Original Article

Journal of Child Neurology
2025, Vol. 40(5) 342-347

DOI: 10.1177/08830738241312262
journals.sagepub.com/home/jcn
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Laser Interstitial Thermal Therapy for the Treatment of Mesial Temporal Lobe Epilepsy in Children

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Abstract

Objective: Few studies have explored the efficacy of laser interstitial thermal therapy in pediatric epilepsy surgery. This study aims to evaluate seizure-free outcomes in children and adolescents with mesial temporal lobe epilepsy who underwent laser interstitial thermal therapy. **Methods:** This was a retrospective cohort study performed at a level 4 epilepsy center. All patients had comprehensive presurgical epilepsy evaluations with a consensus treatment decision made by a multidisciplinary team. Brain magnetic resonance imaging (MRI) data were used to determine lesional vs nonlesional groups. All laser interstitial thermal therapy procedures were performed using Visualase laser ablation systems by the neurosurgical team. Seizure-free outcomes were measured according to the Engel surgical outcome scale. **Results:** This study included 19 patients (12 girls, 7 boys). Age of epilepsy onset ranged from 2 to 17 years (mean 9.9 years), and age at time of surgery ranged from 8 to 20 years (mean 15.1 years). Ten patients (52.5%) had signs of hippocampal sclerosis on MRI (lesional group), and 9 patients (47.5%) had a normal brain MRI (nonlesional group). Engel 1 score was achieved by 14 of 19 patients (73.5%): 9 of 10 patients (90%) in the lesional group and 5 of 9 patients (55.5%) in the nonlesional group. Younger age of seizure onset was a predictor of better postsurgical outcome, but no other outcome predictors could be established. **Conclusion:** Laser interstitial thermal therapy is safe and effective for the treatment of drug-resistant mesial temporal lobe epilepsy in children, rendering more favorable seizure-free outcomes in pediatric patients with hippocampal atrophy than in those with nonlesional mesial temporal lobe epilepsy.

Keywords

Epilepsy, Surgery, Treatment

Received 30 July 2024. Received revised 3 December 2024. Accepted for publication 8 December 2024.

Temporal lobe epilepsy is among the most common types of focal epilepsies with onset in late childhood or early adolescence. The clinical and electrographic features of mesial temporal lobe epilepsy are well established, and brain magnetic resonance imaging (MRI) classically shows hippocampal atrophy. However, patients with clinical and electrographic features of mesial temporal lobe epilepsy can often have a normal brain MRI.

Despite the development of numerous new antiseizure medications, the number of patients achieving seizure freedom with pharmacotherapy alone is suboptimal. Epilepsy surgery should be considered after the failure of 2 tolerated and appropriately dosed antiseizure medications.[1] Laser interstitial thermal therapy is increasingly considered as a less invasive alternative to open craniotomy.

Amygdalohippocampectomy performed by laser interstitial thermal therapy has seizure-free rates comparable to open craniotomy, with the additional benefit of being less invasive, associated with fewer complications and shorter hospital stays.[2–5]

Most data available are based on adult studies, and the efficacy of laser interstitial thermal therapy for mesial temporal lobe epilepsy in children has not been systematically evaluated as robustly. The objective of this study is to evaluate seizure outcome after laser interstitial thermal therapy surgery in

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children with mesial temporal lobe epilepsy and to investigate seizure-free outcome difference in nonlesional patients, or those with normal MRIs, compared to those with radiographically confirmed mesial temporal sclerosis.

Methods

This was a retrospective cohort study conducted at a level 4 epilepsy center. Data were obtained by chart review at a 12-month follow-up, and the study was approved by the institutional review board of our institution. Inclusion criteria were the following: age <20 years at the time of epilepsy surgery, electroclinical diagnosis of mesial temporal lobe epilepsy, diagnosis of drug-resistant epilepsy according to the International League Against Epilepsy (ILAE) criteria[6] (failure of 2 tolerated and appropriately dosed antiseizure medications), available follow-up data, and history of laser interstitial thermal therapy performed at our institution. Patients with brain MRI showing a structural lesion other than hippocampal sclerosis were excluded from the analysis.

The diagnosis of mesial temporal lobe epilepsy was established by a team of pediatric epileptologists after a comprehensive neurologic workup including multiple scalp EEGs, video EEGs, MRI scans, and additional studies performed at the discretion of the treating epileptologist. Neuroimaging evaluation was performed by an experienced neuroradiologist by visual assessment of hippocampal size, signal, internal structure, and shape as well as adjacent mesial temporal structures.[7]

Stereotactic laser ablation of the amygdala and hippocampus was performed in 1 or more stages. Visualase catheters (Medtronic, Inc) for laser ablation were placed in the operating room. Ablation was performed according to the manufacturer's instructions, at 60% to 80% power and with safety markers lining the periphery of the ablation site. The patients were then transferred to the MRI scanner for confirmatory imaging and ablation. Diffusion-weighted imaging and T1-weighted imaging with contrast were used to confirm the complete ablation before removing all catheters (Figure 1).

The radiologic goal of ablation was to target the amygdala, head, and body of the hippocampus as far back as the tectal plate. The aim was to completely ablate the amygdala, and often a second fiberoptic laser catheter orthogonal to the primary hippocampal catheter was placed to accomplish complete amygdala ablation. All patients received steroids for 5-14 days in a slow wean schedule.

Patients were included in 2 groups: group 1 (nonlesional) included patients with normal brain MRI, and group 2 (lesional) included patients with signs of hippocampal sclerosis shown by brain MRI (atrophy and/or hypersignal on T2-weighted / fluid-attenuated inversion recovery sequences and/or abnormal internal structure of the hippocampus). Surgical efficacy was evaluated according to the Engel Surgical Outcome Scale using 12-month postsurgical follow-up data, which was compiled for seizure freedom assessments.

Outcomes were evaluated using a Student *t* test for continuous variables and Fisher exact test for categorial variables.

Results

This study included 19 patients (12 girls, 7 boys). The mean age at onset of epilepsy was 9.9 years and ranged from 2 to 17 years. The mean age at time of surgery was 15.1 years and ranged from 8 to 20 years. Of the 19 patients, 10 patients (52.5%) were included in the lesional group, and had hippocampal sclerosis on MRI, and 9 patients (47.5%) were included in the nonlesional group and had a normal brain MRI. Neurologic examination was normal in all patients. Patient characteristics are shown in Table 1. Both groups had the same characteristics regarding age of seizure onset, age at laser interstitial thermal therapy, and duration of epilepsy (Table 2).

Stereoelectroencephalography was performed in all patients with nonlesional epilepsy and 6 of the 10 patients (60%) with hippocampal atrophy (Table 1).

Fourteen patients (73%) from the entire cohort achieved an Engel 1 score at 12-month follow-up. The lesional group achieved an Engel 1 score in 9 of 10 patients (90%), and the nonlesional group achieved an Engel 1 score in 5 of the 9 patients (55.5%) at 12-month follow-up (Figure 2). There was no difference in seizure control according to the side of ablation (nonlesional group / normal brain MRI: $P = .20$; lesional group / hippocampal sclerosis: $P > .99$).

No complications were observed. Neurologic examination, including visual fields and cranial nerves, were assessed at immediate postoperative and follow-up visits,

Younger age of seizure onset was a predictor for better surgical outcome; however, the age at which laser interstitial thermal therapy was performed and the duration of epilepsy were not (Table 3). Independent analysis including only patients in the lesional group showed that age of seizure onset, age at laser interstitial thermal therapy, and duration of epilepsy did not influence the final postsurgical outcome (Table 4). The sample size precluded the statistical analysis for age of seizure onset, age at laser interstitial thermal therapy, and duration of epilepsy in the lesional group.

Discussion

Mesial temporal lobe epilepsy has been more widely studied in adults, and laser interstitial thermal therapy has been demonstrated to be an effective and common minimally invasive approach for the treatment of mesial temporal lobe epilepsy.[3,8] However specific data regarding mesial temporal lobe epilepsy and laser ablation in children is still limited.

Our data showed that 73.5% of our patients had excellent clinical results with Engel 1 classification scores at 12-month follow-up. Overall postsurgical seizure-free outcomes were similar to data reported in adults with mesial temporal lobe epilepsy. However, this study demonstrates seizure-free outcomes for lesional mesial temporal lobe epilepsy of 90%, which is higher than the frequency reported for adults.[3,9,10] Although this is a preliminary study and our sample size is small, it may suggest that epilepsy surgery for mesial temporal lobe epilepsy due to hippocampal sclerosis has a better prognosis if performed earlier in life.

In addition, our data did not show a correlation between the duration of epilepsy and postsurgical prognosis. One possible explanation is that epilepsy surgery early in life enables a better surgical outcome than the one seen in adults because long-term mesial temporal lobe epilepsy is often associated with a progressive decrease in hippocampal volume and

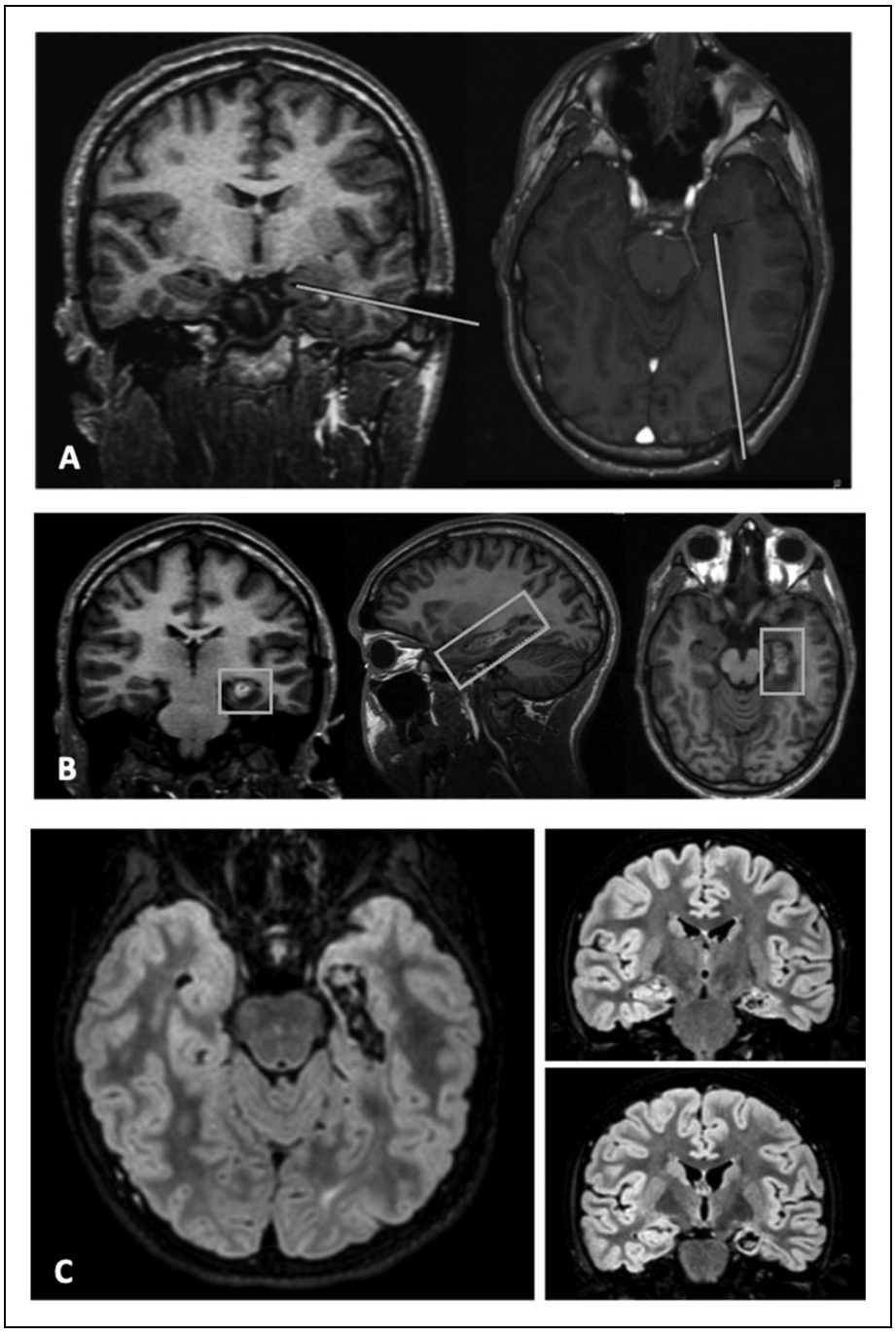

Figure 1. (A) Brain magnetic resonance imaging (MRI) (coronal and axial T1 images) showing probe placement for laser interstitial thermal therapy of the left mesial structures. (B) Brain MRI (coronal, sagittal and axial T1 images) showing acute changes of the left mesial structures after laser interstitial thermal therapy (box). (C) Follow-up brain MRI (axial and coronal fluid-attenuated inversion recovery images) showing left hippocampal ablation (after 2 years of laser ablation).

increased network synchronization that leads to drug-resistant epilepsy.[11–16]

Postsurgical outcomes after laser interstitial thermal therapy in adults with mesial temporal lobe epilepsy usually show similar rates of seizure freedom in patients with normal brain MRI, but confirmed stereoelectroencephalography mesial temporal lobe epilepsy, and hippocampal sclerosis.[10] However, our data showed that the rates of seizure freedom after laser interstitial thermal therapy were higher in those with lesional mesial temporal lobe epilepsy than those with normal imaging. This may be attributable to the fact despite stereoelectroencephalography showing ictal onset on the temporal mesial structures, the epileptogenic zone may extend beyond the amygdala and hippocampi or at additional regions (such as in patient 3, where

Table 1. Patient Characteristics.

ID	Gender	Age at seizure onset, y	Age at LITT, y	Duration of epilepsy until LITT, y	Brain MRI	Seizure frequency before LITT	SEEG / ictal onset	LITT ablation / no. of probes (n)	Engel score at 12 mo	Special notes
1	M	11	16	5	Normal	Daily	Yes/H	Left A/H (2)	4	
2	M	8	12	4	Normal	Daily	Yes/AH	Right A/H/P (3)	1	
3	M	12	17	5	Normal	Weekly	Yes/AH + parietal	Right A/H/P (3)	3	
4	F	11	16	5	Normal	Weekly	Yes/H	Right A/H/P (2)	1	
5	F	12	20	8	Normal	Daily	Yes/AH + neocortical temporal + insula	Left A/H/P (3)	3	Extension into insula (check if neocortical tempo)
6	F	15	17	2	Normal	Weekly	Yes/AH + insula	Left A/H/P (3)	1	Extension into insula
7	M	17	20	3	Normal	Weekly	Yes/AH + posterior insula	Left A/H/P (3)	3	
8	F	12	16	4	Normal	Monthly	Yes /AH + insula	Right H/P (3)	1	Extension into inferior insula
9	M	8	11	3	Normal	Monthly	Yes /A + neocortical temporal + insula	Right A/H (2)	1	
10	F	2	8	7	Left HS	Weekly	No	Left A/H (2)	1	
11	F	4	11	9	Left HS	Daily	No	Left A/H (2)	1	
12	F	4	9	5	Left HS	Weekly	No	Left A/H (2)	1	
13	F	3	8	5	Left HS	Weekly	No	Left A/H (2)	1	
14	F	8	19	9	Right HS	Monthly	Yes/H	Right H (2)	1	
15	M	13	16	2	Right HS	Weekly	Y/H + insula	Right A/H (3)	1	Extension to insula
16	M	10	18	8	Left HS	Monthly	Y/AH	Left A/H (2)	1	
17	M	14	17	3	Right HS	Weekly	Y/H	Right A/H (2)	4	
18	F	13	18	5	Right HS	Weekly	Y/H	Right A/H (2)	1	
19	M	12	19	6	Right HS	Weekly	Y/AH	Right H (1)	1	

Abbreviations: A, amygdala; H, hippocampus; HS, hippocampal sclerosis; LITT, laser interstitial thermal therapy; P, parahippocampus; SEEG, stereoelectroencephalography.

Table 2. Analysis of Variables Between Patients With Lesional and Nonlesional Mesial Temporal Lobe Epilepsy (n = 19).

Variable	Mean	*P* Value [a]
Age at seizure onset, y		.0725
Lesional group	8.3	
Nonlesional group	11.7	
Duration of epilepsy, y		.1064
Lesional group	5.8	
Nonlesional group	4.3	
Age at LITT, y		.3408
Lesional group	16.1	
Nonlesional group	14.3	

Abbreviation: LITT, laser interstitial thermal therapy.
[a]Statistical analysis was performed using Student *t* test.

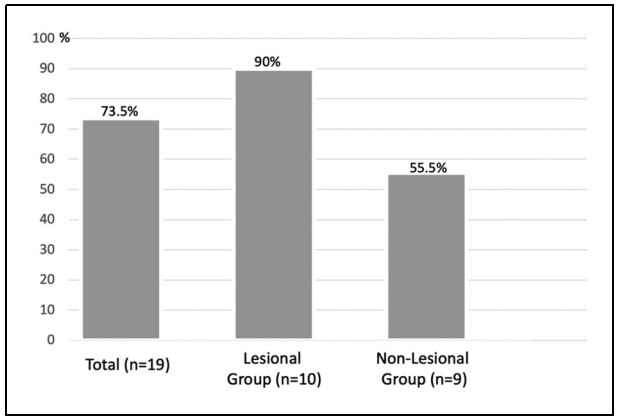

Figure 2. Engel I classification 12 months after laser interstitial thermal therapy procedure among lesional and nonlesional groups.

there was also ictal onset over the parietal region), rendering laser interstitial thermal therapy procedure less effective.[11] Genetic factors are also being explored and hypothesized as possible reasons for poorer seizure freedom rates in nonlesional epilepsies compared with lesional epilepsies.[12]

Seizure recurrence after laser interstitial thermal therapy depends on several factors, and a more medial, anterior, and inferior ablation is likely associated with better disconnection

Table 3. Analysis of Variables Regarding Postsurgical Outcome (n = 19).

Variable	Mean	*P* Value [a]
Age at seizure onset, y		**.0416**
Engel 1	8.79	
Engel 3 and 4	13.2	
Duration of epilepsy, y		.6983
Engel 1	5.21	
Engel 3 and 4	4.80	
Age at LITT, y		.0631
Engel 1	14.1	
Engel 3 and 4	18	

Abbreviation: LITT, laser interstitial thermal therapy.
[a]Statistical analysis was performed using Student *t* test.

Table 4. Analysis of Variables Regarding Postsurgical Outcome in Patients With Normal Brain MRI (Nonlesional Group, n = 9).

Variable	Mean	*P* Value [a]
Age at seizure onset, y		.3521
Engel 1	10.80	
Engel 3 and 4	12.75	
Duration of epilepsy, y		.1684
Engel 1	3.6	
Engel 3 and 4	5.2	
Age at LITT, y		.0515
Engel 1	14.40	
Engel 3 and 4	18.2	

Abbreviation: LITT, laser interstitial thermal therapy
[a]Statistical analysis was performed using Student *t* test.

of mesial structures, thereby providing a better seizure freedom outcome.[13] Ablation of the entire head of the hippocampus, half of the amygdala, and possibly piriform cortex seems to be associated with better seizure freedom outcomes. Although not included in the results because of our follow-up cutoff, patient 1 had seizure recurrence after laser interstitial thermal therapy but is seizure-free after a second ablation of the residual hippocampus including the ipsilateral insula.

In selected patients, we widened the ablation to also include the parahippocampus for more extensive ablation of the piriform cortex. We did this by applying a parallel catheter to the hippocampal catheter. On the other hand, volume of ablation and residual mesial structures (amygdala, hippocampal, entorhinal, and parahippocampal) do not always correlate with seizure outcomes.[14–18]

Although seizure onset was earlier in children with mesial temporal lobe epilepsy due to hippocampal sclerosis, there was no difference between age at laser interstitial thermal therapy and epilepsy duration before surgery. Delaying surgery in patients with normal brain MRI is often due to the misconception that a normal brain MRI is a contraindication for epilepsy surgery. Other techniques (such as positron emission tomography scan, single-photon emission computed tomography, magnetoencephalography, and stereoelectroencephalography) that can help identify the epileptogenic zone should be used.[19] It is likely that children with mesial temporal lobe epilepsy without known MRI lesions may benefit from a procedure at an earlier age.

Conclusion

Although this is a retrospective study, it provides preliminary evidence that children with mesial temporal lobe epilepsy who had epilepsy surgery performed by laser interstitial thermal therapy have seizure freedom rates comparable to the outcomes reported in adults and pediatric patients who had open surgery. The results include both lesional and nonlesional intractable mesial temporal lobe epilepsy, with better outcomes seen in children with mesial temporal lobe epilepsy associated with hippocampal sclerosis. In addition, this study confirmed laser interstitial thermal therapy safe with a very low morbidity rate.

This study suggests the role of laser interstitial thermal therapy in children with both lesional and nonlesional mesial temporal lobe epilepsy, providing a safer and effective alternative to open craniotomy. Future prospective studies including a larger sample and follow-up are needed to better understand seizure-free outcomes using laser interstitial thermal therapy. Future studies are also needed to assess if the volume of ablation, neuropsychological data, proposed epileptogenic zones, or genetic factors may affect the seizure freedom outcomes of laser interstitial thermal therapy in pediatric patients.

Declaration of Conflicting Interests

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

Funding

The authors received no financial support for the research, authorship, and/or publication of this article.

Ethical Approval

This study was approved by the IRB of our institution (#807749).

Author Contributions

DG: acquisition/data interpretation, drafted manuscript/final approval. OKM: acquisition/data interpretation, drafted manuscript/final approval. AF: acquisition/data interpretation, drafted manuscript/final approval. NGE: acquisition/data interpretation, drafted manuscript/final approval. AJ: acquisition/data interpretation, drafted manuscript/final approval. SS: acquisition/data interpretation, drafted manuscript/final approval.

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