Study Title: A Pilot Study to Compare Short-Term Transcutaneous or Epidural Spinal Stimulation for Enabling Motor Function in Humans with Spinal Cord Injury

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MAYO CLINIC

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RESEARCH PARTICIPANT CONSENT AND PRIVACY AUTHORIZATION FORM

Study Title: A Pilot Study to Compare Short-Term Transcutaneous or Epidural Spinal Stimulation for Enabling Motor Function in Humans with Spinal Cord Injury

IRB#: 21-006340

Principal Investigator: Kristin Zhao, Ph.D., and Colleagues

Key Study Information

This section provides a brief summary of the study. It is important for you to understand why the research is being done and what it will involve before you decide. **Please take the time to read the entire consent form carefully and talk to a member of the research team before making your decision.** You should not sign this form if you have any questions that have not been answered.	
It's Your Choice	This is a research study. Being in this research study is your choice; you do not have to participate. If you decide to join, you can still stop at any time. You should only participate if you want to do so. You will not lose any services, benefits or rights you would normally have if you choose not to take part.
Research Purpose	The purpose of this research is to learn more about how electrical spinal stimulation affects and enables the function of motor nerves, and to assess any changes in movement, sensation, and function during four weeks with stimulation, and for 16 weeks after stimulation. You have been asked to take part in this research because you have a spinal cord injury resulting from trauma.
What's Involved	If you agree to participate, you will be assigned to receive either epidural stimulation through temporarily implanted wires (or leads), or transcutaneous stimulation through electrodes placed on the skin. Study participation involves about 1 week of pre-stimulation testing, 4 weeks of rehabilitation sessions with stimulation, 1 week of post-stimulation testing, and then follow-up testing during Week 8 and

	Week 20. If you were assigned to epidural stimulation, a procedure to temporarily implant leads through your skin into the epidural space your lower spine will be performed by a doctor specializing in pain medicine. You will undergo 4 weeks of rehabilitation sessions, 3 times per week, using electrical spinal stimulation. Then, if you were assigned to epidural stimulation, the doctor will remove the leads and clean and dress the incision site. Then you will undergo a week of the same tests and assessments that were done at the beginning of the study. Most of these tests and assessments will be repeated at 4 weeks and 16 weeks after the end of stimulation rehabilitation sessions.
Key Information	The risks associated with study participation are completely described later in this form, be sure to review them carefully. Given the visit frequency and the duration of the study, time expenditure will be the main potential inconvenience; please discuss and concerns or possible conflicts with your study team. With the brief procedure to implant the stimulator leads, there are risks including infection and fluid leakage into adjoining tissues. Additionally, rehabilitation training and weight-bearing tasks can be accompanied by minor skin irritation or abrasions, bruising, and fatigue.
Learn More	If you are interested in learning more about this study, read the rest of this form carefully. The information in this form will help you decide if you want to participate in this research or not. A member of our research team will talk with you about taking part in this study before you sign this form. If you have questions at any time, please ask us.

Making Your Decision

Taking part in research is your decision. Take your time to decide. Feel free to discuss the study with your family, friends, and healthcare provider before you make your decision. Taking part in this study is completely voluntary and you do not have to participate.

If you decide to take part in this research study, you will sign this consent form to show that you want to take part. We will give you either a printed or electronic copy of this form to keep. A copy of this form will be put in your medical record.

For purposes of this form, Mayo Clinic refers to Mayo Clinic in Arizona, Florida and Rochester, Minnesota; Mayo Clinic Health System; and all owned and affiliated clinics, hospitals, and entities.

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Contact Information

If you have questions about …	You can contact …
▪ Study tests and procedures ▪ Materials you receive ▪ Research-related appointments ▪ Research-related concern or complaint ▪ Research-related injuries or emergencies ▪ Withdrawing from the research study	**Principal Investigator:** Kristin Zhao, Ph.D. **Phone:** (507) 284-8942 **Study Team Contact:** Tyson Scrabeck **Phone:** (507) 538-1016 **Institution Name and Address:** Mayo Clinic 200 1st St. SW Rochester, MN 55905
▪ Rights of a research participant	**Mayo Clinic Institutional Review Board (IRB)** **Phone:** (507) 266-4000 **Toll-Free:** (866) 273-4681
▪ Rights of a research participant ▪ Any research-related concern or complaint ▪ Use of your Protected Health Information ▪ Stopping your authorization to use your Protected Health Information ▪ Withdrawing from the research study	**Research Participant Advocate (RPA)** **(The RPA is independent of the Study Team)** **Phone:** (507) 266-9372 **Toll-Free:** (866) 273-4681 **E-mail:** ResearchParticipantAdvocate@mayo.edu
▪ Billing or insurance related to this research study	**Patient Account Services** **Toll-Free:** (844) 217-9591

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

A description of this research study will be available on http://www.mayo.edu/research/clinical-trials. This website will not include information that can identify you. You can search this website at any time.

Why are you being asked to take part in this research study?

You are being asked to take part in this research study because you have sustained a spinal cord injury (SCI) with partial or complete loss of motor function below the injury.

Why is this research study being done?

The purpose of this study is to compare spinal motor nerve response to electrical stimulation delivered directly to the epidural space, and delivered through the skin (transcutaneously), and to measure any changes in motor performance over the course of about 5 months, during and after using one of the two types of stimulation.

The neural stimulation system and electrical leads for direct spinal stimulation are approved for treating pain. They are not approved by the U.S. Food and Drug Administration (FDA) to enable motor function, but the FDA has allowed the use of these devices in this research study.

The plan is to have 8 people take part in this study at Mayo Clinic.

Information you should know

Who is Funding the Study?
The Mayo Clinic Center for Regenerative Medicine is funding the study. The Center for Regenerative Medicine will cover costs related to running the study.

How long will you be in this research study?

You will be in this study for about 5 months.

What will happen to you while you are in this research study?

If you are eligible for the study, we will assign you to receive one of the two treatments: either direct spinal stimulation using temporarily implanted wires (leads), or stimulation delivered through electrodes on the skin (transcutaneous stimulation). You will be assigned to a treatment arm based on availability at the time you participate. If both arms are open, you will be given the choice of which arm you would like to participate in.

The following tests and procedures will be performed over the first week of the study:

Screening

- Evaluation of bone density through an x-ray scan (also called a DEXA scan),
- Assessment of spinal reflexes using transcutaneous (through the skin) electrical stimulation over the lower spine, involving surface-level skin electrodes placed with the option of ultrasound guidance,
- A physical exam to determine your neurological level of injury (also called ASIA),
- A spasticity assessment called the Modified Ashworth Scale,
- Vital signs, including blood pressure, heart rate, and body weight,
- Urinalysis, to detect any signs of infection,
- Computerized tomography (CT) and magnetic resonance imaging (MRI) for visualization of spinal structures.
- Urine pregnancy screening, if you are a female of child-bearing potential,
- A mock-up therapy session utilizing a body weight support (BWS) harness over a treadmill, with trainer assistance, to facilitate stand and step activities while monitoring blood pressure, tolerance, and range of motion.

Pre-Intervention Assessments

- Measurements of joint angles and movement using adhesive motion capture markers, and measurement of foot pressure using shoe insole pressure sensors,
- Electrophysiological tests to detect and record nerve conduction and residual motor and sensory system function, using surface-level skin electrodes (electromyography, or EMG) and, for some assessments, magnets affixed to headgear (transcranial magnetic stimulation, or TMS),
- Assessment of spinal reflexes using transcutaneous (through the skin) electrical stimulation over the lower spine,
- Assessments of your endurance, task performance, and ability to stand and step using body weight support and research staff assistance,

- A balance assessment using motion capture and EMG if you are unable to stand, or a staff-guided objective measurement scale if you are able to stand,
- Bladder function testing (also called urodynamic tests),
- Surveys measuring quality of life, spasticity, bowel and bladder function, and sexual function.

If you have recently had any of these assessments as part of your clinical care, the study team may be able to use those results instead of repeating the testing.

Implantation of Stimulator Leads (for participants assigned to epidural stimulation only)
If you are assigned to receive epidural stimulation, a routine surgical procedure to implant the stimulator electrodes will be performed by a doctor specializing in pain medicine. An incision above your spine will be made at the entry site for the leads, and the leads will be guided in with an insertion needle and fluoroscopic (x-ray) guidance. After the doctor confirms that the positioning is correct, the implantation site will be dressed, and the leads will be secured to your skin with an adhesive bandage. About 1-3 days after implantation, a trained healthcare professional will inspect the incision site. The study team will also inspect the incision site daily for any signs of infection or lead displacement.

Rehabilitation Sessions with Spinal Stimulation
Three days per week over the following four weeks, multiple rehabilitation activities which the research staff deem safe and appropriate for you will be performed with the application of electrical spinal stimulation. Your blood pressure and level of exertion will be monitored routinely by study staff.

- While lying on your back or side, with your legs supported by slings, you will train on and attempt movements of your legs.
- Utilizing parallel bars, an overhead body weight support (BWS) system, and trainer assistance, you will train on and attempt standing tasks.
- Using BWS over a treadmill, you will train on and attempt stepping activity with research trainer assistance. If appropriate for you, this may include overground movement with an assistive device such as a front-wheeled walker with a safety gait belt.
- If stimulation-enabled movement is inconsistent, an x-ray may be performed to determine if the inconsistency is due to the leads changing position.

If you have had stimulator leads implanted, a spine CT will be done during the first week of rehabilitation sessions so the team can visualize the placement of the stimulator leads, and again during the final week of rehabilitation sessions to evaluate any changes in the location of the leads.

Rehabilitation sessions will typically last 2 – 3 hours. The following tests and procedures may be repeated during the Rehabilitation phase in order to continuously improve and fine tune performance with stimulation:

- Measurements of joint angles and movement using adhesive motion capture markers, and measurement of foot pressure and seated pressure using pressure sensors,
- Electrophysiological tests to detect and record nerve conduction and residual motor and sensory system function, using surface-level skin electrodes (electromyography, or EMG) and, for some assessments, magnets affixed to headgear (transcranial magnetic stimulation, or TMS),
- Assessment of spinal reflexes using transcutaneous or epidural electrical stimulation (depending on which you were assigned to),

Lead Removal (for participants assigned to epidural stimulation only)
After completing the Rehabilitation phase, the bandage will be removed, the incision site will be opened, and the leads will be carefully withdrawn. Then the incision site will be cleaned and dressed.

Post-Intervention Assessments and Follow-Up Visits
Over the course of Week 5 of the study, the same tests and procedures performed during the Pre-Intervention Assessments will be repeated. In addition, we will do the ASIA exam again, to re-assess your neurological level of injury.

During Weeks 8 and 20, we will repeat these tests and procedures to evaluate any residual effects of the use of stimulation with training. We will not repeat the urodynamic tests at Weeks 8 and 20.

Tests done only for research purposes are not meant to provide clinical information or help care for you. The results are only important for research. Therefore, the results of tests done with your information and samples will not be provided to you. In the rare event that a finding might affect the health of you or your family, we will contact you and you can choose whether to receive or refuse the information. If you decide to follow up and further medical testing or care is needed, the costs will be billed to you or your insurance.

What are the possible risks or discomforts from being in this research study?

Risks associated with rehabilitation
Risks include skin irritation and minor bruising from pressure applied during trainer assistance and body weight support, muscle and joint soreness, fatigue, and bladder or bowel incontinence due to exertion and abdominal pressure from support harness.

There is a slight risk of fracture in the lower extremities. Lightheadedness or dizziness from a sudden drop in blood pressure is a risk associated with transitioning from sit to stand quickly.

Risks associated with weight-bearing tasks:
Risks include muscle soreness, fatigue, skin irritation, fracture, changes in blood pressure, and potential for a fall.

Risks associated with lead implantation and explantation:
Risks include pain, bleeding, and infection at the site of the implantation.

Risks associated with ES leads
- Undesirable changes in stimulation due to tissue changes around the electrodes, changes in the electrode position, loose electrical connections and/or lead failure,
- Cerebrospinal fluid (CSF) leakage,
- Fluid build-up at the incision site, and fluid drainage,
- Infection,
- Spinal cord compression, and/or paralysis,
- Discomfort due to chest wall stimulation,
- Persistent pain at the electrode site or receiver site.
- Allergic or rejection response to implant materials,
- Lead migration and/or local tissue breakdown,
- Paralysis, weakness, clumsiness, numbness, or pain below the level of implantation.

Risks associated with epidural spinal stimulation following implantation:
Risks include hardware malfunction, discomfort or abdominal tightness during stimulation, increased or decreased spasticity, bowel or bladder incontinence, shortness of breath, and muscle soreness. People with mid-thoracic or higher injuries can experience autonomic dysreflexia (AD), an event in which there is a sudden onset of excessively high blood pressure in combination with a low pulse rate; AD can be accompanied by sweating and nausea.

Risks associated with transcutaneous spinal stimulation:
Risks include skin irritation due to transcutaneous electrical delivery and skin surface electrodes, skin irritation and/or allergic reaction from alcohol used to prepare skin for electrode contact, discomfort or abdominal tightness during stimulation, increased or decreased spasticity, bowel or bladder incontinence, shortness of breath, muscle soreness, or fatigue during or after the stimulation session. Higher-current stimulation or longer stimulation may result in skin irritation or burns, so the electrode sites will be periodically checked during your sessions by the study staff, and the stimulation will be stopped if this is observed. People with mid-thoracic or higher injuries can experience autonomic dysreflexia.

Risks associated with MRI:
There is no radiation associated with MRI, but people who have metal devices like pacemakers cannot have an MRI and will not be able to participate in the study. Some people with claustrophobia may feel too closed in and may not tolerate MRI scanning. If you feel too confined in the MRI scanner you can inform the technologist and the MRI scan will be stopped. The MRI machine makes loud knocking sounds when it is scanning. Because of this you will be asked to wear earplugs while getting your MRI scan. The earplugs minimize discomfort from noise and keep the MRI noise within the safety range.

Risks associated with transcranial magnetic stimulation (TMS):
Risks include seizure, possible hearing changes, headache, and a chance of heating on the skull where the magnet is placed.

Risks associated with urodynamic studies
Urodynamic studies may carry the risk of AD, mild irritation of the urethra, and infection.

Risks associated with EMG
Risks involved with electrophysiological recordings include skin irritation and/or allergic reaction from the adhesive used to apply skin surface sensors, and skin irritation and/or allergic reaction from alcohol used to prepare skin for electrode contact.

Risks associated with CT, DEXA, x-ray, and fluoroscopy:
You will be exposed to radiation from the CTs, x-ray and fluoroscopy. The amount of radiation has a low risk of harmful effects.

Risks associated with blood draw:
The risks of drawing blood include pain, bruising, lightheadedness, and/or fainting, or rarely, infection at the site of the needle stick.

Questionnaires:
If you are uncomfortable answering any of the questions in the surveys, you may skip those you don't want to answer.

Pregnancy:
The effect of electrical spinal stimulation of the mother's spinal cord on a fetus (developing baby still in the womb), or on a breastfeeding infant, is unknown and may be harmful. Because of these risks, women cannot take part in this study if they are pregnant or breastfeeding.

If you are a female, you must have a negative pregnancy test in order to participate in this study unless you cannot become pregnant.

If you are sexually active and able to become pregnant, you must agree to use one of the birth control methods listed below:

- Hormonal methods, such as birth control pills, patches, injections, vaginal ring, or implants
- Barrier methods (such as a condom or diaphragm) used with a spermicide (a foam, cream, or gel that kills sperm)
- Intrauterine device (IUD)
- Abstinence (no sex)

Confidentiality:
As with all research, there is a chance that confidentiality could be compromised; however, we take precautions to minimize this risk.

Photographs and videos will be taken throughout this study and will be used by the study team for data analysis. Your entire body including your face will be included. The photographs and videos will be kept until the end of this study and then destroyed.

If the researchers want to use these images for publications or presentations intended to share the study's findings, you will be asked to sign a separate Mayo Clinic authorization document. Signing this separate authorization form means these images may be available in scientific publications or presentations forever, but you do not have to sign the authorization in order to continue participating in the study.

Are there reasons you might leave this research study early?

You may decide to stop at any time. You should tell the Principal Investigator if you decide to stop, and you will be advised whether any additional tests may need to be done for your safety.

In addition, the Principal Investigator or Mayo Clinic may stop you from taking part in this study at any time:

- if it is in your best interest,
- if you don't follow the study procedures,
- if the study is stopped.

If you decide to stop taking part in the study for any reason after lead implantation, we will ask you to make a final study visit. The final study visit will take less than an hour. At this visit, the bandage will be removed, the incision site will be opened, and the leads will be carefully withdrawn. Then the incision site will be cleaned and dressed.

If you leave this research study early, or are withdrawn from the study, no more information about you will be collected; however, information already collected about you in the study may continue to be used.

We will tell you about any new information that may affect your willingness to stay in the research study.

What if you are injured from your participation in this research study?

Where to get help:
If you think you have suffered a research-related injury, you should promptly notify the Principal Investigator listed in the Contact Information at the beginning of this form. Mayo Clinic will offer care for research-related injuries, including first aid, emergency treatment and follow-up care as needed.

Who will pay for the treatment of research related injuries?
Care for such research-related injuries will be billed in the ordinary manner, to you or your insurance. Treatment costs for research-related injuries not covered by your insurance will be paid by Mayo Clinic.

What are the possible benefits from being in this research study?

You won't benefit from taking part in this research study. It is for the benefit of research. However, others with SCI may benefit in the future from what we learn in this research study.

What alternative do you have if you choose not to participate in this research study?

This study is only being done to gather information. You may choose not to take part in this study.

What tests or procedures will you need to pay for if you take part in this research study?

You won't need to pay for tests and procedures which are done just for this research study. These tests and procedures are:

- Clinical and research evaluations and examinations done for the study
- Urinalysis
- Urodynamic testing
- Magnetic resonance imaging (MRI)
- Computed tomography (CT), x-ray and fluoroscopy
- Nerve conduction studies
- Neurostimulator lead implantation and explantation
- Electromyography (EMG)
- Transcranial magnetic stimulation (TMS)
- Rehabilitation training sessions
- Questionnaires
- DEXA scan
- Pregnancy test

However, you and/or your insurance will need to pay for all other tests and procedures that you would have as part of your clinical care, including co-payments and deductibles.

If you have billing or insurance questions call Patient Account Services at the telephone number provided in the Contact Information section of this form.

Will you be paid for taking part in this research study?

You won't be paid for taking part in this study; however, you will be offered parking and valet passes.

In the event of situations such as inclement weather, or a staggered scheduling timeframe for assessments or procedures over two consecutive days, the study team may offer you a complimentary stay at a local hotel.

Will your information or samples be used for future research?

Identifiable information such as your name, Mayo Clinic number, or date of birth may be removed from your information collected in this study, allowing the information to be used for future research or shared with other researchers without your additional informed consent.

How will your privacy and the confidentiality of your records be protected?

Mayo Clinic is committed to protecting the confidentiality of information obtained about you in connection with this research study. To safeguard your confidentiality, data obtained will be coded, research materials will be stored in cabinets accessible only to the study staff, and digital data will be kept on secure computer servers. If the results of the research are made public, information that identifies you will not be used, unless you authorize this use by signing a Mayo Clinic authorization document.

During this research, information about your health will be collected. Under Federal law called the Privacy Rule, health information is private. However, there are exceptions to this rule, and you should know who may be able to see, use and share your health information for research and why they may need to do so. Information about you and your health cannot be used in this research study without your written permission. If you sign this form, it will provide that permission (or "authorization") to Mayo Clinic.

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Your health information may be collected from:

- Past, present and future medical records.
- Research procedures, including research office visits, tests, interviews and questionnaires.

Your health information will be used and/or given to others to:

- Do the research.
- Report the results.
- See if the research was conducted following the approved study plan, and applicable rules and regulations.

Your health information may be used and shared with:

- Mayo Clinic research staff involved in this study.
- Other Mayo Clinic staff involved in your clinical care.
- The Mayo Clinic Institutional Review Board that oversees the research.
- Federal and State agencies (such as the Food and Drug Administration, the Department of Health and Human Services, the National Institutes of Health and other United States agencies) or government agencies in other countries that oversee or review research.

How your information may be shared with others:

While taking part in this study, you will be assigned a code that is unique to you but does not include information that directly identifies you. This code will be used if your study information is sent outside of Mayo Clinic. The groups or individuals who receive your coded information will use it only for the purposes described in this consent form.

If the results of this study are made public (for example, through scientific meetings, reports or media), information that identifies you will not be used.

In addition, individuals involved in study oversight and not employed by Mayo Clinic may be allowed to review your health information included in past, present, and future medical and/or research records. This review may be done on-site at Mayo Clinic or remotely (from an off-site location). These records contain information that directly identifies you. However, the individuals will not be allowed to record, print, or copy (using paper, digital, photographic or other methods), or remove your identifying information from Mayo Clinic.

Is your health information protected after it has been shared with others?

Mayo Clinic asks anyone who receives your health information from us to protect your privacy; however, once your information is shared outside Mayo Clinic, we cannot promise that it will remain private, and it may no longer be protected by the Privacy Rule.

Your Rights and Permissions

Participation in this study is completely voluntary. You have the right not to participate at all. Even if you decide to be part of the study now, you may change your mind and stop at any time. You do not have to sign this form, but if you do not, you cannot take part in this research study.

Deciding not to participate or choosing to leave the study will not result in any penalty. Saying 'no' will not harm your relationship with your own doctors or with Mayo Clinic.

If you cancel your permission for Mayo Clinic to use or share your health information, your participation in this study will end and no more information about you will be collected; however, information already collected about you in the study may continue to be used.

You can cancel your permission for Mayo Clinic to use or share your health information at any time by sending a letter to the address below:

Mayo Clinic
Office for Human Research Protection
ATTN: Notice of Revocation of Authorization
201 Building 4-60
200 1st Street SW
Rochester, MN 55905

Alternatively, you may cancel your permission by emailing the Mayo Clinic Research Participant Advocate at: ResearchParticipantAdvocate@mayo.edu.

Please be sure to include in your letter or email:

- The name of the Principal Investigator,
- The study IRB number and /or study name, and
- Your contact information.

Your permission for Mayo Clinic to use and share your health information lasts until the end of this study, unless you cancel it. The study does not end until all data has been collected, checked (or audited), analyzed, and reported. Because research is an ongoing process, we cannot give you an exact date when the study will end. Sometimes this can be years after your study visits and/or activities have ended.

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Enrollment and Permission Signatures

Your signature documents your permission to take part in this research.

	/ /	: AM/PM
Printed Name	Date	Time

Signature

Person Obtaining Consent

- I have explained the research study to the participant.
- I have answered all questions about this research study to the best of my ability.

	/ /	: AM/PM
Printed Name	Date	Time

Signature

Signature of a witness to the consent conversation:
I observed the entire consent conversation and confirm that the participant appears to understand the information and was given the opportunity to ask questions.

Witness (Print Name)

		AM/PM
Signature of Witness	Date	Time