



Introduction to the VNS Therapy[®] System

Indications, Contraindications, Warnings, and Precautions

For Healthcare Professionals

April 2010

U.S. Version

Caution: U.S. federal law restricts this device to sale by or on the order of a physician.

Note: This is one part of a multi-part physician'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 physician's manual sections for the VNS Therapy 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.

Table of Contents

1. BRIEF DEVICE DESCRIPTION	5
1.1. Symbols and Definitions	5
2. INTENDED USE / INDICATIONS	6
2.1. Depression	6
2.2. Epilepsy	6
3. CONTRAINDICATIONS	7
4. WARNINGS	8
5. PRECAUTIONS	12
5.1. General	12
5.2. Sterilization, Storage, and Handling	14
5.3. Lead Evaluation and Connection	16
5.4. Environmental and Medical Therapy Hazards	16
5.4.1. Hospital and medical environments	16
5.4.2. Home occupational environments	18
5.4.3. Cellular phones	18
5.4.4. Other environmental hazards	18
5.4.5. Programming Software	18
5.4.6. Pulse Generator and EMI effects on other devices	18
5.4.7. Effects on ECG monitors	19
5.4.8. Pulse Generator disposal	19
6. INFORMATION AND SUPPORT	20

List of Figures

FIGURE 1	ECG ARTIFACT PRODUCED BY PULSE GENERATOR COMMUNICATION	19
----------	---	----

1. BRIEF DEVICE DESCRIPTION _____

The Cyberonics® VNS Therapy® System, used for vagus nerve stimulation (VNS), consists of the implantable VNS Therapy Generator, Lead, and external programming system used to change stimulation settings. The Pulse Generator is an implantable, multiprogrammable pulse generator that delivers electrical signals to the vagus nerve. The Pulse Generator is housed in a hermetically sealed titanium case and is powered by a single battery. Electrical signals are transmitted from the Pulse Generator to the vagus nerve by the Lead. The Lead and the Pulse Generator make up the implantable portion of the VNS Therapy System.

Note: See the Programming Software physician's manual for a list of compatible computers.

The external programming system includes the Programming Wand, the Software, and a compatible computer. This Software allows a physician to place the Programming Wand over the Pulse Generator to read and change device settings.

1.1. Symbols and Definitions

This multi-part physician's manual and accompanying device labeling use these symbols and definitions:



Notice for reader to pay special attention to details that follow



Serial Number



Expiration Date (last day of indicated month)



Single Use Only / Do Not Reuse



Date of Manufacture



Storage Temperature



Contents Sterilized by Ethylene Oxide



Contents Sterilized by Hydrogen Peroxide



Consult Instructions for Use



Sidebar Note (cross-references and other useful information)

2. INTENDED USE / INDICATIONS _____

2.1. Depression

The VNS Therapy System is indicated for the adjunctive long-term treatment of chronic or *recurrent depression* for patients 18 years of age or older who are experiencing a major depressive episode and have not had an adequate response to four or more adequate *antidepressant treatments*.



Note: See the *Glossary* part of this multi-part physician's manual for a definition of terms.

2.2. Epilepsy

The VNS Therapy System is indicated for use as an adjunctive therapy in reducing the frequency of seizures in adults and adolescents over 12 years of age with partial onset seizures that are refractory to antiepileptic medications.

3. CONTRAINDICATIONS _____

- **Vagotomy**—The VNS Therapy System cannot be used in patients after a bilateral or left cervical vagotomy.
- **Diathermy**—Do not use shortwave diathermy, microwave diathermy, or therapeutic ultrasound diathermy (hereafter referred to as diathermy) on patients implanted with a VNS Therapy System. Diagnostic ultrasound is not included in this contraindication.

Energy delivered by diathermy may be concentrated into or reflected by implanted products such as the VNS Therapy System. This concentration or reflection of energy may cause heating.

Testing indicates that diathermy can cause heating of the VNS Therapy System well above temperatures required for tissue destruction. The heating of the VNS Therapy System resulting from diathermy can cause temporary or permanent nerve, tissue, or vascular damage. This damage may result in pain or discomfort, loss of vocal cord function, or even possibly death if there is damage to blood vessels.

Because diathermy can concentrate or reflect its energy off any size implanted object, the hazard of heating is possible when any portion of the VNS Therapy System remains implanted, including just a small portion of the Lead or electrode. Injury or damage can occur during diathermy treatment whether the VNS Therapy System is turned “ON” or “OFF.”

Diathermy is further prohibited because it may also damage the VNS Therapy System components resulting in loss of therapy, requiring additional surgery for system explantation and replacement. All risks associated with surgery or loss of therapy (loss of seizure control) would then be applicable.

Advise your patients to inform all their healthcare professionals that they should not be exposed to diathermy treatment.

4. WARNINGS

Physicians should inform patients about all potential risks and adverse events discussed in the VNS Therapy System physician's manuals.

- **Use (depression)**—This device is a permanent implant. It is only to be used in patients with severe depression who are unresponsive to standard psychiatric management. It should only be prescribed and monitored by physicians who have specific training and expertise in the management of treatment-resistant depression and the use of this device. It should only be implanted by physicians who are trained in surgery of the carotid sheath and have received specific training in the implantation of this device.
- **Use (epilepsy)**—The VNS Therapy System should only be prescribed and monitored by physicians who have specific training and expertise in the management of seizures and the use of this device. It should only be implanted by physicians who are trained in surgery of the carotid sheath and have received specific training in the implantation of this device.
- **Not curative (depression)**—Physicians should warn patients that VNS Therapy has not been determined to be a cure for depression. Patients should be counseled to understand that individual results will likely vary. Beneficial results might not become evident for months. Most patients will continue to require antidepressant medications and/or electroconvulsive therapy (ECT) in addition to VNS Therapy.
- **The VNS Therapy device is not curative (epilepsy)**—Physicians should warn patients that VNS Therapy is not a cure for epilepsy and that since seizures may occur unexpectedly, patients should consult with a physician before engaging in unsupervised activities, such as driving, swimming, and bathing, and in strenuous sports that could harm them or others.
- **Unapproved uses**—The safety and efficacy of the VNS Therapy System have not been established for uses outside the “Intended Use / Indications” section of this multi-part physician's manual, including (but not limited to) patients with:
 - ◆ Acute suicidal thinking or behavior (depression)
 - ◆ History of schizophrenia, schizoaffective disorder or delusional disorders (depression)
 - ◆ History of rapid cycling bipolar disorder (depression)
 - ◆ History of previous therapeutic brain surgery or CNS injury


- ◆ Progressive neurological diseases other than epilepsy or depression
- ◆ 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
- ◆ Only one vagus nerve
- ◆ Other concurrent forms of brain stimulation
- ◆ Pre-existing hoarseness
- ◆ Under 12 years of age (epilepsy)
- ◆ Under 18 years of age (depression)
- ◆ Primary generalized seizures
- **Worsening depression/suicidality (depression)**—Patients being treated with adjunctive VNS Therapy should be observed closely for clinical worsening and suicidality, especially at the time of VNS Therapy stimulation parameter changes or drug or drug dose changes, including either increases or decreases in the stimulation parameters or concomitant treatments. Consideration should be given to changing the therapeutic regimen of VNS Therapy or concomitant treatments, including possibly discontinuing VNS Therapy or the concomitant therapy, in patients whose depression is persistently worse or whose emergent suicidality is severe, abrupt in onset, or was not part of the patient’s presenting symptoms.
- **Dysfunctional cardiac conduction systems**—The safety and effectiveness of the VNS Therapy System in patients with predisposed dysfunction of cardiac conduction systems (re-entry pathway) have not been established. Evaluation by a cardiologist is recommended if the family history, patient history, or electrocardiogram suggests an abnormal cardiac conduction pathway. Serum electrolytes, magnesium, and calcium should be documented before implantation. Additionally, postoperative bradycardia can occur among patients with certain underlying cardiac arrhythmias. Post-implant electrocardiograms and Holter monitoring are recommended if clinically indicated.
- It is important to follow recommended implantation procedures and intraoperative product testing described in the *Implantation Procedure* part of this multi-part physician’s manual. During the intraoperative


System Diagnostics (Lead Test), infrequent incidents of bradycardia and/or asystole have occurred. If asystole, severe bradycardia (heart rate < 40 bpm), or a clinically significant change in heart rate is encountered during a System Diagnostics (Lead Test) or during initiation of stimulation, physicians should be prepared to follow guidelines consistent with Advanced Cardiac Life Support (ACLS).

Additionally, postoperative bradycardia can occur among patients with certain underlying cardiac arrhythmias. If a patient has experienced asystole, severe bradycardia (heart rate < 40 bpm), or a clinically significant change in heart rate during a System Diagnostics (Lead Test) at the time of initial device implantation, the patient should be placed on a cardiac monitor during initiation of stimulation.

The safety of this therapy has not been systematically established for patients experiencing bradycardia or asystole during VNS Therapy System implantation.

- **Swallowing difficulties**—Difficulty swallowing (dysphagia) 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 for such patients.
- **Dyspnea or shortness of breath**—Dyspnea (shortness of breath) may occur with active VNS Therapy. Any patient with underlying pulmonary disease or insufficiency, such as chronic obstructive pulmonary disease or asthma, may be at increased risk for dyspnea and should have their respiratory status evaluated prior to implantation and monitored following initiation of stimulation.
- **Obstructive sleep apnea**—Patients with obstructive sleep apnea (OSA) may have an increase in apneic events during stimulation. Lowering stimulus frequency or prolonging “OFF” time may prevent exacerbation of OSA. Vagus nerve stimulation may also cause new onset sleep apnea in patients who have not previously been diagnosed with this disorder. It is recommended that patients being considered for VNS Therapy 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 or direct current stimulation. Either event could cause nerve damage and other associated problems. Patients should be instructed to use the Magnet to stop stimulation if they suspect a malfunction, and then to contact their physician immediately for further evaluation. Prompt surgical intervention may be required if a malfunction occurs.

 **Note:** See the *MRI with the VNS Therapy System* part of this multi-part physician's manual for details.

 **Note:** Use of the Magnet to activate stimulation is not recommended for patients with depression. The Magnet Mode output current should remain at 0.0mA for patients with depression.

- **MRI**—Patients with the VNS Therapy System or any part of the VNS Therapy System implanted should not have full body MRI. Additional surgery may be required to remove the VNS Therapy system if full body MRI is required.
- **Excessive stimulation**—Excessive stimulation at an excess duty cycle (that is, one that occurs when “ON” time is greater than “OFF” time) has resulted in degenerative nerve damage in laboratory animals. An excess duty cycle can be produced by continuous or frequent Magnet activation (> 8 hours), as determined by animal studies. Do not stimulate at these combinations of ranges.
- **Device manipulation**—Patients who manipulate the Pulse Generator and Lead through the skin (Twiddler’s Syndrome) may damage or disconnect the Lead from the Pulse Generator and/or possibly cause damage to the vagus nerve. Patients should be warned against manipulating the Pulse Generator and Lead.
- **Sudden unexplained death in epilepsy (SUDEP)**—Through August 1996, 10 sudden and unexplained deaths (definite, probable, and possible) were recorded among the 1,000 patients implanted and treated with the VNS Therapy device. During this period, these patients had accumulated 2,017 patient-years of exposure.

Some of these deaths could represent seizure-related deaths in which the seizure was not observed, at night, for example. This number represents an incidence of 5.0 definite, probable, and possible SUDEP deaths per 1,000 patient-years.

Although this rate exceeds that expected in a healthy (nonepileptic) population matched for age and sex, it is within the range of estimates for epilepsy patients not receiving vagus nerve stimulation, ranging from 1.3 SUDEP deaths for the general population of patients with epilepsy, to 3.5 (for definite and probable) for a recently studied antiepileptic drug (AED) clinical trial population similar to the VNS Therapy System clinical cohort, to 9.3 for patients with medically intractable epilepsy who were epilepsy surgery candidates.

5. PRECAUTIONS

Physicians should inform patients about all potential risks and adverse events discussed in the VNS Therapy System physician's manuals.

5.1. General

- Appropriate physician training is very important.
 - ◆ **Prescribing physicians** should be experienced in the diagnosis and treatment of depression or epilepsy and should be familiar with the programming and use of the VNS Therapy System.
 - ◆ **Physicians who implant the VNS Therapy System** should be experienced performing surgery in the carotid sheath and should be trained in the surgical technique relating to implantation of the VNS Therapy System.
- **Use during pregnancy**—The safety and effectiveness of the VNS Therapy System have not been established for use during pregnancy. There are no adequate and well-controlled studies of VNS Therapy in pregnant women. Reproduction studies have been performed using female rabbits stimulated with the commercially available VNS Therapy System at stimulation dose settings similar to those used for humans. These animal studies have revealed no evidence of impaired fertility or harm to the fetus due to VNS Therapy. Because animal reproduction studies are not always predictive of human response and animal studies cannot address developmental abnormalities, VNS Therapy should be used during pregnancy only if clearly needed. Although the operating ranges of the VNS Therapy System and fetal monitors are dissimilar and no interaction would be expected, testing has not been performed. Therefore, the potential may exist for interaction between the VNS Therapy System and fetal monitoring systems.
- The VNS Therapy System is indicated for use only in stimulating the left vagus nerve in the neck area inside the carotid sheath. The VNS Therapy System is indicated for use only in stimulating the **left vagus nerve below where the superior and inferior cervical cardiac branches separate from the vagus nerve**. The safety and efficacy of the VNS Therapy System have not been established for stimulation of the right vagus nerve or of any other nerve, muscle, or tissue.
- It is important to follow infection control procedures. Infections related to any implanted device are difficult to treat and may require that the device be explanted. The patient should be given antibiotics preoperatively. The surgeon should ensure that all instruments are sterile prior to the operation.

Frequent irrigation of both incision sites with generous amounts of bacitracin or equivalent solution should be performed prior to closure.



Note: See the “Physician Training/Information” section of the *Implantation Procedure* part of this multi-part physician's manual.

To minimize scarring, these incisions should be closed with cosmetic closure techniques. Also, antibiotics should be administered postoperatively at the discretion of the physician.

- **Effects on other medical devices**—The VNS Therapy System may affect the operation of other implanted devices, such as cardiac pacemakers and implanted defibrillators. Possible effects include sensing problems and inappropriate device responses. If the patient requires concurrent implantable pacemaker, defibrillator therapy, or other types of stimulators, careful programming of each system may be necessary to optimize the patient’s benefit from each device. Furthermore, when the VNS Therapy System and another stimulator are implanted in the same patient, the two stimulators should be placed at least 10 centimeters (4 inches) apart to avoid communication interference. Users should refer to the product labeling for the concurrent device to determine if there are additional precautions that should be observed.
- **Reversal of Lead polarity has been associated with an increased chance of bradycardia** in animal studies. It is important that the electrodes are attached to the left vagus nerve in the correct orientation. It is also important to make sure that Leads with dual connector pins are correctly inserted (white marker band/serial number to + connection) into the Pulse Generator’s Lead receptacle(s).
- The patient can use a neck brace for the first week to help ensure proper Lead stabilization.
- **Do not program the VNS Therapy System to an ON or periodic stimulation treatment for at least 14 days after the initial or replacement implantation.** Failure to observe this precaution may result in patient discomfort or adverse events.
- Do not use frequencies of 5 Hz or below for long-term stimulation. Because these frequencies generate an electromagnetic trigger signal, their use results in excessive battery depletion of the implanted Pulse Generator and, therefore, should be used for short periods of time only.
- Resetting the Pulse Generator turns the device OFF (output current = 0.0 mA), and all device history information is lost. The device history information should be printed out before resetting.
- Laryngeal irritation may result from stimulation. Patients who smoke may have an increased risk of laryngeal irritation.
- The Lead is available in multiple sizes. Since it is not possible to predict in patients what size Lead will be needed, **Cyberonics recommends that at least one alternate Lead size be available in the operating room.** In addition, backups for Leads should be available in the event of compromised sterility or damage induced during surgery.
- Because the VNS Therapy Lead is an integral component of the VNS Therapy System, the indications, contraindications, and possible



Note: For Lead size availability, see the “Product Specifications” section in the *Technical Information* parts of the Lead physician’s manuals.

complications and adverse events associated with its use are identical to those described in the Physician’s Manual for the Pulse Generator. Possible adverse events specifically related to the Lead include migration, dislodgment, breakage, and corrosion.

- **Potential effects of Lead breaks**—Lead fractures of the VNS Therapy System may prevent patients from receiving therapy. If a Lead fracture is suspected, perform diagnostic testing to evaluate continuity within the system. If diagnostics suggest that a fracture is present, consider turning the VNS Pulse Generator to zero milliamps (0 mA) of output current. Continuing stimulation with a fractured Lead may result in dissolution of the conductor material resulting in adverse events, such as pain, inflammation, and vocal cord dysfunction. The benefits and risks of leaving the Pulse Generator ON (actively stimulating) when a Lead fracture is present should be evaluated and monitored by the medical professional treating the patient.
- **Some complications** may be associated with damage to the vagus nerve.
 - ◆ Hoarseness may be caused by device malfunction, nerve constriction, or nerve fatigue. Nerve constriction should be apparent within a few days after implantation and may require explantation of the Lead. Nerve fatigue usually occurs after intense stimulation parameters have been used, and might not be associated with any other adverse event. If fatigue is suspected, the Pulse Generator should be turned off for several days until hoarseness subsides.
 - ◆ Persistent hoarseness *not* associated with stimulation suggests possible nerve irritation and should be immediately investigated.
 - ◆ Trauma to the vagus nerve at the implantation site could result in permanent vocal cord dysfunction.



Note: For more information on diagnostic testing, see the “Troubleshooting” section in the device-specific *Technical Information* modules or the Programming Software physician’s manual.

5.2. Sterilization, Storage, and Handling

The Pulse Generator, Lead, Accessory Pack, and Tunneler have been sterilized using either hydrogen peroxide (H₂O₂) gas plasma or ethylene oxide (EO) gas, and are supplied in a sterile package to permit direct introduction into the operating field. An expiration (or use-before) date is marked on each package.

A sterilization process indicator is included in each package. Products labeled as sterile should be used only if the color of the indicator is in the range of gold to bronze (in the case of product sterilized with H₂O₂) or gray to green (in the case of product sterilized with EO).



Note: See the exterior package label to ascertain the method of sterilization, which is indicated by the H₂O₂ sterility symbol or the EO sterility symbol (see “Symbols and Definitions” on page 5).

The implantable portions of the VNS Therapy System are nonpyrogenic.

- **Store the VNS Therapy System** between -20°C (-4°F) and +55°C (+131°F). Temperatures outside this range can damage components.
- **Do not store the VNS Therapy System** where it is exposed to water or other liquids. Moisture can damage the seal integrity of the package materials.
- **Do not implant a device** if any of the following has occurred:
 - ◆ The device has been dropped, because dropping it could damage Pulse Generator components.
 - ◆ The color of the sterilization process indicator within the inner package is not in the range of gray to green for product sterilized by EO.
 - ◆ The color of the sterilization process indicator within the inner package is not in the range of gold to bronze for product sterilized by H₂O₂.
 - ◆ The outer or inner storage package has been pierced or altered, because this could have rendered it nonsterile.
 - ◆ The expiration (use-before) date has expired, because this can adversely affect the device's longevity and sterility.
- **Do not ultrasonically clean the Pulse Generator**, because doing so may damage Pulse Generator components.
- **Do not re-sterilize any VNS Therapy System product.** Return any opened devices to Cyberonics.
- The Pulse Generator and Lead are single-use-only devices. **Do not reimplant an explanted Pulse Generator or Lead for any reason**, because sterility, functionality, and reliability cannot be ensured, and infections may occur.

Explanted Pulse Generators and Leads should be returned to Cyberonics for examination and proper disposal, along with a completed Returned Product Report form. Before returning the Pulse Generator or Lead, disinfect the device components with Betadine[®], Cidex[®] soak, or other similar disinfectant, and double-seal them in a pouch or other container properly labeled with a biohazard warning.

- **Do not incinerate the Pulse Generator**; it contains a sealed chemical battery, and an explosion could result.

5.3. Lead Evaluation and Connection

- **Do not use a lead other than** the Cyberonics dual-pin Lead with the Cyberonics dual-receptacle Pulse Generator or a Cyberonics single-pin Lead with the Cyberonics single-receptacle Pulse Generator because such use may damage the Pulse Generator or injure the patient.
- Exercise extreme caution if testing the Lead using **line-powered equipment** because leakage current can injure the patient.
- Do not insert a Lead in the Pulse Generator Lead receptacle(s) without first visually **verifying that the setscrew(s) is sufficiently retracted** to allow insertion. Avoid backing the setscrew(s) out further than needed for Lead insertion.
- Ensure that the hex screwdriver is fully inserted in the setscrew, and then push in on the hex screwdriver and turn it clockwise until it clicks. To avoid damaging (stripping) the setscrew(s) and/or dislodging the setscrew plug(s), insert the hex screwdriver into the center of the setscrew plug, keeping it perpendicular to the Pulse Generator.

5.4. Environmental and Medical Therapy Hazards

Patients should exercise reasonable caution in avoiding devices that generate a strong electric or magnetic field. If a Pulse Generator 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.



Note: See “Other environmental hazards” on page 18.

5.4.1. Hospital and medical environments

- VNS Therapy System operation **should always be checked** by performing device diagnostics after any of the procedures mentioned in this manual. Additional precautions for these procedures are described below.
- **For clear imaging, patients may need to be specially positioned for mammography procedures** because of the location of the Pulse Generator in the chest. (Most routine diagnostic procedures, such as fluoroscopy and radiography, are not expected to affect system operation.)
- **Therapeutic radiation** may damage the Pulse Generator’s circuitry, although no testing has been done to date and no definite information on radiation effects is available. Sources of such radiation include therapeutic radiation, cobalt machines, 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.

- **External defibrillation** may damage the Pulse Generator. Attempt to minimize current flowing through the Pulse Generator and Lead system by following these precautions:
 - ◆ Position defibrillation paddles perpendicular to the Pulse Generator and Lead system and as far from the Pulse Generator as possible.
 - ◆ Use the lowest clinically appropriate energy output (watt-seconds).
 - ◆ Confirm Pulse Generator function after any internal or external defibrillation.
- Use of electrosurgery [electrocautery or radio frequency (RF) ablation devices] may damage the Pulse Generator. During the VNS implantation procedure, do not use electrosurgical equipment after the Pulse Generator has been introduced to the sterile field. When performing other surgical procedures on a patient implanted with a VNS Pulse Generator, attempt to minimize the current flowing through the Pulse Generator and Lead system by following these precautions:
 - ◆ Position the electrosurgery electrodes as far as possible from the Pulse Generator and Lead.
 - ◆ Avoid electrode placement that puts the Pulse Generator or Lead in the direct path of current flow or within the part of the body being treated.
 - ◆ Confirm that the Pulse Generator functions as programmed after electrosurgery.
- Electrostatic Discharge (ESD) may damage the Pulse Generator. Care should be taken when using the hex screwdriver to avoid touching the metal shaft when the screwdriver is engaged with the setscrew of the Pulse Generator. This shaft can serve as a path to conduct electrostatic discharges into the device circuitry.
- **Extracorporeal shockwave lithotripsy** may damage the Pulse Generator. If therapeutic ultrasound is required, avoid positioning the area of the body where the Pulse Generator is implanted in the water bath or in any other position that would expose it to ultrasound therapy. If that positioning cannot be avoided, program the Pulse Generator output to 0 mA for the treatment, and then after therapy, reprogram the Pulse Generator to the original parameters.
- If the patient receives medical treatment for which electric current is passed through the body (such as from a TENS unit), either the Pulse

Generator output should be set to 0 mA or function of the Pulse Generator should be monitored during initial stages of treatment.

- **Therapeutic ultrasound.** Routine therapeutic ultrasound could damage the Pulse Generator and may be inadvertently concentrated by the device, causing harm to the patient.

5.4.2. 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 Pulse Generator. Similarly, most routine diagnostic procedures, such as fluoroscopy and radiography, are not expected to affect system operation. However, because of their higher energy levels, sources such as transmitting antennas may interfere with the VNS Therapy System. It is suggested that the Pulse Generator be moved away from equipment—typically at least 1.8 meters (6 feet)—that may be causing interference.



Caution: The patient should seek medical advice before entering environments that are protected by a warning notice preventing entry by patients implanted with a cardiac pacemaker or defibrillator.

5.4.3. Cellular phones

Based on testing to date, cellular phones have no effect on Pulse Generator operation. Unlike an implanted pacemaker or defibrillator, the Pulse Generator does not sense physiologic signals.

5.4.4. 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 cause accidental Magnet activation. Patients should be cautioned to keep such devices away from the Pulse Generator, typically at least 15 centimeters (6 inches) away.

5.4.5. Programming Software

The Pulse Generator can be programmed using the Model 250 Programming Software. This Software should be used on a laptop or handheld computer dedicated only to programming the VNS Therapy System.



Note: See the Programming Software physician's manual, which includes a list of computers that have been qualified for use with this Software.

5.4.6. Pulse Generator and EMI effects on other devices

During stimulation, the Pulse Generator may interfere with devices operating in the 30 kHz to 100 kHz range, such as pocket transistor radios and hearing aids. This interference is a theoretical possibility, and no effects on hearing aids have yet been reported, although the Pulse

Generator can interfere with a transistor radio. No specific testing has been done to date, and no definite information on effects is available.

The Pulse Generator should be moved—typically at least 1.8 meters (6 feet)—away from equipment with which it may be interfering.

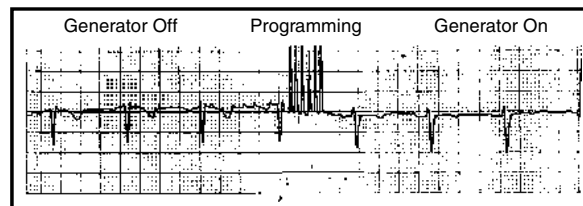
Programming or interrogating the Pulse Generator may momentarily interfere with other sensitive electronic equipment nearby. The Pulse Generator is not expected to trigger airport metal detectors or theft-protection devices that are further than about 1.8 meters (6 feet).

- The Pulse Generator may affect the operation of **other implanted devices**, such as cardiac pacemakers and implantable defibrillators. Possible effects include sensing problems and inappropriate Pulse Generator responses. If the Pulse Generator patient requires concurrent implantable pacemaker and/or defibrillator therapy, careful programming of each system is necessary to optimize the patient's benefit from each device.
- The Magnet provided for activation or inhibition of the Pulse Generator may damage **televisions, computer disks, credit cards, and other items** affected by strong magnetic fields.

5.4.7. *Effects on ECG monitors*

Pulse Generator data communication produces an ECG artifact, an example of which is shown in the ECG tracings in Figure 1:

Figure 1. ECG Artifact Produced by Pulse Generator Communication



5.4.8. *Pulse Generator disposal*

- Do not incinerate the Pulse Generator, because it can explode if subjected to incineration or cremation temperatures.
- Return all explanted Pulse Generators to Cyberonics for examination and safe disposal.
- Do not implant an explanted Pulse Generator in another patient, because sterility, functionality, and reliability cannot be ensured.

6. INFORMATION AND SUPPORT _____

If there are questions regarding use of the VNS Therapy System or any of its accessories, contact Cyberonics:

USA

Cyberonics, Inc.

100 Cyberonics Boulevard

Houston, Texas 77058

Telephone: +1 (281) 228-7200

1 (800) 332-1375 (US and Canada)

Fax: +1 (281) 218-9332

Europe

Cyberonics Europe sa/nv

Belgicastraat 9

1930 Zaventem

Belgium

Telephone: +32 2 720 95 93

Fax: +32 2 720 60 53

For 24-hour Clinical and Technical Support, call:

Telephone: 1 (866) 882-8804 (US and Canada)

+1 (281) 228-7330 (Worldwide)

Internet

www.Cyberonics.com