrode assembly. An electrical stimulation device operably coupled to at least one electrode assembly and the sensor system, the electrical stimulation device including a control system to automatically receive feedback from at least one characteristic of the muscle from the detected muscle response and adjust at least one parameter of the muscle stimulation signal in real-time and in response thereto and a programmed microprocessor for controlling said electrical stimulation and receiving input from said sensor system.



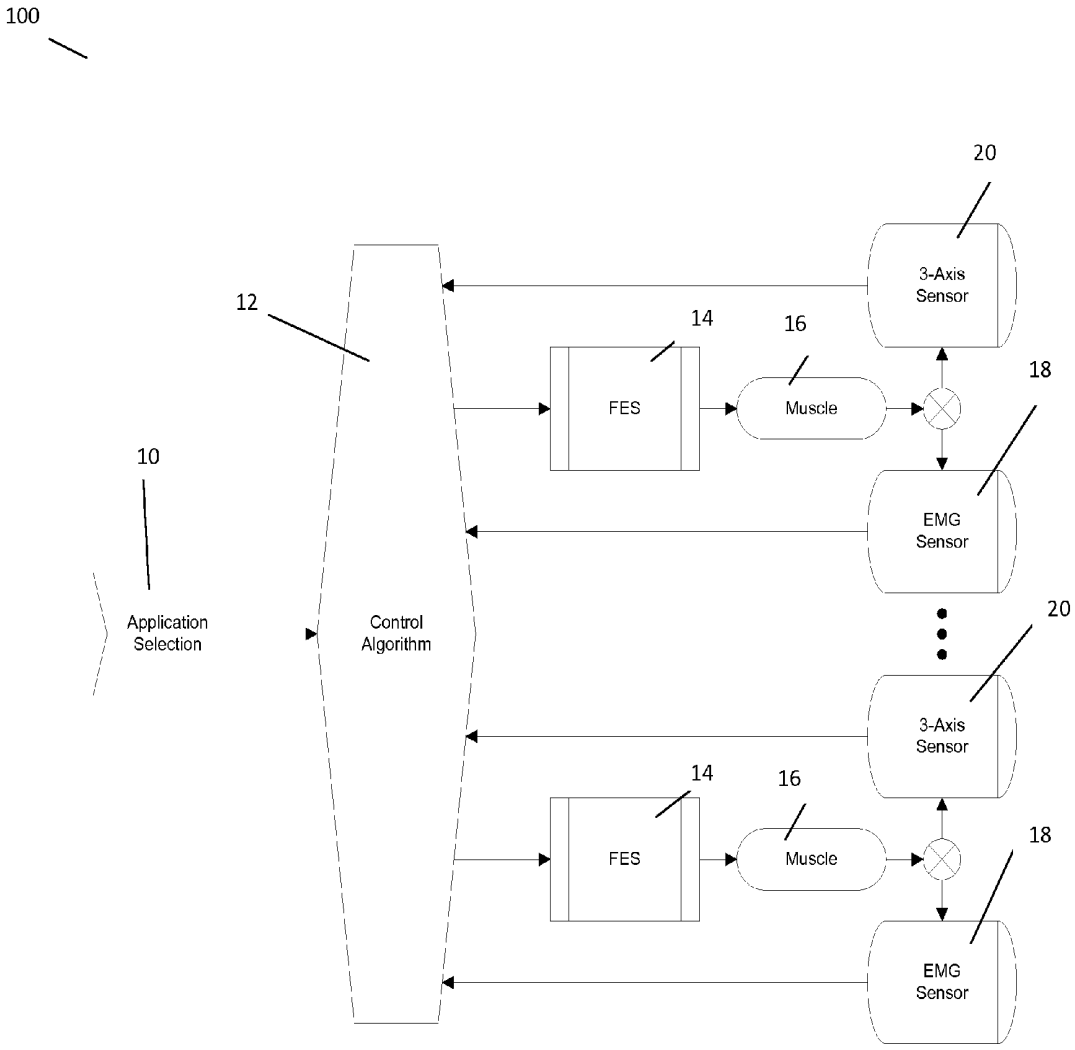

100
20
12
14
16
18
10
3-Axis Sensor
FES
Muscle
EMG Sensor
Application Selection
Control Algorithm
20
3-Axis Sensor
14
16
18
FES
Muscle
EMG Sensor

Fig. 1

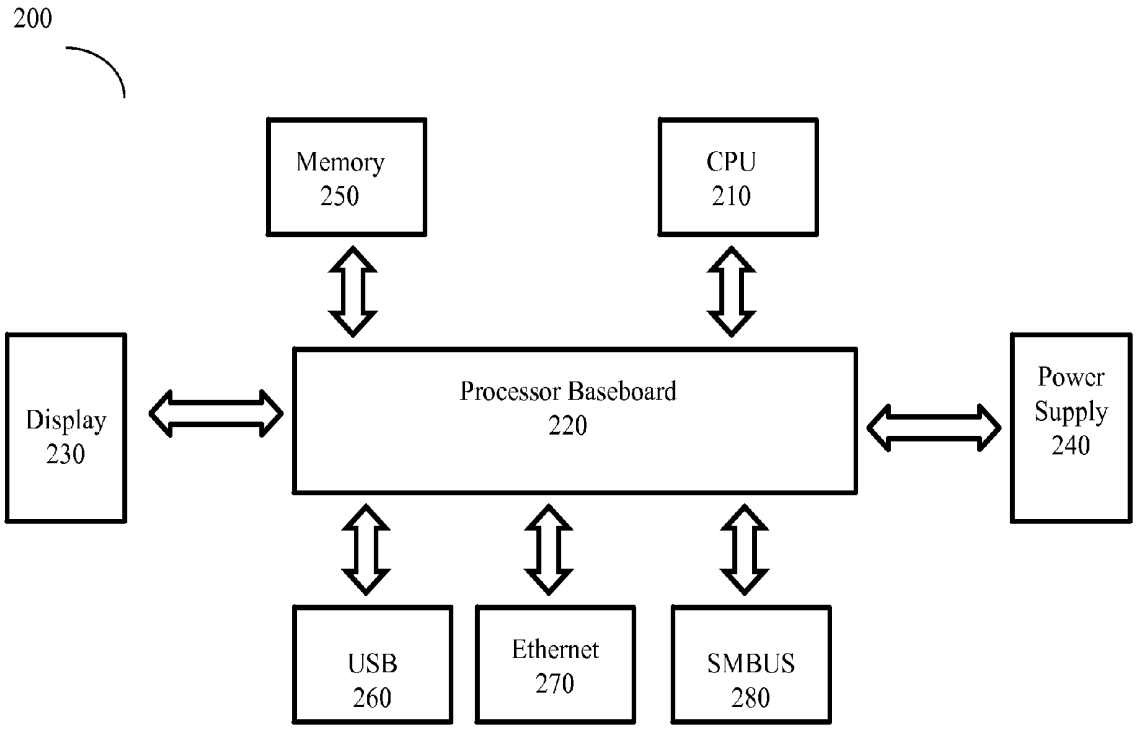

200
Memory
250
CPU
210
Display
230
Processor Baseboard
220
Power
Supply
240
USB
260
Ethernet
270
SMBUS
280

Fig. 2

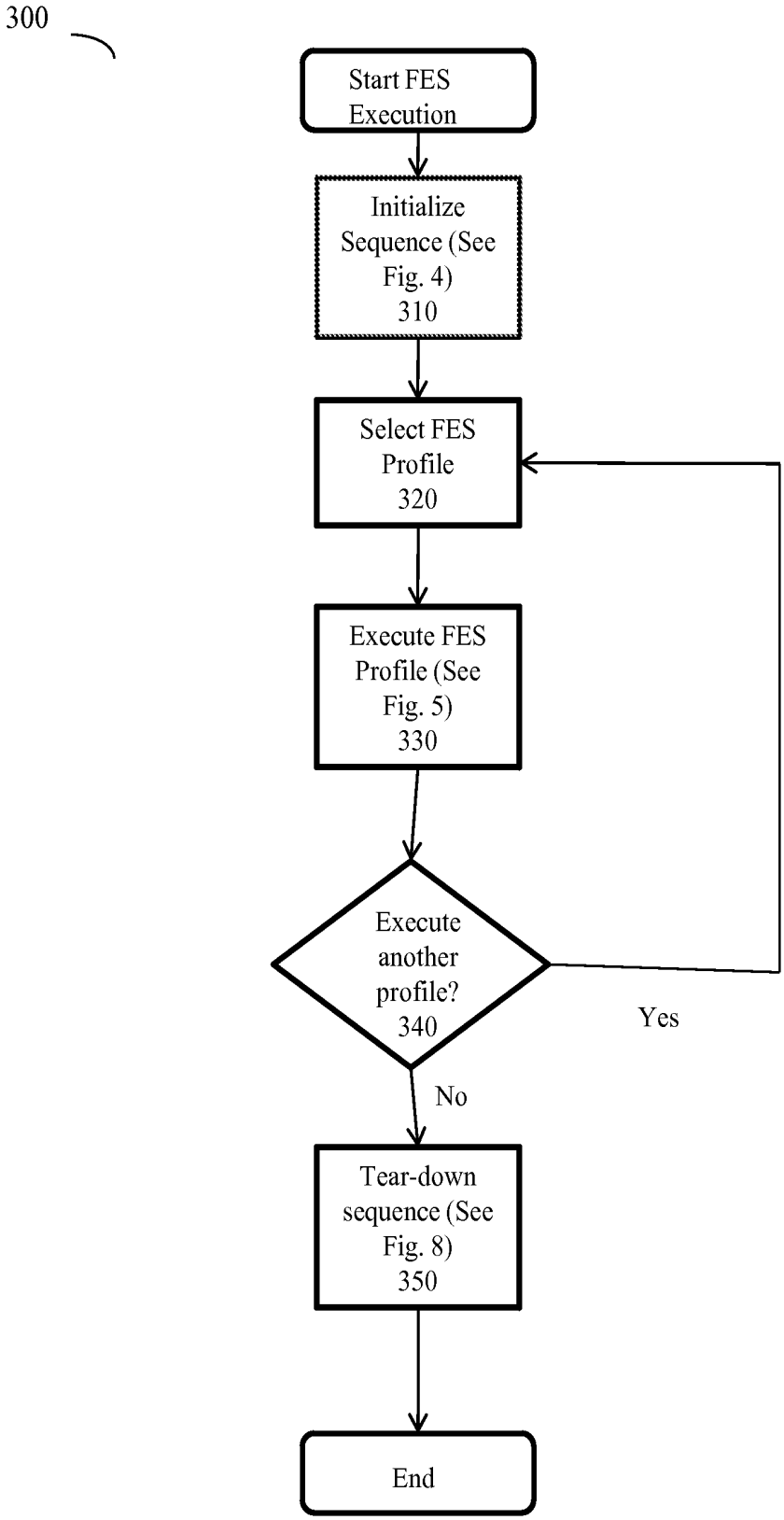

300
Start FES Execution
Initialize Sequence (See Fig. 4) 310
Select FES Profile 320
Execute FES Profile (See Fig. 5) 330
Execute another profile? 340
Yes
No
Tear-down sequence (See Fig. 8) 350
End

Fig. 3

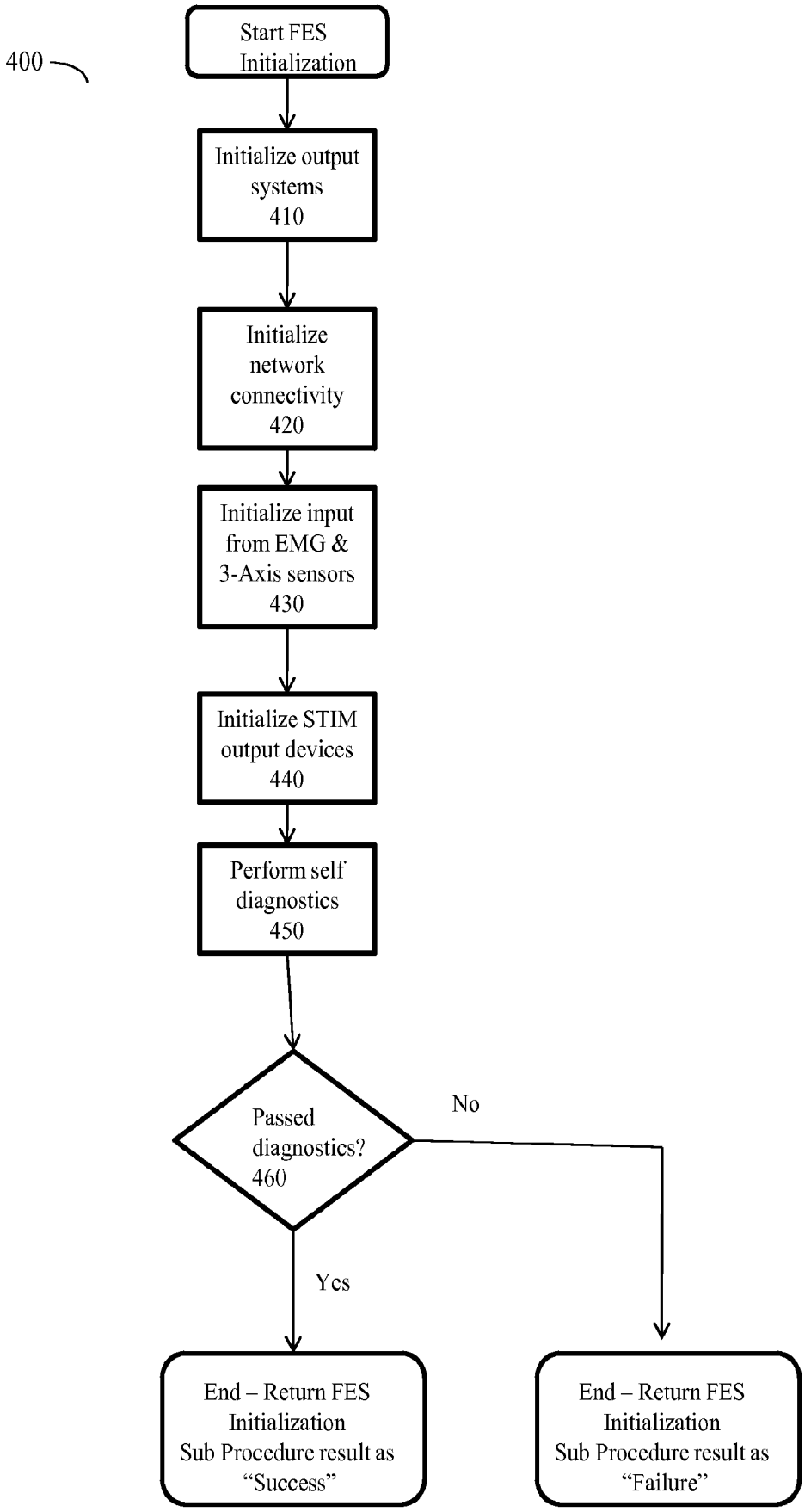

400
Start FES Initialization
Initialize output systems 410
Initialize network connectivity 420
Initialize input from EMG & 3-Axis sensors 430
Initialize STIM output devices 440
Perform self diagnostics 450
Passed diagnostics? 460
No
Yes
End – Return FES Initialization Sub Procedure result as "Success"
End – Return FES Initialization Sub Procedure result as "Failure"

Fig. 4

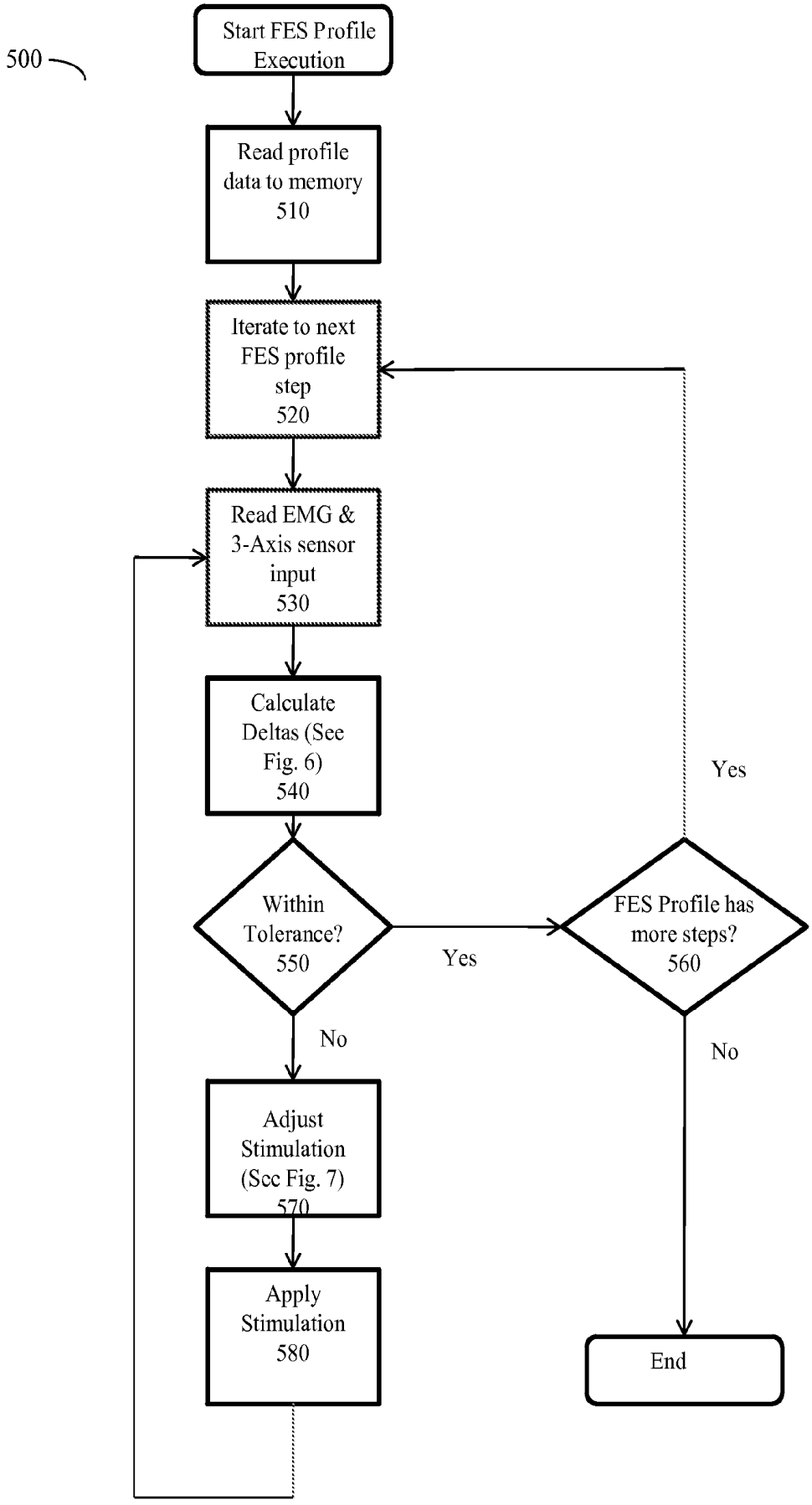

500
Start FES Profile Execution
Read profile data to memory 510
Iterate to next FES profile step 520
Read EMG & 3-Axis sensor input 530
Calculate Deltas (See Fig. 6) 540
Within Tolerance? 550
Yes
No
FES Profile has more steps? 560
Yes
No
Adjust Stimulation (See Fig. 7) 570
Apply Stimulation 580
End

Fig. 5

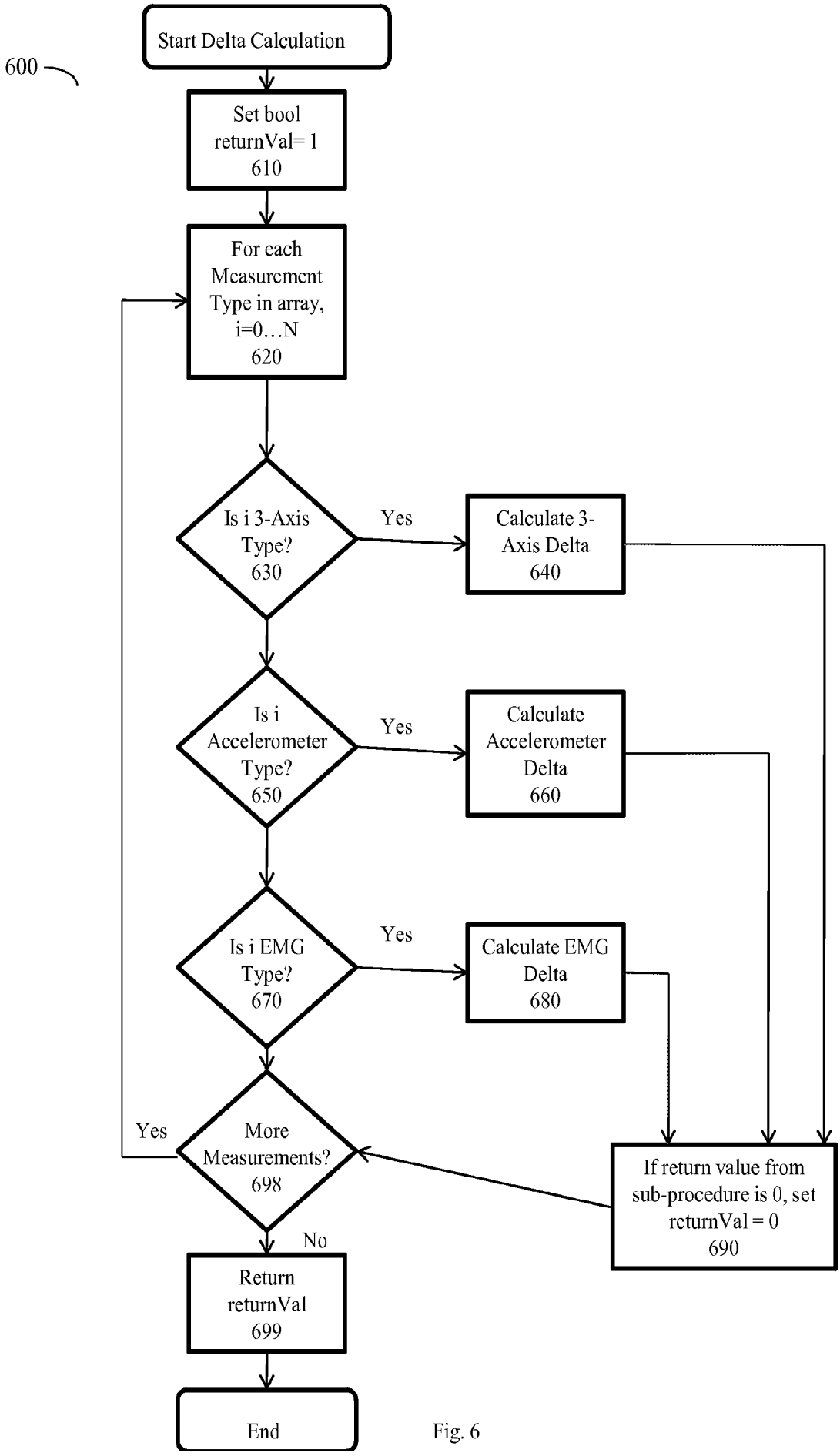

600
Start Delta Calculation
Set bool returnVal= 1
610
For each Measurement Type in array, i=0…N
620
Is i 3-Axis Type?
630
Yes
Calculate 3-Axis Delta
640
Is i Accelerometer Type?
650
Yes
Calculate Accelerometer Delta
660
Is i EMG Type?
670
Yes
Calculate EMG Delta
680
More Measurements?
698
Yes
No
If return value from sub-procedure is 0, set returnVal = 0
690
Return returnVal
699
End

Fig. 6

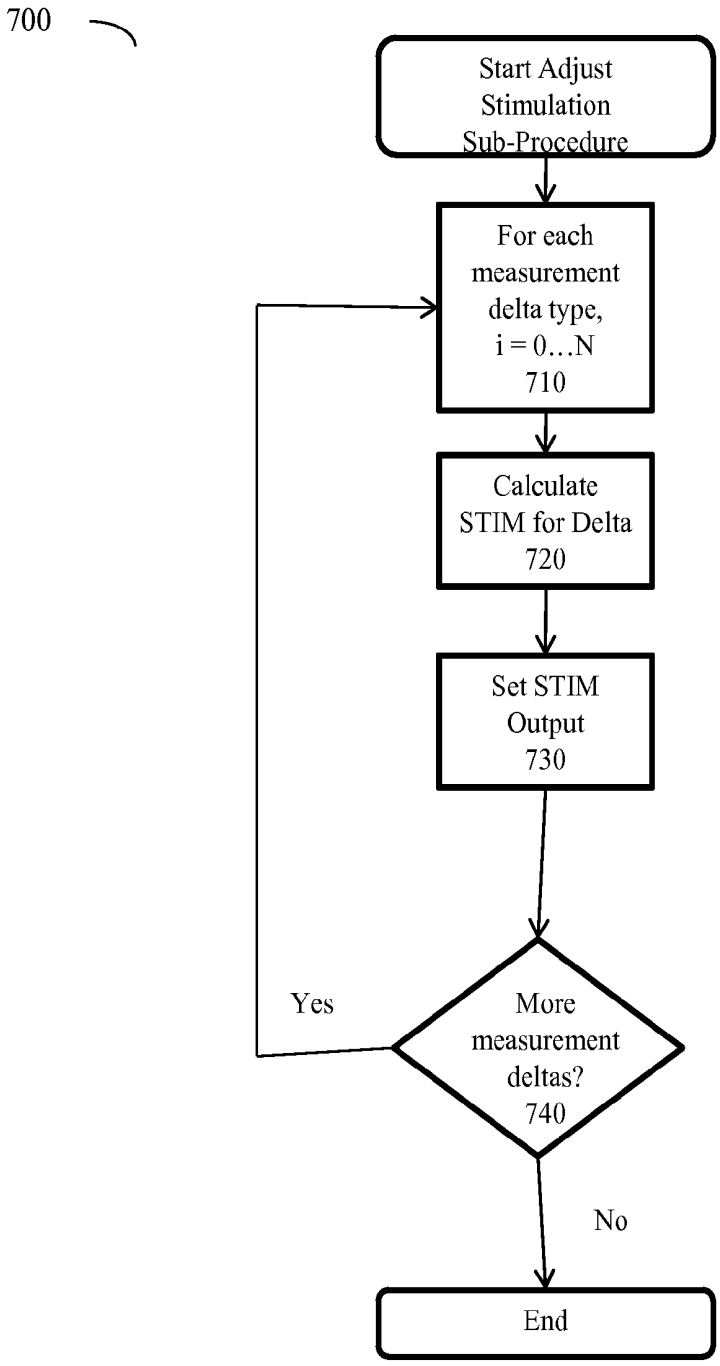

700
Start Adjust Stimulation Sub-Procedure
For each measurement delta type, i = 0…N
710
Calculate STIM for Delta
720
Set STIM Output
730
More measurement deltas?
740
Yes
No
End

Fig. 7

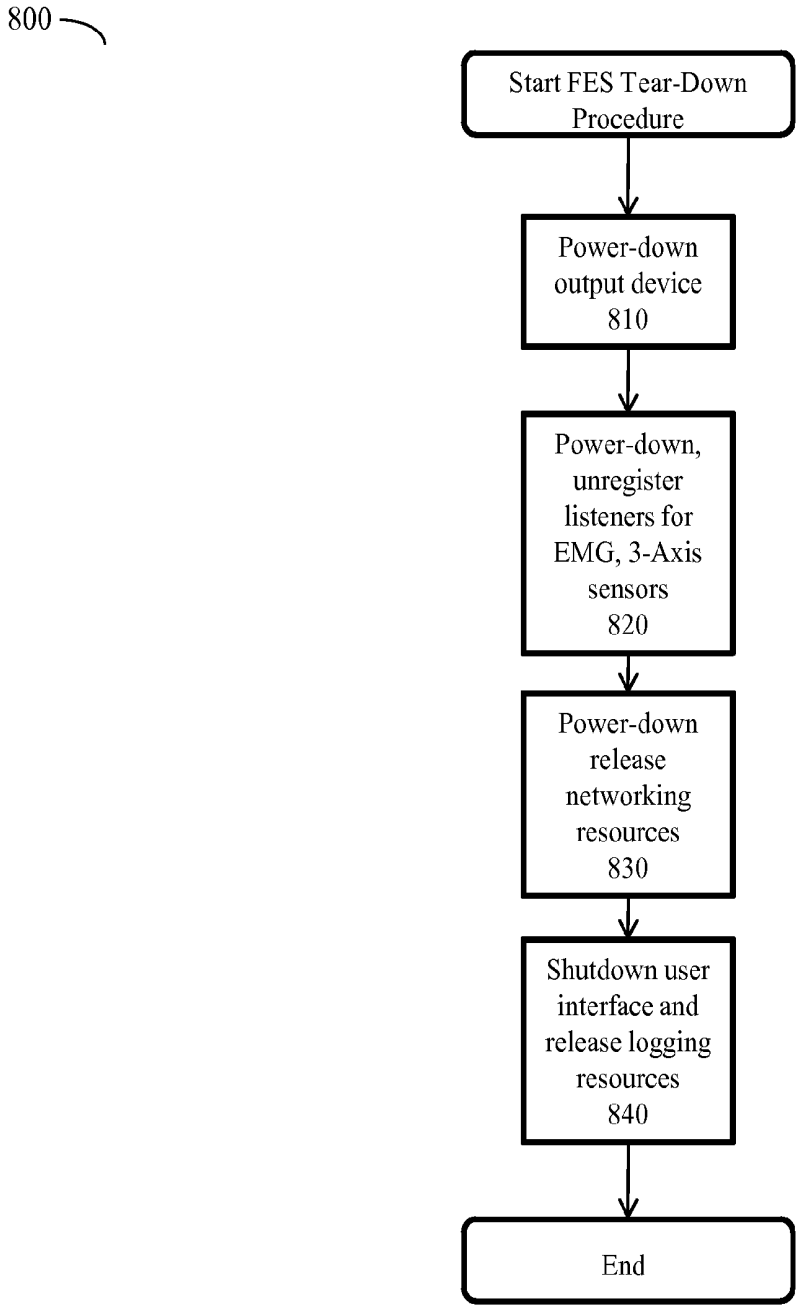

800
Start FES Tear-Down Procedure
Power-down output device 810
Power-down, unregister listeners for EMG, 3-Axis sensors 820
Power-down release networking resources 830
Shutdown user interface and release logging resources 840
End

Fig. 8

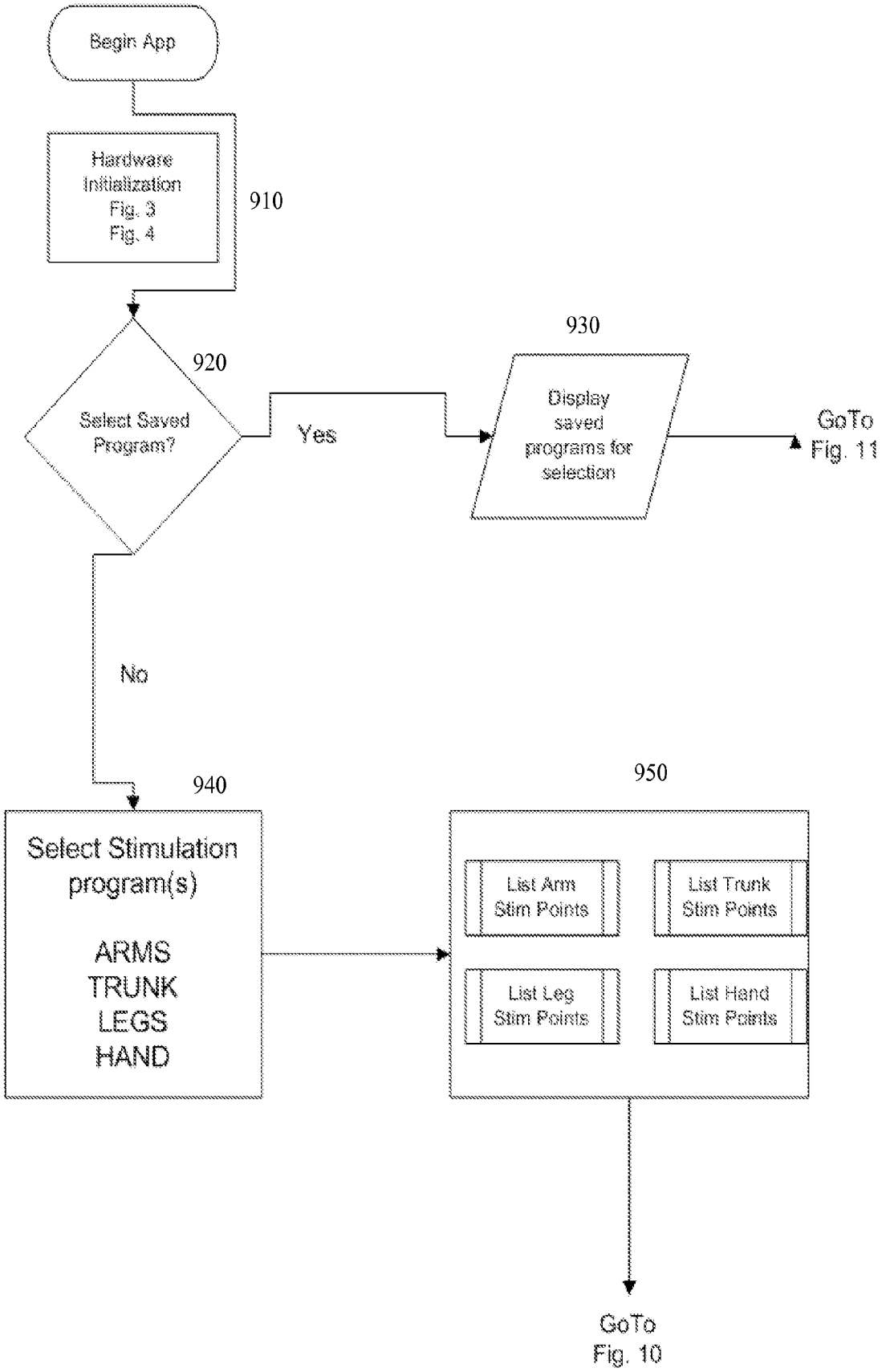

Begin App
Hardware Initialization Fig. 3 Fig. 4
910
920
Select Saved Program?
Yes
930
Display saved programs for selection
GoTo Fig. 11
No
940
Select Stimulation program(s)
ARMS
TRUNK
LEGS
HAND
950
List Arm Stim Points
List Trunk Stim Points
List Leg Stim Points
List Hand Stim Points
GoTo Fig. 10

Fig. 9

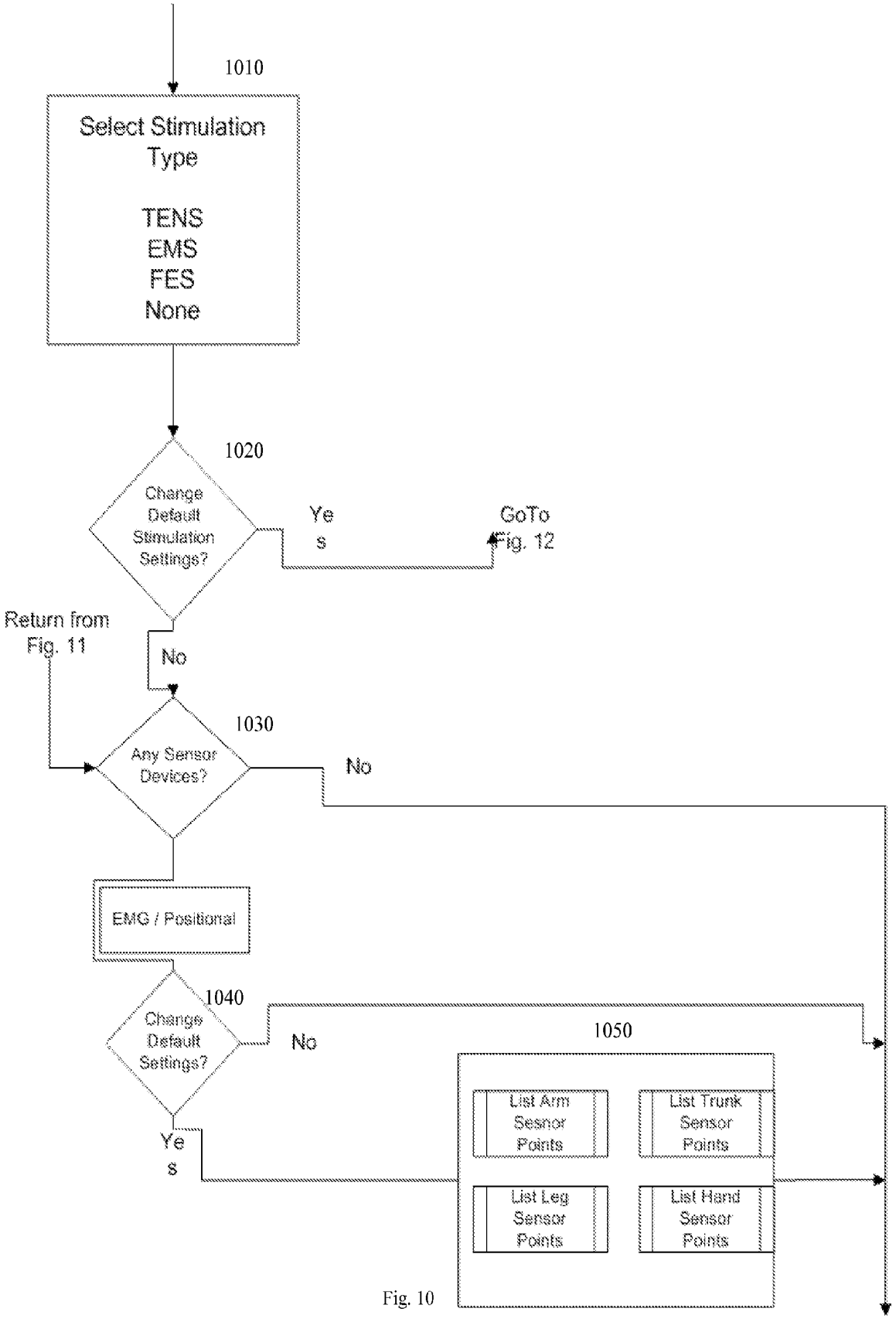

1010
Select Stimulation Type
TENS
EMS
FES
None
1020
Change Default Stimulation Settings?
Ye s
GoTo Fig. 12
Return from Fig. 11
No
1030
Any Sensor Devices?
No
EMG / Positional
1040
Change Default Settings?
No
1050
Ye s
List Arm Sesnor Points
List Trunk Sensor Points
List Leg Sensor Points
List Hand Sensor Points

Fig. 10

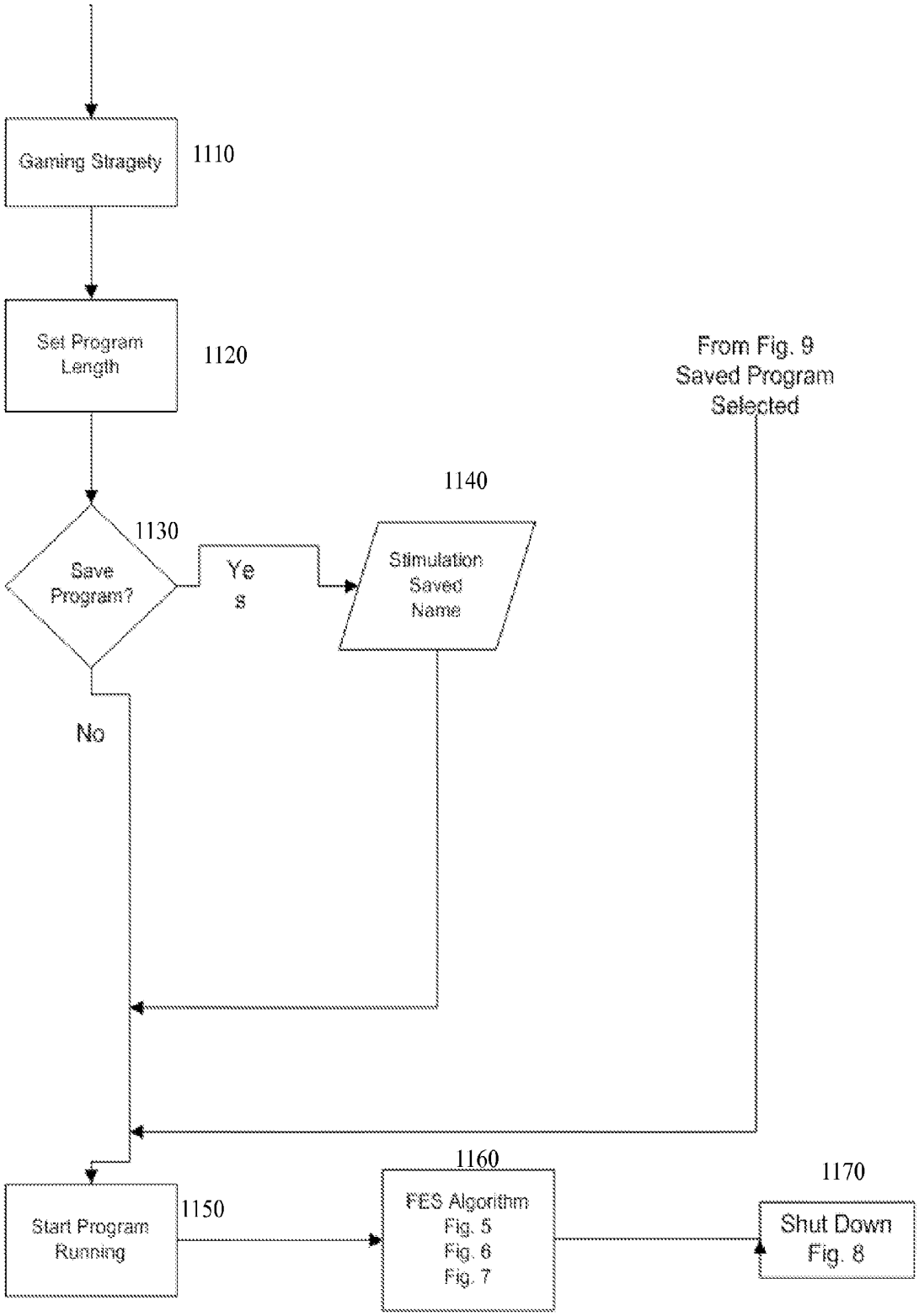

Gaming Stragety
1110
Set Program Length
1120
From Fig. 9 Saved Program Selected
1140
1130
Save Program?
Ye s
Stimulation Saved Name
No
1160
1170
Start Program Running
1150
FES Algorithm Fig. 5 Fig. 6 Fig. 7
Shut Down Fig. 8

Fig.11

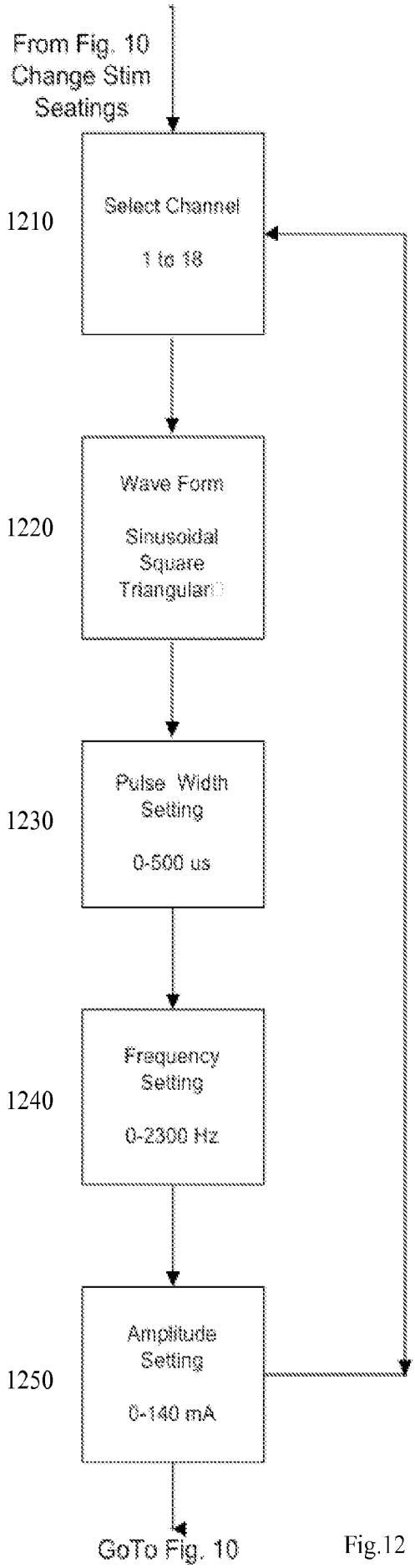

From Fig. 10
Change Stim
Seatings
1210
Select Channel
1 to 18
1220
Wave Form
Sinusoidal
Square
Triangular
1230
Pulse Width
Setting
0-500 us
1240
Frequency
Setting
0-2300 Hz
1250
Amplitude
Setting
0-140 mA
GoTo Fig. 10

Fig.12

UNIVERSAL CLOSED-LOOP ELECTRICAL STIMULATION SYSTEM

RELATED APPLICATIONS

[0001] The present invention claims the priority of provisional patent application Ser. No. 61/360,690 filed on Jul. 1, 2011, the disclosure of which is incorporated herein by reference.

BACKGROUND OF THE INVENTION

[0002] The present invention is to a universal closed-loop, electrical stimulation system which may be integrated with a multi-channel electromyography (EMG) and/or body position sensors (such as, angle accelerometers and gyroscopes) to allow for 1) real-time measurement of body position and movement, 2) autonomous system configuration utilizing closed-loop control and multi-channel capacity, 3) direct operation of neural and muscular structures in the human body and, 4) user-friendly programming capabilities. The electrical stimulation system may produce a variety of electrical outputs such as functional electrical stimulation (FES), transcutaneous electrical nerve stimulation (TENS) and neuromuscular electrical stimulation (NMES). For convenience, the term FES will be used herein to refer to these different electrical stimulation types. The closed-loop FES system of the present invention can also be integrated with wearable garments in its use or combined with electromagnetic devices to deliver further benefits to users.

[0003] FES is a method, undergoing continuing development, to restore function to patients with damaged or destroyed neural pathways with microprocessor controlled electrical neuromuscular stimulation and can be used with or without an orthotic device. FES systems use electronics to generate electrical impulses. These impulses are transcutaneous, typically transferred through surface electrodes to stimulate contraction/activity of the muscles that are otherwise dysfunctional or not operating optimally. In order for useful and controlled movements of limbs to be achieved several muscles must usually be operated in concert and sensory feedback closed-loop control is required to alter stimulation patterns in real-time. The impulse delivery is normally coordinated by an algorithm executed under the control of the FES system, the end result being the delivery of a patterned and timed stimulation sequence.

[0004] FES systems can be used as an assistive device for neural prostheses to restore functions lost because of neural damage. FES facilitates neuromodulation to help restore motor functions and sensory functions. For example, FES can be used to enhance the function of upper and lower limbs in individuals with paralysis related to spinal cord injury (SCI) or stroke. It has been used to allow standing, walking, cycling, grasping, bowel-and-bladder control, male sexual assistance, and respiratory control in individuals with paralysis related to central nervous system disease (i.e. spinal cord disease (SCD), multiple sclerosis (MS), traumatic brain injury (TBI), spinal cord injury (SCI)). Traditionally, in any nervous system (brain or spinal cord) disease that allows for the (partial) preservation of the nerve pathway to the muscle, FES can be considered to improve either organ anatomy (i.e. muscle mass) or function (i.e. bladder evacuation).

[0005] Damage to the mammalian central nervous system ("CNS") can produce devastating physical impairment (paralysis) and associated medical complications and co-morbidities that are life-threatening. Paralysis directly affects most of the organ systems in the body:

[0006] a) respiratory system is affected by decrease lung volumes and decreased ability or inability to take a volitional breath.

[0007] b) cardiovascular system is affected by the inability to regulate the blood pressure and heart rate.

[0008] c) autonomic nervous system is affected and leads to difficulty in regulating body temperature.

[0009] d) gastrointestinal and genitourinary systems are affected by the inability to voluntarily control bowel movements and urination. In addition, sexual function is also significantly impaired, to the point of total loss of function.

[0010] e) musculo-skeletal system is impaired to volitionally control movement or control abnormal movements. For example, trunk weakness after spinal cord injury leads to trunk instability which further leads to poor posture, difficulty doing activities of daily living (ADL) and a primary contributing factor to the development of upper limb pain and injury.

[0011] The use of FES to restore motor function in individuals with neurological impairments is a technique used widely in both clinical practice and paralysis related research institutions. To date however there are very few commercial FES systems that are fully integrated remote systems that adjust stimulation based on sensory feedback in an effort to optimize performance.

[0012] As stated, FES has been used to restore certain functions following neural injury or disease. Examples include enhancing the function of the upper limbs in individuals with paralysis related to spinal cord injury (SCI) or stroke, restoring standing, walking and cycling in individuals with paralysis related to central nervous system disease (i.e. spinal cord disease (SCD), multiple sclerosis (MS), traumatic brain injury (TBI), cochlear implants for restoration of hearing, stimulation of muscles and peripheral nerves to restore motor function including hand grasp and release, breathing, and bladder emptying; and deep brain stimulation to treat the motor symptoms of Parkinson's disease (Grill, Warren M., Kirsch, Robert F., *"Neural Prostheses", Wiley Encyclopedia of Electrical and Electronics Engineering,* 27 Dec. 1999). Each of these applications work by stimulating neural activity in intact neuromuscular systems to restore control to systems where control has been compromised by injury or disease. FES therapy and neural prostheses devices have also been used with or without locomotor training, such as on a treadmill, or cycle training for individuals with motor paralysis to restore or improve walking A neural prosthesis device consists of a microprocessor-based electronic stimulator with one or more channels for delivery of individual pulses transcutaneously. The device may also be integrated with a mechanical brace.

[0013] An algorithm, that may be stored and controlled by the FES microprocessor, activates channels to stimulate peripheral nerves and trigger muscle contractions to produce functionally useful movements that allow patients to sit, stand, walk, and grasp. Closed-loop FES devices are systems, which provide feedback information on muscle activity and/or joint position, thus allowing constant modification of stimulation parameters, which are required for complex activities such as walking. These are contrasted with open-loop systems where an electronic stimulator only controls the output without considering feedback information.

[0014] FES devices have also been developed for patients with foot drop. Foot drop is weakness of the foot and ankle

that causes reduced dorsiflexion and difficulty with ambulation. It is often a result of damage to the central nervous system such as stroke, incomplete spinal cord injury, traumatic brain injury, cerebral palsy and multiple sclerosis. Stimulation of the peroneal nerve has been used as an aid in raising the toes during the swing phase of ambulation. Examples of such devices used for treatment of foot drop are the Innovative Neurotronics (formerly NeuroMotion, Inc.) WalkAide®, Bioness radio-frequency controlled NESS L300™, and the Odstock Foot Drop Stimulator.

[0015] FES can assist standing and primitive walking in SCI individuals has been achieved utilizing the Parastep® Ambulation System. Using this system, only spinal cord injury patients with lesions from T4 to T12 were considered candidates for ambulation as the energy requirements for the individuals with higher injuries were considered prohibitive and individuals with lower neurologic injuries would not respond to the electrical stimulation parameters utilized by the Parastep. Using percutaneous stimulation, the device delivers trains of electrical pulses to trigger action potentials at selected nerves at the quadriceps (for knee extension), the common peroneal nerve (for hip flexion), and the paraspinals and gluteals (for trunk stability). Patients use a walker or elbow-support crutches for further support. The electrical impulses are controlled by a computer microchip attached to the patient's belt that synchronizes and distributes the signals. In addition, there is a finger-controlled switch that permits patient activation of the stepping. Other devices added a reciprocating gait orthosis (RGO) to an FES system but the orthosis used was a cumbersome hip-knee-ankle-foot device linked together with a cable at the hip joint and the use of this device was limited by the difficulties in putting the device on and taking it off (Hirokawa, Gimm, Le, Solomonow, Baratta, Shoji, D'Ambrosia, "*Energy Consumption in Paraplegic Ambulation Using the Recipriocating Gait Orthosis and electrical stimulation of thigh muscles", Arch Phys Med Rehabilitation* 1990 August; 71(9):687-94). Neuromuscular stimulation is also proposed for motor restoration in hemiplegia and treatment of secondary dysfunction (e.g., muscle atrophy and alterations in cardiovascular function and bone density) associated with damage to central motor nerve pathways.

[0016] Despite the described devices, a great need therefore remains for universal, closed-loop, portable, easy to use interchangeable and multi-functional systems that partially or completely restore lost or impaired motor and sensory function in individuals suffering from disruptions of motor and sensory function due to damage of the CNS. The commercial market translation of surface FES systems has been limited in capability and scope. Surface FES systems for general clinical use are limited to 2-4 channel open-loop systems or simple biofeedback closed-loop systems (e.g. NeuroMove™ NM900 and Thought Technology MyoTrac Infiniti). FES cycling uses knowledge from the machine itself (e.g. crank angle and/or cadence) to adjust the timing of muscle activation. A few commercial products have coupled movement sensors such as accelerometers and gyroscopes in a closed-loop fashion with surface FES, but they have limitations, such as for example, Innovative Neurotronics WalkAide which has 1 FES channel and 1 accelerometer. Bioness NESS L300 has 1 FES channel and 1 foot switch. There are a few commercial products that provide multi-channel movement sensors but not in combination with FES (Delsys Trigno Wireless). There are few patents and no closed-loop products that currently target trunk function in SCI. What is needed to improve clinical care and evidence-based user outcomes is a smart multi-channel, 3D position sensor and/or EMG regulated, closed-loop FES system that can automate stimulation (i.e. smart system) to maximize physical reconditioning and spontaneous neurological recovery with the capacity to be used in a clinical center, gym or home-based environment while being monitored at a distance.

[0017] Discovery of new control approaches, which can exploit voluntary movements to drive the body in an intended way, has been of great interest to scientists and clinicians. Electromyographic signals have been investigated to a large extent as a means to predict the level of muscle activation for performing activity or adjusting stimulation upon sensing fatigue. Moreover 3-D movement sensors to automate stimulation signals have been used in several studies (Williamson R and Andrews B J, "*Sensor systems for lower limb functional electrical stimulation (FES) control", Med Eng Phys* 22: 313-325, 2000; Simcox S, Parker S, Davis G M, Smith R W and Middleton J W, "*Performance of orientation sensors for use with a functional electrical stimulation mobility system", J Biomech* 38: 1185-1190, 2005.). Patented invention approaches include (U.S. Pat. No. 7,346,396 Barriskill et al., U.S. Pat. No. 7,162,305 Tong et al.). Despite the substantial evidence that automating stimulation is more effective than using manual methods in a variety of rehab applications, real-time closed-loop FES control of patient parameters is not widely available to clinicians.

[0018] Therefore, a need exists for a universal closed-loop FES system that would measure, monitor, stimulate and provide sensory feedback closed-loop real-time control for the human nervous system. This can be used in sports and fitness for motion capture and analysis; toning, tightening and strengthening muscles; and cardiovascular exercise. It can also be used for people with paralysis strengthening muscles, nerves and restoring motor and sensory function. Scientifically this system can be used to validate outcome measures in SCI related to research. Currently, trunk function assessment in SCI individuals is significantly limited by the inability to perform a detailed clinical examination. There is no current tool to objectively assess the trunk muscle activity. Without a valid and practical means to measure the neurologic function between T2-T12, assessing the safety and efficacy of potential therapeutic interventions in humans will seriously be hampered. Creating a critical outcome assessment tool for thoracic spinal cord function will have the largest impact on future human clinical trials, rehabilitation strategies, and understanding the physiologic basis (neuroplasticity) for activity-based restorative therapies (ABRT).

SUMMARY OF THE INVENTION

[0019] The present invention embodies a novel universal, multi-channel, closed-loop functional electrical stimulation system (closed-loop FES system) that may be integrated with a multi-channel electromyograph (EMG) and body position sensors (such as, angle accelerometers and gyroscopes) and are controlled by a wearable computer system with the bandwidth to process a large amount of data in real-time integrating information through multi-array electrodes systems. The multiple-array electrodes include stimulation and sensory electrodes. The system allows real-time measures, autonomous configuration, closed loop control and multi-channel input/output capacity and end-user programming capabilities. The system provides multiple output stimulation types

such as FES, TENS, NMES and other through the customized software architecture. The system can be further integrated with other devices such as wearable garments or electromagnetic devices to deliver other benefits to users.

[0020] In one embodiment of the present invention an automated adaptive functional electrical closed-loop stimulation system is described, including, at least one electrode assembly adapted to deliver an electrical stimulation signal to the central nervous system, peripheral nervous system, or muscles of a user. The system also includes a sensor system adapted to detect a mechanical response to a muscle stimulation signal of at least one muscle associated with a muscle group stimulated through the nervous system or proximate to the electrode assembly. The system further includes an electrical stimulation device operably coupled to at least one electrode assembly and the sensor system, the electrical stimulation device including a control system operable to automatically receive feedback from at least one characteristic of the muscle from the detected muscle response and adjust at least one parameter of the muscle stimulation signal in real-time and in response thereto to deliver an adjusted muscle stimulation signal. The system also includes a programmed microprocessor for controlling said electrical stimulation and receiving input from said sensor system, including means for comparing said electrical stimulation and said mechanical response based upon the input from the sensor system and the means for comparing, where the electrical stimulation and the detected muscle response comprises a plurality of reaction pulses.

[0021] The present invention stimulates muscle groups selectively, not only to restore motor function to persons with disabilities and/or paralysis, but also address FES exercise for people who are overweight (and those that want to "improve their game") and those looking for ways to optimize the aging process and reverse or prevent loss of cells, neural connections and functional efficiency. The present invention will improve physical conditioning and fitness that will reduce hyperlipidemia, reduce cardiovascular risk factors, reduce stroke risk factors, reduce sensitivity for depression, optimize cognitive performance and improve physical conditioning. The present invention will also improve the longevity of performance in general sports, and/or advanced sports performance by optimizing, extending and tracking training. With the FES closed-loop system, elite athletes can identify areas of need, develop applications for novel training techniques and push themselves to optimize neuromuscular function. Athletes will be able to overcome their body's natural brakes.

[0022] Current FES systems have limited and isolated clinical applications and are largely restricted to center based-treatment and therefore accessible to only a small percentage of patients and restricted temporally in time to the acute and sub acute clinical care setting. Because of the universality and portability of the present invention, it may be used in many fields such as in a rehabilitation setting, outpatient setting, home or in athletic facilities. The present invention can be used for acute and chronic medical issues as well as everyday use for sports performance and fitness. Additionally, the system's customization features allows researchers to develop different tools used as inputs and outputs for different projects.

BRIEF DESCRIPTION OF THE DRAWINGS

[0023] The present invention will now be described by the way of a non-limiting example, with reference to the attached drawings in which:

[0024] FIG. **1** is block diagram showing the FES system of the present invention;

[0025] FIG. **2** is a block diagram of the present invention showing the remote module;

[0026] FIGS. **3-8** are flow diagrams showing an example of an algorithm employed with the present invention.

[0027] FIGS. **9-12** are flow diagrams showing an example process utilizing the algorithm in FIGS. **3-8** employed with the present invention.

DETAILED DESCRIPTION OF THE INVENTION

[0028] The present invention embodies a novel universal closed-loop, multi-channel electrical stimulation system, that can be integrated with multi-channel electromyography (EMG) and body position sensors (such as, angle accelerometers and gyroscopes) and are controlled by a wearable computer system with the bandwidth to process a large amount of data in real-time integrating information through multi-array electrodes systems. The multiple-array electrodes include stimulation and sensory electrodes. The system allows real-time measures, autonomous configuration, closed loop control and multi-channel input/output capacity and end-user programming capabilities. The FES system of the present invention may allow for control of the trunk, upper and lower extremity, pelvic and low back muscles and other parts, or combination of parts, allowing performance of cardiovascular exercise, measurement of predictive movement, muscle enhancement, intermittent stimulation for healing of skin ulcers and deep tissue stimulation.

[0029] The FES system of the present invention will serve as either a passive measurement device, a data-monitoring device or, as a measurement and monitoring device combined with dynamic stimulator all-in-one application integrated with intelligent garments. The system may also be a Continua Health Alliance compliant remote monitoring device. The FES system of the present invention will deliver electrical stimulation to the central nervous system, the peripheral nervous system and directly to the muscles of the user in order to achieve a multitude of end results, including, but not limited to 1) motion capture and movement analysis, 2) cardiovascular exercise, 3) measurement of predictive movement, 3) toning, tightening and strengthening muscles, 4) cardiovascular exercise, 5) providing specific organ functions, including upper and lower limbs and extremity movement and trunk movement and stability, 6) muscle hypertrophy, 7) restoration of lost motor movement and enhancement of current motor function and abilities, 8) control of muscle spasticity, 9) deep tissue stimulation, and 10) healing of skin ulcers. The FES system of the present invention can be further integrated with other devices such as, for example, wearable garments or electromagnetic devices to deliver further benefits to users.

[0030] The present invention can be used to quantify motor and sensory function in neurologic diseases. For example, it can measure motor function of the thoracic spinal cord using a smart sensor device, such as electromyography and motion sensors, and provide a lightweight closed-loop FES system for stimulating the core muscles' functional performance. The present invention enables real-time closed loop control on a modular hardware platform designed to accommodate a

large array of feedback sensors and stimulation channels, enabling capabilities previously inaccessible to clinical practice. Further, the present invention will provide a new quantifiable assessment tool for thoracic motor function using a trunk garment with imbedded electrophysiological sensors, which will record axial muscle recruitment and trunk extension, flexion, lateral flexion, and rotation in individuals with paralysis during unsupported sitting via surface EMGs and measure trunk excursion during specific activity-based tasks (i.e. seated forward reach and lateral lean) using body position sensors.

[0031] The present invention consists of a state-of-the-art embedded system with modular architecture and peripheral sensory devices. For example, the present invention utilizes sensory data on reach and propulsion activities in conjunction with control algorithms from the data collected to provide operation within the requirements for real-world activities. Surface EMG and movement sensor data can be synthesized to determine trunk muscle activity (amplitudes and timing) and sensor thresholds for classifying wheelchair propulsion activity (e.g. ramp ascent versus level propulsion) and cycle phasing. The system receives and drives input/output signals in accordance with design specifications.

[0032] The present invention incorporates 3-axis accelerometers on the body to characterize upper extremity activity and to understand the impact of wheelchair use on the development of repetitive strain injuries. We have found that local peaks in axis and resultant hand acceleration closely match the start instances of recovery (hands off rim) and propulsion (hands on rim) phases detected by the SMART Wheel, which is considered a standard instrument and is used as the reference method. The system of the present invention enables the ability to objectively quantify motor function of the trunk. The present invention employs a system (e.g. surface EMG and 3D sensor data) to match the input with the functional requirements.

[0033] The present invention is directed to an automated adaptive FES system comprising at least one electrode assembly adapted to deliver an electrical stimulation signal to the central nervous system, peripheral nervous system, or muscles of a user, a sensor system adapted to detect a mechanical response to a muscle stimulation signal of at least one muscle associated with a muscle group stimulated through the nervous system or proximate to the electrode assembly, and an electrical stimulation device operably coupled to at least one electrode assembly and the sensor system, the electrical stimulation device including a control system operable to automatically receive feedback from at least one characteristic of the muscle from the detected muscle response and adjust at least one parameter of the muscle stimulation signal in real-time and in response thereto to deliver an adjusted muscle stimulation signal; and a programmed microprocessor for controlling said electrical stimulation and receiving input from said sensor system, including means for comparing said electrical stimulation and said mechanical response based upon the input from the sensor system or a data base of preferred responses and the means for comparing, wherein the electrical stimulation and the detected muscle response comprises a plurality of reaction pulses.

[0034] The present invention, as seen in FIG. **1**, is a modular system **100** that provides closed-loop surface FES functionality. In use, a particular application will be chosen and instructions will be input into an application selection **10**. This can be a touch screen display or other appropriate device. The input from application selection **10** will go to a digital computer system having a computer readable memory and processor which is controlled by a control algorithm **12**. The algorithm will in turn determine the appropriate signal pattern for the functional electrical stimulator (or FES) **14** to apply to the appropriate location in the nervous system and hence to the appropriate muscle(s) **16**. The signal can be transmitted via an electrode placed at the appropriate location(s) for treatment or stimulation. When the muscle responds, an electrical signal is generated by the muscle and the electrode(s), which could be the same or different than those used for the FES, will pass the electrical signal to an electromyograhic sensor **18** which will detect the signal and feed it back to the processor **12**. At the same time, a motion sensor **20**, such as a 3-axis sensor, will provide another feedback signal for the processor **12**. By comparing the required or desired stimulation pattern, as inputted from the application section **10**, the electrical signal to be outputted via the FES **14** can be adjusted. The system can also employ an electrical filter means for eliminating unwanted signals and noise from the input signals. Additionally, a means for amplifying the input signals and controlling the amplification range of the input signals may be employed.

[0035] The present invention will provide versatility via the programming so that it can, for example, be used to stimulate the trunk muscles of a user and then used to stimulate the leg muscles of another user, although not at the same time. Or, it could be used by the same user, but for different muscle groups. Thus, the present invention is versatile and adapting it for different uses is simple. The stimulation of the trunk muscles would be done, for example, to facilitate a person sitting up, improving posture, improving respiration, or moving from one position to another, where there is no longer such functionality in that person, but where the nervous system can be accessed and stimulated. That need would be different from the need to move a leg, but the programming of the processor via the appropriated algorithm would mean that the device and system would not need to be reconfigured to function and the adjustment could be done via the software for the device.

[0036] Further, the capability of the system means that multiple electrodes, or a garment which contains and/or supports electrodes, could be used since the processor can be programmed to go through a selection process to determine the appropriate electrodes for the appropriate procedure. Such procedures are known, such as for example, the one set forth in an article by S.B. O'Dwyer et al., "An electrode configuration technique uses an electrode matrix arrangement for FES-based upper arm rehabilitation systems", *Medical Engineering & Physics* 28 (2006), pages 166-176, which is incorporated herein by reference. Additionally, microelectrode array does not need to be limited to garments but may include technologically advanced skin interface microelectrode systems.

[0037] As seen in FIG. **2**, the system **200** can be a computer, for example a remote module (RM). The RM will support the surface FES peripheral, which provides transcutaneous neuromuscular stimulation. The RM may be based on a processor such as an Intel® Atom Processor, although other appropriate processors could be employed provided they have the high speeds required, and the same versatility, flexibility, and transportability, and which incorporates high speed I/O ports. In one example, the RM may incorporate up to 32 I/O ports

centered on an Altera Stratix-II™ GX field programmable gate array for control. The RM could also employ 6 USB ports and have wireless capability. Further, the RM could be a "flexible computer", which would be one that provides the same processing, but is incorporated in a fabric or is part of a fabric or technically advanced skin interface microelectrode system so that the person being treated could wear the processor without the need for bulk or weight.

[0038] There is no limit to the number of ports, and the ports can be employed to support a star topology, tree topology, or any similar topology, which extends the reach of the sensors/stimulators, thus enabling the attachment for hundreds of sensors for feedback and control. As noted, the system can function as a remote module, e.g., it could be wireless and not be connected via a wire, or it could function as a wired system, depending on the needs involved. The RM will support two types of "peripheral components", for example, a surface Functional Electrical Stimulation—Electromyography (FES-EMG) peripheral which provides transcutaneous neuromuscular stimulation as well as surface electromyography and a peripheral with a combined 3-Axis accelerometer and 3-Axis gyroscope (3-D sensor) which provides time-space limb kinematics feedback in real-time. A modular use of the peripherals allows clinicians or coaches to "mix and match" and "plug and play" any number in any combination to satisfy their needs.

[0039] The present invention will be explained in terms of a 5 port system, but this is only exemplary, and more ports could be employed or fewer ports could be combined with a star topology approach. The present invention is not limited to 5 ports and could comprise more or less ports or could encompass a star, tree, or other topology. Further, the modular approach allows for the combination of several units to obtain the necessary multiplicity. In a preferred embodiment, the present invention may employ more than 10 electrodes. The electrodes may be embedded in the wearable garment associated with the present invention. It is possible to employ more than 100 electrodes. By employing a large number of electrodes, the system is able to stimulate multiple muscles. Preferably, 8 to 10 muscles may be stimulated. Still further, electrodes can be placed in numerous spots, or be available via the use of clothing, covers, wraps and/or advanced skin interfaces to address nerves and muscles and then the system can evaluate which electrodes need to be active for the desired treatment and which electrodes are near vital organs and need to be deactivated.

[0040] FIG. **2** shows an embodiment of the current invention. The system **200** of the present invention is comprised of a CPU **210** and a baseboard **220** that hosts a touch sensitive display **230** for user interaction; input and output ports, such as USB **260**, Ethernet **270**, System Management Bus (SMBUS) **280**, and a power supply **240**. The display **230** may be an 800×480 4.8" TTL TFT display with four-wire touch sensitive overlay. In one embodiment, the CPU **210** operates at a speed of at least 1.0 gigahertz and adjusts FES parameters within 10 milliseconds.

[0041] As can be appreciated, these components exemplify the present invention and so should not be considered limiting. These devices are bundled together into a single mini-chassis that satisfies passive cooling needs. Five high speed serial ports **260** such as 5 USB 2.0 Micro-AB ports support sensor/FES daisy-chain capability. The Ethernet port **270**, such as a GigB Ethernet RJ-45, will provide for secure remote communications. The SMBUS/USB **280** Type A will provide lightweight communication, typically to the power supply **240**. The power supply **240** may be a 1.4-12VDC power supply connected to a Li-Ion battery pack 2S1P, 7.4V 1200 mAH.

[0042] The FES functionalities of the RM **200** have been chosen to facilitate US Food and Drug Administration clearance, and thus has similarities like other FDA cleared surface powered stimulators (e.g., Simcox et al. 2004). The FES functionalities include amplitude of 0-140 mA, a pulse width: 0-500 us, a frequency of 0-500 Hz, a pulse waveform that is biphasic, charged balanced. The EMG functionalities could include, for example and depending upon the treatment, a bandwidth of 0.05 Hz to 150 Hz, 60 Hz/50 Hz suppression, and electrocardiogram (ECG) artifact detection/blanking, as may be required to detect and mark the signals.

[0043] The EMG sensors incorporate electrode conductivity reading. The EMG circuitry shares the same electrode pads as the FES circuitry to minimize electrode placement and maximize EMG muscle feedback quality. The 3-D sensor incorporates both 3-Axix gyro and 3-Axis accelerometer capability into a combined sensor, which is necessary for proper sensing and feedback to the control unit. The 3-D sensor functionalities include sagittal, coronal, and transverse angle, angular velocities in 3-D and accelerations in 3-D. The rotational and accelerometer readings are measurable in one degree increments on all three axes and read via the USB 2.0 port. The 3-D Sensor peripheral USB 2.0 port is based upon industry standards.

[0044] One of the full-speed/low-speed USB ports **260** is dedicated to internal needs, the Touch Sensitive Interface device, display **230**. The Touch Sensitive Interface device, display **230**, requires a USB 1.0 low-speed port for operation. To satisfy this internal need, one of the six ports capable of full-speed and low-speed signaling is internally committed, leaving only five ports for external utilization.

[0045] The system **200** may comprise three Universal Host Controller Interfaces (UHCI) and one Enhanced Host Controller Interface (EHCI). Each UHCI supports two (2) USB 1.1 ports. The EHCI supports two (2) high-speed USB ports (for internal utilization only) and can multiplex over the six UHCI ports. Preferably, the EHCI may support up to fifteen (15) FES/EMG peripherals and sixteen (16) 3-Axis peripheral sensors on a single USB internal Hub port, however the EHCI may support more or less. Additional peripheral components can be accommodated by clustering multiple Remote Modules via GigE Ethernet ports. Up to a dozen RMs can be clustered together.

[0046] The RM **200** operates on a Real Time Operating System (RTOS), and a LCD touch screen with a basic user interface for selecting and tweaking stimulation strategies and sensor channels and parameters. The closed-loop control algorithms are implemented in the RTOS. The software test routine operating on the remote module will adjust and drive every possible parameter and the specification outcome will be validated. The software test routine on the RM will combine every parameter in every combination and validate that the remote module operates as specified. Validation of a control loop latency of 10 ms or better will be employed using the existing internal processor performance clocking mechanisms and the default utilities provided by Wind River.

[0047] The RM **200** utilizes standard protocols for physical signal input and output. Two key aspects of the RM **200** cover all input and output capability. The first key aspect consists of five USB 2.0 ports to drive peripheral components. The sec-

ond key aspect is the Graphical User Interface (GUI) including all programmable device parameters that drive all signal input and outputs.

[0048] The USB 2.0 peripheral component ports are capable of driving any combination of peripheral components. The EMG circuit will use an industry standard EMG wave-form generator (such as is available from Fluke). Input EMG test wave-forms will be read and validated via the USB 2.0 port. These parameters will be driven via the USB 2.0 port. A variable resistor in the test system will be adjusted from zero ohms to 10 mega-ohms in 500 ohm increments for each parameter and, when needed, the output signal can be validated via an oscilloscope reading.

[0049] Because the combination of FES and EMG functions share electrodes, key signal protection circuitry is designed into the EMG input signal path to ensure that high-voltage FES signals do not interfere with EMG sampling Inherent and dynamic changes in electrode to surface skin conductivity are a well-known issue in surface FES. To combat this problem, the FES circuit in the present invention is designed as a current controlled drive. In addition to this, junction conductivity reading circuitry has been designed into the EMG circuit that allows dynamic conductivity readings to be taken in real-time.

[0050] FIGS. **3-8** show examples of an algorithm for use in the present invention. The present invention utilizes an algorithm which reflects outcome measure for functional capacity within various neurologic levels, such as for example, thoracic SCI, and assesses postural control in the seated position in response to perturbations using motion analysis and gyroscope technology. The algorithm facilities providing a trunk core strengthening FES based upon both sensor technologies and closed loop FES controlled stimulation.

[0051] Electrical stimulation signals are applied to the selected muscles at a predetermined frequency, pulse width, and amplitude, and work output by the muscles in response to stimulation signals determined over a fixed period of time. The work output is compared to a defined value which can be a target value or a value measured during a previous stimulation period. The amount of electrical energy coupled into the muscles by the stimulation signals is varied in response to the results of the comparison in order to maximize the amount of work output by the muscles during a treatment period. This is accomplished by adjusting the frequency and/or pulse width during stimulation treatment in response to the work output measured. For example, if it was desired to move a leg, the programmed microprocessor could produce hip movement by generating control signals for stimulation transducers which stimulate the iliacus, hamstring, and gluteal muscles. The microprocessor produces knee movement through generation of control signals for stimulation transducers which stimulate the quadriceps and hamstring muscles. Finally, the microprocessor produces ankle movement through generation of control signals for stimulation circuits which stimulate the gastrocnemius and tibialis muscle groups. As the hip, knee and ankle motion progresses, corresponding feedback signals are generated by sensors mounted on the body, and these feedback signals are applied to the microprocessor for closed-loop control of the stimulation control signals. Movement restriction means are provided for limiting movement of the hips and knees to a common plane, thereby limiting the number of muscle groups requiring stimulation. In addition, motion sensors would provide an additional feedback signal and allow for further adjustment.

[0052] Since an electrical stimulation signal will be affected differently in different people, the feedback is helpful in evaluating whether or not the proper signal was delivered to the proper area. Some of the variance, given as examples and not considered limiting, can be due to a person's tissue properties, physical activity levels, amounts of body fat, tissue layer thickness, depth of nerve in the muscle, and how the electrode is making contact with the skin.

[0053] The present invention provides the capability to apply any type of electro-medical treatment. For example, one exemplary embodiment of the multi-functional electro-medical device in accordance with the present invention is programmed to apply interferential current stimulation, high voltage muscle stimulation as well as pulsed muscle stimulation treatments. With the ability to provide interferential current stimulation, the multi-functional portable electro-medical device of the present invention provides the ability to be used universally for a variety of treatments. Although the term FES is used herein, the multi-functional portable electro-medical device in accordance with the present invention may be programmed to apply many other types of electro-medical treatment such as NEMS, TENS, micro current, high voltage, constant voltage or pulse width, and the like.

[0054] To create real-world "natural" movement via FES, two key capabilities are needed. Most "natural" movement involves a multitude of muscles (more than 4-6) working together in various degrees of contribution and coordinated timing. The present invention is able to drive large numbers of muscles, in varying degrees, and in a coordinated manner. This can be contrasted with crude FES technology which can force muscle movement, but that movement is strongly distorted (i.e. either dysfunctional or "robot like"). Any re-connection through the damaged spinal cord due to neural restoration achieved through therapeutic measures like ABRT will ultimately be limited, therefore only allowing for "robot like" functionality. Sensing of muscle movement, as well as other key factors like fatigue, combined with capabilities for constant FES adjustment based upon that sensing enable real-world "natural" movement. This is facilitated via real-time feedback and closed-loop control. The present invention is a device that is wearable, can drive a large number of muscles, provide sensing for those muscles, and manage real-time closed-loop control via computer processing capability. Further, by emulating real-world "natural" movement, it might be possible to accelerate the re-mylenation and re-growth process.

[0055] A more detailed version of the process and algorithm shown in FIGS. **3-12** will now be described. FIGS. **9-12** show a general selection process that utilizes the algorithm shown in FIGS. **3-8**. In FIG. **9**, the end-user may begin the application and at step **910**, the hardware initiation sequence, shown in FIGS. **3** and **4**, are executed. Procedure **300**, shown in FIG. **3**, includes the steps of initializing the system **310**, selecting a FES profile **320**, executing the FES profile **330**, determining whether to execute another FES profile **340** and a tear down sequence **350**.

[0056] FIG. **4** shows the FES initialization sub-procedure **400**. Sub-procedure **400** includes the steps of initializing output systems **410** and initializing network connectivity **420**, such as wireless or hardwired network. Sub-procedure **400** also includes the steps of initializing input from EMG & 3-Axis sensors **430** and initializing STIM output devices **440**. The sub-procedure **400** may also include performing self-diagnostics at step **450** to ensure that the system and devices

are working properly. If the self-diagnostic test is successful, the sub-procedure **400** returns a result of "Success" and procedure **300** continues. However, if the self-diagnostic test is unsuccessful, the sub-procedure **400** returns a result of "Failure" and the sub-procedure may abort.

[0057] Referring back to FIG. **9**, after initialization, an end-user has the option to select a saved program at **920**. A display of the saved programs for selection may be displayed at **930**. The sequence to save a program is described in more detail in FIG. **11**. If the end-user would like to begin a new program, the end-user selects a stimulation program at **940**. For example, selected program may provide stimulation to the legs, trunk, legs or hands. At **950**, the stimulation points for the selected program are listed and selected. For example, in an arm stimulation program one or more points on one or more muscles may be defined.

[0058] After a stimulation program is selected, a stimulation type may be selected at **1010** in FIG. **10**. The stimulation program may apply stimulation types such as TENS, EMS, FES or no stimulation. The user may change the default stimulation settings at **1020**. FIG. **12** shows the different stimulation attributes that may be changed by the user. For example, at **1210**, the user may select a channel **1** to **18**. At **1220**, the wave form may be selected from sinusoidal, square or triangular. At **1230**, the pulse width setting can be adjusted between 0-500 μs. The frequency setting may be adjusted at 1240 to 0-2300 Hz and the amplitude may be adjusted at 1250 to 0-140 mA.

[0059] After the stimulation settings are adjusted or if no changes are needed, the process resumes at **1030**, where sensor devices are detected, such as EMG and/or body position sensors (angle accelerometers and gyroscopes). At **1040**, those devices default settings may be adjusted. If the settings are adjusted, the sensor points for the selected program (arms, trunk, leg, hands) are listed at **1050**.

[0060] In FIG. **11**, a gaming strategy may be selected at **1110**. At **1120**, the program length is set. A user may save the program at **1130**. The program may be saved under a particular name entered by the user at **1140**. At **1150** the selected program begins, the FES algorithms used therein at **1160** are now described in more detail.

[0061] FIG. **5** shows the program being executed according to sub-procedure **500**. Sub-procedure **500** in FIG. **5** includes the step of reading profile data to memory **510**, and iterating through each FES profile step at **520**. Sub-procedure **500** also includes the step of reading EMG and 3-Axis sensor input **530**, calculating deltas **540** as shown in FIG. **6**, and determining if the deltas are within a tolerance at step **550**. If the delta is within a tolerance, the FES profile is analyzed to see if there are more profile steps to iterate through at step **560**. If the delta is not within the tolerance, the stimulation is adjusted at **570**, as shown in FIG. **7**, and the adjusted stimulation is applied at step **580**.

[0062] FIG. **6** shows sub-procedure **600** for calculating deltas for actual versus ideal body positioning. An example of a definition for sub-procedure **600** follows:

Method Definition:

bool calculateDeltas(struct Measurement Type[ ] currentConfiguration, struct MeasurementType[ ] idealConfiguration, struct MeasurementType[ ]* deltas)

Parameters for the method definition include:

struct MeasurementType[ ] currentConfiguration—an array of measurements observed in real-time representing the current position and state of the measured body.

struct MeasurementType[ ] idealConfiguration—an array of measurements observed in real-time representing the current position and state of the measured body.

struct MeasurementType[ ]* deltas—an out-bound array of measured discrepecies between parallel arrays represented by the currentConfiguration and the idealConfiguration.

Data-Type Definitions:

```
typedef struct Spatial3AxisInstrumentType {
   /*Implementation Data*/
};
typedef struct AccelerometerInstrumentType {
   /*Implementation Data*/
};
typedef struct EMGInstrumentType {
   /*Implementation Data*/
};
typedef union MeasurementInstrumentType {
   struct Spatial3AxisInstrumentType* spatial3AxisInstrument = 0;
   struct AccelerometerInstrumentType accelerometerInstrument = 0;
   struct EMGInstrumentType EMGInstrument = 0;
};
typedef struct MeasurementInstrumentType {
   //Can be any of : MEASUREMENT_TYPE_3AXIS,
   //MEASUREMENT_TYPE_ACCELEROMETER,
```

-continued

```
  //MEASUREMENT_TYPE_EMG
  int measurementInstrument = 0;
  unionMeasurementInstrumentType* = 0;
};
typedef struct MeasurementDealtaType {
  //Can be any of : MEASUREMENT_TYPE_3AXIS,
  //MEASUREMENT_TYPE_ACCELEROMETER,
  //MEASUREMENT_TYPE_EMG
  int measurementInstrument = 0;
  bool isWithinTolerance = 0;
  float deltaValue = o.o;
};
```

Return parameters:

1 if the currentConfiguration array contains no measurements that are out of the profile's defined tolerance. (i.e. Overall body positioning is "close enough" to correct as defined by the clinician's profile).
0 if any single delta is outside of the profile's defined tolerance.

[0063] At step **610** a boolean variable, such as bool calculateDeltas, is set with a return value of 1. At step **620**, for each measurement type in an array, for example for each measurement type in struct MeasurementType[ ]currentConfiguration, struct MeasurementType[ ] idealConfiguration, or struct MeasurementType[ ]* deltas, measurement type i=0 . . . N, and the following decisions are made. At step **630**, if i is a 3-Axis type, the 3-Axis delta is calculated at step **640**. At step **650**, if i is an accelerometer type, the accelerometer delta is calculated at step **660**. At step **670**, if i is an EMG type, the EMG delta is calculated. If the return value of the delta calculation is 0, the return value boolean is set to 0 at step **690**. If there are more measurements, for example if i<=N, then at step **698**, the sub-procedure is directed back to step **620**. If there are no measurements left, the boolean variable return value is returned at **699** and the sub-procedure **600** ends.

[0064] FIG. **7** shows sub-procedure **700** for adjusting stimulation levels if the deltas are not within a tolerance at step **550** of sub-procedure **500**. Sub-procedure **700** includes a loop at step **710** for each measurement delta type, i=0 . . . N. At step **720**, the STIM is calculated for the delta. At step **730**, the STIM output is set based at least upon the calculation at step **720**. If there are more measurement deltas at step **740**, sub-procedure **700** is set back to step **710**. If there are no more measurement deltas, sub-procedure **700** ends. An example of a definition for sub-procedure **700** follows:

Method Definition:

void adjustStimulation(struct StimControlType* step, struct MeasurementDeltaType[ ] deltas, struct StimControltype[ ]* stimControls)

Parameters:

struct ProfileStepType* step—a struct representing the current step in the FES profile.
struct MeasurementDeltaType[ ]* deltas—an array of measured discrepancies between the ideal configuration and the measured (actual) configuration.
struct StimControlType[ ]* stimControls—an out-bound array of stim adjustments to be made to correct for the deltas.

Data-Type Definitions:

```
typedef struct ProfileStepType{
  /*Impplementation Detail */
};
typedef struct MeasurementDealtaType {
  //Can be any of : MEASUREMENT_TYPE_3AXIS,
  //MEASUREMENT_TYPE_ACCELEROMETER,
  //MEASUREMENT_TYPE_EMG
  int measurementInstrument = 0;
  bool isWithinTolerance = 0;
  float deltaValue = o.o;
};
typedef struct StimControlType{
  /*Implementation Detail */
};
```

[0065] FIG. **8** shows FES tear-down sub-procedure **800**. Sub-procedure **800** includes power-down of the output device at step **810**, power-down and unregistration listeners for EMG, 3-Axis sensors at step **820**, power-down release of networking resources at step **830** and shutdown of the user interface and release of logging resources at step **840**.

[0066] The present universal closed-loop FES system invention can be used to restore function in numerous body parts of persons with neurological impairments (e.g. hand function, core strength, walking, etc) and to catapult FES technology beyond clinical setting to telerehabilitation and gym applications with secure, HIPAA compliant, remote home-based fitness and therapy serving people with paralysis in the convenience of clinics, gyms and their homes. Additionally, this technology application will accelerate commercialization of a full-line of efficient, remotely measured and monitored, economical and user-friendly wearable computer and apparel products. These products will serve the growing global population of people who have 1) chronic health conditions, 2) are overweight and interested in exercise fitness, 3) need motion capture and analysis in business, training and advanced sports performance, and 4) monitoring for military personnel and first responders in dangerous environments, although other applications could be included and so the examples should not be limiting.

[0067] The following applications are examples of the use of the present invention, since use of dynamic real-time controls can provide movement, training and regeneration in specified areas, but they are not considered exhaustive:

1. The use of the system for controlling physiological aspects of anatomy under computer control, which enables drive control of muscle tissue with real-time feedback for the purpose of measuring muscle reaction and determining muscle fatigue.

2. The use of a matrix of topical computer controlled (smart) electrodes arranged over a wide area of the anatomy, including analog and digital signaling switch circuitry and movement/placement sensors. The analog and digital signaling switch circuitry enables the driving of FES and the feedback of EMG via the same electrodes. The switch circuitry dynamically enables multiple nodes in the matrix to work in combination to emulate a larger electrode and/or electrodes of varying shape and size and/or and/or advanced skin interfaces.

3. The use of an array of small sensors/electrodes over a large area of anatomy, an autonomous computer controlled algorithm that dynamically stimulates while capturing feedback data to determine an optimal size, shape, and placement of an emulated electrode for the purposes of FES/EMG closed-loop control.

4. The capture of complex muscle movements can be compared to a large template of known movement models.

5. The enablement of movement of disabled parts of an anatomy based upon known good movement models for exercise and therapy.

6. The use of the device to provide real-time integration and control of multi-modalities and machines.

7. The integrated monitoring of vital functions and outcome neurological measures with distance management, while controlling the surface sensory and stimuli system to evaluate, monitor and train a variety of neurological and autonomic functions.

8. The use of the device as a wearable computing system integrated with wearable fabric and/or advanced skin interface encompassed sensory and stimuli measures and deliverables.

9. The use of the device in static cardiovascular exercise, such as for a workout measurement tool and device, the entire body can be covered with a flexible, wearable garment and/or advanced skin interface. Then muscles and large muscle groups are repeatedly activated via FES in an opposing manner to limit physical movement and raise the subject's metabolic rate for the purpose of exercising the heart, build muscle mass, and build bone mass.

10. The use of the present invention as a universal trunk stimulator to help restore motor function to persons with disabilities, and also address FES exercise for people who are overweight and those looking for advanced sports performance.

11. The use of the device in conjunction with constructive electromagnetic interference and/or as a deep tissue stimulation and scanning device.

12. The use of the device as a non-evasive deep tissue stimulation device using a computer controlled array of electrodes surrounding an area of interest, each electrode transmitting an electromagnetic signal into tissue. The overlap of multiple signals creates nodes of both constructive and destructive interference. Computer generation of these signals enables precise placement of interference nodes in the area surrounded by the electrode array.

13. The use of multiple surface electrodes to provide an additive stimulus signal in which a node of constructive interference generates an area of high potential and a node of destructive interference generates an area of low potential. By placing a high potential on one side of a trigger area, and a low potential on the opposite side of a trigger area causes a flow of ions, thus triggering stimulation.

14. The use of a bipolar pair of nodes is placed at a location within the surrounded tissue of an electrode array that can record a reaction (via physical movement and/or EMG feedback). The bipolar pair is then moved a small distance and the process is repeated. Continued movement of the bipolar pair sweeps the entire area of tissue surrounded by the electrode array. Mapping of the corresponding data enables an autonomous means to map out the most optimal sensation points within the area of interest.

15. The use of a computer-controlled array of strategically place EMG electrodes to sample activity and match that activity to movement models enabling accurate prediction of desired movement, other key areas of the anatomy can be electrically stimulated to either cause movement (for the disabled) or enhance movement, and this can enable the movement of disabled and/or paralyzed parts of an anatomy based upon captured and predicted movement of enabled parts of the anatomy.

16. The use of a computer-controlled array of strategically placed (or autonomously configured) EMG electrodes can be used to sample activity and match that activity to movement models enabling accurate prediction of desired movement. Based upon the movement model, other key areas of the anatomy are electrically stimulated via FES to either cause movement (for the disabled) or enhance movement and this will enable the movement of disabled parts of an anatomy based upon captured and predicted movement of enabled parts of the anatomy.

17. The use of the device can be used to maximize stimulation to (or, over stimulate) key muscles and/or muscle groups in an orchestrated and optimized manner to enhance performance at a precise and advantageous moment.

18. The use of the device can be used to dynamically capture complex muscle movements that are then compared to a large template of movement models to predict an activity, then stimulating relative muscles/muscle groups to communicate the best/optimal sequence of movements for a specific activity for learning/training needs.

19. The use of the device can be used for surface stimuli and sensors capabilities to retrain and strengthen body skeletal musculature and associated CNS systems to gain functional control and, where appropriate, to use muscle against muscle to place stress on bone and enhance bone density.

20. The use of the device can be used for dynamic integrated control. These include, but are not limited for trunk, upper and lower extremities, legs, pelvis & shoulder device to facilitate disabled human to computer interface and control by using a select array of EMG electrodes and 3-D sensors measuring muscle and body movements in the upper and lower extremities, shoulder, legs and pelvis.

21. The use of the device to stimulate, repair and control autonomic nervous system function. These may include, but are not limited to, control of bowel and bladder, blood pressure and heart rate, respiration, multiple organ function and sexual function.

22. The use of the system to modulate sensory function via stimulation activity. These include, but are not limited to, light touch, vibration, proprioception and pain.

23. The use of the device to offset aging of the nervous system including limiting or reversing loss of neural cells, neural connections and global CNS function.

24. The use of the device to offset aging or pathological injury to the peripheral nervous system.

25. The use of the device to restore health to end organs such as offsetting aging or reversing injury to end organs. For example, maintaining the multiple organelles of the skin, including vasculature, sensory systems and skin integrity.

[0068] The foregoing embodiments of the present invention have been presented for the purposes of illustration and description. These descriptions and embodiments are not intended to be exhaustive or to limit the invention to the precise form disclosed, and obviously many modifications and variations are possible in light of the above disclosure. The embodiments were chosen and described in order to best explain the principle of the invention and its practical applications to thereby enable others skilled in the art to best utilize the invention in its various embodiments and with various modifications as are suited to the particular use contemplated.

What we claim is:

1. An automated adaptive closed-loop functional electrical stimulation system comprising:

at least one electrode assembly adapted to deliver an electrical stimulation signal to the central nervous system, peripheral nervous system, or muscles of a user;

a sensor system adapted to detect a mechanical response to a muscle stimulation signal of at least one muscle associated with a muscle group stimulated through the nervous system or proximate to the electrode assembly; and

an electrical stimulation device operably coupled to at least one electrode assembly and the sensor system, the electrical stimulation device including a control system operable to automatically receive feedback from at least one characteristic of the muscle from the detected muscle response and adjust at least one parameter of the muscle stimulation signal in real-time and in response thereto to deliver an adjusted muscle stimulation signal; and

a programmed microprocessor for controlling said electrical stimulation and receiving input from said sensor system, including means for comparing said electrical stimulation and said mechanical response based upon the input from the sensor system and the means for comparing,

wherein the electrical stimulation and the detected muscle response comprises a plurality of reaction pulses.

2. The system of claim **1**, wherein said system includes means for remotely receiving said input and directing said electrical stimulation.

3. The system of claim **1**, wherein the system employs more than 10 electrode assemblies.

4. The system of claim **1**, wherein said electrical stimulation device includes means for generating an electrical signal which includes a sequence of pulses having a selected basic pulse sequence frequency, wherein each pulse includes positive and negative excursions relative to a reference voltage;

means for automatically changing the pulses in the pulse sequence between being initially positive-going and initially negative-going upon the successive occurrence of a predetermined number of pulses in the pulse sequence, thereby producing at least one harmonic frequency in the sequence of pulses in addition to the basic pulse sequence frequency; and

the predetermined number of pulses is more than two.

5. The system of claim **1**, wherein the sensor system includes an electromyography transducer adapted to be coupled to a body surface adjacent to the muscle being stimulated for generating an output signal indicating the response of said muscle.

6. The system of claim **1**, wherein the system further includes an electrical filter means for eliminating unwanted signals and noise from said input signals.

7. The system of claim **1**, wherein the system further includes a means for amplifying said input signals and controlling the amplification range of said input signals.

8. The system of claim **1**, wherein the system further includes means for displaying the intensity of said input signals.

9. The system of claim **1**, wherein the sensor system includes an accelerometer and gyroscope for measuring movement of a body part associated with the muscle being stimulated.

11. The system of claim **1**, wherein said electrode assembly is part of a wearable garment and/or advanced skin interface.

12. The system of claim **1**, wherein said electrical stimulation provides a supplement to exercise.

13. The system of claim **1**, wherein said electrical stimulation provides deep tissue stimulation.

14. The system of claim **1**, wherein the system further includes an electromagnetic stimulation device.

15. The system of claim **1**, wherein said electrode assembly is attached to a trunk, upper or lower extremities, pelvis, shoulder, or any combination thereof.

16. The system of claim **1**, wherein the system includes means for confirming the position of the electrode on the

surface of a body and disengaging those electrodes which would affect vital human parts and those electrodes not needed for certain purposes.

17. The system of claim **1**, wherein the sensor system includes 3-axis sensor for measuring movement of a body part.

18. The system of claim **1**, wherein the sensor system includes means for sensing muscle fatigue.

19. An automated adaptive functional electrical stimulation system comprising:

at least one electrode assembly adapted to deliver a spinal cord stimulation signal to the spinal cord of a user;

a sensor system adapted to detect a mechanical response to 1] the muscle stimulation signal of at least one muscle associated with a muscle group which would receive input from the electrode assembly and 2] to a volitional activation of a muscle by the user;

an electrical stimulation device operably coupled to the at least one electrode assembly and one sensor system, the electrical stimulation device including a control system operable to automatically diagnose at least one characteristic of the muscle from the detected mechanical response and/or adjust at least one parameter of the muscle stimulation signal in response thereto to deliver an adjusted muscle stimulation signal; and

a programmed microprocessor for controlling said electrical stimulation and receiving input from said sensor system, means for comparing, in real time, the electrical stimulation and the mechanical response, wherein the detected muscle response comprises a plurality of reaction pulses, and wherein the control system is operable to provide real time analysis and adjust the electrical stimulation based upon the comparison of the electrical stimulation and the input from the sensor system.

* * * * *

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(54) **IMPEDANCE MONITORING DURING ELECTROSTIMULATION**

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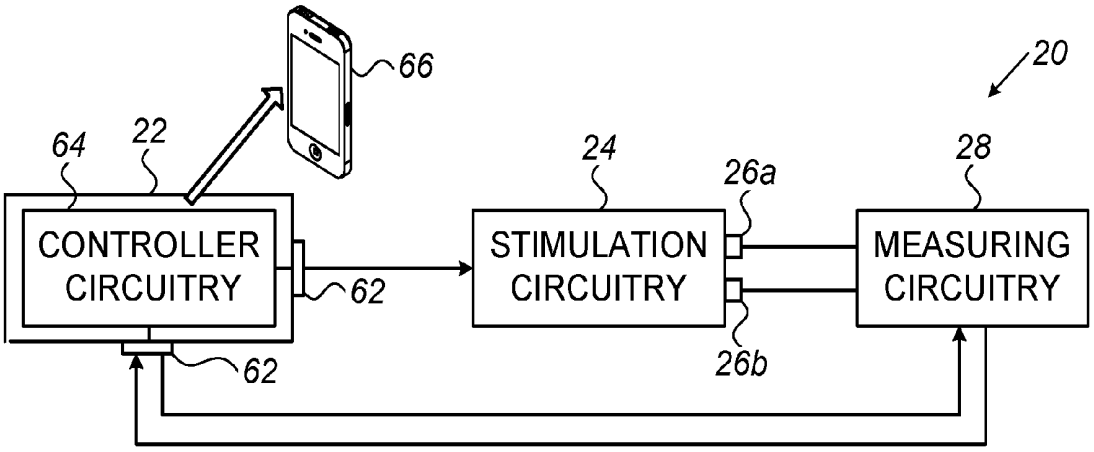
CPC ***A61N 1/08*** (2013.01); ***A61N 1/36014*** (2013.01); *A61N 2001/083* (2013.01)

(57) **ABSTRACT**

Embodiments described herein include a controller (**22**). The controller includes at least one interface (**62**) that couples the controller to stimulation circuitry (**24**), which includes a pair of electrodes (**26***a*, **26***b*), and to measuring circuitry, and further includes controller circuitry (**64**). While the electrodes are coupled to skin (**60**) of a subject, the controller circuitry, via the interface, drives the stimulation circuitry to (i) pass a plurality of stimulating pulses (**32**) between the electrodes, and (ii) pass one or more reference pulses (**34**) between the electrodes, the reference pulses being different from each of the stimulating pulses. The controller receives, from the measuring circuitry, an impedance between the electrodes that is measured using the reference pulses. In response to the impedance measured using the reference pulses, but not in response to any impedance measured using the stimulating pulses, the controller circuitry controls the stimulation procedure. Other embodiments are also described.



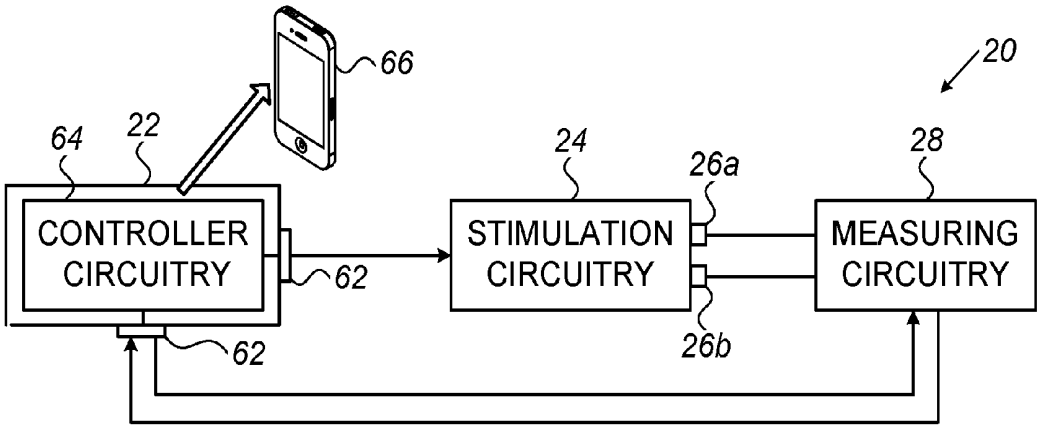

66
20
64
22
24
26a
28
CONTROLLER CIRCUITRY
STIMULATION CIRCUITRY
MEASURING CIRCUITRY
62
62
26b

FIG. 1

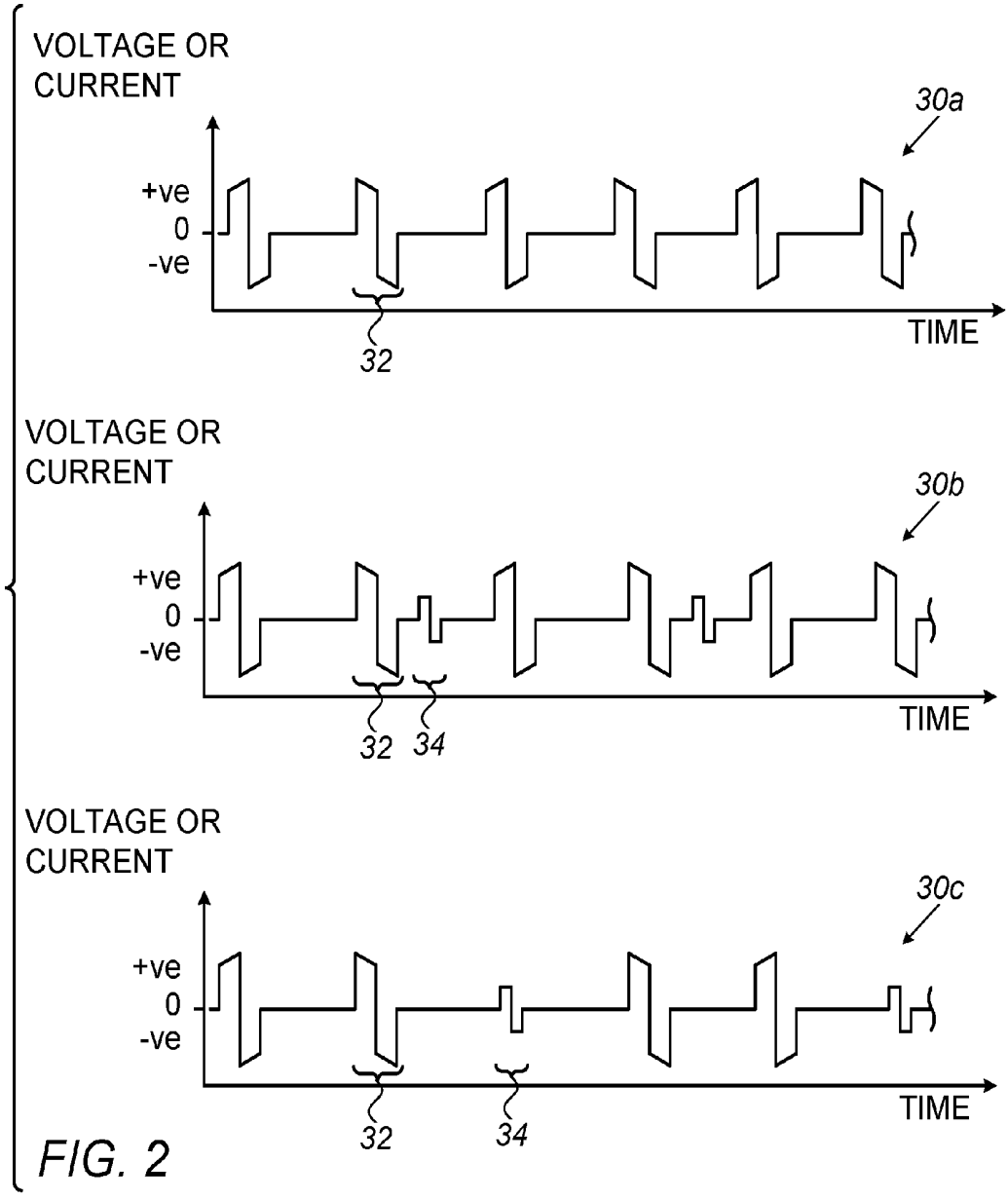

VOLTAGE OR CURRENT
30a
+ve
0
-ve
TIME
32
VOLTAGE OR CURRENT
30b
+ve
0
-ve
TIME
32
34
VOLTAGE OR CURRENT
30c
+ve
0
-ve
TIME
32
34

FIG. 2

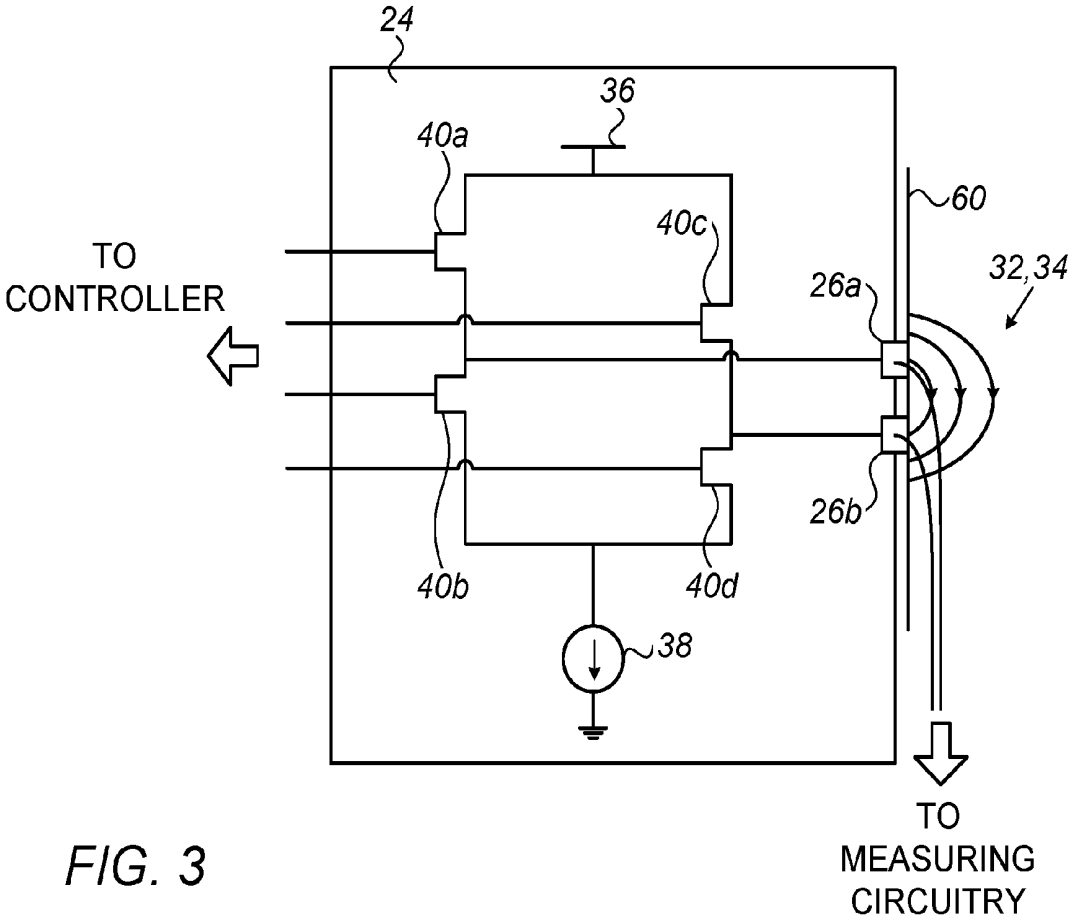

24
36
40a
60
40c
TO
CONTROLLER
32,34
26a
26b
40b
40d
38
TO
MEASURING
CIRCUITRY

FIG. 3

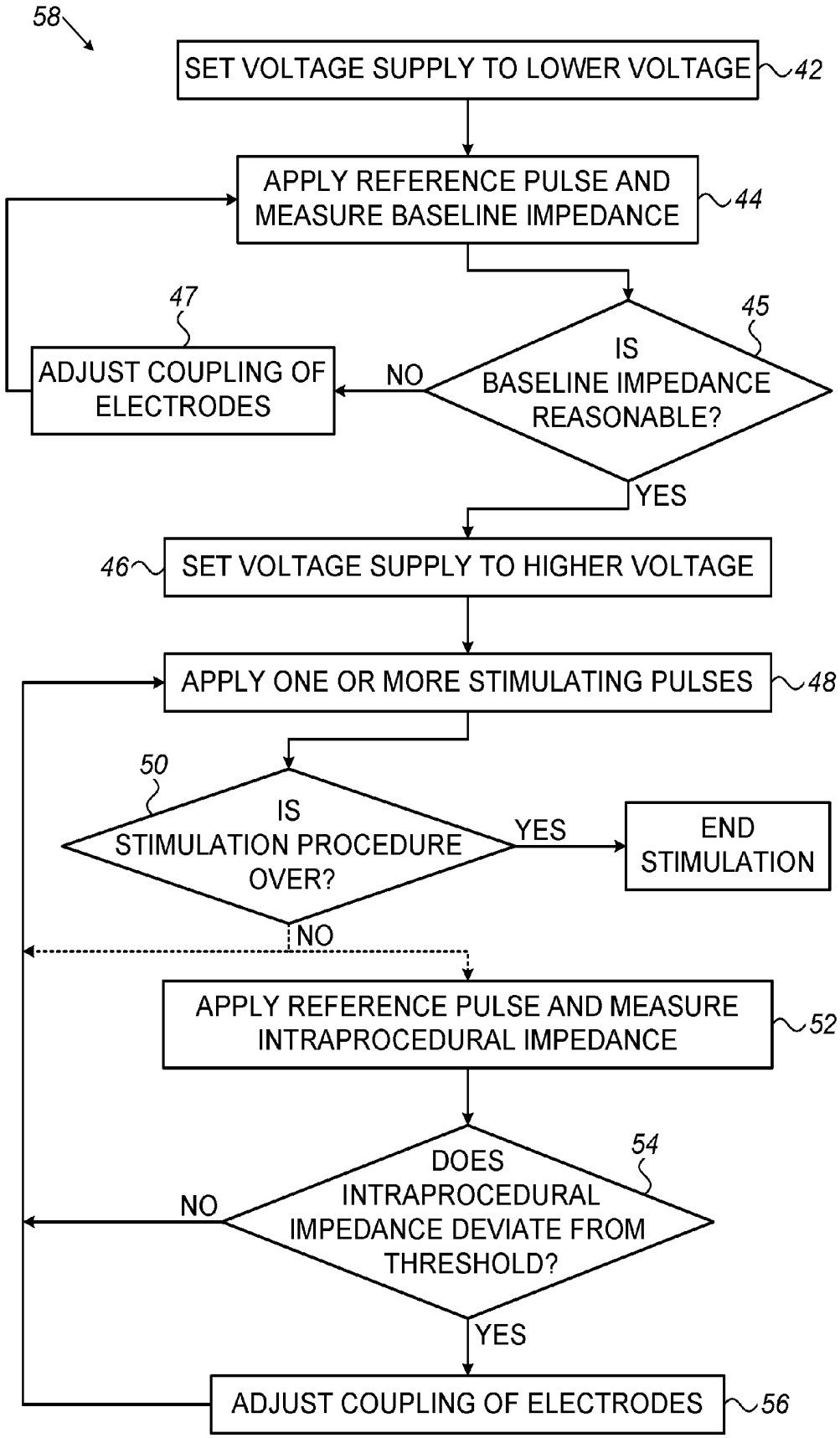

58
SET VOLTAGE SUPPLY TO LOWER VOLTAGE
42
APPLY REFERENCE PULSE AND MEASURE BASELINE IMPEDANCE
44
47
45
ADJUST COUPLING OF ELECTRODES
NO
IS BASELINE IMPEDANCE REASONABLE?
YES
46
SET VOLTAGE SUPPLY TO HIGHER VOLTAGE
APPLY ONE OR MORE STIMULATING PULSES
48
50
IS STIMULATION PROCEDURE OVER?
YES
END STIMULATION
NO
APPLY REFERENCE PULSE AND MEASURE INTRAPROCEDURAL IMPEDANCE
52
54
DOES INTRAPROCEDURAL IMPEDANCE DEVIATE FROM THRESHOLD?
NO
YES
ADJUST COUPLING OF ELECTRODES
56

FIG. 4

IMPEDANCE MONITORING DURING ELECTROSTIMULATION

FIELD OF THE INVENTION

[0001] The present invention relates to medical procedures, and specifically to electrostimulation of tissue.

BACKGROUND

[0002] Transcutaneous electrical nerve stimulation (TENS) is the use of electric current produced by a device to stimulate the nerves for therapeutic purposes. Electrical muscle stimulation (EMS), also known as neuromuscular electrical stimulation (NMES) or electromyostimulation, is the elicitation of muscle contraction using electric impulses.

[0003] U.S. Pat. No. 8,620,434, whose disclosure is incorporated herein by reference, describes a device and method for applying transcutaneous electrical nerve stimulation via an electrode. The device includes the electrode being arranged for detecting a change of a skin impedance and being configured for switching from a stimulation mode of operation for stimulating the nerve, into a recalibration mode of operation upon detection of the changed skin impedance. The device may include a plurality of electrodes being configured for detecting the change of the skin impedance and being configured for adjusting an electrical current flowing through the skin via the plurality of electrodes.

[0004] US Patent Application Publication 2004/0015212, whose disclosure is incorporated herein by reference, describes improved operating features for an electrotherapy device are provided by the use of a peel off detection system which monitors device operation and provides necessary corrective action where appropriate. More specifically, the electrotherapy device monitors the connection characteristics of the electrodes, in order to determine if acceptable connections are being maintained to the patient. In order to monitor these connections, a baseline signal measurement is made when the system is first started. Subsequent measurements are then compared to this baseline measurement, to insure that the magnitude stays within an acceptable range. If the measurement shows a non-acceptable connection condition, the electrotherapy device is shut down and appropriate warning signals are provided to the user. Where multiple output channels are used, isolation circuits are included in the feedback network in order to insure no signal coupling exists.

[0005] An article by Degen and Loeliger, entitled "An improved Method to continuously monitor the Electrode-Skin Impedance during Bioelectric Measurements," published in the Proceedings of the 29th Annual International Conference of the IEEE EMBS, 2007, which is incorporated herein by reference, describes a method that allows to monitor the electrode-skin impedance during bioelectric recordings in a continuous way, without reducing the common mode rejection ratio (CMRR) of the amplifier. The method is based on an additional common mode signal which is superimposed on the bioelectric signal.

[0006] U.S. Pat. No. 6,217,574, whose disclosure is incorporated herein by reference, describes an RF ablation system comprising an irrigated split tip electrode catheter, an RF generator and a signal processor. The catheter comprises four orthogonally arranged electrodes at the distal tip. The catheter is used to map the electrical activity of a heart chamber to locate site(s) of aberrant electrical pathways to be ablated. Once an ablation site has been located, the signal processor activates the RF generator to transmit a low level RF current to each electrode member of the split tip electrode. The signal processor receives signals indicative of the impedance between each electrode member and one or more surface indifferent electrodes and determines which electrode members are associated with the highest impedance. Such electrode members are those in greatest contact with the myocardium. The signal processor then automatically activates the RF generator to transmit an RF ablation current to the electrode members in contact with the myocardium to create a lesion.

SUMMARY OF THE INVENTION

[0007] There is provided, in accordance with some embodiments of the present invention, a method for controlling a stimulation procedure. The stimulation procedure is executed, by passing a plurality of stimulating pulses between a pair of electrodes coupled to skin of a subject. One or more reference pulses are passed between the pair of electrodes, the reference pulses being different from each of the stimulating pulses. An impedance between the electrodes is measured, using the reference pulses. In response to the impedance measured using the reference pulses, but not in response to any impedance measured using the stimulating pulses, the stimulation procedure is controlled.

[0008] In some embodiments, passing the reference pulses includes passing a plurality of reference pulses between respective pairs of the stimulating pulses.

[0009] In some embodiments, passing the plurality of references pulses includes passing the plurality of reference pulses at regular intervals.

[0010] In some embodiments, passing the reference pulses includes passing one or more symmetric reference pulses.

[0011] In some embodiments, passing the reference pulses includes passing one or more asymmetric reference pulses.

[0012] In some embodiments, measuring the impedance between the electrodes includes measuring the impedance by measuring a voltage between the pair of electrodes during the passing of the reference pulses.

[0013] In some embodiments, measuring the impedance between the electrodes includes measuring the impedance by measuring a current between the pair of electrodes during the passing of the reference pulses.

[0014] In some embodiments, passing the stimulating pulses between the pair of electrodes includes passing current-regulated stimulating pulses.

[0015] In some embodiments, passing the stimulating pulses between the pair of electrodes includes passing voltage-regulated stimulating pulses.

[0016] In some embodiments, passing the reference pulse before the stimulation procedure includes passing the reference pulse using a first supplied voltage that is lower than a second supplied voltage that is used to pass the stimulating pulses between the pair of electrodes.

[0017] In some embodiments, passing the reference pulses includes passing the reference pulses by substituting at least one pulse of the stimulation procedure with one of the reference pulses.

[0018] In some embodiments, passing the reference pulses includes passing the reference pulses without substituting any pulse of the stimulation procedure with one of the reference pulses.

[0019] In some embodiments, passing the reference pulses includes passing at least one reference pulse having a lower amplitude than an amplitude of at least one of the stimulating pulses.

[0020] In some embodiments, passing the at least one reference pulse includes passing at least one reference pulse having a current that is less than 15 mA.

[0021] In some embodiments, passing the at least one reference pulse includes passing at least one reference pulse having a current that is less than 10 mA.

[0022] In some embodiments, passing the at least one reference pulse includes passing at least one reference pulse having a current that is less than 5 mA.

[0023] In some embodiments, passing the at least one reference pulse includes passing at least one reference pulse having a voltage that is less than 15 V.

[0024] In some embodiments, passing the at least one reference pulse includes passing at least one reference pulse having a voltage that is less than 9 V.

[0025] In some embodiments, passing the reference pulses includes passing at least one reference pulse having a shorter duration than a duration of at least one of the stimulating pulses.

[0026] In some embodiments, passing the at least one reference pulse includes passing at least one reference pulse having a duration of less than 25 microseconds.

[0027] In some embodiments, passing the reference pulses includes passing at least one reference pulse having an amplitude that varies less than an amplitude of at least one of the stimulating pulses.

[0028] There is further provided, in accordance with some embodiments of the present invention, a controller for use with (i) stimulation circuitry that includes a pair of electrodes, and (ii) measuring circuitry. The controller includes at least one interface configured to couple the controller to the stimulation circuitry and measuring circuitry. The controller further includes controller circuitry, configured to, while the electrodes are coupled to skin of a subject, via the interface, (i) execute a stimulation procedure by driving the stimulation circuitry to pass a plurality of stimulating pulses between the pair of electrodes, (ii) drive the stimulation circuitry to pass one or more reference pulses between the pair of electrodes, the reference pulses being different from each of the stimulating pulses, and (iii) receive, from the measuring circuitry, an impedance between the electrodes that is measured using the reference pulses. The controller circuitry is further configured to, in response to the impedance measured using the reference pulses, but not in response to any impedance measured using the stimulating pulses, control the stimulation procedure.

[0029] In some embodiments, the controller circuitry is configured to control the stimulation procedure in response to the measured impedance by, via the interface, adjusting an amplitude of the stimulating pulses.

[0030] In some embodiments, the controller circuitry is configured to control the stimulation procedure in response to the measured impedance by generating an alert indicative of a required adjustment to the coupling of the electrodes to the skin.

[0031] In some embodiments, the controller circuitry is configured to drive the stimulation circuitry to pass the one or more reference pulses between the electrodes during the stimulation procedure.

[0032] In some embodiments, the controller circuitry is configured to control the stimulation procedure in response to the measured impedance by stopping the stimulation procedure.

[0033] In some embodiments, the controller circuitry is configured to:

[0034] receive, from the measuring circuitry, a baseline impedance between the electrodes and a subsequent impedance between the electrodes, and

[0035] control the stimulation procedure in response to comparing the subsequent impedance to a threshold that is based on the baseline impedance.

[0036] In some embodiments, the controller circuitry is further configured to adaptively adjust the threshold during the stimulation procedure.

[0037] In some embodiments, the controller circuitry is configured to drive the stimulation circuitry to pass one of the reference pulses before the stimulation procedure, the baseline impedance being measured using the reference pulse that is passed before the stimulation procedure.

[0038] In some embodiments, the controller circuitry is configured to drive the stimulation circuitry to pass the reference pulse before the stimulation procedure using a first supplied voltage that is lower than a second supplied voltage that is used to pass the stimulating pulses between the pair of electrodes.

[0039] In some embodiments, the controller circuitry is configured to control the stimulation procedure in response to the measured impedance by, via the interface, controlling a supplied voltage that is used to pass the stimulating pulses between the pair of electrodes.

[0040] The present invention will be more fully understood from the following detailed description of embodiments thereof, taken together with the drawings, in which:

BRIEF DESCRIPTION OF THE DRAWINGS

[0041] FIG. **1** is a block diagram of a system for applying, and monitoring impedance during, electrostimulation, in accordance with some embodiments of the present invention;

[0042] FIG. **2** is a schematic illustration of various pulse sequences that may be passed between electrodes, in accordance with some embodiments of the present invention;

[0043] FIG. **3** is a schematic circuit diagram of stimulation circuitry coupled (e.g., attached) to skin of a subject, in accordance with some embodiments of the present invention; and

[0044] FIG. **4** is a flow diagram showing a method for electrostimulation practiced in accordance with some embodiments of the present invention.

DETAILED DESCRIPTION OF EMBODIMENTS

Overview

[0045] In electrostimulation procedures, at least two electrodes are coupled (e.g., attached) to the skin of the subject, and subsequently, a plurality of stimulating pulses are passed between the electrodes. In current-regulated stimulation, a predefined amount of current is passed between the electrodes during each the stimulating pulses. In voltage-regulated stimulation, a predefined amount of voltage is applied between the electrodes during each of the stimulating pulses.

[0046] In some cases, the electrodes might not be properly coupled (e.g., attached) to the skin before the procedure. Alternatively or additionally, the electrodes may become at least partially uncoupled from the skin, or shorted to one another, during the procedure, e.g., due to movement of the subject or degradation of the adhesive material that keep the electrodes coupled to the skin. Such a scenario may lead to inefficient power consumption, and/or lessen the effectiveness of the stimulation. For example, if the impedance between the electrodes is higher than normal due to improper coupling of the electrodes to the skin, it may be necessary, for current-regulated stimulation, to increase the supplied voltage that supplies the stimulating current, thus consuming more power than would otherwise be necessary. For voltage-regulated stimulation, the increased impedance may cause a smaller amount of current to pass between the electrodes, thus lessening the effectiveness of the stimulation.

[0047] In light of the above, it may be advantageous, before and/or during the stimulation procedure, to measure the impedance between the electrodes, such that, if the measured impedance deviates from a particular threshold, the coupling (e.g., attachment) of the electrodes to the skin may be adjusted. To measure the impedance, the voltage between the electrodes may be measured while a current of known amplitude is passed between the electrodes. Alternatively, the current between the electrodes may be measured while a voltage of known amplitude is applied between the electrodes.

[0048] One implementation of the above-described impedance measurement is to measure the voltage or current between the electrodes while the stimulating pulses are passed between the electrodes. However, pulse parameters that are suitable for stimulation are not necessarily suitable for impedance measurement, and vice versa. For example, in many cases, the amplitude of the stimulating pulses varies over time in an "intra-pulse" and/or "inter-pulse" manner, thus rendering it difficult to use the stimulating pulses to accurately measure the impedance. That is, at least some of the stimulating pulses may have a varying amplitude, and/or the respective amplitudes of the stimulating pulses may be varied during the stimulation procedure, as the subject tries to find his "comfort zone."

[0049] In light of the above, embodiments of the present invention provide an improved implementation, in which one or more reference pulses are passed between the electrodes, in addition to the stimulating pulses. The reference pulses, but not the stimulating pulses, are used for impedance measurement, while the stimulating pulses, but typically not the reference pulses, are used for stimulation. Parameters such as pulse amplitude, duration, and frequency may be "tailored" differently for each type of pulse, thus facilitating effective stimulation and impedance monitoring. For example, in some embodiments of the present invention, the amplitude of the reference pulses is less time-varying than that of the stimulating pulses (and in fact, is often set to a constant value), thus allowing the reference pulses to be used to accurately measure the impedance between the electrodes.

System Description

[0050] Reference is initially made to FIG. **1**, which is a block diagram of a system **20** for applying, and monitoring impedance during, electrostimulation, in accordance with some embodiments of the present invention. System **20** comprises a controller **22** (e.g., a programmable controller configured to execute, for example, microcode), stimulation circuitry **24** comprising at least a pair of electrodes **26***a* and **26***b*, and measuring circuitry **28**. Controller **22** comprises at least one interface **62** (e.g., an electric interface, such as a plug or socket) that couples the controller to stimulation circuitry **24** and measuring circuitry **28**, and further comprises controller circuitry **64**.

[0051] Electrodes **26***a* and **26***b* are coupled (e.g., attached) to skin of the subject who is to be electrostimulated. Subsequently, to execute the stimulation procedure, controller circuitry **64** drives stimulation circuitry **24** to pass a plurality of stimulating pulses between the electrodes. As further described hereinbelow, controller circuitry **64** may also drive the stimulation circuitry to pass one or more reference pulses between the pair of electrodes before and/or during the electrostimulation procedure, the reference pulses being different from each of the stimulating pulses. During the application of the reference pulses, but not during the application of the stimulating pulses, the controller circuitry drives measuring circuitry **28** to measure a voltage or current between the electrodes. The measuring circuitry passes the measured voltage or current to the controller circuitry, which then uses the quantity from the measuring circuitry to measure the impedance between the electrodes. In this manner, the reference pulses, but not the stimulating pulses, are used to measure the impedance. In any case, even if some impedances are measured using the stimulating pulses, the controller circuitry controls the stimulation procedure in response to impedance(s) measured using the reference pulses, but not in response to any impedance measured using the stimulating pulses.

[0052] Typically, at least one of the reference pulses is used to measure a baseline impedance between the electrodes. This reference pulse may be passed before the stimulation procedure (after coupling the electrodes to the skin), or during the procedure (e.g., near the beginning of the procedure). Subsequently, during the procedure, at least one reference pulse is used to measure a subsequent impedance between the electrodes, which, for ease of description, is referred to below as the "intraprocedural impedance." The intraprocedural impedance may be compared to a threshold that is based on the baseline impedance, and, in response thereto, the stimulation procedure may be controlled. For example, if the intraprocedural impedance deviates from the threshold, the controller circuitry may generate an alert that indicates that the coupling of the electrodes to the skin needs to be adjusted. (In some embodiments, the controller circuitry generates the alert by wirelessly or wiredly driving a smartphone **66** of the subject to display an appropriate message to the subject.) Further to receiving the alert, the subject may adjust the coupling (e.g., attachment) of the electrodes to the skin, e.g., by reapplying adhesive material at the electrode-skin interface for at least one of the electrodes.

[0053] In some embodiments, if the intraprocedural impedance deviates from the threshold, the controller circuitry stops the stimulation procedure, alternatively or additionally to generating the alert. While the stimulation procedure is stopped, the coupling (e.g., attachment) of the electrodes to the skin may be adjusted, and subsequently, the stimulation procedure may be restarted.

[0054] The above-described threshold may, for example, be a range of values having a lower bound that is slightly less than the baseline impedance, and an upper bound that is slightly greater than the baseline impedance, such that the intraprocedural impedance is considered to deviate from the threshold whether it is greater than the upper bound or lower than the lower bound. Alternatively, the threshold may be a single value (e.g., the baseline impedance plus or minus some margin), and the intraprocedural impedance may be considered to deviate from the threshold if it is greater than the threshold, or alternatively, if it is lower than the threshold.

[0055] In some embodiments, the threshold is adaptively adjusted during the stimulation procedure. For example, in some embodiments, the threshold is periodically lowered during the stimulation procedure, to account for the expected decrease in impedance during the procedure caused by sweating of the subject. Alternatively or additionally, the threshold may be adjusted in response to any other relevant factors.

[0056] Alternatively or additionally, in response to measuring the baseline and/or intraprocedural impedance between the electrodes, the amplitude of the stimulating pulses may be adjusted. For example, the amplitude of the stimulating current may be set as an increasing function of the measured impedance, since a higher impedance may be indicative of a greater amount of body fat in the subject, which, in turn, indicates that a stronger current is needed to reach the subject's nerve or muscle. Typically, the controller circuitry is configured to differentiate a stable, high-but-normal impedance from an abnormally high and/or increasing impedance. For the former type of impedance, the controller circuitry typically adjusts the amplitude of the stimulating pulses, as described immediately above. For the latter type of impedance, on the other hand, the controller circuitry typically generates an alert and/or stops the procedure, as described above.

[0057] Reference is now made to FIG. **2**, which is a schematic illustration of various pulse sequences that may be passed between electrodes **26***a* and **26***b*, in accordance with some embodiments of the present invention. The pulses shown in FIG. **2** may be voltage pulses used for voltage-regulated stimulation, or alternatively, current pulses used for current-regulated stimulation. (Thus, the units of the vertical axes may be any appropriate unit for voltage or current.)

[0058] First sequence **30***a* is a sequence of stimulating pulses **32**, which may be passed between the electrodes while executing a stimulation procedure. As shown in the figure, stimulating pulses **32** have varying intra-pulse amplitudes, such that it may be difficult to use the stimulating pulses to measure the impedance between the electrodes. (As noted above, the stimulating pulses may also vary in an inter-pulse manner, such that a particular pulse may have a different amplitude from that of a neighboring pulse.) Hence, in embodiments of the present invention, a sequence such as second sequence **30***b* or third sequence **30***c*, each of which includes a plurality of reference pulses **34** between respective pairs of stimulating pulses, is used, instead of first sequence **30***a*.

[0059] Reference pulses **34** typically have an amplitude that varies less than the amplitude of the stimulating pulses. For example, as shown in FIG. **2**, each reference pulse may have a constant (i.e., "flat") positive ("+ve") amplitude, and a constant negative ("−ve") amplitude. Hence, as noted above, reference pulses **34**, rather than stimulating pulses **32**, may be more easily used to measure the impedance. Typically, as shown in FIG. **2**, at least some of the reference pulses are passed at regular intervals (i.e., periodically), such that the impedance may be measured at regular intervals.

[0060] In some embodiments, at least one pulse of the stimulation procedure is substituted with one of the reference pulses. For example, in sequence **30***c*, two of the stimulating pulses of sequence **30***a* are substituted with respective reference pulses. In other embodiments, no pulse of the stimulation procedure is substituted with a reference pulse. For example, in sequence **30***b*, two reference pulses are added to sequence **30***a*, without replacing any of the stimulating pulses. Typically, the references pulses are added to the stimulating-pulse sequence (as in sequence **30***b*), rather than substituted for stimulating pulses (as in sequence **30***c*), unless the frequency of delivery of the stimulating pulses is too high to accommodate the addition of the reference pulses.

[0061] In some embodiments, as shown in FIG. **2**, one or more of the reference pulses are symmetric. That is, for one or more of the reference pulses, the duration and amplitude of the positive portion of the pulse are equal to, respectively, the duration and amplitude of the negative portion of the pulse. Alternatively or additionally, one or more of the reference pulses may be asymmetric. (Even though the integral over an asymmetric pulse is typically zero, the amplitude and duration of the positive portion of the asymmetric pulse are different from the amplitude and duration of the negative portion of the pulse.)

[0062] Typically, as shown in FIG. **2**, the reference pulses have an amplitude that is lower than that of the stimulating pulses, and/or a duration that is shorter than that of the stimulating pulses. Hence, the reference pulses are unlikely to stimulate the subject, and in fact, may not be noticed by the subject at all. For example, in some embodiments, the amplitude of the current of the reference pulses is less than 15 mA, such as less than 10 mA, e.g., less than 5 mA, and/or the voltage of the reference pulses is less than 15 V, e.g., less than 9 V. Alternatively or additionally, the duration of the reference pulses may be less than 25 microseconds.

[0063] Reference is now made to FIG. **3**, which is a schematic illustration of stimulation circuitry **24** coupled (e.g., attached) to skin **60** of a subject, in accordance with some embodiments of the present invention. It is noted that the particular configuration shown in FIG. **3** is provided purely by way of example. In practice, any suitable circuitry may be used to apply the stimulating and reference pulses described herein, for either current-regulated or voltage-regulated applications.

[0064] In some current-regulated stimulation embodiments, stimulation circuitry **24** comprises the half-bridge circuit shown in FIG. **3**. In such a circuit, a current source **38** supplies the current that is passed between electrodes **26***a* and **26***b*, while the voltage between the electrodes is limited to the voltage supplied by voltage supply **36**. (In other words, the current that is passed between the electrodes is the minimum of "I" and "V/R," where "I" is the current supplied by current source **38**, "V" is the voltage supplied by voltage supply **36**, and "R" is the impedance of the tissue.) To generate pulses of current such as the stimulation and reference pulses shown in FIG. **2**, the controller controls switches (e.g., transistor switches) **40***a*, **40***b*, **40***c*, and **40***d*.

In particular, to pass current from electrode **26***a* to electrode **26***b*, the controller closes switches **40***a* and **40***d*, thus connecting electrode **26***a* to voltage supply **36** and electrode **26***b* to current source **38**, while switches **40***b* and **40***c* remain open. Conversely, to pass current from electrode **26***b* to electrode **26***a*, the controller closes switches **40***b* and **40***c*, thus connecting electrode **26***b* to voltage supply **36** and electrode **26***a* to current source **38**, while switches **40***a* and **40***d* remain open.

[0065] The direction of current determines the polarity of the pulse. For example, the respective positive portions of the pulses shown in FIG. **2** may be obtained by passing current from electrode **26***a* to electrode **26***b*, while the respective negative portions may be obtained by passing current from electrode **26***b* to electrode **26***a*. The degree to which the switches are closed determines the amplitudes of the pulses.

[0066] In some embodiments, the voltage supplied by voltage supply **36** is controlled, in response to the measured impedance. For example, in some embodiments, a "calibration procedure" is performed. At least one reference pulse, passed between the electrodes prior to the stimulation procedure, is used to measure the baseline impedance between the electrodes. Subsequently, the voltage supply **36** may be set to a voltage that is slightly higher than the product of the measured baseline impedance and the maximum desired stimulation current.

[0067] The above-described calibration procedure is advantageous, in that it facilitates setting a voltage limit that is high enough to accommodate the stimulation of the subject, yet not too high as to consume a relatively large amount of excess power. In other words, if the voltage supply were set without regard to the baseline impedance, the voltage supply would need to be set, for every subject, as high as needed to accommodate the "worst case scenario," i.e., the highest expected skin impedance. However, some subjects may have a skin impedance that is significantly lower than the highest expected skin impedance. For such subjects, the voltage supply would be too high, such that excess power would be needlessly consumed. Hence, by setting the voltage supply in response to the measured baseline impedance, an appropriate voltage limit may be set for each subject, thus facilitating more efficient consumption of power.

[0068] Typically, when passing the reference pulse that is used to measure the baseline impedance, the voltage supply is set to a lower voltage than the voltage to which it is subsequently set for the stimulation procedure. For example, the voltage supply may be set to a voltage that is slightly higher than the product of the maximum estimated impedance and the desired reference current. Subsequently, in response to the measured baseline impedance, the voltage supply may be increased in order to accommodate the stimulation, as described above. Since the precision of measuring circuitry **28** (FIG. **1**) is typically greater for smaller supplied voltages than for larger supplied voltages, the above-described technique may facilitate a more precise measurement of the baseline impedance. (During the stimulation procedure, however, the voltage supply typically remains at the higher stimulation-accommodating value, even during the application of the reference pulses.)

[0069] For example, reference pulses such as those shown in FIG. **2** may have an amplitude of 10 mA, while skin impedance of human subjects is typically no higher than 1500 Ohm. Thus, during the calibration procedure, the voltage supply may be set to 18 V, which is slightly higher than the product of 10 mA and 1500 Ohm. Stimulation pulses such as those shown in FIG. **2** may have a maximum amplitude of 30 mA. Thus, if, for example, the measured baseline impedance was 1000 Ohm, the voltage supply for the stimulation procedure may be set to 35 V, which is slightly higher than the product of 30 mA and 1000 Ohm.

[0070] Reference is now made to FIG. **4**, which is a flow diagram showing a method **58** practiced in accordance with some embodiments of the present invention. Most of the steps in method **58** were already described above, but, for clarity, are again described hereinbelow, with reference to FIG. **4**.

[0071] Method **58** begins with a first voltage-setting step **42**, in which voltage supply **36** is set to a voltage that is high enough to accommodate a reference pulse, yet lower than the voltage used subsequently during the stimulation procedure. (As noted above, such a lower voltage may facilitate a more precise measurement of the baseline impedance.) Subsequently, in a baseline-impedance-measuring step **44**, at least one reference pulse is applied to the subject by being passed between the electrodes, and during the application of the reference pulse, the baseline impedance is measured, by measuring the voltage between the electrodes. At a first decision step **45**, the controller assesses whether the measured baseline impedance is reasonable, i.e., whether it falls within an expected range of normal human skin impedance, e.g., 300-1500 Ohm. If the baseline impedance is not reasonable (i.e., it is higher than expected, thus indicating that the electrodes may not have been properly coupled to the skin, or it is lower than expected, thus indicating a possible shorting of the electrodes), an alert may be generated, and subsequently, in response to the alert, the coupling (e.g., attachment) of the electrodes to the skin may be adjusted, at a first adjusting step **47**. Subsequently, steps **44** and **45** are repeated. (Steps **42**, **44**, **45**, and **47** collectively form part of the calibration procedure referred to above.)

[0072] Following an assessment that the baseline impedance is reasonable, at a second voltage-setting step **46**, voltage supply **36** is set, in response to the baseline impedance, to a higher voltage that is high enough to accommodate the stimulation. Next, at a stimulating step **48**, one or more stimulating pulses are applied to the subject, by being passed between the electrodes. At a second decision step **50**, the controller, or the subject, decides whether the stimulation procedure is over, i.e., whether enough stimulating pulses have been applied to the subject. If the answer is affirmative, the stimulation procedure ends. Otherwise, depending on the current state of the stimulation procedure, either (i) more stimulating pulses are applied to the subject, at stimulating step **48**, or (ii) at an intraprocedural-impedance-measuring step **52**, at least one reference pulse is applied to the subject, and during the application of the reference pulse, the intraprocedural impedance between the electrodes is measured. Subsequently to (ii), at a third decision step **54**, the controller compares the intraprocedural impedance to a threshold that is based on the baseline impedance. If the intraprocedural impedance deviates from the threshold (i.e., it is higher than the threshold, thus indicating a possible decoupling of the electrodes from the skin, or it is lower than the threshold, thus indicating a possible shorting of the electrodes), an alert may be generated, and subsequently, in response to the alert, the coupling (e.g., attachment) of the electrodes to the skin

may be adjusted, at a second adjusting step **56**. Following the adjustment, the stimulation may continue, at stimulating step **48**.

[0073] In some embodiments, controller circuitry **64** is embodied as a programmable digital computing device comprising a central processing unit (CPU) and random access memory (RAM). Program code, including software programs, and/or data are loaded into the RAM for execution and processing by the CPU. The program code and/or data may be downloaded to the controller in electronic form, over a network, for example, or it may, alternatively or additionally, be provided and/or stored on non-transitory tangible media, such as magnetic, optical, or electronic memory. Such program code and/or data, when provided to the controller, produce a machine or special-purpose computer, configured to perform the tasks described herein.

[0074] It will be appreciated by persons skilled in the art that the present invention is not limited to what has been particularly shown and described hereinabove. Rather, the scope of the present invention includes both combinations and subcombinations of the various features described hereinabove, as well as variations and modifications thereof that are not in the prior art, which would occur to persons skilled in the art upon reading the foregoing description.

1. A method, comprising:

executing a stimulation procedure, by passing a plurality of stimulating pulses between a pair of electrodes coupled to skin of a subject;

passing one or more reference pulses between the pair of electrodes, the reference pulses being different from each of the stimulating pulses;

measuring an impedance between the electrodes, using the reference pulses; and

in response to the impedance measured using the reference pulses, but not in response to any impedance measured using the stimulating pulses, controlling the stimulation procedure.

2. The method according to claim **1**, wherein controlling the stimulation procedure comprises adjusting an amplitude of the stimulating pulses.

3. The method according to claim **1**, wherein controlling the stimulation procedure comprises generating an alert indicative of a required adjustment to the coupling of the electrodes to the skin.

4. The method according to claim **1**, wherein passing the reference pulses comprises passing one or more reference pulses during the stimulation procedure.

5. The method according to claim **4**, wherein controlling the stimulation procedure comprises stopping the stimulation procedure.

6. The method according to claim **4**, wherein passing the reference pulses comprises passing a plurality of reference pulses between respective pairs of the stimulating pulses.

7. The method according to claim **6**, wherein passing the plurality of references pulses comprises passing the plurality of reference pulses at regular intervals.

8. The method according to claim **1**, wherein passing the reference pulses comprises passing one or more symmetric reference pulses.

9. The method according to claim **1**, wherein passing the reference pulses comprises passing one or more asymmetric reference pulses.

10. The method according to claim **1**, wherein measuring the impedance between the electrodes comprises measuring the impedance by measuring a voltage between the pair of electrodes during the passing of the reference pulses.

11. The method according to claim **1**, wherein measuring the impedance between the electrodes comprises measuring the impedance by measuring a current between the pair of electrodes during the passing of the reference pulses.

12. The method according to claim **1**, wherein passing the stimulating pulses between the pair of electrodes comprises passing current-regulated stimulating pulses.

13. The method according to claim **1**, wherein passing the stimulating pulses between the pair of electrodes comprises passing voltage-regulated stimulating pulses.

14. The method according to claim **1**,

wherein measuring the impedance between the electrodes comprises measuring a baseline impedance and a subsequent impedance, and

wherein controlling the stimulation procedure comprises controlling the stimulation procedure in response to comparing the subsequent impedance to a threshold that is based on the baseline impedance.

15. The method according to claim **14**, further comprising adaptively adjusting the threshold during the stimulation procedure.

16. The method according to claim **14**, wherein passing the reference pulses comprises passing one of the reference pulses before the stimulation procedure, and wherein measuring the baseline impedance comprises measuring the baseline impedance using the reference pulse that is passed before the stimulation procedure.

17. The method according to claim **16**, wherein passing the reference pulse before the stimulation procedure comprises passing the reference pulse using a first supplied voltage that is lower than a second supplied voltage that is used to pass the stimulating pulses between the pair of electrodes.

18. The method according to claim **1**, wherein controlling the stimulation procedure comprises controlling a supplied voltage that is used to pass the stimulating pulses between the pair of electrodes.

19. The method according to claim **1**, wherein passing the reference pulses comprises passing the reference pulses by substituting at least one pulse of the stimulation procedure with one of the reference pulses.

20. The method according to claim **1**, wherein passing the reference pulses comprises passing the reference pulses without substituting any pulse of the stimulation procedure with one of the reference pulses.

21. The method according to claim **1**, wherein passing the reference pulses comprises passing at least one reference pulse having a lower amplitude than an amplitude of at least one of the stimulating pulses.

22. The method according to claim **21**, wherein passing the at least one reference pulse comprises passing at least one reference pulse having a current that is less than 15 mA.

23. The method according to claim **22**, wherein passing the at least one reference pulse comprises passing at least one reference pulse having a current that is less than 10 mA.

24. The method according to claim **23**, wherein passing the at least one reference pulse comprises passing at least one reference pulse having a current that is less than 5 mA.

25. The method according to claim **21**, wherein passing the at least one reference pulse comprises passing at least one reference pulse having a voltage that is less than 15 V.

26. The method according to claim **25**, wherein passing the at least one reference pulse comprises passing at least one reference pulse having a voltage that is less than 9 V.

27. The method according to claim **1**, wherein passing the reference pulses comprises passing at least one reference pulse having a shorter duration than a duration of at least one of the stimulating pulses.

28. The method according to claim **27**, wherein passing the at least one reference pulse comprises passing at least one reference pulse having a duration of less than 25 microseconds.

29. The method according to claim **1**, wherein passing the reference pulses comprises passing at least one reference pulse having an amplitude that varies less than an amplitude of at least one of the stimulating pulses.

30. A controller for use with (i) stimulation circuitry that includes a pair of electrodes, and (ii) measuring circuitry, the controller comprising:

at least one interface configured to couple the controller to the stimulation circuitry and measuring circuitry; and

controller circuitry, configured to, while the electrodes are coupled to skin of a subject:

via the interface:

execute a stimulation procedure by driving the stimulation circuitry to pass a plurality of stimulating pulses between the pair of electrodes,

drive the stimulation circuitry to pass one or more reference pulses between the pair of electrodes, the reference pulses being different from each of the stimulating pulses, and

receive, from the measuring circuitry, an impedance between the electrodes that is measured using the reference pulses, and

in response to the impedance measured using the reference pulses, but not in response to any impedance measured using the stimulating pulses, control the stimulation procedure.

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