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Long-term Outcomes of Mesial Temporal Laser Interstitial Thermal Therapy for Drug-Resistant Epilepsy and Subsequent Surgery for Seizure Recurrence: A Multi-center Cohort Study

Brett E. Youngerman[1], **Matei A. Banu**[1], **Farhan Khan**[1], **Guy M. McKhann**[1], **Catherine A. Schevon**[2], **Jonathan R. Jagid**[3], **Iahn Cajigas**[4], **Christian B. Theodotou**[3], **Andrew Ko**[5], **Robert Buckley**[5], **Jeffrey G. Ojemann**[5], **John W. Miller**[6], **Adrian W. Laxton**[7], **Daniel E. Couture**[7], **Gautam S. Popli**[8], **Vivek P. Buch**[9], **Casey H. Halpern**[4], **Scheherazade Le**[10], **Ashwini D. Sharan**[11], **Michael R. Sperling**[12], **Ashesh D. Mehta**[13], **Dario J. Englot**[14], **Joseph S. Neimat**[15], **Peter E. Konrad**[14], **Sameer A. Sheth**[16], **Elliot G. Neal**[17], **Fernando L. Vale**[18], **Kathryn L. Holloway**[19], **Ellen L. Air**[20], **Jason M. Schwalb**[20], **Pierre-François D'Haese**[21], **Chengyuan Wu**[11]

[1]Department of Neurological Surgery, Columbia University Medical Center, New York, New York, USA

[2]Department of Neurology, Columbia University Medical Center, New York, New York, USA

[3]Department of Neurological Surgery, Jackson Memorial Hospital, University of Miami, Miami, Florida, USA

[4]Department of Neurological Surgery, Perelman School of Medicine at the University of Pennsylvania, Philadelphia, Pennsylvania, USA

[5]Department of Neurological Surgery, Harborview Medical Center, University of Washington, Seattle, Washington, USA

[6]Department of Neurology, Harborview Medical Center, University of Washington, Seattle, Washington, USA

[7]Department of Neurological Surgery, Wake Forest University School of Medicine, Winston-Salem, North Carolina, USA

[8]Department of Neurology, Wake Forest University School of Medicine, Winston-Salem,North Carolina, USA

[9]Department of Neurological Surgery, Stanford Neuroscience Health Center, Stanford, California, USA

[10]Department of Neurology, Stanford Comprehensive Epilepsy Center, Stanford, California, USA

Corresponding Author: Brett E. Youngerman, MD, MS, Assistant Professor of Neurological Surgery, The Neurological Institute of New York, Columbia University Irving Medical Center, 710 West 168th Street, 4th Floor, New York, NY 10032, Telephone: (646) 317-2887, Fax: (212) 305-2026, bey2103@cumc.columbia.edu.

Competing Interests: Several centers that contributed data to this study are sites in the Stereotactic Laser Ablation for Temporal Lobe Epilepsy (SLATE) study (NCT02844465) sponsored by Medtronic (Minneapolis, Minnesota, USA). Procedures reported here precede any enrollment in SLATE. This study was not industry sponsored. Dr. Sharan is Chief Medical Officer Medtronic Neuromodulation Operating Unit.

[11]Department of Neurological Surgery, Vickie and Jack Farber Institute for Neuroscience, Thomas Jefferson University, Philadelphia, Pennsylvania, USA

[12]Department of Neurology, Vickie and Jack Farber Institute for Neuroscience, Thomas Jefferson University, Philadelphia, Pennsylvania, USA

[13]Department of Neurological Surgery, Zucker School of Medicine at Hofstra Northwell, Hempstead, New York, USA

[14]Department of Neurological Surgery, Vanderbilt University, Nashville, Tennessee, USA

[15]Department of Neurological Surgery, University of Louisville, Louisville, Kentucky, USA

[16]Department of Neurological Surgery, Baylor College of Medicine, Houston, Texas, USA

[17]Department of Neurological Surgery, University of South Florida Health South Tampa Center, Tampa, Florida, USA

[18]Department of Neurological Surgery, Medical College of Georgia-Augusta University, Augusta, Georgia, USA

[19]Department of Neurological Surgery, Virginia Commonwealth University, Richmond, Virginia, USA

[20]Department of Neurological Surgery, Henry Ford Health, Detroit, Michigan, USA

[21]Rockefeller Neuroscience Institute, West Virginia University, Morgantown, West Virginia, USA

Abstract

Background—Magnetic resonance-guided laser interstitial thermal therapy (MRgLITT) is a minimally invasive alternative to surgical resection for drug-resistant mesial temporal lobe epilepsy (mTLE). Reported rates of seizure freedom are variable and long-term durability is largely unproven. Anterior temporal lobectomy (ATL) remains an option for patients with MRgLITT treatment failure. However, the safety and efficacy of this staged strategy is unknown.

Methods—This multicenter, retrospective cohort study included 268 patients consecutively treated with mesial temporal MRgLITT at 11 centers between 2012–2018. Seizure outcomes and complications of MRgLITT and any subsequent surgery are reported. Predictive value of preoperative variables for seizure outcome was assessed.

Results—Engel I seizure freedom was achieved in 55.8% (149/267) at 1 year, 52.5% (126/240) at 2 years, and 49.3% (132/268) at last follow-up ≥1 year (median 47 months). Engel I or II outcomes were achieved in 74.2% (198/267) at 1 year, 75.0% (180/240) at 2 years, and 66.0% (177/268) at last follow-up. Preoperative focal to bilateral tonic-clonic seizures were independently associated with seizure recurrence. Among patients with seizure recurrence, 14/21 (66.7%) became seizure free after subsequent ATL and 5/10 (50%) after repeat MRgLITT at last follow-up ≥1 year.

Conclusions—MRgLITT is a viable treatment with durable outcomes for patients with drug-resistant mTLE evaluated at a comprehensive epilepsy center. Although seizure freedom rates were lower than with ATL, this series represents the early experience of each center and a

heterogeneous cohort. ATL remains a safe and effective treatment for well-selected patients who fail MRgLITT.

Keywords

Epilepsy, Temporal Lobe [C10.228.140.490.360.290]; Laser Therapy [E02.594]; Drug Resistant Epilepsy [C10.228.140.490.125]; Anterior Temporal Lobectomy [E04.043]; Surgical Procedures, Operative [E04]

INTRODUCTION

Temporal lobe epilepsy is the most common form of focal drug resistant epilepsy (DRE).(1) Open surgical resection with anterior temporal lobectomy (ATL) is the gold-standard treatment, supported by 2 class I clinical trials(2,3) and numerous studies demonstrating 60–80% seizure freedom with 2-year follow up.(2–4) However, epilepsy surgery remains underutilized(5,6) in part due to concerns regarding its invasiveness and the risk of neurocognitive deficits.(6) Several approaches to selectively resect the amygdalohippocampal complex and adjacent mesial structures have been developed, but these technique nonetheless require open surgery, rates of seizure freedom appear lower than with ATL,(4) and neurocognitive benefits have been variable,(7–9) likely due to persistent disruption of overlying cortex or white matter en route to the mesial structures. Less invasive approaches, including stereotactic radiosurgery and radiofrequency ablation, have had disappointing outcomes and not been widely adopted.(10)

Magnetic resonance image-guided laser interstitial thermal therapy (MRgLITT) is growing in popularity as a minimally invasive alternative to open surgical resection for drug-resistant mesial temporal lobe epilepsy (mTLE).(5,11) MRgLITT allows immediate, well-demarcated ablation of the deep mesial structures with minimal disruption of the overlying lateral temporal neocortex and white matter. Several studies suggest MRgLITT yields favorable neurocognitive outcomes.(10,12–15) Real-time MR thermometry minimizes the risk of heat injury to surrounding structures. The procedure is performed via an incision less than 1cm; patients typically have minimal pain and go home the first postoperative day. There is growing evidence in support of the safety and efficacy of MRgLITT for epilepsy and mesial temporal ablation is the most widely reported application.(10,16)

While adoption of MRgLITT is increasing,(5,11) most evidence is still derived from single-center studies with relatively short-term follow-up. Reported rates of seizure freedom are variable, ranging from 36–80% at ≥1 year follow-up,(10,17) but mostly appear to be lower than with ATL and there are few reports of long-term durability.(13) While ATL remains an option for patients with seizure recurrence after MRgLITT, it can be technically challenging due to altered operative anatomy and scarring;(18) the safety and efficacy of this staged strategy has not been widely reported.(18) Risk factors for treatment failure from MRgLITT also remain inconsistently defined in existing studies and meta-analyses.(10,13,15,17,19–25)

In our previous study, we characterized the effects of surgical targeting on seizure outcomes in a multicenter cohort of patients from 11 centers.(20) In the present study, we present longer clinical follow up on the more complete, consecutive series of patients treated at

these centers. We also assess the association between preoperative clinical characteristics and seizure outcomes after initial MRgLITT. Finally, we present outcomes for those patients with seizure recurrence after MRgLITT who underwent subsequent ATL or repeat ablation.

METHODS

Patient Selection

Patients were eligible for inclusion if they were among those treated consecutively at 1 of 11 comprehensive epilepsy centers with mesial temporal MRgLITT for drug-resistant epilepsy between 2012–2018. For most centers, included procedures represent their earliest experience with MRgLITT. For those centers participating in the prospective Stereotactic Laser Ablation for Temporal Lobe Epilepsy (SLATE) study (NCT02844465), procedures reported here precede any enrollment in SLATE. Patients were ineligible if they had a prior resection or ablation for epilepsy or the ablation was primarily targeting a mesial temporal lesion such as a tumor or cavernous malformation rather than the amygdalohippocampal complex and adjacent mesial cortex. Patient selection was otherwise per the interdisciplinary team at each center with no restriction on age or suspected pathology. Patients remaining seizure free with less than 1-year follow-up were excluded from seizure outcomes reporting and analysis, though any procedural complications are reported for the full cohort. This study presents longer duration and more complete follow-up of patients previously included in Wu et al.(20) as well as additional patients previously excluded for insufficient follow-up.

Data were collected per Institutional Review Board (IRB) approval or exemption at each site and deidentified data were analyzed in accordance with Columbia University Medical Center IRB approval with a waiver of informed consent (IRB-AAAT1593).

Variables

Preoperative characteristics were reported by each site based on interdisciplinary case conference consensus and included age at the time of first ablation, gender, handedness, side of ablation, evidence of mesial temporal sclerosis (MTS) on MRI, and presence of a lesion other than MTS on MRI (dual pathology). Results of preoperative fluorodeoxyglucose positron emission tomography (FDG-PET), if performed, were classified as ipsilateral temporal hypometabolism, negative (no hypometabolism), or discordant (including bilateral or contralateral hypometabolism). Focal aware seizures (FAS), focal impaired awareness seizures (FIAS), and focal to bilateral tonic-clonic seizures (FBTC) were identified according to International League Against Epilepsy (ILAE) criteria.(26) Preoperative noninvasive electroencephalogram (EEG) localization was classified as concordant (ipsilateral temporal) or discordant (bitemporal, ipsilateral extra-temporal, contralateral temporal, multifocal, or nonlocalized). Use of intracranial EEG was reported. Patients were classified as having “concordant MTS” if preoperative MRI demonstrated evidence of ipsilateral MTS without contralateral MTS or dual pathology, noninvasive EEG was concordant, and, if performed, FDG-PET and intracranial EEG were not discordant. This definition of “concordant MTS” retrospectively approximates the inclusion criteria of the prospective SLATE study.(27)

Outcomes

Seizure outcomes were reported according to the Engel Epilepsy Surgery Outcome Scale(28) at 6 months and annually until last available follow-up. Class I is defined as free of disabling seizures, class II rare disabling seizures, class III worthwhile improvement, and class IV no worthwhile improvement. Auras, seizures exclusively in the setting of medication withdrawal, and seizures in the first postoperative week were not counted as recurrence.(24) Patients with recurrent seizures and subsequent improvement for at least 2 years were reclassified based on the most recent outcome at last follow-up (Figure 1) but do not recover in survival analysis (Figure 2). Class I and II are collectively referred to as “favorable” outcomes. The semiology of recurrent seizures was classified as same, different, or multiple (with or; and the presence of FAS, FIAS, and FBTC after recurrence was reported. The results of any subsequent diagnostic testing were reported with the same classification applied to preoperative variables. Medication reduction was per clinical discretion and is reported with Engel I outcome.

Procedural and neurological adverse events within 12 months of the procedure and death at any time until last follow up are reported.(29)

Seizure outcomes and adverse events following subsequent ATL or repeat MRgLITT are also reported at last follow up.

Neuropsychological outcomes were collected inconsistently and with heterogenous instruments between sites and are not reported.

Clinical Analysis

Preoperative variables were evaluated for association with Engel I and Engel I or II outcomes at 1 year, 2 years, and last follow-up using univariate and multivariable logistic regression and with time to recurrence using univariate Mantel Cox and multivariable Cox proportional hazards model. All analyses were performed in Stata version 17 (StataCorp LLC, College Station, Texas, USA).

RESULTS

Patient Characteristics

A total of 277 patients were treated consecutively with mesial temporal MRgLITT at 1 of 11 centers. Nine patients were seizure free with less than 1 year follow-up and excluded from seizure outcomes. Characteristics of the remaining 268 patients are presented in Table 1.

Seizure Outcomes

Seizure outcomes after MRgLITT are summarized in Figure 1. Median follow-up was 47 months (range 12–95, IQR 31–61). After initial MRgLITT, Engel I outcome was achieved in 65.9% (170/258) at 6 months, 55.8% (149/267) at 1 year, 52.5% (126/240) at 2 years, and 49.3% (132/268) at last follow-up; 55 patients (20.5%) were Engel IA and 58 (21.6%) were Engel I with medication reduction or elimination (Table S1). Engel I or II outcomes were achieved in 76.0% (196/258) at 6 months, 74.2% (198/267) at 1 year, 75.0% (180/240)

at 2 years, and 66.0% (177/268) at last follow-up. After initial MRgLITT, 8.6% (23/268) of patients underwent ATL and 3.3% (9/268) had repeat MRgLITT. At last follow-up including outcomes after subsequent ATL or repeat MRgLITT, 57.1% (153/268) were Engel I and 75.4% (177/268) were Engel I or II.

Survival curves for initial loss of Engel I and II status after primary MRgLITT are shown in Figure 2. Median Engel I survival was 18 months and median Engel I or II survival was 31 months. Of note, Engel I and II rates are lower on the survival curves (Figure 2) than at last follow-up in Figure 1 because patients who improve for at least 2 years after early seizure recurrence are reclassified at last follow-up (including 16 patients who achieved Engel I outcome) but these “failures” do not recover on the survival curve.

Characteristics of seizure recurrence are included in Table S2. Among 161 patients with seizure recurrence, more than half (n=104, 64.6%) had their first seizure in the initial 6 months after MRgLITT and 131 (86.3%) recurred within 18 months of the procedure. Patients with recurrent seizures were less likely to have impaired awareness (FIAS) (76.6% vs 94.0%, OR 0.208, 95% CI 0.111–0.388, p<0.0001) and more likely to have FAS (38.0% vs 19.0%, OR 2.605, 95% CI 1.673–4.057, p<0.0001) than the preoperative baseline cohort. Among those reporting, 71.3% (92/129) had the same semiology as before surgery and, when video EEG was performed, 82.2% (88/107) had seizures localized to the temporal lobe ipsilateral to the side of ablation.

Predictors of Seizure Recurrence

Results of univariate and multivariable logistic regression are shown in Tables S3 and S4, respectively. In multivariable analysis, the presence of FBTC seizures was most consistently associated with reduced odds of seizure freedom (Engel I: 2-year: OR 0.504, 95% CI 0.286–0.888, p=0.018) or favorable outcome (Engel I or II: 1-year: OR 0.394, 95% CI 0.213–0.730, p=0.003; 2-year: OR 0.491, 95% CI 0.261–0.923, 0.027; last follow-up: OR 0.529, 95% CI 0.296–0.947, p=0.032).

Results of the univariate analysis of time to failure (Mantel-Cox test) and multivariable Cox proportional hazards regression are shown in Tables S5 and S6, respectively. Factors associated with earlier unfavorable outcome (loss of Engel I or II status) were FBTC seizures (HR 1.881, 95% CI 1.214–2.914, p=0.005) and age <43-year median (HR 1.624, 95% CI 1.036–2.546, p=0.034).

MTS, dual pathology on MRI, negative or discordant PET, discordant EEG localization, and concordant MTS were not associated with seizure outcome or time to failure in multivariable analysis.

Adverse Events

Adverse events are reported in Table S7. The most common adverse event was a visual field deficit (n=12, 4.3%), typically a superior quadrantanopia (n=11, 3.8%). Extraocular movement (EOM) dysfunction occurred in 7 (2.5%) patients and was persistent in 3 (1.1%). Hemorrhage was noted on imaging in 5 (1.8%) patients and symptomatic in 1 (0.4%) with transient EOM dysfunction and double vision. There were 3 deaths at any time during

available follow-up: 2 suicides (1 less than 1 year after surgery and the other 4 years after surgery) and 1 case of sudden unexplained death in epilepsy (SUDEP) 12 months after surgery. Given the retrospective nature of the study, details regarding the severity of symptoms were not consistently available. Language and memory deficits were not consistently quantified and are not reported.

Subsequent Surgery

A total of 36 patients with seizure recurrence after MRgLITT underwent 37 subsequent therapeutic surgeries. 22 patients underwent subsequent ATL at 6 of the 11 centers. Characteristics of the cohort and outcomes are presented in Table 2. Engel I outcome was achieved in 66.7% (14/21) at 1 year, 68.6% (11/16) at 2 years, and 66.7% (14/21) at last follow-up (median 25, IQR 19.5–42, range 12–65 months). The median interval between MRgLITT and ATL was 28 months (range 4–58 months). After ATL, 9.1% (2/22) experienced adverse events: 1 ipsilateral visual field deficit and 1 infection.

The cohort was not powered to determine statistically significant predictors of seizure freedom after subsequent ATL. Of note, Engel 1 seizure freedom was observed in 11/12 (91.7%) patients with ipsilateral PET localization, 8/10 (80.0%) with concordant MTS, and 9/11 (81.8%) with the same semiology at seizure recurrence.

Among 10 patients who underwent repeat MRgLITT, 5 (50%) were Engel 1 at last follow-up of at least 1 year (median 19, range 12–48 months). One patient experienced a new visual field deficit. Median interval between initial MRgLITT and repeat MRgLITT was 15 months (range 7–50 months). One patient who failed repeat MRgLITT underwent subsequent ATL and was seizure free at last follow up 48 months after ATL.

Additional subsequent surgeries after failed MRgLITT included 1 combination ATL and adjacent Responsive Neurostimulation (RNS), 1 ipsilateral temporal RNS, and 3 vagus nerve stimulation (VNS) procedures.

DISCUSSION

Key Findings

After primary MRgLITT, nearly half of patients achieved durable freedom from disabling seizures (Engel I outcome) at last follow-up (median 47 months, range 12–95). The rate of Engel I seizure freedom declined slightly over time from 55.8% at 1 year to 52.5% at 2 years and 49.3% at last follow-up. Additional patients had rare disabling seizures, bringing those with a favorable (Engel I or II) outcome to 74.2% at 1 year, 75.0% at 2 years, and 66.0% at last follow up. Other patients had worthwhile improvement and/or elimination of seizures with impaired awareness. The presence of FBTC seizures was associated with unfavorable seizure outcomes after MRgLITT. Among those undergoing subsequent ATL for seizure recurrence after MRgLITT, complications were comparable to upfront open resection and approximately two-thirds achieved seizure freedom. At last follow-up including outcomes after subsequent ATL or repeat MRgLITT, 57.1% (153/268) were Engel I and 75.4% (177/268) were Engel I or II.

Efficacy and Durability

We present the largest multi-center series of patients undergoing laser ablation for drug-resistant mTLE to date with longer follow-up than most smaller studies.(10,16,17) Reported rates of seizure freedom in the literature from smaller, predominantly single center series are highly variable, ranging from 36 to 78% at 1 year.(10,12,13,15,17,21–24) One large, single-center series with relatively long-term follow-up reported 60.4% Engel I outcome among 48 patients with mean follow-up 50 months.(13) Patient and procedural variability may contribute to variable outcomes in smaller series emphasizing the value of multi-center cohorts. Our findings demonstrated slightly lower 1-year seizure freedom but greater long-term durability than a recent meta-analysis, which estimated seizure freedom to be 64% at 1 year, 47% at 2 years, and 42% at 3 years.(17) One explanation is that most recurrences in our series happened in the first 18 months following surgery but some patients with early seizures went on to achieve at least 2 years freedom from disabling seizures (Engel I outcome) at last follow-up.

Our study represents the early experience with MRgLITT at each center and includes a heterogeneous cohort of patients with suspected mTLE. While ATL remains the gold-standard, supported by 2 class I trials(2,3) and numerous studies demonstrating 60–80% seizure freedom with 2-year follow up,(2–4) comparisons to MRgLITT should be made with several caveats.

First, outcomes with ATL are variable(29) and durability of seizure freedom has been reported to fall below the often cited 60–80% range in longer term follow-up.(30,31)

Second, our study included a heterogenous group of patients with factors that predict seizure recurrence after ATL including radiographically normal (non-MTS) MRI, dual pathology on MRI, discordant EEG and PET findings, and FBTC seizures.(32,33) Only 72.8% had MTS and only 50.4% had MTS with fully concordant imaging and EEG.

Third, improved targeting and knowledge of the necessary ablation structures or volume may improve outcomes with MRgLITT in the future. Our earlier series(20) and an independent experience(25) suggest that ablation of anterior and medial structures such as the amygdala, hippocampal head, parahippocampal gyrus, and entorhinal/perirhinal cortex is associated with seizure freedom while ablation of the posterior hippocampal body and tail is relatively independent from outcome. Subsequent work has found that ablation of key structures is associated with favorable connectivity changes that predict seizure outcome.(34) In the present study, we observed several patients with seizure recurrence after initial MRgLITT who became seizure free after repeat ablation, providing further evidence that improved knowledge of an adequate ablation may lead to better outcomes.

Safety and Minimally Invasive Appeal

In comparison to ATL, any reduced chance of seizure freedom with MRgLITT must be weighed against its benefits. The appropriate comparison to MRgLITT for many patients who decline an open procedure is not ATL but continued medical management, which has consistently been shown to have much lower chance of yielding seizure freedom, on the order of 3% or less.(35,36) Despite decades of evidence supporting ATL(2–4) and

guidelines recommending surgical evaluation for drug resistant epilepsy,(37,38) epilepsy surgery remains underutilized owing in part to concerns regarding its invasiveness and the risk of neurocognitive deficits.(5,6) MRgLITT is a minimally invasive procedure performed via a less than 1 centimeter incision. The rate of complications reported in our study and elsewhere compare favorably with open ATL.(39,40). The most common complication observed with MRgLITT, a superior quadrantanopsia, is likely due to injury to the adjacent optic radiations and is seen in as many of 70% of ATL when specifically tested. Cranial nerve palsies are also seen with both procedures.(39,40) Median length of stay is 1 day compared with 3–4 days for ATL.(11,40) MRgLITT also spares the lateral temporal neocortex, which has been associated with neurocognitive benefits.(10,12–15) As evidenced by its growing popularity,(5,11) many patients prefer MRgLITT over an open procedure.

There are several alternative stereotactic approaches. Radiofrequency thermocoagulation has favorable 1–2-year seizure outcomes in a few experienced centers(41,42) but produces smaller ablations with no ability to monitor temperature beyond the probe tip and has not been widely adopted where MRgLITT is available. Stereotactic radiosurgery (SRS) may have a role for poor surgical candidates, but rates of seizure freedom have been similar, or below those with MRgLITT, there is a latent period and possible temporary increase in seizure frequency, and radiation does not contour to fluid in the ventricles and cisterns leading to less discrete lesions.(43,44) Neuromodulation offers an option when the risk of deficit precludes a tissue destructive procedure (e.g., bilateral or dominant MTLE with preserved function) but yields primarily seizure reduction with low rates of seizure freedom.(45)

Subsequent ATL After Failed MRgLITT

We also demonstrate that primary management with MRgLITT does not preclude subsequent safe and effective ATL after treatment failure. ATL after MRgLITT can be technically challenging due to altered operative anatomy including obfuscation of normal temporal horn landmarks and loss of the medial pia arachnoid plane.(18) Scarring and adhesion of brain to surrounding structures may also be a concern. The type and rate of complications in our series of 22 patients (1 ipsilateral visual field deficit and 1 infection) were not out of the ordinary for ATL.(39,40) The 66.7% rate of seizure freedom at last follow-up was consistent with outcomes of upfront ATL.(2–4) These results should be interpreted with caution as they derive from a small, highly selected cohort with surgeries performed at experienced centers. Follow-up is also shorter than that for the larger MRgLITT cohort.

Taken together, the minimally invasive benefits of MRgLITT and ability to safely perform ATL for treatment failures provides the strongest support to date for use of MRgLITT as a first-line surgical therapy despite slightly higher historical rates of seizure freedom with upfront ATL. In practice, the appeal of this stepped approach to therapy must be weighed against the cumulative risk of some patients undergoing two procedures and the risk of delaying or deferring the more definitive ATL procedure. A relatively small portion of patients who failed MRgLITT went on to ATL in our cohort, potentially preventing some patients from achieving their best possible outcome.

When counseling patients, those planning to undergo MRgLITT should be prepared for the possibility that a future ATL may be necessary to achieve seizure freedom and ATL should be considered initially for those who want the best chance of seizure freedom with a single procedure based on current evidence.

Risk Factors for Seizure Recurrence After MRgLITT

The presence of FBTC was most consistently associated with unfavorable outcomes after adjustment for other variables. FBTC has also been associated with failure of ATL.(32) The association with younger age was relatively weak and inconsistent but may be attributable to unmeasured confounders such as greater prevalence of neocortical epilepsy in younger patients. Left handedness was associated with Engel I outcome at a single time point in logistic regression only (1 of 8 analyses) and is likely a spurious finding.

It is notable that several risk factors associated with seizure recurrence after open resection in prior studies(32,33) did not predict recurrence in our MRgLITT cohort, including the absence of MTS on MRI, dual pathology, and discordant video EEG or PET findings. Radiographic MTS is not typically confirmed pathologically with MRgLITT, which might explain its lack of predictive value, but it has been associated with seizure freedom in several single-center studies of the technique.(13,15,23) It is possible that careful patient selection and greater use of intracranial monitoring among patients with traditional risk factors in our cohort (Table 1) allowed for similar outcomes in these patients, as has been suggested by other single-center studies.(21,22)

Limitations

There are several important limitations to our study. This was an open-label, retrospective cohort study with self-reporting from each center. Consequently, patient selection for MRgLITT versus other procedures, the diagnosis of mTLE, and surgical technique were left to each site leading to a heterogenous cohort and intervention. Significant loss to follow-up after 2 years may bias longer term seizure outcomes.13 Retrospective data collection may also underreport adverse events; systematic assessment of visual fields was not performed. We were also unable to report neuropsychological outcomes due to inconsistent follow-up (ie. insurance barriers, patient reluctance) and heterogenous instruments between sites (ie. variable naming and memory tests or versions thereof). The rate of medication reduction or elimination with Engel I outcome was likely influenced by institutional practice and patient preference during adoption of a new surgical technique and may not reflect what is achievable when medication reduction is a clinical priority.

The ongoing SLATE trial will report prospective outcomes including neuropsychological testing in a more homogenous cohort of patients with drug-resistant focal epilepsy with MTS and fully concordant workup with some guidance and constraints on surgical technique.(27) However, the heterogeneity of our cohort, including approximately 50% of patients who would likely not meet SLATE’s inclusion criteria allowed for robust analysis of risk factors for seizure recurrence and better captures real-world applications and outcomes.

Conclusions

Laser ablation is a viable treatment option for well-selected patients with suspected drug-resistant mTLE who prefer a minimally invasive option. Nearly half (49.3%) of patients had durable seizure freedom at last follow-up, 16.7% had rare disabling seizures, and additional patients had worthwhile improvement and/or elimination of impaired awareness with seizures. Our early experience with MRgLITT in a heterogeneous cohort of patients with mTLE offered slightly lower chance of seizure freedom than historical ATL. Outcomes may improve with additional knowledge of ideal patient selection and surgical technique. MRgLITT is also less invasive with a favorable safety profile making it appealing to many patients, including some who would not consider an open surgical option. Moreover, MRgLITT does not preclude future successful ATL or more extensive ablation if seizures persist or recur. There is a need for continued real-world outcomes monitoring as well as prospective studies with standardized inclusion criteria and data collection including neurocognitive outcomes.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Key Messages

What is already known on this topic –

Magnetic resonance-guided laser interstitial thermal therapy (MRgLITT) is a minimally invasive alternative to surgical resection for drug-resistant mesial temporal lobe epilepsy (mTLE). The durability of seizure freedom after MRgLITT and outcomes after subsequent resection are largely unknown.

What this study adds –

Among 268 consecutively treated patients at 11 centers, the largest published series to date, nearly half (49.3%) of patients had durable seizure freedom at last follow-up (median 47, range 12–95 months) and 16.7% had rare disabling seizures. Among patients with seizure recurrence after MRgLITT, 14/21 (66.7%) became seizure free after subsequent anterior temporal lobectomy (ATL) and 5/10 (50%) after repeat MRgLITT.

How this study might affect research, practice or policy –

MRgLITT is a minimally invasive, first-line surgical treatment with durable outcomes for select patients with drug-resistant mTLE, and ATL remains a treatment option for those with persistent seizures after MRgLITT.

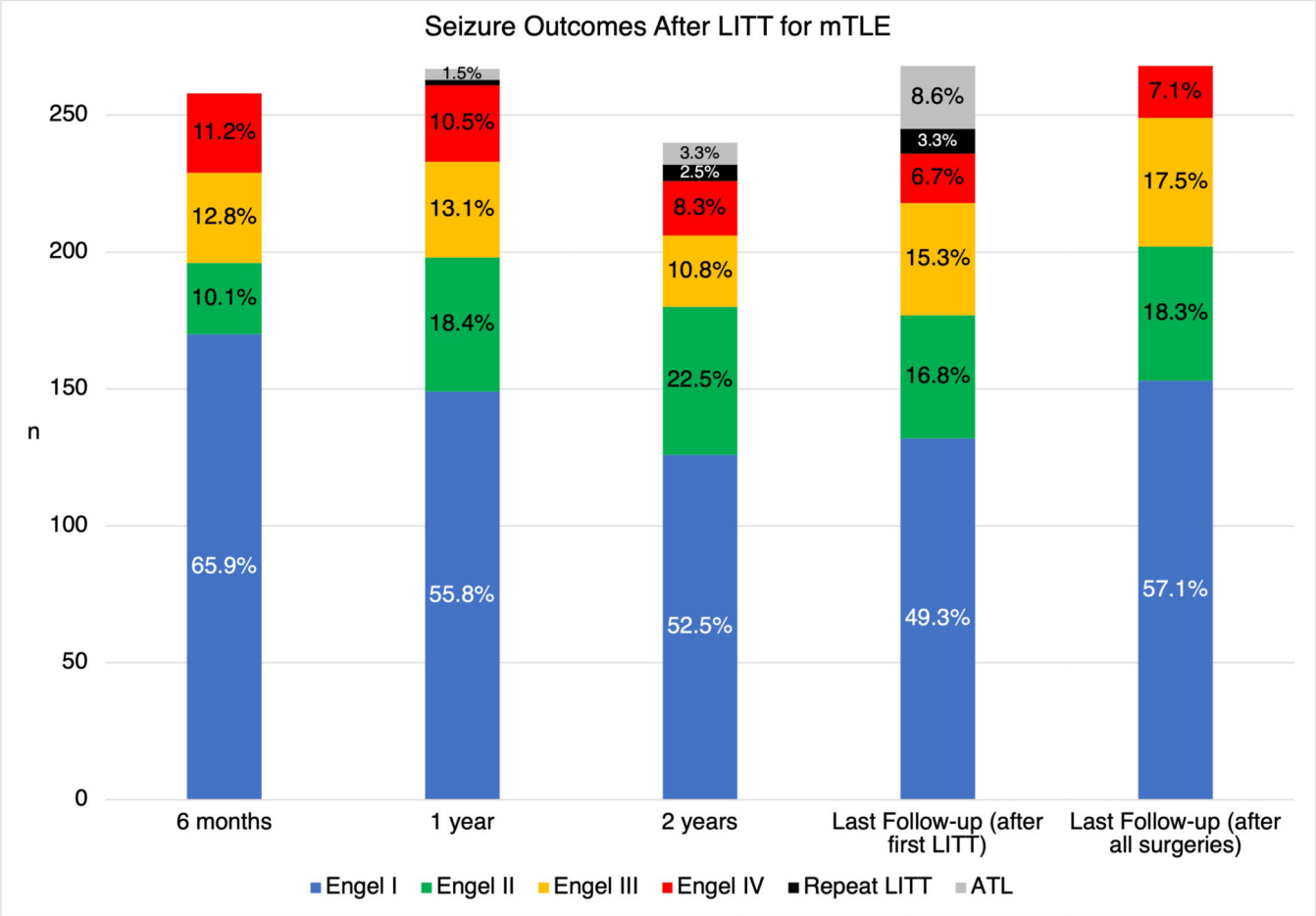

Figure 1. Seizure outcomes after laser interstitial thermal therapy (LITT) for mesial temporal lobe epilepsy (mTLE) (n=268).

After initial LITT, Engel I outcome was achieved in 65.9% (170/258) at 6 months, 55.8% (149/267) a 1 year, 52.5% (126/240) at 2 years, and 49.3% (132/268) at last follow-up ≥1 year (median 47 months, range 12–95 months). Engel I or II outcomes were achieved in 76.0% (196/258) at 6 months, 74.2% (198/267) at 1 year, 75.0% (180/240) at 2 years, and 66.0% (177/268) at last follow-up. At last follow-up, 8.6% (23/268) had undergone anterior temporal lobectomy and 3.3% (9/268) had a repeat LITT with no further surgery. At last follow-up after all surgeries, 57.1% (153/268) were Engel I and 75.4% (177/268) were Engel I or II. Patients with some disabling seizures after surgery but free of disabling seizures for at least 2 years were classified as Engel I at last follow-up. Patients with more than rare disabling seizures after surgery bur rare seizures for at least 2 years were classified as Engel II at last follow-up.

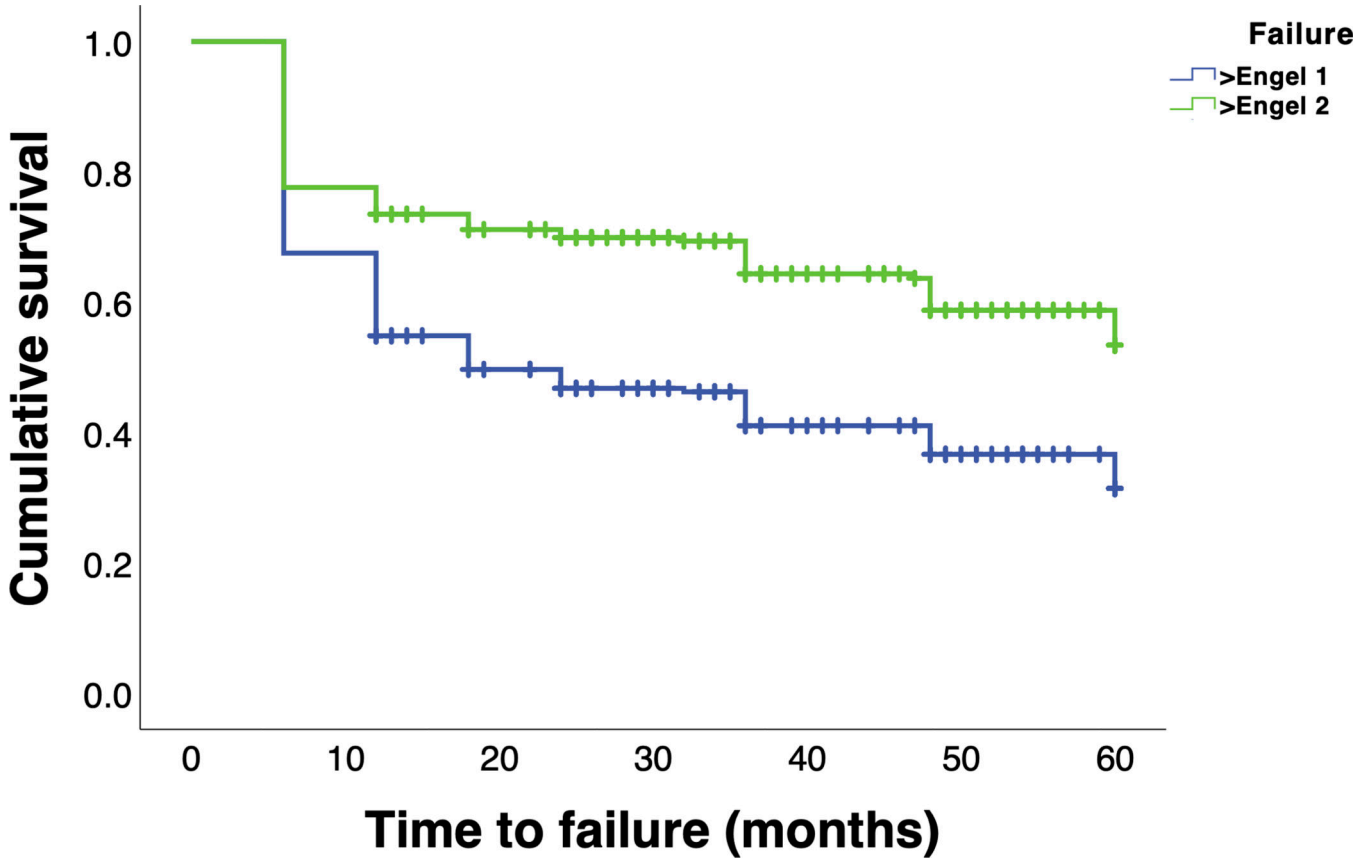

Figure 2. Survival curve for loss of Engel I and Engel II outcome after LITT for mTLE.

The blue curve represents the proportion of patients with surviving Engel I outcome (cumulative survival) over time. The green curve represents patients with Engel I or II outcome (ie. failure is loss of at least Engel II status). Hash marks represent patients censored due to end of follow-up. Note, patients with disabling seizures after the first postoperative week "fail" Engel I status on the survival curve and patients with more than rare disabling seizures "fail" Engel II status even if these outcomes are ultimately achieved with improvement at last follow-up. Engel I and II rates are therefore lower on the survival curves than at last follow-up after primary MRgLITT (Figure 1) because outcomes improved after initial seizure recurrence in some patients but treatment failure does not recover on the survival curve.

Table 1.

Characteristics of patients undergoing MR-guided laser interstitial thermal therapy (MRgLITT) for mesial temporal lobe epilepsy (mTLE) (n=268)

	Cohort (n=268)	
	n	**(%)**
Age<43 years[1]	138	(51.5)
Gender		
Female	144	(53.7)
Male	124	(46.3)
Handedness		
Right	219	(85.6)
Left	37	(14.4)
Side of LITT		
Right	118	(44.0)
Left	150	(56.0)
MTS (Ipsilateral to LITT)	195	(72.8)
Dual pathology on MRI	61	(22.9)
PET hypometabolism	210	(78.4)
Ipsilateral temporal	159	(59.3)
Negative	30	(11.2)
Discordant	21	(7.8)
Bilateral	18	(6.7)
Contralateral	3	(1.1)
Seizure Type		
FAS	51	(19.0)
FIAS	252	(94.0)
FBTC	129	(48.1)
EEG Localization		
Concordant (Ipsilateral Temporal)	206	(76.9)
Discordant	39	(15.9)
Bitemporal	22	(8.2)
Multifocal	5	(1.9)
Non-localized	6	(2.2)
Ipsilateral extratemporal	5	(1.9)
Contralateral temporal	1	(0.4)
Concordant MTS[2]	137	(51.1)
Invasive monitoring	53	(19.8)
Concordant MTS	8	(3.0)

[1]Median 43, interquartile range (IQR) 30–54, range 7–82

[2]MTS ipsilateral to LITT, no dual pathology, concordant semiology/EEG, PET/invasive monitoring not discordant if performed.

EEG, electroencephalogram; FAS, focal aware seizures; FBTC, focal to bilateral tonic clonic seizure; FIAS, focal impaired awareness seizures (FIAS); LITT, laser interstitial thermal therapy; MRI, magnetic resonance imaging; MTS, mesial temporal sclerosis; PET, fluorodeoxyglucose positron emission tomography; SD, standard deviation.

Table 2.

Characteristics and outcomes of patients undergoing anterior temporal lobectomy after failed laser interstitial thermal therapy (n=22).

	ATL after failed LITT, n	Engel I at last follow-up, n (%)
Total (≥1 year follow-up)[1]	21	14 (66.7%)
Age<43 years	12	8 (66.7%)
Gender		
Female	10	7 (70.0%)
Male	11	7 (63.6%)
Handedness		
Right	19	13 (68.4%)
Side of LITT		
Right	10	7 (70.0%)
Left	11	7 (63.6%)
MTS (Ipsilateral to LITT)	16	11 (68.8%)
Dual pathology on MRI		
Yes	6	4 (66.7%)
No	15	10 (66.7%)
PET localization		
Ipsilateral	12	11 (91.7%)
Negative	1	0 (0.0%)
Discordant (Bilateral)	4	2 (50.0%)
Seizure Type		
FAS	4	3 (75.0%)
FIAS	21	14 (66.7%)
FBTC	9	5 (55.6%)
EEG Localization		
Concordant (Ipsilateral Temporal)	18	13 (72.2%)
Discordant (Bitemporal)	2	1 (50%)
Concordant MTS[2]	10	8 (80.0%)
Invasive monitoring	3	2 (66.7%)
Recurrent semiology		
Same	11	9 (81.8%)

[1]The cohort excludes 1 patient who was seizure free when lost to follow-up 3 months after ATL and includes 1 patient who failed repeat MRgLITT prior to ATL.

[2]MTS ipsilateral to LITT, no dual pathology, concordant semiology/EEG, PET/invasive monitoring not discordant if performed.