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Old Diagnostic Meets Newer Therapy; ECoG During LiTT

Intraoperative Electrocorticography During Laser-Interstitial Thermal Therapy Predicts Seizure Outcome in Mesial Temporal Lobe Epilepsy

Chen, B, Grewal SS, Middlebrooks EH, Tatum WO, Ritaccio AL, Sirven JI, Freqund BE, Feyissa AM. *Clin Neurophysiol.* 2023;146:118-123. doi:10.1016/j.clinph.2022.12.003

Background and Objectives: Magnetic resonance-guided laser interstitial thermal therapy (MRLiTT) for treating temporal lobe epilepsy has recently gained popularity. We aimed to investigate the predictive value of pre-and post-MRLiTT epileptiform discharges (EDs) on intraoperative electrocorticography (iECoG) in seizure outcomes for patients with mesial temporal lobe epilepsy (mTLE). Methods: We conducted a pilot, prospective single-center cohort study on seven consecutive patients with mTLE that underwent MRLiTT. Pre- and post-MRLiTT iECoG was performed using a 1×8 contact depth electrode along the same trajectory used for the laser catheter. Findings: The responders had a robust reduction in ED frequency compared to pre-MRLiTT iECoG (86% vs 13%, $p < 0.01$). Clinical characteristics, including risk factors for epilepsy, duration of epilepsy, presence of mesial temporal lobe sclerosis, prior intracranial monitoring, the absolute frequency of pre- or post-MRLiTT EDs, and ablation volume were not significantly associated with responder status. Discussion: This is the first demonstration that intraoperative reduction in EDs during mesial temporal lobe MRLiTT may potentially predict seizure outcomes and may serve as an intraoperative biomarker for satisfactory ablation. However, larger prospective studies are needed to confirm our findings and evaluate the utility of iECoG during MRLiTT.

Commentary

Magnetic resonance-guided laser interstitial thermal therapy (LiTT) is a minimally invasive surgery that is an effective and safe therapy for treatment of drug-resistant mesial temporal lobe epilepsy (mTLE). The effects of location of ablation volume and individual patient anatomy affect surgical outcomes. While the long-term seizure control is comparable to anterior temporal lobectomy (ATL) with resection of the amygdala and hippocampus,[1] the incidence of neuropsychological morbidity seems to be lower, especially for dominant-temporal lobe cases, and the duration of hospital stay favor the use of LiTT.[2] The technique relies on a straight laser catheter to ablate a target. Due to curvature of the hippocampus and variations in temporal lobe anatomy, a compromise on ablation coverage will be required if a single trajectory is to be performed. In some cases, multiple trajectories are required to ablate the ictal focus. This is a critical feature as ablation volume correlates with seizure control.[3]

In some patients undergoing ATL, intraoperative electrocorticography (iECoG) has been used for the identification of interictal epileptiform discharges (IEDs) beyond a lesion or suspected ictal focus and further delineation of the epileptogenic zone. Interictal epileptiform discharges are a manifestation of excessive hyper-synchronization of cortical activity and are considered a marker of potentially epileptogenic tissue.[4] Despite their spatial and temporal variability, which are partly related physiologic state (awake vs asleep), IEDs tend to present a relatively consistent spatial core region.[5] Regions generating IEDs usually overlap with areas that generate seizures. Recent work using a novel computational approach based on the temporal orderings of IEDs reports that the source of interictal activity matches the location of ictal discharges and resection of areas containing both correlates with good seizure outcome.[6] In a single-center study of 140 patients with or without mesial temporal sclerosis (MTS) who underwent temporal lobectomy with a tailored hippocampal resection and were followed for at least 18 months, the presence of residual IEDs predicted a worse outcome independent of the extent (less or greater than 2.5 cm) of the resection.[7] Likewise, in a study of 22 patients who underwent a selective amygdalo-hippocampectomy with at least 12 months of follow-up and studied with pre-and post-resection ECoG for the *mesiobasal* region, the presence of post-resection EDs correlated with a worst outcome.[8]

Despite this data, the use of iECoG has declined over time due to the uptake in the use of stereo-encephalography and improvement of noninvasive techniques to localize the epileptogenic zone, such as magnetoencephalography or electrical source imaging. But the main limitation of iECoG is its reliance on data within the spatiotemporal constraints of surgery. Compounding the short duration of sampling are the inhibitory effects of certain anesthetic agents on IEDs.[9]

This trend in the use of iECoG might change due to the recent report by Chen et al.[10] In an exploratory pilot study, the authors report on the use of pre- and post-LiTT iECoG as a predictor of seizure outcome in patients with mTLE. In this single-center cohort of 7 patients (5 with left mTLE, 2 with MTS, 4 studied with chronic iEEG), an 8-contact depth electrode was placed along the trajectory of the laser fiber used for eventual ablation of the amygdala and hippocampus posteriorly to the level of the mesencephalic sulcus. Visual quantification of IEDs was performed, with a mean duration of pre-ablation iECoG of 6 minutes and of 5.3 minutes post-ablation. Clinical or subclinical seizures were not recorded and the neurosurgeon, but not the epileptologist, was blinded to the results. Univariate analysis was performed to evaluate potential predictors of outcome, using among other LiTT ablation volume and ECoG findings. Mean duration of follow-up was 23.7 months (range 8.8-48.4 months). Four patients (2 with MTS) were considered responders (defined as achieving Engel Class I outcome) despite one having bitemporal lobe IEDs on the presurgical evaluation.

Responders showed a lower number of IEDs pre-LiTT but the difference compared to nonresponders was not statistically different ($P = 0.24$). Surprisingly, the only factor that predicted a good outcome was the percent reduction in IEDs frequency (86% vs 13%; $P < .01$) despite no difference in the mean absolute difference in IED frequency pre- and post-ablation (4 ± 34 IED/minute in responders compared to 9.9 ± 17 for nonresponders ($P = .43$). Mean ablation volume was not significantly different (4.5 cm^3 in responders vs 3.8 cm^3 for nonresponders). This finding is unexpected given the reported correlation between ablation volume and seizure control.[3] The authors conclude that the use of intraoperative iECoG may serve as a biomarker to determine the adequacy of LiTT and improve seizure outcomes.

The study has several limitations, the major one being the small sample size and the inclusion of only adult patients with mTLE; its major strengths are the prospective design and long duration of follow-up. It would have been interesting to visually display the placement of the catheter in relation to the mesial structures and to describe the topographical distribution of the IEDs along the electrode trajectory. Evidently, these results need to be validated in larger patient cohorts. Nevertheless, these results raise several interesting questions: what is the optimal duration of iECoG when performing LiTT; is there a difference in the rate of IEDs when recording while asleep versus awake; should high-frequency oscillations be included in the analysis; would performing post-LiTT iECoG via a different electrode trajectory improve the detection of IEDs; does the presence of post-LiTT IEDs imply the need for additional ablation trajectories that are parallel or tangential to the initial one; is there an insertional effect of the EEG electrode in the induction of IEDs; do these results extend to pediatric patients and other types of pathologies, such as cortical dysplasia?

These are timely questions given the increasing use of LiTT, specially for nondominant mTLE. Only controlled studies with large patient cohorts can answer these questions. If the results reported by Chen et al[10] are replicated, an old diagnostic technique could see a revival and help improve the seizure outcome of an increasingly favored therapeutic intervention for drug-resistant mTLE.

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Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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