Institutional Review Board for Baylor College of Medicine and Affiliated Hospitals

Protocol Number: **H-50753**
Status: Approved
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Approval Period: 12/20/2023 - 12/12/2024

Section Aa: Title & PI

A1. Main Title

TRANSCUTANEOUS ELECTRICAL NERVE STIMULATION FOR LOWER EXTREMITY IN PATIENTS WITH NEUROGENIC PAIN - A PROOF OF CONCEPT RANDOMIZED CLINICAL TRIAL

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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?

Yes

Section Ab: General Information

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A5. Funding Source:

Organization: NATIONAL SCIENCE FOUNDATION (NSF);BAYLOR COLLEGE OF MEDICINE (BCM)

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

BCM: Baylor College of Medicine

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:
NCT05200858

Section B: Exempt Request

B. Exempt From IRB Review

Not Applicable

Section C: Background Information

Neurogenic pain (NP) arises or is caused by central or peripheral nervous system dysfunction. The types of NP can be derived from its origin including: 1) central, due to a lesion derived from the brain and/or spinal cord; 2) neuropathic, due to injury to a peripheral nerve, or 3) deafferentation, due to stemming from loss or interruption of sensory nerve fiber transmissions. Each of these types may manifest with different pain characteristics in relation to frequency, duration, intensity, and severity. The most common NP are peripheral neuropathy or fibromyalgia. Standard of care treatment for these conditions is pharmacologic-derived; however, other alternatives such as transcutaneous electrical nerve stimulation (TENS) have demonstrated its ability to manage pain in patients with peripheral neuropathy (Najafi et al, JDST, 2017) and fibromyalgia (Jamison et al, JPR, 2021).

In this matter, Neurometrix Inc. (Woburn, MA, USA) has created a wireless TENS device (Quell®) to address pain and its associated symptoms (fatigue, reduced gait, sleep). This technology is a portable wireless non-invasive device placed in the lower-extremity that works through the stimulation of nerves that carry non-painful sensations (A-beta fibers) by closing a neurological "gate" in the spinal cord, thus, reducing transmission from pain nerves (A-delta and C fibers) to the brain. This device utilizes a wireless technology manageable through a smart phone application (Quell App) that also tracks symptom-status. Unlike other devices, it utilizes position and motion sensing to automatically adjust stimulation to the patient both day and night. The device is practical by connecting via bluetooth to a smartphone/smartwatch apps that help the patient personalize and control their treatment.

The Quell® device has been employed for treatment of various NP etiologies such as fibromyalgia, chemotherapy induced peripheral neuropathy (CIPN), chronic back pain, post-acute sequelae of Sars-Cov-2 (PASC), neuromyelitis optica spectrum disorder, restless leg syndrome, and painful diabetic neuropathy. Recently, Quell® has received FDA breakthrough device designation for treatment of fibromyalgia and CIPN.

We purpose the use of Quell TENS device to explore its benefits in patients with NP derived by different etiologies.

Study #1: One population that has shown vast symptoms related to NP includes PASC. This is an emerging entity that has been clearly recognized by musculoskeletal pain, fatigue, cognitive, and sleep disturbances, among other symptoms, in patients who have recovered from severe Sars-CoV-2 infection. Hospitalized survivors have reported a significant excess

burden of many of these symptoms up to 8 months after discharge. Particularly in the lower extremity, NP and musculoskeletal illness has been associated with prolonged immobilization, high-risk comorbidities, and the use of glucocorticoids that is commonly administered to these patients. These manifestations are the cardinal symptoms of fibromyalgia, a condition thought to be caused by hyperactive sensory signaling due to central sensitization as well as deficient endogenous pain inhibition, triggered among others, by viral infections. Consequently, fibromyalgia sequelae are one of the most common long-term complications seen in PASC. Thus, it is expected to impose a serious burden on different medical specialties in a near future. In a population that has persistent lack of symptom resolution such as fibromyalgia, adherence to therapy could be challenging. Patients with constant pain, fatigue, and sleep disturbances, are difficult to keep motivated, especially those pain-medication dependents that often present low quality of life. Therefore, we purpose the use of TENS to address pain management and its accompanied symptoms. Since this technology is dose-dependent, we propose a practical daily-basis therapy that patients with persistent associated fibromyalgia due to previous COVID-19 infection could apply at home, thus, addressing PASC without relying only on medication.

Our institution has created the Post-COVID-19 Clinic (McNair Campus, BCM St Luke's, Houston, TX, USA) supervised by specialists in critical and pulmonary care. This Clinic has a high volume of patients that present with PACS, particularly those with associated fibromyalgia (i.e., persistent muscle pain, fatigue, weakness, atrophy, sleep problems, and/or anxiety). Therefore, we believe our institution is a suitable place to perform this pilot study.

Study #2: Chemotherapy and other cancer treatments can cause damage to the peripheral nerves mainly reflected in severe pain in the upper and/or lower extremities. Additional to pain, cancer treatment may cause loss of balance which affects motor capacity and is a major cause of poor quality of life. There are only minimally effective treatments for CIPN despite over 20 years of research. Few recent studies including ours have suggested that exercise intervention could be effective to restore numbness and motor capacity loss because of CIPN. Unfortunately, conventional rehabilitation programs however suffer from poor adherence and those programs for supervised settings have limitation of access for those who live in the remote areas (e.g., rural area), or could be too frail to travel after chemotherapy. This raised a significant disparity for delivering an effective therapy for those who are living in remote areas or those who are too frail to travel. Therefore, we believe the user-friendly design, and wireless practicality of Quell® is a suitable option for our CIPN population at BCM.

Our institution's Duncan Cancer Center (McNair Campus, BCM St Luke's, Houston, TX, USA) supervised by specialists in clinical and surgical oncology, has a high volume of patients that present with CIPN. Therefore, we believe our institution is a suitable place to perform this sub-study. The premise of this sub-study is that daily basis of TENS therapy could be effective to reduce pain, reduce numbness and improve both motor-capacity and mobility performance leading to improve quality of life in those who suffer from CIPN and have limited access to health care.

Section D: Purpose and Objectives

The purpose of the pilot study is to examine acceptability and proof of concept effectiveness of a wireless TENS technology to address NP due to different etiologies.Sample size (n=60) is convenient and designed to explore acceptability and feasibility.

Study #1: PASC associated FM. Eligible participants (N=30) will be screened at the BCM Post-COVID-19 Clinic for inclusion criteria.

Study #2: Patients with CIPN (N=30). Eligibility will be screened at the Duncan Cancer Center at BCM.

Participants, who satisfy the inclusion and exclusion criteria and sign the informed consent form will be randomly assigned with ratio of 1:1 into two groups. One group will utilize TENS functional devices (Active group, AG); the other group will utilize TENS non-functional devices (Placebo group, PG). The baseline measurements will be performed, and the patients will take the programmed device home for a duration of 4 weeks. Then, the patients will come back after four weeks (4W). At this 4th week visit, both groups will be unblinded and the AG will keep their functional device and the PG group will receive a functional device. Both groups will continue to deliver 3-5 hour of stimulation daily, until their final 8th week follow up visit (8W). The primary outcomes will be pain symptoms, sleep and fatigue. Secondary outcomes include limb strength and perfusion, gait assessment (gait speed, stride length, double stance, and gait steadiness), balance, pulse oximetry, and quality of life. The coordinator will utilize a weekly spreadsheet showing utilization (therapy sessions/day, logged in the Quell health Cloud) so compliance can be monitored and those that are not using the device can be encouraged.

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

Groups to be recruited will include:
Patients

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

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

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 60 patients with NP derived from different etiologies (study #1: PASC, study #2: CIPN). Randomization will be done through a computer-generated list followed by sequential allocation.

Patients will be followed-up and monitored for up to 8 weeks. The study will be double-blinded (clinicians and patients) until the 4th week, where study participants will be told of their group assignment.

The following characteristics will be included: 1. Frequency: 3+ hours daily. 2. Patient reported outcomes: Fibromyalgia Diagnostic Criteria (FMS), Symptom Impact Questionnaire (SIQR), Patients Global Impression of Change (PGIC), Brief pain inventory (BPI), Medical Outcome Study Sleep Scale (MOS) questionnaires, and Multidimensional Assessment of Fatigue (MAF), common terminology criteria for adverse events (CTCAE) v5., EORTC-CIPN20, UENS, EORTC-QLQC30 3. Perfusion test: Lower limb calf tissue oxygen saturation (Kent Imaging System) 4. Other measurements: pulse oximetry, muscle calf activation in response to TENS (surface electromyography [sEMG] assessment), muscle calf activation in response to ankle maximum voluntary contraction (sEMG assessment), ankle strength (measured using ankle dynamometer), peripheral neuropathy (DPNCheck), vibration perception threshold (VPT test). 5. Time points: The outcome measures will be obtained at baseline and four weeks. 6. Optional questionnaires collected at each time point: instrumental activity of daily living scale (IADL), daily living independence (KATZ), depression (CES-D), fatigue (FACIT), cognitive assessment (MOCA), pain and mobility, global health (PROMIS), sleep (PSQI), frailty (TSFI), anxiety (BAI), and user acceptability (TAM). 7. Optional assessments of the 6-minute walk test, gait speed, balance, frailty and physical monitoring will be conducted at both study visits using wearable sensors. 8. Optional: Patients keep the device after the study ends

(those who wore sham will get an active device).

The cohorts (per sub-study) will be randomized in two arms: Active group (AG). The AG (n=15) will be undergoing TENS therapy with an active device during 4 weeks. To deliver TENS, a band strap with hydrogel pads will be placed around the calf muscle of one lower-extremity alternating to the other side in a weekly basis. We hypothesize that a high dose nerve stimulation has a widespread effect on pain and other symptoms, not just at the location of stimulation. To get localized effects in both limbs the subjects will alternate limbs. We also recommend this in any case to minimize the risk of skin irritation from the hydrogel pads. According to previous studies, perceived afferent stimulation by the brain from only one limb is able to send efferent signals to both limbs. Therefore, both limbs will be assessed for therapy outcomes.

Placebo Group (PG). The PG (n=15) will be undergoing TENS therapy with a sham device as described in the AG. The sham device is identical to the active device in all respects except that it stimulates for 6 minutes during each therapy session instead of 60 minutes, and is therefore 10% of the dose.

Both groups will receive their respective devices at the initial visit (BL) and will be asked to return in 4 weeks for follow-up assessment (4W visit). At this 4 week visit, study participants will be unblinded and the active group will keep their active device, while the placebo group will receive a placebo device. Study participants will return for a final in-person visit at the 8th week (8W), which will include the assessments described above. Throughout this 8-week period the participants may receive follow-up phone calls assessing their compliance. All subjects will keep their active device after completion of the 8-week study.

Inclusion Criteria:

Study #1: Previous COVID-19 infection Persistent symptoms for lower extremity pain, fatigue, weakness, or poor gait and balance after infection assessed by critical care clinicians on the initial consultation Willing to attend clinic for assessments

Study #2: Patients with chemotherapy induced peripheral neuropathy in current active or having finished treatment for any type of cancer that requires chemotherapy regardless of dosage. Willing to attend clinic for assessments

Exclusion Criteria:

Study #1: Severe cognitive decline reduces their ability to interact with the TENS mobile app Major visual or hearing weakness reduces the ability to interact with TENS mobile app Unable to walk independently for a distance of 10 meter Major foot problems such as active lower extremity wounds, major foot deformity (e.g., Charcot Foot), previous major amputations, and claudication Demand-type cardiac pacemaker, implanted defibrillator, or other implanted electronic devices; and any conditions that may interfere with outcomes or increase the risk of the use TENS based on the judgement of clinicians

Study #2: Severe cognitive decline reduces their ability to interact with the TENS mobile app Major visual or hearing weakness reduces the ability to interact with TENS mobile app Unable to walk independently for a distance of 10 meter Major foot problems such as active lower extremity wounds, major foot deformity (e.g., Charcot Foot), previous major amputations, and claudication Demand-type cardiac pacemaker, implanted defibrillator, or other implanted electronic devices; and any conditions that may interfere with outcomes or increase the risk of the use TENS based on the judgement of clinicians. Patients with metastatic or terminal cancer disease.

F2. Procedure

30 subjects per sub-study (study #1: 30 subjects, study#2: 30 subjects):

Aim 1 (acceptability): To examine feasibility and acceptability of TENS in patients with NP.

At the baseline visit and each of the follow-up visits (at four weeks, 4W; and eight weeks, 8W), electrical stimulation using the TENS device, will be administered by the coordinator. Daily electrical stimulation, between the baseline and follow-up visit, will be administered by the patient at their convenience. They will be asked to use the device at least 3 hours per day for at least 4 days per week. At follow-up study visits (4W and 8W), a Technology Acceptance Model (TAM) survey adopted for tele-health and smart wearables applications perception of benefit, technological anxiety, technology acceptance, trust, facilitation conditions, risk, and attitude of use will be obtained for each subject.

Aim 2 (proof of concept effectiveness): To examine effectiveness of TENS for NP.

At the baseline visit (BL) and each of the follow-up visits (at four weeks, 4W; and eight weeks, 8W), electrical stimulation using the TENS device, will be administered by the coordinator. This trial will have 30 patients divided into two groups. Group 1 (Active group, n=15) will receive a functional Neurometrix Quell Relief Device; Group 2 (Placebo group, n=15) will receive a non-functional Neurometrix Quell Relief Device that will administer 6 minutes of stimulation per hour of stimulation. Lower extremity muscle activation will be assessed by using sEMG (electromyography) at each study visit during the delivery of stimulation. At the 4th week (4W), both groups will be unblinded and the AG will keep their functional device, will the PG will return their non-functional device and receive a functional device. The patients will be monitored for another 4 weeks with a final follow-up visit at 8 weeks (8W). Both the AG and PG will have the option to take home their functional device at the end of the 8-week study

Tissue Oxygen Saturation: near infrared imaging (Kent Imaging System) at pre-, 30min, 60min, and 30min post-treatment (after stopping of EE device) at each study visit.

Patient reported outcomes: Fibromyalgia Diagnostic Criteria (FMS), Symptom Impact Questionnaire (SIQR), Patients Global Impression of Change (PGIC), Brief pain inventory (BPI), Medical Outcome Study Sleep Scale (MOS) questionnaires, and Multidimensional Assessment of Fatigue (MAF), Common Terminology Criteria for Adverse Events (CTCAE) v5., European Organization for Research and Treatment of Cancer Quality of Life Questionnaire-CIPN twenty-item scale (EORTC-CIPN20), Utah Early Neuropathy Scale (UENS), European Organization for Research and Treatment Core Quality of Life questionnaire (EORTC-QLQC30).

Peripheral Neuropathy: Peripheral neuropathy will be assessed at BL, 4W, and 8W using DPNCheck (Neurometrix, Woburn, MA, USA). This is a noninvasive device which will measure conduction velocity and amplitude. Vibration perception threshold (VPT) will also be used to assess sensitivity of patients' lower extremity.

Optional assessments: Oxygen Level Assessment: Oxygen saturation will be measured using a pulse oximeter.

Gait assessment: Gait performance will be assessed using a validated body worn sensors (LegSys, Biosensics LLC, USA). The device uses five sensor modules respectively attached to right and left anterior shins, right and left anterior thighs, and posteriorly to the lower back. Based on the subject's height and using a two-link inverse pendulum model the following spatio-temporal gait parameters will be estimated: velocity, stride length, stride time, double support, single support, stride-to-stride variability, and gait initiation. In addition, the center of mass (COM) range of motion during walking will be calculated by using the data from the sensor attached to lower-back. Gait will be assessed over a distance of 20 meters under 2 conditions: (1) walking at habitual speed (2) walking at maximum speed (fast walking).

Balance assessment: Balance will be quantified using validated body worn sensors (BalanSens, Biosensics LLC, USA). The system measures ankle and hip motion in three dimensions (3D), 2D COM sway as well as RCI in ML and AP directions. Balance will be assessed according to Romberg protocol during eyes-open and eyes-closed condition during double, semi-tandem, and full tandem stances. For those patients who may not be able to do gait and balance test, we will use alternative upper extremity test, which according to our previous studies provide similar results as gait bit do not require subject to walk. (See Attachment)

Upper Extremity Frailty Test: Investigators will measure arm motion from each participant by implementing validated wearable inertial sensors (e.g. accelerometer, gyroscope) such as LegSys (Biosensics LLC, MA, USA), Frailty Meter (Biosensics LLC, MA, USA), or BioStamp (MC10, MA, USA). These inertial sensors will assess respectively kinematic of upper extremities (e.g., arm and shoulder) motion as well as joint coordination. We will be used at least 1 sensor attached on wrist to capture arm motion.

Physical Activity and Health Monitoring: The subject will be given a wearable device (PAMSys) and/or a smart watch (Vivosmart 4) that will be measuring several parameters including number of steps taken, duration of sitting, standing, walking and lying, time taken and number of transitions from sit to stand, and walking speed for a minimum of 48 hours. At the end of the specific visit, the subject will be given the device, if they are given PAMSys it will be attached to pendant to wear around the neck, otherwise they may wear the smart device on their wrist. Investigators will ask the subject to return the wearable device at study completion. Subjects will either return the device at their next research visit or be given a prepaid package to mail the device back.

Optional Questionnaires at each study visit: pain, weakness, sleep, quality of life, frailty, depression, life and space, beck anxiety scale, Katz-daily living, fatigue, and user acceptability.

The supervision of this study will be by pulmonary care specialists (Study #1), and cancer care specialists (study #2) and the location will be at Baylor College of Medicine McNair Campus.

Section G: Sample Size/Data Analysis

G1. Sample Size

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

Local: 60 Worldwide: 60

Please indicate why you chose the sample size proposed:

Convenient and selected based on available resources to demonstrate feasibility and the proof of concept effectiveness of TENS therapy for patients with NP. We plan to recruit 60 eligible subjects.

Study #1: 30 subjects Study #2: 30 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?

Independent t-test, U-test, or Chi-square (depends on type of variables) to compare between groups (AG, and PG for key baseline descriptors including demographics and relevant clinical characteristics. Those descriptors which show statistical

significant difference, baseline value of the outcomes measured in the model, and other variables that are deemed to be prognostic, 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.

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 EMG device will detect level of fatigue and based on that we will determine the length of the sessions.

The devices and technologies are 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 band or hydrogel pads on their legs. We will inform the subject to please notify the investigators if the band or hydrogel pads are 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 TENS therapy could be: (1) Skin related discomfort, such as tingling or (2) Skin reaction to hydrogel pads (irritation, rash).

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 peripheral neuropathy device (DPNCheck) has minimal risks to the subjects as it is non-invasive, safe, non-toxic, and non-ionizing. The subjects may feel a tingling sensation during its use, and if it is too intense, the research staff will stop the test.

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.

Study #1: We cannot promise any benefit to you or to others from you joining this research. However, the proposed treatment may assist in reducing symptoms of PACS associated FM. In addition, the participation in this study may help the investigators better understand how COVID-19 may impact cause neuropathy and how to best help these patients to recover from NP. This may allow physicians to provide personalized care by monitoring chronic pain caused by PASC.

Study #2: We cannot promise any benefit to you or to others from you joining this research. However, the proposed treatment may assist in reducing symptoms of pain associated to your chemotherapy. In addition, the participation in this study may help the investigators better understand how TENS help patients with CIPN. This may allow physicians to provide personalized care by monitoring chronic pain caused by CIPN.

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

As described above, this type of work may allow physicians to provide more personalized care for patients with NP.

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

Study #1:

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 TENS, skin allergy to the TENS band, risk associated with electrical mal-function of the TENS device, and other unknown risks. All TENS devices will be checked before any use to minimize the risk associated with electrical malfunction. All TENS devices are FDA approved for the purpose of temporary relief of pain. However, these devices have not been used before for purpose of managing COVID-19 side effects like the purpose of this study. 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 COVID-19. The peripheral neuropathy device (DPNCheck) has minimal risks to the subjects as it is non-invasive, safe, non-toxic, and non-ionizing. The subjects may feel a tingling sensation during its use, and if it is too intense, the research staff will stop the test.

Study #2:

The risk to participants of this study is considered to be minimal because all that is required is simple walking in a controlled environment with a research staff present (all subjects will be mobile, and walking as a regular part of their activities of daily living this research routine will not place them at higher risk than normal activities of daily living). No more risk of harm or discomfort is associated with these tests than the discomfort normally incurred while walking or during normal muscle stretching. The peripheral neuropathy device (DPNCheck) has minimal risks to the subjects as it is non-invasive, safe, non-toxic, and non-ionizing. The subjects may feel a tingling sensation during its use, and if it is too intense, the research staff will stop the test.

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.

Study #1 Subjects will be recruited from the Post-COVID-19 Clinic (McNair Campus, BCM St Luke's, Houston, TX, USA). 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.

Study #2: Subjects will be recruited from the Duncan Cancer Center (McNair Campus, BCM St Luke's, Houston, TX, USA). 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.

Informed Consent Form signatures will be obtained according to standard Baylor IRB regulations. The PI/research staff will review the study and consent document with the participant, asking questions to gauge comprehension, and answering the subject's questions and concerns. Once the subject completes reviewing the consent and all questions are addressed, the subject and the PI/designee will sign the ICF. The subject will receive a paper copy of the ICF to review. The signed consent form will be stored in the research facility to which only authorized personnel have access.

Reconsent plan (if needed): Currently enrolled subjects will be reconsented at their next in-person, follow up visit. The consent form will be explained and all questions will be answered.

Are foreign language consent forms required for this protocol?
No

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?
No

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 #:
Yes

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 B10.401.

How will such physical research data be secured?
Physical 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:
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.
The planned data to be sent to the sponsor will be non-sensitive (such as: time of device usage, subjective response to device, adverse events experienced during the study, etc), and will be de-identified. This data will be transferred via secured emails. The BCM PI will contact BCM SPO to determine whether a DTA/DUA/MTA is required for the proposed data transfers. Prior to sharing any data externally, these agreements will be established if determined necessary by SPO.

Will you obtain a Certificate of Confidentiality for this study?
No

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

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.
All clinical/standard procedures will be billed to the subject's insurance. These include, physician visits, debridement, medications prescribed by physician.

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:

150

Distribution Plan:

For taking part in this research, the subject may be paid a total of $150. Their compensation will be broken down as follows:

Subjects will be paid $50 for every visit completed visit. There are a total of up to 3 visits. Payments will be done using the ClinCard method. Their SSN will be requested for the research team to issue the payments. The research study will also cover the subject's parking or transportation expenses to go to their research visits.

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: Quell TENS device

Device 2: Trigno Wireless EMG System

Device 3: Snapshot NIR

Device 4: Pulse Oximeter

Device 5: Legsys

Device 6: Frailty Meter

Device 7: Balansens

Device 8: Pamsys

Device 9: Vivosmart 4

Device 10: DPNCheck

Section Q: Consent Form(s)

Transcutaneous Electrical Nerve Stimulation for Lower Extremity in Patients with Post Acute COVID-19 Syndrome

Transcutaneous Electrical Nerve Stimulation for Lower Extremity in Patients with Chemotherapy Induced Peripheral Neuropathy

Section R: Advertisements

None