Responsive Neurostimulation (RNS)

INDICATIONS

FDA approved (2013)

Comparisons of Neuromodulations (RNS, DBS, VNS) – see p. E11

Brochures

- see

Reading


- adjunctive therapy in reducing frequency of seizures in individuals ≥ 18 years**** with partial onset seizures who have undergone diagnostic testing that localized no more than 2* epileptogenic foci, are refractory to ≥ 2 antiepileptic medications, and currently have frequent** and disabling*** seizures.

*Neuropace has receptacle only for two leads.
** ≥ 3 disabling seizures per month over three most recent months (with no month with fewer than two seizures); RNS® System has not been evaluated in patients with less frequent seizures.
***motor partial seizures, complex partial seizures and / or secondarily generalized seizures
****FDA indication for RNS is age > 18 years, but it likely has efficacy in adolescents and children (limitation in young children is skull thickness before it reaches adult size, so it could certainly be used in adolescents).

Summary
a) ≥ 2 foci
b) eloquent areas
c) mesial temporal lobe (uni- or bilateral)
d) difficult to resect (e.g. insula, large regional onsets, interhemispheric)
e) failed previous surgery or VNS

VNS, RNS, and DBS are all palliative and comparable in efficacy, both in pivotal trials and over longer-term trials. VNS is a first choice as it is extracranial. A specific scenario where RNS may have an advantage is bilateral mesiotemporal epilepsy – RNS allows for long-term ECoG recording, which may in turn (occasionally) allow for an eventual resection in a small number of patients.

PATHOPHYSIOLOGY

- Penfield and Jasper noted: inhibitory polarization caused by transmembrane currents of applied current → flattened local electrocorticography pattern.

HARDWARE
- RNS Neurostimulator Kit Model # RNS-300M-K.
- four cortical 5 mm bone screws.

**Device**

- accepts two electrode arrays; if uncertain – may implant more and leave contact end capped (may switch and reconnect later).

<table>
<thead>
<tr>
<th>Feature</th>
<th>model 320</th>
<th>model 300</th>
</tr>
</thead>
<tbody>
<tr>
<td>Battery life</td>
<td>8.4 yrs (on medium settings)</td>
<td>3.9 yrs</td>
</tr>
<tr>
<td>Data capacity</td>
<td>1 MB - stores 8 ECoGs (90 sec duration each)*</td>
<td>0.5 MB</td>
</tr>
<tr>
<td>Price</td>
<td>6000 USD more expensive</td>
<td>25K USD</td>
</tr>
</tbody>
</table>

*still no warning to the patient when memory is full and data is overwritten

Q: who should be getting **model 300**? A: nobody.

**Strips**

- 4 contacts spaced 10 millimeters apart - spans 33 mm
- lead lengths (avoid unnecessarily long lead lengths):
  - 15 cm (model CL-315-10)
  - 25 cm (model CL-325-10)
  - 35 cm (model CL-335-10)

**Depths**

- 4-contacts
- diameter 1.27 mm (same as DBS electrode); slotted cannula 2.1 mm.
- configurations (avoid unnecessarily long lead lengths):
  - 3.5 mm contact spacing, 30 cm length (model DL-330-3.5)
  - 3.5 mm electrode spacing, 44 cm length, (model DL-344-3.5)
  - 10 mm electrode spacing, 30 cm length (model DL-330-10) - spans 33 mm
  - 10 mm electrode spacing, 44 cm length (model DL-344-10) - spans 33 mm

Wider spacing is for hippocampal depths!

**ON IMAGING**

[Image of a medical procedure]

Source of picture: Viktoras Palys, MD

**PREOP COUNSELLING**

I explained the alternative of the VNS, pros and cons of each as well as the risks of surgery to include no change or worsening of seizures, visual fields compromise, memory compromise, or other injury to the brain. I explained that how the computer was placed to replace the skull and the electrodes that pass through the brain to the hippocampus. We talked about shaving some of the head - patient had no problems about that. The patient understands the risk of an infection, which would require removal.

**PROCEDURE – DEPTH ELECTRODE IMPLANTATION**
HIPPOCAMPAL DEPTH

Trajectory (hippocampus cannulation) – see p. E15 >>

- prone in radiolucent Mayfield (standard metal frame has less wiggle than radiolucent frame).
- O-arm
- guidance platform: Nexframe or StarFix or ROSA
- **slotted cannula** is needed for StarFix or ROSA.
- pins (radiolucent) – make sure pins not too posterior – will interfere with bur holes.
- incisions for bilateral leads (keeping in mind scalp blood supply and the battery replacement surgeries):

```
• O-arm (stays for the whole procedure but is also OK to remove after leads are placed):
  N.B. place blue drape towels first, then large DBS drape
• vertical incision (may be separate from device incision), Acra-Cut perforator (undercut laterally using M8 drill bit)
• Medtronic Nexframe (or any other platform) with double Silastic on lateral side (may even need offset bengun).
• if using Nexframe: “at target” DBS cannula with Neuropace electrode is placed into the center track to the full depth to the target along the long axis of hippocampus.
```
do CT and look for contact position (10 mm lead with 4 contacts spans 33 mm) – may need to pull lead back for the best coverage.

Stimloc or Neuropace lead **burhole anchoring device**.

**Implantation of 2 leads**
- if implanting 2 leads in parallel (e.g. second lead in parahippocampal gyrus), aim to keep distance > 10 mm between leads so can stimulate in bipolar mode between contacts in separate leads.
- inner diameter of Neuropace bur hole cover is 10 mm (if using one bur hole for both leads, plan entry points ≤ 10 mm apart).

**PROCEDURE - DEVICE IMPLANTATION**
- two antibiotics: cefazolin, 2 g IV and vancomycin 1 g IV
- plan incision so generator is not under incision.
- if incision is curved, plan generator implant so leads face away from incision; plan for battery replacements – will need to open only flat end of device curving a little bit on the side (opposite where leads exit).
- tunnel leads from other side in shortest way.

**CRANIECTOMY**
N.B. partial thickness craniectomy is not recommended – time consuming, bone grows and pushes device out.
- use template.
- location – anywhere where shape conforms to skull curvature, e.g. parietal area.
- one or two bur holes (some place it where ferule tab is going to be)
- discard bone flap.
- some place dural tack-ups along perimeter.

**IMPEDANCES**
- normal lead impedance range 250-3500 Ohm.

**Case report of implanting in infraclavicular position**
- band pass detection rates increased by 50%, while line length detection rates decreased by 50%.
- number of detections decreased from 1046 to 846, with a resultant decrease in stimulations.
- although there was some compromise of function due to the elevated noise floor, more than 2 yr following the procedure the patient remains free of seizures and infection.

**Case report of implanting inside prosthetic skull implant**
*First In-Human Experience With Complete Integration of Neuromodulation Device Within a Customized Cranial Implant. Chad R Gordon, DO Gabriel F Santiago, MD Judy Huang, MD Gregory K Bergey, MD Shuya Liu, MS Mehran Armand, PhD Henry Brem, MD William S Anderson, PhD, MD. Operative Neurosurgery, Volume 15, Issue 1, 1 July 2018, Pages 39–45*
PROCEDURE - BATTERY REPLACEMENT

- enough to expose only very bottom of generator → undo 2 screws, remove strain relief plate from leads, and reflect leads.
- use Bovie set at 6 if need to dissect leads (Dr. P. Weber); do not use Bovie when new battery is in.

COMPLICATIONS

**Infection** (3.7-3.8%; 1.9% leading to explantations)

**Hemorrhages** (2.7%)

No chronic stimulation side effects!

POSTOPERATIVELY

**CONTRAINDICATED PROCEDURES**

1. **MRI** contraindicated (FDA is evaluating; mainly due to MRI-compatibility of lead and not device).

2. **Diathermy procedures** (any treatment that uses high-frequency electromagnetic radiation, electric currents, or ultrasonic waves to produce heat in body tissues).

3. **Electrosurgery** – conflicting info: some say not to use Bovie (use bipolar at > 2-3 cm away from device); others say it is OK to use **Bovie** (if close to device, it may reset the device – will need to reprogram). It is OK to use **Bovie** on old battery (if close to leads – use lowest settings on Bovie).

4. **Electroconvulsive Therapy** (ECT).

5. **Transcranial Magnetic Stimulation** (TMS).

6. **Radiotherapy**

   Exposure to high levels of radiation may damage the RNS® System.
   The effects of high radiation sources (such as cobalt 60 or gamma radiation) on the RNS® System have not been studied - no studies to determine safe levels of irradiation for their device nor are there any recommendations for safe dose exposures. Neuropace suggests that the patient scan the device daily after each radiation fraction. This information can be transmitted to Neuropace who can determine if software repairs/re-programming can restore any lost functionality (if the device is damaged, it will try to reset itself. If unable to do that, it shuts down to a stable non-functioning state). Neuropace does not recommend prophylactically removing this device prior to radiation therapy.

ANALYSIS & PROGRAMMING

impedances - see above >>
RNS device stores ECoG only at certain triggers (if no triggers, device stores ECoG at certain time every day):

a) patient swipes magnet (e.g. if feels aura) – device stores 60 sec of preceding ECoG and 30 sec of subsequent ECoG
b) amplifier saturation detection (high amplitude)*
c) long episode detection (spikes or fast activity run > set time, e.g. 10 sec)*

*device stores ECoG if triggered stimulation does not abort activity (i.e. device stores ECoG of stimulation failures)

RNS-320 stores 8 ECoGs (90 second duration each); then it starts overwriting the oldest one without warning – so teach patient to regularly upload data to laptop.

**DETECTION**

Detection counts: counts of irregular epileptiform activity detected by the RNS (mostly composed of brief interictal epileptiform events but also include a small number of electrographic seizure onsets).

Long episode counts: counts of a specific type of detection trigger (lasting longer than a pre-specified time period) that often represent electrographic seizures.

N.B. only 10% of RNS triggers are actual seizures! (thus, it is correct to say that “RNS detects electrographic activity” and not “electrographic seizures”)

**STIMULATION**

Device stimulates up to 5 times if redetection happens right away.

**OUTCOMES**

**NEUROPSYCHOLOGICAL**

- some expert concerns that hippocampal (longitudinal) depth electrode placement may affect verbal memory – do neuropsychological testing 2 mos after implantation (before turning stim on).

**SEIZURES**

- after RNS implantation, for 2 months postop seizure frequency may increase.
- RNS uncovered that clinical seizures are only the tip of iceberg.

Neuropace Trial - responder rate:

By seizure type

CPS 27%

Geller 2017. RNS for temporal epilepsy
13% seizure free! (at 8 years: 26% of patients were seizure-free for at least 6 months and 18% for at least a year)

- history of VNS has no influence on outcomes.
- effectiveness is similar for all ages and regardless of where the seizures started.

**STUDIES**

**Feasibility Study**
- n=65

**Pivotal Study**
- randomized, controlled, double-blinded pivotal trial
- n=191

**Long-term treatment (LTT) trial**
- n=256
- at 7 years:
  - 66% responder
  - 72% median seizure reduction
  - at least one seizure-free period lasting:
    - ≥ 3 months - 39% of patients
    - ≥ 6 months - 29% of patients
    - ≥ 1 year - 16% of patients
- at 9 years:
  - 75% median seizure reduction
  - at least one seizure-free period lasting:
    - ≥ 6 months - 28% of patients
    - ≥ 1 year - 18% of patients
  - no chronic stimulation-related adverse effects, no adverse cognitive or neuropsychological effects

**MEDICAL TREATMENT MONITORING**

- typically, it takes many months to know whether a new AED will improve seizure control.
- electrographic data recorded by the RNS may be used to assess whether a new AED is likely to improve seizure frequency in as early as one month.

**Clinical and electrocorticographic response to AED with RNS (correlations between device data and clinical seizure frequency)**


- in patients with RNS, adding clobazam or levetiracetam gave higher clinical benefit (seizure reduction) than starting lacosamide or pregabalin – that correlated with change in interictal spike rate.
BIBLIOGRAPHY for ch. “Epilepsy and Seizures” → follow this LINK