

MRI can be safely performed on patients with VNS Therapy provided that specified guidelines are followed.

VNS Therapy System

The VNS Therapy system (generator and lead), usually located between C7 and T8 vertebrae, must not be exposed to the radio frequency (RF) field.

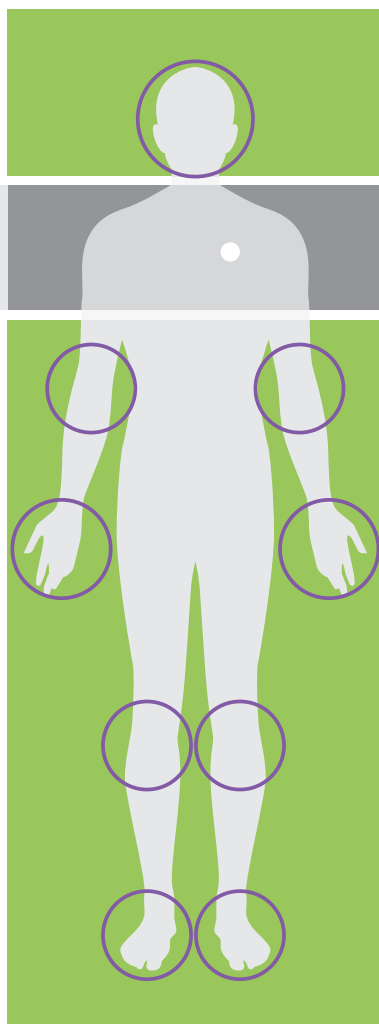
MRI Zone

with local Transmit/Receive coil

MRI Exclusion Zone





 **Local Transmit/Receive coil commercially available**

Note: Imaging techniques such as x-ray, computed tomography, and ultrasound are safe to perform in the MRI exclusion zone.



Safe MRI Conditions

Performing MRI is safe when the guidelines below are followed

	<div><p>Complete VNS Therapy system</p><p>OR</p><p>Suspected lead break</p><p>OR</p><p>Lead only >2 cm remaining</p></div>	<div><p>Lead only ≤2 cm remaining*</p></div>
Allowable imaging zones	See graphic on front cover	Full body
RF coil type	Head or local ONLY	Any
RF coil mode	Transmit/receive ONLY	Any
Static magnetic field	3T or 1.5T	3T or 1.5T
MRI configuration	Closed-bore	Closed-bore
MRI operating mode	Normal	Normal
Spatial gradient field	≤720 gauss/cm	≤720 gauss/cm
Head-averaged SAR	≤3.2 W/kg	≤3.2 W/kg

*Equivalent to clipping the lead at the anchor tether

Additional MRI considerations

- Only the implanted VNS Therapy system components are safe for MRI. All other VNS Therapy components (eg, programming wand, programming computer, patient magnet) are MR unsafe and must not be brought into the MRI scanner room.
- A transmit RF body coil can only be used if the VNS Therapy system has been removed and ≤2 cm of lead remains in the body. Surgical removal of the VNS Therapy system will be required if it is necessary to perform MRI using a transmit RF body coil.

Pre- and Post-MRI Instructions

Pre-MRI instructions

An appropriate healthcare professional with access to a VNS Therapy programming system must prepare the VNS Therapy generator before the patient enters an MR system room.

- ✓ Interrogate the VNS Therapy generator* and record the generator settings
- ✓ Perform System Diagnostics to ensure proper operation of the generator
- ✓ Reprogram the Output Current parameter settings for Normal Mode, Magnet Mode, and AutoStim Mode[†] as follows:
 - Output Current (mA): 0.0
 - Magnet Current (mA): 0.0
 - AutoStim Current (mA): 0.0 and Tachycardia Detection “OFF”
- ✓ Interrogate the generator* to verify that programming was successful
- ✓ Verify that placement of the VNS Therapy system is located between the C7 and T8 vertebrae
- ✓ Instruct the patient to notify the MR system operator of pain, discomfort, heating, or other unusual sensations so the operator can terminate the procedure, if needed

Post-MRI instructions

After the MRI procedure, an appropriate healthcare professional with access to a VNS Therapy programming system should assess the condition of the VNS Therapy system.

- ✓ To assess the VNS Therapy system:
 - Interrogate the VNS Therapy generator
 - If the generator was reset during the scan, reprogram the serial number, patient ID, and implant date, as needed
 - Program the patient’s therapeutic parameters as they were **before the MRI procedure**
 - Perform System Diagnostics. Results should indicate **Impedance=OK**
 - Interrogate the generator again to confirm that reprogramming was successful

* When an interrogation is performed by the programming software, the generator serial number, implant date, stimulation parameters, and generator operating time are automatically logged in the programmer database. This information may be retrieved from the database at any time after interrogation.

† AspireSR Model 106 Only

Your **first choice add-on** for restoring wellness in people with drug-resistant epilepsy because it is **easy to use**, **provides value** and delivers **superior patient outcomes**.



Easy to use

- ✓ Use with approved treatments at any time¹
- ✓ No missed therapeutic opportunities¹

Restoring wellness

- ✓ Reduced seizure frequency that continues to improve over time²
- ✓ Reduced seizure duration^{†3}
- ✓ Decreased seizure severity^{†3}
- ✓ Decreased postictal period³
- ✓ Quality of life improvements, independent of seizure control³
- ✓ Easily tolerated adverse event profile^{4,5,6}

Providing value

- ✓ Reduces patients' consumption of healthcare resources⁷
- ✓ Cost effective⁷
- ✓ Globally accessible and widely reimbursed³



For more information about performing MRI on patients with VNS Therapy, please consult the **VNS Therapy System Physician's Manual**, available at: www.VNSTherapy.com

Please see important safety information and references attached.

† AspireSR Model 106 Only

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To include: MRIGdRef16FU1

Brief Summary¹ of Safety Information for the VNS Therapy® System [Epilepsy Indication] (June 2015)

1. INTENDED USE / INDICATIONS

Epilepsy (US)—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.

2. CONTRAINDICATIONS

Vagotomy—The VNS Therapy System cannot be used in patients after a bilateral or left cervical vagotomy.

Dialtherapy—Do not use short-wave dialtherapy, microwave dialtherapy, or therapeutic ultrasound dialtherapy on patients implanted with a VNS Therapy System. Diagnostic ultrasound is not included in this contraindication.

3. WARNINGS — GENERAL

Physicians should inform patients about all potential risks and adverse events discussed in the physician's manuals. This document is not intended to serve as a substitute for the complete physician's manuals.

The safety and effectiveness of the VNS Therapy System have not been established for uses outside the "Intended Use/Indications" section of the physician's manuals.

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. Post-implant electrocardiograms and Holter monitoring are recommended if clinically indicated.

Postoperative bradycardia can occur among patients with certain underlying cardiac arrhythmias.

It is important to follow recommended implantation procedures and intraoperative product testing described in the *Implantation Procedure* part of the physician's manuals. 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).

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.

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.

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.

Device malfunction could cause painful stimulation or direct current stimulation. Either event could cause nerve damage. 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.

Patients with the VNS Therapy System, or any part of the VNS Therapy System, implanted should have MRI procedures performed only as described in the *MRI with the VNS Therapy System (US)*. Surgery will be required to remove the VNS Therapy System if a scan using a transmit RF body coil is needed.

Excessive stimulation at an excess duty cycle (that is, one that occurs when "ON" time is greater than "OFF" time) and high frequency stimulation (i.e., stimulation at ≥ 50 Hz) has resulted in degenerative nerve damage in laboratory animals.

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.

Cardiac arrhythmia (Model 106 only)—The AutoStim Mode feature should not be used in patients with clinically meaningful arrhythmias currently being managed by devices or treatments that interfere with normal intrinsic heart rate responses (e.g., pacemaker dependency, implantable defibrillator, beta adrenergic blocker medications). Patients also should have a history of chronicotropic intervention (commonly seen in patients with sustained bradycardia (heart rate < 50 bpm)).

Pre-surgical Surface Assessment (Model 106 only)—For anticipated use of the AutoStim feature, it is important to follow the recommended pre-surgical surface assessment described in the *Implantation Procedure* to determine a location for the pulse generator to reside in which it can accurately detect heart beats.

4. WARNINGS — 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.

The VNS Therapy System is not curative. Physicians should warn patients that the VNS Therapy System 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.

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 through this time period 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 — GENERAL

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

Prescribing physicians should be experienced in the diagnosis and treatment of 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.

The safety and effectiveness of the VNS Therapy System have not been established for use during pregnancy. VNS should be used during pregnancy only if clearly needed.

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**.

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 procedure.

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, defibrillatory therapy or other types of stimulators, careful programming of each system may be necessary to optimize the patient's benefit from each device.

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 (while marker band to + connection) into the pulse generator's lead receptacles.

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.

For Models 100, 101, 102 and 102R do not use frequencies of 5 Hz or below for long-term stimulation.

Resetting the pulse generator disables or turns the device OFF (output current = 0 mA). For Model 100, 101, 102 and 102R, resetting the pulse generator will result in device history loss.

Patients who smoke may have an increased risk of laryngeal irritation.

Unintended Stimulation (Model 106 only)—Because the device senses changes in heart rate, false positive detection may cause unintended stimulation. Examples of instances where the heart rate may increase include exercise, physical activity, and normal autonomic changes in heart rate, both awake and asleep, etc. Adjustments to the AutoStim feature's detection threshold should be considered; which may include turning the feature OFF.

Device Placement (Model 106 only)—The physical location of the device critically affects the feature's ability to properly sense heart beats. Care must be taken to follow the implant location selection process outlined in the *Implantation Procedure*.

Battery Drain (Model 106 only)—Talk to your patient about use of the AutoStim feature since use of the feature will result in faster battery drain and the potential for more frequent device replacements. The physician's manual describes the impacts to the battery life. The patient should return to their physician at appropriate intervals to further evaluate whether they are receiving benefit from the current AutoStim settings.

6. 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.

VNS Therapy System operation should **always** be checked by performing device diagnostics after any of the procedures mentioned in the physician's manuals.

For clear imaging, patients may need to be specially positioned for mammography procedures, because of the location of the pulse generator in the chest.

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 ionizing radiation can range from a temporary disturbance to permanent damage, and may not be detectable immediately.

External defibrillation may damage the pulse generator.

Use of electrosurgery [electrocautery or radio frequency (RF) ablation devices] may damage the pulse generator.

Magnetic resonance imaging (MRI) should not be performed with a magnetic resonance body coil in the transmit mode. The heat induced in the lead by an MRI body scan can cause injury. Additionally, in vitro tests have shown that an intact lead without an implanted pulse generator presents substantially the same hazards as a full VNS Therapy System. If an MRI should be done, use only a transmit body coil or lead coil or local coil. MRI compatibility was demonstrated using 1.5T and 3.0T MR systems. Consider other imaging modalities when appropriate. Procedures in which the radio frequency (RF) is transmitted by the body coil should not be done on a patient who has the VNS Therapy System. Thus, protocols must not be used that utilize local coils that are RF receive-only, with RF-transmit performed by the body coil. Note that some RF-head coils are receive-only, and that most other local coils, such as knee and spinal coils, are also RF-receive only. **These coils must not be used in patients with the VNS Therapy System.** See *MRI with the VNS Therapy System* (U.S. version) for details or further instructions for special cases such as lead breaks or partially explanted VNS Therapy systems.

Extracorporeal shockwave lithotripsy may damage the pulse generator. If therapeutic ultrasound therapy 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 should be set to 0 mA or function of the pulse generator should be monitored during initial stages of treatment.

Routine therapeutic ultrasound could damage the pulse generator and may be inadvertently concentrated by the device, causing harm to the patient.

For complete information related to home occupational environments, cellular phones, other environmental hazards, other devices, and ECG monitors, refer to the physician's manuals.

7. ADVERSE EVENTS — EPILEPSY

Adverse events reported during clinical studies as statistically significant are listed below in alphabetical order: ataxia (loss of the ability to coordinate muscular movement); dyspepsia (indigestion); dyspnea (difficulty breathing, shortness of breath); hyposthesia (impaired sense of touch); increased coughing; infection; insomnia (inability to sleep); laryngismus (throat, larynx spasms); nausea; pain; paresthesia (prickling of the skin); pharyngitis (inflammation of the pharynx, throat); voice alteration (hoarseness); vomiting.

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¹ The information contained in this Brief Summary for Physicians represents partial excerpts of important prescribing information taken from the physician's manuals. (Copies of VNS Therapy physician's and patient's manuals are posted at www.cyberonics.com). The information is not intended to serve as a substitute for a complete and thorough understanding of the material presented in all of the physician's manuals for the VNS Therapy System and its component parts nor does this information represent full disclosure of all pertinent information concerning the use of this product, potential safety complications, or efficacy outcomes.

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