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TITLE OF RESEARCH STUDY:

Title: Vagus Nerve Stimulation: A Non-Invasive Treatment to Improve the Health of Gulf Veterans with Gulf War Illness

PRINCIPAL INVESTIGATOR (HEAD RESEARCHER) NAME AND CONTACT INFORMATION:

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WHAT IS A RESEARCH STUDY?

A research study is when scientists try to answer a question about something that we don't know enough about. Participating may not help you or others.

People volunteer to be in a research study. The decision about whether or not to take part is totally up to you. You can also agree to take part now and later change your mind. Whatever you decide is okay. It will not affect your ability to get medical care within the Mount Sinai Health System.

Someone will explain this research study to you. Feel free to ask all the questions you want before you decide. Any new information that develops during this research study that might make you change your mind about participating will be given to you promptly.

Basic information about this study will appear on the website http://www.ClinicalTrials.gov. There are a few reasons for this: the National Institutes of Health (NIH) encourages all researchers to post their research; some medical journals only accept articles if the research was posted on the website; and, for research studies the U.S. Food and Drug Administration (FDA) calls "applicable clinical trials" 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.

PURPOSE OF THIS RESEARCH STUDY:

Gulf War Illness [GWI] is a condition occurring in some veterans who served in the 1990-1991 Gulf War. To date there is no specific treatment for it. A major complaint of veteran subjects with GWI is widespread pain and achiness. Currently some drugs are available to treat these symptoms, but these treatments have three major drawbacks – they don't work on all patients; their effect often does not last more than a few months; and the side effects they produce are often so bad that patients stop taking them. The purpose of this study is to test a new method of treating the widespread pain complaint of Gulf Veterans with GWI using a hand-held neuro-stimulator device that activates a nerve

in the neck called the vagus. The thing that will be determined in this study is if the active device which does stimulate the vagus nerve reduces your widespread pain in comparison to what happens using an inactive device which does not stimulate the vagus nerve. We will also test to see if the active device improves migraine which commonly occurs with widespread pain in GWI. The device has recently been approved for the acute treatment of both cluster and migraine headaches in adult patients in the US; however, the Food and Drug Administration (FDA), which is the regulatory body that determines whether new drugs and devices are safe to use, has not approved the neuro-stimulator device for the treatment of wide spread pain, therefore, although we have obtained special permission from the FDA to use it for this purpose, its use in treating your widespread pain is experimental.

You may qualify to take part in this research study because our colleagues at the New Jersey War Related Illness & Injury Study Center have told us that you are a suitable candidate for this study. They told us that you signed an Informed Consent allowing them to pass your personal health information to the researchers at Icahn School of Medicine at Mount Sinai (ISMMS). Some of that information indicates that you are a Gulf Veteran with Gulf War Illness who suffers from widespread pain. They also told us that they gave you sheets of paper to use to rate your pain in the past 24 hr, called the numerical pain rating going from no pain or zero to worst pain possible or 10, and that they called you four times in the week after you were in the WRIISC to get your response. You were also given a booklet summarizing the study and listing the dates and times of all visits, both phone and face to face. Not every subject with Gulf War Illness can participate in this study because of a set of requirements defining who can participate. If you are excluded, study staff can tell you the reason why this happened. If you are included and do participate, study staff can explain why you fit the requirements to allow you to move ahead with the study.

Funds for conducting this research are provided by the Department of Defense's Congressionally Directed Medical Research Program on GWI. Additional support for the study as well as the study devices is coming from electroCore Ltd, the device manufacturer. Permission to use this device for this study has been requested of the US Food and Drug Administration.

LENGTH OF TIME AND NUMBER OF PEOPLE EXPECTED TO PARTICIPATE

Your participation in this research study is expected to last up to 24 weeks allowing you to participate in the experimental phase for 10 weeks where you may get either a device that does stimulate the vagus or one that does not stimulate the vagus and then in the open label phase for an additional 10 weeks where every eligible subject gets an active device to use. You will then be told if you were receiving the actual unit or the sham unit. The device and diary will be checked to determine if you delivered at least 70% of scheduled stimulations and completed at least 70% of diary entries. If you have done these things, you will be given the active unit and charging station for the open label phase of the study. If you did not do these things, you will exit the study and not receive the active unit in the Open Label phase. The extra 4 weeks allow for some flexibility in scheduling the various encounters.

We plan to get complete data from 40 subjects and will evaluate up to 100 to get to this goal.

DESCRIPTION OF WHAT'S INVOLVED:

We are partnering with a company that has made a hand-held device that allows for stimulation of the vagus nerve which can be self-administered without the need for surgery; it works by the patient putting it on the skin overlying the vagus nerve in their neck and then turning it on for 120 sec periods three times a day on each side of your neck. The device is programmed to deliver only 6 bouts of stimulation per day – one to each side of the neck three times a day and then cannot be activated again until the next day.

The first time you come to ISMMS is for Encounter #6. We will first ask you to sign your informed consent to allow us to move ahead with the study. Then we will briefly review your medical and eligibility information obtained on Encounters #1 through 5. In doing so, we will confirm that you have Gulf War Illness by asking you several questions related to this diagnosis.

Next, you will rate your body-wide pain over the past 24 hours using the same visual analog scale you used previously. Your pain ratings obtained on the 4 phone calls (Encounters #2 through 5) plus the one done today will be reviewed for your eligibility to continue in this study.

Next, we will ask you about which medications you are taking at this time and how much of each. You do not have to stop any medicines you are currently taking while enrolled in this study. If a medical need arises for you to start a new medication or increase a dose of an existing medication, please inform the study team. If this happens, you may not be able to continue in the study. If you feel well enough to reduce or stop a medicine, you can do so but first discuss this with study staff.

While there is no suggestion that nVNS is a danger to a pregnancy, we think it wiser to exclude pregnant woman from this study. Toward that end, during Encounter #6, we will have you complete a urine pregnancy test if you are a woman of childbearing potential. The urine pregnancy test will be repeated during Encounter #14, if, upon review, you are eligible to continue to the open label phase of the study. To be able to continue with this study, you will need to agree to be trained on the features and use of the hand-held device and to comply with all contact/follow-up requirements.

Next, one of our staff will ask you questions to determine if you have migraine, and if so, how many attacks lasting at least 4 hours you have had in the past 2 weeks. We will also conduct a brief medical evaluation for baseline purposes during which we will ask you about your symptoms to determine if you have diagnoses which are often seen in GWI including chronic fatigue syndrome, fibromyalgia, multiple chemical sensitivity, and/or irritable bowel syndrome.

Next, we will ask you to complete the following questionnaires

SF-36: This is a 36 item questionnaire that provides information as to health-related quality of life including pain and overall physical and mental function

Migraine Disability Assessment Test [MIDAS}: This is a five question assessment of the degree to which having migraine headaches have affected you.

Hospital Anxiety and Depression Scale [HADS]: This is a 14 item questionnaire that asks questions to quantify the degree of anxiety and/or depression in the prior week

Next, we will introduce you to the device trainer who will give you the device you are assigned to use over the next 10 weeks [either the active or the sham/inactive device]. The instructions you will receive will be identical for both the active and sham devices. In contrast to the active device which does stimulate the vagus nerve, the inactive or sham device is a "placebo" which does not stimulate the vagus. Determination of which treatment you will get will be chosen by chance, like flipping a coin. You will have an equal chance of being given either study treatment. Neither you nor any of the study personnel will know which device you get, but this information could be obtained in an emergency. The trainer will teach you about the device features and will make sure that you know how to use it, including proper placement on the neck and how to recharge the device. Under your trainer's supervision, you will place the device on your neck and will be instructed on how to turn it on and off and use the controls. This will ensure that you are able to use the device properly to treat at home. Both devices produce similar sensations – a buzzing electrical type stimulation. This electrical current passes through muscle in your neck down to your vagus nerve where it gets stimulated. You will be able to control the intensity of the stimulation.

In order to follow you in using the device, we will provide you with information to access the electronic diary (eDiary). The eDiary will be the primary mode of inputting information about your use of the device. The eDiary can be accessed from any device that is connected to the internet. With the research staff's assistance, your eDiary will be activated and you will be assigned an unique 10 digit identifier. The screen will prompt you to input your email address, phone number, and to create a password. You will use this information to log onto your eDiary.
You should complete the eDiary after giving yourself each of the three treatments you will self-administer each day. The diary will ask you to insert the time you gave yourself the treatment and the intensity of the treatment you selected which is on the device. It will also ask you to indicate if you had a headache lasting at least 4 hours that day and if so to rate its intensity on the zero to ten pain scale. In addition to the eDiary, the trainer will also give you a paper diary and train you on the use of it in case you do not have access to the internet.

You will then go home and begin treating yourself for 120 sec on each side of your neck as you were instructed: shortly after getting up in the morning, approximately 6-8 hours later in the afternoon and then again 6-8 hours later in the evening. To get the best outcome, you should use the device six times a day [three on each side of your neck] as you have been instructed. The device counts the number of times that you have used it. If you use it less than 70% of the times scheduled or if you complete fewer than 70% of all the diary entries over the 10 weeks of this phase of the trial, the researchers will not be able to use any information from your participation, and you will not be allowed to advance to the open label phase of the study when every subject gets to use an active unit.

You will use whichever device you are assigned to for 10 weeks and then regardless of which device you had originally used, you will be given an active device to use for another 10 weeks during the "open label" phase of the study, if you are eligible.

While everyone wants to have the active treatment in any clinical trial, even if unproven, there is a very important reason for the trial to have some subjects receiving an inactive or placebo device for at least sometime. Information provided by subjects using the inactive device will be compared to information provided by subjects using the active device. If the active device is more effective than

the inactive or placebo device, that will mean that the effect of using the active nVNS device is responsible for making subjects feel better – not just because ISMMS personnel are paying attention to them due to their participating in a clinical trial. This determination has never been done for using the device for widespread pain. Your remaining in the treatment phase of the study for the full 10 weeks will make it possible to learn this valuable piece of information.

Encounter # 7 is a phone call in the next week following your visit at ISMMS. During this phone call, staff will call to check to see how you are doing and to learn if you are experiencing any negative effects of the stimulation. If you are, these are called "adverse events" and a health professional will determine if having them presents any risk to you and if so whether the risk is great enough to stop your participating further. The staff member will also ask you about using the diary as instructed.

Encounter #8 is a Phone Call which will be made in the third week of this phase of the study. At that time, the researcher will ask you to rate the severity of your widespread pain in the last 24 hours using the same zero to ten scale that you have used previously. You will also be asked about adverse events and if your pain is sufficiently improved, if you are using your diary and if you would want to reduce any of your current medications.

Encounter #9 is a Phone Call which will be made in the sixth week of this phase of the study. At that time, the researcher will ask you to rate the severity of your widespread pain in the last 24 hours using the same zero to ten scale that you have used previously. You will also be asked about adverse events, if you are using your diary, and if your pain is sufficiently improved that you would want to reduce your current medications.

Encounters #10, #11, #12 and #13 are phone calls which will be made on four separate days in the week before the end of this phase of the study. On the first of these calls, you will be asked about adverse events, if you are using your diary, and if your pain is sufficiently improved that you would want to reduce your current medications. For this and the other three calls, the researcher will ask you to rate the severity of your widespread pain in the last 24 hours using the same zero to ten scale that you have used previously.

Encounter #14: You will return to ISMMS to complete the same questionnaires as you had originally done in your last encounter at ISMMS [#6] and to undergo the same brief medical evaluations as in Encounter #6. In addition, you will be asked to complete the following questionnaires:

Patient Global Impression of Change: This is a 7 item questionnaire in which the research subject indicates whether the treatment produced an effect ranging from marked improvement to marked worsening.

Measure of Certainty: This is a 4 item questionnaire that allows you to indicate how certain you were that you were getting the active treatment.

If you are eligible to continue in the study, you will then be told you will receive a new device, an active one, which will stimulate your vagus nerve with each use. The trainer will reiterate instructions to teach you about the device features and how to use it, including proper placement on the neck and how to recharge it. Under your trainer's supervision, you will place the device on your neck and will be instructed on how to turn it on and off and use the controls. This will ensure that you are able to use the device properly to treat at home. You will continue to use your secure logon information you have

set up at Encounter #6 to access your eDiary. The trainer will also give you a new paper diary to complete in case you do not have access to the internet.

In signing this consent, we ask you to agree **not** to communicate with any other subjects about any difference you might perceive between the actual and the sham unit. If you do this, other subjects who have not yet participated in this study might be alerted to differences and this could impact negatively on the results of this important trial.

Encounter #15 is a phone call in the week after Encounter #14: During the call, staff will call to check to see how you are doing and to learn if you are experiencing any negative effects or "adverse events" from the stimulation. If you are, a health professional will determine if having them presents any risk to you and if so whether the risk is great enough to stop your participating further. The staff member will also ask you about using the diary as instructed.

Encounter #16 is a phone call: To be made in the third week of the open label phase of the study. At that time, the researcher will ask you to rate the severity of your widespread pain in the last 24 hours using the same zero to ten scale that you have used previously. You will also be asked about adverse events, use of your diary, and if you wish to reduce or stop any of your medications due to your having less of a problem with widespread pain.

Encounter #17 is a phone call: To be made in the sixth week of the open label phase of the study. At that time, the researcher will ask you to rate the severity of your widespread pain in the last 24 hours using the same zero to ten scale that you have used previously. You will also be asked about adverse events, use of your diary, and if you wish to reduce or stop any of your medications due to your having less of a problem with widespread pain.

Encounter #18, #19, #20 and #21 are Phone Calls: To be made on four separate days in the week before the end of this phase of the study. For each of these calls, the researcher will ask you to rate the severity of your widespread pain in the past 24 hours using the same zero to ten scale that you have used previously. On the first of these calls, the researcher will ask you about adverse events, use of your diary, and if you want to reduce any of your medications.

Encounter #22: You will come to ISMMS to provide the same data that you provided during Encounter #14, the end of the 10 week trial where you used either the active device or the sham device. You will return your device to the researchers at this time.

Table of Study Encounters:

Period 2: Randomized, blinded phase at ISMMS									
Encounters	E6	E7	E8	E9	E10	E11	E12	E13	E14
Type	Office Visit	Phone Call	Phone Call	Phone Call	Phone Call	Phone Call	Phone Call	Phone Call	Office Visit
Study Week	0	1	3	6	9	9	9	9	10
Informed Consent	x								
Eligibility Check	x								x
Pain VAS	x		x	x	x	x	x	x	x

Period 2: Randomized, blinded phase at ISMMS									
Encounters	E6	E7	E8	E9	E10	E11	E12	E13	E14
Type	Office Visit	Phone Call	Phone Call	Phone Call	Phone Call	Phone Call	Phone Call	Phone Call	Office Visit
Study Week	0	1	3	6	9	9	9	9	10
Diagnosis of GWI	x								
CFS, IBS, & MCS	x								
Medication Review	x		x	x	x				x
Pregnancy test/ screen	x								x
Migraine/Head. Dx	x								x
Medical Evaluation	x								x
Vital signs	x								x
SF 36	x								x
MIDAS	x								x
HADS	x								x
Randomization	x								
Device training/review	x								x
Diary training/review	x	x	x	x	x				x
Dispense device	x								x
Adverse events		x	x	x	x				x
Return Device									x
Device compliance									x
Diary compliance									x
PGIC									x
Measure of Certainty									x
Unblinding									x

Period 3: Open Label Phase at ISMMS								
Encounters	E15	E16	E17	E18	E19	E20	E21	E22
Type	Phone Call	Phone Call	Phone Call	Phone Call	Phone Call	Phone Call	Phone Call	Office Visit
Study Week	11	13	16	19	19	19	19	20
Pain VAS		x	x	x	x	x	x	x
Diagnosis of GWI								x

CFS, IBS, & MCS								x
Medication Review		x	x	x				x
Migraine/Headache Dx								x
Medical Evaluation								x
Vital signs								x
SF 36								x
MIDAS								x
HADS								x
Adverse events	X	x	x	x				x
Diary Training/Review	X	x	x	x				
Return device								x
Device compliance								x
Diary compliance								x
PGIC								x

For Women:

Since you are participating in a study that involves an investigational treatment that could present a risk to a developing fetus, it is recommended, for your protection, that you not become pregnant for the duration of the study; If you are a woman of childbearing potential, we will have you take a pregnancy test, to ensure that you not pregnant. Also, you should not participate if you are breastfeeding. Therefore, practicing effective contraception is important. No individual contraceptive is 100% effective.

Recommended methods of birth control are:

- The consistent use of an approved hormonal contraception (birth control pill/patches, rings),
- An intrauterine device (IUD),
- Contraceptive injection (Depo-Provera),
- Double barrier methods (Diaphragm with spermicidal gel or condoms with contraceptive foam),
- Sexual abstinence (no sexual intercourse) or
- Sterilization.

Hormonal contraceptives, implants, and injections are only considered effective if used properly and started at least one month before you begin the study, continuing throughout the study and for one month after the end of the study. If you are unsure whether the method of birth control you use is acceptable to use while participating in this study, you should ask your study doctor before you begin the study. If you are less than one year post-menopausal, there is the potential that you could become pregnant. If you become pregnant or think you may be pregnant at any time during the trial, it is important that you tell your study doctor immediately. The trial may be stopped and a referral will be made to an obstetrician/gynecologist for follow-up. If you plan to become pregnant in the year following a clinical trial, speak with your study doctor.

If you have any questions about birth control, your study coordinator or study doctor will be able to answer your questions and give you advice.

Should you become pregnant, regardless of the outcome, the sponsor may ask for information on your pregnancy, even if you are withdrawn from the study. Your written consent will be obtained separately in the case that this happens.

YOUR RESPONSIBILITIES IF YOU TAKE PART IN THIS RESEARCH:

If you decide to take part in this research study you will be responsible for the following things:

Coming to scheduled office encounters and completing questionnaires given to you by research staff then.

Responding to phone calls to provide information on any adverse events that might have occurred, on any reductions in medications you might want to make, and on the severity of your pain in the past 24 hours

Calling into research staff if you have questions about using the device or if adverse events occur

Treating yourself with the nVNS device on both sides of your neck for 120 sec each in the morning, afternoon and evening as you have been instructed.

Completing the electronic diary (eDiary) and/or paper diary each time you treat yourself by providing the time of each treatment, the intensity of the stimulation and at the end of the day whether you had a headache lasting at least 4 hours that day; if so, you would rate its severity on the 0 to 10 pain scale.

Following instructions about birth control.

Willingness to not communicate with other subjects about differences you may have detected between the actual device and the sham device. Doing this might compromise the outcome of this study.

COSTS OR PAYMENTS THAT MAY RESULT FROM PARTICIPATION:

If you agree to take part in this research study, we will pay you by check, $100 for each of the three visits you make to ISMMS for your time and effort. We will also reimburse you for travel up to the amount of $85 each time you come to ISMMS. You will need to bring receipts from the travel incurred in order to be reimbursed. In order to issue you a check, research personnel will collect information about you, including your name, address, and social security number. Your information will be kept confidential.

Check processing may take up to 6-8 weeks and will be mailed to the address you specify on the reimbursement form. Checks require some time to be prepared and will be given to you as available.

Tax law may require the Mount Sinai Finance Department to report the amount of payment you receive from Mount Sinai to the Internal Revenue Service (IRS) or other agencies, as

applicable. Generally this reporting would take place if you receive payments that equal $600 or more from Mount Sinai in a calendar year. You would be responsible for the payment of any tax that may be due.

POSSIBLE BENEFITS:

It is important to know that you may not get any benefit from taking part in this research. Others may not benefit either. However, possible benefits may be reduction of your widespread pain and in the number or severity of your migraine headaches. After you complete the study and have returned the nVNS device, it is possible that your symptoms may revert to what they were when you began your participation.

REASONABLY FORESEEABLE RISKS AND DISCOMFORTS:

You may experience side effects and complications associated with gammaCore. These are anticipated to resolve shortly after stopping the stimulation procedure without medical intervention. Occurrence of several of these events can be reduced by repositioning the device on your neck and/or decreasing the stimulation intensity. These potential anticipated adverse events (side effects) include, but are not limited to:

- Application site discomfort – 4.85%
- Application site irritation/redness – 3.74%
- Local pain in your face/head/neck area (including toothache) – 3%
- Muscle twitching and/or contractions in your face/head/neck area (including facial droop and/or lip pull) – 2.74%
- Headache/migraine – 2.56%
- Dizziness – 2%
- Tingling, pricking or a feeling of "pins and needles" on the skin where the device is applied (paresthesia/dysesthesia) – 1.63%

The following risks and complications have been associated with other VNS devices and may potentially occur with gammaCore:

- Coughing
- Gastrointestinal discomfort (stomach ache)
- Headache
- Hoarseness or change in voice
- Irregular heart beat (arrhythmia)
- Nausea
- Shortness of breath (dyspnea)

- Metallic taste

These side effects typically resolve immediately after the stimulation is complete.
Providing information on the questionnaires should not present any risks. It is likely you may be bored by having to complete the daily diary entries but you should understand that doing this accurately and on time will allow the researchers to track your experience with nVNS.

If you receive the inactive device, your symptoms may not improve as much as if you were on the active device over this 10 week part of the study. But we do not know that for sure and learning this is the reason for doing this study – that is, to determine whether the effect of nVNS is due to its stimulating the vagus and is not just a placebo response. Importantly, you will be given the active device to use for an additional 10 week period so you will have any benefit that the active device might confer. If you do not use your device regularly and reliably in the part of the study when you will be on either the active or the sham device, you will not progress to this open label phase of the study.

There is some risk to not allowing you to add or increase any of your medications over the 10 week period when you won't know which device you are using. However, your doctors have worked with you over the years to get you on the best treatment possible and so the likelihood of your needing to change your medications is small. If the treatment helps, you can of course reduce your meds.

There is the risk of loss of private information; this risk always exists, but there are procedures in place to minimize the risk.

OTHER POSSIBLE OPTIONS TO CONSIDER:

You may decide not to take part in this research study without any penalty. The choice is totally up to you. Instead of being in the research study, you may return to your physician for help in managing your pain. Common treatments for these include physical therapy and medications such as anti-inflammatories, antidepressants which also reduce pain, antiepileptic drugs which target pain pathways to reduce their activity and in a few treatment-resistant patients if needed, opioids. In contrast to VNS whose side effects are local to stimulations, drug therapies carry side effects such as sedation and weight gain and with the opioids, drug dependency. But many patients can take these medicines without problems with the benefit of having reduced pain.

IN CASE OF INJURY DURING THIS RESEARCH STUDY:

If you are injured or made sick from taking part in this research study, medical care will be provided. This will be provided at no cost to you by VA unless the injury was due to your not following the study procedures. This does not prevent you from seeking payment for injury related to malpractice or negligence. Contact the investigator at Icahn School of Medicine at Mount Sinai for more information. You may also contactDr. Anays Sotolongo , at 973-676-1000 ext: 2550 at the VA New Jersey HealthCare System if you have questions about any research related injuries.

ENDING PARTICIPATION IN THE RESEARCH STUDY:

You may stop taking part in this research study at any time without any penalty. This will not affect your ability to receive medical care at any of the Mount Sinai Health System hospitals or to receive any benefits to which you are otherwise entitled.

If you decide to stop being in the research study, please contact the Principal Investigator or the research staff. At that point, you will be asked to return to ISMMS to return the device. If you do drop out of the study, you may not receive the full benefit, if any, of the treatment.

If you stop being in the research study, already collected information may not be removed from the research study database and will continue to be used to complete the research analysis.

You may also withdraw your permission for the use and disclosure of any of your protected information for research, but you must do so in writing to the Principal Investigator at the address on the first page. Even if you withdraw your permission, the Principal Investigator for the research study may still use the information that was already collected if that information is necessary to complete the research study. Your health information may still be used or shared after you withdraw your authorization if you have an adverse event (a bad effect) from participating in the research study.

Withdrawal without your consent: The study doctor, the sponsor or the institution may stop your involvement in this research study at any time without your consent. This may be because the research study is being stopped, the instructions of the study team have not been followed, the investigator believes it is in your best interest, or for any other reason. If specimens or data have been stored as part of the research study, they too can be destroyed without your consent.

CONTACT PERSON(S):

If you have any questions, concerns, or complaints at any time about this research, or you think the research has hurt you, please contact the office of the research team at phone number 212-844-6665 and/or Dr Natelson at 212-844-6665.

If you experience an emergency during your participation in this research, contact Michelle Blate, the study nurse practitioner at 917-414-5841, but also go to the emergency room.

This research has been reviewed and approved by an Institutional Review Board. You may reach a representative of the Program for Protection of Human Subjects at the Icahn School of Medicine at Mount Sinai at telephone number (212) 824-8200 during standard work hours for any of the reasons listed below. This office will direct your call to the right person within the Mount Sinai Health System:

- Your questions, concerns, or complaints are not being answered by the research team.
- You cannot reach the research team.
- You are not comfortable talking to the research team.
- You have questions about your rights as a research subject.
- You want to get information or provide input about this research.

DISCLOSURE OF FINANCIAL INTERESTS:

Sometimes, physicians/researchers receive payments for consulting or similar work performed for industry. Effective September 2014 Mount Sinai reviews only payments to an individual totaling more than $5,000 a year per entity when determining potential conflicts of interest. If you have questions regarding industry relationships, we encourage you to talk your physician/researcher or visit our website at http://icahn.mssm.edu/ where Mount Sinai publicly discloses the industry relationships of our faculty.

The company participating in this research study manufactures the device being tested and so has a financial interest that could be affected by the outcome of this research study.

MAINTAINING CONFIDENTIALITY – HIPAA AUTHORIZATION:

As you take part in this research project it will be necessary for the research team and others to use and share some of your private protected health information. Consistent with the federal Health Insurance Portability and Accountability Act (HIPAA), we are asking your permission to receive, use and share that information.

What protected health information is collected and used in this study, and might also be disclosed (shared) with others?

As part of this research project, the research team at the hospital(s) involved in the research will collect your name, address, telephone/fax numbers, birthday, e-mail address, and device identifiers.

The researchers will also get information from your medical record and from their assessment of you from the East Orange NJ VA Medical Center.

During the study the researchers will gather information by:

- taking a medical history (includes current and past medications or therapies, illnesses, conditions or symptoms, family medical history, allergies, etc.)
- doing a physical examination that generally also includes blood pressure reading, heart rate, breathing rate and temperature
- completing the tests, procedures, questionnaires and interviews explained in the description section of this consent.

Why is your protected health information being used?

Your personal contact information is important to be able to contact you during the study. Your health information and the results of any tests and procedures being collected as part of this research study will be used for the purpose of this study as explained earlier in this consent form. The results of this study could be published or presented at scientific meetings, lectures, or other events, but would not

include any information that would let others know who you are, unless you give separate permission to do so.

The Principal Investigator may also use and share the results of these tests and procedures to treat you in collaboration with others in the Mount Sinai Health System.

The research team and other authorized members of The Mount Sinai Health System ("Mount Sinai") workforce may use and share your information to ensure that the research meets legal, institutional or accreditation requirements. For example, the School's Program for the Protection of Human Subjects is responsible for overseeing research on human subjects, and may need to see your information. If you receive any payments for taking part in this study, the Mount Sinai Finance Department may need your name, address, social security number, payment amount, and related information for tax reporting purposes. If the research team uncovers abuse, neglect, or reportable diseases, this information may be disclosed to appropriate authorities.

Who, outside Mount Sinai, might receive your protected health information?

As part of the study, the Principal Investigator, study team and others in the Mount Sinai workforce may disclose your protected health information, including the results of the research study tests and procedures, to the following people or organizations: (It is possible that there may be changes to the list during this research study; you may request an up-to-date list at any time by contacting the Principal Investigator.)

- Collaborators at the NJ War Related Illness & Injury Study Center and at electroCore Ltd, the company that makes the nVNS device and which is participating in doing this study. Both groups need to know of any serious adverse events that might occur with device use.
- The Department of Defense's Congressional Directed Medical Research Program for Gulf War Illness and/or its representative who need to confirm the accuracy of the results submitted to the government or the use of government funds.
- The United States Food and Drug Administration
- The United States Department of Health and Human Services and the Office of Human Research Protection.

In all disclosures outside of Mount Sinai, you will not be identified by name, social security number, address, telephone number, or any other direct personal identifier unless disclosure of the direct identifier is required by law. Some records and information disclosed may be identified with a unique code number. The Principal Investigator will ensure that the key to the code will be kept in a locked file, or will be securely stored electronically. The code will not be used to link the information back to you without your permission, unless the law requires it, or rarely if the Institutional Review Board allows it after determining that there would be minimal risk to your privacy. It is possible that a sponsor or their representatives, a data coordinating office, a contract research organization, may come to inspect your records. Even if those records are identifiable when inspected, the information leaving the institution will be stripped of direct identifiers. Additionally, when applicable, the monitors, auditors, the IRB, the Office of Human Subjects Protection (OHRP) of the Department of Health and Human Services as well as the Food and Drug Administration (FDA) will be granted direct access to your medical records for verification of the research procedures and data. OHRP and FDA are

authorized to remove information with identifiers if necessary to complete their task. By signing this document you are authorizing this access. We may publish the results of this research. However, we will keep your name and other identifying information confidential.

For how long will Mount Sinai be able to use or disclose your protected health information?

Seven years. Your authorization for use of your protected health information for this specific study does not expire.

Will you be able to access your records?

During your participation in this study, you will not be able to access your medical records. This will be done to prevent the knowledge of study results from affecting the reliability of the study. Your information will be available should an emergency arise that would require your treating physician to know this information to best treat you. You will have access to your medical record and any study information that is part of that record when the study is over or earlier, if possible. The investigator is not required to release to you research information that is not part of your medical record.

Do you need to give us permission to obtain, use or share your health information?

NO! If you decide not to let us obtain, use or share your health information you should not sign this form, and you will not be allowed to volunteer in the research study. If you do not sign, it will not affect your treatment, payment or enrollment in any health plans or affect your eligibility for benefits.

Can you change your mind?

You may withdraw your permission for the use and disclosure of any of your protected information for research, but you must do so in writing to the Principal Investigator at the address on the first page. Even if you withdraw your permission, the Principal Investigator for the research study may still use your protected information that was already collected if that information is necessary to complete the study. Your health information may still be used or shared after you withdraw your authorization if you should have an adverse event (a bad effect) from being in the study. If you withdraw your permission to use your protected health information for research that means you will also be withdrawn from the research study, but standard medical care and any other benefits to which you are entitled will not be affected. You can also tell us you want to withdraw from the research study at any time without canceling the Authorization to use your data.

It is important for you to understand that once information is disclosed to others outside Mount Sinai, the information may be re-disclosed and will no longer be covered by the federal privacy protection regulations. However, even if your information will no longer be protected by federal regulations, where possible, Mount Sinai has entered into agreements with those who will receive your information to continue to protect your confidentiality.

If as part of this research project your medical records are being reviewed, or a medical history is being taken, it is possible that HIV-related information may be revealed to the researchers. If that is the case, the following information concerns you. If this research does not involve any review of medical records or questions about your medical history or conditions, then the following section may be ignored.

Notice Concerning HIV-Related Information

If you are authorizing the release of HIV-related information, you should be aware that the recipient(s) is (are) prohibited from re-disclosing any HIV-related information without your authorization unless permitted to do so under federal or state law. You also have a right to request a list of people who may receive or use your HIV-related information without authorization. If you experience discrimination because of the release or disclosure of HIV-related information, you may contact the New York State Division of Human Rights at (888) 392-3644 or the New York City Commission on Human Rights at (212) 306-5070. These agencies are responsible for protecting your rights.

Study ID #: HSM#16-00097/GCO#16-0350 **Form Version Date: 07/15/2019**

Signature Block for Capable Adult

Your signature below documents your permission to take part in this research and to the use and disclosure of your protected health information. A signed and dated copy will be given to you.

DO NOT SIGN THIS FORM AFTER THIS DATE → **8/28/2020**

Signature of subject	Date
Printed name of subject	Time

Person Explaining Study and Obtaining Consent

Signature of person obtaining consent	Date
Printed name of person obtaining consent	Time