University of Pittsburgh
School of Medicine
Department of Neurological Surgery

CONSENT TO ACT AS A PARTICIPANT IN A RESEARCH STUDY

TITLE: **Spinal Cord Stimulation for the restoration of arm and hand function in people with subcortical stroke**

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PURPOSE OF STUDY:

The purpose of our study is to characterize the muscle activation that can be produced by electrical stimulation of the spinal nerves in people who have had a stroke. More specifically we would like to understand if these activations can improve the execution of simple arm and hand movements and if they impact muscle spasticity. The study involves a surgical procedure to temporarily place one to two FDA-approved stimulation electrodes in the space between your spinal cord and the bones in your cervical spine (close to your neck). This surgical procedure will be performed under general anesthesia and will take approximately two to three hours. Afterwards, the electrodes will be connected to an external stimulator and a series of experiments will be performed to characterize the muscle activity generated by pulses of electrical stimulation delivered to the spinal nerves. Over the course of less than 30 days, there will be up to 20 of these experimental sessions. At the end of the final experimental session, the stimulation electrodes will be removed by a final short surgical procedure.

We are inviting you to consider participating in this research because you have had a stroke that caused weakness in your arm and hand. To be able to participate to this study, you must be between the ages of 21 and 70 and at least 6 months post-stroke. Alternatively, we are enrolling healthy control participants who do not have a history of stroke and are between the ages of 21 and 70.

You must be willing to travel to the University of Pittsburgh at least twice per week for 30 days.

You will have to meet certain criteria to be eligible. This will be reviewed with you upon your consent of participation to the study. We will screen 40 people in total and expect that up to 15 individuals with stroke will complete this study. We also plan to enroll up to 20 healthy participants. We plan to recruit subjects with various ranges of impairment after stroke. If there have been an adequate number of subjects enrolled in the same range as you, you may not be eligible for the study.

Drs. Capogrosso, Gerszten, and Pirondini have financial interests in Reach Neuro, Inc., which has an interest in technology being evaluated in this study. This means it is possible that results of this study could lead to personal profit for these investigator(s) and/or the University of Pittsburgh. Any questions you might have about this will be answered fully the Human Subject Protection Advocate of the University of Pittsburgh at (866) 212-2668, or by the Principal Investigator, Lee Fisher at (412) 383-1329, who has no financial conflict of interest with this research.

STUDY PROCEDURES:

As part of this study, you will complete the following procedures that will be conducted during multiple visits to the University of Pittsburgh or UPMC occurring over a period of up to two years. 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. Some baseline testing that is performed for the purpose of determining eligibility may be performed again in the weeks prior to surgery if surgery will be completed more than one month after initial baseline testing. These tests may include the pregnancy test, pre-operative labs and screening, MRI safety screenings, questionnaires, preoperative sensory/motor and spasticity testing, and preoperative strength, range of motion and proprioception/vision testing which are listed and described below."

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 stroke. If, during the course of this review, you are found to be a danger to yourself or others, you will be referred to the appropriate facilities for help with your condition.
- **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 your consent prior to any medical record inquiries. Our study team may contact your medical doctors to discuss medications or medical conditions related to study eligibility.
- **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 stroke and current level of motor and sensory function. We will also ask questions related to your motor ability, spasticity, exercise and quality of life. The questionnaires should take less than 30 minutes. This can be completed in research space at the Rehab Neural Engineering Labs or UPMC.
- **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 labs and screening:** You will undergo standard pre-operative screening. The clinic staff will ask you about your medical history and perform a simple physical examination. If you are currently taking any medications that thin your blood, you will not be eligible for this study. You will be screened for fever/infection. You will be asked to provide a blood sample. Less than 3 teaspoons of blood will be required for the 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. You will also be asked if you are receiving any medication that affects blood coagulation. Additional tests or treatments (such as a chest Xray, MRSA nasal swab, or electrocardiogram may be ordered at the discretion of the principal investigator or study physiatrist to assure your safety. This visit is expected to last 1 hour and will be performed at a UPMC facility within 2 weeks of electrode placement and testing.

Experimental Procedures:

If you qualify to take part in this research study, you will undergo the experimental procedures listed below. Pre-operative procedures will begin 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.

- **MRI Scan Screening:** 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. Also, individuals from the MRI center may 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, spinal cord and brain. The MRI will be used to determine a) whether or not electrodes can be placed near your spinal cord, b) the neural activity level of your brain and spinal cord at the moment of study enrollment. You will undergo two or more scans during this study. 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. One of the scans is named functional MRI. During this particular scan you will be asked close your eyes and stay at rest. While you are resting with eyes closed, the MRI scanner will measure the neural activity in your spinal cord and brain at rest do determine your baseline activity level before commencement of the study.
- **Preoperative sensory/motor and spasticity testing:** You may undergo testing to measure your baseline sensory and motor functions 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. Standard clinical tests to assess spasticity and limb mobility will also be performed: e.g. you will be asked to try to move the arm in a particular position in space or exert a certain force on a dynamometer. 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.
- **Preoperative strength, range of motion and proprioception/vision testing:** The strength and range of motion of your arm joints and your ability to sense where your arm is in space will be assessed using different devices in the lab and through clinical standardized tests. Your visual attention will also be assessed through a pen and paper test. We will use the KINARM robot to evaluate your proprioception and the Humac Norm system and WristBot to measure strength and range of motion of your arm joints. For your hand we will use a standard hand-held dynamometer and pinch gauge. Proprioceptive ability will be assessed prior to implantation, at day 29 before removal of the spinal electrodes and during the follow up visit 2 weeks after electrode removal. Strength and range of motion performances will be tested prior to implantation, throughout the 29 days of testing and at follow up 2 weeks after electrode removal.
- **Transcranial magnetic stimulation:** TMS involves the use of a magnet to stimulate the parts of the brain that control movement. The type of TMS performed in this study is considered experimental. We will ask

you to wear a headband or glasses so that we can keep track of where to put the magnet. Small sensors with wires attached to them will be placed on your arms to record the electricity coming out of your muscles. When the magnet is used, it will be gently placed on top of your head and you will hear a tapping sound and feel tingling on your scalp. Your body may move after each tap. We will move the magnet to different places on your scalp and repeat the process up to 1000 times, each time measuring the electricity from your muscles and how it affects the movements that you make. During TMS, we may also record activity from the implanted electrodes by connecting them to an external system. We may also ask you to squeeze a sensor that measures grip strength while you are receiving TMS.

- **Possible preoperative X-ray**: The study physician will use one of two methods to place the electrodes in your back. One of these methods requires an x-ray of your cervical spine to determine the best way to place the electrodes.
- **Prophylactic antibiotics:** To reduce the risk that an infection occurs during the insertion of the stimulator electrodes, you will be given a dose of antibiotics (cefazolin, 1-2g or vancomycin, 1g) via intra-venous injection within two hours of the procedure. For the same reason, you may also be prescribed an oral antibiotic to take for the duration of the study. A study physician will discuss any potential allergies with you.
- **Pre-Operative intravenous Sedation:** You may receive a small dose of sedation through an IV prior to the stimulator electrode implantation in order to keep you comfortable and relaxed during the implantation procedure. 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 listed on the package inserts.
- **Electrode Placement:** Dr. Gerszten and his team will place up to two spinal cord stimulator electrodes in the space between your spinal cord and the bones in your cervical spine (close to your neck). The procedure will be performed at UPMC Presbyterian Hospital. You will receive general anesthesia. You will be continuously monitored by trained medical personnel for the duration of the procedure. Once in the operating room hair near the insertion point of the electrode may be shaved to minimize the risk of infections. Additionally, small percutaneous needles will be inserted in your arm muscles to record the muscle electrical activity induced by electrical stimulation and ensure correct positioning of the stimulator electrodes. At the end of the procedures these needles will be removed. Dr. Gerszten will use a special epidural needle (14 gauge Tuohy needle) to create an access to the epidural space, without performing an incision of the skin or the muscles around your spine. The position of the needle compared to your spine will be monitored using X-Rays. After that a flexible linear electrode will be gently positioned above the spinal cord. Electrical stimulation will then be applied through the electrode and muscle activation will be measured to verify that the correct spinal nerves are being stimulated. Electrical stimulation will be provided with a device that is FDA-approved. Electrodes will be connected to the stimulator through dedicated commercial clinical connectors. The electrode may be adjusted until the stimulation elicits activity in all the arm/hand muscles that are mostly affected by your stroke. Finally, to avoid movement of the leads the surgeon will secure the cables of the stimulator electrodes under your skin by performing a small skin incision which will be sutured at the end of the procedure. The entire procedure is expected to last approximately 2 to 3 hours. At the end of the procedure, you will be trained to care for the sites where the electrodes enter your skin. The connection through the skin will be maintained for up to 29 days. During that time, you will not be able to perform any strenuous activity. You will be kept in the hospital for the night following the procedure at UPMC Presbyterian Hospital to minimize infection risks and monitor your recovery.
- **X-rays:** Every other week, two to three X-ray images of your upper back and neck 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.

- **Post-operative High-Resolution Computerized Tomography (CT) Scan**: After lead placement, you may have a high-resolution CT scan of the cervical spine to document the 3-dimensional location of the leads. We may use pillows or brace during this CT and the pre-operative MRI to ensure that your spine is in a similar position for both scans.
- **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**.**
- **Stimulation experiments:** For each visit over the duration of the study we will perform experiments up to 5 days per week for up to 8 hours per day, during the 30 days following implantation. Each experiment is described below
- **Experiment 1: Motor Stimulation Testing:** The first part of the experiments does not involve significant physical effort and may also be performed within the days post-implantation. 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 arm and hand. Testing will involve determining the relationship between stimulation of your nerves and the muscle activation. Small pulses of electric current will be sent to the nerves near your spinal cord in order to mimic the signal that the brain sends to the muscles to contract and move limbs. We will attach electrodes to the surface of your skin to measure the activity in the muscles of your arm and hand. We may also attach electrodes to your scalp to measure activity in your brain related to the stimulation. You will be asked questions in regard to the nature of sensations that you may feeling, such as location, smooth/sharpness, temperature, and pain level (if any). You will also be asked to describe any changes in spasticity or limb sensations during stimulation. We may also ask you to perform simple movement with a single joint such as extension and flexion of the elbow or we will passively move your arm while we deliver electrical stimulation and ask you if it feels easier or harder to complete these simple gestures when stimulation is active. 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.
- **Three-dimensional reaching/ simulated Activities of Daily Living (ADL) task:** When Dr. Gerszten determines that you are fully recovered from the electrode placement you will be asked to perform some physical activity with your affected arm. Specifically, you will be asked to move the arm at different positions in space, grasp small objects, perform simple daily living tasks or reach for a lever and pull it. It is possible that robotic or mechanical devices that are routinely used in clinics will be used to help you perform certain movements for example by supporting the weight of your arm. During these tasks you will wear electrodes on your skin that record the electrical activity in your muscles and may also wear wireless gyroscopic sensors that detect movement of your arm. We will then deliver trains of stimulation synchronized to your movement attempts to test the ability of electrical stimulation to improve or deteriorate your motor abilities. You will be given an opportunity to learn to use this system and learn to use the stimulation to improve motor performances. We will test several stimulation parameters during this test and will ask you to report which configurations you felt being more helpful to execute the movement as well as any insurgence of uncomfortable sensations or pain (if any). We will then compare your ability to perform these tasks with and without stimulation. This task will also be executed before surgery as baseline evaluation.
- **Arm movement exercises in Robots**: Periodically throughout the experimental sessions, you will be asked to perform various reaching movements in the Kinarm robot. This robot comfortably supports the weight of your arm at the shoulder level. You may also use the Armeo Power robot or the WristBot, which will assist you to use your arm to play games displayed on a computer screen. These tests will be performed in testing space within the Rehab Neural Engineering Lab at the University of Pittsburgh.
- **Self-Report Questionnaire:** Throughout the study, you will be asked to complete questionnaires about

your current level of spasticity. The questionnaires should take less than 30 minutes. This can be completed in research space at the University of Pittsburgh or UPMC or at your home.

- **Post-operative sensory/motor and spasticity testing:** In the 30 days following the implantation of the stimulator electrodes you may undergo testing to measure your sensory and motor abilities that are similar to those you will perform before the implantation. This may include tests to measure your sensitivity to light touch or vibration, and your ability to feel your limbs moving. Standard clinical tests to assess spasticity and limb mobility will also be performed: e.g. you will be asked to try to move the arm in a particular position in space or push on a device that measures fore. 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.
- **Arm ownership test:** In the 30 days following the implantation of the stimulator electrodes you may undergo testing to measure your arm ownership. The sense of arm ownership refers to the awareness of one's own arm as belonging to oneself and the feeling that the arm belongs to your own body. For this test, we may ask you to wear an Oculus virtual reality system which consists of a head mounted display (HMD). You will be asked to move your arm while a virtual representation of your arm is displayed in the Oculus system with or without spatiotemporal delay. These tests will be performed in testing space within the Rehab Neural Engineering Lab at the University of Pittsburgh.
- **Removal of electrodes:** After completion of testing and no later than 29 days after device placement, the SCS leads will be removed at UPMC Presbyterian. To remove these devices, you will follow a procedure and preparation that is identical to the implantation procedure. However, no testing of muscle activation will be performed. Instead, Dr. Gerszten will gently pull the leads from the spine, slightly open the skin where the contacts were secured, until all leads are removed from your body. Visual inspection of the leads will confirm that they are intact and that no portion of the device remains under the skin. The skin will be sutured, cleaned with Hibiclens or betadine and dried with sterile 4x4 gauze dressings, and a sterile bandage will be placed on the site. You will then receive a follow-up telephone call within 48 hours of the discharge to make sure that the wounds are healing properly.

- **Replacement of electrodes:** In some cases, it is possible that the electrodes may move away from the target nerves. If this occurs, it may be necessary to remove the electrodes before the end of the 29-day period. In this case, if you would like to continue participating in the study, you may undergo the electrode placement procedure one additional time, followed by an additional 29 days of testing as described above. In this case, we may repeat any of the screening and experimental procedures described above.
- **Post-testing follow-up:** After electrode removal, within 2 weeks, the neurosurgery team will monitor the status of your surgery site and remove sutures as needed. Within a month after electrode removal, a research staff member will call you to ask questions about any remaining changes in your spasticity level or motor control and check on how you are feeling. One month after electrode removal, you may be asked to return to the lab for follow-up testing, comprised of approximately four 3-hour sessions. For up to two years after enrollment, testing visits described above may be repeated.

DEVICES:

The following devices will be used in the surgical procedure: Medtronic or Boston Scientific Percutaneous Leads, the Natus Medical Protektor32, which is FDA-approved and used in an "off-label" manner for this study. Alternatively, we might also use the Digitimer DS8 which is approved for research use in humans. Connection to the Stimulators will be performed using clinical connecting systems provided by Ad-Tech Medical Instrument Corporation.

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 and neural stimulation. You will undergo two medical procedures (electrode placement and removal) during the study.

- **Pre-operative blood work and tests.** 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 expected to be rare. A nasal swab for MRSA may cause discomfort in the nostrils. You may have skin discomfort or a rash from an electrocardiogram.
- **Devices for strength and proprioceptive ability assessment**: There may be some risks associated with the use of robotic devices for performance assessment. A robot malfunctioning may cause injuries. The possible injuries from a malfunctioning robot include bruises, pinching, strain, lacerations, dislocations, or bone fractures. The robots used in this study have not caused dislocation or bone fracture in any of our ongoing robot studies. The risk of injury is minimized by the design of the robot limiting its movement and including a safety stop switch that allows staff members to stop the robot if there is any potential for injury. You may feel muscle fatigue or discomfort that fades within minutes.
- **General anesthesia for the electrode placement procedure 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, sore throat from the respiration tubes . Rare risks include low blood pressure and irregular heartbeat. Some of these risks may be severe and even life compromising. Trained specialists will closely monitor you before, during and immediately following implantation to ensure all risks are appropriately addressed and minimalized. If the risk is too great, it may serve as an exclusion factor from the surgery and/or study.
- **Local anesthesia for the electrode placement procedure carries several risks.** A common risk is short term pain at the injection site. An infrequent risk is local skin infection. There is a rare risk of adverse reactions to the injections; including light headedness, dizziness, drowsiness, blurred vision, respiratory depression, edema, low blood pressure, or irregular heartbeat.
- **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.** Infrequent risks include minor cerebrospinal fluid (CSF) leak that may cause a severe headache. In rare cases, a CSF leak may require additional surgery. This emergency surgery would occur at no cost to you. Another infrequent risk is infection of the spinal cord (meningitis) which may occur after the surgical procedure. Additionally, there is a low risk of infection at the site where the electrodes tunnel through the skin. A rare, but potentially severe, risk of electrode placement is nerve damage the can cause neurological dysfunction, although placement of these electrodes is 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. For example, leads may slide down in the space within the vertebra and the spine because of gravity, or movements of the neck. This movement is not likely to result in any medical complications, but it may affect the types of sensations you feel during stimulation and the muscles that are activated by each electrode contact. These changes may prevent further testing of the electrodes, in which

case we will remove them earlier than expected. Since you won't be able to perceive movement of the leads, we will assess the position using X-rays regularly. Also we will be able to notice if electrodes moved if activation of muscles changes over time. These changes 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, in which case they will be removed earlier than expected.

- **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. It is possible you may experience shortness of breath or difficulty breathing. 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 as a result of electrical stimulation, although the stimulation parameters used in this study have been carefully selected to avoid causing any damage.
- **Securing sensors/electrodes with tape:** A common risk of placing surgical tape on the skin is discomfort while removing the tape. Tape will be used conservatively and will be removed with caution and care.
- **Reaching and grasping with stimulation:** Stimulation may cause you to feel unusual or unexpected sensations and movements. During arm movements, these sensations and involuntary movement could be distracting and could impede the desired movement. During initial use of the system, a study investigator will try to exclude use of all stimulation parameters that induce such sensations and movements.
- **Reaching movement with Oculus Rift:** The use of the Oculus device may cause the following symptoms: eye strain, dizziness, disorientation, impaired balance, or other symptoms similar to motion sickness. Some people (about 1 in 4,000) may have seizures or blackouts triggered by light flashes or patterns, and this may occur while they are experiencing virtual reality, even if they have no history of seizures or epilepsy. Such seizures are more common in children and young people. We will frequently ask you how you are feeling and ensure that you are not having any discomfort. A 10-minute break will be provided for every 30 minutes of headset use. If at any moment you are not feeling well, we will take a break and wait until you are feeling better or discontinue the use of the Oculus device.
- **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/C. Difficile (a bacteria), nausea, vomiting, increased liver enzymes, and abnormal blood urea nitrogen or serum creatinine levels, which are related to kidney function.
- **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. For individuals with implanted drug delivery pumps, we must consult with your physician to determine that it is okay to have an MRI scan. These pumps typically will temporarily stall during the scan, which will deprive you of your medicine during that time. Following the scan, you will need to have your pump checked to verify that it has resumed operation. 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. Some subjects will have suffered this reaction, called

claustrophobia, in other situations. Should you develop claustrophobic feelings during the study or for any reason feel that you cannot endure remaining in the scanner, the study can be interrupted and you will be able to rest outside of the enclosed area. You are in voice contact with the staff during the MRI.

- TMS: You may get a headache or feel uncomfortable during parts of the procedure. Permanent side effects have never been reported after magnetic stimulation. Magnetic stimulation over your head feels like a tap on your scalp, may cause some tingling in your scalp or other parts of your body, and may make a part of your body move. There is an extremely small risk of the stimulation causing a seizure. That risk is so small that no seizures have occurred with this type of stimulation in people who do not have seizure disorder. This study does not use MRI-compatible leads. Even though it is considered safe, there is a slight chance of TMS inducing current in the leads (heating and skin burn). There is also the risk of skin irritation at the site of the EMG electrodes used for TMS data collection and the chance of electrical current (DC) less than what would be experienced with a nine-volt battery. There are no known pregnancy risks associated with a TMS procedure.
- **Fluoroscopy, CT scan, and x-ray imaging carries a risk of radiation exposure.** The study physician may need an x-ray of your lower spine prior to placing the electrodes. During the electrode placement procedure, fluoroscopic imaging will be used to assist with targeting the placement of leads. Additionally, throughout the study, we will use x-ray imaging (2 multi-view radiographs) to document the location and any movement of the electrodes. This imaging will exposure you to radiation. The maximum amount of radiation exposure you will receive is 11.2 rem. This is a fraction of the annual radiation exposure (20 rem) permitted to the most sensitive organs of radiation workers by federal regulations. 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. However, the amount of radiation exposure you receive in this study is considered to be low and comparable to everyday risks.
- **Replacement of electrodes.** In the case that the electrodes move or break before the end of the 29 day testing period, you may be offered a second opportunity to have the electrodes reinserted. The electrode replacement is completely voluntary and optional. You do not have to agree to a second electrode insertion. The risks of replacement of the electrodes are similar to the risks involved in the first electrode placement procedure. There is a slight increased risk as a result of the additional exposure to radiation from the fluoroscopic and x-ray imaging. The total radiation exposure is expected to be no more than 2.1 rem, which is a fraction of the annual radiation exposure (20 rem) permitted to the most sensitive organs of radiation workers by federal regulation.
- **Since personal 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 separately. 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***.*** A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.
- **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. We do not believe that pregnancy would carry any additional risks during the study, however this has not been studied and therefore the risks are unknown. If you have questions, you are encouraged to speak with the study doctor or your personal physician.

- **Intravenous line placement.** There is potential risk of inflammation of the vein where the IV is placed. Due to this risk we will avoid, if possible, placing IV lines in your affected arm.

BENEFITS:

This study will provide no direct benefit to you. This study will provide the basis for long-term testing of electrical stimulation to restore movement and enhance motor recovery in people suffering from subcortical stroke.

It is likely that any improvement in limb control that you will experience during electrical stimulation will disappear when the stimulation is off. Any improvement on arm and hand control that you might experience when the electrical stimulation is off might be temporary and might fade away after the end of this experimental protocol.

Additionally, participation to this study will not prevent you to participate to future studies involving the permanent implantation of a stimulator system and a longer rehabilitation protocol.

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 procedures performed for the purpose of this research study (i.e., the Screening Procedures or Experimental Procedures described above). If you undergo replacement electrodes, the procedure will be paid for by the Department of Neurological Surgery at the University of Pittsburgh. 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 36 study visits (consent, pre-operative examination, MRI, lab work, electrode placement and removal, and testing sessions) for which you will be compensated $50 for each visit. The maximum compensation prior to electrode placement and testing is $350. The total maximum compensation you can normally earn in this study is $1800. However, if you are asked to participate in additional visits, such as if leads are replaced or additional testing occurs, 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. 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. .

You will be required to travel to UPMC or the University of Pittsburgh 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 are withdrawn from the study by the investigators due to lead failure or lead migration, you will be compensated for 3 study visits per week for the remainder of the study. For example, if you are withdrawn after three weeks, you will receive an additional $150 ($50 per visit, 3 visits per week, for 1 additional week). If you withdraw from the study for other reasons, 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. 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. Injury as a result of research procedures performed at Carnegie Mellon University, including at the CMU-Pitt BRIDGE Center, will be covered in accordance with CMU policy. CMU offers no financial compensation or payment for costs of medical treatment related to injury. **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 stroke. 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 Research Conduct and Compliance Office 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. Per University policy, data will be maintained up to 7 years after completion of research study"

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.

We may share your de-identified research information with other researchers interested in this topic at the University of Pittsburgh and other centers, such as Carnegie Mellon University.
We might use your research data and your biological samples in future studies. These future studies might be done by us or by other investigators. In most cases, before we use your data or samples, we will remove any information that shows your identity. There still may be a chance that someone could figure out that the information is about you. Carnegie Mellon University may access your identifiable data. We may also share your research data with the company Reach Neuro or with the Food and Drug Administration (FDA). Your data will be shared with Reach Neuro in a de-identified manner. However, the FDA may require access to identifiable data to conduct regulatory reviews.

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. 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.

If you choose not to participate in this study, the alternative is usual medical care.

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.

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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