

Brain-responsive Neurostimulation in Patients with Medically Intractable Seizures Arising from Eloquent and Other Neocortical Areas

JOBST BC, ET AL. EPILEPSIA. 2017 JUN; 58(6): 1005-1014

SUMMARY

- The median percent seizure reduction was 70% in patients with frontal and parietal seizure onsets, and 58% in those with temporal neocortical onsets in the most recent 3 months of data (LOCF).
- Twenty-six percent of patients experienced at least one seizure-free period of 6 months or longer and 14% experienced at least one seizure-free period of 1 year or longer.
- Stimulation parameters used for treatment did not cause acute or chronic neurologic symptoms or deficits, even in eloquent cortical areas.

METHODS

Study Design:¹ Prospective data from the open label period of a randomized, controlled, double-blinded pivotal trial and a long-term treatment (LTT) trial with average follow up of 6.1 years.

Population: 126 patients² with seizures of neocortical onset, representing 774 patient implant years. Additional analyses were performed in those subsets of patients with onsets in eloquent cortex and insula.

Outcome Measures: Median percent change in seizures compared to baseline and responder rate. To control for possible effects of patient withdrawal, last observation carried forward (LOCF) analyses were performed. Safety was assessed by reported adverse events (AE's).

KEY RESULTS

Long-term Seizure Reduction

- 58% median seizure reduction overall (LOCF)
- 55% responder rate overall (LOCF)
- At least one seizure-free period lasting
 - ≥3 months = 37% of patients
 - ≥6 months = 26% of patients
 - ≥12 months = 14% of patients

Long-term Safety

- The overall rate of SAEs due to infection was 0.017 per patient implant year
- 2.4% hemorrhage rate³; no persistent postoperative deficit.

OUTCOMES BY LOBE OF SEIZURE ONSET⁴



FRONTAL
Median Change: -70%
 Responder Rate: 54%
 LOCF n=37



LATERAL TEMPORAL
Median Change: -58%
 Responder Rate: 67%
 LOCF n=27



PARIETAL
Median Change: -70%
 Responder Rate = 58%
 LOCF n=12



OCCIPITAL
 Individual patient results:
-100%, -100%, -38%, -4%
 LOCF n=4

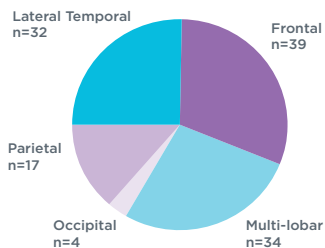


STIMULATION IN ELOQUENT CORTICAL AREAS

Eloquent Area	Seizure Outcomes	Stimulation Effects
Primary Motor ⁵ (n=17)	Median change: -83% (LOCF) Responder rate: 65% (LOCF)	No mild or serious device-related adverse events at therapeutic settings, such as involuntary motor activity in frontal subjects when leads were placed over primary motor cortex.
Broca's Area ⁵ (n=2)	Individual LOCF change in seizures: [-100%, -91%]	No mild or serious device-related adverse events at therapeutic settings, related to language or speech in subjects receiving stimulation in Broca's or Wernicke's Area.
Wernicke's Area ⁶ (n=5)	Individual LOCF change in seizures: [-78%, -54%, -45%, -8%, 56%]	
Primary Visual ⁷ (n=3)	Individual LOCF change in seizures: [-100%, -38%, -4%]	One patient with occipital leads reported a transient experience of brief star-like events (mild) that resolved when the stimulation current was decreased.

PATIENT CHARACTERISTICS

Region of Neocortical Onset



Demographics (mean ± SD):

- Duration of epilepsy: 19.5 yrs ± 10.2
- Number of AEDs at enrollment: 3.1 ± 1.1
- Baseline seizures/month: 88.0 ± 246.7 (median=20.0)

History:

- 37% had prior treatment with vagus nerve stimulation (VNS)
- 52% had prior treatment with epilepsy surgery
- 82% had prior localization with intracranial monitoring
- 55% had lesion on imaging

ADDITIONAL OBSERVATIONS

- Seizure reduction was greater in lesional patients (-77% LOCF median seizure change) as compared with non-lesional patients (-45% LOCF median seizure change), although both groups received benefit (p=0.02).
- There was **no difference in seizure response** for patients:
 - Who had prior intracranial monitoring vs. those who did not (p=0.08)
 - Who had prior surgery vs. those who did not (p=0.12)
 - Who had prior VNS vs. those who did not (p=0.20)

Footnotes

1. Retrospective analysis of ongoing prospective study, with data cutoff of November 1, 2014. The study was not powered to drive conclusions of clinical significance. N values are small and caution must be taken while interpreting results.
2. 18 yrs. or older, refractory to 2 or more AEDs and with no more than 2 foci localized by diagnostic testing
3. Not due to seizure-related head trauma.
4. Patients with multi-lobar seizure onsets had median change of -51% and a responder rate of 52% (LOCF n=33)
5. A subset of the 37 subjects with seizures of frontal onset. An individual subject can be in more than one subset (e.g. data from a subject with a lead in primary motor cortex and one in Broca's Area will be in both groups).
6. A subset of the 27 subjects with seizure onset(s) in the lateral temporal lobe.
7. A subset of the 4 subjects with seizure onset(s) in the occipital lobe.



See important prescribing and safety information in the RNS[®] System labeling. This is intended as supplementary information and should be used in conjunction with the labeling. Refer to the labeling for a description of the RNS[®] System and its components, indications for use, contraindications, warnings, cautions, adverse events and instructions for use. The manuals are available at www.NeuroPace.com.