

Consent and Authorization Document

The Effectiveness of Early Sacral Nerve Stimulation in Improving Bladder Related Complications and Quality of Life After Acute Traumatic Spinal Cord Injury

BACKGROUND

You are being asked to take part in a research study. Before you decide if you want to participate, it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with friends and relatives if you wish. Ask the research doctor or staff if there is anything that is not clear or if you would like more information. Take time to decide whether or not to volunteer to take part in this research study.

Urinary problems (known as urinary or bladder dysfunction and incontinence) place a large burden on patients with spinal cord injury (SCI) in terms of medical management, quality of life, and physical ability. In addition to bladder dysfunction, SCI patients usually have some degree of physical limitation because of their injury that may also decrease their quality of life. Along with these difficulties, a loss of nerve input from the spinal cord results in changes to control of the bladder, which can in turn cause bladder spasms, high bladder pressures and urinary leakage. These symptoms together are known as “neurogenic bladder”.

Over the past 20 years a treatment called sacral neuromodulation has become common and is currently United States Food and Drug Administration (FDA) approved for the treatment of the following symptoms: urinary urge incontinence (an intense urge to urinate resulting in urine leakage from the bladder), urinary frequency, and urinary retention from non-neurogenic (non-nerve related) causes. Sacral neuromodulation involves a surgery that implants a device under the skin that can be programmed to deliver electrical impulses to nerves. In this surgery, the surgeon uses a form of imaging known as fluoroscopy to help place electrodes on a nerve root within the base of the spine (an area known as the “sacral foramen”). A stimulator similar to a heart pacemaker is connected to the electrodes. The nerves are stimulated with electrical impulses of varying patterns and intensity. How these nerves actually work to help control the bladder in humans is not well understood, but it is thought to be through the same nerves that are involved in the development of neurogenic bladder. Sacral neuromodulation is not currently approved by the United States Food and Drug Administration (FDA) for the use in SCI, and therefore the device is used in sacral neuromodulation is an investigational device. The device we are using in this study is called the Interstim® Sacral Neuromodulator, and it is made by Medtronic. While the effectiveness of sacral neuromodulation has been well established in patients with urgency incontinence (a condition in which a person experiences urges to immediately urinate), only some success has been achieved in patients with chronic neurogenic bladder related to SCI.

The purpose of this study is to see what the effect of sacral neuromodulation is on various tests to measure urinary and bladder function in participants with acute spinal cord injury, and to



determine the impact of sacral neuromodulation on patient reported quality of life after acute spinal cord injury.

STUDY PROCEDURES

Randomized Trial: A research trial usually involves comparing different treatments. In a trial, one group will get one treatment and another group will get a different treatment. In a “randomized trial” people are put in one group or the other by random chance. This means that a computer will decide by chance which group a person is in, not the doctors running the trial.

For this study, 60 patients with acute (sudden onset) complete spinal cord injury at either the University of Utah, the University of Minnesota, Allina Health, Hennepin County Medical Center, or the University of Michigan will be enrolled in this study. These 60 patients will be randomized (50:50 chance) to either the intervention arm or to the control arm. If randomized to the intervention arm, a participant will have a surgery during which a surgeon implants electrodes and the battery-controlled medical device called the Interstim® Sacral Neuromodulator within six weeks of complete spinal cord injury. If randomized to the control arm, the participant will receive usual standard of care. Both groups of patients will be followed for one year.

At enrollment, all participants will be provided with the following:

- (1) Catheterization protocols. These are instructions for you to use to insert a catheter to empty your bladder.
- (2) Bladder, bowel, and erectile function diaries to record how long catheterization takes you to perform, amount and time of fluid intake, incontinence events (accidental or involuntary urination), bowel movements, and currently used medications.
- (3) Spinal Cord Injury Quality of Life (SCI-QOL) questionnaires
- (4) A baseline urodynamic study (tests on your bladder and urinary function).

Follow up will consist of a urodynamic study at 3 months, followed by a clinical exam every 3 months for one year. A urodynamic study involves placing a catheter in your bladder and introducing water while monitoring pressure and electrical activity in the bladder muscle. We take fluoroscopic x-ray images of the bladder at the time of these studies. Before each examination, participants will be asked to write a 3-day bladder diary. When a participant arrives in clinic, he or she will be given Spinal Cord Injury Quality of Life (SCI-QOL) questionnaire to fill out. Upper tract imaging with renal ultrasound will be completed at one year. These procedures will be done to monitor for the development of hydronephrosis. Hydronephrosis is when urine builds up in the kidney and cannot drain out, which leads to swelling of the kidney. Serum creatinine to estimate of renal function will be collected every year to test for any problems with your kidneys. Anytime you are treated with antibiotics for a urinary tract infection urine culture results, antibiotic used, and other relevant information will be recorded. If you are treated at an outside institution, you will be asked to forward the information to the study center.

For those that have the Interstim® device in place, plain film x-rays will be taken of the pelvis at your post-operative check within 4 weeks of surgery, and at 3 months and 12 months after surgery.

You will also be asked to provide basic demographic information, other medical conditions, level of spinal cord injury, and urinary tract infections. We will also gather information from bladder tests, which include maximum bladder capacity, bladder reflex volume, maximum detrusor pressure and detrusor compliance.

Your total participation time in the study will be up to 15 months for either group.

MULTIMEDIA RECORDINGS

A video recording of the device implantation surgery will be made in approximately 30% of participants in the intervention (implantation) group, which will be reviewed by the investigator and another urologist who is not part of the study. This will be done to confirm that the procedure is being performed safely and consistently. No identifying features or information will be included in the videos. Recordings will be stored digitally on a secure server, with password-protected access limited to study team members only. All recordings will be deleted within one year of study completion. You will not be compensated for the recording. If you do not wish to be recorded, you should not participate in this research study.

RISKS

There are several risks to surgery, which include infection, pain, and bleeding. Please be aware that any unexpected events (such as an infection) that occur as a result of participating in this study could delay the recovery of your spinal cord injury. There is also a risk associated with general anesthesia, however, overall, it is very safe. Older adults, or those with serious medical problems, particularly those undergoing more extensive surgeries, may be at increased risk confusion after the operation, pneumonia, or even stroke and heart attack.

This research study involves the use of fluoroscopy and x-ray scans. These scans are not standard of care and you are receiving them only because you are enrolled in this research study. These procedures will expose you to radiation. The risk from this radiation exposure is considered to be small and comparable to other every day risks. To give you an idea of how much radiation you will receive, we will compare this radiation to the radiation that you receive from natural sources. Everyone receives a small amount of unavoidable radiation every day. Some of this radiation comes from space while some comes from radiation that is naturally occurring in water, soil, rocks and minerals found in plants and animals. The excess radiation that you will be exposed to in this research study is equivalent to about 600 days of natural background radiation. This amount does not include any radiation exposures that you may receive from other types of tests. Radiation exposure increases health risk such as carcinogenesis and tissue reaction through DNA damage. There is also the risk of local tissue burn related to fluoroscopy.

There are also several risks that are very specific to placement of a sacral neuromodulator:

Infection: the risk of the device becoming infected is low and less than 5% (1 out of 20 patients). If infection occurs the neuromodulator and the electrodes (wires travelling to the nerves in the pelvis through the tailbone) need to be removed in a separate surgery. The combination of removal of the device and antibiotics will cure most infections.

Device failure: the device can fail due to mechanical or electrical failure

Electrode migration: In a study of patients undergoing sacral neuromodulation for treatment of neurogenic bladder, the revision rate of sacral electrodes due to migration was about 30%. If the electrodes migrate (often from lower extremity muscle spasms) than they need to be replaced with a new electrode in a revision outpatient surgery

All of the complications of sacral neuromodulation can generally be resolved by removal of the device which requires a surgical procedure and additional antibiotics.

Additional procedures associated with participation in this study include fluoroscopic urodynamic studies. These will be performed at baseline prior to device implantation, 3-months and 12-months after device implantation. The risks of fluoroscopic urodynamic include urinary tract infection, discomfort during the study, bleeding, and autonomic dysreflexia (high blood pressure or heart rate, headaches, sweating, flushing, and blurred vision). There is also a risk of radiation exposure associated with fluoroscopy during the procedure (this risk is described as above).

In addition to the surgical procedure, there are small risks associated with participating in a clinical trial. Specifically, the other aspects of the study include (1) research team chart review, (2) questionnaire completion, (3) bladder diary completion and (4) 24 hour pad collection. We will also request that you have a renal ultrasound or CT scan at 12 months after device implantation but this is standard care that you would receive if you were under the care of a urologist for your neurogenic bladder.

Psychological Risks: Participants will be asked to provide information regarding their demographic information, self-reported mental and emotional well-being, physical health, and satisfaction with their treatment. These questions have a small psychological risk if participants are upset by questions, which ask them to reflect on their health or emotional issues.

Social Risks: While patient may worry that involvement in this research may impact their employment or insurance status negatively, however, there are no expected risks to either employment or future insurance with participation in the study. Other social risks could be feeling a 'stigma' or awkwardness and shame in social situations from having a bladder

stimulator. The bladder stimulator, however, is not visible and flat against the abdominal wall. With normal clothing the bladder stimulator would not be at all visible.

Images 1 and 2 below are the neurostimulator device and leads that will be implanted in the intervention group. Image 3 shows the Interstim programmer used to control the device.



Image 1- Neurostimulator



Image 2- tined lead



Image 3- programmer

Breach of Confidentiality Risk: There is a small risk of breach of confidentiality with this study as demographic information will be collected and stored by study investigators. All steps will be taken to minimize this risk. Please see “Confidentiality” section below.

REPRODUCTIVE RISKS

Pregnant women will be excluded from participation. It is possible that if the treatment is given to a pregnant woman it will harm the unborn child. Pregnant women must not take part in this study, nor should women who plan to become pregnant during the study. Women who are at risk of pregnancy will be asked to have a pregnancy test before taking part to exclude the possibility of pregnancy. If you could become pregnant, you must use an effective contraceptive during the course of this study. Acceptable methods of birth control include abstinence, oral contraceptives, the contraceptive patch, the contraceptive ring and condoms. If you become pregnant while taking part in the study, you must immediately tell your research doctor. Options will be discussed with you at that time. Whether or not you remain on study treatment, we will follow the outcome of your pregnancy and we will continue to follow you according to the study plan.

UNFORESEEABLE RISKS

Participation in the study may involve risks that are currently unknown. You will be informed during the course of this study, of any risk that may have an effect on your willingness to continue with this study.

BENEFITS

There might be no direct benefits to you from your taking part in this study. There is no financial compensation for participants in this study. The information we get from this study may help us treat future patients in your situation.

ALTERNATIVE PROCEDURES

You may choose not to be in this study. If you do not want to take part in the study, there are other choices that you may discuss with your doctor. Other treatment options include standard of care neurogenic bladder management with medications, catheters and/or surgery as your doctor recommends.

RIGHT OF INVESTIGATOR TO WITHDRAW PARTICIPANTS

The study doctor may choose to withdraw you from the study at any time and for any reason, including the following:

- The conditions and timing of your enrollment are not favorable for you to be in the study,
- The risks of you being in the study outweigh the benefits,
- You do not follow the study treatment schedule/routine,
- There are issues that affect the main endpoint of the study, or
- The study sponsor decides to stop the study.

If you end the study early, any questionnaires will be completed as possible at that time but there will be no other invasive procedures. You will not be required for any additional follow-up if you are withdrawn from the study.

PERSON TO CONTACT

If you have questions, complaints or concerns about this study, you can contact Jeremy B. Myers, MD at 801-213-2700. If you think you may have been injured from being in this study, please call Jeremy B. Myers, MD at 801-213-2700. Dr. Myers can be reached at this number during 8:00 a.m. to 5:00 p.m. Or, you can call the hospital operator at (801) 581-2121 as ask for the urology resident on-call. This last number is answered 24 hours a day, seven days a week.

Institutional Review Board: Contact the IRB if you have questions regarding your rights as a research participant. Also, contact the IRB if you have questions, complaints or concerns which you do not feel you can discuss with the investigator. The University of Utah IRB may be reached by phone at (801) 581-3655 or by e-mail at irb@hsc.utah.edu.

Research Participant Advocate: You may also contact the Research Participant Advocate (RPA) by phone at (801) 581-3803 or by email at participant.advocate@hsc.utah.edu.

RESEARCH-RELATED INJURY

If you are injured from being in this study, medical care is available to you at the University of Utah as it is to all sick or injured people. The University of Utah has not set aside any money to pay the costs for such care. The University will work with you to address costs from injuries. Costs would be charged to you or your insurance company (if you have insurance), to the extent those parties are responsible for paying for medical care you receive. Since this is a research



study, some health insurance plans may not pay for the costs. By signing this consent form you are not giving up your right to pursue legal action against any parties involved with this research. However, the sponsor of this study is not responsible for any research related injuries.

The University of Utah is a part of the government. If you are injured in this study, and want to sue the University or the doctors, nurses, students, or other people who work for the University, special laws may apply. The Governmental Immunity Act of Utah is a law that controls when a person needs to bring a claim against the government, and limits the amount of money a person may recover. See sections 63G -7-101 to -904 of the Utah Code.

VOLUNTARY PARTICIPATION

Research studies include only people who choose to take part. You can tell us that you don't want to be in this study. You can start the study and then choose to stop the study later. We will still give you medical care and answer any questions you have. Your decision will not affect your relationship with your doctor or the study team in any way. If you want to stop being in this study, please let the research doctor know. That way you can find out what should be done about your normal medical care outside of the study.

COSTS AND COMPENSATION TO PARTICIPANTS

There is no financial compensation for participants in this study. The study will be billed for any visits and procedures that are completed just for the purpose of this study. You/your insurance will be billed for any visits and procedures that your doctor would normally perform for people with this condition. The table below shows who will be billed for which visits and procedures, which will be determined by which arm of the study you are randomized to.

	Billed to Patient/Insurance	Billed to Study
Control Arm	<ul style="list-style-type: none">• 3 month visit and procedures• 12 month visit and procedures	<ul style="list-style-type: none">• Baseline visit and procedures
Intervention Arm	<ul style="list-style-type: none">• 3 month visit and procedures, excluding pelvic x-ray• 12 month visit and procedures, excluding pelvic x-ray	<ul style="list-style-type: none">• Baseline visit and procedures• All pelvic x-rays• Investigational device/ components• All device implantation and revision charges

NEW INFORMATION

Sometimes during the course of a research project, new information becomes available about the device that is being studied. If this happens, your research doctor will tell you about it and discuss with you whether you want to continue in the study.

NUMBER OF PARTICIPANTS

We expect to enroll 60 participants in this study with roughly one third coming from the University of Utah.

AUTHORIZATION FOR USE OF YOUR PROTECTED HEALTH INFORMATION

Signing this document means you allow us, the researchers in this study, and others working with us to use some information about your health for this research study. This is the information we will use and include in our research records:

- Demographic and identifying information like name, address, telephone and email.
- Related medical information about you like allergies, current and past medications or therapies, and information from physical examinations, such as blood pressure reading, heart rate, temperature, and lab results
- All tests and procedures that will be done in the study

How we will protect and share your information:

We will do everything we can to keep your information private but we cannot guarantee this. Study information will be kept in a secured manner and electronic records will be password protected. Study information may be stored with other information in your medical record. Other doctors, nurses, and third parties (like insurance companies) may be able to see this information as part of the regular treatment, payment, and health care operations of the hospital. We may also need to disclose information if required by law.

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.

In order to conduct this study and make sure it is conducted as described in this form, the research records may be used and reviewed by others who are working with us on this research:

- U.S. Food and Drug Administration
- U.S. Department of Defense
- Medtronic, the company that makes the Interstim device
- Members of the research team
- University of Utah Health
- The University of Utah Institutional Review Board (IRB), which reviews research involving people to make sure the study protects your rights.
- Other academic research centers and hospitals we are working with: University of Minnesota, University of Michigan, Allina Health, and Hennepin County Medical Center.

If we share your identifying information with groups outside of University of Utah Health, they may not be required to follow the same federal privacy laws that we follow. They may also share your information again with others not described in this form.

If you do not want us to use information about your health, you should not be part of this research. If you choose not to participate, you can still receive health care services at University of Utah Health.

What if I decide to Not Participate after I sign the Consent and Authorization Form?

You can tell us anytime that you do not want to be in this study and do not want us to use your health information. You can also tell us in writing. If you change your mind, we will not be able to collect new information about you, and you will be withdrawn from the research study. However, we can continue to use information we have already started to use in our research, as needed to maintain the integrity of the research. This authorization does not have an expiration date. You have a right to information used to make decisions about your health care. However, your information from this study will not be available during the study; it will be available after the study is finished.

CONSENT

I confirm that I have read this consent and authorization document and have had the opportunity to ask questions. I will be given a signed copy of the consent and authorization form to keep. The U.S. Department of Defense is providing funding for this study.

I agree to take part in this research study and authorize you to use and disclose health information about me for this study, as you have explained in this document.

Participant's Name

Participant's Signature

Date

Name of Person Obtaining Authorization and Consent

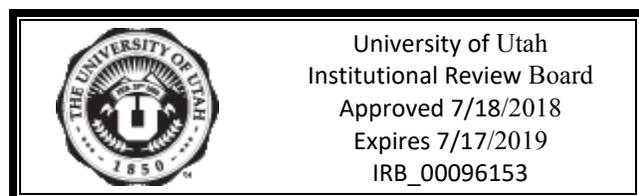
Signature of Person Obtaining Authorization and Consent

Date

WITNESS STATEMENT:

The participant was unable to read or sign this consent form because of the following reason:

The participant is illiterate



- The participant is visually impaired
 The participant is physically unable to sign the consent form. Please describe:

- Other (*please specify*):

I confirm that I was present as a witness for the consent process for this study. I confirm that the participant named above was read the information in the consent document and that the participant has agreed to take part in the research study.

Name of Witness

Signature of Witness

Date

