Three New Things (Maybe)… in EEG

No financial disclosures

Overview

1. Rapid Response EEG (Ceribell)
2. Invasive EEG for surgical evaluation of DRE
3. Thalamic stimulation with responsive neurostimulation (RNS)

#1

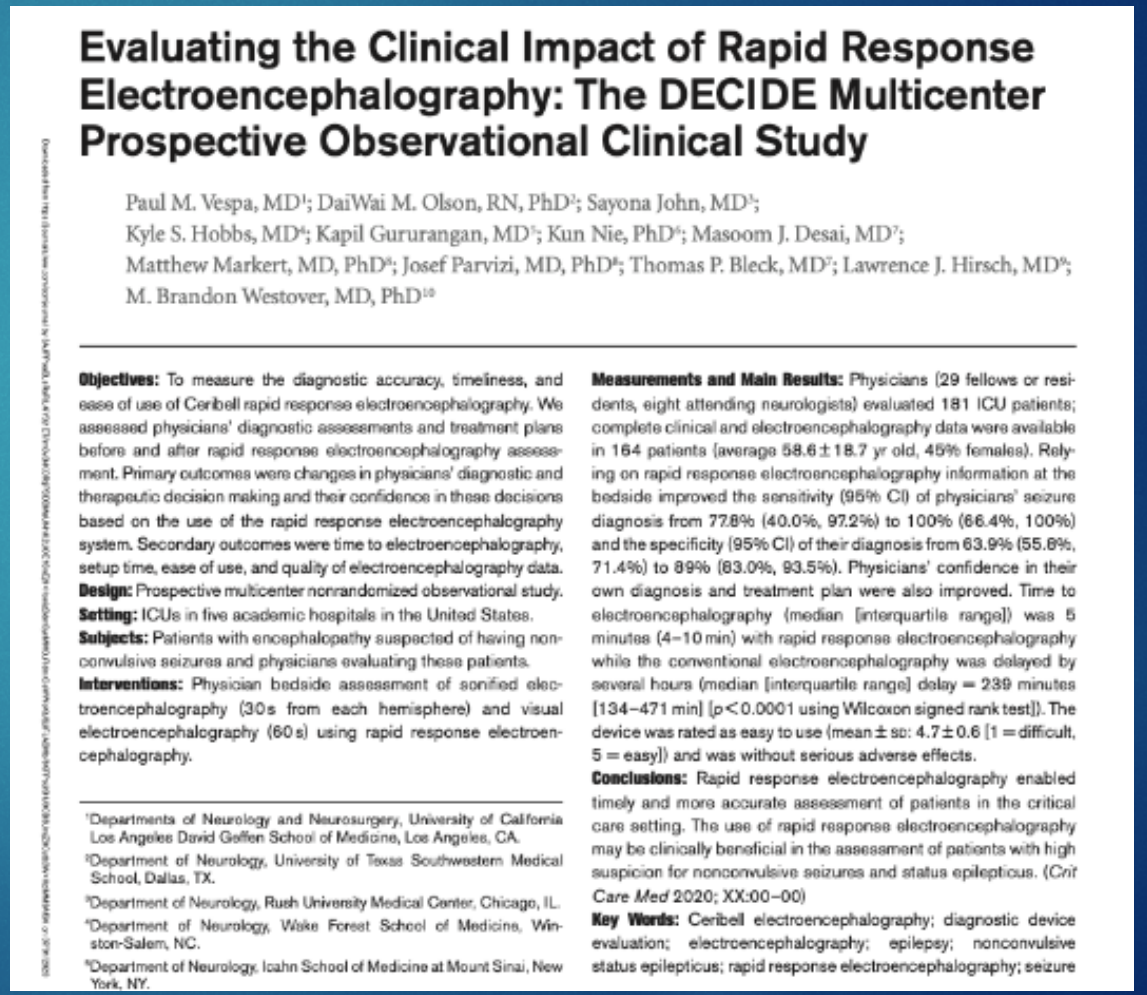
Rapid Response EEG (Ceribell)

Rapid Response EEG (Ceribell)

- 8-channel circumferential EEG system via soft, adjustable headband
- Samples frontal, temporal, and occipital regions
- Connected to EEG recorder that uploads data to HIPAA-compliant cloud portal (via WiFi)
- Designed for earlier diagnosis of status epilepticus and to decrease workforce demands

Ceribell diagnostic utility and physician experience

- Median time to conventional EEG about 239 minutes as compared to 5 minutes with Ceribell
- 90% diagnostic accuracy with Ceribell (sensitivity 100%, specificity 89%) versus 65% using clinical judgement alone (sensitivity 78%, specificity 64%)
- Diagnostic confidence rated as 86% with Ceribell versus 40% using clinical judgement alone



Evaluating the Clinical Impact of Rapid Response Electroencephalography: The DECIDE Multicenter Prospective Observational Clinical Study

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Objectives: To measure the diagnostic accuracy, timeliness, and ease of use of Ceribell rapid response electroencephalography. We assessed physicians' diagnostic assessments and treatment plans before and after rapid response electroencephalography assessment. Primary outcomes were changes in physicians' diagnostic and therapeutic decision making and their confidence in these decisions based on the use of the rapid response electroencephalography system. Secondary outcomes were time to electroencephalography, setup time, ease of use, and quality of electroencephalography data.
Design: Prospective multicenter nonrandomized observational study.
Setting: ICUs in five academic hospitals in the United States.
Subjects: Patients with encephalopathy suspected of having nonconvulsive seizures and physicians evaluating these patients.
Interventions: Physician bedside assessment of sonified electroencephalography (30 s from each hemisphere) and visual electroencephalography (60 s) using rapid response electroencephalography.

Measurements and Main Results: Physicians (29 fellows or residents, eight attending neurologists) evaluated 181 ICU patients; complete clinical and electroencephalography data were available in 164 patients (average 58.6 ± 18.7 *yr* old, 45% females). Relying on rapid response electroencephalography information at the bedside improved the sensitivity (95% CI) of physicians' seizure diagnosis from 77.8% (40.0%, 97.2%) to 100% (66.4%, 100%) and the specificity (95% CI) of their diagnosis from 63.9% (55.8%, 71.4%) to 89% (83.0%, 93.5%). Physicians' confidence in their own diagnosis and treatment plan were also improved. Time to electroencephalography (median [interquartile range]) was 5 minutes (4–10 min) with rapid response electroencephalography while the conventional electroencephalography was delayed by several hours (median [interquartile range] delay = 239 minutes [134–471 min] [$p < 0.0001$ using Wilcoxon signed rank test]). The device was rated as easy to use (mean ± sd: 4.7 ± 0.6 [1 = difficult, 5 = easy]) and was without serious adverse effects.
Conclusions: Rapid response electroencephalography enabled timely and more accurate assessment of patients in the critical care setting. The use of rapid response electroencephalography may be clinically beneficial in the assessment of patients with high suspicion for nonconvulsive seizures and status epilepticus. (*Crit Care Med* 2020; XX:00–00)
Key Words: Ceribell electroencephalography; diagnostic device evaluation; electroencephalography; epilepsy; nonconvulsive status epilepticus; rapid response electroencephalography; seizure

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Ceribell reduces cost in the acute care setting

- Two-armed decision-analytic cost-benefit model comparing Ceribell to clinical suspicion alone for NCSE
- Ceribell reduced hospital LOS by 1.2 days (6.1 versus 7.4 days) and ICU LOS by 0.4 days (1.5 versus 1.9 days)
- Translated into cost savings ranging between $3,971 to $17,290

Modeling the economic value of Ceribell Rapid Response EEG in the inpatient hospital setting

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AIMS Potentially life-threatening diagnosis of non-convulsive status epilepticus (NCSE) can only be confirmed with electroencephalography (EEG). When access to EEG is limited, physicians may empirically treat, risking unnecessary sedation and intubation, or not treat, increasing risk of refractory seizures. Either may prolong hospital length of stay (LOS). The current study aimed to examine the effect of a new EEG system (Ceribell Rapid Response EEG, Rapid-EEG) on hospital costs by enabling easy access to EEG and expedited seizure diagnosis and treatment.

MATERIALS AND METHODS We built a two-armed decision-analytic cost–benefit model comparing Rapid-EEG with clinical suspicion alone for NCSE. Diagnostic parameters were informed by a multicenter clinical trial (DECIDE, NCT03534258), while LOS and cost parameters were from public US inpatient data, published literature, and Center for Medicare and Medicaid Services fee schedules. We calculated reference case estimates from mean values, while uncertainty was assessed using 95% prediction intervals (PI) generated by probabilistic sensitivity analysis (PSA) and ANCOVA sum of squares. All costs were indexed to 2019 US$.

RESULTS Each use case of Rapid-EEG saved $3,971 to $17,290 as it led to reduction in the hospital LOS by 1.2 days (6.1 vs. 7.4 days) and ICU LOS by 0.4 days (1.5 vs. 1.9 days). Using PSA, Rapid-EEG saving was $5,633 per use case (95% PI: $($4,649 to $6,617), as it led to diminished hospital LOS by 1.1 days (95% PI: 0.9–1.4 days) and reduced ICU LOS by 0.5 days (95% PI: 0.4–0.6 days). Cost-savings were demonstrated in 75% of replications. Sixty-four percent of variance in total costs was attributable to LOS for persons incorrectly diagnosed with seizures.

LIMITATIONS Results were obtained from the analysis of existing data and not a prospective outcome trial.

CONCLUSIONS Rapid-EEG alters the treatment course for patients with suspected seizures and will result in cost savings per patient.

Other literature implicating benefits of Ceribell

- Allows EEG-untrained medical providers to rapidly assess for NCSE (Hobbs et al. Neurocrit Care. 2018 Oct; 29(2):302-312)
- High negative predictive value (99%) in differentiating non-epileptiform activity from epileptiform EEG patterns (Kamousi et al. Neurocrit Care. 2021 Jun; 34(3):908-917)
- Of 38 patients at several ED sites, Ceribell changed clinical management (positively) for 20 cases and expedited disposition for 8 cases (Wright et al. Emerg Med J. 2021 Dec; 38(12):923-926)
- Ceribell obviated need for inter-hospital transfer for vEEG in 31 of 33 patients (94%) (Madill et al. Epileptic Disord. 2022 Jun 1;24(3):507-516)

#2

Invasive EEG for surgical evaluation of DRE

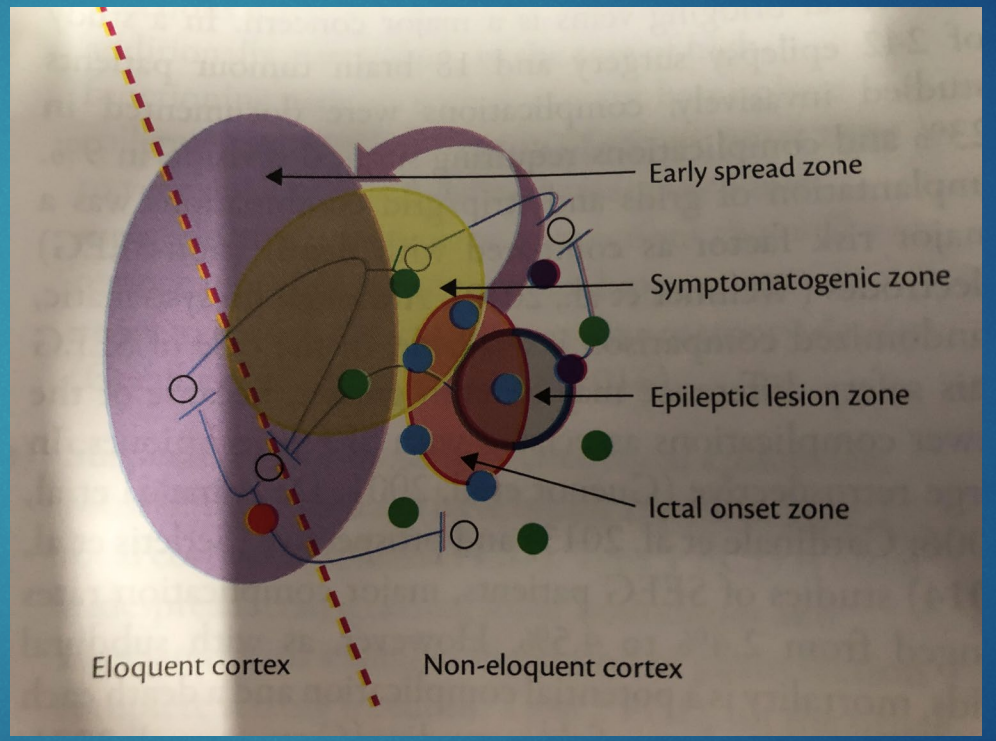
3 main patient groups

1. Suspected mesial temporal (or temporolimbic) epilepsy
2. Suspected MRI-negative neocortical epilepsy
3. Suspected neocortical epilepsies in proximity to eloquent cortex

Invasive Studies of the Human Epileptic Brain, Principles and Practice; Lhatoo, Kahane, Luders, 2019

Choice of approach (subdural grids versus depth electrodes)

- Sampling of…
  - Sulcal regions
  - Deep cortical areas
  - Large brain areas
- Mapping of…
  - Eloquent cortex
  - Ictal onset zone
- Surgical safety



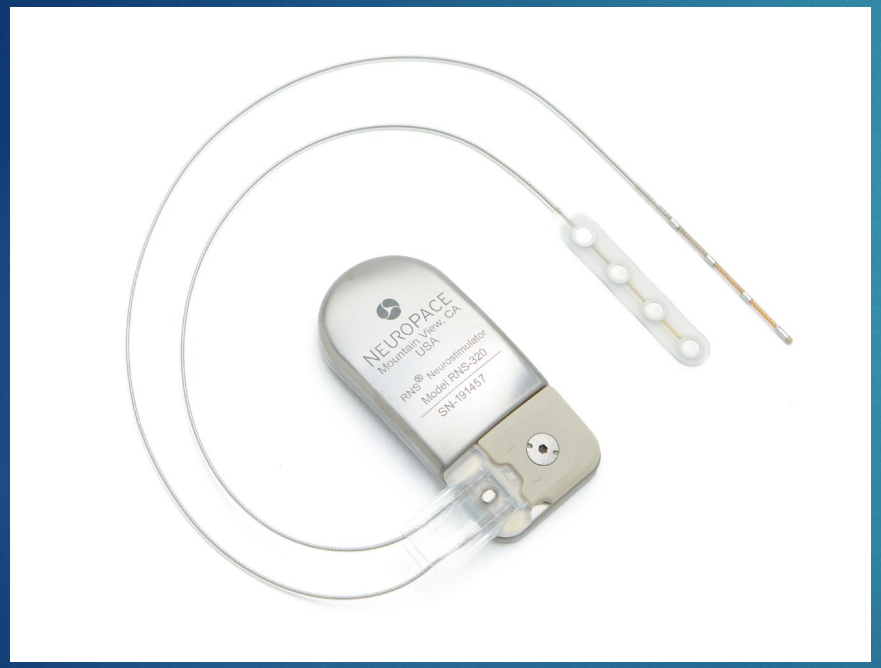
Invasive Studies of the Human Epileptic Brain, Principles and Practice; Lhatoo, Kahane, Luders, 2019

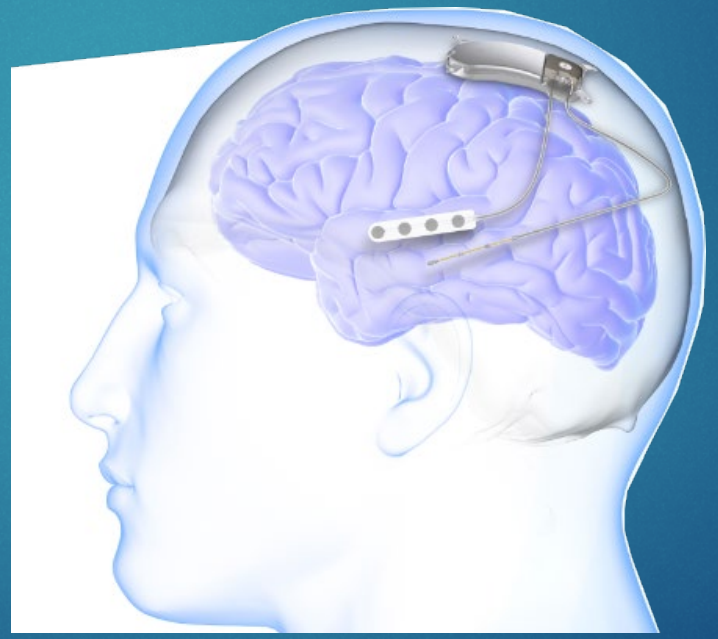
#3

Thalamic stimulation with responsive neurostimulation (RNS)

RNS (responsive neurostimulation)

(AKA Neuropace RNS for focal or multifocal epilepsy)

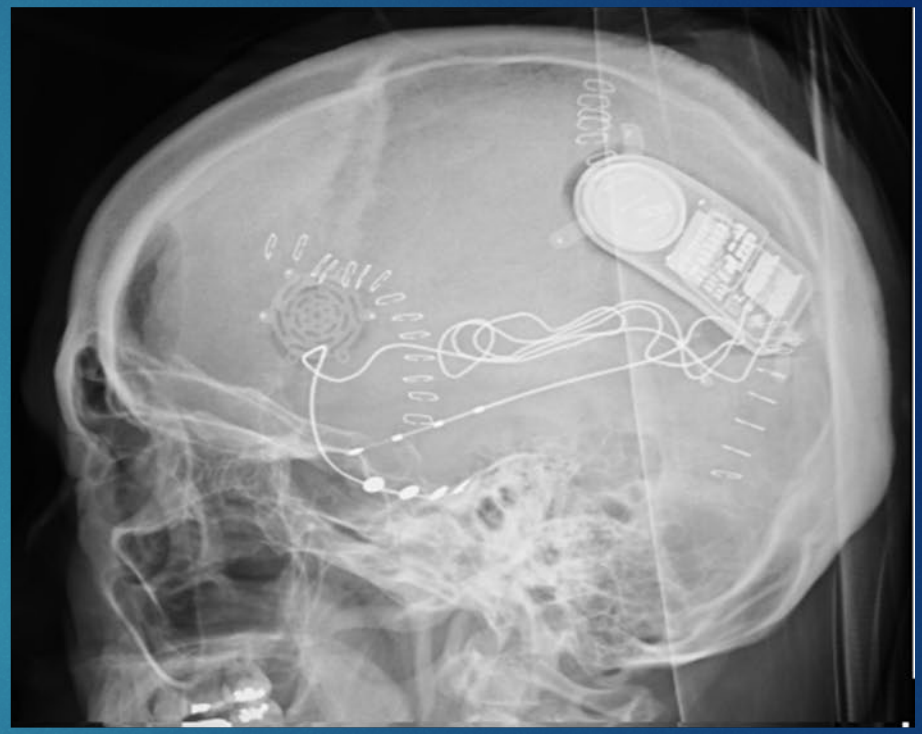




RNS™ system

Components:

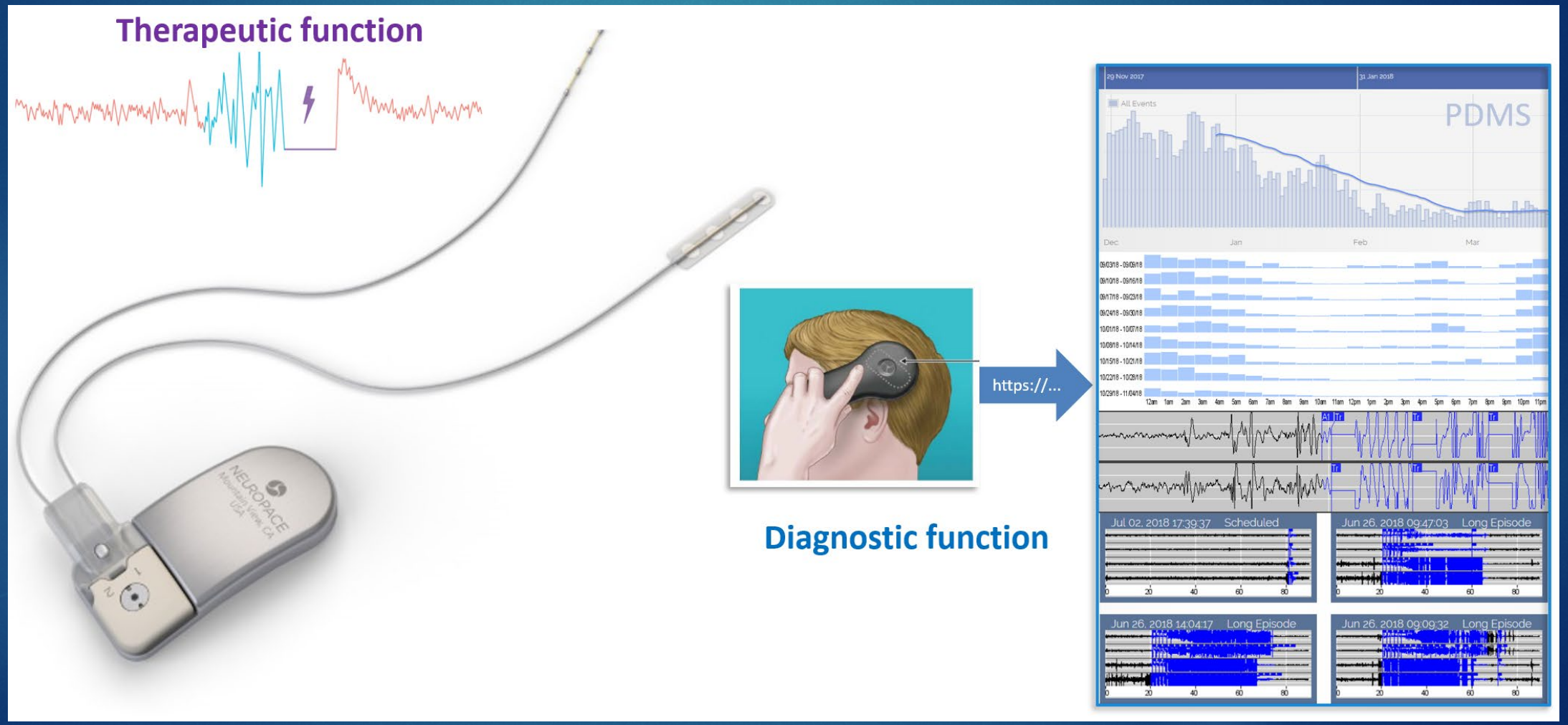
- 2 leads, either intraparenchymal depth leads, or subdural strips, or combination of both.
- Each contains 4 recording & stimulating electrodes.
- Can be bilateral
- Ferrule implanted in the skull which contains the battery, analysis computer, and recording & storage device.
- Battery life approximately 10 years



Long-term iEEG Monitoring

Froedtert & Medical College of Wisconsin

Long-term iEEG



Objective iEEG Data Can Help Optimize Patient Care

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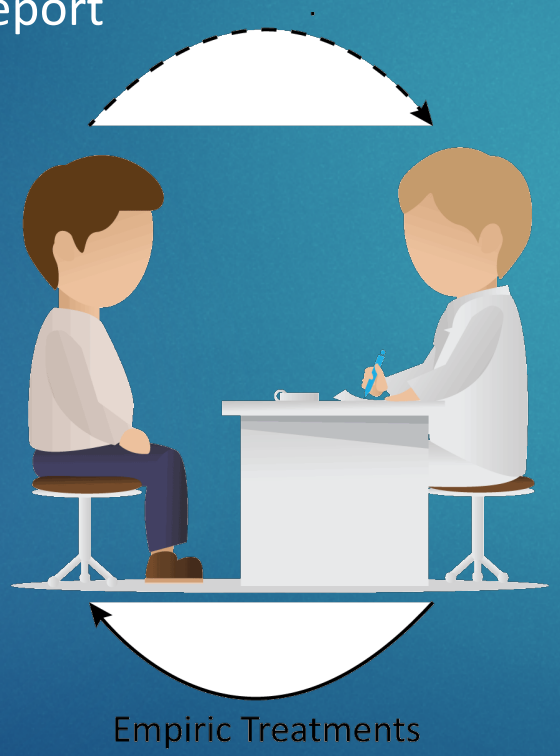
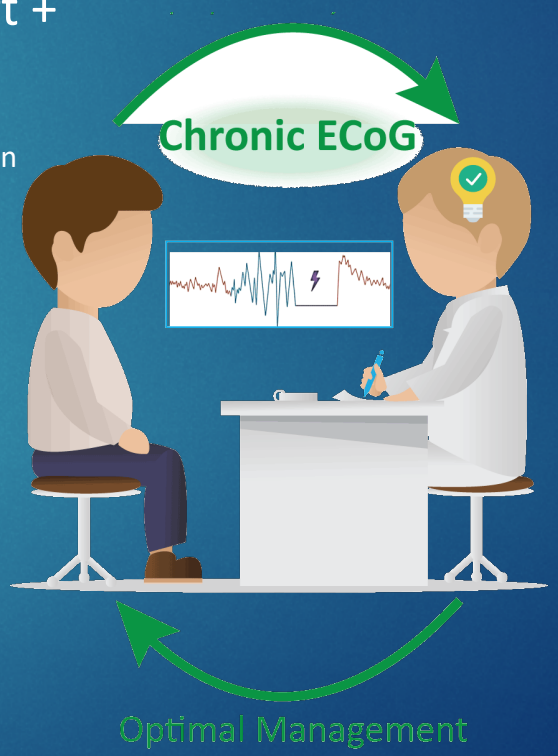
Verbal Report



Verbal Report +

- Subclinical Seizures
- Seizure Lateralization
- Medication Effects
- Epileptic Activity Trends



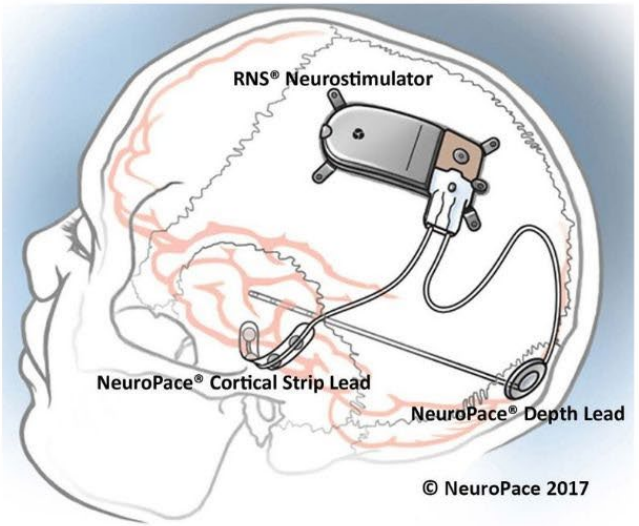
RNS and thalamic stimulation

Froedtert & Medical College of Wisconsin

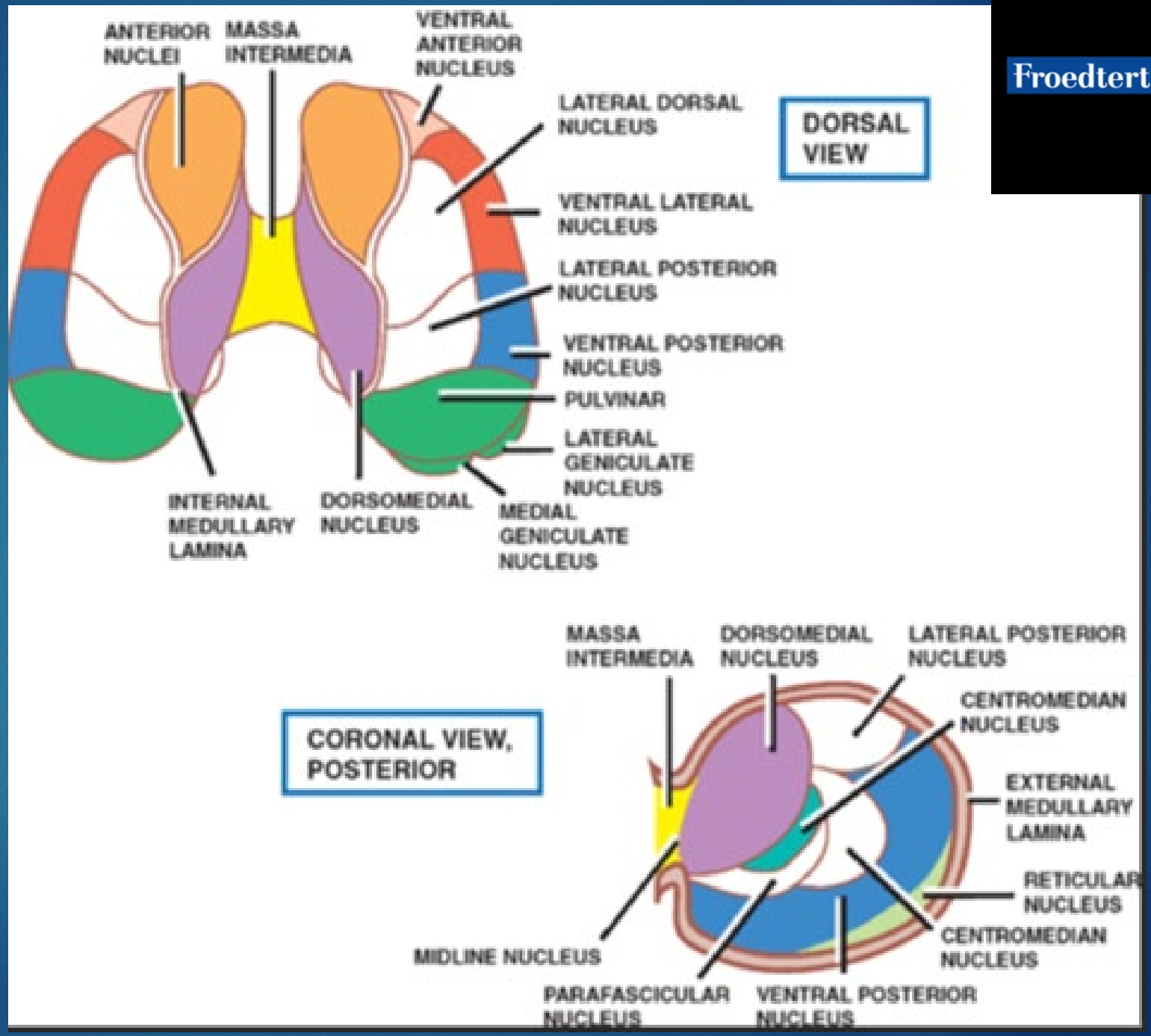
RNS System Labeling

Assuming patient meets the FDA-approved indication for use, placement of a responsive neurostimulation lead in the thalamus is consistent with FDA labeling.

- **Lead placement**: The labeling does not specify lead location. Leads are placed in order to detect an early onset with location based on the physician's judgment.
- **Not studied in pre-approval trials**: RNS System has not been evaluated in a prospective clinical trial in patients with epileptogenic regions located at or caudal to the level of the thalamus.
- **Post-approval study**: There are patients enrolled in the PAS study with corticothalamic RNS lead placements.

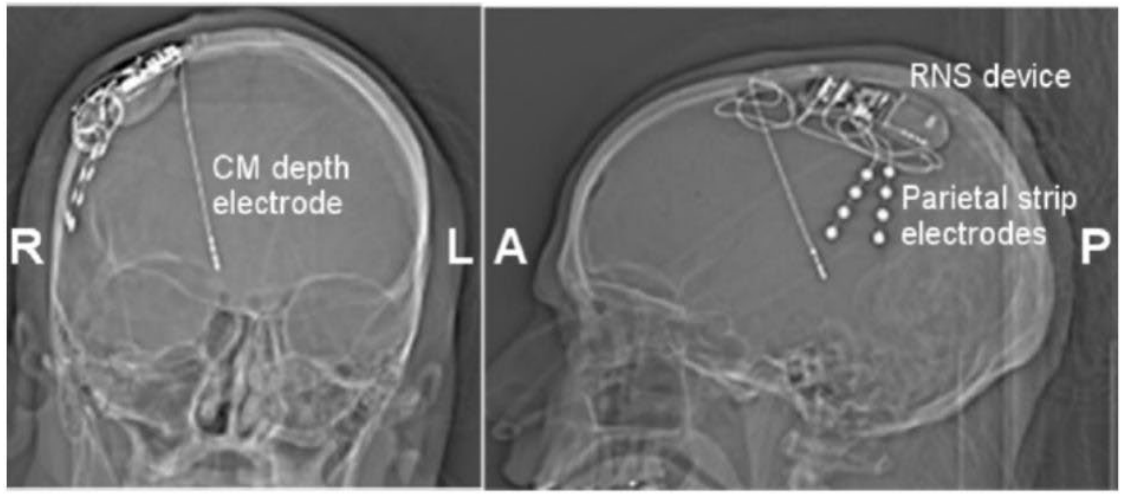


Thalamic nuclei (and subnuclei…)



Typical Corticothalamic Lead Placement

1 cortical lead and 1 ipsilateral thalamic lead



Case Study from Gummadavelli A, Zaveri HP, Spencer DD, Gerrard JL., Front Neurosci. 2018;12:474. 2018 Jul 31.

Cortical strip lead(s) are placed over most active region of seizure onset.*

Depth lead placed in the target thalamic nucleus (CMT in this case).

Cortical and thalamic leads are set up for detection and stimulation.

*While only two leads can be connected to the neurostimulator, up to four leads can be implanted (with no more than two depth leads).

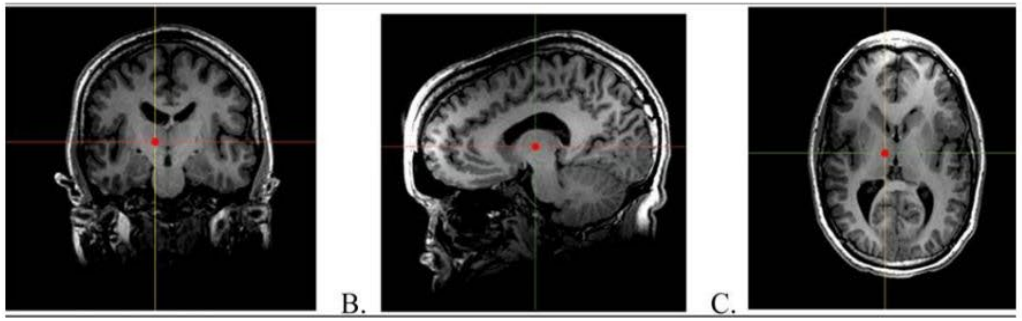
Single Center Case Series Targeting the CMT

ELSEVIER

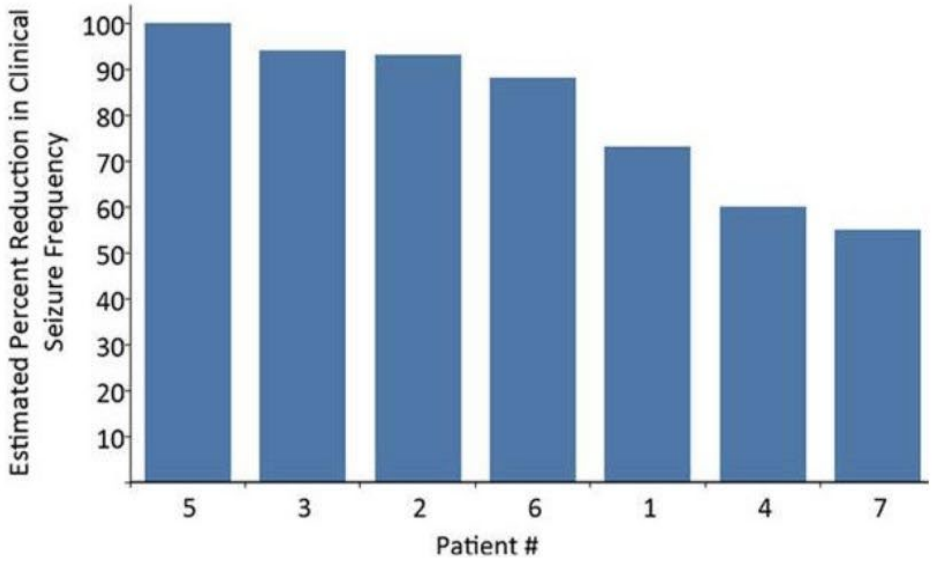
Epilepsy & Behavior
Volume 112, November 2020, 107354

Brain-responsive corticothalamic stimulation in the centromedian nucleus for the treatment of regional neocortical epilepsy

David E. Burdette [a], M. Ayman Haykal [a], Beata Jarosiewicz [b], Rachel R. Fabris [a], Gabe Heredia [a], Kost Elisevich [a], Sanjay E. Patra [a]



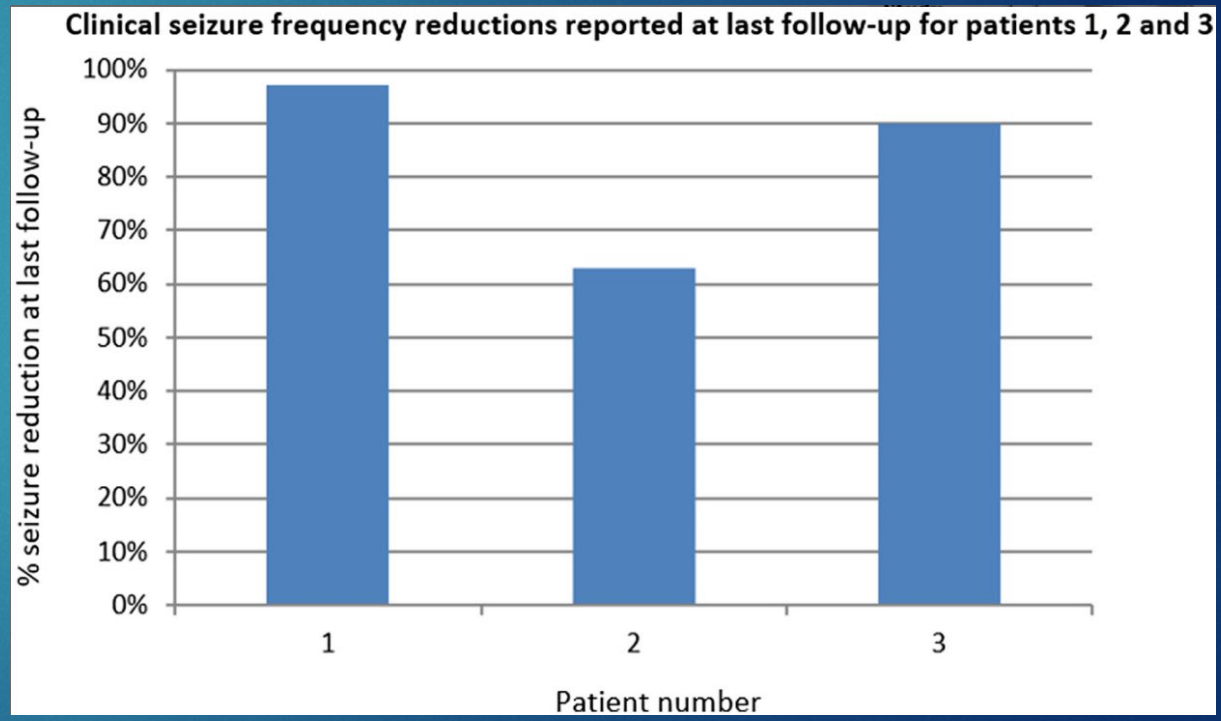
All 7 patients achieved ≥50% reduction in disabling seizures, with no stimulation-related adverse events



Follow up: Avg of 17 months (range: 8-28 months)

Regional onsets: Pulvinar and cortical treatment

- Three patients with one or two regional seizure onsets in the posterior quadrant epilepsy
- Patients treated with cortical-pulvinar neurostimulation for average of 12.5 months
- Electrographic seizure onset or evolution was noted in the pulvinar in all patients
- Responsive stimulation had no negative impact on neuropsychological outcomes in 3 patients and some minor improvements in 2 patients



Burdette, et al. *Epilepsia Open*, 2021

MCW experience with RNS-based thalamic stimulation

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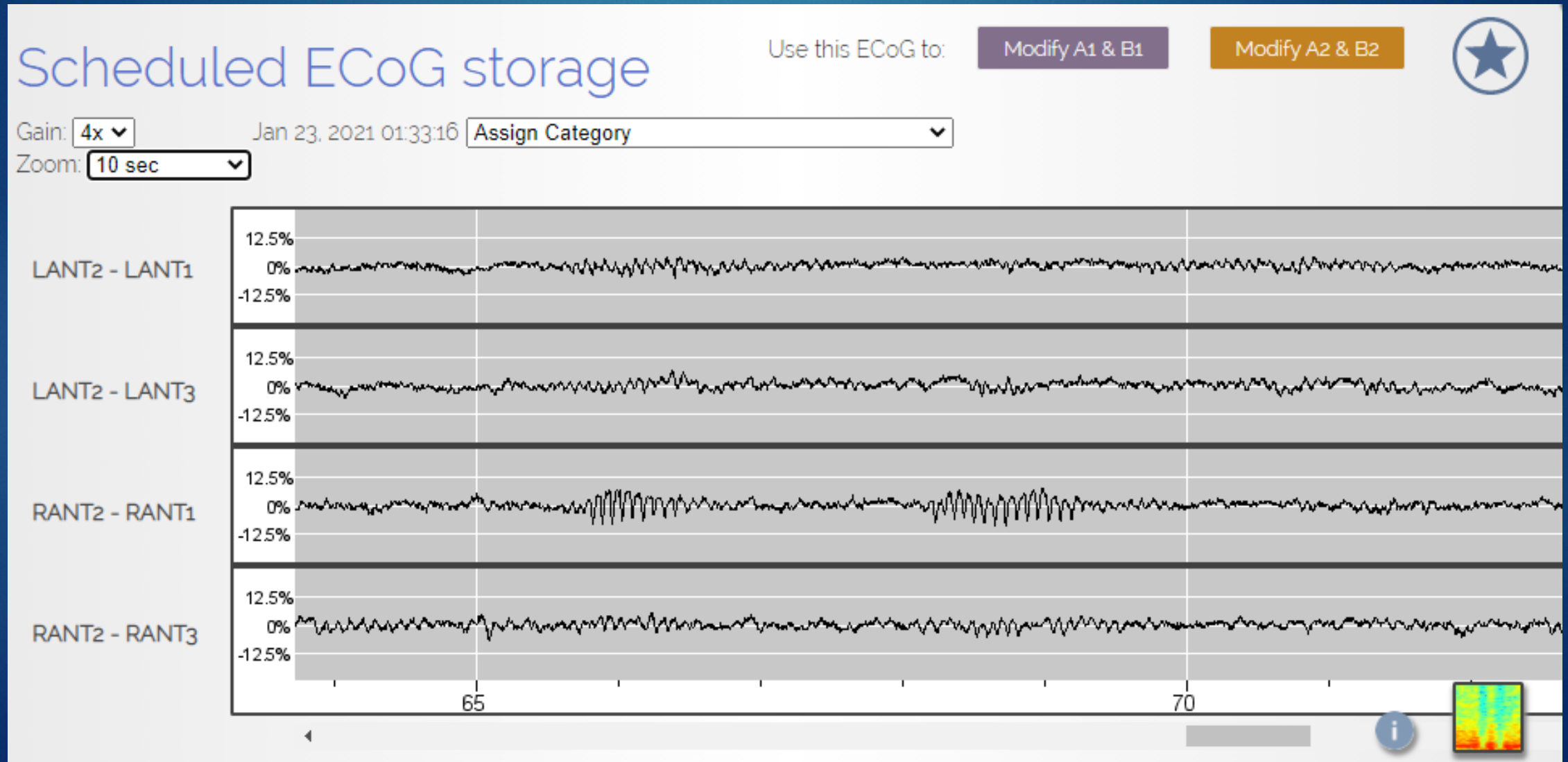
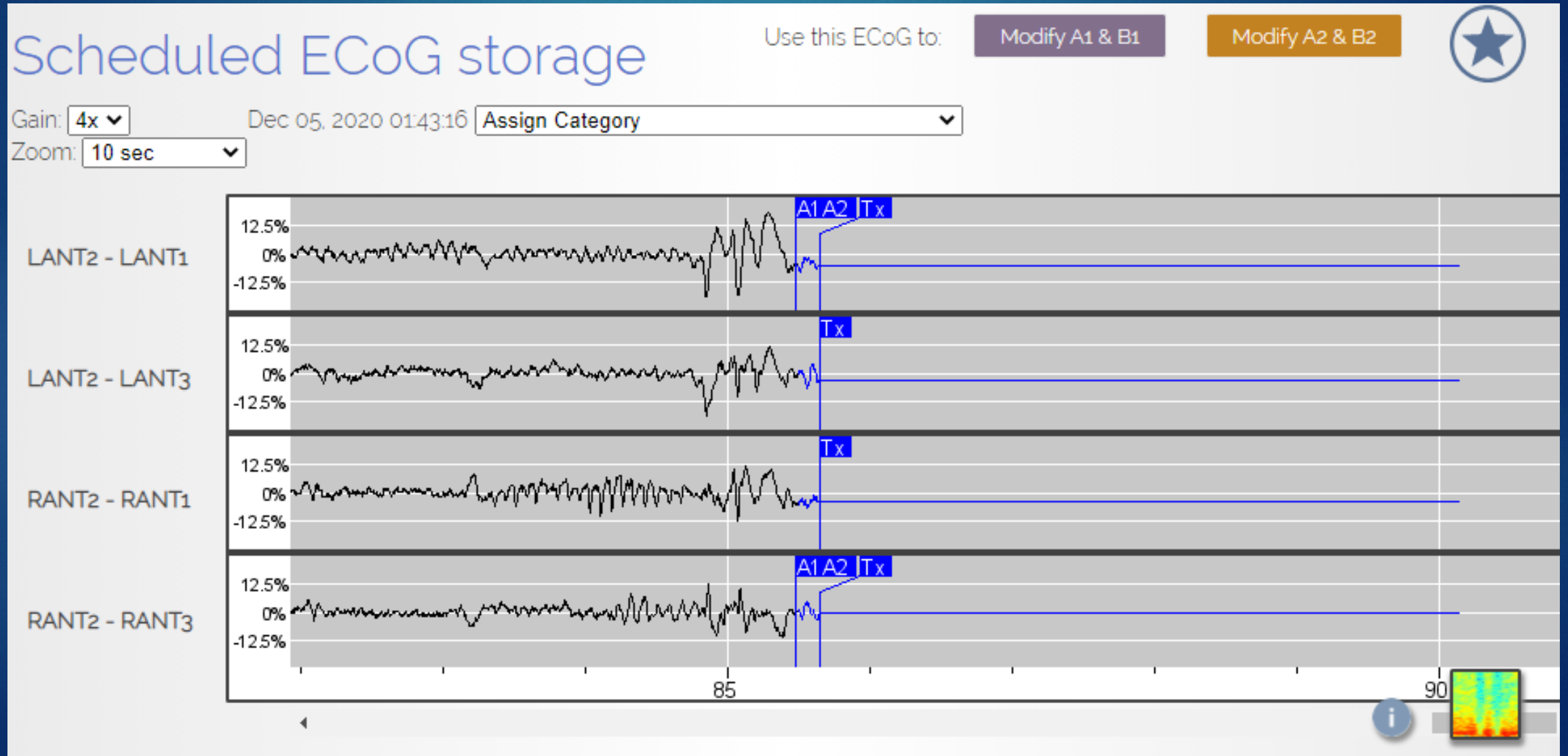
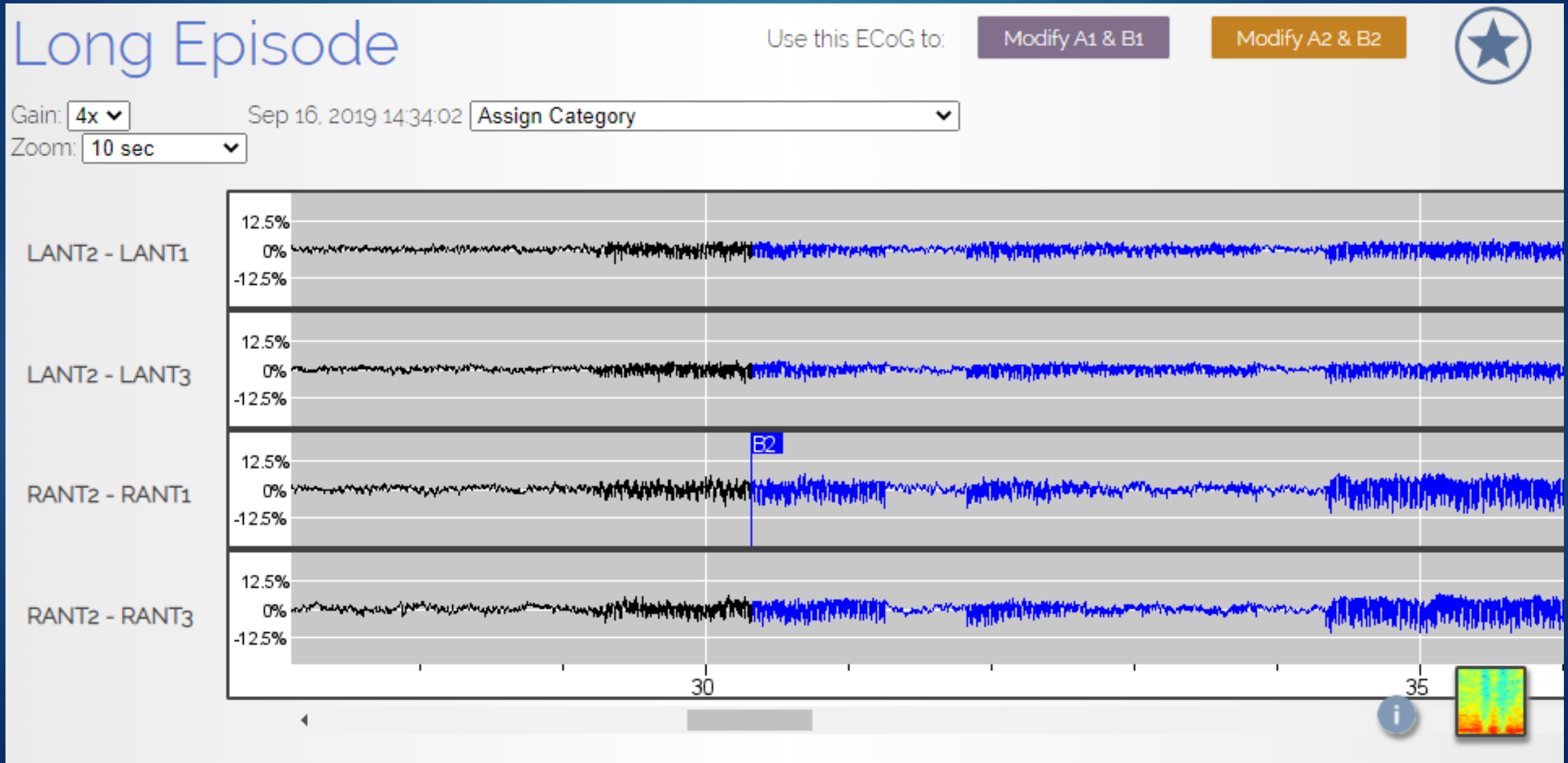
Thalamic EEG: Sleep spindles



‘Gen’ spike-wave being detected and treated



GPFA bursts


Long Episode
Use this ECoG to:
Modify A1 & B1
Modify A2 & B2
Gain: 4x
Sep 16, 2019 14:34:02
Assign Category
Zoom: 10 sec
LANT2 - LANT1
LANT2 - LANT3
RANT2 - RANT1
RANT2 - RANT3
12.5%
0%
-12.5%
B2
30
35

RNS-IGE 3 patient Case Series at Froedtert

3 patients

Normal neurological and physical exam

Normal IQ

Normal MRI

EEG with generalized spike-wave

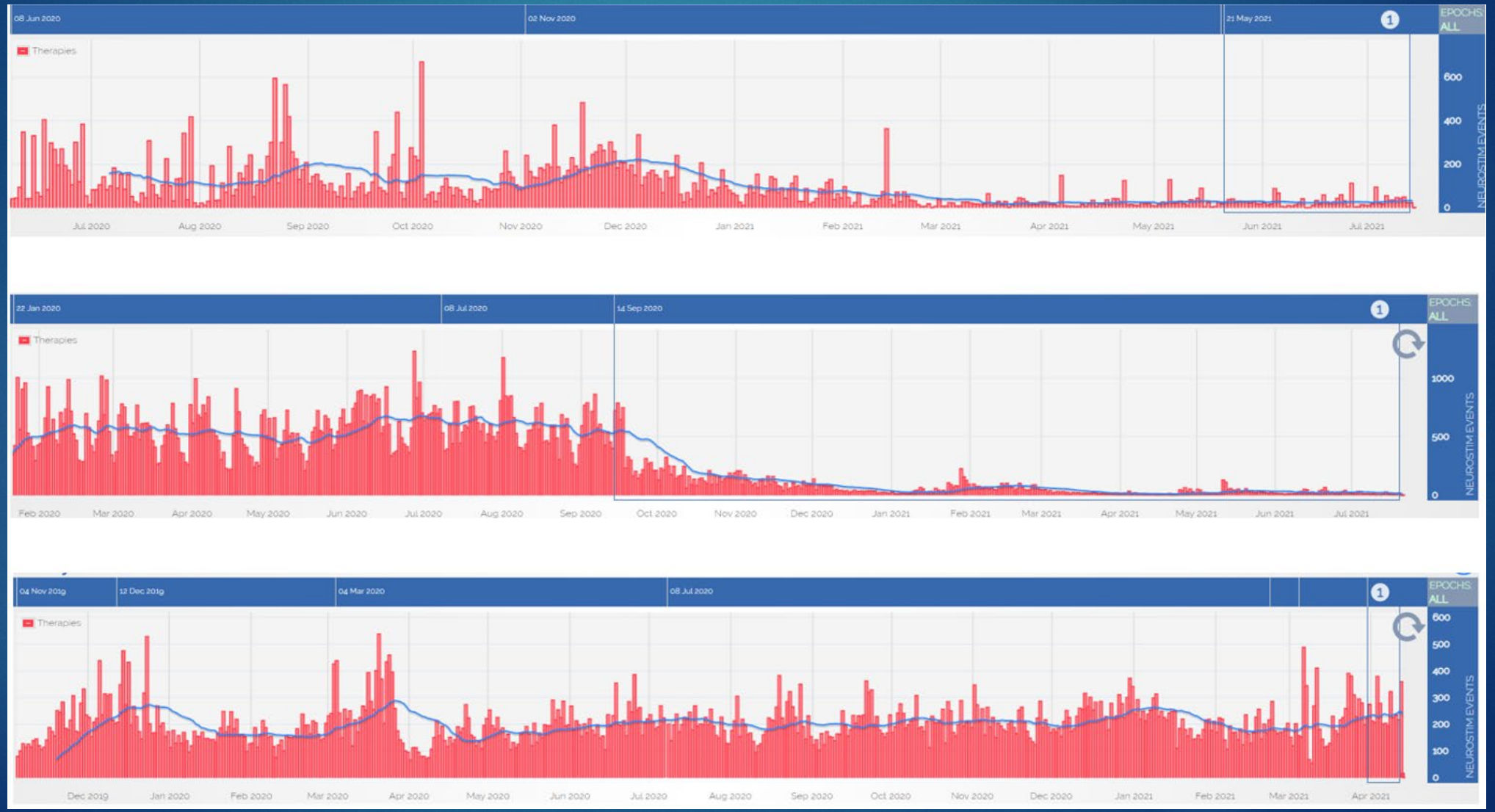
Seizure types: absence, convulsions, myoclonus

PRO00040790

Case Series RNS-IGE Results

Subject ID	Epileptiform Activity Post-'Parameter Optimization'	Long Episodes* Post-'Parameter Optimization'	Epilepsy-Related Hospitalizations Post- RNS Implantation
Patient 1	45% reduction (p= <0.0001)†	61% reduction (p=0.0396)†	76% reduction (p=0.0048)†
Patient 2	89% reduction (p= <0.0001)†	98% reduction (p= <0.0001)†	45% reduction (p=0.2167)
Patient 3	21% increase (p=0.0465)†	128% increase (p=0.1182)	35% increase (p=0.6855)

Case Series RNS-IGE Results (PDMS histograms)



Acknowledgements / Questions

- Thanks to Chris T. Anderson and remainder of epilepsy-based team at Froedtert Hospital / MCW
- Thanks to the WNS committee for organizing this conference

- I'm open to any comments or questions