BU Charles River IRB
Application Form (Full Board and Expedited Review)

SECTION A: PROTOCOL AND CONTACT INFORMATION

Protocol Title:	Next-Generation Neuroprostheses for the Diagnosis and Management of Locomotor Deficits
Principal Investigator **(Name, degrees, licenses, etc.):** ☐ Mr. ☐ Ms.	Lou Awad (PT, DPT, PhD)
Department/School:	Department of Physical Therapy & Athletic Training; College of Health & Rehabilitation Sciences: Sargent College
BU Mailing Address:	635 Commonwealth Ave, Boston, MA 02215
Email:	louawad@bu.edu
Telephone:	617-358-3043
Additional Contact Person:	Lillian Ribeirinha-Braga (Research Coordinator)
Email:	lcrbraga@bu.edu
Telephone:	617-500-3645
☒ YES **(REQUIRED)**	I confirm that I qualify to serve as the Principal Investigator of this study and am in compliance with the following policies: http://www.bu.edu/researchsupport/compliance/human-subjects/

SECTION B: FUNDING

Provide information regarding **ALL** funding sources for this project, including existing funding, pending funding, and funding that has been applied for to support this research.

Please check all that apply:	
☒	This research is funded
☒	Funding has been requested Have you received Just In Time (JIT) Notification? ☐ Yes ☒ No NOTE: Once the funding has been awarded, submit an amendment to the IRB to add the funding source
☐	Research is not funded

If the research is funded or funding has been requested, it is REQUIRED that you complete the box below. If you don't have an award #, please state that in the box below. If you have multiple funding sources, add additional boxes as necessary.

Sponsor Name	Boston University Neuromotor Recovery Laboratory
Title of Grant/Proposal	A soft, hybrid robotic exosuit neuroprosthesis (reNeu) for post-stroke gait assistance and rehabilitation
Sponsor Award # **(REQUIRED)*** *If Award is pending, put "pending".	Not applicable

YES	NO	
☒	☐	Is Boston University the Prime Awardee of the grant?
☐	☒	Is Boston University receiving a sub-award? Name of Prime Recipient:
☐	☒	Is the research being supported by an Industry Contract or Clinical Trial Agreement?

***NOTES:**

- Provide a copy of the grant application, funding proposal, contract/agreement, scope of work, or sub-award agreement supporting the research. If an award is pending, once the funding has been awarded, submit an amendment to the IRB to add the funding source.
- If this research study is for your dissertation, provide a copy of your prospectus (if available).

SECTION C: CONFLCT OF INTEREST

☒ YES **(REQUIRED)**	I confirm that **ALL** those responsible for the design, conduct, or reporting of the proposed research, including at minimum, all Senior/key personnel in the grant application, have completed the financial interest disclosure forms, submitted them to the COI office, and completed training as dictated at: http://www.bu.edu/researchsupport/compliance/conflicts-of-interest/, and as provided under *the Boston University Investigator Conflicts of Interest Policy for Research.* **NOTE: You must attach a copy of the PI's COI submission confirmation email. COI submission confirmation emails for all other study staff should be maintained at the research site.**
Of the financial interest disclosure forms submitted, did you check "yes" to any of the questions on either the FIND1 or NONFIND1 form? ☐ Yes* ☒ No	

***If you checked "yes" to any of the questions on either the FIND1 or NONFIND1 form, the IRB Director will contact the COI office to obtain the disclosure information.**

SECTION D: TYPE OF REVIEW

For Guidance regarding Type of Review please refer to the CRC IRB website

I. **FULL BOARD** ☒
Please refer to the CRC IRB website for Full Board submission deadlines and meeting dates.

II. **EXPEDITED** ☐
In order to qualify for expedited review, the study must be no more than minimal risk* **AND** must fall into one of the categories below. Check all that apply:

1. ☐ Clinical studies of drugs and medical devices only when an investigational new drug application (IND) or investigational device exemption application (IDE) is not required

2. ☐ Collection of blood samples by finger stick, heel-stick, ear stick, or venipuncture as follows:
   a. From healthy, nonpregnant adults who weigh at least 110 pounds. For these subjects, the amounts drawn may not exceed 550 ml in an 8-week period and collection may not occur more frequently than 2 times per week; or
   b. From other adults and children, considering the age, weight, and health of the subjects, the collection procedure, the amount of blood to be collected, and the frequency with which it will be collected. For these subjects, the amount drawn may not exceed the lesser of 50 ml or 3 ml per kg in an 8-week period and collection may not occur more frequently than 2 times per week.

3. ☐ Prospective collection of biological specimens for research purposes by noninvasive means. Examples include hair and nail clippings, saliva or cheek swabs, sweat, etc.

4. ☒ Collection of data through noninvasive procedures (not involving general anesthesia or sedation) routinely employed in clinical practice, excluding procedures involving x-rays or microwaves. Where medical devices are employed, they must be cleared/approved for marketing. Examples:
   - Physical sensors that are applied either to the surface of the body or at a distance and do not involve input of significant amounts of energy into the subject or an invasion of the subject's privacy
   - Weighing or testing sensory acuity
   - Magnetic resonance imaging
   - Electrocardiography, electroencephalography, thermography, detection of naturally occurring radioactivity, electroretinography, ultrasound, diagnostic infrared imaging, doppler blood flow, and echocardiography
   - Moderate exercise, muscular strength testing, body composition assessment, and flexibility testing where appropriate given the age, weight, and health of the individual

5. ☒ Research involving materials (data, documents, records, or specimens) that have been collected, or will be collected solely for non-research purposes (such as medical treatment or diagnosis)

6. ☒ Collection of data from voice, video, digital, or image recordings made for research purposes.

7. ☐ Research on individual or group characteristics or behavior (including research on perception, cognition, motivation, identity, language, communication, cultural beliefs or practices, and social behavior) or research employing survey, interview, oral history, focus group, program evaluation, human factors evaluation, or quality assurance methodologies.

Note: The IRB will make the final determination on the Type of Review

***Minimal risk** means that the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests.

SECTION E: STUDY STAFF AND HUMAN SUBJECTS TRAINING

List **ALL** current members of the research team in the table below. Add more rows as necessary.

STUDENT RESEARCH:
The Faculty Advisor must be listed as a co-investigator in this section and must complete the Human Subjects training requirements. Faculty Advisors are responsible for reviewing the IRB application, agreeing to serve as the Co-PI for this study with the student and are responsible for the ethical conduct of this student's human subjects research. Faculty Advisors must sign this Application prior to it being submitted to the IRB.

BU CHARLES RIVER CAMPUS (CRC) INVESTIGATORS/STUDY STAFF
Note: Boston University Medical Campus (BUMC) investigators/study staff should be listed in the NON-BU INVESTIGATOR/STUDY STAFF section

Name, Degree, Department, School	**Study Role (e.g. co-investigator, research coordinator, research assistant, project manager, lab manager)**	***Training**
Louis Awad (PT, DPT, PhD) Department of Physical Therapy and Athletic Training, College of Health & Rehabilitation Science: Sargent College, Boston University	Principal Investigator	☒ CITI Most Recent Date Completed: 01/03/2020
Terry Ellis (PhD, PT, NCS) Department of Physical Therapy and Athletic Training, College of Health & Rehabilitation Science: Sargent College, Boston University	Co-Investigator	☒ CITI ☐ Other**: HIPAA training completed 9/2/15 Most Recent Date Completed: 07/19/2019
Julie Starr (PT, DPT, CCS) Department of Physical Therapy and Athletic Training, College of Health & Rehabilitation Science: Sargent College, Boston University	Co-Investigator	☒ CITI Most Recent Date Completed: 05/28/2019
Regina Sloutsky Neuromotor Recovery Laboratory	Research Physical Therapist	☒ CITI Most Recent Date Completed: 06/30/2020

Teresa Baker Neuromotor Recovery Laboratory	Research Physical Therapist	☒ CITI Most Recent Date Completed: 06/25/2020
Anna Roto Neuromotor Recovery Laboratory	Research Assistant	☒ CITI Most Recent Date Completed: 08/18/2020
Andy Alvarez Neuromotor Recovery Laboratory	Research Assistant	☒ CITI Most Recent Date Completed: 06/27/2020
Ashlyn Aiello Neuromotor Recovery Laboratory	Research Assistant	☒ CITI Most Recent Date Completed: 04/16/2018
Ashley Collimore Neuromotor Recovery Laboratory	Research Assistant	☒ CITI Most Recent Date Completed: 06/13/2018
Lillian Ribeirinha-Braga Neuromotor Recovery Laboratory	Research Assistant	☒ CITI Most Recent Date Completed: 07/08/2019
Dheepak Arumukhom Revi Neuromotor Recovery Laboratory	Research Assistant	☒ CITI Most Recent Date Completed: 09/11/2019
Michail Theofanidis Neuromotor Recovery Laboratory	Research Assistant	☒ CITI ☐ Other**: Most Recent Date Completed: 05/14/2020
Marc Mitjans I Coma Neuromotor Recovery Laboratory	Research Assistant	☒ CITI ☐ Other**: Most Recent Date Completed: 09/18/2018
Johanna Spangler Neuromotor Recovery Laboratory	Research Physical Therapist	☒ CITI ☐ Other**: Most Recent Date Completed: 9/15/2020
Aaron Horwin Neuromotor Recovery Laboratory	Research Assistant	☒ CITI ☐ Other**: Most Recent Date Completed: 5/9/2021
Tzu Yu Liu Neuromotor Recovery Laboratory	Research Assistant	☒ CITI ☐ Other**: Most Recent Date Completed: 05/02/2021

Kevin Senanayake Neuromotor Recovery Laboratory	Research Assistant	☒ CITI ☐ Other**: Most Recent Date Completed: 8/30/2021
Nicole Geraghty Neuromotor Recovery Laboratory	Research Assistant	☒ CITI ☐ Other**: Most Recent Date Completed: 8/29/2021
Ryan Faiz Neuromotor Recovery Laboratory	Research Assistant	☒ CITI ☐ Other**: Most Recent Date Completed: 08/20/2021
Nick Wendel Neuromotor Recovery Laboratory	Research Physical Therapist	☒ CITI ☐ Other**: Most Recent Date Completed: 8/27/2021
Kara Lydzinski Neuromotor Recovery Laboratory	Research Assistant	☒ CITI ☐ Other**: Most Recent Date Completed: 09/23/2021

- *For more information regarding the Human Subjects Training Policy, refer to the 'Training' section of the Policies & Guidance section IRB website.
- **If the investigator/study staff did not complete CITI, you must submit a copy of his/her training certificate.

NON-BU INVESTIGATORS/STUDY STAFF* ☐ **N/A**

Note: BUMC and BMC staff are considered non-BU staff and should be listed in this section. Add more rows as necessary. All the columns in the box below must be completed. In addition, you must complete the box that follows with a description of the activities for each staff member.

Name, Degree, Institution	Study Role	Staff Information	Will IRB Approval be Obtained from Non-BU Institution?
Conor Walsh (PhD) John A. Paulson School of Engineering and Applied Sciences, Harvard University	Co-Investigator	1. Will this staff interact with subjects? ☒ Yes ☐ No 2.Will this staff have access to identifiable information? ☒ Yes ☐ No	☐ Yes (provide copy of IRB approval letter): ☒ No (provide reason): See note in box below.

		3.Is the work that the staff will complete related to their role or coursework at their institution.? ☒ Yes ☐ No	
Paolo Bonato (PhD) Spaulding Rehabilitation Hospitals	Co-Investigator	1. Will this staff interact with subjects? ☒ Yes ☐ No 2.Will this staff have access to identifiable information? ☒ Yes ☐ No 3.Is the work that the staff will complete related to their role or coursework at their institution.? ☒ Yes ☐ No	☐ Yes (provide copy of IRB approval letter): ☒ No (provide reason): See note in box below.
Dabin Choe John A. Paulson School of Engineering and Applied Sciences, Harvard University	Research Assistant	1. Will this staff interact with subjects? ☒ Yes ☐ No 2.Will this staff have access to identifiable information? ☒ Yes ☐ No 3.Is the work that the staff will complete related to their role or coursework at their institution.? ☒ Yes ☐ No	☐ Yes (provide copy of IRB approval letter): ☒ No (provide reason): See note in box below.
Benjamin Shih Harvard University	Postdoctoral Research Fellow	1. Will this staff interact with subjects? ☒ Yes ☐ No 2.Will this staff have access to identifiable information? ☒ Yes ☐ No	☐ Yes (provide copy of IRB approval letter): ☒ No (provide reason): See note in box below.

		3.Is the work that the staff will complete related to his/her role or coursework at his/her affiliate institution.? ☒ Yes ☐ No	
Dorothy Orzel Harvard University	Functional Apparel Designer	1. Will this staff interact with subjects? ☒ Yes ☐ No 2.Will this staff have access to identifiable information? ☒ Yes ☐ No 3.Is the work that the staff will complete related to his/her role or coursework at his/her affiliate institution.? ☒ Yes ☐ No	☐ Yes (provide copy of IRB approval letter): ☒ No (provide reason): See note in box below.

*If IRB approval will be obtained from the affiliate site, only list the lead investigator from the affiliate on this form.

The box below must be completed. Include a summary for each staff listed in the above box. If any of the investigators listed on this form are not affiliated with BU, provide a summary of the study activities that he/she will conduct. If IRB approval is not being obtained at the affiliate institution, provide an explanation. **NOTE: Non-BU staff may be required to complete an Individual Investigator Agreement (IIA). The IRB will notify you if this form is required.**

Conor Walsh may be present at data collections to observe device performance and interact with participants to ask questions. Additionally, Conor Walsh may look at the collected biomechanical and system data in order to advise further technical development of the device.

Paolo Bonato may be present at data collections to observe device performance and interact with participants to ask questions and provide further clinical guidance in device development.

Dabin Choe will be present at data collections to monitor the device and ensure the device is working correctly. Additionally, Dabin Choe will assist in the collection and processing of biomechanical, clinical, and technical data to inform further development of the device.

Benjamin Shih may be present at data collections to observe device performance and interact with participants to ask questions to guide the translation of the device to community and commercial use.

Dorothy Orzel may be present at data collections to observe participant interactions with the device and to assess user needs to inform developments for functional apparel designs.

*** IRB approval is not being obtained at Harvard University or Spaulding Rehabilitation Hospital due to BU being the lead research site and prior guidance received from the IRB on the preference for single site IRB review of human subjects research. ***

REQUIRED GOOD CLINICAL PRACTICE TRAINING FOR NIH-FUNDED CLINICAL TRIALS

YES*	NO	NIH-FUNDED CLINICAL TRIALS
☐	☒	Is your study NIH-Funded AND meet the definition of a clinical trial as defined in the NIH policy?

SECTION F: LOCATION OF THE RESEARCH

YES*	NO	
☒	☐	Will this research take place at sites/locations other than Boston University? **Note:** If the research will take place at Boston University, state the location (Building and Room number):

*If **YES,** please complete the boxes below

NOTE: You are responsible for obtaining permission/letters of support for research conducted off-site. This may include locations such as schools, workplaces, community organizations, etc. You must submit the letters/documentation of support with this application.

Institution Name and Address (if known)	**Describe Involvement (recruiting, consenting, data analysis, etc.) of the site. If the site or the site staff is not involved (engaged)[1] in research procedures, state NONE.**	**IRB/Ethics Approval/Site Permission Attached? If no[2], explain the plan to obtain this approval. If the site is not engaged in the research, you do not need to complete the box.**
Spaulding Rehabilitation Hospital (300 1st Ave., Charlestown, MA)	Recruiting, consenting, data collection and analysis, administration of primary and secondary screening, and testing visits	SMART IRB submission will be completed once the protocol has been approved.
Harvard University (150 Western Ave, Boston MA 02134; and Allston Science and Engineering Campus)	Recruiting, consenting, data collection and analysis, administration of primary and secondary screening, and testing visits	SMART IRB submission will be completed once the protocol has been approved.

[1]Guidance on Engagement of Institutions in Human Subjects Research
[2]If IRB approval will not be obtained at the site, describe the IRB oversight arrangements here:

YES*	NO	
☒	☐	Is the off-site location requesting that the Boston University IRB review the protocol in place of local IRB review? If **YES**, complete the Single IRB Review Form "Boston University is Institution A"

YES*	NO	
☒	☐	Is the BU PI the lead investigator **OR** is BU the lead site for this research? **Note: This box only needs to be completed if the off-site location is engaged in the research.**

		***If YES**, provide the following information in this box:
		• The plan for collection and management of data from all the sites
		  ○ Data collected at Boston University, Harvard University, and Spaulding Rehabilitation Hospital will be encrypted and password-protected and stored on either a private network drive, SharePoint folder, or REDCap. The private network drive will be used for backup storage. Identifiable information, project documents, and de-identified biomechanical and photo/video data will be stored on the SharePoint folder, which is accessible only by the research team. Clinical documents and surveys will be scanned and uploaded to REDCap. Any documents that are hand-written will be scanned and transported back to BU or shredded once electronically uploaded.
		• The plan for reporting and evaluating:
		  ○ Unanticipated problems
		  ○ Serious and/or continuing non-compliance
		  ○ Suspensions and terminations of research
		  ○ Interim results
		  ○ Protocol modifications
		***** All reporting will be directed to both the individual site PIs and the overall project PI, either at a biweekly team meeting or immediately if the problem or non-compliance is serious or urgent. *****
		• The name of the Principal Investigator from each site
		  ○ Boston University: Lou Awad
		  ○ Harvard University: Conor Walsh
		  ○ Spaulding Rehabilitation Hospitals: Paolo Bonato

YES*	NO	
☐	☒	Will this research be conducted outside of the United States? If **YES**, complete the International Research Form.

SECTION G: STUDY SUMMARY

Summarize the study in lay language (do not copy from the grant/scope of work/proposal, etc.). This summary should include the research design, purpose, objectives, research question, hypothesis, and any relevant background information.

Do not include a list of citations in this section. Please limit this section to no more than 300 words.

Stroke is the leading cause of disability worldwide, resulting in nearly $35B annual costs to the US alone. The restoration of walking is a primary goal of post-stroke recovery, yet existing rehabilitation approaches and assistive technologies fail to sufficiently ameliorate post-stroke gait deficits, resulting in poor long-term outcomes. Muscles are biological motors that have been optimized for bipedal locomotion. Despite their weakened state, the muscles of people post-stroke retain a remarkable capacity to produce large magnitudes of force that patients are unable to voluntarily access during functional activities. Our team of engineers, clinicians, and scientists are working to develop a textile-based neuroprosthesis, the reNeu, that uses a clothing-like human-device interface to harness the power of electricity to bypass the damaged neural circuitry and exploit the residual force generating capacity of post-stroke muscle. In addition to having an immediate effect when worn[1–4], our past research has shown that long-term use of a neuroprosthesis during gait training can lead to durable gait restoration that is not dependent on continued use of the stimulation[5–7].

The aims of this project are two-fold: 1) to create a device that uses electrical stimulation to improve walking after stroke; and 2) to integrate the electrical stimulation device in Aim 1 with a previously developed soft robotic exosuit to optimize the restorative potential of wearable rehabilitation devices.

The electrical stimulation device being developed in Aim 1 (referred to as reNeu) delivers small bursts of electrical current to enable muscles to perform body movements, a technique called functional electrical stimulation (FES). The reNeu will use wearable sensors to detect an individual's unique gait pattern. These sensors, integrated with flexible apparel, will enable electrical stimulation to be delivered adaptively to the muscles of the affected lower limb based on an individual's specific gait pattern. Initial developments of the reNeu will focus on assistance of the ankle, whereas further developments will progress to assistance of the knee, hip, or a combination of lower limb joints.

We believe that both the level and timing of stimulation assistance will affect walking quality and hypothesize that individualized adaptive assistance will improve walking quality compared to fixed assistance (i.e. same level and timing for all individuals). More specifically, we hypothesize that changes in plantarflexor FES will alter the forward propulsion and walking speed of individuals post-stroke. To test the hypotheses, participants will walk with several different stimulation profiles, i.e. combinations of stimulation level (low-high) and timing (early-late). Initial development studies will be performed on the treadmill to determine specific biomechanical mechanisms being altered by the reNeu and will inform further adjustments of stimulation profiles to best assist the user. Testing will progress from treadmill to overground to assess feasibility of using the reNeu in a community setting, and training studies using the reNeu will identify potential therapeutic benefits of the device.

For Aim 2 of the study, the aforementioned stimulation device will be integrated into a soft robotic exosuit previously designed by members of the lab and its affiliates. This new FES-integrated exosuit will combine neuromuscular assistance from FES with mechanical assistance provided by the exosuit. We hypothesize that FES-integrated exosuits will improve walking quality better than either device alone, by improving walking speed and distance while reducing overall energy expenditure. We also hypothesize this hybrid device will reduce device energy costs (e.g. motor power, electrical current) compared to either device alone, by modulating between FES (neuromuscular) and exosuit (mechanical) assistance in response to muscle fatigue and required energy for a particular functional task. These hypotheses will be verified by studies comparing walking with the stimulation device (from Aim 1), the exosuit, and the FES-integrated exosuit. Muscle fatigue and system power consumption will be monitored, as well as metabolic expenditure and biomechanical measures.

Activities performed in this study will be categorized into one of three research phases. Phase 1 consists of Device Development visits which include walking with and without the FES device. These visits are standalone visits to inform development decisions from the research team. Phase 2 consists of Device Testing visits which include walking with and without the FES device with a combination of assistance profiles. These visits may span multiple sessions to validate device developments. Phase 3 consists of Training Studies which include walking with and without the FES device with the intent of providing rehabilitative effect. These visits will span multiple sessions at a pre-defined frequency to provide standardized training for all participants and evaluate long-term rehabilitative effects of the device. Please see Section L for more detail on research phases.

Individuals enrolled in this study will be categorized into one of two groups. Group 1 participants must be currently undergoing active rehabilitation under the guidance of a therapist/physiatrist. This rehabilitation must be active at the time of secondary screening and independent of procedures conducted in this study. Participants identified as Group 1 will remain in Group 1 for as long as their clinical rehabilitation is active. Group 2 participants are those who are not undergoing active rehabilitation at the time of the secondary screening visit and throughout their participation in the study. If a Group 2 participant begins clinical rehabilitation while participating in the study, that participant will become a Group 1 participant. Both Group 1 and Group 2 participants are eligible to participate in any of the activities in the three research phases. Please see Section I for more detail on participant groups.

References:

1. Awad LN, Kesar TM, Reisman D, Binder-Macleod SA. Effects of repeated treadmill testing and electrical stimulation on post-stroke gait kinematics. Gait & posture. 2012.
2. Kesar TM, Perumal R, Jancosko A, Reisman DS, Rudolph KS, Higginson JS, Binder-Macleod SA. Novel patterns of functional electrical stimulation have an immediate effect on dorsiflexor muscle function during gait for people poststroke. Physical therapy. 2010;90(1):55–66.
3. Hakansson NA, Kesar T, Reisman D, Binder-Macleod S, Higginson JS. Effects of fast functional electrical stimulation gait training on mechanical recovery in poststroke gait. Artificial organs. 2011;35(3):217–20.
4. Kesar TM, Perumal R, Reisman DS, Jancosko A, Rudolph KS, Higginson JS, Binder-Macleod SA. Functional electrical stimulation of ankle plantarflexor and dorsiflexor muscles: effects on poststroke gait. Stroke; a journal of cerebral circulation. 2009;40(12):3821–7.

5. Awad LN, Reisman DS, Kesar TM, Binder-Macleod SA. Targeting paretic propulsion to improve poststroke walking function: A preliminary study. Archives of Physical Medicine and Rehabilitation. 2014;95(5):840–848.
6. Awad LN, Reisman DS, Pohlig RT, Binder-Macleod SA. Identifying candidates for targeted gait rehabilitation after stroke: better prediction through biomechanics-informed characterization. Journal of neuroengineering and rehabilitation. 2016;13(1):84.
7. Awad LN, Reisman DS, Pohlig RT, Binder-Macleod SA. Reducing The Cost of Transport and Increasing Walking Distance After Stroke: A Randomized Controlled Trial on Fast Locomotor Training Combined With Functional Electrical Stimulation. Neurorehabilitation and neural repair. 2016;30(7):661–70.

SECTION H: RESEARCH METHODS AND ACTIVITIES (Check all that apply)

☒	Collection of audio, video, digital, or image recordings
☐	Biological samples → Complete Biological Samples Form Examples: blood, hair, cheek swab, urine, tears, saliva, etc.
☐	Collection of data that may be sensitive and if disclosed could put subjects at risk for legal or social harms. (e.g. Illegal behaviors, HIV status, psychiatric illness, information related to sexual behaviors, etc.
☐	Coordinating Center/Lead Site
☐	Deception
☒	Devices → Complete Devices Form
☐	Drugs → Complete Drugs Form
☐	Ethnographic: The study of people in their own environment through the use of methods such as participant observation and face-to-face interviewing
☐	Focus Groups
☐	Genetics Testing → Complete Genetics Form
☐	MRI
☐	Placebo
☐	Pregnancy Testing
☒	Randomization
☒	Surveys, interviews, questionnaires

☐	Secondary Data Analysis
☒	Other (please describe): Common clinical examination approaches will be used to measure cognition, sensorimotor function, and walking ability. Additionally, non-invasive measurements of biomechanical function will be made using common movement analysis tools such as an instrumented treadmill, forceplates, optical motion tracking cameras, and motion tracking sensors attached to the body (see section L for more details).

SECTION I: PARTICIPANT POPULATION

Provide the Number of Participants to be Enrolled. If you have sub-groups or more than one arm, please separate out these enrollment numbers. Note: Please account for participants who may drop out or be withdrawn from the study. Anyone who signs a consent form is considered to be enrolled in the research regardless of whether they complete any study procedures.

This study has a target enrollment of up to 40 participants who have had a stroke and 40 participants who have not had a stroke. Participants with post-stroke hemiparesis will participate in the patient-in-the-loop development of a novel neuroprosthesis that harnesses the power of electricity to exploit the residual force generating capacity of post-stroke muscles during functional activities. These participants may be enrolled into one of two groups (depending on whether they are in an active rehabilitation program) and may participate in as many of the three phases of this study (listed below) as they wish. Healthy participants will also participate in the patient-in-the-loop development of this novel neuroprosthesis and will be enrolled into a healthy participant group. Healthy participants may partake in device development and testing phases of this study. Regardless of participant group or research phase, the target enrollment for the entire study across all approved research sites will not exceed a total of 80 participants. Participants who complete screening at one research site will complete subsequent testing at the same location, or at the testing site that is most convenient for that participant. Participants may switch study sites if they wish, however all visits for a particular sub-study (e.g. a clinical training study in Phase 3) must be conducted at the same site.

Participant Groups:

- Group 1: participants post-stroke currently undergoing rehabilitation under the guidance of a therapist/physiatrist (independent of research procedures for this study). Rehabilitation program must be active at the time of the secondary screening visit.
- Group 2: participants post-stroke not currently undergoing rehabilitation under the guidance of a therapist/physiatrist (independent of research procedures for this study).
- Healthy: participants who have not had a stroke

Research Phases:

- Phase 1: Device Development
- Phase 2: Device Exposure & Testing
- Phase 3: Clinical Training Studies

Check all categories that apply to your participant population:

☒	Adults
☐	Children (< 18 years of age)
☐	Adults with Limited Decision-Making Capacity
☐	Non-English Speaking
☐	Prisoners
☒	BU Employees
☒	BU Students
☐	Wards of the state
☐	Other (please describe):

If a population other than 'Adults' has been checked, describe the additional safeguards that have or will be put in place to protect those individuals, and provide the rationale for including this population in the research study. For information on additional protections, please see the 'Supplemental Guidance' section of the CRC IRB webpage.

BU students and employees may be enrolled if ALL the following conditions are met:

- The student/employee is aware that participation in the study is completely voluntary and will not be used to sway benefits or employment status
- The student/employee has had ample time to read over the consent form
- The investigator taking informed consent must be someone other than the PI and must not be in a senior or supervisory role to the student/employee
- The investigator taking informed consent must be trained in taking consent

No student/employee can consent themselves to participate in this interventional study. Any BU employee, student, or staff *who is a direct member* of any of the research labs leading this study may participate in the study but will not be compensated. BU students who are not directly affiliated with any of the research labs leading this study may participate in the study and will be compensated for their time.

Eligibility Criteria

Inclusion Criteria (Healthy):

- Age 18-80 years old
- No known, self-reported neuromotor disorder, gait pathology, or comorbidity that would interfere with participation (musculoskeletal, cardiovascular, neurological, skin, and vasculature conditions)

Inclusion Criteria (Stroke):

- Age 18-80 years old
- Diagnosis of a stroke
- Observable gait deficits (confirmed at secondary screening visit)
- Independent ambulation (with or without an assistive device) for at least 30 meters (confirmed at secondary screening visit)
- Full range of motion in ankle (confirmed at secondary screening visit)
- Ability to follow a 3-step command (confirmed at secondary screening visit)
- Resting heart rate between 40-100 bpm (confirmed at secondary screening visit)
- Resting blood pressure between 90/60 and 170/90 mmHg (confirmed at secondary screening visit)
- Provide HIPAA Authorization to allow communication with healthcare provider as needed during the study period
- Medical clearance by a physician

Additional Inclusion Criteria (Group 1: active rehabilitation):

- Currently undergoing active rehabilitation (independent of research procedures for this study) under the guidance of a therapist/physiatrist.

Additional Inclusion Criteria (Group 2: no active rehabilitation):

- Not currently receiving active rehabilitation (independent of research procedures for this study) under the guidance of a therapist/physiatrist.

Exclusion Criteria (Healthy):

Note: Exclusion criteria are the specific criteria which would disqualify an individual from participating in the study, not simply the opposite of the inclusion criteria.

- Diagnosed or self-reported neuromotor disorder or gait pathology
- Serious co-morbidities that may interfere with ability to participate in this research (musculoskeletal, cardiovascular, neurological, skin, and vasculature conditions)

Exclusion Criteria (Stroke):

Note: Exclusion criteria are the specific criteria which would disqualify an individual from participating in the study, not simply the opposite of the inclusion criteria.

- History of lower extremity joint replacement (i.e. hip, knee, ankle)
- Severe aphasia and/or speech/language disorder, limiting ability to express needs and comprehend instructions
- Shows signs of neglect or hemianopia
- Serious comorbidities that may interfere with ability to participate in the research (e.g. musculoskeletal, cardiovascular, pulmonary)
- Metal implants, pacemakers, and/or similar implantable devices that could be affected by the FES
- Pressure ulcers or skin wounds located near human-device interface sites
- More than 2 unexplained falls in the previous month

SECTION J: RECRUITMENT

Provide a summary of the recruitment process, including who will recruit, when and where recruitment will occur, and how subjects will be identified

Submit all recruitment materials (e.g. advertisements, brochures, flyers, letters/e-mails, scripts, etc.) as separate documents in either Word or PDF format.

All investigators and research assistants will be involved in recruitment. Recruitment may occur via email (e.g., using IRB-approved language), IRB-approved flyers, promotional videos, or word of mouth through the following:

a. Clinicians at clinics, centers, and institutions with whom the investigators have developed collaborating relationships (e.g., Spaulding Rehabilitation Hospital, the Wyss Institute at Harvard University, Boston University's Center for Neurorehabilitation, New England Rehabilitation Hospital, Braintree Rehabilitation Hospital, and Boston Medical Center) may approach patients who they believe may be interested in participating in the study to inform them about the study.
    i. If these patients are interested, they will be provided with a research flyer which they can use to initiate contact with our study personnel.
b. Clinical research programs in the greater Boston area (e.g., Boston University's Aphasia Resource Center or Spaulding Rehabilitation Hospital's Stroke Research and Recovery Institute). These programs keep the contact information of patients who have had a diagnosed stroke and are interested in participating in research.
    i. Potential participants from these registries will be contacted via email or phone and asked if they wish to learn more about the study. If they are interested, they will be provided with a flyer that they can use to initiate contact with our study personnel.
c. Clinicians at rehabilitation hospitals and clinics in the greater Boston area will be provided with IRB-approved recruitment materials that they can make available to their patients.
    i. Patients that are interested can then use the information in these materials to initiate contact with our study personnel.
d. Study investigators may be invited to speak about the study to relevant organizations, including recreational/social programs, support groups, etc. Study flyers will be left at or provided to these locations for distribution.
    i. Individuals that are interested can then use the information on these flyers to initiate contact with our study personnel.
e. Information about the study may also be distributed via the following methods with prior approval from site staff/managers:
    i. Relevant buildings around Boston, at local businesses (e.g. coffee/sandwich shops), at local health or fitness centers
    ii. Electronic posting on lab website, research opportunities in clinical sites, and other relevant websites such as Craigslist or print papers such as the Boston Metro
    iii. Relevant social media sites or groups (e.g. Facebook)

In cases when an interested participant verbally indicates preference to be contacted by our study team, a member of the study team will contact the participant to provide more information about the study.

SECTION K: CONSENT AND ASSENT

Please refer to the consent and assent form templates on the IRB website when creating your consent/assent documents. The templates include the required elements of consent and will help to ensure that your consent/assent form meets the requirements of the federal regulations and the BU CRC IRB.

STUDENT RESEARCHERS must: 1) indicate in the consent form/information sheet/script that he/she is a student and 2) list the Faculty Advisor as a contact in the form/sheet/script.

Provide a summary of the consent process, including who will consent participants, when and where consent will occur. The summary should include, as appropriate, any waiting period between informing the prospective participant about the research and obtaining consent, such that the prospective participant or the legally authorized representative has sufficient opportunity to consider whether to participate, and steps taken to minimize coercion or undue influence. **Submit copies of all consent forms and scripts; materials should be submitted as separate documents in Word format.**
Potential participants will first undergo an initial phone or in-person screen to determine eligibility for the study. This screen will take under ten minutes and will be conducted by the trained study personnel listed in section E. During this first conversation, the goals of the project will be clearly described, and the potential participant will be asked questions to ascertain whether they meet the study's inclusion/exclusion criteria. If the participant meets the study criteria and remains interested in participating, they will be scheduled for a secondary screening visit. This visit will take place either at the Neuromotor Recovery Laboratory (100 Ashford Street, Boston, MA 02215), Spaulding Rehabilitation Center (300 1st Ave., Charlestown, MA), or Harvard University (150 Western Ave Boston, MA). If the participant prefers a virtual visit, this screening will be conducted virtually through BU Zoom or over the phone. These participants will be emailed the informed consent form to follow along as it is summarized by a research member. The participant will have the ability to sign the informed consent form via REDCap, a secure web-based platform for clinical research and data storage (via eConsent framework), or to print and sign/date the emailed ICF form, which will be returned to the study staff by email. If the consent form is signed via REDCap, the ICF will automatically be stored securely in the REDCap File Repository. A version of the signed/dated eConsent form will be provided to the participant by direct download, email or in hardcopy at their first in-person visit (participant preference). If possible, the HIPAA authorization will also be reviewed and completed by the participant remotely and emailed to study staff. Trained study personnel will conduct the visit. First, the informed consent document will be reviewed in detail with the participant. All procedures will be explained, and voluntary participation will be confirmed with signed consent prior to the initiation of data collection. Study participants will be asked to confirm their preference on the collection of photo/video during testing via a check-off box on the consent form. Photo and video refer to the audiovisual media taken primarily of the participant's lower body during walking with or without the reNeu device. Photo/video will not contain identifiable information, such as participant names, and will be stored on an encrypted and password-protected SharePoint folder accessible only by the research team. If any photo/video captures a participant's face or other identifiable landmark, that area will be blurred out if used for publications, presentations, training purposes, or

promotional purposes. Photo/video may also be used for visual assessment and correlation with other biomechanical outcome measures obtained during data collection.

Consent to participate in the study is obtained during the secondary screening visit, along with the participant's HIPAA authorization. After HIPAA authorization is obtained, the research team will put together a medical clearance packet to send to the participant's primary care physician. This packet includes the following:

a. Medical clearance form (Appendix IV)
b. HIPAA authorization form with participant's signature
c. Cover sheet asking physician to review and sign in the notes section

Once the packet is prepared, it will be faxed to the primary care physician for the physician's signature. Once this clearance is obtained, the participant may begin testing visit procedures described in Section L, Part (d).

Indicate the consent and/or assent process and document(s) to be used in this study.
Check all that apply

Consent: Adults (≥18 years old); One of the following MUST apply	**N/A ☐**
☒	Consent Form/Information Sheet
☐	Verbal Consent (Script) **Note:** If written consent will not be obtained, complete the 'Waiver of Written Documentation Consent' box (Box 1) located further down in this section
☐	Consent will not be obtained **Note**: If consent will not be obtained, complete the 'Waiver or Alteration of Consent' box (Box 2) located further down in this section

Assent of Children (≤ 18 years old); One of the following MUST apply	**N/A ☒**
☐	Assent Form **OR** Parent Consent Form/Information Sheet (older children may sign the parent consent form along with their parents as long as the consent form is written at the grade level of the subjects)
☐	Verbal Assent (Script)
☐	Assent will not be obtained; one of the following conditions must exist: 1. ☐ The capability of some or all of the children is so limited that they cannot reasonably be consulted; 2. ☐ The children are too young to provide assent; 3. ☐ The intervention or procedure involved in the research holds out the prospect of direct benefit to the health or well-being of the children and is available only in the context of the research

	4. ☐ The research meets the same conditions as those for waiver or alteration of informed consent in research involving adults, as specified in the regulations at 45 CFR 46.116(d)*. **(Complete the 'Waiver or Alteration of Consent' box (Box 2) located further down in this section)**

Guidance on age requirements for obtaining assent:

- **Parental Permission for minors under 6 years old**
- **Verbal assent for minors 6-11 years old**
- **Written assent from minors ages 12-17 (unless verbal consent is approved for the parents/adult subjects**

Parental Permission; One of the following MUST apply	**N/A ☒**
☐	Parental Consent Form
☐	Parental Verbal Consent (Script) **Note:** If written consent will not be obtained, complete the 'Waiver of Written Documentation of Consent' box (Box 1) located further down in this section
☐	Parental permission will not be obtained; **one of the following conditions must exist:** 1. ☐ The research protocol is designed to study conditions in children or a subject population for which parental or guardian permission is not a reasonable requirement to protect the subjects (for example, neglected or abused children). 2. ☐ The research meets the same conditions as those for waiver or alteration of informed consent in research involving adults, as specified in the regulations at 45 CFR 46.116(d)*. **(Complete the 'Waiver or Alteration of Consent' box (Box 2) located further down in this section).**

Consent: Adults with Limited Decisional Capacity to Consent (≥18 years old) N/A ☒ **Describe the consent and/or assent process for enrolling adults with limited decisional capacity to consent to research. Including how decisional capacity will determined, and who will serve as Legally Authorized Representative.**
Assent will be obtained from: ☐ All Subjects ☐ Some participants, specify: ☐ No participants. If no participants will assent, provide a rationale:

☐	Consent will be obtained from the subject's Legally Authorized Representative (LAR) **(REQUIRED).** **Who will serve as LAR:**

CONSENT OF NON-ENGLISH SPEAKING SUBJECTS N/A ☒ **Describe the process for obtaining consent from non-English speaking subjects. List the individual who will serve as the interpreter and his/her qualifications.** **NOTE:** A copy of the translated consent along with the Attestation Form for Translation of Consent must be submitted. The Attestation Form can be located on the IRB website.

BOX 1—WAIVER OF WRITTEN DOCUMENTATION OF CONSENT

WAIVER OF WRITTEN DOCUMENTATION OF CONSENT N/A ☐ **Either Criteria 1 or 2 must be met in order to qualify**	**Yes**	**No**
☐ **Criteria 1**		
The research is **NOT** FDA Regulated	☐	☐
The only record linking the subject and the research would be the consent document	☐	☐
The principal risk would be potential harm resulting from a breach of confidentiality	☐	☐
Each subject will be asked whether the subject wants documentation linking the subject to the research and the subject's wishes will govern	☐	☐
A written statement/information sheet will be provided to subjects. **If NO**, provide rationale for not providing this information:	☐	☐
☐ **Criteria 2**		
The research is **NOT** FDA Regulated	☐	☐
The research presents no more than minimal risk of harm to subjects	☐	☐
The research involves no procedures for which written consent is normally required outside of the research context	☐	☐
A written statement/information sheet will be provided to subjects. If **NO**, provide rationale for not providing this information:	☐	☐
☐ **Criteria 3**		
The research is **NOT** FDA Regulated	☐	☐
The research presents no more than minimal risk of harm to subjects	☐	☐
The subjects or legally authorized representatives are members of a distinct cultural group or community in which signing forms is not the norm	☐	☐
There is an appropriate mechanism for documenting that informed consent was obtained	☐	☐
A written statement/information sheet will be provided to subjects. If **NO**, provide rationale for not providing this information:	☐	☐

BOX 2—WAIVER OR ALTERATION OF CONSENT

NON-FDA REGULATED STUDIES

WAIVER OR ALTERATION OF CONSENT N/A ☐ **45 CFR 46.116 Waiver or alteration of consent. The IRB may approve a consent procedure which does not include, or which alters, some or all of the elements of informed consent set forth in this section, or waive the requirements to obtain informed consent provided the IRB finds and documents ALL of the criteria listed below:**	**Yes**	**No**
The research involves no more than minimal risk to the subjects;	☐	☐
The waiver or alteration will not adversely affect the rights and welfare of the subjects;	☐	☐
The research could not practicably be carried out without the waiver or alteration;	☐	☐
If the research involves using identifiable private information or identifiable biospecimens, the research could not practicably be carried out without using such information or biospecimens in an identifiable format;	☐	☐
Whenever appropriate, the subjects will be provided with additional pertinent information after participation. **If NO**, provide rationale for not providing this information:	☐	☐
Provide the justification/rationale for why this study meets the above criteria for waiving or altering consent (REQUIRED):		

FDA-REGULATED STUDIES

Per FDA guidance issued in July 2017, the IRB may waive or alter informed consent requirements for certain minimal risk clinical investigations when the IRB finds and documents ALL of the criteria listed below:	**Yes**	**No**
The clinical investigation involves no more than minimal risk (as defined in 21 CFR 50.3(k) or 56.102(i)) to the subjects;	☐	☐
The waiver or alteration will not adversely affect the rights and welfare of the subjects;	☐	☐
The clinical investigation could not practicably be carried out without the waiver or alteration	☐	☐
Whenever appropriate, the subjects will be provided with additional pertinent information after participation. **If NO**, provide rationale for not providing this information:	☐	☐
Additional Comments:		

SECTION L: STUDY PROCEDURES

In the box below provide a detailed description of the study procedures to be performed (preferably in sequential order). Be sure to specify which procedures are for research

purposes and which procedures are part of standard of care, if applicable. Be sure to include the following information:

- **Methods of data collection**
- **Details regarding research activities/procedures/interventions**
- **Number, frequency, duration and types of subject contacts (visits, phone calls, internet surveys, mailings, etc.)**
- **Time required from each subject**
- **Use of equipment (eye-tracker, treadmill, sensors, etc.). Provide a brief description of equipment that will be used in the study.***

***Note: The IRB may request more information about the equipment (including equipment manuals) and/or request that you submit Appendix C: Device Form.**

Submit copies of all surveys, interview questions, assessments, screening scripts, etc. that will be used during the conduct of this study; materials should be submitted as separate documents in either Word or PDF format.

Study Aims:

The first aim of this study is to develop and validate an intuitive, targeted, and adaptive multi-channel functional electrical stimulation (FES) neuroprosthesis that assists treadmill and overground walking after stroke. Development efforts for this neuroprosthesis (which we will refer to as the reNeu) will begin using a commercial, customizable 4-channel neuromuscular electrical stimulator (Hasomed RehaMove3) combined with wearable sensors and novel algorithms to control FES assistance provided to ankle, knee, and hip joints during walking-related activities on the treadmill. Our initial efforts will focus on the reNeu controller, which will include development of calibration algorithms and adaptive gait detection to adjust stimulation assistance delivered by the commercial stimulator. As research and development progress, we will focus on automatic optimization of stimulation parameters for each individual and the design of functional apparel for user comfort. The testing performed in this study will inform the development of a wearable, adaptive system for overground walking in the lab, clinic, and community.

The second aim of this study is to develop and optimize a novel FES-integrated exosuit (i.e., an exosuit that combines FES and robotic assistance). Our first merger of soft exosuits with FES will focus on multi-modal cooperative assistance to the paretic ankle during walking. The hybrid system will then extend to other joints (e.g. knee and hip) and movements (e.g. sit-to-stand). Compared to exosuits alone, FES integration will reduce the exosuit's motor requirements (i.e. joint mechanical work delivered) and power needs (i.e. electrical power consumed) to produce the same or better biomechanical response. We hypothesize that FES-integrated exosuits will enable faster and more symmetrical mobility compared to no device, participants' usual device, FES only, or exosuits only.

Research Phases:

Due to both developmental and experimental aspects of this project, research-based testing activities are categorized into three research phases that span the continuum from early development efforts to device testing and therapeutic studies. The current research phase is determined by the research team depending on the particular aspects of development and testing necessary for the progression of the device. Participants enrolled in this study compose the

participant pool from which the research team may select a subset to participate in study visits of a particular phase. Specific quantity of study visits and research procedures are determined by the research phase of the study. For example, participants will be asked to perform as few as 1 study visit (e.g. for Phase 1 device development) or **up to 3 study visits per week for up to 12 weeks** (e.g. for Phase 3 clinical training study). All participants will be informed of the specific study visit procedures for the current research phase and will be given the opportunity to decide whether or not they wish to participate. Please see Section L, Part (d) for a more detailed description of the three research phases and the different types of study visits and research procedures involved in each phase.

Phase 1: Device Development – This phase focuses on device development. Development will be informed by repeated single visit testing of different device designs and iterations. Activities in this phase will be light-to-moderate in intensity, and we will target keeping study participants within 60% of their heart reserve, computed using their age-predicted maximum heart rate. Both Healthy, Group 1, and Group 2 participants may participate in this research phase.

Phase 2: Device Exposure & Testing – This phase focuses on testing or training with the device at fixed stages in the development process. Study visits will be discovery-based, designed to test working hypotheses or to inform further refinement of the device. Participants who are suitable for moderate-to-high intensity activities (as determined by the research physical therapist) will be eligible to participate in this phase, and we will target keeping participants within 80% of their heart reserve, computed using their age-predicted maximum heart rate. Both Healthy, Group 1, and Group 2 participants may participate in this research phase.

Phase 3: Clinical Training Studies – This phase focuses on developing and studying novel therapeutic interventions that use the device. Participants who are suitable for moderate-to-high intensity activities (as determined by the research physical therapist) will be eligible to participate in this phase. Study visits will be used to assess potential long-lasting therapeutic benefits of training with the device. We will target keeping participants in this phase within 80% of their heart reserve, computed using their age-predicted maximum heart rate. Only Group 1 and Group 2 participants may participate in this research phase.

Enrolled participants who have had a stroke are eligible for all research phases, whereas participants who have not had a stroke are eligible for research phases 1 and 2. These research phases can be conceptualized as a categorization of the testing procedures being performed for the current development goals of the project. Due to the fluidity of device development and the need for reiteration, testing throughout this study may not follow a linear trajectory from Phase 1 to Phase 3. Rather, we will draw from the pool of enrolled participants to perform testing to inform the development of the reNeu neuroprosthesis, which may be development, testing, or training in nature. Enrolled participants may decline to participate in any of the phases, or they may participate in more than one phase. Participants who perform testing in one research phase will not be asked to repeat procedures in that same phase.

Study Visit Procedures:
Figure 1 provides an overview of the study flow. All eligible participants who have had a stroke will complete primary screening and secondary screening before being enrolled in the appropriate

group. Medical clearance and consent will also be obtained prior to testing. All eligible participants who have not had a stroke will complete primary screening before being enrolled in the Healthy group.

In-person visits will:

- Take place at one of the IRB-approved study locations, which include Boston University, Harvard University, or Spaulding Rehabilitation Hospital.
- Be conducted under the supervision of a trained investigator who will actively monitor the participant to ensure that physiological parameters stay within the established guidelines found on Table 1.
- All participants will follow exercise intensities determined based on an age-predicted heart rate (HR) maximum calculation[1]: max HR = 208 – (0.7*age); and a HR reserve calculation using Karvonen's formula[2]: HR reserve = max HR – resting HR. Training intensities will be set at 60-80% of HR reserve. A training HR at 60% of HR reserve is calculated as: resting HR + 0.6*(208 – 0.7*age – resting HR). A training HR at 80% of HR reserve is calculated as: resting HR + 0.8*(208 – 0.7*age – resting HR). If a participant is taking beta blockers, HR parameters will be reduced by 10 bpm. These parameters are adapted from a clinical trial that implemented stepping practice in stroke at high intensities[3].
  - Participants will remain at or under 60% of HR reserve for Phase 1 study visits.
  - Participants will remain at or under 80% of HR reserve for Phase 2 study visits.
  - Participants will remain at or under 80% of HR reserve for Phase 3 study visits.
- Utilize safety belts and harnesses as necessary to minimize the risk for trips/falls.
- Provide seated or standing rest periods as needed or requested by the participant.
- Sessions that involve use of an exosuit will use either the exosuit developed by the Harvard Biodesign Lab (V2) or the commercial adaptation of the exosuit (ReWalk ReStore). These devices are functionally comparable.

Table 1: Physiological Parameter Maximums allowed During Walking Activities	
BP	Systole: 200 mmHg; Diastole: 110 mmHg or increase > 10 mmHg; or pulse pressure narrowing > 10 mmHg
HR	60-80% of HR reserve: resting HR + (208 – 0.7*age – resting HR)*[60-80%]
RPE	> 15 on a 20-point scale

Surveys, questionnaires, and clinical tests/measures may be collected either on paper documents, or electronically by direct entry into a secure REDCap server. REDCap links for surveys/questionnaires may be sent to the participant via email, allowing the participant to respond to the survey questions directly. Hard copies will be scanned and uploaded to a secure Sharepoint folder or to REDCap.

*** Note that all study procedures will be conducted in accordance with site-specific COVID-19 protocols corresponding to the research site at which the visits are completed. For example, study procedures performed at the Neuromotor Recovery Laboratory will follow the guidelines outlined in the NRL Return to Research Plan submitted to Boston University in response to COVID-19. Similarly, visits performed at Harvard University will follow Harvard's approved procedures, and visits performed at Spaulding Rehabilitation Hospital will follow the SRH guidelines. Please see

Appendix XVIII for the approved COVID-19 laboratory operating procedures for each research site. For research sites other than Boston University, the BU research team will ask for and retain a record of the site's approval to recruit and enroll research participants. An example set of guidelines may include the following (from the NRL Return to Research Plan for visits performed at Boston University): Participants will be required to wear a surgical mask throughout the study visit and should not remove the mask at any time unless drinking water or absolutely necessary. All researchers present at the visit will wear surgical masks throughout the visit. If a researcher or physical therapist must come into close proximity (< 6 feet) of the participant, such as during guarding or placement of sensors, that researcher will don appropriate personal protective equipment (PPE), which includes gloves, gown, and goggles or face shield in addition to the surgical mask. Throughout the visit, researchers and physical therapists will minimize number of people interacting with the participant and time spent in close proximity to the participant, as is outlined in the Return to Research Plan. Given the unpredictability of COVID-19 policies that may change regularly with short notice, if this guidance changes at any point, the research team will follow the most recent guidance provided. ***

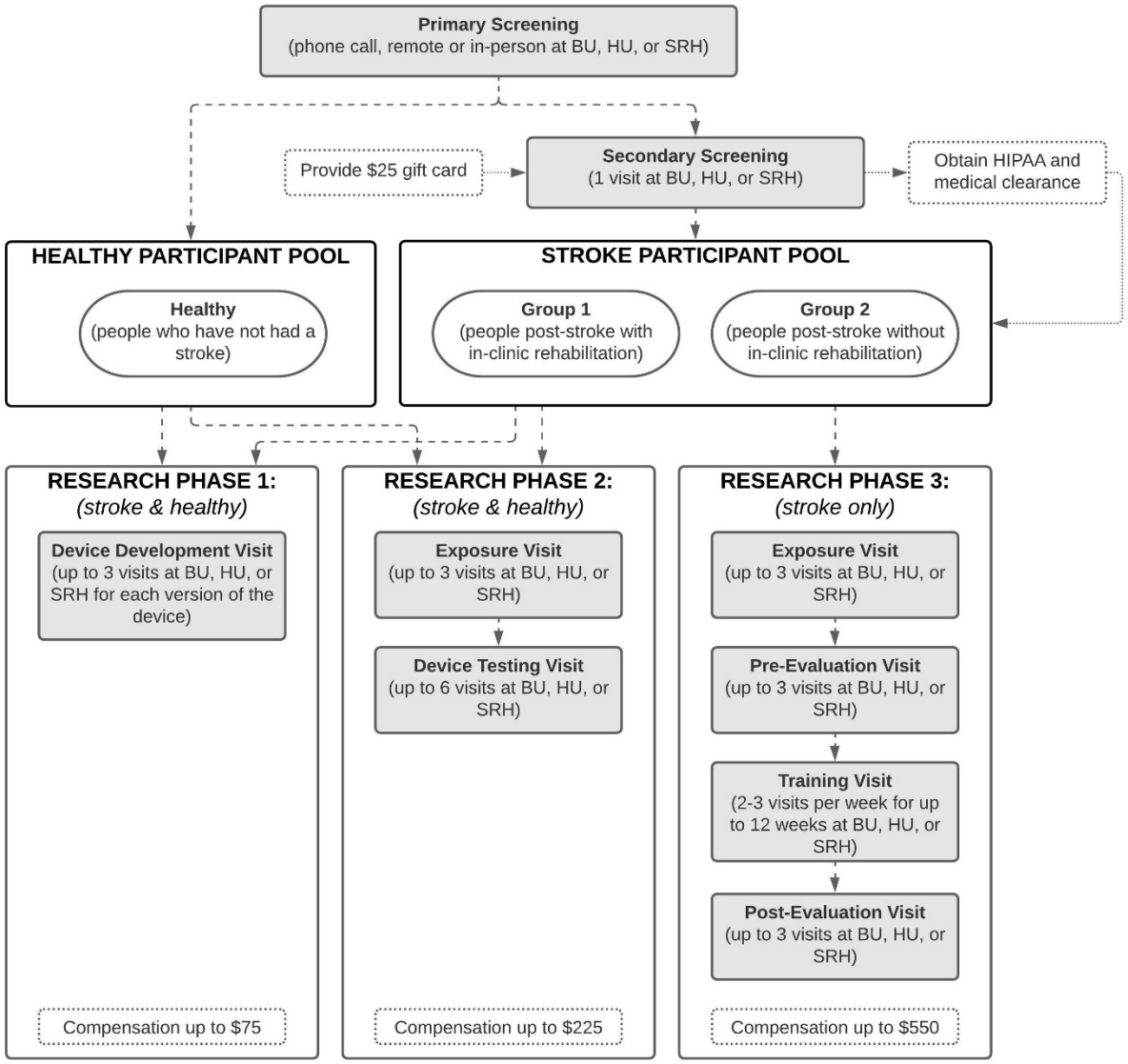

Figure 1: Enrollment and study flow for participants testing at Boston University (BU), Harvard University (BU), and Spaulding Rehabilitation Hospital (SRH).

Study Visit Workflow:

a. Primary Screening *(1 visit; over the phone or in-person at Boston University, Harvard University, or Spaulding Rehabilitation Hospital)*

The first contact with an interested participant will take place over phone (**up to 10-15 minutes**). If the potential participant is already at Boston University, Harvard University, or Spaulding Rehabilitation Hospital (e.g. currently participating in a research study or clinical care), the participant may opt to perform the primary screen in-person. This primary screening does not count toward the total number of sessions. During the primary screening, the study will be explained in detail, and any questions that the participant has will be answered. If the participant maintains interest in participating in the study, he/she will be asked the questions from the primary screening form to determine consideration for the study.

- Case-specific information useful to the physical therapist or trained investigator's assessment of each participant may also be collected. This information includes knowledge of any serious comorbidities or medical conditions that may affect participation in the study, general walking ability, and prior experience with electrical stimulation. The collected information will help physical therapists and the research team to confirm eligibility and to better prepare for subsequent study visits.
- **Note on participants previously known to Boston University through participation or screening in other studies at Boston University:** Participants who have recently participated or have been screened for other studies at Boston University may be contacted to determine their interest in participating in this research study. We will only contact participants who have expressed interest and given permission to be contacted for additional research studies at Boston University. If the participant agrees to participate, information already known to Boston University may be used to complete the primary and/or secondary screening documentation. Study staff may reach out to participants to fill in any gaps and update information as needed on a case-by-case basis. Participants who are actively involved in other studies that have potential effects on walking performance will be eligible for consideration in Phase 1 and 2 of this study and will not be eligible for Phase 3 until after completion of the other study.
- **Note on participants known to Boston University through participation or screening in studies with a collaborating institution:** Participants who have recently participated or have been screened for a research study at one of our collaborating institutions may be referred to us via a collaborator. If the participant agrees to participate in our study, information already known to our collaborators may be shared with Boston University to complete the primary and/or secondary screening documentation. Study staff may reach out to participants to fill in any gaps and update information as needed on a case-by-case basis. This may include identifiable data such as screening forms, medical history, and study data.

If the individual is deemed eligible for Group 1 or Group 2, they will be scheduled for a secondary screening visit to confirm eligibility and review the Informed Consent Form.

If the individual is deemed eligible for the Healthy group, they will be able to review the study's Informed Consent Form with the study team member at the end of this primary screening visit.

Informed Consent:
For the participant's convenience, the Informed Consent Form and HIPAA Authorization Form, if applicable, can be completed either in person (at this visit or at the beginning of the next visit) or remotely (online, by mail, or using BU Zoom). If remote consenting is preferred, participants can choose one of the following options:

1. Secure eConsent - Participants may sign the Informed Consent Form and HIPAA Authorization Form via REDCap (via eConsent framework) or to print and sign/date the emailed consent form, which will be returned to the study staff by email. Consent forms signed in REDCap will automatically be stored securely in the REDCap File Repository. A version of the signed/dated eConsent form will be provided to the participant by direct download, email, or as a hardcopy at their first in-person visit (participant preference).

2. Zoom/Phone - The researcher will email the consent form and HIPAA authorization to the participant and will review the documents with the participant over phone call or BU Zoom video call. The participant can electronically sign the documents or print the forms, sign them, then scan and email them back to the research team.
3. Mail - Participants may request a paper copy of the consent form and HIPAA authorization by mail which will include a pre-stamped, pre-paid return envelope. They should read and sign the forms and mail them back to the research team.

The participant will be able to check a box on the Informed Consent Form to indicate whether or not they agree to having photo/video taken during study visits.

If the individual is not deemed eligible at the end of the primary screening visit, they will not be able to participate in the study. Any data collected will be de-identified and may be used as part of a baseline cross-sectional dataset (e.g., to characterize individuals' baseline function, or identify characteristics of individuals who were versus were not eligible for the study).

b. Secondary Screening *(1 visit; in-person at Boston University, Harvard University, or Spaulding Rehabilitation Hospital)*

The purpose of this visit is to confirm study eligibility and collect clinical measurements that can be used to characterize participants who have had a stroke and to help place them in the appropriate testing group if they are eligible for the study.

This visit will last **up to 3 hours.** Participants who have had a stroke will be asked to complete a medical history and physical examination to assess neurological complications and medical comorbidities, stroke-specific weakness/balance impairment, cognitive or behavioral issues, and communication issues. For example, participants will be asked to complete the following:

a. NIHSS Cognitive Screen (only Question 1b and 1c)
b. Medical History
c. Walking and range of motion assessments (Functional Gait Assessment, Fugl-Meyer)
d. Assessments to understand participant's physical activity and comfort performing various tasks (Activities-Specific Balance Confidence scale, International Physical Activity Questionnaire (IPAQ))
e. Overground comfortable walking speed (CWS) and fast walking speed (FWS) assessed using three 10-meter walk tests for each speed
f. Overground long-distance walking ability using the 6-minute walk test
g. Brief, harnessed, treadmill walking

We may also collect sensor data (e.g. movement-related) and/or vitals (e.g. heart rate and blood pressure) during the visit.

If the individual is deemed eligible, they will review and sign the study's Informed Consent Form and a HIPAA Authorization Form that allows their physician to disclose protected health information for research purposes, which is necessary to obtain medical clearance and communicate with the physician's office during the course of the study, if necessary. Procedures for reviewing and signing these forms are described under the primary screening visit in Section L, Part (a).

Medical Clearance:
We will seek medical clearance for qualifying individuals who are eligible for Group 1 or Group 2 based on the primary and secondary screening visits. Medical Clearance will be sought annually from the individual's primary healthcare provider (i.e., primary care physician, neurologist, cardiologist, nurse practitioner, or physician assistant) as indicated on the HIPAA Authorization Form. This process is described in the Medical Clearance Standard Operating Procedure (Appendix XI).

Individuals who are eligible for the Healthy group who self-report a medical condition that might pose a risk to participation in this research study will be excluded.

*** Note: Participants who were enrolled, screened, and medically cleared while this study was approved under the Harvard IRB (Harvard IRB19-0878) are permitted to forgo conducting those same procedures before conducting further study procedures under this protocol. Since the process of obtaining medical clearance and the procedures conducted during screening and subsequent research visits has not been altered from the original protocol under the Harvard IRB, this will not affect data integrity or subject safety and willingness to participate in the study. The research team will send a note to the primary physicians of enrolled participants to notify them of this change and provide them an opportunity to contact us with any questions or concerns. The note will let physicians know that 1) the protocol has transferred from Harvard to Boston University, 2) the research team, goals, procedures, and risks remain the same, and 3) they can contact the research team at any time if they have questions or concerns. ***

If the individual is not deemed eligible at the end of this secondary screening visit, they will not be able to participate in the study. Any data collected will be de-identified and may be used as part of a baseline cross-sectional dataset (e.g., to characterize individuals' baseline function, or identify characteristics of individuals who were versus were not eligible for the study).

c. <u>Subsequent Screening</u> *(over the phone or in-person before subsequent study visits at Boston University, Harvard University, or Spaulding Rehabilitation Hospital)*

Eligibility criteria for all participants will be re-assessed during a phone/email screening prior to each subsequent study visit to verify that no change in eligibility has occurred between visits (using a Pre-Visit Screening Form). If the participant is unreachable prior to the study visit, the Pre-Visit Screening Form will be completed at the beginning of the subsequent visit. At the discretion of the study physical therapist, assessments conducted during the Secondary Screening Visit may be re-administered to confirm eligibility. Treating healthcare provider contact information will also be confirmed at subsequent visits using the Pre-Visit Screening Form.

d. <u>Research Visits</u> *(at Boston University, Harvard University, or Spaulding Rehabilitation Hospital)*

For all research visits from this point on, all participants will be selected from Group 1 if the research goal targets a population undergoing active in-clinic rehabilitation, all from Group 2 if the research goal targets a population not currently receiving in-clinic rehabilitation, or all from the Healthy group if the research goal targets a population that has not sustained a stroke. No single study will include participants from a combination of Group 1, Group 2, and Healthy.

Concurrent studies may occur, such as development studies with Healthy and clinical studies with Group 1, however the data will not be merged between groups.

During research visits, participants will be harnessed without body weight support during treadmill walking (or as needed), and we will take photos and videos if the participant provided consent. If metabolic data is being collected at the study visit, we will ask participants to fast (refrain from eating) up to 1 hour before study visits. Food consumption changes the composition of gases in the air we breathe, thus altering our metabolic measurements. Therefore, we request that participants refrain from eating at most 1 hour prior to visits with metabolic collections. Participants who are asked to fast will be allowed to drink water within the 1 hour before the study visit and throughout the study visit.

Once we have obtained medical clearance from the participant's healthcare provider, participants are eligible for research visits conducted according to the Phase 1, Phase 2, and Phase 3 procedures overviewed previously and described below. Each visit will begin with a study investigator reviewing with the participant their medical and physical history to assess any changes since the screening visit.

Participants will then be asked to perform walking-related activities while clinical, biomechanical, and physiological measurements are made. These activities include:

- Walking on a treadmill or walking overground
- Walking at comfortable, fast, or changing speeds
- Wearing electrodes while electrical stimulation activates relaxed muscles
- Walking with and without electrical stimulation at comfortable, fast, or changing speeds on treadmill or overground
- Dynamic Gait Index – walking over a marked distance while performing various tasks (e.g. changing speeds, turning, climbing stairs)
- Timed Up and Go (TUG) or TUG Cognitive (walking with a cognitive task)
- Functional Gait Assessment (FGA) – balance tasks and backward walking
- 2 Minute Walk Test, 6 Minute Walk Test, 12 Minute Walk Test – walking for the prescribed duration at comfortable or fast walking speeds on treadmill or overground
- 10 Meter Walk Test –walking overground over a marked distance
- Mini-Balance Evaluation Systems Test (BEST), Berg Balance Scale, Functional Independence Measure, Fugl-Meyer Assessment, 4 Square Step Test – activities to assess balance and everyday function
- Walking While Talking Test – walking while performing verbal tasks
- Ankle Brachial Index (ABI) – use of ultrasound and BP cuff to evaluate risk of peripheral artery disease
- Capillary Refill Test – monitoring blood flow to tissue
- Borg Rating of Perceived Exertion (RPE), Activities-Specific Balance Confidence (ABC) Scale, Falls Efficacy Scale, Stroke Impact Scale, Physical Activity Scale – self-reported questions on perceived effort, balance confidence, or quality of life
- Stretching – self-administered or with a physical therapist

For additional descriptions of assessments that may be used during testing visits across the three phases of the project, please see Appendix XII.

The exact activities performed during these visits will vary depending on the research phase of the study. Please see Appendix XIII for an example Device Development visit plan. Activities and study flow for research Phases 2 and 3 will follow a similar format.

The study is designed to help our team better understand how people respond to stimulation assistance (Aim 1) and a combination of stimulation and robotic assistance (Aim 2) after stroke, in order to inform and develop translational electrical stimulation paradigms to best assist people with post-stroke hemiparesis during functional activities such as walking. The measurements taken during these study visits will be used to inform the development of algorithms that trigger the delivery of electrical stimulation to adaptively assist in the completion of that movement.

Equipment – The Neuromotor Recovery Laboratory (NRL) at Boston University, the Motion Capture Laboratory (MCL) at Harvard University, and Spaulding Rehabilitation Hospital have access to the following equipment which may be used during any of the study visits:

- Inertial measurement units (IMUs). These wearable sensors gather positional and inertial information (orientation, acceleration, angular velocity, earth-magnetic field, and static pressure) and are secured to body segments (i.e. foot, lower leg, thigh, pelvis, and torso) using Velcro straps. A system of IMUs can be used to determine kinematics and 3D motion of the body in space (limb position, joint angle/velocity, etc.).
- Optical motion capture (Qualisys). This system gathers information about the 3D motion of reflective markers affixed to different segments on the body. Biomechanics software enables the calculation of kinematics (e.g. limb position, joint angle/velocity, and spatiotemporal metrics) and can be coupled with force plates to determine kinetics (e.g. ground reaction forces, joint moment/power).
- Electromyography (EMG). This system measures muscle activation using small sensors affixed over target muscles. For accurate EMG readings, the research team may need to shave small areas on the participant's body where EMG sensors are to be placed (e.g. thigh, calf, and shin).
- Metabolic unit for indirect calorimetry testing (COSMED). The system measures metabolic data (e.g. energy expenditure) by measuring O2 consumption and CO2 production on a breath-by-breath basis through a mask worn over the mouth and nose.
- Force plates (Bertec). These devices are embedded into the floor and measure 3D ground reaction forces during overground activities such as walking.
- An instrumented split-belt treadmill (Bertec). This device measures 3D ground reaction forces during treadmill walking. The right and left belts of the treadmill can be controlled independently to modulate right or left limb speed (split-belt walking) or measure right or left limb forces. Instrumented handrails allow measurement of 3D forces exerted by the participant's hands during treadmill walking.
- Soft robotic exosuit (V2 and ReWalk ReStore). This system is an unobtrusive and lightweight textile device that applies cable-driven assistive torques to the participant's joints in parallel with the underlying musculature to enhance the functional capacity of the paretic limb.

- Electrical stimulation unit (Hasomed RehaMove3). This commercial 4-channel electrical stimulator enables control of current amplitude, pulse duration, and frequency of electrical pulses delivered to muscles through non-invasive surface electrodes. The Hasomed RehaMove3 has also been approved under protocol #4440 in the NRL.
- Heart rate monitor (Polar). This device is worn around the wrist/chest to measure heart rate.
- Blood pressure (BP) cuff and Doppler. The BP cuff measures blood pressure using an arm band and sphygmometer, whereas the Doppler system measures blood pressure using a small portable ultrasound device placed on the participant's skin. For accurate Doppler readings, a small amount of ultrasound gel may need to be put on the participant's skin to enhance the coupling between ultrasound transducer and the skin. Typically, the BP cuff is sufficient for seated or standing measurements, whereas the Doppler system is more conducive for measuring BP during walking.
- Gait walkway. This system is typically a portable electronic walkway designed to measure temporal and spatial parameters during walking via embedded pressure activated sensors. The walkway top cover is typically made of an anti-slip vinyl material.
- Goniometer. This tool, in its simplest form, is operated similar to a ruler or protractor to manually measure joint angles and range of movement. More complex instruments such as electronic and twin axis goniometers can provide continuous or multi-dimensional measurements. These sensors are robust, lightweight, flexible, and can be comfortably worn under clothing without hindering movement of the joint.
- Dynamometer. Lower extremity muscle strength will be assessed in a seated, supine, or prone position using a stationary dynamometer, a hand-held dynamometer, or similar device.

Phase 1: Device Development *(up to 3 visits per device iteration at any testing site)*
Device development visits will be no more than **5 hours each** in total duration. These visits will consist of no more than 60 minutes of cumulative walking, including no more than 15 minutes of continuous walking at one time. On average, participants will walk for less than 6 minutes continuously and will be provided with resting breaks between subsequent walking trials. Data may be collected while the participant is performing activities or while in a seated or supine position. The activities performed during each visit will vary depending on the design objective and the participant's functional abilities. However, most study visits will include electrode placement and tuning, inertial sensor and/or EMG donning, treadmill and/or overground walking with and without varying levels and durations of FES assistance. Rest breaks will be provided as needed, and physiological/stimulation parameters will be verified by a physical therapist to ensure the safety and comfort of participants. If the participant is unable or unwilling to complete a particular activity, that task is dropped from the visit plan, and the study team will assess whether it is safe and/or feasible to modify or continue with the rest of the visit.

Research in this development phase will facilitate the design of adaptive FES systems for post-stroke gait rehabilitation. Participants may be tested across multiple visits to facilitate evaluation of the reliability of the system and algorithms. System prototypes will be tested in the lab (e.g. at BU or HU), clinic (e.g. at SRH), or in the community (e.g. a neighborhood).

Electrode Placement Procedures – At the beginning of visits involving electrical stimulation, inspection and preparation of the skin will be conducted before applying the electrodes. To maximize comfort, care will be taken to ensure the skin underlying the electrodes is intact. If there is concern about the participant's hair interfering with the electrode-skin interface, a safety razor will be used to trim the hair close to the skin, being careful not to damage the skin itself. The participant may be instructed to shave the area at least 24 hours before the next session. The skin will be cleaned using an alcohol wipe to remove lotion, oils, makeup, or dead skin. The skin will be fully dried before applying before applying a topical anesthetic (to reduce discomfort) and the electrodes, and small amounts of stimulation will be delivered with verbal consent from the participant to elicit a muscle contraction and confirm proper placement.

To ensure consistency of electrode placement for participants coming in for subsequent visits, the team may mark the location of the electrodes on the participant's skin using a UV skin marker. This marker utilizes ink that is invisible unless viewed under a UV light so as to minimize impact on the participant's life outside of the study visit.

Electrical Stimulation Procedures – We will use a commercial multi-channel electrical stimulation device to deliver electrical pulses to target muscles via non-invasive surface electrodes. Stimulation assistance will target the lower extremity musculature, including: ankle dorsiflexor, eversion, and plantarflexion muscles; knee flexor and extensor muscles; and hip flexor, extensor, and abductor muscles. Stimulation parameters (i.e. current amplitude, pulse duration, and frequency) will be tuned appropriately for each participant to produce the desired physiological response. For example, to help with ground clearance, we would target stimulation of the tibialis anterior muscle to produce a neutral ankle angle while the person is walking. Parameter tuning will first be performed in a static position (supine, sitting, or standing) depending on the muscles being stimulated and then fine-tuned during walking.

Maximum Force Generating Capacity Testing – In addition, we may tune the stimulation parameters as a percentage of the muscle's maximum force-generating capacity. To assess the muscle's maximum force-generating capacity, a short burst of stimulation pulses may be delivered while the participant is contracting the target muscle maximally for under five seconds, and with the foot placed against a force transducer to allow recording of the force produced by the muscle's activation. With the participant's consent, the amplitude of stimulation will be increased until the resulting force begins to plateau (i.e. a maximum force is determined). Rest breaks will be provided between each assessment to minimize muscle fatigue.

Muscle Activity – We will use wireless surface EMG sensors to better understand the underlying muscle activation patterns that produce observable movements or to identify effects on muscle activity produced by FES and/or exosuit assistance. The skin will be cleaned using an alcohol wipe to remove lotion, oils, makeup, or dead skin. If needed, sticky tape will be used to remove excess dead skin and ensure the area is properly prepared prior to placing the sensors. If there is concern about the participant's hair interfering with the EMG-skin interface, a safety razor will be used to trim the hair close to the skin, being careful not to damage the skin itself.

The participant will be asked to perform muscle contractions of the muscle of interest in a seated, supine, or standing position. This will enable proper location and placement of the EMGs over the

muscle belly. After the sensors are placed, the participant will be asked to repeat the muscle contractions while researchers view real-time muscle activity and determine adequate placement and signal clarity. EMGs are affixed to the skin via a sticky material that can be removed by hand. An alcohol wipe will be used to remove any residue left behind after removal of the EMGs.

Phase 2: Device Exposure & Testing *(up to 3 exposure visits and up to 6 testing visits at any testing site)*

Exposure Visits (up to 3 visits):

Exposure visits will be no more than **4 hours each** in total duration. These visits will consist of no more than 60 minutes of cumulative walking, including no more than 15 minutes of continuous walking at one time. On average, participants will walk for less than 6 minutes continuously and will be provided with resting breaks between subsequent walking trials. Data may be collected while the participant is performing activities or while in a seated or supine position. Activities will consist of device fitting, stimulation tuning, and static/dynamic activities performed while wearing the exosuit and/or FES system in either the active or passive states. The purpose of these visits is to provide the participant with exposure to the exosuit and/or FES systems, including the donning/doffing process, stimulation tuning method, and different assistance profiles administered by the exosuit and FES systems. This visit is important for assessing feasibility, participant acceptability, ease of use, and comfort during walking, sitting, and standing activities.

Up to three separate exposure visits may take place in order to ensure that the participant is adequately prepared for device testing visits using the FES system and/or exosuit. We will collect biomechanics and movement-related data during walking with the devices in three modes:

- No Device: Walking will be performed without any devices. This provides a baseline walking assessment which is used to compare walking ability before, after, or between interventions with the FES/exosuit systems.
- Passive: FES and/or exosuit will be worn, but none of the device components will provide assistance to the paretic limb.
- Active: FES and/or exosuit will be worn and provide mechanical/stimulation assistance to the paretic limb.

Device Testing Visits (up to 6 visits):

Similar to the device development visits in Phase 1, device testing visits will be no more than **5 hours each** in total duration. These visits will consist of no more than 60 minutes of cumulative walking, including no more than 15 minutes of continuous walking at one time. On average, participants will walk for less than 6 minutes continuously and will be provided with resting breaks between subsequent walking trials. As usual, electrode placement and tuning will be performed prior to the assessment portion of the visit. Assessments will be similar to device development visits in Phase 1, however device testing visits in Phase 2 will be a more focused extension of Phase 1 in order to answer a specific research and/or development question. For example, device testing visits will assess the effect of changes in stimulation amplitude or timing over the course of multiple visits, whereas device development visits in Phase 1 would only assess the immediate outcomes from a single visit for each participant to determine if the device is capable of doing what it was designed to do. Rest breaks will be provided as needed, and physiological/stimulation parameters will be verified by a physical therapist to ensure the safety and comfort of participants.

If the participant is unable or unwilling to complete a particular activity, that task is dropped from the visit plan, and the study team will assess whether it is safe and/or feasible to modify or continue with the rest of the visit.

Phase 3: Clinical Training Studies *(up to 3 exposure visits, up to 3 pre-evaluation visits, 2-3 training visits per week for up to 12 weeks, and up to 3 post-evaluation visits at any testing site)*
Exposure Visits (up to 3 visits):
These visits are the same as Phase 2 exposure visits and will be no more than **4 hours each** in total duration. These visits will consist of no more than 60 minutes of cumulative walking, including no more than 15 minutes of continuous walking at one time. On average, participants will walk for less than 6 minutes continuously and will be provided with resting breaks between subsequent walking trials. Data may be collected while the participant is performing activities or while in a seated or supine position. Activities will consist of exosuit fitting, stimulation tuning, and static/dynamic activities performed while wearing the exosuit and/or FES system in either the active or passive states. The purpose of these visits is to provide the participant with exposure to the exosuit and FES system, including the donning/doffing process, stimulation tuning method, and different assistance profiles administered by the exosuit and FES systems. This visit is important for assessing feasibility, participant acceptability, ease of use, and comfort during walking, sitting, and standing activities.

Up to three separate exposure visits may take place in order to ensure that the participant is adequately prepared for device testing visits using the FES system and/or exosuit. We will collect biomechanics and movement-related data during walking with no device mode, passive mode, and active mode as described in Phase 2.

Pre-Evaluation Visits (up to 3 visits):
A baseline evaluation of participant's gait will be performed prior to training. Evaluations will be no more than **3-4 hours each** and will include:

- clinical tests, including measures of gait, mobility, and motor function
- biomechanical assessments, including the use of motion capture, force plates, electromyography, and inertial sensors
- gait assessments, including walking without wearing any devices (no device mode), wearing exosuit, FES system, or FES-integrated exosuit while powered off (passive mode), and wearing exosuit, FES system, or FES-integrated exosuit while powered on (active mode)
- physiologic measurements such as cardiac data
- qualitative measurements using standard and custom questionnaires
- exosuit data, including suit-generated force, position, and timing measures
- an extra visit with the anticipation of technical issues

Training Visits (2-3 visits per week for up to 12 weeks):
Participants will be asked to come in for 2-3 training visits per week for up to 12 weeks for training visits. Each visit will be no more than **3-4 hours** in total duration.

The purpose of the training visits is to understand the therapeutic effects of training with exosuit/FES assistance (Active Training condition) compared to training without the exosuit or FES system (Control Training condition). Prior to beginning training, participants will be *randomly assigned* to either Active Training or Control Training. Randomization procedures will be the same for Group 1 (current in-clinic rehabilitation) and Group 2 (no in-clinic rehabilitation). Both training conditions (active and control) will implement gait training within a range of moderate-to-high intensity walking speeds.

Utilizing concepts in motor learning, training is designed to be high intensity and task-specific. Training will progress based on the participant's capacity by increasing variability and complexity of training environments. An example training progression might begin within controlled environments such as a quiet, temperature-controlled laboratory space. Over the course of training, activities will progress to more open, real-world environments such as a common hallway or an open gym where external factors such as noise, foot traffic, curved paths, and other distractions approximate those of real-world scenarios.

Gait training at fast walking speeds typically involve exercising in higher intensities. From a cardiovascular standpoint, as previously described, we will aim to keep participants within a range of 60 - 80% of their heart rate reserve, computed using their age-predicted heart rate (HR) maximum calculation (HR_{max} = 208 – [0.7*age])[x]. If a participant is taking beta blockers, HR parameters will be reduced by 10 bpm. These parameters are adapted from a clinical trial that implemented stepping practice in stroke at high intensities [xii].

Each of the training sessions will consist of sensor placement, donning/doffing the exosuit and/or FES system, and walking activities with data collection. The participant will do no more than 60 minutes of cumulative walking during any particular training session and no more than 15 minutes of continuous walking at one time. On average, participants will walk for less than 6 minutes continuously and will be provided with resting breaks between subsequent walking trials. In some circumstances, study sessions may extend to 4 hours total to allow completing data collection in the event of technical, human, or other within-session delays. To quantify walking performance during training, we will collect movement data using motion capture, wearable sensors, or any of the equipment described in Section L.

Post-Evaluation Visits (up to 3 visits):
To examine effects of training, participants will undergo a post-training evaluation. These visits will be no more than **3-4 hours each** in total duration and will include the same activities as pre-evaluation visits**.** Evaluations will include:

- clinical tests, including measures of gait, mobility, and motor function
- biomechanical assessments, including the use of motion capture, force plates, electromyography, and inertial sensors
- gait assessments, including without wearing any devices (no device mode), wearing exosuit and/or FES system while powered off (passive mode), and wearing exosuit and/or FES system while powered on (active mode)
- physiologic measurements such as cardiac data
- qualitative measurements using standard and custom questionnaires
- exosuit data, including suit-generated force, position, and timing measures

- an extra visit with the anticipation of technical issues

References:

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3. Hornby TG, Henderson CE, Plawecki A, et al. Contributions of Stepping Intensity and Variability to Mobility in Individuals Poststroke. *Stroke*. 2019;50:2492-2499. doi:10.1161/STROKEAHA.119.026254

SECTION M: RISKS

Describe any expected risks to subjects. Consider physical, psychological, social, political, legal, economic, or other risks that are related to the study.

Risks associated with participating in this study are categorized by procedure/device.

Questionnaire/Survey Risks

Participants may feel emotional or upset when answering some of the survey questions related to perceived comfort/discomfort with electrical stimulation, prior history of using assistive devices, or thoughts about different aspects of the assistance and study procedures. The participants will be instructed to tell the interviewer at any time if they want to take a break or stop the survey. They will be instructed that they do not have to answer any questions that make them feel uncomfortable. Please refer to Appendix XIV for an outline of survey questions.

Mobility Testing Risks

Walking and/or standing tests are not anticipated to be exhausting or physically hard for the participant. However, the participant may become fatigued, or experience joint soreness in their hip, knee, ankle or foot. When the participants are not wearing the suit, the tasks we will ask them to complete should not pose any physical risks to the participants that theywould not experience in everyday life. Some of the tasks may be mild to moderately physically demanding. It is possible that the participant could become tired, or experience a fall, common muscle pull or pain. The participants take a break or stop the testing at any time.

Risk of anxiety is possible with mobility testing as some participants may perceive them as novel and unfamiliar. Theyare free to end testing or procedures that cause anxiety or discomfort at any time, this will not affect any remuneration or transportation they are entitled to.

Walking Without Usual Assistive Devices

If participants typically wear a brace or other assistive device, they may be asked to not wear it during parts of the study sessions. There may be risks that fall in line with ordinary risks that participants may encounter when walking overground without their brace (e.g. minor ankle rolls, tripping, knee hyperextension, etc). When walking without a brace, a participant's lower limb joints (i.e. ankle, knee, hip) may not be as stable, resulting in decreased walking confidence and increased risk of tripping, rolling an ankle, or hyperextending the knee. If a participant typically wears a brace, the researchers will ensure that the participant can safely walk without it before performing data collection activities.

Exosuit Risks

The exposure visits and fit/comfort tests should not be physically difficult for the participants to complete. As with any assistive device, there is a length of time required to feel comfortable wearing it. Participants will be given as much time as they need to feel comfortable while wearing the suit. They may experience minor redness, chafing, rubbing, blistering, swelling, numbness, or tingling due to the tightness of the suit. These are only temporary effects and should disappear over time. Participants may also get blisters on their feet due to the rubbing/movement of feet in the shoes we provide. The person conducting the exosuit fittings and exercise training will inspect the skin on participants' legs and feet prior to and after each study visit. If participants are uncomfortable or wish to stop at any time during the study, they will be able to do so.

Individual electronic devices and sensors of the exosuit will be safety certified by staff engineers and undergo a safety checklist before being applied and worn. The motor controllers have built-in safety measures to detect shorted or unconnected phases and cut power to the system. We have also designed an emergency stop switch that can be used by the operator to instantly cut the power to the motor phases in case of unexpected error. Any assistance participants may experience from the suit will be similar to or less than what a healthy adult can naturally exert.

It is also possible, but unlikely, that the external surfaces of the body-worn actuator could overheat and cause a burn in the event of accidental contact with the skin. The body-worn actuator has built-in safety measures to detect and prevent incidents of overheating, and the actuator is separated from participant by an insulating layer to minimize any accidental contact.

Some of our systems are powered by batteries which, if shorted, could have a risk of fire. In order to lessen this risk, the batteries are protected by a fuse to minimize the effects of a short. The battery connector geometry is designed so that the batteries can only be connected in the correct orientation, and battery charging and setup will only be performed by trained research staff.

Exosuit Fans
Some of our systems use fans to prevent them from overheating. These fans are similar to what is found in a desktop computer. A protective grill prevents objects from contacting the fan blades, but it is possible that long hair could become entangled in the fan or that someone could fit a small finger through the grill. The fans are low powered and should not cause serious injury and will be monitored by our team to ensure that they are placed in a way that lessens the risk of long hair or other body parts coming into contact with them.

Exercising with Exosuit
When participants are wearing the exosuit, it is possible that they could experience a fall while performing the tasks. In the passive mode, the device will not be providing any active assistance to the participant, so the risk of a fall due to the device in this mode of testing is similar to what the participant would experience in daily life. Safety harnessing will be available for all modes of testing that involve treadmill walking in the Neuromotor Recovery Lab at the Boston University or other approved locations. When the harness system is used, we will ensure that it is secure and comfortable for the participant. Unharnessed testing, such as walking overground or outside the laboratory, will only take place if our study team has determined it is safe to do so. Research personnel will be present to provide additional support, guarding and/or monitoring during the tasks. Loss of balance or experiencing a fall with unharnessed and harnessed walking are possible

risks within this study. Risk of anxiety is possible with the suit as some participants may perceive them as novel and unfamiliar. Participants are free to end testing or procedures that cause anxiety or discomfort at any time, this will not affect any remuneration or transportation the participants are entitled to.

Functional Electrical Stimulation (FES)

Although the amplitude of electrical stimulation will be well within safety limits and have been previously used without incident, it is possible that joints, muscles, ligaments, or other tissues could be damaged as a result of the electrical currents. The commercial stimulator that we use in this study has implemented an upper limit on stimulation amplitude to reduce the risk of injury from electrical currents. There is also the potential for electrical shock resulting from equipment malfunction, however stimulation exposure durations necessary to cause permanent harm are not likely to occur. In addition, because the stimulator delivers electric current through electrodes attached to the surface of the skin, there is a risk of localized electrical burns. These risks are minimized by safety circuitry built into the stimulator to limit current density, and we will take care in preparation and placement of the electrodes to minimize discomfort of the skin. Stimulation may also cause muscle cramping, and a licensed physical therapist will guide participants in proper body positioning to minimize the risk of cramping during stimulation tuning.

Topical Anesthetic

To reduce discomfort on the skin from using electrical stimulation, a local anesthetic can be applied to the skin as a cream, wipe, or spray. The anesthetic is intended to reduce sensation in a small area. This may cause altered sensation and numbness at the application site or skin irritation.

Phase 3 Training Risks

As with any exercise, there is the possibility that abnormal responses could occur. The maximum heart rate that participants are allowed to train at during walking activities is higher for Phases 2 and 3 than for Phase 1. The increased intensity of exercise training in Phases 2 and 3 may be associated with risks that include nausea, shortness of breath, fatigue, muscle cramps, or muscle soreness (sometimes lasting days after a testing session), as well as unexpected changes in blood pressure, irregular heart rate, fainting, or joint injury. Rare risks associated with exercise could include heart problems or hospitalization. There could be additional risks if participants have a known history of Deep Vein Thrombosis (blood clots, typically in the lower extremity). Sometimes these clots can detach and travel to the lungs, causing a pulmonary embolism, stroke or death. People who have had a stroke are at higher risk. Blood thinning medications might increase the risk of bleeding and bruising if participants experience a fall.

Our physical therapist or trained investigator will monitor vital signs (heart rate and blood pressure) at each study visit and check for symptoms of distress. Additionally, we will take blood pressure readings as needed before and after each walking bout, or whenever deemed necessary based on symptoms. For all visits we will monitor participants' heart rate while walking.

We will be providing the participants with instructions, or cues, while they walk. With the potential use of cueing there may be a risk of unintentional distraction or dizziness as they may be asked to focus on the cues (e.g. on a screen or projection) while walking.

Electromyography (EMG) Risks:
EMG sensors measure the electrical signals generated by muscles when individuals move. We use a commercial wireless EMG system in this study, however some of the EMG sensors may have wires connecting two parts of the sensor. These wires are covered to minimize risk of electric shock or discomfort on the skin. The sensors are placed on participants' skin using double-sided medical tape, and the tape may cause slight skin redness or irritation and may pull body hair when removed. This is a normal reaction and will disappear with time. The tape can be removed with hypoallergenic/alcohol wipes if preferred.

EMG sensors may also be wrapped with an elastic material (e.g. PreWrap or Coban) to ensure the sensor remains securely attached to the skin during dynamic activities. Pressure indentation, skin redness, or soreness may result from the pressing of the sensor onto the skin. This is a normal reaction and will disappear with time. If discomfort does not subside after a few days, we will recommend they contact the research team or their primary physician.

Although these sensors are purely observational and do not apply any electrical current to the body, there may be a very rare risk of discomfort or shock from the electronic components. Although the likelihood of system malfunction is rare, we have periodic equipment and data checks in place to minimize this risk. As an additional safety measure, individual electronic devices and sensors will be safety certified by staff engineers and undergo a safety checklist before being applied and worn by a human subject.

Shaving Risks
We may ask to shave a small area of the body (thigh, calf, shin, chest) where EMG sensors are placed. A research team member may help with shaving to lessen any effects of the razor on the skin (e.g. bleeding, cuts, razor burn). Some sensors or devices have edges that may irritate or cause abrasions on skin.

Loss of Confidentiality
The main risk of allowing us to use and store participants' information for research is a potential loss of privacy. We will protect participants' privacy by labeling their information with a de-identified participant ID. The master key relating identifiable information and participant IDs will be kept in an encrypted and password-protected folder on SharePoint.

Describe the plan to minimize risks. Include in the description the availability of any medical or psychological resources.

The PI and co-investigators have extensive experience with clinical research involving individuals poststroke. Many of the investigators have a clinical background in physical therapy and many study personnel and students have training in CPR and first aid. All of the aforementioned risks will also be mitigated through the following:

- Potential participants will be provided with the consent form and be provided ample time to read it and ask questions. The research team will address any concerns. Participants will be told that participation in the study is completely voluntary and they have the right to withdraw from the study at any time.
- Adequate rest periods and water will be provided to optimize comfort and reduce fatigue.

- Total walking time per session will be limited to one hour.
- Trained investigators will monitor vital signs and check for symptoms of distress at each study visit. Procedures will be halted as physiologic signs clinically warrant activity cessation. Any findings out of the ordinary will be reported to the participant's primary healthcare provider, concluding the study visit procedures.
- Trained investigators will use overhead harness when possible. Treadmill and over-ground walking tests will be completed with overhead harnessing to prevent a fall. There might be situations where harnessing is not possible such as when transitioning between activities or when harness is not available, when testing activities occurring outside of the lab in the hallway, or when harnessing is not clinically necessary (e.g. training progression to reduce reliance on external balance support to improve balance during walking). During these situations when harness is not used, an investigator will provide close guarding and will use a gait belt if indicated.
- Trained investigators will ensure that participants are safe to walk without their usual brace (e.g. ankle foot orthosis). The determination will be based on clinical assessment of participant's gait, such that the participant would be able to walk without high risk for toe catches, tripping, or ankle instability (e.g. ankle rolling).
- For poststroke participants, we will obtain medical clearance from their primary healthcare provider prior to enrollment in the study.
- A research team member will offer to assist with shaving, if needed, to further minimize any effects of the razor on the skin (e.g., bleeding, cuts, razor burn).

All participants are free to end testing or procedures that cause anxiety or discomfort at any time, this will not affect any remuneration or transportation they are entitled to.

SECTION N: BENEFITS

Describe the potential benefits to subjects related to the study. State if there are no direct benefits. NOTE: Compensation and/or course credit are not considered benefits.
There are no direct benefits to participants as a result of participating in device development and testing visits during Phase 1 and Phase 2 of this study. However, there are potential benefits such as improved walking speed, efficiency, and neuromuscular activation as a result of participating in the training studies during Phase 3 of this study. The aforementioned potential benefits may also result from participating in Phase 2 study visits that constitute a small-scale training study (e.g. in preparation for Phase 3 of this study).
Describe the potential benefits to society and/or others related to the study
This project will facilitate the development of a new device that can improve poststroke walking ability through specific action on impairments that limit mobility and participation after stroke.

SECTION O: COSTS/PAYMENTS

YES*	NO	
☐	☒	Are there any costs to subjects as a result of participating in this study? **If YES**, provide a description of the costs: Participants will be responsible for any up-front costs related to traveling to any of the three study sites. Parking vouchers will be distributed as needed for garage parking. In the event that a participant is unable to cover up-front costs

		for transportation to/from study visits, the study staff can schedule and pay for a rideshare to transport subjects to/from study visits on behalf of the participant. If transportation costs are covered in this manner or reimbursed (as described below), the participant may not be eligible for the study compensation (i.e. if the transportation cost exceeds the amount noted for study compensation via gift card).
☒	☐	Will subjects be compensated for participating in the study? Compensation may include cash, checks, gift cards, lotteries, course credit, etc. Payments should be prorated to compensate subjects for time and procedures completed **If YES**, provide a description of the compensation: All Group 1 and Group 2 participants as well as healthy participants who are not direct members of any of the research labs leading this study will be compensated for their participation in research visits and for garage parking as outlined below. Healthy participants who are direct members of the research labs leading this study will not be eligible to receive compensation. **Secondary Screening Visit:** Participants will receive a $25 gift card at the secondary screening visit (1 visit). **Device Development:** For a given version of the device, participants will receive a $25 gift card for each study visit attended (i.e. up to $75 across the 3 visits). For each new version of the device, participants may receive up to $75 for participating in the Device Development visits associated with that version of the device. **Device Exposure & Testing:** Participants will receive a $25 gift card for each study visit attended (i.e. up to $225 across the 9 visits). **Clinical Training Studies:** Participants will receive up to $550 in gift cards across 45 visits: • One $25 gift card for each exposure visit (i.e. up to $75 across 3 visits) • One $25 gift card for each pre-evaluation visit (i.e. up to $75 across 3 visits) • Four $50 payments throughout the course of training (i.e. up to $200 across 36 visits) • One $200 gift card after completing all post-evaluation visits (up to 3 visits) Participants should ask the study team if they have any questions about how many study visits they may attend and if they want to know the amount of potential compensation. If participants drive to the study visit, they will receive a garage parking voucher to park for free at each study site. Participants may use other modes of transportation, such as rideshares (e.g. Ride, Uber, Lyft) or public transportation

		(e.g. bus, T, etc.) to transport to/from the study visit. For participants that cannot afford to cover this transportation cost and have no other way to access transportation for participation in the research study, they can be reimbursed for transportation costs that exceed the reimbursement amount for the study visit via check or gift card.
☐	☒	Will identifiable information be sent to Central University departments (e.g. Accounts Payable, Post Award Financial Operations, etc.) for payment purposes? **If YES**, this information must be disclosed in the consent form.

SECTION P: CONFIDENTIALITY OF DATA

Describe how data will be stored (e.g. paper, electronic database, etc.)
Research participants will be informed that all data collected for study purposes will be held in strict confidence and used for research purposes only. Records may be paper or electronic. ***Paper Documents*** **–** Screening information may be kept in paper format and stored in a locked file cabinet that only the research team has access to. There will be a different locked file cabinet at each approved research site. Participant files will also be scanned and stored on an encrypted, password-protected SharePoint folder or REDCap server, with access provided only to the PI and key research personnel. ***Photos/Videos*** **–** All photos and videos will be kept on an encrypted password-protected SharePoint folder. ***REDCap*** **–** Electronic forms of study documents such as e-consent forms, screening forms, surveys, questionnaires, data from walking measurements, medical information, in-session clinical documentation, physician communication, and any notes generated related to the study will also be kept on a secure REDCap server. Other biomechanical data, photo/video, project documents, and identifiable information will be retained on an encrypted and password-protected SharePoint folder. Backups of data, if applicable, will be stored on an encrypted private network drive. ***De-Identified Participant ID Number*** **–** Data collected during this research will be labeled using a de-identified participant ID number. ***Research Data*** **–** Data collected from study visits, including biomechanics, metabolics, FES/exosuit device metrics, and photos/videos, will be de-identified and stored on an encrypted, password-protected SharePoint folder accessible only by the research team. Photos/videos may be transferred as a local copy to encrypted password-protected personal computers for processing or to prepare media material for publications, presentations, training purposes, or for promotional purposes.

YES*	**NO**	
☒	☐	Will you collect identifiable information? (e.g. names, social security numbers, addresses, telephone numbers, etc.). **If YES**, complete the box below.
Describe the coding system that will be used to protect the information including who will have access to the code. Coding systems are used to: 1) protect the confidentiality of the research		

data and 2) allow the investigator to link subjects to their responses. Each subject is assigned a unique study ID at the beginning of the study. A separate document (key) should be maintained that links the names of the subjects to the study ID numbers.
To ensure confidentiality of all data collected, each subject will be assigned a unique alphanumeric participant ID. Only the PI and designated research personnel associated with the project will have access to the master-key with the corresponding names and identifiers. The master-key will be kept on an encrypted password-protected folder in SharePoint. Photos/videos will be labeled with the participant ID and never in conjunction with identifiable information such as the participant's name.

YES*	NO	
☒	☐	Will you share data with others outside of the study? **If YES**, complete the box below.

Describe how data will be transferred and how confidentiality will be maintained (e.g. identifying information will not be sent outside, etc.):
It is possible a participant's identifiable data may be shared between collaborating institutions including the School of Engineering and Applied Sciences at Harvard University and Spaulding Rehabilitation Hospital when/if participants are interested in multiple research studies in the area, possibly at the same time. This may include screening forms, medical history, study results, etc. This will be done in order to better meet the needs of the participant and synchronize enrollment across multiple studies for which they are interested in participating. Any identifiable data shared with collaborating institutions will be transferred through secure email or server, and will be stored on a secure server at the collaborating institution. Any data provided to Boston University will be treated as identifiable data and will be stored appropriately. The request to share information beyond the study team will be an option to participants on the Informed Consent form. Participants will be able to take part in the study even if they do not want their information shared beyond the study. Information will not be shared, and participants will not be contacted for additional studies, unless they have given their permission via the consent form.

Describe how you will maintain the confidentiality of the data (e.g. locked cabinet, password-protected files, encryption, etc.). Note: Confidentiality refers to the researcher's agreement with the participant about how the subject's identifiable private information will be handled, managed, and disseminated. For further assistance and/or access to resources regarding information security, please refer to the BU Information Security website**.**
Only the PI and a few designated research personnel will have access to identifiable research data. The PI and all study personnel (listed in section E) will have access to all coded data housed on a password-protected secured network drive. Paper forms will be stored in a locked filing cabinet in a locked office. No names or identifiers of subjects will be contained on paper forms or entered into a database. REDCap will be used for data collection and only accessible to study personnel. No identifiable data will be shared with non-study personnel including students, professional colleagues, outside institutions or study sponsors. No identifiable data will be used in scholarly presentations, in future research projects and in publications.

Per Boston University (BU) Record Retention Policy, records concerning human subjects must be retained for 7 years. As the investigator, you must also adhere to all applicable requirements as defined by regulatory agencies (e.g. FDA, etc.) or sponsors.

SECTION Q: CERTIFICATE OF CONFIDENTIALITY

In 2017 the NIH updated its policy for issuing **Certificates of Confidentiality**. Under the policy, all **eligible** research studies funded by the NIH are automatically issued a certificate of confidentiality. Investigators whose research is not funded or supported by the NIH may request and obtain from the NIH a Certificate of Confidentiality. Investigators who request and receive Certificates must follow the NIH and PHS policies governing such certifications.

YES	NO	
☐	☒	Is your research funded by the NIH and eligible for a Certificate of Confidentiality?
☐	☒	If your research is not funded by the NIH, will you be applying for a Certificate of Confidentiality?

SECTION R: PRIVACY

Describe how you will protect the privacy of subjects (e.g. where will consent procedures take place, if interviews or other interventions, where will these procedures take place)
Privacy of participants will be protected by conducting all in-person interactions in a semi-private or private space. No personally identifiable information will be discussed in common areas. ***Photos/Videos*** **–** Participants will be asked to confirm their preference on the collection of photo/video during testing via a check-off box in the consent form. • All photo/video will not contain participant names or other identifiable information and will be stored on an encrypted password protected SharePoint folder with access limited to the research team. • Any photo/video that captures a participant's face or other identifiable landmark will be blurred out if used for publications, presentations, training purposes, or promotional purposes. ***Personal Health Information*** **–** Any medical records obtained during the course of the study will be de-identified and labeled only with a letter/number combination for each participant.

SECTION S: MONITORING STUDY DATA

How will data be monitored? **Note:** The Data and Safety Monitoring Plan should be tailored to the nature, size, and complexity of the research protocol, the expected risks of the research, and the type of subject population being studied.	
☒	Principal Investigator
☐	Monitor/Monitoring Group
☐	Data and Safety Monitoring Board (DSMB) Note: The DSMB Charter must be submitted with this Application. For more information regarding a DSMB, please refer to the NIH website.

Describe the plan for monitoring study data. This should include a description of how data will be collected and analyzed as the project progresses to assure the appropriateness of the research, its design, and subject protections.
Data will be collected and de-identified (using participant ID number only). This de-identified data will be processed and analyzed by the PI and research team (Section E). Occurrences of adverse events will be described and recorded and any medical attention sought will be documented. If a deviation in data collection/usage, adverse or unanticipated event involving risks to participants or others, or a breach in confidentiality is suspected or found, the study will be halted until a resolution is determined in accordance with the IRB. The following definitions will be applied to the present study to monitor adverse events: **Adverse Event:** Any untoward or unfavorable physical or psychological occurrence in a participant, including any abnormal sign (e.g., abnormal physical exam or laboratory finding),

symptom, or disease temporally associated with participation in the research, whether or not considered related to participation in the research. The PI will be notified when any adverse event is identified and will report this to the IRB.

Serious Adverse Event: Any adverse event that:

i. results in death
ii. is life-threatening (places the participant at immediate risk of death)
iii. results in hospitalization
iv. results in a persistent or significant disability/incapacity
v. results in a congenital anomaly/birth defect
vi. may jeopardize the participant's health and may require medical or surgical intervention to prevent one of the other outcomes listed in this definition.

Unexpected Adverse Event: Any adverse event occurring in one or more participants, the nature, severity, or frequency of which is not consistent with either:

i. the known or foreseeable risk of adverse events associated with the procedures involved in the research that are described in (a) the protocol-related documents, such as the IRB-approved protocol, any applicable investigator brochure, and the current IRB-approved informed consent document, and (b) other relevant sources of information, such as product labeling and package inserts.

SECTION T: HIPAA

Health Insurance Portability and Accountability Act

YES*	NO	

☒	☐	Is this research being conducted in a covered entity?
		The following BU CRC Departments are considered covered entities:
		• Sargent College Rehabilitation Services
		  ○ Physical Therapy Center at the Ryan Center for Sports Medicine and Rehabilitation
		  ○ Sargent Choice Nutrition Center
		• The Danielsen Institute
		• Boston University Health Plan
		*If YES, contact the IRB office for assistance.

SECTION U: FAMILY EDUCATIONAL RIGHTS AND PRIVACY ACT (FERPA)

FERPA is the federal law that protects the privacy of student education records. Research funded by the Department of Education or research conducted in educational institutions that receive funds from the Department of Education (for research or other purposes) must comply with FERPA.

YES*	NO	
☐	☒	Does this study involve collection of information from student school/university records? *If YES, refer to the following websites for guidance on FERPA: • http://www.bu.edu/researchsupport/compliance/human-subjects/ • http://www.bu.edu/reg/general-information/ferpa/

		• http://www2.ed.gov/policy/gen/guid/fpco/ferpa/index.html **If FERPA applies, you must complete the box below:**
In accordance with FERPA, written consent must be obtained to access student records. The consent must: • Specify the records that may be disclosed • State the purpose of the disclosure • Identify the person or class of parties to whom the disclosure can be made		
☐ YES **(REQUIRED)**		I confirm that I will comply with the FERPA policy that is in place at the educational institution where I am conducting my research. This includes, if applicable, the requirements for written agreement when requesting a waiver of consent for personally identifiable information. **If an agreement is required, this agreement must be submitted to the IRB.**

SECTION V: PROTECTION OF PUPIL RIGHTS AMENDMENT (PPRA):

PPRA is a federal law that affords certain rights to parents of minor students with regard to surveys that ask questions of a personal nature. Research funded by the Department of Education or research conducted in educational institutions that receive funds (for research or other purposes) from the Department of Education must comply with the PPRA.

YES*	NO	
☐	☒	Does PPRA apply to this study? If YES, refer to the following websites for guidance: • http://www2.ed.gov/policy/gen/guid/fpco/ppra/index.html • http://www.bu.edu/researchsupport/compliance/human-subjects/ **If PPRA applies, you must complete the box below:**
In accordance with PPRA, written parental consent must be obtained prior to subjects participation in the study.		
☐ YES **(REQUIRED)**		I confirm that I will comply with the PPRA policy that is in place at the educational institution where I am conducting my research.

SECTION W: CLINICAL TRIALS REGISTRATION:

The Food Drug and Administration Amendments Act (known as FDAAA 801) requires that "applicable clinical trials" be registered and have results reported on clinicaltrials.gov. In addition, the International Committee of Medical Journal Editors (ICJME) and the National Institutes of Health (NIH) also have requirements for registration. Please see box below to determine if your study requires registration in accordance with either FDAAA 801, ICJME, or NIH.

YES	NO	FDAAA 801 Requirements
☐	☒	Does your study meet the definition of an applicable clinical trial (ACT) and require registration **AND** results submission in accordance with FDAAA 801? ACTs include: • Trials of drugs and biologics: Controlled clinical investigations, other than phase 1 clinical investigations, of drugs or biological products subject to Food and Drug Administration (FDA) regulation • Trials of devices (see note): 1) Controlled trials with health outcomes of devices subject to FDA regulation, other than small feasibility studies, and 2) pediatric post-market surveillance required by FDA

		Note: If your study meets the requirement for registration and reporting, you must submit the National Clinical Trial (NCT) Identifier # to the IRB prior to IRB approval**.** NCT #:
YES	**NO**	**ICMJE Requirements**
☒	☐	Does your study meet the definition of a clinical trial and require registration in accordance with ICMJE? **Note:** If your study meets the requirement for registration, you must submit the National Clinical Trial (NCT) Identifier # to the IRB prior to IRB approval. NCT #: Phases 1 and 2 of this study do not meet the definition of a clinical trial. However, some research activities conducted as part of Phase 3 of this study (Clinical Training Studies) may qualify. Because we are currently in the early development stages of this device, we have not finalized the technology that would be used in potential clinical trials. When the technology has been developed and appropriately tested, we will register any Phase 3 procedures of this study that would be defined as a clinical trial in accordance with ICMJE.
YES	**NO**	**NIH Requirements**
☐	☒	Does your study meet the definition of an applicable clinical trial and require registration **AND** results submission in accordance with NIH? For more information on this policy please refer to: • NIH Policy on the Dissemination of NIH-Funded Clinical Trial Information • Checklist **Note:** If your study meets the requirement for registration and reporting, you must submit the National Clinical Trial (NCT) Identifier # to the IRB prior to IRB approval. NCT #:

Certification / Signatures

- By submitting this protocol I attest to the fact that all research activities to be implemented related to human subjects have been completely and accurately described herein.
- I agree to conduct the describe research in an ethical manner.
- I agree to comply with all institutional policies and procedures related to human subjects research and will not begin any human subjects research activities until I have obtained full approval from the IRB.
- I agree to conduct the research as described in this protocol and not to make any changes (except to eliminate immediate harm to subjects) without first obtaining approval for the changes from the IRB.
- I agree to immediately report any unanticipated problems involving risks to subjects or others, any subject complaints, and any incidents of non-compliance with the requirements of this protocol as soon as I become aware of them.
- I agree to comply with any relevant HIPAA and FERPA regulations if applicable.
- I verify that all those responsible for the design, conduct, or reporting of the proposed program, including at minimum, all Senior/key personnel in the grant application, have completed the financial interest disclosure forms and completed training as dictated at http://www.bu.edu/orc/coi/forms/, and returned the forms to the Office for Research Compliance COI Unit. **NOTE: If anyone checked "yes" to any of the questions on either the FIND1 or NONFIND1 form, the IRB Director will contact the COI office to obtain the disclosure information.**

PI Printed Name: Lou Awad

PI Signature:  **Date:** 8-24-2020

Submission: This form can be completed, signed, scanned and submitted to the IRB at irb@bu.edu. Faxed documents and handwritten materials are not accepted. Be sure to include all relevant attachments.

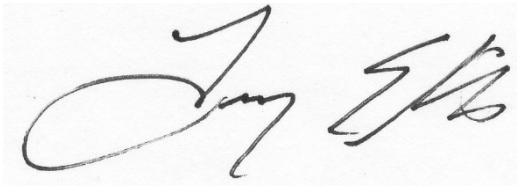
FACULTY Research:

The Department Chair signature is required: This application must be signed by the Department Chair for all faculty researchers. If the PI is the Department Chair, then signature by the appropriate Dean is required. Department Chair signature is not required for student research.

By signing this form you are indicating that you have reviewed the application, the faculty/staff person listed as PI on this protocol is a member of your department, hat he/she is qualified to serve as the PI for this study, he/she has the adequate resources, and the research utilizes acceptable practice for the discipline.

Department Chair (print name): Terry Ellis

Department/School: Department of Physical Therapy & Athletic Training; College of Health & Rehabilitation Sciences: Sargent College

Signature: 

Date: 8-25-2020