INFORMED CONSENT AND RESEARCH AUTHORIZATION

Task and Physiological Specific Stimulation for Recovery of Autonomic Function, Voluntary Movement and Standing using Epidural Stimulation and Training after Severe Spinal Cord Injury

Surgical Implantation and Intervention Consent

Funding Agency name & address:	Christopher & Dana Reeve Foundation 636 Morris Avenue Short Hills, NJ 07078 The Leona M. and Harry B. Helmsley Charitable Trust 230 Park Avenue, Suite 659 New York, NY 10169
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Site(s) where study is to be conducted:	Kentucky Spinal Cord Injury Research Center University of Louisville Hospital University of Louisville Department of Neurological Surgery
Phone number for subjects to call for questions:	(502) 581-8675

Introduction and Background Information

You are invited to take part in a research study because you have been diagnosed with a disease or injury to the spinal cord which has impaired your ability to walk. The study is being conducted under the direction of Susan Harkema, PhD, Claudia Angeli, PhD, Maxwell Boakye, MD, Alexander Ovechkin, PhD, Charles Hubscher, PhD, April Herrity, PhD, and Enrico Rejc, PhD at the University of Louisville**.** Approximately 36 individuals with spinal cord injury will complete this study.

Purpose

The purpose of this study is to evaluate the effects of epidural stimulation of the spinal cord on cardiovascular function, voluntary movement, and standing, as well as respiratory, bowel, bladder and sexual function in individuals with spinal cord injury. We will also evaluate how these interventions affect quality of life.

Procedures

Your participation in this study may last about 24 months. You will have an epidural stimulator implanted and will complete assessments and interventions for at least 12 months. After interventions have concluded and assessments have been completed, you will be given the choice to have the stimulator removed or to leave it in place. If you choose to leave the stimulator in place, you will be given the option to participate in Home and Community Integration for about 2 additional months. If

you consent, you will be randomized, have the stimulator surgically implanted, and may have the following procedures while you are in this study.

I. Surgery:

- Spine surgery will be performed at University of Louisville Hospital by the neurosurgeon. You will also be asked to sign an additional surgical consent form required by University Hospital. This requires an operation on your lower back performed under sedation by intravenous medications injected into your body.
- A four to six inch cut will be made in your lower back and electrodes (devices to produce electrical stimulation) measuring approximately ½ x 3" will be inserted in your spinal canal.
- During this four to five hour operation, several electrical stimulations will be given to your spinal cord in order to determine the best place for the sensor.
- Battery (generators) measuring 3"x1/2" will be placed under your skin through a cut placed in the lower back. You will get to choose which side it is placed. You and the study team will be able to adjust the electrical stimulator using an external device.
- Approximately half a cup of blood will be used during the operation, either from the surgical cuts or by the anesthesiologist who will draw blood to perform routine laboratory tests.
- The electrode(s) and battery system will remain in place during your participation in the study and may be removed after you have completed the study.
- You will be monitored following your operation in the recovery room at University of Louisville Hospital between four and 24 hours.
- A second surgery may be necessary if the electrode wires become disconnected from the stimulator or if an electrode needs to be removed.

After your surgery, you will have a rest period of at least two weeks. After the rest period, you will participate in a series of mapping tests to determine the ideal epidural stimulation settings for each of the training interventions.

<u>Epidural Mapping</u>

- You will have epidural stimulation conducted in the laboratory to identify your spinal cord and muscle responses to various stimulation settings.
- Sensors pasted to your skin will record the electrical activity of your muscles and the position of your limbs. We may have to shave areas of your skin in the spots where we place the sensors.
- We may use a needle to insert a fine wire into some muscles to record the electrical activity.
- We may measure continuous blood pressure, breathing rate and temperature with different sensors.
- In this test, you will be lying down, sitting, standing or stepping.
- You will have the opportunity to rest at any time during any of these experiments.
- We may ask you to participate in these assessments throughout the study.
- These assessments will take approximately two to three hours.

After you complete the mapping tests you will be randomized into a training intervention. You will then undergo the study assessments. Assessments may then be repeated weekly, at mid-point, post-interventions, and follow-up visits.

II. Interventions:

a. You will be randomized (like a flip of a coin) into one of four intervention groups.

i. Group A1 will complete sessions of epidural stimulation during voluntary leg and trunk movements while sitting or lying down. Each session will be six hours per day, approximately five to seven days per week.
ii. Group A2 will complete sessions of epidural stimulation for blood pressure during sitting or lying down. Each session will be six hours per day, approximately five to seven days per week.
iii. Group B1 will complete sessions of epidural stimulation during voluntary leg and trunk movements while sitting or lying down and will also complete sessions of epidural stimulation to contract muscles during standing. Each session of epidural stimulation for voluntary movement will be six hours per day, approximately five to seven days per week. Each session of epidural stimulation to contract muscles for standing will be two hours per day, approximately five days per week.
iv. Group B2 will complete sessions of epidural stimulation for blood pressure during sitting or lying down and will also complete sessions of epidural stimulation to contract muscles during standing. Each session of epidural stimulation for blood pressure will be six hours per day, approximately five to seven days per week. Each session of epidural stimulation to contract muscles for standing will be two hours per day, approximately five days per week.

After completing at least 80 sessions of your group intervention, clinical and neurophysiological assessments will be repeated. Some assessments may be performed more often. You will then complete at least 80 sessions of a second intervention as follows:

If you started in Group A1, you will transition to Group B1; if you started in Group A2, you will transition to Group B2; if you started in Group B1, you will stay in Group B1; if you started in Group B2 you will stay in Group B2. You will complete at least 80 sessions of the second intervention.

Table 1. Interventions for research participants (n=36)

(n=18) Group A		(n=18) Group B	
Intervention #1			
N=9 **A1** Vol-scES 6 hours	**N=9** **A2** CV-scES 6 hours	**N=9** **B1** Vol-scES 6 hours ***and*** Stand-scES + weight bearing training 2 hours	**N=9** **B2** CV-scES 6 hours ***and*** Stand-scES + weight bearing training 2 hours
Intervention #2			
B1 Vol-scES 6 hours ***and*** Stand-scES + weight bearing training 2 hours	**B2** CV-scES 6 hours ***and*** Stand-scES + weight bearing training 2 hours	**B1** Vol-scES 6 hours ***and*** Stand-scES + weight bearing training 2 hours	**B2** CV-scES 6 hours ***and*** Stand-scES + weight bearing training 2 hours
Home and Community Integration			

Completion of the first intervention and the second intervention will each take from five to six months.

Kessler Foundation

You will have the option to complete the second intervention, home and community integration, and/or follow-up visits at the Kessler Foundation in East Orange, NJ.
Assessments:

1. Random Comprehensive Drug Screen (at random time points)
   - You will be asked to provide a urine sample for drug screening at random time points.
   - You may be asked to do this multiple times throughout your study participation.
   - Your results from this test may cause you to be withdrawn from the study.

2. Blood Collection
   - You will have your blood drawn after the completion of your Usual Care, prior to surgery, after Intervention #1 and Intervention #2, and at your 6-month and 12-month follow-up visits. The blood collected prior to surgery will be used to test for infections as well as liver tests, vitamin D, coagulation, and markers of inflammation. You will also give a urine sample prior to surgery to test for infection. The blood

collected at every other time point will be used for liver tests, markers of inflammation, blood fat, blood sugar, nicotine, and vitamin D levels. If you are female, we will also conduct a blood pregnancy test at each time point. Overall, about 4 ½ tablespoons of blood will be taken at each time point.

3. Testing for Infections
    - You may be asked to have a small cotton swab placed into your nose and another in your rectum to test for infections.
    - We may also ask you to provide some urine for a urinalysis and urine culture test also looking for the presence of infections.
    - If infections are found to be present, we will recommend treatment in the form of antibiotics or other methods provided by our study physician.

4. 12-Lead Electrocardiogram
    - The electrocardiogram (ECG) is a test that gives a measure of your heart's electrical activity.
    - You will be asked to lie flat on a table and several small electrode pads (like stickers) will be placed on the left side of your chest, both arms, and both legs.
    - This test will last approximately 10 minutes.

Voluntary Movement Assessments:

1. Functional NeuroPhysiological Assessment (FNPA)
    - You may be asked to participate in one or more assessments that will show us how your neurological system is able to control your movement.
    - We will ask you to try to perform several different movements while you are lying on your back.
    - Sensors will be adhered to your skin to record the electrical activity of your muscles.
    - Muscles recorded will be in your arms, trunk, legs, neck, or a combination.
    - Leg muscle reflexes may also be performed.
    - This assessment may be performed with and without epidural stimulation.
    - This assessment will take approximately three hours.

2. Neuromuscular Recovery Scale (NRS):
    - This assessment consists of 11 items performed in sitting and standing and 3 items performed while standing over a treadmill equipped with a harness and an overhead lift system that supports some of your body weight.
    - When we use EMG, sensors pasted to your skin will record the electrical activity of your muscles and the position of your limbs. We may have to shave areas of your skin in the spots where we place the sensors.
    - We may use a needle to insert a fine wire into some of the muscles to record the electrical activity.
    - We may measure continuous blood pressure, breathing rate, and temperature with different sensors.
    - Research staff will provide assist as needed throughout the assessment for safety.
    - This assessment may be performed with and without epidural stimulation.
    - This assessment will take approximately 2 hours to perform. You will have the opportunity to rest at any time during the experiment.

3. Neuromuscular Voluntary Movement Assessments:
    - Sensors pasted to your skin will record the electrical activity of your muscles and the position of your limbs. We may have to shave areas of your skin in the spots where we place the sensors.
    - We may use a needle to insert as fine wire into some muscles to record the electrical activity.
    - We may measure continuous blood pressure, breathing rate and temperature with different sensors.
    - In this test, you will be lying down on your back or sitting on a mat, and we will ask you to move your legs or trunk.
    - We may ask you to look at a computer and follow a line on the computer with your movement. We may also send a tone over headphones and ask you to move your legs at the same rhythm and intensity as the tone.
    - These assessments may be performed with and without epidural stimulation.
    - You will have the opportunity to rest at any time during any of these experiments.
    - We may ask you to participate in these assessments throughout the study.
    - These assessments will take approximately two hours.

4. Lower Extremity Torque Assessment with Electromyography (EMG)
    - You will be asked to sit and/or lie down in an adjustable chair/mat.
    - You may be strapped at the waist and/or chest. Your leg may also be strapped into the chair just above your knee and above your ankle.
    - You will be asked to tighten your muscles.
    - You may receive epidural stimulation to help you do this.
    - We may place an accelerometer over the muscle belly (fixed on the skin by tape) to measure peak acceleration.
    - Sensors pasted to your skin will record the electrical activity of your muscles and the position of your limbs. We may have to shave areas of your skin in the spots where we place the sensors.
    - You may be asked to repeat this assessment multiple times to assess different movements.
    - This assessment will take approximately 3 hours.
    - These assessments may be performed with and without epidural stimulation.
    - If you are in the voluntary movement training group we may ask you to practice moving your legs while sitting or lying down in the adjustable chair.

Cardiovascular Assessments:

5. Ambulatory Blood Pressure and Heart Rate Monitoring:
    - Blood pressure and/or heart rate may be recorded over a 24 hour period of time outside the lab. We will use a standard arm blood pressure cuff and/or sensors placed on your chest to record your heart rate.
    - The arm cuff is connected to a small program box that buckles around your waist with a nylon strap.
    - The heart rate chest sensors are also connected to a similar small portable box.
    - Blood pressure readings at set intervals will be taken during the day and at night while heart rate will be monitored continuously.

- You will be asked to perform your normal daily activities and your regular sleep schedule.
- We will give you a diary to make notes and record regular activities or events of interest.
- We will also ask you to fill out a questionnaire about your blood pressure stability, heart rate stability, and other health related events.
- This assessment takes 24 hours to perform.

6. Baseline Systolic and Diastolic Blood Pressure:
   - We will measure your blood pressure three times in a row in the morning while you are seated and calculate your average blood pressure.
   - This assessment will take approximately 10 minutes.

7. Orthostatic Stress Test:
   - During this assessment we will record your blood pressure from your arm and your finger, heart rate with small sensors that stick to your chest, and the movement of your chest and abdomen with belts.
   - The assessment will begin with you lying down on your back. At some point, you will be moved suddenly from lying down to either the sitting position in a special chair or the vertical position on a tilt table.
   - We will record all of the parameters mentioned above throughout these position changes.
   - During the assessment, certified personnel may take blood samples (approximately 4 tablespoons) from a small catheter inserted in your arm vein.
   - During this recording, heart ultrasound, pulse wave velocity, vascular ultrasound and/or transcranial doppler assessments may also be performed.
   - These assessments may be performed with and without epidural stimulation.
   - This assessment will take approximately 2 hours.

8. Echocardiogram:
   - You will be asked to not eat or drink (water is permitted) 4 hours before your visit.
   - No caffeine and alcohol 12 hours before your visit.
   - No smoking (cigarettes/marijuana) 12 hours before your visit.
   - No physical activity/exercise 24 hours before your visit.
   - Take medications & vitamins as usual, avoid medications not prescribed by your doctor (i.e. allergy medications, Tylenol, etc.)
   - The assessment looks at different areas of the heart.
   - You will be lying on your left side in a gown with a bolster supporting you while on a padded table for most of the test. We will also have you on your back and sitting at an 80 degree angle.
   - We will be examining your heart structure non-invasively by placing gel on a probe which will then be placed on your chest, left side, neck and abdomen.
   - These assessments may be performed with and without epidural stimulation.
   - The assessment will last about 1.5 hours.

9. Arterial Pulse Wave Velocity:
   - This assessment looks at arterial muscle and wall properties using pressure detecting technology.

- The assessment will be performed while you are lying down on your back.
- We will be examining your arterial structure and/or your arterial stiffness non-invasively by placing sensors on the arteries in your neck, hip, wrist, and foot.
- The purpose of the exam is NOT to assess overall cardiovascular health or to diagnose unknown diseases. However, if abnormalities are inadvertently observed that may put your health at risk, we may report these findings to our study physician.
- These assessments may be performed with and without epidural stimulation.
- The assessment will take approximately one hour.

10. Vascular Ultrasound
    - You will be asked to sit and/or lie down on a padded table.
    - You will be asked to remain quiet while the vessels in your neck, arm, abdomen, and/or leg will be measured by Doppler ultrasound.
    - Blood pressure will be measured by an inflated cuff on your arm and/or finger.
    - Electrical activity of the heart will be measured from electrodes on your chest.
    - You may be asked to repeat this assessment.
    - These assessments may be performed with and without epidural stimulation.
    - This assessment will take approximately 1 hour to complete.

11. Venous Occlusion Plethysmography (VOP)
    - You will be asked to lie down on a padded table while your right leg is propped up on a foam block.
    - A strain gauge (small rubber band) will be placed around your calf at its widest point.
    - A pressure cuff will be placed around your ankle and another will be placed around your thigh.
    - The cuff around your ankle and thigh will be inflated encouraging blood to pool between the cuffs.
    - The strain gauge sensor around your calf will measure the change in volume of your lower leg as blood accumulates between the cuffs.
    - The cuffs may stay inflated for approximately 5 minutes as we obtain our measurements.
    - The cuffs will be deflated and then an approximately 5 minute long rest break will follow.
    - After the rest break, we may repeat the assessment up to two times.
    - This assessment may take approximately 45 minutes to complete.

Stand Assessments:

12. Dual Energy X-ray Absorptiometry (DXA):
    - The DXA scan measures the density of your bones and composition of your body.
    - You will have your entire body, and individual body parts, scanned by a large machine while lying on your back and/or side and/or while sitting.
    - You will have to lie still during the assessment.
    - This assessment will take approximately 1 hour.

13. Standing Assessment (EMG):
    - We will measure the activity of your trunk and leg muscles while you are standing.

- We may ask you to stand on a treadmill, while wearing a harness that is attached to an overhead suspension device that will support the weight of your body.
- We may ask you to stand on an over ground apparatus with horizontal bars for support and balance.
- Trainers will provide assistance as needed.
- Sensors pasted to your skin will record the electrical activity of your muscles and the position of your limbs. We may have to shave areas of your skin in the spots where we place the sensors.
- We may use a needle to insert a fine wire into some muscles to record the electrical activity.
- We may measure continuous blood pressure, breathing rate and temperature with different sensors.
- Sensors pasted to your skin and surrounding your fingers and chest may be used to record temperature, blood pressure and respiration.
- These assessments may be performed with and without epidural stimulation.
- You will have the opportunity to rest at any time during any of these experiments.
- We will ask you to participate in these experiments throughout the study.
- These experiments will last from 2-3 hours. You will have the opportunity to rest at any time during the experiment.

Respiratory Assessments:

14. Pulmonary Function Test (PFT):
    - We will record your lung volume, airflow, and airways pressure by using a mouth piece while you are sitting in your personal wheelchair and/or lying down.
    - You will be asked to inhale and exhale into the mouth piece when your nose is closed with a plastic clip.
    - This assessment will last about 30 minutes.

15. Respiratory Motor Control Assessment (RMCA)
    - We will record your lung volume, airflow, and airway pressure by using a mouth piece while you are sitting and/or lying down.
    - You will be asked to inhale and exhale into the mouth piece when your nose is closed with a plastic clip.
    - We will also record the muscle activity from your neck, chest, arms, legs, abdomen and back by placing adhesive sensors over your muscles and heart.
    - We may ask your permission to shave skin at the sites of sensor placement.
    - We will record how you are breathing by placing elastic belts around your chest and abdomen.
    - We will record your blood pressure and heart rate using a finger cuff.
    - This assessment may be performed with and without epidural stimulation.
    - This assessment will take approximately three hours.

16. Resting Metabolic Rate (RMR)
    - We will measure your metabolic activity (calories you burn) at rest.
    - You will be asked to fast for 10-12 hours before the assessment and refrain from exercise that day.
    - You will be asked to lie down on a bed on your back quietly and to remain still.

- A plastic canopy hood will be placed over your head and shoulders to contain the air you are breathing.
- We will measure the gases in the air you exhale to examine how much energy your body uses at rest.
- The assessment will take approximately one hour.

Bladder Assessments:

17. Urodynamic Evaluation:
    - You will need to avoid taking your bladder medication/s at least 24 hours prior to assessment.
    - If you are able to urinate voluntarily, you may be asked to arrive to the appointment with a comfortably full bladder so that we can take a measurement of your urinary flow.
    - A urine specimen will be obtained to screen for bacteria as well as analyze it in the lab for various biomarkers.

    Yes, you may keep my urine samples:

    _____
    Signature of Participant Date

    No, you may not keep my urine samples:

    _____
    Signature of Participant Date

    - We will measure the pressure inside your bladder.
    - We will drain your bladder completely and fill it with room temperature physiologic saline using a special catheter that can measure the internal pressure.
    - We will insert another catheter in your rectum in order to measure abdominal pressure.
    - As the bladder fills with saline, you will be asked to tell the nurse when you first feel something in the bladder, when it feels full and when it feels like you cannot hold anymore.
    - You will be asked to empty your bladder while we measure the pressures or your bladder will be emptied using a catheter.
    - While pressures are being recorded, we will place sensors around your urethra to measure your bladder activity. Sensors may also be placed on your legs to record muscle activity during the testing.
    - The Urodynamic equipment, and with a rectal balloon catheter in place, may also record pressure measurements of the anal sphincter muscles, the sensation of the rectum, and activity of the reflex pathways that are needed for normal bowel movements.
    - We will measure your blood pressure and heart rate.
    - Your skin will also be inspected to ensure that all areas exposed during the assessment are dry.
    - You may also be asked to complete a short questionnaire regarding your bladder, bowel, and sexual health function.

- You may complete the questionnaire in a private area and may take about 15 minutes to complete.
- After the procedure, it is recommended that you drink an 8 oz glass of water every half-hour for two hours to help reduce any discomfort after the assessment. You can continue with your daily activities.
- This assessment may be performed with and without epidural stimulation.
- The assessment will take approximately one hour and 30 minutes.

18. Bladder and Kidney Ultrasound:
    - Ultrasound is a safe and painless assessment that will use sound waves to make images of your kidneys, ureters, and bladder.
    - You may be asked not to eat or drink anything for several hours before the assessment.
    - If the ultrasound requires the participant to have a full bladder; you will be given specific instructions on what to do.
    - The ultrasound machine will send sound waves into the kidney and bladder area and images will be recorded on a computer.
    - The black-and-white images will show the internal structure of the kidneys and related organs.
    - The assessment is painless and you may resume your daily activities following the procedure.
    - This assessment will take approximately 45-60 minutes.

Bowel Assessments:

19. Anorectal Manometry:
    - You will be asked to perform either a Fleet® enema or to complete your bowel program the morning of the assessment so that you arrive to the appointment with an empty rectum.
    - You will need to avoid eating anything 2 hours before your appointment.
    - While lying on your side, a small, flexible tube, about the size of a thermometer, with a balloon at the end will be inserted into the rectum.
    - The catheter is connected to equipment that measures pressure. A small balloon attached to the catheter may be inflated in the rectum to assess muscle responses.
    - You will be asked to relax, squeeze, and push at various times.
    - The anal sphincter muscle pressures are measured during each of these muscle contraction/relaxation actions.
    - Surface patch EMG sensors will be placed near the buttocks to evaluate muscle activity of the anal sphincter.
    - A measurement of the time it takes to expel a small balloon from the rectum is recorded.
    - Your blood pressure and heart rate will be measured throughout the procedure.
    - Following the assessment, you will be able to go about your normal daily activities.
    - The assessment will take approximately 60 minutes.

iv. Quality of Life

Researchers from Boston University will administer three quality of life questionnaires over the phone just prior to you being surgically implanted with the device (in conjunction with your pre-

implant assessments) and at 6, 12, 18, and 24 months after the first administration. The Quality of Life questionnaires are the Spinal Cord Injury Quality of Life (SCI-QOL), Spinal Cord Injury Functional Index (SCI-FI), and PROMIS Sexual Satisfaction. The questionnaires will be administered using a computer program and your responses will be entered into the program. Your name and phone number may be shared with the researchers from Boston University so they can call you to administer these questionnaires over the phone.
You will also complete the European Quality of Life questionnaire (EQ-5D-3L) which is a short, two page questionnaire that you will fill out at the same time points as the other quality of life questionnaires.

You may choose to decline to answer any question that makes you feel uncomfortable.

1. SCI-QOL will collect information about you on the following:
    a. Depression
    b. Anxiety
    c. Ability to participate in social roles/activities
    d. Bladder Management
    e. Bowel Management
    f. Pain Interference

2. SCI-FI will collect information about you on the following:
    a. Basic Mobility
    b. Ambulation
    c. Wheelchair Mobility
    d. Self-care
    e. Fine Motor

3. PROMIS will collect information regarding your overall satisfaction with your sexual function.

4. EQ-5D-3L will collect information on you about the following:
    a. Mobility
    b. Self-care
    c. Pain/discomfort
    d. Anxiety/depression
    e. Usual Activities

At the end of your participation in the study, researchers from Boston University will conduct a qualitative interview with you to better understand the impact of epidural stimulation on your quality of life. Specifically, they will ask you to describe your experience with epidural stimulation in four areas: 1) ability to move, 2) ability to do every day activities, 3) effects on other body systems, and 4) psychological and emotional effects.

v. *Health Economics*

We will collect Explanation of Benefits (EOB) statements from your insurance company from two years prior to beginning epidural stimulation to two years after beginning epidural stimulation. This will allow us to determine if there is a reduction in healthcare costs and/or the utilization of healthcare resources as a result of epidural stimulation. We may ask you to

contact your insurance company to obtain a consent to allow us to gather all EOB statements from them. Or, you can choose to obtain them yourself and provide us with copies.

Potential Risks

Any study can have risks involved. We will try to inform you of the risks and encourage you to ask questions about anything that you wish. The risks are placed into categories based on how severe the risk is and the seriousness of the harm that could happen. The severity can depend on your age, individual physical status as well as the medication or intervention itself. Minimal risk would be the level of risk similar to those you would encounter in daily life or during routine doctor exams or tests. A minor risk is slightly increased and you may feel some discomfort from these events. A moderate risk event is more serious and could require medical intervention, treatment, and follow up. The harm is reversible in these cases. A severe risk is much higher and the harm may not be reversible. Risks can be potentially severe depending on the nature of the event.

The frequency is an estimated range of the likelihood that the risk will occur to you. These are general ranges. Rare (0-10%), Less likely (11-30%), Likely (more than 30%) chance that these risks may occur from you being in the study. At any time depending on your condition, a risk may increase to another level to be more severe. Again, please ask us if you are concerned about any particular risk and we will try to answer all your questions. There may also be new risks that we have not anticipated.

This study may involve the following physical risks and/or discomforts:

Surgical Risks
Surgical procedures are associated with numerous risks, including death. Usually surgery requires some form of anesthesia which also has risk. You will sign a separate consent form for surgical procedures. Risks associated with surgery include, but are not limited to:

Likely
- Mild discomfort
- Bruising
- Development of scar tissue
- Bleeding
- Constipation

Less Likely
- Skin infection at the incision site
- Infection at the incision site with washout
- Ileus

Rare
- Open wound
- Infection resulting in explant
- Seroma – pocket of clear fluid that can develop in body after surgery
- Complications from anesthesia
- Lung infection (pneumonia)
- Bleeding into spinal cord without causing pressure
- Bleeding in spinal cord requiring surgery
- Skin erosion
- Hematoma (swelling of clotted blood) without compression
- Hematoma (swelling of clotted blood) requiring surgery
- Cerebrospinal fluid leak results from a hole or tear in the dura – the outermost tissue that covers the spinal cord and brain

- Blindness
- Excessive blood loss
- Heart attack
- Death

Electrode/Device Risks

Less Likely
- Undesirable change in stimulation
- Jolting or shocking

Rare
- Allergic response
- Hardware malfunctions
- Migration
- Erosion
- Breakage or failure resulting in further injury to the spinal cord

Risks of Assessments and Interventions
Particular interventions are specific to stimulation group. If you have any questions, please ask you Investigator/Study doctor for clarification.

Likely
- Skin irritation from hand placements of trainers
- Skin irritation from adhesive tape, sensors, wires, and/or pads
- Tingling feeling from the stimulation
- Dizziness during sitting, standing or stepping
- Skin irritation from vein needle and/or fine wire insertion
- Slight discomfort from the pressure of the ultrasound probe
- Skin irritation from ECG sensor placement
- Slight discomfort during inflation of the pressure cuffs

Less Likely
- Bleeding and/or bruising from fine wire insertion and/or blood draw
- Pain and/or infection from blood draw
- Skin abrasion from hand placements of trainers
- Feelings of fear of being in closed spaces
- Shortness of breath
- Significant changes in heart rate and/or blood pressure
- Muscle and joint soreness

Rare
- Chest pain
- Joint sprain or muscle strain
- Nausea
- Discomfort and/or pain from stimulation
- Fall
- Broken bones requiring medical treatment
- Broken bones requiring surgical treatment and long-term medical follow-up

Risks of Bladder Assessments

Likely
- Feeling of shyness
- Significant changes in heart rate and/or blood pressure
- Autonomic dysreflexia symptoms (sudden high blood pressure) that resolves when the cause is removed (*individuals with an injury level above T6 and in those who have previously experienced these symptoms)

Less Likely
- Mild discomfort, especially during urination after assessments of the bladder
- Urinary tract infection requiring oral antibiotics
- Discomfort from lying still for ultrasound

Rare
- Autonomic dysreflexia symptoms (sudden high blood pressure) but the cause cannot be identified and the high blood pressure does not resolve and medical intervention is required (*individuals with an injury level above T6 and in those who have previously experienced these symptoms)
- Urinary tract infection requiring intravenous antibiotics
- Excessive pain, fever, chills

Risk of Bowel Assessments

Likely
- Feeling of shyness
- Significant changes in heart rate and/or blood pressure
- Autonomic dysreflexia symptoms (sudden high blood pressure) that resolves when the cause is removed (*individuals with an injury level above T6 and in those who have previously experienced these symptoms)

Rare
- Autonomic dysreflexia symptoms (sudden high blood pressure) but the cause cannot be identified and the high blood pressure does not resolve and medical intervention is required (*individuals with an injury level above T6 and in those who have previously experienced these symptoms)
- Bleeding of the rectum
- Bowel infection requiring oral antibiotics
- Bowel perforation (tearing) in those with previous rectal surgery, bowel inflammation, or bowel obstruction

Risk of Sexual Function Assessments (Questionnaire)

Likely
- Feeling of shyness

DXA Risks: You will be exposed to minimal amounts of radiation during the DXA scan. We are exposed to radiation on a daily basis both from natural (sun, earth, etc.) and man-made sources. The average radiation dose from these sources for those living in the United States is about 300 millirem per year. By comparison, your dose will be less than 200 millirem from the DXA scan. The radiation

dose that you will receive from this study is well below the levels that are thought to result in a significant risk of harmful effect.

In addition, you may suffer harms that we have not seen before. If you should have any of these difficulties during assessments, we will stop. There no reasonably foreseeable psychological risks, social risks, and/or legal risks. This study may involve risks that are currently unforeseeable.

Possible Pregnancy Risks

Pregnant women are excluded from this study, as the risk to the fetus is unknown. Women of child bearing age will be given a pregnancy test. You should discuss these risks with your doctor before signing this consent form. Talk to your doctor about the best method of birth control to use while you are in this study. If you are pregnant or become pregnant, your unborn child may suffer harms that we have not seen before. It is important that you contact someone on the research team at (502) 581-8675 right away if you become pregnant during the course of this study. If you become pregnant, you will be terminated from the study by the study doctor.

Benefits

We do not know the benefits of this study. Although there are no guarantees of benefits occurring during this experimental study, the information obtained from your participation in this study may help you and/or other patients who have/or will sustain spinal cord injuries in the future.

Alternatives

Instead of taking part in this study, you could choose to not participate.

Research Related Injury

If you are injured by being in this research study, the study doctor will arrange for you to get medical treatment. Your study doctor has not set aside money to pay for treatment or any injury. You and your insurance will be billed for the treatment of these injuries. Before you agree to take part in this research study you should find out whether your insurance will cover an injury in this kind of research. You should talk to the study doctor or staff about this. If you are injured, there is not money set aside for lost wages, discomfort, disability, etc. You do not give up your legal rights by signing this form. If you think you have a research related injury, please call your study doctor, Sarah Wagers MD, at (502) 899-3623 (24 hour number).

Compensation

You will be paid by prepaid card for travel based on the federal mileage rate and parking fees up to $75 dollars per day while you are in the study. Because you will be paid to be in this study, the University of Louisville may collect your name, address, social security number, and keep records of how much you are paid. You may or may not be sent a Form 1099 by the University. This will only happen if you are paid $600 or more in one year by the University. This will not include payments you may receive as reimbursement for actual expenses based on receipts or actual miles traveled. We are required by the Internal Revenue Service to collect this information and you may need to report the payment as income on your taxes.

Costs

You will not be billed for the office visits, tests and procedures that are done for this research study. The charges for these items will be paid for by the Sponsor. These include visits study related physician visits, intervention sessions and assessments.

You or your insurance company will be billed for all office visits, tests, medications and procedures that are part of your routine medical care outside of this research study. You will be responsible for paying your co-pay that is associated with any office visit, test, medication or procedure. Some insurance companies will not pay for medical bills for people who participate in a research study. It is your responsibility to find out what costs, if any, your insurance company will cover before taking part in the study. If you need help finding out what your insurance company will cover, please ask your study doctor for assistance. If your insurance company does not pay for your bills associated with this study, you will be responsible for paying them.

HIPAA Research Authorization

The Health Insurance Portability and Accountability Act of 1996 (HIPAA) provides federal safeguards for your protected health information (PHI). Examples of PHI are your name, address, and birth date together with your health information. PHI may also include your medical history, results of health exams and lab tests, drugs taken and results of this research study. Your PHI may not be used or shared without your agreement, unless it meets one of the HIPAA exceptions.

State and federal privacy laws protect your health information. In most cases, health information that identifies you can be used or shared by the research team only if you give your permission by signing this form.

If you sign this form your health information will be used and shared to answer the research questions described above and to make sure that the research was done correctly. The time period when information can be used or shared ends when all activities related to this study are completed. Your access to your health information will not be limited during this study.

You do not have to sign this form. If you do not sign this form you may not participate in the study and health information that identifies you will not be shared with the research team.

Site(s) where health information about you will be used or shared for this research:

In our research, the research team will look at and may share information about you and your health. Federal law requires that health care providers and researchers protect the privacy and security of health information that identifies you. We may ask for your health information from the following:

Affiliated Sites:
University of Louisville
Frazier Rehab Institute
University of Louisville Hospital

Unaffiliated Sites:
Labcorp (Laboratory Corporation of America)
Quest Diagnostics
Drexel University
Kessler Foundation

Any physician offices, emergency rooms, healthcare providers where you may seek treatment during the course of this study.

Protected health information (PHI) that will be used or shared for research

Diaries and questionnaires
Records of your operation(s)

Discharge summaries
Healthcare provider orders
History and physical exams
Laboratory, x-ray and other tests
Medical progress notes
Photos, videotapes, digital or other images
Records about the study device

Revocation of Research Authorization

You may cancel the permission you have given to use and share your protected health information at any time. This means you can tell us to stop using and sharing your protected health information. If you cancel your permission:

- We will stop collecting information about you.
- You may not withdraw information that we had before you told us to stop.
  - We may already have used it or shared it.
  - We may need it to complete the research.
- Staff may ask your permission to follow-up with you if there is a medical reason to do so.

To cancel your permission, you will be requested to complete a written "Revocation of Research Authorization" form located at the end of this document. You may also obtain a copy from your study doctor, designated personnel or from the Human Subjects Protections Program Office website (http://louisville.edu/research/humansubjects/links-to-forms).

Information Available on ClinicalTrials.gov

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

Confidentiality

Total privacy cannot be guaranteed. We will protect your privacy to the extent permitted by law. If the results from this study are published, your name will not be made public. Once your information leaves our institution, we cannot promise that others will keep it private.

Your information may be shared with the following:

- Christopher & Dana Reeve Foundation and the Leona M. and Harry B. Helmsley Charitable Trust
- Organizations that provide funding at any time for the conduct of the research
- The University of Louisville Institutional Review Board, Human Subjects Protection Program Office, Privacy Office and others involved in research administration at the University
- The local research team
- People who are responsible for research and HIPAA oversight at the institutions where the research is conducted
- People responsible for billing, sending and receiving payments related to your participation in the study
- Government agencies, such as:
  - Office for Human Research Protections
  - Office of Civil Rights
  - Food and Drug Administration
- Data Safety Monitoring Board(s) related to the study
- Others: Medtronic, Drexel University, Kessler Foundation
- Boston University researchers

Medtronic will keep your health information confidential in accordance with all applicable laws and regulations. Medtronic may use your health information for its business purposes, such as overseeing and improving the performance of its device, new medical research and proposals for developing new medical products or procedures, and another business purposes. Any reports or publications about the study or any other research will not include your name or a description of you. Information received during the study will not be used to market to you; your name will not be placed on any mailing lists or sold to anyone for marketing purposes.

Security

Your information will be kept private by being stored in a locked cabinet behind closed door with limited access. Electronic data is stored on a password protected computer with limited access in a locked area.

Conflict of Interest

This research study utilizes devices that are licensed to Power NeuroRecovery. The person or persons running this study has a relationship with Power NeuroRecovery. If you have any questions about this conflict of interest, please talk to Holly Symonds Clark at (502) 852-2965. This person is not a member of the study team and does not have a conflict of interest related to the study.

Voluntary Participation

Taking part in this study is completely voluntary. You may choose not to take part at all. If you decide not to be in this study, you won't be penalized or lose any benefits for which you qualify. If you decide to be in this study, you may change your mind and stop taking part at any time. If you decide to stop taking part, you won't be penalized or lose any benefits for which you qualify. You will be told about any new information learned during the study that could affect your decision to continue in the study.

Termination

Your study investigator or study doctor or the study sponsor has the right to stop this study at any point. Your study investigator or study doctor may take you out of this study with or without your okay. Reasons why this may occur include circumstances that arise which warrant doing so. The decision may be made either to protect your health and safety, or because it is part of the research plan that people who develop certain conditions may not continue to participate. If the study doctor believes that the pain or discomfort might pose a risk to you, you will be terminated from the study. If you become pregnant you will be terminated from this study.

Participation in Other Research Studies

You may take part in this study if you are currently in another research study that does not interfere with this study. It is important to let your study team know if you are in another research study.

Contact Persons

If you have any questions, concerns, or complaints about the research study, please contact Susan Harkema, Ph.D. at (502) 581-8675. Once you are enrolled in this study, you will be given additional contact numbers that are answered 24/7 to reach a designated research staff member if you need immediate assistance.

Research Subject's Rights

If you have any questions about your rights as a research subject, you may call the Human Subjects Protection Program Office at (502) 852-5188. You may discuss any questions about your rights as a research subject, in private, with a member of the Institutional Review Board (IRB). You may also call this number if you have other questions about the research, and you cannot reach the study doctor, or want to talk to someone else. The IRB is an independent committee made up of people from the University community, staff of the institutions, as well as people from the community not connected with these institutions. The IRB has approved the participation of human subjects in this research study.

Concerns and Complaints

If you have concerns or complaints about the research or research staff and you do not wish to give your name, you may call the toll free number 1-877-852-1167. This is a 24 hour hot line answered by people who do not work at the University of Louisville.

Acknowledgment and Signatures

This informed consent document is not a contract. This document tells you what will happen during the study if you choose to take part. Your signature indicates that this study has been explained to you, that your questions have been answered, and that you agree to take part in the study. You are not giving up any legal rights to which you are entitled by signing this informed consent document. You will be given a copy of this consent form to keep for your records.

Participant Name (Please Print)	Signature of Participant	Date Signed
Printed Name of Legal Representative (if applicable)	Signature of Legal Representative	Date Signed
Relationship of Legal Representative to Participant		
Printed Name of Person Explaining Consent Form	Signature of Person Explaining Consent Form (if other than the Investigator)	Date Signed
Printed Name of Investigator	Signature of Investigator	Date Signed

List of Investigators:
Susan Harkema, PhD

Phone Numbers:
(502) 581-8675

REVOCATION OF AUTHORIZATION FOR USE AND DISCLOSURE OF YOUR HEALTH INFORMATION FOR RESEARCH

Return To:

PI Address:	**220 Abraham Flexner Way, 15th Floor** Louisville, KY 40202
PI Phone:	502-581-8675

OR

Institutional Review Board
MedCenter One, Suite 200
501 E. Broadway
Louisville, KY 40202

Do not sign this letter unless you are withdrawing from this research. You will be sent confirmation that this notice was received.

To Whom It May Concern:

I would like to discontinue my participation in the research study noted above. I understand that health information already collected will continue to be used as discussed in the Authorization I signed when joining the study.

Your options are (***choose one***):

☐ **Withdraw from Study & Discontinue Authorization:**

Discontinue my authorization for the future use and disclosure of protected health information. In some instances, the research team may need to use your information even after you discontinue your authorization, for example, to notify you or government agencies of any health or safety concerns that were identified as part of your study participation.

☐ **Withdraw from Study, but Continue Authorization:**

Allow the research team to continue collecting information from my personal health information. This would be done only as needed to support the goals of the study and would not be used for purposes other than those already described in the research authorization.

_____ _____
Printed Name and Signature of Participant | Date Signed

_____ _____
Signature of Participant's Legal Representative (if subject is unable to sign) | Date Signed

_____ _____
Printed Name of Participant's Legal Representative | Birthdate of Participant

_____
Relationship of Legal Representative to Participant

_____ _____
Participant's Address | Participant's Phone Number

Optional:
I am ending my participation in this study because: