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

CONSENT TO ACT AS A PARTICIPANT IN A RESEARCH STUDY

TITLE: **Spinal Cord Stimulation for Restoration of Function in Lower-Limb Amputees**

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ClinicalTrials.gov Identifier: NCT04547582

SOURCE OF SUPPORT: National Institute of Neurological Disorders and Stroke

This research study is conducted under Investigational Device Exemption G200203 and is regulated by the Food and Drug Administration (FDA).

KEY INFORMATION

This research study involves the surgical implantation of electrodes near the spine **for up to 90 days** and testing of stimulation to produce sensations in your missing limb. This study will test if electrical stimulation of the lumbar spinal cord decreases your level of phantom limb pain and improves your ability to balance and walk. Stimulation will be applied to the implanted electrodes to determine the effects of stimulation on sensation and movement. At the completion of testing, the implanted electrode leads will be surgically removed.

This is an FDA-regulated study under an Investigational Device Exemption (IDE) to test the safety and efficacy of a spinal cord stimulation system, made up of spinal cord stimulation leads, a stimulator, and sensors that can be attached to your prosthesis. Since placement of the leads and use of the system is temporary, **there is no direct benefit to you**.

Eligible individuals for this study will have an amputation of one leg, below the

knee and above the ankle, and be between the ages of 22 and 70. The amputation must have occurred more than 6 months ago. Individuals must be willing to travel to the Rehabilitation Neural Engineering Labs at the UPMC Mercy Pavilion at least twice a week for 90 days. Eligible individuals will not have implants such as cardiac pacemakers, cardioverter defibrillators, or implanted drug infusion pumps, as systems used during testing may affect the activity of these devices.

We will screen participants to determine eligibility. Screening procedures include a verbal self-report of eligibility criteria, questionnaires, review of your medical records, a pregnancy test, and a complete physical exam with a study physician. If a participant expresses severe depressed or anxious mood, resources will be provided to assist in seeking appropriate mental health treatment.

Participants determined to be eligible for implantation will undergo several pre-operative procedures. You will have blood drawn to assess your suitability for surgery. You will also undergo pre-operative MRIs, CT scans, and x-rays to determine the location of electrode placement. A pre-operative EKG may be performed to determine if you can receive sedation during surgery. Testing of somatosensory function may also be performed prior to surgery. Somatosensory function is the ability to interpret bodily sensation. Sensation takes a number of forms, including touch, pressure, vibration, temperature, itch, tickle, and pain.

Electrode placement is a surgical procedure and will occur following the completion of all pre-operative screening procedures. This is an outpatient procedure and is expected to take approximately 2 to 3 hours.

Following placement of the electrodes, **you will come into our lab for research testing 2-5 times per week for up to 8 hours a day.** Testing will include self-report questionnaires, sensory testing involving stimulation of the implanted electrodes, and monitoring changes in your ability to balance during standing and walking.

A physician will monitor you during the course of this study. You will meet with a study physician at least once a week to assess the electrode placement site.

Approximately 90 days after implantation, the electrodes will be surgically removed. A member of the study team will contact you shortly after electrode removal to monitor your recovery. You will also meet with a study physician two weeks following removal to check the lead removal site and to discuss any additional follow-up.

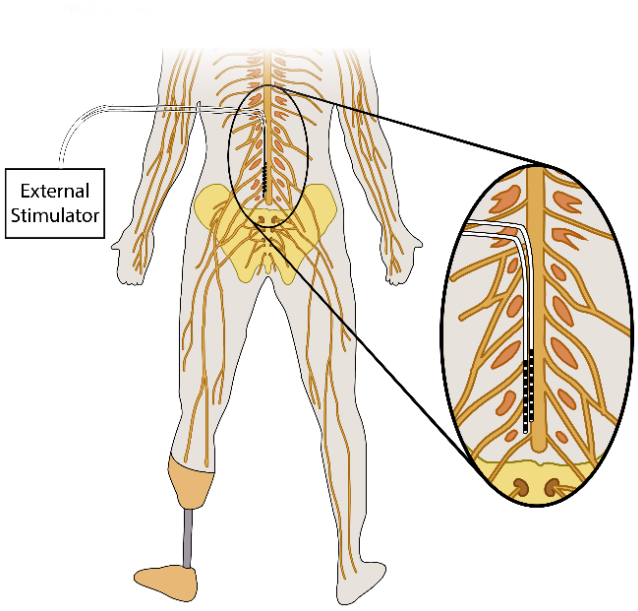
This is a greater than minimal risk study. Most of the risks are associated with placement of the electrodes and the presence of the electrodes themselves. There are also risks related to the x-rays and MRI scans completed prior to electrode placement. Other risks involve falling and uncomfortable sensations during balance and gait and stimulation testing, and confidentiality breach. As this study requires a surgical procedure with the inherent risks of surgery, the study surgeons will be available to answer any questions you might have, in person or via teleconference software, such as Zoom, Skype, or FaceTime.

You will be compensated for participation in this study at a rate of $50 per study

visit, in addition to reimbursement for travel. The maximum compensation you can generally receive for this study is $3,300.

Your participation in this study is voluntary. Our study team will explain the study procedures to you and will answer any questions that you might have. You will be provided with as much time as necessary to decide to participate. You may withdraw from the study at any time.

PURPOSE OF STUDY:



The purpose of this research study is to determine if a neuroprosthetic device which provides a sense of "feeling" to your missing limb can enable you to walk better or with greater ease. A **neuroprosthetic** is a prosthetic limb that is able to provide sensory feedback to the user. We want to characterize the types of sensations that can be produced by stimulating the spinal nerves in persons with lower limb amputations, and use stimulation to reduce phantom limb pain.

The study involves a medical procedure to temporarily place one to three stimulation electrodes in the space near the spinal cord. This medical procedure will be performed under local anesthesia and will take approximately 3-4 hours. Afterwards, the electrodes will be connected to an external stimulator and sensors will be mounted on your current prosthesis. Then, a series of experiments will be performed to characterize the types of sensations which are generated by electrical stimulation of the spinal cord and spinal nerves, as well as to measure the effect of stimulation on phantom limb sensations and phantom limb pain. Over the course of 90 days, we will ask you to come to the lab 2-5 days per week for experimental sessions. At the end of the final experimental session, the stimulation electrodes will be removed.

We are inviting you to consider participating in this research because you have a lower-limb amputation. You must be between the ages of 22 and 70 and at least 6-months post-amputation. You must be willing to travel to the Rehabilitation Neural Engineering Labs at least twice per week for 90 days.

You will have to meet certain criteria to be eligible. This will be reviewed with you upon your consent. We will screen 15 people and expect that up to 10 individuals will complete this study.

STUDY PROCEDURES:

As part of this study, you will complete the following procedures that will be conducted during multiple visits to UPMC occurring over a period of up to nine months. While it may be possible to schedule some of the procedures on the same day, you should plan to allow for a separate visit for each listed procedure. We will work with you to determine the testing schedule as early as possible.

Screening Procedures:

Procedures to determine if you are eligible to take part in a research study are called "screening procedures." For this research study, the screening procedures include:

- **Eligibility review:** We will ask you questions regarding your eligibility for this research study. This will include information about serious diseases or disorders, pregnancy and/or breast-feeding, current medications and allergies to medications, age and information about your amputation.
- **Brief Symptom Inventory questionnaire:** We will ask you to complete an 18-question survey to screen for anxious or depressed mood. This survey is known as the Brief Symptom Inventory-18. Due to the sensitive nature of the questions included in the survey, we will ask you to complete it in person at your first screening visit. Mental health resources will be made available to you at the time of the survey.
- **Medical record review:** You cannot have any serious diseases or disorders that affect your ability to participate in this study. We may need to access your medical records if additional information is required to assess your health. We will ask you for specific written consent prior to any medical record inquiries.
- **Self-report questionnaire:** You will be asked to provide basic information about yourself (age, weight, height, etc.) as well as medical history information including the date of your injury and current level of function and phantom limb sensations/pain. We will also ask questions related to your level of function, quality of life, mental health, and prosthetic limb usage. The questionnaires should take less than 30 minutes. This may be completed in research space at the UPMC Mercy Pavilion, other UPMC hospitals, or at your home.
- **Pregnancy test:** Women who are pregnant, plan to become pregnant, or are breastfeeding during the study cannot be included. Prior to any procedure, such as an x-ray, MRI, or fluoroscopy that may potentially involve risk to an unborn child, we will ask females of child-bearing potential to undergo a urine pregnancy test. If found pregnant, you will be withdrawn from the study.
- **Pre-operative x-rays:** You may be asked to undergo X-rays of your chest, upper back and lower back prior to surgery.
- **Pre-operative labs and screening:** You will undergo standard preoperative screening at a UPMC facility. UPMC clinic staff and a study physician will review your medical history and perform a clinical evaluation. This clinical evaluation

will include a detailed physical examination to evaluate your muscle and nerve function in your intact and residual limbs, and to screen for any signs of fever or active infection. You will also be asked if you are taking any medication that thins your blood or affects the way your blood clots. If you are currently taking any medications that thin your blood, you will not be eligible for this study.

We will also ask you to provide blood samples as part of this screening. Less than 4 teaspoons of blood will be required for each blood sample. Standard lab tests will be run on these samples to ensure that you do not have risk factors that would make you an unsuitable candidate for this study, including elevated blood sugar levels. As higher blood sugar levels may increase your risk of infection, we will test to make sure your levels are low enough for surgery with blood samples taken up to 6-months before surgery. For your safety, you will not be eligible for implant surgery if your blood sugar levels are too high.

Additional tests or treatments, such as a urinalysis, pregnancy test, or a MRSA swab, will be ordered to assure your safety. All preoperative screening procedures, with the exception of the initial clinical exam and drawn blood samples for blood sugar monitoring, will be completed within 2 weeks of electrode placement and testing. Preoperative screening visits are expected to last about 1 hour.

Experimental Procedures:

If you qualify to take part in this research study, you will undergo the experimental procedures listed below. Pre-operative procedures, electrode placement and testing will occur within 6 months after the screening procedures are completed. We will work with you to determine the best testing schedule. You may be photographed or videotaped during any of the experimental procedures for research or educational purposes.

- **Magnetic Resonance Imaging (MRI) scan:** You will have a MRI scan at a UPMC facility. Prior to arriving for this MRI scan, we will ask you about possible metallic devices and shrapnel which may be in your body, as these can interfere with the image quality and, more importantly, your safety. In the case of some implants, a pre-MRI x-ray may be required. Individuals from the MRI center will go over this information again, in order to protect you.
- **Preoperative MRI scan:** MRI uses a large magnet to take a picture of your spine and spinal cord. The MRI will be used to determine whether or not electrodes can be placed near your spinal cord. You will undergo one or two scans during this study. During one, you will have a contrast agent injected through an IV in order to improve the image quality. Each MRI, including preparation time, is expected to take less than 1 hour. If MRI images of your spine and spinal cord already exist, we may access your medical records to view those images instead of performing a new MRI scan.
- **Preoperative sensory testing:** You may undergo testing to measure your baseline sensory function before placement of the spinal cord stimulator leads. This may include tests to measure your sensitivity to light touch or vibration,

and your ability to feel your limbs moving. These tests will either be performed manually, by one of the study team members, or by a machine that is specifically designed to perform the test.

If you have already completed sensory testing in another study, such as our study "Balance and Gait Testing Baselines in Lower-Limb Amputees", you will not have to repeat it for this study. Your research data will be shared between studies to prevent repeat testing.

- **Preoperative 12-lead EKG**: You may undergo a 12-lead Electrocardiogram, or EKG, prior to lead placement. During an EKG, sensors are placed on the surface of your chest. These sensors can detect the electrical activity of your heart and can be used to detect heart problems. The EKG will show us that your heart is healthy enough for you to receive sedation during the lead anchoring procedure.
- **Infection prevention procedures**: We will ask that you shower each day for 5 days including the morning prior to your implant surgery. Our study physician may also recommend an ointment to use around your nose during this period. We will provide you with additional information regarding care of your incision.
- **Prophylactic antibiotics:** To reduce the risk of infection, you will be given an intravenous dose of antibiotics (cefazolin or similar) within two hours of the procedure. A study physician will discuss any potential allergies with you.
- **Videotaping of test sessions:** We will photograph or video portions of the experimental sessions. We will use images of your face and or recordings of your voice, with your consent, for research purposes. We may also use the photographs to document experimental setup and to document responses to stimulation. You may indicate your consent or not at the end of this document**.**
- **Electrode placement:** The study surgeon and their team will place up to three spinal cord stimulator electrodes in the space between your spinal cord and the bones in your spine (epidural space) in your lower back. The procedure will be performed at UPMC Mercy. You will be given antibiotics (cefazolin and/or vancomycin) through an IV prior to the procedure, as is standard protocol, to minimize the risk of infection. Lidocaine, a local anesthetic, will be injected near the site where the electrodes are inserted. You will also see an anesthesiologist to receive a small amount of sedatives through an IV prior to the procedure. Hair near the insertion site may be shaved to minimize the risk of infection. Once the skin on your back is numb, a needle will be inserted into the epidural space in your spine, using fluoroscopic imaging (x-ray movie) to view the location of the needle tip. A spinal cord stimulator electrode will be fed through the needle and tunneled in the epidural space to the target spinal nerve. Electrical stimulation will be applied through the electrode and you will be asked to describe the location on your body where you feel the stimulation. The electrode may be adjusted until you feel sensations seemingly coming from your amputated leg. We will use fluoroscopic (continuous x-ray) imaging to make sure there is no lead migration during this process. The needle will be removed and the electrode will be secured to your skin with tape. Based on the amount of time this process takes and our success in targeting the spinal nerves in your

lower back, the study physician may decide to repeat this procedure with up to two more electrodes (three total). The entire procedure is expected to last approximately 3-4 hours. At the end of the procedure, you will be trained to care for the sites where the electrodes enter your skin. During normal use of these electrodes to treat back pain, a connection through the skin is maintained for approximately 7 days, and then the devices are either removed or permanently implanted. During this study, the connection through the skin will be maintained for up to 90 days. During that time, you will not be able to perform any strenuous activity, such as heavy lifting (greater than 10 pounds), hard exercise, or operating heavy equipment, unless otherwise indicated by the study physicians. Detailed hospital discharge instructions will be provided to you.

- **Intravenous sedation:** You may receive a small dose of sedation through an IV prior to the lead anchoring procedure in order to keep you comfortable. The two drugs that may be used are called Fentanyl and Versed. Fentanyl will help stop any pain that may occur during and/or after the procedure. Versed is a sedative that will keep you calm. Both of these drugs are FDA-approved. These drugs will be used according to the instructions on the package inserts.
- **General anesthesia:** You may receive general anesthesia if you request it and the anesthesiologist approves it. A combination of medications put you in a sleep-like state before the medical procedure. Under general anesthesia, you don't feel pain because you're completely unconscious.
- **Lead anchoring procedure:** Once the electrodes have been placed, the doctors will secure the leads to prevent them from moving. The leads will be secured to a membrane in your lower back through a small incision.
- **Post-operative pain medication:** We may prescribe you a low dose of pain medication for you to take if you are uncomfortable after the leads are placed. The pain medication that may be prescribed to you, Norco 5-325, is FDA-approved. You will be instructed to use this medication according to the instructions on the packaging label.
- **Post-operative high resolution Computerized Tomography (CT) scan**: After lead placement, you will have a high-resolution CT scan of the lumbar spine to document the 3-dimensional location of the leads. We may use pillows or brace during this CT and the second pre-operative optional MRI to ensure that your spine is in a similar position for both scans.
- **Weekly x-rays:** Multi-view x-rays of your middle and/or lower spine will be taken to document the location of the electrodes and any movement that may have occurred. This will occur during testing visits and will take approximately 30 minutes including wait time. These x-rays will be taken once per week for the first 4 weeks of the study, and once every two weeks after that.
- **Weekly clinical exams:** You will meet with a physician at least once a week to check the site where the electrodes were inserted for infection. If you were only given vancomycin during the placement procedure, you will meet with a physician at least twice a week. The physician will inspect the site for any

redness, swelling, or pus, and will check to make sure you do not have a fever. The physician may use a swab at the insertion site for a culture or ask that you have more blood work drawn if they suspect you may have an infection. You may also be given oral antibiotics to take for 5-7 days if infection is suspected. If you have a severe infection, or if your infection does not resolve within 3 days, we will remove the electrodes closest to the infected area. Clinical exams may occur either in-person at a UPMC facility or our laboratory, or via telemedicine at our laboratory or at your home, whichever is most convenient for you and the physician. Clinical exams are expected to take less than 1 hour of your time.

- **Psychological discussions:** Throughout the study, you will have the opportunity to talk to a psychologist, to discuss any concerns you may have regarding the study. The psychologist may ask you questions about your mood and discuss plans with you for after the devices are removed at the end of the study.
- **Sensory stimulation testing:** Testing will be repeated at each visit over the duration of the study, up to 5 days per week, for up to 8 hours per day. Rest, meals, and other breaks will be scheduled as needed. During each testing session, we will connect an external stimulator to the electrodes and our system will stimulate your nerves, which may provide sensations that feel like they originate from your leg. Testing will involve determining the relationship between stimulation of your nerves and your perceived sensation. Small pulses of electric current will be sent to the nerves near your spinal cord in order to mimic the aspects of touch and feel in relation to physical interaction with objects or people. We may also attach electrodes to the surface of your skin to measure the activity in the muscles of your legs, or to your scalp to measure activity in your brain related to sensation. You will be asked questions in regard to the nature of the feeling, such as location, smooth/sharpness, temperature, and pain level (if any). You will also be asked to describe any changes in phantom limb sensations or phantom limb pain during stimulation. We may also electrically or mechanically stimulate your residual limb or your intact limb and ask you to compare the sensations to those generated by spinal cord stimulation. Electrical stimulation of your limb will be delivered with a different device than the spinal cord stimulator. Impedance (electrical resistance) testing may also be conducted during the testing session to assess electrode function. You will likely not feel any sensations as a result of this testing.
- **Control of a sensorized prosthetic limb:** Using your own prosthesis, a different prosthetic foot, or a virtual reality version of a foot, you will be asked to perform tasks that test your ability to use sensory stimulation in activities of daily living. If your own prosthesis is used, sensors will be temporarily attached to the ankle and sole of the foot of the device to detect movement speed and position. These sensors will be removed at the end of the experimental session and do not on their own influence your movements or control of your prosthetic. Electrodes may be placed on your skin over the muscles of your residual limb to detect muscle activity. You will be asked to contract those muscles to produce control signals for the prosthetic foot. We may also place markers on your skin that allow us to track the motion of your limbs controlling the prosthesis. You

will be given an opportunity to learn to use this system. Afterwards, you will be asked to perform tasks such as moving your limb to a specific point in space or applying force. During some of these tasks, you will be provided sensory feedback through electrical stimulation of your spinal nerves. We will compare your control of the prosthetic limb with and without this electrical stimulation. The sensations that you feel as a result of your movements may help you to improve your gait.

- **Balance control and gait stability:** Using your own prosthesis, you will be asked to perform tasks that measure your ability to balance during standing and walking. Sensors will be temporarily attached to the ankle and sole of the device. These sensors will be removed at the end of the experimental session. You will be instructed to perform tasks such as standing quietly with eyes open or closed, walking forwards or backwards, or standing on a moving or rotating platform. Motion capture markers and electrodes may be attached to your skin to measure limb movement and muscle activity. We will compare your performance during these tasks with and without stimulation. We may ask you to complete these tasks before and during the implant period. These tests will be performed under direct supervision of a physical therapist and/or with the use of a safety harness system.
- **Clinic-based prosthetic training and assessment:** As part of this study we will ask you to perform some tasks at home to determine how the device affects your normal daily activities. These at home tasks will occur over a 2-week period. Before you take the device home, we will ask you to visit the University of Pittsburgh's Physical Therapy Clinical and Translational Research Center (PT-CTRC) to see how well you are able to perform certain tasks associated with daily life, such as sitting, standing, and using stairs. We may ask you questions regarding how your home is set up and if you have someone at home who assists you with certain tasks. You will undergo 1-5 sessions of physical therapy and gait training with the sensorized prosthesis before you can take it home with you. For your safety, a physical therapist will be present during this training. You have the option to use an app on your mobile device to adjust the stimulation settings. The study team will collect the data from the app and will train you on the use. The data transmitted via Bluetooth will be de-identified. The PI will provide his direct cell number, so you will be able to contact the researchers at any time during this week if you have problems with the system, and you can also deactivate the system at any time and use your prosthesis as you usually do.
- **Community use of sensorized prosthesis:** We will attach sensors to your current prosthesis that will help monitor your activity. These sensors will allow the stimulator and spinal cord leads to generate sensations that should feel similar to the sensations you feel in your intact leg. You may be able to use the device outside the lab for up to two weeks to see if it improves your ability to move, such as when standing and walking.
- **Self-report questionnaire:** Throughout the study, you will be asked to complete questionnaires about your current level of phantom limb pain. The questionnaires should take less than 30 minutes. This can be completed in

research space at the Mercy Pavilion, UPMC, or at your home.

- **Removal of electrodes:** After the completion of the final day of testing, and less than 90 days from the date of electrode placement, the electrodes will be removed by the study physician(s) who placed the electrodes. This will involve pre-op testing, and another procedure at UPMC Mercy. You will be given antibiotics prior to the procedure to minimize the risk of infection. Lidocaine, a local anesthetic, will be injected near the site where the electrodes were inserted. You will also see an anesthesiologist to receive a small amount of sedatives through an IV prior to the procedure. One of the study surgeons will inspect each lead to ensure that it is intact and was completely removed from your body. If there are any concerns about incomplete removal, fluoroscopic imaging can be used during the procedure to visualize the epidural space and guide decisions about next steps, which will be determined by the surgeon. The entire removal procedure is expected to last approximately 1 hour.
- **Post-removal follow-up visit:** We will ask you to see a study physician two weeks after the leads are removed. The study physician will remove any remaining sutures and inspect the area where the leads were to make sure that you are healing properly.
- **Post-removal follow-up calls:** Within 48 hours after electrode removal, a research staff member will call you to see how you are feeling. Within a month after electrode removal, a research staff member will call you to ask questions about any remaining changes in your phantom limb sensations or phantom limb pain and check on how you are feeling.

RISKS and BENEFITS:

There are a number of possible risks, side effects, and discomforts associated with participation in this research study. As with any investigational study, there may be risks of adverse events or side effects that are currently unknown and it is possible that certain unknown risks could be serious, permanent, severe or life threatening.

STUDY RISKS:

The most significant risks of this study are related to the electrode placement procedures performed under local anesthesia and neural stimulation. You will undergo two medical procedures (electrode placement and removal) during the study.

- **Pre-operative blood work.** The insertion of the needle to draw blood may cause temporary discomfort, bruising from where the needle enters the vein, or soreness. There is a slight risk of infection. Fainting may occur, but this risk is rare.
- **Pre-operative EKG:** You may experience minor discomfort when the adhesive EKG sensors are removed from your skin.
- **Local anesthesia for the electrode placement and removal procedures carries several risks.** Common risks, which are minor and typically temporary,

include increased pain at the injection site and local skin infection. Infrequent risks include lightheadedness, dizziness, drowsiness, blurred vision, respiratory depression, and swelling. Rare risks include low blood pressure and irregular heartbeat.

- **Using general anesthesia carries several risks.** There is a risk of increased pain and/or local infection at the injection site. There are also risks of side effects such as nausea, vomiting, chills, confusion for a few days, breathing problems including pneumonia, injury to the teeth, and a sore throat caused by a breathing tube. General anesthesia will only be used if you request it and the anesthesiologist approves it.
- **There are risks associated with the sedatives you may receive prior to electrode placement.** Common risks associated with these sedatives include nausea and vomiting, urinary retention, and pruritus "itchiness." Uncommon risks include respiratory depression and temporary hypotension (low blood pressure). An anesthesiologist will be present to make sure that you are safe while you are sedated. For your safety, the study physicians and their medical staff will monitor you during and after the lead placement procedure.
- **The procedure to place electrodes near the spinal cord carries several risks including some rare, but severe, risks.** Common risks include fluid buildup, called seroma, and bruising at the insertion site. This bruising and buildup is harmless, but may be uncomfortable. There is a low risk of infection at the site where the electrodes tunnel through the skin. Meningitis, or swelling of the brain and spinal cord membranes due to infection, is a rare but potentially serious risk. The risks of infection may increase the longer the electrodes remain implanted. Other rare but serious risks include pain, numbness, or weakness in your arms, hands, legs, or feet, which may come on gradually or suddenly, and bleeding from the space between spine and spinal cord. Study physicians and UPMC surgical staff will closely monitor you during surgery for any complications. The method of lead insertion used during placement will reduce the risks associated with the surgical placement of the electrodes and study physicians will monitor the insertion site following surgery for any signs of infection.
- **There are risks associated with the implanted electrodes.** Infrequent risks include pain at the electrode sites, allergic reaction in response to the implanted leads, or minor cerebrospinal fluid (CSF) leaks that may cause severe headaches. Allergic reactions may cause itchiness, redness, or swelling. CSF leaks may rarely require emergency surgery, which would occur at no cost to you. A rare but potentially severe risk of electrode placement is nerve damage that can cause neurological dysfunction, including paralysis, although placement of these electrodes is a common clinical practice with a low risk of these side effects. There is also a risk that, over the course of the study, the electrodes will move within your back to a new location. Movement of the electrodes may affect the types of sensations you feel during stimulation. These changes in sensations may prevent further testing of the electrodes, in which case we will remove them earlier than expected. Similarly, it is unlikely, but possible, that the electrodes may break or otherwise fail to deliver appropriate stimulation, in

which case they will be removed earlier than expected. If a lead breaks, a study physician may need to perform additional surgery, possibly including additional x-ray exposure and removal of a small amount of bone on the back of your spine to retrieve any fragments of the lead from your body.

- **The procedure to remove electrodes near the spinal cord carries several risks including some rare, but severe, risks.** There is a risk of post-implantation infection of the skin where the electrodes were placed. Meningitis, or swelling of the brain and spinal cord membranes due to infection, is a rare but potentially serious risk. The study physician will check the lead site for infection during your follow-up visit.
- **There are risks associated with electrical stimulation of your nerves.** A risk of electrical stimulation is that on some electrodes, the evoked sensations may be unpleasant or painful, or limbs may involuntarily move and then subside after several minutes. Prior to stimulation tests, it is not possible to know on which electrodes this may occur. Therefore, stimulation intensity will be increased slowly to minimize the chance of eliciting these sensations. If these sensations occur, stimulation on that electrode will be stopped. There is a rare risk of damage to your nerves or prolonged phantom limb pain as a result of electrical stimulation, although the stimulation parameters used in this study have been carefully selected to avoid causing any damage. Additionally, any reductions in phantom limb pain that you experience as a result of stimulation may not be permanent. Any phantom limb pain you experienced prior to implantation of the electrodes may return after the electrodes are removed.
- **Observing a 3D virtual environment:** There is a risk that you will experience dizziness or nausea while looking at the 3D virtual environment, such as in closed-loop control testing. This risk will be mitigated by providing frequent breaks or ending the virtual reality experiment.
- **Securing sensors/electrodes with tape:** A common risk of placing surgical tape on the skin is discomfort when removing the tape. Tape will be used conservatively and will be removed with caution and care.
- **Standing and walking with stimulation:** Stimulation may cause you to feel unusual or unexpected sensations. During standing and walking, these sensations could be distracting and could cause a loss of balance. During initial use of the system, a study investigator will stand nearby to assist with any loss of balance. Any challenging tasks such as walking with eyes closed or walking backwards will be performed near a study investigator and under the supervision of a physical therapist.
- **Malfunctions associated with mechanical prostheses:** There is a risk that interactions between your prosthetic and our stimulation system could cause temporary malfunctions in your prosthesis. This may increase your risk of tripping or falling. If you have an electrically powered prosthesis, before walking with our system, we will turn it on near your prosthesis to look for any malfunctions. During walking, research staff will stand near you to provide support, and we will keep cabling as short as possible to prevent any possible

snagging or breaking. If any malfunctions occur, stimulation will cease and your prosthetic will continue to operate normally.

- **Connecting electrodes to the stimulator:** It is possible to incorrectly connect the leads to the wrong channel. This could cause feedback or generate painful sensations. We will color-code the leads to match specific channels to prevent this from occurring.
- **Antibiotics may cause side effects.** We will follow the standard clinical procedures to minimize the risks associated with surgical implantation or removal of electrodes. For example, antibiotic prophylaxis administration (cefazolin or similar) is usually initiated for the patient approximately two hours before the surgery and will be maintained as directed by the study physiatrist and their clinical team. We have excluded pregnant females and those with renal failure as they may be at an increased risk for complications resulting from administration of the antibiotics. Antibiotic ointment and sterile dressings will be applied to the implantation site to minimize the risk of infection. Standard sterile surgical techniques will be followed for this study. Common side effects include pain, swelling, skin rash or a hard lump at the injection site. Other side effects include: fever, seizure, rash, itching, diarrhea associated with *C. difficile* (a bacteria) infection, nausea, vomiting, increased liver enzymes, and abnormal blood urea nitrogen or serum creatinine levels, which are related to kidney function.
- **Pain medication may cause side effects.** We will follow standard clinical procedures to keep you as comfortable as possible while the leads are in place. You may feel some pain and/or discomfort in the first few days following the lead placement procedure. In order to keep you comfortable, the study physician may prescribe a pain medication called Norco 5-325. The pain relief from this medication should last 4-6 hours, though side effects may be present up to a day after the last dose. A common side effect of Norco 5-325 is drowsiness. Uncommon side effects include nausea, vomiting, constipation and/or diarrhea, pruritus ("itchiness"), rash, dizziness, and confusion. The risk of these uncommon side effects is low. There is a risk of tolerance, physical dependency, and psychic dependency associated with administration of this drug; however, this risk is lowered when Norco 5-325 is taken as prescribed for only short periods of time. Signs of dependency and tolerance include requiring increasingly larger doses of the drug to reduce your pain. You should notify a member of the study team if you experience any side effects, including signs of dependency.

  Prior to prescribing Norco 5-325, we will ask you to answer a questionnaire to measure your risk for dependency. Based on the results from this questionnaire, you may be prescribed Tylenol or a lesser opiate drug.
- **MRI scanning is associated with several risks.** There is the potential risk related to the machine itself attracting metal. Therefore, if you have metal within your body (e.g. aneurysm clips or pacemakers) that is not compatible with MRI, you will be excluded from this study. Participants with dental fillings and most spinal fixators can be studied without risks. The magnet will make

intermittent, loud, knocking noises that could cause ear discomfort in some people. Also, the rapidly switched magnetic fields used during imaging may cause nerve stimulation (e.g., an uncontrolled twitch or tickle near the waist). Because you must lay inside the narrow scanner tube, you may become anxious and frightened in the enclosed space. If you feel claustrophobic during the scan, you can alert the staff during the MRI at any time. The study can be stopped and you can rest outside of the enclosed area.

- **A contrast agent will be injected into your arm through a needle during one of the MRIs. This carries additional risks.** The contrast agent contains a material called gadolinium. Injection of contrast may cause discomfort, tingling, or warmth in the lips, metallic taste in the mouth, tingling in the arm, nausea, or headache. These symptoms occur in less than 1% of people and go away quickly. There is a small risk of an allergic reaction to gadolinium, although a severe allergic reaction occurs in less than one in 300,000 people. Insertion of the needle to inject the gadolinium may cause minor pain, bruising, and/or infection at the injection site. People with severe kidney failure who receive gadolinium are at risk for developing Nephrogenic Systemic Fibrosis/Nephrogenic Fibrosing Dermopathy (NSF/NFD) (formation of excess connective tissue of skin, joints, eyes and internal organs that can create large areas of hardened skin). If you have kidney failure, you will be excluded from this study. Please notify the research staff, a doctor, nurse, or technician if you are allergic to gadolinium, if you have any kidney problems, or if you experience any side effects so that they can determine if you are at risk for developing NSF/NFD. There is evidence that repeated MRI scans with gadolinium can result is some accumulation of it in the brain. The significance of this and possible effect on health is not known.

- **Fluoroscopy, CT scan, and x-ray imaging carries a risk of radiation exposure.** During the electrode placement procedure, fluoroscopic imaging will be used to assist with targeting the placement of leads. Periodically throughout the study, we will use x-ray imaging to document the location and any movement of the stimulation leads. A chest x-ray may occur prior to surgery, then multi-view x-rays of the thoracic and/or lumbar spine will occur weekly for the first four weeks, and then every other week for the remainder of the study, resulting in an additional four multi-view x-rays, for a total of eight multi-view thoracic and/or lumbar spine x-rays. This imaging will expose you to radiation. The maximum amount of radiation exposure you will receive during this study is as much as 39.01 mSv effective dose. This is in addition to the average yearly exposure for Americans, which is 6.2 mSv. For comparison, the annual whole body radiation limit is 50 mSv for a radiation worker. There is no minimal level of radiation exposure that is recognized as being totally free of the risk causing genetic mutation (abnormal cells) or cancer, but participation in this study involves medical procedures with radiation exposure higher than for the average American and lower than the maximum allowed for radiation safety workers. Throughout the study, we will monitor your radiation exposure to ensure the total effective dose is less than 50 mSv. We will also share this dose with you so that you can inform your doctor about this study-related dose before undergoing any other medical procedures involving radiation in the next year.

- **Community-use trial:** There may be a risk of falling while walking and standing with the sensorized prosthesis. There is also a risk of system failure due to technical/software issues or power malfunction, which may distract you and cause a fall. Falling may result in injuries ranging from minor (for example: scrapes, bruises, cuts) to major (for example: broken bones, head injury). We will teach you about the most likely types of failures and you will practice responding to them while under the supervision of our study team. You will have contact information for the team in case there is an issue with any of the equipment.
- **Since identifiable information is collected, there is a risk of breach of confidentiality.** 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 to protect your private information. Contact information and other identifiable information will be stored separate from research data. Photographs and videotapes will be stored digitally on our password-protected server. Hard copies may be stored in a locked file cabinet. At the end of this consent form is a space for you to give your permission (or deny permission) for pictures or videos that include images of your face to be used in research presentations or publications.
- **Women who are pregnant during the study are excluded due to potential risks to the unborn fetus or themselves.** These risks include radiation exposure during fluoroscopic imaging which may lead to birth defects, mental impairment, cancer, or miscarriage. There are no known risks associated with undergoing an MRI scan while pregnant and the risks of MRI to the fetus are felt to be very small, but are, nevertheless, also not known. Any complications during medical procedures would put the fetus at risk for distress. If you have questions, you are encouraged to speak with a study doctor or your personal physician. A urine pregnancy test will be given to females of child-bearing potential. If pregnant, you will be excluded from the study.

BENEFITS:

This study will provide no direct benefit to you. This study will provide the basis for long-term testing of electrical stimulation to provide sensation in those with amputations.

It is likely that any reduction in pain that you experience during stimulation will be temporary. If you currently have phantom limb pain and experience a significant reduction in that pain during stimulation, you may be referred to a neurosurgeon to discuss further options for permanent implantation of a spinal cord stimulator system.

There are other appropriate alternative procedures or treatments that may help in the reduction of your phantom limb pain. Non-surgical treatments for phantom limb pain include oral medications, rehabilitative therapy and behavioral modifications, transcutaneous electrical nerve stimulation, and neurolysis. Transcutaneous electrical nerve stimulation (TENS) is the use of electrical nerve

stimulation through electrodes placed on the surface of your skin. Neurolysis is the application of physical or chemical agents to a nerve in order to cause a temporary degeneration of targeted nerve fibers. Oral medications for phantom limb pain include over-the-counter pain relievers, such as acetaminophen and non-steroid anti-inflammatory drugs (NSAIDs), narcotic pain medications, muscle relaxants, beta-blockers, anticonvulsants, and antidepressants. Surgical treatments, in addition to implanted spinal cord stimulation systems, include sympathectomy, or the severing of nerve pathways responsible for your phantom limb pain. You are encouraged to speak with a study doctor or your personal physician about any of these treatments that may be helpful to you.

NEW INFORMATION:

You will be promptly notified if we learn of any new information about study risks or other clinically relevant research results that could affect your health or otherwise cause you to change your mind about continuing to participate.

COST AND PAYMENTS:

Neither you, nor your insurance provider, will be charged for the costs of any of the procedures performed for the purpose of this research study (i.e., the Screening Procedures or Experimental Procedures described above). If you get a bill or believe your health insurance has been billed for something that is part of the study, notify a member of the research team. Any procedures performed for routine medical care will still be billed to you or your insurance company; you will be responsible for any co-payments.

You will be compensated for participating in this research study. You will be reimbursed on a reloadable debit card**.** You will participate in up to 50 study visits (consent, pre-operative examination, MRI, lab work, electrode placement and removal, testing sessions, and physician follow-up appointment) for which you will be compensated $50 for each visit. The maximum compensation prior to electrode placement and testing is $150. The total maximum compensation you can normally earn in this study is $3,300. If you are asked to participate in additional visits, you will be compensated $50 per visit for each additional visit. For lengthy study visits that occur during meal times, meals will also be provided to you. Please know that if compensation for research is greater than $600, it is reported to the IRS as income.

Participants who do not provide a social security number may still participate in the research, but the IRS requires that 26% of the payment be sent by the institution to the IRS for 'backup withholding;' thus you would only receive 74% of the expected payment.

You will be required to travel to UPMC or our research lab for study procedures. If you have your own personal transportation, you will be reimbursed for mileage costs at the standard IRS rate and 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. We will also reimburse airfare for you and a caregiver for screening or study visits.

We may also provide housing or housing reimbursement for overnight accommodations for study-related visits. This may include up to 7 days a week for study visits for the duration of your participation.

If you withdraw from the study for any reason, 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.

Your data from this research study may contribute to a new discovery or treatment. In some instances, these discoveries or treatments may be of commercial value and may be sold, patented, or licensed by the investigators and the University of Pittsburgh for use in other research or the development of new products. You will not retain any property rights nor will you share in any money that the investigators, the University of Pittsburgh, or their agents may receive.

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. Lee Fisher, 240-620-1420. 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. Imaging studies (such as x-rays), 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 result in identifiable information that will be placed into your medical records held at UPMC Presbyterian. The nature of the identifiable information resulting from your participation in this research study that will be recorded in your medical record includes any imaging study results (x-rays, etc.) or medical procedures. Authorized representatives of the UPMC hospitals or other affiliated health care providers may have access to identifiable information related to your participation in this research study for the purpose of (1) fulfilling orders, made by the investigators, for hospital and health care services (e.g., laboratory tests, diagnostic procedures) associated with research study

participation; (2) addressing correct payment for tests and procedures ordered by the investigators; and/or (3) for internal hospital operations (i.e. quality assurance).

This research study will involve the recording of, past, current and/or future 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 any changes to your health related to your amputation. This information will be used for the purpose of assessing potential changes related to study procedures. In special cases, investigators may access previous medical records to assess your ability to participate in this study.

Authorized representatives of the University of Pittsburgh Office of Research Protection may review your identifiable information for the purpose of monitoring the appropriate conduct of this research study. Additionally, the **Food and Drug Administration** may inspect your records and identifiable information as part of monitoring this 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.

You may access medical information that results from participation in this study. In accordance with the UPMC Notices of Privacy Practices document that you have been provided, you are permitted access to information contained within your medical records filed with your health care provider.

This research is covered by a Certificate of Confidentiality from the National Institutes of Health. Most people outside the research team will not see your name on your research information. This includes people who try to get your information using a court order. One exception is if you agree that we can give out research information with your name on it. Other exceptions are information about child abuse or neglect and harm to yourself or others.

Your de-identified research information and data may be shared with other researchers performing data analysis as part of this study at the University of Pittsburgh, and Carnegie Mellon University. In addition, de-identified data may be shared in secure data repositories or databases such as the DABI: Data Archive BRAIN Initiative, which is funded by the National Institutes of Health. Researchers from outside this project may have access to the de-identified data in those data repositories.

As a result of your visits at the Clinical and Translational Research Center, a research record will be created in your name with the PT-CTRC System in

order to log your visit. No test results will be stored in this record.

We might use or share your research data in similar studies, such as our study on balance and gait. These studies might be done by us or by other investigators. Before we use or share your data, we will remove any information that shows your identity.

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.

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 completely voluntary. 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. Whether or not you provide your consent for participation in this research study will have no effect on your current or future medical care at a UPMC hospital or affiliated health care provider or your current or future relationship with a health care insurance provider.

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 or medical information 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.**

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. Your decision to withdraw your consent for participation in this research study will have no effect on your current or future medical care at a UPMC hospital or affiliated health care provider or your current or future relationship with a health care insurance provider.

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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.

VOLUNTARY CONSENT

The above information has been explained to me and all of 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**