Neurostimulation for Drug-Resistant Epilepsy

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Disclosures

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Antiepileptic drugs: The more things change...

Coatsworth (1971): 6 drugs, 38% refractory
Gowers (1881): 1 drug, 36% refractory

Brodie (2012): 26 drugs, 32% refractory
Kwan & Brodie (2000): 15 drugs, 37% refractory

Pre-surgical evaluation for drug-resistant epilepsy

Scalp EEG 3T MRI PET MEG SPECT Wada

Stereo-EEG
Stimulation mapping

Grid electrodes
Epilepsy surgery can be highly effective

Epilepsy surgery has limits

CASE: Bitemporal Seizures
66F with 30-year history of epilepsy and cognitive decline
Frequent focal dyscognitive seizures
Multiple hospitalizations for status epilepticus
Failed 10 antiepileptic drugs

Severe bilateral hippocampal sclerosis

CASE: Eloquent Cortex
18F with epilepsy onset at age 5, focal seizures 3-4x/week
Semiology: aphasia, choking, RUE clonus +/- generalization
Scalp EEG: LEFT frontotemporal onset, MRI: normal
Failed VNS
CASE: Prior Surgery
34M h/o severe TBI (R temporal ICH), epilepsy onset age 12 s/p RIGHT ATL, seizures improved but persisted
Semiology: L head turn, RUE tonic extension with clonus
Scalp EEG: Bitemporal spikes, poorly lateralized ictal onset

Neurostimulation for epilepsy
- Electrical modulation of neural activity without removal of brain tissue
- Possible therapeutic mechanisms:
  - Raise threshold for seizure initiation
  - Limit seizure propagation
  - Facilitate early seizure termination
  - Plasticity, network-level effects

Patient Selection for Neurostimulation
1. Failure of ≥ 2 AEDs
2. Presurgical evaluation
3. Surgical option?
Patient Selection for Neurostimulation

I. Multiple foci
   A. Bilateral (e.g., Bitemporal)
      i. Lesional
      ii. Non-lesional
   B. Unilateral
      i. Dual pathology

II. Unresectable focus
   A. Eloquent
      i. Language
      ii. Sensorimotor
      iii. Vision
   B. Prior Surgery
      i. ATL
   C. Extensive / Deep Lesion
      i. PVNH
   D. Other
      i. Cognitive risks
      ii. Patient preference

Vagus Nerve Stimulator

- Open-loop stimulation of the left vagus nerve
- No need to localize seizure onset zone
- Magnet swipe triggers additional stimulation
- 44% median seizure frequency reduction at 3 y
- Effective for focal and generalized epilepsy
- Side effects: cough, hoarseness, sleep disruption
- Battery life: 3–8 y

‘Closed-loop’ VNS (AspireSR®)

- EEG desynchronization?
Responsive Neurostimulation

Records brain activity
Detected abnormal activity
Stimulates to stop activity

Electrodes (depths/strips):
- Record neural activity (EEG)
- Stimulate to reduce seizures

Lead wires

Neurostimulator:
- Cranially implanted
- Electronics and battery

The RNS® System

Providers
Patients

https://

RNS System implantation

- Leads (strips and/or depths) placed at the seizure focus/foci
- Neurostimulator implanted in the skull
Chronic ambulatory electrocorticography

Remote Wand Telemetry

Patient collects data from the neurostimulator and uploads it to a secure website.

Online Data Review

Provider logs in to secure website to view patient’s ECoG data.

Chronic ambulatory ECoG can inform surgical planning

CASE
44-year old male veteran with epilepsy onset at age 21

Focal dyscognitive seizures 2x/week; GTCS 2x/year
IQ 140, Mensa member, cognitively demanding job
vEEG: usu. LEFT temporal, 1 episode RIGHT temporal status

Bilateral hippocampal sclerosis
Declined palliative LEFT ATL
RNS System: bilateral hippo depths

Chronic ambulatory ECoG for spell characterization

CASE: 38M multifocal left hemispheric peri-Rolandic seizures

- Called clinic to report episodes of suddenly “slumping” to one side
- Spell type not previously captured during IC-EEG
- Patient swiped magnet over neurostimulator to trigger ECoG storage

Magnet swipe
Chronic ambulatory ECoG for spell characterization

**CASE: 18F** multifocal left hemispheric seizures, RNS strips left temporal and parietal lobes
- Called clinic on post-op day 10 to report abrupt onset of right hand numbness x hours
- Concern for vascular process
- Patient swiped magnet over neurostimulator to trigger ECoG storage

Focal sensory status epilepticus
Symptoms resolved with benzo’s

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Chronic ambulatory ECoG to capture rare events

**CASE: 26F w/ perinatal MCA stroke, R MTS, 2 sz types, s/p R ATL, RNS over motor strip**
- Seizure-free for 7 months after ATL and RNS implantation
- Found down at home by her mother, ?post-ictal
- Mother downloaded and transmitted device data from the ER

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Hyperacute seizure reduction by the RNS System

**Responsive Stim OFF**

**Responsive Stim ON**

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Subacute seizure reduction by the RNS System

**Change in Seizure Frequency during Blinded Period (Treatment vs. Sham)**

- Sham (n=94)
- Treatment (n=97) (p = 0.012, GEE)

*Adlard B. et al., Neurology (2011)**
Chronic seizure reduction by the RNS System

Seizure-free Intervals:
- ≥ 6 mo: 29%
- ≥ 1 yr: 16%

UCSF RNS System Patients (N=22)

**UNRESECTABLE FOCUS**
- Bilateral hippocampal (5)
- PVNH (1)
- Eloquent cortex (4)
  - Broca’s area (1)
  - Wernicke’s area (1)
  - Sensorimotor (1)
  - Primary Visual (1)

**RESECTIVE SURGERY**
- Prior ATL (3)
- Concurrent resection (3)
- Future surgery (2)

**REGIONAL ONSET**
- Frontal (1)
- Parietal (2)
- Insular (1)

RNS System vs. VNS

**RNS System Advantages:**
- Imperceptible stimulation
- Records brain activity (ECoG)
- Works locally, on-demand
- May be more effective

**RNS System Disadvantages:**
- More invasive (intracranial)
- Must localize seizure onset zone(s)
- Not indicated in children or primary generalized epilepsy
- MRI contraindicated
Deep Brain (Anterior Thalamus) Stimulation

- Approved in Europe and Canada, soon to be approved in U.S.
- Open-loop bilateral DBS of anterior thalamic nuclei
- 69% median seizure frequency reduction at 5 y (SANTE trial)
- Temporal lobe epilepsy may respond best
- May have adverse effects on mood, memory, and sleep

Fisher and Velasco, Nat Rev Neurol 2015
Fisher et al., Epilepsy 2010 May;51(5):899-908

Drug-Resistant Epilepsy

- Seizures localized?
  - YES
  - NO
  - How many foci?

  - Safe to resect?
    - YES
    - NO
    - Low cognitive risks?

    - YES
    - NO
    - Will it be curative?

    - YES
    - NO
    - Patient willing?

    - YES
    - NO
    - Reactive Surgery or Laser Ablation

RNS System

- Combination therapies
  - VNS Therapy

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