Vivistim® SYSTEM

# Vivistim® Paired VNS™ System

## Manual for Patients


## Your Vivistim® System

MicroTransponder

NOTE: This page identifies the parts included in this Patient's Manual. The information contained herein is not intended to serve as a substitute for a complete and thorough understanding of the material presented in all of the manuals for the Vivistim® Paired VNS™ System and its component parts, nor does this represent full disclosure of all pertinent information concerning use of this product, potential safety complications, or efficacy outcomes. Copies of all Vivistim® Paired VNS™ System manuals are included with the system for full disclosure; copies are also available from MicroTransponder, Inc.

26-0002-0004 Rev. 2



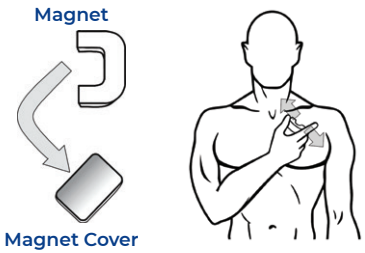
PAT. www.microtransponder.com/patents

Rx Only

# Vivistim® Paired VNS™ System

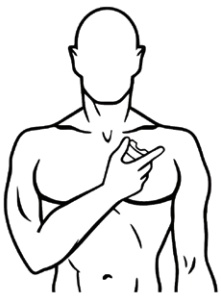
## Quick Start Guide for Patients

1. To turn on your IPG, remove the magnet cover, if applicable, and swipe the magnet once across your chest, above where the IPG is implanted. The IPG will then stimulate your vagus nerve for a therapy session typically lasting 30 minutes.[1] The device will automatically stop stimulation and shut off at the time programmed by your health care provider. NOTE: You may not feel stimulation.




2. To stop the stimulation during a session, hold the magnet over the IPG. Continue holding – it will take approximately 30 seconds for the stimulation to stop. When you remove the magnet, stimulation will continue until your therapy session end time.

3. If you wish to stop the stimulation for the rest of your therapy session, you must hold the magnet over your chest until your therapy session end time.[2]



*Continued on page 4*

[1] Your health care provider may program the session to be shorter or longer than 30 minutes.
[2] For example, if your health care provider programmed the session to last 30 minutes and you started your session at 8:00 am, then your session would end at 8:30 am. If you want to completely stop stimulation starting at 8:20 am, then you would need to hold the magnet in place for 10 minutes, which is until the pre-programmed session time would end at 8:30 am.

| | |
|---|---|
| 4. If you lose your magnet, you will need to contact your clinician for a new one or replace it with a magnet that is strong enough. A commercial magnet with a pull force rated at 4.5 kg or greater is sufficient. | **Magnet Force: 4.5+ kg** |
| 5. The magnet provided to you may damage TVs, computer disks, credit cards, and other items affected by strong magnetic fields | **Please keep the magnet away from such items.** |

Contact your clinician for medical care and medical advice, or if you have any questions about your MicroTransponder® Vivistim® Paired VNS™ System.

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# 1 Your MicroTransponder® Vivistim® Paired VNS™ System

The MicroTransponder® Vivistim® Paired VNS™ System (Vivistim® System) is an active implantable medical device that is made up of 4 main components: (1) an Implantable Pulse Generator (IPG), (2) an implantable Lead, (3) Physician software, and (4) a Wireless Transmitter (WT). The IPG and Lead are the implantable components; the software and WT are the non-implantable components and are used by your clinician only and are not provided to patients.

The (Vivistim® System), when used as intended, provides a drug-free way to treat upper extremity motor deficits associated with stroke by pairing rehabilitation movements with Vagus Nerve Stimulation (VNS); the Vivistim® System delivers a mild electrical pulse to the vagus nerve in your neck. The Lead electrodes are attached to the left vagus nerve in your neck. The Lead is tunneled from the neck to the chest, where it is connected to the IPG, and the IPG is placed subcutaneously (under the skin) or sub-muscularly (under the muscle) in the pectoral region. The software, via the WT, allows the clinician to change the settings of the IPG (e.g., amplitude, frequency, pulse width) and read the status and history of the IPG. The software also stores the number of stimulations, task performed, and IPG status that occur for each rehabilitation activity for future review by the clinician.

The (Vivistim® System) allows the implanted components (the IPG and Lead) to stimulate the vagus nerve while a rehabilitation movement occurs. The therapist initiates the stimulation using a USB push button or mouse click, which synchronizes the stimulation with an appropriate timepoint during your rehabilitation movements. When directed by a clinician and with appropriate programming to the IPG, you can initiate at-home use by swiping a magnet over the IPG implant site. This activates the IPG to deliver stimulation for about 30 minutes while rehabilitation movements are performed. At-home use does not require the use of software or the WT. In addition, the magnet provided to you to initiate home therapy also has a safety feature: holding the magnet over the IPG stops any inadvertent stimulation for as long as it is held over the IPG. You will be trained on how to use the magnet.

The IPG and Lead placement of the Vivistim® System is shown in Figure 1.1.

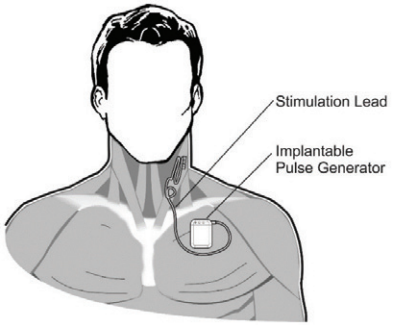


**Figure 1.1:** Device Placement

## 1.1 Symbols and Definitions

This manual and accompanying device labeling use these symbols and definitions.

| | |
|---|---|
| ⚠ | Caution, pay special attention to the information following the symbol |
| **RX only** | For prescription use only |
| | Manufacturer |
| MR | MR Conditional |

# 2 Intended use

The MicroTransponder® Vivistim® Paired VNS™ System is intended to be used to stimulate the vagus nerve during rehabilitation therapy in order to reduce upper extremity motor deficits and improve motor function in chronic ischemic stroke patients with moderate to severe arm impairment.

# 3 Contraindications

**Vagotomy**
The Vivistim® System cannot be used if you have had a left cervical vagotomy.

# 4 Warnings

You should talk to your clinician, physician, or therapist about all potential risks and adverse events discussed in this manual as well as any other concerns you have.

- **Not curative:** The Vivistim® System has not been determined to be a cure for upper extremity motor deficits associated with ischemic stroke. Individual results will likely vary. Beneficial results might not become evident for months or may never occur.

- **Unapproved uses:** The safety and efficacy of the Vivistim® System have not been studied for uses outside of its intended use, and it has not been used in certain patient populations including, but not limited to, people with:

  - Acute suicidal thinking or behavior
  - History of schizophrenia, schizoaffective disorder, or delusional disorders
  - History of rapid cycling bipolar disorder
  - History of previous therapeutic brain surgery or CNS injury
  - Progressive neurological diseases other than stroke
  - Cardiac arrhythmias or other abnormalities
  - History of dysautonomias
  - History of respiratory diseases or disorders, including dyspnea and asthma
  - History of ulcers (gastric, duodenal, or other)
  - History of vasovagal syncope (fainting)
  - Only 1 vagus nerve
  - Other concurrent forms of brain stimulation
  - Pre-existing hoarseness

- **Diathermy:** Inform anyone treating you that you CANNOT have any shortwave diathermy, microwave diathermy, or therapeutic ultrasound diathermy (hereafter referred to as diathermy) because you have an implanted Vivistim® System. It can cause damage to your nerve and/or the device system whether your Vivistim® System is turned "ON" or "OFF". Diagnostic ultrasound is not included in this warning. Check with your clinician if you have questions about this.

- **Worsening depression/suicidality:** Patients being treated with adjunctive Paired VNS™ who have moderate or severe depression should be observed closely for clinical worsening and suicidality. Talk to your doctor if you feel depressed or suicidal.

- **Dysfunctional cardiac conduction systems:** If you have cardiac conduction difficulties, evaluation by a cardiologist is recommended. Please talk to your doctor. Care should be taken if you have cardiac difficulties.

- **Swallowing difficulties:** Difficulty swallowing may occur with active stimulation, and aspiration may result from the increased swallowing difficulties. Patients with pre-existing swallowing difficulties are at greater risk for aspiration. Appropriate aspiration precautions should be taken. Talk to your doctor about this.

- **Dyspnea or shortness of breath:** Shortness of breath may occur at high stimulation settings. Also, if you have underlying pulmonary disease, such as chronic obstructive pulmonary disease or asthma, you may be at increased risk for shortness of breath. Talk to your doctor about this.

- **Obstructive sleep apnea:** As of May 2020, worsened apnea has not been reported with Paired VNS™ but has been reported with VNS Therapy®. People with obstructive sleep apnea (OSA) may have an increase in apneic events during stimulation. Lowering stimulus frequency or increasing the Train Period may prevent exacerbation of OSA. Vagus nerve stimulation may also cause new onset sleep apnea in people who have not previously been diagnosed with this disorder. It is recommended that patients being considered for Paired VNS™ who demonstrate signs or symptoms of OSA, or who are at increased risk for developing OSA, should undergo the appropriate evaluation(s) prior to implantation.

- **Device malfunction:** Device malfunction could cause painful stimulation, inflammation, vocal cord dysfunction, or longer than normal stimulation. Any of these events could cause nerve damage and other associated problems. If you suspect a malfunction, contact your clinician immediately for further evaluation, and do not continue therapy.

- **Magnetic resonance imaging (MRI):** People with the Vivistim® System are able to have MRI under certain conditions. Please contact your doctor if you need an MRI.

- **Device manipulation:** Do not manipulate the IPG or Lead through your skin. Contact your clinician immediately if you notice significant movement of the IPG when you move your arm; this may damage the Lead or your vagus nerve.

- **Surgery:** Post surgery, you may experience pain, swelling, and/or tenderness at the surgery site. Other risks of surgery include bleeding, seroma/hematoma, bruising, permanent numbness or other sensations, vocal cord paralysis (ongoing hoarseness), itching, infection, dry eye and tearing, and allergic response to the implanted materials. Let your surgeon know if you experience any of these symptoms.

- **Medications:** It is possible that some medications may interfere with the mechanism of action of VNS and may impact effectiveness of the therapy. Please talk to your doctor about what medications you are taking and if you should consider switching any that might interfere.

# 5 Precautions

## 5.1 General

- Use during pregnancy—The safety and effectiveness of the Vivistim® System have not been established for use during pregnancy. Contact your clinician if you become pregnant while using the Vivistim® System.

- Do not touch or open your incision sites in order to prevent possible infections. Your surgeon should prescribe antibiotics preoperatively and postoperatively.
- Effects on other medical devices—The Vivistim® System has not been tested with, and may affect the operation of, other implanted devices, such as cardiac pacemakers and implanted defibrillators. Possible effects include, but are not limited to, sensing problems for the other implanted devices and inappropriate device responses.
- Your surgeon may suggest that you use a neck brace for the first week to help ensure proper Lead stabilization.
- Laryngeal irritation may result from stimulation. People who smoke may have an increased risk of laryngeal irritation. Additionally, nicotine may decrease any benefits gained from Paired VNS™; it is recommended that Paired VNS™ patients not smoke.
- Potential effects of Lead breaks—Lead fractures may prevent you from receiving therapy. If a Lead break is suspected, your clinician or therapist can use their Physician software to check this. Contact your clinician if you suspect a Lead break. Replacement surgery may be necessary if a Lead break is suspected.
- Some surgical complications may be associated with damage to the vagus nerve (such as hoarseness or swallowing difficulties). These can occur due to surgery even if your device is functioning properly.
- Hoarseness should be apparent within a few days after implantation (your voice will be hoarse). This may require another surgery, although your system may just be turned off for a few days to see if the hoarseness subsides.
- Persistent hoarseness not associated with stimulation suggests possible nerve irritation; contact your clinician immediately if you have persistent, ongoing hoarseness even when the device is not in use.
- Trauma to the vagus nerve at the implantation site could result in permanent vocal cord dysfunction or other difficulties due to a damaged nerve.
- Do not have metal objects implanted near the IPG or Lead, since they may interfere with device communication or may migrate and damage the IPG or Lead.

## 5.2 Environmental and Medical Therapy Hazards

Please exercise reasonable caution in avoiding devices that generate a strong electric or magnetic field. If your IPG ceases operation while in the presence of a strong electric or magnetic field, moving away from the source may allow it to return to its normal mode of operation.

### 5.2.1 Hospital and Medical Environments

Your Vivistim® System operation should always be checked by your clinician after any of the medical procedures mentioned in this manual. Additional precautions for these procedures are described below.

- If you need imaging in your neck or chest (e.g., for a mammography procedure), notify the technician about your Vivistim® System so that they can take care when positioning you for the image.
- Most routine diagnostic procedures, such as fluoroscopy and radiography, are not expected to affect system operation.
- Therapeutic radiation and nuclear imaging may damage the IPG's circuitry. Sources of such radiation include therapeutic radiation, brachytherapy, stereotactic radiosurgery, cobalt machines, PET scans, and linear accelerators. The radiation effect is cumulative, with the total dosage determining the extent of damage. The effects of exposure to such radiation can range from a temporary disturbance to permanent damage and may not be detectable immediately. Notify your clinician if you are having any of these procedures.
- External defibrillation may damage the IPG. Notify your clinician if you have had defibrillation performed on you.
- Extracorporeal shockwave lithotripsy may damage the IPG. Notify your clinician if you need therapeutic ultrasound.
- Notify your doctor if you need TENS (Transcutaneous Electrical Nerve Stimulation) treatment, FES (Functional Electrical Stimulation), or other treatment where electric current is passed through the body. Although patients have used these treatments without issue in the clinical studies, it is important

not to put the treatment electrodes directly over the device; you may need your IPG checked or monitored during initial stages of treatment.

- Routine therapeutic ultrasound could damage the IPG and may be inadvertently concentrated by the device, causing you harm. Contact your clinician if you need therapeutic ultrasound.
- Other therapies that utilize electrical or RF energy could damage the IPG and may be inadvertently concentrated by the device, causing you harm. If such therapy is required, consult your clinician.
- You should seek medical advice before entering environments that are protected by a warning notice preventing entry by people implanted with a cardiac pacemaker or defibrillator.


**Magnetic Resonance Imaging (MRI) Conditional**

People with the Vivistim® System are able to have MRI under certain conditions. Please contact your doctor if you need an MRI. The specific conditions permitted for MRI procedures with an implanted Vivistim® system are detailed in the manuals provided to your physician.

### 5.2.2 Home Occupational Environments

Properly operating microwave ovens, electrical ignition systems, power transmission lines, theft-prevention devices, and metal detectors are not expected to affect the Vivistim® System. You should exercise reasonable caution in avoiding devices that generate a strong electric or magnetic field. If your stimulator (IPG) ceases operation while in the presence of electromagnetic interference (EMI), moving away from the source may allow it to return to its normal mode of operation.

### 5.2.3 Cellular Phones

Cellular phones should have no effect on Vivistim® System operation.

### 5.2.4 Pressure Hazards

Entering environments where the pressure may exceed 150 kPa absolute pressure may damage the implanted device. To avoid this pressure, do not swim at depths greater than 15 m (50 ft).

### 5.2.5 Contact Sports

Playing certain contact sports (such as boxing) may damage the implanted Vivistim® System.

### 5.2.6 Other Environmental Hazards

Strong magnets, hair clippers, vibrators, loudspeaker magnets, Electronic Article Surveillance (EAS) System tag deactivators, and other similar electrical or electro-mechanical devices, which may have a strong static or pulsing magnetic field, can interact with your device. The magnetic fields could either inadvertently start or stop your therapy (depending on how your clinician programmed the IPG). Keep magnets away from your IPG, typically at least 15 cm (approximately 6 in) away.

**CAUTION:** Do not use the Vivistim® System in an environment where explosive or flammable gases are present.

### 5.2.7 Rehabilitation Equipment

Passive hand/arm splints have been used safely with the Vivistim® System by patients in the clinical studies. Please contact your Vivistim® System clinician if you wish to use electric stimulation therapies such as FES and TENS combined with the Vivistim® System.

### 5.3 Implantable Pulse Generator (IPG) and EMI Effects on Other Devices

The IPG may affect the operation of other implanted devices, such as cardiac pacemakers and implantable defibrillators. Possible effects include sensing problems for the other implanted devices and inappropriate device responses.

The magnet provided to you to start and stop at-home therapy may damage televisions, computer disks, credit cards, and other items affected by strong magnetic fields. Please keep the magnet away from such items.

# 6 Your Vivistim® System


**Figure 6.1:** Vivistim® System IPG and Lead

- The IPG, sometimes called a stimulator, is a small, battery-powered electronic device that is implanted inside the body.
- The Lead connects the IPG to the vagus nerve. It is attached to the vagus nerve on the left side of the neck.
- The Lead and IPG are implanted during an operation that often lasts 1-2 hours.

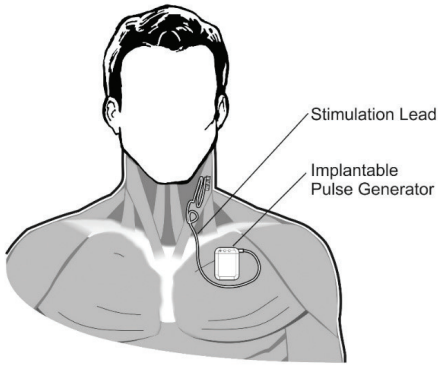


**Figure 6.2:** Device Placement

# 7 Applicable Commercial Devices for Use with Vivistim® System

A commercial magnet with a pull force rated at 4.5 kg is sufficient to close the reed switch within the IPG. Closing the reed switch stops stimulation (holding the magnet over the IPG); closing and opening the reed switch (swiping the magnet) can start stimulation (with appropriate IPG programming by the clinician) as described in the Directions for Use section.

Contact your clinician if you have questions about the magnet.

# 8 Directions for Use

You shall perform at-home therapy as directed by your physician or therapist.

Verify that you can use your magnet appropriately during the first session with your clinician when stimulation is started. Also verify that you are given a magnet to take home for this use.

## 8.1 How to Start Therapy at Home

For at-home therapy, the IPG is typically programmed by your physician or therapist to deliver stimulation for 30 minutes once it is triggered by a magnet swipe. Stimulation begins immediately following the magnet swipe.

You may or may not feel the stimulation based on the programmed settings of your IPG or whether or not you have grown accustomed to the stimulation.

Begin your rehabilitation tasks immediately after the magnet swipe and continue your rehabilitation tasks throughout the duration (~30 minutes) of the stimulation per your physician's or therapist's instructions. Contact your physician or therapist right away if there is any discomfort or concern with the stimulation.

The stimulation can be stopped by using the magnet. See the **How to Stop the Stimulation** section.

**NOTE:** To begin the stimulation, remove the magnet cover, if applicable, and swipe the magnet across your chest where the IPG is located. Since you are starting the stimulation, do not hold the magnet in place over the IPG for more than 30 seconds. Doing so will temporarily stop stimulation.

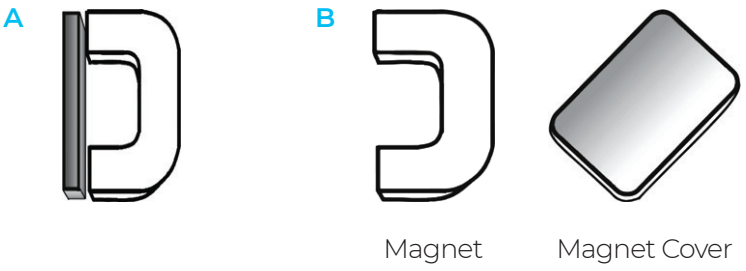


**Figure 8.1:** Magnet with Cover Attached (A) and Detached (B)

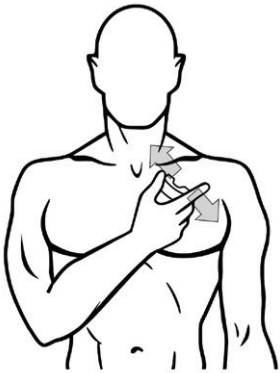

**Figure 8.2:** Magnet Swipe

## 8.2 How to Stop the Stimulation

In the event that stimulation is too strong or becomes uncomfortable for any reason, including IPG malfunction, you can stop the stimulation by holding the magnet over the IPG (see next paragraph). Your physician or therapist will also have a magnet available. To stop stimulation, place the magnet over your chest where the IPG is located and hold it in place. After 30 seconds, the stimulation will stop. When you remove the magnet, stimulation will continue until your therapy session end time.

To stop the stimulation for the rest of your therapy session, you must hold the magnet over your chest until your therapy session end time.

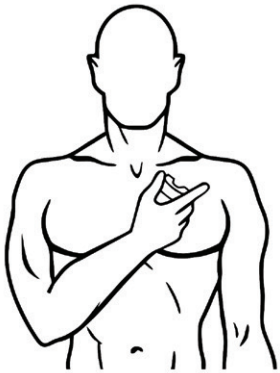

**Figure 8.3:** Hold Magnet

**NOTE:** To stop stimulation, hold the magnet to your chest where the IPG is located. Continue holding – it will take approximately 30 seconds for the stimulation to stop.

If stimulation does not stop after you have held the magnet in place for greater than 30 seconds, you should contact your physician, clinician, or therapist for an immediate appointment so that the device can be deactivated and tested further to ensure it is functioning properly.

**CAUTION:** In the event that you hold the magnet in place for greater than 30 minutes and stimulation comes back after you have removed the magnet from your chest, hold or tape the magnet over your chest again, where the IPG is located, to stop the stimulation. The magnet should be held in place and your physician contacted for further instruction. In this situation, stimulation will be stopped for as long as the magnet is held in place.

# 9 Guidelines for Follow-up

## 9.1 Follow-up After Surgery

During the first few weeks after implantation, you should be seen by your clinician to confirm wound healing and proper Vivistim® System operation. Your clinician will determine your settings. Although there are target settings, your clinician will set the device to tolerable settings. In fact, there is some evidence that more stimulation is not necessarily better.

Your clinician will work with you to set your rehabilitation session schedule. Your therapist will work with you to do rehabilitation movements and will start VNS while you are in the clinic. The clinician or therapist will give you proper training on how to use the magnet to initiate stimulation. See the **How to Start Therapy at Home** section of this manual.

### 9.2 After Treatment Begins

Call your doctor right away if any of the following occur:

- Your voice is constantly hoarse.
- The stimulation becomes painful or irregular.
- The stimulation causes any choking, trouble with breathing, trouble with swallowing, or change in heart rate.
- You or someone else notices changes in your level of consciousness (e.g., you become constantly drowsy).
- You notice anything new or unusual that you relate to the stimulation.
- The feeling that you usually have during stimulation becomes stronger or weaker.

## 10 Device Lifetime

### 10.1 IPG Lifetime, Removal, and Replacement

The anticipated life of the IPG battery varies, depending on the IPG settings and the interaction of the Lead and vagus nerve over time. At typical settings, the battery is predicted to last approximately 5 years. Your specific situation and settings may result in shorter or longer battery life.

During your visits to your clinician, the clinician will use their Physician software to check the status of your IPG. The software will display warning messages if the battery is nearing its depletion.

All MicroTransponder IPGs eventually require surgical replacement as a result of battery depletion. When the battery is depleted, communication with the IPG or continued treatment will not be possible. IPG replacement does not, of itself, require Lead replacement unless a Lead discontinuity (a break) is suspected. IPG replacement or removal requires an additional surgery to open of the IPG's pocket in your chest,

with care being taken not to damage or cut the Lead. Replacement of the IPG typically requires 60 minutes or less. Contact your clinician to discuss removal or replacement of your IPG.

### 10.2 Lead Lifetime, Removal, and Replacement

A Lead requires replacement when a Lead discontinuity (a break) is suspected. Events in your control that can shorten the life expectancy of the Lead are as follows:

- Blunt trauma to the neck and/or any area of the body beneath which the Lead is implanted
- Twisting or picking (Twiddler's Syndrome) at either the implanted Lead or the IPG

**CAUTION:** Lead replacement or removal—Replacing or removing Leads because of lack of efficacy is a medical judgment that includes your desires and health status and must be carefully weighed against the known and unknown risks of surgery. At present, no known long-term hazards or risks are associated with leaving the Lead implanted, beyond those already mentioned in this manual. All precautions and contraindications still should be observed.

Contact your clinician to discuss removal or replacement of your Lead.

## 11 Study Information

Three studies (MT-St-01, MT-St-02 and MT-St-03) have been performed on the MicroTransponder® Vivistim® System. The first 2 studies were smaller pilot studies with 9 and 17 patients implanted with the device. Since these 2 studies were positive a larger study (Study MT-St-03) of 108 implanted subjects at 19 study sites (14 US, 5 UK) was performed.

Talk to your clinician or doctor if you have questions about the Vivistim® System clinical study results. The studies provided evidence of safety and efficacy so that the device is commercially available. The studies showed that VNS plus rehabilitation provides about twice the benefit of rehabilitation alone.

# 12 Safety Information

This section discusses events reported as of May 2020.

## 12.1 Extent of Exposure

The data from all 108 implanted patients were analyzed for safety effects. At the time of this analysis, these patients were exposed to the device for an average of 14.5 months each (range 0.52 to 28.8) and a total exposure of more than 100 years.

## 12.2 Adverse Events (AEs)

This type of device and surgery are similar to a device and surgery used for epilepsy and depression since 1997. Since this similar device has been used for a long time and in many patients, it is useful to review what type of events occur with that device and surgery.

The typical expected events seen in VNS for epilepsy or depression would be the type seen in any surgery – pain and bruising at an incision site, any effects of anesthesia, the possibility of infection due to the surgery or implant, and the possibility of any problems from the actual surgery (e.g., nerve damage when the electrode is placed). The typical types of events seen from VNS usage (stimulation) are hoarseness, coughing, shortness of breath, neck pain, swallowing difficulty, throat pain, skin tingling, and nausea. The events discussed below are those actually reported during the pivotal study already discussed.

### 12.2.1 Summary of Adverse Events from MT-St-03

Most patients (79%) reported some adverse events during the study, although most were not related to VNS and most were only mild or moderate. No new or unexpected events were reported. Most events were either unrelated to surgery or stimulation; where events were at least possibly related, most were thought due to surgery.

There was only 1 serious adverse event (SAE) due to surgery – 1 patient experienced dysphonia (from vocal cord paresis) due to the implant surgery. The dysphonia (sustained hoarseness) was reported as resolved after approximately 5 weeks and was verified as resolved via videoendoscopy a couple of months later. This is the only major event reported due to the device therapy (VNS) or surgery. Other reported serious events were either related to the patient's underlying condition (stroke or other comorbid issue) or unrelated to VNS (such as a fall or a UTI). None of the serious events are ongoing. One patient who was thin did decide to withdraw because the IPG (stimulator) bothered him where it was placed in his chest.

The only events reported in more than 5% of VNS subjects were pain due to implant (22.6%), bruise/fall (11.3%), general pain (9.4%), muscle pain (9.4%), general hoarseness (7.5%), fracture (7.5%), headache (5.7%), hoarseness after surgery (5.7%), rash (5.7%), low mood (5.7%), dizziness (5.7%), throat irritation (5.7%), UTI (5.7%), and fatigue (5.7%). Most events resolved within a few weeks of the surgery and therapy initiation.

### 12.2.2 Other Information

VNS did not have any negative impact on weight, heart rate, blood pressure, or temperature. VNS subjects did have a slight reduction in their average depression score when compared to the control group.

## 12.3 Device Performance

No significant IPG (stimulator) complications were reported. Two subjects had Leads that indicated high-impedance within about 1 week of original surgery and had replacement surgeries (a second surgery was required). Communication issues were resolved by repositioning the WT or patient location or by restarting the computer

and software. Most device issues were resolved on the day of the initial report. Very few issues were reported overall, and none impacted the study data. Your clinician should have a back-up transmitter and software to use if needed.

## 12.4 Safety Conclusion

Adverse events were as expected based on the pilot studies and less than the reported rates in VNS for epilepsy and depression. In general, adverse events were mild or moderate, transient, and well tolerated. Most patients could not feel stimulation or barely noticed stimulation, especially after the first few days of treatment. Most events resolved within a few weeks of the surgery and therapy initiation. There were no significant adverse events related to the device reported during randomized phase or long-term portion of the study; the only significant event reported due to implant surgery was a report of dysphonia (vocal cord paresis) that recovered within about 5 weeks after surgery. This type of event (hoarseness or dysphonia associated with implant surgery) is expected and appears to occur in about 1 out of every 100 surgeries of this type.

No new event types due to surgery or stimulation were seen, and no unanticipated events were reported. Subjects did experience the typical pain, swelling, and bruising after surgery. No significant events related to stimulation were reported.

No long-term events appear to be related to the device use or surgery; events are typically due to the patients' ongoing condition. There were no serious events reported as related to stimulation.

In summary, the safety results from this study are consistent with those already known to exist for vagus nerve stimulation and its implant surgery. The results support the safety of Paired VNS™ using the Vivistim® System for upper limb improvements after an ischemic stroke.

# 13 Counseling Information

In the unlikely event of uncomfortable adverse events, continuous stimulation, or other malfunction, you should first stop stimulation. See the **How to Stop the Stimulation** section of this manual. If any event continues, hold or tape the magnet directly over the implanted IPG to prevent additional stimulation; then notify your clinician immediately.

Remember, do not manipulate the device or Lead through your skin, as this could damage the device. Pulling on the Lead may move the electrode from your nerve and cause possible nerve damage. Additionally, do not pick at your surgical scars, as this may cause infection.

# 14 Information About Surgery

Surgical side effects are discussed above. Surgery itself often lasts 1-2 hours, depending on the surgeon and on your specific anatomy. Each person's anatomy is slightly different.

Your doctor should have you take antibiotics before and after surgery. If it matters to you, you should talk to your doctor about the scars and exactly where your device is placed. It is your surgeon's decision about placement and scar location, but they may be able to accommodate your preference. Your doctor may want you to limit activity or wear a neck brace for a few days after surgery to ensure that your recovery goes smoothly. Surgery is typically performed using general anesthesia. Depending on your recovery and anesthesia effects, you may be released from the hospital within a few hours after surgery; most people are released the same day or after an overnight stay (within 24 hours).

# 15 MRI Guidance

Non-clinical testing has demonstrated that the Vivistim® System is Magnetic Resonance Imaging (MRI) Conditional (MR Conditional). This means MRI may be performed under certain conditions. However, these conditions are very specific – so, unless they are met exactly, MRI should not be performed.

The Vivistim® system is designated as an MR Conditional device that has been demonstrated to present no known hazards when exposed to a specific magnetic resonance (MR) environment that meets specific conditions of use as described in the manuals provided to your physician. Do not have an MRI without guidance from the physician you work with on the Vivistim® system.

**MR UNSAFE:** Do not carry metal (for example magnets, jewelry, etc.) into the MR scanner room. Metal objects can become dangerous flying objects if attracted by the strong magnetic field of the MRI scanner.

**CAUTION:** Potential risks of performing MRI with your implanted Vivistim® system include:

- Movement, vibration, or rotation of the IPG, resulting in discomfort during the MRI scan
- Lead electrode or IPG heating, resulting in patient discomfort, tissue damage, or serious injury
- Functional impairment of the IPG, sustained beyond the end of an MRI-scanning session
- Unintended stimulation during the MRI scan
- Image distortion and artifacts of IPG and Lead over regions where diagnostic information required

**CAUTION:** If during the MRI scan, you have any pain, discomfort, heating, or other unusual sensations, notify the MRI operator so the MR procedure can be stopped immediately.

# 16 Information and Support

**MicroTransponder, Inc.**
2802 Flintrock Trace, Suite 226
Austin, TX 78738
www.microtransponder.com
info@microtransponder.com
Phone: (855) 628-9375

# 17 Glossary

**AE (Adverse Event):** Any symptom, sign, illness, or experience that develops or worsens in severity and/or frequency during the course of the study (i.e., any changes from baseline).

**Electrode:** The mechanical and electrical interface of the Vivistim® System to the vagus nerve. The electrode is part of the Lead.

**EMI:** Electromagnetic interference

**High Lead Impedance:** Any impedance above 10,000 Ω is considered high. High Lead impedance can be caused by any of the following: possible fibrosis between the nerve and electrode, dry nerve (during surgery), Lead fracture, Lead disconnection from the IPG, or high battery impedance approaching end of life (EOL).

**IPG (Implantable Pulse Generator):** The stimulator portion of the Vivistim® System, typically implanted in the chest below the left clavicle. The IPG provides stimulation to the vagus nerve through a connected Lead and Lead electrodes.

**Lead:** An implantable part of the Vivistim® System; delivers electrical impulses from the IPG to the electrodes attached to the vagus nerve; contains flexible conductive wires within a bio-compatible insulating sheath.

**Low Lead Impedance:** Lower than expected resistance to the flow of output current produced by the IPG potentially caused by a short-circuit condition resulting from a break within the Lead body insulation or connector insulation.

**Magnet:** A magnet is provided to allow people to start stimulation at their home (a swipe over the device will start a 30-minute stimulation session). When placed over the device and left in place, the magnet stops all stimulation. This second use is a safety feature (can stop stimulation if it is bothersome).

**MRI:** Magnetic Resonance Imaging

**MR Conditional:** Item that has been demonstrated to pose no known hazards in a specified MR environment with specified conditions of use.

**MR Unsafe:** An item that poses hazards in all MRI environments.

**Paired VNS™:** VNS delivered by the MicroTransponder Paired VNS™ System. The Vivistim® System pairs VNS with standard rehabilitation therapy.

**Pulse Width:** Duration of a single pulse within a train of stimulation; measured in μs.

**SAE (Serious Adverse Event):** Any adverse event that resulted in any of the following outcomes: death, a life-threatening adverse experience, in-patient hospitalization or prolongation of existing hospitalization, a persistent or significant disability/incapacity, a congenital anomaly/birth defect, or any medical intervention that prevents one of the above.

**Vivistim®:** Trade name of the Vivistim® System intended to reduce upper extremity motor deficits and improve motor function associated with ischemic strokes.

**Train:** Duration (in seconds) that the signal frequency is output from the IPG.

**Vagus nerve:** Either of the pair of tenth cranial nerves arising from the medulla and supplying mainly the viscera, especially with autonomic sensory and motor fibers.

**VNS:** Vagus Nerve Stimulation

**VNS Therapy®:** VNS delivered by the LivaNova/Cyberonics VNS Therapy® System. Paired VNS™ is delivered by the MicroTransponder® Vivistim® System.

**WT (Wireless Transmitter):** A radio frequency device that is used in conjunction with the Physician software to provide communication with the IPG.

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**MR Conditional Device:**
This person is implanted with a Paired VNS™ System. MRI can be safely performed but only under very specific conditions. Scanning under different conditions may result in severe patient injury or device malfunction. The programming physician is required to program the device before and after a MRI. Full MRI information is available in the Healthcare Professionals Manual and at www.microtransponder.com.

**To stop the stimulation:** Place the magnet over the patient's chest where the IPG is located and hold the magnet in place for at least 30 seconds. Stimulation may resume if magnet is removed depending on device settings.
**In an emergency:** Contact a physician and call the local emergency number or go to nearest emergency room.
**MicroTransponder® cannot provide medical care or advice**
Healthcare providers may contact MicroTransponder® for more information.
www.microtransponder.com

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Vivistim® SYSTEM

**Have a question?**

Contact a Vivistim representative or visit **Vivistim.com**

info@vivistim.com
**(855) 628-9375**

Vivistim®

## Patient Identification Card

This person is implanted with a vagus nerve stimulator

Name of Patient: _____

| | Model | Serial # | Implantation Date |
|---|---|---|---|
| **Generator** | | | |
| **Lead** | | | |

Physician Name: _____

Phone Number: _____

Implanting Center: _____

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