VNS Therapy™

MRI Guidelines for VNS Therapy™

The MRI labeling allows patients with an implanted VNS Therapy System to receive MRI scans, including scans that use Body Coils*, so long as specific guidelines are followed.

*only for DemiPulse™ Model 103, Aspire HC™ Model 105, AspireSR™ Model 106, SenTiva™ Model 1000 or SenTiva Duo™ Model 1000-D with scan conditions as listed on page 2

Safe MRI Conditions with the usage of **Transmit Body Coil**

100% of brain MRI

90% of all MRI scans performed on people with epilepsy

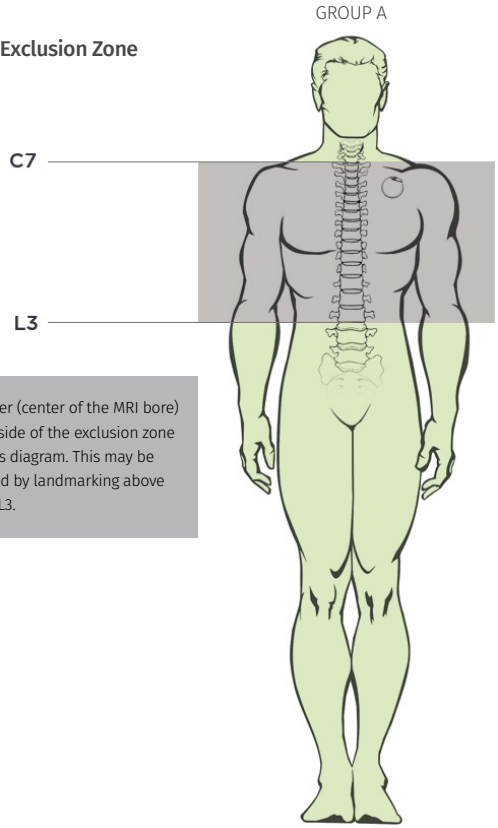
Any MRI center close by

Performing MRI with a body coil is safe when the below conditions are followed:

No local transmit-receive coil required

Permissible Scan Area

MRI Exclusion Zone



The iso-center (center of the MRI bore) must be outside of the exclusion zone shown in this diagram. This may be accomplished by landmarking above C7 or below L3.

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

† Patients with implants in other locations must follow alternate scan conditions as listed on page 4

DemiPulse™ Model 103, Aspire HC™ Model 105, AspireSR™ Model 106, SenTiva™ Model 1000 or SenTiva Duo™ Model 1000-D and the generator location according to LivaNova implanting guidelines in the upper left chest at or above armpit (above anterior rib 4)†

MR Conditional	Yes
Static Magnetic Field Strength	1.5T or 3T
Scanner Type	Horizontal field, cylindrical closed-bore clinical system for hydrogen proton imaging
Operating Mode	Normal Operating Mode
Exclusion Zone	**Body coil:** C7-L3 **Transmit-receive head or extremity coil:** C7-T8*
Spatial Field Gradient	≤3000 Gauss/cm
Max Slew Rate	200 T/m/s
RF Coil	**Transmit:** Body coil or Transmit-receive head or extremity coils **Receive:** No Restrictions
Max SAR	**Transmit head coil:** 3.2 W/kg **Transmit body coil:** 2.0 W/kg
System Programming	Stimulation OFF Sensing OFF* *for select models with AutoStim mode Optional device features OFF (Model 1000 and Model 1000-D only)
Exposure Time	**Transmit head or extremity coil:** No restrictions **Transmit body coil:** ≤15 minutes of active scan time within a 30 minute window
Additional Restrictions	**Transmit head or extremity coil:** none **Transmit body coil:** Circularized Polarized mode only

*see next page for scanning with Transmit-Receive Local Coil

Review the most current labelling prior to performing an MRI scan. For full MRI safety information, refer to MRI Instructions for Use at **www.vnstherapy.co.uk/physician-manuals**

Safe MRI Conditions with **Transmit-Receive Local Coil**

100% access to brain MRI

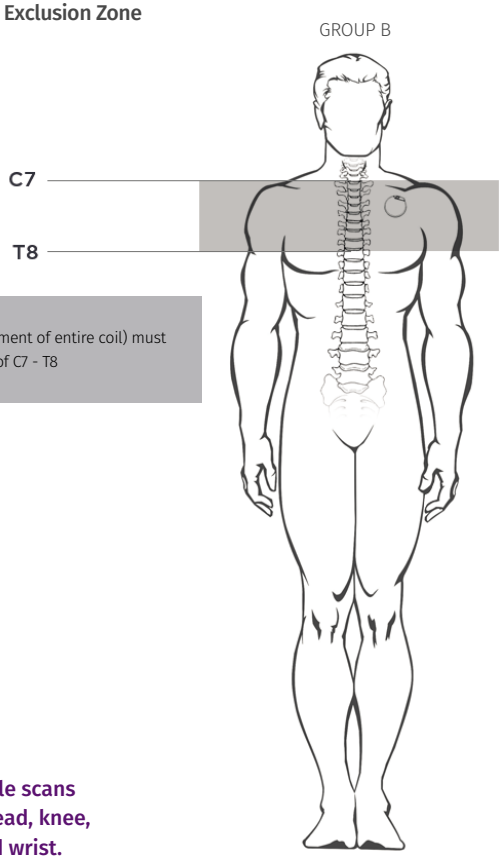
Requires special local transmit-receive coils

Access to extremity scans including knee, ankle, and wrist

Performing MRI with a transmit-receive coil is safe when the below conditions are followed:

Local transmit-receive coil required

MRI Exclusion Zone



Scan (placement of entire coil) must be outside of C7 - T8

Permissible scans include head, knee, ankle, and wrist.

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

Pulse™ Model 102, Pulse Duo™ Model 102R, DemiPulse Duo™ Model 104 **AND** DemiPulse™ Model 103, AspireHC™ Model 105, AspireSR™ Model 106, SenTiva™ Model 1000 or SenTiva Duo™ Model 1000-D **NOT** located in the upper left chest, at or above armpit (above anterior rib 4).

MR Conditional	Yes
Static Magnetic Field Strength	1.5T or 3T
Scanner Type	Horizontal field, cylindrical closed-bore clinical system for hydrogen proton imaging
Operating Mode	Normal Operating Mode
Exclusion Zone	C7-T8
Spatial Field Gradient	≤3000 Gauss/cm
Max Slew Rate	200 T/m/s
RF Coil	Transmit-receive head or extremity coils
Max SAR	**Transmit-receive head coil:** 3.2 W/kg
System Programming	Stimulation OFF Sensing OFF* *for select models with AutoStim mode Optional device features OFF (Model 1000 and Model 1000-D only)
Exposure Time	**Transmit-receive head or extremity coil:** No restrictions
Additional Restrictions	None

Review the most current labelling prior to performing an MRI scan. For full MRI safety information, refer to MRI Instructions for Use at www.vnstherapy.co.uk/physician-manuals

Special MRI scenarios

Performing MRI is safe when the guidelines below are followed:

Suspected Lead Break	OR	Lead Only > 2cm remaining (no generator)
		
MR Conditional	Yes	
Static Magnetic Field Strength	1.5T or 3T	
Scanner Type	Horizontal field, cylindrical closed-bore clinical system for hydrogen proton imaging	
Operating Mode	Normal Operating Mode	
Exclusion Zone	C7-T8	
Spatial Field Gradient	≤3000 Gauss/cm	
Max Slew Rate	200 T/m/s	
RF Coil	Transmit-Receive head or extremity coils only	
Max SAR	**Transmit-Receive head coil:** 3.2 W/kg	

Lead Only ≤ 2cm remaining* (no generator)

MR Conditional: Yes
Static Magnetic Field Strength: 1.5T or 3T
Scanner Type: Horizontal field, cylindrical closed-bore clinical system for hydrogen proton imaging
Operating Mode: Normal Operating Mode
Exclusion Zone: None
Spatial Field Gradient: ≤3000 Gauss/cm
Max Slew Rate: 200 T/m/s
RF Coil: **Transmit:** Body or transmit-receive head or extremity coils **Receive:** No Restrictions
Max SAR: **Transmit-Receive head coil:** 3.2 W/kg **Transmit body coil:** 2.0 W/kg

* Equivalent to clipping the lead at the anchor tether

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.

1. Interrogate the VNS Therapy generator and record the generator settings.
2. Perform System Diagnostics to ensure proper operation of the generator.
3. Reprogram the Output Current parameter settings for Normal Mode, Magnet Mode, and AutoStim Mode† as follows:
   - Normal Output Current : 0 mA
   - Magnet Current : 0 mA
   - Model 106, 1000 and 1000-D only
     - Detection “OFF”
     - AutoStim Output Current: 0 mA
4. Turn off any other optional device features (Model 1000 and Model 1000-D only).
5. Interrogate the generator to verify that programming was successful.
6. Verify that placement of the VNS Therapy system is located between the C7 and T8 vertebrae.

The device has been evaluated for MRI induced risks, including heating, unintended stimulation, force, torque, device malfunction and device vibration and has been determined to be safe under the conditions specified in labeling; however, the patient may feel sensations of warmth or vibration at the implant site during the MRI scan.

† for select models with AutoStim mode

* 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.

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:

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

For patients with Tuberous Sclerosis currently MRI is considered the modality of choice for the evaluation of the brain. Computer Tomography is the modality of choice for evaluating renal lesions.[1]

To ensure effective communication with the MRI centre, complete the Patient MRI Form.

Send with the patient to their MRI appointment. Form can be downloaded at **www.vnstherapy.co.uk/mri**

Brief Summary[1] of Safety Information for the VNS Therapy™ System

[Epilepsy Indication] (February 2021)

1. INTENDED USE / INDICATIONS

Epilepsy (Non-US)—The VNS Therapy System is indicated for use as an adjunctive therapy in reducing the frequency of seizures in patients whose epileptic disorder is dominated by partial seizures (with or without secondary generalization) or generalized seizures that are refractory to seizure medications. AspireSR™, SenTiva™ and SenTiva DUO™ feature an Automatic Stimulation Mode which is intended for patients who experience seizures that are associated with cardiac rhythm increases known as ictal tachycardia.

2. CONTRAINDICATIONS

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

Diathermy—Do not use short-wave diathermy, microwave diathermy, or therapeutic ultrasound diathermy 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 efficacy of the VNS Therapy System have not been established for uses outside the "Intended Use/Indications" chapter 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 chapter of the 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).

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 instructions for use. In some cases, 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 (i.e., one that occurs when "ON" time is greater than "OFF" time) and high frequency stimulation (i.e., stimulation at ≥50Hz) has resulted in degenerative nerve damage in laboratory animals.

Patients who manipulate the generator and lead through the skin (Twiddler's Syndrome) may damage or disconnect the lead from the generator and/or possibly cause damage to the vagus nerve.

The Wand, Programmer, and patient magnet are MR unsafe devices. These devices are projectile hazards and must not be brought into the MR scanner room.

Generators with AutoStim only — The AutoStim Mode feature should not be used in patients with clinically meaningful arrhythmias or who are using treatments that interfere with normal intrinsic heart rate responses (e.g., pacemaker dependency, implantable defibrillator, beta adrenergic blocker medications). Patients also should not have a history of chronotropic incompetence [commonly seen in patients with sustained bradycardia (heart rate < 50 bpm)].

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 unexpected death in epilepsy (SUDEP): Through August 1996, 10 sudden and unexpected 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 — 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 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.

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. Children (<12 years of age) may have a greater risk for infection when compared to adolescent and adult patients (≥ 12 years). Careful monitoring for site infection as well as the avoidance of manipulation of the surgical site post implant in children should be stressed.

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 (white marker band to + connection) into the 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 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.

Generators with AutoStim only — For devices that sense changes in heart rate, false positive detection may cause unintended stimulation. Examples of instances where heart rate may increase include exercise, physical activity, and normal autonomic changes in heart rate, both awake and asleep, etc.

Generators with AutoStim only — For the AutoStim feature, the physical location of the device critically affects this its ability to properly sense heart beats. Therefore, care must be taken to follow the implant location selection process outlined in the Implantation Procedure. Note that this implant location selection procedure may be performed preoperatively as part of the patient's surgical work-up.

M1000/1000-D only — Since the Scheduled Programming feature allows the generator to apply therapy increases at scheduled intervals, it may not be appropriate for use in patients who are nonverbal or are unable to use the patient magnet to stop undesired stimulation. Similarly, exercise caution for use of this feature in patients with a history of obstructive sleep apnea, shortness of breath, coughing, swallowing difficulties, or aspiration.

6. ENVIRONMENTAL AND MEDICAL THERAPY HAZARDS

Patients should exercise reasonable caution in avoiding devices that generate a strong electric or magnetic field. If a 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 generator in the chest.

Therapeutic radiation may damage the generator's circuitry. 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 generator.

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

Magnetic resonance imaging (MRI) should not be performed using a transmit RF body coil for certain VNS Therapy device configurations or under certain specific conditions. In some cases, heating of the lead caused by the transmit RF body coil during MRI may result in serious injury. Static, gradient, and radio frequency (RF) electromagnetic fields associated with MRI may change the generator settings (i.e., reset parameters) or activate the VNS device if the Magnet Mode output remains "ON". Note that certain magnetic resonance (MR) system head coils operate in receive-only mode and require use of the transmit RF body coil. Other MR systems use a transmit/receive RF head coil. Local or surface coils may also be receive-only RF coils that require the transmit RF body coil for MRI. **The use of a receive RF coil does not alter hazards of the transmit RF body coil**. Exposure of the VNS Therapy System to any transmit RF coil must be avoided. Do not perform MRI scans using any transmit RF coil in the defined exclusion zones. See the MRI with the VNS Therapy System instructions for use for details or further instructions for special cases such as lead breaks or partially explanted VNS Therapy systems.

Extracorporeal shockwave lithotripsy may damage the generator. If therapeutic ultrasound therapy is required, avoid positioning the area of the body where the 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 generator output to 0 mA for the treatment, and then after therapy, reprogram the 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 generator should be set to 0 mA or function of the generator should be monitored during initial stages of treatment.

Routine therapeutic ultrasound could damage the 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); hypoesthesia (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. Adverse events reported in clinical investigation of the AutoStim feature were comparable.

26-0009-0100/6 (OUS) — 1

References :

1. Bennett S Greenspan, MD et al.; Medscape Nov 30, 2015 Tuberous Sclerosis Imaging; Overview http://emedicine.medscape.com/article/385549-overview

[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.livanova.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.

Not approved in all geographies. Consult your labeling.

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