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Research Participant Informed Consent Form

Title of Study:	Mechanisms of paired vagus nerve stimulation in chronic stroke: a randomized, blinded, sham-controlled, single-center mechanistic trial s24-00751
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1. About volunteering for this research study

You are being invited to take part in a research study because you previously had a stroke and now have limitations in the movement of your upper limb. Your participation is voluntary which means you can choose whether or not you want to take part in this study.

People who agree to take part in research studies are called “subjects” or “research participants.” These words are used throughout this consent form. Before you can make your decision, you will need to know what the study is about, the possible risks and benefits of being in this study, and what you will have to do in this study. You may also decide to discuss this study and this form with your family, friends, or doctor. If you have any questions about the study or about this form, please ask us. If you decide to take part in this study, you must sign this form. We will give you a copy of this form signed by you for you to keep.

2. What is the purpose of this study?

The purpose of this study is to test the safety and effects (good and bad) of using the ReStore System to deliver vagus nerve stimulation (VNS) during physical therapy of the upper limb in people with a history of stroke. This study will also try to understand how VNS works to potentially improve movement after a stroke. The vagus nerve is like a messenger between the brain and the body's organs, and it helps the body relax and rest.

The ReStore System is a device that's still being tested, which means it hasn't been approved by the Food and Drug Administration (FDA) for use outside of research studies like this one. It has a very small stimulator that is put on top of the vagus nerve in the neck during surgery. It uses two devices outside the body to activate the VNS. The VNS then activates parts of the brain that might help learning during therapy exercises.

During the study, there will be a time when you will get active VNS with your therapy. There will also be a time when you will get a placebo (inactive) VNS with your therapy. This is done to see how you respond to the active VNS being tested compared to the placebo VNS.

We will use a few different tools to see how the brain changes after the VNS treatment. One is called transcranial magnetic stimulation (TMS), which uses magnetic pulses to check how your brain circuits are working, and it doesn't hurt. Another is magnetic resonance imaging (MRI), which takes pictures of your brain. We will also do some clinical tests to check your movement, thinking, and feelings.

There is a commercially available VNS device, called the Transponder VNS system, which is FDA-approved to treat motor deficits after stroke. The Transponder VNS system requires implantation of three components: a stimulator on the vagus nerve, a battery to power the stimulator, and wires in the neck connecting the two. We are not using this system in this study because it requires a longer surgery and post-operative recovery time. Importantly, this system is not compatible with TMS or MRI, which would keep us from learning how the brain changes from the treatment.

3. How long will I be in the study? How many other people will be in the study?

The study will last about 9 months and will involve about 42 visits. When possible, we will also perform a long-term assessment of safety for up to 2 years after your implant date, consisting of twice-yearly phone call check-ins.

The study overall will last 5 years. We expect to enroll 45 individuals with stroke at NYU Langone Health.

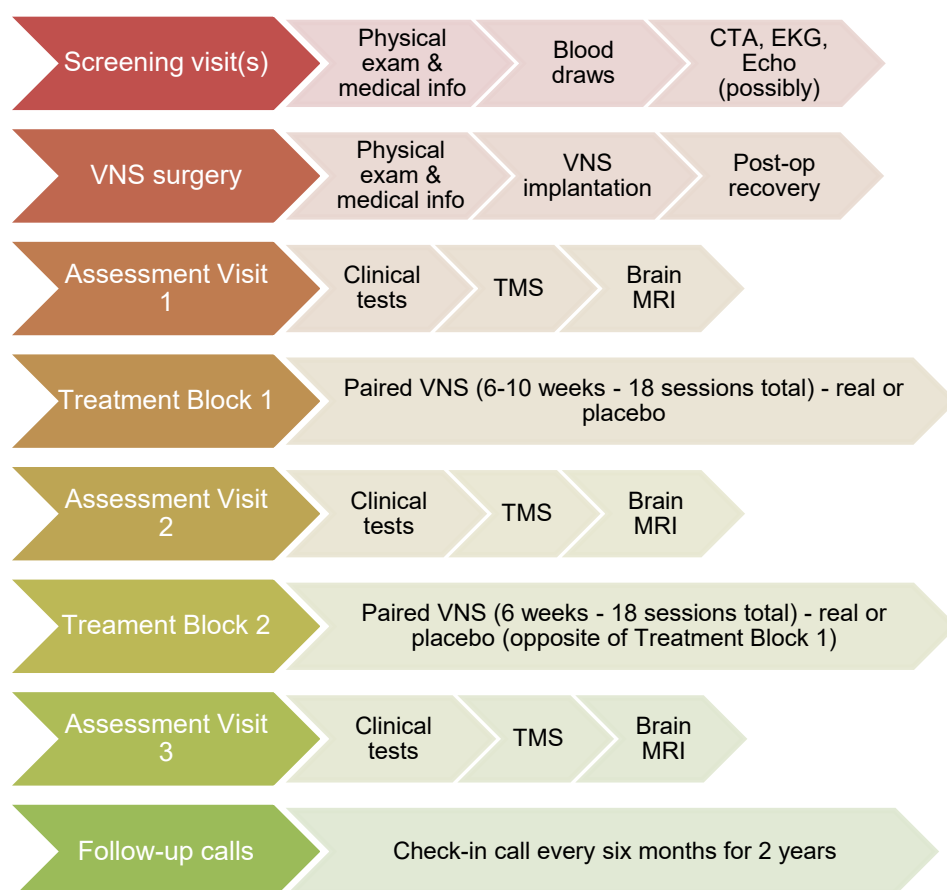
This study will be both an in-patient and an out-patient study. This means some of the study will happen in the hospital. Most of the study visits will be as an out-patient at NYU Tisch or NYU Brooklyn.

4. What will I be asked to do in the study?

If you choose to take part in the study and are eligible, we will ask you to sign this consent form before you have any procedures with the study staff that are part of the study.

Overview. You will be asked to attend about 42 study visits. **See the flow chart.** You will first undertake screening, consent, and pre-operative assessments, which could take up to four months. Once cleared, you will undergo the surgery to place the vagus nerve stimulator on the vagus nerve in the neck, followed by up to one month of recovery.

You will then receive two treatment blocks. In one treatment block, you will receive active VNS stimulation during upper limb rehabilitation. In the other treatment block, you will receive placebo (sham or inactive) stimulation during upper limb rehabilitation.



You will be assessed at visits before and after each of the treatment blocks. We will collect information about changes in your brain circuitry, brain anatomy, and behavioral functions.

Pre-operative screening Visit(s). After you sign this consent to take part in the study, some exams, tests, and/or procedures may be performed (described below) to find out if you can continue in the study;

this is called pre-operative screening. We may also be able to use the results of exams, tests, and/or procedures you completed before enrolling in this study. You may have 2 or more visits, and each will take 1-2 hours. These will take place in an outpatient setting. We will complete some or all of the following in preparation for your surgery.

- Brief physical exam and medical history - this will be completed by a medical professional. We will ask for information about your demographics (e.g. age, sex, ethnicity, handedness, and education level), the medications you take, and will check your heart, pulse, and blood pressure. It is meant to assess your overall health and ability to take part in the study. This will take 20 minutes.
- Brief neurological examination - this exam will be completed by a medical professional, and includes checking your ability to move your arm and how tight your muscles are. This will take 30 minutes.
- Blood draw - blood (about two tablespoons) will be taken from a vessel in your arm to count the number of red blood cells and white blood cells, to measure the amount of sugar/cholesterol in your blood, and to determine your overall, general health. If you are capable of becoming pregnant, a blood pregnancy test will also be done. This will take 15 minutes.
- Other tests - in addition, your doctor may request other tests in order to clear you to receive surgery, such as EKG, echocardiogram, or CT angiography of the brain. These tests will require separate visits.

The results of the screening exams, tests, and/or procedures will be reviewed to determine whether you will be allowed to continue in the study. You will be assessed for the inclusion and exclusion criteria as well as medical history and physical exam. If you meet the criteria and give consent, you will be enrolled in the study. If you are not allowed to continue in the study, the researcher will discuss the reasons with you.

VNS surgery visit. If you are determined to be medically eligible for the study, and it is determined that your stroke injury meets the study criteria and your eligibility for surgery is verified (which includes physical exams, plus a pregnancy test if you are capable of becoming pregnant), the study team will schedule your surgery for the implantation of the ReStore System (i.e., the vagus nerve stimulator).

- Brief physical exam and medical history - this will be completed by a medical professional, and includes checking your heart, pulse, and blood pressure. It is meant to assess your overall health and ability to undergo the surgery. This will take 15 minutes.
- Surgery - the surgery is expected to take less than 60 minutes and involves one incision on the left side of your neck. The surgery will take place in the operating room in outpatient surgery. After you receive anesthesia and are asleep, the surgeon will locate the vagus nerve on the left side of your neck and then will place the stimulator next to the vagus nerve. It will be held in place by a silicone cuff. Your incisions will be closed with stitches or medical skin glue. After surgery you will recover for 2-4 weeks or as directed by your doctor. Once you have recovered, you will start your study treatment.

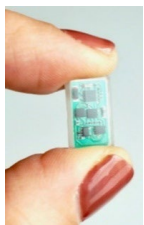
Assessment visits. The week before and after each of your treatment blocks, you will undergo the following in an assessment visit. The visit might be split up into two days.

- Clinical assessments of motor, cognitive, and emotional functions - tests of motor function will take up to 4 hours. You will be tested on your muscle strength, muscle tightness, and how well you can control your wrist movements. These tests involve moving your wrist while we record your movements with wearable reflectors. We will tape surface EMG electrodes (sensors) to parts of your arm to record muscle activity. We will also score your arm's movement quality and its ability to move objects with clinical tests and will ask you about the impact of your stroke on your daily function. Tests of cognitive function will take up to 2 hours. You will be tested on your thinking, attention, and memory with a video game and paper assessment. Your positive and negative emotions and depression levels will also be assessed with questionnaires.

- **Transcranial magnetic stimulation (TMS)** - TMS tests will take up to 3 hours. They will measure changes in the strength of your brain pathways. We use a plastic coil that is held on the surface of your head and generates a magnetic pulse that stimulates the brain. You will hear a click and may feel a pulling sensation on the skin under the coil, and there may be a twitch in muscles of the face, arm, or leg. During the stimulation, we may ask you to tense certain muscles slightly or perform other simple actions. The TMS device (Magstim) is considered an investigational device because it is not cleared by the Food and Drug Administration (FDA) for therapeutic use for stroke recovery. We are able to use it for research purposes. As part of this assessment, we may also stimulate a nerve in your arm that moves your wrist. We would apply a small electrical pulse through an electrode placed on the skin of your elbow, which will cause your wrist to twitch.
- **Magnetic resonance imaging (MRI)** – the MRI will take up to 30 minutes. You will first complete an MRI safety screening worksheet, which will determine your eligibility for this portion of the study. You will be taken into a changing room and asked to remove all metal from your body and change into a gown. You will be instructed on how to lay on the MRI imaging table, and will be provided with an emergency squeeze ball which will allow you to communicate with the MRI technicians. You will be monitored throughout your MRI visit by a trained MRI technologist.

Treatment visits. You will receive two treatment blocks, each lasting 6-10 weeks. Each block has 18 treatment visits. One block will give you active VNS during rehabilitation and the other block will give you placebo VNS during rehabilitation.

- **Randomization** - you will have a one in two chance of being randomly selected (like the flip of a coin) to initially receive either the active VNS or the placebo VNS. Following your Treatment Block 1, you will automatically receive the opposite stimulation condition in Treatment Block 2. You will receive upper limb rehabilitation in both treatment blocks. Most people getting the active stimulation in previous studies did not sense the stimulation after the first few trials. You will be instructed that you may initially perceive stimulation, but the perception may fade. Because of this, neither you nor the researchers will know whether you are receiving the active stimulation or placebo. In the event of an emergency, there is a way for the researcher to find out which are you receiving.
- **Treatment sessions** – for each treatment block, you will receive 18 sessions total of rehabilitation with VNS, which will take 6-10 weeks to complete. Each session is 90 minutes with a licensed occupational therapist. At the start of each session, the therapist will place the power and communications module (PCM) in a collar around your neck. The PCM wirelessly powers and drives the implanted stimulation electrode. The therapist will deliver a stimulation at the completion of a training movement by the weak arm. The therapist presses a button on a smart device which communicates wirelessly with the PCM to trigger this stimulation (**see figure below**). The treatment sessions will be videotaped to document when stimulation is given during your arm movement.



Vagus Nerve Stimulation (VNS) Device



(A) VNS device in the cuff is surgically placed on the vagus nerve in the neck; (B) the Power and Communication Device (PCM) is worn in a removable neckband; (C) the smart device triggers stimulation by the PCM during a rehabilitation movement (D).

- **Long-term follow-up calls.** Phone assessments will be performed twice annually for two years after the date of implant. There is no plan to stimulate during this period.

Removal of VNS device. You are free to decide to have the device removed at any time during the study. The cost of this will be covered within two years of your date of implant. Upon completion of the study, even if you have not experienced any issues with the device, it is your choice whether to leave the device implanted or have the device removed. After those two years, you will be responsible for paying the cost of the surgery to remove the device.

Optional storage of your data and samples for future research studies:

This study is collecting data and biospecimens from you, including TMS, MRI, behavioral tests, and video recordings of your rehabilitation treatment. We would also like to make your data and/or specimens available for future research studies or other data and/or specimen repositories. These studies may be done by researchers at this institution or other institutions, including for-profit companies. It is your choice whether to let researchers share your data and/or specimens for future research. In order to obtain your data and/or specimens, future researchers must seek approval from Dr. Schambra and NYU Langone Health. Researchers must agree not to try to identify you. If you say “yes,” you can change your mind later. If you say “no,” you can still fully participate in this study. With your permission, we will store your data and/or specimens. We plan to keep your data and/or specimens indefinitely on an encrypted, password- and firewall-protected research drive.

Sharing data and/or specimens is part of research and may increase what we can learn from this study. Because science constantly advances, we do not yet know what future use of research data and/or specimens may include. These data could be used for research into stroke, its complications and other conditions for which individuals with stroke are at increased risk, and to improve treatment or for other purposes. This future research may be done by other research centers or institutions, for-profit companies, government agencies, or other research partners. It is unlikely that what we learn from these studies will have a direct benefit to you, but these studies may provide additional information that will be helpful in understanding stroke or other diseases or conditions, including research to develop new tests, treatments, drugs or devices or other products or services with commercial value. There are no plans to provide financial compensation to you should this occur.

We protect your information to the extent possible by limiting the researchers’ use and the type of information that is shared and making sure we have data and/or specimen sharing agreements in place. We do not think that there will be further risks to your privacy and confidentiality by sharing your data and/or specimens with repositories or other researchers.

All MRI, TMS, and behavioral data will be coded to protect your identity before they are shared with other researchers. Dr. Schambra will have a code key that can be used to link your identifying information. The code key will be securely stored. The videos of your treatment session will also be coded to protect your identity, but your face may be visible. Therefore, video data are potentially identifiable.

After data are coded, it may be used for future research studies or shared with other external collaborators and we will not request additional informed consent from you to use it.

Please check and initial next to your choice:

_____ **Yes**, you may use all of my data, my treatment session videos, and other specimens for possible other and future research studies.

_____ **Yes**, you may use my data and other specimens **but NOT my videos** for possible other and future research studies.

_____ **No**, you may NOT use any of my data, video, or specimens for possible other and future research studies.

5. What are the possible risks or discomforts?

While on this study, you are at risk for reactions that are listed below. Medicines may be given to make them less serious and uncomfortable. Many of these reactions go away shortly after the VNS is stopped, but in some cases, they can be serious or long-lasting and permanent. You should discuss these with the researcher and/or your regular doctor. There also may be other reactions that we cannot predict. These unknown reactions could also be to your unborn child if you are pregnant or become pregnant while on this study.

Risks associated with VNS surgery include:

Likely, some may be Serious (in 100 people, about 21-100 may have):

- Pain caused by the incision (surgical cut)
- Inflammation or irritation of the skin (area around the incision site becomes red, swollen, and sometimes painful)
- Nausea
- Formation of scar tissue

Less Likely, some may be Serious (in 100 people, about 2-20 may have):

- Blood Clot
- Formation of cysts
- Infection
- Facial numbness (losing feeling in your face)
- Facial paralysis (weakness in your face)
- Edema (swelling near the incision site)
- Paresthesia (numbness, tingling)
- Hematoma (solid swelling of clotted blood)
- Hoarseness/vocal cord paresis/paralysis
- Tissue reaction (tissue becomes inflamed i.e., red and swollen)

Rare and Serious (in 100 people, about 1 or fewer may have):

- Nerve damage
- Side effects from the anesthesia
 - Breathing and heart problems
 - Collapsed lung (pneumothorax)
 - Drug reactions
 - Aspiration (accidentally inhaling food or liquid into your airway)
 - Nerve damage
 - Cardiac arrest (heart stops beating)
 - Brain damage
 - Paralysis
 - Permanent organ damage
 - Memory dysfunction/memory loss
 - Injury to vocal chords, teeth, lips, eyes
 - Awareness during the procedure
 - Death
- Parasthesia (tingling, pricking, chilling, burning, or numb sensation on the skin)
- Skin or other tissue having a reaction to the surgery or the device

Risks associated with vagus nerve stimulation include:

Likely, some may be Serious (in 100 people, about 21-100 may have):

- Pain in the throat or neck
- Muscle twitching during stimulation

- Hoarseness
- Pharyngitis (sore throat)
- Cough
- Irritation of the skin

Less Likely, some may be Serious (in 100 people, about 2-20 may have):

- Diarrhea
- Dyspepsia (upset stomach)
- Dysphagia (difficulty or discomfort with swallowing)
- Ear ache
- Hiccup
- Laryngospasm (spasm of the vocal cords)
- Nausea and vomiting

Rare and Serious (in 100 people, about 1 or fewer may have):

- Respiratory effects
- Histotoxicological reaction (reaction to the device, i.e. an allergic reaction to the materials or redness and swelling around the device)
- Dyspnea (difficult breathing)

At much higher and longer doses of VNS than will be used in this study (for epilepsy subjects), some subjects noted brief changes in pulse, but clinically relevant cardiac effects have not been observed in controlled studies. In addition, although not shown to be definitely related to stimulation, a small number of subjects in studies for other indications that used substantially higher stimulation intensity and duration have reported cardiac abnormalities after stimulation was initiated. Based on a large body of preclinical and clinical literature and our own clinical investigations using lower-intensity VNS stimulation similar to this study, cardiac effects are not expected in this study.

Risks associated with VNS device removal. It is recommended that you talk to your doctor to determine whether to leave the device implanted or have it removed. The risks of leaving the device implanted long-term are currently unknown.

If adverse events are experienced, the team of surgeons and clinical investigators will determine if the device warrants removal during or at completion of the study. If device removal is warranted, the study team will make a strong recommendation to you to have it removed.

Device removal may have increased risks compared with the original implantation surgery because of potential scar tissue from the original operation. In reported series, removal of the implanted electrode (a different device that wrapped wires around the vagus nerve) resulted in a slightly higher incident of nerve injury compared to implantation (4.9 vs 3.6%). As explained in the section on the risks of implantation, damage to the nerve may result in issues such as hoarseness, difficulty with swallowing, and cough.

If you choose to leave the device in place, you may be contacted annually by phone to check on you, and you may also be contacted about relevant future studies.

Risks associated with rehabilitation training. The risk of rehabilitation is potential soreness or fatigue from being more active than usual. You will be given rest breaks to prevent fatigue.

Risks associated with motor, cognitive, and emotion questionnaires and tests. The risk of this testing is potential discomfort or fatigue from sitting down and making movements or answering questions for a few minutes at a time. You will be given rest breaks as needed.

Risks associated with TMS. Most people do not find TMS painful, but sometimes strong contractions of scalp muscles can cause discomfort or headache. If you find the procedure too uncomfortable, you may discontinue it at any time. Headaches usually go away with over-the-counter pain medication. TMS has rarely been associated with seizure. TMS can interfere with implanted medical devices and will not be

used if you have a pacemaker, implanted pump, stimulator, or have metal objects (besides dental work) inside the eye or skull. Please inform the investigators if you have any of these. Stimulation of the elbow with the electrical stimulus may produce a stinging or tingling sensation and the wrist will twitch. You might experience some pain during the nerve stimulation. If you find this stimulation too uncomfortable, you may choose not to complete this procedure.

Risks associated with MRI.

Magnetic Field Risk. MRI uses strong magnetic fields and radio waves to make images of the inside of your body. MRI does NOT involve high-energy radiation (like X-rays). For most people MRI is very safe. However, if you have anything made of metal on your skin or inside your body, MRI may not be safe for you, and you must tell study personnel before your scan. Also, if you have any electronic devices on the outside or inside of your body, you must tell study personnel about those too. Some things, like tattoos, may have metal materials in them even though you might not realize it. For this reason, study personnel will give you a checklist of things that have metal or electronic parts in them. You must read the list carefully before your scan and put a checkmark next to everything that applies to you.

The following paragraphs will describe the possible risks of MRI. To reduce many of these risks, you will be given an emergency squeeze ball to hold in your hand during the scan. If you feel any discomfort you should squeeze the ball. This sets off an alarm that the technologist can hear. The technologist will then talk to you and will stop the scan if you want. There is a microphone in the scanner so that you can communicate with the technologist. However, the scanner makes a lot of noise when it is running and the technologist may not always hear what you say. If you need to get the technologist's attention, you should squeeze the ball.

Remember, if at any point you feel uncomfortable and want to stop the scan, just squeeze the ball and tell the technologist.

Risks from metal. The strong magnetic field in the scanner will pull on things that contain certain types of metal. If someone takes a metal object into the scan room, it might fly towards the scanner and hurt you. For this reason, everyone (including you) must remove everything metal from their clothes and pockets before going into the scan room. Also, the door to the scan room will be kept closed during the scan to prevent unauthorized people from walking in.

If you have something metal inside your body, the scanner might pull on it and make it move. You must tell study personnel before your scan if you have anything metal inside your body.

Some types of metal might heat up when the scanner is running. If you feel any burning sensation during the scan, you should squeeze the emergency ball and the technologist will stop the scan.

Risks from electronic devices. If you have any electronic devices on the inside or outside of your body, the scanner might make them stop working properly. For this reason, you must tell study personnel before your scan if you have anything electronic on or in your body.

Burns. Metal is not the only thing that can cause burns in MRI. It's possible (although very rare) to get burned by touching the inside walls of the scanner or by making skin-to-skin contact. The technologist will give you a blanket or cushions so that you don't touch the inside walls of the scanner. You should also avoid letting your hands or legs touch each other. Remember, if you feel any burning sensation during the scan, you should squeeze the emergency ball and the technologist will stop the scan.

Tinnitus (ringing in the ears) and hearing loss. The scanner makes very loud sounds while it is running. You will be given earplugs or headphones to wear during the scan. Make sure you roll the earplugs tightly and let them expand in your ears so that they work properly. If the sound of the scanner is still so loud that it causes you discomfort, squeeze the emergency ball and tell the technologist. This is important because very loud sounds can cause ringing in the ears or even hearing loss.

Feeling warm or hot. The radio waves used in MRI are like those your cellphone uses, but much stronger. Sometimes they are strong enough to make you feel warm (just like standing in bright sunshine

makes you feel warm). MRI scanners are designed to try to avoid you getting too hot. However, if you start to feel uncomfortable, squeeze the emergency ball and tell the technologist.

Peripheral nerve stimulation (tingling or twitching). The magnetic field inside the scanner changes very quickly while the scanner is running. If it changes too quickly, it can give you tingling sensations or make you twitch. MRI scanners are designed to try to avoid this. However, if you experience tingling or twitching, squeeze the emergency ball and tell the technologist.

Claustrophobia (discomfort in enclosed spaces). Some people get panic attacks inside enclosed spaces. This is called 'claustrophobia', which means 'fear of confined spaces'. If you know that you are claustrophobic, tell study personnel before your scan. Some people only find out they are claustrophobic when they have an MRI for the first time. If you feel anxious or panicky inside the scanner, squeeze the emergency ball and the technologist will get you out.

Quench. In very rare circumstances, the scanner can lose its magnetic field. This happens very suddenly and is known as a 'quench'. The helium that helps keep the magnetic field strong will then escape from the scanner. The scanner is connected to a vent so that the helium will go outside the building. However, if for some reason the vent doesn't work properly, helium might fill the scan room, making it difficult to breathe. In the very unlikely event of a quench, the technologists will get you out of the scanner immediately.

Loss of confidentiality risks. Risks could occur if your information is released by mistake. The measures being taken to protect your privacy are taken seriously and make this possibility unlikely. However, releasing this information to others, such as including it in your medical record, may pose a possible risk of discrimination, or increased difficulty in obtaining or maintaining disability, long-term care, or life insurance.

Unforeseeable Risks. The research may involve risks that are currently unforeseeable.

6. Can I be in the study if I am pregnant or breastfeeding?

You should not become pregnant while taking part in this study because we do not know how the activated vagus nerve stimulator could affect a fetus. Examples of acceptable birth control options include hormonal contraceptives (combined oral contraceptives, patch, vaginal ring, injectable and implants), intrauterine device (IUD), vasectomy, tubal ligation, and complete abstinence. You should not nurse your baby while in this study. Ask about counseling and more information about preventing pregnancy. The study device has not been adequately studied on pregnant women and the effects on the fetus/unborn baby are unknown. After the study, you may opt to keep in the vagus nerve stimulator long-term. It cannot be activated without the external PCM and a smart device to trigger it, which you will not have access to. The risks of an inactive stimulator on fetal health or breastfeeding are unknown.

7. What if new information becomes available?

During the course of this study we may find more information that could be important to you. This includes information that might cause you to change your mind about being in the study. We will notify you as soon as possible if such information becomes available.

In some cases, an imaging scan of will reveal an abnormality with (or without) a clinical significance. Each scan done in this study is reviewed by a licensed radiologist, who might then detect an abnormality. If clinically useful information is uncovered, either the Principal Investigator or another clinician on the study will speak to you in person or on the telephone regarding the new information. The findings will also be included in your medical record, which means that anybody authorized to see your medical record (i.e. your treating doctor) will have access to these findings.

8. What are the possible benefits of the study?

It is possible that some study participants who receive VNS from the ReStore device may experience an improvement in their arm function during the study. However, if you receive such benefit, because the

ReStore device is not FDA-approved for the treatment of stroke impairment, your doctor cannot prescribe it after you finish the study. Also, you may not get any benefit from being in this research study. Others with stroke may benefit in the future from what we learn in this study.

9. What other choices do I have if I do not participate?

You do not have to take part in this research study to be treated for stroke deficits. If you decide not to participate, your decision will not interfere with your future care, payment for your health care, or your eligibility for health care benefits. Other treatments or procedures that are available to treat stroke deficits include:

- VNS with the Transponder VNS system, which is commercially available and has been approved by the FDA, when paired with rehabilitation training, to treat motor deficits after stroke. Surgery and rehabilitation training with the device may be covered by your insurance company. The Transponder VNS system requires the surgical implantation of three components: a stimulating electrode wrapped around the vagus nerve, a battery under the skin on the left chest wall, and wires connecting the two in the neck. By comparison, the ReStore VNS system in this study requires the surgical placement of an electrode on top of the vagus nerve; there is no implanted battery or wires.
- Standard out-patient rehabilitation therapy.

10. Will I be paid for being in this study?

You will be paid \$20 per hour. You will be paid half-way through the study (after about 21 study visits) and at the end of the study (after another 21 study visits). If you choose to leave or are withdrawn from the study for any reason before finishing the entire study, you will be paid for each completed visit.

As is required by the laws that apply to NYU Langone Health, in order for you to receive a payment (i.e. check or ClinCard), you need to give the study staff either your Social Security number or your Alien Registration number and will be asked to complete a W-9 form issued by the Internal Revenue Service (IRS). If you do not have either of these numbers or are not willing to complete the W-9, you may be in the study but will not receive any payment.

We will pay for pre-operative screening tests, the VNS surgery, and your rehabilitation sessions with a certified occupational therapist. We will also pay for your travel costs to and from the study site (e.g. Lyft car services) for your treatment and assessment visits. We will pay to remove the VNS device up to two years after the implantation, if you decide to remove it.

11. Will I have to pay for anything?

You and/or your health insurance may be billed for the costs of medical care during this study if these expenses would have happened even if you were not in the study. If you have health insurance, the cost of these services will be billed to your insurance company. If your insurance does not cover these costs or you do not have insurance, these costs will be your responsibility.

12. What happens if I am injured from being in the study?

For medical emergencies contact 911. If you think you have been injured as a result of taking part in this research study, tell the principal investigator as soon as possible. The principal investigator's name and phone number are listed at the top of page 1 of this consent form.

We will offer you the care needed to treat injuries directly resulting from taking part in this research. We may bill your insurance company or other third parties, if appropriate, for the costs of the care you get for the injury, but you may also be responsible for some of them. There are no plans for NYU Langone Health to pay you or give you other compensation for the injury. You do not give up your legal rights by signing this form.

13. When is the study over? Can I leave the Study before it ends?

This study is expected to end after all participants have completed all visits, and all information has been collected. This study may also be stopped or your participation ended at any time by your physician, the study sponsor, or the U.S. Food and Drug Administration (FDA) without your consent because:

- The principal investigator feels it is necessary for your health or safety. Such an action would not require your consent, but you will be informed if such a decision is made and the reason for this decision.
- You have not followed study instructions.
- The study sponsor, the principal investigator, the FDA, or other body responsible for monitoring the safety of the study has decided to stop the study.

If you decide to participate, you are free to leave the study at any time. Leaving the study will not interfere with your future care, payment for your health care or your eligibility for health care benefits.

If you no longer wish to have us store or share your data and/or specimens for future research studies, you should contact Dr. Schambra. We will do our best to accommodate your request and retrieve any data and/or specimens that have been shared with other researchers. However, there may be circumstances where this is not possible, such as when identifying information has been removed and we are no longer able to identify your data and/or specimens. In addition, if your data and/or specimens have already been used for other research purposes, the information from that study may still be used. We will discard any data and/or specimens we currently have or are able to retrieve.

14. How will you protect my confidentiality?

Your medical information is protected health information, or "PHI," and is protected by federal and state laws, such as the Health Insurance Portability and Accountability Act, or HIPAA. This includes information in your research record as well as information in your medical record at NYU Langone Health. In compliance with NYU Langone Health policies and procedures and with HIPAA, only those individuals with a job purpose can access this information.

Medical information created by this research study may become part of your medical record. We may include your research information in your medical record for several reasons, including for the billing of services provided in connection with the study, to securely document any medical services you receive, and so that other members of the NYU Langone Health community who may treat you have access to important information about your health.

You have a right to access information in your medical record. In some cases, when necessary to protect the integrity of the research, you will not be allowed to see or copy certain information relating to the study while the study is in progress, but you will have the right to see and copy the information once the study is over in accordance with NYU Langone Health policies and applicable law.

Certificate of Confidentiality

To help us further protect your confidentiality, this research is covered by a Certificate of Confidentiality from the National Institutes of Health (NIH). The NIH has issued a Certificate of Confidentiality for this research. This adds special protection for the research information (data, documents, or biospecimens) that may identify you.

Research information protected by this Certificate of Confidentiality cannot be disclosed to anyone else who is not connected with the research, without your consent. With this Certificate of Confidentiality, the researchers may not disclose or use research information that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other action, suit, or proceeding, or be used as evidence, for example, if there is a court subpoena, without your consent. However, disclosure, without your consent, is still necessary if there is a federal, state, or local law that requires disclosure (such as to report child abuse or communicable diseases).

The Certificate of Confidentiality cannot be used to refuse a request for information from appropriate government agencies responsible for project oversight.

The Certificate of Confidentiality does not prevent you from releasing information about yourself and your involvement in this research, including for your medical treatment. Federal regulations may also allow for the use or sharing of information for other scientific research.

By agreeing to be in this research and signing below, you are giving your consent to share research information with others at NYU Langone Health. This means that your research information, including lab results, TMS, MRIs, information about the investigational device used in this study, may be included in your NYU Langone Health electronic medical record.

15. HIPAA Authorization

As noted in the Confidentiality section above, federal law requires us, and our affiliated researchers, health care providers, and physician network to protect the privacy of information that identifies you and relates to your past, present, and future physical and mental health conditions. We are asking for your permission (authorization) to use and share your health information with others in connection with this study – in other words, for purposes of this research, including conducting and overseeing the study.

Your treatment outside of this study, payment for your health care, and your health care benefits will not be affected even if you do not authorize the use and disclosure of your information for this study.

What information may be used or shared with others in connection with this study?

All information in your research record for this study may be used and shared with those individuals listed in this section. Additionally, information in your medical record that the research team believes may be important to the study may be accessed by those listed here. This includes, for example, results from your physical examinations, laboratory tests, questionnaires, and therapy sessions.

Who may use and share information in connection with this study?

No one outside of NYU will have access to your identifiable information without your permission. The following individuals may use, share, or receive your information for this research study:

- The research team at NYU, including the Principal Investigator, trainees, study coordinators, and personnel responsible for the support or oversight of the study
- Affiliated researchers at other institutions who are under the regulatory oversight of their institution's IRB and have a legal data sharing agreement in place with us
- The study sponsor: National Institutes of Health
- Governmental agencies responsible for research oversight (e.g., the U.S. Food and Drug Administration or FDA).
- Health care providers, including your doctors and others who provide services to you in connection with this study, and laboratories or other individuals who analyze your health information in connection with this study.
- Data and Safety Monitoring Board

Your information may be re-disclosed or used for other purposes if the person who receives your information is not required by law to protect the privacy of the information.

What if I do not want to give permission to use and share my information for this study?

Signing this form is voluntary. You do not have to give us permission to use and share your information, but if you do not, you will not be able to participate in this study.

Can I change my mind and withdraw permission to use or share my information?

Yes, you may withdraw or take back your permission to use and share your health information at any time for this research study. If you withdraw your permission, we will not be able to take back information that has already been used or shared with others. To withdraw your permission, send a written notice to

the principal investigator for the study noted at the top of page 1 of this form. If you withdraw your permission, you will not be able to stay in this study.

How long may my information be used or shared?

Your permission to use or share your personal health information for this study will never expire unless you withdraw it.

16. The Institutional Review Board (IRB) and how it protects you

The IRB reviews all human research studies – including this study. The IRB follows Federal Government rules and guidelines designed to protect the rights and welfare of the people taking part in research studies. The IRB also reviews research to make sure the risks for all studies are as small as possible. The NYU Langone Health IRB Office number is 212-263-4110. The NYU Langone Health IRB is made up of doctors, nurses, non-scientists, and people from the community.

17. Who can I call with questions, or if I'm concerned about my rights as a research participant?

If you have questions, concerns or complaints regarding your participation in this research study or if you have any questions about your rights as a research participant, you should speak with the Principal Investigator listed on top of page 1 of this consent form. If a member of the research team cannot be reached or you want to talk to someone other than those working on the study, you may contact the Institutional Review Board (IRB) at (212) 263-4110.

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

NYU Langone Health is committed to providing a safe, productive, and welcoming environment for participants and researchers in all research studies and interactions. All participants will be treated with respect and consideration, and in turn, we ask that you please treat fellow participants and research staff with respect.

Please refer to the NYU Langone [Statement on the Conduct of Participants](#) in Research Studies for further information.

When you sign this form, you are agreeing to take part in this research study as described to you. This means that you have read the consent form, your questions have been answered, and you have decided to volunteer.

Name of Participant (Print)

Signature of Participant

Date

Name of Person Obtaining Consent (Print)

Signature of Person Obtaining Consent

Date

Witness to Consent Process for Non-English-Speaking participants (using a translated consent form OR “Short Form” in participant’s Spoken Language)**Statement of Witness**

As someone who understands both English and the language spoken by the participant, I represent that the English version of the consent form was presented orally to the participant in the participant’s own language, and that the participant was given the opportunity to ask questions.

Name of Witness (Print)

Signature of Witness

Date