Stereotactic Laser Amygdalohippocampotomy for Mesial Temporal Lobe Epilepsy

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Objective: To evaluate the outcomes 1 year and longer following stereotactic laser amygdalohippocampotomy for mesial temporal lobe epilepsy in a large series of patients treated over a 5-year period since introduction of this novel technique.
Methods: Surgical outcomes of a consecutive series of 58 patients with mesial temporal lobe epilepsy who underwent the surgery at our institution with at least 12 months of follow-up were retrospectively evaluated. A subgroup analysis was performed comparing patients with and without mesial temporal sclerosis.
Results: One year following stereotactic laser amygdalohippocampotomy, 53.4% (95% confidence interval [CI] = 40.8–65.7%) of all patients were free of disabling seizures (Engel I). Three of 9 patients became seizure-free following repeat ablation. Subgroup analysis showed that 60.5% (95% CI = 45.6–73.7%) of patients with mesial temporal sclerosis were free of disabling seizures as compared to 33.3% (95% CI = 15.0–58.5%) of patients without mesial temporal sclerosis. Quality of Life in Epilepsy-31 scores significantly improved at the group level, few procedure-related complications were observed, and verbal memory outcome was better than historical open resection data.
Interpretation: In an unselected consecutive series of patients, stereotactic laser amygdalohippocampotomy yielded seizure-free rates for patients with mesial temporal lobe epilepsy lower than, but comparable to, the outcomes typically associated with open temporal lobe surgery. Analogous to results from open surgery, patients without mesial temporal sclerosis fared less well. This novel procedure is an effective minimally invasive alternative to resective surgery. In the minority of patients not free of disabling seizures, laser ablation presents no barrier to additional open surgery.

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Mesial temporal lobe epilepsy (MTLE) represents roughly one-quarter of all cases of epilepsy, approximately one-third of which are refractory to medication.[1] The standard surgical treatment of drug-resistant MTLE has been open surgical resection of the medial temporal lobe, including most of the hippocampus and amygdala as well as the parahippocampal gyrus. This can be performed with an anterior temporal lobectomy (ATL)[2] or via a more "selective" approach (selective amygdalohippocampectomy [SAH]), which avoids resection of the anterior temporal lobe, gaining access to the medial temporal lobe by transection through a white matter corridor. A recent meta-analysis comparing ATL and SAH demonstrated 1-year rates of freedom from disabling seizures of 75% and 67%, respectively (determined from the reported risk ratios and absolute risk reductions).[3] The

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analysis showed that 13 patients needed to be treated to render 1 additional patient seizure-free after ATL.

ATL has been associated with cognitive impairments and focal neurological deficits,[4–10] particularly with regard to verbal memory[11] and aspects of naming ability.[8–10] The rationale to perform a more selective resection (ie, SAH) has been, at least in part, to minimize neurocognitive impact related to resection of the anterior temporal lobe. However, SAH has not clearly prevented cognitive declines.[7–9,12–14] On the dominant side, SAH has been associated with greater declines in verbal learning than ATL, which has been related to the degree of "collateral damage" within the temporal stem resulting from its transgression during the approach to the medial temporal structures.[15] Novel surgical approaches that minimize the degree of collateral injury during ablation of medial temporal structures may reduce cognitive impact, but perhaps at a cost to seizure outcome. That tradeoff may determine the relative benefits of such a minimally invasive approach.

Stereotactic laser amygdalohippocampotomy (SLAH) utilizes minimally invasive stereotactic access for insertion of a cooled catheter through which an optical fiber delivers laser energy. Laser heating, controlled by real time magnetic resonance (MR)-guided thermal mapping, produces thermocoagulative necrosis of the hippocampus, subiculum, amygdala, and uncus, while relatively sparing other medial, basal, and lateral temporal structures.[16,17] In early studies, SLAH has shown promise for stopping seizures while avoiding neurocognitive declines typically associated with ATL and SAH.[18] To better determine the safety and effectiveness of this procedure, we report outcomes at 1 year following SLAH in 58 patients with MTLE, with or without mesial temporal sclerosis (MTS), treated over the first 5 years after the introduction of the laser ablation for epilepsy.

Patients and Methods

Patient Selection

All patients who underwent SLAH for MTLE between July 1, 2011 and June 30, 2016 were included in this retrospective analysis, which was performed under a protocol approved by the Emory University Institutional Review Board. Candidates for surgical treatment underwent a standard diagnostic epilepsy evaluation comprised of long-term inpatient scalp video electroencephalographic (EEG) monitoring, 3T (unless contraindicated) MR imaging (MRI) including coronal T2 and T2 fluid-attenuated inversion recovery (FLAIR) sequences, 18-fluorodeoxyglucose positron emission tomography, and neuropsychological testing. The preoperative MRI scans were evaluated by neuroradiologists and neurosurgeons for presence of MTS, defined as atrophy of the hippocampus with loss of internal architecture and/or presence of increased signal on T2 and/or T2 FLAIR sequences. If necessary, additional testing was performed, including language lateralization determination via functional MRI; intracarotid amobarbital (Wada) testing; and/or invasive EEG monitoring via depth, strip, grid, and/or foramen ovale electrodes. Final vetting for surgery was determined in a multidisciplinary conference that included epileptologists, neurosurgeons, neuroradiologists, and neuropsychologists. Patients who had electrographic evidence of unilateral anterior temporal onsets on scalp EEG and/or medial temporal onsets on invasive EEG, with concordant MTS, if present, and/or concordant temporal hypometabolism on PET, were offered a choice of open resection or SLAH, although later in the series the option of open temporal surgery was not offered to patients with dominant hemisphere onsets.

Surgical Procedure

One of 2 surgeons (R.E.G. and J.T.W.) performed SLAH with patients under general anesthesia using the Visualase system (Medtronic, Lewiston, CO) for laser energy delivery and MR thermal imaging, as previously described.[19–21] Some patients underwent implantation of the laser catheter in the operating room using a standard stereotactic head frame (CRW; Integra Neurosciences, Plainsboro, NJ), but the majority of patients underwent implantation of the catheter in the MRI scanner using an MRI-guided trajectory frame (ClearPoint ScalpMount SmartFrame; MRI Interventions, Irvine, CA). Trajectories were chosen to penetrate the central portion of the hippocampus from the body at the level of the tectal plate through the head, continuing through the amygdala to the medial temporal pole. The laser fiber was inserted and adjusted if the location was suboptimal. Thermal maps were acquired continuously throughout the laser energy delivery to monitor the target and surrounding tissue temperatures. A 15W 980nm wavelength diode laser was used to generate the laser light, first as a low-power subablative test pulse to verify position of the heating, and then at ablative intensities. Multiple pulses were generated along the surgical tract to create a contiguous overlapping ablation zone via manual translation of the fiber within the catheter until the entire target was lesioned. A second tract was employed when anatomically necessary in a minority of cases. After postablation imaging with various sequences including gadolinium-enhanced T1, the probe was removed. Patients were typically monitored overnight in a standard hospital room, except for a few patients early in the series who were monitored in the intensive care unit for 1 day, and most patients were discharged on postoperative day 1. Figure 1 presents a series of images outlining the course of the procedure for a representative patient, including preoperative workup, intraoperative thermal imaging, immediate postoperative imaging, and 1-year follow-up imaging.

Patients who were not free of disabling seizures following the procedure were considered for further surgical intervention, including open resection and, for patients in whom review of an interval postoperative MRI scan showed a remnant region of the hippocampus and/or uncus thought to be responsible for ongoing seizures, repeat ablations. The latter were performed in a fashion similar to the initial ablation but from a more lateral entry, targeting the remnant medial temporal structures.

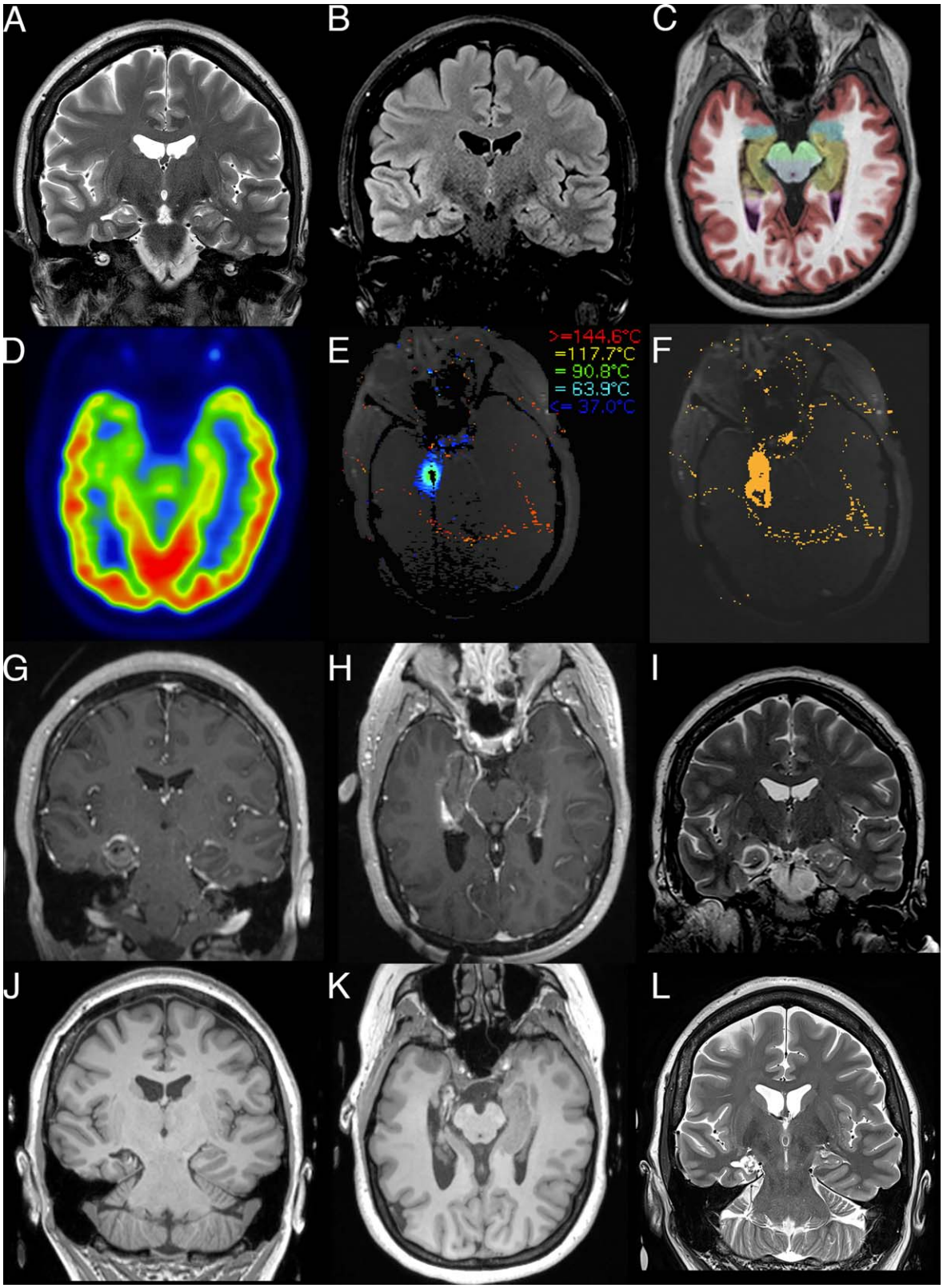

FIGURE 1: Representative magnetic resonance (MR) images from the pre- and postoperative course of a representative stereotactic laser amygdalohippocampotomy patient with right mesial temporal sclerosis (MTS). Preablative diagnostic workup demonstrates the characteristic findings of MTS being hippocampal atrophy with increased T2 (A, coronal) and T2 fluid-attenuated inversion recovery (B, coronal) intensity. This is further highlighted by NeuroQuant (CorTechs Laboratory, San Diego, CA) segmentation (C, axial) with the colorized medial temporal lobe structures (hippocampus in brown and amygdala in blue) overlaid on T1 imaging. Preoperative 18-fluorodeoxyglucose positron emission tomography (D, axial) demonstrates hypometabolism in the right medial temporal structures, consistent with right MTS. Intraoperative MR thermometry is utilized to guide the procedure (E, axial screenshot of Visualase thermal map generated during laser interstitial thermal therapy (LITT) of the amygdala) and assess the thermal damage following the procedure (F, axial screenshot of Visualase irreversible damage estimation). Immediate postablative imaging demonstrates T1 hypointensity of the ablation target with peripheral contrast enhancement (G, coronal and H, axial; magnetization-prepared rapid acquisition gradient echo [MPRAGE]) and T2 (I, coronal) hypointense rings surrounding the ablation. Twelve-month follow-up imaging demonstrates necrosis and volume reduction of the target tissue with the resulting cavitation on T1 (J, coronal and K, axial; MPRAGE) and T2 hyperintensity (L, coronal).

Patients who failed a repeat ablation were again considered for open surgical procedures.

Outcome Categorization

All patients had follow-up by a neurosurgeon and/or neurologist typically at 6 weeks, 3 months, 6 months, 12 months, and then every 12 months. Assessments included postoperative complications, seizure frequency, antiepileptic medication doses, and quality of life (Quality of Life in Epilepsy Inventory-31 [QOLIE-31]). Surgical outcomes using Engel's classification scheme[22] were determined by retrospectively analyzing clinic notes and patient correspondence. For patients who underwent additional surgical procedures, such as repeat SLAH or ATL, the last observation prior to the second surgery was carried forward, with the following exception; patients who attained 12 months of outcome following a second SLAH procedure on the same target (ie, the medial temporal lobe; n = 9) were recategorized with respect to that second procedure, with the initial procedure having been considered a technical failure. Patients who underwent a subsequent ATL (n = 4) continued to be categorized as not seizure-free with respect to the previous SLAH. Only patients who had generalized convulsive seizure(s) immediately following antiepileptic drug withdrawal were categorized as Engel ID, following the original classification scheme. A 95% confidence interval (CI) was generated for the proportion of the patients who remained seizure-free for at least 12 months following SLAH.

The postoperative progression of seizure freedom within our cohort was also examined via a Kaplan–Meier analysis, with events being defined as recurrence of debilitating seizures and censorship at the point of last follow-up. For those patients having undergone a repeat SLAH, the analysis was performed with respect to the repeat procedure.

Quality of life was determined from administration of the QOLIE-31 before SLAH and at 1-year follow-up. Only data from patients having QOLIE-31 data before and after SLAH, but before an open resection, if applicable, and having passed performance validity measures, are included. For this inventory, patients' responses were scored on a point scale from 0 to 100, with a higher number indicating a more positive outcome in terms of quality of life. Raw scores were then converted to T scores scaled against the mean of a cohort of epilepsy patients originally used to develop the inventory, with the mean of that original cohort set at 50. Thus, a score > 50 would indicate a more favorable outcome in terms of quality of life than is generally experienced among epilepsy patients; a score < 50 would indicate a lower quality of life. Overall quality of life was examined through descriptive statistics, as well as through the 3 subcategories believed to be the most relevant to the outcomes following a surgical intervention: seizure worry, cognitive function, and emotional well-being. A 2-tailed repeated measures *t* test was performed for the overall quality of life as well as the subcategories.

Verbal memory was assessed using the Rey Auditory Verbal Learning Test (RAVLT), a standard measure of verbal learning and memory used regularly in the context of epilepsy surgery.[23,24] The RAVLT requires free recall of words from a list of 15 unrelated words, which are repeated over 5 separate trials. Recall is tested at the end of each of 5 trial presentations. An alternative word list is then presented and tested, followed by an immediate recall of the words from the original list. This is followed by another free recall at the end of a 30-minute delay period filled with other unrelated tasks. This test was administered at presurgical baseline and an average of 6.4 (standard deviation = 1.5) months after surgery (range = 5–11 months). We examined the 5-trial learning total and delayed recall scores from the RAVLT, using reliable change index scores.[25] We also used paired sample *t* tests to determine whether pre- to postablation change was significant at the group level. Forty-nine of the 58 patients had these data available for evaluation.

Results

Patient Demographics and Diagnostic Data

A total of 58 patients underwent SLAH, including 33 females and 25 males, ranging in age from 16 to 67 years (mean = 40 ± 15 years) at the time of first SLAH (Table 1). Thirty patients underwent right-sided and 28 left-sided procedures. MRI demonstrated MTS in 43 patients, 3 of whom had bilateral MTS, which was greater on the operated side. An additional 3 patients had signal increase in the hippocampus on T2 and/or FLAIR imaging, but lacked hippocampal atrophy. The Supplementary Table presents each patient's presurgical diagnostic data. Several patients had imaging findings possibly suggestive of secondary epileptogenic foci.

A total of 67 laser ablation procedures were performed: 58 initial procedures and 9 repeat procedures in 9 patients. Two patients with recurrent seizures following SLAH elected to undergo ATL as a secondary procedure, and 2 additional patients underwent ATL following unsuccessful repeat SLAH. Repeat SLAH was performed 12.9 ± 11.9 months following the initial procedure. The ATLs were performed 8.5 ± 4.5 months (mean) after the initial or, if performed, repeat SLAH. The mean length of stay was 1.4 ± 0.7 days following both initial and 1.3 ± 0.5 days following repeat SLAH procedures.

Seizure Outcomes

Thirty-one of 58 patients (53.4%, 95% CI = 40.8–65.7%) were free of disabling seizures (Engel I) for $\geq$12 months following SLAH (Fig 2A), including 3 patients who were initially not seizure-free but achieved Engel I outcomes for $\geq$12 months following repeat ablation of remaining medial temporal tissue. Of patients with MTS, 26 of 43 (60.5%, 95% CI = 45.6–73.7%) were free of disabling seizures at $\geq$12 months, only 1 of whom underwent repeat ablation. Conversely, only 5 of 15 (33.3%, 95% CI = 15.0–58.5%) patients without

TABLE 1. Patient Demographics

Characteristic	Value
Female, %	56.9, n = 33
Age, yr, mean ± SD	
At SLAH	40.4 ± 15.1
At first nonfebrile seizure	17.1 ± 14.2
Left-sided procedures, %	48.3, n = 28
Radiological findings, %	
Unilateral MTS only	48.3, n = 28
Other[a]	6.9, n = 4
Both MTS and other[a]	25.8, n = 15
Normal	19.0, n = 11
Prior surgery for epilepsy, %[b]	5.2, n = 3

[a]Other radiological findings included temporal lobe–gray white matter blurring, dysmorphic temporal lobe, dysmorphic hippocampi, temporal asymmetry, hippocampal asymmetry, diffuse atrophy (temporal and parietal), atrophic fornix and mammillary body, encephalomalacia (frontal periventricular, temporal, and occipital), gliosis, parietal arachnoid cyst, parietal calvarium lesion, subependymal gray matter heterotopia (periventricular and frontal), bifrontal contusions, temporal bone fracture, microhemorrhages (corpus callosum, thalamus, frontal cortex, and subcortex), microvascular ischemic changes, resection of parieto-occipital meningioma, and traumatic brain injury.

[b]Surgeries included an anterior two-thirds corpus callosotomy, an amygdalohippocampectomy, and resection of a temporal juvenile pilocytic astrocytoma. None of these occurred in patients with unilateral MTS only or magnetic resonance imaging–normal patients. Two of these surgeries were performed in patients with MTS plus other radiological findings.

MTS = mesial temporal sclerosis; SD = standard deviation; SLAH = stereotactic amygdalohippocampotomy.

MTS achieved Engel I outcomes. Following repeat ablation, 7 of 9 patients experienced improved outcomes, with 3 of those achieving freedom from disabling seizures (Engel IB; see Fig 2B, C). Of the 31 patients who achieved freedom from disabling seizures, 22 were completely seizure-free (Engel IA), 7 had nondisabling simple partial seizures (Engel IB), 1 had a single generalized convulsive seizure with antiepileptic drug withdrawal (Engel ID), and 1 had generalized convulsive seizure associated with hyponatremia secondary to carbamazepine use (Engel ID).

Four patients underwent ATL following SLAH, 2 after a single SLAH procedure and 2 following repeat ablations. After 1 year, only 1 such patient achieved seizure freedom (a single simple partial seizure occurred at 6 weeks); the others experienced a reduction in seizure frequency (Engel II [n = 1] and Engel III [n = 2]). Notably, none of these 4 patients had MTS on MRI.

Only 4 of 27 patients not free of disabling seizures underwent open resections. Reasons for not having subsequent open surgery varied, including (1) nearly seizure-free or only nocturnal seizures (n = 11), (2) not interested in further surgery (n = 6), (3) moved or lost to follow-up (n = 3), (4) possible contralateral onsets (n = 1), (5) underwent callosotomy (n = 1), and (6) ATL is scheduled to be performed.

Open Resections during the Study Period

To determine whether there was a selection bias in the SLAH cohort, we tabulated the open temporal lobe resections during the 5-year study period, comprising 22 patients who underwent either ATL (n = 20) or SAH (n = 2). Reasons varied for undergoing open resection. Six underwent ATLs following failed medial temporal surgeries: 4 SLAH (as noted above) and 2 other medial temporal procedures. Eight ATLs were performed at the completion of invasive monitoring with subdural grid electrodes, along with removal of the electrodes; of these, 2 had onsets found to be medial temporal. Five patients were offered ATL but not SLAH, for the following reasons: 1 due to the presence of an ipsilateral visual field deficit from a contralateral occipital stroke (contraindicating an ipsilateral occipital lobe procedure), 2 due to the presence of other temporal lobe lesions (occipital–temporal gyrus calcified lesion; basal temporal encephalocele), 1 due to another possible epileptic focus, and 1 out of concern for patient inability to return for follow-up (this patient never returned for follow-up after surgery). This latter patient, therefore, was the only surgical patient during the timespan of this series who was not offered SLAH despite being a bona fide candidate. Finally, 3 patients who had been offered both options chose open surgery over SLAH (1 ATL and 2 selective amygdalohippocampectomy). Overall, 11 of 22 (50%; 1 lost to follow-up was categorized as not seizure-free) were seizure-free (8 Engel IA, 2 Engel IB, 1 Engel ID) at 1 year following open temporal surgery. Of these 22, 12 patients could be considered equivalent to the SLAH patients: offered SLAH but chose open resection (n = 3), only offered ATL for reasons other than having a possible alternative epileptic zone (n = 2), underwent ATL after invasive monitoring that identified mesial structures as the sole onset zone (n = 2), or underwent but failed SLAH (n = 4; ie, were originally considered SLAH candidates) or another medial temporal procedure (n = 1) prior to ATL. Six of these 12 patients (50%) were seizure-free, all being Engel IA; 6 of the remaining 10

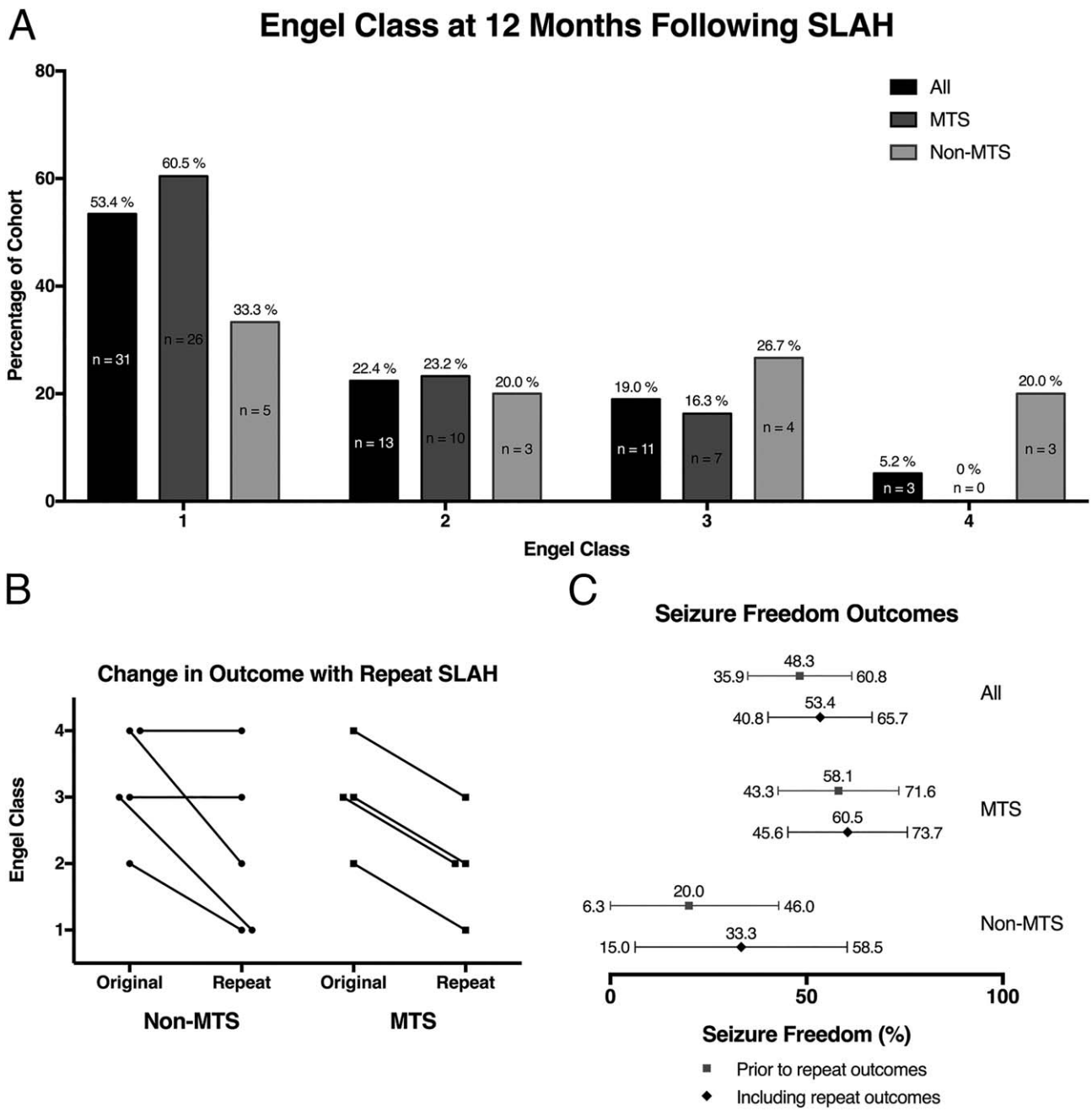

FIGURE 2: Outcome following stereotactic laser amygdalohippocampotomy (SLAH) at 12-month follow-up. (A) Distribution of 12-month patient outcomes by Engel class with respect to last SLAH procedure. The numbers above the bars indicate the percentage of patients in each class, and the numbers within the bars equal the number of patients (bar color: all, black; mesial temporal sclerosis [MTS], dark gray; non-MTS, light gray). (B) Comparison of 12-month patient outcomes as stratified by Engel class for patients having undergone repeat SLAH with the 12-month outcomes following the first SLAH (Original) compared with the 12-month outcome following the repeat SLAH (Repeat), demonstrating sustained or improved outcome following the repeat procedure. Non-MTS and MTS groups are presented. (C) The 1-year seizure freedom rates observed for all patients with the 95% confidence intervals. The black diamonds are the outcomes with respect to the last SLAH procedure (ie, including repeat procedures), and the gray squares are the outcomes with respect to only the first procedure. All patients are presented, as well as the subgroups of MTS and Non-MTS.

(ie, not equivalent) patients who underwent ATL (60%) were also free of disabling seizures. These data suggest that the results in the SLAH cohort were not due to selection bias, and that these results represent the wide range of patients who present for surgery for MTLE at a high-volume epilepsy center.

Seizure Freedom Survival Analysis

A Kaplan–Meier analysis of the time until seizure recurrence was performed to determine the long-term efficacy of SLAH. As per the Engel classification scheme, seizures within the first month were excluded. The recurrence rate was greatest within the first 6 months following SLAH. Seizure recurrence occurred at a lower but steady rate through 24 months (seizure freedom = 34.3%, 95% CI = 19.7–49.3%), after which point seizure recurrence was no longer observed. The longest follow-up without seizure recurrence was 53 months (Fig 3A). When comparing non-MTS patients to those with MTS, the Mantel–Cox log-rank test indicated that there was a significant difference between the seizure-free survival curves (chi-square = 6.636, $df = 1$, $p = 0.01$), with non-MTS patients being 3.32 (Mantel–Haenszel hazard ratio; 95% CI = 1.33–8.29) times more likely to have seizure recurrence than those with MTS (see Fig 3B).

Quality of Life Outcomes

At the group level, patients (n = 41) who underwent SLAH experienced improved quality of life as compared to their presurgical states. Follow-up ranged from 5 to 28 months post-SLAH, with a mean of 12.4 ± 4.0 months. All 9 patients who underwent repeat SLAH are included here, with the follow-up outcomes of 8 following the repeat SLAH and 1 following the first SLAH (ie, before the repeat procedure). For overall quality of life, a significant improvement was observed following SLAH ($p < 0.002$). There were also significant improvements observed in all of the explored subcategories, including seizure worry ($p < 0.0001$), cognitive functioning ($p = 0.001$), and emotional status ($p < 0.05$).

Complications

Five visual field deficits (VFDs) occurred (5/58 = 8.6%), only 1 of which was persistent and symptomatic (1.7%; see Supplementary Table). This was a nearly complete homonymous hemianopia that followed a repeat ablation, and may be attributable to thermal spread to the ventral thalamus, in the region of the lateral geniculate nucleus. The second VFD was a superior quadrantanopia secondary to an intraparenchymal hematoma in the occipital region; although persistent on formal visual field and confrontation testing, it was asymptomatic on last follow-up. A third patient complained of vague visual difficulties and had a mild incongruous hemianopic central depression, thought to be at the level of the optic tract, but follow-up formal and confrontation visual field testing were normal. The other 2 VFDs were mild superior quadrantanopias that were asymptomatic on follow-up confrontation testing; formal field testing was persistent in 1, and not obtained in the other. These mild quadrantanopias are believed to have resulted from the most posterior ablations having encroached upon the optic radiation in the external sagittal stratum. After this etiology had been recognized, it did not occur in the last 33 of 58 patients. In addition to the 1 intraparenchymal

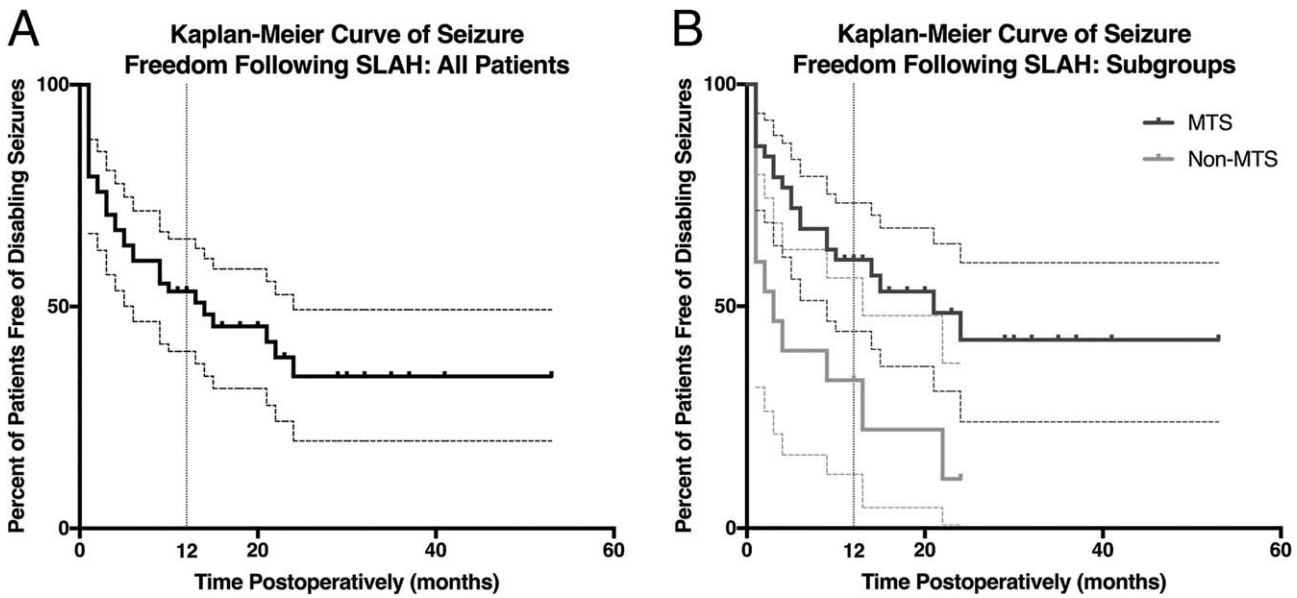

FIGURE 3: Long-term seizure outcomes. Kaplan–Meier depiction is shown of the time to recurrent seizures following last stereotactic laser amygdalohippocampotomy (SLAH). All patients (A) are presented, as well as a comparison (B) of the patients with mesial temporal sclerosis (MTS; dark gray) to those without (light gray). Dashed lines corresponding in color to their solid line counterparts indicate 95% confidence intervals. Tick marks indicate censorship. A vertical gray dashed line is presented to indicate the 12-month time point.

TABLE 2. Verbal Memory Outcomes

	RAVLT–Learning		RAVLT–Delayed Recall	
	Pre-SLAH	**Post-SLAH**	**Pre-SLAH**	**Post-SLAH**
All subjects, n = 49	41.8 ± 10.8 (14–65)	41.9 ± 11.6 (11–59)	5.9 ± 3.9 (0–15)	6.5 ± 4.1 (0–14)
Language dominant hemisphere SLAH, n = 20	37.4 ± 10.7 (14–62)	35.3 ± 12.7 (11–56)	4.6 ± 3.7 (0–13)	4.2 ± 3.4 (1–12)
Nondominant hemisphere SLAH, n = 29	44.9 ± 10.0 (33–65)	46.6 ± 8.3 (22–59)	6.6 ± 3.9 (1–15)[a]	8.2 ± 3.7 (0–14)[a]

Scores are presented as mean ± standard deviation (range).
[a]Scores differed significantly across pre- and postsurgical ablation time points ($p < 0.05$).
RAVLT = Rey Auditory Verbal Learning Test; SLAH = stereotactic laser amygdalohippocampotomy.

hematoma noted, there was 1 additional hemorrhage, an acute subdural hematoma that was operatively addressed immediately following ablation; it was not associated with a neurologic deficit. Four patients (4/58 = 6.9%) experienced transient nondisabling partial cranial nerve palsies (III and IV), believed to have resulted from thermal injury spreading medially at the tentorium when ablating the uncus, subiculum, and/or entorhinal cortex. All 4 patients were treated with steroids and recovered completely.

Memory Outcomes

Four of 49 (8.2%) patients experienced a decline on 1 (n = 3) or both (n = 1) subscores of the RAVLT (verbal memory) measure. This included 3 of 20 (15%) patients undergoing SLAH involving their language-dominant cerebral hemisphere and 1 of 29 (3.4%) patients undergoing a nondominant SLAH. Of the 3 language-dominant SLAH patients to significantly decline on this memory measure, 2 declined on the learning trial only and the third declined on both the learning and delayed recall trials. Notably, 2 of the patients who declined had dual pathology involving the lateral temporal lobe region (1 of these patients also had MTS), and 1 patient had normal neuroimaging. The single nondominant SLAH patient to experience significant decline involved a patient with right MTS who exhibited a decline on the learning trial only. In contrast, significant improvements were observed in 2 of 20 (10%) patients undergoing language-dominant SLAH and 7 of 29 (24.1%) patients undergoing nondominant SLAH. Improvements were typically in the delayed recall score of the RAVLT (8 of 9 cases). At the group level, the only significant change following ablation was the improvement seen in delayed verbal recall by the nondominant SLAH group ($t = -2.08$, $p < 0.05$; Table 2).

Discussion

Stereotactic laser amygdalohippocampotomy, a minimally invasive approach to medial temporal lobe surgery using MR-guided laser interstitial thermal therapy, eliminated disabling seizures in 53.4% (95% CI = 40.8–65.7%) of all patients with MTLE, and 60.5% (95% CI = 45.6–73.7%) of patients with MTS, at 1 year following surgery. These results mirror and expand our early results[19] and those of others in smaller uncontrolled cohorts (Table 3). In the aggregate of our series and those currently published series' 1-year outcomes, 56 of 98 patients overall (57.1%) and 42 of the 69 patients with MTS (60.8%) became free of disabling seizures at 1-year follow-up. It should be noted that series such as these, describing the outcome of a novel approach and representing a center's initial cohort of patients, are prone to be nonrepresentative of a mature technique, reflecting each individual center's "learning curve" with respect to patient selection and technical performance.

By contrast, there is an extensive experience with both ATL and selective amygdalohippocampectomy. Two randomized controlled trials compared ATL to best medical therapy in single-blinded designs. The Canadian trial found that 58% of patients in the surgical arm (n = 40, intent-to-treat group) and 64% of operated patients (n = 36) became free of disabling seizures for 1 year following surgery, versus 8% in the medical arm.[2] The second, the Early Resective Surgery for Epilepsy Trial (ERSET), found that 73% of highly selected operated patients (intent-to-treat group, n = 15; 85% of patients with a complete dataset) remained free of disabling seizures in the second year following surgery, versus no subjects in the control arm.[26] In contrast to these studies, however, the present cohort represents a "real-world" series of patients, not a selected subset. This is evident by

TABLE 3. Published SLAH Series

Study	No.	Age Range, yr	Mean LOS, days	Complications	Mean Follow-up, mo	Outcomes
Curry 2012[16]	1	16	4.0	None	12.0	Engel ID: 1/1 (100%); patient with MTS
Willie 2014[19] (included in this series)	13	16–64	1.5; repeat: 1.0	1 VFD, 1 acute SDH (without neurodeficit)	15.2[a]	Engel I: all, 7/13 (53.8%); MTS, 6/9 (66.7%)
Waseem 2015[31]	7	54–67	1.6	2 partial VFD	12.0	Engel I: 4/5 (80.0%)
Kang 2016[30]	20	11–66	1.2	1 VFD (superior quadrantanopsia due to an IPH), 1 transient fourth CNP, 1 suicide	13.1	Engel I at 1 year: all, 4/11 (36.4%); MTS, 4/10 (40.0%)
Jermakowicz 2017[27]	23	12–37	1; 75% 1–3 (range)[b]	1 VFD (homonymous hemianopia)	22.4	Engel I: all, 16/23 (69.6%); non-MTS, 5/8 (62.5%); MTS, 11/15 (73.3%)
Gross 2018 (this series)	58	16–67	1.4; repeat: 1.3	3 VFD (2 superior quadrantanopsias[c] and 1 homonymous hemianopsia after repeat SLAH, 1 acute SDH and 1 acute IPH with no neurodeficits, 4 transient partial CNP (1 third nerve and 3 fourth nerve[c])	≥12	Engel I: all, 31/58 (53.4%); non-MTS, 5/15 (33.3%); MTS, 26/43 (60.5%)

[a]With respect to last SLAH procedure if 12-month outcome achieved.
[b]Only data reported.
[c]One patient had both a superior quadrantanopsia after initial SLAH and a transient fourth nerve palsy after repeat SLAH.
CNP = cranial nerve palsy; IPH = intraparenchymal hematoma; LOS = length of stay; MTS = mesial temporal sclerosis; SDH = subdural hematoma; SLAH = stereotactic laser amygdalohippocampotomy; VFD = visual field deficit.

the paucity of patients in this period who underwent open resection rather than SLAH; that is, we did not exclude patients less likely to experience better outcomes from the treatment. This is reflected in the seizure-free rate among the contemporaneous open-resection group of 50%. In contrast, both randomized trials contained criteria that would have excluded many of the patients in our series, although such patients are in reality treated with temporal lobe surgery at many epilepsy centers and can derive benefits from surgery. For example, whereas 26% of our patients did not have MTS, only 15% of patients in the surgical arm in the Canadian trial had "normal" MRI results, and the ERSET trial specifically excluded all such patients.

A more appropriate comparison than randomized clinical trials (RCTs) is a recent meta-analysis comparing outcomes following ATL and SAH, comprised of studies less than half of which collected data prospectively.[3] Back calculation of the rates of freedom from disabling seizures from risk ratios and absolute risk reductions derived overall rates of 75% after ATL and 67% after SAH. Of note, 1,092 of the 1,203 patients (91%) had hippocampal sclerosis, as compared to 75% in our series, rendering the seizure-free rate in that study more comparable to our MTS-positive cohort than our complete cohort. A similar back calculation of seizure freedom rates in the MTS subgroup from the meta-analysis yields a 73% rate following ATL and 66% following SAH. By comparison, we observed that 60.5% of MTS patients treated with SLAH were free of disabling seizures at 12 months. Thus, assuming that the MTS cohorts are comparable among these studies, it appears that ATL is somewhat

superior to SAH, and SAH is somewhat superior to SLAH, at least with respect to seizure outcome at 12 months alone.

Only 1 prior series directly compares outcomes of open temporal lobe surgery with SLAH. While describing select cognitive outcomes, we previously reported similar seizure outcomes following open resection (ATL or SAH) as compared to SLAH.[18] In that series, 39 patients underwent open surgery (all but 3 of them prior to availability of SLAH) and 19 underwent SLAH; there were no significant demographic differences between the cohorts. Engel I status at 12 months following surgery was achieved in 24 of 39 (62%) open surgeries and 11 of 19 (58%) SLAH patients, comparable to the larger series reported here (53.4% of 58 patients). In the present study, we analyzed the contemporaneous group of 22 patients undergoing open resections (all but 2 of which were ATL), the outcomes of which (50% free of disabling seizures) were comparable to the SLAH group (53.4%), with a similar number of patients completely seizure-free (Engel IA: 38% vs 43%, respectively). However, when we excluded from the analysis of the open-resection group those patients who were not strictly comparable to the patients offered SLAH, although still 50% were free of disabling seizures, all of those were completely seizure-free (Engel IA), suggesting that open-resection may be more effective for eliminating auras, which may originate outside of the zone of laser ablation, for example, within extramesial temporal regions. In sum, just as it appears that the chance of becoming free of seizures after SAH is somewhat less than after ATL, a reasonable interpretation of our results and those of others is that there is a further but small reduction of the achievement of seizure freedom after SLAH. More definitive data will require larger prospective trials.

The relative advantages and disadvantages of SLAH versus open resective surgery merit consideration. First and foremost are the comparative surgical risks against which benefits must be weighed. Only 1 patient (1.7%) experienced a permanent disabling complication: homonymous hemianopia following repeat SLAH, likely due to thermal injury to the lateral geniculate nucleus. This occurred during the sixth procedure in our series and, with improvements in stereotactic and ablative technique (reflecting learning curve), no similar complications have been seen in 61 subsequent procedures, including 8 other repeat ablations. This complication was reported by another group after de novo SLAH, and the specific anatomical and trajectory-related circumstances contributing to this avoidable complication were discussed.[27] Four other patients in our series experienced visual field deficits, none of which was persistently symptomatic. One resulted from an intraparenchymal hematoma (of which there was only 1 in the series), and 1 was a transient and mild injury to the optic tract. The remaining 2 likely resulted from thermal injury to the optic radiation near the posterior hippocampal body. Recognition of circumstances contributing to this complication (excessive ablation of this region) also makes it avoidable, and none occurred in the final 33 patients. By contrast, in the Canadian RCT 1 patient (2.8%) sustained unexpected permanent deficits from a thalamic infarct, and 55% of patients experienced nondisabling superior quadrantanopias. Again, more definitive risk information awaits larger prospective studies, but it appears that the surgical risks of SLAH are less than those of open procedures, particularly after surmounting the initial technical learning curve.

A second set of risks to consider includes the unintended consequences of open temporal lobe surgery on structures and functions not intrinsic to the seizure onset zone—so-called "collateral damage."[15] We recently demonstrated that, whereas 88% of patients following open resection (ATL or SAH) experienced cognitive declines in naming or object recognition, none of our first 19 patients experienced decline in any measure following SLAH.[18] Furthermore, based on outcome data presented in our current sample, there appears to be less risk of decline in verbal memory following SLAH than after open resection (ie, 8.2% of total sample, 15% of language-dominant TLE cases). These numbers are far below the 30 to 60% rates of decline reported in the research literature for patients undergoing open resection.[11,28,29] Two of the 3 language-dominant TLE cases experiencing decline had dual pathology involving their lateral temporal lobe and/or pole, and 1 had normal neuroimaging. These findings should provide caution that verbal memory decline can occur in a minority of SLAH patients, and that specific patient characteristics should be prospectively studied in outcome studies to determine the relative risk of decline for the individual patient. Sparing more of what is presumed to be a broad network supporting verbal memory appears to more often contribute to preserved memory. Overall, these cognitive advantages of SLAH likely derive from avoiding transgression and/or resection of the anterior, lateral, and basal temporal structures. Other groups report preserved naming following language-dominant SLAH,[27,30–32] and although verbal memory can decline following SLAH, preliminary results from currently published small series hint at better outcomes than those typical of open resection as well.[27,30–32] Thus, on balance, although SLAH may yield a marginal decrease in the chance of freedom from disabling seizures, and possibly in the rate of being

completely seizure-free, as compared to open resection, the cognitive benefits and safety profile of SLAH make it an attractive alternative, especially when considering surgery on the dominant hemisphere. An analysis taking into consideration the advantages associated with fewer cognitive and other adverse effects suggested that seizure-free rates must be greater than 43% for those advantages to outweigh the disadvantages of a lower rate of seizure freedom.[33] In the present study, SLAH surpasses that threshold; both the actual rate of freedom from disabling seizures, and the lower bound of the CI for those patients with MTS, exceed 43%.

Third, the socioeconomic advantages and disadvantages of a minimally invasive approach to medial temporal surgery warrant consideration. Although socioeconomic costs in medical decision-making are complex and take into account numerous factors beyond the scope of this article (eg, subsequent health care utilization, living independently, rates of return to work), we note that the mean length of stay after SLAH was 1.4 days, whereas the length of stay for a craniotomy is at minimum 2 days, and usually longer.

In the foregoing discussion, comparisons were made between laser amygdalohippocampotomy and more invasive open resections, in terms of seizure and neurocognitive outcomes. However, no direct randomized comparison has been made, nor is such a trial feasible in the absence of patient equipoise: many patients and/or care providers (including referring neurologists) are unwilling to fully consider open temporal lobe surgery. Conventional epilepsy surgery is known to be underutilized for fear of discomfort, disfigurement, surgical risks, and cognitive side effects. In our own series, several patients conveyed reluctance to undergo open surgery as an alternative to laser ablation, a sentiment still present even in patients with recurrent seizures after SLAH. Only 5 of these patients agreed to undergo open surgery (4 have been completed; 1 is scheduled). Six other patients with persistent seizures who would be candidates for further surgery have thus far refused further surgical treatment. This may reflect bias on both the part of patients, who are increasingly aware of the availability of laser ablation for epilepsy, and the part of care givers, including neurologists, neurosurgeons, and advanced practice providers. At our center, we stopped offering open resection as an initial option for patients with left mesial temporal onsets due to the high incidence of decline in naming ability[10,18]; in the first half of the period of this study, we performed 7 left-sided and 9 right-sided open resections, whereas during the second half we only performed 1 left-sided resection as compared to 5 right-sided resections. The advent of U.S. Food and Drug Administration–approved neurostimulation has also contributed to the decline in our left-sided open as well as laser ablative procedures.[34] These considerations raise the question of the most appropriate comparator groups for SLAH (and other less-invasive ablative procedures); for patients and practitioners who do not embrace conventional open surgery, the appropriate comparator for ablation is not open surgery but best medical therapy or neurostimulation. Undoubtedly, a seizure-free rate of at least 53.4% is significantly superior to the historical cohorts randomized to best medical management, yielding only a 0 to 8% chance of prolonged seizure control, as well as to cohorts in studies of hippocampal neurostimulation.[34–36] Yet it remains a concern that patients who elect thermal ablation risk being left with a suboptimal result if they do not become seizure-free and then reject subsequent open surgery, as the foregoing discussion indicates they have a tendency to do.

Stereotactic laser ablation represents a paradigm shift in the surgical management of epilepsy. With careful consideration and technical execution, this generally low-risk, high-reward approach minimizes recovery time and cognitive risk while still providing a high chance of seizure control. As SLAH presents no barrier to subsequent ablation, open surgery, or other procedures, SLAH now fills an important gap between the "all or none" considerations of continued medical management and open resection. It provides a practical iterative approach to surgical epilepsy when patient need or desire dictates, and its availability improves utilization of potentially curative epilepsy surgery.

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Author Contributions

R.E.G., M.A.S., J.T.W., and D.L.D. contributed to the conception and/or design of the study; R.E.G., M.A.S., J.T.W., R.E.F., A.M.S., B.P.S., N.P.P., and D.L.D. contributed to the acquisition and/or analysis of the data; R.E.G., M.A.S., J.T.W., A.M.S., B.P.S., and D.L.D.

contributed to the drafting of the text and/or preparation of the figures.

Potential Conflicts of Interest

R.E.G. has served as a consultant to Medtronic, Monteris, MRI interventions, Visualase, and Zimmer Biomet, which manufacture products related to the research described in this paper and may be affected by this study, and receives compensation for these services; received research support from Medtronic as part of the SLATE trial (their multisite prospective trial evaluating SLAH); and has received research grants from Visualase and MRI Interventions. The terms of these arrangements have been reviewed and approved by Emory University in accordance with its conflict of interest policies. J.T.W has served as a consultant to Medtronic and MRI Interventions and has received compensation for these services, and receives research support from Medtronic as part of the SLATE trial. The terms of these arrangements have been reviewed and approved by Emory University in accordance with its conflict of interest policies. R.E.F. receives research support from Medtronic for the SLATE trial. D.L.D. has received a research grant from Medtronic through Emory University and currently serves as the core laboratory director for their SLATE trial. The terms of these arrangements have been reviewed and approved by Emory University in accordance with its conflict of interest policies.

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