Neurostimulation for Epilepsy

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Neurostimulation for Epilepsy

- Vagus Nerve Stimulation (VNS)
- Deep Brain Stimulation (DBS)
- Future Systems: Closed-Loop Stimulation
Neurostimulation for Epilepsy

- Vagus Nerve Stimulation (VNS)
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- Future Systems: Closed Loop Stimulation
Vagus Nerve Stimulation

• Advantages:
  – FDA approved since 1997
  – Low risk surgery
  – Possible Mood Benefits

• Disadvantages:
  – Mild to moderate impact on seizures
  – Vocal side effects
  – No significant control over device
Vagus Nerve Stimulation

• Historical Data:
  – 1980’s: Desynchronization of EEG by VNS in animals
  – 1990’s: Device concept and pilot testing
    • European Outcomes Study (EOS) 1-5
  – 1997: FDA approval for patients with medically refractory CPSz and generalized seizures
Vagus Nerve Stimulation

- Implantable pulse generator and lead
- Mild electrical pulses applied to the left vagus nerve in the neck
- Automatic intermittent stimulation
- Magnet use allows patient/caregiver
  - On-demand stimulation
  - On-demand side effect control
- Simple in-office programming
- Easy maintenance
Vagus Nerve Stimulation

• Outcomes:
  – Reduction in seizure frequency, duration, spread.
    • EO3 and EO5 studies demonstrated 23-31% of patients had >50% reduction in seizure number. (at 3 months)
    • Rate of seizure reduction may increase with stimulation out to 1 year and beyond with up to 61% of patients responding.
    • Patients report improved Quality of Life.
  – Improved interictal level of consciousness
  – Moderate chance of medication reduction
  – No cure for seizures
Intended Use / Indications

• 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 which are refractory to antiepileptic medications.

• Generalized onset seizures have been treated with VNS in Europe but are not FDA approved.
Bipolar Lead: The Electrode

NOTE: Sutures are for placement, not tying.

--Negative Electrode
--Positive Electrode
--Anchor Tether
Pulse Generator:

- Model 100: Thickness: 0.52” (13.2 mm), Volume: 31 cc
- Model 101: Thickness: 0.41” (10.3 mm), Volume: 26 cc
- Model 102/102R: Thickness: 0.27” (6.9 mm), 14/16 cc
- Model 103: Thickness: 0.27” (6.9 mm), 8 cc

Source: Neurosurg Focus © 2009 American Association of Neurological Surgeons
# Pulse Generator: Parameters

<table>
<thead>
<tr>
<th>Parameter</th>
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<tbody>
<tr>
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<tr>
<td>Signal On-time</td>
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<tr>
<td>Signal Off-time</td>
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</table>
VNS system: Implantation Procedure
VNS System Implant: Overview

- Approach similar to carotid endarterectomy
- Approximately 2 hour case length
- Typically general anesthesia
- Patients may go home same day
VNS System Implantation

Clavicle

Anterior fold of axilla incision site option

Neck incision site
VNS System Implant:
The Exposed Carotid Sheath
VNS System Implant:

- Anchor
- Tether
- Negative Electrode
- Positive Electrode
With the hex screwdriver inserted, fully insert the lead connector(s) into the generator header.

When tightening the set screw(s), make sure the hex screwdriver remains fully inserted.

Hold the lead as close as possible at the entry point to the header. Make sure to insert the positive electrode (white marker) into the positive port if dual pin lead.
VNS System Implant: Closure

- To minimize scarring, a subcuticular closure is typically used/
VNS Therapy Surgical Complications

Epilepsy Clinical Studies (n=454)

• Surgical Complications ≥0.5% ¹
  • Infection without explant ¹ 1.8%
  • Infection with explant ¹ 1.1%
  • Hoarseness/temporary vocal cord paralysis ¹ 0.7%
  • Hypesthesia/lower left facial paresis ¹ 0.7%

• Mortality 0.0%

VNS Therapy Surgical Complications

Post approval (n=17,019)

- Infection (with and without explant) 1.3%
- Hoarseness/temporary vocal cord paralysis 1.1%
- Mortality 0.0%

Asystole from VNS Stim in Surgery

- Incidence of asystole during routine intraoperative lead test
  - Reported rate $\approx 1$ in 1000 patients
  - Full recovery for all patients
- Similar events are not reported in epilepsy clinical trials
- Reason: anatomic differences, lead placement, anesthesia, or collateral current spread?

Replacement of the VNS Generator

- Typical battery life of 5-7 years.
- Can be performed under local or mild general anesthesia
- 30-45 minute procedure
- Routine battery replacement only involves replacing the generator, not the lead
- >1,500 generator replacements
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Deep Brain Stimulation

- Cerebellar stimulation in 1970’s effective in seizure reduction
- Anecdotal trials since 1980
- Modulated targets include STN, medial thalamus, amygdala, hippocampus.
- SANTE multicenter trial completed in 2008.
- FDA approval anticipated...maybe

Deep Brain Stimulation

• Surgical Concepts:
  – Stereotactic methods
  – Targeting based on physiology
  – High frequency stimulation “jams” seizure spread
Deep Brain Stimulation

• Surgical Advances
  – Newer Stereotactic frames improve patient comfort and accuracy.
  – Physiological mapping may improve technique efficacy.
  – Combined anatomic and physiological approach maximizes success.
Deep Brain Stimulation

- Outcomes: SANTE Trial
  - 110 patients randomized, double-blind design.
  - 60% of treated patients had >50% seizure reduction in first 3 months.
  - By 3 years patients had 68% average seizure reduction.
  - At 1 year 9% were seizure free
  - 44.5% had prior VNS, 24.5% had prior surgery
Deep Brain Stimulation

• Advantages:
  – Moderately better outcomes than VNS.
  – More targeted control at seizure spread
  – Known surgical technique
  – No vocal hoarseness

• Disadvantages:
  – Complications rare but potentially more severe than VNS
  – Open Loop design
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Responsive Brain Stimulation

• Historical Data:
  – High frequency stimulation (>100Hz) peri-ictally can arrest seizures in animal models¹
  – Automated seizure detection algorithms exist since mid-1990’s
  – Human pilot studies show proof of principle since 1999²

Responsive Brain Stimulation

- **Surgical Concepts:**
  - Focus of seizure activity is restricted
  - Localized detecting electrodes feed signals to control circuitry
  - High Frequency Stim applied to region of seizure focus within 2 sec.
Preemptive Brain Stimulation

• Surgical Concepts:
  – Neuropace™ study
  – Electrodes implanted:
    • Cortical strip
    • DBS
  – Generator: embedded in the skull.
  – Software loadable algorithms for detection and therapy
Responsive Brain Stimulation

Preliminary results:

• Multi-center trial of 191 patients at 31 sites

• In 3 month blinded phase patients had 29% average reduction in sz.

• At 1 year 47% had >50% reduction in seizure frequency.

• Minimal adverse events.
Preemptive Brain Stimulation

• Advantages:
  – Addresses non-resectable, focal seizure disorder.
  – Open ended architecture. Therapy may improve as algorithms get smarter.
  – Minimized stimulation allows long battery life and may minimize stimulation side effects.

• Disadvantages:
  – Major surgery needed for implant
  – Risks similar to DBS surgery
  – Final study results and FDA approval pending.
Implant procedure
Subdural Strip Lead Implant
Depth Lead Implant Example
Neurostimulation for Epilepsy

Summary:

• VNS is the only neurostimulation system currently available.
• DBS and Closed-Loop Stimulation systems may be available as soon as this summer.
• Stimulation may be a useful treatment when medications fail and resection is not an option.
• If seizure detection improves future Responsive systems could provide even greater seizure control.