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Example - Early Feasibility Investigational Device Exemption

IDE Section:

Informed Consent Document

11.0 Informed Consent Document

Introduction

You are being asked to participate in this research study. Before you can decide whether or not to volunteer for this study, you must understand 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 or its doctors.

If you decide to participate in this study you will be told about any new information learned during the course of the study that might cause you to change your mind about staying in the study.

You are being asked to participate in this study because you have a cervical-level spinal cord injury.

Why is this study being done?

[redacted] are conducting a research study involving Functional Neuromuscular Stimulation (FNS), also known as Functional Electrical Stimulation (FES). The goal of the research is to develop practical FNS techniques for providing improved functional grasp and reach to individuals with cervical level spinal cord injury. The investigators are evaluating the use of an implantable muscle stimulation system that electrically activates paralyzed upper extremity muscles in order to restore lost

hand and arm function. This study is based on work that has been ongoing in this field since the early 1970's at Case Western Reserve University, MetroHealth Medical Center and the Louis Stokes Cleveland VA Medical Center. Financial support for the study is primarily provided by the National Institutes of Health (NIH).

How many people will take part in the study?

Approximately 100 subjects may be screened to be involved in this study. It is expected that up to 10 subjects will undergo surgery to receive the implanted system.

What is involved in the study?

The study procedures will be performed at [redacted]. The objective of this research is to provide functional movement of grasp and reach through the use of electrical stimulation. This technique is known as Functional Neuromuscular Stimulation (FNS), or Functional Electrical Stimulation (FES). For this study, a network of implantable electronic components will be placed under your skin in the abdomen, chest area, and arm during a surgical procedure. Stimulating electrodes will be surgically placed in the muscles of your hand, arm, shoulder and trunk. As many as twenty stimulating electrodes will be implanted. Wires from the electrodes and the stimulator (also known as "leads") will be tunneled beneath your skin and connected to small stimulator devices that will be located in your forearm, upper arm and torso. Each stimulator device delivers an electrical stimulus to the muscles through the electrodes. In addition, as many as four electrodes will be placed on muscles that you can control already. These electrodes will record the muscle activity that occurs when you contract the muscle, known as the "myoelectric signal" or "electromyographic signal" (EMG). You will control the electrical stimulation using movement(s) that you can still make voluntarily, which will be measured by the recording electrodes. Following implantation of the device, periodic evaluations will be performed to assess your condition, and the operation and usefulness of the device.

The implantable stimulator to be used in this study, known as the Upper Extremity Networked Neuroprosthetic (UE NNP) System, is a new implant design that is composed of a variety of modules that are connected similar to a computer network. The modules communicate with each other inside the body in order to coordinate their activity. The different modules that make up the NNP System include a "power module", which contains rechargeable batteries, a "stimulator module" and a "sensor module". Each stimulator module is connected to four stimulating electrodes. Each sensor modules is connected to two recording electrodes. The power module is placed in either your abdomen or chest. In order to recharge the batteries inside the power module, you will need to place a coil on the skin over the power module. Depending on your usage level, you may need to recharge the batteries in the power module every night.

The stages of this study include: screening, muscle conditioning, surgical reconstruction (if appropriate), implantation of the NNP System, post-surgical stabilization, exercise and training in use of the device, and follow-up evaluation of device function. In some cases, surgical reconstruction and implantation of the device can be performed during a single surgical procedure.

Muscle Conditioning: You will undergo approximately four weeks of exercise using a commercially-available muscle stimulator which delivers current through electrodes placed

on your skin. This surface stimulation exercise program will build muscle strength and endurance that will help [redacted] determine the best placement of electrodes in your implant surgery.

Surgical Reconstruction: Surgical reconstruction means the use of surgical techniques to restore some degree of hand function. Examples include:

- *"Arthrodeses"* where joints are fixed in one position to stabilize them (For example, a thumb joint could be fused to make it more rigid and useful.);
- *"Tenodeses"* where tendons are anchored to provide passive movement at the joints they cross (For example, in a patient who retains wrist movement, the tendons which normally would move the fingers could be anchored to the forearm bones. If the wrist was then flexed [i.e., bent downward], the finger extensors would tighten, causing the fingers to extend [i.e., open]; if the wrist was extended [i.e., bent upward], the finger flexors would tighten, causing the fingers to flex [i.e., close].);
- *"Tendon Anastomoses"* where several tendons are tied together to achieve synchronous movement and/or improve strength (For example, the tendons of the fingers could be tied together so that they move at the same time, thus causing the fingers to open and close as a group rather than individually.);
- *"Tendon Transfers"* where tendons are rerouted to permit muscles that are still under voluntary control to accomplish new functions (For example, muscles that normally would move the wrist could be transferred so that they would move the fingers instead.); and
- *"Rotational Osteotomies"* where a forearm bone is rotated to position the hand in a more functional posture. The surgical procedures are individualized to the needs of each patient.

You will be examined by [redacted] in order to determine if you would benefit from surgical reconstruction. They will discuss any appropriate procedures with you in detail. If you consent to undergo reconstructive surgery, a standard pre-operative physical examination will be performed, and normal surgical operative and post-surgical management protocols will be followed. Although "Surgical Reconstruction" is identified as a distinct stage of this study, the surgery may be, and usually is, performed at the same time that the NNP System is implanted (described below). [redacted] will advise you about whether reconstructive surgery and device implantation should be performed at the same time or during two different surgical sessions.

Implantation of the NNP System: A comprehensive medical history will be taken, and a standard pre-operative physical examination will be performed prior to any surgery. These tests include drawing blood for analysis, and pregnancy tests for females. In addition, a series of clinical evaluation tests will be performed to document the motor and sensory function of your hand and arm. Upon satisfactory completion of all pre-operative tests, and having granted informed consent, you will be an operative candidate. For the surgery itself, you will be anesthetized and prepared for implantation of the NNP System, which will be implanted under sterile conditions by [redacted]. In addition, a technical support team will be present to evaluate the operation of the system. The system will have previously passed a rigorous series of operational tests before being approved for implantation. During surgery, a final check is performed to confirm that the device is operating properly. You will be hospitalized for approximately 2-4 days immediately following the implantation surgery, and x-rays will be taken to document the position of the implanted hardware.

Exercise and Training: Post-operatively, your arm will be in a cast for approximately three weeks to allow wound healing and stabilization of the implanted device. After the cast has been removed, active muscle stimulation and unloaded, unresisted exercise (i.e., exercise without the use of weights or resistance that you push or pull against) will be initiated to build up muscle fatigue resistance (i.e., to condition the muscles so they don't tire out quickly). Progressive resistive exercises will be initiated when appropriate, at which time functional use of the implanted hand and arm and the stimulation system is also permitted. Following a period of several more weeks of full-strength exercise, you will undergo formal training in functional use of the system. Training and initial evaluations will be performed either during an inpatient visit of up to three weeks duration or on an outpatient basis over a longer period of time. Training consists of working with a therapist to learn the best ways of performing everyday tasks. You will control the stimulator, and hence movement of your hand and arm, through voluntary movement(s) that you retain in order to perform these tasks. Each training session is expected to last 2-4 hours.

Follow-up Evaluation of Device Function: In addition to being evaluated during your training period, you will be asked to report to the hospital at approximately six and twelve months after your surgery, and then annually thereafter up to 3 years, so that a series of follow-up evaluations can be performed. (If problems are encountered with the NNP System, you may be required to return to the hospital on a more frequent basis so that the nature of the problems can be identified and corrected.) Evaluations include: 1) a clinical assessment, which is a series of standard clinical tests performed to evaluate the motor and sensory function of your implanted hand and arm; 2) a technical assessment, which is a series of non-invasive measurements performed to evaluate the operation of the implanted device; and 3) a functional assessment, which is a series of functional tests performed to evaluate the effectiveness of the device in restoring hand grasp and reaching function (these tests measure your ability to move and manipulate objects, and to perform activities of daily living). Not all tests are performed at the same time. They are divided up so that a typical testing session should last 2-4 hours.

What happens if I discontinue or withdraw from the study?

You are free to participate in this study for as long as you like unless [redacted] believe it would be in your best interest to discontinue your participation (which they may do without your consent). Conversely, you may withdraw from the study at any time. If you choose to withdraw, the investigators may ask that the portable control tower be returned to the investigators. Although this would render the implantable device non-functional, the implant would not necessarily have to be removed. The device would be removed if you request that it be, or if the investigators deem it necessary to do so. If the investigators decide that the device should be removed, they will discuss the reasons with you. As long as the device remains implanted, its condition and integrity should be periodically assessed as part of your regular medical checkups. This should be done annually at least.

What are the risks of this study?

Your participation in this study may involve the following risks:

Inconvenience

You will be hospitalized for 2-4 days immediately following surgery to implant the device. This study also requires periodic visits to the hospital to participate in training and

evaluation experiments, as described above. The initial training and evaluation is performed either during an inpatient visit of up to three weeks duration or on an outpatient basis over a longer period of time. Follow-up evaluations are performed at six and twelve months, and may involve a brief (1-3 days) inpatient visit. A typical testing session will last 2-4 hours.

Surgery
There are some risks associated with any surgical procedure and the use of general anesthesia. Examples include the possibilities of infection, bleeding, tissue scarring, and an adverse reaction to the anesthetic. To minimize these risks, the procedure will be performed by a qualified surgeon and anesthesiologist, and complete monitoring will be performed during the operation to ensure your safety.

Blood draw
When blood is drawn from a vein, there may be some temporary discomfort, local bruising, infection or blockage of the vein. Rarely fainting occurs. Suitable precautions will be taken to minimize these risks.

Radiation exposure
The amount of radiation you will be exposed to from the x-rays is relatively small. Such doses of radiation may be potentially harmful, but the risks are so small that they are difficult to measure. If you have already had many x-rays, you should discuss the potential added risk from more radiation with the researchers before agreeing to be in the study.

Infection
The implanted device could become infected. You will be taught how to identify possible infections. To reduce the likelihood of infection, special procedures set up for implanting artificial devices will be used. If an infection occurs, antibiotics will be used to try to eliminate it. If this is unsuccessful, the device may have to be removed in another surgical procedure. Less than 1% of the electrodes implanted in this program have become infected. About 2% of similar implanted stimulators utilized in this program have become infected.

Device malfunction
The implanted device could fail to operate properly due to failure of the device itself or of the leads or electrodes. Manufacturing procedures have been established to reduce the likelihood of malfunction. If failure should occur, procedures have been established to analyze the failure and replace the faulty component. This would require another surgical procedure. You may choose to have the failed part replaced, leave it in place, or have the entire device removed. In previous studies using similar electrodes, about 1% of the electrodes have failed. We do not have any previous experience with the modules that make up the NNP System. Based on similar implanted electronic devices, the failure rate is likely to be less than 5%.

Device rejection
Your body's reaction may be to reject the implanted device. To reduce this possibility, all materials used in the implant are commonly-used biomaterials (materials designed for implantation in the body) that have previously been used in other implantable devices cleared for marketing by the FDA. Despite this selection of materials, some unknown process could cause rejection. If this were encountered, you would be counseled regarding

the nature of the problem and the device would be removed. We have utilized similar materials in other devices we have studied and have not observed any adverse tissue reaction or rejection of the materials.

Tissue breakdown
The skin over the implant or leads could break down from mechanical abrasion and allow the device to protrude through the skin. The device is designed to minimize the possibility of tissue deterioration. The surgical placement of the power module is similar to that for a drug pump or pacemaker and is intended to reduce the possibility of such breakdown. If the tissue did break down, you would be counseled regarding the nature of the problem and any device components at the site of the breakdown would be removed. If you request, the entire device would be removed.

Overheating
The implant (power module) could heat up during recharging or if there is damage to the battery. The external charger and internal charging circuitry are designed to prevent the battery from heating excessively under any circumstances. You will be taught how to check for heating during recharging and what to do if the recharging coil feels too hot.

Fibrosis and scarring
Tissue around the implant stimulator or electrodes could become excessively scarred from the surgical procedure, the presence of the device, or the injection of current over long periods of time. Adverse tissue reactions will be indicated by changes in the performance of the device. In animal studies, the investigators have not encountered such reactions and they do not anticipate them in the human studies. Levels of stimulation will be kept within limits that have not caused damaging effects on the surrounding tissue in animals. If such a change did occur and did not allow the device to function properly, or in any way compromised your safety, you would be informed about the nature of the problem. The components at the site of the tissue reaction could be removed and replaced, or the device removed in its entirety.

Electrical safety
There is a possibility of a shock hazard. The electronic circuitry in the device is designed to stop generating electrical current in the case of a failure of the circuitry. This is to ensure that potentially damaging current levels will not be generated. You have been provided with a magnet to place over power module in case the system appears to operate improperly or if you cannot shut it down using the normal methods. The magnet will disconnect the batteries from the power module and it will immediately stop functioning. Any stimulation will stop immediately. In order to restart the NNP System after you use the magnet, it will be necessary to return to the laboratory for evaluation and reset of the system. The NNP System also uses a radio frequency connection that is known to be safe at the transmitted energy levels. Other sources of radio frequency transmission are unlikely to affect your implant because of the way the transmitted signals are encoded.

Additional surgery
Following implant surgery and recovery, your resulting hand grasp and arm function could be different than that which was observed during surgery. In addition, usage of your hand and arm in normal activities can cause changes in your grasp and arm function over time. There is also a possibility that components of the implanted device may need to be repositioned. The implant surgical procedures are designed to ensure careful placement of

the implant and electrodes as well as careful modification of your hand to provide functional grasp. In addition, post-surgical management protocols are designed to promote proper healing. If [redacted] feels that revision surgery is necessary, you would be counseled regarding the reasons, and you would be advised of all options available to you. If you choose not to undergo revision surgery, you will still be provided with appropriate training and support in the use of your NNP System.

Unknown risks
There may be other risks that are currently unknown. The investigators will inform you of any new information learned during the course of the study that might cause you to change your mind about continuing your participation.

Reporting side effects
If side effects occur or other complications arise, you will report them immediately so that you can be properly treated. Follow-up of any side effects or complications will be carried out in a timely manner.

Precautions after implantation

- You should not have a Magnetic Resonance Imaging (MRI) performed on any part of your body. The implant stimulator and electrodes have not been tested for safety within an MRI machine.
- You should not have ultrasound imaging, or a sonogram, applied directly over the implanted modules.
- Do not use surface stimulation such as Transcutaneous Electrical Nerve Stimulation (TENS) or Neuromuscular Electrical Stimulation (NMES) without first contacting one of the investigators in this study. There is a risk of inducing current flow through the implanted stimulator that could result in damage to the device.
- Avoid placing needles or catheters into the arm with implanted electrodes and modules. There is a risk that the needle will puncture one of the electrode leads.
- Avoid placing blood pressure cuffs on the arm with the implanted leads. The pressure induced by the cuff will put stress on the connectors and leads in the arm.
- Contact one of the study investigators before undergoing any surgery near the implant or before undergoing implantation of orthopaedic or cardiovascular devices (such as artificial hips or pacemakers).
- Inform one of the study investigators if you develop any infection, such as a pressure sore or a urinary tract infection (UTI).

Are there benefits to taking part in the study?

This study is part of a research program and there may be no immediate personal benefit to you. It is possible that you will benefit from improved upper extremity function and/or improved trunk stability. Future patients may benefit from the results of this study as well.

What other options are there?

For some spinal cord injury patients, there are also alternative methods available for restoration of some degree of certain upper extremity functions. These methods include surgical reconstruction and external orthotics.

Surgical Reconstruction: A variety of surgical reconstructive techniques can be used to restore some degree of hand function to people with tetraplegia who retain voluntary

control of certain muscles. These were discussed previously. Some of these techniques also can be used to provide other upper extremity functions as well. Such procedures are effective for many people with high-level tetraplegia, depending on the overall condition of their paralyzed hand and arm, but they cannot be applied effectively to many others.

Although these techniques may not be sufficient in themselves to restore adequate hand and arm function, they may be used in conjunction with electrical stimulation to provide the desired level of function. [redacted] will determine which reconstructive techniques could provide you with better hand grasp and arm function, both with and without electrical stimulation, and will discuss the procedure(s) and anticipated result(s) with you.

External Orthotics: Hand splints have been developed for patients having no voluntary hand control. These devices use electric motors to power an external brace or a ratchet on a splint to control hand and finger position. Acceptance and continued use of such splints has only been moderate. Problems inhibiting their use include functional limitations (i.e., their usefulness for certain functions is limited) and complexity of operation. If you choose to utilize orthotic devices or bracing, the NNP System will not interfere with your ability to do so. You may use some simple orthoses in conjunction with the NNP System to provide the desired level of function.

What are the costs?

There is no cost to you or your insurance company for the NNP System components. 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 revision surgery to replace or repair electrodes or other implanted 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?

Medical care (including hospitalization) is available if you are injured or become ill because of the research procedures. This medical care is not free. You will be responsible for the costs. However, many forms of insurance, including Medicare, cover items or services needed for the diagnosis and treatment of any complications that result from your participation in this research trial. We will work with you to ensure that any care is billed appropriately. You may call the Director of Risk Management at [redacted] if you have any questions about the cost of treatment in your case.

Will I be paid for participating in this study?

You will receive no payment for participating in this study. However, you may be eligible for reimbursement for the costs of participating in this study.

What about Confidentiality?

We will make every effort to keep your research records confidential, but confidentiality cannot be assured. The data collected during this study will remain under the control of the investigators. 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
- National Committee for Quality Assurance

Your records may also be looked at by the National Institutes of Health (NIH), Department of Veterans Affairs (VA), Case Western Reserve University (Case), and the Cleveland FES Center (FESC). Authorized representatives of these institutions, including auditors and monitors, may also review your records related to research participation.

If the results of the study are published or presented in public, your name will not be used without your permission.

If the study personnel find evidence that suggests that you have been physically or sexually abused or they find evidence of child or elder abuse or neglect, they are required by law to report this to local law authorities.

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 unless you give your specific permission on a separate form.

All videotapes, audio tapes, and photographs will be kept indefinitely.

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 permission, you will continue to be followed and clinical data will continue to be collected from your medical records. A Data Safety and Monitoring Board (a group of experts) will be reviewing the data from this research throughout the study.

If you choose 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.

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

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

This study is being sponsored by grants from the National Institutes of Health. Portions of the investigators' and their research team's salaries are being paid by this grant.

Whom do I call if I have questions or problems?

The investigators for this study are: [redacted]. [redacted] is the primary contact. [redacted] are the surgeons/physicians. The investigators will answer, at any stage of this study, questions concerning any of the procedures and may be reached at the CWRU Rehabilitation Engineering Center, Department of Orthopedics, MetroHealth Medical Center, 2500 MetroHealth Drive, Cleveland, Ohio 44109-1998, telephone number [redacted].

If you have questions about any part of the study now or in the future, you should contact [redacted], who may be reached at [redacted]. If you experience any side effects or injuries while participating in this study, please contact [redacted], who may be reached at [redacted] For after hours, weekends and/or holidays, call [redacted], at [redacted] If you have any questions about your rights as a research participant, contact the MetroHealth Medical Center's Institutional Review Board (which is a group of people who review the research to protect your rights) at [redacted].

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 understand it. I agree to participate in this study. I have been given a copy of this consent form.

_____ _____

Patient/Subject Signature Date

_____ _____

Signature of Person Obtaining Informed Consent Date