

# Laser Interstitial Thermal Therapy for Epilepsy



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## KEYWORDS

• Laser interstitial thermal therapy (LITT) • Epilepsy • Minimally invasive

## KEY POINTS

- Laser interstitial thermal therapy (LITT) has a diverse use in epilepsy.
- Offers a minimally invasive option attempting to limit approach-related comorbidity.
- Long-term data are yet lacking compared with open surgical data.

## INTRODUCTION

In recent years, laser interstitial thermal therapy (LITT) has emerged as an alternative to open surgery for many patients with drug-resistant epilepsy or neoplasm. Increasing neurosurgeon experience is creating potential for more widespread implementation for epilepsy management. The basic physical premise is that high-density light is converted to heat energy within the tissue of a confined and controllable region, monitored with magnetic resonance thermometry.

Advantages of LITT include a less-invasive approach with faster recovery, increased tissue preservation, the potential to recruit patients who might decline open surgery, and preserved ability to re-treat with either LITT or open surgery if needed. LITT may be particularly useful for areas of relatively high surgical risk or complexity, such as the insular targets. Nonetheless, surgical outcomes remain superior for some indications, and there is relatively little prospective or long-term data. For most indications, the preponderant publications remain based on small case series.

Use for treating epilepsy is unique in that the primary treatment endpoint may be either complete ablation of a lesion or functional disconnection. Specific focal lesions are numerous and include malformations of cortical development, low-grade neoplasms such as dysembryoplastic neuroepithelial tumor, hypothalamic hamartoma (HH), tubers, cavernous malformations, and temporal lobe encephaloceles. Functional disconnection is sought with temporal lobe epilepsy (TLE; either nonlesional or with mesial temporal lobe sclerosis [MTS]), corpus callosotomy, stereotactic electroencephalogram (sEEG)-positive/MRI-negative seizures, and encephalomalacia-related seizures.

A key consideration is that the treatment is ideally the result of a rigorous multidisciplinary evaluation. Neurologists serve a central role in the initial diagnosis, medical treatment optimization, semiology evaluation, and EEG interpretation. Neuroradiologists optimize and tailor anatomic and functional imaging protocols for diagnosis and procedure planning. Neurosurgeons synthesize this information to formulate and offer

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appropriate surgical treatment options. At our institution, complex cases are evaluated for procedure candidacy with a full review of all pertinent information by a multidisciplinary committee. A team approach during and after the procedure was also implemented. This article will review the key technical, clinical, radiologic, and neurosurgical considerations for LITT management of epilepsy, emphasizing the advantages of a multidisciplinary approach.

## **Background**

Thermal ablation with resultant necrosis and cytor-education is the primary mechanism used for LITT for epilepsy. However, other potential mechanisms are being explored for LITT more broadly, such as blood-brain barrier opening effects. According to the Arrhenius equation, tissue necrosis depends on temperature and time. In brief, necrosis does not occur less than 43°C and is instantaneous at 60°C. At 100°C, water vaporization and carbonization can result in tissue cavitation, referred to as a “steam event.”

Near real-time MR thermometry based on temperature-dependent features of MRI signal, typically with proton resonance frequency shift imaging,<sup>1</sup> permits the creation of heat maps and estimated cell damage maps during the procedure. Temperature-limit markers are strategically placed to avoid damage to nearby critical structures and to prevent vaporization in the hottest region.

Laser fibers are produced by 2 major vendors, each with unique designs, placement methods, ablation patterns, and cooling methods. These can be placed by a variety of standard stereotactic techniques. Also varying by vendor, laser applicators are available with varying diameters, laser wavelength, diffusing tip length, and power levels. Optical fiber diffusing tips are also available in isotropic or directional variants depending on the vendor. Specifics of available LITT equipment continue to evolve. Trajectory planning and placement are the key steps to a technically successful procedure.

## **DISCUSSION**

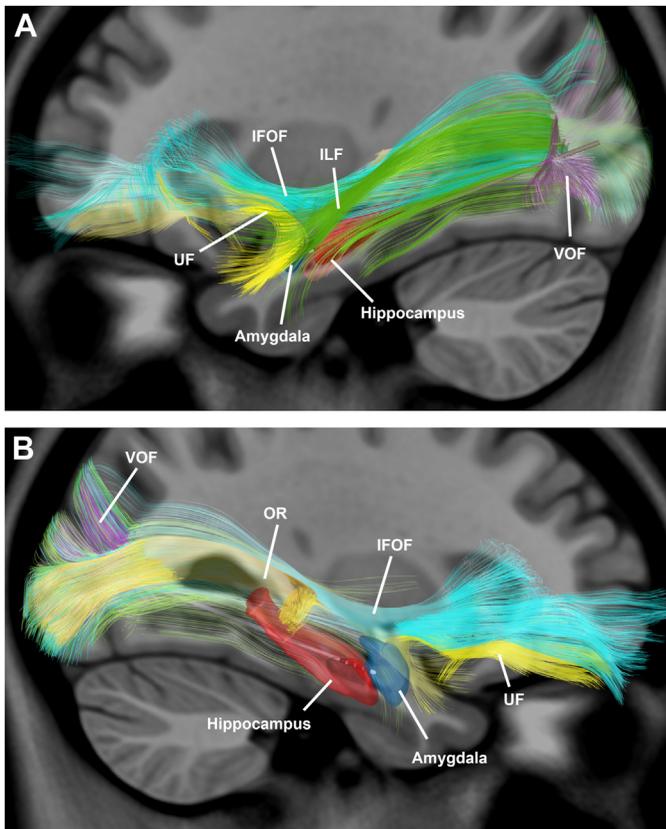
### **Temporal Lobe Epilepsy—Lesional**

TLE is one of the most common variants of focal epilepsy. Anterior temporal lobectomy (ATL) was reported as a surgical option in treating medically refractory temporal lobe epilepsy in 1950. Many still consider this the gold standard surgical treatment of TLE.<sup>2</sup> As techniques progressed, selective amygdalohippocampectomy was popularized for mesial temporal lobe epilepsy (MTLE) treatment. Compared with ATL, a selective amygdalohippocampectomy

leads to seizure-free outcomes that are within 10% of seizure-free rates of ATL.<sup>3</sup> However, visual field and verbal memory deficits with ATL seem greater than selective amygdalohippocampectomy (43% vs 31%).<sup>4</sup> The potential for effectiveness balances seizure freedom with the risk of “collateral damage” incurred by neocortical resection of the anterior temporal lobe.<sup>5</sup> MTS is the most common pathologic condition in patients with MTLE.<sup>6–10</sup> For treating patients with MTLE, many centers have transitioned from ATL and selective amygdalohippocampectomy to LITT. The surgical approach is typically performed by occipital insertion of the LITT catheter following an extraventricular trajectory along the long axis of the hippocampal formation (**Fig. 1** Hippo). Following this, the hippocampus and amygdala ablation is performed with concomitant MRI monitoring. Currently, there is no class I evidence to compare the efficacy and complication rates observed with selective laser amygdalohippocampectomy (SLAH) and ATL. However, there is currently enrolling a Medtronic Industry Sponsored study, Stereotactic Laser Ablation for Temporal lobe Epilepsy (SLATE), to provide level one evidence. Available literature from retrospective case series studies (Class III data) suggest an efficacy rate of SLAH that is comparable but slightly less than outcomes seen after ATL (38%–70%), whereas surgical complication rates for SLAH that are less than that for ATL.<sup>11–22</sup> Studies have suggested that LITT has resulted in a lower rate of neuropsychological deficits compared with traditional approaches. However, there may be no significant difference in postoperative visual field deficits.<sup>13,20–24</sup> A large analysis of 234 patients undergoing MRgLITT at multiple institutions found a hemorrhage rate of 1.5% with a rate of persistent neurological complications in 11% of patients (majority visual field deficits).<sup>25</sup> Studies have performed a volumetric analysis of patients undergoing MRgLITT and found no correlation between total ablation volume and seizure outcome. However, in patients with persistent seizures following SLAH, there may be an association of mesial hippocampal head sparing with persistent disabling seizures.<sup>13,20,21</sup> As there has been no significant correlation between length of ablation or volume of ablation and seizure freedom, there remains some controversy as to the ideal ablation. Depending on the curvature of the mesial temporal lobe structures, an adequate ablation could require multiple trajectories, as has been suggested by some studies.

### **Nonlesional temporal lobe epilepsy**

It is well recognized that nonlesional epilepsy has consistently demonstrated worse surgical outcomes than lesional epilepsy, making this an important area for improvement in our diagnostic



**Fig. 1.** hippo: T1-weighted sagittal images with MR tractography demonstrating the relevant tract anatomy for LITT ablation of the amygdalohippocampus. (A) Lateral projection showing the relationship of the inferior fronto-occipital fasciculus (IFOF; cyan), uncinate fasciculus (UF; yellow), inferior longitudinal fasciculus (ILF; green), and vertical occipital fasciculus (VOF; purple), which lie lateral to the hippocampus (red) and amygdala (blue). The UF, IFOF, and ILF may be transgressed in open approaches to resection the amygdala and hippocampus with potential for neurological consequence. (B) Medial projection also reveals the close association of these tracts plus the optic radiations (OR; light orange). The laser trajectory typically traverses these tracts but limits injury as opposed to open resection.

and surgical approaches.<sup>26</sup> The use of LITT as a surgical ablation strategy for epilepsy patients without an identifiable lesion detected on MRI is increasingly used because of lower morbidity than open resection. However, this technique requires a precise sEEG-mapped seizure onset to target in most cases. Further, the optimal extent of ablation around an sEEG-mapped seizure zone is unknown.

Laser ablation of the mesial temporal structures provides the largest reported experience with LITT for nonlesional epilepsy. Moreover, the reported rate of seizure freedom across studies using stereotactic laser amygdalohippocampectomy (SLAH) in cases without MTS is highly variable, ranging from 30% to 58%. In the largest series of SLAH procedures ( $n = 234$  patients), Wu and colleagues<sup>25</sup> found no significant differences in seizure freedom rate in those with imaging evidence of hippocampal sclerosis compared with those without after 24 months of follow-up. Additionally, across all patients, invasive intracranial monitoring was not associated with an improvement in seizure outcome, although the rate of intracranial monitoring in nonhippocampal sclerosis patients was not separately reported. In a

large single institution series of 58 SLAH patients, only 5/15 (33%) patients without MTS achieved Engel I outcomes after at least 12 months of follow-up.<sup>27</sup> This reported outcome was comparable to the 3 of 10 non-MTS patients achieving Engel I with mesial temporal LITT in a similar series of 21 patients.<sup>28</sup> The question of whether non-MTS patients who receive LITT benefit from preablation sEEG was recently addressed in a retrospective series. In this small study, Engel I was observed in 7 of 12 (58%) non-MTS mesial temporal lobe cases confirmed via sEEG, compared with 10 of 18 (56%) MTS cases with confirmatory sEEG, after 16 and 17 months of follow-up, respectively.<sup>29</sup> There is insufficient evidence to state that sEEG should be routinely used to tailor laser ablation whose semiology and scalp EEG are strongly right temporal in the nonlesional setting. However, both the Wu and colleagues<sup>25</sup> study of laser ablation and the recent Sone and colleagues<sup>30</sup> study reporting outcomes of open temporal lobectomy have associated the ablation and resection of specific hippocampal subregions with seizure outcome. Taken together, these data provide a conceptual basis by which sEEG could be used to interrogate tissue along the axis of the

hippocampus to tailor a laser ablation. Further standardization and study of hippocampal amygdalar network sEEG before LITT will be needed to determine its ability to improve outcomes in nonlesional cases.

### ***Extratemporal Nonlesional LITT***

The efficacy of LITT for MRI-negative nonlesional epilepsy is sparsely reported outside of the temporal lobe. Further, there is a lack of systematic description of the sEEG electrographic onset patterns associated with targets for LITT therapy in nonlesional patients. Outside of the mesial temporal lobe, LITT targeting electrographic seizure onsets in the insula and cingulate gyrus has been commonly reported, although most series do not report differential outcomes by anatomic region of seizure onset. Recently, Gupta and colleagues<sup>31</sup> described 35 patients with extratemporal epilepsy targeted by LITT, and of these, 6 (17%) were nonlesional. In this series, 33% of nonlesional patients achieved Engel I compared with 63% of lesional patients. Uniquely, this study captured electrographic seizure onset patterns from sEEG data in a subset of 24 patients (lesional and nonlesional). The authors found that low-voltage fast activity, a well-characterized sensitive biomarker of the epileptic cortex, was associated with improved LITT outcomes in both lesional and nonlesional cases. In another series of 20 patients with 70% nonlesional onsets, a small subset of 7% underwent LITT treatment immediately after the sEEG mapping.<sup>32</sup> Of these nonlesional patients, 55% achieved Engel I or II seizure outcomes at a mean of 17.2 months postop. Finally, Gireesh and colleagues<sup>33</sup> reported a series of 9 patients with nonlesional epilepsy mapped to the insula or cingulate. Five patients had LITT targeted at the insula alone, 3 at the cingulate alone, and operculum. In this series, 6 of 9 patients (66%) had Engel I, 2 of 9 Engel II, and 1 of 9 Engel III, respectively. As reported outcomes vary widely for nonlesional LITT, different strategies for seizure onset zone determination by epileptologist and neurosurgeons, and the extent of ablation remain potential sources of variability that may underlie differences in outcome across series.

LITT within eloquent areas such as the insula or near motor areas has a substantial advantage. It is helpful to monitor critical and nearby structures with low-temperature limits, typically around 43°C. These limits serve as posts to limit lesioning temperatures within, for instance, the internal capsule, extreme capsule, or motor cortex. Accordingly, LITT has been a beneficial strategy for treating lesions such as cavernomas within

these regions alternatively mapped cortical areas by sEEG that would benefit by reducing approach-related morbidity.

HHs are discussed in a separate article and therefore, not covered here.

### ***Corpus Callosotomy***

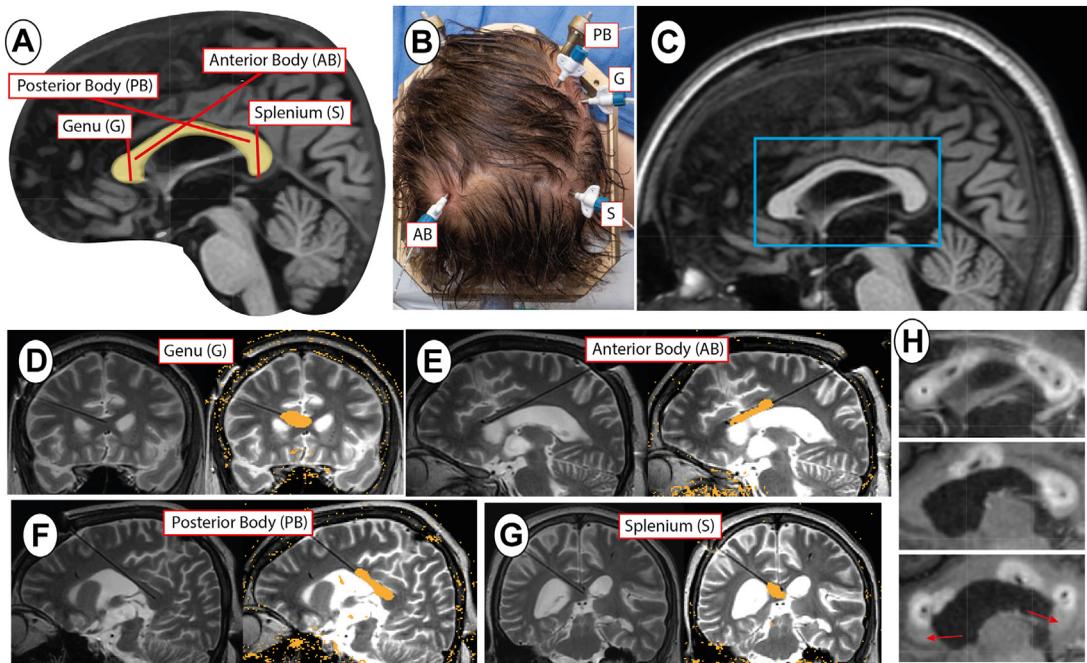
Corpus callosotomy is reserved for the most extreme cases of intractable epilepsy. The procedure involves disconnecting the 2 hemispheres by sectioning the corpus callosum. It is effective specifically for the therapy for drop attack seizures, both tonic and atonic.<sup>34</sup> This disconnection may produce a variety of side effects resulting from the inability of the 2 sides of the brain to coordinate cognition, sensory, or motor processing.<sup>35</sup> To mitigate these adverse effects, partial callosotomies sparing the anterior or posterior portions of the corpus callosum have been developed.<sup>36,37</sup> When performing these via an open craniotomy, there may be morbidity beyond the expected collateral syndromes created by isolating the hemispheres due to transgressing the scalp, skull, and dura, retracting a cerebral hemisphere, and manipulating vasculature. The advent of LIIT allows the surgeon to perform the callosotomy under MRI guidance and attempt to minimize morbidity.

Using up to 4 laser trajectories separately targeting the genu, the anterior body of the corpus callosum, the posterior body of the corpus callosum and isthmus, the splenium, and a complete corpus callosotomy may be performed minimally invasively (Fig. 2 CC).<sup>38</sup> Fewer trajectories are needed in many cases. However, this will depend on each patient's anatomy. A 2-trajectory laser intervention may effectively complete the full disconnection without reopening the prior craniotomy and dissecting through a scarred operative field for patients who have previously undergone a partial corpus callosotomy.<sup>39</sup>

### ***Neurologist Role***

The relationship between neurology and neurosurgery is arguably closer in epilepsy than in any other neurologic disease. Their combined efforts can dramatically change lives but individually neither can adequately care for patients with drug-resistant epilepsy. The neurologist's role is vital for setting up patients and neurosurgeons for success.

The most crucial role of the neurologist is confirming the diagnosis of epilepsy, the type of epilepsy, and for focal epilepsies, localizing seizure onset. Although this seems obvious, it bears mentioning as poor seizure characterization and



**Fig. 2.** CC: A 4-trajectory approach to laser corpus callosotomy. (A) Stereotypical trajectories for performing a complete interhemispheric disconnection, separately targeting the genu, anterior body, posterior body, and splenium. (B) Insertion sites for each trajectory. (C) The corpus callosum of the patient, with blue box indicating the location of the panels in (H). (D) Genu trajectory, showing the insertion on the left with the damage estimate in gold on the right. (E) As in (D) but for the anterior body trajectory. (F) As in (D) but for the posterior body trajectory. (G) As in (D) but for the splenium trajectory. (H) Postprocedure parasagittal sections through the corpus callosum, illustrating thermal ablation sites on a T1-weighted postcontrast MRI. Because ablations are ultimately produced in varying lateralities in the corpus callosum due to the angles of the trajectories required, multiple imaging views are needed to fully appreciate the complete ablation. Note that the most ventral aspect of both the genu and splenium are ablated at particular locations along the left-right traversal of their callosal fibers, though the nonablated portions of those same fibers will not have immediate postprocedure contrast enhancement (red arrows). This appearance could be misleading if the entire width of the corpus callosum is not evaluated.

localization prevent any chance of success with surgical interventions. Once seizures are characterized and localized, a risk assessment is performed to weigh the potential of seizure freedom against clinically significant deficits. This requires an informed seizure-onset hypothesis with input from anatomic, electrophysiologic, functional, and neuropsychologic data. Therefore, a multidisciplinary approach is mandatory, involving neurologists, neurosurgeons, neuroradiologists, and neuropsychologists.

The eventual intervention counseling is shared between the patient's neurologist and neurosurgeon. Communication between the neurologist and neurosurgeon must ensure consistent messaging with the patient. The neurologist counsels on the surgical option or options deemed appropriate and expected rates of seizure freedom or, if appropriate, palliation as well as the types of deficits and chances of their occurrence. The neurosurgeon is instrumental in

counseling on the performance of any offered procedure, limitations after surgery, expected recovery, and discussion of potential deficits. It is important to remember that surgery does not need to be completely without risk to be performed, only likely beneficial enough to outweigh the risks involved based on the anticipated change to the quality of life that surgery may provide. The patient ultimately determines this through an informed discussion of the risks and benefits.

Presurgical counseling from the neurologist is also essential to set expectations for postoperative antiseizure medication (ASM) management. Many patients undergo surgical evaluations with the goal of not just seizure freedom but also freedom from ASMs. Neurologist counseling ahead of surgery, and ideally at the start of the surgical evaluation, should be clear that the goal of any surgical intervention is to benefit seizure control but not necessarily eliminate medications. Patients on multiple

medications often can reduce doses and eliminate some ASMs over time following successful epilepsy surgery<sup>40,41</sup> but complete ASM removal is not a specific treatment aim.<sup>42</sup>

Immediately following surgery, the neurologist provides inpatient support for any necessary medical management. The neurologist also provides longitudinal follow-up with the timing based on the patient's epilepsy and potential needs. Although timing is not standardized, it is common to perform postoperative EEG over the months and years following surgery to help guide management and assist in prognosis, although data on its utility is mixed.<sup>43,44</sup> Postoperative neuropsychology testing should also be performed within the first 6 to 12 months after surgery to document any new "baseline" cognitive changes compared with preoperative functioning. The decision to reduce or stop ASMs over time can be made at the neurologist's and patient's discretion based on shared decision-making. Early versus late reductions may not alter the overall likelihood of seizure freedom but earlier recurrence may be more likely with earlier reductions.<sup>40</sup>

### **Neuroradiology Considerations**

Neuroradiology plays a central role in the preoperative, operative, and follow-up phases of care for patients undergoing LITT. Preoperative imaging generally consists of standard seizure protocol MRI examinations and potentially single-photon emission computerized tomography (SPECT). An MRI examination should include volumetric images with high spatial resolution and sequences tailored to assess subtle findings. The primary purpose of the initial examination is diagnostic, which should include contrast. High-resolution sequences highlighting gray-white differentiation, such as double inversion recovery or edge enhancing gradient echo, help detect subtle malformations of cortical development (MCDs) that may not be identifiable on other sequences. However, it may also be used for fusion with subsequent nuclear medicine examinations or neurosurgical procedural planning.

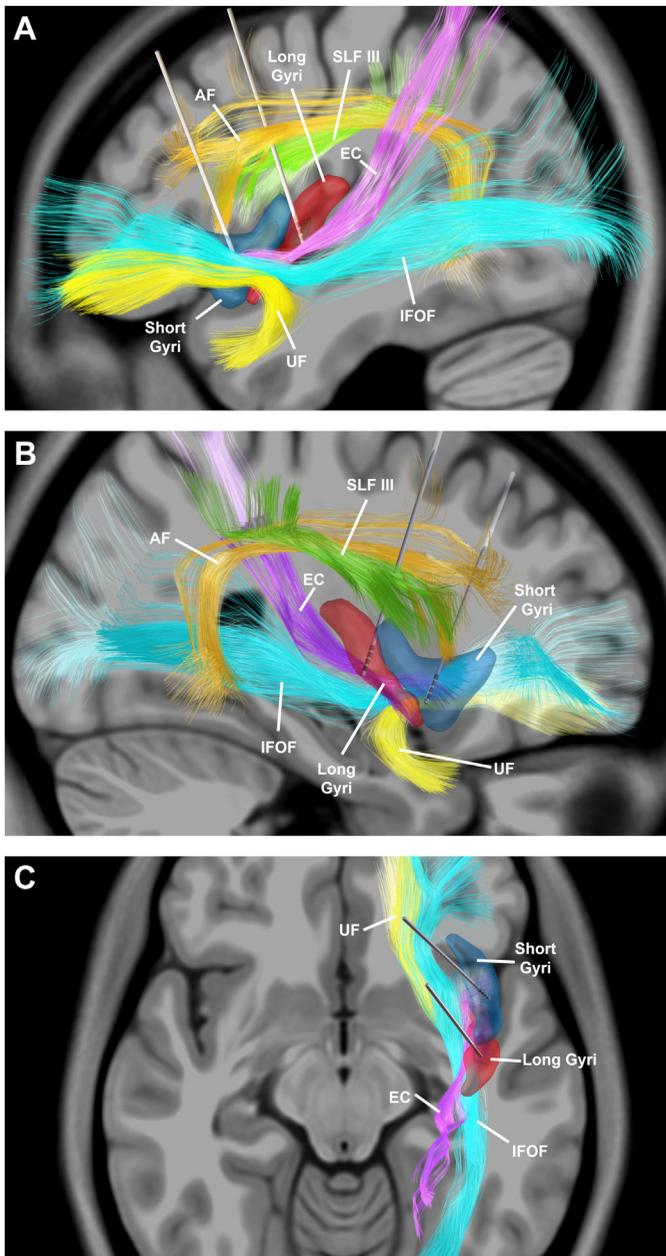
Scrutiny of images for subtle abnormalities such as peri-insular MCDs, subtle MTS, dual pathologic condition, and temporal lobe encephalocoeles is critical. When these become available, some findings are only confidently detectable on rereview in the context of nuclear medicine, semiology, and electrophysiologic data.

Additional advanced imaging may be useful for select cases, such as 7 Tesla imaging, diffusion tensor imaging (DTI) with tractography, fluorodeoxyglucose (FDG)-positron emission tomography

(PET)/MRI, or functional MRI (fMRI). For example, delineation of the white matter tracts near the insula, such as the arcuate fasciculus with tractography for a left-sided (language dominant) peri-insular ablation planning (Fig. 3 Insula). The neurosurgeon should be aware that the depicted results of advanced functional imaging methods such as fMRI and DTI with tractography depend on numerous technical and user-dependent parameters. The precise depicted border of white matter tract streamlines, or BOLD activity cannot be assumed to be discrete ground-truth borders. False negatives and false positives occur in all such advanced or mechanistic MRI techniques. This distinction is critical in LITT, as opposed to open, awake craniotomy, where extensive intraoperative mapping can be performed to validate fMRI and tractography findings further. A low threshold for in-person discussion with the neuroradiologist is prudent.

Intraoperative imaging requires stereotactic planning, ablation monitoring, and immediate postablation assessment. Stereotactic images with contrast (MRI or computerized tomography [CT]) are used to plan the trajectories and predicted ablation regions. Routes are selected to avoid blood vessels or pre-existing postoperative material and minimize the traversal of sulci and ventricles. There are several additional case-specific or pathology-specific considerations. For example, it is useful to review any advanced imaging performed, such as tractography for trajectories or target areas near eloquent areas; if this is unavailable, detailed knowledge of the expected location of key functional areas of the cerebral cortex as well as white matter tracts on high-resolution anatomic imaging is invaluable.<sup>45</sup> For cavernous malformations, delineating of any associated developmental venous anomalies is useful. For sEEG+/MRI cases, the correlation of planned targets to sEEG lead positions and implicated contacts is vital.

Once the laser fiber(s) are placed, intraoperative MRI is required to confirm fiber position and exclude significant hematoma. The planes and sequences used to monitor ablation are optimized to sequentially depict each fiber's extent of ablation and vulnerable anatomy. During the laser activation for each trajectory, MR thermometry allows near real-time assessment of tissue temperature and an estimated ablation zone with thermal damage threshold lines. One can monitor in 1 to 3 planes; however, as more planes are added, the update time makes the monitoring less "real-time." Low-temperature limits are placed on vulnerable anatomy (eg, 43°C–48°C), and high-temperature limits (eg, 90°C) are set near the laser fiber diffusing tip to surveil for excessive heating or



**Fig. 3.** *Insula: T1-weighted sagittal images with MR tractography demonstrating the relevant tract anatomy for LITT ablation of the insula.* Sagittal T1-weighted imaging from the (A) lateral and (B) medial projections shows the relationship of the long (red) and short (blue) gyri with the arcuate fasciculus (AF; light orange), superior longitudinal fasciculus part III (SLF III; green), extreme capsule (EC; purple), inferior fronto-occipital fasciculus (IFOF; cyan), and uncinate fasciculus (UF; yellow). The UF and IFOF traverse the ventral aspect of the claustrum and EC. (C) Axial projection with AF and SLF III removed showing the relationship of UF, EC, and IFOF with the insula.

catheter fracture. Commonly protected structures such as the optic tracts or lateral geniculate nucleus can be more difficult to visualize directly on intraoperative imaging, requiring firm knowledge of cross-sectional anatomy to identify confidently. The treating surgeon must constantly visually monitor the heating during each laser ablation to surveil for vapor events should the heating increase more than 100°C. The laser should be immediately turned off. Because PRFS MR thermometry is gradient echo-based, it is important

to recognize causes of susceptibility artifacts that may degrade the thermometry, such as blood products (commonly postbiopsy or cavernous malformation) or proximity of the skull base. Lesions that are superficial in the brain may be difficult to evaluate with MR thermometry during LITT if an artifact from a titanium skull anchor bolt is near.

Immediate postprocedure diagnostic imaging with the laser fiber(s) in place helps assess the extent of ablation. Multiple zones of the ablated region have

been described. The primary consideration is whether the edge of ablation adequately addresses the lesion or target anatomy for disconnection. This edge is seen as rim enhancement on postgadolinium T1-weighted imaging, T2-weighted FLAIR hyperintensity, and a rim of restricted diffusion surrounding a necrotic core with facilitated diffusion. Recent postablation imaging analyses have suggested that the patients with increased apparent diffusion coefficient (ADC) intensity values on postablation imaging have improved seizure reduction rates after mesial temporal LITT.

The exact evolution of imaging findings over time can vary. Generally, peri-lesional edema increases with a peak around 1 to 3 days and can persist for weeks.<sup>46</sup> Peripheral enhancement persists for months with eventual involution. The volume of ablation can temporarily increase after ablation of focal lesions with subsequent involution and resolution of enhancement, although this is better described for the treatment of neoplasms.<sup>47</sup> One systematic review found that the size of cavernous malformations decreased by 59% on average.<sup>48</sup> Follow-up may also be useful to monitor for recurrence or new lesions when applicable. Downstream effects of network disruption may also indicate successful ablation in some applications, such as a greater decrease in ipsilateral mammillary body size after ablation of the hippocampus in patients with seizure freedom.<sup>22</sup> DTI and tractography might also be useful to directly assess such connectivity changes, although limited data are currently available.<sup>49</sup> In a small series where 4 patients had DTI performed before and after completion of callosotomy, crossing fibers persisted on postop day diffusion imaging in 3 of 4 despite intraoperative imaging demonstrating contrast extravasation in the intended region of the residual corpus callosum. In one patient, no crossing fibers were predicted on postop day one imaging but was detectable on follow-up imaging. Thus, the relationship between the region of LITT lesioning as predicted by intraoperative contrast enhancement and subsequent disconnection gauged by DTI still needs to be fully understood, and further research will be required to identify imaging sequences ideal for the prediction of durable functional disconnection.

A special-case consideration is planning and performing a case in the setting of an implanted medical device such as responsive Neurostimulation (RNS) or vagal nerve stimulation (VNS). Consultation with the radiology MRI safety team, including medical physicists, is imperative. The team can help determine if the procedure can be safely performed (typically at 1.5 Tesla) with a device in place or pulled back or if device removal

would be needed. Additionally, tests can be performed to predict the likely extent and degree of resultant artifact in the areas of interest. This process also helps guide appropriate informed consent. Limited reports of LITT in the setting of implanted devices are available.<sup>50</sup>

### **Neuropsychology considerations**

Neuropsychological assessment is an important component of a comprehensive presurgical epilepsy evaluation. Current recommendations for neuropsychological assessment include administering objective and subjective measures of cognition, emotional, psychosocial, and adaptive functioning.<sup>51</sup> The neuropsychological evaluation provides a cognitive baseline, can help lateralize and localize various cognitive functions, and inform the risk of proposed surgical intervention. In addition, neuropsychological assessment can identify any health-related concerns or psychiatric comorbidities that may need to be addressed preoperatively and/or postoperatively because untreated symptoms of depression and anxiety can influence the quality of life independent of seizure control.<sup>52</sup>

From a cognitive perspective, LITT offers a promising alternative to traditional open resection, such as ATL. Early studies suggest that LITT is associated with fewer postoperative deficits in naming, verbal fluency, and object recognition measures compared with open resection.<sup>12,23</sup> Although there is still the risk of verbal memory decline with LITT in the dominant temporal lobe, there is some evidence of improved memory outcomes. However, research is still ongoing, and further studies with larger samples are needed.<sup>23,53</sup> One critical consideration for surgical planning is whether there are structural abnormalities on neuroimaging because an earlier case study suggests patients with MRI-negative epilepsy may be more likely to experience memory decline following LITT, although this was not replicated in another independent sample.<sup>21,54</sup> Interestingly, a recent study by Kanner and colleagues<sup>55</sup> demonstrated that some patients with preexisting mood and anxiety disorders had improved symptoms following LITT. Furthermore, those with reduced anxiety and depression postoperatively achieved better seizure control. Additionally, in 2 patients with refractory posttraumatic MTLE and post-traumatic stress disorder (PTSD), the amygdala in the ablation zone reduced PTSD-associated psychiatric symptoms, suggesting that tailoring LITT targeting may have the ability to reduce seizures as well as ameliorate common comorbidities (REF 32259241). These studies provide early but encouraging evidence that LITT offers an alternative to open resection that may reduce cognitive morbidity and improve functional outcomes.

Whether patients pursue LITT or open resection, it is critical to consider individual patient characteristics during surgical planning and counseling. No procedure is entirely without risk, and patients have varying risk aversions. It is particularly important to consider each patient's cognitive abilities and level of functioning during the shared decision-making process because previous study shows that those with higher baseline functioning are more likely to experience a decline.<sup>56</sup> Finally, postoperative monitoring is necessary to identify any decline or changes in functional status to facilitate appropriate referrals for additional treatment, such as cognitive rehabilitation or psychotherapy.<sup>51</sup>

## SUMMARY

Other forms of thermal ablation are beginning to be used more frequently, such as radiofrequency (RF) and MR-guided ultrasound. However, LITT in epilepsy is by far the most used of these in the United States. Europe, however, has had success historically with RF ablation, and currently, LITT is becoming more popular in areas outside the United States. Because LITT ablations are “tailored” resections that are markedly smaller than what typically occurs in open resections, their seizure freedom rates currently tend to be 10% to 20% less than standard open procedures. From a patient perspective, therapies such as LITT with significantly lower side effect profiles, despite their comparably modest seizure reduction, may render comparable larger improvements in quality from seizure reduction because these gains are not tempered by the quality of life debits from treatment-associated morbidities.<sup>57</sup> However, this is matched by reduced side effects from surgery and fewer complications, which is invaluable to the individual patient. As we improve the targeting of LITT by further studying our interventions at this time and developing ways to improve our tailored techniques with LITT, we hope to find an excellent balance eliminating of seizures with fewer overall complications.

## CLINICS CARE POINTS

- LITT has a prominent role in MTLT as a minimally invasive effective technique that may improve patient verbal memory outcomes compared to open selective approaches.
- LITT has an emerging role in corpus callosotomy; however, long-term efficacy has not been proven.

## DISCLOSURES

*J.J. Van Gompel M.D:* named inventor for intellectual property licensed to Cadence Neuroscience Inc, which is coowned by Mayo Clinic; Investigator for the Medtronic EPAS trial, SLATE trial, and Mayo Clinic Medtronic NIH Public Private Partnership (UH3-NS95495), also with consulting contract; Stock Ownership and Consulting Contract with Neuro-One Inc.; site Primary Investigator in the Polyganics ENCASE II trial; Site Primary Investigator in the NXDC Gleolan Men301 trial; Site Primary Investigator in the Insightec MRgUS EP001 trail. *E.H. Middlebrooks MD:* consultant for Boston Scientific Corp. and Varian Medical Systems, Inc.; receives research funding from Varian Medical Systems. and Vigil Neuroscience, Inc. *D.B. Burkholder MD;* *J.J. Parker MD, PhD;* *S.S. Grewal MD;* *V.T. Lehman MD;* *K.J. Miller MD, PhD;* *E.C. Alden PhD;* and *T.J. Kaufmann MD, MS.*

## REFERENCES

1. Blackwell J, Kraśny MJ, O'Brien A, et al. Proton resonance frequency shift thermometry: a review of modern clinical practices. *J Magn Reson Imaging* 2022;55(2):389–403.
2. Penfield W, Flanigin H. The surgical therapy of temporal lobe seizures. *Trans Am Neurol Assoc* 1950; 51:146–9.
3. Josephson CB, Dykeman J, Fiest KM, et al. Systematic review and meta-analysis of standard vs selective temporal lobe epilepsy surgery. *Neurology* 2013;80(18):1669–76.
4. Helmstaedter C. Temporal lobe resection—does the prospect of seizure freedom outweigh the cognitive risks? *Nat Clin Pract Neurol* 2008;4(2): 66–7.
5. Drane DL, Ojemann GA, Aylward E, et al. Category-specific naming and recognition deficits in temporal lobe epilepsy surgical patients. *Neuropsychologia* 2008;46(5):1242–55.
6. Gastaut H, Gastaut J, Silva GE, et al. Relative frequency of different types of epilepsy: a study employing the classification of the International League Against Epilepsy. *Epilepsia* 1975;16(3): 457–61.
7. Labate A, Ventura P, Gambardella A, et al. MRI evidence of mesial temporal sclerosis in sporadic “benign” temporal lobe epilepsy. *Neurology* 2006; 66(4):562–5.
8. Kim WJ, Park SC, Lee SJ, et al. The prognosis for control of seizures with medications in patients with MRI evidence for mesial temporal sclerosis. *Epilepsia* 1999;40(3):290–3.
9. Kurita T, Sakurai K, Takeda Y, et al. Very long-term outcome of non-surgically treated patients with

- temporal lobe epilepsy with hippocampal sclerosis: a retrospective study. *PLoS one* 2016;11(7): e0159464.
10. Picot MC, Baldy-Moulinier M, Daurès JP, et al. The prevalence of epilepsy and pharmaco-resistant epilepsy in adults: a population-based study in a Western European country. *Epilepsia* 2008;49(7):1230–8.
  11. Gross RE, Willie JT, Drane DL. The role of stereotactic laser amygdalohippocampotomy in mesial temporal lobe epilepsy. *Neurosurg Clin N Am* 2016; 27(1):37–50.
  12. Drane DL, Loring DW, Voets NL, et al. Better object recognition and naming outcome with MRI-guided stereotactic laser amygdalohippocampotomy for temporal lobe epilepsy. *Epilepsia* 2015;56(1): 101–13.
  13. Jermakowicz WJ, Kanner AM, Sur S, et al. Laser thermal ablation for mesiotemporal epilepsy: analysis of ablation volumes and trajectories. *Epilepsia* 2017;58(5):801–10.
  14. Kang JY, Wu C, Tracy J, et al. Laser interstitial thermal therapy for medically intractable mesial temporal lobe epilepsy. *Epilepsia* 2016;57(2): 325–34.
  15. Waseem H, Osborn KE, Schoenberg MR, et al. Laser ablation therapy: An alternative treatment for medically resistant mesial temporal lobe epilepsy after age 50. *Epilepsy Behav* : E&B 2015;51:152–7.
  16. Petit GT, Wharen RE, Feyissa AM, et al. The impact of stereotactic laser ablation at a typical epilepsy center. *Epilepsy Behav* 2018;78:37–44.
  17. Xue F, Chen T, Sun H. Postoperative outcomes of magnetic resonance imaging (mri)-guided laser interstitial thermal therapy (LITT) in the treatment of drug-resistant epilepsy: a meta-analysis. *Med Sci Monit* 2018;24:9292–9.
  18. Tatum WO, Thottempudi N, Gupta V, et al. De novo temporal intermittent rhythmic delta activity after laser interstitial thermal therapy for mesial temporal lobe epilepsy predicts poor seizure outcome. *Clin Neurophysiol* 2019;130(1):122–7.
  19. Le S, Ho AL, Fisher RS, et al. Laser interstitial thermal therapy (LITT): seizure outcomes for refractory mesial temporal lobe epilepsy. *Epilepsy Behav* 2018;89:37–41.
  20. Grewal SS, Zimmerman RS, Worrell G, et al. Laser ablation for mesial temporal epilepsy: a multi-site, single institutional series. *J Neurosurg* 2018;1–8. <https://doi.org/10.3171/2018.2.JNS171873>.
  21. Donos C, Breier J, Friedman E, et al. Laser ablation for mesial temporal lobe epilepsy: surgical and cognitive outcomes with and without mesial temporal sclerosis. *Epilepsia* 2018;59(7):1421–32.
  22. Grewal SS, Gupta V, Vibhute P, et al. Mammillary body changes and seizure outcome after laser interstitial thermal therapy of the mesial temporal lobe. *Epilepsy Res* 2018;141:19–22.
  23. Drane DL. MRI-Guided stereotactic laser ablation for epilepsy surgery: promising preliminary results for cognitive outcome. *Epilepsy Res* 2018;142:170–5.
  24. Jermakowicz WJ, Ivan ME, Cajigas I, et al. Visual deficit from laser interstitial thermal therapy for temporal lobe epilepsy: anatomical considerations. *Oper Neurosurg (Hagerstown)* 2017;13(5):627–33.
  25. Wu C, Jermakowicz WJ, Chakravorti S, et al. Effects of surgical targeting in laser interstitial thermal therapy for mesial temporal lobe epilepsy: A multicenter study of 234 patients. *Epilepsia* 2019;60(6): 1171–83.
  26. Téllez-Zenteno JF, Hernández Ronquillo L, Moien-Afshari F, et al. Surgical outcomes in lesional and non-lesional epilepsy: a systematic review and meta-analysis. *Epilepsy Res* 2010;89(2–3):310–8.
  27. Gross RE, Stern MA, Willie JT, et al. Stereotactic laser amygdalohippocampotomy for mesial temporal lobe epilepsy. *Ann Neurol* 2018;83(3):575–87.
  28. Tao JX, Wu S, Lacy M, et al. Stereotactic EEG-guided laser interstitial thermal therapy for mesial temporal lobe epilepsy. *J Neurol Neurosurg Psychiatr* 2018;89(5):542–8.
  29. Youngerman BE, Oh JY, Anbarasan D, et al. Laser ablation is effective for temporal lobe epilepsy with and without mesial temporal sclerosis if hippocampal seizure onsets are localized by stereoelectroencephalography. *Epilepsia* 2018;59(3):595–606.
  30. Sone D, Ahmad M, Thompson PJ, et al. Optimal surgical extent for memory and seizure outcome in temporal lobe epilepsy. *Ann Neurol* 2022;91(1):131–44.
  31. Gupta K, Cabaniss B, Kheder A, et al. Stereotactic MRI-guided laser interstitial thermal therapy for extratemporal lobe epilepsy. *Epilepsia* 2020;61(8): 1723–34.
  32. Perry MS, Donahue DJ, Malik SI, et al. Magnetic resonance imaging-guided laser interstitial thermal therapy as treatment for intractable insular epilepsy in children. *J Neurosurg Pediatr* 2017;20(6):575–82.
  33. Gireesh ED, Lee K, Skinner H, et al. Intracranial EEG and laser interstitial thermal therapy in MRI-negative insular and/or cingulate epilepsy: case series. *J Neurosurg* 2020;1–9. <https://doi.org/10.3171/2020.7.Jns201912>.
  34. Graham D, Tisdall MM, Gill D. Corpus callosotomy outcomes in pediatric patients: a systematic review. *Epilepsia* 2016;57(7):1053–68.
  35. Jea A, Vachhrajani S, Widjaja E, et al. Corpus callosotomy in children and the disconnection syndromes: a review. *Childs Nerv Syst* 2008;24(6):685–92.
  36. Oguni H, Olivier A, Andermann F, et al. Anterior callosotomy in the treatment of medically intractable epilepsies: a study of 43 patients with a mean follow-up of 39 months. *Ann Neurol* 1991;30(3): 357–64.
  37. Paglioli E, Martins WA, Azambuja N, et al. Selective posterior callosotomy for drop attacks: a new

- approach sparing prefrontal connectivity. *Neurology* 2016;87(19):1968–74.
38. Miller KJ, Fine AL. Decision-making in stereotactic epilepsy surgery. *Epilepsia* 2022. <https://doi.org/10.1111/epi.17381>.
  39. Ho AL, Miller KJ, Cartmell S, et al. Stereotactic laser ablation of the splenium for intractable epilepsy. *Epilepsy Behav Case Rep* 2016;5:23–6.
  40. Yardi R, Irwin A, Kayyali H, et al. Reducing versus stopping antiepileptic medications after temporal lobe surgery. *Ann Clin Transl Neurol* 2014;1(2):115–23.
  41. Lamberink HJ, Otte WM, Blümcke I, et al. Seizure outcome and use of antiepileptic drugs after epilepsy surgery according to histopathological diagnosis: a retrospective multicentre cohort study. *Lancet Neurol* 2020;19(9):748–57.
  42. Parker JJ, Zhang Y, Fatemi P, et al. Antiseizure medication use and medical resource utilization after resective epilepsy surgery in children in the United States: a contemporary nationwide cross-sectional cohort analysis. *Epilepsia* 2022;63(4):824–35.
  43. Hodges S, Goldenholz DM, Sato S, et al. Postoperative EEG association with seizure recurrence: analysis of the NIH epilepsy surgery database. *Epilepsia Open* 2018;3(1):109–12.
  44. Rathore C, Wattamwar PR, Baheti N, et al. Optimal timing and differential significance of postoperative awake and sleep EEG to predict seizure outcome after temporal lobectomy. *Clin Neurophysiol* 2018;129(9):1907–12.
  45. Kaufmann TJ, Lehman VT, Wong-Kisiel LC, et al. The utility of diffusion tractography for speech preservation in laser ablation of the dominant insula: illustrative case. *J Neurosurg Case Lessons* 2021;1(19):Case21113.
  46. Schwabe B, Kahn T, Harth T, et al. Laser-induced thermal lesions in the human brain: short- and long-term appearance on MRI. *J Comput Assist Tomogr* 1997;21(5):818–25.
  47. Alattar AA, Bartek J Jr, Chiang VL, et al. Stereotactic laser ablation as treatment of brain metastases recurring after stereotactic radiosurgery: a systematic literature review. *World Neurosurg* 2019;128:134–42.
  48. Yousefi O, Sabahi M, Malcolm J, et al. Laser interstitial thermal therapy for cavernous malformations: a systematic review. *Front Surg* 2022;9:887329.
  49. Huang Y, Yecies D, Bruckert L, et al. Stereotactic laser ablation for completion corpus callosotomy. *J Neurosurg Pediatr* 2019;1–9. <https://doi.org/10.3171/2019.5.Peds19117>.
  50. Buch VP, Mirro EA, Purger DA, et al. Magnetic resonance imaging-guided laser interstitial thermal therapy for refractory focal epilepsy in a patient with a fully implanted RNS system: illustrative case. *J Neurosurg Case Lessons* 2022;3(21):Case22117.
  51. Baxendale S, Wilson SJ, Baker GA, et al. Indications and expectations for neuropsychological assessment in epilepsy surgery in children and adults: Executive summary of the report of the ILAE Neuropsychology Task Force Diagnostic Methods Commission: 2017–2021. *Epilepsia* 2019;60(9):1794–6.
  52. Hamid H, Blackmon K, Cong X, et al. Mood, anxiety, and incomplete seizure control affect quality of life after epilepsy surgery. *Neurology* 2014;82(10):887–94.
  53. Gross RE, Mahmoudi B, Riley JP. Less is more: novel less-invasive surgical techniques for mesial temporal lobe epilepsy that minimize cognitive impairment. *Curr Opin Neurol* 2015;28(2):182–91.
  54. Dredla BK, Lucas JA, Wharen RE, et al. Neurocognitive outcome following stereotactic laser ablation in two patients with MRI-/PET+ mTLE. *Epilepsy Behav* 2016;56:44–7.
  55. Kanner AM, Irving LT, Cajigas I, et al. Long-term seizure and psychiatric outcomes following laser ablation of mesial temporal structures. *Epilepsia* 2022;63(4):812–23.
  56. Helmstaedter C. Cognitive outcomes of different surgical approaches in temporal lobe epilepsy. *Epileptic Disord* 2013;15(3):221–39.
  57. Mahajan UV, Parker JJ, Williams NR, et al. Adjunctive repetitive transcranial magnetic stimulation delivers superior quality of life for focal epilepsy compared to anti-epileptic drugs: a meta-analytic utility prediction study. *Brain Stimul* 2020;13(2):430–2.