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.

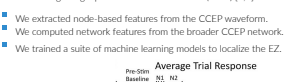

Figure 1 Left: CCEP Electodes Implants Right: Typical CCEP Response [3]

Data

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

Results

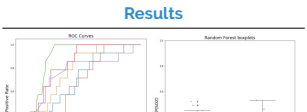

Figure 2.
Left: ROC Curves for 6 ML models. Random Forest AUC = 0.87. Right: Random Forest Model Boxplot, showing clear separation between non-EZ (blue) and EZ (orange). Sensitivity = 0.92, Specificity = 0.75

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

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