Version Date: October 24, 2023	**Page: 1 of 12**
Subject Name:	**Informed Consent Date:**
Principal Investigators: Dr. Jill Wecht, EdD	**VAMC: James J Peters**

Protocol #: 1727500

Title of Study: Autonomic Effects of Transcutaneous Spinal Cord Stimulation in Veterans with SCI (Study 2)

INTRODUCTION

You are being asked to participate in a research study that is being performed at JJPVAMC. Before you decide to take part, it is important for you to know why the research is being done and what it will involve. This includes any potential risks to you, as well as any potential benefits you might receive.

Please read the information below closely, and discuss it with your family and friends.. You can also ask one of the study staff members to explain anything that is not clear to you in more details. Please take your time to decide. If you do decide to take part in this study, your signature on this consent form will show that you received all of the information, and that you were able to discuss any questions and concerns you had with a member of the study team.

1. Purpose of study and how long it will last:

You are being asked to participate in the study because you have a spinal cord injury and you are at least 18 years old. Persons with spinal cord injury usually have difficulty maintaining a steady body temperature (98.6° F) and feeling warm and comfortable when in a cool environment.

The purpose of this research study is to compare the effects of electricity being delivered through surface electrodes (sticky pads on your skin), called active transcutaneous spinal cord stimulation (TSCS), compared to sham TSCS (sticky pads with electricity initially turned on but then turned off) on your ability to 1) keep your body temperature stable and 2) feel comfortable, while in a cool environment (cool room at 64° F) for 90 minutes. We will assess your thermal sensation by asking you if overall you feel cold, cool, neutral, warm, or hot and your comfort level by asking you to grade your thermal comfort (how comfortable or how uncomfortable you feel) when you are seated in a thermoneutral room (80° F) and again in the cool room with active TSCS compared to the cool room with sham TSCS. The results will help guide experimental studies aimed at improving health and longevity in the population with SCI. If you choose to participate in this study, there will be 2 study visits that last about 3-4 hours each. A copy of this form will be given to you and a copy will be kept by the JJPVAMC research team. This study is sponsored and funded by the VA Rehabilitation Research and Development Service. You will be one of about 20 participants in the study at JJPVAMC.

Inclusion criteria:

- You are above the age of 18 years old
- You have a SCI between C3-T6
- You have been injured longer than 1 year
- You have an American Spinal Injury Association injury classification scale (AIS) A, B, C

- Your prescription medications have not changed for at least 30 days

Exclusions: You cannot participate in this research if any of the following statements apply to you. You need not tell the research staff which statements apply to you. If you choose to tell the investigator which of the statements apply to you, the information will be kept strictly confidential. Please inform the researcher if any of the following statements apply to you.

- You have a history or seizures
- You have an acute illness or infection
- You have diabetes
- You have untreated thyroid disease
- You have a neurological condition other than SCI (Alzheimer's disease, dementia, stroke, multiple sclerosis, Parkinson's disease, etc.)
- You have history of heart or vascular disease (coronary artery disease, congestive heart failure, peripheral artery disease,)
- You have a history of moderate or severe head trauma (TBI) or diagnosed with cognitive impairment
- You have a present or history of a psychological disorder
- You have contraindications to electricity over your spine
- You are dependent on a ventilator to breathe or have an open tracheostomy site
- You have a recent history of substance abuse (within the past 3 months)
- You have open wounds over the spine at the level targeted for stimulation
- You are pregnant

2. Description of the Study Including Procedures to be Used:

If you consent to participate in this research study, you will visit the research center in Suite 7A-13 of the JJPVAMC main hospital building located in the Bronx, NY. During the day of testing, you will report to the thermal laboratory located in the SCI Research Department. For each visit you will be asked to empty your bladder before your arrival and again upon arrival, if needed. You will be asked to avoid caffeinated and alcoholic beverages and heavy exertion for 24 hours before testing. When you are ready to start, you will be set up with the instruments necessary to measure your body temperatures and skin blood flow. During the study, you will be asked to wear only shorts and a T-shirt.

Baseline Instrumentation:

Body temperature will be measured by a disposable sensor taped to your forehead (Bair Hugger thermometer) and an earplug thermometer (StarBoard disposable ear thermistor). Skin temperature will be measured by temperature sensors (Isothermex thermocouples) taped to your skin at different places on the front and back of your trunk (chest and stomach) and on each hand and foot (total of 14 skin temperature sensors). A laser sensor will be used to measure blood flow in the skin of your hand and foot. A blood pressure cuff will be placed above one elbow to measure your blood pressure (BP) and heart rate (HR). A perfusion index sensor will be placed on another finger to measure blood flow changes in your finger.

Baseline Collection (15 Minutes): After resting in the seated position in your wheelchair for 30 minutes (acclimation period) in the set-up room at a neutral room temperature (80° F), we will start collecting baseline data for 15 minutes. Your core body temperature (internal body temperature, e.g., ~98.6° F) will be measured with a forehead sensor (Bair Hugger system) and an ear thermistor (ear plug with temperature measuring wire) every minute.. Your skin temperature at 15 different areas on your body will be measured with skin sensors every minute as well. Skin blood flow will be measured for a 5-minute period every 10 minutes. Your inner ear temperature (handheld tympanic thermometer), blood pressure (BP), blood oxygen saturation, and heart rate (HR) will be measured every 5 minutes. BP will be measured before and after each laser doppler skin blood flow measurement. You will be asked about your general sensation of temperature on a 9-point scale (feeling very cold, cold, cool, slightly cool, neutral, slightly warm, warm, hot or very hot) and how comfortable you feel with the temperature (thermal comfort) on a 6-point scale (very comfortable, comfortable, just comfortable, just uncomfortable, uncomfortable, very uncomfortable), every 10 minutes. At the end of the 15-minute baseline period, you will be given a memory test (delayed recall task). For this test, you will be given five simple words to remember and asked to repeat them immediately and again after a 5-minute period.

Thermal Challenge (90 minutes): When you complete the 15-minute Baseline, you will be wheeled into a cool (64°F) thermal room (thermal challenge), where you will remain seated throughout the 90-minute session. TSCS surface electrodes will be placed at the location on the spine that was found to be best for normalizing your BP in Study 1 (*Targeted Transcutaneous Spinal Cord Stimulation to Restore Autonomic Cardiovascular Health in Individuals with Spinal Cord Injury)*. Stimulation will be turned on for active TSCS, using the best electrical settings identified for you in Study 1, for 90 minutes. Core body temperature (forehead sensor and earplug thermistor) and skin temperature (skin sensors) will be collected continuously, skin blood flow will be measured for a 5-minute period at 15-minute intervals (6 times total), and inner ear temperature, BP, blood oxygen saturation, and HR will be measured every 10 minutes. BP will be measured right before and after laser skin blood flow measurements. You will be asked about the general sensation of temperature that you feel (Thermal sensation) on a 9-point scale and

general feeling of comfort related to your sensation of temperature (Thermal comfort) on a 6-point scale, every 10 minutes. At the end of the thermal challenge, you will be given the delayed recall task in the same way as before, but with 5 different simple words.

Once you complete the cool thermal challenge, you will be transferred to a room at a neutral temperature (80° F) and provided with warm fluids. You will be monitored for a minimum of 30 minutes during the recovery period to ensure your core body temperature returns to within 1% of what it was during baseline.

If at any time your core body temperature measured by the Bair Hugger or earplug thermistor sensor decreases to 95° F or if you feel discomfort, the protocol will be terminated for that day. You will be transferred to the thermoneutral room (80° F), covered with warm blankets, and provided with warm fluids. If symptoms persist Dr. Noam Harel will assess you and provide the appropriate care.

During Visit 2, you will do the exact same thermal challenge with either active TSCS (electricity on) or sham TSCS (electricity initially on but then turned off), whichever condition you have not done yet.

Procedure Details:

Active Transcutaneous Spinal Cord Stimulation: electrodes that stick to your skin (surface electrodes) will be placed on the location on the spine that produced the most normal seated systolic BP (the top number of a 120/80 mmHg BP reading) in the prior study, *Targeted Transcutaneous Spinal Cord Stimulation to Restore Autonomic Cardiovascular Health in Individuals with Spinal Cord Injury*. For the active TSCS session the electricity will then be turned on using the settings that produced the most normal seated systolic BP in the prior study. The electrical stimulation will remain on for up to 90 minutes.

Sham TSCS session: during the sham TSCS session (control session), the electrodes will also be placed at the same site and the electrical stimulation will be briefly ramped up over 30 seconds to the same level as the active stimulation, but then ramped down and turned off for the 10-minute seated recording. The stimulator and electrodes will remain attached to you during the study visit, just like the active TSCS session.

Skin Temperature: Skin temperature will be measured by sensors taped to your skin at 15 areas (index finger, hand, upper arm, big toe, foot, thigh, chest, abdomen, underarm). Skin temperatures will be measured continuously for 10 minutes during Baseline and continuously throughout the cool thermal challenge session (90 minutes).

Inner Ear Temperature: Inner ear temperature (tympanic temperature) will be measured using an infrared heat-sensing thermometer. It will be measured every 5 minutes during Baseline and every 10 minutes during the thermal challenge for every visit.

Blood Pressure (BP), Blood Oxygen Saturation and Heart Rate (HR): Blood Pressure will be measured at your upper arm (brachial BP). Baseline BP will be measured every 5 minutes during baseline and every 10 minutes during the thermal challenge for every visit. BP will be measured immediately before and after measurement of skin blood flow (laser doppler). The amount of oxygen your blood is carrying (blood oxygen saturation) will be measured at the tip of your index finger every 10 minutes during baseline and the thermal challenge.

Thermal Sensation: You will be asked to rate how warm or cool your body feels on a 9-point scale: +4 (very hot), +3 (hot), +2 (warm), +1 (slightly warm), 0 (neutral), -1 (slightly cool), -2 (cool), -3 (cold), -4 (very cold) every 10 minutes during baseline and every 10 minutes during the thermal challenge for each visit.

Thermal Comfort: You will be asked to rate how comfortable your body temperature feels on a 6-point scale: +3 (very comfortable), +2 (comfortable), +1 (just comfortable), -1 (just uncomfortable), -2 (uncomfortable), -3 (very uncomfortable) every 10 minutes during baseline and every 10 minutes during the thermal challenge for each visit.

Skin Blood Flow: The blood flow to your skin will be measured by a laser light-emitting diode taped to the skin on the back of your hands and feet. Skin blood flow will be recorded for 5 minutes at 5-minute intervals during baseline and for 5 minutes at 15-minute intervals during the thermal challenge for each visit.

Core Body Temperature: Core temperature will be measured using 2 methods, 1) a disposable sensor taped to your forehead (Bair Hugger thermometer) and 2) an disposable earplug thermometer (StarBoard disposable ear thermistor). Your body's core temperature will be measured every minute throughout baseline and the thermal challenge.

Pain Likert Scale: Questions will be asked every 5-minutes during the thermal challenge test both with active and sham stimulation to report if you are experiencing any pain. The 11-point rating scale is 0 = no pain to 10 = sever pain.

While you are being tested in this study, investigators may identify test results that they believe should be reviewed by your primary care doctor. If that happens, they will call you within a week of the test to let you know. If you agree, the research team will send the test results to your primary care doctor. You acknowledge that the researchers are not specifically looking for any medical problems, so it is unlikely that they will find any underlying issues. You understand that the tests for this study are not the same tests done as part of regular medical care.

3. Description of any Procedures that may Result in Discomfort or Inconvenience:

You have been told that the study described above may involve the following risks and/or discomforts:

Inner Ear Temperature: Inner ear temperature measurement is non-invasive and should not cause any discomfort. You may feel some pressure of the thermometer in your ear canal.

Skin Temperature: Skin temperature measurement is non-invasive and should not cause any discomfort. Removing the tape for the sensor may be uncomfortable at the end of each visit.

Blood Pressure (BP) and Heart Rate (HR): BP and HR measurements are non-invasive and should not cause any discomfort. You may find the pressure of the cuff around your upper arm uncomfortable.

Thermal Sensation: Measurement of how warm/cool you feel is non-invasive and should not cause any discomfort.

Thermal Comfort: Measurement of how comfortable you feel is non-invasive and should not cause any discomfort.

Skin Blood Flow: Measurement of blood flow in your skin is non-invasive and should not cause any discomfort.

Core Body Temperature: The core body temperature sensors are 1) a disposable sensor taped to your forehead (Bair Hugger thermometer) and 2) an earplug thermistor (StarBoard disposable ear thermometer). The forehead sensor should not cause any discomfort. You may feel some pressure in your ear from the earplug thermistor.

Transcutaneous spinal cord stimulation: You may get some skin breakdown, skin irritation and burns at the electrode placement site, or experience severe pain from the transcutaneous stimulation. If any of these potential risks occur, the stimulation will stop immediately and the investigators will monitor the situation. We are using protective electrodes to minimize the risk of skin irritation and burns.

Autonomic Dysreflexia: There is a small chance that you could have an episode of autonomic dysreflexia (uncontrolled rise in BP) while participating in this study. These episodes usually include headache, goose bumps, flushing (red face), and a potentially dangerous increase in blood pressure. The investigators will be monitoring your blood pressure and other vital signs the entire time, and if there are significant symptoms or changes in your vital signs, they will stop the procedure immediately and provide appropriate medical care. The investigators are very experienced in treating episodes of autonomic dysreflexia in persons with SCI.

4. Expected Risks of Study:

Inner Ear Temperature: Inner ear temperature measurement is non-invasive and is not associated with risks.
Skin Temperature: Skin temperature measurement is non-invasive and is not associated with risks.
Blood Pressure (BP), Blood Oxygen Saturation, and Heart Rate (HR): BP, oxygen saturation, and HR measurements are non-invasive and not associated with risks.
Thermal Sensation: Measurement of how warm/cool you feel is non-invasive and not associated with risks.
Thermal Comfort: Measurement of how comfortable you feel is non-invasive and not associated with risks.
Skin Blood Flow: Skin blood flow measurement is non-invasive and not associated with risks.
Core Body Temperature: The disposable sensor taped to your forehead (Bair Hugger thermometer) and the earplug thermistor (StarBoard disposable ear thermometer) are not associated with any risks. The earplug that is attached to the thermistor is a soft foam plug to protect the wire (thermistor) from touching your eardrum.
Thermal Challenge: There is a risk of hypothermia (low body temperature: $\leq 95°$ F) from being in a cool room (64°F) for 90 minutes. To decrease this risk, we will check core body temperature continuously for your safety. We will also check BP, HR, and thermal sensation and comfort every 10 minutes. If your core body temperature goes down to 95°F or if you feel uncomfortable, we will stop the study and bring you to a warm room (80° F). We will cover you with blankets and give you warm fluids to drink. If you are still cold, the study physician will assess the situation and provide the appropriate care. If you finish the thermal challenge, we will bring you to a warm room (80° F) and cover you with blankets and give you warm fluids to drink.
Transcutaneous spinal cord stimulation: You may get skin breakdown, skin irritation and burns at the electrode placement site or severe pain. If any of these potential risks occur, we will stop the stimulation immediately and the investigators will monitor the situation. We are using protective electrodes to minimize the risk of skin irritation and burns.
Autonomic Dysreflexia: There is a small chance that you could have an episode of autonomic dysreflexia while participating in this study. These episodes usually include headache, goose bumps, flushing (red face), and a potentially dangerous increase in blood pressure. The investigators will be monitoring your blood pressure and other vital signs the entire time, and if there are significant symptoms or changes in your vital signs, they will stop the procedure immediately and provide appropriate medical care. The investigators are very experienced in treating episodes of autonomic dysreflexia in persons with SCI.

Subject modesty: You will wear a standard T-shirt and pair of shorts during the study. This may cause potential embarrassment, but we limit your exposure to the area of the study and only to the few research team members.

As with any research, there may be unforeseen risks and discomforts. The study physician associated with the study, will be available during testing for clinical intervention if necessary or to treat any medical emergency.

5. Expected Benefits of the Study

There may be no direct benefit to you from this study, but any information that the researchers get from this study may help others.

6. Other Treatments Available:

Participation in the study is voluntary and the alternative to this study is to not participate and seek clinical advice from your doctor.

7. Use of Research Results:

The researchers will let you and your physician know of any significant new findings made during this study which may affect your willingness to participate in this study. All research material generated from the study will remain in the possession of Dr. Jill Wecht and her study team at the JJP VAMC. Your medical records will be maintained according to this medical center's requirements and all electronic and hardcopy. All electronic and hardcopy Records will be retained according to National Archives and Records Administration, Records Schedule RCS-10-1.

Access to the research materials generated from the study will be restricted to Dr. Jill Wecht and her study team. If results of this study are reported in medical journals or at meetings, you will not be identified by name, by recognizable photograph, or by any other means without your specific consent. No information by which you can be identified will be released or published unless required by law. In order to comply with federal regulations, research records identifying you may be reviewed by the following:

□_____ By checking this box and initialing, you agree to be contacted by the Principal Investigator or her investigative team at a future date for additional studies being conducted in the Spinal Cord Damage Research Center.

Authorized representatives of the JJPVAMC (e.g., Institutional Review Board, Research Compliance Officer) and VA, including the Office of Research Oversight (ORO), Federal Agencies such as the Government Accounting Office (GAO), VA Office of Inspector General (OIG), and Office for Human Research Protections (OHRP) may have access to your research records. If this research involves articles regulated by the FDA, the FDA may choose to inspect and copy research records that identify individual research subjects.

Clinical Trials:

A description of this clinical trial will be available on http://www.ClinicalTrials.gov. This website will not include any information that can identify you. At most, the website will include a summary of the results. You can search this website at any time using the NCT# (NCT05664646) to locate this study.

8. Special Circumstances:

Your participation in this study will be included in the VHA health record. A copy of the signed informed consent form and signed HIPAA authorization for participation in the study will be in your health record. The study staff has no real or apparent conflicts of interest involving this study

9. Compensation and/or Treatment in the Event of Injury:

The VA must provide necessary medical treatment to a research subject injured by participation in a research project approved by a VA R&D Committee and conducted under the supervision of one or more VA employees. Further information about compensation and medical treatment may be obtained from the medical administration service at this VA medical center.

10. Voluntary Participation:

You are not required to take part in this study; your participation is entirely voluntary. You can refuse to participate in this study or withdraw your participation in this study after you consent without penalty or loss of VA or other benefits to which you are entitled.

11. Termination of Participation:

You can refuse to participate now or you can withdraw from the study at any time after giving your consent. This will not interfere with your regular medical treatment, if you are a patient. The investigator also has the right to withdraw you from the study at any time for reasons including, but not limited to, medical concerns (your health and safety are in jeopardy with continued participation in the

study), non-compliance (you miss several scheduled appointments without notification) and protocol deviations (exclusion/inclusion criteria change and you are no longer eligible to participate).

12. Costs and Reimbursements:

As a veteran or non-veteran, you will not be charged for any treatments or procedures that are part of this study. For veterans who are required to pay co-payments for medical care and services provided by VA, these co-payments will continue to apply for medical care and services provided by VA that are not part of this study.

You will receive up to $400 compensation for participation in this research study according to the following schedule:

Visit 1: $200 Visit 2: $200

You will also receive up to $75/per visit compensation for travel if necessary, or a total of $150

13. Contact Person(s):

To obtain answers to questions about the research, report or seek treatment for a research-related injury, or to voice concerns or complaints about the research contact the following:

- **During the Day: Jill Wecht, EdD (718) 584-9000 x3122**
- **After Hours: Matthew Maher, MS (201) 566-0291**

I understand that should I wish to discuss my participation in this study with any other doctor or layperson, I can contact Mary Sano, Ph.D., Associate Chief of Staff (ACOS) R&D Program at the JJP VAMC by requesting an appointment at (718)741-4228 hospital extension 4228, first floor in the research building, Room 1F-01 If I have questions, concerns, and/or complaints or to offer input.

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Subject Name:	**Informed Consent Date:**
Principal Investigators: Dr. Jill Wecht, EdD	**VAMC: James J Peters**

Protocol #: 1727500

Title of Study: Autonomic Effects of Transcutaneous Spinal Cord Stimulation in Veterans with SCI (Study 2)

RESEARCH SUBJECTS' RIGHTS: I have read or have had read to me all of the above. Dr. Jill Wecht or her delegate has explained the study to me and answered all of my questions. I have been told of the risks or discomforts and possible benefits of the study. I have been told of other choices of treatment available to me.

I understand that I do not have to take part in this study, and my refusal to participate will involve no penalty or loss of rights to which I am entitled. I may withdraw from this study at any time without penalty or loss of VA or other benefits to which I am entitled.

The results of this study may be published, but my records will not be revealed unless required by law. This study has been explained to me. I have had a chance to ask questions. I voluntarily consent to participate in this study. I will receive a signed copy of this consent form.

_____	_____	_____
Subject Signature	Date	Time

_____	_____	_____
Person Obtaining Informed Consent (Print Name) (Investigator or Delegate as indicated on Assurance Page)	Signature of Person Obtaining Informed Consent	Date

JJPVAMC IRB
Effective Date: December 7, 2023

VERBAL CONSENT IF THE PARTICIPANT LACKS UPPER LIMB FUNCTIONS TO COMFORTABLY WRITE

_____ is unable to sign the consent form due to impaired arm function. I certify that I have carefully explained the purpose and nature of this research to him/her in appropriate language and he/she has had an opportunity to discuss it with me in detail. I have answered all of his/her questions and he/she has consented to participate in this research. I, therefore, am signing the consent form to document that he/she has given his/her consent to participate in this research study.

Person Obtaining Consent:

Name: _____

Signature: _____

Date: _____

Witness Name: _____

Signature: _____

Date: _____