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What Is the Best Target for Ablation of Mesial Temporal Lobe Epilepsy?

Effects of Surgical Targeting in Laser Interstitial Thermal Therapy for Mesial Temporal Lobe Epilepsy: A Multicenter Study of 234 Patients

Wu C, Jermakowicz WJ, Chakravorti S, Cajigas I, Sharan AD, Jagid JR, Matias CM, Sperling MR, Buckley R, Ko A, Ojemann JG, Miller JW, Youngerman B, Sheth SA, McKhann GM, Laxton AW, Couture DE, Popli GS, Smith A, Mehta AD, Ho AL, Halpern CH, Englot DJ, Neimat JS, Konrad PE, Neal E, Vale FL, Holloway KL, Air EL, Schwalb J, Dawant BM, D′Haese PF. *Epilepsia*. 2019;60(6):1171-1183. doi:10.1111/epi.15565.

Objective: Laser interstitial thermal therapy (LITT) for mesial temporal lobe epilepsy (mTLE) has reported seizure freedom rates between 36% and 78%, with at least 1 year of follow-up. Unfortunately, the lack of robust methods capable of incorporating the inherent variability of patient anatomy, the variability of the ablated volumes, and clinical outcomes have limited 3-dimensional quantitative analysis of surgical targeting and its impact on seizure outcomes. We therefore aimed to leverage a novel image-based methodology for normalizing surgical therapies across a large multicenter cohort to quantify the effects of surgical targeting on seizure outcomes in LITT for mTLE. Methods: This multicenter, retrospective cohort study included 234 patients from 11 centers who underwent LITT for mTLE. To investigate therapy location, all ablation cavities were manually traced on postoperative magnetic resonance imaging (MRI), which were subsequently nonlinearly normalized to a common atlas space. The association of clinical variables and ablation location to seizure outcome was calculated using multivariate regression and Bayesian models, respectively. Results: Ablations including more anterior, medial, and inferior temporal lobe structures, which involved greater amygdalar volume, were more likely to be associated with Engel class I outcomes. At both 1 and 2 years after LITT, 58.0% achieved Engel I outcomes. A history of bilateral tonic-clonic seizures decreased chances of Engel I outcome. Radiographic hippocampal sclerosis was not associated with seizure outcome. Significance: Laser interstitial thermal therapy is a viable treatment for mTLE in patients who have been properly evaluated at a comprehensive epilepsy center. Consideration of surgical factors is imperative to the complete assessment of LITT. Based on our model, ablations must prioritize the amygdala and also include the hippocampal head, parahippocampal gyrus, and rhinal cortices to maximize chances of seizure freedom. Extending the ablation posteriorly has diminishing returns. Further work is necessary to refine this analysis and define the minimal zone of ablation necessary for seizure control.

Commentary

There are many operative techniques used to treat mesial temporal lobe epilepsy (MTLE), one of the most common epilepsy syndromes that are refractory to pharmacological treatment. These include anterior temporal lobectomy (ATL) and selective amygdalohippocampectomy which can result in long-term seizure-free rates between 60% and 80%, with higher rates in patients with radiographic evidence of mesial temporal sclerosis (MTS).[1] Unfortunately, patients who undergo dominant ATL can have a 37% decline in verbal memory.[2]

Laser interstitial thermal therapy (LITT) has emerged as an alternative treatment to ATL, the gold standard therapy, for patients with medically refractory MTLE. Laser interstitial thermal therapy involves stereotactic placement of a laser fiber and magnetic resonance imaging (MRI) thermometry for real-time feedback of the ablation. The therapy has been used in patients with MTLE, both with or without radiographic evidence of MTS,[3] when resective therapy has been deemed not to be appropriate due to the concern for excessive morbidity or risk for damage to eloquent cortex. For patients with MTS, this includes minimizing injury to visual or memory function.

In the initial report describing the use of LITT in patients with MTLE, 7 of 13 patients achieved seizure freedom when followed for a median of 14 months after ablation of a mean 54% volume of the amygdalohippocampal complex.[4] Subsequently, seizure-free outcomes from small case or single-institution series have varied between 54% and 80%. These reports have utilized protocols targeting different locations and ablation volumes as well as imaging techniques to quantify the volume of ablation. For example, Kang et al[5] used multiple software packages to process image fusion, user-defined segmentation, and transposition of segmented volumes to perform the volume-based analysis. In contrast, Jermakowicz et al[6] performed manual tracings for volumetric analysis applying a nonrigid, deformable brain atlas for spatial normalization of images into a common reference atlas to perform group comparisons.

In most of these reports, the efficacy of LITT correlated with ablation of the anterior structures of the temporal lobe, with emphasis on the amygdala and medial aspect of the head of the hippocampus. An exception is a multisite, single-institution retrospective review of 23 patients with MTLE, utilizing pre- and postablation volumes measured with an open source software suite for processing and analyzing MRI images (FreeSurfer) and a supervised spline-based edge detection algorithm. After a median follow-up of 34 months, there was no correlation between ablation volume of either the amygdala or hippocampus and seizure outcome.[7] Given that specific therapy location is subject to variability in patient anatomy and the surgery itself, it has been difficult to compare clinical outcomes among these small series of patients. Appropriate indications and predictors of safety and efficacy have not been well characterized in larger series.

Wu et al present a novel methodology using nonlinear normalization and statistical models that aims to provide guidance for the optimal use of LITT in MTLE. The authors performed a multicenter, retrospective study of 234 patients who had a minimum follow-up of 1 year to assess efficacy and tolerability of the procedure. The procedure was not standardized across institutions, but all patients were required to have standardized pre- and postoperative MRI of the brain so as to clearly identify the ablation cavity. Clinical outcomes that were explored included seizure outcomes at 6-month intervals, the presence of intracranial hemorrhage postablation and postoperative complications, excluding neuropsychological assessments. Ablation cavities were traced in a blinded fashion with regard to seizure outcomes. Images were normalized to a common reference space and the cavities were superimposed over anatomical structures to allow calculation of the percentage of amygdala and hippocampus ablation. Statistical analysis including uni- and multivariate logistic regressions was performed on clinical variables as well as on ablation location. A theoretical favorable ablation zone with the dimensions of a typical ablation was then generated.

At 1 year postoperatively, 58% of patient achieved seizure freedom. The presence of hippocampal sclerosis did not affect the outcome. The incidence of visual disturbances (5.1%) and worsening of preexisting affective disorder (4.3%) were the most common complications. The authors conclude that ablations involving the amygdala, head of the hippocampus, parahippocampal gyrus, and rhinal cortices, in contrast to more posterior ablations of the hippocampus, were associated with better seizure outcomes. These results mirror the findings on the topographic distribution of seizure onset in patients with hippocampal atrophy studied with intracranial electroencephalogram; 80% of ictal onsets involved the amygdala and anterior half of the hippocampus, despite the presence of atrophy of these segments in only 40% of the patients.[8]

Limitations of the study include the retrospective design; the lack of standardized neuropsychological evaluation among the different centers precluded an adequate assessment of the effects of LITT on neuropsychological outcomes; and the dependency on the image-based analysis on the accuracy of the nonlinear registration algorithm.

As seizure outcome has been associated with the extent of amygdalar and hippocampal ablation, it is important to select a safe trajectory optimizing involvement of both structures; however, variations in temporal anatomy significantly affect the overall complexity of planning. The curvature of the hippocampus and the presence of potential heat sinks, such as cerebral spinal fluid, may prevent adequate ablation of the epileptogenic network in some individuals. A small case series recommends utilizing a protocol for long-axis AHC cannulation that maintains an extraventricular trajectory to minimize hemorrhage risk and targets the center of the amygdala and head of the hippocampus to optimize ablation volumes.[9]

What about neuropsychological outcomes? Limiting collateral damage to the lateral temporal neocortex, parahippocampal gyrus, and subcortical white matter fiber tracts has been suggested to improve neuropsychological outcomes when treating dominant MTLE. Preliminary data from a 2 center, nonrandomized series suggest that LITT may preserve important category-related recognition and naming abilities that are often affected by ATL.[10] The authors postulate that preservation of white matter pathways and neocortical regions with LITT is the reason for the improved neuropsychological outcomes.

In conclusion, LITT seems to be a reasonable effective and safe alternative to ATL in some patients with MTLE, particularly in patients with dominant temporal lobe ictal onsets. The ideal structures for ablation and optimal ablation volume remain to be defined. Until the results of the Stereotactic Laser Ablation for Temporal Lobe Epilepsy trial—an ongoing, large prospective cohort study— are available, data presented by Wu et al provides some guidance on how to use LITT in patients medically refractory MTLE.

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