CLINICAL STUDY



Magnetic resonance-guided laser interstitial thermal therapy for posterior fossa neoplasms

Omar Ashraf¹ • Grant Arzumanov¹ · Evan Luther² · J. Tanner McMahon³ · James G. Malcolm³ · Samuel Mansour⁴ · Ian Y. Lee⁵ · Jon T. Willie³ · Ricardo J. Komotar² · Shabbar F. Danish¹

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Abstract

Purpose Magnetic resonance-guided laser interstitial thermal therapy (LITT) has been increasingly used to treat a number of intracranial pathologies, though its use in the posterior fossa has been limited to a few small series. We performed a multi-institutional review of targets in the posterior fossa, reporting the efficacy and safety profile associated with laser ablation in this region of the brain.

Methods A retrospective review of patients undergoing LITT in the posterior fossa was performed from August 2010 to March 2020. Patient demographic information was collected alongside the operative parameters and patient outcomes. Reported outcomes included local control of the lesion, postoperative complications, hospital length of stay, and steroid requirements.

Results 58 patients across four institutions underwent LITT in the posterior fossa for 60 tumors. The median pre-ablation tumor volume was 2.24 cm³. 48 patients (50 tumors) were available for follow-up. An 84% (42/50) overall local control rate was achieved at 9.5 months median follow up. There were two procedural complications, including insertional hemorrhage and laser misplacement and 12/58 (21%) patients developed new neurological deficits. There was one procedure related death. The median length of hospital stay was 1 day, with 20.7% of patients requiring discharge to a rehabilitation facility. **Conclusions** LITT is an effective approach for treating pathology in the posterior fossa. The average target size is smaller than what has been reported in the supratentorial space. Care must be taken to prevent injury to surrounding structures given the close proximity of critical structures in this region.

Keywords Laser interstitial thermal therapy · Tumor ablation · Posterior fossa

- ☐ Shabbar F. Danish shabbar.danish@rutgers.edu
- Department of Neurosurgery, Rutgers Robert Wood Johnson Medical School, 10 Plum St. 5th Floor, New Brunswick, NJ 08901, USA
- Department of Neurological Surgery, University of Miami Miller School of Medicine, Miami, FL 33101, USA
- Department of Neurosurgery, Emory University School of Medicine, Atlanta, GA 30322, USA
- Charles E. Schmidt College of Medicine, Florida Atlantic University, Boca Raton, FL 33431, USA
- Department of Neurosurgery, Henry Ford Hospital, Detroit, MI 48202, USA

Introduction

The posterior fossa presents a unique challenge for neurosurgeons given the anatomic complexity and high eloquence of tissue confined to this small space. Surgery in this area carries greater morbidity and mortality compared to its supratentorial counterpart and is an independent risk factor for poor clinical outcomes following resection [1–3]. With risk of postoperative complications such as CSF leak, cranial nerve palsy, and hydrocephalus, surgical resection for infratentorial lesions presents unique challenges.

Magnetic resonance-guided laser interstitial thermal therapy (LITT) is a minimally invasive surgical technique that uses an optical fiber to transmit nonionizing radiation from a laser source to the target [4]. Its use for primary brain tumors, radiation necrosis/recurrent metastasis, and pediatric brain tumors is well documented [5–13]. However, the



literature on laser ablation in the posterior fossa is limited to a few small case series [14–16]. Establishing the efficacy and safety profile of LITT in the posterior fossa is crucial as this treatment modality gains momentum in the field of neuro-oncology. In this study, we report the largest series to date of patients who underwent LITT in the posterior fossa for a variety of oncologic pathologies. We report on local control, procedural complications, hospital length of stay (LOS), and pre-/postablation steroid use.

Methods

Patient selection

We retrospectively reviewed patients who underwent LITT for a posterior fossa neoplasm from October 2010 to March 2020. Patients were evaluated by a multidisciplinary team to determine their eligibility for laser ablation given their pathology and treatment history; LITT was considered if resection posed a high risk, the tumor was surgically inaccessible, or the lesion failed maximal radiation therapy. All patients were enrolled in an institutional review board-approved protocol at their respective institution.

Surgical procedure

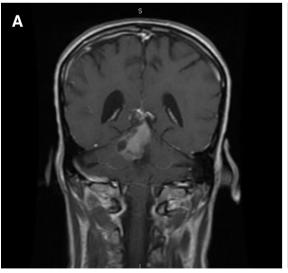
The procedure for LITT using the Visualase thermal therapy system (Medtronic Inc., Dublin, Ireland) has been previously reported [17–19]. Method of insertion was at the discretion

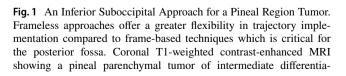
of the operating surgeon, and all surgeons were experienced with the technology. Laser insertion was performed via frameless and framed approaches, with robotic assistance and with the ClearPoint system (ClearPoint Neuro, Irvine, California). For the purposes of this study, the decision to proceed with ablation based on the accuracy of laser insertion was determined by the operating surgeon. Biopsy was not routinely performed at some institutions during LITT based on their own institutional protocols. 51/60 laser placements included in this study were completed using the Medtronic Vertek Arm and Precision Aiming Device using a frameless approach [19].

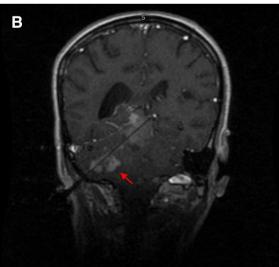
While a number of approaches for laser insertion were utilized in this study, we have found that some tumors may be more appropriately treated by a certain technique. In our experience, frame-based techniques offer exceptional precision, though the bulk introduced by these systems often limits more robust trajectories. The frameless approach allows for more flexibility in trajectory implementation, especially for more inferior trajectories (Fig. 1). Beyond the decision of which targeting system to use, trajectory planning involves a thorough evaluation of the anatomy. This will allow for more effective targeting of brainstem tumors (Fig. 2) and enable the operator to bypass traditional anatomic boundaries (Fig. 3).

Data collection

Demographic information, pathology, tumor location, presenting problem, preoperative symptoms, and operative







tion (left) in the pineal region and an inferior suboccipital trajectory (right) with insertional hemorrhage (arrow). A frameless approach enabled a sufficiently inferior trajectory for laser insertion across the long axis of the tumor which likely would not have been possible with a frame-based technique



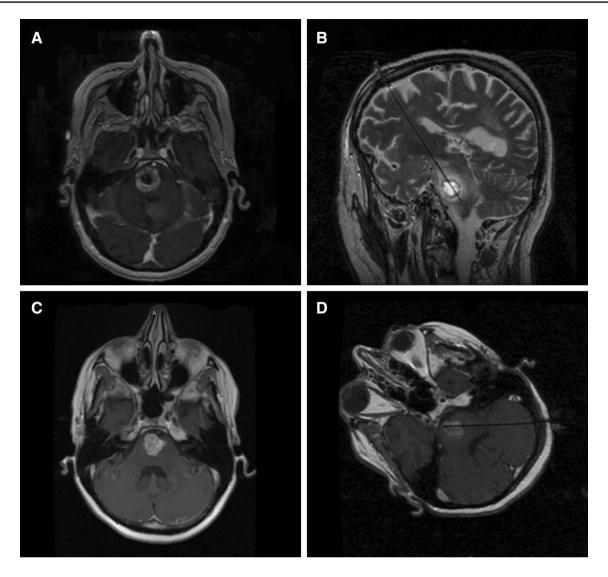


Fig. 2 A Comparison Between a Frontal and Transcerebellar Trajectory for Pontine Tumors. Pontine tumors can typically be approached by either a frontal or transcerebellar trajectory, with the decision in which trajectory to use dictated by the morphology of the tumor. Axial T1-weighted MRI with gadolinium (**a**) showing tumor local-

ized to the right pons. Trajectory implementation involved utilizing a frontal approach to the pons through the midbrain (\mathbf{b}) . Axial T1-weighted image (\mathbf{c}) shows an anterior pontine tumor in another patient to demonstrate an alternative transcerebellar approach (\mathbf{d})

variables were gathered from hospital charts. The presenting problem was considered the primary reason the patient presented (i.e. the predominating symptom or radiographic progression via serial imaging), whereas preoperative symptoms incorporated all of the patient's reported symptoms. Infield recurrence was considered to be recurrence within a previously radiated field following stereotactic radiosurgery for a metastatic tumor; it may represent radiation necrosis, recurrent metastasis, or both [6, 10, 20].

End points included local control, postoperative complications, hospital LOS, 30-day readmission rate, and steroid use. Hospital LOS was defined as the amount of days spent in the hospital post-ablation, since some patients were admitted the day before the procedure for preoperative imaging. The 30-day readmission rate was measured by identifying readmissions directly related to LITT. Postoperative complications were defined as inpatient events only. Any resolution in new neurological deficits was assessed through outpatient records. Local control was defined as lack of tumor progression after LITT. Progression was defined as enhancement that increased in size by a minimum of 25% in two dimensions on two consecutive MRI scans (contrastenhanced T1) 4–12 weeks apart, or enhancement accompanied by symptoms necessitating intervention. Long-term steroid use was considered to be dexamethasone use beyond the postoperative taper (typically a 1–2 week taper).



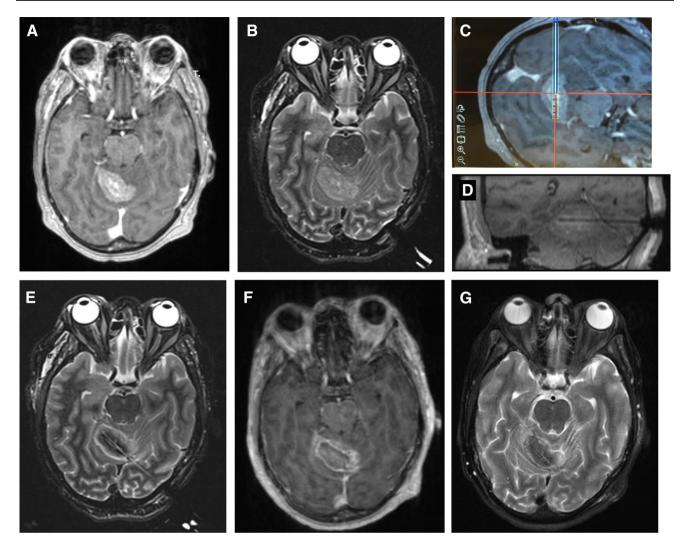


Fig. 3 Transoccipital Transtentorial Stereotactic Laser Ablation of Cerebellar Vermian Metastatic Tumor. Traditional anatomic boundaries such as the tentorium can be traversed if the morphology of the tumor demands a transtentorial approach. Shown is the preoperative gadolinium-enhanced axial T1 image (a) and preoperative axial T2 image (b). Preoperative stereotactic trajectory view (c) demonstrates a transtentorial approach which would allow adequate ablation of the

tumor, and intraoperative direct MRI guidance view shows transtentorial placement (\mathbf{d}) of the laser apparatus. E Immediate post-treatment effects visualized with axial T2 image. F 6-week postoperative gadolinium-enhanced axial T1 image showing treatment effects without progression of lesion. G 6-week postoperative axial T2 image showing treatment effects with decreased edema and mass effect

Imaging protocol and analysis

Exact institutional imaging protocols varied, but each center obtained at least two MRIs during each hospitalization: within 24 hr pre-operatively and within 24 h after LITT. After discharge, patients obtained sequential MRIs every 4–12 weeks, though this interval was increased in the cases of exceptional long-term control following laser ablation. The extent of ablation was quantified by calculating the 24-h postablation-to-preablation tumor volume ratio; this ratio was used to assess the effect that extent of ablation has on local control and the development of postoperative neurological deficits. Tumor dimensional and volumetric analysis

was carried out with OsiriX MD (Pixmeo SARL, Geneva, Switzerland) [21].

Statistical analysis

Statistical analyses were done using Prism 8.2.1 (Graph-Pad Software, La Jolla, California). Categorical data are reported as percentages, and continuous data are presented as the mean with standard error of the means. Comparisons in demographics, operative parameters, and outcomes between cerebellar and brainstem lesions were considered separately; outcomes were also compared between patients with primary and secondary brain tumors. Differences are



considered significant with p < 0.05. Statistical analysis was completed via Student's t-test for continuous data and Fisher's exact tests for categorical data.

Results

Patient demographics

A total of 58 patients with 60 tumors underwent LITT in the posterior fossa. Patient demographics, tumor pathology, and operative parameters are summarized in Table 1. There were a total of 15 primary tumors and 45 secondary tumors (44 cases of infield recurrence and one untreated metastatic tumor). Of the patients with infield recurrence, primary tumor pathology included breast cancer (n = 18), non-small-cell lung cancer (n = 16), melanoma (n = 4), neuroendocrine tumor, cholangiocarcinoma, small-cell lung cancer, renal cell carcinoma, ovarian cancer, and cervical cancer (n = 1 each). Preoperative symptoms among all patients, beyond the presenting complaint, included balance difficulty (n = 14), headache (n = 13), motor weakness (n = 7), dizziness (n = 3), vision problems (n = 3),

Table 1 Patient demographics information, operative parameters, and ablation volumes

	Total	Location			
		Brainstem	Cerebellum	Pineal region	
Number of tumors	60	7	52	1	
Sex (n, %)					
Male	18 (31%)	5	12	1	
Female	40 (69%)	2	38	0	
Age (range)	56.4 ± 2.2 [4-90]	46.0 ± 9.7 [4-75]	$58.0 \pm 2.2 [23-90]$	51	
Pathology (n, %)					
Infield recurrence of a previously radiated metastatic tumor	44 (73.3%)	2	42	0	
Glioblastoma	4 (6.7%)	4	0	0	
Pilocytic astrocytoma	3 (5%)	0	3	0	
Low grade glioma	2 (3.3%)	0	2	0	
Hemangioblastoma	2 (3.3%)	0	2	0	
Anaplastic astrocytoma	2 (3.3%)	0	2	0	
Ependymoma	1 (1.7%)	1	0	0	
PPTID	1 (1.7%)	0	0	1	
Untreated metastatic tumor (breast)	1 (1.7%)	0	1	0	
Presenting problem (n, %)					
Radiographic progression	34 (58.6%)	0	34	0	
Balance difficulty	9 (15.5%)	2	6	1	
Headache	9 (15.5%)	0	9	0	
Motor weakness	3 (5.2%)	3	0	0	
Sensory deficit	2 (3.4%)	2	0	0	
Nausea	1 (1.7%)	0	1	0	
Operative parameters					
Preoperative target volume (cm ³)	2.24 ± 0.21	3.24 ± 0.59	2.11 ± 0.22	2.32	
Laser power (Watts)	$9.93 \pm .0.26$	9.3 ± 0.56	10.0 ± 0.3	10.4	
Ablation time (Seconds)	404.3 ± 44.6	406.7 ± 87.1	400.1 ± 51.0	570	
Number of ablations	2.94 ± 0.27	3.57 ± 0.72	2.74 ± 0.29	4	
Trajectory length* (mm)	70.3 ± 3.9	$123.3 \pm 6.5*$	61.9 ± 3.1 *	110.8	
24-hour postablation volume (cm ³)	3.92 ± 0.28	3.73 ± 0.63	3.97 ± 0.31	2.81	
Postablation-to-preablation volume ratio	2.38 ± 0.28	1.17 ± 0.08	2.57 ± 0.32	1.21	

PPTID pineal parenchymal tumor of intermediate differentiation



^{*}Reached statistical significance (p < 0.05)

sensory deficit (n=2), nausea (n=2), hearing difficulty, and cognitive decline (n=1 each).

53 patients (91%) had undergone prior intervention for their tumor. Patients with primary tumors previously underwent craniotomy (n=6), radiotherapy (n=1), or both craniotomy and radiotherapy (n=3). Secondary brain tumors were previously treated by stereotactic radiosurgery (n=34) or both craniotomy and stereotactic radiosurgery (n=9). Among the patients who had not received prior intervention, primary pathology was glioblastoma (n=2), hemangioblastoma, pilocytic astrocytoma, and metastatic breast cancer (n=1 each).

Local control

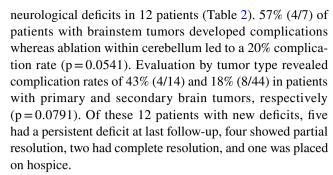
Ten patients did not have follow-up records for the subsequent reasons: one patient had the procedure aborted following improper placement of the laser and underwent subsequent resection; five patients continued care at outside hospitals; two patients died prior to follow-up (one patient died secondary to procedural complications and another patient with primary NSCLC died due to pneumonia); two patients were placed on hospice care due to extracranial disease progression. The remaining 48 patients (50 tumors) were available for clinical and radiographic follow up.

The median duration of follow-up was 9.5 months (range 0.6–81.5) for 48 patients. LITT resulted in an overall local control rate of 84.0% (42/50). Stratifying patients by tumor location revealed a local control rate of 50.0% (2/4) for brainstem tumors and 87.0% (40/46) for cerebellar locations (p=0.115). Primary and secondary brain tumors demonstrated local control rates of 60% (6/10) and 90.0% (36/40), respectively (p=0.0407). The 24-h postablation-to-preablation volume ratio was lower in patients with recurrence than in those without recurrence (1.67 \pm 0.26 vs 2.54 \pm 0.36, p=0.3057). The median time from laser ablation to recurrence was 5.5 months (range 2.8–14.6). Five patients with recurrence pursued further treatment: two patients underwent craniotomy, one patient opted for radiosurgery, and two patients had changes made to their chemotherapy regimen.

Local control among patients with infield recurrence was 89.7% (35/39). Biopsy was employed in 13 of these cases, revealing recurrent metastasis in seven cases, radiation necrosis in four cases, and mixed recurrent tumor and radiation necrosis in two cases; local control was 100% for each of these histopathologic diagnoses at median follow-ups of 11.5 months (recurrent metastasis), 9.6 months (radiation necrosis), and 7.6 months (mixed tumor/radiation necrosis).

Procedural complications

There was a total of 14 complications in this study (24.1%), consisting of two procedural complications and new



Catheter misplacement occurred in a patient who had LITT for a cerebellar hemangioblastoma. Imaging confirmed the catheter was inserted superior to the target, and the patient then opted for resection. Another patient was noted to have a superficial insertional hemorrhage which required evacuation following ablation. There was one procedure-related mortality in this cohort. The patient had LITT for a midbrain glioblastoma, and subsequently died 8 weeks later secondary to refractory edema.

The 24-h postablation-to-preablation tumor volume ratio was compared between patients with and without new postoperative neurological deficits. Interestingly, patients that developed postoperative complications had a lower postablation-to-preablation tumor volume ratio compared to patients without deficits, though this difference was not statistically significant (1.34 \pm 0.09 vs 2.66 \pm 0.35, respectively; p=0.0502). There was no association between the development of complications and catheter insertion approach (p=0.6786) or pre-ablation tumor volume (p=0.6445).

Hospital stay and readmissions

The mean hospital LOS was 2.50 ± 0.42 days (range 1–22, median 1). Analysis by target location revealed those with ablation in the brainstem had a mean LOS of 5.5 ± 2.52 days (range 1–22, median 2), which was longer than patients with cerebellar ablation who had a mean LOS of 2.0 ± 0.24 days (range 1–8, median 1) (p=0.0416). Patients with complications had higher LOS than those without, with an average stay of 4.79 ± 1.42 days compared to 1.75 ± 0.25 days, respectively (p=0.0013). At the time of discharge, 12 patients (20.7%) were sent to a rehabilitation facility, and 46 patients were sent home (79.3%). The 30-day readmission rate was 0%.

Steroid use

18 of the 48 patients (37.5%) in this study with long-term follow-up were taking steroids preoperatively. Post-procedurally, 46 patients (95.8%) were placed on 1 to 2-weeks steroid tapers. Among the patients that had been on steroids pre-operatively, 50% achieved steroid freedom on follow-up. 9/30 (30%) patients that had not been taking steroids



Table 2 Postprocedural neurological deficits

Target location	Pathology	Pre-ablation lesion volume (cm ³)	Neurological deficit following ablation	Degree of resolu- tion of new neuro- logical deficit	Pre-ablation ster- oid dose	Post-ablation steroid course
Right midbrain	Glioblastoma	6.20	Refractory cerebral edema	Persistent	2 mg twice daily	2 mg twice daily until death
Right pons	Infield recurrence	1.91	Hemiparesis	N/A, patient placed on hos- pice	4 mg twice daily	2-week taper to off
Right cerebellar peduncle	Infield recurrence	1.01	Facial nerve palsy (House-Brack- mann V)	Persistent	4 mg four times daily	4 mg twice daily
Right cerebello- pontine angle	Pilocytic astrocy- toma	0.69	Hearing loss	Persistent	None	2-week taper to off
Right midbrain	Glioblastoma	3.70	Facial droop and hemiparesis	Partial	None	1 mg daily
Anterior pons	Infield recurrence	1.86	Facial droop and hemiparesis	Persistent	None	4 mg four times daily
Right cerebellum	Infield recurrence	1.68	Arm weakness	Partial	1 mg twice daily	1 mg twice daily
Left cerebellar peduncle	Pilocytic astrocy- toma	3.56	Hearing loss	Persistent	None	1-week taper to off
Right cerebellar peduncle	Infield recurrence	1.90	Dysmetria and slurred speech	Partial	None	6 mg four times daily
Cerebellar vermis (2 targets)	Anaplastic astrocytoma	1.51, 2.47	Truncal ataxia and scanning speech	Partial	2 mg twice daily	4 mg four times daily for 11 months
Left cerebellum	Infield recurrence	3.35	Diplopia	Complete	None	2-week taper to off
Left cerebellum	Infield recurrence	1.83	Speech impairment and balance difficulty	Complete	3 mg once daily	2 mg once daily

preoperatively required long-term steroids, typically due to persistence of symptomology. There was no significant difference between these two groups (p=0.222).

When looking at each subset of patients, there was no significant difference in preoperative and long-term postoperative steroid use in patients with brainstem and cerebellar lesions (p = 0.486 and p = 0.825, respectively).

Discussion

As more neurosurgeons incorporate LITT into their practice, elucidating the capabilities and limitations of this technology is critical for optimizing the treatment of intracranial tumors. To that end, we present a multi-institutional series of patients that underwent LITT for a number of oncologic pathologies within the posterior fossa.

Local control rate was 84% with a median follow-up of 9.5 months, consistent with another study published by Borghei-Razavi et al. [14] They presented a series of 8 patients who underwent LITT for infratentorial metastases, radiation necrosis, pilocytic astrocytomas, and glioblastoma with a local control rate of 75%. In addition, Dadey

et al. [15] published a series of five patients, two of which underwent LITT in the posterior fossa for gangliogliomas; neither experienced recurrence. Both of these studies are in contrast to the findings presented by Traylor et al. [16] who investigated the use of LITT infratentorially for five cases of radiation necrosis and eight cases of metastases. Overall, there was recurrence in 69.2% of the subjects. While this recurrence rate is higher than the studies previously discussed, there is notable heterogeneity between these studies in terms of the specific tumor pathologies treated. Overall, more research is needed to investigate the efficacy of LITT for specific tumor pathologies. Furthermore, control rates are much more a function of the underlying histopathology than the specific location.

Postoperative complications secondary to LITT can be categorized as either secondary to thermal ablation (due to hyperthermia, post-ablation edema, or ablation-induced hemorrhage) or laser insertion [4, 6, 9]. In this study, we encountered a complication rate of 24.1%. Two complications were secondary to laser insertion, specifically insertional hemorrhage and catheter misplacement; neither patient had lasting effects from these complications. The remaining 12 complications were related to thermal ablation



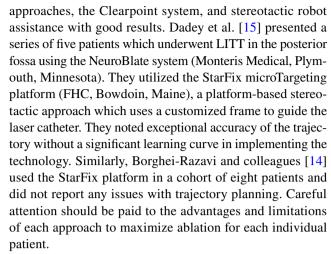
resulting in new neurological deficits, of which 5 patients had persistent deficits at last follow-up. The one procedure-related mortality occurred in a patient with a 6.2cm³ midbrain glioblastoma, preoperatively putting him at high-risk for ablation-related complications. Three prior studies evaluating LITT in the posterior fossa with 5, 8, and 13 patients reported complication rates of 0%, 37.5%, and 7.7%, respectively [14–16]. While our results fall within this range, it is difficult to draw any definitive conclusions given the high variability and small sample size in these reported cases.

Upon risk-stratifying patients before intervention, we have found that patients with symptomatic improvement with steroids preoperatively typically do not develop complications following ablation, as their initial symptomology was likely due to edema as opposed to infiltration. The compactness of the gray and white matter in the posterior fossa indicates that the sensitivity of target location is more critical than the volume. Several patients that developed permanent deficits despite low volume ablation had involvement of facial and motor tracts in close proximity to the target. 4/12 patients with new deficits had brainstem tumors. Overall these findings serve to illustrate the higher risk associated with LITT in the brainstem and closer to the midline in the posterior fossa. The volumetric analysis did show that the majority of tumors in the posterior fossa that underwent LITT were smaller (<4cm³) than those targeted in the supratentorial space, emphasizing the lower volume threshold for treatment of infratentorial targets.

Assessing the ability of LITT to reduce rates of steroid dependence is an important component of its overall efficacy given the consequences of long-term dexamethasone treatment [22]. Of the patients on steroids preoperatively, 50% were successfully weaned off dexamethasone following LITT. However, 30% of patients that did not require preoperative steroids had been on steroids at last follow-up. This highlights the utility of LITT in helping patients achieve steroid freedom, though also suggests that it may not prevent long-term steroid use among patients that did not require them preoperatively.

LITT has been shown to have a shorter hospital LOS when compared to surgical resection [9, 23], and this holds true for patients undergoing thermal ablation in the posterior fossa. Our findings show a median LOS of 1 day, with previous series demonstrating a similar trend [14–16]. This is in contrast to patients with infratentorial tumors who are treated with resection, in which one study with 152 patients reported a median LOS of 7 days [24]. Moreover, there were no reported complications of CSF leak or infection in this series, a notable advantage over resection in the posterior fossa [1].

While the majority of patients presented in this study underwent bone-fiducial-based frameless stereotaxy, individual surgeons also chose to utilize frame-based



This study has several limitations. Ten patients (ten tumors, 17.2%) that underwent ablation were unavailable for follow-up, potentially introducing a source of survivorship bias and affecting the local control rate and steroid requirement analysis. Furthermore, our series featured nine different tumor pathologies split between 58 patients. While this illustrates the potential wide breadth of LITT, it lacks the power to adequately demonstrate the efficacy or safety profile of laser ablation for any single diagnosis. Our cohort also had a preponderance of secondary brain malignancies, making our results less generalizable to primary tumor pathologies. The majority of patients treated for infield recurrence did not undergo a biopsy due to certain institutional care algorithms in which biopsy would not change the treatment plan [6]. While this potentially limits the understanding of the underlying pathology, the overall control rate in this series exceeds 80% when considered in aggregate. This is a result of institutional heterogeneity in how the procedure is performed and could potentially be solved in the context of a prospective trial. In addition, this study employed a number of LITT targeting techniques. This demonstrates the feasibility of each system for infratentorial LITT, but the small number of cases with some systems precluded a detailed analysis of how certain approaches may be associated with target location and trajectory planning.

Conclusions

This multi-institutional study demonstrates the efficacy and safety of LITT as a treatment modality for posterior fossa neoplasms, particularly secondary tumors. Care must be taken to prevent damage to surrounding neural structures as long-term neurological morbidity and death may occur, especially for targets in the brainstem. Proper patient selection, coupled with careful trajectory planning, is essential to preventing complications while maximizing thermal ablation, thereby allowing long-term tumor control. While this



work provides a deep look into the capabilities of LITT in targeting infratentorial lesions, larger studies are necessary to assess its efficacy amongst different tumor pathologies and its safety profile within subregions of the posterior fossa.

Author contributions Conceptualization: SFD, OA, GA; Methodology: OA, SFD; Formal analysis and investigation: OA, GA, EL, JTM, SM; Writing—original draft preparation: OA, GA, SFD; Writing—review and editing: JTW, IYL, RJK, JGM, EL, JTM, SM; Funding acquisition: N/A; Supervision: SFD, JTW, IYL, RJK, JGM.

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Data availability The datasets analyzed during the current study are available from the corresponding author on reasonable request.

Compliance with ethical standards

Conflicts of interest Dr. Danish and Dr. Willie have received Honoraria from Medtronic Inc., for educational lectures. Dr. Willie serves as site Primary Investigator for the Stereotactic Laser Ablation Trial for Epilepsy (SLATE) sponsored by Medtronic, Inc.

Ethical approval This study was approved by the IRB at each respective institution

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