



RNS vs Surgery Among Patients with Epilepsy in Eloquent Foci

Erica Hartmann, MPH (c), MMS (c)
Faculty Advisor: Lisa Murphy, PA-C, MSPAS
Department of Medical Science



Abstract

Over **50 million people** worldwide suffer from epilepsy. Up to 40% of cases are refractory to medical management. Historically, these patients were offered surgery to control symptoms at the risk of losing critical human functions such as language and motion. Neuropace Responsive Neurostimulation (RNS) is a minimally invasive novel device that detects and responds to seizure activity.

(P) Among patients with refractory epilepsy with seizures involving eloquent cortices
(I) is RNS or
(C) surgical resection
(O) safer and more effective in reducing seizures.

Introduction

Seizure Classification: 2017 International League Against Epilepsy

- ❖ **Focal Onset:** *Originating in one hemisphere*
 - ❖ Aware vs Impaired Awareness
 - ❖ Motor vs nonmotor
- ❖ **Generalized Onset:** *Originating in both hemispheres*
 - ❖ Motor vs nonmotor (absence)
- ❖ **Unknown Onset**
 - ❖ Motor vs nonmotor
- ❖ **Epilepsy:** ≥2 unprovoked seizures more than 24 hours apart

Treatment Options

- ❖ **Medical management:** up to 40% of epilepsy cases are refractory to medical management with two or more medications
- ❖ **Surgical Resection:** Traditional standard of care for refractory epilepsy
- ❖ **RNS:** Electrodes placed near seizure foci detect and respond to abnormal brain activity. Neuropace RNS is the only FDA approved device for refractory epilepsy.

Eloquent Foci

- ❖ Areas of the brain responsible for language, vision, sensorimotor and mobility
- ❖ Located in the cortex, hypothalamus, internal capsule and brainstem

Methods

Literature Search

- September 2018
- Google Scholar
 - PubMed
 - EBSCOhost

Search terms:

- “Neuropace and Epilepsy”
- “Neuropace and Eloquent Epilepsy”
- “Responsive Neurostimulation”
- “Surgical Resection and refractory epilepsy”

Inclusion Criteria

- Human Research
- Adult and child participants
- Full text
- Case studies, cohort studies, randomized clinical trials

Exclusion Criteria

- Animal Research
- Methodological Analysis
- Systematic reviews or meta analysis

Results

1. **Dwivedi R, Ramanujam B, Chandra PS, et al. Surgery for Drug-Resistant Epilepsy in Children. New England Journal of Medicine. 2017;377(17):1639-1647. doi:10.1056/nejmoa1615335.**
 - Non blinded RCT (N= 116) assessed seizure freedom and quality of life among children with epilepsy who received surgical resection or medical management.
2. **Morrell MJ. Responsive cortical stimulation for the treatment of medically intractable partial epilepsy. Neurology. 2011;77(13):1295-1304. doi:10.1212/wnl.0b013e3182302056**
 - Double blinded RCT (N =191) assessed seizure reduction among adults with epilepsy who received Neuropace RNS or medical management.
3. **Heck CN, King-Stephens D, Massey AD, et al. Two-year seizure reduction in adults with medically intractable partial onset epilepsy treated with responsive neurostimulation: Final results of the RNS System Pivotal trial. Epilepsia. 2014;55(3):432-441. doi:10.1111/epi.12534.**
 - Prospective Cohort (N= 175) evaluated seizure reduction among adults with epilepsy for two years who received Neuropace RNS compared to baseline.
4. **Engel J, McDermott MP, Wiebe S, et al. Early surgical therapy for drug-resistant temporal lobe epilepsy: a randomized trial. JAMA. 2012;307(9):922-30**
 - Non blinded RCT (N= 37) assessed seizure freedom and quality of life among adults with epilepsy who received surgical resection or medical management.
5. **Jobst BC, Kapur R, Barkley GL, et al. Brain-responsive neurostimulation in patients with medically intractable seizures arising from eloquent and other neocortical areas. Epilepsia. 2017;58(6):1005-1014. doi:10.1111/epi.13739.**
 - Prospective cohort study (N=120) evaluated seizure reduction and quality of life among adult participants who received Neuropace RNS compared to baseline.
6. **Miller KJ, Burns TC, Grant GA, Halpern CH. Responsive stimulation of motor cortex for medically and surgically refractive epilepsy. Seizure. 2015;33:38-40. doi:10.1016/j.seizure.2015.10.011. Accessed January 12, 2019.**
 - Case study evaluated seizure frequency in a 38 y/o F who received Neuropace RNS after failed surgical resection and vagus nerve stimulation.
7. **Geller EB, Skarpaas TL, Gross RE, et al. Brain-responsive neurostimulation in patients with medically intractable mesial temporal lobe epilepsy. Epilepsia. 2017;58(6):994-1004. doi:10.1111/epi.13740. Accessed March 10, 2019.**
 - Prospective cohort study (N= 111) evaluated seizure frequency and quality of life among adult patients with epilepsy who received Neuropace RNS.

Study	Design	N	Baseline Seizure frequency	Age (median)	Seizure Foci location	Treatment	Control/ comparison	Outcome Measures
Dwivedi R (2017) ¹	RCT	116	2/ day	9.5	UL, BL, TL, NTL	SR	MM	S Freedom QoL
Morrell (2011) ²	RCT	191	>3/ month	35	UL, BL, TL, NTL	RNS	MM	S Frequency QoL
Heck (2014) ³	Prospective Cohort	175	>3/ month	35	UL, BL, TL, NTL	RNS	Seizures at Baseline	S Frequency QoL
Engel (2012) ⁴	RCT	37	>2/ week	26	TL	SR	MM	S Freedom QoL
Jobst (2017) ⁵	Prospective Cohort	120	20/ month	34	UL, BL, TL, NTL	RNS	Seizures at Baseline	S Frequency QoL
Miller (2015) ⁶	Case Study	1	8/ day	38	Motor Cortex	RNS s/p SR	Seizures at baseline	S Frequency
Geller (2017) ⁷	Prospective Cohort	111	7.7/ month	37	BL, UL, TL	RNS	Seizures at baseline	S Frequency QoL

Design: RCT = Randomized clinical trial
 Foci Location: TL = Temporal lobe, NTL = Non temporal lobe, UL = Unilateral, BL = Bilateral
 Treatment: SR = Surgical Resection of seizure foci, RNS = Responsive Neurostimulation, RNS s/p SR = RNS placed after surgical resection
 Control: MM = Medical Management
 Outcome: S Freedom = Seizure Freedom, S Frequency = Seizure frequency, QoL = Quality of Life

Study	Seizure Frequency	Seizure Freedom	QoL	Endurance of Therapy	Severe Adverse Events (% of N)
Dwivedi R (2017)	S	S	S	A	33%
Morrell (2011)	S	N/A	S	I	5.2%
Heck (2014)	S	N/A	S	A	7%
Engel (2012)	S	S	S	A	43%
Jobst (2017)	S	N/A	S	A	11.6%
Miller (2015)	S	N/A	N/A	M	0
Geller (2017)	S	N/A	S	A	11.7%

Seizure Frequency: S = Significant reduction compared to control, NS = Not significant reduction compared to control, N/A = not applicable
Seizure Freedom: S = Patients with treatment were significantly more likely to be free of seizures compared to controls, NS = Patients with treatment were not significantly more likely to be free of seizures compared to controls, N/A = not applicable
QoL (Quality of Life) improvement: S = Significant improvement compared to control, NS = Not significant improvement compared to control, N/A = not applicable
Endurance of Therapy: A - Significant improvement compared to controls for > 12 months, M - Significant improvement compared to controls for > 6 months, I - Significant improvement compared to controls for < 6 months, N/A - Not measured
Severe Adverse Events: Among the intervention groups what was the frequency of deaths / permanent physical disability / hospitalization longer than 1 day

Discussion

OUTCOMES	Surgical Resection	Neuropace RNS
Seizure Reduction (RCTs)	Not Evaluated	Significant improvement vs MM (reduced by 41%)
Seizure Elimination (RCTs)	Significant improvement vs MM (77% Seizure Free)	Not Evaluated
Quality of Life	Significant Improvement over MM	Significant Improvement over MM
Adverse Events	33%-43%	5.2%-11.7%

LIMITATIONS

- No direct comparison between RNS and Surgical Resection
 - Differences in N, baseline seizure frequency, age of participants, and seizure foci location do not permit comparisons between studies of RNS and surgical resection.
- Blinding was only achieved in Morell (2011)
 - Blinding reduces participant and research bias

Conclusions

- Both Surgical Resection and RNS reduce seizures compared to medical management alone.
- Longitudinal prospective studies reveal the safety and relatively few adverse events associated with Neuropace.
- Certain populations may benefit from Neuropace over Surgical resection (those with seizure foci in eloquent cortices)
- Providers should be aware of options available for treatment of refractory seizures.