Clinical Trials Registration Cover Page

Study: Neuromodulation in Lower Limb Amputees

NCT#: NCT04543786

Document type: Informed Consent Form

Most recent update and approval of document: Jan. 24, 2022

University of Pittsburgh | Department of Physical Medicine and Rehabilitation
School of Medicine

CONSENT TO ACT AS A PARTICIPANT IN A RESEARCH STUDY

TITLE: **Spinal excitability changes and transcutaneous spinal cord stimulation in lower limb amputees**

Principal Investigator:	Lee Fisher, PhD Rehab Neural Engineering Lab 3520 Fifth Avenue Keystone Building, suite 300 Pittsburgh, PA 15213 Phone: 412-383-1329 E-mail: lef44@pitt.edu
Research Coordinator:	Alayna Schwerer **Phone: 412-648-4035**
Study Physicians:	George Wittenberg, MD, PhD; Michael Boninger, MD
Study Team Members:	Ashley Dalrymple, PhD; Debbie Harrington; Karen Greenwald; Ian Smith

SOURCE OF SUPPORT: National Institutes of Health: National Center of Neuromodulation for Rehabilitation

RESEARCH STUDY KEY INFORMATION

Spinal excitability changes and transcutaneous spinal cord stimulation in lower limb amputees

Dr. Lee Fisher, PhD – Principal Investigator
Refer to the full consent form for detailed information.

You are being asked to take part in a **research study**. Research Studies include only people who choose to take part. The study team members will explain the study to you and will answer any questions you might have. You should take your time to make your decision. The duration of the study is 5 to 8 days.

This research study involves the placement of stick-on electrodes on the lower back and legs each day for 5 days in one week. We will apply electrical stimulation through the electrodes on your back for 30-60 minutes. You will describe your experiences with phantom limb pain. We will also record the activity in the muscles of your legs to look at reflexes. We may also request additional sessions where we only record the activity in your muscles using the stick-on electrodes. Session durations will range from 4 to 9 hours. All the electrodes will be removed at the end of each session.
This is not a treatment study. **There is no direct benefit to you**.

ELIGIBILITY: Individuals who may qualify must have a below-knee amputation in one of both legs and experience phantom limb pain as a result of the amputation.

QUESTIONNAIRES: We will ask you about your experience with phantom limb pain using questionnaires.

RESEARCH TESTING: We will use a clinical device to press on your skin to measure your pain response. We will also record the activity in your legs using stick-on electrodes. We will record the activity while you are at rest and while we electrically stimulate the nerves on your leg or on your lower back. This is called reflex testing and allows us to test for any changes in your spinal cord as a result of your amputation.

ELECTRICAL STIMULATION: We will apply electrical stimulation through electrodes on your lower back for 30-60 minutes. You will be lying comfortably on your back during the electrical stimulation. We will slowly increase the electrical stimulation to give you a change to get used to the feeling of the stimulation. The stimulator that will deliver the electrical stimulation is CE safety certified for use in human research studies.

RISKS: There is a risk of a brief painful sensation while testing your pain response. A common risk of placing surgical tape or stick-on electrodes on the skin is discomfort while removing them. There is a risk of unpleasant sensations near the electrode location during electrical stimulation. There is a rare risk of skin irritation or burns as a result of electrical stimulation. Other risks include confidentiality breach.

COMPENSATION: You will be compensated for your participation in this research study: $50 per session for up to 8 sessions for a maximum of $400.

PURPOSE OF STUDY:

The purpose of this study is to investigate how a lower limb amputation and phantom limb pain can change the reflexes in the remaining muscles in the amputated leg. This study also investigates the use of electrical stimulation over the lower back as a method to change the reflexes and reduce phantom limb pain. This study involves several testing methods to measure pain and reflexes, as well as repeated stimulation sessions using stick-on electrodes. Testing and stimulation will take place over 5 days in 1 week. Up to 3 additional testing only sessions may be requested. No electrodes will be left on the participant and no devices will leave the lab area.

ELIGIBILITY:

We are inviting you to consider participating in this research study. Research Studies include only people who choose to take part. The study team members will explain the study to you and will answer any questions you might have. You should take your time to make your decision. You are being invited to participate in this research study because you have a below-knee amputation in at least one leg and experience severe phantom limb pain as a result of your amputation. You must be between the ages of 21 and 70. You must be willing to travel to the University of Pittsburgh 5 times in 1 week. Up to 3 additional recording sessions may be requested. Sessions range in duration from approximately 4 hours to up to 9 hours. A meal will be provided for longer sessions which occur over a mealtime. You will have to meet certain criteria to be eligible. This will be reviewed with you upon your consent.

STUDY PROCEDURES:

As part of this study, you will complete the following assessments that will be conducted at the University of Pittsburgh. Most of these assessments will occur at each session, while others will occur only at the beginning and the end of the week. We will work with you to determine the testing schedule as early as possible. You may be photographed or videotaped during any of the study procedures for presentation and publication purposes. All study procedures will take place at the Rehab Neural Engineering Labs at the University of Pittsburgh.

- **Eligibility review:** We will ask you questions regarding your eligibility for this research study. This will include information about serious diseases or disorders, pregnancy, age, and information about your limb amputation. This will take approximately 10 minutes to complete. Pregnancy will be determined via self-report or by pregnancy test and female participants are encouraged to avoid getting pregnant throughout the duration of the research study. We suggest that female participants of child-bearing potential use a method of birth control to avoid pregnancy while enrolled in the research study.
- **General Questionnaire and Medical History:** You will complete a basic questionnaire to collect information such as your age, weight, and height. This questionnaire will also include questions about your medical history and current medications. This will be completed on the first day of the program. This will take approximately 10 minutes to complete.
- **Pain Testing**: You will be asked to complete questionnaires about your current level of pain. Two questionnaires, called the McGill Pain Questionnaire and the Groningen Questionnaire

Problems after Leg Amputation (GQPLA), should take about 10 minutes to complete and will be given on the first and last day of the study. A shorter questionnaire, called the visual analog scale (VAS) will take less than 2 minutes to complete. The VAS asks you to rate your pain on a scale of 0 to 10 and will be completed daily prior to stimulation. We will test your pain threshold using a clinical test which includes pressing on your skin with a pressure-sensing clinical instrument, called an algometer. This test will take place on the first and last day of stimulation. This will take approximately 5 minutes to complete.

- **Surface EMG Monitoring:** We will use surface electromyography (EMG) to monitor the electrical activity of your muscles. We will apply adhesive electrodes to your skin of either or both legs to measure the electrical activity of your muscles while you are standing, sitting, or lying down for 60 minutes. EMG recording will also take place during reflex testing.
- **Peripheral Nerve Stimulation:** We will use electrical stimulation to measure your reflexes. We will place stick-on electrodes on your legs and connect them to an external stimulator equipment. You may feel a tingling sensation while you are receiving stimulation. This tingling sensation will go away once stimulation stops. Reflex testing will occur each day. Reflex testing may take between 1 and 4 hours to complete, with a longer duration on the first testing day and less time at later days. The first day may take longer because the nerves in your residual limb may be difficult to locate and stimulate and we may need to explore more than one nerve. Between 130 and 150 stimulation pulses will be delivered over several hours.
- **Electrical Stimulation:** Electrical stimulation will be delivered using adhesive surface electrodes that are placed next to your spine and on your hip bones. Electrodes will be secured to your trunk using a comfortable wrap. You will be asked to lie down as this is often more comfortable. Electrical stimulation over this area will cause tingling and prickling sensations and muscle contractions near the electrode regions. You will be given several opportunities to get used to the stimulation before it is increased. As the stimulation is increased, the sensations and contractions will become stronger, and you may feel sensations in your legs, as well as muscle contractions in your legs. We will monitor this activity continuously. Once at a comfortable level that does not cause muscle contractions in your legs, the stimulation will remain on for 30-60 minutes, with breaks and skin checks every 15 minutes, unless you wish to stop earlier. When stimulation is turned off, you may feel some fatigue in the muscles near the electrodes. Electrical stimulation will also be used to measure reflexes. This will include short bursts of stimulation through the same electrodes. Reflex testing may take between 1 and 2 hours to complete, with a longer duration on the first testing day and less time at later days.
- **Videotaping of Test Sessions:** We will photograph or video portions of the experimental sessions. We will blur or block out any images of your face from photos and videos to protect your confidentiality. We may use the photographs to document experimental setup and to document responses to stimulation. The purpose of the photographs and videos is for publication and presentation purposes. You may choose not to be photographed or videoed and still participate in the study. Please inform the study team.

STUDY RISKS

- **Securing Sensors/Electrodes with Tape:** A common risk of placing surgical tape or stick-on electrodes on the skin is discomfort while removing them. Tape will be used conservatively and will be removed with caution and care.
- **Pain Threshold Testing:** There is a risk of brief pain or discomfort may be felt when the skin is pressed with the indenter of the clinical device. Care will be taken while administering this test to limit the number of locations and repetitions of pressing on the skin with the clinical device.
- **Reflex Testing:** Uncomfortable sensations including sharp poking and/or skin irritation are uncommon risks related to electrical stimulation during reflex testing. As with EMG electrodes, these electrodes may cause skin discomfort when removed. We will only use as many electrodes as is necessary and will remove them carefully. If you experience any uncomfortable sensations, we can lower the amount of stimulation you are receiving. During testing trials, the stimulus will be applied in very short durations (up to 1 ms). Minor irritation of the skin may occur due to sticky electrodes used to deliver stimulation and with recording EMG in the legs. Adhesive electrodes will be removed with caution and care. There is a rare risk of skin irritation or burns as a result of electrical stimulation, although the stimulation parameters used in this study have been carefully selected to avoid causing any damage. Trained personnel will be using a CE certified stimulator, which has passed safety testing and is approved for use in human research studies. The CE certification indicates that the stimulator has passed health, safety, and environmental protection standards within the European Economic Area, and is frequently found on electronic products sold globally.
- **Transcutaneous Spinal Cord Stimulation:** Transcutaneous Spinal Cord Stimulation uses electrical stimulation to record reflexes and to provide longer duration stimulation over the back. There is a rare risk of skin irritation or burns as a result of electrical stimulation, although the stimulation parameters used in this study have been carefully selected to avoid causing any damage. Trained personnel will be using the same CE certified stimulator described above (Reflex Testing), which has passed safety testing according to European regulations and is designed for use in human research studies. There is a risk of unpleasant sensations near the electrode location and repeated short duration stimulation can result in moderate discomfort. Unpleasant sensations may include sharp poking or buzzing. Stimulation intensity will be increased slowly to allow acclimation to the sensations and to minimize discomfort. If extreme discomfort occurs, stimulation will be stopped. You will be asked to rate your discomfort on a scale of 0-10. Minor irritation of the skin may occur due to the sticky electrodes used to deliver transcutaneous spinal cord stimulation. Adhesive electrodes will be removed with caution and care.
- **Breach of Confidentiality.** Since personal information will be collected, there is a risk of breach of confidentiality, which means someone could see your private information that is not authorized. We will take the necessary steps to protect your information to the best of our ability. Research data will be collected using a coded ID instead of your name to protect your private information. Contact information and other identifiable information will be stored separately. Photographs and videotapes will be stored digitally on our password-protected

server. Hard copies will be stored in a locked file cabinet.

- **Text Messaging.** Text messages will be used for testing session appointment reminders between you and the PI and/or the study coordinator. Personal identifier information such as your name will not be transmitted via text messages. Text messages are not encrypted or secure during their transmission and could be intercepted.

STUDY BENEFITS:

This study will provide no direct benefit to you. This study will provide the basis for investigating a non-invasive method of electrical stimulation to measure the changes in the spinal cord as a result of your amputation and to reduce phantom limb pain.

This is not a treatment study. You may experience improvement in pain during or after electrical stimulation. That effect may or may not continue after the stimulation is completed.

NEW INFORMATION:

If we learn of any new information about study risks that could cause you to change your mind about continuing to participate, we will notify you promptly.

COST AND PAYMENTS:

Neither you, nor your insurance provider, will be charged for the costs of any of the testing procedures performed for the purpose of this research study (i.e., the Screening Procedures or Experimental Procedures described above).

You will be compensated for participating in this research study. You will be reimbursed on a reloadable debit card**.** In this study, you will participate in up to 8 study visits (testing sessions) for which you will be compensated $50 each, for a maximum of $400. For lengthy study visits that occur during mealtimes, meals will also be provided to you.

You will be required to travel to the University of Pittsburgh for study procedures. If you have your own personal transportation, you will be provided with validated parking tickets for UPMC parking garages for study visits. If you use public or contracted transportation, you will be reimbursed for the travel costs or we may be able to have the transportation company bill us directly.

Since you are being compensated for your participation in this study, your name, address, and social security number will be released to the Accounting Office. If the total reimbursement for your participation in research is greater than $600 in a year, this will be reported to the Internal Revenue Service (IRS) as income.

If you are withdrawn from the study by the investigators, you will be compensated for all completed study visits at the rates described above. Please contact a research team member if you have questions about payment.

COMPENSATION FOR INJURY:

If you believe that the research procedures have resulted in an injury to you, immediately contact the Principal Investigator who is listed on the first page of this form. Emergency medical treatment for injuries solely and directly related to your participation in this research study will be provided to you by the hospitals of UPMC. Your insurance provider may be billed for the costs of this emergency treatment, but none of those costs will be charged directly to you. If your research-related injury requires medical care beyond this emergency treatment, you will be responsible for the costs of this follow-up care. At this time, there is no plan for any additional financial compensation. **You waive no legal rights by signing this consent.**

CONFIDENTIALITY:

Any information about you obtained from this research will be kept as confidential (private) as possible. All paper records related to your involvement in this research study will be stored in a locked file cabinet. Your identity on these records will be indicated by a coded ID rather than by your name, and the information linking these case numbers with your identity will be kept separate from the research records. Photographs and videotapes will also be stored electronically using your case number on our password-protected server. Any hard copies will be stored in a locked file cabinet with the rest of the research data. All electronic records will be stored on a password-protected server.

This research study will involve the recording of past identifiable medical information from your hospital and/or other (e.g., physician office) records. The information that will be recorded will be limited to information concerning your medical history to determine if you are eligible.

Authorized representatives of the University of Pittsburgh Office of Research Protections may review your identifiable information for the purpose of monitoring the appropriate conduct of this research study. **The study sponsor and our collaborators** may access your research records for the purpose of protecting human subjects and analyzing the study data.

Your information will be maintained by the investigators after your participation is completed. The investigators may continue to use and disclose, for the purposes described above, identifiable information (which may include your identifiable medical information) related to your participation in this research study for a minimum of seven years after final reporting or publication of a project.

We may share your de-identified or coded research information with other researchers interested in this topic at the University of Pittsburgh and other centers, including Carnegie Mellon University.

We might use your research data in future studies. These future studies might be done by us or by other investigators. Before we use your data, we will remove any information that shows your identity. There still may be a chance that someone could discern that the information is about you.

A description of this clinical trial will be available on http://www.clinicaltrials.gov, as is required by U.S. Law. This website will not include information that can be used to identify you. At most, the website will include a summary of the results. You can search this website at any

time.

In addition to the investigator listed on the first page of this consent form and the research staff, the following individuals will or may have access to identifiable information related to your participation in this research study:

- In unusual cases, the investigators may be required to release your identifiable research information (which may include your identifiable medical record information) in response to an order from a court of law. If the investigators learn that you or someone with whom you are involved is in serious danger or potential harm, they will need to inform the appropriate agencies, as required by Pennsylvania law.

This research is covered by a Certificate of Confidentiality from the National Institutes of Health. This means that the researchers cannot release or use information, documents, or samples that may identify you in any action or suit unless you say it is okay. They also cannot provide them as evidence unless you have agreed. This protection includes federal, state, or local civil, criminal, administrative, legislative, or other proceedings. An example would be a court subpoena.

There are some important things that you need to know. The Certificate DOES NOT stop reporting that federal, state or local laws require. Some examples are laws that require reporting of child or elder abuse, some communicable diseases, and threats to harm yourself or others. The Certificate CANNOT BE USED to stop a sponsoring United States federal or state government agency from checking records or evaluating programs. The Certificate DOES NOT stop disclosures required by the federal Food and Drug Administration (FDA). The Certificate also DOES NOT prevent your information from being used for other research if allowed by federal regulations.

Researchers may release information about you when you say it is okay. For example, you may give them permission to release information to insurers, medical providers or any other persons not connected with the research. The Certificate of Confidentiality does not stop you from willingly releasing information about your involvement in this research. It also does not prevent you from having access to your own information.

RIGHT TO PARTICIPATE or WITHDRAW FROM PARTICIPATION:

Your participation in this research study, to include the use and disclosure of your identifiable information for the purposes described above, is <u>completely voluntary</u>. Whether or not you provide your consent for participation in this research study will have no effect on your current or future relationship with the University of Pittsburgh or UPMC.

You may withdraw, at any time, your consent for participation in this research study, to include the use and disclosure of your identifiable information for the purposes described above. Any identifiable research recorded for, or resulting from, your participation in

this research study prior to the date that you formally withdrew your consent may continue to be used and disclosed by the investigators for the purposes described above. **If the investigators feel that you cannot complete the study requirements safely, they may withdraw you from the study.** Reasons for this may include serious medical complications, demonstrating poor understanding of the study, or non-compliance with study procedures.

To formally withdraw from this research study, you should provide a written and dated notice of this decision to the principal investigator of this research study at the address listed on the first page of this form. Your decision to withdraw your consent for participation in this research study will have no effect on your current or future relationship with the University of Pittsburgh or UPMC.

PHOTOGRAPH / VIDEO CONSENT:

By participating in this study, I understand that I will be photographed, videotaped or recorded. These pictures, videos or voice recordings may be used for research or educational purposes. Pictures, videos or voice recordings will not be used for potential media stories until I sign a separate consent form. By initialing below,

_____ I give my permission to use photographs, videos or recordings that contain images of my face or recordings of my voice for research or educational purposes.

_____ I **do not** give my permission to use photographs, videos or recordings containing images of my face or recordings of my voice for research or educational purposes. I understand that I will still be photographed, videotaped and/or recorded as part of this study.

_____ I **do not** give my permission to be photographed, videoed or recorded as part of this study.

****

VOLUNTARY CONSENT

The above information has been explained to me and all my current questions have been answered. I understand that I am encouraged to ask questions about any aspect of this research study during the course of this study, and that such future questions will be answered by a qualified individual or by the investigator(s) listed on the first page of this consent document at the telephone number(s) given. I understand that I may always request that my questions, concerns or complaints be addressed by a listed investigator.

I understand that I may contact the Human Subjects Protection Advocate of the IRB Office, University of Pittsburgh (1-866-212-2668) to discuss problems, concerns, and questions; obtain information; offer input; or discuss situations that have occurred during my participation.

By signing this form, I agree to participate in this research study and for the use and disclosure of my medical record information for the purposes described above. A copy of this consent form will be given to me.

Participant's Signature	Printed Name of Participant	Date

CERTIFICATION of INFORMED CONSENT

I certify that I have explained the nature and purpose of this research study to the above-named individual(s), and I have discussed the potential benefits and possible risks of study participation. Any questions the individual(s) have about this study have been answered, and we will always be available to address future questions as they arise. I further certify that no research component of this protocol was begun until after this consent form was signed.

Printed Name of Person Obtaining Consent	Role in Research Study
Signature of Person Obtaining Consent	Date