Evaluation of Pulsed Radiofrequency Ablation of the Superior Hypogastric Plexus for Treatment of Bladder Pain Syndrome: A Randomized, Placebo-Controlled Pilot Study

Principal Investigator: Eli Medvescek, MD

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Walter Reed National Military Medical Center, Bethesda, MD

CONSENT TO PARTICIPATE IN RESEARCH

Title: *Evaluation of Pulsed Radiofrequency Ablation of the Superior Hypogastric Plexus for Treatment of Bladder Pain Syndrome: A Randomized, Placebo-Controlled Pilot Study*

Principal investigator: LT Eli Medvescek, MD

You may be eligible to take part in this research study. This form gives you important information about the study.

Please take time to carefully review this information. You should talk to the researchers about the research study and ask them any questions you have. You may also wish to talk to others (for example, your friends, family, or your personal physician) about your potential participation in this research study. You do not have to take part in this study. Participation is voluntary. You may also leave the research study at any time without penalization.

1. KEY INFORMATION

Many women suffer from bladder pain syndrome (BPS). There are a variety of treatments, but there is no one universally effective option. The purpose of this study is to explore the use of electrical energy directed towards a group of nerves, called the superior hypogastric plexus, for treatment of BPS. There is data from many different studies that suggest that this kind of therapy might provide relief of BPS symptoms.

Participants will be asked to participate for a total of six months from the date of their first nerve treatment. At the first appointment, they will be evaluated in the Walter Reed Chronic Pain clinic and asked several questions about the severity and personal management of their symptoms. The procedure will then be performed by inserting two needles into the back (one on either side of the spine) and directing extremely short bursts of electrical microcurrent towards the target nerve. Some participants will receive treatment, whereas others will receive sham (placebo). Participants will not be informed of their treatment group until the conclusion of the study.

Following this initial appointment, participants will be asked about their symptoms at 1-, 3-, and 6-month follow-up appointments. Participants will be asked about pain, mood

symptoms, sexual function, and measures of bladder irritation. The procedure will only be performed once.

The main requirements of study participants include timely scheduling and attendance of follow-up appointments and participation during these appointments in filling out questionnaires about the symptoms listed above.

Benefits of this study may include possible relief of BPS symptoms. This may help to advance research about treatments for BPS. This is a novel approach to the treatment of BPS and as such may provide benefits greater than those found in treatment outside of the study. However, conventional treatment strategies for BPS – such as lifestyle and dietary modifications, medications, and surgery – are also available modalities which may provide relief of symptoms.

Risks of participation include possible damage to structures inside the abdomen while performing the procedure. This is a very rare complication. Other risks include possible loss of personal information that is given to investigators; however, several safeguards will be established to minimize the risk of information loss.

Consent for this study is being sought for research purposes only; participation is voluntary and alternative treatments are available.

Your decision will not affect your future care at Walter Reed National Military Medical Center. If you decide to take part in this research study, you will be asked to sign this document. Before you sign this document, be sure you understand what the research study is about in all sections of the consent form, including the risks and possible benefits to you.

Please tell the researchers if you are taking part in another research study.

2. WHAT IS THE PURPOSE AND DURATION OF THIS RESEARCH AND WHO WILL TAKE PART?

You are being asked to take part in this research study because you have been diagnosed with bladder pain syndrome. The purpose of this research study is to learn about the role of the superior hypogastric plexus, a nerve bundle that provides pain sensations to the bladder and nearby structures, and its relationship to the pain and urinary symptoms experienced in bladder pain syndrome. The duration of participation per visit is about 1-1.5 hours for the initial intake session, and about thirty minutes at three follow-up sessions.

There will be 38 people taking part in the study at Walter Reed, over a period of two years.

During the study, you will have four visits with researchers in the Chronic Pain clinic. You may need to return to Walter Reed at 1-, 3-, and 6-month intervals following your initial appointment. Follow-up appointments may also be available via telehealth encounters.

This study is looking at using extremely short bursts of electrical microcurrent, directed at the superior hypogastric plexus through a small needle. This procedure has not been well-studied for treatment of bladder pain syndrome. However, many studies exist evaluating this procedure for other types of chronic pain. This means that the procedure is considered experimental for bladder pain syndrome.

At the end of this research study the clinical results, including research results about you, *will be* shared with you. Results shared will include your treatment group (placebo or intervention). After analysis of the data, if researchers find that the intervention was effective, you will be notified and offered the treatment if you were originally in the placebo group. You have no obligation to take this offer.

3. SCREENING PROCESS TO QUALIFY FOR PARTICIPATION IN THIS STUDY

In order to participate in this study, you must be a DEERS-eligible adult biological female with a diagnosis of BPS. Exclusion criteria include current enabled implantable neurostimulator device (such as TENS or Interstim), bladder Botox therapy within the last 3 months, current pregnancy, current active pelvic or gynecologic cancer, bleeding disorder, local or systemic infection, severe cardiac disorders, bladder dysfunction due to spinal cord injury, or other abnormalities of the spinal cord that prevent the procedure from being performed. No tests or other laboratory data are necessary prior to participation.

4. WHAT WILL HAPPEN IF YOU DECIDE TO BE IN THIS RESEARCH?

You will first be seen in Walter Reed Chronic Pain clinic for an intake appointment. The first part of this intake appointment will be used to get to know you. Researchers will administer questionnaires and ask questions about your BPS, including questions about your pain, urinary symptoms, mood symptoms, current modalities used to treat your condition, and overall satisfaction with your care. The second part of the intake appointment will be used to perform the procedure. During this procedure, you will be attached to medical monitors and lie on your stomach while researchers insert two needles in your back, one on either side of your spine. Local numbing solution will be used to minimize discomfort. These needles will be inserted into a space just in front of your spine using advanced x-ray guidance. At this point, electrical microcurrent or sham (placebo) will be performed, and the needles will be withdrawn. You will stay in the Chronic Pain clinic for 30 minutes after the procedure to ensure that you feel well

afterwards. This first appointment should take about 1-1.5 hours. Before departing the clinic, you will be asked to schedule a 1-month follow-up.

At your 1-, 3-, and 6-month follow-up appointments, you will be asked questions about your symptoms. Many of these questions will be identical to those asked at your intake. No additional nerve blocks are necessary at these follow-up appointments, and they may be done virtually at your discretion. These follow-up appointments should take 30 minutes or less.

You will be randomly assigned to one of two groups. Randomization is a process like flipping a coin and means you will have a chance of being assigned to either of the groups. You will be randomized into a treatment or placebo group prior to your first appointment.

You will have a one in two chance of being in the treatment group. The treatment is electrical microcurrent directed through a needle tip. The medical term for this is “pulsed radiofrequency ablation.” This procedure causes disruption on a microscopic level of nerve fibers that send pain sensations to the bladder and other organs in the pelvis.

You will have a one in two chance of being in the sham group. A sham is a placebo – this intervention looks like the research study intervention described above, but contains no electrical microcurrent.

This research study is a single blind study, which means that you will not know whether you are receiving the research study medication or a placebo.

5. WHAT ARE THE RISKS OR DISCOMFORTS FROM BEING IN THIS RESEARCH?

If you choose to take part in this study, risks include bleeding, or accidental injury to blood vessels or organs when inserting the needle. There is also a slight possibility of infection at the site where the blood is drawn. The rate of these risks is not known, however, in many previous studies performing the same procedure, no major complications occurred. Guidance with sophisticated imaging tools and sterile techniques are used to decrease the risk of accidental injury, bleeding, and infection.

Although very rare, participants may experience a brief period of low blood pressure during the procedure which can be managed rapidly by an experienced physician at the bedside if necessary.

During your participation in this research study, you will be exposed to radiation from scheduled x-rays and/or imaging scans. The total exposure resulting from these imaging studies is calculated to be (approximately 3.5 mSv). This amount is less than

you would receive from one year of natural background exposure within the United States, which is approximately 6.2 mSv.

The principal investigator for this research study has determined and verified that all/most/some of the x-rays and/or imaging scans prescribed for this study would typically be performed as part of the standard medical care required to adequately monitor your current illness. If you are especially concerned with radiation exposure, or you have had a lot of x-rays or imaging scans already, you should discuss this with the principal investigator for this study, Dr. Eli Medvescek.

There may be some discomfort associated with needle insertion during the procedure. This may include physical or psychological discomfort, since many people do not like needles. Investigators will use a local numbing solution prior to the procedure to decrease your level of physical discomfort. You may have a bruise or be sore at the site where the needle is inserted. There may also be non-specific discomforts after the procedure, such backache, nausea, or temporary numbness/tingling of the legs, which may be treated supportively as needed.

There is a risk that the nerve procedure does not lead to resolution of symptoms associated with BPS.

There is also a risk of loss of confidential information. Investigators have several safeguards in place to minimize the risk of confidential information. Although efforts are made to protect your research study records, there is always a risk that someone could get access to the personal information in your medical records or other information researchers have stored about you.

You may not receive the nerve therapy if you are currently pregnant. However, if you become pregnant during the study after the nerve therapy, you will still be able to participate. **If you suspect that you may be pregnant, please notify the research team before signing this consent form.** There are no anticipated future risks to pregnancy as a result of receiving the electrical microcurrent therapy. The numbing medications used in the study have not been shown to cause birth defects in humans.

There may also be other risks of taking part in this study that we do not yet know about. **If your bladder pain returns or worsens after receiving the procedure, or you experience any other adverse or severe symptoms, please contact the study Principal Investigator, Dr. Eli Medvescek, at 520-780-6888 or eli.d.medvescek.mil@health.mil.**

6. WHAT ARE THE POSSIBLE BENEFITS FROM THIS RESEARCH?:

The possible benefits to you as a research participant in this research study are relief from bladder pain symptoms. However, there is no guarantee that you will benefit from being in this research. Furthermore, others may benefit in the future from the information learned during this study. The possible benefit to others is using this nerve therapy for future treatment of bladder pain syndrome, if it is found to be effective.

7. WHAT ARE THE ALTERNATIVES TO TAKING PART IN THIS RESEARCH?

There may be other options for treating your condition. Alternative treatments that may be available to you include: dietary modification, stress management, physical therapy, oral medications, bladder instillations (medicine instilled directly into the bladder), hydrodistension (stretching the bladder with fluid while you are sedated), implanted electrical stimulation device, or onabotulinumA toxin injections. Your urogynecologist will describe these and other alternative treatment options to you in alignment with the recommendations of the American Urogynecologic Society. Taking part in this study may not preclude you from using one or many of these other options.

Choosing not to take part in this research study is also an option.

There may be other research studies involving experimental treatments that could be helpful to your condition.

8. IS THERE COMPENSATION FOR YOUR PARTICIPATION IN THIS RESEARCH?

No, you will not receive any compensation for participating in this study.

9. ARE THERE COSTS FOR PARTICIPATING IN THIS RESEARCH?

No, there are no costs to you for taking part in this research study other than getting yourself to the clinic or hospital for scheduled in-person visits. The Walter Reed Chronic Pain clinic will provide the therapy at no cost to you during this study.

10. PRINCIPAL INVESTIGATOR (the person(s) responsible for the scientific and technical direction of the study):

LT Eli Medvescek, MD, Department of Anesthesiology, WRNMMC

Cell: 520-780-6888. Email: eli.d.medvescek.mil@health.mil

11. STUDY SPONSOR (the organizations or persons who oversee the study and are responsible for analyzing the study data):

Department of Defense - Walter Reed National Military Medical Center

As the sponsor of this research, the Department of Defense may have access to your research data in accordance with DoDI 3216.02.

12. SOURCE OF FUNDING: None.

13. LOCATION OF THE RESEARCH:

Walter Reed National Military Medical Center (WRNMMC) Urogynecology and Chronic Pain Clinics.

14. DISCLOSURE OF FINANCIAL INTERESTS AND OTHER PERSONAL ARRANGEMENTS: None.

15. WHO WILL SEE MY INFORMATION (PRIVACY) AND HOW WILL IT BE PROTECTED (CONFIDENTIALITY)?

Records of your participation in this research study may only be disclosed in accordance with state and federal law, including the Federal Privacy Act, 5 U.S.C.552a, and its implementing regulations. DD Form 2005, Privacy Act Statement - Military Health Records, contains the Privacy Act Statement for the records. A copy of DD Form 2005 can be given to you upon request, or you can read on-line at: https://www.esd.whs.mil/Portals/54/Documents/DD/forms/dd/dd2005.pdf

The research team will keep your research records. These records may be looked at by research team members from the Department of Anesthesia and Urogynecology Division in the Department of Gynecologic Surgery and Obstetrics, the Institutional Review Board (IRB), and the DoD Higher Level Review as part of their duties. These duties include making sure that the research participants are protected. Confidentiality of your records will be protected to the extent possible under existing regulations and laws but cannot be guaranteed.

Procedures to protect the confidentiality of the data in this study include but are not limited to: storage of physical data in a single secure locked drawer in the office of a research team member, removal of personal information when storing data on electronic resources, password protection of computers, shredding physical data at the conclusion of the study period, and creation of barriers within the computer to protect information from being viewed by unauthorized people (firewalls).

All paper research records will be stored in a locked cabinet inside of a locked room accessible only by authorized staff. Your coded study data will be entered into a spreadsheet housed on the Walter Reed National Military Medical Center servers that is

secure, access-controlled, and accessible only by authorized staff. At the conclusion of the study, the master list associating your data with your identity will be destroyed, and your data will become de-identified.

Researchers will make every effort to protect your privacy and confidentiality; however, there are risks of breach of information security and information loss.

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 results. You can search this Web site at any time.

Complete confidentiality cannot be promised for military personnel, because information regarding your health may be required to be reported to appropriate medical or command authorities to ensure the proper execution of the military mission, including evaluation of fitness for duty.

Study Principal Investigator and research team members in the Department of Anesthesia and Department of Gynecologic Surgery and Obstetrics – Urogynecology Division.

Those listed above will have access to your records and agree to safeguard your protected health information by using and disclosing it only as permitted by you in this consent or as directed by state and federal law.

Information gained from your participation in this research study may be published in literature, discussed for educational purposes, and used generally to further science. You will not be personally identified when your information is shared in these ways; all information will de-identified.

16. LONG TERM USE OF DATA

The investigator has requested to save selected data collected from your participation in this research study for possible use in future research. This data will be de-identified, meaning it cannot be linked back to you. This future research may be in the same area as the original study, or it may be for a different kind of study. You will be provided an option at the end of this consent form to approve or deny use of your de-identified data in future research studies. If you decline the future use of your de-identified data, it will be destroyed at the conclusion of the study.

Any future research using your retained data will require a research protocol for the proposed study approved by an Institutional Review Board (IRB) (a committee

responsible for protecting research participants) or other authorized official responsible for protecting human subjects of research. The data protections for privacy and confidentiality described in this consent form will apply to any future use of your stored data.

17. INCIDENTAL FINDINGS

There is a low possibility that, while performing your procedure, we may see an abnormality that we did not expect to see in this study. This is what is called an "incidental finding." We will let you know if we see such an incidental finding. Depending on the type of incidental finding, we may contact you by phone. In the case of a potential serious emergency, the researcher will inform you right away. We will also give information about this incidental finding to your primary doctor, or we will refer you to an appropriate doctor for further evaluation.

The costs for any care that will be needed to diagnose or treat an incidental finding would not be paid for by this research study. These costs would be your responsibility. If you are a DoD beneficiary, you will have access to care through standard Military Health System and TRICARE procedures. You may not opt out on receiving information on incidental findings.

18. VOLUNTARY PARTICIPATION

The decision to take part in this research study is completely voluntary on your part which means you do not have to take part if you do not want to. You may also leave the research study at any time. If you choose not to take part in this research study or if you leave the study before it is finished, there will be no penalty or loss of benefits to which you are otherwise entitled.

You will be informed if significant new findings develop during this research study that may relate to your decision to continue participation.

19. WHAT HAPPENS IF I WITHDRAW FROM THIS RESEARCH?

Should you choose to withdraw, you must *notify the research team.* If you decide to withdraw from this research study, the researcher may still use or disclose any already obtained health information as necessary to maintain the integrity or reliability of this research.

Please note that withdrawing your consent to participate in this research does not fully revoke your HIPAA Authorization Form to use/disclose your protected health information. To make that revocation, please send a letter to the principal investigator as discussed in the HIPAA Authorization Form.

The principal investigator of this research study may terminate your participation in this research study at any time if he determines this to be in your best interest, if you are unable to comply with the procedures required, or if you no longer meet eligibility criteria.

20. WHAT HAPPENS IF YOU ARE INJURED AS A RESULT OF THIS RESEARCH?

If you think that you have a research-related injury, notify your Principal Investigator immediately using the contact information in the section below.

If you are injured because of your participation in this research and you are a DoD healthcare beneficiary (e.g., active-duty military, dependent of active duty military, retiree), you are authorized space-available medical care for your injury within the DoD healthcare system, as long as you remain a DoD healthcare beneficiary. This care includes, but is not limited to, free medical care at DoD hospitals or DoD clinics.

If you are injured because of your participation in this research and you are not a DoD healthcare beneficiary, you are authorized space-available medical care for your injury at a DoD hospital or an DoD clinic; medical care charges for care at a DoD hospital or a DoD clinic will be waived for your research-related injury. If you obtain care for research-related injuries outside of a DoD or DoD hospital or clinic, you will not be reimbursed for those medical expenses.

For DoD healthcare beneficiaries and non-DoD healthcare beneficiaries: Transportation to and from hospitals or clinics will not be provided or paid for by DoD. Unless you are covered by TRICARE, no DoD reimbursement is available if you incur medical expenses to treat research-related injuries. No compensation is available for research-related injuries. You are not waiving any legal rights.

21. CONTACT INFORMATION:

Principal Investigator (PI)

The Principal Investigator or a member of the research staff will be available to answer any questions throughout this study.

Principal Investigator: Eli Medvescek, MD. Cell: 520-780-6888

Walter Reed National Military Medical Center Human Research Protection Program (HRPP) Office

The Human Research Protection Program Office Point of Contact and/or Human Protections Administrator (HPA) will be available to answer questions or discuss concerns you may have about this research study.

Human Protections Administrator/HRPP Phone: 301-295-8239\

Institutional Review Board (IRB) Office

If you have any questions about your rights as a research participant or if you have concerns or complaints about the research study, please contact the WRNMMC IRB Office at:

WRNMMC Department of Research Programs, Bldg 17B, 3rd floor, Ste C, 4650 Taylor Road, Bethesda, MD 20889.

Phone 301-295-8239

IF THERE IS ANY PORTION OF THIS DOCUMENT THAT YOU DO NOT UNDERSTAND, ASK THE INVESTIGATOR BEFORE SIGNING. YOU MAY CONSULT WITH YOUR PERSONAL PHYSICIAN OR LEGAL ADVISOR, IF YOU WISH.

A signed and dated copy of this document will be given to you.

SIGNATURE OF PARTICIPANT

By signing below, I agree that I have been provided time to read the information describing the research study in the consent form. The content and meaning of this information has been explained to me. I have been provided with the opportunity to ask questions. I voluntarily consent to participate in this study.

By signing this form, I have not given up any of my legal rights as a research participant.

☐ By checking this box, I DECLINE the use of my de-identified study data for use in future research studies (see Section 16).

_____

Printed Name of Participant

_____ _____

Signature of Participant Date

SIGNATURE OF INDIVIDUAL ADMINISTERING CONSENT

(Can only be signed by an investigator or staff approved to administer consent)

_____

Printed Name of Administering Individual

_____ _____

Signature of Administering Individual Date