Laser ablation of abnormal neurological tissue using robotic neuroblate system (LAANTERN): Procedural safety and hospitalization

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Laser Ablation of Abnormal Neurological Tissue Using Robotic Neuroblate System (LAANTERN): Procedural Safety and Hospitalization

BACKGROUND: Stereotactic laser ablation (SLA) has demonstrated potential utility for a spectrum of difficult to treat neurosurgical pathologies in multiple small and/or retrospective single-institutional series. Here, we present the safety profile of SLA of intracranial lesions from the Laser Ablation of Abnormal Neurological Tissue using Robotic NeuroBlate System (LAANTERN; Monteris Medical) multi-institutional, international prospective observational registry.

OBJECTIVE: To determine the procedural safety of SLA for intracranial lesions.

METHODS: Prospective procedural safety and hospitalization data from the first 100 treated LAANTERN patients was collected and analyzed.

RESULTS: Mean age and baseline Karnofsky Performance Status (KPS) were 51 (±17) yr and 83 (±15), respectively. In total, 81.2% of patients had undergone prior surgical or radiation treatment. Most patients had a single lesion (79%) ablated through 1 burr hole (1.2 ± 0.7 per patient), immediately following a lesion biopsy. In total, >90% of the lesion was ablated in 72% of treated lesions. Average total procedural time was 188.2 ± 69.6 min, and average blood loss was 17.7 ± 55.6 ccs. The average length of intensive care unit (ICU) and hospital stays before discharge were 38.1 ± 62.7 h and 61.1 ± 87.2 h, respectively. There were 5 adverse events (AEs) attributable to SLA (5/100; 5%). After the procedure, 84.8% of patients were discharged home. There was 1 mortality within 30 d of the procedure (1/100; 1%), which was not attributable to SLA.

CONCLUSION: SLA is a safe, minimally invasive procedure with favorable postprocedural ICU and hospital utilization profiles.

KEY WORDS: Stereotactic laser ablation, Neuro-oncology, Safety

Stereotactic laser ablation (SLA), also known as laser interstitial thermotherapy (LITT), is a minimally invasive procedure where a laser probe is stereotactically inserted into an abnormal target tissue. Laser activation triggers thermocoagulation and focused tissue destruction.1 The extent of thermocoagulation is monitored under near real-time magnetic resonance thermometry to minimize the risk of injury to the surrounding cerebrum.2-5 Emerging data support the safety and clinical efficacy of SLA as treatment for a spectrum of neurosurgical pathologies including low- and high-grade gliomas, brain metastases, radiation necrosis, and seizure foci (Table 1).3-18 However, these datasets are mostly small (<50 patients) and/or retrospective reports of single-institutional series. Moreover, there is significant heterogeneity in these studies in terms of quality assurance, definition of complications, and data validation. These challenges limit the generalizability of the reported data. Additionally,
interpretation of this data set is often confounded by various forms of biases inherent in retrospective, institutional studies.

To address these issues, we initiated a prospective, multi-institutional registry to track, analyze, and report unfiltered patterns of use and clinical outcomes for patients undergoing intracranial SLA, using a common set of definitions for complications and multi-step mechanisms for quality assurance and data validation. This ongoing study, termed Laser Ablation of Abnormal Neurological Tissue using Robotic NeuroBlate System (LAANTERN; Monteris Medical) is collecting indication, safety, efficacy, and quality of life data on a target population of 1000 total SLA patients. We have previously reported the clinical indications for the first 100 SLA-treated patients enrolled in LAANTERN. Here, we present the procedural safety profile for this patient cohort.

METHODS

Study Design, Participants, and LAANTERN Registry

Details pertaining to the LAANTERN registry (ClinicalTrials.gov study ID # [NCT02392078 for review]) were previously described. This registry includes consenting SLA patients (or those with a legally authorized proxy), who are expected to comply with clinical follow-up. More than 15 centers are actively participating in this study. The institutional review boards (IRB) of all participating centers reviewed and approved the study protocol. As previously described, pretreatment clinical parameters, postoperative neurologic condition, length of intensive care unit (ICU) stay, length of hospital stay, complications, discharge location, and other pertinent clinical parameters are collected by the site PI. At predefined follow-up intervals, the site PIs assess the patient and complete clinical outcome and quality of life surveys, as well as assess follow-up MRIs. Routine audits are performed to ensure compliance and data accuracy. This manuscript was prepared in accordance with STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) guidelines.

The LAANTERN study was designed to identify complications that occur at >0.1% frequency, with the target sample size of 1000 patients commonly used in observational studies aiming to characterize the safety of novel interventions.

MRI-Guided Biopsy and SLA

The protocol for both MRI-guided biopsy and SLA using stereotaxis has been previously described, and all procedures are performed based on institutional standards of care. Briefly, patients undergo general anesthesia, are pinned with an MRI-compatible head frame, positioned, cleaned, and prepared. An MRI-visible grid is used to localize the entry site, and a frameless MRI-compatible stereotactic targeting cannula is aligned to the desired trajectory. A small Burr hole and durotomy are created, and a ceramic stylet is moved to the target site. The stylet is removed after MRI confirmation, and replaced by a biopsy needle if biopsies are performed. The SLA probe is then inserted to the target site for thermal ablation under real-time MR thermometry as previously described.

Clinical Variables Collected

The following parameters were extracted from the LAANTERN central data registry: age, baseline Karnofsky Performance Status (KPS), postprocedure KPS, prior surgical or radiation treatment, number of lesions treated, whether biopsies were performed prior to SLA, indication for surgery, percent of lesion ablated, total procedural time, total time spent in the ICU/hospital (immediate postoperative level of care was based on physician assessment), preprocedure medical conditions, and postprocedure morbidities.

Main Outcome: Adverse Events (AEs) and Complications

Study AEs (defined as any deviation from the normal or anticipated postoperative course) occurring within the initial 30-d postprocedure window were examined. Each AE could contain 1 or more complication(s). Subsequent to reporting, AEs were further broken down into specific complications based on the categorization schema for craniotomies introduced by Sawaya et al, with all potential contributing factors also listed. This modified complication classification scheme was chosen for our initial AE data analysis and presentation to ensure capture of all potential complications related to each aspect of the procedure, and is summarized in Tables 2 and 3. While SLA is performed through a Burr hole, many of the lesion treated would have been approached through an open craniotomy if SLA were not available. In this context, we were interested in comparing the safety profile of SLA vs an open craniotomy approach. We adopted the AE schema developed for craniotomies in this context. For cases where the relative contribution of the biopsy and thermo-coagulation (SLA) could not be easily determined (Table 3), both were listed as contributing factors.

To further assess the safety of SLA, AEs were classified by all participating authors of this manuscript based on their most likely etiology into the following: (1) medical AEs, (2) AEs related to surgical manipulation and the known risks of biopsy, and (3) AEs likely related to thermo-coagulation injury by laser ablation.

Statistical Analysis

Continuous variables are reported as mean ± standard deviation (SD) or standard error of the mean (SEM) (median and ranges reported for selected parameters). Patients with incomplete data were excluded from pertinent categorical analyses.
<table>
<thead>
<tr>
<th>Authors</th>
<th>Year</th>
<th>Total patients</th>
<th>Total targets</th>
<th>Study design</th>
<th>Institution</th>
<th>Clinical indication</th>
<th>Intracranial location</th>
<th>Lesion volume (cm$^3$) (median [range] or mean ± SD)</th>
<th>Pre-operative KPS (median [range] or mean ± SD)</th>
<th>Procedural time (minutes) (mean ± SD)</th>
<th>ICU stay (days) (median [range] or mean ± SD)</th>
<th>Hospital stay (days) (median [range] or mean ± SD)</th>
<th>Overall complication rate</th>
<th>Neurologic complication rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carpentier et al$^9$</td>
<td>2008</td>
<td>6</td>
<td>6</td>
<td>Prospective case series</td>
<td>Single-institution</td>
<td>BMs</td>
<td>Frontal, temporal, parietal, occipital lobes</td>
<td>N/a</td>
<td>68.3 ± 23.1</td>
<td>N/a</td>
<td>N/a</td>
<td>N/a</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>Carpentier et al$^9$</td>
<td>2011</td>
<td>7</td>
<td>15</td>
<td>Prospective case series</td>
<td>Single-institution</td>
<td>BMs</td>
<td>N/a</td>
<td>62 mean</td>
<td>135 mean</td>
<td>N/a</td>
<td>11 (mean)</td>
<td>26%</td>
<td>13%</td>
<td></td>
</tr>
<tr>
<td>Carpentier et al$^9$</td>
<td>2012</td>
<td>4</td>
<td>4</td>
<td>Prospective case series</td>
<td>Single-institution</td>
<td>HGGs</td>
<td>Frontal, temporal lobes, CC</td>
<td>2.0 ± 2.0</td>
<td>N/a</td>
<td>N/a</td>
<td>N/a</td>
<td>N/a</td>
<td>50%</td>
<td>50%</td>
</tr>
<tr>
<td>Hawasli et al$^6$</td>
<td>2013</td>
<td>17</td>
<td>17</td>
<td>Prospective case series</td>
<td>Single-institution</td>
<td>HGGs, BMs, Epilepsy</td>
<td>Frontal, parietal lobes, insula, thalamus, BG, CC</td>
<td>11.6 ± 9.6</td>
<td>74.1 ± 9.4</td>
<td>301 ± 88 for single trajectory; 480 ± 77 for multi-trajectory</td>
<td>1.8 ± 17</td>
<td>5.0 ± 6.4</td>
<td>41%</td>
<td>35%</td>
</tr>
<tr>
<td>Sloan et al$^14$</td>
<td>2013</td>
<td>10</td>
<td>10</td>
<td>Prospective phase I trial</td>
<td>Multi-institution</td>
<td>HGGs</td>
<td>Frontal, temporal, parietal lobes</td>
<td>6.8 ± 5.0</td>
<td>80 (70-90)</td>
<td>N/a</td>
<td>N/a</td>
<td>3 (median)</td>
<td>N/a</td>
<td>30%</td>
</tr>
<tr>
<td>Mohammadi et al$^3$</td>
<td>2014</td>
<td>34</td>
<td>34</td>
<td>Retrospective case series</td>
<td>Multi-institution</td>
<td>HGGs</td>
<td>Frontal, parietal, temporal lobes, insula, thalamus</td>
<td>10.1 (0.7-49.9)</td>
<td>80 (50-90)</td>
<td>N/a</td>
<td>N/a</td>
<td>3 (1-29)</td>
<td>30%</td>
<td>20%</td>
</tr>
<tr>
<td>Rao et al$^8$</td>
<td>2014</td>
<td>14</td>
<td>15</td>
<td>Retrospective case series</td>
<td>Single-institution</td>
<td>BMs</td>
<td>Frontal, parietal, temporal lobes, cerebellum</td>
<td>3.6 ± 6.1</td>
<td>N/a</td>
<td>136 ± 27</td>
<td>N/a</td>
<td>12 (1-5)</td>
<td>13%</td>
<td>6%</td>
</tr>
<tr>
<td>Ali et al$^7$</td>
<td>2016</td>
<td>23</td>
<td>26</td>
<td>Retrospective case series</td>
<td>Multi-institution</td>
<td>BMs</td>
<td>Frontal, parietal, occipital lobes, insula, thalamus, BG, cerebellum</td>
<td>4.9 (0.4-28.9)</td>
<td>N/a</td>
<td>N/a</td>
<td>N/a</td>
<td>N/a</td>
<td>22%</td>
<td>13%</td>
</tr>
<tr>
<td>Rennert et al$^5$</td>
<td>2016</td>
<td>10</td>
<td>10</td>
<td>Retrospective case series</td>
<td>Single-institution</td>
<td>HGGs</td>
<td>Frontal, temporal, parietal lobes, CC</td>
<td>10.2 ± 8.8</td>
<td>N/a</td>
<td>254 ± 28 for single trajectory; 33 ± 85 for 2-trajectory; 436 ± 102 for 3-trajectory</td>
<td>N/a</td>
<td>N/a</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>Thomas et al$^10$</td>
<td>2016</td>
<td>21</td>
<td>21</td>
<td>Retrospective case series</td>
<td>Single-institution</td>
<td>HGGs</td>
<td>Parietal, temporal lobes, insula, thalamus, CC</td>
<td>14.6 to 22.4 (mean by clinical grouping)</td>
<td>80 to 85 (mean by clinical grouping)</td>
<td>N/a</td>
<td>N/a</td>
<td>N/a</td>
<td>9%</td>
<td>9%</td>
</tr>
<tr>
<td>Authors</td>
<td>Year</td>
<td>Total patients</td>
<td>Total targets</td>
<td>Study design</td>
<td>Institution</td>
<td>Clinical indication</td>
<td>Intracranial location</td>
<td>Lesion volume (cm³)</td>
<td>Pre-operative KPS (median [range or mean ± SD])</td>
<td>Procedural time (minutes)</td>
<td>ICU stay (days)</td>
<td>Hospital stay (days)</td>
<td>Overall complication rate</td>
<td>Neurologic complication rate</td>
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</tr>
<tr>
<td>Kang et al.</td>
<td>2016</td>
<td>20</td>
<td>20</td>
<td>Prospective case series</td>
<td>Single-institution</td>
<td>Epilepsy</td>
<td>Mesial temporal lobe</td>
<td>3.2 to 5.4 (mean by clinical grouping)</td>
<td>N/a</td>
<td>N/a</td>
<td>N/a</td>
<td>N/a</td>
<td>N/a</td>
<td>50%</td>
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<tr>
<td>Patil et al.</td>
<td>2016</td>
<td>102</td>
<td>102</td>
<td>Retrospective case series</td>
<td>Single-institution</td>
<td>HGGs, BMs, Epilepsy, Chronic pain</td>
<td>N/a</td>
<td>N/a</td>
<td>171 ± 34</td>
<td>1.8 ± 3.4</td>
<td>3.6 ± 5.4</td>
<td>26%</td>
<td>13%</td>
<td>11%</td>
</tr>
<tr>
<td>Kamath et al.</td>
<td>2017</td>
<td>120</td>
<td>133</td>
<td>Prospective case series</td>
<td>Single-institution</td>
<td>LGGs, HGGs, BMs, Epilepsy, Radionecrosis</td>
<td>Frontal, temporal, parietal, occipital lobes, insula, thalamus, CC, intraventricular, pons, pineal region, cerebellum</td>
<td>10.2 (0.3-62.8)</td>
<td>N/a</td>
<td>225 ± 110</td>
<td>1.2 to 1.9 (mean by clinical grouping)</td>
<td>2.2 to 4.0</td>
<td>13%</td>
<td>11%</td>
</tr>
<tr>
<td>Donos et al.</td>
<td>2018</td>
<td>43</td>
<td>43</td>
<td>Retrospective case series</td>
<td>Single-institution</td>
<td>Epilepsy</td>
<td>Mesial temporal lobe</td>
<td>N/a</td>
<td>N/a</td>
<td>N/a</td>
<td>N/a</td>
<td>N/a</td>
<td>&lt;24 h for all pts</td>
<td>2%</td>
</tr>
<tr>
<td>Grewal et al.</td>
<td>2018</td>
<td>25</td>
<td>25</td>
<td>Retrospective case series</td>
<td>Multinstitution</td>
<td>Epilepsy</td>
<td>Mesial temporal lobe</td>
<td>6.8 (3.0-11.5)</td>
<td>N/a</td>
<td>N/a</td>
<td>N/a</td>
<td>N/a</td>
<td>N/a</td>
<td></td>
</tr>
<tr>
<td>Ahluwalia et al.</td>
<td>2018</td>
<td>42</td>
<td>45</td>
<td>Prospective case series</td>
<td>Multinstitution</td>
<td>BMs, Radionecrosis</td>
<td>Frontal, temporal, parietal, occipital lobes, thalamus, BG, cerebellum</td>
<td>6.4 (0.4-38.6)</td>
<td>82.1 ± 13.0</td>
<td>180 (84-562)</td>
<td>N/a</td>
<td>N/a</td>
<td>83%</td>
<td>28%</td>
</tr>
</tbody>
</table>

*reported or calculated based on total patients treated
*reported or calculated based on target lesions treated

**Abbreviations:** BG: basal ganglia; BM: brain metastases; CC: corpus callosum; HGG: high grade glioma; KPS: Karnofsky Performance Status; LITT: laser interstitial thermotherapy; LGG: low grade glioma; N/a: not applicable; SD: standard deviation; SLA: stereotactic laser ablation.
RESULTS

Participants and Demographic Data

The demographics of the first 100 LAANTERN patients was previously reported.\textsuperscript{19} For ease of readership, this previously published data is included in Table 4. In brief, there were 58 male and 42 female patients, with a mean age of 51 yr (± 17). Average body mass index (BMI) was 28.0 ± 6.9. Regarding co-morbidities, 36.9% were current or former smokers, 13.6% had a history of cardiovascular disease, 7.6% had a history of coagulopathy, 28.8% had a history of hypertension, and 12.1% had a history of diabetes. In total, 49.2% of patients had a significant co-morbidity. Baseline KPS was 83.1 ± 14.7. In total, 87.8% of patients had neurological symptoms pre-operatively, ranging from subjective (24.4%), to mild objective (48.8%), to objective limiting independence/function (8.5%). A total of 81.2% of the patients had undergone prior treatments for the target lesion, including surgery, radiation, and chemotherapy in the 2 yr prior to SLA, with nearly 45% of these treated lesions considered difficult to access through open surgery.\textsuperscript{19} As

<table>
<thead>
<tr>
<th>TABLE 4. Summary of Patient Characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Measure</td>
</tr>
<tr>
<td>--------</td>
</tr>
<tr>
<td>Gender</td>
</tr>
<tr>
<td>Female</td>
</tr>
<tr>
<td>Male</td>
</tr>
<tr>
<td>Age (years)</td>
</tr>
<tr>
<td>Race (N = 98)</td>
</tr>
<tr>
<td>White</td>
</tr>
<tr>
<td>African American</td>
</tr>
<tr>
<td>Asian</td>
</tr>
<tr>
<td>Native American</td>
</tr>
<tr>
<td>Unknown</td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
</tr>
<tr>
<td>Medical history smoker</td>
</tr>
</tbody>
</table>

*Data rows with N other than 100 as indicated. Reproduced with permission from Rennert et al\textsuperscript{19} CC BY-NC-ND 4.0.
SAFETY OF NEURONAL LASER ABLATION

FIGURE 1. Number of lesions present per patient. Most patients had a single lesion (79%) ablated through 1 burr hole (1.2 ± 0.7 per patient). The maximum number of lesions treated in a single procedure was 2, even in patients with 3+ lesions.

Previously published, 48% of the treated patients had primary intracranial tumors, 34% suffered from brain metastases, 16% received SLA for epilepsy, and 2% of the patients were treated for other indications. SLA target location for this study cohort has also already been reported, with 46% of treated lesions classified as deep.

Procedural Outcomes and Hospitalization Data

Most patients underwent SLA for a single lesion (79%) through a single burr hole (1.2 ± 0.7 per patient; Figure 1). Sixty-six (66%) percent of patients underwent a lesional biopsy immediately preceding the SLA. The “blue” thermal damage lines on the M*Vision Pro™ Software (Monteris Medical) indicate regions of irreversible thermal damage. Average target lesion volume was 9.8 ± 23.5 cm³, and greater than 90% of the lesion was ablated to the “blue” thermal line in 72% of treated lesions. The average total procedural time was 188.2 ± 69.6 min, and average blood loss was 17.7 ± 55.6 ccs (Figure 2).

Twenty-one patients (25%) spent no postoperative time in the ICU (Table 5). The LAANTERN registry did not collect information on the specifics of the level of care that these patients required. The average length of ICU and hospital stays before discharge were 38.1 ± 62.7 h (median 21.5 [0.0, 335.6]; Figure 3) and 61.1 ± 87.2 h (median 27.0 [6.0, 612.0]), respectively. Upon discharge, 84.8% of patients went home, 7.6% to a rehabilitation facility, 4.3% to a skilled nursing facility, 1.1% to another acute care hospital, 2.2% to other locations, and 0% to hospice.

Main Results: SLA and Safety

At 1 mo of follow-up, there were 11 study AEs that occurred in 9 patients. To better understand the nature of these AEs, they were first categorized based on the schema published by Sawaya et al,22 with an additional listing of all potential contributing factors (Table 6).

AEs were also classified based on their most likely etiology into medical, surgical, or SLA-related. Based on this final classification, 2 of the 11 AEs (2/100 or 2%) were medical conditions (AE2 [hypoxia] and AE8 [wide-complex tachycardia], with AE2 related to sedation and AE8 occurring in a patient with a prior history of cardiac arrhythmias).
Four of the 11 AEs (4/100 or 4%) were likely related to surgical manipulation (AE4 [wound dehiscence], AE 6 [subdural hematoma], AE 9 [bacteremia], and AE 11 [intraventricular hemorrhage]), with AEs 4 and 6 attributed to the surgery rather than the SLA since the target site for the SLA was located >2 cm away from the site of the dehiscence and the subdural hematoma, respectively. AE 9 was attributed to surgical manipulation as the infectious risk for these procedures is largely derived from skin entry. AE 11 is discussed in detail below.

Energy deposition from laser ablation likely contributed to 5 of the AEs (AEs 1, 3, 5, 7, and 10). Of these, there were 2 new neurologic deficits (1 patient with abnormal gait [AE 3] and 1 patient with hemibody weakness and sensory changes [AE 5]). There were 2 patients with postoperative seizures [AE 1 and AE 7] referable to increased peri-SLA edema or intraparenchymal hemorrhage after the procedure. AE 10 was a delayed intraparenchymal hemorrhage. While this AE may be the result of disease progression or SLA, we cannot exclude contribution from laser ablation. Since all of these patients underwent stereotactic biopsy as well as laser ablation, it was also not possible to determine the relative contributions of these procedures.

There was 1 death within the 30-d postoperative period (Patient 1). In this patient, intraventricular hemorrhage [AE 11] involving the lateral, third, and fourth ventricles with associated hydrocephalus was noted on MRI immediately after biopsy, but before SLA. The surgeon opted to proceed with the SLA with a total lasing time of 1 min. The bleeding arrested after SLA and an external ventricular drain was placed. Subsequent head computed tomography (CT) showed no evidence of hemorrhagic progression, however, despite adequate cerebrospinal fluid (CSF) drainage the patient was made comfort measures only and expired on postoperative day 9.

DISCUSSION

Key Results

Here, we report the procedural safety and hospitalization data for SLA for intracranial pathologies from the first 100 patients enrolled and treated in the LAANTERN study. Overall, the safety profile in this registry appears favorable, with 4 AEs (4%) related to surgical manipulation and 5 AEs (5%) potentially attributable to laser ablation. The average hospital stay before discharge was 61.1 ± 87.2 h, with the majority of patients discharged home within 2 d of the procedure. Compared to previously published SLA studies,3-7,13,15,24,25 the majority of LAANTERN patients harbor more severe baseline comorbidities and neurologic complaints. Moreover, nearly half of the lesions treated were considered difficult to access through conventional surgical approaches.19 These results highlight the utility of a prospective registry for assessing the real-world uses and outcomes of an emerging technology like SLA compared to the more restricted and often less generalizable data associated with randomized clinical trials (or for patient populations not amenable to randomization), as well as the clinical potential of this technique.

Interpretation

The 9% rate of potentially referable AEs to the combination of surgical manipulation/stereotactic biopsy and laser ablation represents an estimate of the complication rate directly associated with SLA as performed in the LAANTERN patient cohort. Including all recorded AEs, the per patient overall complication rate in this cohort was also 9%. These findings are within the wide range of previously reported 0% to 83% overall, and 0% to 50% neurologic complication rates with SLA (Table 1),3-11,13-18 and slightly lower than the 13% to 26% overall and 11% to 13% neurologic complication rates of recent larger cohort studies (n > 100 patients).16,18 In fact, our findings are comparable to the published complication rates of up to 7% for stereotactic biopsy alone,24,26-28 suggesting that the addition of laser ablation to stereotactic biopsy may not significantly elevate the risk of postoperative morbidity relative to patients treated with biopsy only. Notably, our complication rate is lower than that reported for open craniotomies as treatment for difficult to access tumors.22,23 Average blood loss was also trivial with SLA (mean of 17.7 ± 55.6 cc’s), consistent with the minimally invasive nature of this technique.

Regarding the overall complication rate for this cohort, we believe a per-patient calculation (9 patients with 11 total AEs, or a 9% overall complication rate [Table 6]) is reasonable. As an example of the potential pitfalls of including multiple complications per patient in this calculation, if half of a theoretical patient cohort suffered 2 complications, summing the total number of complications and dividing by the total number of patients would yield a 100% complication rate. However, this number is misleading, as a 100% complication rate is likely to be interpreted that all patients (rather than half) in the theoretical cohort...
suffered a complication. Nevertheless, only 2 patients in this series had multiple AEs, and the overall complication rate is not significantly changed using either calculation.

Our interim analysis also provides data pertaining to hospital resource utilization measures, including OR time, time in the ICU, and time in the hospital. The average total procedural time for stereotactic biopsy plus SLA was 188.2 ± 69.6 min, which is comparable to previously published series.5,8,16,17 This time estimate for procedure completion is approximately 30 to 60 min longer than the reported average time required for stereotactic biopsy without laser ablation,29,30 suggesting that the incorporation of SLA into a stereotactic procedure did not significantly increase anesthetic time.

The <24 h of ICU utilization in the majority of patients and the 61-h average overall hospital stay is consistent with the published literature for SLA (Tables 1 and 5),3,6,8,9,16-18 and comparable or shorter than the ICU and hospital stays associated with open cranial surgery.31-35 The observation that 1 quarter of patients did not require postoperative ICU care suggests future opportunities to de-escalate the level care for selected postablation patients. These results support the cost-effectiveness of SLA in the context of the documented benefits of shortened, less acute hospitalizations for both the patient36 and the hospital system.37

**Limitations**

The disease progression within 30 d of SLA in patient H is a reminder that ablation should not be misrepresented as a “cure” for tumors with microscopic disease extension beyond what is visualized on MRI. Despite the >90% lesional ablation achieved in the majority of patients in the study, this situation is analogous to the high recurrence rates of gliomas even after a surgical gross total resection,38,39 and is reflective of the

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### TABLE 6. Description of Adverse Event (AEs) Occurring Within 30 d With Assigned Complication Categorizations and Contributing Factors

<table>
<thead>
<tr>
<th>Adverse event#</th>
<th>Patient ID</th>
<th>Adverse event description</th>
<th>Days to event</th>
<th>Complications</th>
<th>Contributing factor(s)</th>
<th>Resolution (days to resolution)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>A</td>
<td>Intraparenchymal hemorrhage and increased seizure activity</td>
<td>0</td>
<td>Neurologic: Seizure, Regional: Bleeding/Hemorrhage</td>
<td>-Pre-existing condition (seizure) -SLA</td>
<td>Resolved (7)</td>
</tr>
<tr>
<td>2</td>
<td>A</td>
<td>Hypoxia</td>
<td>0</td>
<td>Systemic: Respiratory</td>
<td>-Sedation</td>
<td>Resolved (7)</td>
</tr>
<tr>
<td>3</td>
<td>B</td>
<td>Abnormal gait</td>
<td>1</td>
<td>Neurologic: Deficit: Abnormal Gait/Ataxia</td>
<td>-Surgical procedure -SLA</td>
<td>Ongoing</td>
</tr>
<tr>
<td>4</td>
<td>C</td>
<td>Wound dehiscence</td>
<td>22</td>
<td>Regional: Wound dehiscence</td>
<td>-Surgical procedure</td>
<td>Ongoing</td>
</tr>
<tr>
<td>5</td>
<td>D</td>
<td>Postoperative left hemineglect and hemiplegia (3/5 strength in left lower extremity; 0/5 in left lower extremity)</td>
<td>0</td>
<td>Neurologic: Deficit: Motor, Neurologic: Deficit: Sensory</td>
<td>-Surgical procedure -SLA</td>
<td>Ongoing</td>
</tr>
<tr>
<td>6</td>
<td>E</td>
<td>Small subdural hematoma at operative site; postoperative right lower extremity mild weakness and paresthesia; mild expressive aphasia</td>
<td>1</td>
<td>Regional: Hemotoma, Neurologic: Deficit: Ataxia, Neurologic: Deficit: Sensory, Neurologic: Deficit: Aphasia/Dysphasia</td>
<td>-Surgical procedure</td>
<td>Ongoing</td>
</tr>
<tr>
<td>7</td>
<td>F</td>
<td>New onset seizure associated with imaging findings of worsening cerebral edema</td>
<td>1</td>
<td>Neurologic: Seizure, Regional: Edema/Swelling</td>
<td>-Surgical procedure -SLA</td>
<td>Ongoing</td>
</tr>
<tr>
<td>8</td>
<td>G</td>
<td>Postoperative wide complex tachycardia without hemodynamic instability. Condition managed medically</td>
<td>0</td>
<td>Systemic: Cardiac</td>
<td>-Pre-existing medical condition (arrhythmia)</td>
<td>Ongoing</td>
</tr>
<tr>
<td>9</td>
<td>H</td>
<td>MSSA bacteremia</td>
<td>8</td>
<td>Systemic: General systemic infection</td>
<td>-Surgical procedure</td>
<td>Resolved (9)</td>
</tr>
<tr>
<td>10</td>
<td>H</td>
<td>Intraparenchymal hemorrhage with surrounding edema affecting the left basal ganglia and left frontal lobe</td>
<td>29</td>
<td>Regional: Bleeding/Hemorrhage, Regional: Edema/Swelling</td>
<td>-Surgical procedure -SLA</td>
<td>Ongoing</td>
</tr>
<tr>
<td>11</td>
<td>I</td>
<td>Intraventricular hemorrhage with ventriculomegaly</td>
<td>0</td>
<td>Regional: Bleeding/Hemorrhage</td>
<td>-Biopsy -Disease progression</td>
<td>Death (9)</td>
</tr>
</tbody>
</table>

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infiltrative nature of primary brain tumors. Accordingly, rapid disease progression adjacent to ablation sites has been previously reported in glioblastoma patients who underwent SLA but failed to respond to subsequent chemotherapy. As such, it should be clearly communicated to patients in these settings that therapeutic efficacy is expected only if the tumor subsequently responds to chemotherapy and/or radiation.

The unusual cases of excessive blood loss (300 ccs) and prolonged ICU stays (>12 d) warrant further comment. These data points represent unusual outcomes for SLA, which is performed through a burr hole. Because of their unusual nature, these data points were confirmed before entry into the registry. Unfortunately, the clinical context surrounding these events were not collected in LAANTERN. In terms of blood loss, we speculate that if a Burr hole is placed such that a venous lacunae is violated, excessive blood loss can occur prior to hemostasis. As in most real-world surgical situations, the reported blood loss likely also includes a contribution from irrigation used during hemostasis. This blood loss was reviewed by independent reviewers and not considered an AE because of the following: (1) it did not trigger hemodynamic instability requiring transfusion or resuscitation, and (2) the patient emerged from surgery neurologically intact. In terms of prolonged ICU stays, we hypothesize these rare patients are likely related to the AEs described in the manuscript (see Table 6).

**Generalizability**

Despite the inherent shortcomings related to an interim analysis of a prospective registry (eg, limited clarifying details of data point outliers), the concordance of the data provided here with independent published series suggests the robust nature of our observations. That said, continued assessments of safety and resource utilization data is warranted as the LAANTERN registry continues to accrue patients. Two other areas of assessment are needed in the future, including the following: (1) efficacy of impact on the underlying disease process, and (2) effects on the patient’s quality of life. Both of these information sets are being actively collected as a part of the LAANTERN effort and will soon be available.

**CONCLUSION**

Analysis of the first 100 patients from the LAANTERN registry suggests that SLA is a safe, minimally invasive procedure for the treatment of intracranial pathologies. The morbidity and hospitalization time profiles compare favorably to those previously reported for conventional craniotomies.

**Disclosures**

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**REFERENCES**


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