Introducing Vagus Nerve Stimulation for Epilepsy

The Most Proven Neuromodulation Therapy For Drug-Resistant Epilepsy Patients
Drug-Resistant Epilepsy
A complex disease needs a comprehensive approach

1 in 3 of your patients will not respond adequately to anti-epileptic drugs (AEDs)\(^1\)

The rate of Drug-Resistant Epilepsy (DRE) has not been significantly reduced over the last 20 years despite the entry of new AEDs with unique mechanisms of action (MOAs)\(^1\)

DRE: The failure of two appropriately chosen and tolerated AEDs (whether as monotherapy or in combination)\(^2\)
**Consequences** of Drug-Resistant Epilepsy extend beyond seizures\(^3,4,7\)

- Seizure-related injuries
- Increased hospital stays
- Increased mortality & morbidity including SUDEP

- Depression, anxiety & sleep disturbance
- Cognitive & memory impairment
- Adverse effects with long-term AED use

Impaired ability to:
- Obtain education
- Work
- Develop and maintain social relations
Treatment options and treatment goals\textsuperscript{2,5,6}

Newly diagnosed

1 AED Trial
Monotherapy

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2 AED Trial
Monotherapy or Combination

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Comprehensive Epilepsy Evaluation

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Resective Surgery

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VNS Therapy

\rightarrow

Combination

\rightarrow

Diet

\rightarrow

Other

\rightarrow

Treatment Goal:\textsuperscript{8}
- No seizures
- No side effects

Treatment Goals for Drug-Resistant Epilepsy:\textsuperscript{9,10}
- Optimize seizure-control
- Minimize seizure severity
- Maximize Quality of Life
- Reduce AED side-effects
- Ensure adherence
A treatment gap exists for Drug-Resistant Epilepsy patients*

New strategies are needed to improve patient wellbeing

* Data on file: longitudinal cohort study using data from the German statutory health insurance system, 2010
** All epilepsy surgeries
VNS Therapy: clinically proven treatment that is easy to use

The generator sends electrical impulses to the brain via the left vagus nerve in the neck at regular intervals all day, every day.

The stimulation has an anti-convulsive effect via several pathways:
- Desynchronises ictal EEG patterns
- Alters neurotransmitter expression and release (↑ Norepinephrin, ↑ GABA, ↑ Serotonin, ↓ Aspartate)
- Increases Cerebral Blood Flow in the Thalamus and in the Cortex

Easy to use treatment:
- Short procedure, typically 1-2 hours
- Can be safely used in combination with any approved therapy at any time
- Built-in compliance
- No drug interactions
VNS Therapy is customisable to patient needs

**Standard Mode**

*Ongoing delivery of mild pulses*

to the vagus nerve. Treatment is delivered at regular intervals.

**Magnet Mode**

*Manual delivery of an extra dose*

of therapy as needed. Magnet Mode may be used during Standard Mode and Detect & Respond Mode.

**Detect & Respond Mode***

*Responsive automatic delivery* of an extra dose of therapy when a rapid increase in heart rate is detected that may be associated with seizures.

VNS Therapy 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*.

*Also known as Auto Stimulation Mode/Available for AspireSR® only*
Optimising treatment outcomes with VNS Therapy

- Reduced seizure frequency
- Reduced seizure duration
- Improved comorbidities: Mood, Alertness/Energy, Cognition
- Fewer side effects
- Lower drug burden
- Reduced seizure severity & intensity
- Impact on seizure onset & propagation

Reduced seizure frequency

Patient wellbeing

Severity

Consequences

Reduced seizure duration
Shortened post-ictal recovery period
Why wait for wellbeing?

Earlier use is proven to enhance seizure control. Earlier use is proven to enhance seizure control.

Reduction in Seizure Frequency (All) at 3 months

- Early Use (N=120)*
- Control (N=2,785)**

- ≥50%: 50.8% vs 49.6%
- ≥75%: 35.0% vs 28.2%
- ≥90%: 25.8% vs 14.3%
- 100%: 15.0% vs 4.4%

* VNS Therapy within 5 years of epilepsy onset
** VNS Therapy after 5 years of epilepsy onset, mean 21 years
Long-term efficacy of VNS Therapy

Adult Patients

Responder rate

NO MEDICATION CHANGES WERE ALLOWED DURING THE STUDY PERIOD

<table>
<thead>
<tr>
<th>Study</th>
<th>Responder Rate</th>
<th>Mean Follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>LABAR17 (N=269)</td>
<td>57%</td>
<td>12 Months</td>
</tr>
<tr>
<td>CHAYASIRISOBHON18 (N=39)</td>
<td>64%</td>
<td>24 Months</td>
</tr>
<tr>
<td>De HERDT19 (N=138)</td>
<td>59%</td>
<td>44 Months</td>
</tr>
<tr>
<td>ELLIOTT20 (N=436)</td>
<td>64%</td>
<td>59 Months</td>
</tr>
</tbody>
</table>

PERCENTAGE OF PATIENTS ≥50% SEIZURE FREQUENCY REDUCTION
Long-term efficacy of VNS Therapy
Paediatric Patients

PERCENTAGE OF CHILDREN WITH ≥50% SEIZURE FREQUENCY REDUCTION

**Maintained at mean follow-up of 41 months**
Early reductions in seizure frequency that continued to improve over time

Improvements in seizure frequency were seen in a highly intractable patient population\textsuperscript{25}

- 2.8 AEDs at baseline (median)
- 6 AEDs failed (mean)
- 20 years mean duration of epilepsy
- 31\% prior brain or epilepsy surgery

![Graph showing mean % seizure reduction over time](image-url)
Reductions in **seizure severity** and duration

CHANGES IN SEIZURE SEVERITY OF PREDOMINANT SEIZURE TYPE

- **34.8%** children with decrease in duration of seizures
- **38.2%** children with decrease in ictal severity
- **42.6%** children with decrease in postictal severity

<table>
<thead>
<tr>
<th>Time Period</th>
<th>Percentage of Children</th>
</tr>
</thead>
<tbody>
<tr>
<td>6 MONTHS (N=284)</td>
<td>34.8%</td>
</tr>
<tr>
<td>12 MONTHS (N=338)</td>
<td>39.5%</td>
</tr>
<tr>
<td>24 MONTHS (N=195)</td>
<td>42.3%</td>
</tr>
</tbody>
</table>

**Children with decrease in duration of seizures**

**Children with decrease in ictal severity**

**Children with decrease in postictal severity**
Significant improvements in quality of life

Adult Patients

Achievements: 30%
Memory: 34%
Verbal Skills: 41%
Seizure Clusters: 44%
Mood: 45%
Postictal: 55%
Alertness: 62%

Improvement was defined as patient being “better” or “much better” at 12 months (N=2,229)
Significant improvements in quality of life

Paediatric Patients

Improvement was defined as patient being “better” or “much better” at 12 & 24 months (N=109)\(^2\)

<table>
<thead>
<tr>
<th>Category</th>
<th>12 Months (N = 200)</th>
<th>24 Months (N = 109)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Memory</td>
<td>16%</td>
<td>25%</td>
</tr>
<tr>
<td>Development of life skills</td>
<td>23%</td>
<td>30%</td>
</tr>
<tr>
<td>Progress with school work</td>
<td>25%</td>
<td>31%</td>
</tr>
<tr>
<td>Verbal Communication</td>
<td>28%</td>
<td>34%</td>
</tr>
<tr>
<td>Mood</td>
<td>41%</td>
<td>43%</td>
</tr>
<tr>
<td>Energy</td>
<td>43%</td>
<td>43%</td>
</tr>
<tr>
<td>Concentration</td>
<td>35%</td>
<td>42%</td>
</tr>
<tr>
<td>Alertness</td>
<td>55%</td>
<td>61%</td>
</tr>
<tr>
<td>Energy</td>
<td>66%</td>
<td>66%</td>
</tr>
</tbody>
</table>

\(^2\) Improvement was defined as patient being “better” or “much better” at 12 & 24 months (N=109)
Proven safety and tolerability

Non-pharmacological side effect profile

- Occur only during stimulation and generally diminish over time\textsuperscript{27,28}
- May be diminished or eliminated by the adjustment of parameter settings\textsuperscript{27,29}

MOST COMMON VNS THERAPY SIDE EFFECTS
(ADULTS AND CHILDREN, N=440)\textsuperscript{28}

- Incidence of adverse events following stimulation (>5%) were dysphonia, convulsion, headache, oropharyngeal pain, depression, dysphagia, dyspnea, dyspnea exertional, stress, and vomiting.
**VNS Therapy reduces** hospitalisations and health-related events

### Post-VNS Therapy Reductions in Hospitalisations and Health-Related Events

<table>
<thead>
<tr>
<th>Event</th>
<th>Impact</th>
</tr>
</thead>
<tbody>
<tr>
<td>Head Trauma</td>
<td>-27%</td>
</tr>
<tr>
<td>Fractures</td>
<td>-34%</td>
</tr>
<tr>
<td>Emergency Room Visits</td>
<td>-39%</td>
</tr>
<tr>
<td>Hospitalisations</td>
<td>-41%</td>
</tr>
<tr>
<td>Number of Hospital Days</td>
<td>-43%</td>
</tr>
</tbody>
</table>

**POST-VNS THERAPY REDUCTIONS IN HOSPITALISATIONS AND HEALTH-RELATED EVENTS N=1,655  AVERAGE FOLLOW-UP 30.4 MONTHS**


The most proven neuromodulation therapy in use for Drug-Resistant Epilepsy patients\textsuperscript{30}

- 85,000 Patients treated
- 77\% Reimplantation Rate
- 81\% report VNS Therapy to be worthwhile, irrespective of seizure response and psychosocial outcomes \textsuperscript{31} (N=21)
- 1000 Peer-reviewed publications
Why wait for patient wellbeing?

- **Seizure reduction** that continues to **improve over time**
- Decreased seizure **severity** and **duration**
- Improves quality of life
- Decreased hospitalisation
- **Non-pharmacological side effects** that typically diminish over time
- **Easy to use** treatment
VNS THERAPY EUROPEAN INDICATION FOR USE

VNS Therapy 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. The Model 106 AspireSR® (Seizure Response) features the Automatic Stimulation Mode, which is intended for patients who experience seizures that are associated with cardiac rhythm increases known as ictal tachycardia.

CONTRAINDICATIONS:
The VNS Therapy system cannot be used in patients after a bilateral or left cervical vagotomy. Do not use short-wave diathermy, microwave diathermy, or therapeutic ultrasound diathermy on patients implanted with the VNS Therapy system. Diagnostic ultrasound is not included in this contraindication. Cardiac arrhythmia (Model 106 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.

WARNINGS:
Physicians should inform patients about all potential risks and adverse events discussed in the VNS Therapy Physician Manuals, including information that VNS Therapy may not be a cure for epilepsy. Since seizures may occur unexpectedly, patients should consult with a physician before engaging in unsupervised activities, such as driving, swimming, and bathing, or in strenuous sports that could harm them or others.

A malfunction of the VNS Therapy system could cause painful or direct current stimulation, which could result in nerve damage. Removal or replacement of the VNS Therapy system requires an additional surgical procedure. Patients who have pre-existing swallowing, cardiac, or respiratory difficulties (including, but not limited to, obstructive sleep apnea and chronic pulmonary disease) should discuss with their physicians whether VNS Therapy is appropriate for them since there is the possibility that stimulation might worsen their condition. Postoperative bradycardia can occur among patients with certain underlying cardiac arrhythmias. MRI can be safely performed; however, special equipment and procedures must be used.

ADVERSE EVENTS:
The most commonly reported side effects from stimulation include hoarseness (voice alteration), paresthesia (prickling feeling in the skin), dyspnea (shortness of breath), sore throat and increased coughing. The most commonly reported side effect from the implant procedure is infection.

*The information contained here represents partial excerpts of important prescribing information from the product labeling. Patients should discuss the risks and benefits of VNS Therapy with their healthcare provider. Visit www.VNSTherapy.com for more information.

References:
15. Vonck et al. Seizure. 2008;05.001
18. Chayassrisobhon S et al. J Neurol Neurophysiol. 2015, 6:1
30. Data on File, LivaNova, Houston, TX.