MRI-Guided Interstitial Laser Ablation for Intracranial Lesions: A Large Single-Institution Experience of 133 Cases

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Keywords

Laser ablation · Laser interstitial thermal therapy · Intracranial lesions · Survival · MRI · Brain tumors

Abstract

Background: Managing difficult-to-access lesions or surgically accessible lesions in fragile patients is a central problem in neurosurgery. MRI-guided interstitial laser ablation (ILA) is a minimally invasive option that may provide a safe means of treating these challenging patients. **Objective:** We aim to (1) evaluate safety, efficacy, and preliminary outcomes with a diverse and large series of ILA treatments; and (2) report technical details and operative trends that proved useful over time in the authors' experience and that may be of use to neurosurgeons who perform ILA. **Methods:** A retrospective evaluation of ILA patients was performed in terms of demographics, surgical techniques, and clinical outcomes. **Results:** A total of 133 intracranial lesions in 120 patients were treated with ILA, including glioblastomas (GBM), other gliomas,

metastases, epilepsy foci, and radionecrosis. The rate of complications/unexpected readmission was 6.0%, and the mortality rate was 2.2%. With high-grade tumors, tumor volumes >3 cm in diameter trended toward a higher rate of complication ($p = 0.056$). Median progression-free survival (PFS) and overall survival (OS) for recurrent GBM were 7.4 and 11.6 months, respectively. As a frontline treatment for newly diagnosed GBM, median PFS and OS were 5.9 and 11.4 months, respectively. For metastases, median PFS was not yet reached, and OS was 17.2 months. **Conclusion:** Our series suggests that ILA is a safe and efficacious treatment for a variety of intracranial pathologies, can be tailored to treat difficult-to-access lesions, and may offer a novel alternative to open craniotomy in properly selected patients.

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Published by S. Karger AG, Basel

Portions of this work were presented in slideshow form at the Southern Neurosurgical Society Annual Meeting, Orlando, FL, USA, on February 23, 2017.

Introduction

Interstitial laser ablation (ILA) has been utilized in the treatment of solid tumors in various organ systems [1, 2]. In recent years, ILA has been brought to the field of neurosurgery [3–6, 10]. The technology uses a magnetic resonance imaging (MRI)-compatible optical fiber that transmits the light through a sapphire tip, which is inserted via stereotactic guidance into the centroid of a brain lesion. The laser then produces a focused thermal

injury by heating the surrounding tissue. This is performed with real-time MRI thermometry, which allows for monitoring and cessation of ablation in a controlled fashion. ILA therefore provides a promising alternative to open surgery and may also afford opportunities as a treatment modality to patients who are not optimal candidates for traditional craniotomy. Previous case series of ILA have been limited by small sample sizes and short follow-up, largely due to the relatively recent introduction of thermoablative techniques in neurosurgery. Our institu-

Fig. 1. Exemplar case of patient with a large left frontal glioblastoma who was a candidate for interstitial laser ablation. **a** Preoperative MRI of the left frontal tumor. Scalp fiducials and artifact from a recent needle biopsy are visible. **b** Postlaser interstitial thermal therapy day 1 MRI shows slight expansion of the tumor mass

and surrounding edema. **c** 6-month postoperative MRI shows resolution of edema and isointense postablation changes without residual contrast enhancement seen (the ventricular enlargement was felt to represent ex vacuo changes from chemoradiation, as the patient had no clinical signs of hydrocephalus).

Fig. 2. Exemplar case of patient with right insular thalamic glioma who was a candidate for interstitial laser ablation. T2 sequence demonstrates the tumor. Various functional sites are identified with resting-state functional magnetic resonance imaging (rs-fMRI) and diffusion tensor imaging (DTI), including speech network, somatomotor network, corticospinal tract, and arcuate fasciculus. **a** Axial view. **b** Coronal view.

tion previously reported a series of 17 patients treated with MRI-guided ILA [3]. In this work, we now report on our cohort of 133 intracranial lesions treated with MRI-guided ILA during 2010–2016 at Washington University in St. Louis. We found that generally the procedure was well tolerated, efficacious for multiple oncologic and epilepsy indications, and associated with a short hospital stay. The experience of using ILA in over 100 patients has also provided clinical and technical insights into its application that may benefit the wider patient population.

Methods

Study Design and Data Collection

Institutional review board approval was obtained for retrospective human subjects research (IRB ID: 201609152). A retrospective database of ILA patients was maintained including patient demographics, age, sex, indication, and lesion type/location/dimensions, as well as operative data including date, number of trajectories used, and operative time. Postoperative complications and readmissions within 30 days were also recorded via chart review. The database was updated with follow-up information including survival and progression-free time for tumor pa-

Fig. 3. **a** Thalamic lesion, showing a common interstitial laser ablation (ILA) trajectory to the thalamus. The approach involved a mid- to high-parietal cortical entry posterior to the sensory cortex. There tended to be a narrow (1–1.5 cm) region between the anterior portion of trigone of the lateral ventricle and the high posterior aspect of the insula. This entry zone is called the ventricular-insular corridor, which afforded the best access to the thalamus while avoiding the corticospinal tract. Left, axial view; right, coronal view. **b** Insular lesion, showing a common ILA trajectory to the insula. The insula has an oval-discoid (i.e., a “flattened football”) shape that is angled downward from posterior to anterior in the sagittal plane and leans medial to lateral in the coronal plane. To

best access the entirety of the insula (if required), a trajectory with a high medial parietal entry, posterior to the sensory cortex, in the plane between the putamen medially and the insula laterally was used. This corridor we putatively term the putaminal-insular corridor. Left, side view; right, coronal view. **c**, **d** Common ILA trajectories to the corpus callosum. **c** Unilateral corpus callosum lesion. **d** Bilateral corpus callosum lesion. There were several considerations, depending on the location of the lesion in the corpus callosum and whether the lesion was unilateral or bilateral. If the lesion was more unilateral in nature a higher frontal or parietal trajectory was taken (**c**). If more bilateral in distribution, a lower trajectory was taken to more fully cross the corpus callosum (**d**).

Fig. 4. Stereotactic frames used for supratentorial targets. **a** The Monteris® Mini-Bolt which has a lower profile (142 mm with fiber driver) but is limited to a single trajectory. **b** The Monteris Axiis® frame which has a higher profile (197 mm with fiber driver), but is more versatile for multiple trajectories (images courtesy of Monteris Medical Corporation).

tients, and Engel class for epilepsy patients. Patients in whom the procedure was cancelled or aborted due to issues unrelated to the procedure itself were excluded. Data from the Monteris® workstation were used for the volumetric analysis of tumors. After slice-by-slice reconstruction, the slices were interpolated to build a 3D model of the target lesion. The lesion volumes as well as the treatment area volumes were calculated by the workstation's proprietary software (Monteris Medical Corporation, Plymouth, MN, USA). The treatment area was monitored via standard thermal dose threshold (TDT) lines, with the yellow TDT line signifying the thermal dose equivalent of 43°C for 2 min and the blue signifying 43°C for 10 min. The primary ILA database was maintained as a deidentified list in Microsoft Excel (Microsoft Corporation, Redmond, WA, USA). Excel was used for basic statistics and figures including statistical significance using the Student *t* test and a threshold (α) of 0.05 to indicate significance. We constructed Kaplan-Meier curves and calculated median survival via linear interpolation in MATLAB (MathWorks Inc., Natick, MA, USA).

Patient Selection and Indications

Patients selected for ILA fell into 2 broad categories: (1) ILA would be a "salvage" treatment modality for previously treated, progressive, or recurrent disease; and (2) ILA was a frontline therapy for a newly discovered brain lesion. For recurrent lesions where a diagnosis of tumor recurrence versus radiation necrosis was unclear, or in which a diagnosis would influence subsequent clinical management, a needle biopsy was taken at the time of ILA.

In general, characteristics that made a lesion favorable for ILA treatment included (1) deep location including lobar, basal gan-

glia/thalamus, periventricular, and corpus callosum, among others; (2) lesion morphology, such that lesion volume could be mostly or totally encompassed within a 3-cm-diameter cylinder; (3) average/low vascularity of the lesion; (4) a safe trajectory with the ability to avoid eloquent structures or transgression of a ventricle or vascular plane (e.g., Sylvian fissure, interhemispheric); and (5) adequate clearance for the patient and affixed fiber apparatus within the bore of the MRI. Additionally, it is worth noting that while surgical deeply located inaccessible lesions were predominantly treated, more superficial lesions also were considered. Factors that would favor treating lesions that could theoretically be reached with open surgery would include thin scalp, wound-healing risks, and tenuous functional status of the patient. An example would include a patient with recurrent glioblastoma (GBM) who has had previous open craniotomy, thinned scalp due to radiation, and a borderline Karnofsky performance score. Conversely, characteristics that made ILA less favorable included (1) diffuse lesions which were bilateral or involved multiple lobes; (2) very large lesions in which only subtotal treatment would be possible; (3) hypervascular lesions; and (4) advanced stage of disease and poor functional status. ILA procedures were performed primarily by 2 neurosurgeons (E.C.L. and A.H.K.). The NeuroBlate® system (Monteris Medical Corporation), consisting of a CO₂-cooled fiber optic laser probe, was exclusively used.

Operative Techniques

The ILA technique used at our institution has been previously described [3, 4]. Here, we aim to provide highlights of our operative workflow after experience with the patients reported in this series.

Fig. 5. Stereotactic frame used for posterior fossa, brain stem, and hippocampal targets. **a** Customized frame made for target in the brain stem (ganglioglioma). **b** MRI of fiber placed within the target. **c** Tumor before interstitial laser ablation (ILA) treatment. **d** Tumor after ILA treatment.

Supratentorial Lesion Ablation Technique

For the majority of procedures, Stealth (Medtronic Inc., Minneapolis, MN, USA) was used for trajectory planning and lesion targeting via frameless stereotaxy. Scalp fiducials were used for registration with a registration error of less than 2 mm used as a general goal. Care was taken during positioning to ensure that the patient's head with affixed ILA apparatus would fit into the bore of the intraoperative MRI (IMRIS Inc., Minnetonka, MN, USA). The trajectory was then examined to ensure avoidance of sulci and blood vessels. An example of a supratentorial frontal lobe ablation is shown (Fig. 1). In addition to anatomic information, all patients received advanced functional MRI (fMRI) imaging. Typically, this included resting-state fMRI to define somatomotor and speech networks [7, 8] and diffusion tensor imaging (DTI) mapping of the corticospinal tracts and the arcuate fasciculus (Fig. 2). Based on this integrated information, a trajectory for the target and entry site was determined.

For deep-seated lesions there were several approaches that merit attention. Clearly, every lesion is unique and trajectories must be designed on a case-by-case basis. However, there are general trajectories into specific locations that over time were found

to be useful in the authors' experience. First, thalamic tumors were the most common type of difficult-to-access lesions encountered. Most were located in the posterior thalamus/pulvinar. The typical approach involved a mid- to high-parietal cortical entry posterior to the sensory cortex. There tended to be a narrow (1–1.5 cm) region between the anterior portion of trigone of the lateral ventricle and the high posterior aspect of the insula. We term this the “ventricular-insular corridor” (VIC). This afforded the best access to the thalamus while avoiding the corticospinal tract (Fig. 3a). The second most common location of deep lesions was the insula. The insula has an oval-discoid shape that is angled downward in the sagittal plane and leans medially in the coronal plane (Fig. 3b). To best access the entirety of the insula, a trajectory with a high medial parietal entry in the plane between the putamen medially and the insula laterally was used. This corridor we putatively term the “putaminal-insular corridor” (PIC). Finally, the corpus callosum was also treated with some frequency. If the lesion was unilateral in nature a higher trajectory was taken. If it was more bilateral in distribution, then a lower trajectory was taken to more fully cross the corpus callosum (Fig. 3c).

Table 1. Demographics

<i>Sex, n (%)</i>	
Male	70 (58)
Female	50 (42)
Total	120
<i>Average age, years</i>	
	51.8 (5–79)
<i>Lesions, n (%)</i>	
Glioblastoma	57 (42.5)
Metastasis	35 (26.3)
WHO III glioma	10 (7.5)
WHO II glioma	10 (7.5)
WHO I glioma	6 (4.5)
Epilepsy focus	8 (6.0)
Radiation necrosis	5 (3.8)
Teratoma	1 (0.8)
Encephalocele	1 (0.8)
Total	133
<i>Location, n (%)</i>	
Lobar	90 (67.7)
Lobar-frontal	34 (25.6)
Lobar-parietal	31 (23.3)
Lobar-occipital	2 (1.5)
Lobar-temporal	23 (17.3)
Deep	40 (30.8)
Thalamic	18 (13.5)
Insular	11 (8.3)
Corpus callosum	8 (6.0)
Intraventricular	2 (1.5)
Pineal	1 (0.8)
Pontine	1 (0.8)
Cerebellar	2 (1.5)
Total	133

There are 2 stereotactic technologies used for placement of the laser fiber: (1) the Monteris® Mini-Bolt which has a lower profile (142 mm with driver) but is limited to a single trajectory; and (2) the Monteris Axiis® frame, which has a higher profile (197 mm with fiber driver) but is more versatile for multiple trajectories (Fig. 4). The most common technique was the placement of the Monteris® Mini-Bolt. Typically, the stereotactic trajectory was aligned using the Medtronic Vertek® stereotactic arm (Medtronic). A Stryker hand drill (Stryker, Kalamazoo, MI, USA) was used to make a twist drill burr hole 4.5 mm in diameter, and the bolt was screwed into the skull through the Vertek® arm along the planned trajectory. This technique was used for the following situations: (1) high expectation of single trajectory to treat the lesions in the supratentorial space; (2) lateral trajectories at or below the superior temporal line where the protuberance of laser placement could threaten a collision with the inner bore of the MRI; and (3) posterior fossa lesions. As an alternative, the Monteris Axiis frame was typically reserved for the following situations: (1) high expectation

for multiple trajectories; and (2) salvage for those cases in which the Monteris® Mini-Bolt trajectory was misaligned when screwed into the skull. For all the cases reported, 3.3-mm diffusion tip or side-fire tip laser fibers were used.

Posterior Fossa, Brainstem, and Hippocampal Ablation Technique

Tumors in the posterior fossa – within the cerebellum or brainstem – and lesions of the mesial temporal lobes require exquisitely precise targeting to achieve appropriate treatment and avoid adjacent critical tissues. In our practice, a registration error of less than 1 mm was used as a general goal for these locations. The STarFix microTargeting (mT) platform offered a highly accurate laser fiber insertion that can accommodate extremely oblique trajectories in the skull, particularly for posterior fossa and medial temporal lobe targets. By using bone fiducials and rapid-prototyping 3D printing technology, STarFix mT platforms can be designed and manufactured to fit the unique cranial anatomy of each patient [9]. The procedure was performed in 2 phases. The first phase of the procedure involved placement of bone fiducials, which would serve as anchors for the STarFix frame. For the second phase of the procedure (1 week later), the customized STarFix mT frame was mounted on the bone fiducials. The NeuroBlate system (Monteris Medical Corporation) was then combined with the STarFix frame, which was used as the base to guide the laser fiber driver (Fig. 5).

Results

Participants

A total of 133 ILA treatments were performed in 120 patients between 2010 and 2016 at Washington University in St. Louis (Table 1). There were 70 males and 50 females, and the average age was 51.8 (± 17.8) years (range 5–79). There were several lesion types, in order of frequency: GBM ($n = 57$), metastases ($n = 25$), WHO grade III gliomas ($n = 12$), WHO grade II gliomas ($n = 12$), epilepsy foci ($n = 11$), WHO grade I gliomas ($n = 8$), radiation necrosis ($n = 6$), teratoma ($n = 1$), and encephalocele ($n = 1$) (Fig. 6a). The majority of the lesions ($n = 90$) were lobar and were primarily based in the frontal ($n = 34$), parietal ($n = 31$), occipital ($n = 2$), or temporal ($n = 23$) lobes. Other locations included thalamic ($n = 18$), insular ($n = 11$), corpus callosum ($n = 8$), intraventricular ($n = 2$), cerebellum ($n = 2$), pineal ($n = 1$), and pontine ($n = 1$) sites. A total of 18 patients were lost to follow-up (15 GBM patients and 3 metastasis patients).

Indications and Operative Details

ILA was chosen as a first-line therapy in 36 cases; 97 cases had prior treatment, with ILA chosen as a secondary or a salvage therapy. The location of the lesion was the primary reason for ILA over open craniotomy in 64 cases, while advanced age, poor functional status, and failure of

Fig. 6. Clinical summary. **a** Types of lesions treated. **b** Case duration relative to the number of cases performed. Redline indicates linear regression. **c** Hospital stay and ICU stay comparing the first 50 cases versus the second 50 cases. The latter 50 cases demonstrate shorter stays, respectively. **d** Tumor size comparison of patients with and without complications. The size difference approaches significance ($p = 0.056$).

prior treatments were the primary reasons for ILA in 69 cases. There were 19 patients in whom 2 trajectories were required in one procedure to achieve treatment coverage. Eleven patients had preplanned 2-stage procedures, and 1 patient underwent a 3-stage procedure for a complex insular glioma. The remaining patients all had a single trajectory treatment in one procedure ($n = 108$). The average operating time – defined as skin puncture to the application of the final dressing – was 225 min (± 110 min). Over time, a downward trend in operative time was apparent (Fig. 6b). Specifically, the first 60 procedures took an average of 262 min, while the latter 60 procedures took an average of 191 min ($p < 0.001$). This trend was also conserved when separating cases by performing surgeon.

The average lesion volume was 10.17 cm³ (range 0.27–62.77). Treatment volumes were monitored with the goal of complete ablation, with supramarginal ablation sometimes performed in the case of lesions in noneloquent

brain areas. Fifty patients (43%) had complete or supra-marginal coverage of the lesion by the yellow TDT line. The remainder (57%) had an average of 88.3% coverage of the lesion. Twenty-five patients (21%) had complete or supramarginal coverage by the blue TDT line, while the remainder (79%) had an average of 85% lesion coverage. Broken down by lesion type, the average volume for GBM was 12.36 cm³ with 88% blue TDT line ablation achieved, and the average volume of other gliomas was 8.77 cm³ with 86% ablation achieved. The average volume of metastasis was 7.88 cm³ with 94% ablation achieved, and the average volume of epilepsy targets was 6.23 cm³ with 84.3% ablation achieved. Ablation was terminated either for encroachment on eloquent regions, or for inability to reach peripheral areas of the lesion as limited by fiber placement. An MRI was obtained on postoperative day 1 for all patients for qualitative evaluation of the success of ablation and to establish a posttreatment baseline.

Table 2. Complications

Patient	Pathology	Age, years	Sex	Location	Volume, cm ³	Type	POD	Complication	Management
1	GBM	36	F	occipital	17.51	perioperative	2	right-sided hemiparesis, edema	mannitol
2	GBM	52	M	thalamic	3.15	perioperative	0	hydrocephalus, meningitis	EVD, antibiotics – expired
3	Metastatic	60	M	frontal	10.09	perioperative	0	new seizure	antiepileptics
4	GBM	53	M	corpus callosum	19.72	perioperative	1	hydrocephalus	EVD, no shunt needed
5	GBM	78	M	parietooccipital	16.23	perioperative	2	lesional hemorrhage	supportive care – expired
6	GBM	73	F	temporoparietal	1.13	perioperative	0	edema	mannitol
7	GBM	46	M	temporoparietal	42.22	perioperative	0	hyponatremia	fluid management
8	Radiation Necrosis	78	M	thalamic	19.77	perioperative	1	seizures	antiepileptics
9	GBM	37	F	thalamic	14.03	readmission	28	seizures	antiepileptics
10	GBM	74	M	temporoparietal	34.37	readmission	6	hyponatremia	fluid management
11	Metastatic	56	M	frontal	8.91	readmission	4	mild confusion	none
12	Metastatic	59	F	parietal	12.8	readmission	8	edema	steroids
13	Metastatic	58	F	parietal	5.24	readmission	10	hyponatremia	fluid management
14	GBM	68	M	thalamic	6.54	readmission	20	hydrocephalus	EVD, no shunt needed
15	Metastatic	65	M	parietal	24.59	readmission	16	AMS/seizures	supportive care – expired
16	GBM	54	F	temporal	1.25	readmission	21	seizures	antiepileptics

AMS, altered mental status; EVD, external ventricular drain; GBM, glioblastoma; POD, postoperative day of complication.

Complications

The ILA procedures of 4 patients were cancelled or aborted due to reasons unrelated to the procedure itself. There were 8 perioperative complications (6.0%) and 8 unplanned readmissions (6.0%) in our series (Table 2). Of these, there were 3 perioperative mortalities (2.2%). One patient suffered from fulminant meningitis with *Enterobacter aerogenes*. An analysis traced this problem back to a sterile processing-related contamination. The second mortality occurred in a patient with a large parietooccipital GBM which hemorrhaged postoperatively. The third occurred in a patient with a recurrent parietal metastatic lesion who was discharged without incident and readmitted on postprocedure day 16 with seizures and altered

mental status, for whom the family elected for comfort measures. Our analysis found that patients who suffered perioperative complications or unplanned readmissions tended to have larger tumors (mean volume 14.5 ± 12 cm³) compared to those without complications (mean volume 9.3 ± 11 cm³) ($p = 0.056$).

Operational Efficiency

Patients undergoing ILA tended towards shorter ICU and overall hospital stays during the course of the series (Fig. 6c). Two patient groups were defined a priori; patients 1 through 50 stayed in the ICU an average of 1.98 days and overall in the hospital 4.06 days. In contrast, patients 51 through 100 stayed in the ICU an average of 1.21

Fig. 7. Glioblastoma (GBM) outcome with interstitial laser ablation (ILA). Fifty-seven GBM tumors were treated by ILA. The majority of these were lobar in location. There were also thalamic ($n = 8$), corpus callosum ($n = 8$), and insular ($n = 2$) lesions treated. Median follow-up was 9.5 months, with the longest follow-up being 25.5 months. Twenty-three patients underwent ILA as a frontline treatment for newly diagnosed GBM. Median progression-free survival (PFS) was 5.9 months, and median overall survival (OS) was 11.4 months. Thirty-six patients underwent ILA as a secondary or “salvage” treatment. Median PFS and OS in this group were 7.7 and 11.8 months, respectively.

days and in the hospital for 2.29 days. Both ICU and hospital lengths of stay were shortened over time by a significant amount ($p = 0.008$ and 0.03 , respectively).

Outcome Data

Fifty-seven GBM tumors were treated by ILA. Sites included lobar ($n = 39$), thalamic ($n = 8$), corpus callosum ($n = 8$), and insular ($n = 2$) locations. Median follow-up was 9.5 months (range 2.5–25.5 months). Fifteen patients were lost to follow-up. Median progression-free survival (PFS) after ILA for all GBM was 7.3 months, and median overall survival (OS) was 11.5 months. Twenty-three patients underwent ILA as a frontline treatment, 9 of which were deep-seated. In this frontline cohort, median PFS was 5.9 months, and median OS was 11.4 months (8.1 and 9.1 months for deep-seated). Thirty-four patients underwent ILA as a secondary treatment in the setting of disease progression or recurrence, typically after standard-

Fig. 8. Metastasis outcome with ILA. Twenty-five metastatic tumors were treated by interstitial laser ablation: 15 lung, 3 melanoma, 2 breast, 2 colon, 1 ovarian, 1 prostate, and 1 adenocarcinoma of unclear primary origin. The majority of these lesions were located in the frontal or parietal lobes. There was 1 insular lesion, 2 thalamic lesions, and 1 cerebellar lesion. Median follow-up for these patients was 9.8 months, with the longest follow-up being 24 months. Median progression-free survival (PFS) was not reached; median overall survival (OS) was 17.2 months.

of-care craniotomy and chemoradiation; of these, 9 were deep-seated. Median PFS and OS in this group were 7.7 and 11.8 months, respectively (Fig. 7) (7.3 and 11.7 months for deep-seated). When separating all patients into lobar and deep GBM, the PFS/OS were 7.7/11.4 months and 8.1/10.7 months, respectively.

Twenty-five metastatic tumors were treated by ILA after failure of stereotactic radiosurgery to achieve local disease control: 15 lung, 3 melanoma, 2 breast, 2 colon, 1 ovarian, 1 prostate, and 1 adenocarcinoma of unclear primary origin. The lesions were lobar, insular, thalamic, and cerebellar in location. Median follow-up for these patients was 9.8 months, with the longest follow-up being 24 months. Three patients were lost to follow-up. Median OS was 17.2 months and median PFS was not reached (Fig. 8).

Eleven epilepsy patients were treated with ILA. Five patients had temporal lobe epilepsy (45%) due to cortical

dysplasia ($n = 3$), mesial temporal sclerosis ($n = 1$), or temporal encephalocele ($n = 1$). Six patients had extra-temporal lobe epilepsy (55%) due to cortical dysplasia ($n = 2$), insular epilepsy ($n = 3$), and low-grade glioma ($n = 1$). Among the 11 patients, the average follow-up was 13.5 months (range 3–40 months) and none were lost to follow-up. An Engel class I outcome was achieved in 5 patients (45%), Engel class II in 4 patients (36%), and Engel class III in 2 patients (18%).

Discussion

We describe in this work one of the largest single institutional experiences of using ILA to treat a multitude of different pathologic lesions in the brain. Taken together, the use of ILA is emerging as a powerful surgical tool to treat moderate-sized lesions in the brain with low morbidity, short length of stay, and clinically meaningful outcomes.

Despite the diversity of age, pathology, and location in this experience, there were some technical trends that emerged. Thalamic lesions had a more lateral parietal approach, but entered the posterior thalamus through the VIC, which avoided the ventricle and the corticospinal tract (Fig. 3a). Many lesions in the insula were successfully accessed via a high parietal approach through the PIC, which enabled maximal volumetric coverage of this region of the brain while avoiding the putamen and branches of the middle cerebral artery (Fig. 3b). Lesions in the posterior fossa, brainstem, or hippocampus, which had very little tolerance for variability of fiber position, were treated using STarFix customized stereotactic frames (Fig. 5). Across all lesions the use of resting-state fMRI and DTI tractography was useful for defining anatomic areas to avoid for the fiber trajectory (Fig. 2).

Generally, the patients tolerated the ILA procedure well with low morbidity (6.0%) and mortality (2.2%) rates. Additionally, after an initial learning curve, the operative time was approximately 3 h, with an average ICU stay of 1.21 days and hospital stay of 2.29 days. Hospital stays may have shortened over the series due to physicians, nurses, and ancillary staff becoming more comfortable with the postoperative workflow in laser interstitial thermal therapy patients; due to the low rate of adverse events, patients moved from the ICU to hospital floor to discharge more quickly over time.

It appears that complications correlated with the volume of the treated lesion, which approached significance ($p = 0.056$; Fig. 6d). From a practical standpoint, these

were lesions larger than 3 cm in maximal diameter. Similar considerations of lesion volume have been reported in the radiosurgery literature [11, 12]. While we do not propose precluding larger lesions, it is important to counsel patients that the procedure may be associated with a longer operative time, longer hospital stay, and a higher risk for a surgical complication. These larger lesions may merit additional minimally invasive debulking, as has been previously described [13, 14]. With regard to clinical outcome, there were several diagnoses that had sufficient clinical numbers for which more objective observations could be made.

Glioblastomas

In total, 57 GBM were treated with ILA. Although this was not a controlled study between ILA and traditional treatment, we report here some descriptive outcome statistics from our series that may be of interest and prompt future studies into the efficacy of ILA in GBM. Twenty-three patients underwent ILA as a frontline treatment followed by standard chemoradiation (temozolomide and radiation therapy). In this cohort, median PFS was 5.9 months, and median OS was 11.4 months. While this is a shorter median OS when compared to the current median OS of 14.6 months for open surgical resection followed by standard chemoradiation [15], most patients treated with ILA as frontline therapy were not candidates for craniotomy due to tumor location or the patient's medical status. Rather, they would have been treated with a biopsy followed by standard chemoradiation. Stupp et al. [15] showed this cohort to have a median survival of 9.4 months, compared to the median of 11.4 months when adding frontline ILA. Thus, ILA may add a meaningful outcome benefit when seen in this light. A similar difference was observed in the setting of recurrent GBM. Thirty-four patients with recurrent GBM, who were not candidates for redo craniotomy, underwent ILA as a "salvage" treatment followed by bevacizumab. Median PFS and OS in this group were 7.7 and 11.8 months, respectively. Currently, there is a high degree of variability in how recurrent GBM are treated. At this stage they are often much more functionally fragile and worse candidates for surgical resections. In the absence of surgery, the first line of therapy is bevacizumab, for which the median OS is 9.2 months. In our series, the average OS when adding ILA was 11.8 months. Again, it should be noted that these are descriptive values, and a true comparison of survival would require a controlled study between groups, accounting for factors such as tumor location. Additionally, in the current age, substantive conclusions about survival

must take into account the molecular heterogeneity of these tumors such as isocitrate dehydrogenase status, MGMT methylation status, and others. Further studies which examine ILA in the context of these factors will be very useful.

Metastases

Twenty-five metastatic tumors were treated by ILA. All of these tumors were treated after a failure of initial stereotactic radiation to achieve disease control. As with GBM, in cases of ambiguity as to true recurrence versus radionecrosis, or when a diagnosis would influence subsequent management, a needle biopsy was performed at the time of ILA. The majority of tumors were from lung cancer. Our outcome data for metastases showed a median OS of 17.2 months after ILA, and the median PFS had not yet been reached, suggesting that these patients tended to succumb to their systemic cancer rather than the intracranial metastasis.

Epilepsy

A smaller number of patients were treated for medically refractory epilepsy; 9 of 11 patients had good outcomes (Engel class I and II). Previous reports have shown the utility of ILA for hippocampal ablation in seizure control [16]. Our experience, while limited, suggests the utility of this approach for treating extratemporal seizure foci with good clinical control.

In this series, we used 3.3-mm fibers. These larger-diameter fibers were more rigid. This was felt to be an advantage in that they were less likely to be perturbed when passing the fiber into the brain. In the past, concerns have been raised that the larger-diameter fibers might have a higher risk for hemorrhage. The experience in this series contradicts this notion in that bleeding risk for this series was 0.75%. Most complications were associated with the after-effects of the ILA rather than the technical procedure of fiber placement.

This is a single-institution descriptive study and is thus subject to some inherent limitations. We report our experience with ILA in treating several intracranial pathologies, with the intent of providing an introduction to the versatility and safety profile of ILA. Further comparative studies looking at the role of ILA in treating each of these disease entities will be useful. In addition, the experience of one center cannot be readily generalized to all patients undergoing thermoablative therapy, and as the majority of cases were performed by a single surgeon (E.C.L.), the experience from other institutions may vary. Specifically, this clinical population largely consists of an adult oncologic patient population, thus pathologies that are more representative in pediatric or epilepsy populations (e.g., hamartomas) may not be as well represented, nor on which we can make inferences. Larger, multicenter studies with controlled groups will be essential for validating the role of ILA as a treatment for intracranial lesions.

Conclusion

Despite the limitations inherent to a descriptive single-institution study, our series suggests that ILA is a safe and efficacious treatment for a variety of intracranial lesions, and may offer a novel alternative to traditional open craniotomy in properly selected patients. Further studies will be useful in guiding therapy as ILA solidifies its role in the treatment paradigms for various neurosurgical pathologies.

Disclosure Statement

Dr. Eric Leuthardt has a consulting relationship with Monteris Medical. There were no gains, financial or otherwise, related to the production of this paper, which was produced independently of Monteris Medical. All other authors certify that they have no disclosures or conflicts of interest to report.

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