A. COVER PAGE

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Human Subjects: Yes **HS Exempt:** NA **Exemption Number:** **Phase III Clinical Trial:** NA	**Vertebrate Animals:** NA
hESC: No	**Inventions/Patents:** No

CONSENT TO PARTICIPATE IN BIOMEDICAL RESEARCH

NIH Study of Neural Control of a Bionic 2-DoF Ankle-Foot Prosthesis

You are asked to participate in a clinical research study led by [redacted] at the Biomechatronics group at the Media Lab at the Massachusetts Institute of Technology (M.I.T.). You are selected as a possible participant for this study because you are a healthy person either with a below knee amputation who is capable of walking with variable cadence using prosthetic devices or biologically-intact limbs.
You should read the information below, and ask questions about anything you do not understand before deciding whether or not to participate.

- **PARTICIPATION AND WITHDRAWAL**

Your participation in this study is completely VOLUNTARY and you are free to choose whether to be in it or not. If you choose to participate in this study, you may subsequently withdraw from it at any time without penalty or consequences of any kind by notifying the Principal Investigator, [redacted] hherr@media.mit.edu If you choose not to participate, this will not affect your relationship with M.I.T. or your right to health care or other services to which you are otherwise entitled or will not cause you to lose your research compensation.

- **PURPOSE OF THE STUDY**

The purposes of this study are to explore the use of your lower limb muscles as a neural control source for a new ankle-foot prosthesis system, and the role neural feedback can play in your capability to perceive the position and motion of your prosthetic limb. Long term goals of the work are to provide increased freedom of motion and new capabilities for sensory perception to individuals with below knee amputations. Our goal, through the participation of biologically-intact individuals, is to establish baselines for biomimetic gait and motor control strategies. These baselines will serve as the foundation for the development and evaluation of a new neurally-controlled ankle-foot prosthesis system.

- **PROCEDURES**

Overview:

The study design calls for an experimental group of eleven participants who received two agonist-antagonist myoneural interfaces (AMIs) that were surgically constructed during a modified transtibial amputation procedure, and a control group of eleven matched participants who received standard transtibial amputations. The study design also calls for a separate, eleven biologically-intact individuals (non-amputees; intact cohort). The study protocol involves one or more of the following activities:
1. Collection of electromyography (EMG) data from participants' lower limbs to characterize muscle activation and create maps specific to individual participants,
2. Investigation of participants' capabilities to use an experimental ankle-foot prosthesis that is

designed to allow independent actuation of the ankle and subtalar joints, and offers EMG-modulated control over prosthetic joint position and stiffness, and
3. Exploration of AMIs as a means of communicating information between the participant and the new prosthesis using a system involving EMG, functional electrical stimulation, and ultrasound. 4. Investigation of motor control strategies of the intact cohort during various motor tasks to establish baseline for prosthetic control evaluation.
The hypothesis is that transtibial amputations involving AMIs can offer improved motor control of the new prosthesis while also enabling proprioceptive sensation (perception of the position, movement, and torque of the affected limb and prosthetic joint). The AMIs are expected to improve voluntary prosthetic control, improve prosthetic terrain adaptations, and offer new possibilities for bi-directional communication across the human-device interface.

Experimental Sessions:
Biomedical data are collected from study participants in the Biomechatronics space within the MIT Media Lab in Cambridge, MA. Experimental group participants attend five or six sessions, with four sessions lasting approximately 4 hours each and the other one or two session(s) lasting up to 8 hours. Control group participants attend four sessions lasting approximately 4 hours each. Intact group participants attend up to four sessions lasting approximately 4 hours each.

Experiments for AMI and control groups

During Session 1, you are given information about the trial, we answer your questions, and, if you decide to participate, you are asked to sign this informed consent form. Next, we collect data from your lower limbs using a large number of noninvasive surface EMG electrodes. These EMG electrodes are positioned on your skin at locations that are distributed over your lower limb surfaces. You are instructed to move your phantom or biological foot through the ankle and/or subtalar joint spaces - plantar flexion, dorsiflexion, eversion, and inversion. Data are collected to characterize muscle activations and create maps specific to individual study participants.

During Session 2, we collect data from your lower limbs using a small number of noninvasive surface EMG electrodes that are positioned on your skin at specific target locations. We also collect data from other sensors, including small motion and/or pressure sensors strapped or taped to your legs. You are instructed on how to follow position trajectories while seated. You are asked to perform target-tracking tasks that involve pointing your phantom foot toward specified positions in free space, and/or stiffening your biological and/or phantom joints for specified time intervals. Data are collected to evaluate your capability for voluntary prosthetic joint control in free space.

During Session 3, we collect EMG data from your residual limb muscles using a small number of surface EMG electrodes, as described for Session 2. EMG leads are threaded between your skin and the liner to exit the socket, and used to control an experimental ankle-foot prosthesis that allows independent actuation of powered ankle and subtalar joints and EMG-modulated control of prosthetic joint position and stiffness. The experimental prosthesis will initially be attached to a test apparatus and then used in place of your customary prosthesis. You are allowed as much time as you need to become accommodated to the prosthesis - sitting, standing, and

then walking.

During Session 4, we collect data from your limb muscles using a small number of noninvasive surface EMG electrodes that are positioned on your skin as described for Session 3 and used to control the experimental ankle-foot prosthesis that is used in place of your customary prosthesis. We also collect data from other sensors, including small motion and/or pressure sensors strapped or taped to your legs, small reflective balls attached to your clothes or skin, and/or pressure-sensitive shoe inserts. We may record video of your movements as you walk, using special motion cameras to track and record the positions of the reflective markers. We may also collect images using standard video and still cameras. You are asked perform three ambulatory tasks - stair ascent, stair descent, and navigating an obstacle presented in your path as you walk on level ground. Based on your performance and comfort level, you may be asked to perform jogging, running, single-leg balancing, jumping, and jump roping. Data are collected to evaluate your capabilities for voluntary and involuntary (reflexive) prosthetic joint control.

During Session 5 and an optional Session 6, the experimental ankle-foot prosthesis is attached to a test apparatus. We turn on and off a system that provides you with force feedback from the prosthesis through functional electrical stimulation (FES). We evaluate the efficacy of our system in communicating information to you from sensors on-board the prosthesis, and ask you questions about your prosthetic control experience. You are asked to perform tasks while seated, including pedal-pushing tasks where you are asked to move your phantom foot to press down on the pedal at various effort levels against mechanical resistance. You may be asked to "mirror" (i.e., simultaneously perform tasks using both your affected and unaffected limbs. You may be asked to perform the tasks while looking directly at the prosthesis or while blindfolded. As you perform the tasks, we apply FES to your limb, causing limb muscle contractions.

We collect data using fine-wire electrodes that are temporarily inserted into your limb muscles, surface EMG electrodes that are placed on your skin, and an ultrasound probe. Two fine-wire electrodes are placed into muscles of your affected or unaffected limb for FES application, and two additional fine-wire electrodes may also be placed into other muscles of your affected or unaffected limb for EMG recording. An experienced clinician (Dr. Carty or another experienced clinician) locates the target muscle sites and places the fine-wire electrodes in each muscle of interest. These electrodes are placed at MIT, in a secluded office. A needle is temporarily used for fine-wire electrode placement and this needle is removed immediately after placement. This electrode itself is very fine, with a diameter of only 0.051 mm. Muscle stimulation involves the use of small, controlled bursts of electricity. Sensations associated with muscle stimulation are typically described as "tingly" and we expect you to feel your muscle contracting. In the event that two trials are scheduled over two consecutive days, the fine-wire electrodes may remain in place overnight. If this is to happen, the clinician will apply local antibiotic ointment to the needle insertion points, and will bandage your limb. It will be important that you not use your socket overnight, or try to bear weight on your residual limb while it is bandaged. It will also be essential that the bandaging does not get wet, and that you do not remove it. We will provide you with crutches or a wheelchair to use during the overnight period, depending on your preference. In the event that you have any problems or concerns with your electrodes overnight, the clinician will be available by phone. The electrodes will be left in place for a maximum of two trial days, or one overnight period.

During an optional Session 7, we will collect neurally-controlled prosthetic gait data in outdoor settings, utilizing the same system described in Session 4. Only individuals who are comfortable performing neurally-controlled prosthetic gait inside of the lab settings and have demonstrated stable gait performances will be invited for this session. You will be asked to perform walking and terrain adaptation tasks on the MIT campus and in a park. Additionally, you will be required to wear a safety helmet while walking outside of the lab settings. The data collected during this session will be used to assess the neural controllability of your prosthesis in real-world environments.

Experiments for the intact group

During Session 1, you are given information about the trial, we answer your questions, and, if you decide to participate, you are asked to sign this informed consent form. Next, we collect data from your lower limbs using a large number of noninvasive surface EMG electrodes. These EMG electrodes are positioned on your skin at locations that are distributed over your lower limb surfaces. We collect data from non-invasive sensors, including small motion and/or pressure sensors strapped or taped to your legs, small reflective balls attached to your clothes or skin, and/or pressure-sensitive shoe inserts. We may also collect images using standard video and still cameras. You are asked perform various ambulatory tasks – walking, jogging, running, single-leg balancing, jumping, jump roping, stair ascent, stair descent, and navigating an obstacle presented in your path as you walk on level ground. Data are collected to serve as a baseline for evaluating prosthetic joint control.
During Session 2, we will collect your walking and terrain adaptability data in outdoor settings. You will be asked to perform walking and terrain adaptation tasks on the MIT campus and in a park. The data collected during this session will be identical to that of Session 1 and will serve as a baseline for evaluating prosthetic joint control.

- **POTENTIAL RISKS AND DISCOMFORTS**

The ankle-foot prosthesis is investigational, and there may be risks that are currently unknown and/or unanticipated. In the case that a malfunction does occur, then the prosthesis defaults from an active state to an inactive state, becoming nearly rigid and much like a standard passive ankle-foot prosthesis.

Attaching sensors or reflective markers to the skin uses adhesives or adhesive tape that may result in skin irritation when the sensor or marker is removed. Please note that the EMG data are collected for research and not medical purposes, however, if we think your EMG data include any information that may be clinically relevant then we will pass on this information to you and advise you to discuss it with your physician.

As with any prosthetic device used for walking, there is a small risk of falling during the study sessions. This is minimized by the presence of a member of the research team who will stand next to you at all times during ambulatory sessions. Also, our lab is equipped with handrails, parallel bars and a safety harness attached to the ceiling.

You may become fatigued during the study. If you become too fatigued, you may ask to take a break, or ask us to stop the study at any time.

You may experience muscle discomfort when the clinician places the fine-wire electrodes, and during the muscle stimulation study which involves the use of small, controlled bursts of electricity. Sensations associated with muscle stimulation are typically described as "tingly" and we expect you to feel your muscle contracting. This risk is minimized by maintaining all stimulation settings within historically safe limits, and tuning the intensity for each participant. Specifically, we begin at low stimulation amplitude and pulse width, and slowly increase intensity until you tell us that we have reached your limit of comfortable stimulation or until we reach the limit of what is historically safe (whichever comes first). Once we determine this limit, we set up our stimulation system to ensure that this limit is never surpassed. If you become too uncomfortable, you may ask to take a break, or ask us to remove the electrodes or stop the stimulation at any time. If muscle stimulation becomes at all painful, please let us know immediately.

We do not anticipate risk of infection from the placement of fine-wire electrodes because the clinician performing the procedure has substantial experience and sterile electrodes are used. In the event that sessions are scheduled over two consecutive days, the fine-wire electrodes may remain in place overnight. If this is to happen, the clinician will apply local antibiotic ointment to the insertion points, and will then bandage your residual limb. It will be important that you not use your socket overnight, or try to bear weight on your residual limb while the limb is bandaged. It will also be essential that the bandaging does not get wet, and that you do not remove it. We will therefore ask that you not shower during the overnight period between consecutive session days. We will provide you with either crutches or a wheelchair to use for this overnight period, depending on your preference. In the event that you have any problems or concerns during the overnight period, the clinician will be available by phone. In this scenario, the electrodes are removed at the end of the second day, and are left in place for a maximum of two session days, or one overnight period.

Confidential information about you will be collected as part of this study. Although significant efforts are made to safeguard your confidential information, as described in the "Privacy and Confidentiality" section below, there exists a risk that your confidential information may be disclosed.

The research may involve risks that are currently unforeseeable.

- **ANTICIPATED BENEFITS**

You will receive no immediate benefit for participating in this study. The prosthetic device and control systems we are using are prototypes and would not be immediately available. There may be potential benefits to society and the advancement of science as the findings could inform procedures or technologies relating to limb loss.

- **ALTERNATIVES TO PARTICIPATION**

The purpose of this research is not intended to affect your current medical condition. You have the option to not participate in this study and, if applicable, to continue with the standard of care determined by your physician.

- **PAYMENT FOR PARTICIPATION**

You will receive $20 per hour in monetary compensation for your time and effort. To receive compensation, you must complete the informed consent process (of which this document is a part) and participate for a minimum of 1 hour. We can assist in arranging your transportation but are unable to pay your transportation costs. You should receive payment for your participation approximately one month after the study has been completed. Should you decide to withdraw from the study, or are withdrawn by the investigator, you will be paid $20/hour for the time and effort put in prior to withdrawal.

- **POSSIBLE COMMERCIAL PRODUCTS**

The technologies developed based on this research may one day be implemented in commercial products, and the institutions or researchers may benefit if this happens.

- **FINANCIAL OBLIGATION**

Neither you nor your insurance company will be billed for your participation in this research.

- **PRIVACY AND CONFIDENTIALITY**

The only people who will know you are participant in this clinical trial are members of the research team and, if appropriate, your physicians and nurses. Identifiable information may be shared with members of the Biomechatronics group who are actively working on human subject research, for the purposes of recruitment to our other studies and reliable record-keeping. The data will exist in an individually password-protected MIT Media Lab network hub folder that is managed by the Media Lab IT Department. Only Biomechatronics group MIT personnel with valid Institutional Review Board (IRB) training will have access to this folder. There are currently eighteen IRB-trained Biomechatronics group members who will have access to the data. Individuals without valid training certificates, or who leave the group, will no longer be granted access this folder. Identifiable data will not be copied to local computers or shared in any other way. No information about you, or provided by you during the research, will be disclosed to others outside of the aforementioned group without your written permission, except, if necessary to protect your rights or welfare, or if required by law.

Once the study is completed, data will remain in the MIT Media Lab Biomechatronics group for future processing and reference. When the research results are published or reported, no information will be included that can reveal your identity. If photographs, videos, or audio- tape recordings of you will be used for educational purposes, your identity will be protected or disguised by blurring or blocking your face. If any other uses of the data are contemplated, you will be contacted by phone, mail or Email requesting your specific consent to do so.

This trial is posted on the public ClinicalTrials.gov website (NCT03913273) in accord with the National Institutes of Health policy for human clinical trials. Authorized representatives of the Food and Drug Administration (FDA) or the National Institutes of Health may need to review records of individual subjects. As a result, they may see your name; but they are bound by rules of confidentiality not to reveal your identity to others. The research team will not be able to delete your data already collected as part of your participation before the required data retention period. This includes photographs, video or audio recordings. After the required data retention period has passed, the research team will delete any data upon your request if it is feasible. If you choose to withdraw, your data up until the point of withdraw will be retained as part of the study records. No additional data will be collected from you for this study.

- **WITHDRAWAL OF PARTICIPATION BY THE INVESTIGATOR**

The Principal Investigator may withdraw you from participating in this research if circumstances arise which warrant doing so. If you experience any side effects or if you become ill during the research, you may have to drop out, even if you would like to continue. The Principal Investigator will make the decision and let you know if it is not possible for you to continue. The decision may be made either to protect your health and safety, or because it is part of the research plan that people who develop certain conditions may not continue to participate.

If you must drop out because the Principal Investigator asks you to or because you have decided on your own to withdraw, you will still receive your pre-agreed upon compensation to compensate you for the time you have already spent.

As stated in the "Privacy and Confidentiality" section, if you choose to withdraw (or have been withdrawn by the Principal Investigator), your data up to the point of withdraw will be retained as part of the study records. No additional data will be collected from you for this study.

- **NEW FINDINGS**

During the course of the study, you will be informed of any significant new findings (either good or bad), such as changes in the risks or benefits resulting from participation in the research or new alternatives to participation that might cause you to change your mind about continuing in the study. If new information is provided to you, your consent to continue participating in this study will be re-obtained.

- **EMERGENCY CARE AND COMPENSATION FOR INJURY**

If you feel you have suffered an injury, which may include emotional trauma, as a result of participating in this study, please contact the person in charge of the study as soon as possible.

In the event you suffer such an injury, M.I.T. may provide itself, or arrange for the provision of, emergency transport or medical treatment, including emergency treatment and follow-up care, as needed, or reimbursement for such medical services. M.I.T. does not provide any other form of compensation for injury. In any case, neither the offer to provide medical assistance, nor the actual provision of medical services shall be considered an admission of fault or acceptance of

liability. Questions regarding this policy may be directed to MIT's Insurance Office, (617) 253-2823. Your insurance carrier may be billed for the cost of emergency transport or medical treatment, if such services are determined not to be directly related to your participation in this study.

- **IDENTIFICATION OF INVESTIGATORS**

In the event of a research related injury or if you experience an adverse reaction, please immediately contact one of the investigators listed below. If you have any questions about the research, please feel free to contact [redacted] 75 Amherst Street Room 374N, Cambridge MA.

- **RIGHTS OF RESEARCH SUBJECTS**

You are not waiving any legal claims, rights or remedies because of your participation in this research study. If you feel you have been treated unfairly, or you have questions regarding your rights as a research subject, you may contact the Chairman of the Committee on the Use of Humans as Experimental Subjects, M.I.T., Room E25-143B, 77 Massachusetts Ave, Cambridge, MA 02139, phone 1-617-253 6787.

SIGNATURE OF RESEARCH SUBJECT OR LEGAL REPRESENTATIVE

I have read (or someone has read to me) and understood the information provided above. I have been given an opportunity to ask questions and all of my questions have been answered to my satisfaction. I agree to participate in this study. I have been given a copy of this form.

_____

Name of Subject

_____

Name of Legal Representative (if applicable)

_____ _____

Signature of Subject or Legal Representative Date

SIGNATURE OF INVESTIGATOR

I have explained the research to the subject or his/her legal representative and answered all of his/her questions. I believe that he/she understands the information described in this document. In my judgment the subject is voluntarily and knowingly giving free, informed consent and possesses the legal capacity to give informed consent to participate in this research study.

_____

Name of Investigator

_____ _____

Signature of Investigator Date