Safety of stereotactic laser ablations performed as treatment for glioblastomas in a conventional magnetic resonance imaging suite

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OBJECTIVE Stereotactic laser ablation (SLA) is typically performed in the setting of intraoperative MRI or in a staged manner in which probe insertion is performed in the operating room and thermal ablation takes place in an MRI suite.

METHODS The authors describe their experience, in which SLA for glioblastoma (GBM) treatment was performed entirely within a conventional MRI suite using the SmartFrame stereotactic device.

RESULTS All 10 patients with GBM (2 with *isocitrate dehydrogenase 1* mutation [*mIDH1*] and 8 with wild-type *IDH1* [*wildIDH1*]) were followed for > 6 months. One of these patients underwent 2 independent SLAs approximately 12 months apart. Biopsies were performed prior to SLA for all patients. There were no perioperative morbidities, wound infections, or unplanned 30-day readmissions. The average time for a 3-trajectory SLA (n = 3) was 436 ± 102 minutes; for a 2-trajectory SLA (n = 4) was 321 ± 85 minutes; and for a single-trajectory SLA (n = 4) was 254 ± 28 minutes. No tumor recurrence occurred within the blue isotherm line ablation zone, although 2 patients experienced recurrence immediately adjacent to the blue isotherm ablation line. Overall survival for the patient cohort averaged 356 days, with the 2 patients who had *mIDH1* GBMs exhibiting the longest survival (811 and 654 days).

CONCLUSIONS Multitrajectory SLA for treatment of GBM can be safely performed using the SmartFrame stereotactic device in a conventional MRI suite.

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KEY WORDS intraoperative MRI; stereotactic laser ablation; neurooncology; MR thermography

STEREOTACTIC laser ablation (SLA) refers to a procedure in which a fiberoptic probe with laser-firing capacity is inserted into an intended target site, followed by tissue destruction through induction of thermocoagulation.^{6,10} Landmark studies have demonstrated the feasibility and safety of this approach for the treatment of challenging neurooncological lesions that cannot be safely treated via conventional surgical approaches.^{2,5,10} Although the procedure has fundamentally reshaped the landscape of neurosurgery, the safety of thermal ablation requires real-time MRI monitoring of thermocoagulation by using a technique called MR thermometry.⁶

Because of this requirement, SLA is mostly performed in specialized surgical suites with built-in MRI scan-

ners,^{5,10} or interventional MRI suites with modified air ventilation to mimic the operating room's sterile environment. For institutions that do not have access to these specialized suites, SLA is achieved by inserting the probe in the operating room, transporting the patient to the MRI suite, and performing thermal ablation under real-time MRI monitoring.² This solution requires reservation of and complex coordination between the operative and the MRI suites as well safe transportation between the 2 sites. Here we describe our experience in which SLA is performed entirely within a conventional MRI suite using the SmartFrame stereotactic device (MRI Interventions). We demonstrate the accuracy of the SmartFrame device for guiding multitrajectory SLA in a conventional MRI suite.

ABBREVIATIONS GBM = glioblastoma; RT = radiation therapy; SLA = stereotactic laser ablation; TMZ = temozolomide.

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TABLE 1. Demographic and clinical characteristics in 10 patients with GBMs treated with SLA

Case No.	Age (yrs)	Sex	Pathology	Location	Indication	Survival After Treatment (days)	Cause of Death	No. of Trajectories	Time in Room (mins)	Procedure Time (mins)
1	69	F	GBM	Lt frontal	Progression on Avastin	97	Local recurrence	3	594	492
2	46	M	GBM	Lt temporal	Progression after TMZ/RT	311	Distant progression	2	558	430
3	63	M	GBM	Lt parietal	Progression after TMZ/RT	811		1	317	281
3*				Lt temporal	Progression after TMZ/RT	549	Distant progression	1	317	275
4	65	F	GBM	Lt parietal	Newly diagnosed	654	Distant progression	3	358	318
5	48	M	GBM	Rt temporal	Progression on Avastin	119	Local recurrence	1	320	220
6	54	M	GBM	Corpus callosum	Progression after TMZ/RT	266	Distant progression	3	663	499
7	46	F	GBM	Lt temporal	Progression after TMZ/RT	335	Distant progression	2	468	346
8	55	M	GBM	Rt frontal	Progression after TMZ/RT	249	Distant progression	2	433	270
9	34	F	GBM	Rt parietal	Progression after TMZ/RT	198	Alive	1	324	243
10	52	F	GBM	Lt parietal	Newly diagnosed	184	Distant progression	2	553	240

* Note that the patient in Case 3 underwent a second SLA procedure 9 months after the initial SLA.

Methods

Patient Population

This is a retrospective series of 10 consecutive patients with glioblastoma (GBM) who underwent SLA treatment. The study was conducted with the approval of the institutional review board. All procedures were performed by the senior author of this manuscript (C.C.C.). Patient characteristics are as shown in Table 1.

Magnetic Resonance Imaging–Guided Biopsy and SLA

The procedures were performed in a diagnostic 3T General Electric (GE Healthcare) MRI suite. A terminal clean protocol was instituted on the evening prior to the procedure.⁸ In brief, this procedure involves temporarily removing all detachable equipment, cleaning lighting and air ducts, and washing all walls, furniture, and equipment. No diagnostic MRI studies were performed after the cleaning prior to the procedure. The specific terminal clean protocol will be provided by the corresponding author upon request.

SmartFrame stereotaxis has been described in detail in other reports.⁷ Briefly, the patients were placed under general anesthesia, followed by head pinning using the Monteris AtamA head frame (Monteris Medical). The head was positioned to avoid collision of the MRI bore and the SLA probe. The intended entry site was prepared. The patient was then moved into the MRI unit, the surgical site was again prepared, and the MRI bore was draped. A grid containing MRI-visible fluid (SmartGrid, MRI Interventions) was placed on the planned surgical site, and an MR image was obtained. On identification of the optimal entry site, an MRI-compatible stereotactic frameless device (SmartFrame) was mounted over this site. The SmartFrame device contains an MRI-visible targeting cannula and 3 MRI-visible fiducial markers.

Based on MR images acquired in real time, the cannula was aligned to achieve the desired trajectory. A stab incision was then placed at the intended entry site. A handheld MRI-compatible drill was inserted into the stab incision

through the cannula for the creation of a small bur hole. The drill was removed, and an MRI-compatible lance was inserted to achieve the durotomy. A ceramic stylet was then inserted and advanced to the target site. The stylet was removed after MR images were obtained to verify the target location. An MRI-compatible needle (Ad-Tech Medical) was inserted to the site of the lesion and biopsies were performed.

In the patient in Case 4, cyst drainage was performed by redirecting the biopsy needle to the center of the cyst and aspirating. The trajectory was then readjusted to the center of the contrast-enhancing region after cyst drainage was complete, before thermal ablation was performed. In all other patients, the SLA probe was inserted to the target site after removal of the biopsy needle. Thermal ablation was performed under real-time MR thermometry as previously described.¹⁰ Yellow isotherm lines indicate tissue heated to 43°C for ≥ 2 minutes, and blue isotherm lines indicate tissue heated to 43°C for ≥ 10 minutes, or to a higher temperature for a shorter period. When multiple-trajectory thermal ablation was required, the SLA probe was removed after each ablation, and the SmartFrame readjusted to the new trajectory. The SLA probe was then inserted to the prescribed depth. After completion of the SLA, the incisions were closed using Dermabond (Ethicon, Inc.).

Results

Patient Demographic Data

Ten patients with GBM underwent SLA during the study period. One of the patients underwent 2 procedures 9 months apart. The average age of the patients was 55 ± 11 years (range 34–69 years). There were 5 male and 5 female patients (Table 1). All patients were followed for > 6 months from the time of the last SLA procedure.

Details of SLA

Single-trajectory SLA was performed in 4 procedures; 2-trajectory SLA was performed in 4 procedures; and 3-trajectory SLA was performed in 3 procedures. The av-

TABLE 2. Treatment results in 10 patients with GBM metastases

Case No.	Target Vol (cm ³)	Treatment Contour (cm ³)		Untreated Tumor Vol (cm ³)		% Treated	
		Yellow Isotherm Line	Blue Isotherm Line	Yellow Isotherm Line	Blue Isotherm Line	To Yellow Isotherm Line	To Blue Isotherm Line
1	26.2	18.4	15.4	7.8	10.8	70.23	58.78
2	13.2	14.8	12.4	0.0	0.8	100.0	93.94
3	12.2	19.6	13.9	0.0	0.0	100.0	100.0
3*	0.22	0.3	0.24	0.0	0.0	100.0	100.0
4	13.2	12.12	9.7	1.08	3.5	91.82	73.48
5	9.1	15.3	10.3	0.0	0.0	100.0	100.0
6	4.3	8.6	6.4	0.0	0.0	100.0	100.0
7	24.0	23.6	17.4	0.4	6.6	98.33	72.5
8	2.3	5.6	3.7	0.0	0.0	100.0	100.0
9	0.19	0.51	0.22	0.0	0.0	100.0	100.0
10	7.0	8.8	6.2	0.0	0.8	100.0	88.57

* Note that the patient in Case 3 returned for a second procedure due to progression.

erage time for a 3-trajectory SLA ($n = 3$) was 436 ± 102 minutes; for a 2-trajectory SLA ($n = 4$) it was 321 ± 85 minutes; and for a single-trajectory SLA ($n = 4$) it was 254 ± 28 minutes (see Tables 1 and 2 for full patient and SLA characteristics).

Surgical Outcomes

There were no perioperative complications, surgical infections, or unplanned 30-day readmissions. No disease recurrence was observed in the ablation cavity defined by the blue isotherm line. However, in 2 patients (Cases 1 and 5), new contrast enhancement was observed in the region immediately surrounding the ablation cavity 1 month after SLA. We refer to this form of recurrence as local recurrence. In most of our treated patients (70%), recurrence developed in sites distant to the SLA site.

Overall survival for the patient cohort averaged 356 days, with the 2 patients who had *mIDH1* GBMs exhibiting the longest survival (811 and 654 days). The shortest survival was observed in the patient who presented with progression after Avastin treatment (97 days).

Illustrative Cases

Case 3

A 63-year-old man initially presented with a left periaxial cystic lesion with a contrast-enhancing nodule. The specimen secured from biopsy of the nodule revealed an *IDH1* mutated GBM. The patient underwent concurrent temozolomide (TMZ) and radiation therapy (RT). His clinical course was complicated by the development of nonobstructive hydrocephalus, requiring a ventriculoperitoneal shunt placement. The patient remained in remission until 9 months after therapy, when he began suffering from progressive aphasia. An MRI study performed at that time revealed enlargement of the contrast-enhancing nodule. The lesion was associated with hemispheric FLAIR signal abnormalities extending across the corpus callosum (Fig. 1A). The patient was placed on Decadron therapy, with symptomatic improvement. The patient subsequently

underwent laser thermal ablation of the contrast-enhancing nodule. The blue isotherm line covered the entire nodule. The patient's neurological status gradually improved over 1 month posttreatment. The MR images obtained 1 month posttreatment revealed significant improvement in the FLAIR signal abnormality (Fig. 1B). The patient was weaned off the Decadron over the ensuing months and lomustine therapy was initiated. He suffered progressive receptive aphasia approximately 19 months after lomustine therapy began. Follow-up MRI revealed a new $0.8 \times 0.9 \times 0.3$ -cm FLAIR signal abnormality in the left superior temporal gyrus that did not enhance after the administration of contrast (Fig. 1C). The entire lesion was ablated to the isotherm line. The patient's neurological status remained unchanged postprocedure. An MR image obtained 1 month after the procedure is shown in Fig. 1D. The patient was subsequently placed on Avastin. He died 9 months later with multifocal recurrence.

Case 4

A 65-year-old woman with a remote history of Stage I breast cancer presented with progressive headaches. Results of her neurological examination were nonfocal. Her MRI studies revealed a $3.8 \times 2.6 \times 3.3$ -cm left temporoparietal cystic lesion with a contrast-enhancing nodule (Fig. 2A). The patient underwent a planned MRI-guided biopsy, cyst drainage, and SLA of the nodular lesion. The first step of the procedure involved biopsy of the nodular portion of the lesion (Fig. 2B). Pathological analysis of the specimen secured in the biopsy procedure revealed findings consistent with GBM (Fig. 2C) (subsequent genomic analysis revealed that the tumor harbored an *IDH1* mutation). A second trajectory was planned to target the center of the cystic lesion to drain its contents (Fig. 2D). Finally, a third trajectory was planned to place the fiberoptic probe in the center of the contrast-enhancing lesion for SLA. The entirety of the lesion was ablated to the blue isotherm line. The patient emerged from the surgery neurologically nonfocal. The patient subsequently underwent TMZ and RT. An MRI study obtained 1 year after the treatment is

FIG. 1. Case 3. Laser ablation course. **A:** Postcontrast T1-weighted (panels i–iii) and FLAIR (panel iv) MRI studies demonstrating enlargement of a known left peri-atrial cystic lesion. **B:** One month after laser ablation, postcontrast T1-weighted (panels i–iii) and FLAIR (panel iv) MRI studies demonstrating significant improvement in the lesion's FLAIR signal. **C:** FLAIR MRI studies demonstrating delayed development of a $0.8 \times 0.9 \times 0.3$ -cm FLAIR signal abnormality in the left superior temporal gyrus that did not enhance after administration of contrast. **D:** FLAIR MRI sequences obtained 1 month after laser ablation of the left superior temporal gyrus lesion.

shown in Fig. 2E. The patient suffered multifocal recurrence 20 months posttreatment and died soon after she was started on Avastin therapy.

Case 5

A 48-year-old man with a known GBM status-post gross-total resection of a right temporal tip lesion (Fig. 3A) developed a $1.3 \times 1.3 \times 1.2$ -cm right periventricular contrast-enhancing lesion (Fig. 3B). The results of the patient's neurological examination were nonfocal. The patient underwent SLA of the lesion, with the blue isotherm line completely covering the lesion. He emerged from the procedure neurologically unchanged. An MRI study taken 1 month after the procedure revealed the expected ablation (Fig. 3C). However, significant extension of contrast enhancement was observed immediately surrounding the ablation cavity. The patient died approximately 5 months after the procedure.

Discussion

We report our experience with SLA performed using the Monteris NeuroBlate system and SmartFrame stereotaxis in a conventional diagnostic MRI suite. In contrast to previous studies in which the procedures were performed in the setting of an intraoperative MRI unit,^{5,10} in an MRI suite with modified ventilation,⁸ or in a staged manner with the probe inserted in the operating room followed by ablation in the MRI suite,² our procedures were performed entirely in the setting of an unmodified diagnostic MRI suite. Importantly, all of our patients underwent SLA during which the biopsy forceps or the fiberoptic probes were repeatedly removed, repositioned, and reinserted into the cranium. Due to complex lesion morphology, 70% of our patients underwent multitrajectory SLA to achieve adequate tumor ablation. These aspects of our SLA fundamentally differ from those previously reported for treat-

FIG. 2. Case 4. Laser ablation course. **A:** Axial (panel i) and coronal (panel ii) postcontrast T1-weighted MR images, and a sagittal T1-weighted MR image obtained without contrast (panel iii) demonstrating a 3.8 × 2.6 × 3.3-cm left temporoparietal cystic lesion with a contrast-enhancing nodule. **B:** A first trajectory was used to obtain a biopsy sample of the nodular portion of the lesion. **C:** Photomicrograph showing a moderate to highly cellular pleomorphic and mitotically active glioma. H & E, original magnification ×40. **D:** A second trajectory (panel i) was used, targeting the center of the cystic lesion for drainage (serial axial T1-weighted MR images demonstrating cyst drainage seen in panels ii–iv). **E:** T1-weighted postcontrast MRI sequences obtained 1 year posttreatment.

FIG. 3. Case 5. Laser ablation course. **A:** Postcontrast axial T1-weighted MRI before (panel i) and after (panel ii) gross-total resection of a right temporal tip lesion. **B:** Postcontrast axial and coronal T1-weighted MRI sequences demonstrating the development of a $1.3 \times 1.3 \times 1.2$ -cm right periventricular contrast-enhancing lesion. **C:** One month after ablation, postcontrast axial and coronal T1-weighted MRI studies demonstrating post-SLA changes, with significant contrast enhancement seen surrounding the ablation cavity.

ment of epilepsy foci, where a single-pass, single-trajectory approach was used.^{9,15} During every probe insertion and reinsertion (a total of 21 such stereotactic insertions), we found the accuracy of the SmartFrame stereotaxis to be submillimeter. All patients have been followed for > 6 months without report of infection, perioperative morbidities, or unplanned 30-day readmission. These results suggest the accuracy of SmartFrame stereotaxis and the safety of performing SLAs in the setting of a diagnostic MRI suite.

Our study further provides a resource for time allocation to SLA performed in conventional MRI suites as well as a cost estimation related to this time interval. Our experience indicates that a single-trajectory SLA can be completed in approximately 4 hours, with 1 hour added for each trajectory thereafter. An additional 1–2 hours should be added for intubation, extubation, line placement, and other anesthesia considerations. Because specialized anesthesia equipment and preparation are required for patient care in the MRI suite, failure to prepare appropriately will inevitably lengthen the time in the MRI suite. For instance, the significant discrepancy between the SLA procedure time (240 minutes) and time in the MRI suite (553 minutes) for the patient in Case 10 resulted from issues related to anesthesia equipment malfunction and inadequate preparation.

Interpretation of the overall survival data in a 10-patient series warrants extreme caution. Nevertheless, we

would like to provide the following discussion points in the context of the broader GBM literature. First, the observation that patients with *IDH1*-mutated GBM exhibit the longest overall survival is generally consistent with the published literature.^{3,14} To the extent that increased tumor resection improves the overall survival of patients with *IDH*-mutated tumors,¹ and tumor ablation was achieved by SLA, our results suggest that SLA is of benefit in patients with *IDH*-mutated GBM. To our knowledge, this is the first documentation of SLA in patients with *IDH*-mutated GBM. Second, the poor survival of patients who underwent SLA after Avastin treatment failed is also consistent with published reports about the aggressive behavior of Avastin-resistant GBM.^{4,11,12} Thus, although our data suggest that SLA can be performed in this setting, a judicious risk-benefit analysis is warranted in considering the procedure. Finally, the immediate development of contrast-enhancing lesion adjacent to the blue isotherm line is a grim reminder that microscopic GBM foci exist outside of the visible contrast-enhancing volume.^{13,16} In this context, SLA should only be considered if performed in the context of an integrated regimen of chemotherapy, immunotherapy, targeted therapy, and/or RT.

As a case series with a small sample size, our study is subject to the limitations inherent in this study design. Despite these limits, our study demonstrates the safety of performing SLA in a conventional, unmodified MRI suite. Moreover, when our study is interpreted in the context of

the published GBM literature, insights emerge to provide the basis for consequential discussions and for rational design of future trials. Meaningful use of the procedural time and MRI suite time reported here require adjustment for differences in institutional workflow as well as time associated with performing a new procedure.

Conclusions

Our study demonstrates the accuracy of the Smart-Frame device for guiding multitrajectory SLA, and it supports the safety of performing these procedures in a conventional MRI suite.

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Disclosures

Dr. Chen is a consultant for Monteris Medical and has consulted for MRI Interventions.

Author Contributions

Conception and design: Chen. Acquisition of data: Chen, Rennert, Hamelin, Chang, Lemkuil. Analysis and interpretation of data: Chen, Rennert, Carroll, Ali. Drafting the article: Chen, Rennert, Carroll, Ali. Critically revising the article: Chen, Rennert, Carroll, Ali, Hamelin, Chang. Reviewed submitted version of manuscript: all authors. Approved the final version of the manuscript on behalf of all authors: Chen.

Supplemental Information

Videos

Video Abstract. <https://vimeo.com/182693913>.

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