IRB #: IRB15-00014
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EVALUATION OF SPINAL CORD STIMULATION WITH WIRE LEADS TO RESTORE COUGH IN PATIENTS WITH SPINAL CORD INJURY

Introduction

You are being asked to participate in a research study entitled "Evaluation of Spinal Cord Stimulation with Wire Leads to Restore Cough in Patients with Spinal Cord Injury." Before you can decide whether or not to volunteer for this study, you must be informed of the purpose of the research study, how this study may help you, any risks to you, and what is expected of you. This process is called informed consent.

You do not have to participate in this study. You may stop your participation in this study at any time without changing your current or future relations with MetroHealth Medical Center (MHMC) or its doctors.

If you decide to participate in this study, you will be told about any new information learned during the study that might cause you to change your mind about staying in the study. If you withdraw we will still provide you with information regarding possible impacts to your health status or future health care decisions.

Individuals with spinal cord injury and impaired ability to cough are being asked to be involved in this research study to investigate the efficacy of a device to produce cough.

Why is this study being done?

The purpose of this study is to attempt to provide an artificial cough by stimulating your expiratory muscles (muscles responsible for coughing). These include the intercostal muscles (muscles in between the ribs) of the lower rib cage and the abdominal muscles. We plan to place wire leads over the surface of the spinal cord on the lower back to stimulate the expiratory muscles and restore your cough. If successful, this technique should provide you with a means of removing airway secretions, help prevent respiratory tract infections, and reduce caregiver support for secretion management. We plan to study 16 adults with cervical spinal cord injury. No pregnant women will be studied. Active participation in this study should take approximately 24 months. However, if the device remains implanted, its integrity and function may be assessed periodically thereafter.

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What is involved in the study?

This study will involve a screening visit, a surgical visit, followed by a post-operation visit, 11 additional visits to assess air pathways over the course of 24 months.

Visits at MHMC	Procedures	Est. Duration
Screening/Pre-surgical testing	EKG, spirometry, respiratory pressures, X-ray, MRI, blood draw, urine sample, study-related forms	4-5 hours
Surgery	Implantation	1-2 days
Post-surgery follow-up	Assessment of surgery wound(s)	1 hour
Week 3	Expiratory Muscle Assessment, study-related forms, X-ray	1-2 hours
Week 7	Expiratory Muscle Assessment, study-related forms	1-2 hours
Week 11	Expiratory Muscle Assessment, study-related forms	1-2hours
Week 15	Expiratory Muscle Assessment, study-related forms	1-2hours
Week 20	Expiratory Muscle Assessment, study-related forms	1-2hours
Week 24	Expiratory Muscle Assessment, study-related forms, X-ray	1-2hours
Week 28	Expiratory Muscle Assessment, study-related forms	1-2hours
Week 40	Expiratory Muscle Assessment, study-related forms	1-2hours
Week 52	Expiratory Muscle Assessment, study-related forms, X-ray	1-2hours
18 months	Expiratory Muscle Assessment, study-related forms	1-2hours
24 months	Expiratory Muscle Assessment, study-related forms	1-2hours

Screening Visit at MHMC:

After an evaluation of your medical history and brief physical examination, we will perform some initial testing. Routine breathing tests will be done to measure the amount and speed of air movement which you can achieve voluntarily. We will also measure the strength of your respiratory muscles by having you make maximal efforts during inhalation and exhalation while your airway is blocked for brief periods. It will be necessary for you to breathe through a mouthpiece and wear nose clips for us to obtain accurate measurements.

You will complete forms that assess your quality of life, how you are managing your secretions and bowel routine, and how often you are having respiratory infections. This should take approximately 10 minutes to complete. Caregivers will also complete forms that assess caregiver burden and responsibility. All forms should take approximately 10 minutes to complete. You will be given a respiratory management log to complete on a daily/as needed basis. These should take a few minutes to complete.

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Within two weeks before surgery, you will have routine tests performed. These include an electrocardiogram (ECG), which measures the electrical activity of your heart, a chest X-ray, MRI (or CT myelogram), and blood and urine samples. This visit will last approximately 4-5 hours.

Surgical Visit at MHMC:

Depending on the time of your surgery, you may be admitted to METROHEALTHY Medical Center the night prior to your surgery. On the day of surgery, the surgeon will make an incision over the spine to place two needles through which two leads will be passed and implanted on the surface of the spinal cord. A receiver will be implanted just under the skin over the chest or abdominal wall and connected to the leads. Moderate IV sedation will be provided during this procedure. Stimulation will be applied in the operating room to observe muscle contraction.

After surgery, you will stay at MetroHealth Medical Center for approximately 1 day. Following your discharge, several visits will take place at the CRU to collect data. In addition to these scheduled visits (outlined below), more frequent assessments may be necessary. Although unlikely, it is possible that a surgical adjustment may be necessary to obtain optimal results.

You will be asked to return to the CRU 10-14 days after your surgery to assess the surgical wounds. This visit will last approximately 1 hour.

Expiratory Muscle Assessment Visits at MHMC:

You will be asked to return to the CRU for 11 visits (1-2 hours per visit) during the study. During these visits, spinal cord stimulation will be applied for brief periods to assess expiratory muscle strength by measuring airway pressure and airflow changes at your mouth or tracheal opening. During stimulation, we will monitor your heart rate, blood pressure and oxygen saturation.

- These visits will occur at weeks #3, 7, 11, 15, 20, 24, 28, 40, 52, and at 18 and 24 months.
- At weeks #20 and 24 following implantation, you will complete a form that assesses how you are managing your secretions. This will take a minute to complete.
- At weeks #7, 11, 15, 20, 24, 28, 40 and 52 and at 18 months and 24 months following implantation, you will complete a variety of forms that assess your quality of life, how you are managing your secretions, and how often you are having respiratory infections. This should take approximately 10-30 minutes to complete.

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- At weeks #3, 24 and 52, a T-spine x-ray will be obtained.
- At 2 weeks and 1 week prior to your Week #3 visit, you will be asked to complete a form that assesses your bowel routine. This will then be completed weekly for 4 weeks, then monthly for 4 months (Weeks # 11, 15, 20, 24). A total of 10 forms will be completed. This should take approximately 5 minutes to complete and can be completed during a normally scheduled visit or sent to the study team via email or fax.

For Caregivers: During the Expiratory Muscle Assessment visits at weeks #28, 40, 52, and 18 and 24 months, you will be asked to complete forms that assess caregiver burden and responsibility. These forms should take approximately 5 minutes to complete.

Spinal Cord Stimulation – Home:

It is anticipated that the expiratory muscles have atrophied (decreased in size and strength) due to your spinal cord injury. In order to restore and maintain strength of these muscles, you and your caregiver will be trained on how to stimulate them for short periods at a time, approximately 5-15 minutes, twice daily. Additionally, you will be able to use the device as needed for clearing your throat or evacuating secretions.

For Caregivers: During the study, you will be asked to fill out daily home stimulation and respiratory management logs, and a bowel routine log, as noted in the prior section. These forms should take no more than a few minutes a day to complete.

What happens if I discontinue or withdraw from the study?

If you withdraw from the study before its completion, you will be asked to return the external components of the investigational device, and for your safety, to come in for a final study visit in order to assess that the implanted components are not damaged. If you chose to withdraw from the study and to end all contact with the study team, we will not be available should you have any complaints regarding the implanted components. If you agree to stay in contact with the study team, we will be available to address any future concerns with the implanted components of the investigational device.

Your participation in this project may be terminated if you are not compliant with the research performed or if you are not benefiting from this research.

What are the risks of this study?

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Screening:

When blood is drawn from a vein, there will be some temporary discomfort. Suitable precautions will be taken to minimize the following risks:

- Local bruising, infection, or blockage of the vein may happen, but is uncommon.
- Fainting may occur, but is rare.

Because the MRI machine acts like a large magnet, it could move iron-containing objects in the MRI room during your examination that could possibly harm you. Precautions have been taken to minimize such an event from happening. Loose metal objects, like pocketknives or key chains, are not allowed in the MRI room. If you have a piece of metal in your body, such as a fragment in your eye, aneurysms clips, ear implants, spinal nerve stimulators, or a pacemaker, you will not be allowed into the MRI room and cannot have a MRI. Having an MRI may mean some added discomfort for you.

- Feeling claustrophobia (being closed in a small space) may happen but is uncommon.
- Temporary hearing loss by the loud banging noise during the test may occur, but is rare. This is why you will be asked to wear earplugs.

At times during the test, you may be asked to not swallow for a short time, which can be uncomfortable. If at any time you experience any unusual sensation or muscle activity, alert the technician.

If you cannot have an MRI, a CT myelogram is a suitable substitute. You may experience uncommon symptoms such as headache, itching, nausea, or, rarely, hives, or inflammation from the spinal needle.

Risks associated with X-rays include rare tissue effects such as skin reddening, cataracts, and hair loss, and a small increase in the development of cancer later in life.

Surgical:

Every effort to minimize surgical risks will be taken before, during, and after the procedure. The following risks are possible during and after surgery:

- Development of a pocket of fluid (seroma) around the implanted materials may occur, but is uncommon. If infected, the implants may have to be removed.
- Your body may reject the implanted materials, but this is rare. If this occurs, the implants would have to be removed.

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- Infection and bleeding during surgery may happen, but is rare.
- Breakage of the stitches holding the leads or receiver in place, causing these to shift in position, may occur but is rare. There is also the potential risk of lead migration and leakage of cerebrospinal fluid.

Spinal Cord Stimulation:

Possible side effects from the initial application of spinal cord stimulation are elevated blood pressure and decreased heart rate, symptoms of autonomic dysreflexia, which should subside quickly with temporary discontinuation of stimulation. In our recent clinical trial, these symptoms occurred in about 20% of subjects. Other signs and symptoms of autonomic dysreflexia (headache, blotchy skin and sweating) are rare and were not observed in previous studies. You may also experience some leg movement with stimulation. In our recent clinical trial, this was well tolerated in each subject. Less common risks during spinal cord stimulation include:

- The receiver may erode through the skin if the antenna is worn continuously for excessive periods, increasing the risk of infection, but this is uncommon. The antenna should be removed, and your skin should be inspected daily for redness and/or irritation. Immediately report any abnormalities to the study team.
- Device malfunctions, while uncommon, may occur. Specific device malfunctions include:
    - Fibrosis (thickening or scarring of connective tissue) at the electrode-tissue interface may occur, but is rare.
    - Activation of the receiver by an external source may occur, but is rare.
- Bowel or bladder discharge due to contraction of the abdominal muscles during stimulation may occur, but is rare.
- Spasm of the expiratory muscles during stimulation, which may restrict your breathing, could happen but is rare and should not last long. Use of sedatives or other drugs which interfere with muscular activity could reduce the effectiveness of this technique. We may attempt to avoid these medications and/or reduce the dose if you are currently taking them.
- Electrically induced tissue damage may occur, but is rare. This is unlikely because stimulation is very brief, and the ranges of the electrical stimulation are known to be safe.

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- It is possible that placement of the device may worsen spasticity after implantation. This is rare and may ultimately require removal of the device.
- Temporary or transient sensory changes, such as electric like sensations, may be present during stimulation. These are uncommon and well tolerated, but can be lessened with changes in the stimulation parameters.

The implanted components may block the view of anatomical structures during x-rays or scans. However, an MRI cannot be conducted safely after implantation of this system. The study team will provide you with a letter from the manufacturer regarding MRI recommendations.

You will be told of any new information learned during the study that might cause you to change your mind about staying in the study.

Are there benefits to taking part in the study?

Participation in this research study might be a direct benefit to you. No guarantee of benefit or any other result can be made. The potential benefits to you from participating in this study may include restoration of an effective cough. This would allow you to clear airway secretions more easily. Lung infections are a significant cause of hospitalizations and death in spinal cord injured patients. Restoration of cough may allow you to clear secretions more normally, hopefully improve your level of comfort and prevent respiratory complications.

Potential benefits may also include a decrease in the need for caregiver support, a reduction in the occurrence of respiratory tract infections such as bronchitis or pneumonia, aspiration of food particles or secretions, and hospitalizations for respiratory tract infections. You may also experience an improvement in your spasticity and ability to remove foreign bodies from your airway.

What other options are there?

There are currently a number of ways to clear your secretions including suctioning, assisted cough, gravity, pneumo-belt, and insufflator-exsufflator device. Unfortunately, all of these have limitations that reduce their effectiveness. We have also recently conducted a clinical trial using spinal cord stimulation with disc electrodes for expiratory muscle activation. Each subject was able to produce an effective cough. There was a significant improvement in secretion management, fewer respiratory tract infections, reduced need for caregiver support for secretion management, and improvement in overall quality of life. However, this surgical

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procedure was lengthy and required an invasive surgical procedure. In contrast, use of wire leads (in this study) can be placed using minimally invasive techniques. This procedure, which is in current clinical use for other indications including pain control, is much less invasive, therefore safer, and may potentially provide the same significant clinical benefits.

What are the costs?

There is no cost to you or your insurance company for the Cough System components (stimulator, electrodes, external transmitter and coil). You and/or your insurance company will be billed for the surgery to implant the device, and related services such as anesthesia, x-rays, and blood work. Follow-up procedures, such as a revision surgery to replace or repair electrodes or other implanted components, or removal surgery, if it becomes necessary to remove one or more components, will also billed to you and/or your insurance company. Prior to any intervention, we will review all planned procedures with you in detail. Before any procedure, we will work with you and/or your insurance company to determine any anticipated costs to you. If you do not have insurance, or if your insurance does not fully cover the cost of any of the procedures related to your participation in this research study, the costs will be reviewed by the research team to determine if funding can be obtained from other sources, such as public or private foundations or through donations. We will outline all expected costs and the expected source of funding for each cost so that you will know the total cost to you prior to surgery.

What happens if I am injured while participating in this study?

All research involves a chance that something bad might happen to you. This may include the risk of personal injury. In spite of all safety measures, you might develop a reaction or injury from being in this study. If such problems occur during the study, you must contact the study doctor, Dr. Anthony F. DiMarco at (216) 778-3906. Necessary medical care will be provided to you by The MetroHealth System. The MetroHealth System has not set aside funds to pay you for any such reactions or injuries or for the related medical care. This medical care is not free. The cost of all treatments due to medical complications that might arise as a result of participating in the study will be billed, wherever allowable, to your health plan (Medicare, Medicaid, Bureau of Worker's Compensation, etc.) and/or your insurance company. You will be responsible for paying any deductible, co-insurance, or co-pays, for those services. If you do not have insurance, or your insurance company will not cover the costs associated with the treatments, you will be responsible for the costs. You may also still try to collect compensation for injury related to malpractice, fault, or blame on the part of those involved in the research, including the hospital. To help avoid injury, it is very important to follow all study directions.

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Will I be paid for participating in this study?

You will be reimbursed for your transportation and parking expenses. You will be reimbursed at the IRS standard mileage rate for transportation in your private vehicle. Reimbursement will be paid in the form of a check issued to you. Parking in MHMC visitors parking lots/garages will be covered by validating your parking pass for each study visit. If you do not have a private vehicle, transportation will be provided to you at the discretion of the study team. If you live in a health care facility which provides transportation, that service may be used, and if this service would result in any direct cost to you, the cost will be covered by the funding source of this study.

You will receive no special compensation for participating in the regularly scheduled aspects of this research project required to install, maintain or monitor the performance of the device. You will only be reimbursed for legitimate travel expenses.

What about Confidentiality?

We will make every effort to keep your research records private, but confidentiality cannot be assured. The MetroHealth System has no control over the use of this information once it is released. The information about you that is collected in this study will be shared with the study sponsor and may be combined with information gathered from public sources or other research studies. This information may be used for purposes unrelated to this research and could potentially be used to identify you.

Records that identify you and this consent form may be looked at by a regulatory agency such as the Food and Drug Administration (FDA), Department of Health and Human Services agencies, MetroHealth Institutional Review Board, Data Safety Monitoring Board and National Committee for Quality Assurance.

If the results of the study are published or presented in public, your name will not be used.

What will happen to video or audio records upon completion of the study?

We may publish or present photographs, audio recordings, and videos of you, including your face. No other personal information about you will be included in the presentation. All videotapes, audio tapes, and photographs will be maintained for future use in advertising material, presentations at professional meetings or publications. Prior to obtaining this material, you will need to sign a consent form which will detail how the material will be used.

What are my rights as a study participant?

Taking part in this study is voluntary. You have the right to choose not to take part in this study. If you do not take part in the study, your doctor will still take care of you. You will not lose any benefits or medical care to which you are entitled. If you withdraw from the study, with your written permission, clinical data will continue to be collected from your medical records.

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If you are an employee or student, whether you take part in this study will not affect your job, current or future medical care, or studies.

A Data Safety and Monitoring Board (an independent group of experts) will be reviewing the data from this research throughout the study.

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.

If you chose to take part, you have the right to stop at any time. You will be told of any new findings from this or other studies that may affect your health, welfare, or willingness to stay in this study. By signing this consent, you are not waiving any of your legal rights.

Does MetroHealth or any member of the research team have a financial conflict of interest in this study?

The principal investigator of this study, Dr. Anthony F. DiMarco, has a significant financial interest as the owner of patented technology used in this study. Dr. DiMarco has the potential to realize a financial gain should he market the technology related to this research study.

Whom do I call if I have questions or problems?

If you have questions about any part of the study now or in the future, or if you wish to communicate concerns or a complaint, you should contact Dr. Anthony F. DiMarco, who may be reached at (216) 778-3906, Monday through Friday. If you experience any side effects or injuries while participating in this study, please contact Dr. DiMarco at (216) 778-3906 during the week. For after hours, weekends, and/or holidays, Dr. DiMarco can be reached at (440) 248- 3125. If you have any questions about your rights as a research participant, or if you wish to express any concerns or complaints, please contact the MetroHealth Medical Center's Institutional Review Board (which is a group of people who review the research to protect your rights) at (216) 778-2021.

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Patient/Subject Acknowledgement:

The procedures, purposes, known discomforts and risks, possible benefits to me and to others, and the availability of alternative procedures regarding this research study have been explained to me. I have read this consent form, or it has been read to me, and I have been given the opportunity to ask questions or request clarifications of anything I do not understand. I voluntarily agree to participate in this study. I have been given a copy of this consent form.

Patient/Subject Signature	Date	Time

OR

Printed Name of Legally Authorized Representative

Description of Legally Authorized Representative's Authority

Legally Authorized Representative's Signature	Date	Time

AND

Signature of Person Obtaining Informed Consent	Date	Time

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