Real-Time Magnetic Resonance-Guided Stereotactic Laser Amygdalohippocampotomy for Mesial Temporal Lobe Epilepsy

BACKGROUND: Open surgery effectively treats mesial temporal lobe epilepsy, but carries the risk of neurocognitive deficits, which may be reduced with minimally invasive alternatives.

OBJECTIVE: To describe technical and clinical outcomes of stereotactic laser amygdalohippocampotomy with real-time magnetic resonance thermal imaging guidance.

METHODS: With patients under general anesthesia and using standard stereotactic methods, 13 adult patients with intractable mesial temporal lobe epilepsy (with and without mesial temporal sclerosis [MTS]) prospectively underwent insertion of a saline-cooled fiberoptic laser applicator in amygdalohippocampal structures from an occipital trajectory. Computer-controlled laser ablation was performed during continuous magnetic resonance thermal imaging followed by confirmatory contrast-enhanced anatomic imaging and volumetric reconstruction. Clinical outcomes were determined from seizure diaries.

RESULTS: A mean 60% volume of the amygdalohippocampal complex was ablated in 13 patients (9 with MTS) undergoing 15 procedures. Median hospitalization was 1 day. With follow-up ranging from 5 to 26 months (median, 14 months), 77% (10/13) of patients achieved meaningful seizure reduction, of whom 54% (7/13) were free of disabling seizures. Of patients with preoperative MTS, 67% (6/9) achieved seizure freedom. All recurrences were observed before 6 months. Variances in ablation volume and length did not account for individual clinical outcomes. Although no complications of laser therapy itself were observed, 1 significant complication, a visual field defect, resulted from deviated insertion of a stereotactic aligning rod, which was corrected before ablation.

CONCLUSION: Real-time magnetic resonance-guided stereotactic laser amygdalohippocampotomy is a technically novel, safe, and effective alternative to open surgery. Further evaluation with larger cohorts over time is warranted.

KEY WORDS: Epilepsy, Laser therapy, Magnetic resonance imaging, Minimally invasive surgical procedures, Stereotactic techniques, Temporal lobe, Thermometry

Surgical resection is the gold standard treatment for drug-resistant focal epilepsy, including mesial temporal lobe epilepsy (MTLE) and other focal cortical lesions with correlated electrophysiological features. Anterior temporal lobectomy with amygdalohippocampectomy (ATALH) has been shown to be more efficacious than continued medical therapy in a randomized, controlled trial. Focal resections, including ATLAH and selective amygdalohippocampotomy (SAH), yield 60% to 80% seizure freedom rates in highly selected patients, such as those found to have mesial temporal sclerosis (MTS) on preoperative imaging, but resections are associated with cognitive impairments or focal neurological deficits. 

ABBREVIATIONS: AHC, amygdalohippocampal complex; ATLAH, anterior temporal lobectomy with amygdalohippocampectomy; DWI, diffusion-weighted imaging; EEG, electroencephalography; FDA, Food and Drug Administration; FDG, 18-fluorodeoxyglucose; FLAIR, fluid-attenuated inversion recovery; MRTI, magnetic resonance thermal imaging; MTLE, mesial temporal lobe epilepsy; MTS, mesial temporal sclerosis; RF, radiofrequency; SAH, selective amygdalohippocampotomy; SLAH, stereotactic laser amygdalohippocampotomy; SRS, stereotactic radiosurgery

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Minimally invasive approaches to treating MTLE might achieve seizure freedom while minimizing adverse effects. Magnetic resonance (MR)-guided stereotactic laser ablation is a minimally invasive alternative that uses small applicators amenable to stereotactic delivery. Heating is dependent on source wavelength such that a source laser can be chosen to produce rapid and localized heating of tissue with sharp boundaries at relatively low powers. Because optical fibers and laser energy are MR imaging (MRI) compatible, simultaneous MR thermal imaging (MRTI), with accuracy on the order of ±0.2°C, in a number of tissue types enables real-time feedback control of laser output and tissue ablation. MR-guided stereotactic laser ablation has been safely used for ablation of intracranial lesions including tumors and certain epileptogenic foci in children, and the requisite device has been cleared by the US Food and Drug Administration (FDA) for tissue ablation in neurosurgery.

Using standard stereotactic methods, including either a rigid stereotactic head frame or an MR-guided trajectory frame, we describe our technical approach and early clinical results using minimally invasive MR-guided stereotactic laser ablation of the amygdala and hippocampus (stereotactic laser amygdalohippocampotomy [SLAH]). We report our first 15 ablations in 13 adult patients with MTLE, including patients both with and without MTS on preoperative imaging.

METHODS

Patient Selection

All patients were evaluated by a standard protocol of noninvasive studies including 3-T MRI, 18-fluorodeoxyglucose (18-FDG) positron emission tomography (PET), neuropsychological testing, and inpatient video electroencephalographic (EEG) monitoring. Functional MRI and intracarotid amobarbital (Wada) testing were often performed to lateralize language dominance and predict risk of postoperative memory deficits. A multidisciplinary committee of epilepsy neurologists, neuropsychologists, and neurosurgeons reviewed results for level of concordance of noninvasive studies and to provide consensus recommendations regarding surgery. Additional intracranial electrode monitoring was performed on 2 patients in this series. All patients in whom preoperative studies were consistent with focal unilateral seizure onsets within mesial temporal structures were considered candidates for mesial temporal lobe surgery. These included patients with diverse preoperative MRI findings including MTS (mesial temporal atrophy with T2/FLAIR sequence signal change), mesial temporal atrophy only, mesial temporal signal change only, or normal. Patients with previous temporal lobe surgery, depth electrode intracranial monitoring, or other intracranial abnormalities were not excluded. Both standard open temporal lobe surgery and minimally invasive SLAH were offered to 17 consecutive patients, 13 of whom chose SLAH. Twelve SLAH patients provided informed written consent for prospective research procedures (collection of patient information such as seizure diaries, additional imaging, and neuropsychological testing); 1 SLAH patient underwent limited retrospective examination only. Over the same time period, 4 of 17 patients who were offered SLAH actually selected open procedures, and 7 additional patients who underwent craniotomies for subdural grid electrodes placement followed by open temporal lobe resections were not offered SLAH. The Emory University Institutional Review Board approved all procedures. Separate standard informed surgical consent was obtained for SLAH itself, which is an ablative procedure using an FDA-cleared surgical device. Two surgeons (J.T.W. and R.E.G.) performed SLAH on patients between July 2011 and June 2013 (with 1 patient undergoing a second procedure in December 2013) using MRI-guided laser treatment after laser applicator placement by either of the 2 following standard stereotactic approaches.

Laser Applicator Placement Using a Standard Stereotactic Frame

Nine of 13 patients underwent placement of an MR-compatible stereotactic head frame (CRW; Integra Neurosciences, Plainsboro, New Jersey) after administration of general endotracheal anesthesia. The frame was affixed to the cranium in standard fashion with 4 cranial pins, but with 10° to 15° of axial rotation and inferior placement of ipsilateral posterior cranial pins into the mastoid region to avoid collision with an occipital approach. The MRI fiducial localizer was secured to the base frame, and volumetric image series (T2/FLAIR and T1 post-contrast) were acquired using a 1.5-T MRI scanner (Magnetom Espree, Siemens HealthCare, Malvern, Pennsylvania).

Each patient was transported to the operating room, positioned supine sitting with the neck flexed, and the CRW (Integra Neurosciences) base ring was affixed to the operating table via a Mayfield adapter. Stereotactic planning was performed using FrameLink software (Stealth Treon or S7 workstations, Medtronic, Louisville, Colorado). Linear trajectories from the lateral occipital region (starting ~4 to 6 cm superior to the inion and 4 to 6 cm lateral to midline) through the long axis of the hippocampal body and into the pes hippocampus were selected, terminating in the amygdala. The posterior extent of hippocampal penetration extended at least to the level of the lateral mesencephalic sulcus. Optimal trajectories avoided cortical and sulcal vasculature and the choroid plexus; ventricle penetration was occasionally required, but could generally be avoided by creating inferior or lateral approaches.

The planned entry site was minimally clipped and widely prepped. The sterile CRW arc set to appropriate frame coordinates was mounted over the draped base ring, the entry site was infused with local anesthetic, a small stab incision was made, and a 3.2-mm inner diameter drill guide tube was lowered into the incision and braced against the bone. A craniotomy-durotomy was performed with a 3.2-mm twist drill. The guide was replaced with a 1.9-mm reducing cannula through which a 1.6-mm stereotactic alignment rod was inserted and used to guide insertion into the twist-drill hole of a threaded polycarbonate anchor bolt with a 3.2-mm outer diameter and 1.8-mm inner diameter (Figure 1A). The alignment rod was then inserted through the anchor bolt and into the brain during live lateral fluoroscopic visualization to verify alignment with stereotactic frame center. The distance to target from the top of the bolt was calculated. The Visualase laser applicator assembly (Visualase Inc, Houston, Texas) comprises an outer 1.6-mm diameter clear (light-transmitting) polycarbonate cooling catheter and an inner 0.73-mm diameter flexible laser optical fiber with 10-mm long diffuser tip (Figure 1A). After removing the alignment rod from the anchor bolt, the cooling catheter (marked at the distance-to-target) containing a stainless steel stiffening stylet (Figure 1A) was inserted to the target under lateral fluoroscopic visualization (Figure 1B). The stylet was then removed, and the laser optical fiber with diffuser tip was inserted at the end of the closed-ended cooling catheter. The laser applicator assembly was secured.
in place via a Touhy-Borst adapter (Martech Medical, Harleysville, Pennsylvania) on the proximal end of the anchor bolt. The stereotactic arc was detached, the drapes were removed, and the patient was then transported to the MRI suite and placed supine within the magnet with the head turned to situate the treatment side up to protect the laser transport. An entry-marking divot in the cranium was created by puncturing through the grid and scalp into bone using a marking trocar. The grid was removed, the scalp was infused with local anesthetic, and a minimal linear incision was made with a scalpel. An approximately 14-mm burr hole centered on the marking divot was drilled using an MR-compatible high-speed air drill. The MRI-guided trajectory frame base was affixed overlying the burr hole with self-tapping screws. A minimal durotomy was opened in cruciate fashion. The trajectory frame components were assembled including a hand controller. A series of short planning scans were obtained, and the workstation computed suggested adjustments in x, y, and pitch and roll that were used to align the frame cannula with the planned trajectory. A ceramic rod was inserted part way to confirm accurate trajectory alignment, and then the Visualase cooling cannula with stiffening stylet was inserted through a reducing cannula, locked in place (Figure 1C) and confirmed with volumetric imaging. The stylet was removed and replaced with the optical fiber.

**MR-Guided Laser Treatment**

In all cases, the laser fiber and cooling lines were routed from the patient to the control room and connected to the proprietary Visualase workstation, which combines a 15-W 980-nm diode laser with an image-processing workstation for real-time MRtI and modeled estimates of the thermal necrosis zone. Initially, volumetric 3-dimensional T1-weighted sequences were acquired to verify proper positioning through the hippocampus and to select appropriate imaging planes for monitoring during ablation. User-defined specific temperature safety limits were set relative to the monitoring image in the inferior lateral thalamus, basal ganglia, and lateral mesencephalon (Figure 2A) to automatically terminate laser delivery if these structures exceeded 45°C, avoiding off-target thermal injury (Figure 2B). The initial lesion was made anteriorly in the amygdalohippocampal complex (AHC) during real-time MRTI and modeling of the necrotizing zone (Figures 2C and 2D). The laser fiber was then retracted in approximately 1.0-cm increments, and as many as 5 overlapping focal ablations were created, resulting in a confluent tubular ablation zone (Figure 2F) encompassing the AHC posteriorly to at least the lateral mesencephalic sulcus (posterior landmark visualized on axial imaging) (Figure 2G).

Postprocedure MRI including diffusion-weighted imaging (DWI), FLAIR, and T1 postgadolinium contrast (Figures 2G and 2H) were acquired, verifying the final lesion location and volume. Laser applicators and anchor bolts were completely removed, a titanium burr hole cover was affixed, incisions were closed with resorbable suture, and stereotactic frames were removed. Patients were typically admitted to the hospital for observation, administered dexamethasone for 24 hours, and discharged with a 1-week oral dexamethasone taper.

**Clinical and Imaging Follow-up**

Patients were evaluated at 2, 6, 12, and 24 months post-treatment. Follow-up visits included collection of patient seizure diaries, evaluation for
complications, verification of medication status, and quality-of-life surveys. Repeat MRI was performed at 6 months post-treatment (Figures 2I and 2J). Partial neuropsychological evaluation was performed at 6 months and a full evaluation at 12 months. A full description of neuropsychological outcomes for SLAH in this cohort is the subject of additional reports.  

**Image Processing**

Using a BrainLab workstation and the iPlan 3.0 application (BrainLab AG, Feldkirchen, Germany), the amygdala and hippocampus on the targeted side were manually segmented and volumes reconstructed from preprocedure T1 gadolinium-contrasted volumetric images using standard anatomic definitions in 3 planes as described by Pruessner et al., with slight modification (the alveus and fimbria were not included in the hippocampal volume, as these structures were not universally visualized). Likewise, postoperative ablation volumes were generated by manually segmenting the ring-enhanced ablation zone. Pre- and postprocedure image sets were spatially coregistered, allowing direct volumetric comparison of ablation zones vs anatomic targets (Figure 3). The

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**FIGURE 2.** Illustrative treatment cycle. A, patient 4 was stereotactically implanted from an occipital approach along the long axis of the amygdalohippocampal complex. Using the Visualase workstation, multiple points (3 shown in this plane) were demarcated for intraoperative magnetic resonance imaging thermal measurement: red circle (in the ablation zone), white square (anterior mesencephalon), and blue diamond (lateral mesencephalon). B, measurement of the temperature at the 3 points during ablation. Pink dotted line indicates ablation temperatures greater than 90°C, above which thermal spread is considered unpredictable and which triggers cycle termination by the workstation. Note that the brainstem temperature does not increase during the procedure. Real-time temperature measurements (left) and estimated ablation areas (right) at 25 seconds (C), 75 seconds (D), and 130 seconds (E). F, after retracting the laser applicator and ablating at a second site, the final estimate of the total ablated area was calculated. Immediate postoperative T1-weighted imaging with contrast highlights the borders of the lesion in the axial (G, red arrow) and coronal (H) planes. I, J, 6 months after the procedure, the amygdalohippocampal complex demonstrates well-circumscribed nonenhancing pseudocystic atrophy.
amount of each target showing evidence of ablation was calculated and expressed as a percentage.

RESULTS

Demographics and Diagnostic Findings

Patient demographics and preoperative diagnostic findings are displayed in Table 1. Seventeen consecutive MTLE patients deemed to be candidates for mesial temporal resections (without previous subdural grid electrode placement) were offered either a standard open temporal resection or minimally invasive SLAH. Although 4 patients elected to undergo open surgery, 13 selected SLAH and were enrolled (6 male and 7 female patients; age range, 16-64 years; median age, 24 years). Two patients (patients 6 and 7) had undergone placement of vagal nerve stimulators before current surgical evaluation, and 2 patients (patients 10 and 12) had undergone previous open temporal lobe surgeries at other institutions. Specifically, patient 10 had remote craniotomy for complete resection of a juvenile pilocytic astrocytoma in the posterior lateral temporal lobe, but epilepsy subsequently developed; intracranial monitoring with subdural strip and intraparenchymal depth electrodes confirmed seizures emanating from preserved mesial temporal structures (anterior hippocampus) rather than encephalomalacia contiguous with the resection cavity. Patient 12 had undergone attempted SAH with sparing of mesial temporal structures, after which seizures persisted. Two patients in this series with equivocal preoperative imaging or other discordant features (patients 10 and 13, Table 1) underwent intracranial monitoring (bilateral strip and depth electrodes) for localization of seizure onsets before laser ablation.

Patients had sufficient concordance of seizure semiology (complex partial seizures) and diagnostic studies (ie, MRI, 18FDG-PET hypometabolism, neurocognitive profile, and EEG onset) to recommend surgical treatment of MTLE (Table 1). Nine of 13 patients met strict radiological criteria for ipsilateral MTS (both hippocampal atrophy and increased T2/FLAIR signal intensity) including patient 6 with bilateral MTS (EEG onset from the more radiologically abnormal left side). Four patients did not meet strict radiological criteria for MTS: patient 1 (mesial temporal T2/FLAIR signal change without atrophy), patient 2 (neither signal change nor atrophy, whose MRI could be characterized as

FIGURE 3. Volumetric reconstruction of ablation zone with respect to the amygdala and hippocampus. A, axial segmentation of the amygdala (yellow boundary), hippocampus (green), and ablation zone (red) of patient 4. Laser applicator trajectory (blue and white dashed line) is also marked. B, sagittal segmentation of the same tissue as well as the applicator track (blue). C, 3-dimensional reconstruction of the amygdala (yellow) and hippocampus (green), as well as the path of the fiber optic (blue) through the tissue. D, 3-dimensional reconstruction from segmented sections of the ablated tissue (red) within the amygdala and hippocampus.
**TABLE 1.** Patient Demographics and Preoperative Diagnostic Results

<table>
<thead>
<tr>
<th>Patient</th>
<th>Sex</th>
<th>Age at SLAH, y</th>
<th>Age at Onset, y</th>
<th>Seizure Type</th>
<th>MRI</th>
<th>(^{18})FDG-PET Hypometabolism</th>
<th>Memory Impairment</th>
<th>Neuropsychological Testing</th>
<th>Intracarotid Amobarbital (Wada) Test</th>
<th>Video EEG Temporal Lobe Seizure Onset</th>
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<tr>
<td>1</td>
<td>F</td>
<td>45</td>
<td>36</td>
<td>CPS</td>
<td>R MT-T2</td>
<td>R</td>
<td>Bilateral (mild deficits in complex learning only)</td>
<td>R &gt; L</td>
<td>R</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>M</td>
<td>22</td>
<td>14</td>
<td>CPS</td>
<td>MT-normal</td>
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<td>R &gt; L</td>
<td>R</td>
<td>R</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>M</td>
<td>30</td>
<td>3</td>
<td>CPS</td>
<td>L MTS</td>
<td>L</td>
<td>L &gt; R</td>
<td>L</td>
<td>L</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>M</td>
<td>18</td>
<td>6</td>
<td>CPS</td>
<td>L MTS</td>
<td>L</td>
<td>L &gt; R</td>
<td>L</td>
<td>L</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>F</td>
<td>24</td>
<td>21</td>
<td>CPS + PNES</td>
<td>L MTS</td>
<td>R &gt; L</td>
<td>L &gt; R</td>
<td>L</td>
<td>L &gt; R</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>F</td>
<td>55</td>
<td>9</td>
<td>CPS</td>
<td>Bilateral MTS (L &gt; R)</td>
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<td>L</td>
<td>L</td>
<td></td>
<td></td>
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<tr>
<td>7</td>
<td>F</td>
<td>64</td>
<td>5</td>
<td>CPS</td>
<td>R MTS</td>
<td>R</td>
<td>R</td>
<td>Not performed</td>
<td>R</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>F</td>
<td>58</td>
<td>13</td>
<td>CPS</td>
<td>L MTS</td>
<td>L</td>
<td>L</td>
<td>L (mild)</td>
<td>L</td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>M</td>
<td>30</td>
<td>1</td>
<td>CPS + GTC</td>
<td>L MTS</td>
<td>L (mild)</td>
<td>L (mild)</td>
<td>R</td>
<td>R (ICM with depth and strip electrodes implicated hippocampus)</td>
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</tr>
<tr>
<td>10</td>
<td>F</td>
<td>21</td>
<td>16</td>
<td>CPS</td>
<td>MT-normal; atrophic R fornix and MB; R posterior temporal encephalomalacia</td>
<td>L (mild)</td>
<td>L (mild)</td>
<td>R (ICM with depth and strip electrodes implicated hippocampus)</td>
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<tr>
<td>11</td>
<td>M</td>
<td>23</td>
<td>&lt;1</td>
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<td>L MTS</td>
<td>L &gt; R</td>
<td>Bilateral</td>
<td>Not performed</td>
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<td></td>
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<tr>
<td>12</td>
<td>M</td>
<td>16</td>
<td>12</td>
<td>CPS + GTC</td>
<td>R MTS, previous SAH sparing AHC</td>
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<td>Unavailable</td>
<td>Not performed</td>
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<tr>
<td>13</td>
<td>F</td>
<td>18</td>
<td>10</td>
<td>CPS + GTC</td>
<td>L &gt; R MTA; R parietal encephalomalacia</td>
<td>L</td>
<td>L &gt; R</td>
<td>L (ICM with depth and strip electrodes implicated hippocampus)</td>
<td></td>
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</table>

\(^{18}\)SLAH, stereotactic laser amygdalohippocampotomy; MRI, magnetic resonance imaging; \(^{18}\)FDG-PET, \(^{18}\)-fluorodeoxyglucose positron emission tomography; EEG, electroencephalography; F, female; CPS, complex partial seizure; R, right; MT-T2, mesial temporal signal change on T2 sequence MRI (without atrophy); L, left; M, male; MT-normal, no mesial temporal atrophy or signal change; MTS, mesial temporal sclerosis (T2 signal change and atrophy); PNES, psychogenic nonepileptic seizure; GTC, general tonic-clonic seizure; MB, mammillary body; ICM, intracranial electrode monitoring used for confirmation; SAH, open selective amygdalohippocampectomy; AHC, amygdalohippocampal complex; MTA, mesial temporal atrophy (without signal change).
“normal”), patient 10 ("normal" mesial temporal structures, but with contiguous posterior lateral temporal encephalomalacia), and patient 13 (mesial temporal atrophy without signal change). Except for patient 5, the remaining patients had unilateral or predominant 18FDG-PET hypometabolism on the side concordant with other findings. Similarly, neurocognitive deficits were concordant in all patients except patient 12, for whom preoperative data were not available. Electroencephalography recorded seizure onsets unilaterally in all patients except patient 5, who had preoperative evidence of bilateral temporal (left > right) seizure onsets (concordant with left MTS but right > left 18FDG-PET hypometabolism).

Technical and Imaging Results

Applicator placement and thermal imaging were accomplished in all cases. Applicator placement relative to location of specific safety temperature limits, a complete thermal treatment cycle, and final acute and chronic ablation results are illustrated specifically for patient 4 (Figure 2). Illustrative ablation imaging is demonstrated for all 15 procedures in 13 patients (see Figure, Supplemental Digital Content 1, which shows laser applicator placement, final integrated ablation estimates, and actual ablation for all 15 SLAH procedures in 13 patients, http://links.lww.com/NEU/A616). In all but the first procedure (patient 1, discussed in the following) the laser assembly was accurately placed within the amygdala and anterior hippocampus extending posteriorly to a point parallel to the lateral mesencephalic sulcus from a single trajectory.

Patient group treatment summaries are displayed in Table 2; individual patient treatment details are available (see Table, Supplemental Digital Content 2, which shows individual and group SLAH treatment summaries, http://links.lww.com/NEU/A617). Overall, patients were treated with a median of 3 contiguous ablation zones (Table 2) along a single trajectory per surgical session to achieve a total ablation area involving the amygdala and hippocampus. The hippocampal ablation extended at least as posterior as the lateral mesencephalic sulcus in all patients (see Figure, Supplemental Digital Content 1, http://links.lww.com/NEU/A616). Ongoing thermal imaging maps and integrated estimates of ablation zone were viewed in real time on the Visualase workstation. The desired treatment areas were generally achieved with laser power of 12 W (rarely as high as 14 W) and a mean exposure time of 9.6 ± 6.4 minutes (range, 3.4-26.1 minutes) (Table 2) (see Table, Supplemental Digital Content 2, http://links.lww.com/NEU/A617). Cycle time was user defined to balance the spread of ablation while maintaining a tissue treatment temperature lower than 90°C.

During the SLAH procedure, the lateral ventricle appeared to have an insulating heat sink effect, with ablation zones generally spreading to conform to the superior surface of the hippocampus without thermal spread across cerebrospinal fluid spaces (temporal horn, transverse cerebral fissure, or ambient cistern), sparing medial structures (basal ganglia, thalamus, optic tract, or mid-brain). Moreover, ablation zones (as confirmed by immediate postprocedure FLAIR, DWI, and contrast-enhanced T1 signal

<table>
<thead>
<tr>
<th>Side</th>
<th>Stereotactic Platform</th>
<th>Treatment Zones</th>
<th>Laser Treatment Time, min</th>
<th>No. of Laser Treatments</th>
<th>Side of Ipsilateral Ablation</th>
<th>Proportion of Structure(s) Ablated, %</th>
<th>Ablation Volume, cm³</th>
<th>Proportion of Structure(s) Ablated, %</th>
<th>Ablation Volume, cm³</th>
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<td>0.04-0.4</td>
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<td>L</td>
<td>72.5</td>
<td>5.3</td>
<td>60.5</td>
<td>5.3</td>
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<td>R</td>
<td>CPSF</td>
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<td>72.5</td>
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<td>72.5</td>
<td>5.3</td>
<td>60.5</td>
<td>5.3</td>
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</table>
intensity) tended to incorporate large portions of the hippocampus, medial to lateral, at any given coronal location, forming an eccentric volume with respect to the laser assembly, apparently delimited by the ependymal lining (superiorly and laterally), the transverse cerebral fissure (medially), and, more variably, the hippocampal sulcus or subiculum (inferiorly). Indeed, safety limit set points, which were user defined in the software interface to terminate laser delivery if any point on the brainstem, optic apparatus, and/or thalamus exceeded 45°C, never changed from baseline temperatures (Figures 2A and 2B). Individual cycles were terminated when on-target temperatures reached 90°C, thus avoiding the risk of char and thermal gassing in target tissues.

Thermal and anatomic imaging overlays yielded integrated ablation zone estimates that correlated well with immediate post-procedure gadolinium-contrasted T1 images (Figure 2) (see Table, Supplemental Digital Content 2, http://links.lww.com/NEU/A616). Likewise, MRI scans obtained at 6 months post-procedure (in all but patients 5 and 12) revealed evidence of nonenhancing pseudocystic atrophy confined to treated mesial temporal structures, as illustrated in patient 4 (Figures 2I and 2J). (See Video, Supplemental Digital Content 3, http://links.lww.com/NEU/A621: Illustrative treatment cycle of magnetic resonance thermometry-guided stereotactic laser thermal amygdalohippocampectomy [SLAH] for epilepsy. Patient 4 [see also text Figure 2] was stereotactically implanted via a twist drill hole from an occipital approach along the long axis of the amygdalohippocampal complex with a saline-irrigated cooling cannula containing the optical fiber with 10 mm-long diffusion tip [Visualase]. Laser energy [15 Watt, 980 nm diode laser] was delivered by the Visualase workstation while MR thermal imaging data was acquired and fed back for real time presentation and safety monitoring. Data is presented within 4 seconds of acquisition in two formats: color thermal map [left] and total irreversible damage estimate [right, see text for details]. The color thermal map [left screen] allows visualization of laser thermal energy deposition (values shown) with corresponding tissue ablation. Percentages for temperature limits (77°C, red; >67°C, yellow; >57°C, green; >47°C, light blue; >37°C, dark blue) during 2 treatment cycles. The first treatment was performed anteriorly, then the optical fiber was withdrawn by 1 cm, and a second treatment cycle was performed. User-defined safety monitoring points [not shown] placed at off-target structures [eg, borders of thalamus, mesencephalon, etc.] were set to automatically trigger therapy discontinuation should off-target temperatures reach undesirable temperatures. Contemporaneously, the workstation provides an integral of locations maintaining ablative temperatures over time [right screen, orange pixels overlaid on a T1 anatomic image]. Axial planes are presented here, but other user-defined planes may be monitored simultaneously. Videographic image is sped up 40x. Total laser treatment time was 6.7 minutes in this case. The final three static axial images demonstrate laser fiber location [T1, left image], final ablation zone estimate [acquired as described above, middle image], and immediate postprocedure ring-enhancing ablation zone [gadolinium enhanced T1, right image].)

From immediate postprocedure gadolinium-contrast T1 images, the mean final hippocampal length ablated was 2.5 ± 0.44 cm (Table 2) (range, 1.55-3.07 cm) (see Table, Supplemental Digital Content 2, http://links.lww.com/NEU/A617), and the final mean total ablation volume was 5.3 ± 1.1 cm³ (Table 2) (range, 3.52-7.59 cm³) (see Table, Supplemental Digital Content 2, http://links.lww.com/NEU/A617). Post hoc anatomically segmented volumetric reconstruction of hippocampus and amygdala (as illustrated in Figure 3) revealed the mean percentage of ablations of these individual structures of 63 ± 10% (range, 49%-86%) and 54 ± 27% (range, 4%-88%), respectively, with a mean cumulative AHC ablated volume of 60 ± 9.7% (range, 49%-76%) (Table 2) (see Table, Supplemental Digital Content 2, http://links.lww.com/NEU/A617).

Patients 1 and 13 in the series had initial ablations of AHC that were judged by imaging to be insufficient after seizures persisted; both underwent repeat SLAH with the aim of additional AHC ablation. In the case of the first procedure in patient 1, the laser fiber assembly had been passed inferiorty through the parahippocampal region rather than the hippocampus, which was recognized on MR imaging after insertion. We nevertheless proceeded with ablation within the parahippocampal gyrus anticipating superior spread into the AHC. This ablation, however, appeared to be limited superiorly by the hippocampal sulcus, encompassing 50% of the AHC, including 59% of the hippocampus but only 4.4% of the amygdala (see Table, Supplemental Digital Content 2, http://links.lww.com/NEU/A617). Six months later, SLAH was repeated with hippocampus-centered fiber placement, achieving an AHC ablation of 69% (67% of hippocampus ablated and 66% of amygdala ablated) (see Table, Supplemental Digital Content 2, http://links.lww.com/NEU/A617). Likewise, in the case of patient 13, despite an initial 66% AHC ablation (55% hippocampus ablated and 83% amygdala ablated) (see Table, Supplemental Digital Content 2, http://links.lww.com/NEU/A617), seizures persisted, and 6-month imaging indicated a rim of spared mesial temporal tissue. We therefore repeated SLAH more medially, increasing ablation volumes to 76% (AHC), 69% (hippocampus), and 88% (amygdala).

Patient 5 underwent a technically successful SLAH (see Table, Supplemental Digital Content 2, http://links.lww.com/NEU/A617), but seizures persisted, and she underwent open ATLAH at 5 months post-SLAH, yielding pathological specimens (hippocampus and parahippocampal gyrus (Figures 4A and 4B). Although laser-treated hippocampal tissue was completely infarcted, parahippocampal tissue appeared viable. Likewise, another surgical specimen of the mesial temporal lobe was obtained 3 months after stereotactic laser ablation of the parahippocampal region in a patient who did not participate in the prospective study (Figures 4C and 4D). Contiguous intact and infarcted tissues were sharply demarcated from each other by a pial border containing arterioles. This confirms the impression from imaging that laser ablation can be relatively delimited by anatomic pia/arachnoid boundaries.

**Seizure Outcomes**

Thirteen patients had post-SLAH follow-up ranging from 5 to 26 months (median, 14 months) (Table 3). The 2 procedures (in
patients 1 and 5) with only 5 months of outcome are presented, as neither patient was ever seizure free, and each underwent subsequent procedures (repeat SLAH and open ATLH, respectively) at the 5-month time points; all others procedures presented have greater than 6-month outcome. Individual outcome duration curves demonstrate time to failure (loss of seizure freedom) for 14 procedures in 13 patients (Figure 5A). This analysis demonstrates that all failures to achieve seizure freedom occurred either immediately or within an interval of no more than 6 months in this series.

Overall, at the time of last follow-up, in 10 patients (77%) meaningful seizure reduction was achieved, with 7 patients (54%) classified as Engel I (free of disabling seizures), 3 (23%) as Engel III (worthwhile improvement), and 3 (23%) as Engel IV (no worthwhile improvement) (Figure 5A, Table 3). Patients with Engel III outcomes saw significant seizure reductions by 85% to
92% per patient seizure diaries. Notably, 1 patient (patient 2) with an Engel IIIA outcome (worthwhile seizure reduction) had a seizure-free interval of less than 2 months followed by recurrence with a change in seizure semiology (preceding déjà vu) and well-documented onsets emerging exclusively contralaterally to the treated side (preoperative studies had not indicated bilaterality) (Tables 1 and 3). When taken into account, an overall 8 of 13 patients (62%) appeared to maintain seizure freedom from the ablated side.

Three patients were Engel IVB (no appreciable change) (Figure 5A, Table 3). Of these, patient 1, who preoperatively experienced daily seizures, underwent 2 laser ablation procedures (separated by 5 months) ultimately encompassing both the AHC (see Table, Supplemental Digital Content 2, http://links.lww.com/NEU/A617) and parahippocampal region, resulting in a 3-month seizure-free interval before recurrence of daily seizures (Table 3, Figure 5A). She underwent open right ATL at 14 mo after second SLAH procedure: currently seizure free. Underwent open left ATL at 5 mo post-SLH; still not seizure free.

Patient 13 underwent repeat SLAH targeting residual mesial tissue (see Table, Supplemental Digital Content 2, http://links.lww.com/NEU/A617), but follow-up of the second procedure was too early (4 months) to determine outcome. Patient 5 was medically noncompliant and continued to have self-reported events after SLAH (Table 3). Repeated video EEG examinations documented frequent psychogenic nonepileptic seizures and, with reduction in medications, infrequent bilateral

<p>| TABLE 3. Clinical Outcomes of SLAH for Each Patienta |
|-----------------|----------------|----------------|----------------|----------------|----------------|</p>
<table>
<thead>
<tr>
<th>Patient</th>
<th>ICU Stay, d</th>
<th>Total Hospital Stay, d</th>
<th>Complications or Adverse Events within 30 d</th>
<th>F/U, mo</th>
<th>Engel Class After SLAH</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1</td>
<td>2</td>
<td>None (first procedure)</td>
<td>6</td>
<td>IVB</td>
<td>First SLAH: continued frequent seizures after incomplete amygdalohippocampotomy.</td>
</tr>
<tr>
<td>0</td>
<td>1</td>
<td>Homonymous hemianopia (second procedure)b</td>
<td>14</td>
<td>IVB</td>
<td>Second SLAH: continued frequent seizures despite adequate amygdalohippocampotomy. Underwent open right ATL at 14 mo after second SLAH procedure: currently seizure free.</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>1</td>
<td>2</td>
<td>Emergency visit for seizure (missed AED)</td>
<td>26</td>
<td>IIIA</td>
<td>Initially seizure free (5 mo), then emergence of new semiology (less frequent) with new contralateral onset by video-EEG.</td>
</tr>
<tr>
<td>3</td>
<td>1</td>
<td>1</td>
<td>None</td>
<td>25</td>
<td>IIIA</td>
<td>Minimal amygdalotomy. Seizure recurrence (same semiology, reduced frequency) by 6 mo postoperatively.</td>
</tr>
<tr>
<td>4</td>
<td>0</td>
<td>1</td>
<td>Emergency visit for seizure (missed AED)</td>
<td>25</td>
<td>ID</td>
<td>Seizures &lt;1 mo postoperatively with improper AED discontinuation only.</td>
</tr>
<tr>
<td>5</td>
<td>0</td>
<td>1</td>
<td>Multiple emergency visits and readmissions for PNES</td>
<td>5c</td>
<td>IVB</td>
<td>Poor medication compliance, continued bilateral temporal seizures and PNES. Underwent open left ATL at 5 mo post-SLH; still not seizure free.</td>
</tr>
<tr>
<td>6</td>
<td>1</td>
<td>Acute SDH (no neurological deficits)d</td>
<td>20</td>
<td>IIIA</td>
<td>Seizure recurrence (same semiology, reduced frequency) at 4 mo postoperatively.</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>0</td>
<td>1</td>
<td>None</td>
<td>23</td>
<td>IB</td>
<td>Nondisabling auras only.</td>
</tr>
<tr>
<td>8</td>
<td>0</td>
<td>1</td>
<td>None</td>
<td>17</td>
<td>IA</td>
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</tr>
<tr>
<td>9</td>
<td>0</td>
<td>3</td>
<td>None</td>
<td>14</td>
<td>IA</td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>0</td>
<td>2</td>
<td>None</td>
<td>8</td>
<td>IA</td>
<td></td>
</tr>
<tr>
<td>11</td>
<td>0</td>
<td>1</td>
<td>None</td>
<td>7</td>
<td>IA</td>
<td></td>
</tr>
<tr>
<td>12</td>
<td>0</td>
<td>1</td>
<td>None</td>
<td>7</td>
<td>ID</td>
<td>Single GTC at 3 mo postoperatively with improper AED wean.</td>
</tr>
<tr>
<td>13</td>
<td>0</td>
<td>None (first procedure)</td>
<td>6</td>
<td>IVB</td>
<td>First SLAH: continued frequent seizures after incomplete amygdalohippocampotomy.</td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>1</td>
<td>None (second procedure)</td>
<td>1</td>
<td>Too early to determine</td>
<td>Second SLAH: adequate amygdalohippocampotomy achieved. Outcome &lt;4 mo.</td>
<td></td>
</tr>
</tbody>
</table>

aSLAH, stereotactic laser amygdalohippocampotomy; ICU, intensive care unit; F/U, follow-up; ATL, anterior temporal lobectomy with amygdalohippocampotomy; AED, antiepileptic drug; EEG, electroencephalography; PNES, psychogenic nonepileptic seizure; SDH, subdural hematoma; SLAH, stereotactic laser amygdalohippocampotomy. 
bSee text for details. 
cPatient underwent anterior temporal lobectomy at 5 months post-SLH.
temporal-onset epileptic seizures. Given the inability to self-report reliable seizure frequency data, she was classified as Engel IVB and underwent open left ATLAH at 5 months post-SLAH. After this procedure and despite improved medical compliance, she has not achieved seizure freedom. Thus, 2 patients (patients 2 and 5) in this series failed to achieve seizure freedom, in part due to bilateral temporal lobe epilepsy.

When analyzed by preoperative imaging status (MTS vs non-MTS) (Figure 5B), 6 of 7 patients with Engel I outcome had preoperative MTS, whereas 3 patients who failed to achieve seizure freedom (Engel III and IV) had preoperative MTS. Thus, in the select MTS population, 6 of 9 patients (67%) achieved Engel I outcome, whereas 2 (22%) were Engel III and 1 (11%) was Engel IV.

Although the volumes ablated of the amygdala, hippocampus, and AHC in each procedure are shown (see Table, Supplemental Digital Content 2, http://links.lww.com/NEU/A617), the distribution of volumes of amygdalohippocampal ablation are specifically categorized by clinical outcome in Figure 5C. Notably, the mean ablation volumes of the procedures associated with each outcome (seizure free, 58.0 ± 10.7%; not seizure free, 58.4 ± 7.6%) were not significantly different (t test, P = .42). Likewise, the length of hippocampus ablated for each procedure (see Table, Supplemental Digital Content 2, http://links.lww.com/NEU/A617) did not correlate with clinical outcome (seizure free, 2.41 ± 0.39 cm; not seizure free, 2.54 ± 0.49 cm; t test; P = .63). Thus, neither amygdalohippocampal ablation volumes nor lengths of hippocampus ablated were particularly predictive of outcome in this series.

Over the 2.5-year period of this study, a total of 23 patients underwent therapeutic temporal lobe procedures for nonlesional epilepsy and MTS at our tertiary care institution (Figure 6). Seven of these patients had a diagnosis of temporal lobe epilepsy in the context of having craniotomies for the placement of diagnostic subdural grid electrode arrays followed immediately by open grid removal and resection. The remaining 18 patients diagnosed with MTLE were eligible for surgical resection either on the basis of noninvasive studies alone or after intraparenchymal depth and subdural strip electrodes or percutaneous transforamen ovale
subdural electrodes. Seventeen of these patients were capable of consenting to and participating in the prospective study, and all were offered the choice of open temporal lobe surgery or SLAH. Four of these chose open surgery (3 with MTS), and 13 selected SLAH (9 with MTS). Overall, 7 of 13 SLAH patients (54%) were free of disabling seizures (Engel I), and 6 of 9 SLAH patients with MTS (67%) were free of disabling seizures (Figure 6). Thus, our only exclusions from consideration for SLAH were inability to provide research consent (n = 1) or having already undergone craniotomy for subdural grid electrodes (n = 7). The SLAH cohort represents a “real-world” sample of temporal lobe epilepsy patients presenting for surgical consideration.

Intensive Care Unit Admission and Hospital Length of Stay

After the first 3 procedures, patients were admitted to the intensive care unit for observation (Table 3). All 3 patients denied headaches or other neurological symptoms, and hospital courses were unremarkable. Subsequently, patients were admitted directly to the hospital ward with the exception of patient 6, whose procedure was complicated by a small acute subdural hematoma (see the following). Thus, length of hospital admissions averaged 1.6 days (median, 1 day; range, 1-3 days (Table 3). This compares favorably with the routine intensive care unit admissions (median, 2 days) and longer postoperative hospital admission (median, 5 days) for the last 12 open temporal lobe resections at our institution over an overlapping period of time.

Adverse Events

One major complication (homonymous hemianopia) and 1 minor complication (small acute subdural hemorrhage) were associated with the stereotactic insertion procedure in this series (Table 3). During the second SLAH procedure in patient 1, failure to adequately thread the anchor bolt into bone resulted in initial superior deviation of the stereotactic alignment rod, which was recognized on lateral fluoroscopy. The deviation was corrected, the remainder of the procedure was technically successful, and MRI confirmed ablation confined to the mesial temporal structures. The patient awoke with left subtotal homonymous hemianopia, presumably from the initial errant alignment rod placement in the lateral geniculate nucleus or optic tract. Nevertheless, no postoperative hematoma or edema could be identified in these off-target structures by MRI, nor was there evidence of contrast enhancement or DWI signal change that would suggest encroachment of the ablation zone into these structures. The deficit persisted at last follow-up.

In patient 6, MRI during the laser ablation revealed a slowly expanding acute occipital subdural hematoma localized near the applicator entry site (Table 3). After completion of a technically successful SLAH, we elected to evacuate the subdural hematoma via a small craniotomy, which revealed bleeding from a superficial cortical artery. Hemostasis was achieved, and the hematoma evacuated without neurological sequelae.

DISCUSSION

Stereotactic laser thermal ablation is a minimally invasive alternative to open epilepsy surgery. We report the technical and early clinical results of MR-guided real-time stereotactic laser amygdalohippocampotomy for MTLE. Two surgeons (J.T.W. and R.E.G.) performed 15 procedures on 13 patients; all but 1 was studied prospectively. This cohort belonged to a larger group of 23 temporal lobe epilepsy patients surgically treated at our tertiary referral center over the same time period (Figure 6). Thus, SLAH candidates did not require subdural grid electrode arrays to be considered for a definitive resection. The 13 patients presented in this study include all of the 17 patients who selected SLAH over open temporal lobe surgery. This patient sample represents a “real-world” cross section of patients presenting for epilepsy surgery and includes patients with and without MTS (Figure 6).

We found that ablation of the AHC is safe, associated with brief hospitalizations, and effective: most patients achieved seizure freedom. This study is novel in several respects: it constitutes the largest series of stereotactic laser ablation for epilepsy to date, it is the first reported series of SLAH for MTLE, and it is the first reported convergence of 2 independent FDA-cleared technologies: an MRI-guided stereotactic laser ablation system (Visualase, Inc) and an MRI-guided trajectory frame (MRI Interventions).

Technical Considerations

The stereotactic laser ablation method, using a diffuser-tipped, 15-W, 980-nm diode laser applicator system, appears readily adaptable to delivery via distinct types of stereotactic platforms in current practice, including traditional rigid fixation head frames (eg, CRW and Leksell [Elekta, Stockholm, Sweden]), image-guided frameless stereotaxis (eg, Medtronic Stealth and BrainLab), and MRI-guided miniframe systems (eg, ClearPoint SmartFrame [MRI Interventions]). Our technique required a median of 3 treatment cycles to conform to the AHC with direct imaging confirmation of ablation. We achieved a mean hippocampal treatment length of 2.5 cm with a mean 60% of the total amygdalohippocampal volume ablated. The use of MR thermometry via the Visualase workstation to monitor both target and collateral tissue temperatures provides automatic feedback control. Although time-dependent tissue injury occurs at tissue temperatures of 45 to 60°C, rapid irreversible ablation occurs at tissue temperatures greater than 60°C. Feedback control prevented superheating (>100°C), which is associated with charring, tissue gassing, and unpredictable heat spread to off-target tissue. Finally, immediate postprocedure confirmation by direct anatomic imaging is facilitated before removing the laser applicator. The result is a powerful approach that is measured, safe, and effective for neural tissue ablations in the setting of MTLE.

We observed that ablation zones tended to conform to anatomic boundaries of the targeted structures and can be delimited by pial boundaries; an impression from imaging that was confirmed in pathological specimens. The ablation dynamics in our study resembled those experienced by Curry et al when using the same laser ablation system. This conformal result is not immediately
intuitive, given that the laser applicator emits light circumferentially around the distal 1 cm of the optical fiber, and the amygdalohippocampal volume is curved and tubular rather than spherical. The thermodynamic factors most likely responsible for this respect for anatomic boundaries include the presence of surrounding cerebrospinal fluid-containing ventricle and cisterns, acting as a heat sink around the hippocampus, and either small amounts of CSF within arachnoidal boundaries (eg, the hippocampal sulcus) or, more likely, light reflectance at such boundaries. Our ability to ablate the AHC posteriorly, at least to the level of the lateral mesencephalic sulcus, along the natural curved anatomy of the hippocampus, and using only a single trajectory was likely feasible due to these favorable local anatomic/thermodynamic features.

In this series, we successfully performed the procedure using either a traditional stereotactic frame (CRW) or an MRI-guided trajectory frame (ClearPoint SmartFrame). The latter enables performance of the entire procedure within an interventional MRI environment. More importantly, it provides an ideal technique for MRI-based radiological verification of accurate localization of the laser fiber assembly during insertion. In contrast, use of the stereotactic frame, in our hands, only allowed for 2-dimensional fluoroscopic radiological control, which does not provide any mediolateral information or information with respect to tissue anatomy. In fact, it is likely that stereotactic technique, at least in part, contributed to the 1 major adverse effect in this series. This complication, a subtotal homonymous hemianopia, likely resulted from inadequately maintaining the stereotactic trajectory by improper placement of the anchor bolt. The alignment rod inserted through the anchor bolt deviated superiorly as visualized on fluoroscopy. This experience resulted in better recognition of the tactile feedback of a fully threaded anchor bolt during subsequent procedures. However, improved 3-dimensional visualization during insertion (which was not available with the CRW-based deployment) could have helped to detect the deviation before fully deploying the rod. In contrast, the MRI-based trajectory frame allows more confident deployment with 3-dimensional anatomic
control of the laser assembly. Notably, neither this complication nor that of a subdural hematoma appeared to result from the laser ablation step itself, but rather from either the stereotactic approach or the craniostomy method used, and both are known complications of analogous procedures such as stereotactic depth electrode insertion and deep brain stimulation.

**Preoperative Patient Factors Predict Seizure Outcome**

Overall, 7 of 13 SLAH patients (54%) were free of disabling seizures (Engel I), and 6 of 9 SLAH patients with MTS (67%) were free of disabling seizures. All SLAH patients had had a diagnosis preoperatively of unilateral MTLE except 1 (patient 5), who had evidence of bilateral temporal epilepsy but was considered for surgical palliation, given the less invasive nature of the proposed intervention. However, our clinical results with respect to seizure freedom (Table 3) may correlate with preoperative patient factors (Table 1). All patients with Engel I outcomes (patients 4, 7-9, 11, and 12), with the exception of patient 10, had in common unilateral seizure onset and MTS with concordant lateralized $^{18}$FDG-PET hypometabolism and memory dysfunction. Patient 10 did not have MTS, but did have previous confirmation of seizure onset to mesial structures via depth electrodes.

**Potential Explanations for SLAH Failures**

There are known or potential explanations for unfavorable outcomes in the patients in this series with Engel III/IV unfavorable outcomes (patients 1-3, 5, 6, and 13) (Table 3), including discordant or bilateral findings on preoperative workup (Table 1) and possibly suboptimal ablation volumes.

**Low Ablation Volumes**

Overall, total proportions of the entire AHC ablated did not correlate with seizure outcomes, as represented in Figure 5C. Likewise, the volumes of hippocampus ablated did not differentiate patients who achieved seizure freedom (seizure free, 63.2 ± 7.8% of volume vs not seizure free, 62.8 ± 11.5% of volume). Regarding the amygdala, the proportions ablated were generally more variable with smaller mean ablation volumes than those achieved in the hippocampus (Table 2). When amygdala ablation volumes were compared by outcome (seizure free, 53.5 ± 21% of volume vs not seizure free, 54.8 ± 32% of volume), no overall difference was observed. However, 2 patients did not achieve seizure freedom after notably low-volume amygdala ablations (4% after first ablation in patient 1 [Engel IV] and 12% in patient 3 [Engel III]). When patient 1 underwent a second ablation procedure, her amygdala ablation increased to 66%, but she still did not achieve seizure freedom (remained Engel IV until undergoing open ATLAH, which resulted in seizure freedom). Thus, no firm conclusions can be drawn from these preliminary observations regarding relationships of outcome to ablation volumes.

Patient 6 (Engel III) had left-sided onset seizures with left $^{18}$FDG-PET hypometabolism and left memory dysfunction and bilateral MTS on MRI. After ablation, seizures recurred at a reduced frequency without change in semiology, possibly suggesting failure to adequately ablate the seizure network rather than bilaterality of seizures, although postoperative video EEG monitoring has not been performed. Of note, this patient had the second lowest ablation volumes in the series with only 41% of the amygdala ablated and 51% of the total AHC.

**Bilateral Seizure Onsets**

Patient 2 (Engel III) had 9 seizures recorded from the right anterior temporal region on preoperative scalp video electroencephalography in the setting of bilateral temporal hypometabolism on PET. Seizures were reduced 85%. Postoperative video-EEG demonstrated a left-sided temporal seizure (with a distinct semiology), contralateral to the ablated right side.

Patient 5 (Engel IV) had left MTS, but bilateral $^{18}$FDG-PET hypometabolism and bilateral memory dysfunction (left > right). Bilateral seizure onsets were recorded preoperatively, although right-sided onsets were only observed after weaning antiepileptic medications, and psychogenic nonepileptic seizures were recorded as well. It was decided to offer palliative surgery, and SLAH was performed. Postoperative video electroencephalography demonstrated left and right onsets and psychogenic nonepileptic seizures. Left ATLAH was performed after 5 months, but seizures have continued and not been further characterized. This patient highlights the consequences of studying a new procedure in the “real-world” context, that is, SLAH was offered to all patients for whom resective temporal lobe surgery was determined to be the recommended treatment course at our comprehensive epilepsy surgery conference.

**More Extended Seizure Network**

SLAH alone, mostly sparing the parahippocampal region, was sufficient to produce seizure freedom in the majority of patients in this small series. Similarly, Malikova et al. concluded that the parahippocampal region was not critical for seizure freedom after radiofrequency (RF) ablation, suggesting that the amygdala and hippocampus were generally sufficient. Nevertheless, the patients without MTS in our series were less likely to be seizure free after SLAH alone. Notably, patient 1 (non-MTS; Engel IV) underwent 2 ablation sessions, ultimately encompassing both the AHC and also the parahippocampal gyrus without eliminating seizures; seizure freedom was achieved only after open ATLAH (follow-up >6 months). Indeed, a recent meta-analysis showed that 8% more patients became seizure free after ATLAH compared with SAH, suggesting that, in some patients with resection of neocortical structures beyond the mesial temporal region (amygdala, hippocampus, and parahippocampal/entorhinal cortices) have a greater likelihood of seizure freedom. Perhaps generating more widespread ablation zones via 2 or more laser trajectories to encompass the parahippocampal region (entorhinal cortex, perihippocampal cortex, and parahippocampal gyrus) might improve the chance of seizure freedom in select patients. However, it is also possible that ablating additional regions will adversely affect cognitive outcome.


Comparison of SLAH With Other Surgical Approaches to MTLE

This small series shows promise for the effectiveness of SLAH, which we expect to improve with more technical experience and appropriate patient selection. Likewise, a full assessment of the true risk of adverse effects requires a greater number of cases, making detailed comparisons with other surgical approaches premature. With these caveats, some potential advantages and disadvantages include the following.

Open Surgical Resection (ATLAH, SAH)

Seizure-free rates from open surgical resection have varied from 60% to 80%, the benchmark being 64% as found in the only randomized, controlled study of highly select patients. It would not be surprising to find in a larger series a somewhat lower rate of seizure freedom compared with ATLAH in light of the findings of a recent meta-analysis that ATLAH is associated with an 8% greater rate of seizure freedom compared with the more limited SAH resection. However, the possibly greater effectiveness of open resection must be balanced against the potentially greater risk of neuropsychological decline from collateral injury to the temporal stem. In fact, we have observed improved outcomes on neuropsychological testing at 6 months and 1 year with respect to naming and object recognition (left and right SLAH, respectively) compared with open resections. An additional advantage of SLAH over open resective procedures is minimal recovery times and decreased short-term health-care use with respect to intensive care unit and hospital lengths of stay.

Stereotactic Radiosurgery

Although stereotactic radiosurgery (SRS) for MTLE has produced rates of seizure freedom comparable to those of open resection, therapeutic effects are delayed up to 2 years compared with the immediate results from SLAH, which does not involve ionizing radiation. Moreover, potential complications from radiation necrosis after SRS require close postoperative monitoring and may require intensive medical or surgical management. A recent prospective, randomized clinical trial of SRS for MTLE was discontinued due to low enrollment.

Stereotactic RF Ablation

RF ablation is the procedure most comparable to SLAH. Although earlier results were disappointing, a more recent series using an occipital approach and length of hippocampus ablation similar to those in SLAH demonstrated 78% of 32 MTLE patients were seizure free over 2 years. Complications were low, and the cohort exhibited no evidence of cognitive decline with standard testing. Limitations of RF ablation include difficulty conforming thermal energy to sensitive anatomic structures, the need to perform a large number of lesions, and lack of real-time imaging verification. Moreover, the “string electrode” used in this recent series is no longer commercially available. Stereotactic delivery of laser thermal energy not only facilitates MRI real-time monitoring, but may also offer superior thermodynamic properties for more safely and effectively conforming ablations to anatomically distinct structures.

In sum, SLAH has significant potential advantages compared with alternative procedures, including the gold-standard open resection, SRS, and RF ablation. Whether seizure-free rates are high enough and the complication rates low enough to justify this minimally invasive procedure must await a larger series, and a multicenter study is under way to examine this question. Because neuropsychological sequelae appear to be lower compared with open resection, a reasonable approach may be to perform SLAH first, as the majority of patients can expect to become seizure free. Should a patient fail to achieve seizure freedom after SLAH, the patient may still be a candidate for more extensive ablation or open resection, an approach that we took in 3 of our patients.

CONCLUSION

This report demonstrates the technical feasibility and encouraging early results of SLAH, a novel approach to eliminating seizures while minimizing collateral injury in patients with MTLE. Efficacy appears to approach that of open resection, especially in patients with MTs. Such minimally invasive techniques may be more desirable to patients and result in increased use of epilepsy surgery among the large number of medically intractable epilepsy patients. A larger, longer term multicenter study of seizure and cognitive outcomes after SLAH is currently under way.

Disclosure

Funding was provided to Emory University by way of a clinical study agreement from Visualase, Inc, which develops products related to the research described in this paper. In addition, Dr Gross serves as a consultant to Visualase and receives compensation for these services. The terms of this arrangement have been reviewed and approved by Emory University in accordance with its conflict of interest policies. Dr Gowda is an employee and stockholder in Visualase, Inc. Dr Drane receives funding from the NIH/NINDS (K02 NS07960), which provides support for his work. The other authors have no personal financial or institutional interest in any of the drugs, materials, or devices described in this article.

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However, 1 patient had a symptomatic homonymous field cut and 1 had safety of the method, which is supposed to be minimally invasive. radiosurgery after a learning curve period. The authors highlight the these results may turn out to be more comparable to microsurgery or microsurgical resection or radiosurgery. However, Table 3 indicates an improvement of the results with increasing operator experience, and these results are quite modest compared with those achieved by microsurgical amygdalohippocampectomy and temporal lobectomy, respectively) when the MTLE is on the dominant side. Interestingly, despite this very good safety/efficacy notion that laser ablation will lead to improved neuropsychological outcomes and look forward to more information in this regard.

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In patients presenting with mesial temporal lobe epilepsies (MTLEs), it is now well established that microsurgical resection of the anterior parahippocampal cortex, amygdaloid complex, and hippocampus results in high rate of seizure cessation at the price of a very modest morbidity. Apart from visual field deficits, the only concern about resection is the risk of verbal memory deficit (30.9% and 43.4% after anterior amygdalohippocampectomy and temporal lobectomy, respectively) when the MTLE is on the dominant side. Interestingly, despite this very good safety/efficacy profile, neurosurgeons have felt the need to develop alternatives that are supposed to be less invasive such as thermocoagulation and radiosurgery. In particular, radiosurgery using the Gamma-knife has demonstrated through 2 multicenter prospective trials, in dominant-side MTLE, to be advantageous in terms of verbal memory sparing. In this paper, the authors have provided us with their preliminary experience with the use of stereotactic laser thermocoagulation in MTLE. Results obtained in 13 patients showed promising data in terms of seizure reduction. This study provides the scientific community valuable new data in terms of feasibility. However, this is a small cohort of only 13 patients with rather short-term follow-up (as short as 5 months for some patients) with no objective evaluation of toxicity (no systematic visual field assessment) and no report of neuropsychological outcome. An interesting comparison that is not provided here would be verbal memory scores pre- and postoperatively for the dominant side nonlesional MTLE patients. With 7 of 13 patients without disabling seizures (Engel I = 54%) including only 4 patients completely seizure free (Engel IA = 30.8%), these results are quite modest compared with those achieved by microsurgical resection or radiosurgery. However, Table 3 indicates an improvement of the results with increasing operator experience, and these results may turn out to be more comparable to microsurgery or radiosurgery after a learning curve period. The authors highlight the safety of the method, which is supposed to be minimally invasive. However, 1 patient had a symptomatic homonymous field cut and 1 had

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Comments

T his is an important work that demonstrates the feasibility of laser ablation of the mesial temporal lobe in a prospective group of patients with temporal lobe epilepsy. Advantages to this technique include the minimally invasive approach and reduced postoperative pain and hospitalization time. It is unclear whether the technique is equal to open resection via cortico-amygdalohippocampectomy; longer follow-up times will answer this question. Disadvantages of the laser technique include an inability to adequately ablate the majority of the amygdala, hippocampus, and parahippocampal tissue due to the curved anatomy and the presence of the ventricle, which acts as a “heat sink” during laser treatment. An additional important disadvantage is the lack of tissue procurement for histopathological analysis. Finally, the presence of dual pathology (usually cortical dysplasia in the temporal pole) in these patients means that patient selection will be all important in maximizing outcomes. I am still somewhat skeptical of the notion that laser ablation will lead to improved neuropsychological outcomes and appear in the printed text and are provided in the HTML and PDF versions of this article on the journal’s Web site (www.neurosurgery-online.com).

Supplemental digital content is available for this article. Direct URL citations appear in the printed text and are provided in the HTML and PDF versions of this article on the journal’s Web site (www.neurosurgery-online.com).

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a subdural hematoma that needed to be evacuated; such complications are perhaps not altogether surprising for a destructive technique requiring intracranial probe insertion.\(^5\)

In terms of patient selection, the small series described here seems to indicate a better chance of seizure freedom in treated patients who have clear-cut evidence of underlying hippocampal sclerosis, because 6 of the 7 patients with class I outcome had mesial temporal sclerosis (MTS), and only 1 of the 9 MTS patients did not have significant improvement after laser amygdalohippocampectomy. This is in keeping with data from conventional surgical series. The heterogeneity of MTLE has recently been highlighted\(^6\) and surgical failures may often be due to the presence of wider areas of dysfunction that extend beyond the pathological lesion.\(^6\) Such wider areas of dysfunction are likely due to more distributed epileptogenic networks, particularly in terms of entorhinal\(^7,8\) or temporal neocortex\(^9\) involvement. This point is important to keep in mind when selecting patients for focal treatment of epilepsy. One of the most challenging groups for future study are those patients with negative or nonspecific MRI findings,\(^10\) which were among those with a poorer outcome in this study. Future work could identify positive predictors of focal organization of the seizure onset zone in such patients, such as \(^11\)FDG-PET,\(^11\) to further optimize patient selection. Indeed this issue of how to best treat patients with “nonhippocampal sclerosis MTLE” may become increasingly important if, as has been suggested, the incidence of MTLE due to hippocampal sclerosis is now on the decline.\(^12\)

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