This changes everything.
Treating patients with drug-resistant epilepsy just got easier.

Smart Technology. Customizable Therapy. Proven Results.

Built on more than 20 years of proven experience.

>100,000 patients treated
>30,000 children treated (≤18y)
Why choose VNS Therapy?

Early reductions in seizure frequency that continue to improve over time\(^2\)

- Multicenter, open-label, long-term, prospective observational study
- >90% follow-up rate

**Early use of VNS Therapy offers proven long-term outcomes**

- Patients having seizures for less than 10 years responded better to VNS Therapy\(^1\)
- VNS Therapy early use results in better outcomes\(^1\)

**Why wait?**
Significant improvements in quality of life
Confirmed across multiple prospective studies

Patients have a better quality of life with VNS Therapy than with medicine alone\(^5\)

Less severe seizures with improved post-ictal recovery time in both adult and pediatric patients\(^1,6\)

Proven safety and tolerability

Nonpharmacological side effect profile

- Typically occur during stimulation and generally diminish over time\(^7,8\)
- May be diminished or eliminated by the adjustment of parameter settings\(^7,9\)

Incidence of adverse events following stimulation (>5%) were dysphonia, convulsion, headache, oropharyngeal pain, depression, dysphagia, dyspnea, dyspnea exertion, stress, and vomiting.
Why choose SenTiva?

SenTiva is the smallest and lightest responsive therapy for treatment of drug-resistant epilepsy

SenTiva with AutoStim responds to heart rate increases that may be associated with seizures\textsuperscript{10}

At a 20\% threshold, AutoStim detected 80\% of seizures and stimulated 5 seconds post seizure onset (median latency)\textsuperscript{1}
Stimulation-associated desynchronization of focal seizure*1

Threshold choice affects timing of stimulation*11

Earlier stimulation correlates with shorter seizures*1

*VNS Therapy with AutoStim

**Individual study patient example. Results may vary.
Treating patients with drug-resistant epilepsy just got easier

Confidently deliver VNS Therapy with one touch

Guided Programming

- Based on an FDA-approved protocol
- Safe and easy pathway towards achieving targeted therapy levels through one-touch programming
  - Parameter defaults chosen to minimize side effects

Scheduled Programming

- Optional feature allowing the healthcare provider to program a titration schedule in one office visit
- Titration changes will be applied at the defined intervals while the patient lives their life

Do your patients:

- Miss dosing appointments?
- Have difficulties with travel to appointments?
Reaching a therapeutic range quickly may result in early and sustained improvements in outcomes.\(^\text{12}\)

Rapid Titration Protocol*  

No AED changes were allowed  
6 MONTHS  
mean follow-up (N=28)  
75% Responder rate

24 MONTHS  
mean follow-up (N=28)  
68% Responder rate

- Age at implant: ≤ 21 years  
- 9 AEDs failed (mean)  
- 64% failed ketogenic diet

NOTE: Rapid titration protocol in study is not the same as the FDA-approved protocol used in Guided Programming and Scheduled Programming  
*6 week titration to 1.5 mA

Side effects occurred in 68% of patients, most were mild and transient and diminished over time

No missed therapeutic opportunities with VNS Therapy.\(^\text{10}\)

- Automatic delivery of therapy
- Acute delivery of therapy at time of seizure symptoms

Non-adherence to drug treatment is associated with worse patient outcomes \(p < 0.05\).\(^\text{11}\)

<table>
<thead>
<tr>
<th></th>
<th>Emergency Department Visits</th>
<th>Hospitalizations</th>
<th>Inpatient Days</th>
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<tbody>
<tr>
<td>% increase in healthcare utilization</td>
<td>19%</td>
<td>39%</td>
<td>76%</td>
</tr>
</tbody>
</table>

Treatment with VNS Therapy reduces hospitalizations and health-related events.\(^\text{14}\)

<table>
<thead>
<tr>
<th></th>
<th>Emergency Room Visits</th>
<th>Seizure-related Hospitalizations</th>
<th>Number of Hospital Days</th>
</tr>
</thead>
<tbody>
<tr>
<td>% reduction</td>
<td>-39%</td>
<td>-47%</td>
<td>-43%</td>
</tr>
</tbody>
</table>

33,658 patient records were collected and reviewed January 1997 - June 2006.  
Average length of observation = 4.65 years  
Adherence evaluated per quarter  
N = 1655  
Average follow-up = 30.4 months
Quickly visualize patient trends

Events & Trends

- Quickly view data at follow-up visits on events that may be associated with seizures
- Easily export patient data and trends

Customized control for when your patients need it

Day and Night Programming

- Two independent sets of parameters can be customized and will alternate based on time of day
- Select which parameters will change, what time the change will occur, and the duration of the change

Which patients could benefit from this customized control?
VNS Therapy is a cost-effective therapeutic solution\(^\text{14}\)

Increased access to 1.5T and 3T MRI with the latest VNS Therapy technology\(^*\text{10}\)

VNS Therapy is the only device for drug-resistant epilepsy that is FDA-approved for MRI

Patients now have access to:

- 7,000 MRI centers
- 90\% of ALL MRI scans performed on people with epilepsy
- An MRI center within 4 miles of their neurologist’s office, on average
- 100\% of brain MRI
- MRI without the need for special equipment/coils

Performing MRI is safe as long as specific guidelines are followed

*AspireHC model 105, AspireSR model 106, SenTiva model 1000
VNS Therapy is the #1 prescribed implantable device to treat epilepsy

Now FDA-approved for people as young as 4


Why wait?
References

1. Data on File, LivaNova, Houston, TX
10. VNS Therapy Physician’s Manual, October 2017, LivaNova, Houston, TX
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 patients 4 years of age and older 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.

Double-Blind—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 has not been established for uses outside the Intended Use/Indications section of the physician's manuals.

4. WARNINGS—EPILEPSY

Postoperative bradycardia can occur among patients with certain underlying cardiac arrhythmias. Patients should be monitored closely for signs of bradycardia for several days after surgery.

Device malfunction could cause painful stimulation or direct current stimulation. Either event could cause serious injury. Patients should be instructed to use the magnet to stop stimulation if they suspect malfunction, and then to contact their physician immediately for further evaluation.

Patients who have a 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 Instruction Manual. In use, some surgeries will require to remove the VNS Therapy System if a scan using a transmit RF body coil is needed.

Excessive stimulation at an excessive duty cycle (that is, one that occurs when "ON" time is greater than "OFF" time) may result in degenerative nerve damage in laboratory animals. Patients who manipulate the generator and lead through the skin (Twidder's Syndrome) may damage or disrupt the lead and/or lead connector pins. The VNS Therapy System has not been tested in patients with neurosensory function impaired by a previous injury to the vagus nerve.

Generators with AutoStim only—The AutoStim Mode feature should not be used in patients with clinically meaningful atrial arrhythmias currently being managed by devices or treatments that interfere with normal atrial conduction. It is important that patients with suspected aortic stenosis be evaluated to determine if the use of an AutoStim feature is appropriate. This mode may be used in patients with atrioventricular (AV) block who require an AV pacemaker/automatic implantable cardioverter-defibrillator (AICD) or in patients requiring dual-chamber pacing.

Generators with AutoStim 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 generator pocket and a site post implant in children should be stressed.

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 prescribing information contained in the physician's manuals. It is important that the electrodes are attached to the left vagus nerve in the correct orientation. It is also important that the electrodes are correctly orientated since incorrect orientation may limit efficacy of therapy. The VNS Therapy System may affect the operation of other implanted devices, such as cardiac pacemakers and implantable defibrillators. Possible effects include sensing problems and inappropriate device response. 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.

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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 that the electrodes are correctly orientated since incorrect orientation may limit efficacy of therapy. The VNS Therapy System may affect the operation of other implanted devices, such as cardiac pacemakers and implantable defibrillators. Possible effects include sensing problems and inappropriate device response. 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.

6. ENVIRONMENTAL AND MEDICAL THERAPY HAZARDS

Patients who have a VNS Therapy System operation should always be checked by performing diagnostic evaluations 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, although no testing has been done to date. Defibrillation (RF) electromagnetic fields associated with MRI may change the generator settings (i.e., reset parameters) or activate the VNS device if the Magnet Mod output remains "ON." Note that certain magnetic resonance imaging (MRI) system head coils operate in receive-only mode and require use of the transmit RF body coil. Other MRI systems use a transmit/receive RF head coil. Local or surface coils may also be used in some MRI systems to improve image quality. Such devices may cause heating of the generator and leads.

7. ADVERSE EVENTS—EPILEPSY

Adverse events reported during clinical studies as statistically significant are listed below in alphabetical order. In these cases, the data is incompletely reviewed or the adverse event not necessarily related to the therapy 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 number of absorbed gray increasing proportionally with the total number of treatments. For patients with a history of obstructive sleep apnea, shortness of breath, coughing, swallowing difficulties, or aspiration.

8. THE VNS THERAPY SYSTEM

9. MRI WITH THE VNS THERAPY SYSTEM

Mercury vapor lamps, high-intensity discharge (HID) lamps, fluorescent light fixtures, and strobe lights may cause the device to malfunction. These types of lighting should be avoided. The patient can take a number of additional steps to reduce the risk of misdiagnosis, including:

10. THERAPEUTIC ULTRASOUND

The device 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. During the intraoperative Implantation Procedure, patients should be instructed to use the magnet to stop stimulation if they suspect malfunction, and then to contact their physician immediately for further evaluation.

11. RISK OF SUDEP

Sudden unexpected death in epilepsy (SUDEP): Through August 1996, 10 sudden and unexpected deaths among patients implanted with a VNS Therapy System. Diagnostic ultrasound is not included in this contraindication.

12. MAGNETIC RESONANCE IMAGING

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 Mod output remains "ON." Note that certain magnetic resonance imaging (MRI) system head coils operate in receive-only mode and require use of the transmit RF body coil. Other MRI systems use a transmit/receive RF head coil. Local or surface coils may also be used in some MRI systems to improve image quality. Such devices may cause heating of the generator and leads.

13. THERAPEUTIC ULTRASOUND

External defibrillation 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 Mod output remains "ON." Note that certain magnetic resonance imaging (MRI) system head coils operate in receive-only mode and require use of the transmit RF body coil. Other MRI systems use a transmit/receive RF head coil. Local or surface coils may also be used in some MRI systems to improve image quality. Such devices may cause heating of the generator and leads.

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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.livanova.com.) The information is not intended to serve as a substitute for a complete and thorough understanding of the material presented in 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.