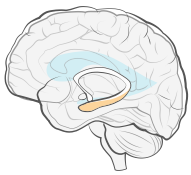
NEUROPACE

Brief Statement →

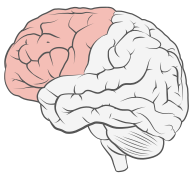
**REFERENCE GUIDE**

# RNS® System Patient Selection



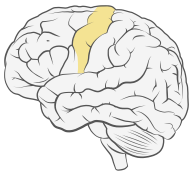
MESIAL TEMPORAL LOBE (MTL) → **PAGE 04**

**CASE STUDIES**: MTL Unilateral | MTL Bilateral



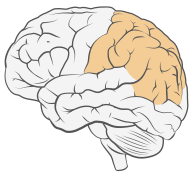
FRONTAL LOBE → **PAGE 11**

**CASE STUDIES**: Lateral Frontal | Interhemispheric



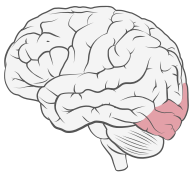
PRIMARY MOTOR → **PAGE 18**

**CASE STUDY**: Primary Motor



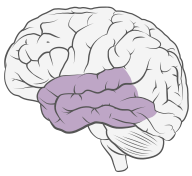
PARIETAL LOBE → **PAGE 22**

**CASE STUDY**: Parietal



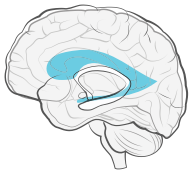
OCCIPITAL LOBE → **PAGE 26**

**CASE STUDY**: Occipital



TEMPORAL LOBE → **PAGE 30**

**CASE STUDIES**: Lateral Temporal | Insula



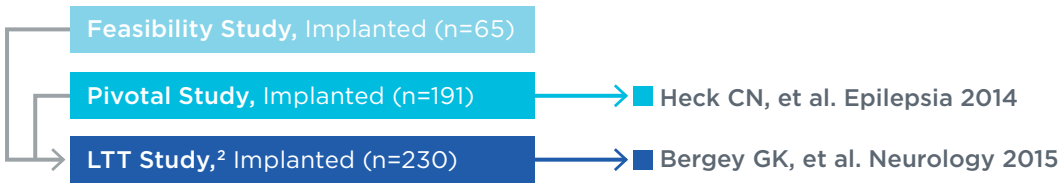
PERIVENTRICULAR NODULAR HETEROTOPIA (PVNH) → **PAGE 37**

**CASE STUDY**: PVNH

# RNS® System Clinical Studies

The safety and efficacy of the RNS® System is supported by **Class I Evidence** from a multi-center, prospective, randomized, controlled, double-blinded pivotal trial.[1]

The long-term prospective open label study (LTT Study) follows patients through 9 years, representing 1,389 patient implant years.[2]




## INDICATION FOR USE

The RNS® System is an adjunctive therapy in reducing the frequency of seizures in individuals 18 years of age or older with partial onset seizures who have undergone diagnostic testing that localized no more than 2 epileptogenic foci, are refractory to two or more antiepileptic medications, and currently have frequent and disabling seizures (motor partial seizures, complex partial seizures and/or secondarily generalized seizures). The RNS® System has demonstrated safety and effectiveness in patients who average 3 or more disabling seizures per month over the three most recent months (with no month with fewer than two seizures), and has not been evaluated in patients with less frequent seizures.

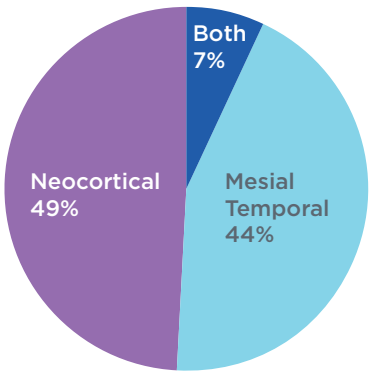
### References


1. Morrell et al., *Neurology*, 2011
2. Bergey et al., *Neurology*, 2015

# Long-term Safety (n=256)

## PATIENT CHARACTERISTICS[1]

### Region of Seizure Onset




### Among mesial temporal patients:

- 28% unilateral
- 72% bilateral

### Among neocortical patients:

- 45% non-mesial temporal
- 38% frontal
- 13% parietal
- 4% occipital

### History

- 32% had prior treatment with vagus nerve stimulation (VNS)
- 34% had prior treatment with epilepsy surgery
- 65% had prior localization with intracranial monitoring

## SAFETY

- SUDEP rate (probable or definite) was 2.0 per 1,000 patient stimulation years (CI 0.7-5.2).[2]
- 3.7% infection rate per neurostimulator procedure. All infections were superficial soft tissue infections. There were no chronic neurologic or medical consequences.[3]
- 2.7% of subjects reported intracranial hemorrhage not due to seizures. There were no persistent, clinically significant neurologic sequelae.[3]


**References**

1. Bergey, GK. et al. Neurology. 2015 Feb24; 84(8):810-7.
2. Devinsky O et al., SUDEP Rate in Patients with Medically Intractable Partial Onset Seizures Treated with Brain Responsive Neurostimulation. *American Epilepsy Society*
3. Weber PB, et al. Infection and Erosion Rates in Trials of a Cranially Implanted Neurostimulator Do Not Increase with Subsequent Neurostimulator Placements. *Stereotact Funct Neurosurg*. 2017;95(5):325-329.


Note: Retrospective analysis of ongoing prospective study. The study was not powered to drive conclusions of clinical significance. N values are small and caution must be taken while interpreting results.

CLINICAL EXPERIENCE

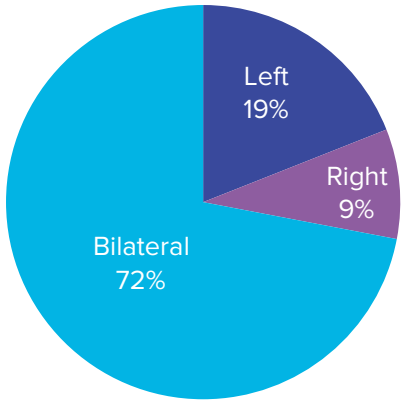
# Mesial Temporal Lobe

## PATIENT POPULATION[1]

**111 adults** with accumulated experience of 671 implant years. All data reported through 11/01/2014.

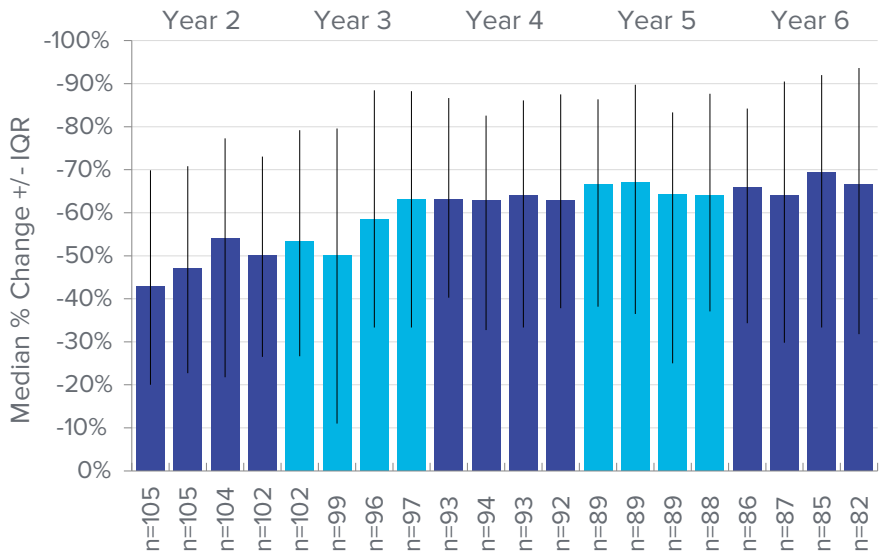
| Patient Characteristics | Mean (min–max) or % |
|---|---|
| Follow-up | 6.1 years<br>(5 weeks–10.4 years) |
| Seizure frequency at baseline (seizures/month) | 15 (1–217)<br>Median = 8 |
| Prior intracranial monitoring | 46% |
| Prior epilepsy surgery | 12% |
| Prior vagus nerve stimulation | 24% |
| Mesial temporal sclerosis on MRI | 55% |

**Seizure Onsets**




# Mesial Temporal Lobe

## SEIZURE REDUCTION[1]




**Last observation carried forward analyses (n=106)**

- 70% median reduction in seizures
- 66% responder rate (95% CI 57%–74%)

**No statistically significant differences in efficacy with**

- Prior epilepsy surgery
- Prior VNS
- Prior intracranial monitoring
- Mesial temporal sclerosis
- Bilateral onsets vs. unilateral onsets

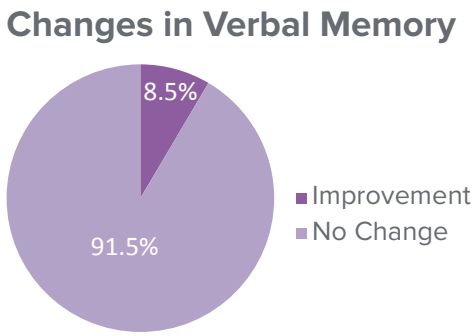
**Seizure-free Intervals**

- ≥ 3 months: 45% of patients
- ≥ 6 months: 29% of patients
- ≥ 1 year: 15% of patients

# Mesial Temporal Lobe

## COGNITIVE OUTCOMES[2]

- MTL onset patients showed statistically significant improvements in verbal memory (AVLT) (n=86; p=0.005)
- At 2 years, 8.5% demonstrated improvements in verbal memory and no patients demonstrated a decline (based on reliable change indices)




## SAFETY

Serious adverse events (SAEs) of particular interest in this group[1] (device related or relation uncertain)

- (1) suicide (patient with prior history of depression)
- (2) suicidal depression (both patients with a prior history of depression; one with a prior suicide attempt)

Serious adverse events for this subgroup were consistent with SAEs reported for all patients in the RNS® System clinical trials.


**References**

1. Geller et al., Brain-responsive neurostimulation in patients with intractable mesial temporal lobe epilepsy. *Epilepsia*. 2017 Jun;58(6):994-1004. doi: 10.1111/epi.13740. Epub 2017 Apr 11.
2. Loring, D. et al. *Epilepsia*. 2015 Sep 19. Doi: 10.1111/epi.13191.


CASE STUDY

# Mesial Temporal: Unilateral

32 year old woman presents with 3 to 4 seizures a month characterized by a rising epigastric sensation followed by loss of awareness and manual automatisms.

## HISTORY

**Seizure onset:** 15 years of age

**Seizure risk factors:** none

**Prior treatments:** failed trials of 4 antiepileptic medications

**Scalp EEG:** remarkable for interictal left temporal spikes (F8/T4); video-EEG captured 3 typical seizures with left anterior temporal ictal onset

**MRI:** normal

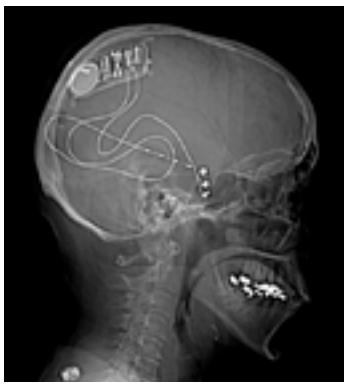
**Intracarotid Amytal (Wada) test:** left hemisphere language dominant

**Neuropsychological testing:** normal visual and verbal memory

## EVALUATION & PLAN

- Partial onset seizures of left mesial temporal lobe origin
- At risk for memory and language deficits following left temporal lobe resective surgery
- Candidate for RNS System with left mesial temporal responsive stimulation

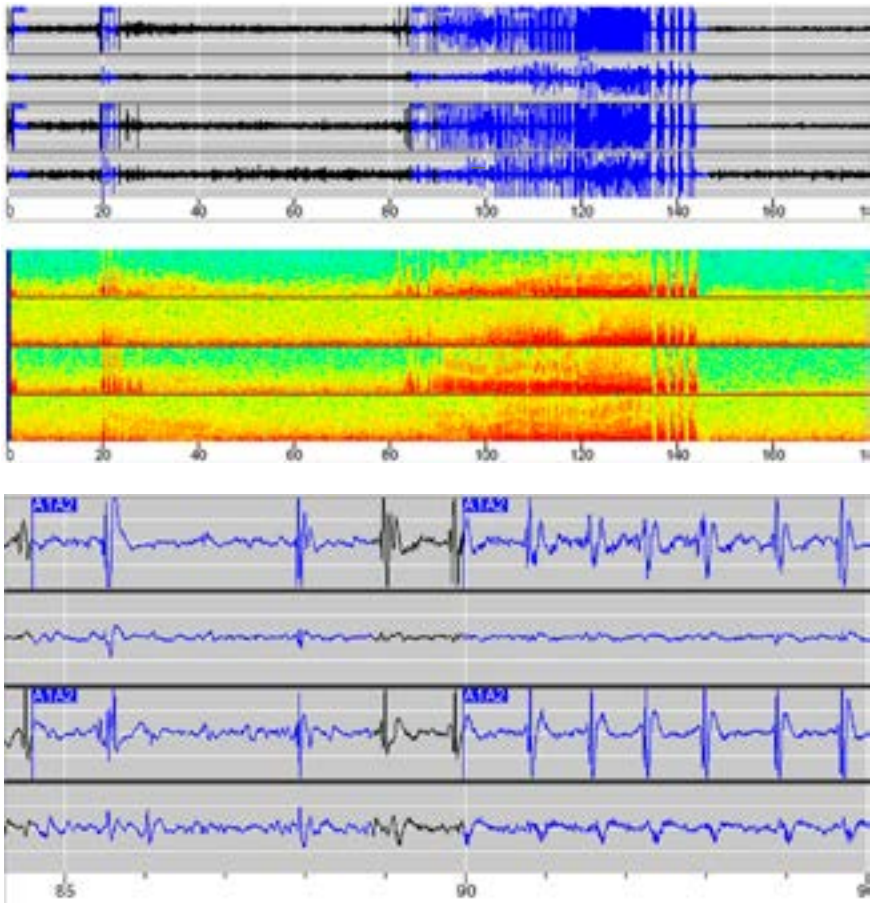
## SURGICAL APPROACH



- 1 hippocampal depth lead: occipital approach along long axis of hippocampus
- 1 subtemporal cortical strip lead

## ECOG

Electrographic seizure detected before neurostimulator has been programmed to provide responsive stimulation. The top 2 channels are recording from the hippocampal depth lead and the bottom 2 channels from the subtemporal strip lead. A1A2 marker indicates the simultaneous detection of hypersynchronous activity on the depth and strip leads. The ECOG and corresponding Fast Fourier Transform (FFT) are shown above an expanded view of the ECOG. Time is indicated on the X axis.




*This case study is a composite adapted from actual case files and results are not necessarily representative of the patient population.*

CASE STUDY

# Mesial Temporal: Bilateral

32 year old woman presents with 3 to 4 seizures a month characterized by characterized by a feeling of dread, then loss of awareness and nonsensical vocalizations.

## HISTORY

**Seizure onset:** 14 years of age

**Seizure risk factors:** none

**Prior treatments:** failed trials of 3 antiepileptic medications

**Scalp EEG:** interictal right temporal spikes (F4/T6) and infrequent left temporal sharps (F3/T3); video-EEG after antiepileptic medications were withdrawn captured 3 typical seizures with right anterior temporal ictal onset and one nocturnal generalized tonic clonic seizure with a left anterior temporal onset

**MRI:** hippocampal sclerosis on right and slight atrophy of left hippocampus

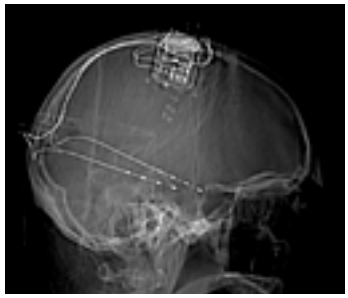
**Intracarotid Amytal (Wada) test:** left hemisphere language dominant, impaired recall after left and right injections

**Neuropsychological testing:** significant impairment of visuospatial memory, slight impairment of verbal memory

## EVALUATION & PLAN

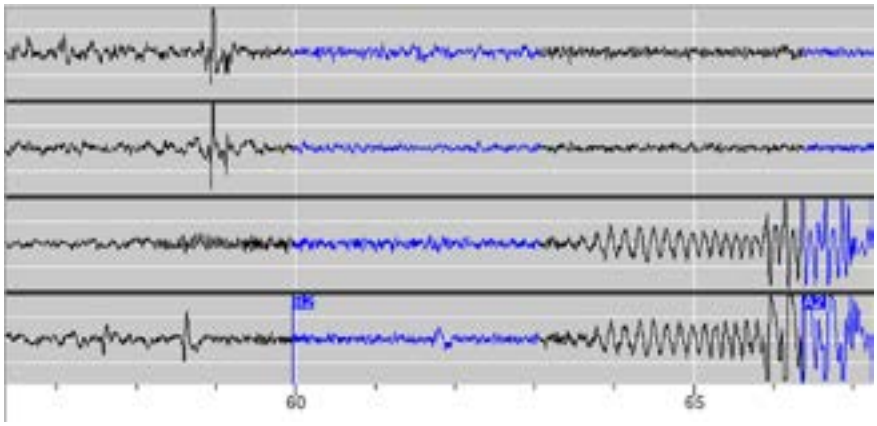
- Partial onset seizures of right mesial temporal lobe origin and possible left temporal origin as well
- Risk of substantial memory deficits following right temporal lobe resection
- Candidate for RNS System with left and right mesial temporal responsive stimulation

## SURGICAL APPROACH

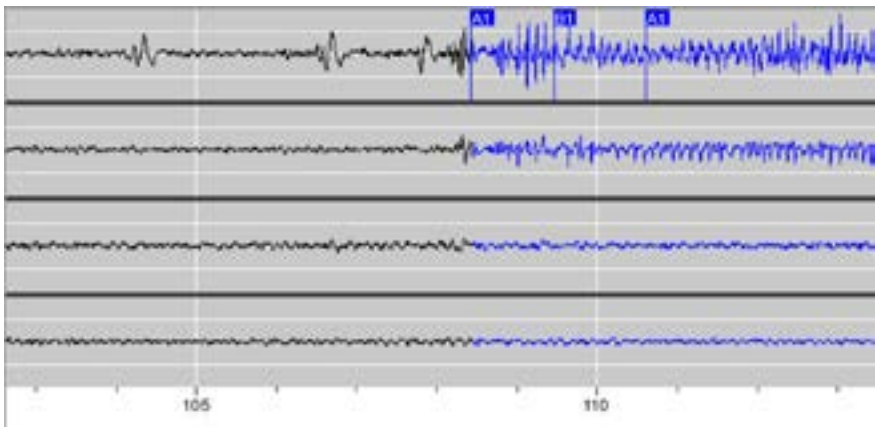


Right and left hippocampal depth leads: occipital approach along long axis of hippocampus

Electrographic seizure detected before neurostimulator has been programmed to provide responsive stimulation. The top 2 channels are recording from the left hippocampal depth lead and the bottom 2 channels from the right hippocampal depth lead. B2 indicates the detection of low voltage fast activity on the right depth lead.




Electrographic seizure detected before neurostimulator has been programmed to provide responsive stimulation. The top 2 channels are recording from the left hippocampal depth lead and the bottom 2 channels from the right hippocampal depth lead. A1 and B1 indicate the detection of increased amplitude rhythmic activity.




*This case study is a composite adapted from actual case files and results are not necessarily representative of the patient population.*

CLINICAL EXPERIENCE

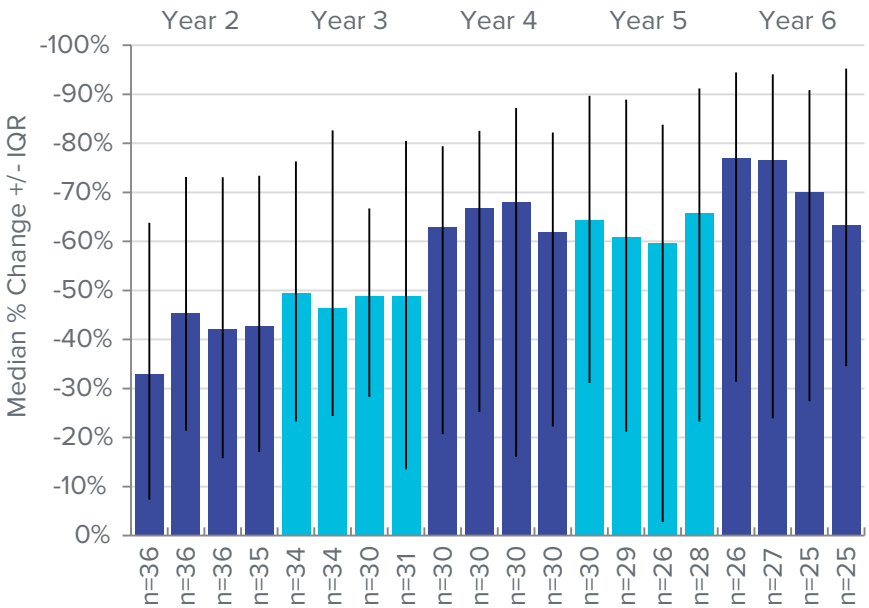
# Neocortical: Frontal

## PATIENT POPULATION[1]

**39 adults.** All data reported through 11/01/2014.

| Patient Characteristics | Mean (min–max) or % (n/N) |
|---|---|
| Seizure frequency at baseline (seizures/month) | 101 (4–723)<br>Median = 37 |
| Prior intracranial monitoring | 95% (37/39) |
| Prior epilepsy surgery | 44% (17/39) |
| Prior vagus nerve stimulation | 44% (17/39) |
| Anatomical abnormality on MRI | 49% (19/39) |

## SEIZURE REDUCTION[2]



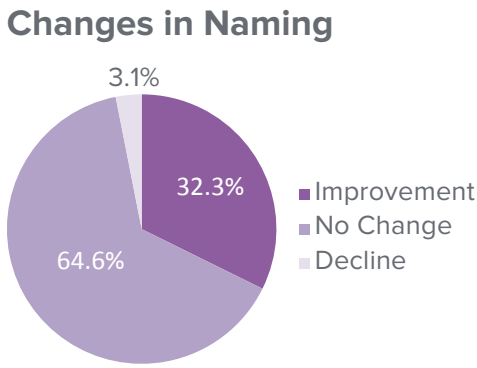

**Last observation carried forward analyses (n=37)**

- 70% median reduction in seizures
- 54% responder rate (95% CI 38–69%)

# Neocortical: Frontal

## COGNITIVE OUTCOMES[3]

- Neocortical onset patients showed statistically significant improvements in naming (BNT) (n=76; p<0.001)
- At 2 years, 32% demonstrated improvements in naming and 3% demonstrated declines (based on reliable change indices)




## SAFETY

**No serious device-related adverse events related to motor function, language, or mood.**[2]

Serious adverse events (SAEs) for this subgroup were consistent with SAEs reported for all patients in the RNS® System clinical trials.

### References


1. Data on file.
2. Jobst et al,. Brain-responsive neurostimulation in patients with medically intractable seizures arising from eloquent and other neocortical areas. *Epilepsia*. 2017 Jun;58(6):1005-1014. doi: 10.1111/epi.13739. Epub 2017 Apr 7.
3. Loring, D. et al. *Epilepsia.* 2015 Sep 19. Doi: 10.1111/epi.13191.


CASE STUDY

# Neocortical: Lateral Frontal

A 51 year old man experiences 5 to 10 seizures a month that often cluster and begin with forced turning of the eyes and head to the left followed quickly by blinking and twitching of the left face, then extension of the left arm and leg and then generalized tonic clonic movements.

## HISTORY

**Seizure onset:** 12 years of age

**Prior treatments:** failed trials of 5 antiepileptic medications and VNS (no longer implanted)

**Scalp EEG:** typical seizure captured with diffuse attenuation over right frontal lobe followed by muscle artifact

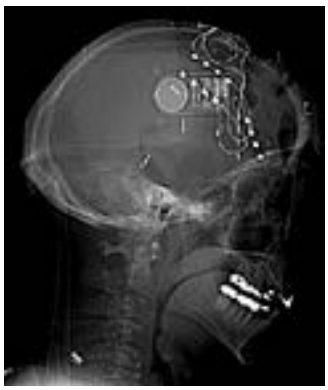
**MRI:** cortical dysplasia in the right lateral frontal lobe

**Intracranial EEG monitoring:** ictal onset adjacent to region of dysplasia; mapping elicits eye deviation to the left followed by left face twitching

## EVALUATION & PLAN

- Focal motor seizures involving right frontal eye fields with rapid propagation to right motor cortex
- At risk for deficits in eye movements and left face motor function with resection
- Candidate for RNS System with strips placed over region of dysplasia

## SURGICAL APPROACH

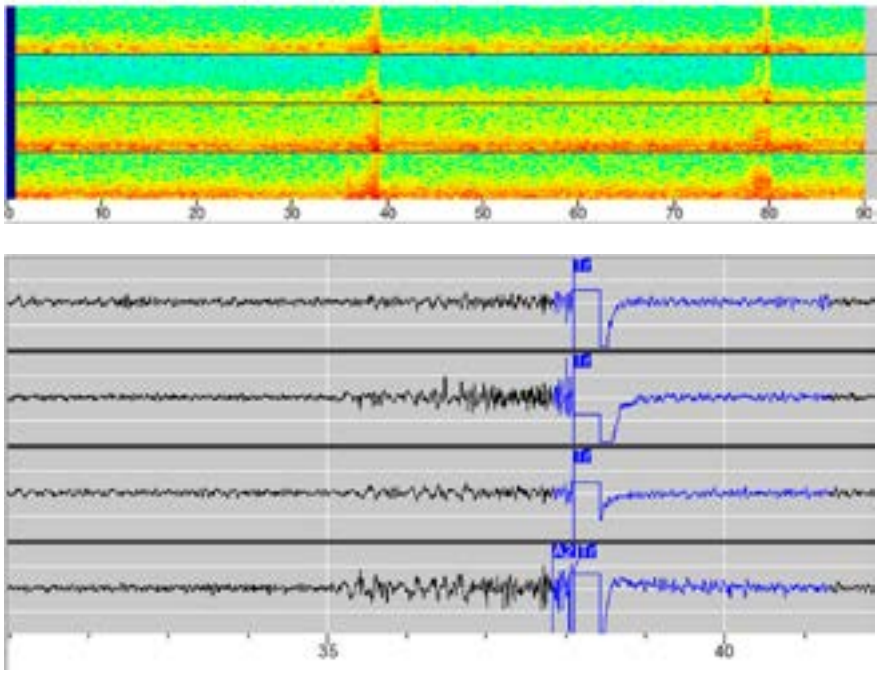


4 subdural strip leads placed*:

- 2 subdural strip leads in the lateral prefrontal region including the frontal eye fields
- 2 subdural strip leads spanning premotor and motor cortex (1 superior, 1 inferior)

## ECOG

Detection of brief epileptiform event (A2) followed by stimulation (Tr). The top 2 channels are recording from a frontal eye field strip lead and the bottom 2 channels from the superior frontal motor strip lead.




*Only 2 leads are connected to the neurostimulator at once.

*This case study is a composite adapted from actual case files and results are not necessarily representative of the patient population.*

CASE STUDY

# Neocortical: Interhemispheric

25 year old man presents with 5 to 9 nocturnal generalized tonic clonic seizures a month.

## HISTORY

**Seizure onset:** 19 years of age

**Seizure risk factor:** MVA related head trauma with loss of consciousness > 48 hours

**Neurological exam:** subtle right pronator drift

**Prior treatments:** failed trials of 5 antiepileptic medications

**MRI:** normal

**Scalp video-EEG:** remarkable for seizures characterized by right arm stiffening followed by generalized tonic stiffening and subsequent clonic movements, ictal EEG shows diffuse left frontal attenuation followed by muscle artifact

**Intracranial monitoring:**

- Subdural grid over left frontal pre- and post-central gyrus, left interhemispheric strips
- Diffuse ictal onset over left anterior quadrant
- Onset correlates with left supplementary motor cortex

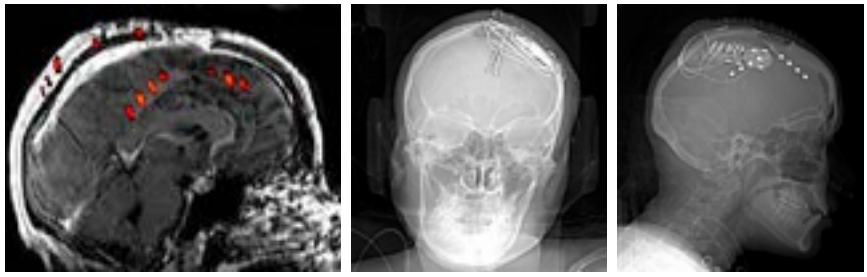
## EVALUATION & PLAN

- Partial onset seizures left supplementary motor cortex
- At risk for right hand and arm motor deficits following resection
- Candidate for RNS System with left supplementary motor strips

## SURGICAL APPROACH

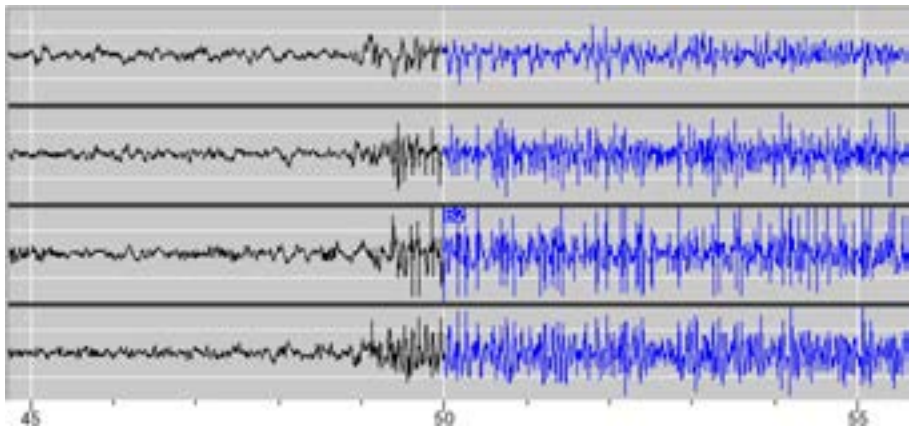
3 cortical strip leads placed*:

- 1 in the anterior and 1 in the posterior interhemispheric space spanning left supplementary motor cortex
- 2 over the lateral frontal convexity spanning the central gyrus (1 superior and 1 inferior)

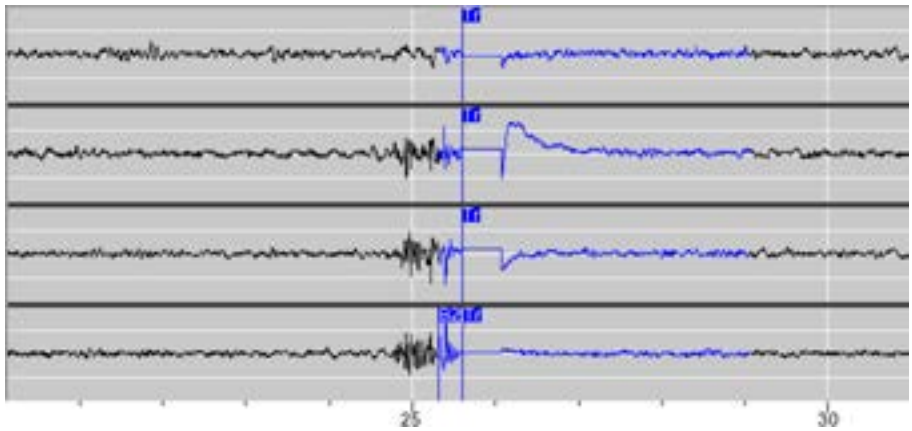


## ECOG

Electrographic seizure detected before stimulation is enabled. The top 2 channels are recording from the anterior interhemispheric strip and the bottom 2 channels from the superior lateral frontal strip. B2 indicates detection.




Electrographic discharge detected at B2 and treated with responsive stimulation (Tr).



## TREATMENT EXPERIENCE

**8 adults.** Data through 11/01/2014.

**Seizure reduction, last observation carried forward analyses**[1]

- Patient 1: **-100%**
- Patient 2: **-95%**
- Patient 3: **-89%**
- Patient 4: **-40%**
- Patient 5: **-23%**
- Patient 6: **-3%**
- Patient 7: **+1%**
- Patient 8: **+65%**

**Safety**

- Serious adverse events (SAEs) for this subgroup were consistent with SAEs reported for all patients in the RNS® System clinical trials.

**References**

1. Data on file.

*Only 2 leads are connected to the neurostimulator at once.

*This case study is a composite adapted from actual case files and results are not necessarily representative of the patient population.*

CLINICAL EXPERIENCE

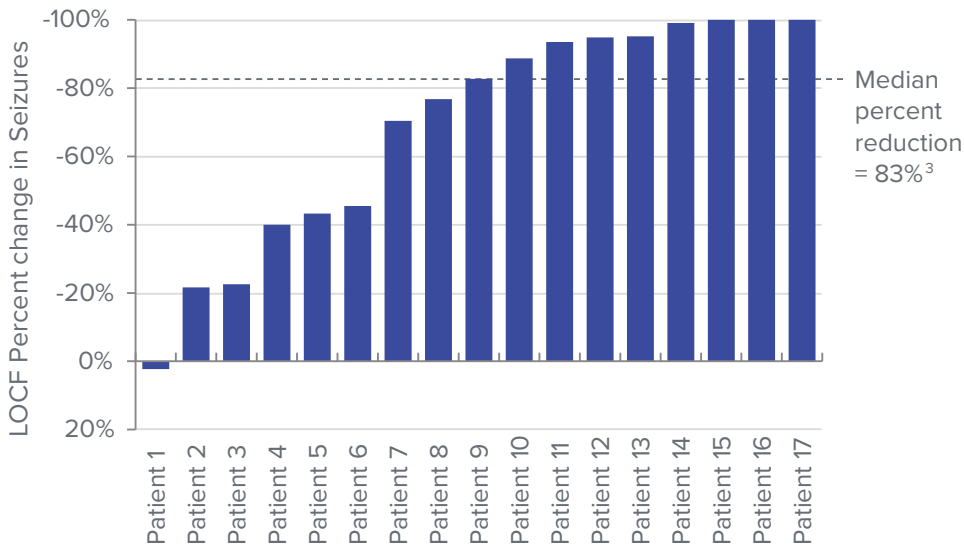
# Neocortical: Primary Motor

## PATIENT POPULATION[1]

**17 adults** who had simple partial motor seizures at baseline. All data reported through 11/01/2014.

| Patient Characteristics | Mean (min–max) or % (n/N) |
|---|---|
| Seizure frequency at baseline (seizures/month) | 91 (37–326)<br>Median = 37 |
| Prior intracranial monitoring | 100% (17/17) |
| Prior epilepsy surgery | 47% (8/17) |
| Prior vagus nerve stimulation | 41% (7/17) |
| Anatomical abnormality on MRI | 59% (10/17) |

## SEIZURE REDUCTION[2]




Last observation carried forward analyses (n=17) showing individual patient responses.

# Neocortical: Primary Motor

## SAFETY

**No serious device-related adverse events related to motor function.**[2]

Serious adverse events (SAEs) for this subgroup were consistent with SAEs reported for all patients in the RNS® System clinical trials.

### References


1. Data on file.
2. Jobst, B. et al. Long-Term Outcome of Adults with Medically Intractable Frontal Lobe Seizures Treated with Responsive Neurostimulation. *American Epilepsy Society.* Philadelphia. December 2015.
3. Jobst et al,. Brain-responsive neurostimulation in patients with medically intractable seizures arising from eloquent and other neocortical areas. *Epilepsia*. 2017 Jun;58(6):1005-1014. doi: 10.1111/epi.13739. Epub 2017 Apr 7.


CASE STUDY

# Neocortical: Primary Motor

34 year old right handed man presents with 10 to 20 simple partial motor seizures a month beginning with left hand clonic movements spreading to left arm and face.

## HISTORY

**Seizure onset:** 30 years of age

**Prior treatments:** failed trials of 3 antiepileptic medications

**MRI:** right frontal cryptic arteriovenous malformation (AVM) with margin of hemosiderin

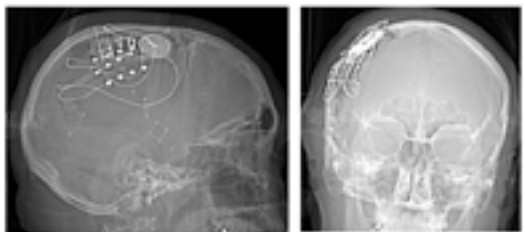
**Intracranial EEG:** ictal onset corresponds to lesion; functional mapping indicates that ictal onset overlaps with primary motor cortex

**Resection of AVM** with posterior margin of resection anterior to left hand area; seizure frequency not changed

## EVALUATION & PLAN

- Partial onset seizures arising from right primary motor cortex, hand area
- Lesionectomy did not achieve seizure control; at risk for weakness in left hand with additional resection
- Candidate for treatment with the RNS System with responsive stimulation to primary motor cortex

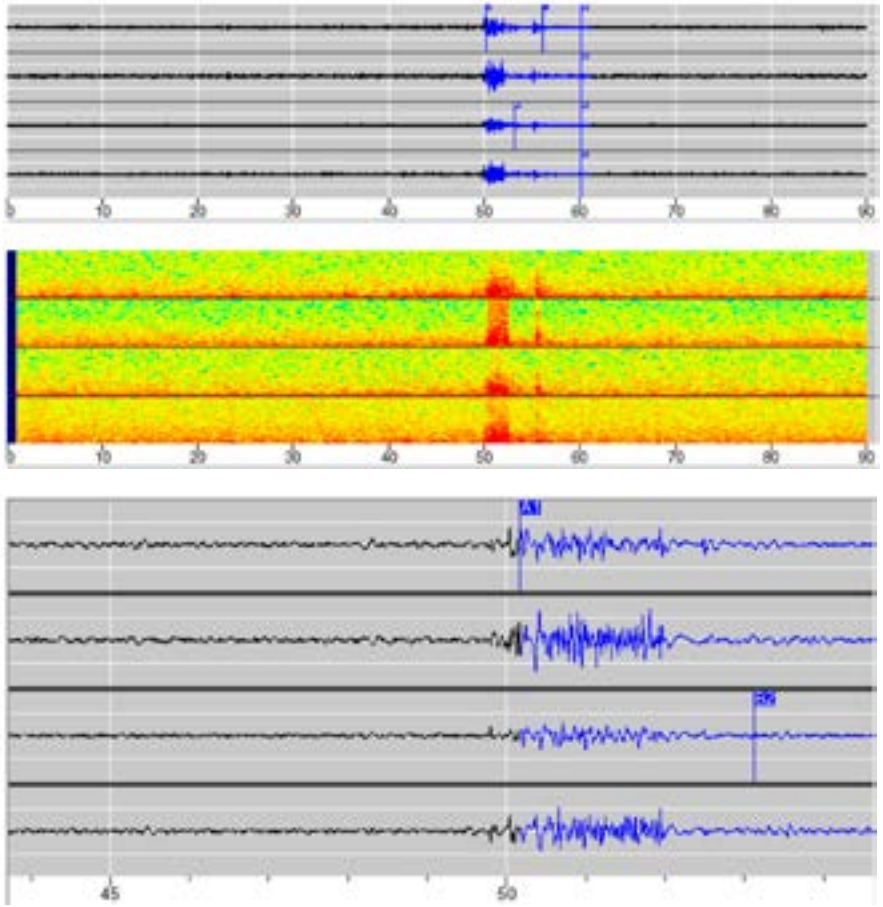
## SURGICAL APPROACH



3 frontoparietal strips*; middle and inferior strips connected to neurostimulator

## ECOG

ECOG recordings before neurostimulator has been programmed to provide responsive stimulation. Epileptiform discharges are detected in electrodes from the middle (A1) and inferior (B2) strips. The ECOG and corresponding Fast Fourier Transform (FFT) are shown above an expanded view of the ECOG.




*Only 2 leads are connected to the neurostimulator at once.

*This case study is a composite adapted from actual case files and results are not necessarily representative of the patient population.*

CLINICAL EXPERIENCE

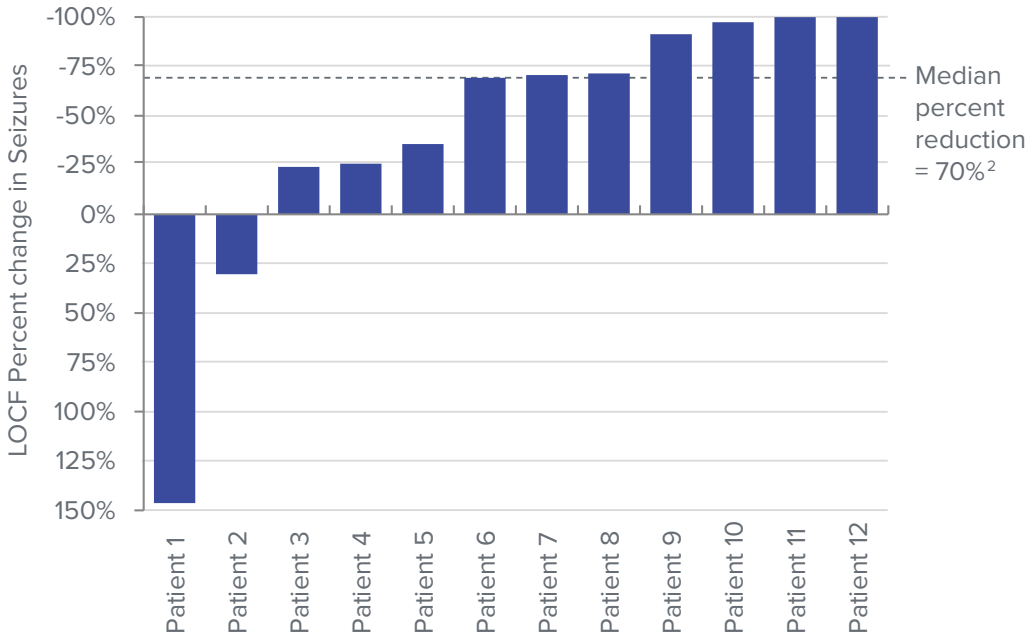
# Neocortical: Parietal

## PATIENT POPULATION[1]

**17 adults.** All data reported through 11/01/2014.

| Patient Characteristics | Mean (min–max) or % (n/N) |
|---|---|
| Seizure frequency at baseline (seizures/month) | 209 (0–2319)<br>Median = 33 |
| Prior intracranial monitoring | 76% (13/17) |
| Prior epilepsy surgery | 71% (12/17) |
| Prior vagus nerve stimulation | 24% (4/17) |
| Anatomical abnormality on MRI | 88% (15/17) |

## SEIZURE REDUCTION[1]




Last observation carried forward analyses (n=12) showing individual patient responses.

# Neocortical: Parietal

## SAFETY

Serious adverse events (SAEs) for this subgroup were consistent with SAEs reported for all patients in the RNS® System clinical trials.


### References

1. Data on file.
2. Jobst et al,. Brain-responsive neurostimulation in patients with medically intractable seizures arising from eloquent and other neocortical areas. *Epilepsia*. 2017 Jun;58(6):1005-1014. doi: 10.1111/epi.13739. Epub 2017 Apr 7.


CASE STUDY

# Neocortical: Parietal

36 year old woman with 5 to 10 seizures a month that awaken her from sleep with left arm and abdominal pain lasting 15 seconds, after which she loses awareness. Her husband reports that she has heavy labored breathing and staring and is often incontinent of urine. Generalized tonic clonic seizures occur about twice a month.

## HISTORY

**Seizure onset:** 32 years of age coincident with a pregnancy

**Prior treatments:** Failed trials of 2 antiepileptic medications

**MRI:** evidence for small cortical lesions in the post-central gyrus and lateral temporal lobe consistent with right mesial cerebral artery emboli

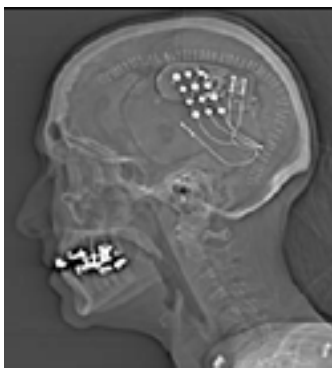
**Scalp EEG:** wide spread rhythmic theta over C4, P4, T4 and T6 with seizure

**Intracranial EEG and mapping:** grid over right frontal and parietal lobe indicates ictal onset corresponds to left arm primary sensory cortex

## EVALUATION & PLAN

- Partial onset seizures of right primary sensory cortex
- At risk for left arm sensory deficits with resection of seizure focus
- Candidate for RNS System with responsive stimulation to post-central gyrus corresponding to left arm sensory cortex

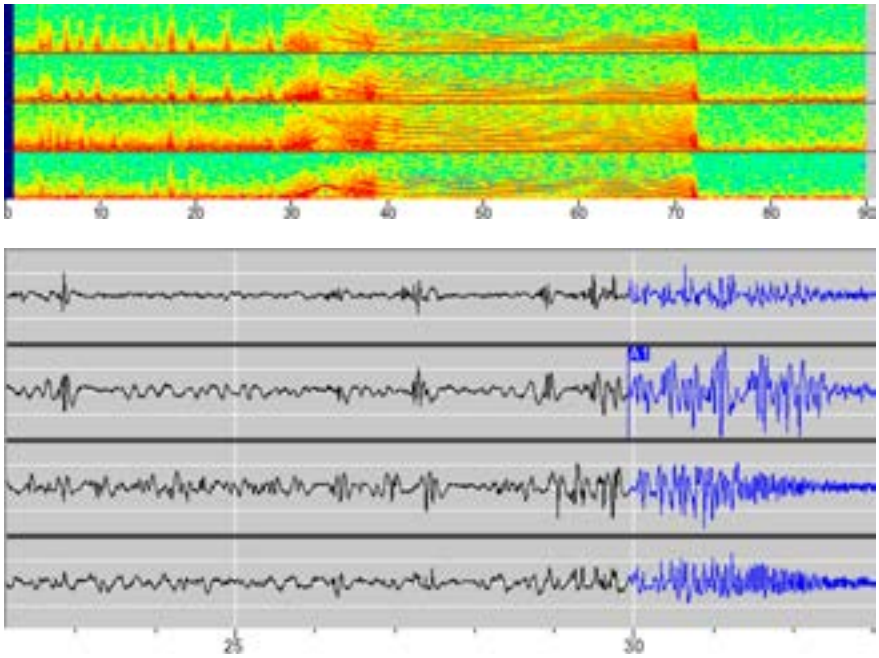
## SURGICAL APPROACH



3 parietal strip leads*

## ECOG

Electrographic seizure obtained from strip leads placed anterior (top 2 channels) and posterior (bottom 2 channels) to cortical dysplasia. The detection occurs at A1. The top image is a spectral array display (Fourier transform) and the bottom image is an ECOG display. Time is indicated on the X axis.




*Only 2 leads are connected to the neurostimulator at once.

*This case study is a composite adapted from actual case files and results are not necessarily representative of the patient population.*

CLINICAL EXPERIENCE

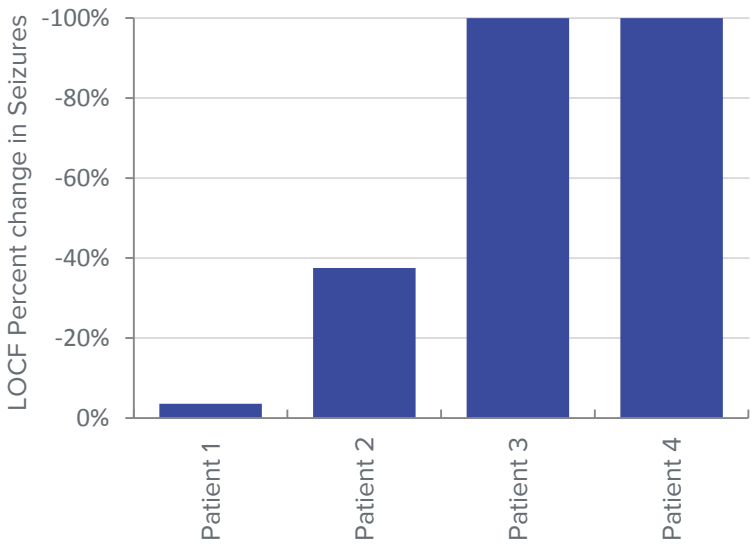
# Neocortical: Occipital

## PATIENT POPULATION[1]

**4 adults.** All data reported through 11/01/2014.

| Patient Characteristics | Mean (min–max) or (n/N) |
|---|---|
| Seizure frequency at baseline (seizures/month) | 6 (4–10)<br>Median = 5 |
| Prior intracranial monitoring | 3 out of 4 |
| Prior epilepsy surgery | none |
| Prior vagus nerve stimulation | none |
| Anatomical abnormality on MRI | 2 out of 4 |

## SEIZURE REDUCTION[2]




Last observation carried forward analyses (n=4) showing individual patient responses.

# Neocortical: Occipital

## SAFETY

**No serious device-related adverse events related to vision.**[2]

Serious adverse events (SAEs) for this subgroup were consistent with SAEs reported for all patients in the RNS® System clinical trials.

### References


1. Data on file.
2. Jobst et al,. Brain-responsive neurostimulation in patients with medically intractable seizures arising from eloquent and other neocortical areas. *Epilepsia*. 2017 Jun;58(6):1005-1014. doi: 10.1111/epi.13739. Epub 2017 Apr 7.


CASE STUDY

# Neocortical: Occipital

23 year old woman with 4 to 5 clusters of seizures a month characterized by unformed visual phenomenon in right visual field and 3 nocturnal complex partial and/or generalized tonic clonic seizures a month.

## HISTORY

**Seizure onset:** 10 years of age

**Seizure risk factors:** no risk factors except for premature birth (29 weeks)

**Prior treatments:** failed trials of 4 antiepileptic medications

**Neurological exam:** partial right inferior quadrant visual field defect

**Scalp EEG:** interictal left occipital spikes; video-EEG captured 3 typical seizures with left anterior temporal ictal onset

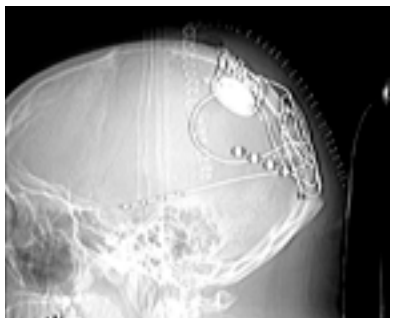
**MRI:** left occipital encephalomalacia

**Intracranial monitoring:** ictal onset in region of encephalomalacia with rapid spread to left hippocampus, mapping indicated that removal of the entire ictal onset zone could complete the right quadrantonopisa

## EVALUATION & PLAN

- Partial onset of seizures of left occipital origin and early involvement of left hippocampus
- At risk for significant visual field deficit with resection
- Candidate for RNS System with responsive stimulation to left occipital region and left hippocampus

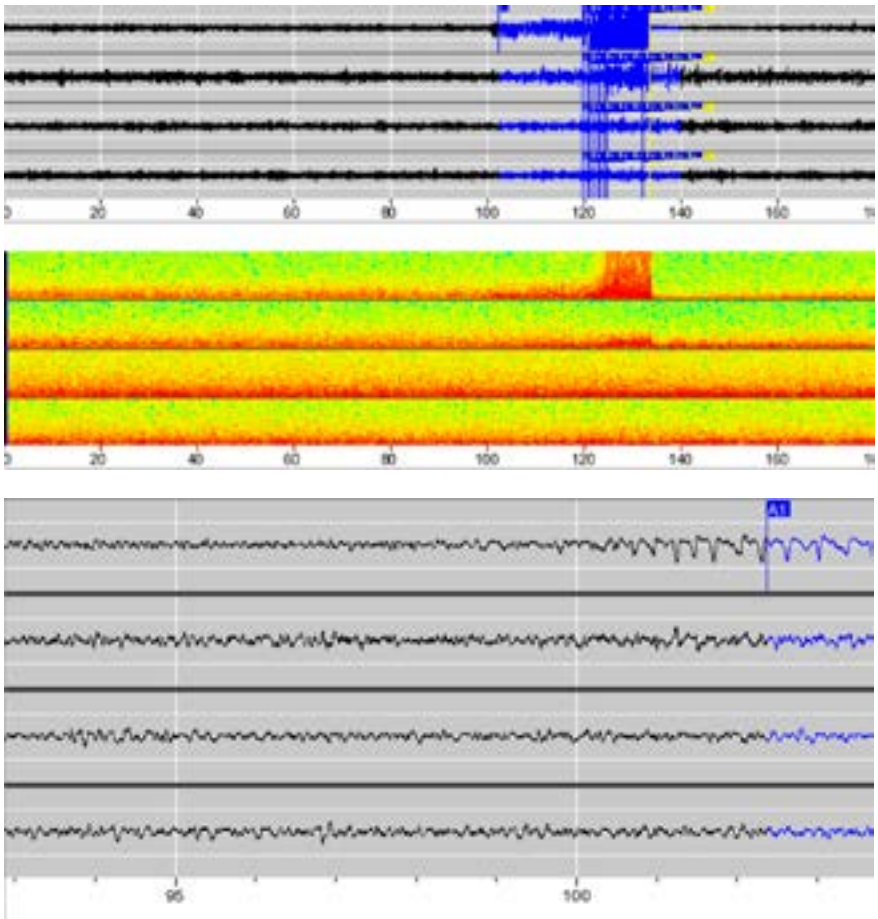
## SURGICAL APPROACH



- 1 depth lead in the hippocampus
- 1 subdural strip lead targeting the left occipital lobe

## ECOG

Electrographic seizure detected before stimulation was enabled. The top two channels are recording from the occipital strip lead and the bottom 2 channels from the hippocampal depth lead. A1 indicates detection. The ECOG and corresponding Fast Fourier Transform (FFT) are shown above an expanded view of the timeseries.




*This case study is a composite adapted from actual case files and results are not necessarily representative of the patient population.*

CLINICAL EXPERIENCE

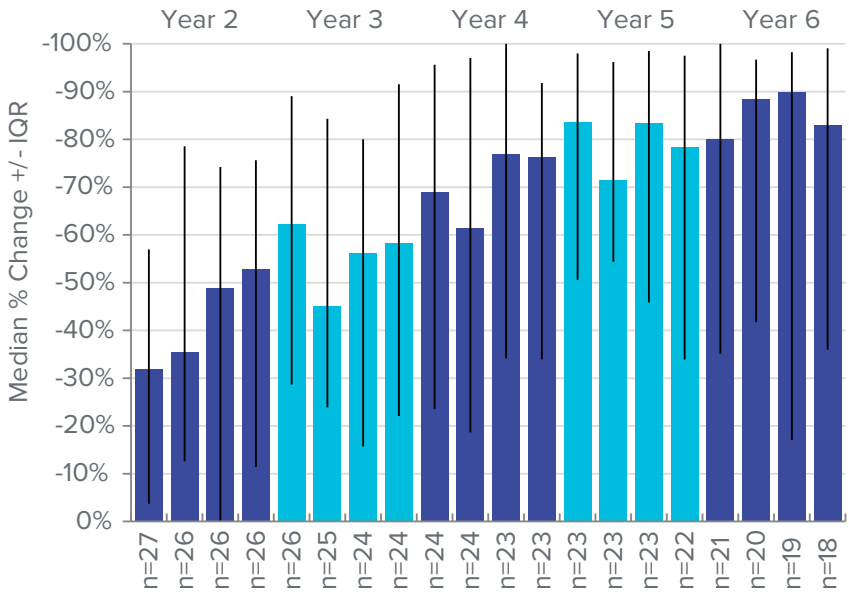
# Neocortical: Temporal (Non-Mesial)

## PATIENT POPULATION[1]

**32 adults**. All data reported through 11/01/2014.

| Patient Characteristics | Mean (min–max) or % (n/N) |
|---|---|
| Seizure frequency at baseline (seizures/month) | 26 (0–294)<br>Median = 7 |
| Prior intracranial monitoring | 78% (25/32) |
| Prior epilepsy surgery | 56% (18/32) |
| Prior vagus nerve stimulation | 38% (12/32) |
| Anatomical abnormality on MRI | 44% (14/32) |

## SEIZURE REDUCTION[2]




**Last observation carried forward analyses (n=27)**

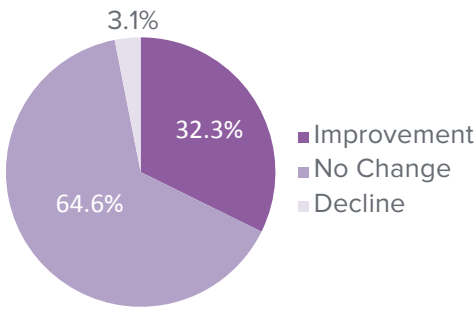
- 58% median percent reduction in seizures
- 67% responder rate (95% CI 48-81%)

# Neocortical: Temporal (Non-Mesial)

## COGNITIVE OUTCOMES[3]

- Neocortical onset patients showed statistically significant improvements in naming (BNT) (n=76; p<0.001)
- At 2 years, 32% demonstrated improvements in naming and 3% demonstrated declines (based on reliable change indices)

**Changes in Naming**




## SAFETY

**No serious device-related adverse events related to language or auditory function.**[2]

Serious adverse events (SAEs) for this subgroup were consistent with SAEs reported for all patients in the RNS® System clinical trials.

### References


1. Data on file.
2. Jobst et al,. Brain-responsive neurostimulation in patients with medically intractable seizures arising from eloquent and other neocortical areas. *Epilepsia*. 2017 Jun;58(6):1005-1014. doi: 10.1111/epi.13739. Epub 2017 Apr 7.
3. Loring, D. et al. Epilepsia. 2015 Sep 19. Doi: 10.1111/epi.13191.


CASE STUDY

# Neocortical: Lateral Temporal

43 year old woman presents with 10 to 20 simple partial seizures a month beginning with a buzzing sound that increases in volume over 15 seconds. The auditory phenomenon progresses to a complex partial seizure with loss of awareness, a blank stare and manual automatisms about 3 times a month.

## HISTORY

**Seizure onset:** 39 years of age

**Seizure risk factors:** none

**Prior treatments:** failed trials of 2 antiepileptic medications; has difficulty tolerating medication side effects

**Scalp EEG:** remarkable for left lateral temporal spikes (T3/T5); 3 typical auditory simple partial seizures begin with left mid-temporal rhythmic theta

**MRI:** evidence for small vessel disease

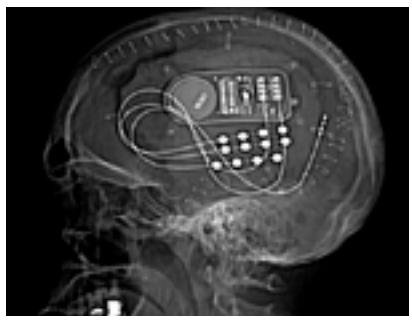
**Functional MRI for language:** left hemisphere language dominant, region of ictal onset corresponds to Wernicke's area

**Neuropsychological testing:** normal visual and verbal memory

## EVALUATION & PLAN

- Partial onset seizures of left lateral temporal lobe origin, probably Heschell's gyrus
- At risk for language deficits following left lateral temporal lobe resection
- Candidate for RNS System with left lateral temporal responsive stimulation

## SURGICAL APPROACH

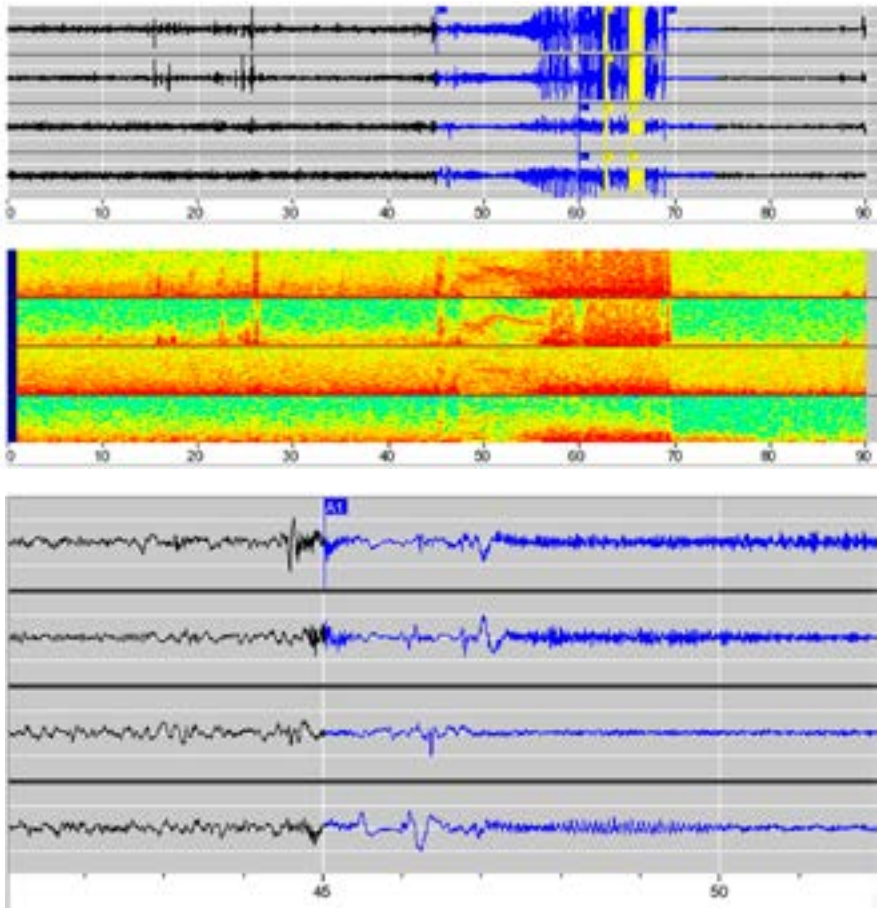


3 left lateral temporal cortical strip leads*

- Superior (connected)
- Middle (connected)
- Inferior (not connected)

## ECOG

Electrographic seizure detected before neurostimulator has been programmed to provide responsive stimulation. The top 2 channels are recording from the superior lateral temporal strip lead and the bottom 2 channels from the middle lateral temporal strip lead. A1 indicates detection. The ECOG and corresponding Fast Fourier Transform (FFT) are shown above an expanded view of the ECOG.




*Only 2 leads are connected to the neurostimulator at once.

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CASE STUDY

# Neocortical: Insula

42 year old man with 20 year history of seizures 4 to 5 times a month characterized by throat constriction, mouth and tongue dysesthesias, and dysarthria that sometimes progresses to focal clonic activity of the left face and arm. Once every 2 to 3 months, he will lose consciousness.

## HISTORY

**Seizure onset:** 22 years of age

**Seizure risk factors:** none

**Prior treatments:** failed trials of 5 antiepileptic medications as well as vagus nerve stimulation therapy

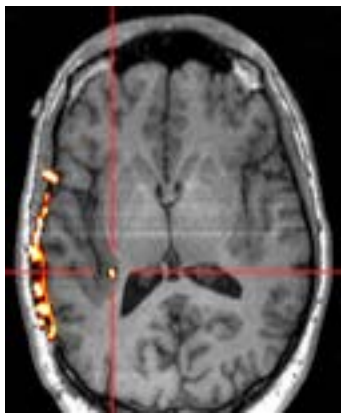
**Scalp video-EEG:** ictal onset involves mid and lateral temporal lobe electrodes as well rapid involvement of frontal lobe electrodes

**Intracranial EEG:** Earliest ictal changes in insula by SEEG with rapid hippocampal spread

## EVALUATION & PLAN

- Simple and complex partial seizures from insular cortex
- Because of the risks of surgery in the insular cortex, it was elected to proceed with treatment with the RNS System with a depth lead placed in the left insula

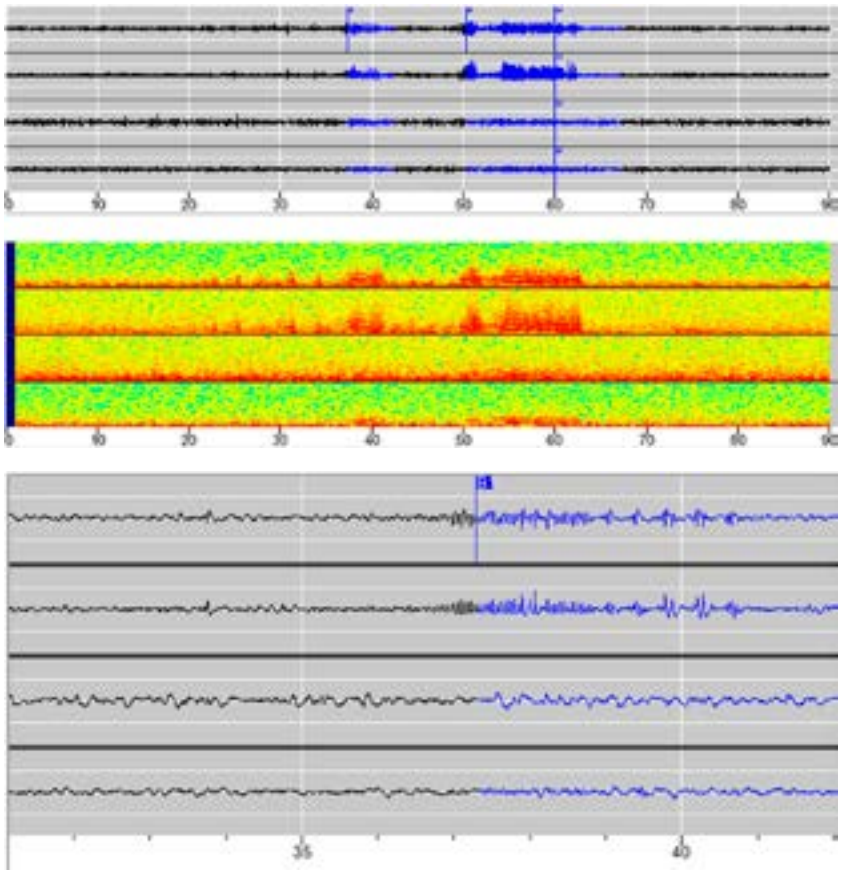
## SURGICAL APPROACH



- 1 depth lead targeting the left insular cortex
- 1 left frontal cortical strip lead

## ECOG

Epileptiform discharges detected before neurostimulator has been programmed to provide responsive stimulation. Insula depth lead is the top two channels and left frontal cortical strip lead is the bottom 2 channels. Detection in electrodes from the insular cortex is denoted by B1. The ECOG and corresponding Fast Fourier Transform (FFT) are shown above an expanded view of the ECOG.



**6 adults had onsets in the Insula.** 4 of these received stimulation in the Insula. Data through 11/01/2014.

**Seizure reduction, last observation carried forward analyses**[1]

- Patient 1: **-96.9%**
- Patient 2: **-93.2%**
- Patient 3: **-91.6%**
- Patient 4: **261%** (Physician noted that the lead might have been unintentionally pulled out of the insula during a lead revision procedure)

**Safety**

- There were no serious device related adverse events in these 4 patients[1].
- Serious adverse events (SAEs) for this subgroup were consistent with SAEs reported for all patients in the RNS® System clinical trials.

**References**

1. Data on file.

*This case study is a composite adapted from actual case files and results are not necessarily representative of the patient population.*

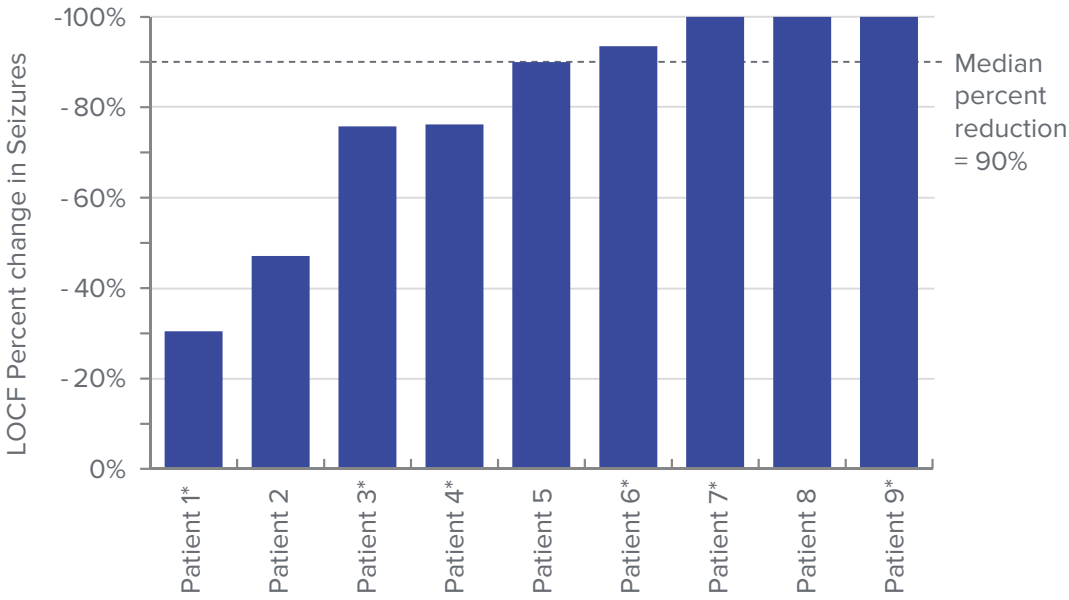
# Periventricular Nodular Heterotopia

## PATIENT POPULATION[1,2]

**9 adults.** All data reported through 11/01/2014.

| Patient Characteristics | Mean (min–max) or % (n/N) |
|---|---|
| Seizure frequency at baseline (seizures/month) | 28 (3–111)<br>Median = 8 |
| Prior intracranial monitoring | 56% (5/9) |
| Prior epilepsy surgery | 22% (2/9) |
| Prior vagus nerve stimulation | 22% (2/9) |

## SEIZURE REDUCTION[2]




*Lead in PVNH

Last observation carried forward analyses (n=9) showing individual patient responses.

# Periventricular Nodular Heterotopia

## SAFETY

Serious adverse events (SAEs) for this subgroup were consistent with SAEs reported for all patients in the RNS® System clinical trials.

### References


1. Data on file.
2. Van Ness P. et al. Electrographic seizure detection and effectiveness of responsive neurostimulation in periventricular nodular heterotopia. *American Epilepsy Society*, December 2015.


CASE STUDY

# Periventricular Nodular Heterotopia

29 year old man with 5 to 6 seizures a month characterized by unformed visual phenomenon without impaired awareness, 3 seizures a month with loss of awareness and right hand dystonic posturing, and rare generalized tonic clonic seizures.

## HISTORY

**Seizure onset:** 15 years of age

**Seizure risk factors:** none

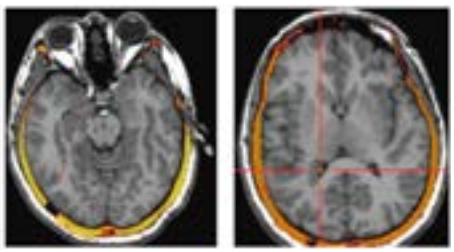
**Prior treatments:** failed trials of 5 antiepileptic medications

**Scalp EEG:** interictal right anterior temporal spikes and right posterior quadrant sharps; video-EEG captured simple partial visual seizures with right posterior quadrant rhythmic slowing and 2 complex partial seizures with right anterior temporal ictal onset

**MRI:** right temporal periventricular nodular heterotopia

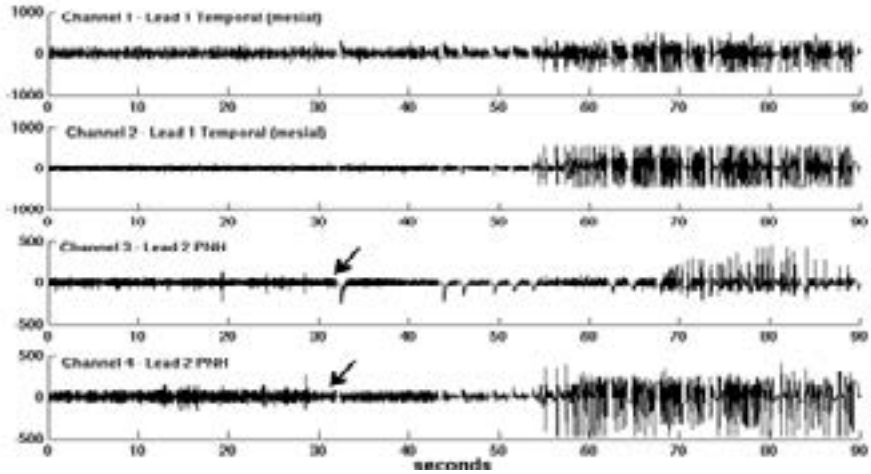
**Neuropsychological testing:** normal

## EVALUATION & PLAN

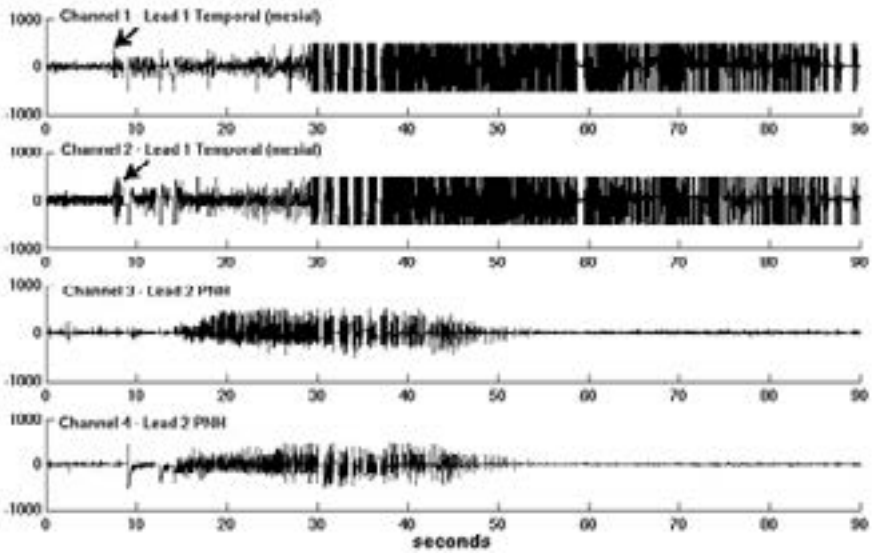


- Partial onset seizures of right occipital and/or right mesial temporal lobe origin, possibly related to PVNH
- Candidate for RNS System with leads in PVNH and right hippocampus

**Example 1:** Electrographic seizure beginning in a PVNH and spreading to the hippocampus. Channels 1 and 2 are recording from a depth lead placed in the right hippocampus. Channels 3 and 4 are recording from a depth lead placed in a PVNH.




**Example 2:** Electrographic seizure beginning in the hippocampus and spreading to a PVNH. Channels 1 and 2 are recording from a depth lead placed in the right hippocampus. Channels 3 and 4 are recording from a depth lead placed in a PVNH.




*This case study is a composite adapted from actual case files and results are not necessarily representative of the patient population.*

## NEUROPACE® RNS® SYSTEM

# Brief Statement

**Indication for Use**
The RNS® System is an adjunctive therapy in reducing the frequency of seizures in individuals 18 years of age or older with partial onset seizures who have undergone diagnostic testing that localized no more than 2 epileptogenic foci, are refractory to two or more antiepileptic medications, and currently have frequent and disabling seizures (motor partial seizures, complex partial seizures and / or secondarily generalized seizures). The RNS® System has demonstrated safety and effectiveness in patients who average 3 or more disabling seizures per month over the three most recent months (with no month with fewer than two seizures), and has not been evaluated in patients with less frequent seizures.

**Contraindications**
The RNS® System is contraindicated for patients at high risk for surgical complications, with medical devices implanted that deliver electrical energy to the brain, and those who are unable (or do not have the necessary assistance) to properly operate the NeuroPace® Remote Monitor or Magnet. For patients with an implanted RNS® System the following medical procedures are contraindicated:

- Magnetic Resonance Imaging (MRI) – The RNS® System is MR Unsafe
- Electroconvulsive Therapy (ECT)
- Transcranial Magnetic Stimulation (TMS)
- Diathermy procedures (any treatment that uses high-frequency electromagnetic radiation, electric currents or ultrasonic waves to produce heat in body tissues)

**Warnings and Precautions**
The RNS® System is not compatible with non-NeuroPace leads and/or pulse generators. Electrical shock may occur with incorrect use of the Programmer or Remote Monitor. Do Not Resterilize and Do Not Reuse the implantable products.

**Clinical Use**
The RNS® System should only be implanted at Comprehensive Epilepsy Centers by neurosurgeons with adequate experience in the implantation of subdural and stereotactic implantation of intraparenchymal electrodes and in the surgical treatment of intractable epilepsy. The RNS® System should only be used by neurologists and neurosurgeons with adequate experience in the management of intractable epilepsy and in the localization of epileptic foci. They must complete a NeuroPace® RNS® System training program and demonstrate specific expertise related to epilepsy, video- EEG monitoring, interpretation of electrocorticograms (ECoGs), the pharmacology of antiepileptic medications and selection of patients for epilepsy surgery. In some instances Neurologists who meet the experience and certification requirements but do not practice at Comprehensive Epilepsy Centers could be qualified by NeuroPace to provide post-implant programming.

**Surgical**
Implantation of the RNS® System and associated surgical procedure risks may cause, but are not limited to, infection, intracranial hemorrhage, tissue damage, temporary pain at the implant site, CSF leakage, seroma, and paralysis.

**RNS® System and Therapy**
The safety and effectiveness has not been studied in pregnant women. The effects of long-term brain stimulation are not completely known. Strong electromagnetic interferences (EMI) can result in serious patient injury or death, damaged brain tissue, loss or change in symptom control, reoperation, stimulation to turn on or off, a return of symptoms, or a momentary increase in stimulation felt by the patient. In addition EMI, such as security screening devices and radio frequency identification, can result in delivering the programmed stimulation to the patient and appear as sensing artifacts on the ECoG recordings. The RNS® System could interact with implanted cardiac devices and result in inappropriate device response or device damage. Additional surgical procedures can result from battery malfunction, electrical short, open circuit, lead fracture, lead insulation failure, damage as a result of head trauma, or lead migration. Severe brain tissue damage can result from exposure to battery chemicals if the Neurostimulator is ruptured or pierced due to outside forces. The patient must collect data from the Neurostimulator once a day and send data to the PDMS once a week.

**Medical Environment**
Electrolysis on the head and neck should be avoided. Prior to the administration of Extracorporeal Shock Wave Lithotripsy or high radiation sources the administering physician should consult with the physician prescribing the RNS® System. Read the user manual to understand the steps to be taken before, during and after computerized tomography (CT) scans.

**Potential Adverse Events**
Serious adverse events occurring in ≥ 2.5% of patients and those of particular relevance reported during the RNS® System clinical studies include EEG monitoring, infection, change in seizures, medical device removal, death, device lead damage or revision, antiepileptic drug toxicity, hemorrhage, psychiatric events, status epilepticus and seizure-related injury. Refer to the product labeling for a detailed disclosure of other reported adverse events.

*Rx Only. Refer to the product labeling for a detailed disclosure of specific indications, contraindications, warnings, precautions and adverse events.*



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For more information, visit our website at
**www.NeuroPace.com**



NeuroPace, Inc. 455 N. Bernardo Ave. Mountain View, CA 94043 NP 160001 Rev 3 / Rev Date: 2017-10

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