Magnetic Resonance Imaging-Guided Laser Interstitial Thermal Therapy for the Treatment of Hypothalamic Hamartomas: A Retrospective Review

David S. Xu, MD*
Tsinsue Chen, MD*
Randall J. Hlubek, MD*
Ruth E. Bristol, MD‡
Kris A. Smith, MD*
Francisco A. Ponce, MD*
John F. Kerrigan, MD§
Peter Nakaji, MD*

*Department of Neurosurgery, Barrow Neurological Institute, St. Joseph's Hospital and Medical Center, Phoenix, Arizona; ‡Department of Neurosurgery, Barrow Neurological Institute, Phoenix Children's Hospital, Phoenix, Arizona; §Department of Pediatric Neurology, Barrow Neurological Institute, Phoenix Children's Hospital, Phoenix, Arizona

Correspondence:
Peter Nakaji, MD,
c/o Neuroscience Publications,
Barrow Neurological Institute,
St. Joseph's Hospital and Medical Center,
350 W Thomas Rd,
Phoenix, AZ 85013.
E-mail: Neuropub@dignityhealth.org

Received, December 20, 2016.
Accepted, November 27, 2017.
Published Online, January 13, 2018.

BACKGROUND: Hypothalamic hamartomas (HH) are rare lesions associated with treatment-resistant epilepsy. Open surgery results in modest seizure control (about 50%) but has a significant associated morbidity. Radiosurgery is limited to a subset of patients due to latent therapeutic effects. Magnetic resonance imaging-guided laser interstitial thermal therapy (LITT) offers a novel minimally invasive option.

OBJECTIVE: To evaluate a single center's outcomes for the LITT treatment of HH.

METHODS: We retrospectively reviewed our experience with LITT for the treatment of HH using our institution's prospectively maintained patient database.

RESULTS: Eighteen patients (mean age, 21.1 yr; median age, 11 yr) underwent 21 total LITT treatments for HH. Mean follow-up was 17.4 mo. The length of stay was 1 night for 16 (89%) patients. At the end of follow-up, 11 of 18 patients (61%) had full disconnection of the HH, and 12 of 15 (80%) patients with gelastic seizures and 5 (56%) of 9 patients with nongelastic seizures were seizure free (International League Against Epilepsy Class 1). Immediate complications included a 39% (7/18) incidence of neurological deficits, including 1 case of hemiparesis. At the end of follow-up, 22% of patients (4/18) had persistent deficits. The hypothyroidism that occurred was delayed in 11% of patients (2/18), as was short-term memory loss (22%, 4/18) and weight gain (22%, 4/18).

CONCLUSION: LITT therapy for HH can achieve excellent rates of seizure control with low morbidity and a short postoperative stay in a majority of patients. Additional research is needed to assess the durability of results and the full spectrum of cognitive outcomes.

KEY WORDS: Epilepsy, Gelastic seizure, Hypothalamic hamartoma, Laser ablation, Stereotactic neurosurgery

Neurosurgery 83:1183–1192, 2018 DOI:10.1093/neuros/nyx604 www.neurosurgery-online.com

A hypothalamic hamartoma (HH) is a rare developmental nonneoplastic lesion associated with a well-characterized epileptic syndrome involving gelastic seizures refractory to medical therapy.[1,2] Surgical resection of HHs has been the definitive treatment for gelastic epilepsy, but because lesions are deep and close to critically eloquent structures, surgery remains treacherous, with variable success and high morbidity.[3-5] Stereotactic radiosurgery is an alternative noninvasive treatment, but radiation effects require months to emerge. Thus, its use is limited in pediatric patients.[6,7] Recently, magnetic resonance imaging (MRI)-guided laser interstitial thermal therapy (LITT) has emerged as a promising minimally invasive treatment for HH.[8,9] Early proof-of-concept trials with short-term follow-up (<1 yr) have shown LITT to be a safe and efficacious treatment for HH.[8-10] This retrospective review examines our experience using LITT to treat HH patients and provides detailed long-term neurological and seizure-control outcomes.

缩略语，请翻译

ABBREVIATIONS: HH, hypothalamic hamartomas; **ILAE,** International League Against Epilepsy; **LITT,** laser interstitial thermal therapy; **MRI,** magnetic resonance imaging; **RFA,** radiofrequency ablation; **SD,** standard deviation.

METHODS

Patient Selection and Follow-up

Through the Hypothalamic Hamartoma Center at Barrow Neurological Institute, a multidisciplinary team evaluates patients with HH,

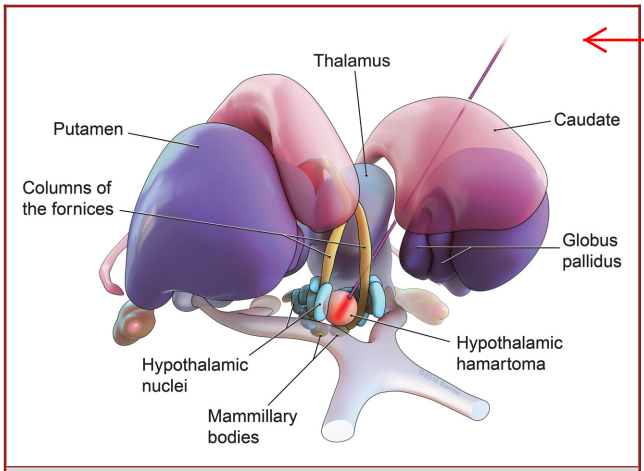


FIGURE 1. *Artist's illustration showing the trajectory of the ablation catheter in reference to critical neurological structures surrounding the hypothalamic hamartoma. Used with permission from Barrow Neurological Institute.*

provides consensus management plans, and prospectively collects clinical data using an active research protocol. After reports of LITT for HH first emerged in 2012,[10] we began offering it as a first-line therapy for patients harboring a discrete lesion of at least 1 cm^3 and less than 2 cm in diameter that could be accessed through a safe stereotactic tract (Figure 1). These criteria included mostly Delalande type II and III (or Regis type II and III) lesions. To assess long-term outcomes, we retrospectively reviewed all HH patients treated with LITT at our institution between January 1, 2012 and December 31, 2015, who had at least 1 yr of follow-up. This study was conducted after receiving Institutional Review Board approval; informed consent was waived due to the retrospective nature of this project.

Preoperatively, patients underwent MRI of the brain and detailed neurological, endocrinologic, and cognitive behavioral evaluations. Postprocedure clinical and radiographic data were collected prospectively. HH disconnection was evaluated on a postoperative MRI at least 6 mo after therapy to evaluate the amount of residual HH attached to the wall of the third ventricle and the mammillary tubercle. Seizure outcomes were determined in person or through a mailed survey and telephone interview based on the International League Against Epilepsy (ILAE) treatment scale.[11] We defined good seizure control as an ILAE class 1 to 3 outcome.

Operative Technique

The Visualase MRI-guided laser ablation system (Medtronic, plc, Dublin, Republic of Ireland) was used, and our operative workflow has previously been described.[12] The laser catheter trajectory was planned by projecting a line from the center of the HH through the epicenter of its connection interface with the hypothalamus toward the surface of the brain. This trajectory was subject to several constraints that included (1) avoiding forniceal fibers that arch over the top of the hypothalamus; (2) avoiding the posterior limb of the internal capsule; (3) not crossing through the ventricle by a margin of at least 4 mm; (4) not exiting in eloquent cortex; and (5) avoiding cortical veins. These constraints were verified against the image guidance system MRI in 3 planes and the probe's eye and trajectory views, resulting in a customized trajectory for each patient. After finalization of the plan, the laser catheter was

stereotactically introduced to the treatment site by a fixed frame system an ll bolt.

red into an intraoperative MRI suite, wh nd ablation was performed. Real-time ab l by a computational Arrhenius rate process model to produce color-coded thermal and damage images of the surrounding target tissue.[13] The target was treated to a temperature threshold of 55°C around its distal margin, with safety zones drawn on the interface of the HH with local tissue, such as the mammillary tubercle, to shut off treatment if they exceeded a temperature threshold of 45°C.

Statistical Methods

Basic descriptive statistics of outcomes were performed in SPSS Statistics for Windows, Version 22.0 (IBM Corp, Armonk, New York). Data are presented as numbers and percentages, means ± standard deviations (SDs), and medians.

RESULTS

Patient Demographics

Eighteen patients (mean age, 21.1 yr; median age, 11 yr) were identified during the study period; demographic data are summarized in Table 1. Fifteen patients underwent 1 ablation treatment, and 3 patients underwent repeat therapy for a total of 21 treatment sessions. In the cohort, males were predominant (14/18, 78%), and half the patients were adults (≥18 yr). Nine (50%) patients had impaired cognitive development, as determined by neurocognitive assessments. Two patients had a diagnosis of Pallister–Hall syndrome, a genetic disorder associated with HH development. Nine (50%) patients had gelastic seizures only, 3 (17%) had nongelastic seizures only, and 6 (33%) experienced both. When lesions were categorized by the Delalande classification system,[14] 2 (11%) lesions were class 1; 9 (50%) were class 2; 6 (33%) were class 3; and 1 (6%) was class 4. Six (33%) patients had attachments to the hypothalamus on the left side, 7 (39%) had attachments on the right, and 5 (28%) had bilateral attachments.

Immediate Postoperative Complications

Immediate postoperative outcomes are outlined in Table 2. Seven (39%) of the 18 patients (5 pediatric [71%] and 2 adult [29%]) had new postoperative neurological deficits. Six patients had strength deficits contralateral to the side of intervention, and 2 had unilateral Horner's syndrome. No patient developed diabetes insipidus. These deficits affected hospital length of stay only for patient 11. After emerging from anesthesia, he had 4/5 rated left-sided weakness and severe orthostatic hypotension, requiring a 10-night stay and transfer to inpatient rehabilitation. Although patient 4 did not experience postprocedure deficits, she developed a small-bowel obstruction due to a large pancreatic pseudocyst and required prolonged medical and surgical treatment (50-night stay).

表格，请翻译，包括表头、表格中的英文文字、表注

TABLE 1. Demographic Characteristics of Patients With Hypothalamic Hamartoma Selected for LITT

Pt	Sex	Age at LITT (years)[a]	Genetic syndrome	Previous surgeries	Previous radio-therapy	Cognitive delay	Precocious puberty	Daily gelastic seizures	Nongelastic seizures	Delalande type	Attachment side
1	M	60.9				Yes	Yes	No	Tonic-clonic	4	Left
2	M	49.0				Yes		Yes	Tonic-clonic	2	Left
3	M	29.8			1			No	Complex partial	2	Right
4	F	7.3	Pallister-Hall			Yes		No	Tonic-clonic	1	Bilateral
5	M	23.0				Yes		Yes	Complex partial	2	Bilateral
6	M	29.1	Pallister-Hall	3		Yes		Yes	0	2	Left
7	M	8.5		1		Yes		Yes	Complex partial	2	Right
8	M	68.9						Yes	Complex partial	3	Right
9	M	13.6				Yes		Yes	Complex partial	3	Left
10	F	40.6		1	1			Yes	0	2	Bilateral
11	M	7.1		1	1			Yes	0	3	Bilateral
12	F	25.6		1		Yes		Yes	0	3	Bilateral
13	M	8.3				Yes		Yes	0	3	Right
14	F	11.0						Yes	0	2	Right
15	M	27.6						Yes	0	2	Left
16	M	3.3 and 3.9						Yes	0	1	Right
17	M	8.4 and 9.1					Yes	Yes	Complex partial	2	Right
18	M	3.9 and 4.6						Yes	0	3	Left

Abbreviations: F, female; LITT, laser interstitial thermal therapy; M, male; Pt, patient.
[a]Patients 16, 17, and 18 underwent 2 LITT procedures each.

Intermediate and Long-Term Complications

Patient follow-up data summarized in Table 3 include outcomes at the first follow-up appointment (mean ± SD, 6.3 ± 4.8 mo; median, 3.7 mo) and either at the last follow-up on record or immediately before additional treatment (mean ± SD, 17.5 ± 7.5 mo; median, 17.4 mo). At the first follow-up, neurological deficits were observed in 5 (28%) patients. Two of these deficits were new: patient 15 reported a sensory loss in his right leg, and patient 17 had partial loss of his left temporal visual field. Five (28%) patients had short-term memory deficits, 3 of which were new. Two (11%) had newly diagnosed hypothyroidism, and 4 (22%) demonstrated weight gain from increased appetite.

At the last follow-up, persistent neurological deficits were observed in 4 (22%) of 18 patients. Functional impact was noted only in patient 11, who required orthotic assistance for ambulation. Other complications at long-term follow-up included hypothyroidism in 2 (11%) patients, short-term memory issues in 4 (22%), and persistent weight gain in 4 (22%). A comparison of the adult and pediatric patients revealed that neurological deficits occurred in 1 adult patient and in 3 pediatric patients, hypothyroidism occurred in 1 patient in each group, memory deficits occurred exclusively in 4 adults, and weight gain was observed in 3 adult patients and in 1 pediatric patient.

Gelastic Seizure Control

Fifteen patients suffered from gelastic seizures, and at the first follow-up, 11 (73%) of these patients had good seizure control (ILAE class 1-3). At the latest follow-up, 12 (80%) patients had good seizure control. The 3 patients with failed therapy had substantial residual HH tissues with hypothalamic connections and underwent repeat LITT. After the second treatment, all 3 had near-complete radiographic ablation of HH-hypothalamus connections, and 2 achieved immediate, sustained seizure control at first follow-up. Ultimately, 14 (93%) of 15 patients achieved well-sustained gelastic seizure control, and 12 (80%) were seizure free. Between the 2 age groups, good seizure control was observed in 7 (88%) of 8 pediatric patients and in all 7 adults. Interestingly, among the 14 patients with good gelastic epilepsy outcomes, all had residual HH tissue on MRI, and 6 of the 14 (43%) had residual connections to the hypothalamus after their last treatment.

TABLE 2. Immediate Postoperative Adverse Effects for Patients With Hypothalamic Hamartoma Treated With LITT

Patient	Side treated	Full disconnection	Immediate new deficits	Endocrine deficits	Behavioral and cognitive deficits	LOS (nights)
Single treatment						
1	Left	No				1
2	Left	Yes			Short-term memory loss	1
3	Right	Yes				1
4	Right	No				50
5	Left	No	Left Horner's	No		1
6	Left	No	0	No		1
7	Right	No	Left 4+/5	No		1
8	Right	Yes	0	No	Short-term memory loss	1
9	Left	No	0	No		1
10	Left	Yes	0	No		1
11	Right	No	Left 4/5	No		10
12	Right	Yes	0	No		1
13	Right	No	0	No		1
14	Right	Yes	0	No		1
15	Left	Yes	Right leg 4+/5	No		1
Multiple treatment						
16	Right	No	0	No		1
16	Right	Yes	Left 4+/5	No		1
17	Right	No	Left 4+/5	No		1
17	Right	No	0	No		1
18	Left	No	Right 4+/5, Left Horner's	No		1
18	Left	Yes	0	No		1

Abbreviations: LITT, laser interstitial thermal therapy; LOS, length of stay.

表格，请翻译，包括表头、表格中的英文文字、表注

Nongelastic Seizure Control

Nine patients suffered from nongelastic seizures. After LITT therapy, 5 (56%) of the 9 patients initially had good seizure control, but deterioration eventually occurred in 2 patients. Patient 1, who initially had daily generalized tonic–clonic seizures, remained seizure free for >2 yr after therapy until weekly seizures returned. Patient 8, who experienced daily complex partial seizures, remained seizure free for >1 yr before weekly seizures recurred. Conversely, patients 5 and 7 initially demonstrated ILAE class 5 and 4 results, respectively, but improved to ILAE class 2 and 1 at last follow-up. Patient 17 initially had no change in seizure frequency but experienced sustained control immediately after a second LITT treatment. In summary, for nongelastic seizure control, initial outcomes were stable in only 5 (56%) of the 9 patients, and 6 (67%) patients ultimately achieved good seizure control. Between age groups, 3 (75%) of 4 pediatric patients and 3 (60%) of 5 adults had good nongelastic seizure control at last follow-up.

Case Examples

Case 1: Delayed Seizure Freedom After LITT

Patient 5, a 23-yr-old man with a history of cognitive delay, had treatment-resistant daily gelastic seizures and weekly complex partial seizures. Preoperative MRI demonstrated a 9 × 6 × 11-mm Delalande type 2 HH with bilateral but predominantly left attachments (Figure 2A). The patient underwent LITT with 2 ablations (Figures 2B-2D). Postoperatively, he developed left-sided Horner's palsy and was discharged home the following morning.

At 3-mo postprocedure, the patient's Horner's palsy had resolved, but he continued having weekly gelastic and complex partial seizures (ILAE class 4 and 5, respectively). At the 6-mo MRI, a small residual HH tissue connection was found and considered for repeat LITT (Figure 2E). Fortunately, weeks after the MRI, the patient became gelastic seizure free and only experienced auras associated with complex partial seizures (ILAE class 1 and 2, respectively). At his most recent follow-up (20.5 mo), the patient remained seizure free.

Case 2: Seizure Freedom After Repeat LITT

Patient 17, an 8-yr-old boy, began having daily gelastic seizures and weekly partial complex seizures at age 7. MRI of the brain demonstrated a Delalande type 2 HH with right-sided attachment (Figures 3A and 3B). The patient underwent right-sided LITT with 2 ablations (Figure 3C). Immediately after

TABLE 3. Follow-up Outcomes for Patients With Hypothalamic Hamartoma Treated With LITT

		First follow-up							Last follow-up						
Pt#	Full disconnection	First follow-up (mo)	ILAE: gelastic seizures	ILAE: nongelastic seizures	Neurological deficits	Endocrine deficits	Behavioral/cognitive deficits	Wt gain	Last follow-up (mo)	ILAE: gelastic seizures	ILAE: nongelastic seizures	Neurological deficits	Endocrine deficits	Behavioral/cognitive deficits	Wt gain
Single treatment															
1	Yes	7.2	NA	1					28.6	NA	5				
2	Yes	11.5	1	1			Short-term memory		25.1	1	1			Short-term memory	
3	Yes	7.9	NA	1					24.4	NA	1				
4	No	5.2	NA	4					17.4	NA	5				
5	No	3.0	4	5					20.5	1	2				
6	No	3.3	1	NA			Short-term memory		18.4	1	NA				
7	No	4.9	1	4	Left foot 4+/5				17.2	1	1	Left foot 4+/5			
8	Yes	14.0	1	2		Hypothyroidism	Short-term memory	Yes	17.4	1	4		Hypothyroidism	Short-term memory	Yes
9	No	13.3	3	1					26.6	2	1				
10	Yes	3.5	1	NA				Yes	12.8	2	NA				Yes
11	No	14.9	1	NA	Left arm and leg 4/5				26.2	1	NA	Left leg 4/5			
12	Yes	3.4	1	NA			Short-term memory		23.6	1	NA			Short-term memory	
13	No	2.4	1	NA					10.9	1	NA				
14	Yes	16.1	1	NA					13.5	1	NA				
15	Yes	2.2	1	NA	Right leg sensory loss and subjective weakness		Short-term memory	Yes	7.9	1	NA	Subjective right foot weakness		Short-term memory and word finding	Yes
Multiple treatments															
16	No	3.2	5	NA					6.7	5	NA				
16	Yes	3.5	5	NA					28.1	5	NA				
17	No	3.7	5	5				Yes	5.7	5	5		Hypothyroidism		Yes
17	Yes	5.7	1	1	Left temporal visual field impairment	Hypothyroidism			18.3	1	1		Hypothyroidism		
18	No	2.7	5	NA	Left Horner's				7.9	5	NA	Left Hor			
18	Yes	0.4	1	NA					9.5	1	NA				

Abbreviations: LITT, laser interstitial thermal therapy; LOS, length of stay; NA, not applicable; Pt, patient; Wt, weight.

表格，请翻译，包括表头、表格中的英文文字、表注

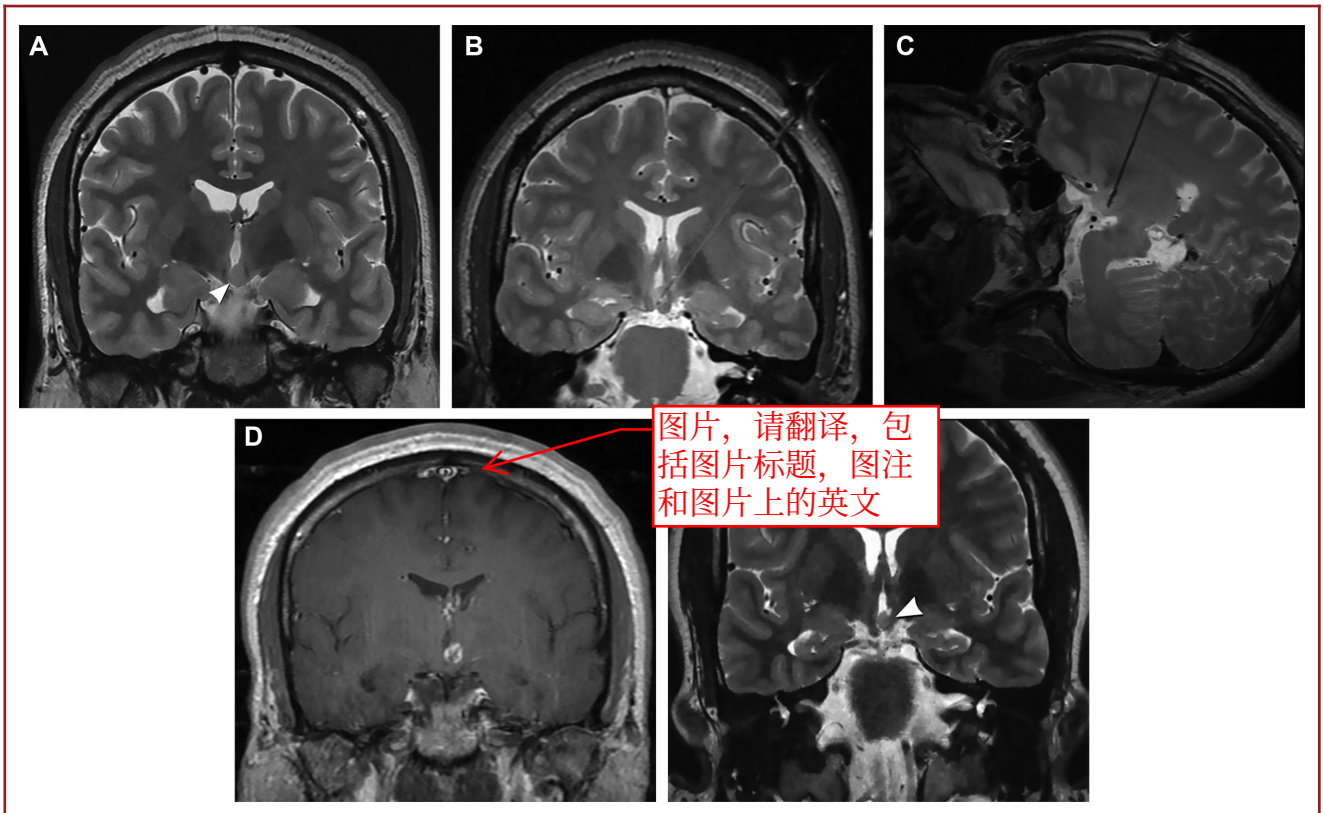


FIGURE 2. *MRI, patient 5.* **A**, *Coronal T2-weighted MRI demonstrates a Delalande type 2 HH (*arrowhead*) on the left wall of the third ventricle with greater left-sided than right-sided attachments. During LITT,* **B**, *coronal and* **C**, *oblique sagittal T2-weighted MRIs parallel to the length of the ablation catheter demonstrate targeting of the left side of the HH.* **D**, *Immediate postoperative coronal T1-weighted MRI with gadolinium contrast reveals the zone of ablation around the laser catheter involving the HH and its left-sided attachments.* **E**, *At 6-mo follow-up after LITT, a repeat coronal T2-weighted MRI demonstrates residual HH tissue (*arrowhead*) and a small amount of encephalomalacia along the left side of the lesion's connection. Used with permission from Barrow Neurological Institute.*

the procedure, the patient had mild left-side weakness. He was discharged home the following day.

At 5.7 mo post-LITT, the patient's left-sided weakness resolved; however, his seizure frequency was unchanged. He also gained 18 kg and developed hypothyroidism. MRI of the brain demonstrated persistent HH tissue with hypothalamic connection (Figure 3D), prompting repeat LITT with 5 ablations (Figure 3E). After the procedure, he emerged without any deficit and was seizure free. At last follow-up (18.3 mo after the second procedure), the patient remained seizure free (ILAE class 1), and imaging demonstrated near-complete disconnection of the HH (Figure 3F).

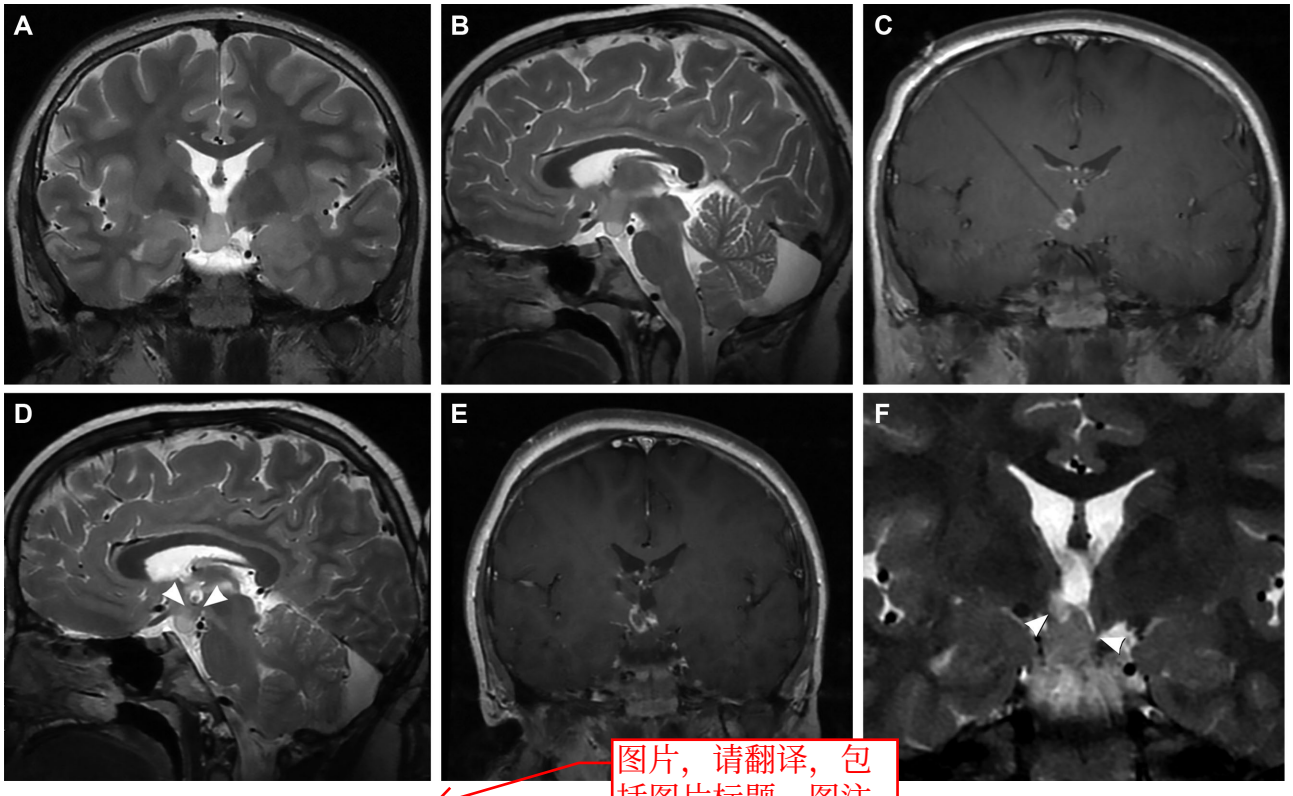
Case 3: Late Delayed Return of Gelastic Seizures After LITT

Patient 1, a 61-yr-old man with cognitive impairment, experienced weekly treatment-resistant generalized tonic-clonic seizures. MRI of the brain demonstrated a giant Delalande type 4 HH with left-sided attachment (Figure 4A). The patient was offered open craniotomy for resection or LITT. Given the patient's poor baseline function, he and his caregiver elected to proceed with left-sided LITT that proceeded without complication (Figures 4B and 4C). Immediately after surgery, the patient was noted to be seizure free, and he remained stable until 23 mo later when he experienced a sudden recurrence of weekly seizures. Repeat MRI demonstrated residual HH tissue and connection with the hypothalamus (Figures 4D and 4E). He was reevaluated and is choosing to defer repeat LITT at the time of this writing.

DISCUSSION

Existing HH Therapies

The clinical features associated with HH include gelastic seizures and a progressive epileptic encephalopathy characterized by the onset of additional seizure subtypes leading to cognitive regression.[1] Targeted resection of the HH or disconnection of its attachments to the hypothalamus is the mainstay of therapy.[14,15] Previous publications indicate that open surgical approaches with or without endoscopic assistance achieve seizure freedom in about 50% of cases, depending on the approach and HH anatomy.[16,17]



图片，请翻译，包括图片标题，图注和图片上的英文

FIGURE 3. *MRI, patient 17.* **A**, *Coronal and* **B**, *sagittal T2-weighted MRIs* [illegible] *HH eccentric to the right side.* **C**, *After LITT, on coronal T1-weighted MRI with gadolinium contrast enhancement, the ablation* [illegible] *lesion.* **D**, *At 6-mo follow-up after LITT, a sagittal T2-weighted MRI demonstrates encephalomalacia along the previous ablation site, but persistent connections between the HH and the hypothalamus* (arrowheads). **E**, *During repeat LITT, coronal T1-weighted MRI with gadolinium contrast reveals further ablation along the left-sided HH attachment.* **F**, *Three months later, a follow-up coronal T2-weighted MRI reveals near-complete disconnection of the HH, with 2 small foci of attachment* (arrowheads). *Used with permission from Barrow Neurological Institute.*

Complications from open surgery for HH vary, but overall morbidity is high, with most patients experiencing at least transient neurological or cognitive deficits. For 26 patients undergoing a transcallosal approach, Ng et al[16] reported transient memory disturbances in 15 (58%), with persistent impairment in 2 (8%) and endocrine disturbances in 2 (8%). Abla et al[18] reported on 10 patients undergoing orbitozygomatic craniotomy for HH; 1 (10%) patient each experienced postoperative hemiplegia, visual field deficits, and persistent diabetes insipidus. Of 37 patients undergoing transcortical transventricular endoscopic HH resection, Ng et al[17] reported residual short-term memory loss in 3 (8%) and symptomatic thalamic infarcts in 2 (5%).

Stereotactic radiosurgery is a less invasive alternative, but due to delays in treatment effect, it is typically limited to older patients with less clinical impairment. HHs must be small, have distinct anatomic boundaries, and be located away from radiosensitive or eloquent structures such as the fornices. Abla et al[6] reported on 10 HH patients treated with Gamma Knife radiosurgery (Elekta AB, Stockholm, Sweden). Four (40%) patients achieved seizure freedom without neurological deficits; however, 2 (20%) experienced weight gain due to increased appetite. In a series of 27 HH patients treated with Gamma Knife radiosurgery, Régis et al[7] reported that 10 (37%) achieved seizure freedom and 6 (22%) had significant reductions in seizure frequency. Complications were minor and included temporary worsening of seizures in 4 (15%) patients and transient poikilothermia in 3 (11%).

Radiofrequency ablation (RFA) is also reported to be safe and successful for HH treatment in case reports[19-22] and in 1 large case series of 25 patients reported by Kameyama et al.[23] Similar to LITT, RFA can be introduced stereotactically into the HH or through a minimally invasive endoscopic approach, and it may be less expensive and more widely available than LITT. However, RFA cannot be monitored in real time, requiring more conservative ablation that may necessitate multiple passes with the catheter. Kameyama et al[23] reported a mean of 3.8 catheter tracks in their series of 25 patients, whereas each of our patients had only 1. RFA seizure outcomes appear to be good, with gelastic

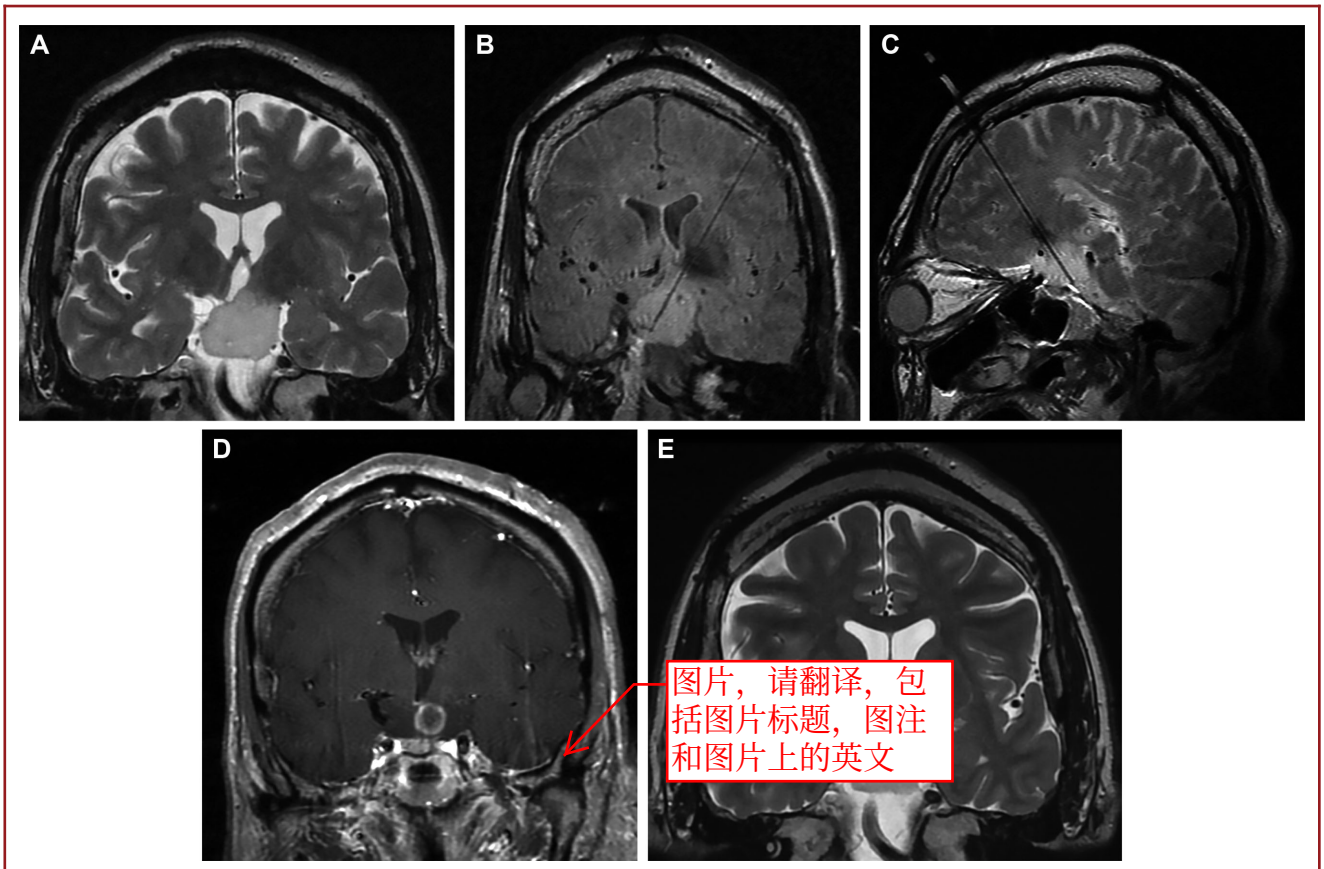


FIGURE 4. *MRI for Patient 1.* **A**, *Coronal T2-weighted MRI demonstrates a giant Delalande type 4 HH with predominantly left-sided attachments.* **B**, *Intraoperative coronal and* **C**, *sagittal fluid-attenuated inversion recovery sequences show the trajectory of the treatment catheter through the left-sided HH attachment into the mass itself.* **D**, *A postoperative coronal T1-weighted MRI demonstrates a large zone of ablation along the left-sided attachment.* **E**, *At 2-yr follow-up, a coronal T2-weighted MRI shows a large area of encephalomalacia within the HH and along its left-sided attachment, but with significant residual connections* (arrowheads). *Used with permission from Barrow Neurological Institute.*

seizure freedom obtained in 76% of reported cases and behavioral and memory changes observed in only 4 (16%) patients.

Study Outcomes

In contrast to traditional HH therapies, our LITT outcomes demonstrated superior seizure control with a similar incidence of unintended side effects. Of 15 patients who underwent treatment for gelastic seizures, 14 (93%) achieved an ILAE class 1 to 3 response at a mean follow-up of 17.5 mo, with the majority (12/15, 80%) requiring only 1 treatment. Furthermore, 12 (80%) patients were completely seizure free. For the 9 patients treated for nongelastic seizures, an ILAE class 1 to 3 response was observed in 5 (56%) patients at the latest follow-up. However, one-half of the patients with nongelastic seizures had eventual changes in seizure control, leading us to recommend close follow-up and delaying repeat treatments until patients have clinically stabilized. Additionally, residual HH tissue with hypothalamic connections was found on follow-up imaging in almost one-half of the patients who had good outcomes for gelastic seizure control. This finding suggests that there may be a threshold of ablation or disconnection for achieving seizure freedom that precludes the need for total disconnection.

Complications

Complications and adverse events after LITT therapy were common, but most were minor and transient. Immediate complications included a 39% (7/18) incidence of new neurological deficits and an 11% incidence (2/18) of short-term memory issues. At last follow-up, many patients with initial neurological deficits had improved, with 22% (4/18) having persistent deficits but only 1 (6%) patient experiencing functional impact. Hypothyroidism was the only long-term endocrine deficit (11%, 2/18). Over time, some patients (22%, 4/18) reported new subjective short-term memory issues, weight gain, or increased

appetite. Interestingly, we did not encounter diabetes insipidus, a complication commonly seen after the treatment of hypothalamic lesions, which may be due to minimal disruption of hypothalamic structures outside the ablation and catheter tract. Nonetheless, the incidence of immediate postprocedure deficits is higher than expected, especially given the absence of unintended injury to adjacent structures based on postoperative imaging. Furthermore, differences appear to exist between adult and pediatric patients, with adults more likely to experience memory deficits and pediatric patients more likely to experience neurological, endocrine, and weight aberrations. A more detailed study on the stereotactic trajectory, the relation of the targeting area to the hypothalamic subnuclei, and the ablation settings is warranted to refine the safety of LITT.

Our results are consistent with other reports in the literature. Wilfong and Curry[8] reported 14 patients undergoing LITT for HH with a mean follow-up of 9 mo. In their series, 90% of patients with follow-up longer than 6 mo achieved seizure freedom. They reported no neurological, endocrinologic, or cognitive complications at final follow-up. Possible reasons for this difference include a shorter length of follow-up (mean, 9 mo vs 17 mo), since many of the endocrine and memory deficits in our patients were detected after the first follow-up period (mean, 6.3 mo), and variations in the technical parameters of LITT. Additional analysis of the stereotactic, volumetric, and ablation settings in LITT with a larger collaborative cohort may shed light on the determinants of patient outcome.

Limitations

The retrospective nature of this study and the small number of patients preclude definitive conclusions on the efficacy of LITT for HH. Furthermore, many patients were unable to undergo formal neuropsychiatric evaluation postoperatively, which limits the accurate assessment of cognitive outcomes, particularly in pediatric patients.

CONCLUSION

Our initial experience with LITT for the treatment of HH has shown excellent seizure control outcomes that exceed previously reported rates for open surgical and radiosurgical techniques. The advantages of LITT include a typical 1-night postoperative hospital stay and immediate seizure control for gelastic epilepsy, as opposed to clinical latency with radiosurgery. LITT remains a promising treatment modality for HH that requires further study to determine long-term seizure control and neuropsychological outcomes. Although new postoperative deficits were common, the majority were mild, transient, and comparable to incidences reported for other surgical procedures.

Disclosure

The authors have no personal, financial, or institutional interest in any of the drugs, materials, or devices described in this article.

REFERENCES

1. Berkovic SF, Arzimanoglou A, Kuzniecky R, Harvey AS, Palmini A, Andermann F. Hypothalamic hamartoma and seizures: a treatable epileptic encephalopathy. *Epilepsia*. 2003;44(7):969-973.
2. Boudreau EA, Liow K, Frattali CM, et al. Hypothalamic hamartomas and seizures: distinct natural history of isolated and Pallister-Hall syndrome cases. *Epilepsia*. 2005;46(1):42-47.
3. Palmini A, Chandler C, Andermann F, et al. Resection of the lesion in patients with hypothalamic hamartomas and catastrophic epilepsy. *Neurology*. 2002;58(9):1338-1347.
4. Wait SD, Abla AA, Killory BD, Nakaji P, Rekate HL. Surgical approaches to hypothalamic hamartomas. *Neurosurg Focus*. 2011;30(2):E2.
5. Pati S, Abla AA, Rekate HL, Ng YT. Repeat surgery for hypothalamic hamartoma in refractory epilepsy. *Neurosurg Focus*. 2011;30(2):E3.
6. Abla AA, Shetter AG, Chang SW, et al. Gamma knife surgery for hypothalamic hamartomas and epilepsy: patient selection and outcomes. *J Neurosurg*. 2010;113(Suppl):207-214.
7. Regis J, Scavarda D, Tamura M, et al. Gamma knife surgery for epilepsy related to hypothalamic hamartomas. *Semin Pediatr Neurol*. 2007;14(2):73-79.
8. Wilfong AA, Curry DJ. Hypothalamic hamartomas: optimal approach to clinical evaluation and diagnosis. *Epilepsia*. 2013;54(suppl 9):109-114.
9. Lewis EC, Weil AG, Duchowny M, Bhatia S, Ragheb J, Miller I. MR-guided laser interstitial thermal therapy for pediatric drug-resistant lesional epilepsy. *Epilepsia*. 2015;56(10):1590-1598.
10. Curry DJ, Gowda A, McNichols RJ, Wilfong AA. MR-guided stereotactic laser ablation of epileptogenic foci in children. *Epilepsy Behav*. 2012;24(4):408-414.
11. Wieser HG, Blume WT, Fish D, et al. ILAE Commission Report: proposal for a new classification of outcome with respect to epileptic seizures following epilepsy surgery. *Epilepsia*. 2001;42(2):282-286.
12. Xu DS, Rosenfeld A, Ponce FA, Nakaji P, Bhardwaj RD. Cerebral peduncle tumor ablated by novel 3-mm laser tip. *Stereotact Funct Neurosurg*. 2015;93(1):38-41.
13. McNichols RJ, Gowda A, Kangasniemi M, Bankson JA, Price RE, Hazle JD. MR thermometry-based feedback control of laser interstitial thermal therapy at 980 nm. *Lasers Surg Med*. 2004;34(1):48-55.
14. Delalande O, Fohlen M. Disconnecting surgical treatment of hypothalamic hamartoma in children and adults with refractory epilepsy and proposal of a new classification. *Neurol Med Chir (Tokyo)*. 2003;43(2):61-68.
15. Likavec AM, Dickerman RD, Heiss JD, Liow K. Retrospective analysis of surgical treatment outcomes for gelastic seizures: a review of the literature. *Seizure*. 2000;9(3):204-207.
16. Ng YT, Rekate HL, Prenger EC, et al. Transcallosal resection of hypothalamic hamartoma for intractable epilepsy. *Epilepsia*. 2006;47(7):1192-1202.
17. Ng YT, Rekate HL, Prenger EC, et al. Endoscopic resection of hypothalamic hamartomas for refractory symptomatic epilepsy. *Neurology*. 2008;70(17):1543-1548.
18. Abla AA, Rekate HL, Wilson DA, et al. Orbitozygomatic resection for hypothalamic hamartoma and epilepsy: patient selection and outcome. *Childs Nerv Syst*. 2011;27(2):265-277.
19. Wang W, Guo X, Zeng Y, Jiang X. Hypothalamic hamartoma causing gelastic seizures treated with stereotactic radiofrequency thermocoagulation. *Epileptic Disord*. 2009;11(4):333-338.
20. Fukuda M, Kameyama S, Wachi M, Tanaka R. Stereotaxy for hypothalamic hamartoma with intractable gelastic seizures: technical case report. *Neurosurgery*. 1999;44(6):1347-1350.
21. Parrent AG. Stereotactic radiofrequency ablation for the treatment of gelastic seizures associated with hypothalamic hamartoma: case report. *J Neurosurg*. 1999;91(5):881-884.
22. Fujimoto Y, Kato A, Saitoh Y, et al. Stereotactic radiofrequency ablation for sessile hypothalamic hamartoma with an image fusion technique. *Acta Neurochir (Wien)*. 2003;145(8):697-700; discussion 700-691.
23. Kameyama S, Murakami H, Masuda H, Sugiyama I. Minimally invasive magnetic resonance imaging-guided stereotactic radiofrequency thermocoagulation for epileptogenic hypothalamic hamartomas. *Neurosurgery*. 2009;65(3):438-449; discussion 449.

COMMENTS

With technological advances and shifts toward minimally-invasive techniques, magnetic resonance guided laser interstitial thermal therapy (LITT) has become an essential technique for tumor surgery. The authors of this study report a modest case series of LITT for the treatment of refractory epilepsy due to hypothalamic hamartomas. The study reports improved seizure control in patients with classic gelastic seizures compared to targeted resection of hypothalamic hamartomas. This series remains one of the largest series utilizing this new technique for such a rare difficult disease. However, the authors' experience using LITT therapy does seem to carry modest surgical morbidity including persistent neurological deficits, memory loss, and endocrinopathies. LITT for hypothalamic hamartomas still remains an exclusive technique that is limited by surgeon experience with LITT and their knowledge of diencephalic anatomy. Nevertheless, surgeons should exercise a patient-specific approach when selecting treatment options for refractory seizures due to this pathology. We commend the authors for contributing for expanding the applicability of LITT for this rare subset of patients; we eagerly await prospective multi-institutional studies that may help corroborate the safety and efficacy of LITT for hypothalamic hamartomas.

Ashish H. Shah
Ricardo J. Komotar
Miami, Florida

This is very well written paper regarding the application of LITT in a rare and difficult to access tumor (hypothalamic hamartoma) that traditionally has limited treatment options with suboptimal outcome. The authors described the procedure very well and their long-term outcomes regarding seizure control (80% seizure free in patients with gelastic seizures) could be considered favorable to other treatment modalities like open/endoscopic surgery or radiosurgery. On top of that, with the advantage of this treatment modality in terms of postoperative hospital course and immediate complications compared to those associated with open surgery, and the added benefit of immediate seizure control compared to radiosurgery, LITT could be considered an attractive treatment option for patients with hypothalamic hamartoma.

Of note, despite being a minimal-access surgery, LITT induced hyperthermia can cause permanent damage to normal tissue and, as described explicitly in this paper, many factors need to be taken into account to minimize morbidity while maximizing long-term seizure control. For instance, precise trajectory planning is needed to prevent eloquent structures from the entry point to the target as well as sufficient extent of ablation to achieve maximal tumor coverage while minimizing overlap with adjacent eloquent structures. Needless to say, case selection is very important based upon the size, location, and presenting symptoms.

LITT has emerged as a novel minimally invasive treatment modality in the fields of neuro-oncology and epilepsy surgery with promising initial reports. However, like any other treatment modality, LITT has its own limitations and learning curve. Studies like this will be helpful to set benchmarks regarding risk/benefit of this treatment modality compared to other available alternative options.

Alireza M. Mohammadi
Michael A. Vogelbaum
Cleveland, Ohio

点评，请翻译