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CLINICAL ARTICLE

Magnetic resonance imaging–guided stereotactic laser ablation therapy for the treatment of pediatric epilepsy: a retrospective multiinstitutional study

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OBJECTIVE The authors of this study evaluated the safety and efficacy of stereotactic laser ablation (SLA) for the treatment of drug-resistant epilepsy (DRE) in children.

METHODS Seventeen North American centers were enrolled in the study. Data for pediatric patients with DRE who had been treated with SLA between 2008 and 2018 were retrospectively reviewed.

RESULTS A total of 225 patients, mean age 12.8 ± 5.8 years, were identified. Target-of-interest (TOI) locations included extratemporal (44.4%), temporal neocortical (8.4%), mesiotemporal (23.1%), hypothalamic (14.2%), and callosal (9.8%). Visualase and NeuroBlate SLA systems were used in 199 and 26 cases, respectively. Procedure goals included ablation (149 cases), disconnection (63), or both (13). The mean follow-up was 27 ± 20.4 months. Improvement in targeted seizure type (TST) was seen in 179 (84.0%) patients. Engel classification was reported for 167 (74.2%) patients; excluding

ABBREVIATIONS AED = antiepileptic drug; DOS = dichotomized outcome score; DRE = drug-resistant epilepsy; eEEG = extracranial EEG; HH = hypothalamic hamartoma; iEEG = intracranial EEG; ILAE = International League Against Epilepsy; LITT = laser interstitial thermal therapy; MCD = malformation of cortical development; MEG = magnetoencephalography; POD = postoperative day; SLA = stereotactic laser ablation; TOI = target of interest; TST = targeted seizure type.

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the palliative cases, 74 (49.7%), 35 (23.5%), 10 (6.7%), and 30 (20.1%) patients had Engel class I, II, III, and IV outcomes, respectively. For patients with a follow-up ≥ 12 months, 25 (51.0%), 18 (36.7%), 3 (6.1%), and 3 (6.1%) had Engel class I, II, III, and IV outcomes, respectively. Patients with a history of pre-SLA surgery related to the TOI, a pathology of malformation of cortical development, and 2+ trajectories per TOI were more likely to experience no improvement in seizure frequency and/or to have an unfavorable outcome. A greater number of smaller thermal lesions was associated with greater improvement in TST.

Thirty (13.3%) patients experienced 51 short-term complications including malpositioned catheter (3 cases), intracranial hemorrhage (2), transient neurological deficit (19), permanent neurological deficit (3), symptomatic perilesional edema (6), hydrocephalus (1), CSF leakage (1), wound infection (2), unplanned ICU stay (5), and unplanned 30-day readmission (9). The relative incidence of complications was higher in the hypothalamic target location. Target volume, number of laser trajectories, number or size of thermal lesions, or use of perioperative steroids did not have a significant effect on short-term complications.

CONCLUSIONS SLA appears to be an effective and well-tolerated treatment option for children with DRE. Large-volume prospective studies are needed to better understand the indications for treatment and demonstrate the long-term efficacy of SLA in this population.

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KEYWORDS magnetic resonance imaging–guided stereotactic laser ablation; laser interstitial thermal therapy; drug-resistant epilepsy; minimally invasive technique; pediatric epilepsy; seizure focus; functional neurosurgery

Drug-resistant epilepsy (DRE) is a debilitating condition that may respond to surgery for resection or disconnection of the seizure focus. To increase treatment options for difficult-to-access locations and to minimize complications related to traditional open surgery, newer minimally invasive approaches are constantly emerging.

MRI-guided stereotactic laser ablation (SLA) or laser interstitial thermal therapy (LITT) has become increasingly popular in the treatment of tumors and DRE over the last 10 years. The application of SLA in the management of both lesional and nonlesional epilepsy has been reported; however, most of the available data involve heterogeneous adult populations.[1–4] Pediatric-specific data for SLA in epilepsy are limited by small case volumes, short follow-up times, and/or narrow epilepsy types and target localizations.[5–10] Thus, there are currently no commonly accepted guidelines or indications for the use of SLA in pediatric patients with DRE.

In this multiinstitutional study, we evaluated the safety and efficacy of SLA for the treatment of DRE in children.

Methods

Seventeen North American centers were enrolled in the study. Data for pediatric patients with DRE who had been treated with SLA between 2008 and 2018 were retrospectively reviewed. Patient selection and recommendations for laser ablation over other treatment options were made at each center after review by their respective multidisciplinary epilepsy team.

Ethical Review and Approval

This multiinstitutional retrospective study was reviewed and approved by our local IRB, and IRB approval was obtained for all participating centers.

Inclusion and Exclusion Criteria

Patients 21 years of age or younger and who had been treated via SLA for a diagnosis of DRE between 2008 and 2018 were included. Patients older than 21 years of age and/or treated via SLA for a diagnosis other than DRE were excluded.

Data Collection

Data collection included demographics, SLA system and stereotactic system used, diagnosis, pathology, history of prior cranial surgeries, treatment goals (e.g., ablation vs disconnection, seizure freedom vs palliation, etc.), size and location of the target of interest (TOI), number of laser trajectories, characteristics of the thermal lesions created, anesthesia time, day of discharge, complications, steroid use, post-SLA follow-up time, post-SLA cranial surgery, pre- and post-SLA antiepileptic drug (AED) use, outcome for targeted seizure type (TST), and post-SLA seizure frequency (i.e., International League Against Epilepsy [ILAE] and Engel classification scales).[11,12]

Procedural Definitions and Dichotomized Outcome Score

In this study, we adhered to definitions outlined in a previous publication:[13] "procedure," a single anesthesia/day; "TOI," a contiguous volume of tissue targeted for ablation and/or disconnection; "lesion," a contiguous volume of tissue that was ablated and may or may not be equal to a TOI; "trajectory," a single tract through the brain with the laser catheter; and "burn," the delivery of energy via laser to a unique location. Note that the TOI locations were categorized as extratemporal, temporal neocortical, mesiotemporal, hypothalamic, or callosal.

The dichotomized outcome score (DOS) indicated a favorable outcome (i.e., Engel classes I and II) or an unfavorable outcome (Engel classes III and IV).

MRI-Guided SLA Systems

Two Food and Drug Administration–cleared technologies were utilized by the participating centers: the Visualase system (Medtronic Inc.)[14] and the NeuroBlate system (Monteris Medical Corp.).[15,16] The operative techniques used with these systems have been described elsewhere.[6,13,14,17–20]

Statistical Analysis

Group comparisons were made using chi-square, Wilcoxon rank-sum, and t-tests. Multivariable logistic regression models for improvement in TST and for DOSs were determined using forward selection, with factors included at the 0.10 level. Note that all callosotomy cases were considered palliative and thus were not included in the univariable or multivariable analysis of treatment efficacy. Missing data groups were used to include cases with partial missing data in the multivariable analysis. All 225 cases were included in the analysis of complications. Patient characteristics were compared across complications (yes vs no) using a t-test for continuous variables and chi-square test for categorical variables.[13] The analysis was performed using SAS version 9.4 (SAS Institute). A $p < 0.05$ was considered statistically significant.

Results

Population Characteristics

A total of 225 patients (mean [± standard deviation] age 12.8 ± 5.8 years; 45.8% females, 54.2% males) were included in the study. All patients had a confirmed diagnosis of DRE. Treatment locations included extratemporal (44.4%), temporal neocortical (8.4%), mesiotemporal (23.1%), hypothalamic (14.2%), and callosal (9.8%). The various etiologies included malformation of cortical development (MCD), hypothalamic hamartoma (HH), mesial temporal sclerosis, brain tumor, cavernous malformation, cortical tuber, encephalomalacia, and other (includes nonlesional seizure foci identified via intracranial EEG [iEEG] or extracranial EEG [eEEG] or otherwise not specified; Supplemental Table 1). All tumors in this series were low-grade (WHO grade I or II) primary CNS tumors. In 3 cases, the tumors were biopsied in a separate procedure, 1 was a presumed diagnosis based on imaging findings, and the rest were biopsied in the same setting as the ablation procedure. Overall, a total of 59 (26.2%) patients had a history of pre-SLA cranial surgery, which was related to TOI in 51 (86.4%) cases. Invasive monitoring for localization of the seizure foci was not considered pre-SLA surgery. The TOI was identified via MRI in 94.7% of patients. iEEG monitoring was used for TOI identification and/or confirmation in 32% of patients. Target identification and/or confirmation was achieved via other diagnostic modalities (e.g., magnetoencephalography [MEG], eEEG) in 63.6% of patients. The mean hospital stay was 2.0 ± 1.9 days (median 1.0 day, range 1–11 days). More than 90% of patients were discharged within the first 4 days from surgery, with 50% of patients discharged on postoperative day (POD) 1 (Supplemental Table 1). Five (2.3%) patients were discharged after POD 10. One of these patients experienced motor deficits, which improved after inpatient rehabilitation. A second patient with a history of factor V Leiden developed venous thrombosis requiring treatment. A third medically complex patient developed endocrinopathy after treatment of an HH, requiring a prolonged inpatient stay. No details were available for the other 2 patients.

Procedural Characteristics

The mean number of SLA procedures for epilepsy per center was 12.7 ± 15.4 (range 1–63). The Visualase system[14] and NeuroBlate system[15,16] were used in 88.4% and 11.6% of cases, respectively. Framed-based targeting systems were more commonly utilized (64.9%), followed by robotic (23.6%) and frameless (11.6%) systems. Procedural goals included ablation (66.2%), disconnection (28.0%), or both (5.8%). The mean anesthesia time was 6.16 ± 1.7 hours. The mean number of laser trajectories used was 1.6 ± 0.7. The within-center number of trajectories ranged from 1 to 2 with a mean of 1.36 ± 0.37. The mean number of thermal lesions created was 3.6 ± 3.2 (Supplemental Table 1).

Follow-Up Time

The mean follow-up for the entire cohort was 27.0 ± 20.4 months (median 24.4 months, range 1.0–71.2 months). Excluding the palliative cases, the mean follow-up was 29.5 ± 19.9 months (median 28.4 months, range 3–71.2 months). All reported palliative cases involved callosotomies. For this subgroup, the mean follow-up was 12.2 ± 16.4 months (median 4.7 months, range 1–42.7 months).

Treatment Efficacy: Engel and ILAE Outcome Scales and DOSs

Engel classification data were reported for 167 (74.2%) patients. After excluding the palliative cases, Engel class data were available for 149 patients, 74 (49.7%) of whom had a class I outcome at the latest follow-up (Table 1). ILAE outcome scale data were reported for 89 (39.6%) patients. Excluding palliative cases, ILAE outcome data were available for 83 patients, 43 (51.8%) of whom had class 1 or 2 at the latest follow-up.

Excluding the palliative cases, the DOS was calculated for 149 (73.4%) patients, 109 (73.2%) of whom had a favorable outcome (Table 2). The within-center proportion of good outcomes ranged from 0 to 1 with a mean of 0.45 ± 0.35. In the palliative subgroup, data for calculation of the DOS were available for 18 of the 22 patients. Of these, 7 patients had a favorable outcome.

Multivariable analysis of significant periprocedural risk factors identified in the univariable analysis revealed that a history of pre-SLA cranial surgery, a greater number of laser trajectories (i.e., 2+ vs 1), the number of lesions created (1–3 vs 4+), and a reliance on the target identification mode of "other" were significant predictors of an unfavorable outcome. The patients with 2+ laser trajectories had 5.842 (OR 5.842, $p = 0.0021$) times higher odds of having an unfavorable outcome compared to the patients with only 1 laser trajectory, after adjusting for pre-SLA surgery. The patients with a history of pre-SLA surgery related to TOI had 4.102 (OR 4.102, $p = 0.0127$) times higher odds of having an unfavorable outcome compared to patients with no pre-SLA surgery, after adjusting for the number of laser trajectories. Patients treated with 4+ lesions per TOI had a lower risk of an unfavorable outcome (OR 0.076, $p = 0.0003$) than those treated with 1–3 lesions per TOI. Thus, patients treated with 1–3 lesions per TOI had a greater risk of having an unfavorable outcome (OR 13.1, $p = 0.0003$) than those treated with 4+ lesions per TOI. Finally, patients whose target identification was

TABLE 1. Postoperative seizure outcomes

Variable	≥3-Mo FU	≥12-Mo FU	≥24-Mo FU	≥36-Mo FU	≥48-Mo FU
Improved TST					
Yes	164/192 (85.4)	56/60 (93.3)	40/41 (97.6)	26/26 (100.0)	18/18 (100.0)
No	28/192 (14.6)	4/60 (6.7)	1/41 (2.4)	0/26 (0)	0/18 (0)
AED need					
Decreased	74/194 (38.1)	28/61 (45.9)	20/42 (47.6)	13/26 (50.0)	9/18 (50.0)
Stable/unchanged	106/194 (54.6)	27/61 (44.3)	19/42 (45.2)	12/26 (46.2)	9/18 (50.0)
Increased	14/194 (7.2)	6/61 (9.8)	3/42 (7.1)	1/26 (3.8)	0/18 (0)
Engel class					
I	74/149 (49.7)	25/49 (51.0)	17/36 (47.2)	11/25 (44.0)	8/19 (42.1)
II	35/149 (23.5)	18/49 (36.7)	14/36 (38.9)	11/25 (44.0)	9/19 (47.4)
III	10/149 (6.7)	3/49 (6.1)	3/36 (8.3)	3/25 (12.0)	2/19 (10.5)
IV	30/149 (20.1)	3/49 (6.1)	2/36 (5.6)	0/25 (0)	0/19 (0)
ILAE class					
1	31/83 (37.3)	15/43 (34.9)	10/33 (30.3)	8/24 (33.3)	5/19 (26.3)
2	12/83 (14.5)	10/43 (23.3)	9/33 (27.3)	7/24 (29.2)	7/19 (36.8)
3	24/83 (28.9)	13/43 (30.2)	10/33 (30.3)	7/24 (29.2)	5/19 (26.3)
4	7/83 (8.4)	3/43 (7.0)	3/33 (9.1)	2/24 (8.3)	2/19 (10.5)
5	7/83 (8.4)	1/43 (2.3)	1/33 (3.0)	0/24 (0)	0/19 (0)
6	2/83 (2.4)	1/43 (2.3)	0/33 (0)	0/24 (0)	0/19 (0)
Neuropsychological tests post-SLA					
Stable	27/44 (61.4)	9/11 (81.8)	6/6 (100)	2/2 (100)	0
Improved	16/44 (36.4)	2/11 (18.2)	0/6 (0)	0/2 (0)	0
Worsened	1/44 (2.3)	0/11 (0)	0/6 (0)	0/2 (0)	0

FU = follow-up.
For all categories, palliative callosotomy cases are excluded. Values are expressed as number/total (%).

achieved via other modality (e.g., MEG, eEEG, etc.) had a greater risk of an unfavorable outcome (OR 6.05, p = 0.0027; Tables 2 and 3).

Post hoc multivariable analysis of significant patient-specific risk factors identified in the univariable analysis revealed that a history of pre-SLA cranial surgery and a pathology of MCD were significant predictors of an unfavorable outcome (Table 2). The patients with a history of pre-SLA surgery related to the TOI had 7.416 (OR 7.416, p < 0.0001) times greater odds of an unfavorable outcome than the patients with no pre-SLA surgery, after adjusting for the pathology MCD. Patients with MCD had 2.591 (OR 2.591, p = 0.0247) times greater odds of an unfavorable outcome than those with other diagnoses, after controlling for a history of pre-SLA surgery.

Treatment Efficacy: Improvement in TST

Outcomes for the specific TST were reported for 213 (94.7%) patients. Of these, 179 (84.0%) patients reported improvement in the TST. Excluding the palliative cases, a total of 192 patients had outcome data for the TST. Of these, 164 (85.4%) patients reported improvement in TST (Tables 1 and 4). For patients with at least 12 months of follow-up, 56 (93.3%) reported improvement in the TST.

Group comparisons revealed significant effects for gender, MCD pathology, goal of procedure, number of trajectories, number of thermal lesions, size of the lesion, and history of pre-SLA cranial surgery (Table 4). Improvement in TST occurred with greater frequency in males (91/100 [91.0%]) than in females (73/92 [79.3%]). For patients with a pathology of MCD, 28.8% (19/66) had no improvement in TST, which was significantly more than for other etiologies.

Larger lesion sizes were associated with less or no improvement in the TST. In contrast, a greater number of lesions appeared to be associated with greater improvements in TST. Patients with a history of pre-SLA surgery were more likely to show less or no improvement in the TST (Tables 4 and 5).

After multivariable logistic regression analysis of significant risk factors identified in our univariable analysis, a pathology of MCD (OR 3.922, p = 0.0034) and a history of pre-SLA surgery related to TOI (OR 3.852, p = 0.0048) were the most significant predictors of no improvement in the TST. After controlling for pre-SLA surgery, a pathology of MCD, and gender, no other variables showed a significant effect (Tables 4 and 5).

In the palliative subgroup, data on TST were available for 21 of 22 patients, 15 (71.4%) of whom were reported to have improvement in TST.

Treatment Efficacy: AED Regimen

AED requirements were assessed by calculating the difference in the number of AEDs required prior to SLA treatment and at the latest follow-up. Excluding the pallia-

TABLE 2. DOSs and associated descriptive variables

Variable	Total	Unfavorable Outcome (Engel class III/IV)	Favorable Outcome (Engel class I/II)	p Value
No. of patients	149	40	109	
Age in yrs	12.8 ± 5.1	12.6 ± 5.1	12.9 ± 5.1	0.769*
Gender				0.145†
F	71 (47.7)	23 (57.5)	48 (44.0)	
M	78 (52.3)	17 (42.5)	61 (56.0)	
Target location				0.804†‡
Extratemporal	75 (50.3)	22 (55.0)	53 (48.6)	
Hypothalamic	26 (17.4)	5 (12.5)	21 (19.3)	
Mesiotemporal	33 (22.1)	9 (22.5)	24 (22.0)	
Temporal neocortical	15 (10.1)	4 (10.0)	11 (10.1)	
Pathology				**0.034†‡**
Primary brain tumor	14 (9.8)	1 (2.6)	13 (12.5)	
CM	3 (2.1)	1 (2.6)	2 (1.9)	
Cortical tuber	16 (11.2)	2 (5.1)	14 (13.5)	
Encephalomalacia§	1 (0.7)	0 (0.0)	1 (1.0)	
HH	26 (18.2)	5 (12.8)	21 (20.2)	
MCD	59 (41.3)	25 (64.1)	34 (32.7)	
MTS	13 (9.1)	4 (10.3)	9 (8.7)	
Other	11 (7.7)	1 (2.6)	10 (9.6)	
Missing data	6	1	5	
Pathology: mode of diagnosis				0.566†
Biopsy proven	32 (22.4)	10 (25.6)	22 (21.2)	
Presumed diagnosis	111 (77.6)	29 (74.4)	82 (78.8)	
Missing data	6	1	5	
MCD				**<0.001†**
No	90 (60.4)	15 (37.5)	75 (68.8)	
Yes	59 (39.6)	25 (62.5)	34 (31.2)	
Target ID via MRI				>0.99†‡
No	10 (6.7)	3 (7.5)	7 (6.4)	
Yes	139 (93.3)	37 (92.5)	102 (93.6)	
Target ID via iEEG				0.313†
No	99 (66.4)	24 (60.0)	75 (68.8)	
Yes	50 (33.6)	16 (40.0)	34 (31.2)	
Target ID via other modality				**0.019†**
No	44 (29.5)	6 (15.0)	38 (34.9)	
Yes	105 (70.5)	34 (85.0)	71 (65.1)	
Goal of procedure				**0.020†‡**
Ablation	101 (67.8)	34 (85.0)	67 (61.5)	
Both	8 (5.4)	1 (2.5)	7 (6.4)	
Disconnection	40 (26.8)	5 (12.5)	35 (32.1)	
Ablation				**0.017†**
No	40 (26.8)	5 (12.5)	35 (32.1)	
Yes	109 (73.2)	35 (87.5)	74 (67.9)	
Disconnection				**0.006†**
No	101 (67.8)	34 (85.0)	67 (61.5)	
Yes	48 (32.2)	6 (15.0)	42 (38.5)	

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TABLE 2. DOSs and associated descriptive variables

Variable	Total	Unfavorable Outcome (Engel class III/IV)	Favorable Outcome (Engel class I/II)	p Value
No. of trajectories				**0.020¶**
Median	1.0 (1.0–2.0)	2.0 (1.0–2.0)	1.0 (1.0–2.0)	
Mean	1.5 ± 0.7	1.7 ± 0.8	1.5 ± 0.7	
Trajectory: 1 vs 2+				**0.011†**
1	82 (55.8)	15 (38.5)	67 (62.0)	
2+	65 (44.2)	24 (61.5)	41 (38.0)	
Missing data	2	1	1	
Trajectory no.				**0.032†‡**
1	82 (55.8)	15 (38.5)	67 (62.0)	
2	54 (36.7)	21 (53.8)	33 (30.6)	
3	7 (4.8)	1 (2.6)	6 (5.6)	
4	4 (2.7)	2 (5.1)	2 (1.9)	
Missing data	2	1	1	
No. of lesions				0.091¶
Median	2.0 (1.0–5.0)	2.0 (1.0–3.0)	2.0 (1.0–6.0)	
Mean	3.6 ± 3.5	2.5 ± 2.6	4.0 ± 3.7	
Lesion no.				0.169†
1	63 (43.8)	18 (47.4)	45 (42.5)	
2	23 (16.0)	10 (26.3)	13 (12.3)	
3	11 (7.6)	5 (13.2)	6 (5.7)	
4	8 (5.6)	1 (2.6)	7 (6.6)	
5	4 (2.8)	0 (0.0)	4 (3.8)	
6	7 (4.9)	1 (2.6)	6 (5.7)	
7	2 (1.4)	0 (0.0)	2 (1.9)	
8	4 (2.8)	0 (0.0)	4 (3.8)	
9	3 (2.1)	0 (0.0)	3 (2.8)	
10	2 (1.4)	1 (2.6)	1 (0.9)	
11	17 (11.8)	2 (5.3)	15 (14.2)	
Missing data	5	2	3	
Lesion vol in cm^3				0.072*
Mean	10.0 ± 12.7	13.3 ± 15.7	8.6 ± 11.0	
Median	5.8 (2.9–12.8)	7.8 (4.2–14.4)	5.6 (2.3–11.3)	
Pre-SLA surgery				**<0.001†‡**
None	113 (75.8)	18 (45.0)	95 (87.2)	
Not related to TOI	6 (4.0)	3 (7.5)	3 (2.8)	
Related to TOI	30 (20.1)	19 (47.5)	11 (10.1)	
FU in mos				0.432*
Mean	29.1 ± 22.0	24.0 ± 19.1	29.9 ± 22.5	
Median	28.4 (8.8–48.7)	20.7 (5.1–40.1)	29.4 (8.8–52.8)	

CM = cavernous malformation; ID = identification; MTS = mesial temporal sclerosis.
Values are expressed as mean ± standard deviation, number (%), or median (Q1–Q3), unless indicated otherwise. Boldface type indicates statistical significance.
* t-test.
† Chi-square test.
‡ Exact test.
§ For example, poststroke or posttrauma.
¶ Wilcoxon rank-sum test.

TABLE 3. Multiple logistic regression: DOS indicating an unfavorable outcome

Variable	OR	95% Wald Confidence Limits	p Value
Pre-SLA surgery unrelated to TOI vs none	5.872	0.809–42.642	0.0801
Pre-SLA surgery related to TOI vs none	4.102*	1.352–12.447	**0.0127**
Trajectories 2+ vs 1	5.842†	1.901–17.954	**0.0021**
Lesions 1–3 vs 4+	13.1	0.019–0.308	**0.0003**
Target ID w/ other modality: yes vs no	6.054	1.866–19.644	**0.0027**

An unfavorable outcome is Engel class III or IV. Analysis excludes palliative cases.
* After adjusting for the number of laser trajectories.
† After adjusting for pre-SLA surgery.

tive cases, data on pre-SLA and post-SLA AED requirements were available for 194 (95.6%) patients. The mean numbers of AEDs per patient pre- and post-SLA were 5.3 ± 1.6 and 3 ± 4.2, respectively. AED requirements decreased, remained unchanged, and increased in 38.1%, 54.6%, and 7.2% patients, respectively (Table 1).

For the palliative subgroup, data on pre-SLA and post-SLA AED requirements were available for 21 (95.5%) patients. The mean numbers of AEDs per patient pre- and post-SLA were 2.5 ± 0.71 and 3 ± 1.4, respectively. AED requirements decreased, remained unchanged, and increased in 28.6%, 71.4%, and 0% patients, respectively.

Treatment Efficacy: Subsequent Surgery

After excluding palliative cases, data on surgery after SLA were available for 193 patients. Post-SLA cranial surgery was reported for 20% of patients. These included iEEG monitoring (3 cases), lesionectomies (9), unspecified surgery for epilepsy (26), and surgery for tumor debulking/resection (1). In the palliative subgroup, 2 (9.1%) patients required post-SLA surgery.

Neuropsychological Outcomes

Data on neuropsychological testing pre- and post-SLA were available for 44 (19.6%) patients, all of whom had at least 6 months of follow-up. Neuropsychological testing was reported as stable, improved, or worsened in 61.4%, 36.4%, and 2.3% of patients, respectively (Table 1).

Complications

Data regarding short-term or acute complications occurring within 30 days from surgery were available for all 225 patients. A total of 51 short-term complications in 30 (13.3%) patients were reported (Table 6). The permanent neurological deficits reported included visual and memory deficits from 2 mesiotemporal TOIs and a motor deficit from treatment of a large/complex hypothalamic TOI.

Frameless targeting systems were used in the 3 cases of reported malpositioned catheters. One of the malpositioned catheters, used for a mesiotemporal target, required replacement. The other 2 cases of malpositioned catheters, used for complex/large hypothalamic lesions, were deemed unusable for ablation but were not replaced; instead, a second preplanned trajectory was used in each of these cases. Thus, the lesions created were reported as smaller than planned. One of these cases required subsequent surgery with repeat SLA.

Excluding the palliative cases, the hypothalamic target location appeared to have a higher relative incidence of complications than the other locations (28% patients, p = 0.029); however, the difference did not reach statistical significance when considering the entire population. Age, gender, history of pre-SLA surgery, pre-SLA target volume, number of laser trajectories, number or size of thermal lesion(s) created, or use of perioperative steroids did not appear to have a significant effect on the incidence of short-term complications (Table 7).

Only 1 patient was reported to experience worsened neuropsychological testing results with persistent memory deficits at 6 months (Table 1). In this case, the patient was treated for a mesial temporal lobe lesion with a presumed diagnosis of a low-grade glial tumor.

Discussion

There is a scarcity of large-volume studies evaluating outcomes of SLA for the treatment of DRE in children. Most data on the use of SLA for epilepsy involve heterogeneous adult populations.[1–4] Currently available pediatric-specific data on SLA in epilepsy are limited by small case volumes, limited follow-up times, and/or narrow epilepsy types and target localizations.[5–10] The present study represents the largest series evaluating the outcomes of SLA for pediatric DRE with a variety of epilepsy types and target localizations. As primary goals of this study, we sought to evaluate 1) current utilization of this technology in North America and 2) its safety and efficacy in this population.

We identified 225 pediatric patients with a variety of epilepsy etiologies and target localizations. Improvement in the TST was reported for 179/213 (84%) patients. Overall, an Engel class I outcome was attained in 74/149 (49.7%) patients with a follow-up ≥ 3 months and 25/49 (51%) patients with a follow-up ≥ 12 months. Seizure freedom or near seizure freedom (Engel class I/II, favorable outcome) was attained by 43 (87.7%), 31 (86.1%), 22 (88.0%), and 17 (89.5%) patients at follow-ups ≥ 12, 24, 36, and 48 months, respectively. Regarding pathology-specific outcomes, an Engel class I outcome was attained in 23 (39.0%) patients with MCD, 18 (69.2%) patients with HH, 7 (53.8%) patients with MTS, 9 (64.3%) patients with brain tumors, 2 (66.6%) patients with cavernomas, 5 (31.3%) patients with cortical tubers, and 6 (54.5%) patients with nonlesional epileptic foci. Except for the HH subgroup, which had lower rates of seizure freedom compared to rates in other series,[7] our

TABLE 4. Improvement in TST and associated descriptive variables

Variable	Total	No Improvement	Improvement	p Value
No. of patients	192	28	164	
Age in yrs	12.8 ± 5.3	11.8 ± 5.3	13.0 ± 5.3	0.291*
Gender				**0.022†**
F	92 (47.9)	19 (67.9)	73 (44.5)	
M	100 (52.1)	9 (32.1)	91 (55.5)	
Target location				0.320†
Extratemporal	95 (49.5)	18 (64.3)	77 (47.0)	
Hypothalamic	32 (16.7)	2 (7.1)	30 (18.3)	
Mesiotemporal	49 (25.5)	6 (21.4)	43 (26.2)	
Temporal neocortical	16 (8.3)	2 (7.1)	14 (8.5)	
Pathology				**0.045†**
Primary brain tumor	15 (8.5)	2 (7.1)	13 (8.7)	
CM	6 (3.4)	1 (3.6)	5 (3.4)	
Cortical tuber	21 (11.9)	2 (7.1)	19 (12.8)	
Encephalomalacia‡	2 (1.1)	0 (0.0)	2 (1.3)	
HH	32 (18.1)	2 (7.1)	30 (20.1)	
MCD	66 (37.3)	19 (67.9)	47 (31.5)	
MTS	22 (12.4)	1 (3.6)	21 (14.1)	
Other§	13 (7.3)	1 (3.6)	12 (8.1)	
Missing data	15	0	15	
Pathology: mode of diagnosis				0.095†
Biopsy proven	36 (20.5)	9 (32.1)	27 (18.2)	
Presumed diagnosis	140 (79.5)	19 (67.9)	121 (81.8)	
Missing data	16	0	16	
Pathology of MCD				**<0.001†**
No	126 (65.6)	9 (32.1)	117 (71.3)	
Yes	66 (34.4)	19 (67.9)	47 (28.7)	
Target ID via MRI				0.595†
No	11 (5.7)	1 (3.6)	10 (6.1)	
Yes	181 (94.3)	27 (96.4)	154 (93.9)	
Target ID via iEEG				0.373†
No	124 (64.6)	16 (57.1)	108 (65.9)	
Yes	68 (35.4)	12 (42.9)	56 (34.1)	
Target ID via other modality				0.133†
No	65 (33.9)	6 (21.4)	59 (36.0)	
Yes	127 (66.1)	22 (78.6)	105 (64.0)	
Goal of procedure				**0.026†**
Ablation	138 (71.9)	26 (92.9)	112 (68.3)	
Both	12 (6.3)	0 (0.0)	12 (7.3)	
Disconnection	42 (21.9)	2 (7.1)	40 (24.4)	
No. of trajectories				**0.040¶**
Median	1.0 (1.0–2.0)	2.0 (1.0–2.0)	1.0 (1.0–2.0)	
Mean	1.5 ± 0.7	1.7 ± 0.6	1.5 ± 0.7	
Trajectory: 1 vs 2+				**0.019†**
1	109 (57.7)	10 (37.0)	99 (61.1)	
2+	80 (42.3)	17 (63.0)	63 (38.9)	
Missing data	3	1	2	

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TABLE 4. Improvement in TST and associated descriptive variables

Variable	Total	No Improvement	Improvement	p Value
No. of trajectories				0.057†
1	109 (57.7)	10 (37.0)	99 (61.1)	
2	65 (34.4)	15 (55.6)	50 (30.9)	
3	10 (5.3)	2 (7.4)	8 (4.9)	
4	5 (2.6)	0 (0.0)	5 (3.1)	
Missing data	3	1	2	
No. of lesions				**0.024¶**
Mean	3.5 ± 3.2	2.2 ± 2.0	3.8 ± 3.4	
Median	2.0 (1.0–5.0)	2.0 (1.0–2.0)	2.0 (1.0–5.0)	
Lesion no.				0.196†
1	68 (36.8)	12 (46.2)	56 (35.2)	
2	36 (19.5)	9 (34.6)	27 (17.0)	
3	17 (9.2)	2 (7.7)	15 (9.4)	
4	17 (9.2)	1 (3.8)	16 (10.1)	
5	8 (4.3)	0 (0.0)	8 (5.0)	
6	8 (4.3)	1 (3.8)	7 (4.4)	
7	3 (1.6)	0 (0.0)	3 (1.9)	
8	5 (2.7)	0 (0.0)	5 (3.1)	
9	2 (1.1)	0 (0.0)	2 (1.3)	
10	2 (1.1)	1 (3.8)	1 (0.6)	
11	19 (10.3)	0 (0.0)	19 (11.9)	
Missing data	7	2	5	
Lesion vol in cm^3				**0.007***
Mean	9.7 ± 11.4	15.2 ± 16.9	8.6 ± 9.7	
Median	6.0 (3.2–12.8)	9.7 (5.0–17.3)	5.8 (2.9–11.6)	
Pre-SLA surgery				**<0.001†**
None	144 (75.0)	12 (42.9)	132 (80.5)	
Not related to TOI	7 (3.6)	2 (7.1)	5 (3.0)	
Related to TOI	41 (21.4)	14 (50.0)	27 (16.5)	
FU in mos				0.339*
Mean	27.3 ± 20.6	18.7 ± 9.6	27.8 ± 21.0	
Median	23.3 (9.2–40.6)	15.2 (13.1–22.3)	25.9 (8.8–42.7)	

Analysis excludes palliative cases. Boldface type indicates statistical significance.
* t-test.
† Chi-square test.
‡ For example, poststroke or posttrauma.
§ "Other" includes nonlesional seizure foci identified via iEEG or otherwise not specified.
¶ Wilcoxon rank-sum test.

study results are consistent with the available literature on SLA for DRE.

Fayed et al. reported seizure freedom (Engel class I) in 66.7% patients and "either seizure freedom or worthwhile improvement (Engel I/II) in 83.3% of patients" from a mixed cohort of 12 patients.[19] Curry et al. reported a case series of 71 pediatric patients with gelastic seizures secondary to HH treated with SLA in which 93% of patients were free of gelastic seizures at the 1-year follow-up.[7] Perry et al. reported a series of 20 patients who had undergone a total of 24 LITT procedures for intractable insular epilepsy, 50% of whom attained an Engel class I outcome with a mean follow-up of 20 months.[8] Hale et al. described a pediatric series of 26 patients with medically refractory insular/opercular epilepsy, 14 of whom were treated via LITT and 12 of whom underwent open resection.[9] In that series, 43% of patients treated with LITT attained an Engel class I outcome compared to 50% of patients in the open insular resection group.

In our study, gender appeared to have an effect on the reported improvement of TST; however, this association did not reach statistical significance in the multivariable analysis (Tables 4 and 5), and no such difference was seen when comparing DOSs (Table 2). Patients with a history of pre-

TABLE 5. Multiple logistic regression: improvement in TST

Variable	OR	95% Wald Confidence Limit	p Value
Gender: F vs M	2.283	0.911–5.722	0.0783
MCD pathology: yes vs no	3.922	1.572–9.786	**0.0034**
Lesion size (per unit size difference)	0.948	0.841–1.069	0.3929
Pre-SLA surgery (unrelated to TOI vs none)	3.647	0.544–24.475	0.1828
Pre-SLA surgery (related to TOI vs none)	3.852	1.508–9.842	**0.0048**

Boldface type indicates statistical significance.

SLA surgery related to TOI were more likely to experience no improvement in their TST (Tables 4 and 5) and to have an unfavorable outcome (i.e., Engel class III/IV; Tables 2 and 3). Similarly, patients whose reported pathology was MCD were more likely to experience no improvement in their TST and to have an unfavorable outcome (Tables 2, 4, and 5). In the subgroup of patients with MCD, 23 (39.0%) patients had an Engel class I outcome, 11 (18.6%) had class II, 2 (3.4%) had class III, and 23 (39%) had class IV. These results appear to be in line with those of Lewis et al.,[10] who reported outcomes for a cohort of 17 pediatric patients with heterogeneous surgical substrates, 11 of whom were positive for focal cortical dysplasia. In their series, the Engel outcome was class I in 7 (41%) patients, II in 1 (6%), III in 3 (18%), and IV in 6 (35%). These authors noted a predominance of prior cranial surgery for resection in the patients with Engel class III/IV outcomes; however, they found no statistically significant association, likely because the study was underpowered.[10] Landazuri et al. recently published the 1-year outcomes for a prospective multicenter study (Laser Ablation of Abnormal Neurological Tissue Using Robotic NeuroBlate System [LAANTERN]).[3] In that study, 31 (73.8%) patients were "considered responders (Engel I/II)," and prior cranial surgery (specifically anterior temporal lobectomy) was found to be a negative predictor.

The number of laser trajectories was a significant predictor of outcomes regarding seizure control. Patients with a TOI requiring 2+ laser trajectories were more likely to experience an unfavorable outcome (Tables 2 and 3). Although not significant in the multivariable analysis, larger thermal lesions were associated with an increased risk of no improvement in the TST. This finding suggests that larger targets may be more refractory to treatment. In contrast, a greater number of thermal lesions appeared to be associated with greater improvements in seizure control. These results suggest that aiming for a greater number of smaller lesions for coverage of the ablation or disconnection target may in turn help to improve seizure control, perhaps by more accurately conforming the lesion(s) created to the target as opposed to creating one large lesion that is less conforming.

Overall, 30 (13.3%) patients in this series experienced 51 short-term complications (Tables 6 and 7). Consistent with the literature, the complication rates in our study are lower than those reported for open epilepsy surgery, particularly in cases with temporal lobe epilepsy and HH.[7,21–23]

The rate of adverse events in our series is comparable to rates in adult SLA series[3] and lower than rates reported in several pediatric SLA series.[7,8,10,13] In our series of SLA-treated pediatric brain tumors, 23 (26.7%) patients experienced short-term complications.[13] Lewis et al. reported a 23.5% adverse event rate in their series of 17 pediatric patients.[10] Perry et al. reported adverse events in 7 (35%) patients.[8] Curry et al. reported adverse events in 18 (25%) patients with HH treated using SLA.[7] These results appear comparable to those in our series for the hypothalamic target location, which had a higher relative incidence of complications than the other locations (28% patients, p = 0.029) after excluding the palliative callosotomy cases.

We found no significant predictors for the incidence of complications. This contrasts with findings in our previ-

TABLE 6. Incidence of short-term complications by TOI location

Complication	All Locations (n = 30)	Extratemporal (n = 13)	Temporal Neocortical (n = 2)	Mesiotemporal (n = 3)	Callosal (n = 3)	Hypothalamic (n = 9)
Unplanned ICU stay	5	3	—	—	2	—
Unplanned 30-day readmission	9	4	—	3	1	1
Malposition of laser catheter	3	—	—	1	—	2
Symptomatic perilesional edema	6	1	—	—	—	5
ICH	2	1	—	—	1	—
Transient neurological deficit	19	9	3	2	2	3
Permanent neurological deficit	3	—	—	2		1
CSF leakage	1	—	—	—	1	—
Hydrocephalus	1	1	—	—	—	—
Wound infection	2	1	—	—	1	—
Total	51	20	3	8	8	12

ICH = intracranial hemorrhage; n = number of patients.
A total of 51 acute/short-term complications were reported in 30 of 225 patients. Short-term complications are acute complications occurring within 30 days from surgery.

TABLE 7. Short-term complications and associated descriptive variables

Variable	Total	No Complication	Complication	p Value
No. of patients	225	195	30	
Age in yrs	12.8 ± 5.8	12.8 ± 6.0	13.3 ± 4.5	0.679*
Missing data	44	42	2	
Gender				0.495†
F	103 (45.8)	91 (46.7)	12 (40.0)	
M	122 (54.2)	104 (53.3)	18 (60.0)	
Pre-SLA surgery				0.692†‡
None	166 (73.8)	142 (72.8)	24 (80.0)	
Not related to TOI	8 (3.6)	7 (3.6)	1 (3.3)	
Related to TOI	51 (22.7)	46 (23.6)	5 (16.7)	
Target location				0.063†‡
Corpus callosum	22 (9.8)	19 (9.7)	3 (10.0)	
Extratemporal	100 (44.4)	87 (44.6)	13 (43.3)	
Hypothalamic	32 (14.2)	23 (11.8)	9 (30.0)	
Mesiotemporal	52 (23.1)	49 (25.1)	3 (10.0)	
Temporal neocortical	19 (8.4)	17 (8.7)	2 (6.7)	
Pathology				0.167†‡
Primary brain tumor	17 (8.4)	14 (8.0)	3 (10.3)	
CM	12 (5.9)	11 (6.3)	1 (3.4)	
Cortical tuber	22 (10.8)	21 (12.1)	1 (3.4)	
Encephalomalacia§	3 (1.5)	3 (1.7)	0 (0.0)	
HH	32 (15.8)	23 (13.2)	9 (31.0)	
MCD	79 (38.9)	71 (40.8)	8 (27.6)	
MTS	22 (10.8)	19 (10.9)	3 (10.3)	
Other	16 (7.9)	12 (6.9)	4 (13.8)	
Missing data	22	21	1	
Pathology: mode of diagnosis				0.228†
Biopsy proven	39 (19.4)	31 (18.0)	8 (27.6)	
Presumed diagnosis	162 (80.6)	141 (82.0)	21 (72.4)	
Missing data	24	23	1	
Goal of procedure				0.402†‡
Ablation	149 (66.2)	128 (65.6)	21 (70.0)	
Both	13 (5.8)	10 (5.1)	3 (10.0)	
Disconnection	63 (28.0)	57 (29.2)	6 (20.0)	
No. of trajectories				0.282‡¶
Median	1.0 (1.0–2.0)	1.0 (1.0–2.0)	1.0 (1.0–2.0)	
Mean	1.6 ± 0.7	1.6 ± 0.7	1.4 ± 0.6	
Missing data	13	10	3	
Trajectory no.				
1	121 (57.1)	103 (55.7)	18 (66.7)	
2	70 (33.0)	63 (34.1)	7 (25.9)	
3	16 (7.5)	14 (7.6)	2 (7.4)	
4	5 (2.4)	5 (2.7)	0 (0.0)	
Missing data	13	10	3	
No. of lesions				0.095‡¶
Median	2.0 (1.0–5.0)	2.0 (1.0–5.0)	2.0 (1.0–3.0)	
Mean	3.6 ± 3.2	3.8 ± 3.4	2.2 ± 1.4	
Missing data	20	17	3	

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TABLE 7. Short-term complications and associated descriptive variables

Variable	Total	No Complication	Complication	p Value
Lesion no.				
1	74 (36.1)	63 (35.4)	11 (40.7)	
2	38 (18.5)	32 (18.0)	6 (22.2)	
3	20 (9.8)	14 (7.9)	6 (22.2)	
4	19 (9.3)	17 (9.6)	2 (7.4)	
5	10 (4.9)	9 (5.1)	1 (3.7)	
6	9 (4.4)	8 (4.5)	1 (3.7)	
7	3 (1.5)	3 (1.7)	0 (0.0)	
8	6 (2.9)	6 (3.4)	0 (0.0)	
9	3 (1.5)	3 (1.7)	0 (0.0)	
10	2 (1.0)	2 (1.1)	0 (0.0)	
11	21 (10.2)	21 (11.8)	0 (0.0)	
Missing data	20	17	3	
Size of lesion in cm^3				0.148‡¶
Median	5.9 (3.0–12.2)	6.1 (3.1–12.8)	4.3 (1.6–10.3)	
Mean	10.5 ± 20.2	10.8 ± 21.0	8.7 ± 14.9	
Missing data	42	38	4	
Steroid use before day of surgery				0.159†‡
No	191 (85.7)	168 (87.0)	23 (76.7)	
Yes	32 (14.3)	25 (13.0)	7 (23.3)	
Missing data	2	2	0	
Steroid use day of surgery				>0.99†‡
No	5 (2.2)	4 (2.1)	1 (3.3)	
Yes	218 (97.8)	189 (97.9)	29 (96.7)	
Missing data	2	2	0	
Planned postop steroid use				0.746†‡
No	22 (9.9)	20 (10.4)	2 (6.7)	
Yes	201 (90.1)	173 (89.6)	28 (93.3)	
Missing data	2	2	0	

Values are expressed as mean ± standard deviation, number (%), or median (Q1–Q3), unless indicated otherwise.
* t-test.
† Chi-square test.
‡ Exact test.
§ For example, poststroke or posttrauma.
¶ Wilcoxon rank-sum test.

ously published series of SLA-treated pediatric brain tumors,[13] in which "the odds of complications increased by 14% (OR 1.14, p = 0.0159) with every 1-cm^3 increase in the volume of the [thermal] lesion created." As we noted in our previous series,[13] the number of neurological deficits reported in the current study (19 transient, 3 permanent) far exceeded the number of intracranial hemorrhages (2 symptomatic, 0 asymptomatic) or the number of confirmed instances of symptomatic perilesional edema (6 cases). On the basis of these findings, one may deduce that these deficits are likely secondary to the proximity of eloquent brain to the thermal lesion(s) created, associated edema, and/or direct damage.[13] This highlights the importance of operator experience in the evaluation of damage estimates and the placement of temperature monitors on adjacent eloquent tissue. In this study, the average number of SLA procedures for epilepsy was 13 per center (range 1–63) and included each center's early experience in the use of this technology. We expect that the complication rates for SLA will go down as the neurosurgical community gains more experience with this technology and the indications for patient selection.

Finally, the mean length of stay was 2.0 ± 1.9 days, with 50% patients discharged on POD 1. These results are consistent with reports from other groups.[3,7,8,24] However, the 30-day readmission rate in our series (4%) was considerably lower than the 30-day readmission rate (11.5%) following open epilepsy surgery recently reported by Rumalla et al.[23] This is an important point since shorter hospital stays and reduced complication rates with lower readmis-

sion rates may decrease perioperative medical costs. Taken together with the traditional benefits of minimally invasive surgical approaches (e.g., decreased blood loss, less scarring, and less postoperative pain), this makes SLA a desirable treatment option for pediatric patients with DRE.

This retrospective study has several limitations. To start, a comparison with traditional therapies was not possible given the absence of a control population. Data on patient comorbidities were not readily available to allow analysis of preoperative risk factors. Our data collection had insufficient granularity to evaluate the associated risk of target proximity to eloquent brain or to draw conclusions concerning optimal thermal dosing regimens (i.e., units of thermal energy needed per target tissue volume, ablation times, etc.). There is significant variability in the number of cases per center; however, the effect of center volumes on seizure outcomes or complications was not addressed in this study. Furthermore, with less than half of the patients having more than 12 months of follow-up, it is difficult to draw conclusions on long-term efficacy.

Conclusions

This study represents the largest series on SLA outcome data in pediatric epilepsy patients and highlights the efficacy and low morbidity of this treatment option. Seizure freedom was achieved in 50% of patients, and more than 86% of patients experienced either seizure freedom or near seizure freedom (Engel class I/II) at the 1-year follow-up and beyond.

Larger thermal lesions were associated with increased risks of no improvement in the TST, likely a reflection of the difficulty in completely ablating large and/or irregularly shaped targets. A greater number of smaller lesions for coverage of the ablation or disconnection target may help to improve seizure outcomes.

Furthermore, a history of pre-SLA surgery related to TOI, a pathology of MCD, and targets requiring 2+ laser trajectories for coverage may constitute negative predictors for attaining seizure freedom. Still, even in the presence of these risk factors, most patients in this cohort, including palliative cases, experienced a significant improvement in seizure control.

SLA appears to be an effective and well-tolerated treatment option for children with DRE. Large-volume prospective studies are needed to better understand the indications for treatment and demonstrate the long-term efficacy of SLA in this population. Future efforts will focus on developing and validating scoring systems based on predicted outcome probabilities and evaluating the effects of institutional case volumes and learning curves on general patient outcomes and complication profiles.

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Dedication

This article is dedicated to one of our contributors, Dr. Sanjiv Bhatia. He is dearly missed.

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Disclosures

Dr. Tovar-Spinoza is a consultant for Monteris. Dr. Smyth is a consultant for and receives personal fees from Monteris, outside the submitted work. Dr. Perry receives personal fees from Zogenix, Stroke Therapeutics, Greenwich Biosciences, Biomarin, Marinus, Taysha, Neurelis, NobelPharma, Eisai, and Bright Minds, outside the submitted work. Dr. Barnett receives personal fees from Monteris Medical outside the submitted work. Dr. Muh receives personal fees from Livanova LLC during the conduct of this study and has a patent for a ventriculoperitoneal shunt. Dr. Thompson is a paid scientific advisor for Oncoheroes Biosciences outside the submitted work.

Author Contributions

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Supplemental Information

Online-Only Content

Supplemental material is available with the online version of the article.

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