Identification and Validation of a CCEP-Derived Computational Marker of the Epileptogenic Zone

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Introduction

Medically Refractory Epilepsy

- Medically refractory epilepsy affects 20M globally and accounts for 80% of $16B total epilepsy spend.

Standard of Care & Innovation

- SOC is surgical removal of the epileptogenic zone (EZ). EZ localization is a challenge, with surgery success ranging from 30-70%.
- Actively measured CCEP data is novel compared to current passive localization (EEG, MRI). Computational EZ localization is also novel.
- Current EZ localization focuses on individual channels. CCEPs allow for understanding and analysis of the broader epileptogenic network.

Methods

Cortico-Cortical Evoked Potentials (CCEPs) actively measure neuronal connections through single pulse electrical stimulation (SPES) [1,2].

- We extracted node-based features from the CCEP waveform.
- We computed network features from the broader CCEP network.
- We trained a suite of machine learning models to localize the EZ.

Data

This CCEP data consists of 40 patients and was collected and processed from the JHU Department of Neurology.

Results

Figure 1. Left: CCEP Electodes Implants Right: Typical CCEP Response [3]

Figure 2. Left: ROC Curves for 6 ML models. Random Forest AUC = 0.87. Right: Random Forest Model Boxplot, showing clear separation between non-EZ (blue) and EZ (orange). Sensitivity = 0.92, Specificity = 0.75

Figure 3. Unsuccessful Surgical Outcome. Clinicians struggled with localization. Our model predictions differed from clinical prediction, perhaps indicating the true EZ. (green = clinically-predicted, red = model-predicted)

Figure 4. Unsuccessful Surgical Outcome. Clinicians identified lesion of interest but were not able to resect (red circle). Model predicted all key areas of interest. (right, green = clinically-predicted, bold = model-predicted)

Conclusion

- CCEPs have been used to map regions of brains, but they have never been used for EZ localization.
- We show that CCEP-based modeling (Random Forest model) can be a promising tool to aid passive EEG / MRI EZ localization methods.
- AUC = 0.87, Sensitivity = 0.92, Specificity = 0.75. Boxplot shows that the RF can differentiate between EZ (orange) and non-EZ (blue).
- Limitations include EZ overestimation in ground truth labels, sparse sampling networks, and inter-patient variability.
- These can be overcome by increasing sample size and standardizing CCEP measurement guidelines.

References