# NeuroPace, Inc. Investor Day

January 28, 2025

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# 2025 Investor Day Agenda

**9:00** **Welcome and Introductions (Rebecca Kuhn)**

**9:05** **NeuroPace Overview (Joel Becker)**
Mission, Unmet clinical need, Vision and key strategic opportunities

**9:15** **The NeuroPace RNS System and Efficacy in Focal Epilepsy (Martha Morrell, MD)**
Epilepsy defined, Responsive neurostimulation in focal epilepsy

**9:30** **Power of the RNS Data (Vikram Rao, MD, PhD)**

**9:45** **RNS Clinical Applications (Mark Richardson, MD, PhD)**

**10:00** **Living with the RNS System (Michael McKenna, MSW)**

**10:10** **Q and A**

**10:20** **Break**

**10:30** **RNS System Clinical Trials (Martha Morrell, MD)**
**Platform and Data Applications (Martha Morrell, MD)**
**Potential Future Applications (Sameer Sheth, MD, PhD)**

**11:00** **Product Development**

- Overview and Strategy
  (Dylan St. John, Chief Operations and Development)
- AI-powered software; Remote programming; Next gen platform
  (Brett Wingeier, PhD, VP Research and Development)

**11:15** **Market Development (Katie Keller, VP Marketing)**

**11:30** **NeuroPace Vision, Plans and Expectations (Joel Becker/Rebecca Kuhn)**

**11:45** **Q and A**

**12:00** **Conclude and Lunch**



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# Speakers

## Special Guest Speakers

**Mark Richardson, MD, PhD**
Associate Professor, Neurological Surgery at Harvard Medical School

**Vikram Rao, MD, PhD**
Associate Professor, Neurology at UCSF Weill Institute for Neurosciences

**Sameer Sheth, MD, PhD**
Professor and Vice-Chair of Research, Department of Neurosurgery at Baylor College of Medicine

**Mike McKenna, MSW**
Senior Patient Engagement Specialist at NeuroPace

## NeuroPace Management

**Joel D. Becker**
CEO and Board Member

**Rebecca Kuhn**
Chief Financial Officer, Vice President, Finance and Administration

**Martha Morrell, MD**
Chief Medical Officer

**Dylan St. John**
Chief, Operations and Development

**Katie Keller**
VP Marketing

**Brett Wingeier, PhD**
VP Research and Development



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# NeuroPace Overview

Joel Becker

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# Disclaimer

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**Transform the lives of people suffering from epilepsy by reducing or eliminating the occurrence of debilitating seizures.**

# NeuroPace: Strong Fundamentals and Positioned for Growth

| | |
|---|---|
| **Large, underpenetrated market** | **>$55B total U.S. addressable market; >$2B annual core market opportunity within Comprehensive Epilepsy Centers with additional upside from expanding outside Level 4 centers** |
| **Unique technology** | Closed loop, brain-responsive neuromodulation system |
| **Compelling clinical evidence** | Differentiated outcomes that continue to improve over time; additional clinical data from Post-approval Study (PAS) and idiopathic generalized, pediatric focal, and LGS trials |
| **Operating execution** | Focused on revenue, gross margin and operating expense management; 2024 revenue growth 20%+ |
| **Healthy balance sheet** | Sufficient capital to support key operating priorities |
| **Future growth opportunities** | Market expansion within and outside of Level 4 centers; indication expansion into the generalized epilepsy and pediatric focal patient populations |

[1]U.S., Center for Disease Control, August 10, 2017; Chen, Z., et al., JAMA Neurology, 2018; Hauser, et al., 1993. Incidence of Epilepsy and Unprovoked Seizures in Rochester, Minnesota: 1935-1984. Epilepsia 34, 453–458; DEFINITIVE HEALTHCARE CLAIMS DATA, https://patientfinder.defhc.com as of 12/31/20



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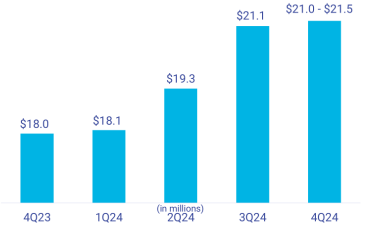
# 2024 in Review

- Revenue grew over 20%
  - Preannounced $79.4 - $79.9 million in revenue, growth of **21% - 22%**
  - Excluding sales from the NAUTILUS trial in 2023, revenue grew **25%+**
  - Revenue growth accelerated in 2H vs 1H
- Delivered strong gross margins at high end of guidance range
- Maintained operating expenses at low end of guidance range
- RNS active prescribers increased to new record highs
- Project CARE pilot demonstrated increasing momentum in 2H
- Completed implants in NAUTILUS trial
- Initiated development of AI enabled software tools

2024 results are preliminary, unaudited, and subject to change.



**Financial Performance**




| | Preliminary 4Q24 (unaudited) | Preliminary FY2024 (unaudited) |
|---|---|---|
| Revenue<br>Revenue growth (y/y) | $21.0M - $21.5M<br>17% - 19% | $79.4M - $79.9M*<br>21% - 22% |

*initial 2024 revenue guidance: $73M - $77M

Total Cash and Short-term Investments of approximately $52.8M (as of 12/31/2024) provides sufficient capital to support key operating priorities



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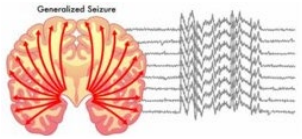
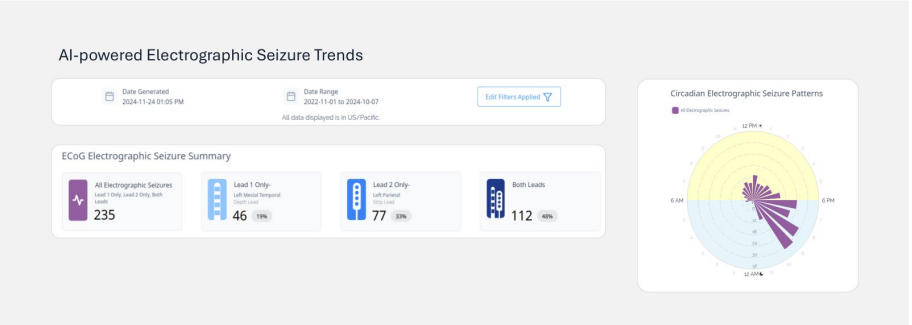
NAUTILUS: Idiopathic Generalized Epilepsy




**AI seizure classifier creates insights for patient care**




Renderings; features not available in the approved RNS System.



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## "We are just getting started..."

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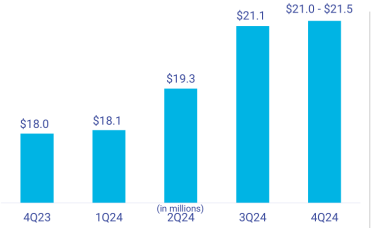


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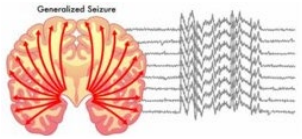
NAUTILUS: Idiopathic Generalized Epilepsy

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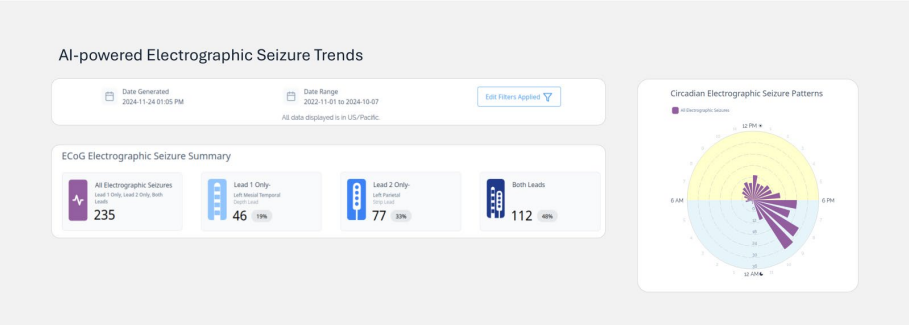


Renderings; features not available in the approved RNS System.



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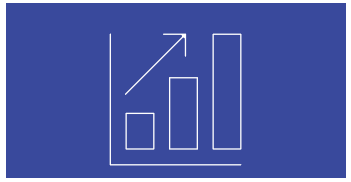
# NeuroPace Long Range Plan: Vision

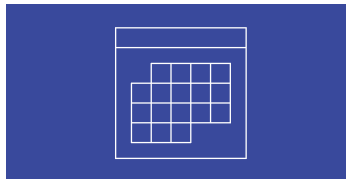
**To become the recognized leader in drug-resistant epilepsy therapy and fully develop the potential of the RNS System**

# Long Range Plan:  Key Areas of Focus



### Market Expansion and Revenue Growth

- IGE and Pediatric Indication
- Project CARE Site of Service Expansion
- Direct to Patient and Referral Marketing Expansion
- Level 4 CEC Adoption and Utilization Growth



### Financial Discipline

- Gross Margin Improvements
- Operating Expense Allocation
- Incremental Commercial Organizational Investment
- Operating Leverage – Commercial Team
- Balance Sheet Flexibility

### Operating Execution

- Expanded Indications Approval and Launch
- Commercial Execution – Level 4 Adoption/Utilization, CARE, New Indications
- Product Development Pipeline
- Direct to Consumer and Referral Network Expansion



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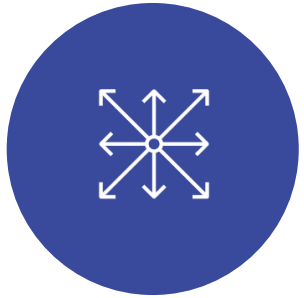
# Multiple Growth Initiatives Underway



## Clinical Development

- PAS – Adult Focal
- NAUTILUS – IGE
- NEST – Pediatric Focal
- LGS

## Product Development

- Annual AI SW Releases
- Remote Programming
- Next Generation Platform

## Market Development

- Incremental Sales Force Expansion
- Project CARE
- Expanded Direct to Patient
- Increased Professional Education



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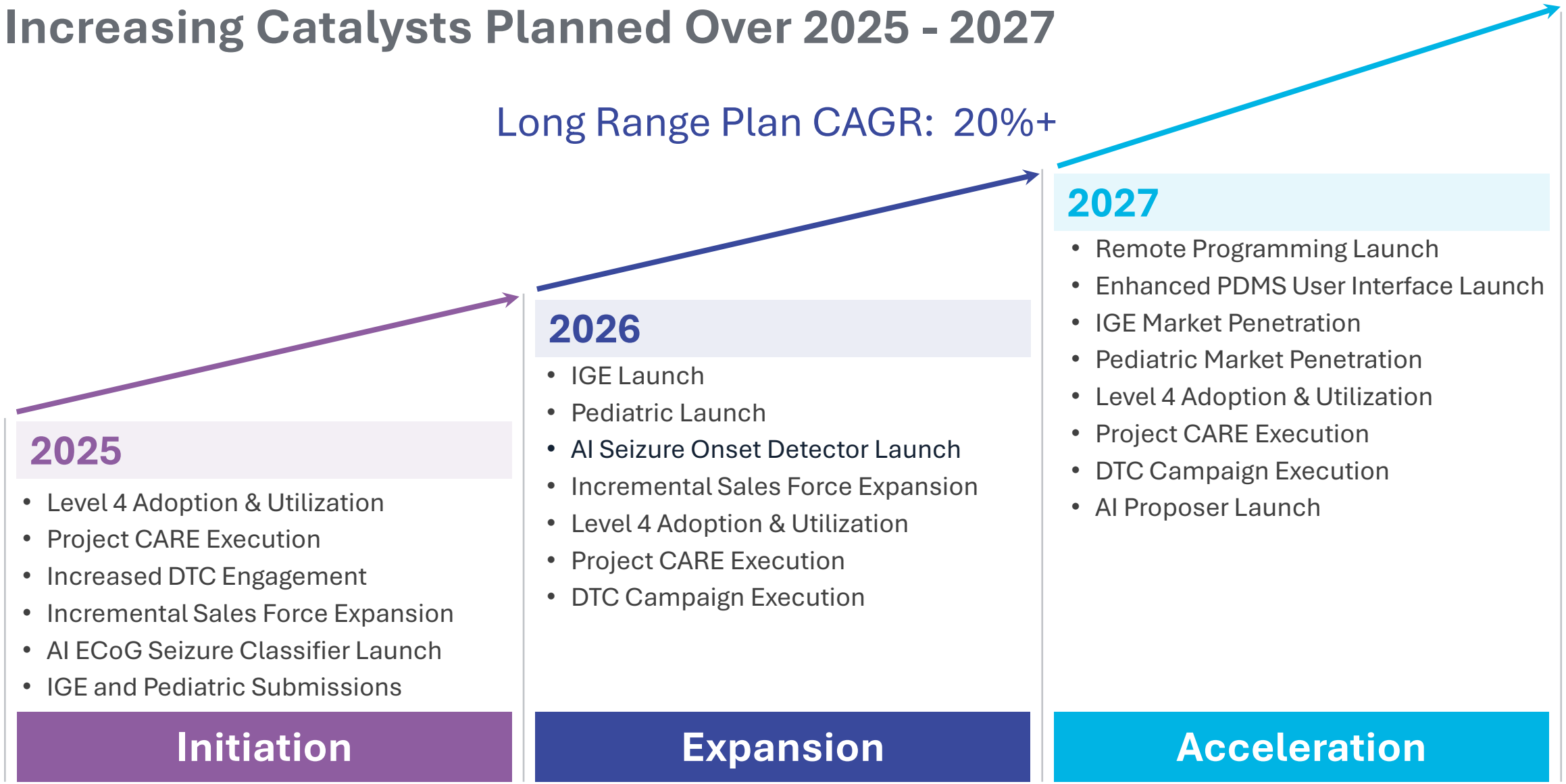
# Increasing Catalysts Planned Over 2025 - 2027




Hardware and software releases, clinical trial submissions, and clinical approval launches are anticipated during the time periods shown above.



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# NeuroPace Vision and Long Range Plan Objectives

Market Leader with LRP Revenue Growth of 20%+ CAGR

Indication expansion to Idiopathic Generalized and Pediatric DRE patients

Neuromodulation category leader in efficiency and ease of use with AI Tools and Remote Programming

Significantly expanded patient and referral awareness and access through direct-to-consumer campaigns and Project CARE

Cash Flow Break Even



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# The NeuroPace RNS System and Effectiveness in Focal Epilepsy

Martha Morrell, MD

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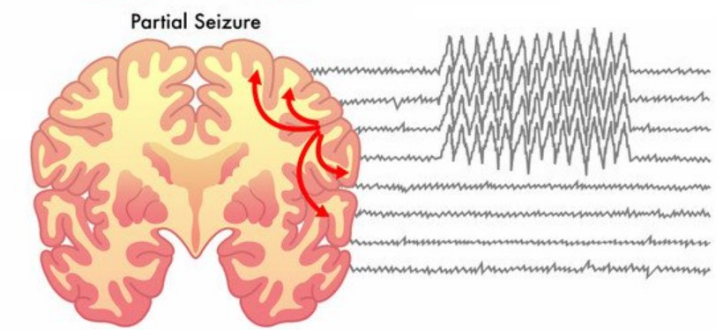
# Epilepsy: a brain disorder that causes recurring, unprovoked seizures

- 4th most common brain disorder; > 3.6 M persons in US[1]
- Seizures caused by abnormal brain electrical activity
- 30-40% of persons with epilepsy are drug resistant

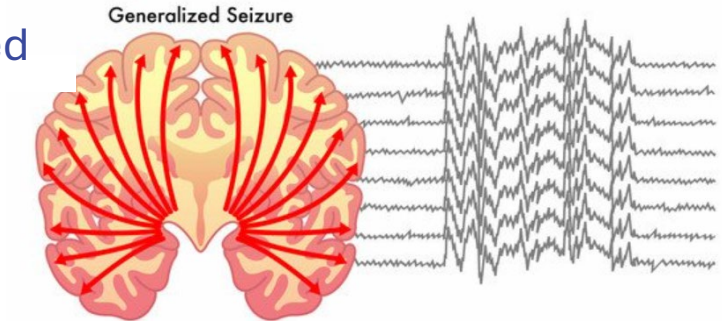
Focal Epilepsy




**Treatment options**

- More medication
- VNS/DBS/RNS
- Surgery/ablation

Generalized Epilepsy




**Treatment option**

- More medication

[1]Kobau et al., 2024



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# Drug-Resistant Epilepsy

## International League Against Epilepsy[1]

"failure of adequate trials of two tolerated, appropriately chosen and used antiepileptic drug schedules (whether as monotherapies or in combination) to achieve sustained seizure freedom"

## Treatment of drug-resistant epilepsy

The expected standard of epilepsy care

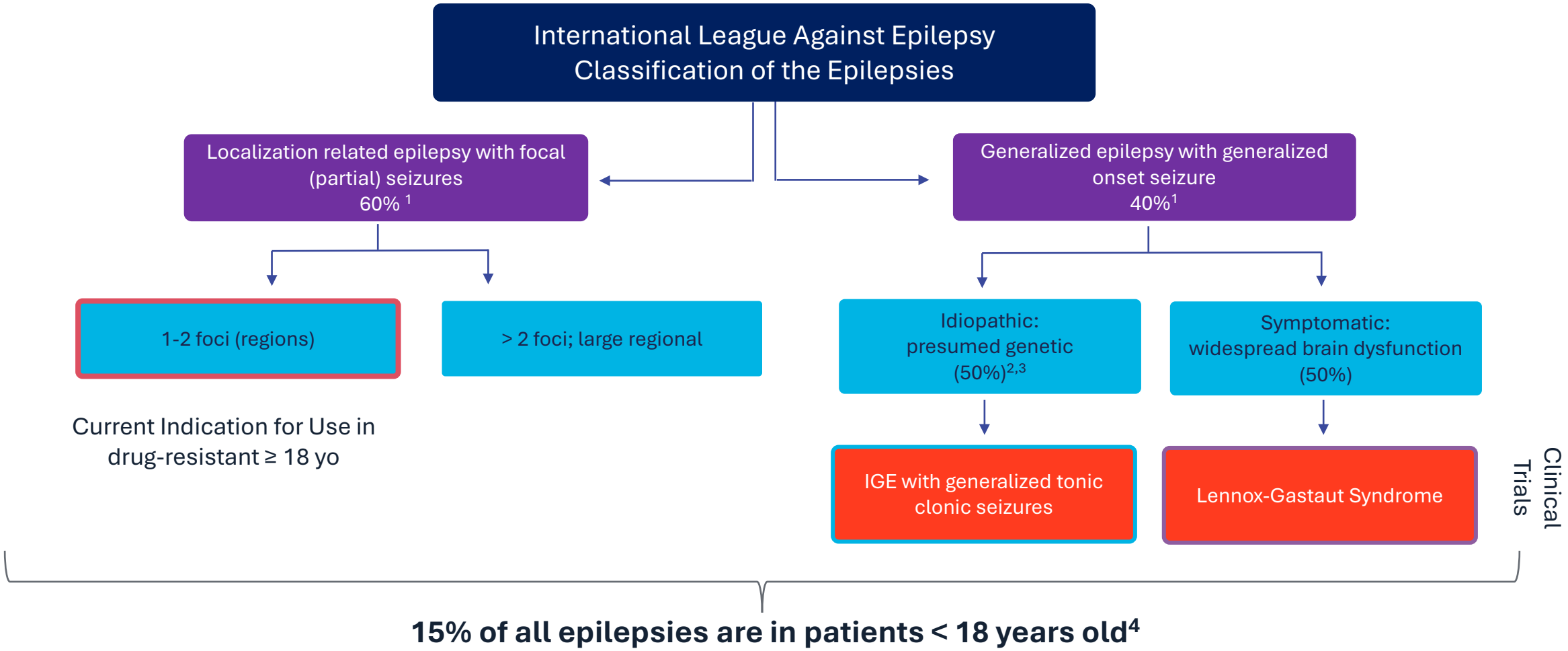
- 2 drugs, referral to epilepsy center to consider neuromodulation, surgery, or resection

The reality of epilepsy care

- Multiple drug trials, > 10 years of intractable epilepsy
- No referral to epilepsy center

[1]Kwan et al., 2010

# Epilepsy Syndromes




[1]Linehan, Berg 2021; [2] Jallon et al. 2005; [3]Vanderwiubecke et al. 2022; [4]Zack et al. MMWR 2017



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# Responsive Neuromodulation – The RNS® System

**Monitors** brain activity continuously

**Recognizes & Responds** to patient-specific seizure patterns

**Records** ongoing iEEG data for physicians to review

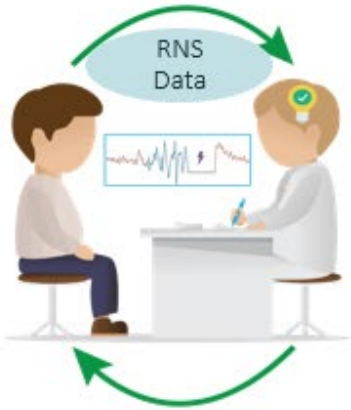
Implantable Device

Physician Programmer


Patient Remote Monitor


Patient Data Management System

Detection and stimulation adjusted using RNS System brain data




Optimal Management



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# An Unprecedented Window to the Brain

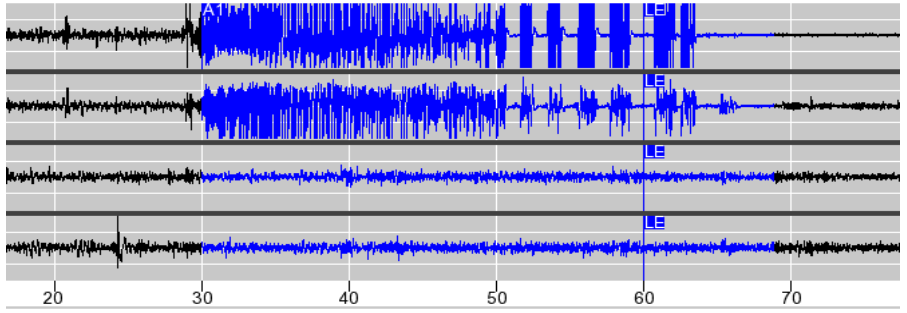
**Patient sends RNS data via internet to the secure Patient Data Management System (PDMS)**

## Data includes:

- Samples of intracranial EEG
- Numbers and times of detections

## Data used to:

- Personalize detection and stimulation
- Monitor the stimulation response


iEEG recording


# of detections



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# Benefits of Choosing RNS System Treatment

- **Novel, differentiated** therapy
- **Excellent safety and efficacy** outcomes
- **Personalized** and **modifiable**
- **Non-destructive**; does not preclude other options
- Delivers **therapy** and provides **data** to help inform treatment decisions
- **Flexible** tool that enables many different treatment strategies



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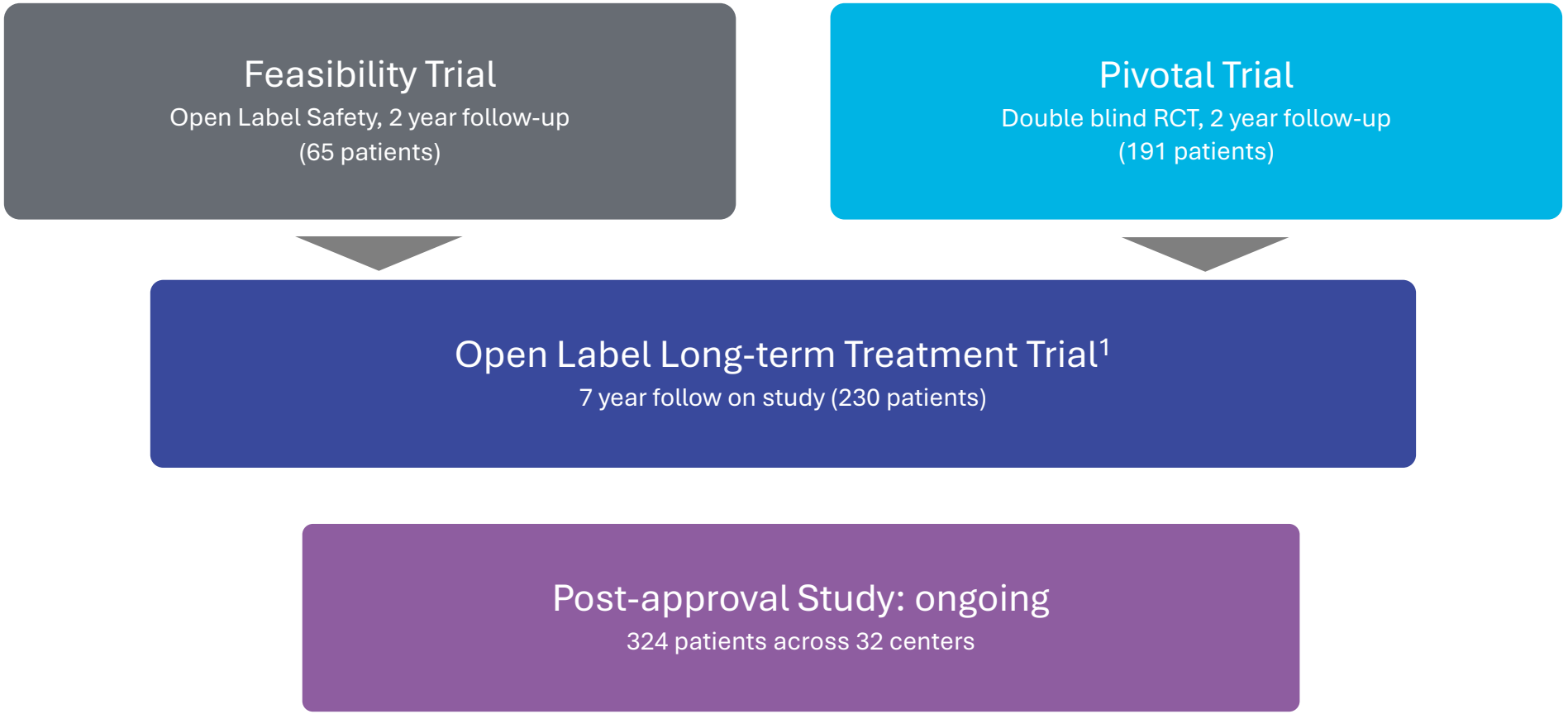
# Rigorous Clinical Trials Provide Rich Data

## 580 patients followed prospectively in RNS System trials[1]




[1] Initial implanted patients from Feasibility, Pivotal, and Post-approval Trials



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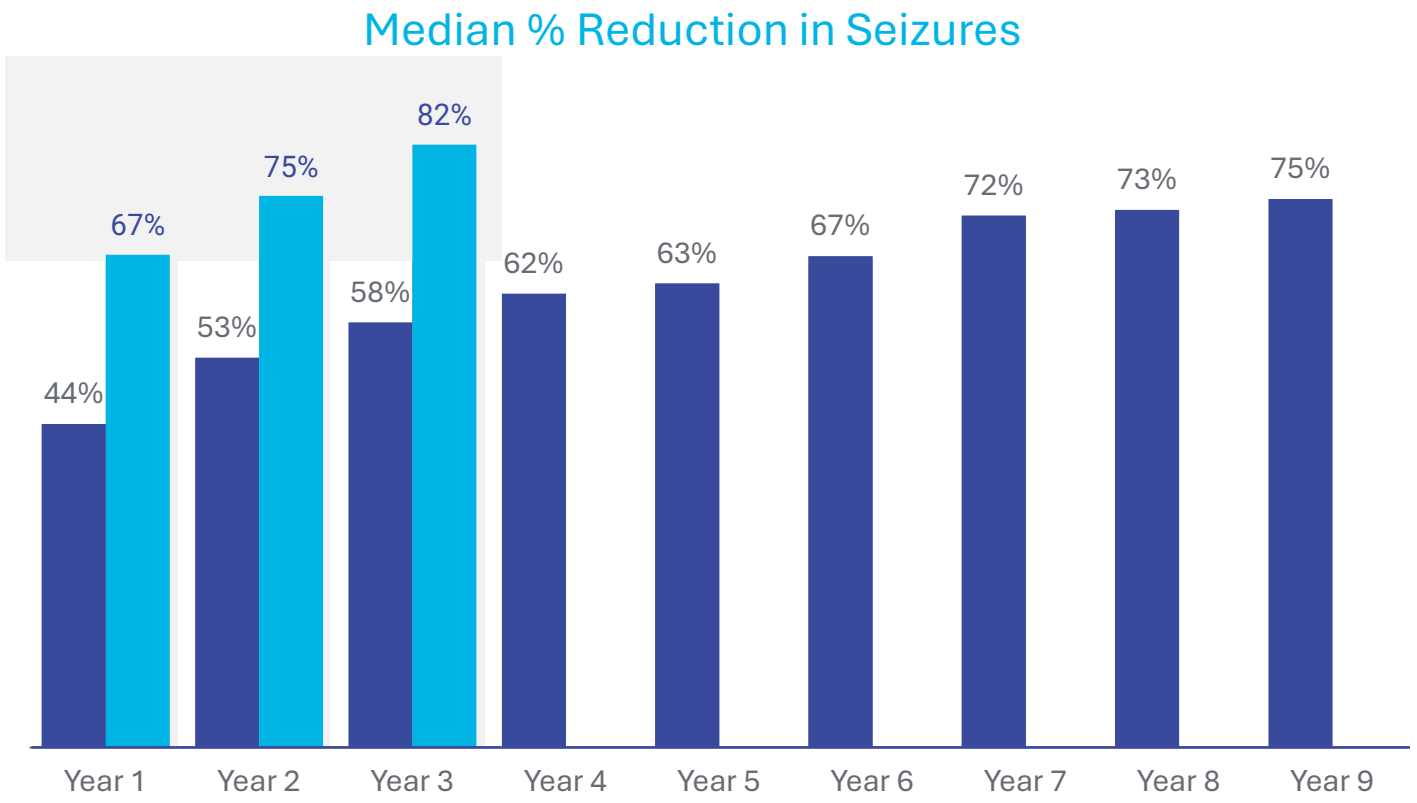
# Impressive Seizure Reductions Improve Over Time




**Original FDA Study Results:**[1,2]

- Statistically greater seizure reduction than sham therapy at 5 months
- 75% median seizure reduction at 9 years
- 28% of patients achieved ≥ 6 months of seizure freedom

**Real World & FDA Post Approval Study Results:**

- 67% median seizure reduction at 1 year[3,4]
- 75% median seizure reduction at 2 years[4]
- 82% median seizure reduction at 3+ years[4]
- ~1 in 3 patients with > 90% reduction in seizures[4]

Improvements shown in: Cognitive Function | Quality of Life | Mental Health | SUDEP

[1]Morrell, M, et al. Neurology, 2011. [2]Nair, D, et al., Neurology, 2020 and Heck et al., Epilepsia , 2014. [3]Szaflarski, JP, et al., Presented at American Epilepsy Society, 2019. [4]Razavi, B, et al., Epilepsia, 2020.



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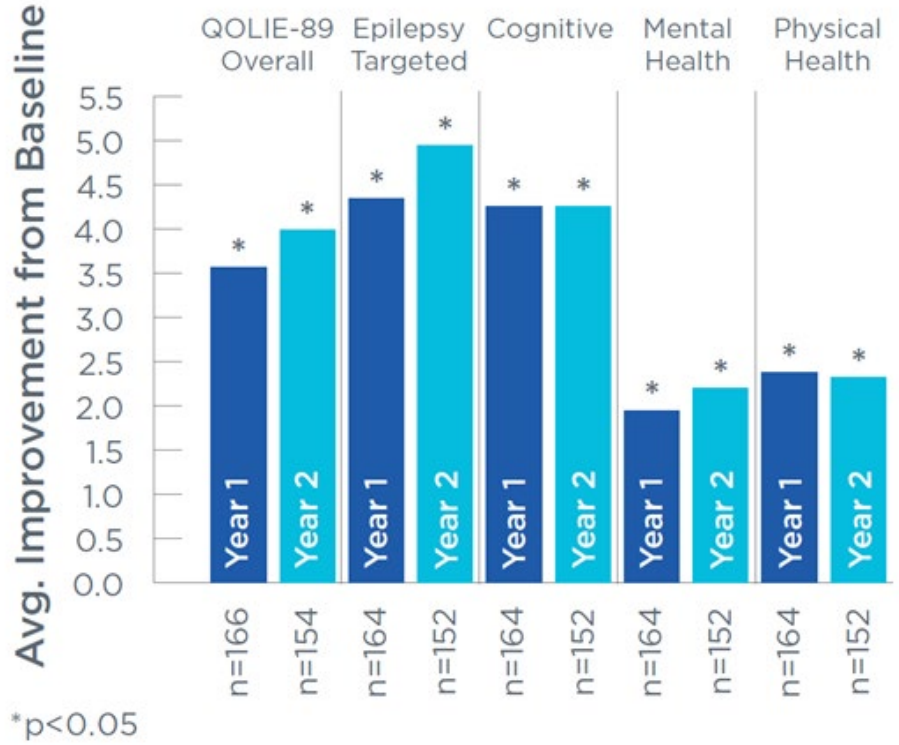
# Cognitive and Quality of Life Improvements Differentiate RNS from Other Neuromodulation Therapies

- Group improvements in **overall QOL** and in subdomains, including **cognitive function and mental health**[1]
- **No negative mood or cognitive effects**[2]
- **Significant cognitive improvements** in:
  - Naming ($p<0.001$)
  - Verbal learning ($p=0.03$)
  - Visual memory ($p=0.03$)
  - Executive function ($p\leq 0.009$)




[1] Meador et al., Epilepsy & Behavior, 2015
[2] Loring et al., Epilepsia, 2015



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# Power of the RNS Data

Vikram Rao, MD, PhD

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# The Clinical Value of the RNS Data

**Data drives patient improvement**

- Informs detection and stimulation programming for each patient
- Data provides opportunity to improve programming for all patients

**Diagnostic Capabilities**

- Long-term ambulatory intracranial EEG monitoring

**Clinical value today-** Improved patient care with data (periodicities, drug response, etc.)

**Clinical value tomorrow** is driven by AI efforts today



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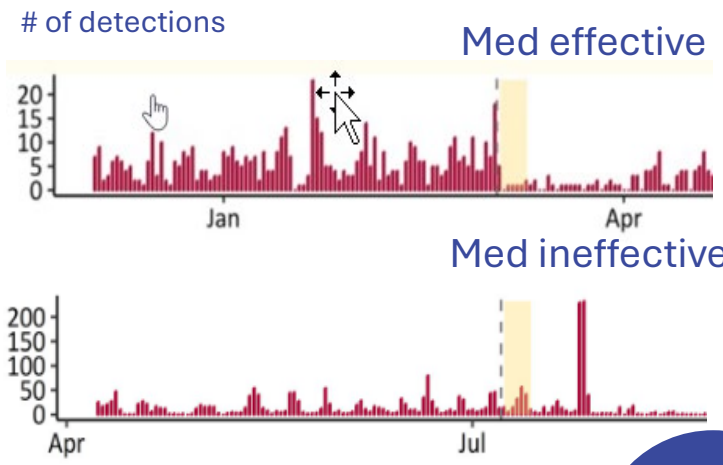
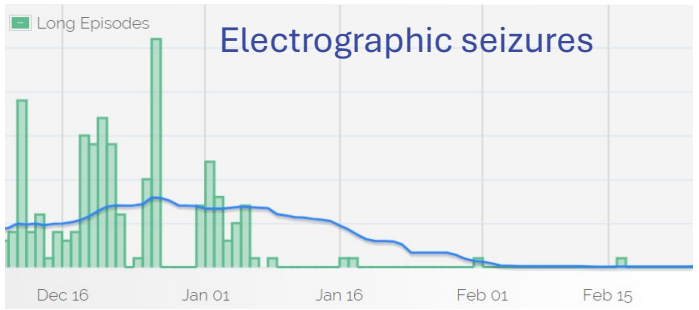
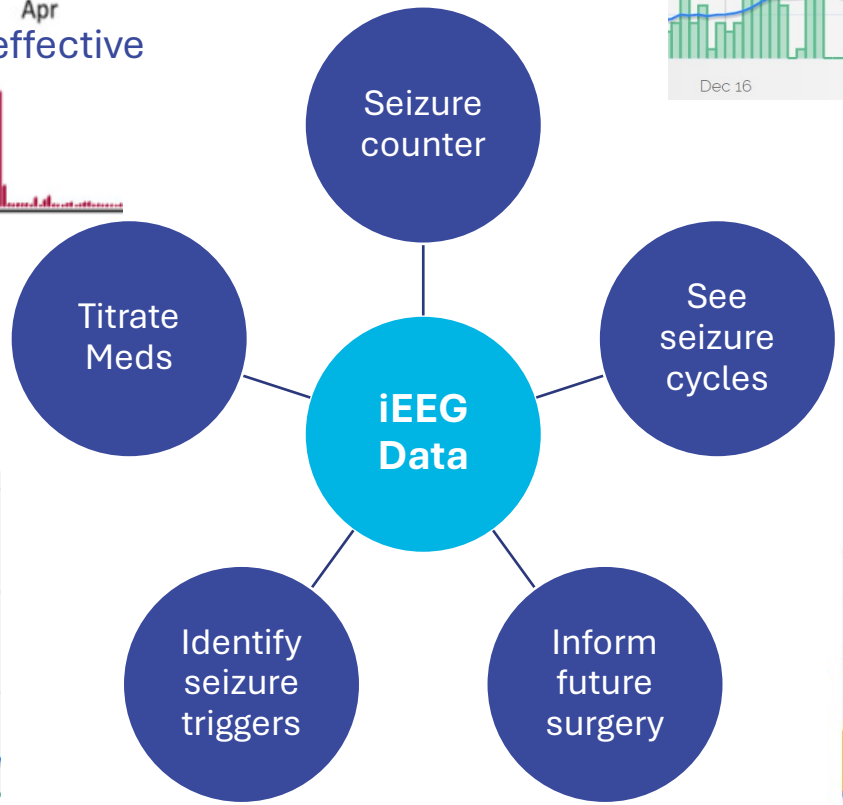
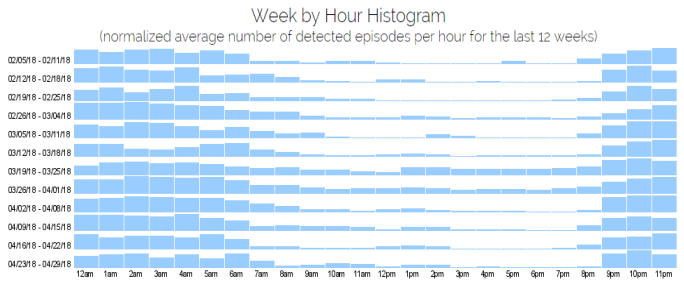
# RNS System Data Contributes to Better Epilepsy Management Today



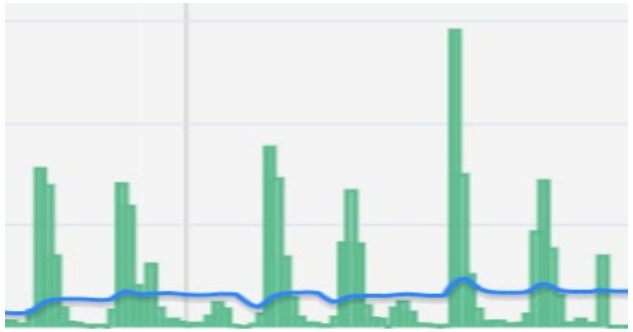



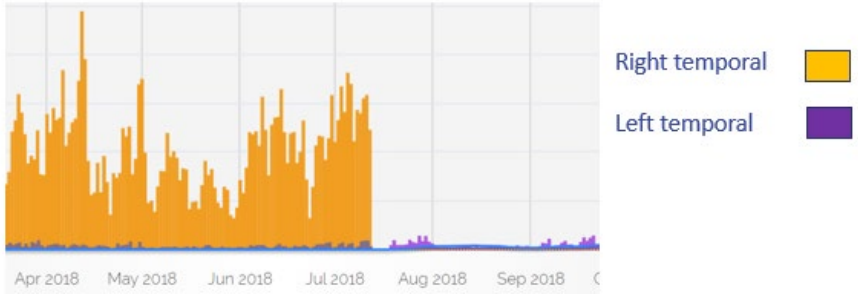

Hours of day/ week over week




Menstrual cycle trigger



Right temporal resection



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# Diagnostic Value of RNS System

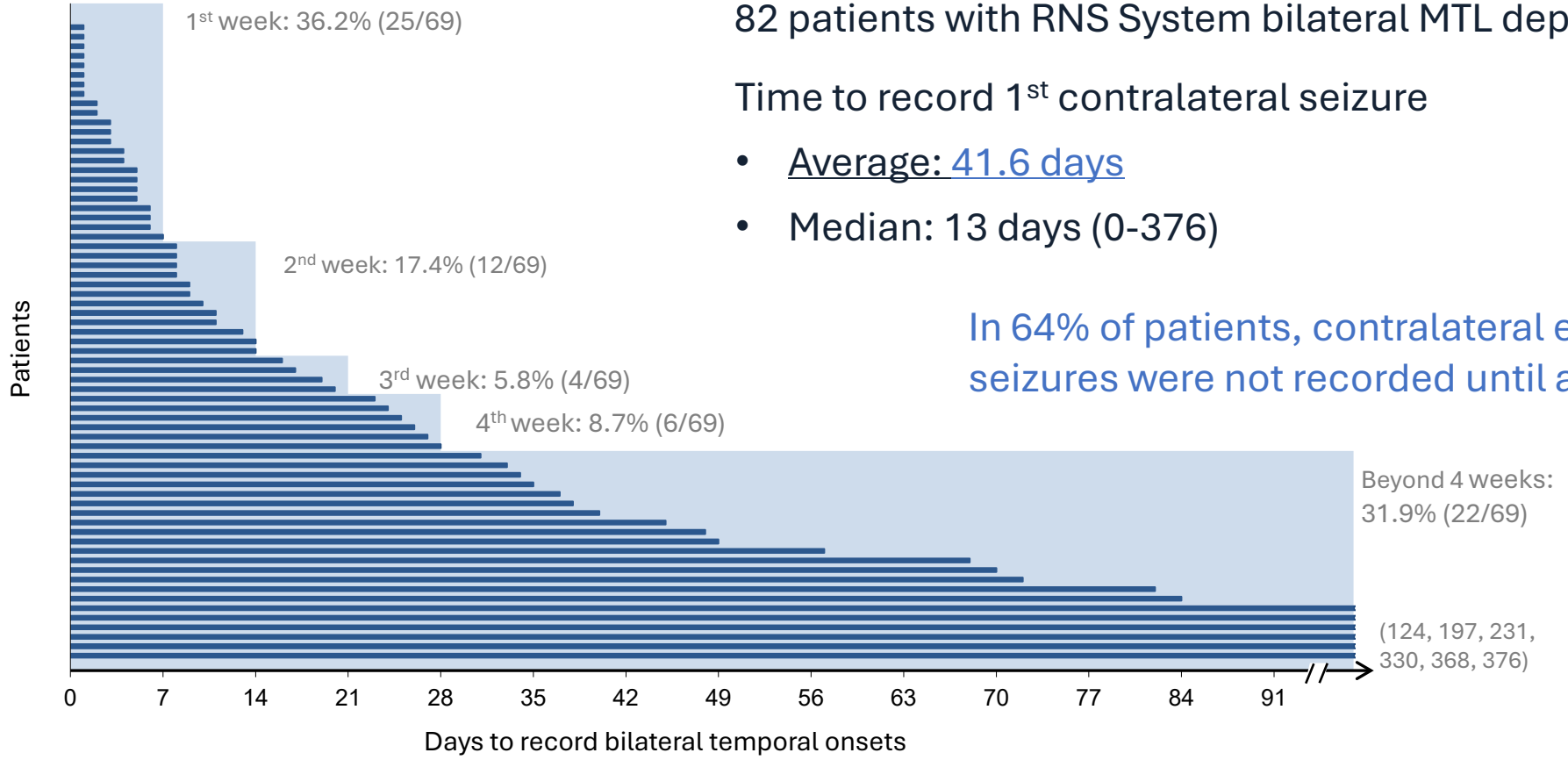
## Enhanced temporal sampling

1-2 weeks in EMU; weeks, months, years with RNS System

## Benefits:

- Track outcomes using electrographic data, as well as patient reported seizures
- Monitor response to addition or removal of a medication using electrographic data– before patient experiences the clinical change
- Identify seizure cycles and times of higher seizure risk
- Confirm localization of seizure onset
  - Particularly important in patients with mesial temporal onsets

# Lateralization of Mesial Temporal Lobe Epilepsy with Chronic Ambulatory Electrocorticography




82 patients with RNS System bilateral MTL depth leads

Time to record 1st contralateral seizure

- Average: 41.6 days
- Median: 13 days (0-376)

In 64% of patients, contralateral electrographic seizures were not recorded until after week 1

King-Stephens et al., Epilepsia 2015



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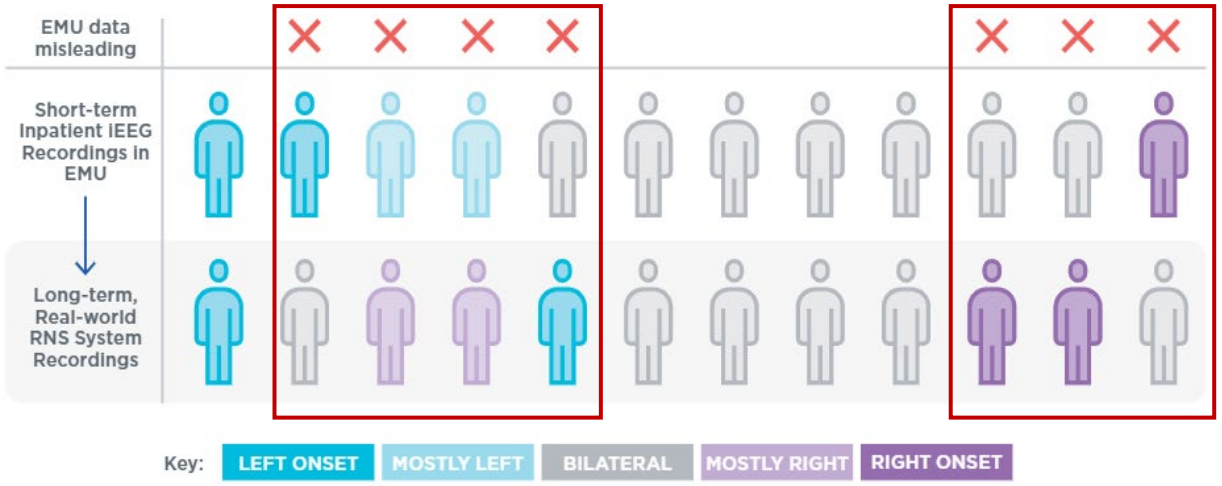
# RNS System Data Reveals Lateralization in Temporal Lobe Patients




Incorrect lateralization can lead to incorrect surgical decisions

RNS System's long-term data can be more accurate than inpatient EMU monitoring

Data from the EMU was misleading in 7 out of 12 patients (58%) who had both intracranial EEG monitoring in the EMU and ambulatory monitoring with the RNS System[2]

1. King-Stephens, D., et al. Epilepsia, 2015 2. Hirsch, L. et al. Epilepsia, 2020



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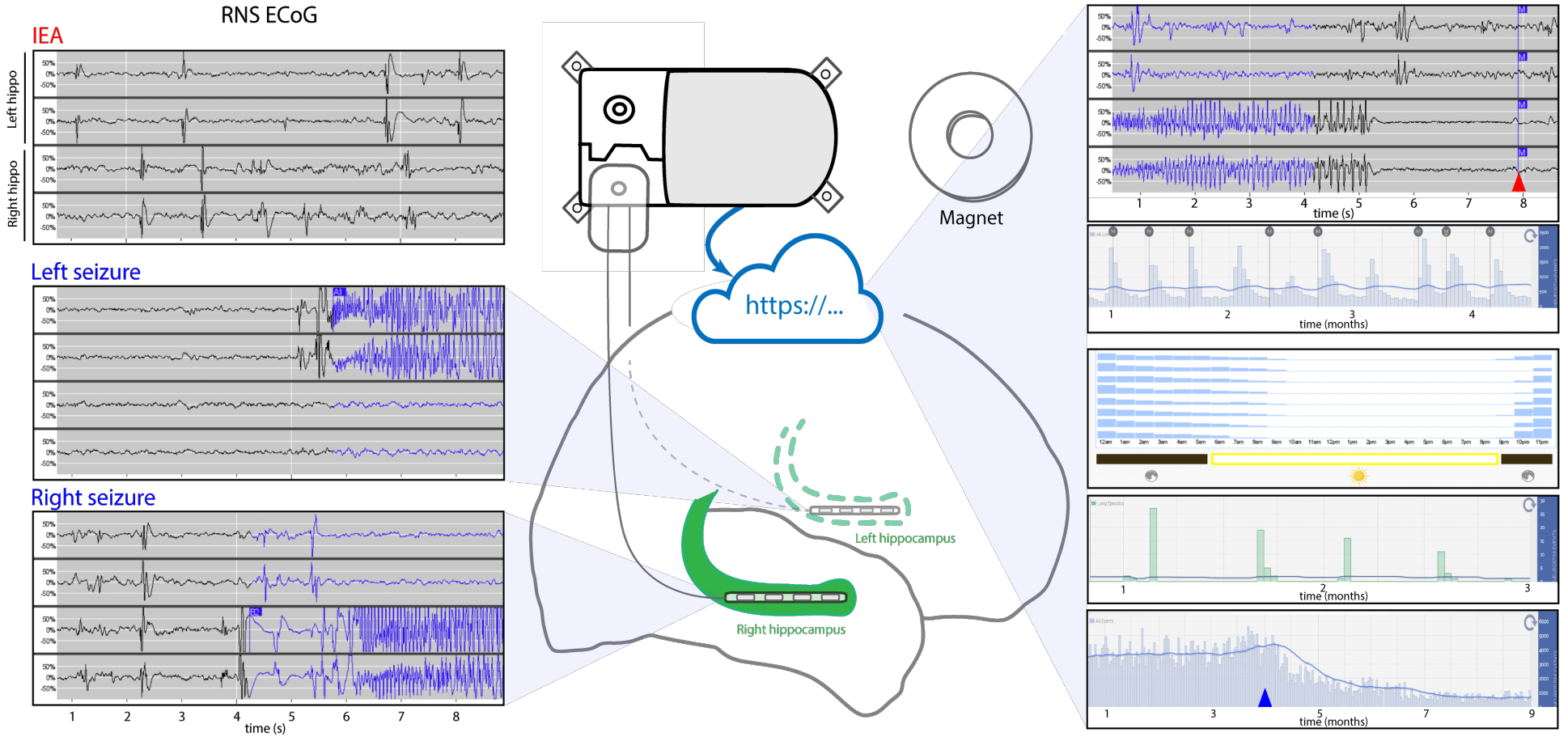
# Types of Data Collected by RNS System




Rao VR. Exp Rev Med Dev (2021) 18(11):1093-1105.



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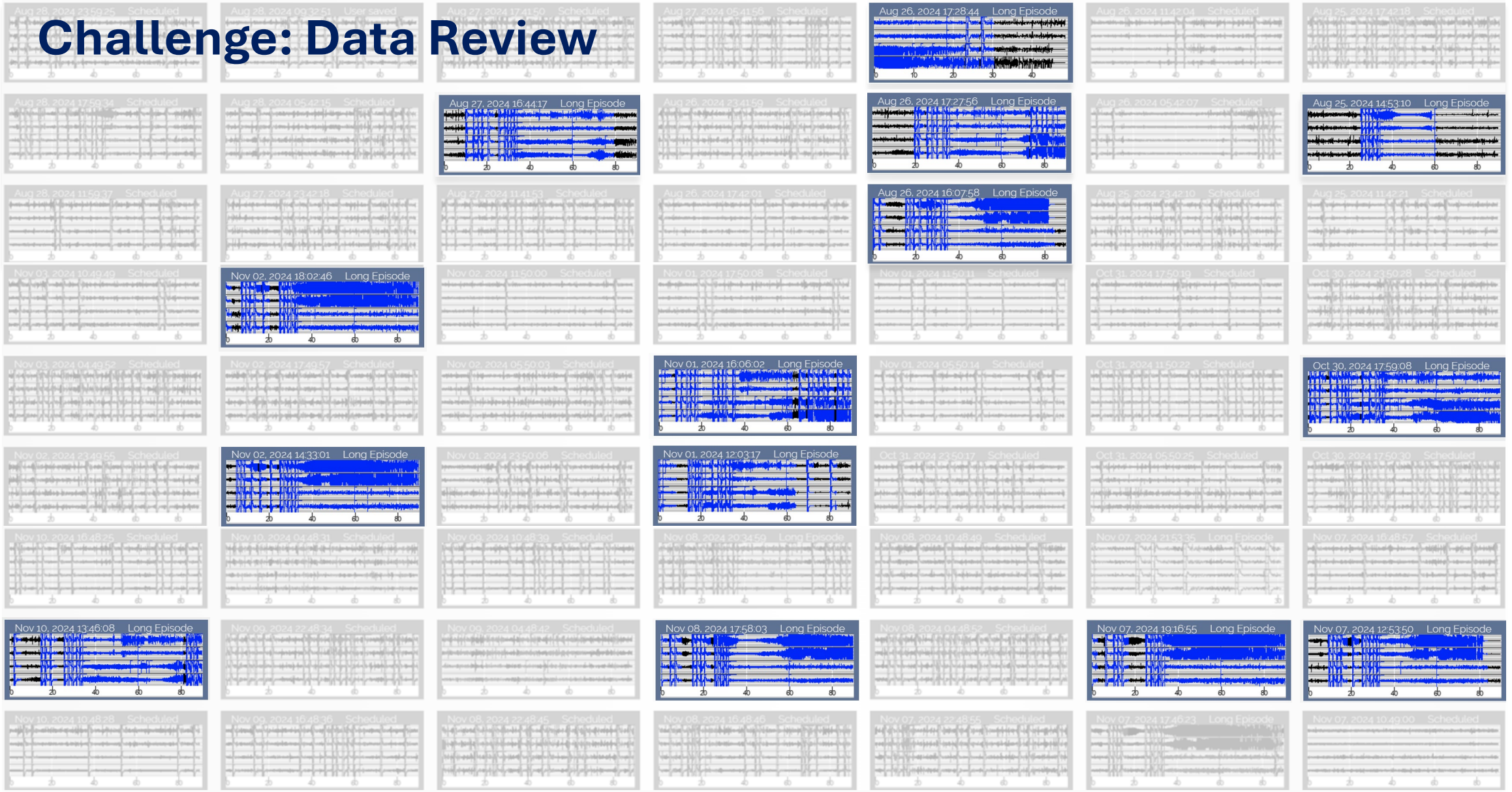
# Challenge: Data Review






NEUROPACE

Last Interrogated: 04/05/2024 17:50:07 Last Data Sync: 04/05/2024 09:17:13 Patient: Sample Patient Logged in: FCE_140

# PDMS

NEUROPACE

## Patient & Neurostim Info

Age:0

Time zone: EDT

Impedance: N/a
Battery: 2.98V

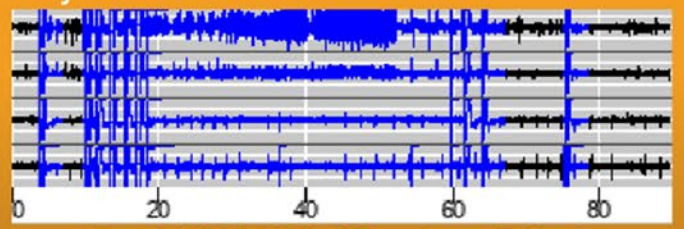
## AI-Powered Seizure Trends

## Activity

## Programming

Detection:Enabled
Stimulation: Enabled

## ECoG Library




March 1, 2024 19:54:37 Long Episode

## Live ECoGs

Conceptual renderings, not approved for use



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# AI-Powered Seizure Review Reduces Physician Burden

## Goal: help clinicians identify electrographic seizures and important trends efficiently

- Validated AI model to sort types of iEEG recordings
  - Non-Seizure
  - Electrographic Seizure Lead 1, 2 or both leads
- Integrated with PDMS physician platform
- Simplifies physician review of iEEG data


Conceptual renderings, not approved for use



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# AI-Powered Seizure Detection Improves Accuracy and Reduces Physician Burden

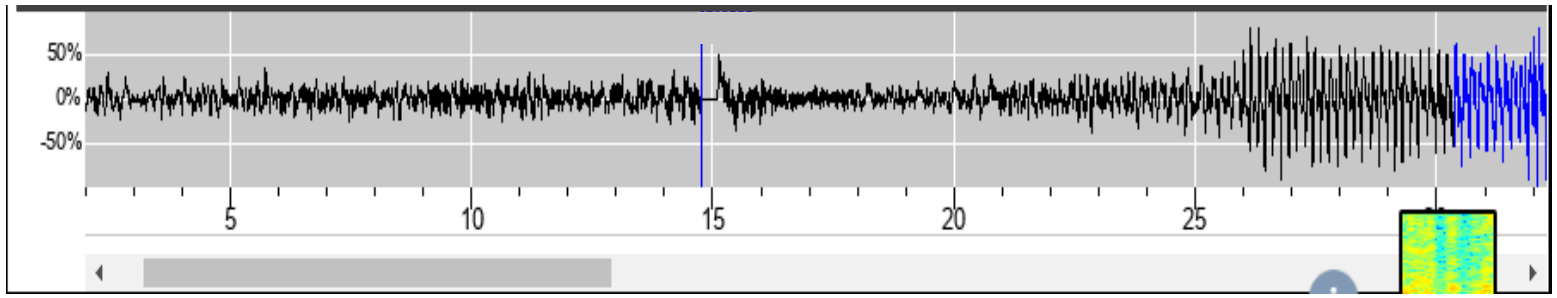
## Current practice

1. Physician looks at iEEG and decides when seizure begins
2. Manually selects detection settings

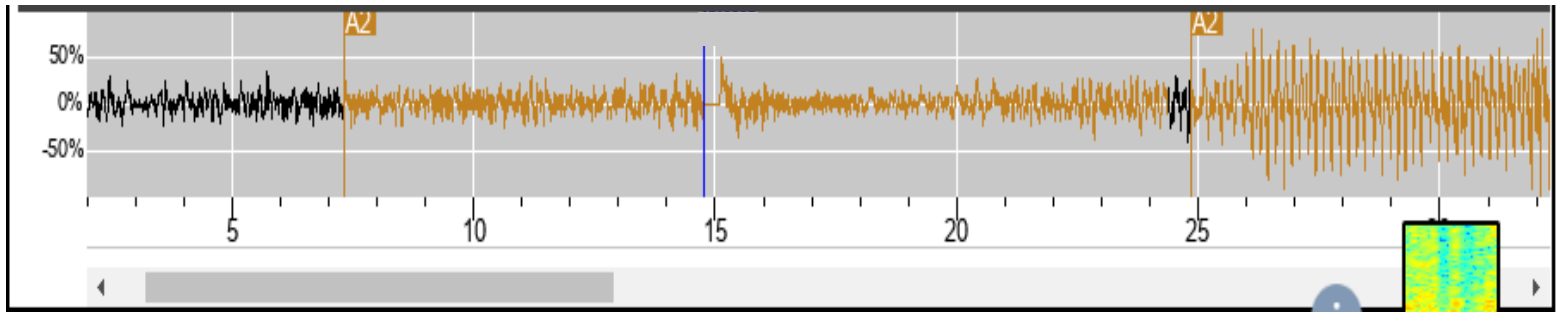
## AI-proposed detections

1. Vision Transformer model identifies seizure onset
2. Automatically proposes detection settings

Physician selected onset




AI selected onset



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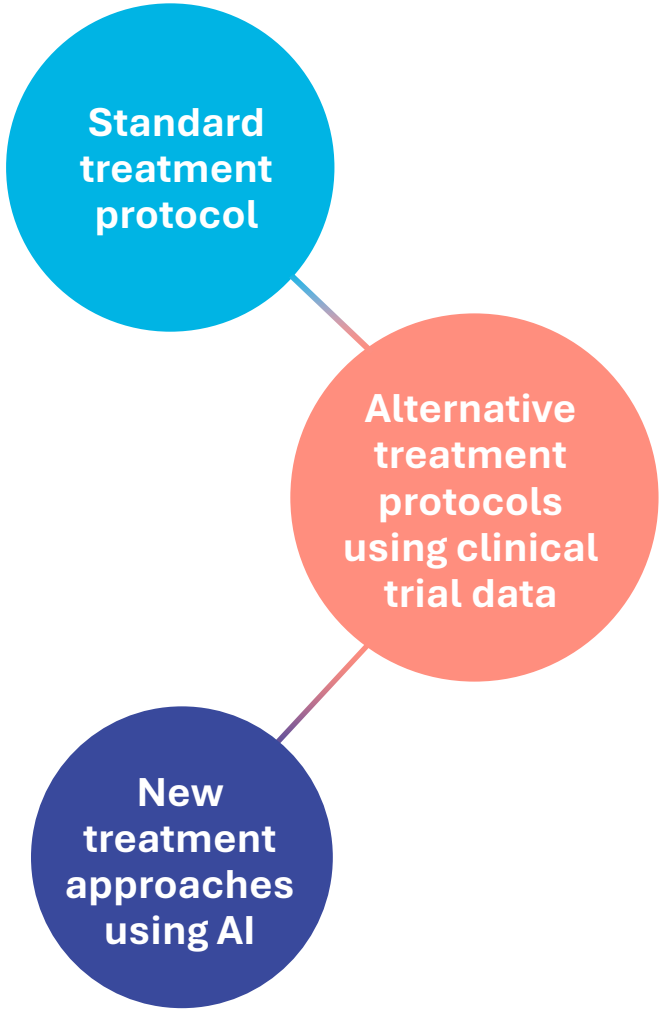
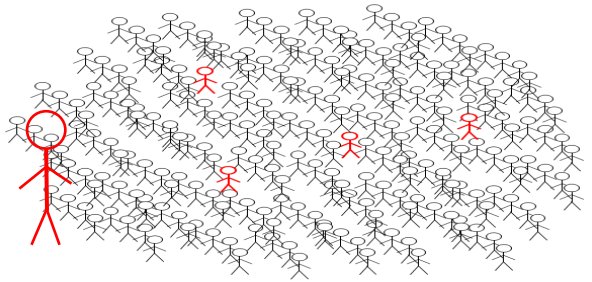
# AI Data Tools: Designed to Improve Outcomes and Ease of Use



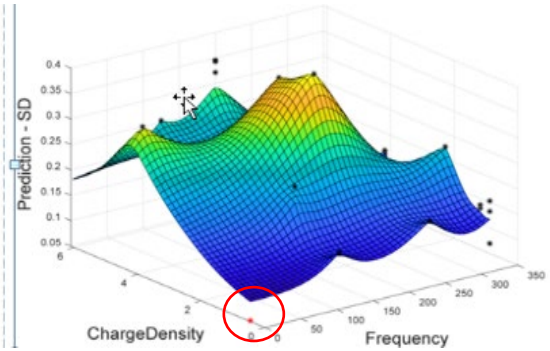

## Machine and Deep Learning

Propose stimulation settings based on response of other similar patients



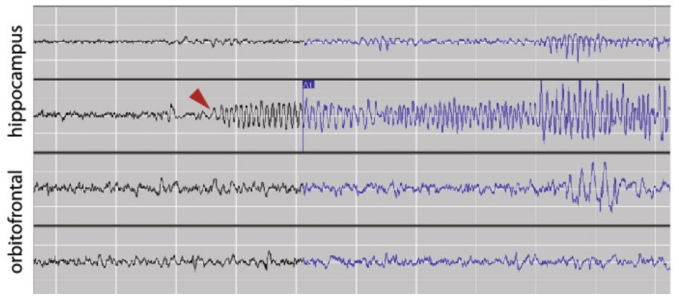
## Bayesian Optimization

Use data from every patient to predict next best settings for one patient




## Detection Proposer

Use AI to reveal seizure onset and propose detection settings



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# RNS System Clinical Applications

Mark Richardson, MD, PhD

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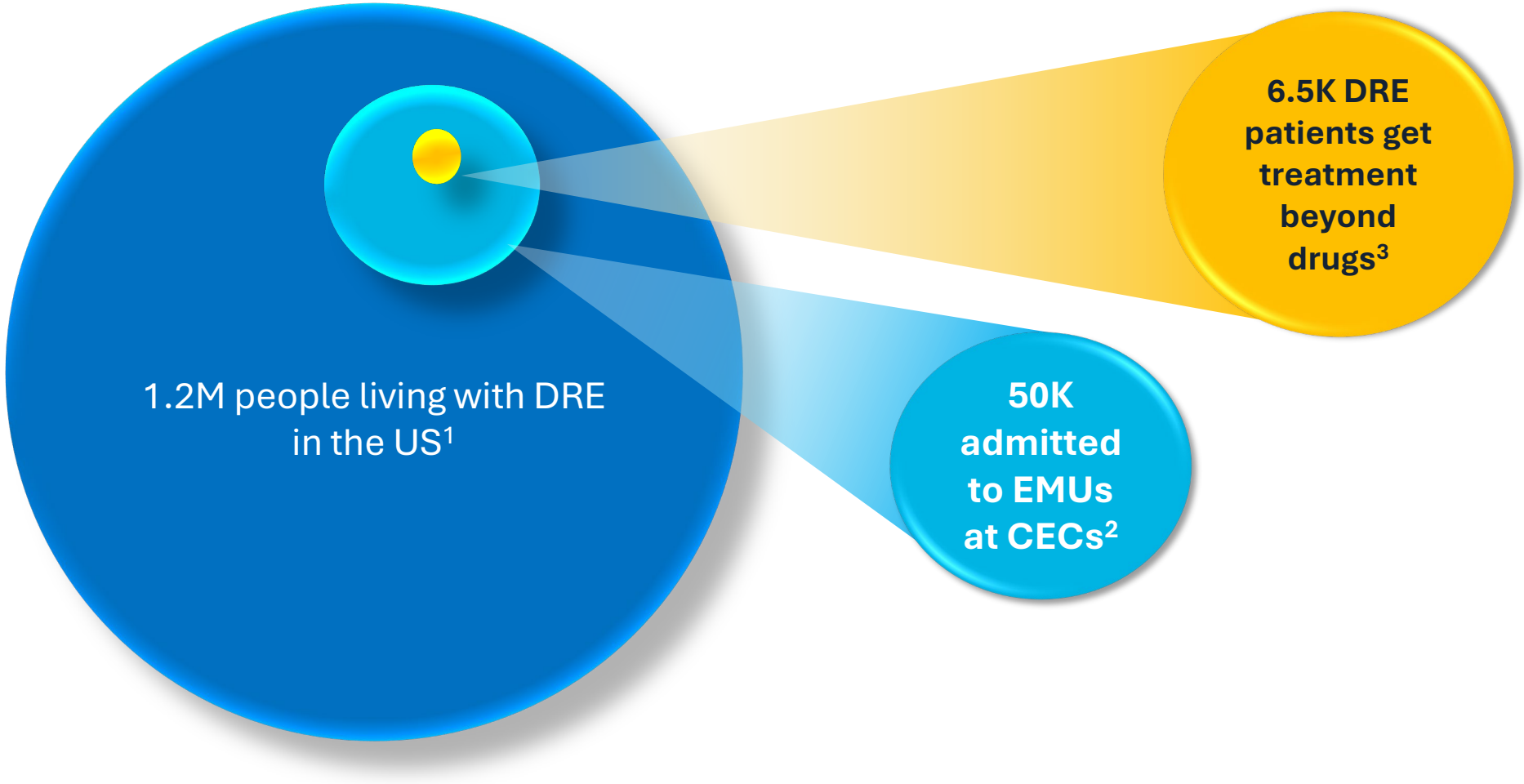
# There is a Substantial Treatment Gap for DRE Patients




1.Chen, Z., et al., JAMA Neurology, 2018.
2.Definitive Health
3.Ostendorf, et al, Neurology, 2022



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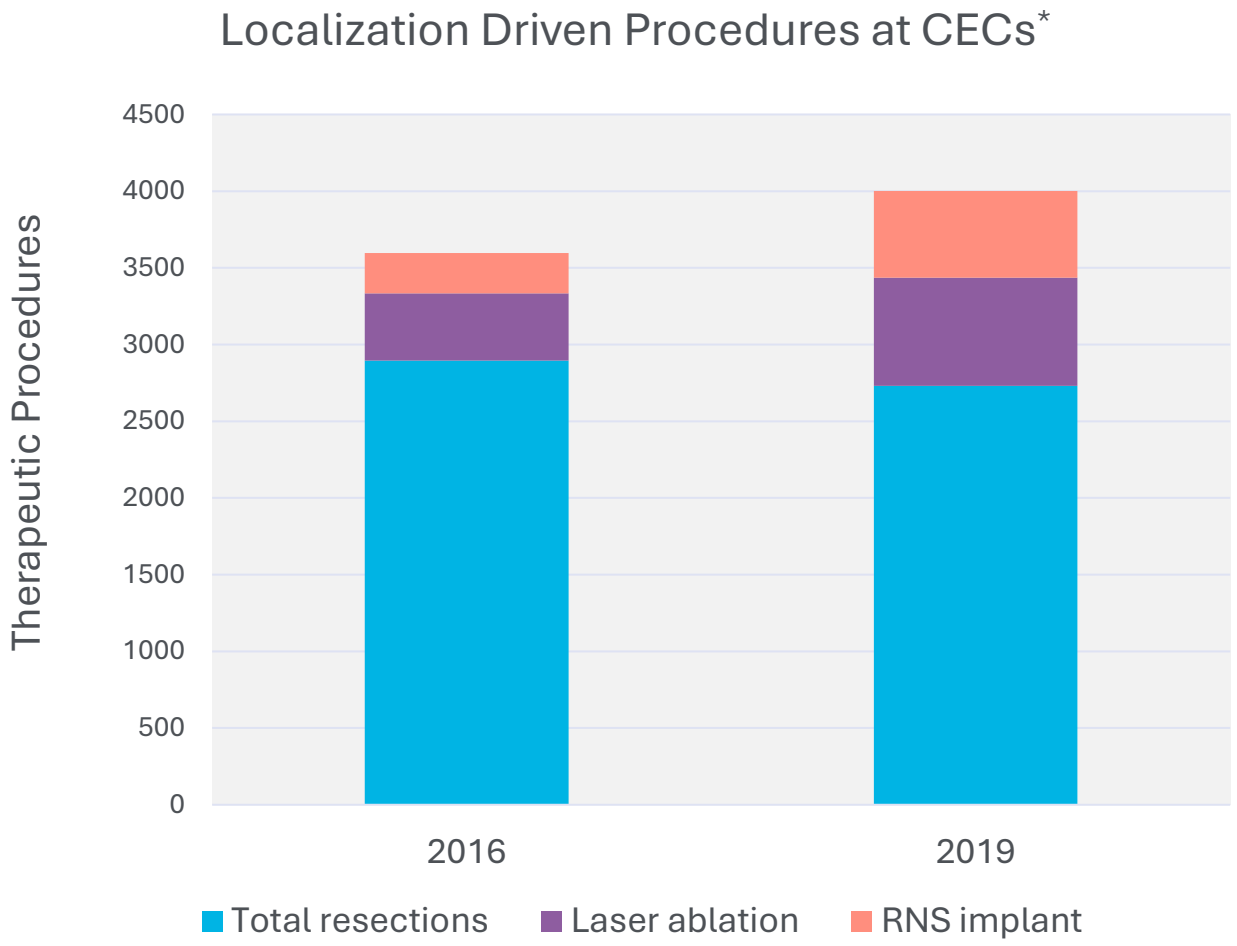
# Minimal Growth in Surgical Procedures

## Epilepsy procedures at CECs 2016 – 2019[1]

- EMU admissions +5% per year
- Intracranial monitoring +8% per year
- Localization related interventions +4% per year
  - Decrease in resection offset by increase in LITT
  - RNS System utilization increased




1. Ostendorf, et al, Neurology, 2022

* figure derived from data presented in (1) Ostendorf et al., Neurology, 2022



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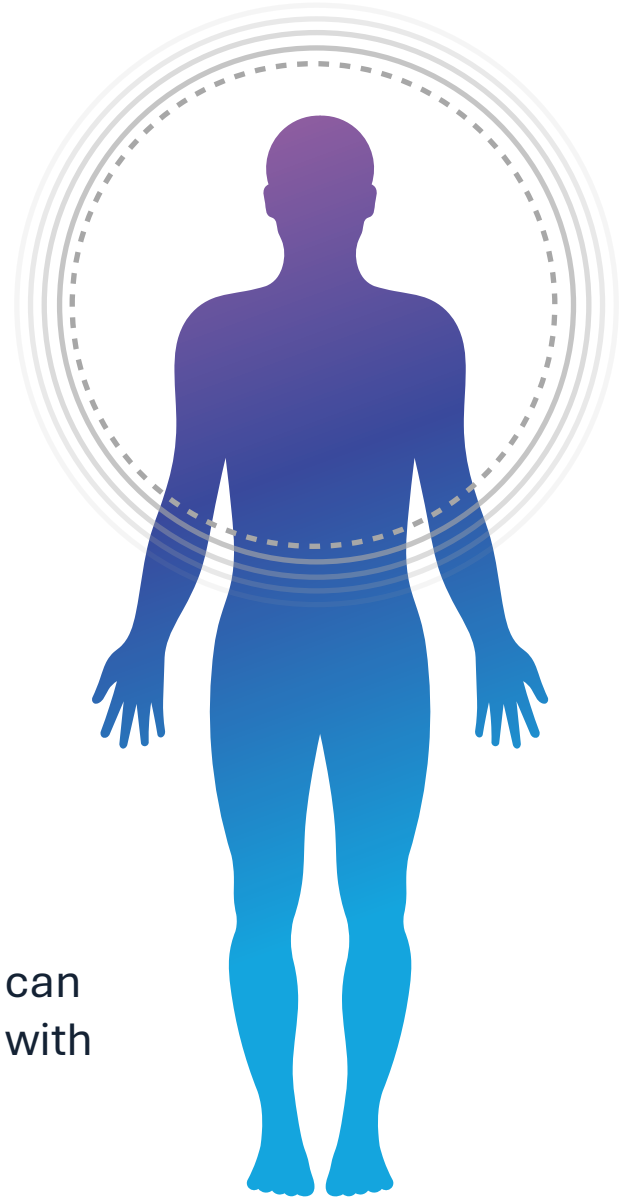
# Why does the surgical Treatment Gap Persist?

**Many patients with localized seizures do not get resection/LiTT because their seizure onset is…**

- Bilateral
- In eloquent cortex
- Part of a regional network
- Too large for complete resection
- Multi-focal



Many of these patients can benefit from treatment with the RNS System

Tomson, et al., Lancet Neurol. 2008
Solli, et al., Epilepsia, 2020
Loring, et al., Epilepsy & Behav, 2021



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# Expanded Thinking

## Paradigm Shifts in Epilepsy

”These paradigm shifts may facilitate closure of the surgical treatment gap in DRE”[1]

| | | Not only... | | But also... |
|---|---|---|---|---|
| **DEFINING SUCCESS** | → | Seizure freedom | + | **Maximize QOL for every patient** |
| **TREATMENT APPROACH** | → | Complete removal of seizure foci | + | **Modulate seizure network to disrupt seizure propagation** |
| **LOCALIZATION GOALS** | → | Inform resection | + | **Inform neuromodulation options** |
| **PATIENT MANAGEMENT** | → | Subjective patient reports | + | **Objective, long-term iEEG** |

1. Richardson, et al., Neurologic Clinics, 2022



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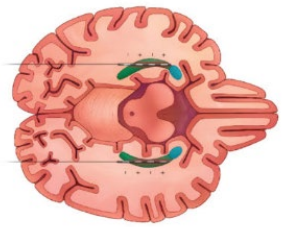
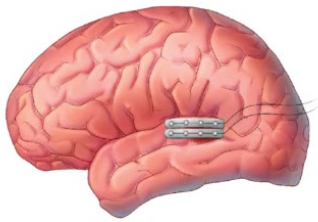
# Flexible Lead Placement Enables Diverse Stimulation Approaches for a Broad Group of Focal DRE Patients

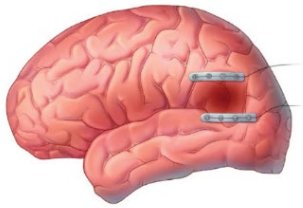
**TARGETED STIMULATION**
for discrete onsets

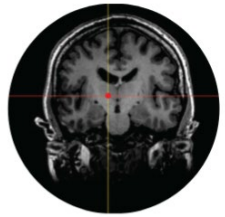
**NETWORK STIMULATION**
for regional onsets

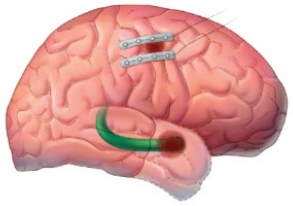
**THERAPY COMBINATIONS**
to augment surgery











MTL Onsets

Discrete Cortical Onsets

Regional Neocortical Stimulation

Corticothalamic Stimulation**

Large or Multifocal* Onsets

*The RNS System is indicated to treat up to 2 epileptogenic foci. Expand treatment area by combining partial resection with the RNS System (Tran, DK. et al., Frontiers in Neurology, 2020).
**RNS System clinical trials did not assess safety and effectiveness in patients with epileptogenic regions at or caudal to the level of the thalamus
Images courtesy of Ma BB and Rao VR., from Epilepsy & Behavior, 2018



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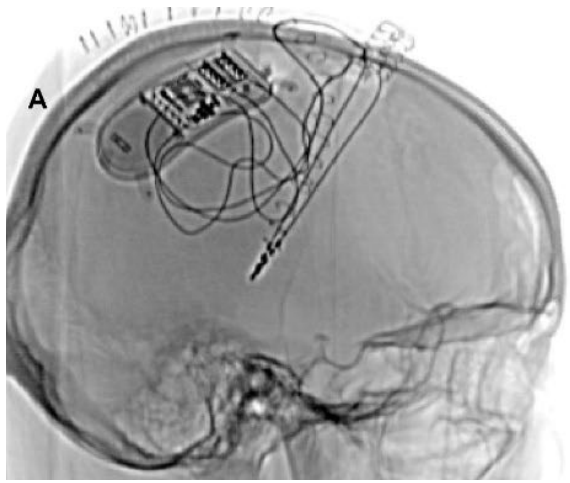
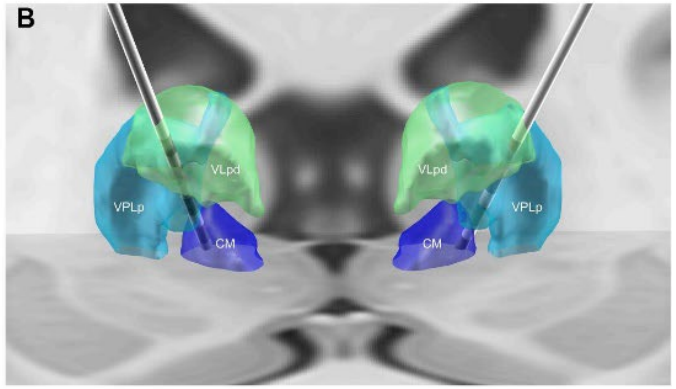
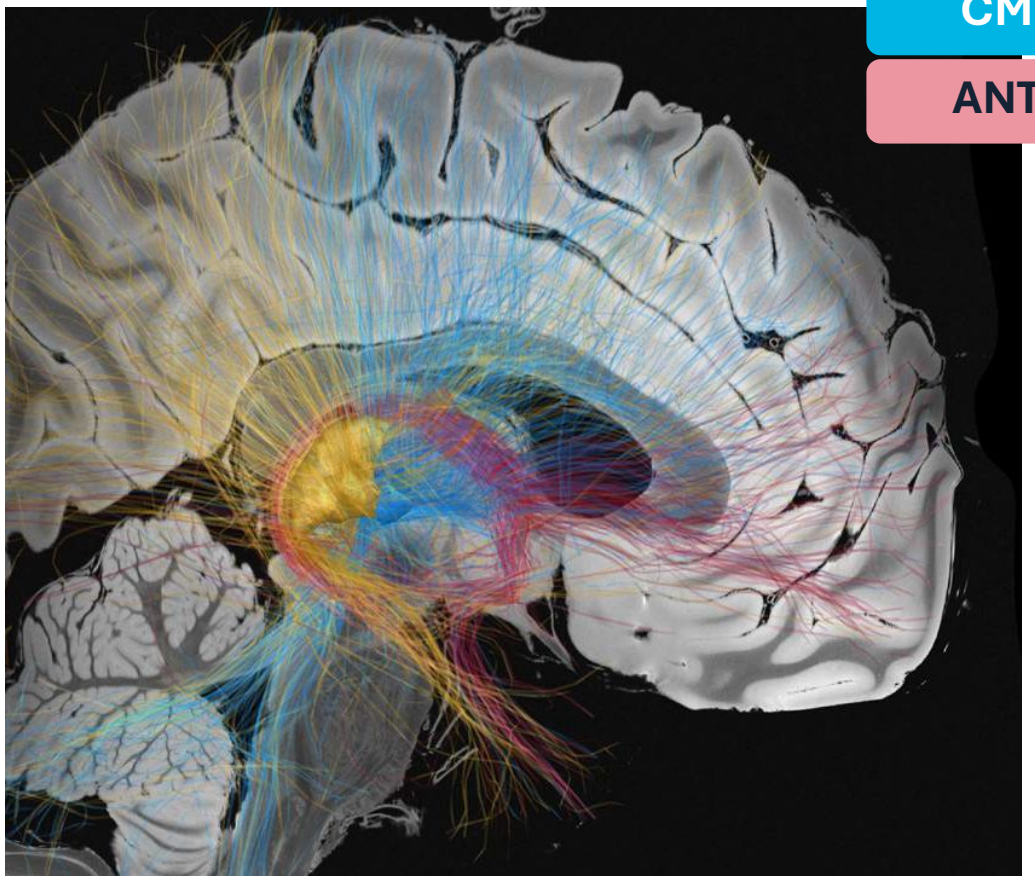
# Treating the Seizure Network with Corticothalamic Stimulation

- Treat spatially extensive seizure foci by targeting a deep nucleus that projects diffusely to cortex
- Target thalamic nuclei based on networks




Kokkinos, et al, Neurosurgery, 2020; Herlopian, et al, Ann Clin Transl Neurol, 2019; Elder, et al, Epilepsia Open, 2019



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# Responsive v. Open-Loop Stimulation

## Advantages of the responsive stimulation approach

### RNS System intracranial EEG (iEEG) data:

- Ictal patterns are seen in the cortex, hippocampus and thalamus
- iEEG data used to guide stimulation settings and pathways

### RNS System studies show no acute or chronic side effects of therapeutic stimulation

### Less stimulation may produce fewer side effects:

- RNS System responsive approach provides minutes of stimulation/day v. hours/day with open-loop stimulation
- Open-loop ANT stimulation side effects:
- Sleep arousals are 3X more frequent[1]
- Self-reported depression and subjective memory impairment[2, 3]

1. Voges et al., Epilepsia, 2015, n=9
2. Sprengers, et al., Cochrane Review of Deep Brain and Cortical Stimulation for Epilepsy, 2017
3. Kaufmann, et al., Epilepsia, 2024

# The Epilepsy Treatment Gap Persists:

## 2022 ILAE Consensus Recommendations

Goal: Identify ways to address DRE patient treatment gaps and clarify when to initiate surgical evaluation

Received: 1 March 2022 | Revised: 25 June 2022 | Accepted: 27 June 2022
DOI: 10.1111/epi.17350

Epilepsia

SPECIAL REPORT

**Timing of referral to evaluate for epilepsy surgery: Expert Consensus Recommendations from the Surgical Therapies Commission of the International League Against Epilepsy**

Lara Jehi[1] | Nathalie Jette[2] | Churl-Su Kwon[3] | Colin B. Josephson[4] | Jorge G. Burneo[5] | Fernando Cendes[6] | Michael R. Sperling[7] | Sallie Baxendale[8] | Robyn M. Busch[1] | Chahnez Charfi Triki[9] | J. Helen Cross[10] | Dana Ekstein[11] | Dario J. Englot[12] | Guoming Luan[13,14,15] | Andre Palmini[16] | Loreto Rios[17] | Xiongfei Wang[13,14,15] | Karl Roessler[18] | Bertil Rydenhag[19] | Georgia Ramantani[20] | Stephan Schuele[21] | Jo M. Wilmshurst[22,23] | Sarah Wilson[24] | Samuel Wiebe[4]

## Key Recommendations

1. Referral for surgical evaluation should be offered to every DRE patient (up to 70 years)
   a. Regardless of epilepsy duration, sex, socioeconomic status, seizure type, epilepsy type, comorbidities
   b. Patients who may not appear to be appropriate candidates for resective surgery should be referred so other options (like neuromodulation) may be offered
2. Surgical referral should not be delayed if
   a. Therapies other than ASMs have not been tried
   b. Surgery is expected to be “palliative”
   c. Patient had prior resection, but still has seizures
   d. Failure of ASM trials was due to unacceptable side effects

Jehi, et al., Epilepsia, 2022



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# The Cost of Doing Nothing or Delaying Treatment

- SUDEP kills 1 in 150 people with uncontrolled seizures each year.[1]
- 20 years of lost quality of life for DRE patients spent on ineffective anti-seizure medications.[2]
- Delayed intervention reduces the potential impact of treatment.[2,3]
  - Early treatment patients (<10 yr after epilepsy onset) had significant improvements in QoL and mood
  - Late treatment patients (≥20 yr after epilepsy onset) not only failed to show these improvements but also declined in the emotional QoL subscale despite similar substantial reductions in seizure frequency

1. Tomson, et al., Lancet Neurol. 2008
2. Solli, et al., Epilepsia, 2020
3. Loring, et al., Epilepsy & Behav, 2021



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# Living with the RNS System

Mike McKenna, MSW

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# Patient Educator Introduction

## Mike McKenna, MSW

- Over eight years ago, I joined NeuroPace as a Patient Educator, after volunteering as an RNS Ambassador for about two years.
- I've seen the importance of patient education for patients who are considering, or moving forward, with the RNS System. Patients and families have shared they appreciate all the educational resources available to them.
- I’ve lived with epilepsy for over 25 years and have been using the RNS System for over 16 years.
- During my RNS journey, I earned a graduate degree in Social Work from ASU and Mayo Clinic School of Health Sciences and worked as a Social Worker at Mayo Clinic – Arizona before moving to Portland, OR.



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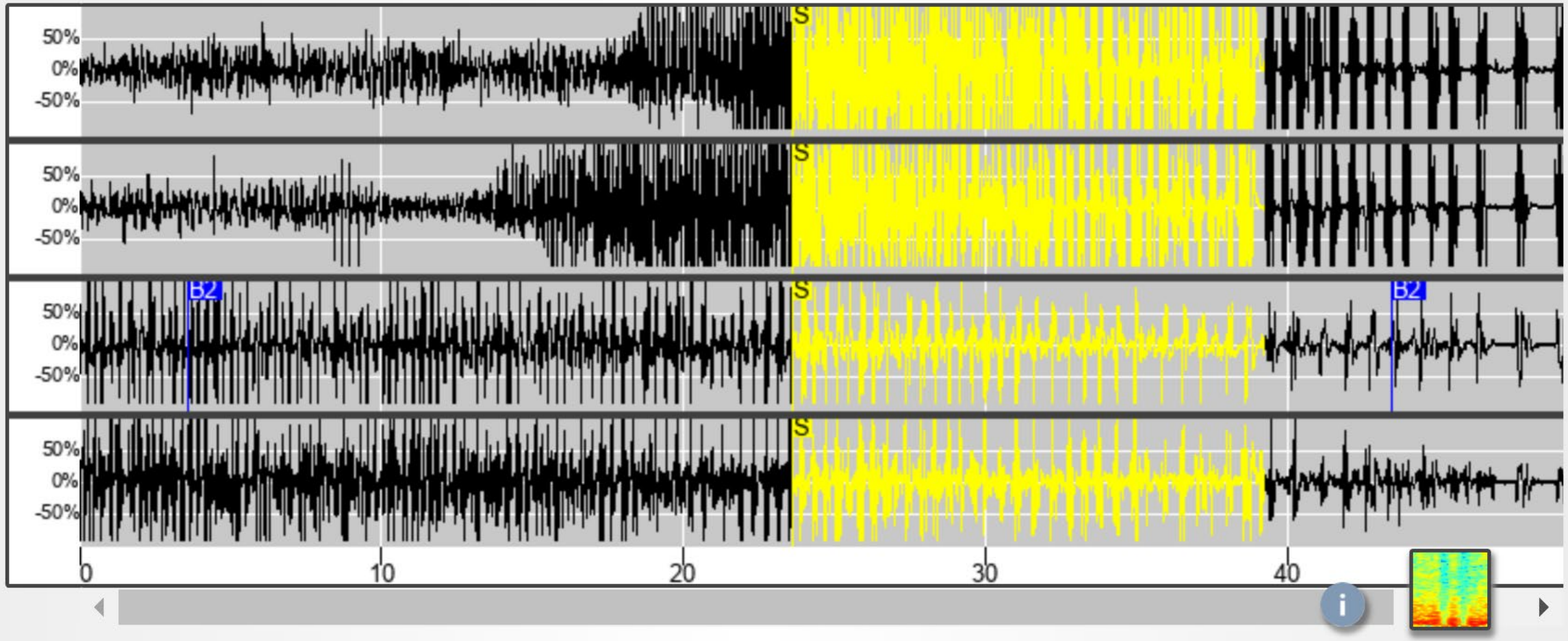
# Oct 26, 2008: First Seizure Recorded

## Saturation

Gain: 1x  Oct 26, 2008 00:57:50  Assign Category

Zoom: Entire ECOG

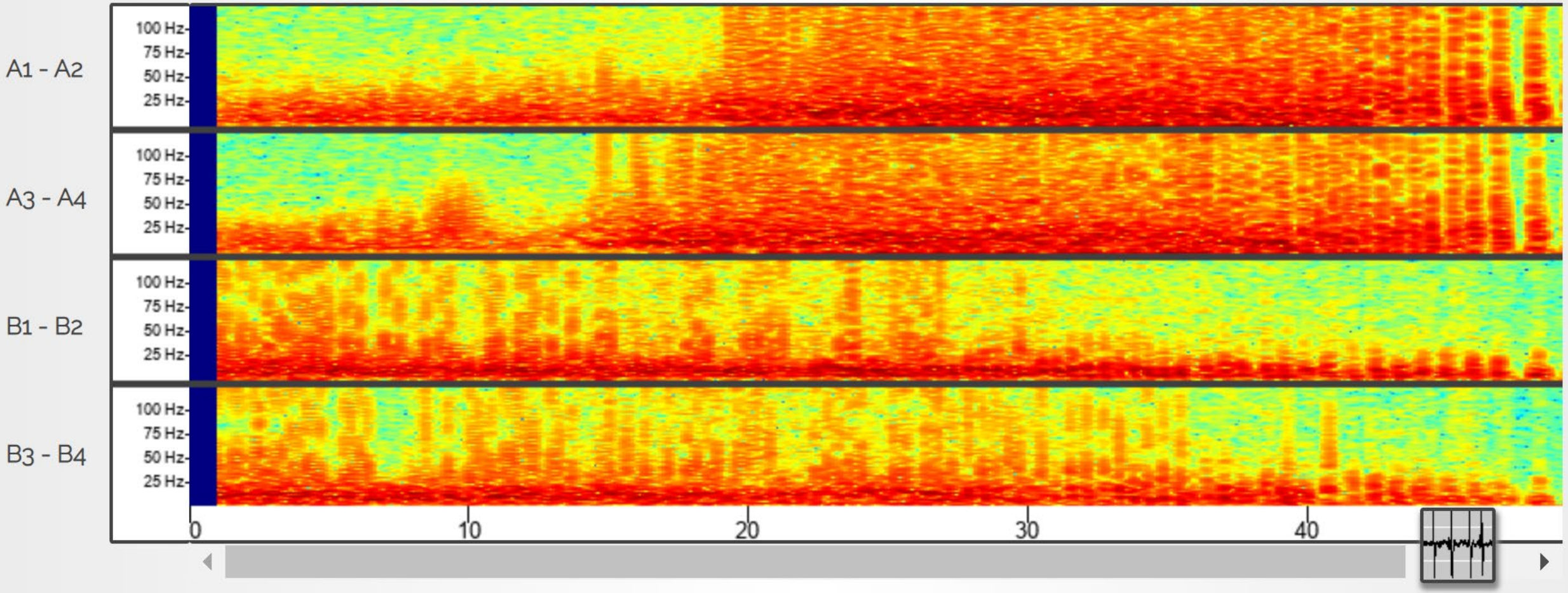


# Oct 26, 2008: First Seizure Recorded Spectrogram

## Saturation

Gain: 1X  Oct 26, 2008 00:57:50  Assign Category

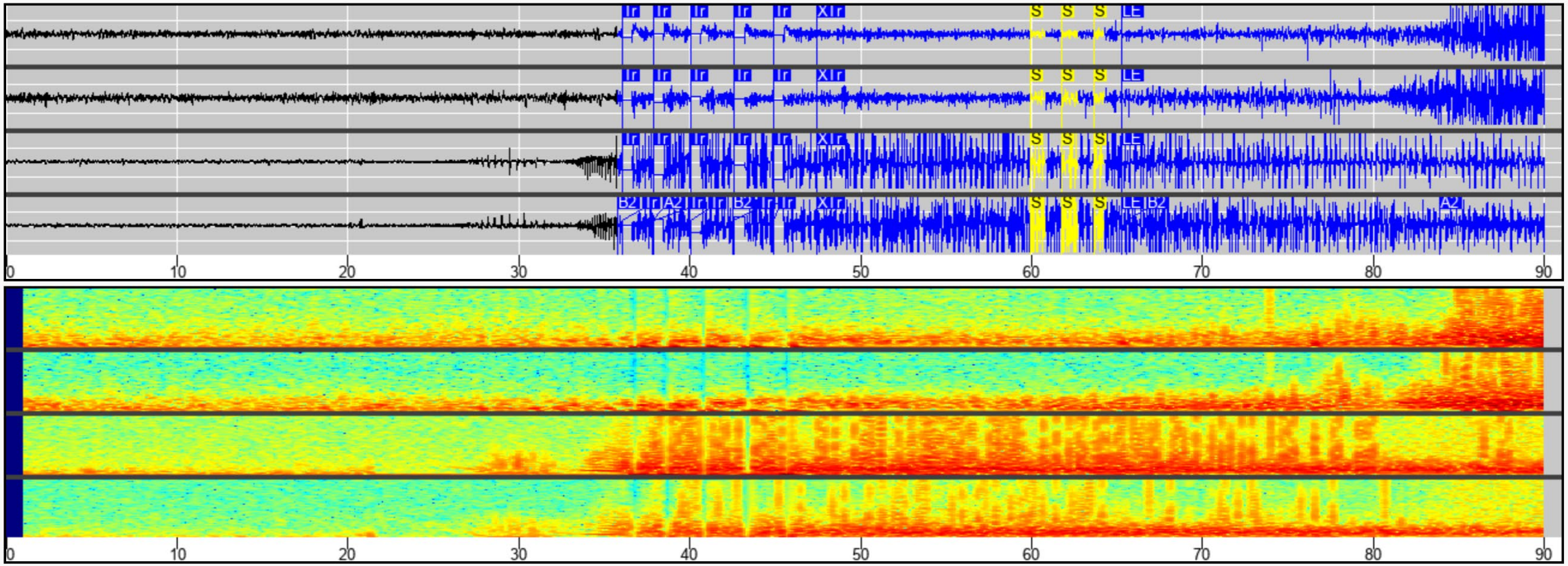
Zoom: Entire ECOG



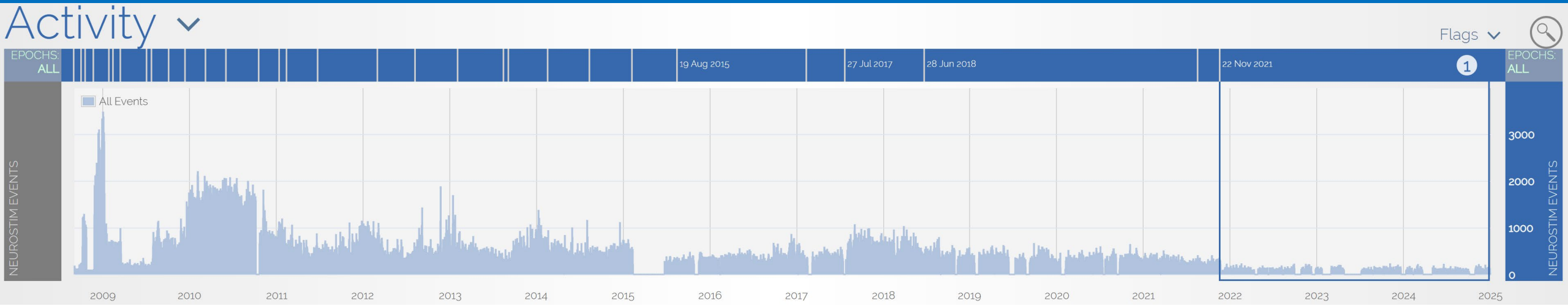
# May 28, 2012: Last Seizure Recorded

Saturation

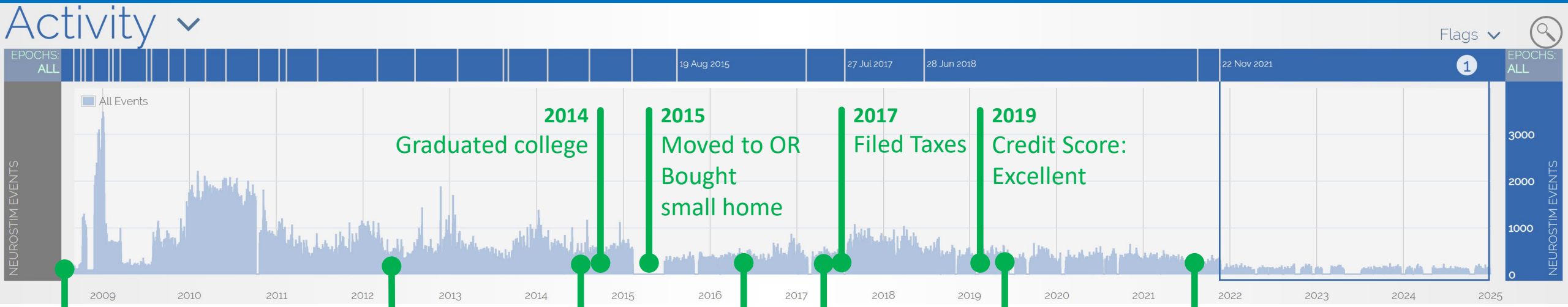
05/28/2012 05:56:39



# 2008 - 2025: All Events Recorded



# 2008 - Beyond: Health & Life Transformation Histogram




**2008**
Started Pivotal Study
Started college

**2012**
Last seizure

**2014**
Graduated college

**2014**
Last Mayo Clinic appointment

**2015**
Moved to OR
Bought small home

**2016**
Started work at NeuroPace

**2017**
Filed Taxes

**2017**
Stopped SSDI

**2019**
Credit Score: Excellent

**2019**
Driver's license reinstated

**My Future**
Investing & planning for retirement


DON'T
settle

# Questions?

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# Break

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# RNS System Clinical Trials and Applications for RNS Data

Martha Morrell, MD

NEUROPACE

# RNS System Clinical Discovery: Clinical Trials and AI

## Clinical Trials to Collect Data and Expand Indications

- **Five-year post-approval study** in adults with focal epilepsy for additional safety and effectiveness data
- Randomized controlled trial in **Idiopathic Generalized Epilepsy**
- Feasibility trial in **Lennox Gastaut Syndrome**
- Collaboration with FDA and NEST to use real-world data to support expansion to **Pediatric Focal Epilepsy**

## AI to Drive Continued Improvement in Effectiveness

- Find device-provided **objective neural biomarkers**
- Use device delivered biomarkers to **personalize detection and stimulation**
- Combine patient reports with biomarker data to **track clinical response**



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# Post-Approval Study

## Largest FDA required prospective post-approval study in neuromodulation for epilepsy

- Five-year post-approval multicenter study: 324 patients implanted at 32 centers
- Primary effectiveness endpoint at 3 years and primary safety at 5




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# Post-Approval Study: Patient Baseline Data

**PAS patients**

- 271 completed 3 years
- Median baseline seizure frequency was 5.7/month

**Seizure onsets similar to Piv/LTT trials**

- 67% had two seizure foci
- Lead locations
  - Mesial temporal only = 178
  - Neocortical only = 110
  - Mesial temporal plus neocortical = 36

**One third of patients did not have intracranial monitoring**

- 67% had prior intracranial monitoring
  - 65% in PIV/LTT trials[1]

**PAS patients more likely to receive RNS first**

- 19.4% had a prior epilepsy surgery
  - 34% in PIV/LTT trials[1]
- 7.7 % had prior treatment with VNS
  - 32% in PIV/LTT trials[1]

[1]Nair et al., Neurology 2020



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# Primary Efficacy Endpoint by Time from Implant

| Time after Implant | N | Median % Change in Seizure Frequency Compared to Baseline[1] (1st quartile, 3rd quartile) |
|---|---|---|
| Months 0-6 | 314 | -62.5% (-91.6%, -11.8%) |
| Months 6-12 | 292 | -62.3% (-93.3%, -14.6%) |
| Months 12-18 | 282 | -68.2% (-97.4%, -15.5%) |
| Months 18-24 | 273 | -69.4% (-98.4%, -19.4%) |
| Months 24-30 | 260 | -75.0% (-99.2%, -25.8%) |
| Months 30-36 | 255 | -82.0% (-100.0%, -29.2 %) |

- 42.5% of patients were seizure free for at least 6 months
- 22% of patients were seizure free for at least 1 year



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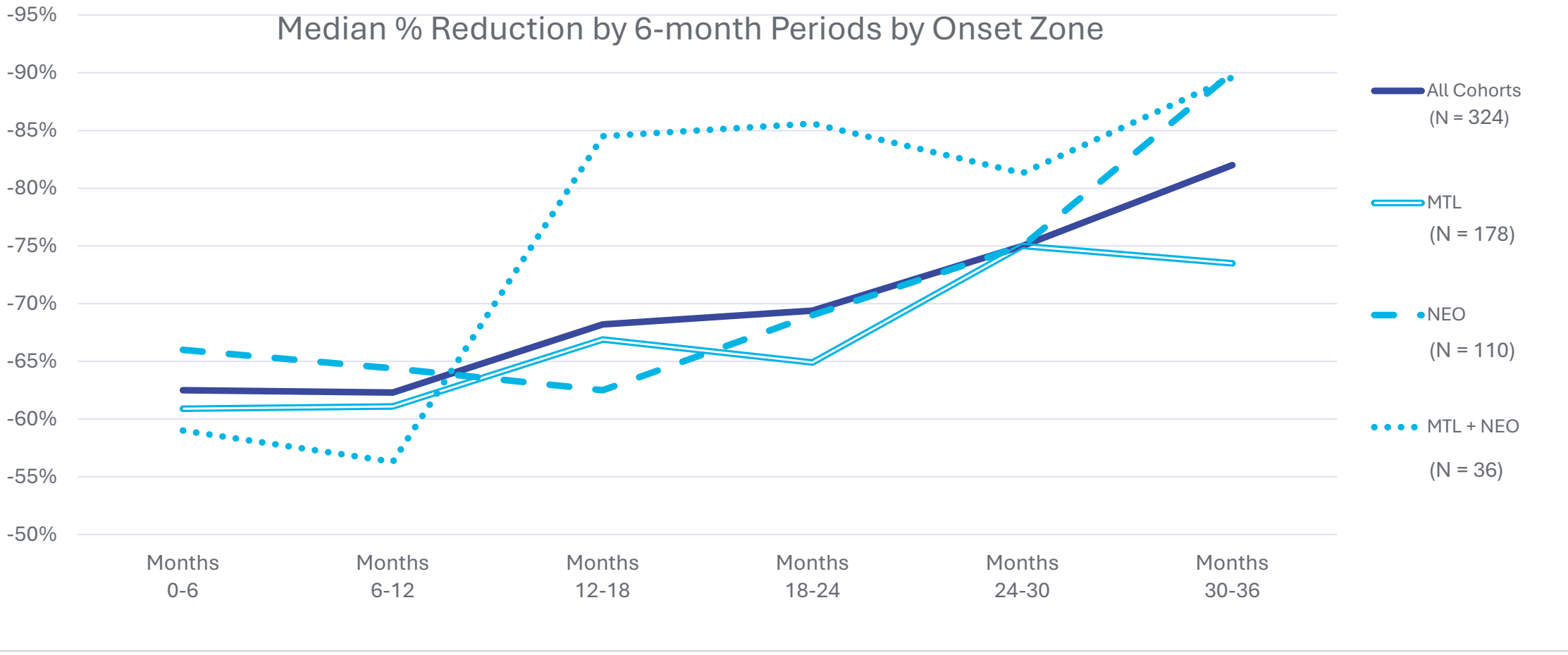
# Seizure Reductions Similar for All Seizure Onset Zones

## Improvement in seizure frequency for patients with mesial temporal, neocortical, and mesial temporal + neocortical onset seizures



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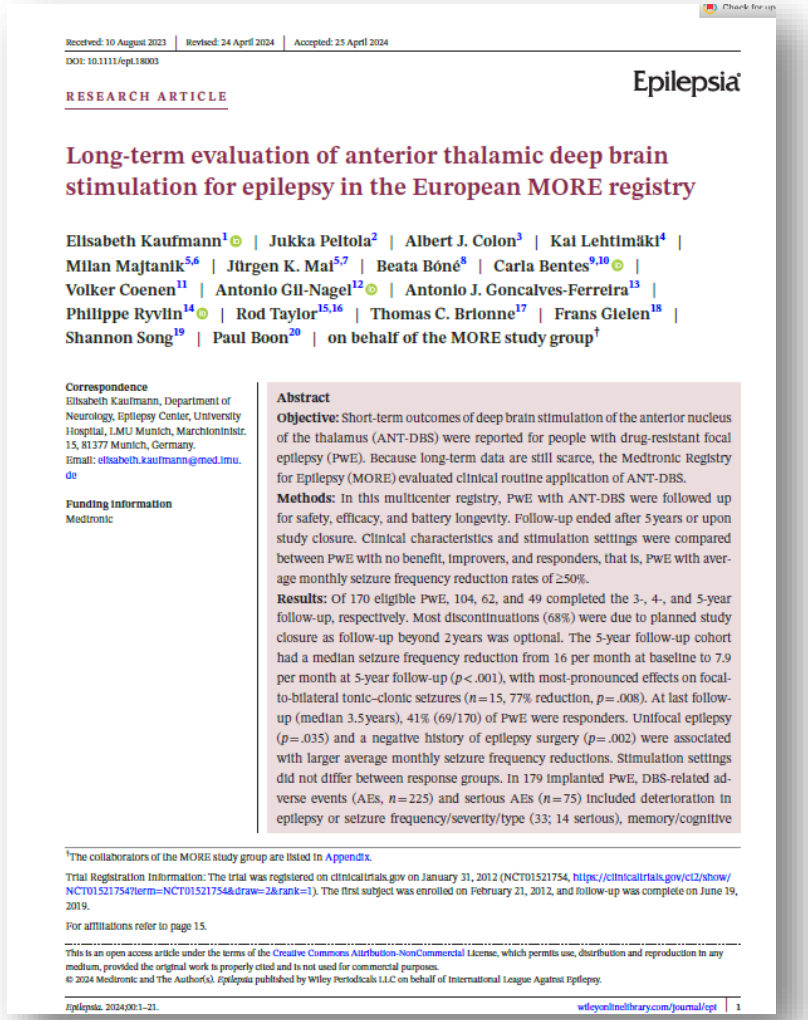
# Real World DBS Study

- Medtronic Registry for Epilepsy (MORE) of long term outcomes of DBS in clinical practice
  - Prospective and retrospective observational study



Received: 10 August 2023 | Revised: 24 April 2024 | Accepted: 25 April 2024
DOI: 10.1111/epi.18003

Epilepsia

RESEARCH ARTICLE

## Long-term evaluation of anterior thalamic deep brain stimulation for epilepsy in the European MORE registry

Elisabeth Kaufmann[1] | Jukka Peltola[2] | Albert J. Colon[3] | Kai Lehtimäki[4] | Milan Majtanik[5,6] | Jürgen K. Mai[5,7] | Beata Bóné[8] | Carla Bentes[9,10] | Volker Coenen[11] | Antonio Gil-Nagel[12] | Antonio J. Goncalves-Ferreira[13] | Philippe Ryvlin[14] | Rod Taylor[15,16] | Thomas C. Brionne[17] | Frans Gielen[18] | Shannon Song[19] | Paul Boon[20] | on behalf of the MORE study group†

**Correspondence**
Elisabeth Kaufmann, Department of Neurology, Epilepsy Center, University Hospital, LMU Munich, Marchioninistr. 15, 81377 Munich, Germany.
Email: elisabeth.kaufmann@med.lmu.de

**Funding information**
Medtronic

**Abstract**

**Objective:** Short-term outcomes of deep brain stimulation of the anterior nucleus of the thalamus (ANT-DBS) were reported for people with drug-resistant focal epilepsy (PwE). Because long-term data are still scarce, the Medtronic Registry for Epilepsy (MORE) evaluated clinical routine application of ANT-DBS.

**Methods:** In this multicenter registry, PwE with ANT-DBS were followed up for safety, efficacy, and battery longevity. Follow-up ended after 5 years or upon study closure. Clinical characteristics and stimulation settings were compared between PwE with no benefit, improvers, and responders, that is, PwE with average monthly seizure frequency reduction rates of ≥50%.

**Results:** Of 170 eligible PwE, 104, 62, and 49 completed the 3-, 4-, and 5-year follow-up, respectively. Most discontinuations (68%) were due to planned study closure as follow-up beyond 2 years was optional. The 5-year follow-up cohort had a median seizure frequency reduction from 16 per month at baseline to 7.9 per month at 5-year follow-up ($p < .001$), with most-pronounced effects on focal-to-bilateral tonic–clonic seizures ($n = 15$, 77% reduction, $p = .008$). At last follow-up (median 3.5 years), 41% (69/170) of PwE were responders. Unifocal epilepsy ($p = .035$) and a negative history of epilepsy surgery ($p = .002$) were associated with larger average monthly seizure frequency reductions. Stimulation settings did not differ between response groups. In 179 implanted PwE, DBS-related adverse events (AEs, $n = 225$) and serious AEs ($n = 75$) included deterioration in epilepsy or seizure frequency/severity/type (33; 14 serious), memory/cognitive

†The collaborators of the MORE study group are listed in Appendix.

Trial Registration Information: The trial was registered on clinicaltrials.gov on January 31, 2012 (NCT01521754, https://clinicaltrials.gov/ct2/show/NCT01521754?term=NCT01521754&draw=2&rank=1). The first subject was enrolled on February 21, 2012, and follow-up was complete on June 19, 2019.

For affiliations refer to page 15.

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Link: https://onlinelibrary.wiley.com/doi/10.1111/epi.18003



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# Impressive Seizure Reductions with RNS System

| | RNS System PAS[1] | DBS MORE Registry[2] |
|---|---|---|
| Median Seizure Reduction at Year 1 | 62.3% (N=292) | 25.3% (N=163) |
| Median Seizure Reduction at Year 2 | 69.4% (N=273) | 33.1% (N=155) |
| Median Seizure Reduction at Year 3 | 82.0% (N=255) | 39.6% (N=101) |

[1]RNS System Post-Approval Study. Results to be presented at American Academy of Neurology April 5-9, 2025. Prospective open label observational study; results provided and accepted by FDA October 2024. Analysis using last observation carried forward.

[2]Kaufmann, et al., Epilepsia, 2024. MORE Registry: open-label, prospective and retrospective observational study. Analysis without imputation for missing data.



NEUROPACE

# RNS Post-Approval Study: Effectiveness Conclusions Based on 3-Year Results

## RNS System therapy is observed to be effective for all types of focal epilepsy

- Efficacy improves over time
- Seizure reduction in upper quartile
  - Exceeds 90% within 6 months of implant
  - 100% at 3 years

## Results better than Pivotal Study because we learn from the data

- Patterns that should be detected
- Lead locations and stimulation targets
- Initial stimulation strategies
- Fine-tuning therapy based on clinical response and biomarkers

# RNS System Treatment of Drug-Resistant Focal Epilepsy in Children



NEUROPACE

# Response Study: Prospective Open-Label Study in Pediatric Patients with Focal Epilepsy

- NeuroPace is committed to expanding use of the RNS System to pediatric patients with drug-resistant focal epilepsy
- Response Study: FDA required prospective open label trial
  - NeuroPace faced typical challenges in enrollment in a pediatric trial of a therapy widely available to adults

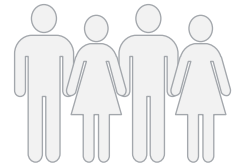
**New Strategy**: pursue use of existing real-world data

to support expanded indication for use in children with drug-resistant focal epilepsy



NEUROPACE

# A New Approach: Use Real World Data to Expand RNS System Treatment to Pediatrics



FDA U.S. FOOD & DRUG ADMINISTRATION

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NEST
NATIONAL EVALUATION SYSTEM FOR HEALTH TECHNOLOGY

**Consortia:**

RNS System data from 27 Pediatric Epilepsy Centers

PEDIATRIC EPILEPSY RESEARCH CONSORTIUM

> 25 peer reviewed publications about RNS System use in pediatrics

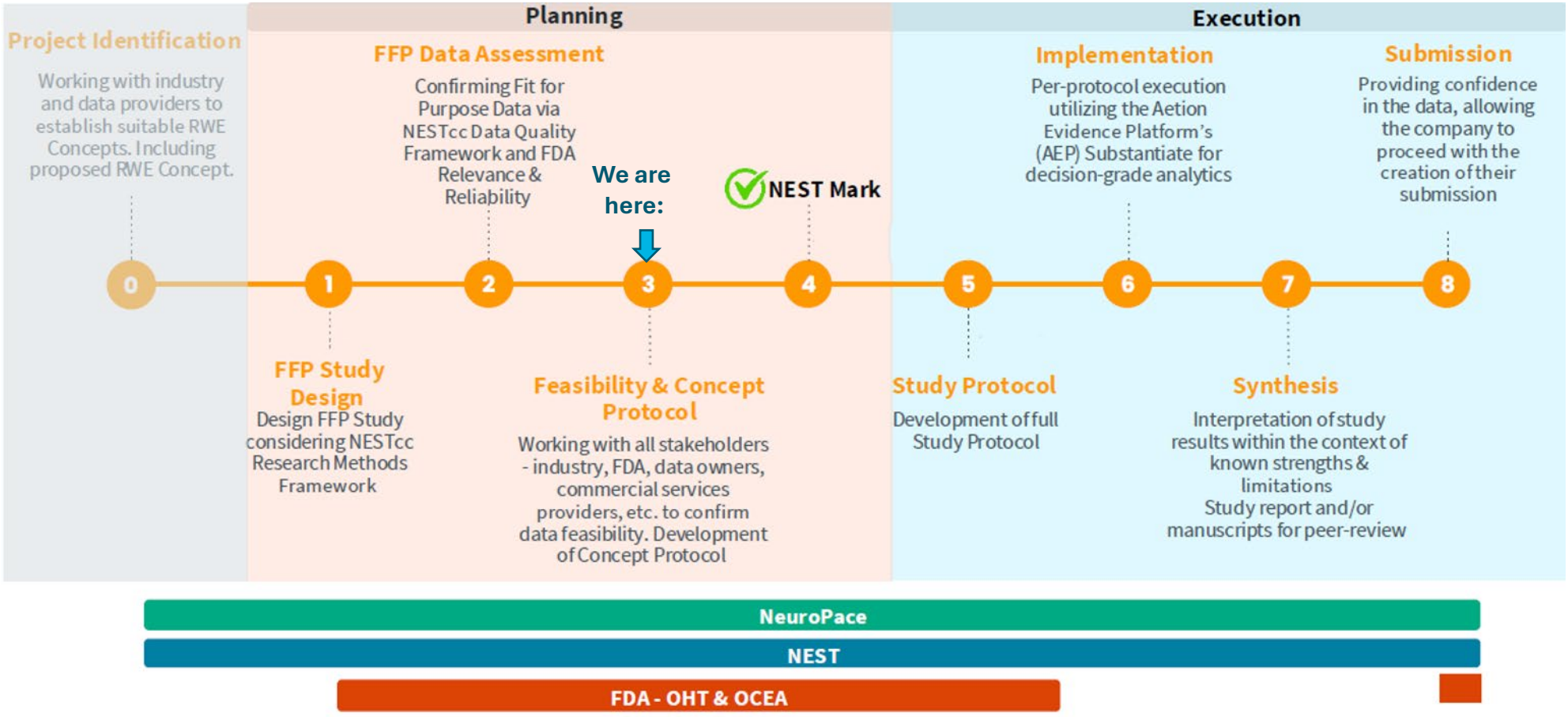
PubMed®

**Advocacy Group Support**

- AES Pediatric Special Interest Group
- Lennox-Gastaut Foundation
- Epilepsy Foundation

# Pursuing a Pediatric Indication Using Real World Data: Collaboration with NEST and FDA

*Submission planned 2H 2025*



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# Idiopathic Generalized Epilepsy

- Majority of patients are cognitively and neurologically normal
- Generalized tonic-clonic, absence, and/or myoclonic seizures
- Confident diagnosis by clinical history and outpatient EEG
  - Intracranial EEG is not necessary
- Serious life consequences:
  - Challenges to cognition, emotional health, social functioning, and educational and occupational achievement
  - High risk for injury and SUDEP
    - North American SUDEP registry: Median onset of IGE = 13 years and median age at SUDEP = 26 years (IQR 20–34 years)[1]

**RNS System treated patient**

[1] Verducci et al., Neurology 2019



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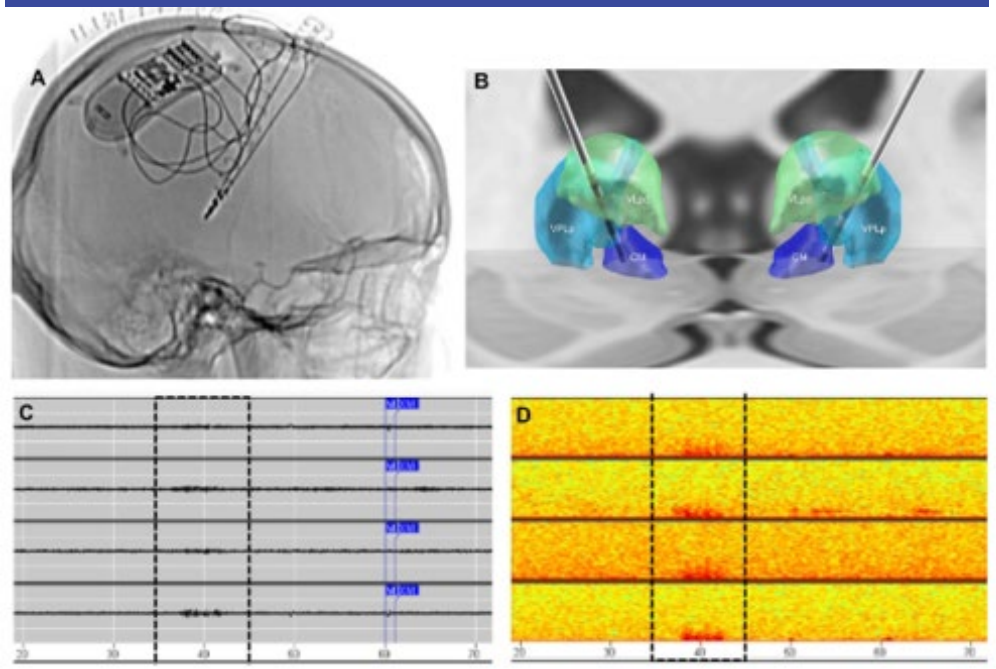
# RNS® System Responsive Thalamic Stimulation for Primary Generalized Seizures (NAUTILUS) Study

Adjunctive therapy for the treatment of generalized seizures in individuals 12 years of age or older who have drug-resistant idiopathic generalized epilepsy

Prospective, multicenter, single-blind, randomized, sham stimulation controlled pivotal study

100 participants enrolled; 87 implanted across 23 centers

**Bilateral centromedian nucleus of thalamus (CM) responsive stimulation**



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# NAUTILUS Study Timeline

2021: FDA Grants Breakthrough Designation

First Site Initiation Aug 2022

First Enrollment Aug 2022

Last Enrollment Dec 2023

Final Implant Mar 2024

Primary endpoint safety and effectiveness evaluations to be performed following completion of follow-up visits in March 2025

- Data monitoring and lock
- Submission planning with regulatory and statisticians
- Dry and final run analyses on mock data
- Data inspections, modification with sites as necessary
- FDA submission writing
- FDA Sprint Meetings (2)
- Data Readout

FDA Submission (2H 2025)

Final patient completes 2 years (1H 2026)

Note: Hardware and software releases, clinical trial submissions, and clinical approval launches are anticipated during the time periods shown above.



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# Thalamocortical Responsive Neurostimulation for the Treatment of Lennox Gastaut Syndrome (LGS)

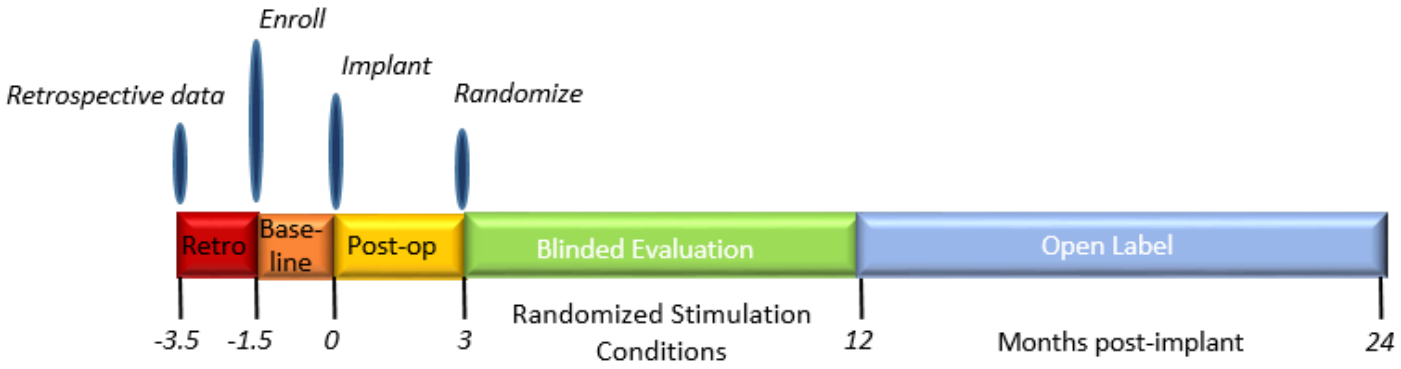
- Devastating generalized epilepsy with frequent seizures and progressive cognitive decline
- Medically intractable, surgery not effective
- NIH Brain Initiative Grant[1]

Clinical Goal: provide preliminary evidence for safety & efficacy of RNS® System treatment of LGS[2]

1 NIH UH3NS109557-01
2 Clinicaltrials.gov NCT05339126

# Treatment of Generalized Seizures in LGS: Responsive stimulation of bilateral thalamocortical networks

- Prospective two-stage single-blind feasibility cross-over IDE study
- All 20 patients implanted
  - Acceptable safety profile to date
- Grant funds
  - AI biomarker discovery
  - Computational methods to aid in lead implant targeting
- Grant completed May 2026



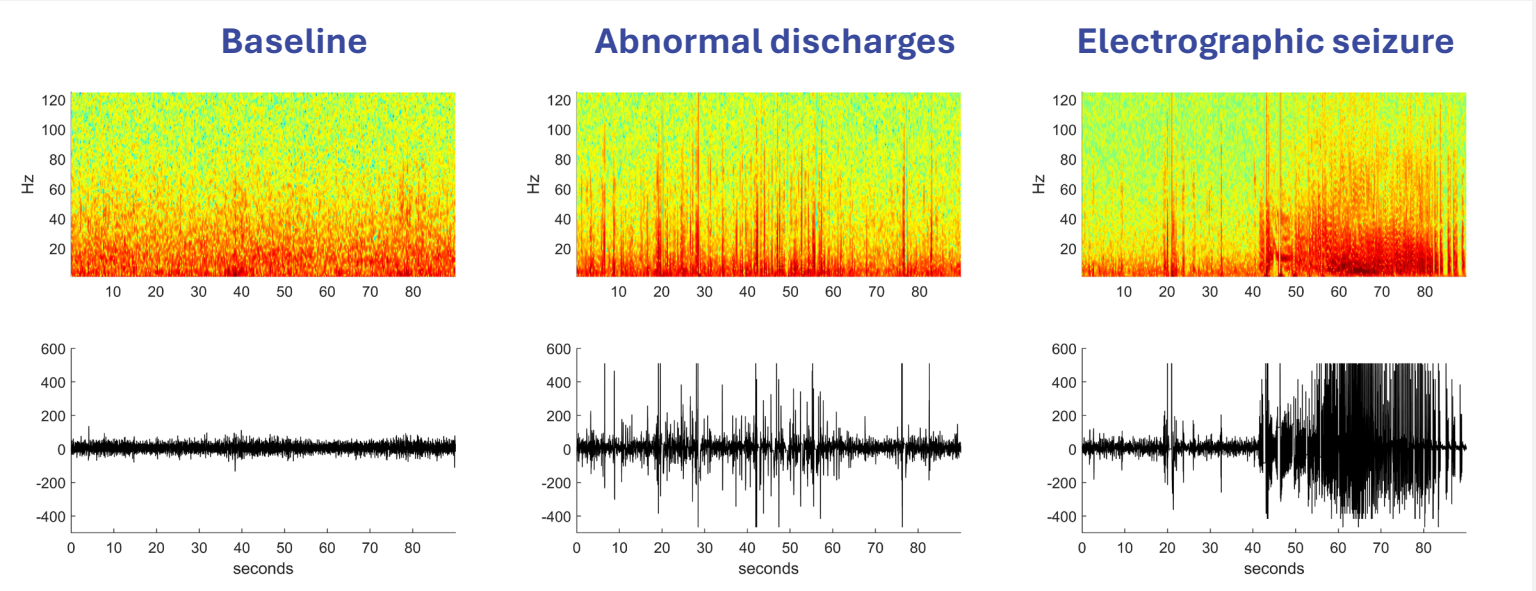

Note: Hardware and software releases, clinical trial submissions, and clinical approval launches are anticipated during the time periods shown above.



NEUROPACE

# An Unprecedented Dataset of Chronic Ambulatory iEEG

- Chronic ambulatory iEEG data in > 6500 patients
- > 19M stored intracranial EEG samples
- Baseline, interictal and ictal samples




**NeuroPace-developed AI algorithms identify activity that is correlated with patient reported seizures**

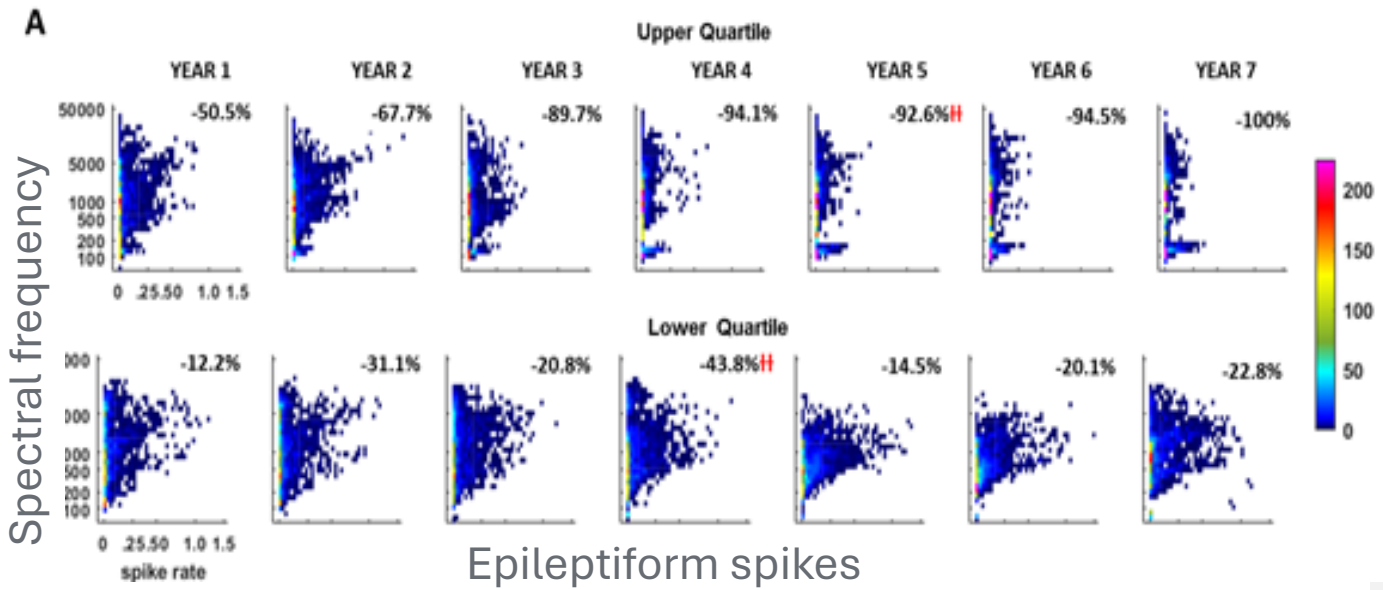


NEUROPACE

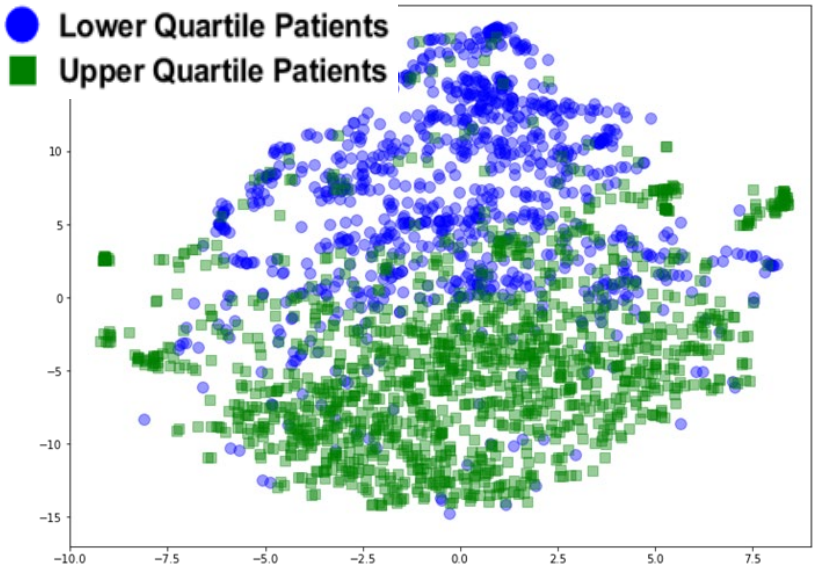
# AI-Fueled Discovery: Guide RNS System Treatment Using Biomarkers

## Machine learning shows biomarker trends in in the best responders

Epileptiform spikes go down in MTLE best responders




## Deep Learning finds features that distinguish the best responders




Desai et al., Clin Neurophys 2019



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# Using RNS System Data to Assess Effects of Anti-Seizure Medications

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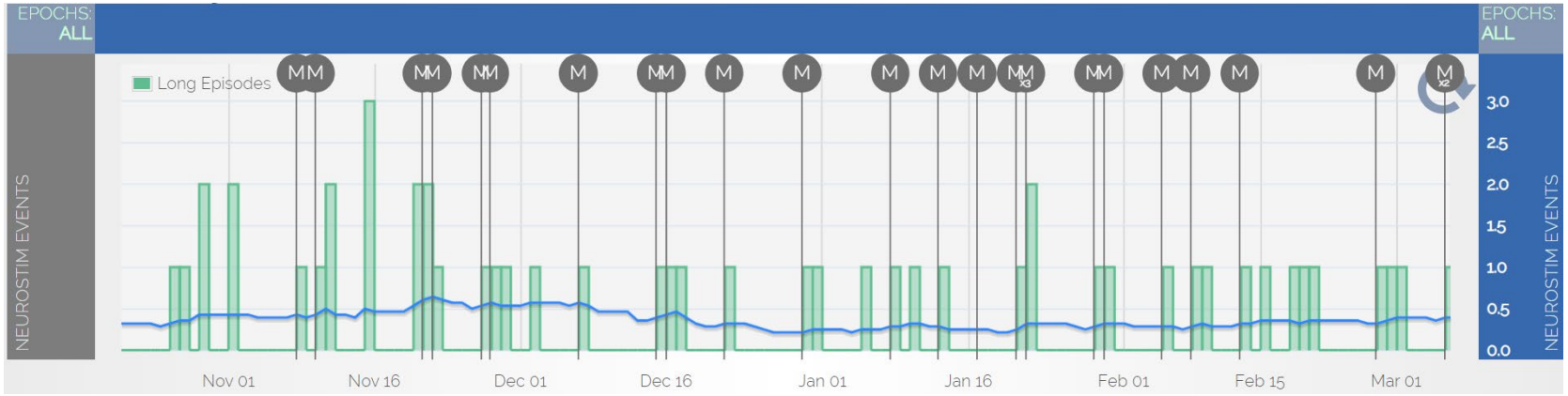
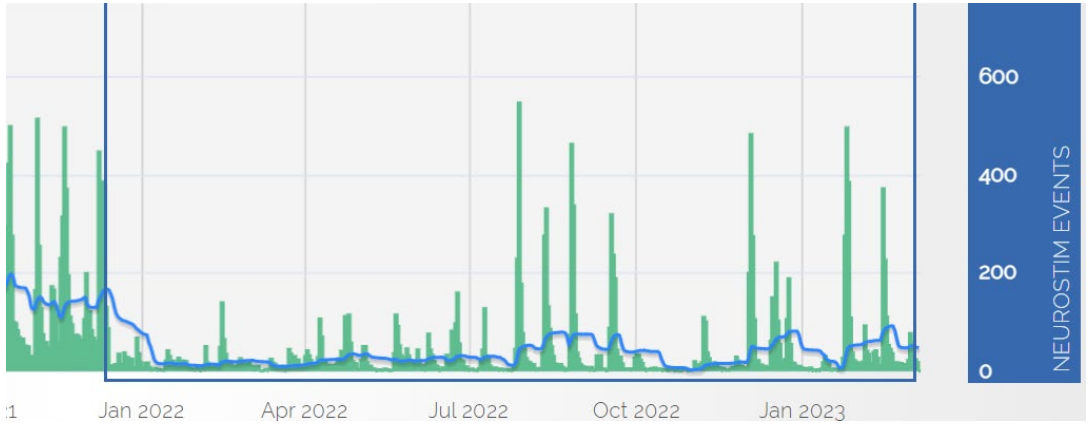
# Gold Standard for Seizure Counts Are Patient Reports

**One patient knows she has seizures (M= magnet swipe)…**




**And one patient does not.**



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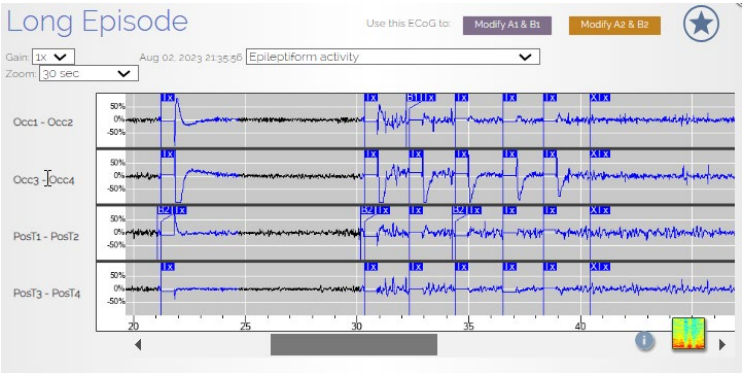
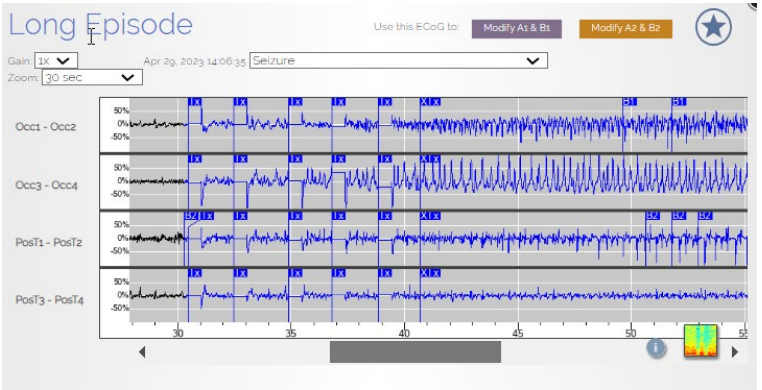
# Moving Beyond the Seizure Diary:

## Patient reported seizures correlate with RNS System detected events

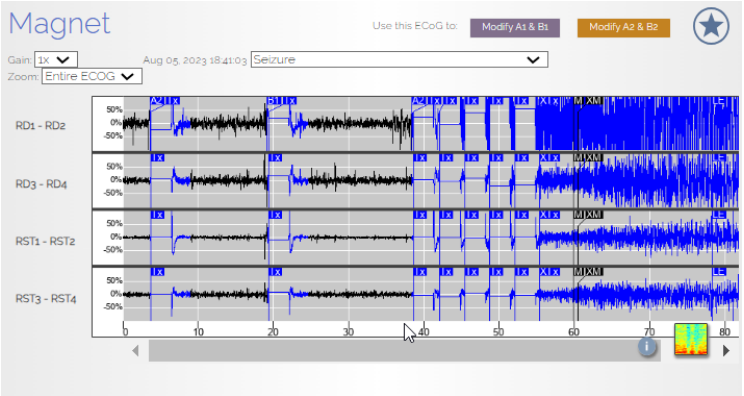
**LE= Prolonged epileptiform activity**




**Electrographic seizure not identified by patient as seizure**




**Electrographic seizure identified by patient as seizure**




**LEs are more frequent, but are strongly correlated with patient-reported seizures (r=-.38; p= 0.00008)**

Quigg et al. Epilepsy Research, 2020



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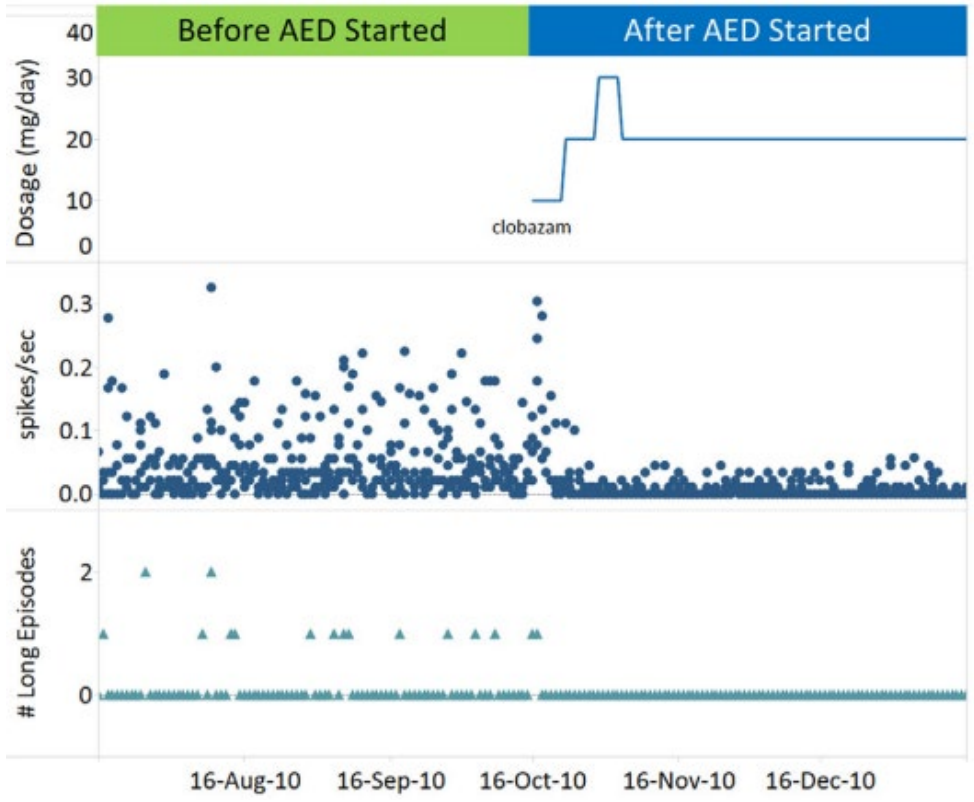
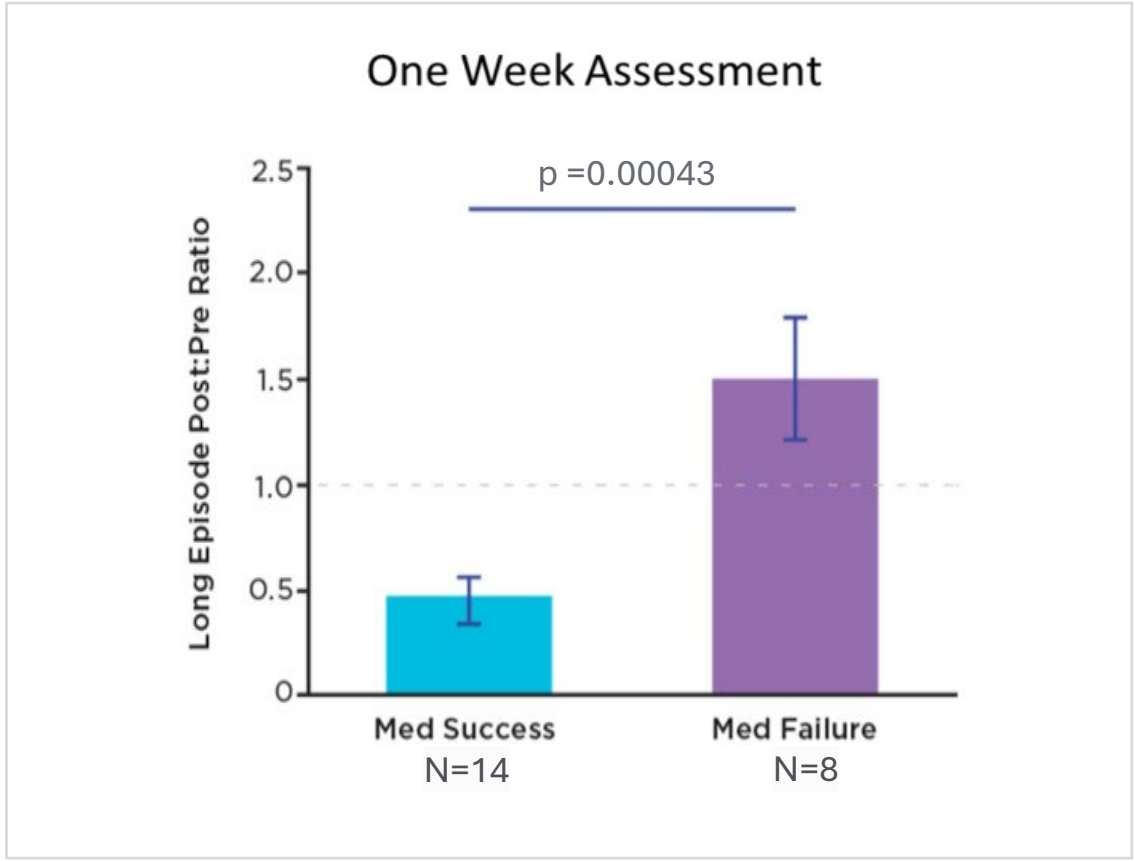
# RNS System Data May Provide Biomarker for Early Effects of Antiseizure Medications (ASMs) within 1-2 Weeks




Skarpaas et al., Epilepsy & Behavior, 2018
Quraishi IH, et al., Epilepsia, 2020



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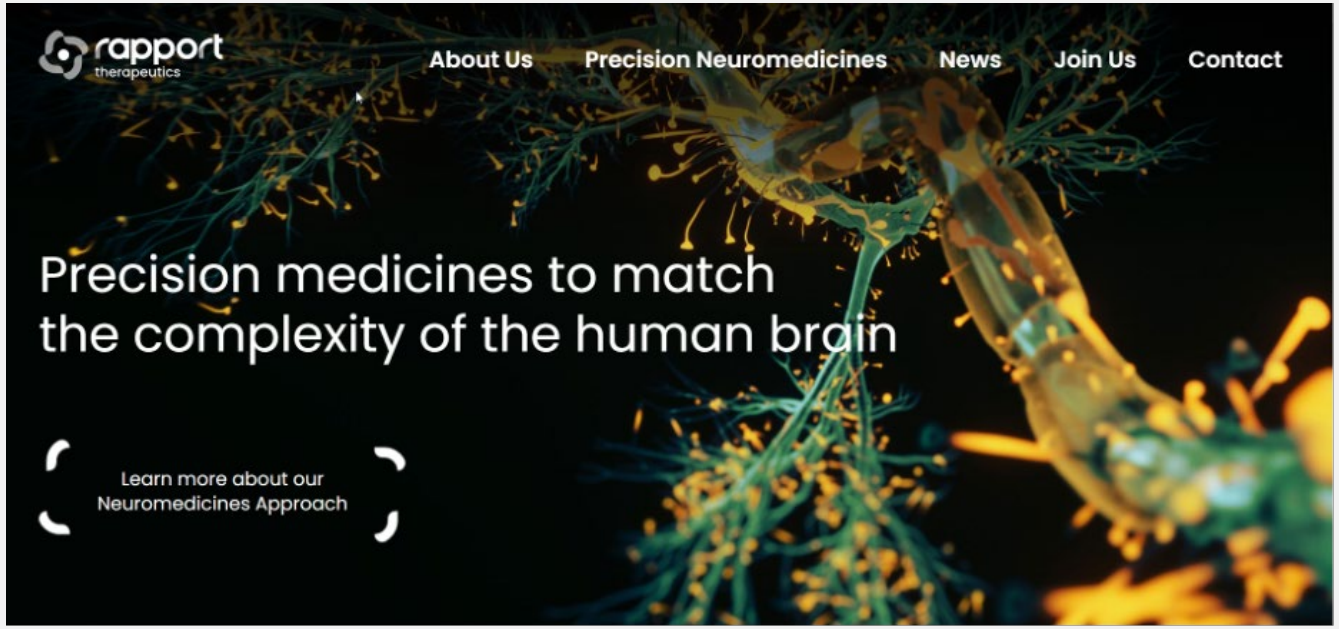
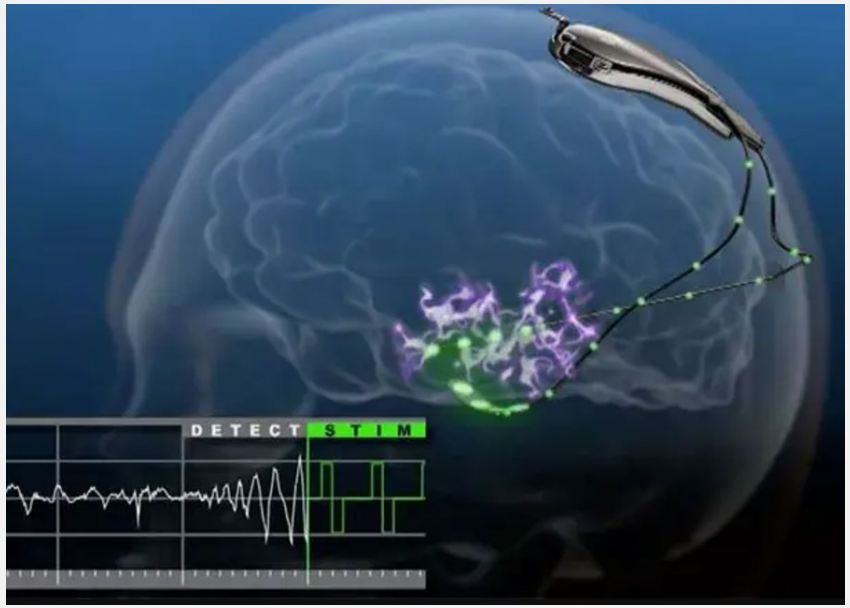
# Rapport and NeuroPace Collaboration: Demonstrating Meaningful Target Engagement

Rapport is conducting a first in epilepsy trial of a novel, neuroanatomically specific, negative allosteric modulator of AMPA receptors for focal epilepsy




Long episodes, an objective, electrophysiological biomarker in patients treated with the NeuroPace RNS System, are the endpoint of the study



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# Potential Future Applications

Martha Morrell, MD
Sameer Sheth, MD, PhD

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# RNS Platform Technology Provides Opportunities Beyond Epilepsy

- FDA approved treatment with **extensive clinical efficacy and safety data** set for focal onset seizures
- **Long-term monitoring of brain electrical activity** in persons with any brain disorder
- **Targeted and personalized** therapy
- **Biomarker** discovery and tracking
- Ability to **treat before clinical symptoms**; intervention to restore normalcy



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# Investigator-Initiated Externally Funded Studies Outside of Epilepsy:

## Neuropsychiatric Disorders

RNS for ***Depression***: Mt. Sinai NY

RNS for ***Depression***: UCSF Medical Center

RNS for ***Loss of Control Eating***: Hospital of the University of Pennsylvania

RNS for ***PTSD***: UCLA Medical Center

RNS for ***PTSD***: Stanford Hospital and Clinics

RNS for ***PTSD***: Hospital of the University of Pennsylvania

# Investigator-Initiated Externally Funded Studies Outside of Epilepsy:

## Memory and Cognition

RNS for ***Spatial Navigation***: UCLA Medical Center

RNS for ***Navigation & Free Recall*** : Dartmouth

RNS for ***Navigation and Memory*** Boston Medical Center

RNS for **Cognitive Assessment** : UC Berkeley

RNS and **Brain Plasticity** to Improve Cognitive Function: UCSF Medical Center

RNS for ***Conscious Perception*** Thalamic Stim: Yale New Haven Hospital

RNS for ***Hippocampal memory encoding*** : Yale New Haven Hospital

RNS for ***Autism***: Mt. Sinai NY

# Opportunities for Responsive Neurostimulation

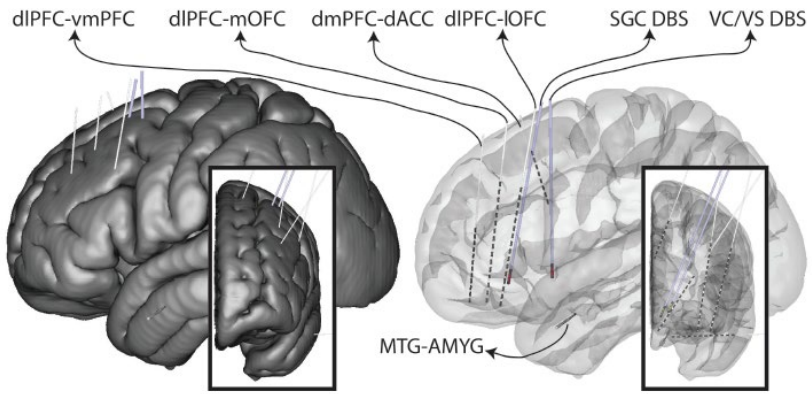
## Disorders with slowly evolving pathophysiology

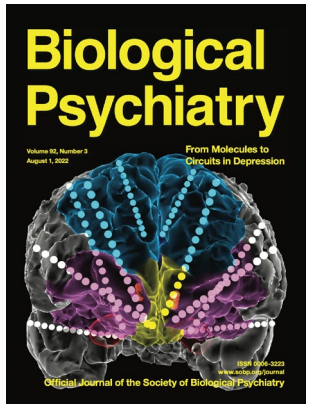
- Derisking has begun
- Philosophy: stimulation adjusts to (slowly evolving) neural biomarkers
- Individualization of neural biomarkers (as in epilepsy) may be critical
- Examples:
  - Depression
  - Memory disorders
  - OCD and anxiety disorders

# Depression

## Neural biomarkers of mood state

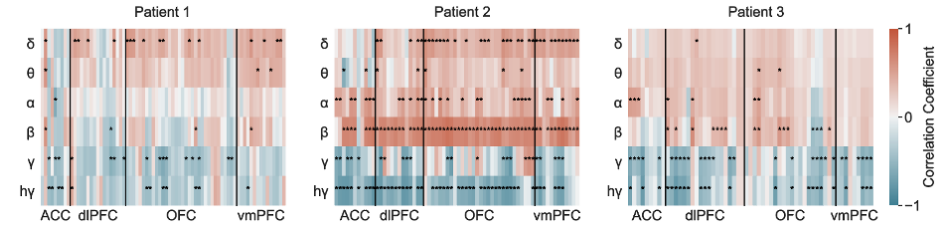
- NIH BRAIN Initiative grant (UH3 NS103549)



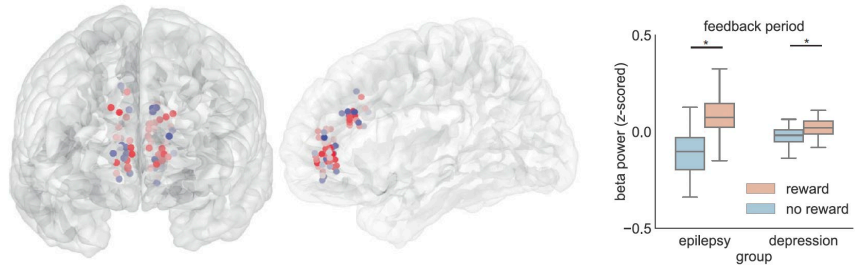

- Necessary information is at the macro (clinical) electrode scale
- Neural biomarkers have some general features (feasibility) and some specific features (individualization)
- Behavioral biomarkers are an exciting and rich source of state information
- Next step: trial testing the hypothesis that adjusting stimulation output based on continuously measured neural/behavioral biomarkers will maintain healthy state
    - Also enable remote monitoring of mood state by clinician

**Decoding Depression Severity From Intracranial Neural Activity**



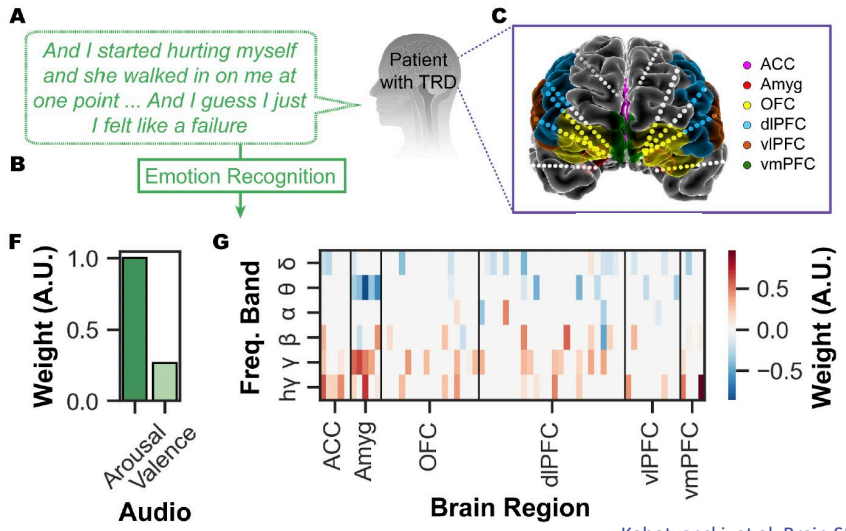

Xiao et al. Biol Psych 2023

**Beta activity in human anterior cingulate cortex mediates reward biases**




Xiao et al. Nat Comm 2024

**Towards objective, temporally resolved neurobehavioral predictors of emotional state**




Kabotyanski et al. Brain Stim 2024

# Summary Thoughts

## Opportunities for Responsive Neurostimulation beyond epilepsy

- Continuous monitoring of neural biomarkers of target state
  - Mood, memory, etc.
- Adjustment of stimulation output in response to evolving neural biomarkers
  - Paroxysmal or slowly evolving
- Remote monitoring by clinical team
  - Objective measures are notably lacking for many neuropsychiatric disorders
  - Beyond subjective symptom-based therapy to objective biomarker-based therapy
- Patient engagement
  - Empower patients to be informed about their health

# Product Development

Dylan St. John
Brett Wingeier, PhD

NEUROPACE

# Key Opportunities

**Therapy Effectiveness**

**Clinic Efficiency**


**Patient & Clinician Ease of Use**



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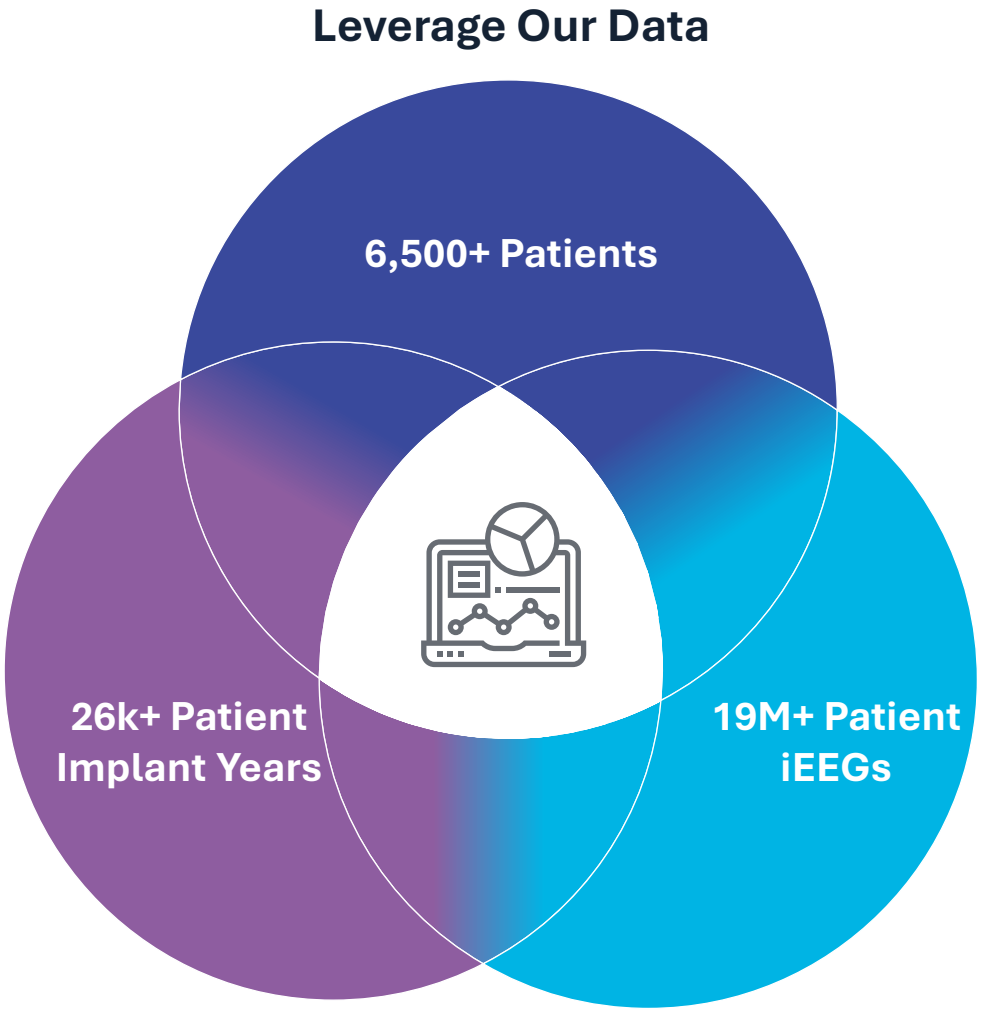
# Product Development Focus Areas



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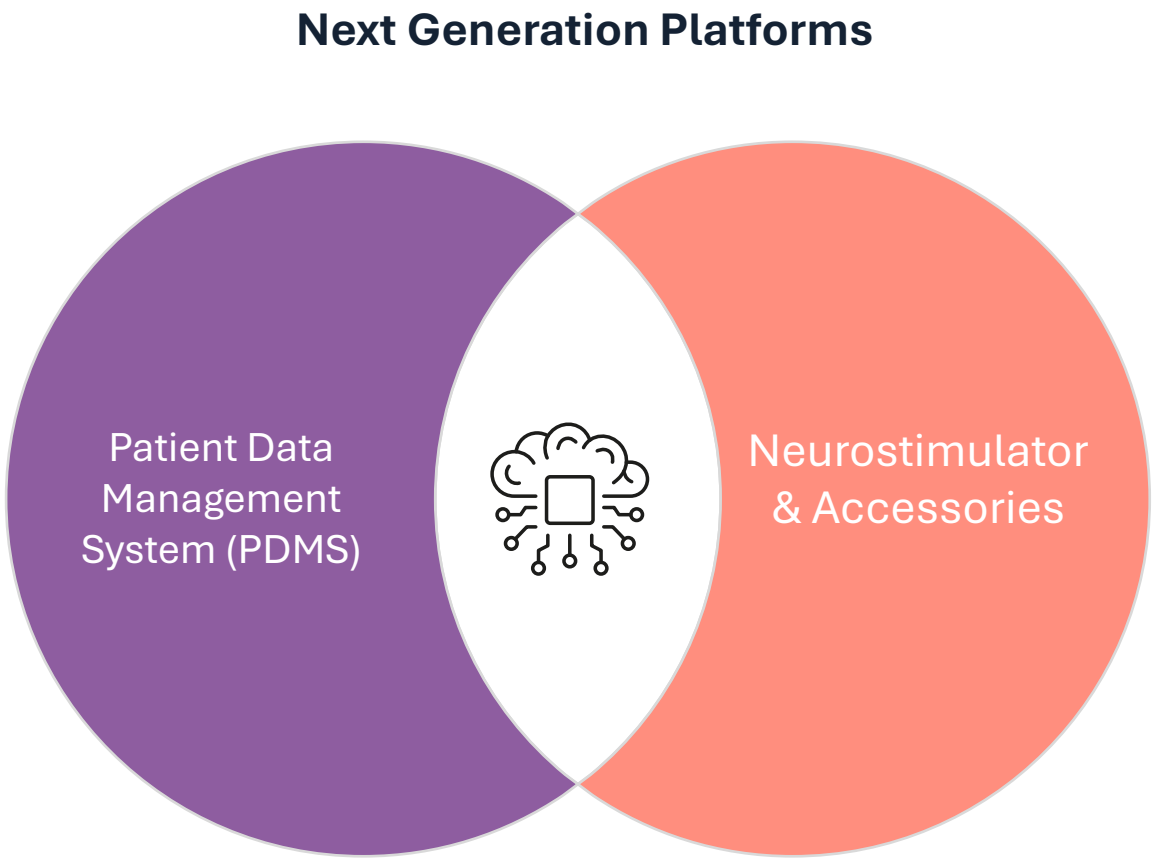
# Product Development Focus Areas




Next generation platforms and features are anticipated and not yet approved.



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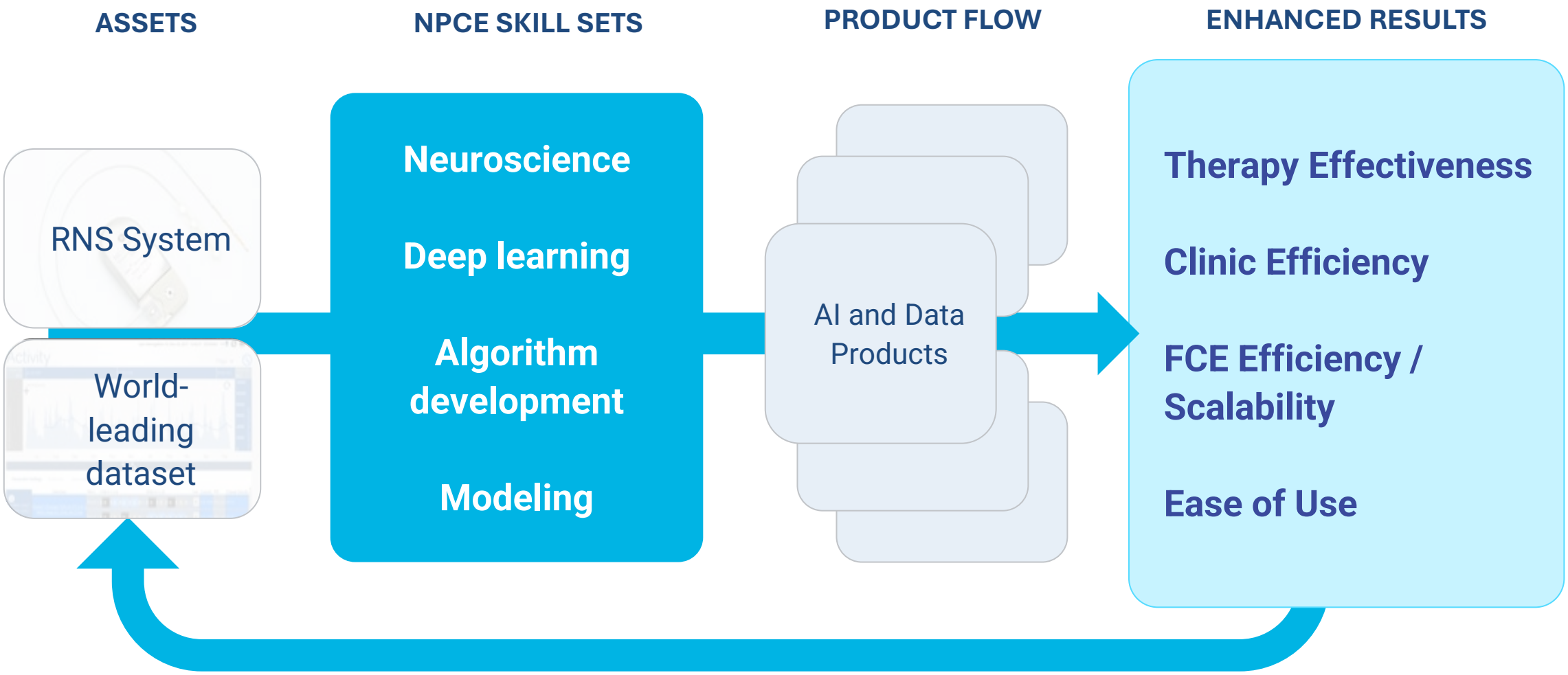
# Data Enable Continuously Improving Results




Renderings; features not available in the approved RNS System. Next generation platforms and features are anticipated and not yet approved.



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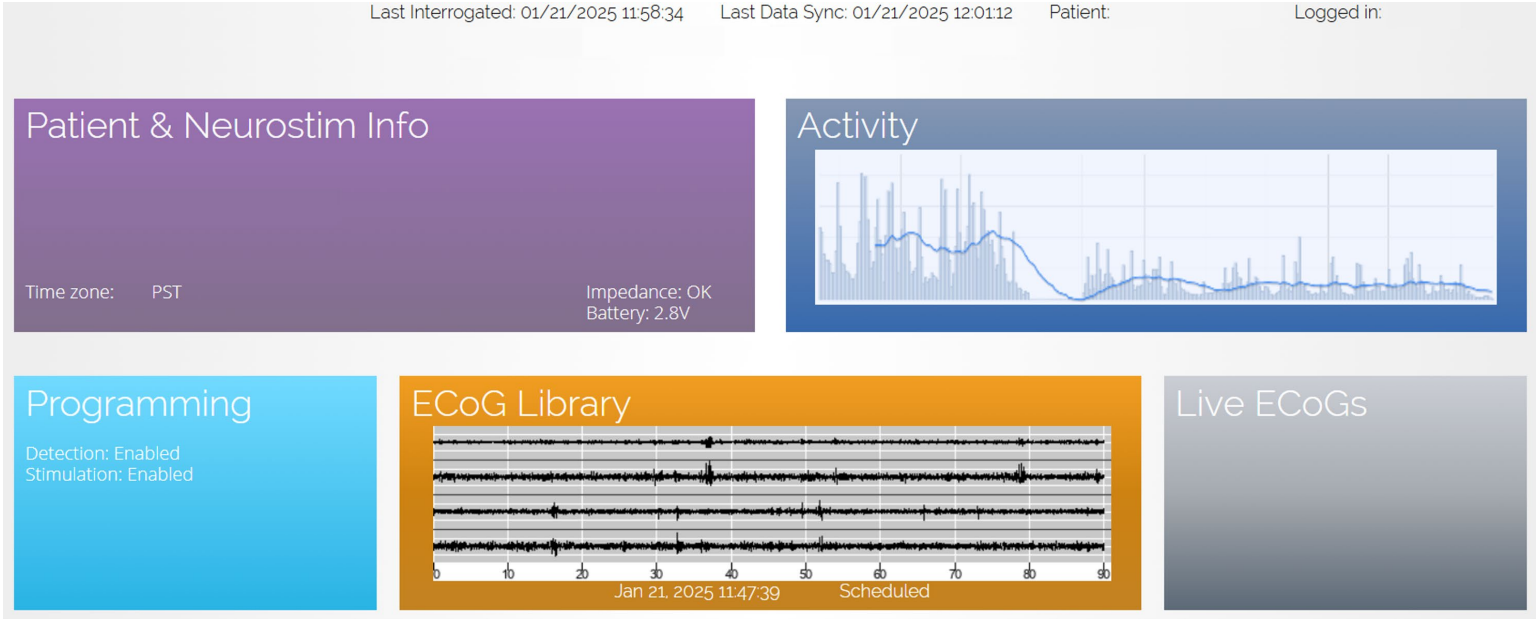
# NeuroPace Patient Data Management System (PDMS)

**Supports review of data and settings**

**19M+ iEEG recordings, 19B+ event records**

**Foundation of NeuroPace research programs**



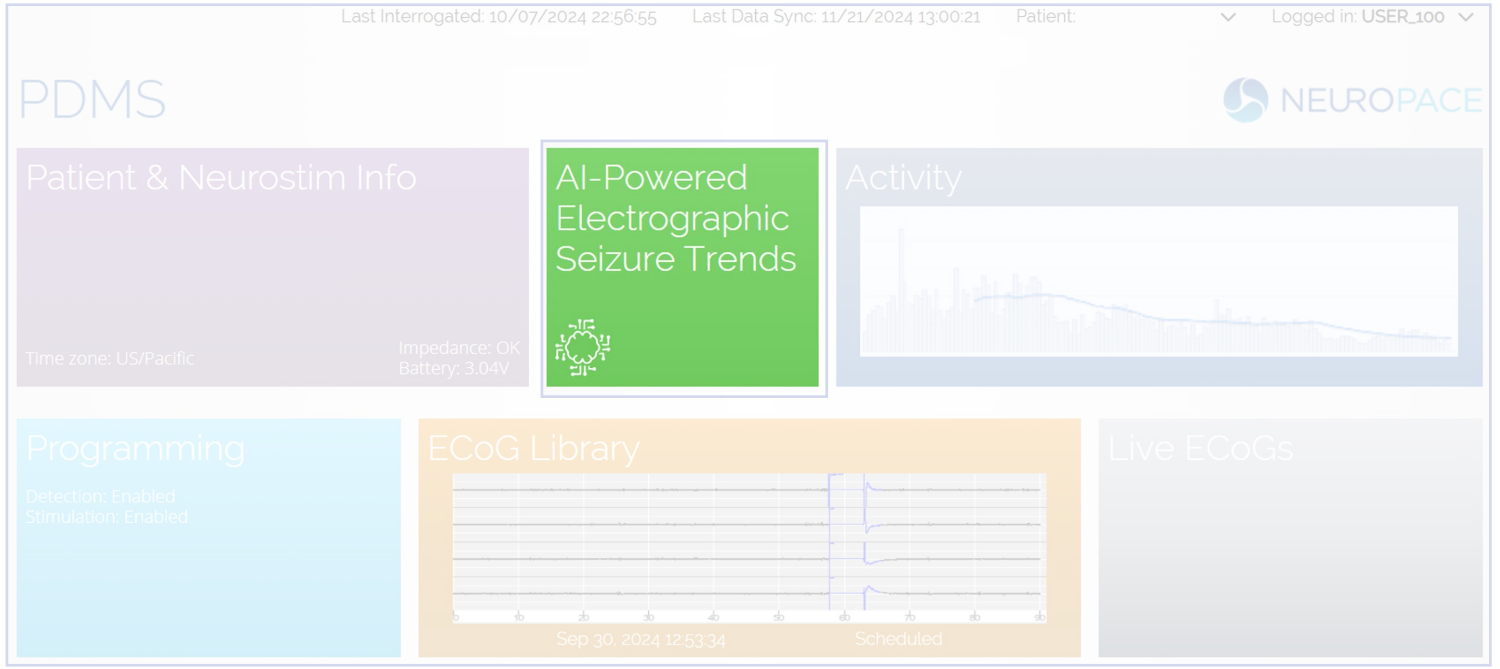



NEUROPACE

# Next-generation PDMS Architecture

**Scalable for growth**

**Platform enables cadence of data products and usability improvements**



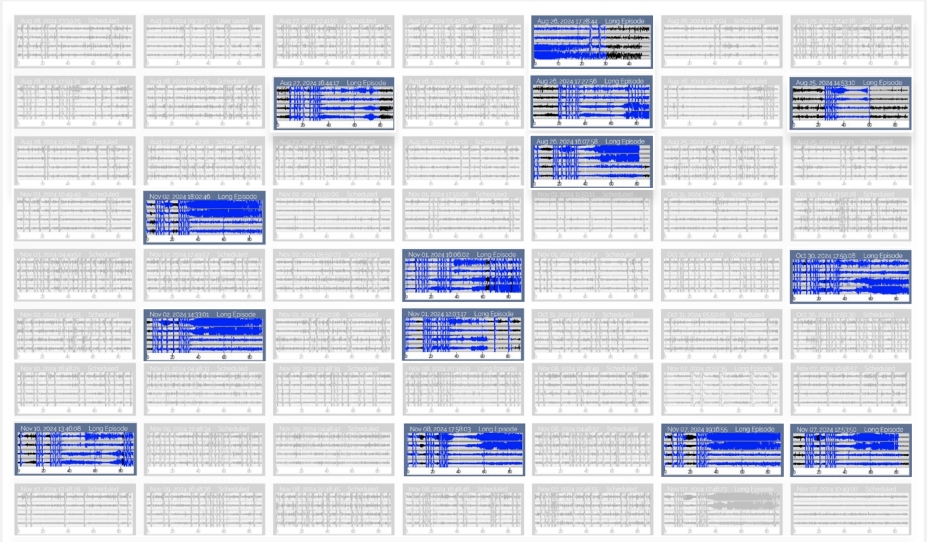

Renderings; features not available in the approved RNS System. Next generation platforms and features are anticipated and not yet approved.



NEUROPACE

# AI-Powered Seizure Classifier

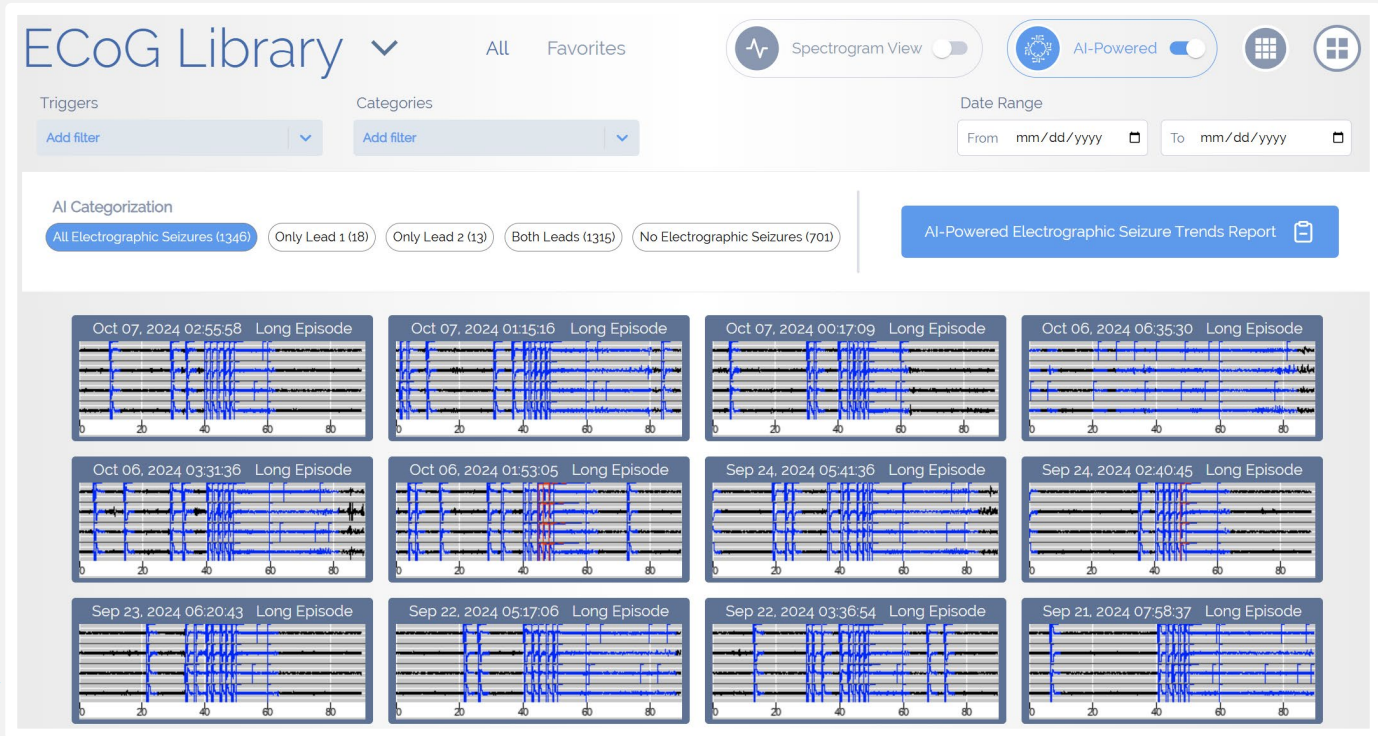
## Present



Validated AI model identifies electrographic seizures

**Simplifies review of iEEG by presenting relevant data for streamlined patient care**

## Future




Renderings; features not available in the approved RNS System.

Renderings; features not available in the approved RNS System. Next generation platforms and features are anticipated and not yet approved.



NEUROPACE

# AI seizure Classifier Creates **Insights for Patient Care**

## AI-powered Electrographic Seizure Trends

Date Generated
2024-11-24 01:05 PM

Date Range
2022-11-01 to 2024-10-07

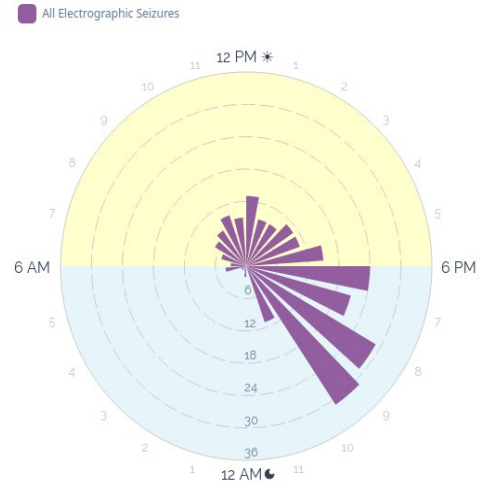
Edit Filters Applied

All data displayed is in US/Pacific.

### ECoG Electrographic Seizure Summary

| All Electrographic Seizures | Lead 1 Only- | Lead 2 Only- | Both Leads |
|---|---|---|---|
| Lead 1 Only, Lead 2 Only, Both Leads | Left Mesial Temporal Depth Lead | Left Parietal Strip Lead | |
| 235 | 46 19% | 77 33% | 112 48% |

### Circadian Electrographic Seizure Patterns

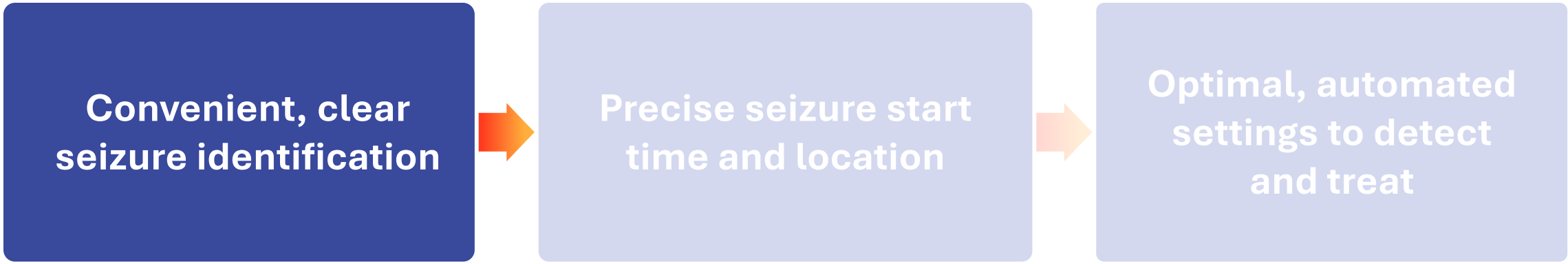



Renderings; features not available in the approved RNS System. Next generation platforms and features are anticipated and not yet approved.



NEUROPACE

# NeuroPace Dataset Enables Cadence of Tools for Therapy Effectiveness, Efficiency, and Ease of Use




Next generation platforms and features are anticipated and not yet approved.



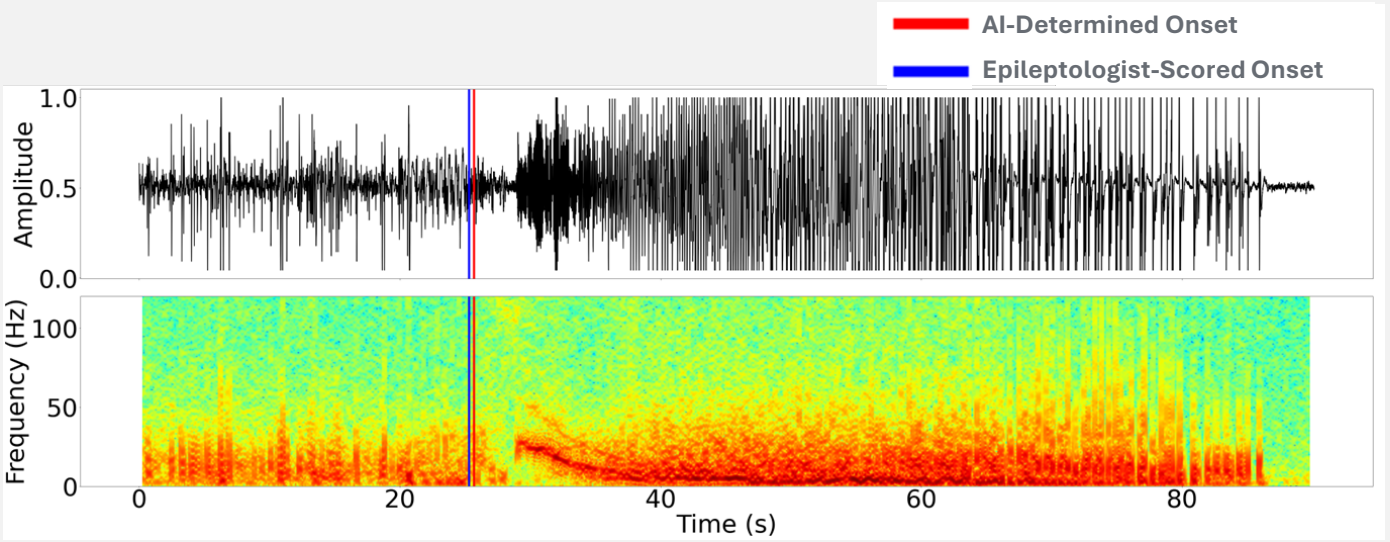
NEUROPACE

# AI Seizure Onset Detection Brings Precision, Insight, and Efficiency

Convenient, clear seizure identification → **Precise seizure start time and location** → Optimal, automated settings to detect and treat

## NeuroPace model identifies seizure onset time, location

## Accurate to within 1 second of clinician-reviewed onsets




Renderings; features not available in the approved RNS System. Next generation platforms and features are anticipated and not yet approved.



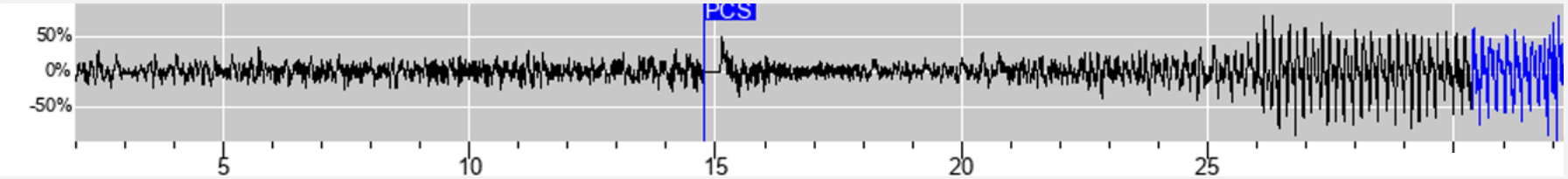
NEUROPACE

# Automated Proposal of Detection and Treatment Settings

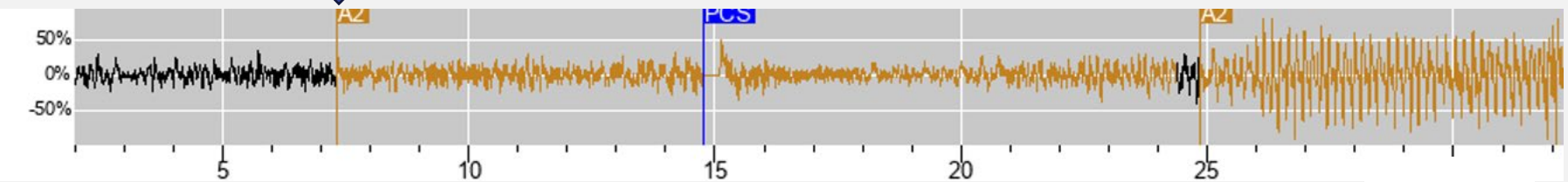
Convenient, clear seizure identification → Precise seizure start time and location → **Optimal, automated settings to detect and treat**

- ✓ **Effectiveness**
- ✓ **Efficiency**
- ✓ **Ease of Use**

Physician setup




AI-proposed setup

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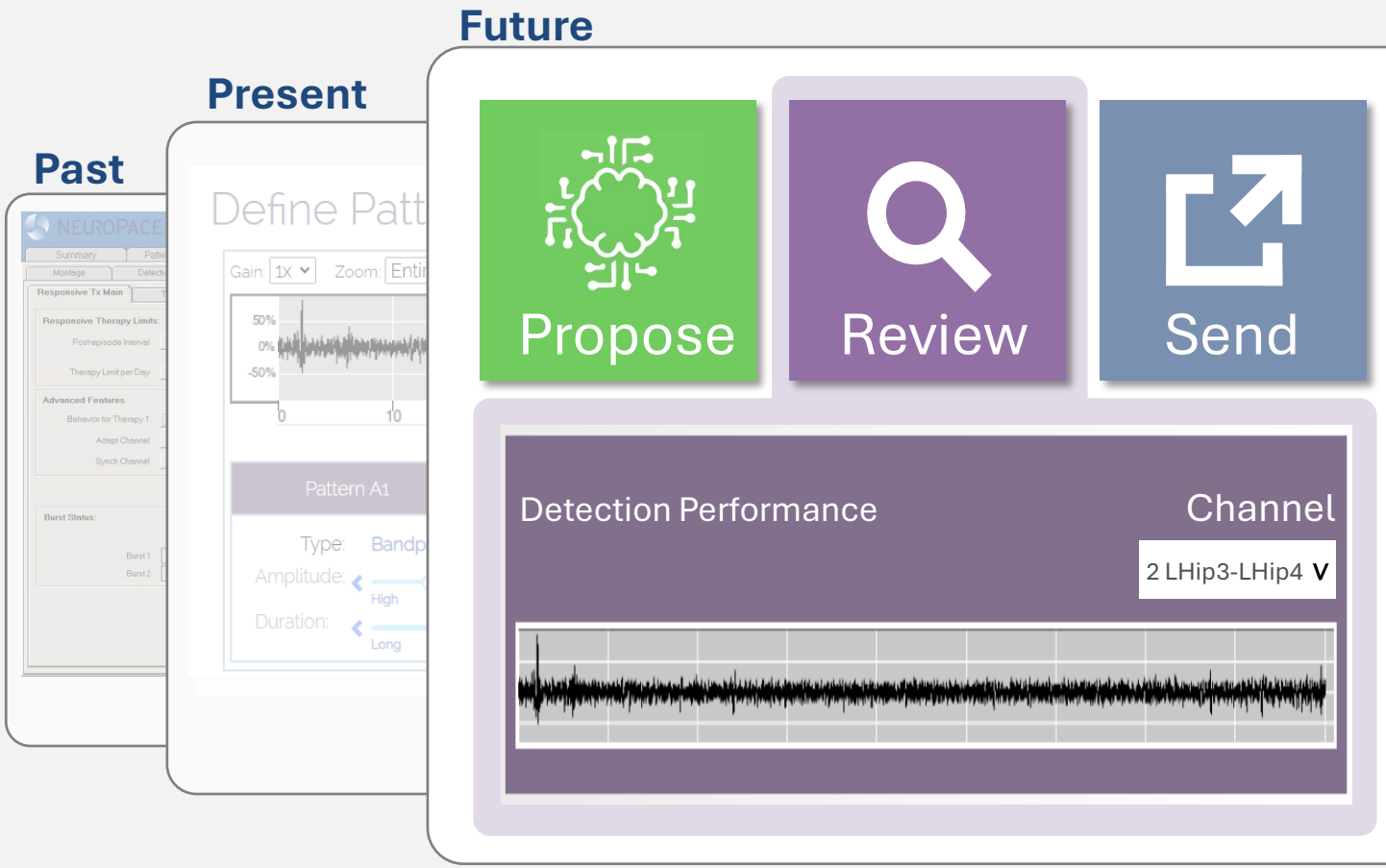
NEUROPACE

# Automated Proposal of Detection and Treatment Settings

Convenient, clear seizure identification → Precise seizure start time and location → **Optimal, automated settings to detect and treat**




AI tools improve **clinic efficiency and ease of use**

System proposes **personalized settings** based on seizure morphology and treatment history, for physician to review and finalize

Improved efficiency means physicians can **treat more patients** with the RNS System

Therapy settings sent and updated via **remote programming**

Renderings; features not available in the approved RNS System. Next generation platforms and features are anticipated and not yet approved.



NEUROPACE

# Remote Programming Solves for Patient Travel, Inconvenience

| | |
|---|---|
| **Problem** | For many patients, the nearest clinic is hours away |
| **Solution** | Remote monitor can receive and update treatment settings<br>Expands use of existing programming functionality |
| **Benefits** | More **efficient** patient care and **greater adoption** with telehealth programming; reduces patient travel |


Next generation platforms and features are anticipated and not yet approved.



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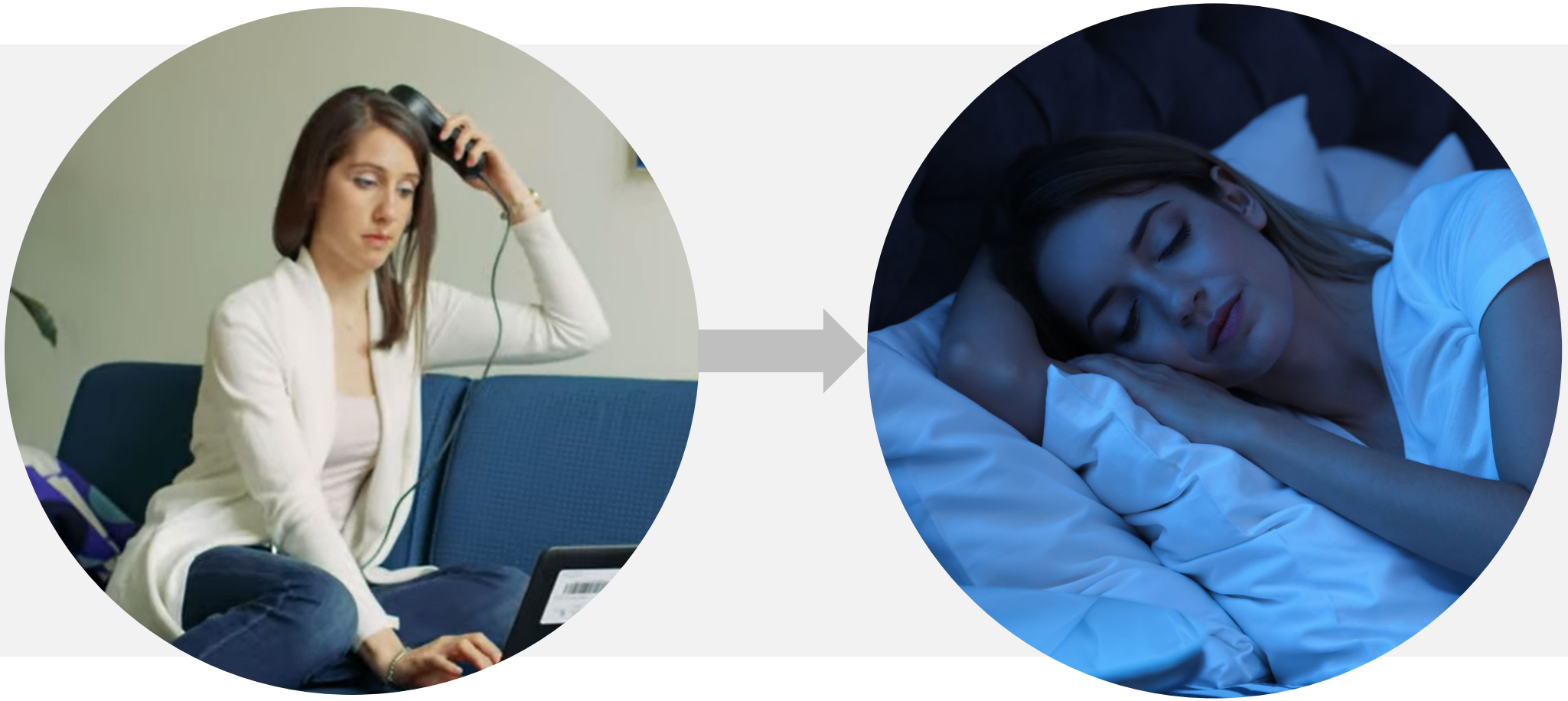
# Next-generation Neurostimulator Enables **Automatic Data Transfer**

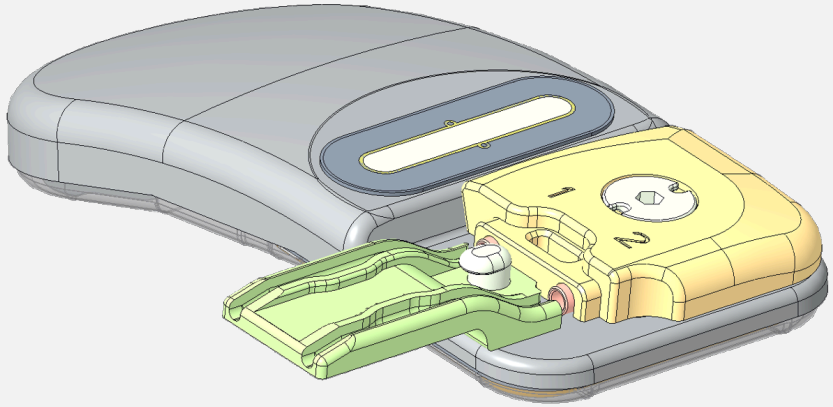


Renderings; features not available in the approved RNS System. Next generation platforms and features are anticipated and not yet approved.

# Next-generation Platform for **Effectiveness, Efficiency, and Innovation**

Automated, overnight data transfer **improves patient experience** and expands adoption

Next-gen hardware **supports future innovation** in detection and therapy



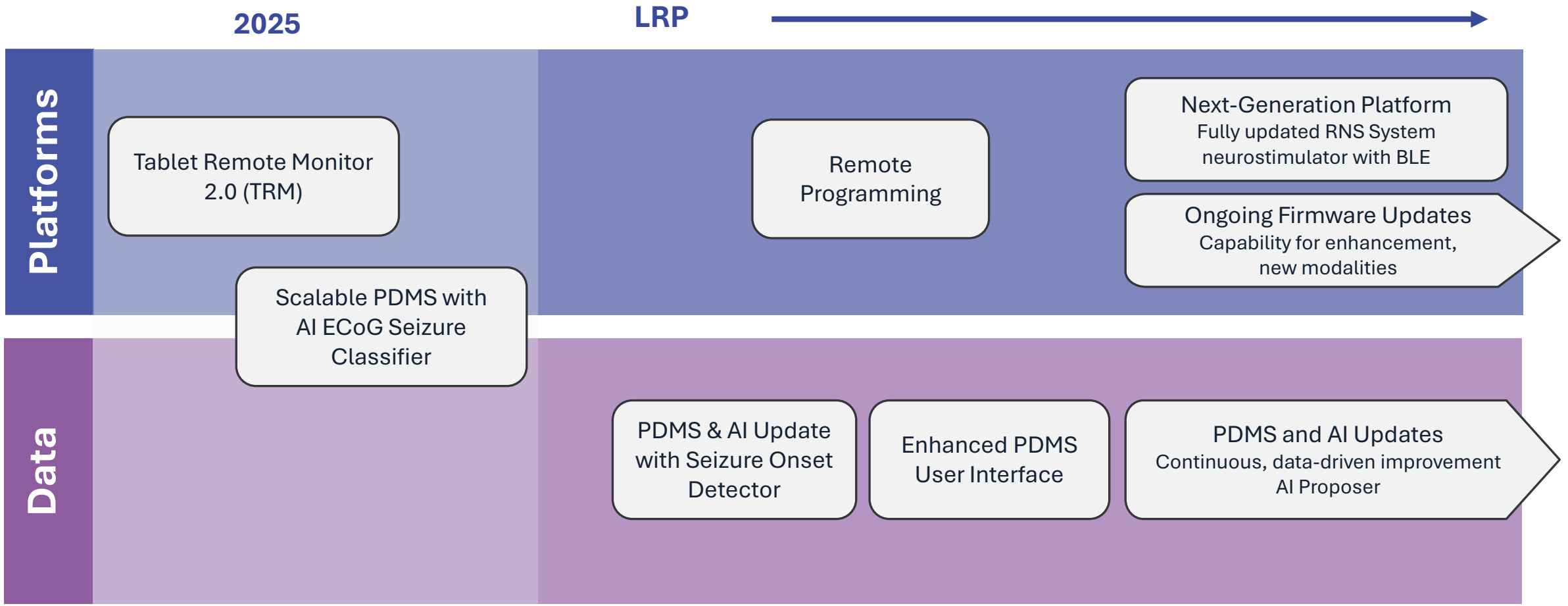
Adds BLE; modernizes microprocessor, ASIC

Maintains MRI conditional labeling

No change to mechanical envelope or RNS System compatibility

Renderings; features not available in the approved RNS System. Next generation platforms and features are anticipated and not yet approved.

# Data and Platform Roadmap




Note: Hardware and software releases, clinical trial submissions, and clinical approval launches are anticipated during the time periods shown above.



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# Market Development

Katie Keller

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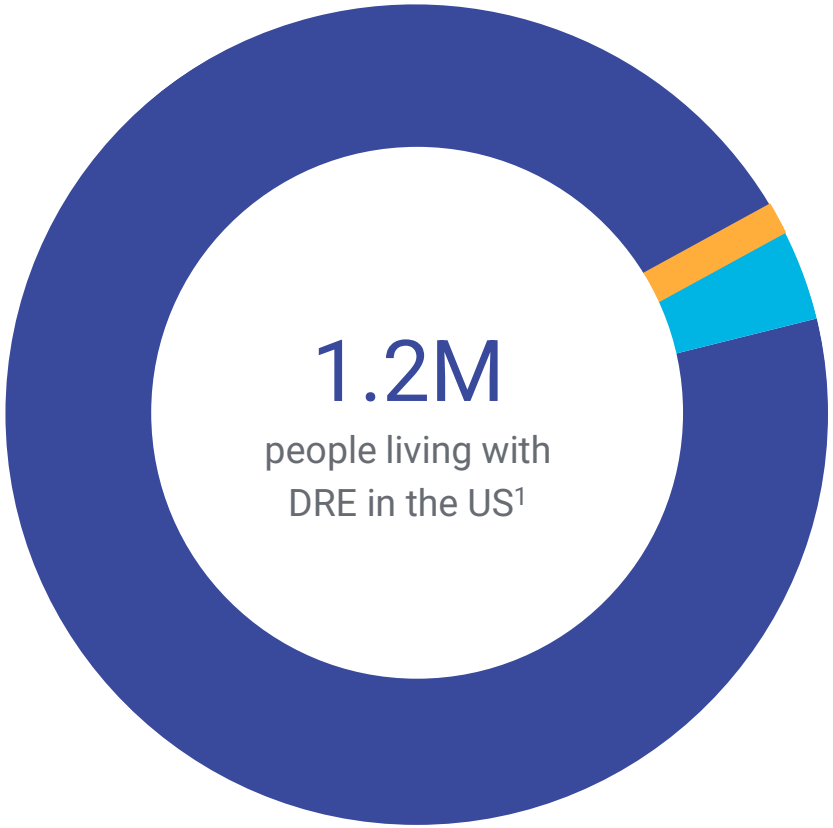
# Current Patient Population Focus




**6.5K**
DRE patients get treatment beyond drugs annually[3]

**50K DRE**
patients admitted to Comprehensive Epilepsy Centers annually[2]

Significant Opportunity Exists to Close the Treatment Gap!

[1]Chen, Z., et al., JAMA Neurology, 2017. [2]Definitive Healthcare Claims Database for Epilepsy Patients who received Inpatient VEEG in 2019. [3]Ostendorf, et al, Neurology, 2022.



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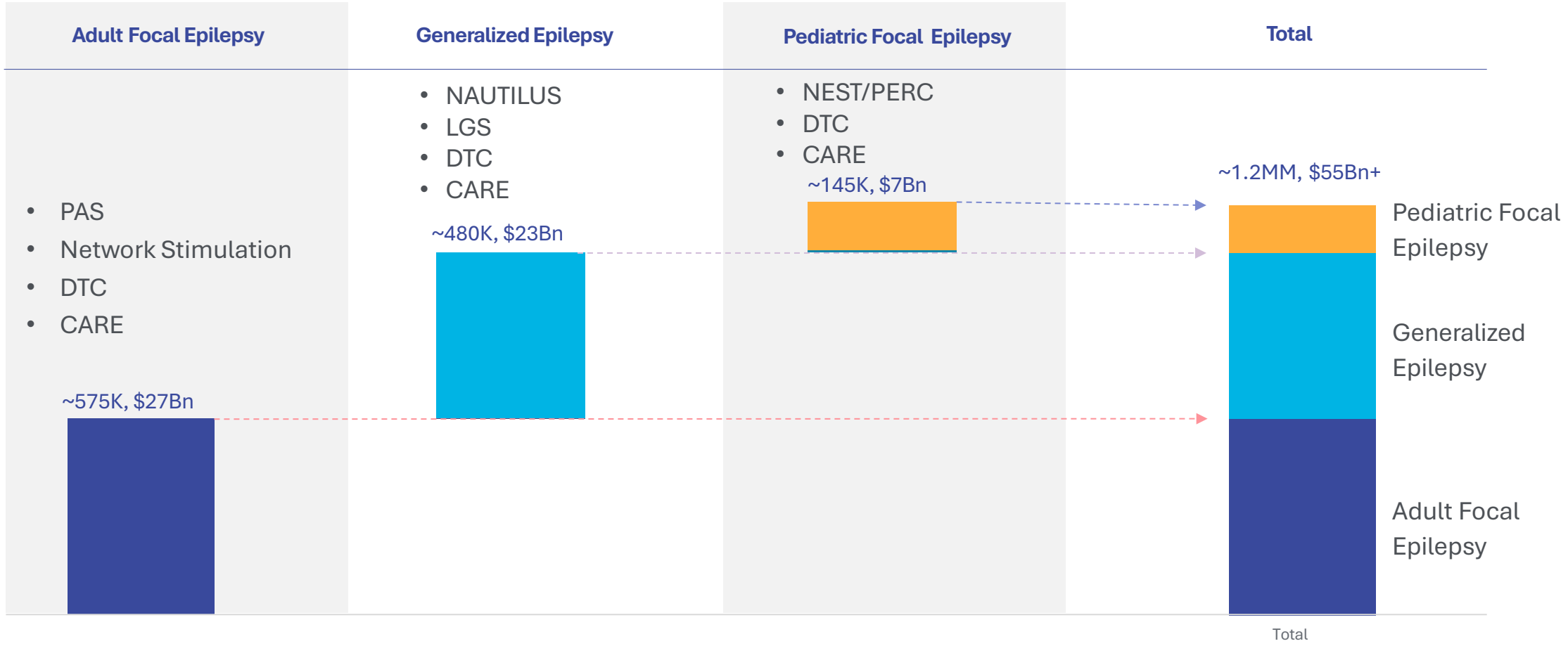
# RNS Addressable Market Segments: Current and Untapped

## RNS Addressable Markets **(Patients, $ market size)**




***Significant programs are underway to expand access to and develop RNS within each of these segments**

Chen, Z., et al., JAMA Neurology, 2017. https://www.cdc.gov/epilepsy/about/; www.childhealthdata.org; https://pmc.ncbi.nlm.nih.gov/articles/PMC9480957/; $ market size calculated using ASP of ~$47,000.



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# Closing the Treatment Gap: Enhanced RNS Therapy Access

| | |
|---|---|
| Patient Indication Expansion: RNS System Access for Generalized Epilepsy | • 40% of DRE Patients<br>• Completed implants in ongoing NAUTILUS and LGS trials<br>• IGE submission after 1-year post-implant follow up<br>• Potential to be first device in U.S. with generalized indication |
| Community Expansion: RNS System Access outside of Level 4 CECs / building referral pathways | • Expansion to additional 1,800 epileptologists and all functional neurosurgeons within current indications<br>• Significant expansion of RNS TAM<br>• 2024: Pilot Activities / 2025: Program Expansion |
| CECs: Focus on Adoption Across Clinicians and Expanded Therapy Utilization by current prescribers | • Build on encouraging initial implant growth<br>• Network stimulation<br>• PAS: new clinical evidence |

2023 2024-2025 2025-2026



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# Fewer Seizures. More Living.

82% seizure reduction at 3 years[1]

Improvements in cognitive function[2]

Significant quality of life improvements after just 1 year[3]

1. Razavi, et al., Epilepsia, 2020
2. Loring DW et al., Epilepsia, 2015. No group decline on any of 14 objective neuropsychological measures after blinded period or at 1 and 2 years (n=175).
3. Meador, et al., Epilepsy Behavior, 2015. Based on QOLIE-89.



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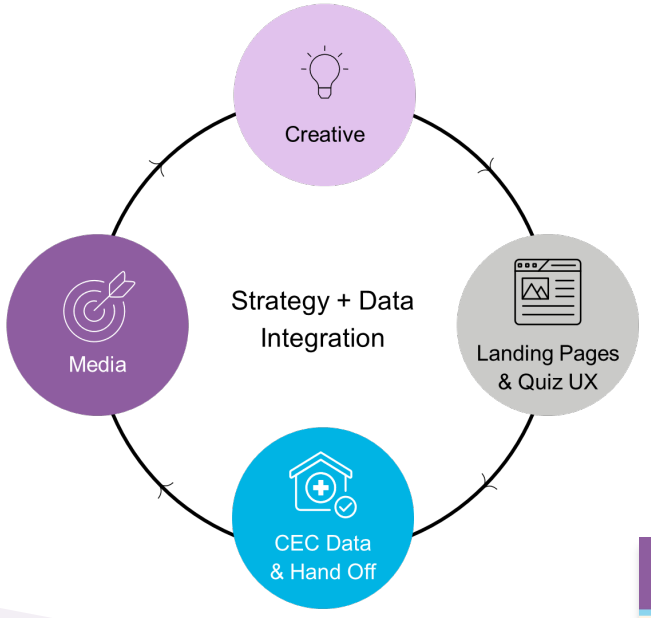
# Direct to Consumer Strategy

**Own patient engagement from diagnosis to implant, providing education and access to care for the RNS System**

- Expanding digital advertising targeting both patients in CEC & the community
- Adding Nurse Navigators & focusing on patients considering surgery
- Maximizing conversion with sales focus
- 50% reduction in cost per lead with mature targeting processes
- Email campaigns for ongoing education
- Activate local patient education programs with physicians




Digital Advertising Drives Awareness of RNS

Patients take Quiz to segment

Nurse Navigator Education

Qualified Leads to Sales

RNS System Implants

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# Patient Education

## Extensive focus on patient education

- Nurse Navigators
  +1600 educations last year
- Patient Educator +500 educations
  +90% move to RNS implant
- Community Chats
- Patient Ambassadors
- Field rep education for patients & families


Michael McKenna, MSW
NeuroPace Patient Educator



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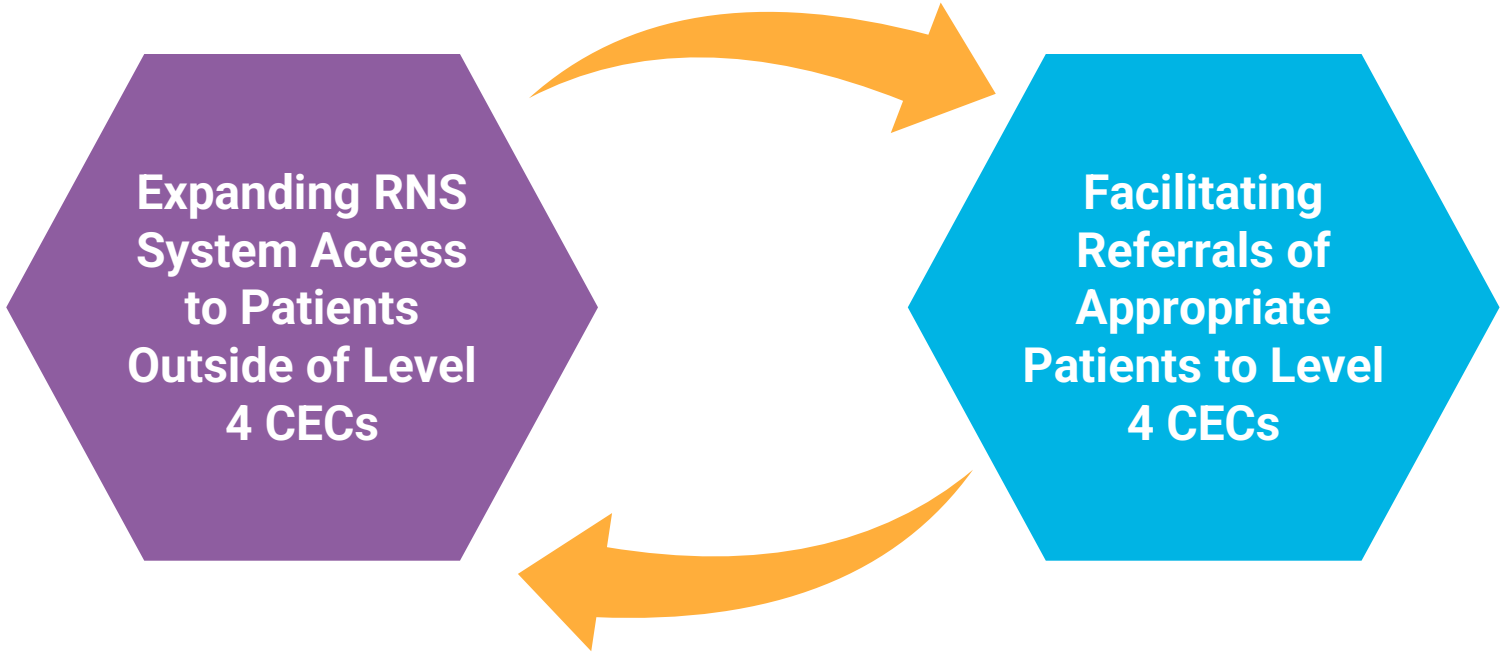
# Market Expansion: Project CARE

## Bringing the RNS System into the Community

**Community Expansion - Making the RNS System Accessible outside of Level 4 CECs**

- Expanding to additional 1,800 epileptologists and all functional neurosurgeons practicing outside of Level 4 CECs
- Goal: more than double implants and referrals from CARE accounts in 2025
- New referral marketing materials
- Digital marketing to referring physicians
- Expanded professional education



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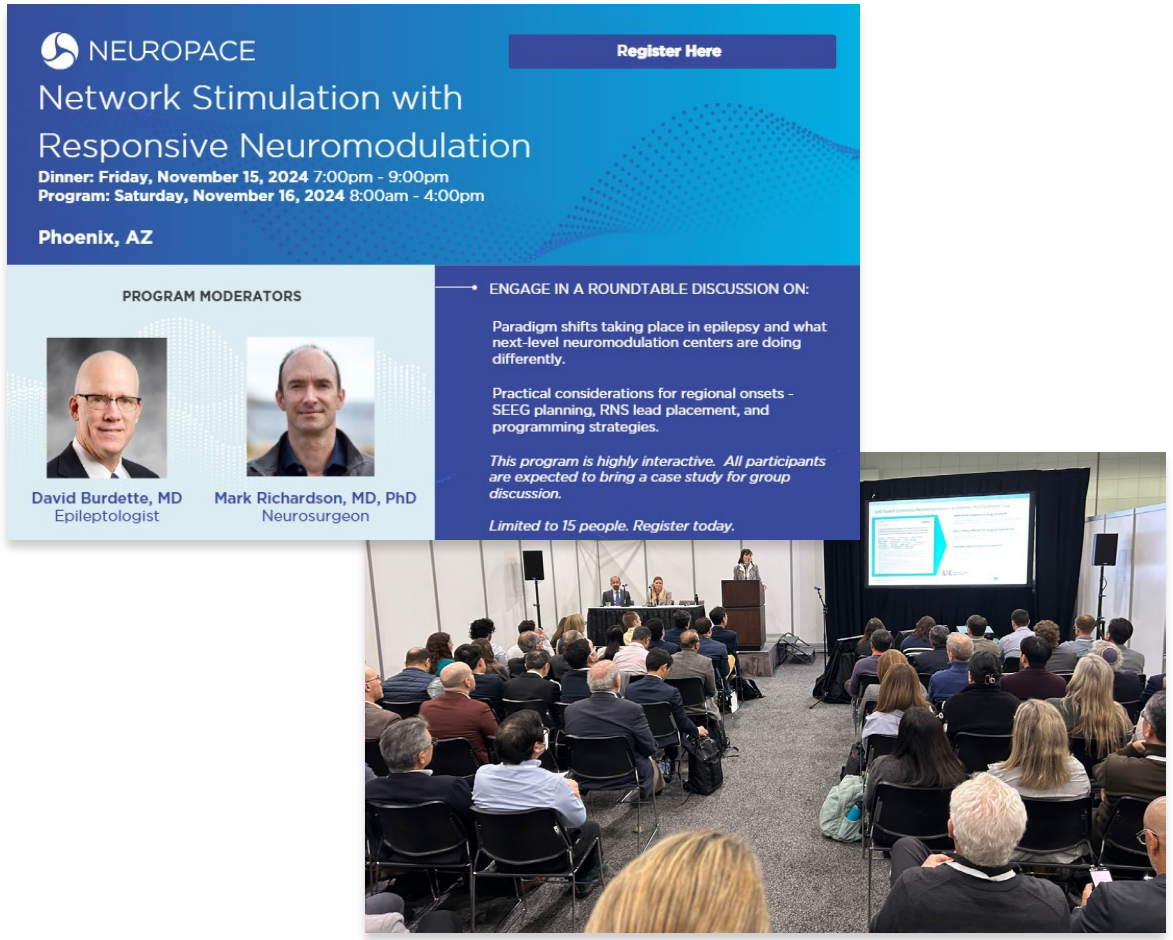
# Professional Education and Podium Presence

## 2024 Highlights

- 572 Physicians educated
- 78 Courses and Events
- American Epilepsy Society (AES)
  - + 553 physician engagements
  - +70 publications and podium sessions on RNS
- RNS reaching a tipping point

## 2025 Focus

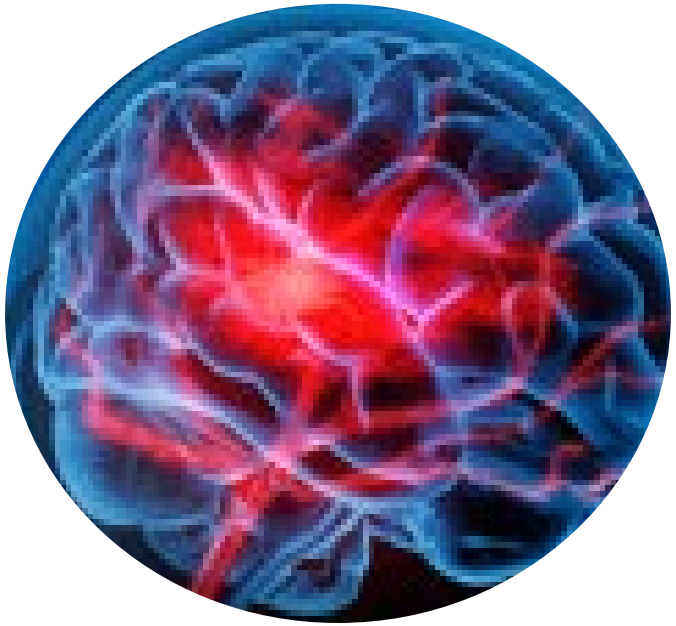
- Network Stimulation
- Differentiated Seizure reduction outcomes
- Proctorships
- Continued Fellows education
- Small group peer-to-peer



# Indication Expansion:  Generalized Epilepsy

**Patient Eligibility Indication Expansion – RNS System indication for Generalized Epilepsy**

- 40% of DRE market
- Shorter diagnostic process
- Shorter time from patient identification to implant



## Generalized Epilepsy Clinical Trials

### NAUTILUS

- Breakthrough Device Designation status
- Enrollment and implants complete
- One-year follow-up to be complete in March 2025

### Lennox-Gastaut Syndrome (LGS)

- NIH-funded feasibility study
- Enrollment and implants complete

2023 — 2024-2025 — 2025-2026



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# Preparing for Generalized Epilepsy Launch

### Prepare the Market Now

- CARE program builds centers ready for implanting IGE patients
- Educate HCPs on generalized epilepsy, NAUTILUS clinical trial design and RNS mechanism of action

### Launch Strong

- Peer-to-peer KOL education
- Comprehensive collateral on IGE
- Patient materials
- HCP materials For Epileptologists, Neurologists, Neurosurgeons
- Multi-faceted PR & social media campaign to create buzz & generate awareness


Clinical trial submissions and clinical approval launches are anticipated during the time periods shown above.



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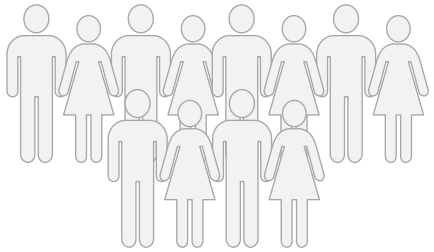
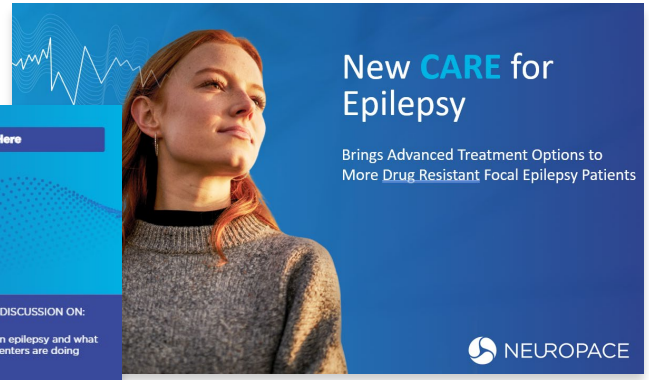
# Scaling for Growth








## Developing Sales & Marketing to drive and sustain growth

- Ongoing incremental increases in sales & marketing teams
- Developing teams with launch excellence
- Drive adoption & differentiation
- Capitalize on CARE community expansion
- Launch data and new products
- Prepare for potential indication expansion (IGE and Pediatric)
- Run educational programs and workshops



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# Vision, Plans and Expectations

Joel Becker
Rebecca Kuhn

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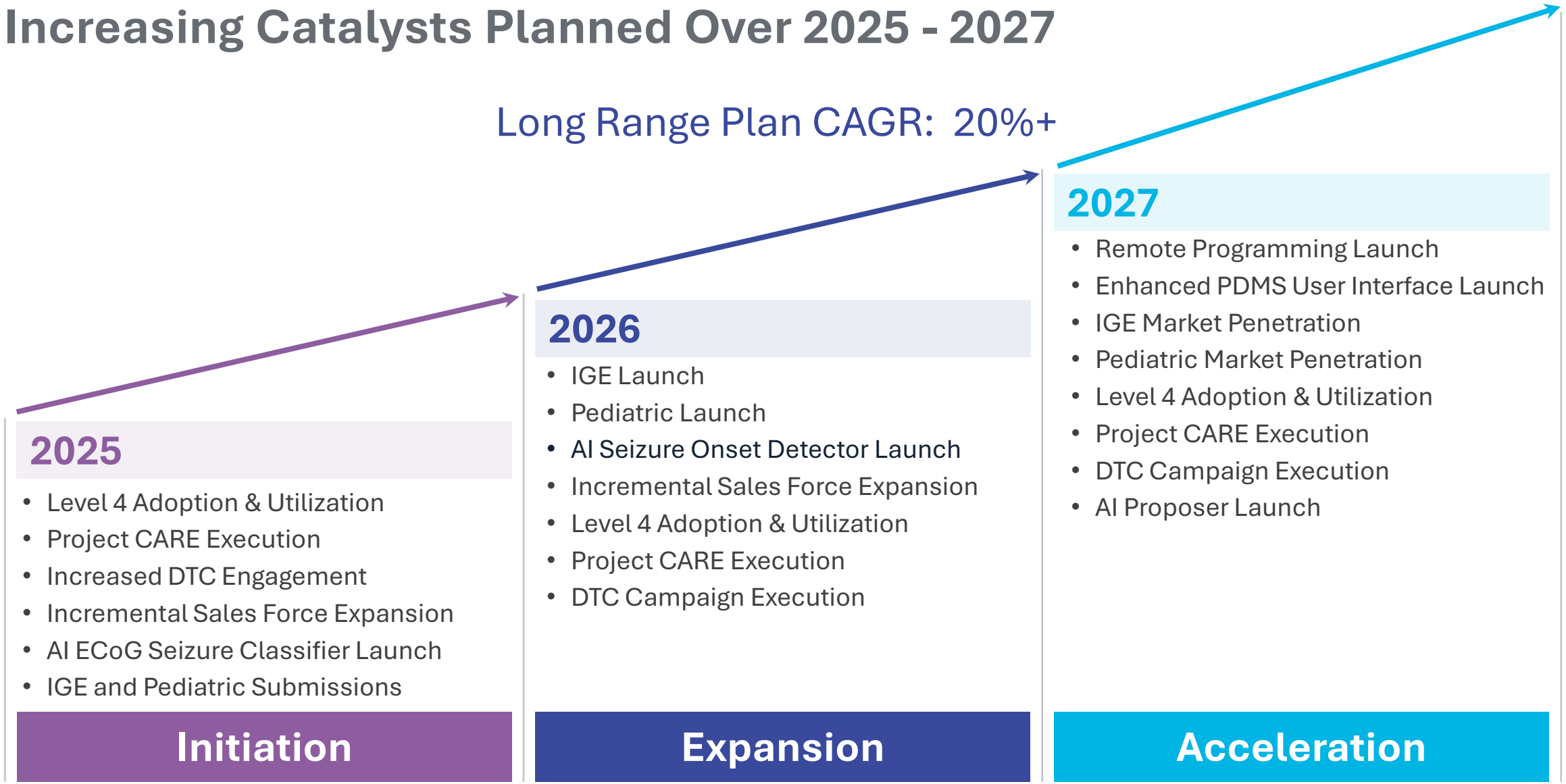
# NeuroPace Long Range Plan: Vision

**To become the recognized leader in drug-resistant epilepsy therapy and fully develop the potential of the RNS System**

# Increasing Catalysts Planned Over 2025 - 2027




Hardware and software releases, clinical trial submissions, and clinical approval launches are anticipated during the time periods shown above.



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# NeuroPace Vision and Long Range Plan Objectives

Market Leader with LRP Revenue Growth of 20%+ CAGR

Indication expansion to Idiopathic Generalized and Pediatric DRE patients

Neuromodulation category leader in efficiency and ease of use with AI Tools and Remote Programming

Significantly expanded patient and referral awareness and access through direct-to-consumer campaigns and Project CARE

Cash Flow Break Even



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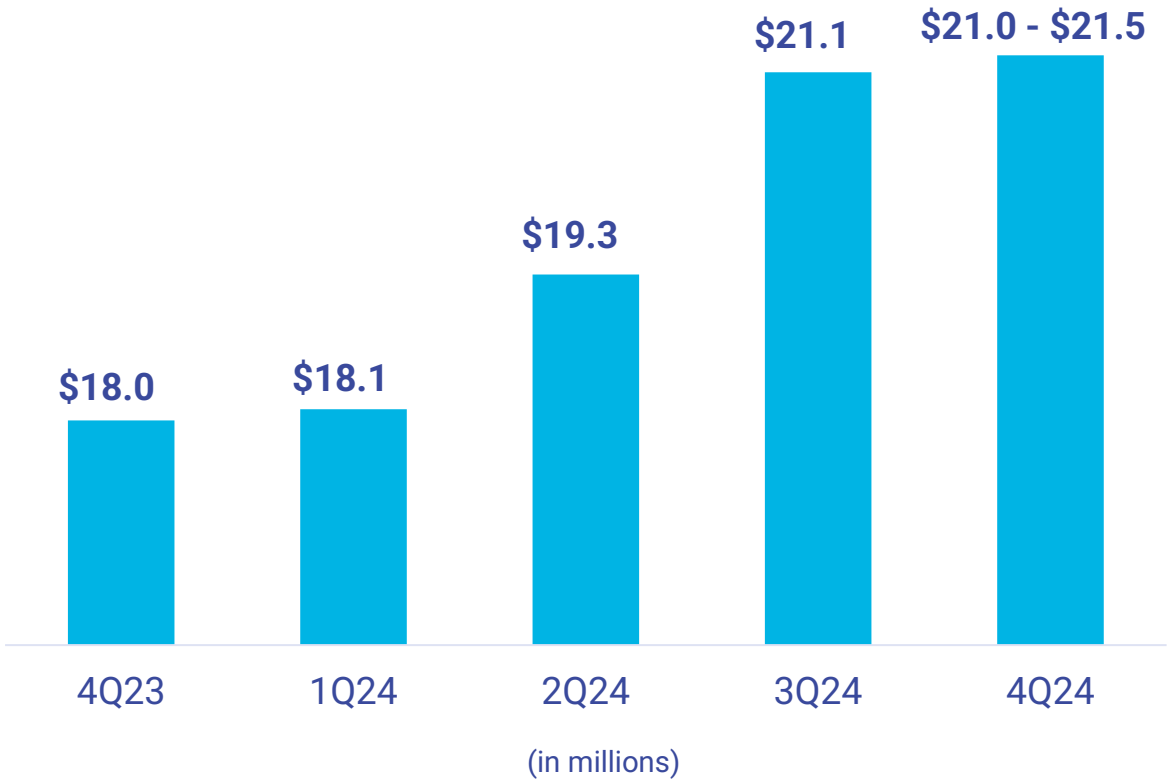
# Financial Performance

## Total Cash Balance of approximately $52.8M (as of 12/31/2024) provides sufficient capital to support key operating priorities




| | Preliminary 4Q24 (unaudited) | Preliminary FY2024 (unaudited) |
|---|---|---|
| **Revenue** | **$21.0M - $21.5M** | **$79.4M - $79.9M*** |
| Revenue growth (y/y) | 17% - 19% | 21% - 22% |

*initial 2024 revenue guidance: $73M - $77M

4Q24 and FY2024 results are preliminary, unaudited, and subject to change



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# 2025 Guidance

| | |
|---|---|
| Revenue | $92 million - $96 million |
| Gross Margin | 73% - 75% |
| Operating Expenses | $92 million - $95 million including approximately $11 million in stock-based compensation |

**Key Revenue Assumptions**

- Growth primarily driven by sales of RNS System
- No contribution from approved new indications
- DIXI distribution agreement continues per current terms
- Substantially all revenue in the US



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# The Brain is the Next Frontier

- I feel about the Brain today the way I felt about the left atrium and the left ventricle in 1995 – I believe that the Brain is the next frontier in Med Tech
- RNS System is only closed loop neuromodulation system
- Multiple clinical, product and market development initiatives underway provide potential for increasing growth catalysts
- Uniquely well positioned to lead in the development of epilepsy treatment and beyond
- Expanding indications and applications for the RNS platform and expanding access to RNS for DRE patients and beyond

# Questions?

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# Thank you!

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