Institutional Review Board for Baylor College of Medicine and Affiliated Hospitals

Protocol Number: H-52968
Status: Draft
Initial Submit Date: 1/9/2023

Section Aa: Title & PI

A1. Main Title

NEUROMODULATION FOR PREVENTION OF INTENSIVE CARE UNIT ACQUIRED WEAKNESS AND POST INTENSIVE CARE SYNDROME - PROOF OF CONCEPT RANDOMIZED CONTROLLED TRIAL

A2. Principal Investigator

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A3a. Financial Conflict of Interest

Does any member of study personnel (Investigator (including investigator's spouse and/or dependent children)) that are involved in the design, conduct, or reporting of the research have a Significant Financial Interest (SFI) that would reasonably appear to be affected by the research for which funding is sought and/or associated with an entity/business that would reasonably appear to be affected by the research?

No

Section Ab: General Information

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A5. Funding Source:

Baylor College of Medicine (Internal Funding Only)

A6a. Institution(s) where work will be performed:

BCM: Baylor College of Medicine
Baylor St. Luke's Medical Center (BSLMC)

A6b. Research conducted outside of the United States:

Country:
Facility/Institution:
Contact/Investigator:
Phone Number:

If documentation of assurances has not been sent to the Office of Research, please explain:

A7. Research Category:

A8. Therapeutic Intent

Does this trial have therapeutic intent?
Yes

A9. ClinicalTrials.gov Registration

Does this protocol/trial require registration on ClinicalTrials.gov due to it: meeting the definition of an Applicable Clinical Trial, being required under the terms and conditions of an award, or being proposed to be published in ICMJE journals?
Yes

Who will be responsible for registering and maintaining the registration of this Applicable Clinical Trial?
The BCM PI will register the trial because either:

- the trial is BCM PI-initiated,
- BCM is the lead site of this multicenter trial, or,
- the industry sponsor has instructed the BCM PI to register the trial, or,
- registration of this trail is required as a term and condition of the reward by the funding agency.

ClinicalTrials.gov Identifier:
NCT

Section B: Exempt Request

B. Exempt From IRB Review

Not Applicable

Section C: Background Information

Post-intensive care syndrome (PICS) is a collection of new or worsening physical, cognitive and psychiatric symptoms that continue to persist after a patient leaves the intensive care unit (ICU). PICS is mainly triggered by serious conditions such as respiratory failure, sepsis, multisystem organ failure, use of endotracheal tubes, mechanical ventilators, use of sedative and intravenous corticosteroids, post-surgical complex procedures, and prolonged duration of the bed-restore. Previous

studies have reported a 64%-84% prevalence of PICS up to 12 months in patients with at least 2 days of ICU length of stay and/or mechanical ventilation. Therefore, patients do not return to their former level of function for weeks, months and even years. This has led PICS to be recognized as a public health burden.

Particularly, the physical problems of PICS are of high concern because of its consequences regarding functional impairment. This include neuromuscular weakness with no plausible cause other than critical illness described as flaccid and symmetric paralysis provoked by polyneuropathy (axonal loss of motor and sensory fibers), myopathy (myosin loss) or a combination of both. Ultimately, ending in joint and muscle contractures that worsens with malnutrition. Experts refer to this condition as ICU-Acquired weakness (ICUAW), possibly seen in any extremity. However, the lower level attributes to the worse consequences post-ICU discharge.

In ICUAW, affection to the lower extremity can be seen in 32.3%. Mainly due to prolonged periods of immobilization or sedation, that lead to atrophy and dysfunction in the quadriceps and gastrocnemius muscles. The consequences are reduced 6-minute walk test distance, reduced ability to perform activities of daily living, and reduced ability to return to driving and paid employment. In healthy individuals, strict bed rest causes a 1% decrease in muscle strength per day. Casting limbs such as in orthopedic injuries has been shown to result in 25% decrease in muscle strength in 7 days. Therefore, in ICU patients, this problem should be approached as prompt as admission. A recent systematic review (Qin ES et al) in 10 studies (n = 985) found that early mobilization decreased the incidence of ICUAW at hospital discharge, increased the number of patients who were able to stand, and increased the number of ventilator-free days during hospitalization. However, reduced hospital staff or increased burden can be a limitation for providing assisted mobilization.

A practical solution to address these limitations is the use of electrical stimulation (E-Stim). In this matter, AVAZZIA Inc. (Dal, TX, USA) has created an E-Stim device (Tennant Biomodulator PRO) that works on a high voltage alternative pulsed current (HVAPC) to address lower-extremity muscle weakness, endurance, pain, and neuropathy. This technology works through a symmetric biphasic waveform that achieves deep stimulation of the muscle fibers. In our previous trial in ICU COVID-19 patients (NCT04685213, H-47781-A), we demonstrated HVAPC improves gastrocnemius muscle endurance without burnout of oxygen consumption. Other ICU studies (Nussbau et al.) have demonstrated E-Stim is feasible to preserve strength and muscle mass, and reduce muscle degradation leading to maintenance of functional capacity. Its benefit has seen to be higher when placed in hams and calf muscles bilaterally, in a supine position, and administered 5-7 days a week or until extubation or hospital discharge. Another benefit has been linked to neural adaptations.

Studies have reported a series of measurements to demonstrate the efficacy of E-stim therapy such as thigh circumference, strength of lower extremity muscles (isometric or isotonic dynamometry, MRC score), and quality of life questionnaires. In our previously mentioned trial (NCT04685213, H-47781-A), dynamometer tests were difficult to obtain due to patient sedation, medical paralyzation or intubation. Moreover, calf circumference was altered in patients with present edema. Even though we did not assess MRC score or quality of life questionnaires, lack of feasibility also applies for this measurements because it requires awareness of the patient. Therefore, objective measurements that do not depend or interfere with the patient status are needed to evaluate the progress/effectiveness of E-Stim therapy.

Quantitative neuromuscular ultrasound is emerging as a potential research and diagnostic tool but is not a clinical standard of care. Although creatinine kinase may be elevated in patients with ICUAW, there are no validated biomarkers used for diagnosing ICUAW. In our previous trials (NCT04685213, H-47781-A; NCT05198466, H-47781-B), surface electromyography (sEMG) has been able to detect muscle endurance in response to E-Stim. This parameter was associated with a decreased likelihood to fall at the time of ICU discharge, and an increase in muscle perfusion of Post-COVID-19 patients with neuromuscular sequelae. This suggests that sEMG can be an objective and feasible muscle assessment for ICU patients regardless of awareness. Moreover, Moss et al. reported that sural sensory nerve conductive assessment yielded a sensitivity of 100% with a specificity of 81% to diagnose neuromyopathy due to ICUAW. Therefore, we purpose to utilize a nerve conductive/amplitude assessment tool of the sural nerve called DPN Check device (Neurometrix Inc.).

Lastly, our institution has a high volume of intensive care units (N=10) (Baylor St Luke’s Medical Center, Houston, TX, USA) supervised by specialists in critical, intensive, and post-surgical care. Therefore, we believe our institution is a suitable place to perform this study.

Section D: Purpose and Objectives

Aim 1. Acceptability: To examine feasibility and acceptability of lower extremity neuromodulation in patients at risk of ICUAW. H1.1: The adherence to daily use of lower extremity neuromodulation is more than 80% among the IG. Adherence is defined as the use of lower extremity neuromodulation at least one hour per day for at least 4 days per week. H1.2: The perceived acceptability, and perceived benefit would be high among IG.

Aim 2. Proof of concept effectiveness: To examine effectiveness of lower extremity neuromodulation for intubated patients at risk of ICUAW H1.1: E-Stim will improve motor function including muscle endurance and thickness, nerve conductivity and amplitude, by utilizing objective assessments (surface electromyography, ultrasound, dynamometry), after 4 weeks of application or hospital discharge, whichever comes first. H1.2: E-Stim will improve lower extremity nerve function and tissue perfusion after 4 weeks of application or until hospital discharge, whichever comes first. The nerve function parameters will be measured with assessed with a digital test (DPN Check) for peripheral neuropathy and the perfusion parameters will be assessed using a near infrared spectroscopy using a validated imaging system (Kent Imaging System).

Section E: Protocol Risks/Subjects

E1. Risk Category

Category 1: Research not involving greater than minimum risk.

E2. Subjects

Gender:
Both

Age:
Adult (18-64 yrs), Geriatric (65+ yrs)

Ethnicity:
All Ethnicities

Primary Language:
English, Spanish

Groups to be recruited will include:
Patients

Which if any of the following vulnerable populations will be recruited as subjects?
Cognitively impaired

Vulnerable populations require special protections. How will you obtain informed consent, protect subject confidentiality, and prevent undue coercion?

Due to the cognitive impairment of intubated patients under ventilatory assistance, the consent will be obtained from the patient legal authorized representative (LAR). The LAR is determined as an individual or judicial or other body authorized under applicable law to make decisions on behalf of another individual. The LAR may provide consent on behalf of a prospective subject to the subject's participation in research. The terms surrogate decision maker or surrogate consent are also sometimes used. The LAR may be a family member or caregiver who has the legal authority to grant consent on behalf of another who has been invited to participate in research. The LAR will give consent by agreeing with the procedures/ benefits/ risks and participation. All questions/doubts from the LAR about the study will be clarified. When the patient regain consciousness or ability to consent, he/she will be fully informed about the study, and the research staff will obtain their signature. In order to reconsent, the patient will need to be fully aware in time, space, and person. The signed consent form will be maintained in research records.

The subject and/or LAR will be informed if he/she can withdraw from the study at any time without loss of benefits. Consent forms will be signed and dated by the subject, LAR and by the Principal Investigator or Investigators. The original consent will be maintained per IRB policy. Any critical information will be sent for inclusion in the medical records, if it affects patient's well-being and any future treatment. A signed copy of the consent form will be provided to the patient and LAR. Informed consent will be obtained prior to performance of any study procedures. Specifically: 1. No minors will be consented. 2. Subjects' LAR are given as much time as needed to ask questions and read over the consent. They are will be given a copy of the consent and can return at a later date if they need to discuss it with family members, etc. There will be an attachment in section S for the waiver of consent the form was retrieved from Section J- Adult assent.

Sub-population: We will recruit patients undergoing surgery in need of post-surgical ICU admission at BSLMC. This population is at risk of ICUAW. Patients will be consented either before surgery, or by a LAR on the day of surgery as described above.

E3. Pregnant woman/fetus

Will pregnant women and/or fetuses (as described in 45 CFR 46 Subpart B) be enrolled in the research?
No

E4. Neonates

Will neonates of uncertain viability or nonviable neonates (as described in 45 CFR 46 Subpart B) be enrolled in the research?
No

E5. Children

Will children be enrolled in the research?
No

Section F: Design/Procedure

F1. Design

Select one category that most adequately describes your research:

c) Pilot

Discuss the research design including but not limited to such issues as: probability of group assignment, potential for subject to be randomized to placebo group, use of control subjects, etc.

We will prospectively recruit 40 patients at risk of ICUAW. Sample size is convenient and designed to explore acceptability and feasibility of objective tools for measurement. Eligible participants will be screened at BSLMC. Those who satisfied the inclusion and exclusion criteria and signed the informed consent form will be randomly assigned with ratio of 1:1 into two groups. Consenting will be performed with a legal authorized representative (LAR) that is present. When the subject regains consciousness and is aware in time, space, and person, he/she will be re-consented. If the subject decline to continue participation in the study, the subject will be withdrawn. The informed consent will obtained from all participants and their LAR.

Sub-population: Post-surgical patients that are admitted to the ICU will be consented either before surgery, or by a LAR on the day of surgery as described above.

The study will be double-blinded (clinicians and patients) in intervention (IG) and control (CG) group. Both cohorts will be followed-up and monitored at 3 days, and then weekly for a total period of 4 weeks or until hospital discharge, whichever comes first. • Intervention group (IG). The IG (n=20) will be undergoing E-Stim therapy with an active device during the hospitalization period until 4 weeks or discharge, whichever comes first. To deliver E-Stim, 2 electrodes will be placed in each proximal gastrocnemius and Achilles tendons. • Control Group (CG). The CG (n=20) will be undergoing E-Stim therapy with a placebo device (5-10% currents) as described in the IG.

Inclusion Criteria:

-Any patient older than 18 years old admitted to the ICU within two days. -Patient can be intubated with ventilatory assistance or not.

Exclusion Criteria:

- Less than 48 hours of ICU stay - Major foot problems such as active lower extremity wounds, major foot deformity (e.g., Charcot Foot), and/or previous major amputations - Demand-type cardiac pacemaker, implanted defibrillator, or other implanted electronic devices - Any conditions that may interfere with outcomes or increase the risk of the use neuromodulation therapy based on the judgement of clinicians

F2. Procedure

Patients admitted to the ICU within 2 days will be eligible and enrolled in the study after obtaining consent form as previously indicated.

Then, we will perform baseline measurements that include:

(Primary outcomes) Myopathy test: gastrocnemius muscle endurance (surface electromyogram, Trigno Delsys) in response to 5 minutes of neuromodulation; and muscle thickness (gastrocnemius muscle ultrasound, Vscan Air).

(Secondary outcomes) Perfusion test: Plantar foot perfusion parameters (near infrared spectroscopy, Kent Imaging System). The Snapshot NIR camera is a non-invasive imaging device that visualizes and maps tissue oxygen saturation, oxyhemoglobin, and deoxyhemoglobin from the microvascular network of a particular area of the skin. The SnapShot NIR camera is classified as an oximeter, tissue saturation device. As indicated in the 510 (k) summary by Kent Imaging, the NIR SnapshotNIR is a class II device intended for use by healthcare professionals as a non-invasive tissue oxygenation measurement system that reports an approximate value of: - oxygen saturation (St02), - relative oxyhemogoblin level (Hb02), and - relative deoxyhemoglobin (Hb) level. SnapshotNIR is based on multispectral imaging technology and performs spectral analysis at each point in a two-dimensional scanned area producing an image displaying information derived from the analysis. In the present study, this device has no diagnostic, decision making, nor treatment intent, it is an assessment camera for tissue perfusion status in real time. The camera is positioned 30-50 cm away from the desired skin area, and a picture is taken. The pictures will be collected from the plantar foot of the patients as in our previous protocols for electrical stimulation (H-47781, H-50753). The data collected will determine whether lower-extremity electrical electrical stimulation improves perfusion to the distal foot by comparing each time point vs baseline and by group comparison (placebo vs active device).

Neuropathy test: Sural nerve conduction/amplitude assessment (neuropathy, DPNCheck Device by Neurometrix Inc)

Biomarkers tests: Creatinine kinase, C-reactive protein, creatinine, potassium, myosin, serum lactate, arterial SpO2, dupplex ultrasound for DVT will be collected from the electronic medical records. If biomarkers were not collected as a standard/regular procedure in the ICU; data will not be extracted from the electronic medical records. Research staff will not draw any blood samples.

Then, the patients will receive an individually programmed device to deliver neuromodulation to both gastrocnemius muscles simultaneously. The frequency of therapy will be 1 hour daily, and the duration will be up to 4 weeks or until hospital discharge, whichever comes first.

The coordinator will provide the ICU staff with a weekly spreadsheet showing utilization (therapy sessions/day) so compliance can be monitored. Also, the devices will monitor the time of usage to confirm hours of effective neuromodulation therapy to the skin.

Follow-up assessments will be performed at 3 days, and then weekly until 4 weeks or until hospital discharge, whichever comes first, by the research staff. The follow-up assessment will be identical to the baseline assessment.

In the final visit, we will assess muscle strength (ankle dynamometer, RoMech Digital Hanging Scale).

Additional measurements: - 1-month post-hospital discharge phone questionnaires: instrumental activity of daily living scale (IADL), community engagement (the Life Space Questionnaire), independence in daily living activities (KATZ), and anxiety (BAI).

Section G: Sample Size/Data Analysis

G1. Sample Size

How many subjects (or specimens, or charts) will be used in this study?

Local: 40 Worldwide: 40

Please indicate why you chose the sample size proposed:

Sample size is convenient and selected based on available resources to demonstrate feasibility and the proof of concept effectiveness of neuromodulation therapy for patients admitted to ICU and post-ICU. We plan to recruit 40 eligible subjects.

G2. Data Analysis

Provide a description of your plan for data analysis. State the types of comparisons you plan (e.g. comparison of means, comparison of proportions, regressions, analysis of variance). Which is the PRIMARY comparison/analysis? How will the analyses proposed relate to the primary purposes of your study?

Statistical Design: Independent t-test, U-test, or Chi-square (depends on type of variables) will be used to compare between groups (IG, and CG for key baseline descriptors including demographics and relevant clinical characteristics). Those descriptors which showed statistical significant difference will be considered as covariates for adjusting the results in the following assessments. Appropriate mixed models (linear for continuous or Generalized Estimating Equations (GEEs) for non-continuous or non-parametric variables) will be used to test the intervention effect for each of the primary or secondary outcomes. Results will be adjusted by covariates as described above.

P-values of 0.05 or less will be considered statistically significant based on a two-sided test unless otherwise noted. All variables will be tabulated descriptively at each scheduled time point (baseline, follow up and discharge date). For each continuous variable, the analyses will include the mean, standard deviation, minimum and maximum. For each categorical variable, the summary will include frequencies and percentages. Each variable will be analyzed using all available data. Baseline variables will be summarized using descriptive statistics. We assume that a successful intervention is also helpful to maintain subjects muscle mass, reduce neuromyopathy signs and increase perfusion. The measured parameters (e.g. sEMG, US, strength, Kent imaging, DPN Check, etc.) should change substantially from baseline to the end of the intervention. For example, the EMG amplitude values should show increased voltages. Next, for all continuous variables, pre-treatment scores will be regressed on post-treatment scores to form residualized change scores (e.g. sEMG, US, strength, Kent imaging, DPN Check, etc.). Correlations will then be generated among these scores to determine whether changes in sEMG factors are related appropriately with increases in (clinically assessed) functional capacities and self-report measures of activities at 1 month post-hospital discharge. ANOVA test will be used to examine significant difference between patients with severe risk factors for prolonged ICU stage (e.g. age, BMI, cardiovascular morbidities). Moderator effects will also be examined for exploratory purposes.

Section H: Potential Risks/Discomforts

H1. Potential Risks/Discomforts

Describe and assess any potential risks/discomforts; (physical, psychological, social, legal, or other) and assess the likelihood and seriousness of such risks:

The risk to participants of this study is considered to be minimal in a controlled environment with an attendant present. This research routine will not place subjects at higher risk than normal activities of daily living, and no more risk of harm or discomfort is associated with these tests than the discomfort normally incurred while performing normal muscle stretching. Subjects will be allowed rest time between trials as needed.

The devices and technology is completely non-invasive, safe, non-toxic and non-ionizing. The potential risks to subject are minimal. However, like any battery powered systems, there is a minimum risk of sensor malfunctioning. In addition, the

study devices are not waterproof, and although they use a low powered battery (similar to a cellphone battery), in order to avoid any risk of shock the monitor should not be submerged or saturated with fluids during operations or cleaning. It does not emit any radiation to the human body, and does not offer any significant risk to the subject.

Subjects may experience mild discomfort from the sensor on their legs. We will inform the subject to please notify the investigators if the sensor is uncomfortable.

All information we will collect about the subject will be stored in a secure location and coded in a way to maintain confidentiality. Only study personnel will have access to their records. Data collected during the study may be published and made publicly available. Data may also be shared with other research groups. However, data that could in any way identify them will not be made public or shared.

Some of potential risks of using neuromodulation therapy could be: * Skin related discomfort, such as tingling * Skin reaction to adhesive patch.

Some of potential risks of using DPN Check could be: * Skin related discomfort, such as tingling *

If the tingling sensation is too intense for the participant, they have the ability to reduce the intensity for their best level of comfort.

The risk to participants due to the optional assessments and surveys is considered minimal because all that is required is simple walking and balance movements in a controlled environment with an attendant present. This research routine will not place subjects at higher risk than normal activities of daily living, and no more risk of harm or discomfort is associated with these tests than the discomfort normally incurred while performing normal muscle stretching. Subjects will be allowed rest time between trials as needed.

Potential risk to the subject due to the pulse oximeter optional test is considered minimal; this device is non-invasive, non-toxic, and non-ionizing. The device will be placed on the subject's finger, and monitor their oxygen levels.

H2. Data and safety monitoring plan

Do the study activities impart greater than minimal risk to subjects?

No

H3. Coordination of information among sites for multi-site research

Is the BCM Principal Investigator acting as the SPONSOR-INVESTIGATOR for this multi-site research?

No or Not Applicable

Is BCM the COORDINATING CENTER for this multi-site research?

No or Not Applicable

Section I: Potential Benefits

Describe potential benefit(s) to be gained by the individual subject as a result of participating in the planned work.

There is potential benefit of prevention or improvement of hospital acquired weakness due to ICU stay, based on previous studies the neuromodulation therapy will improve blood flow, tissue perfusion and muscle activation. In addition, the participation in this study may help the investigators better understand the prevention of ICU-acquired weakness and post-ICU syndrome and may determine if this therapy has an impact in daily leaving and activities after getting discharged from the hospital.

Primary outcomes include myopathy (sEMG) and neuropathy (DPN Check) assessment. Secondary outcomes include perfusion (Kent Imaging), and biomarkers. This therapy will also help to determine if hospital length of stay, and time for extubating can be reduced (patient health record). The primary and secondary outcomes will be assessed at baseline, 3 days, and then weekly after completing 4 weeks or until hospital discharge, whichever comes first. Appropriate mixed models (linear for continuous or Generalized Estimating Equations (GEEs) for non-continuous or non-parametric variables) will be used to test the intervention effect for each of the primary or secondary outcomes.

Also, participation may help the investigators design a practical assessing method to identify the impact of neuromyopathy in the hospital setting and the prevention or reduction of post-ICU syndrome. This may allow physicians to provide personalized care by monitoring muscle loss and limb complications caused by prolonged hospital length of stay.

Describe potential benefit(s) to society of the planned work.

As described above, this work may allow physicians to provide more personalized care for hospitalized patients in need of physical therapy for continuous and prolonged periods, specially when having a severe illness.

Do anticipated benefits outweigh potential risks? Discuss the risk-to-benefit ratio.

This study brings no more than minimal risk to subjects as it only involves a non-invasive device. There are some risks associated with lack of comfort from neuromodulation, skin allergy to the neuromodulation sticky patches/electrode pads that are used for delivering neuromodulation therapy, risk associated with electrical mal-function of neuromodulation, and other unknown risks. All neuromodulation devices will be checked before any use to minimize the risk associated with electrical malfunction. All neuromodulation devices are FDA approved for the purpose of pain reduction and have been used for lower extremity muscle weakness prevention in our previous trial for ICU COVID-19 patients (Zulbaran-Rojas et al, Frontiers in Medicine, 2022). However, these devices have not been used before for purpose of reducing or preventing post-ICU syndrome. Although there is no direct benefit for participating in the study, their participation may help the investigators design a practical assessing method to identify the impact of Neuromyopathy in the hospital (ICU) setting.

Section J: Consent Procedures

J1. Waiver of Consent

Will any portion of this research require a waiver of consent and authorization?

No

J1a. Waiver of requirement for written documentation of Consent

Will this research require a waiver of the requirement for written documentation of informed consent?

No

J2. Consent Procedures

Who will recruit subjects for this study?

PI

PI's staff

Describe how research population will be identified, recruitment procedures, any waiting period between informing the prospective participant and obtaining consent, steps taken to minimize the possibility of coercion or undue influence and consent procedures in detail.

Subjects will be recruited from the hospital. They may get some referrals from other collaborators. In order to recruit or identify subjects, we will screen our patient charts for eligible subjects. The COI will identify eligible subjects and alert the coordinator. The coordinator will review all the details of the study with the subject and/or their family. If the subject agrees to participate in the study, they will be screened and then enrolled into the study. The recruitment process will be the same for English and Spanish patients, we are only adding the Spanish consent in the event a subject who's primary language is not English can be consented. We have a bilingual Research Coordinator who will explain the consent and conduct the visit in the subjects primary language.

We will be conducting the study during the first 48 hours of intubation at the ICU. Consent will be obtained from the patient legal authorized representative (LAR). The LAR is determined as an individual or judicial or other body authorized under applicable law to make decisions on behalf of another individual. The LAR may provide consent on behalf of a prospective subject to the subject’s participation in research. The terms surrogate decision maker or surrogate consent are also sometimes used. The LAR may be a family member or caregiver who has the legal authority to grant consent on behalf of another who has been invited to participate in research. The LAR will give consent by agreeing with the procedures/ benefits/ risks and participation. All questions/doubts from the LAR about the study will be clarified. When the patient regain consciousness or ability to consent, he/she will be fully informed about the study, and will the research staff will obtain their signature. In order to reconsent, the patient will need to be fully awake in time, space, and person. The signed consent form will be maintained in research records.

The subject and/or LAR will be informed if he/she can withdraw from the study at any time without loss of benefits. Consent forms will be signed and dated by the subject, LAR and by the Principal Investigator or Investigators. The original consent will be maintained per IRB policy. Any critical information will be sent for inclusion in the medical records, if it affects patient's well-being and any future treatment. A signed copy of the consent form will be provided to the patient and LAR. Informed consent will be obtained prior to performance of any study procedures. Specifically: 1. No minors will be consented. 2. Subjects' LAR are given as much time as needed to ask questions and read over the consent. They are will be given a copy of the consent and can return at a later date if they need to discuss it with family members, etc. There will be an attachment in section S for the waiver of consent the form was retrieved from Section J- Adult assent.

Are foreign language consent forms required for this protocol?

Yes

Which of the following ways will you document informed consent in languages other than English?

A full-length informed consent document

J3. Privacy and Intrusiveness

Will the research involve observation or intrusion in situations where the subjects would normally have an expectation of privacy?
No

J4. Children

Will children be enrolled in the research?
No

J5. Neonates

Will non-viable neonates or neonates of uncertain viability be involved in research?
No

J6. Consent Capacity - Adults who lack capacity

Will Adult subjects who lack the capacity to give informed consent be enrolled in the research?
Yes

J7. Prisoners

Will Prisoners be enrolled in the research?
No

Section K: Research Related Health Information and Confidentiality

Will research data include identifiable subject information?
Yes

Information from health records such as diagnoses, progress notes, medications, lab or radiology findings, etc.
Yes

Specific information concerning alcohol abuse:
No

Specific information concerning drug abuse:
No

Specific information concerning sickle cell anemia:
No

Specific information concerning HIV:
No

Specific information concerning psychiatry notes:
No

Demographic information (name, D.O.B., age, gender, race, etc.):
Yes

Full Social Security #:
No

Partial Social Security # (Last four digits):
No

Billing or financial records:
No

Photographs, videotapes, and/or audiotapes of you:
Yes

Identifiable biospecimens
No

Other:
No

At what institution will the physical research data be kept?

The physical research will be kept in our BCM offices housed in the McNair Building room B01.529.

How will such physical research data be secured?

Data will be kept in locked file cabinets that only the research team has access to.

At what institution will the electronic research data be kept?

Data will be kept locked on network computers in our BCM offices, under the password protected server. Address:\\discovery1.ad.bcm.edu\bcm-dept-icamp

Additional electronic data may be stored on REDCap. REDCap is hosted by Baylor College of Medicine - Institute for Clinical & Translational Research.

Such electronic research data will be secured via BCM IT Services- provided secured network storage of electronic research data (Non-Portable devices only):

Yes

Such electronic research data will be secured via Other:

Yes, (describe below):
Electronic data will be stored using the REDCap (Research Electronic Data Capture) software. This software is used to electronically collect and manage research data. REDCap is a secure, web-based platform.

Electronic data will also be stored and secured under the password protected server provided by BCM IT Services.

Will there be anyone besides the PI, the study staff, the IRB and the sponsor, who will have access to identifiable research data?

Yes, identify the classes of the persons:
People who ensure quality from the institutions where the research is being done, federal and other regulatory agencies will have access to all of the research data.

Please describe the methods of transmission of any research data (including PHI, sensitive, and non-sensitive data) to sponsors and/or collaborators.

Transmissions, if any, will only happen via secure emails.

Will you obtain a Certificate of Confidentiality for this study?

No

Please further discuss any potential confidentiality issues related to this study.

N/A

Section L: Cost/Payment

Delineate clinical procedures from research procedures. Will subject's insurance (or subject) be responsible for research related costs? If so state for which items subject's insurance (or subject) will be responsible (surgery, device, drugs, etc). If appropriate, discuss the availability of financial counseling.

There will be no research procedures charged to the subject or their insurance. This includes, the research device, materials provided by the research team, visits with the research team.

If subjects will be paid (money, gift certificates, coupons, etc.) to participate in this research project, please note the total dollar amount (or dollar value amount) and distribution plan (one payment, pro-rated payment, paid upon completion, etc) of the payment.

Dollar Amount:

0

Distribution Plan:

N/A

Section M: Genetics

How would you classify your genetic study?

Discuss the potential for psychological, social, and/or physical harm subsequent to participation in this research. Please discuss, considering the following areas: risks to privacy, confidentiality, insurability, employability, immigration status, paternity status, educational opportunities, or social stigma.

Will subjects be offered any type of genetic education or counseling, and if so, who will provide the education or counseling and under what conditions will it be provided? If there is the possibility that a family's pedigree will be presented or published, please describe how you will protect family member's confidentiality?

Section N: Sample Collection

None

Section O: Drug Studies

Does the research involve the use of ANY drug* or biologic? (*A drug is defined as any substance that is used to elicit a pharmacologic or physiologic response whether it is for treatment or diagnostic purposes)

No

Does the research involve the use of ANY gene transfer agent for human gene transfer research?

No

O1. Current Drugs

Is this study placebo-controlled?

No

Will the research involve a radioactive drug?

No

Section P: Device Studies

Does this research study involve the use of ANY device?

Yes

Device 1: Trigno Wireless EMG System

Device 2: Tennat Biomodulator

Device 3: Snapshot NIR

Device 4: DPNCheck

Device 5: Vscan Air

Section Q: Consent Form(s)

Neuromodulation Therapy for Lower Extremity in ICU Patients

Section R: Advertisements

None