Responsive Neurostimulator Implantation Outcomes in Idiopathic Generalized Epilepsy

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Introduction

- Idiopathic generalized epilepsy (IGE) accounts for nearly 20% of epilepsy cases, and up to 30% remain drug-resistant despite appropriate anti-seizure medications. Because seizures often arise from broad, bilateral networks, most patients are not candidates for resective surgery.
- Neuromodulation therapies offer an alternative approach, but available evidence remains limited.
- This study evaluates outcomes in adults with drug-resistant IGE treated with responsive neurostimulation of the centromedian thalamic nucleus (RNS-CMN).

Aims and Objectives

Primary

- Evaluate the percent reduction in generalized tonic-clonic seizures from baseline to last follow-up.

Secondary

- Determine responder rate (≥50% seizure reduction).
- Compare seizure outcomes at 6 months vs. last follow-up using Engel classification.
- Compare outcomes across different stimulation frequency ranges.
- Evaluate charge density in relation to seizure outcomes.

Methods

Inclusion criteria	Exclusion criteria
1. ≥ 18 years of age 2. Diagnosed with medically intractable idiopathic generalized epilepsy 3. Has undergone implantation of a responsive neurostimulator device at Beaumont Hospital, RO (from 01/01/2020 to 11/30/2023)	1. < 18 years of age 2. Not diagnosed with medically intractable idiopathic generalized epilepsy 3. Has not undergone implantation of a responsive neurostimulator device at Beaumont Hospital, RO 4. Pregnant women

Retrospective EMR Review

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Patient Information

- Demographics
- Epilepsy history
- MRI/EEG findings
- Surgical parameters
- Device programming settings
- Clinic follow-up duration

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RNS Implantation

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Outcomes

- Percent reduction in generalized tonic-clonic seizures
- Responder rate (≥50% reduction)
- Last clinic follow-up
- Engel classification at 6 months
  - I-II = good
  - III-IV = poor

Results & Discussion

Table 1: General Patient Information

Patient	Sex	Age (y/o)	Age at Epilepsy Onset (y/o)	Age at RNS implant	Epilepsy Duration Before Implantation	Epilepsy Risk Factors	Seizure Types	EEG Findings	Brain MRI	Electroclinical Syndrome	ASMs (total #)	Previous ASMs (total #)	VNS (Y/N)
1	F	39	4	33	29	FS	M, GTC	3 Hz Generalized S/PSW, GPFA	No epileptic lesions	JME	CNB, BRV, LTG, VPA (4)	CBZ, TPM, ETS, ZNS, LCM, CBD, GBP, CLB (8)	Y
2	F	32	6	28	22	None	A, M, GTC	3-4 Hz Generalized S/PSW	No epileptic lesions	JME	LTZ, ZNS (2)	ETS, LEV (2)	N
3	F	44	4	41	37	FHx	A, M, GTC	3-4 Hz Generalized S/PSW, GPFA	No epileptic lesions	JME	BRV, LTG, ZNS, CZP (4)	VPA, CBD, LEV, TPM, PER, ETS (6)	N
4	M	54	38	50	12	FHx	A, GTC	4-5 Hz Generalized S/PSW, GPFA	No epileptic lesions	JAE	BRV, CBD, LTG (3)	VPA, TPM, ZNS, LCM (4)	N
5	F	28	15	25	10	None	A, GTC	3.5 Hz Generalized S/PSW	No epileptic lesions	JAE	TPM, ETS (2)	CBZ, VPA, LEV, LTG, CZP, BRV, CBD, CNB, LCM, PER (10)	N
6	F	40	15	38	23	FHx	A, GTC	Generalized S/PSW in sleep architecture	No epileptic lesions	JAE	LCM (1)	ZNS, TPM, VPA, LEV, PB, PHT, CBZ, LTG, BRV, ETS (10)	N
7	M	25	10	23	13	FHx	M, GTC	3-5 Hz Generalized S/PSW, GPFA	No epileptic lesions	JME	LCM, CLB, ETS (3)	BRV, LEV, VPA, LTG, TPM (5)	N
8	F	24	19	22	3	None	M, GTC	3-4 Hz Generalized S/PSW	No epileptic lesions	JME	LTG, CLB (2)	TPM, LEV, PER, BRV, ZNS, CNB (6)	N
9	F	27	12	26	14	None	A, M, GTC	3-4 Hz Generalized S/PSW	Cerebellar volume loss, nonspecific white matter changes	JME	LTG (1)	ETS, LEV, VPA, BRV, ZNS, PER, LCM, CBD, CLB, CNB (10)	N
10	M	49	9	47	38	FHx	A, GTC	3 Hz Generalized S/PSW, GPFA	No epileptic lesions	JAE	OXC, ZNS (2)	PHT, VPA, LTG, LCM, LEV (5)	N

Table 2: Patient Outcomes

Patient	Age at RNS Implant (y/o)	Age of Epilepsy Onset to RNS implantation (years)	RNS post-operative follow up (months)	Pre-RNS GTC Frequency (Avg)	Post-RNS GTC Frequency (at last follow up)	Percent Change	Longest GTC-free interval (months)	Percent-time of GTC-freedom after RNS implantation (%)	Medication Reduction (Y/N)	VNS Therapy Changes (Y/N)
1	33	29	63	4/year	4/year	No change	18	29	Y	Y - IPG at EOS
2	27	21	55	1/year	0/year	100 decrease	55	100	Y	N/A
3	41	37	46	5/year	0/year	100 decrease	24	52	N	N/A
4	50	12	42	1/year	2/year	100 increase	21	50	N	N/A
5	25	10	40	9/year	4/year	56 decrease	9	23	Y	N/A
6	38	23	27	6/year	0/year	100 decrease	14	52	Y	N/A
7	23	13	23	1/year	0/year	100 decrease	21	91	Y	N/A
8	22	3	22	24/year	4/year	83 decrease	7	32	N	N/A
9	26	14	16	60/year	7/year	88 decrease	8	50	Y	N/A
10	48	39	14	6/year	3/year	50 decrease	6	43	Y	N/A

Figure 1: Pre- and Post RNS Implantation Average GTC/year

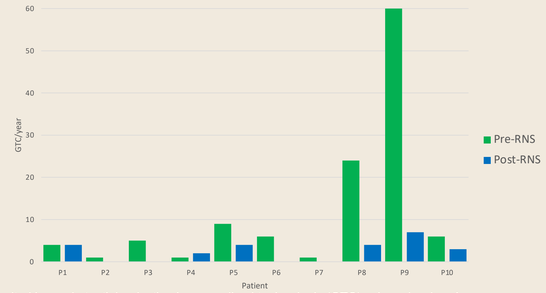


Figure 1. Pre- and post-RNS implantation GTC frequency. RNS therapy in patients with drug-resistant IGE resulted in a substantial reduction in generalized tonic–clonic (GTC) seizure burden. Across all ten patients, the average annual GTC frequency decreased from 11.7 to 2.4 seizures/year, reflecting a 79.5% reduction after implantation. Notably, 80% of the cohort achieved ≥50% seizure reduction, and 40% were GTC-free at last follow-up, demonstrating robust and durable seizure control following bilateral CMN neuromodulation.

Figure 2 A-D: Patient 1 (No change in pre/post-RNS implantation average GTC frequency)

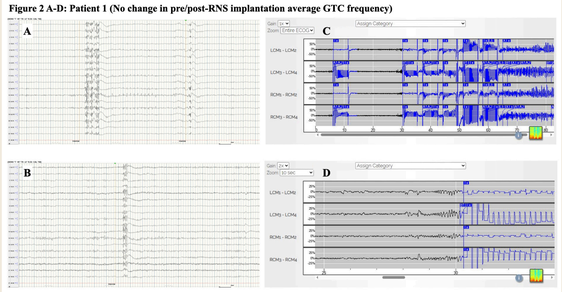
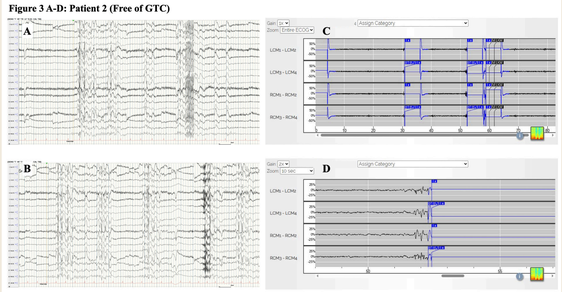


Figure 3 A-D: Patient 2 (Free of GTC)



Figures 2–3. Electrocorticography (ECoG) and representative clinical outcomes following RNS implantation. Patient 1, who averaged 1 GTC per year pre-implantation (Table 2), demonstrated no net change in annual frequency but achieved an 18-month GTC-free interval and a reduction in antiseizure medication burden (Fig. 2A–D). Patient 2, whose baseline frequency was 2 GTCs per year, became GTC-free throughout follow-up (Fig. 3A–D). These cases illustrate the variability of clinical benefit observed with bilateral CMN RNS in drug-resistant IGE.

Figure 4 A-D: Patient 5 (56% decrease in GTC/year)

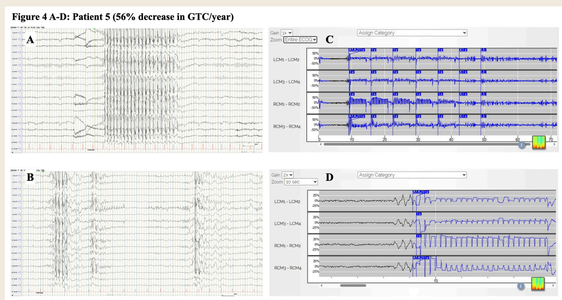
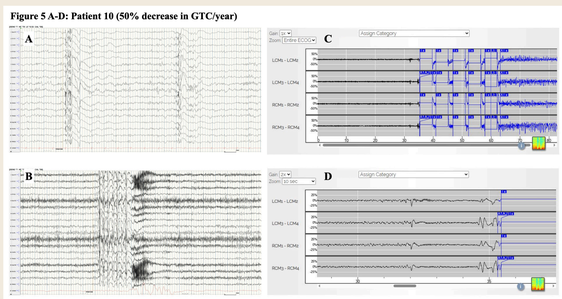


Figure 5 A-D: Patient 10 (50% decrease in GTC/year)



Figures 4–5. Electrocorticography (ECoG) and clinical outcomes in patients with partial GTC reduction. Patient 5 demonstrated a 56% decrease in annual GTC frequency, improving from 9 to 4 GTCs per year (Table 2), with sustained reductions throughout follow-up (Fig. 4A–D). Patient 10 achieved a 50% decrease in GTCs, from 6 to 3 per year, reflecting a stable partial response to RNS therapy (Fig. 5A–D). These cases represent intermediate outcomes within the cohort, illustrating meaningful seizure reduction even when complete remission is not achieved.

Conclusions

- RNS may reduce seizures through acute interruption and long-term neuromodulation[1], potentially via inhibitory neurotransmitter release or depolarization block[2].
- The stimulation frequencies used in this cohort (≤40 Hz) differ from prior IGE RNS studies but maintained charge densities comparable to published series[3,4].
- Evidence from animal and human studies supports low-frequency stimulation (LFS) as a suppressor of epileptic activity[5-7], potentially through alignment with thalamo-cortical network dynamics[2].
- In this series, LFS (≤10 Hz) was associated with >50% GTC reduction in most recipients, suggesting its potential applicability in CMN neuromodulation for drug-resistant IGE.
- RNS within the bilateral CMN produced a **79.5% average reduction** in GTCs and prolonged seizure-free intervals, consistent with emerging data in drug-resistant IGE[3,8].
- These findings support RNS as a safe, promising neuromodulatory option for drug-resistant IGE, with additional insight anticipated from NAUTILUS.

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