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# Evaluating laser interstitial thermal therapy for newly diagnosed, deep-seated, large-volume glioblastoma: survival and outcome analysis

**Adham M. Khalafallah, MD,[1] Khushi H. Shah, BS,[1] Maxon V. Knott, BS,[1] Chandler N. Berke, BS,[1] Ashish H. Shah, MD,[1,2] Ricardo J. Komotar, MD,[1,2] and Michael E. Ivan, MD[1,2]**

[1]Department of Neurological Surgery, University of Miami Miller School of Medicine, Miami; and [2]Sylvester Comprehensive Cancer Center, University of Miami Health System, Miami, Florida

**OBJECTIVE** Laser interstitial thermal therapy (LITT) has emerged as an alternative for treating glioblastoma (GBM) in patients deemed unsuitable for resection due to deep-seated or eloquent location, age, or comorbidities. However, its safety and efficacy in large-volume, deep-seated, newly diagnosed GBM (nGBM) tumors remain insufficiently studied. Therefore, the authors aimed to assess the outcomes of LITT in the treatment of deep-seated, large-volume nGBM.

**METHODS** A retrospective analysis of patients with nGBM who underwent LITT between February 2013 and August 2023 was conducted. Patients with deep-seated tumor volume ≥ 10 $cm^3$ treated with LITT were compared to patients with deep-seated tumor volume < 10 $cm^3$. Demographic, perioperative, and follow-up data were collected and compared among both groups. Kaplan-Meier survival analysis and Cox proportional hazards regression were performed to evaluate the impact of various clinical and treatment-related factors on patient survival.

**RESULTS** A total of 33 patients in the study group (mean ± SD age 65.7 ± 10.2 years, 58% male) with mean tumor volume 36.0 ± 21.6 $cm^3$ were compared to 23 controls (mean age 67.0 ± 12.5 years, 61% male) with mean tumor volume 5.2 ± 2.7 $cm^3$. There were no significant differences in hospital length of stay (p = 0.494), temporary neurological deficits and edema within 30 days (p = 0.705 and p > 0.999, respectively), 30-day readmissions (p = 0.139), < 30-day complications (p = 0.918), complications between 30 days and 3 months (p = 0.903), and new motor and speech deficits within 3 months (p = 0.883 and p > 0.999, respectively) between the study and control groups. Kaplan-Meier analysis did not reveal any statistically significant difference in overall survival (OS) between groups (p = 0.227). Multivariate analysis indicated that tumor volume did not significantly affect the hazard ratio for individuals undergoing LITT (HR 1.16, 95% CI 0.83–3.29, p = 0.150).

**CONCLUSIONS** This pilot study suggests that LITT is safe for treating patients with large-volume, deep-seated nGBM compared to those with small-volume tumor. Although there appears to be improved OS in patients with smaller lesions with greater EOA, significance was not achieved in this cohort.

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**KEYWORDS** glioblastoma; laser interstitial thermal ablation; large volume; management; complications; newly diagnosed

Glioblastoma (GBM) remains the most common malignant primary brain tumor, with an incidence of 3.19 cases per 100,000 individuals, a high recurrence rate, and a median overall survival (OS) of approximately 15 months despite aggressive treatment.[1,2] According to National Comprehensive Cancer Network guidelines, maximal safe resection followed by radiotherapy with concurrent and adjuvant chemotherapy is the standard of care for newly diagnosed GBM (nGBM).[3,4] Challenges such as tumor location in eloquent areas or deep areas such as the basal ganglia or crossing the corpus callosum, along with concerns about surgery tolerance due to age and comorbidities, complicate resection.[5–8] Although extent of resection (EOR) correlates with OS, aggressive resection poses risks to eloquent brain and may adversely affect survival.[9]

Laser interstitial thermal therapy (LITT) has emerged as a minimally invasive, ablative technique for cytoreduction of unresectable or recurrent GBM, offering an alternative to traditional craniotomy.[10–14] Beyond cytoreduction, LITT-induced thermal disruption of the blood-brain barrier enhances local and systemic drug delivery, potentially

**ABBREVIATIONS** EOA = extent of ablation; EOR = extent of resection; GBM = glioblastoma; KPS = Karnofsky Performance Scale; LITT = laser interstitial thermal therapy; mFI-11 = modified 11-item frailty index; nGBM = newly diagnosed GBM; OS = overall survival; PFS = progression-free survival.

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increasing progression-free survival (PFS).[12,15,16] Most literature on LITT for GBM focuses on tumor volumes typically ranging from 1 to 60 $cm^3$, with a median volume of approximately 10 $cm^3$ across recent studies.[14,17–20] Some studies hypothesize that larger initial tumor sizes (> 10 $cm^3$) may impact LITT efficacy due to the risk of incomplete ablation.[15,21,22] However, to date, no study has specifically analyzed LITT outcomes and efficacy in large nGBM. Therefore, our study aimed to compare LITT outcomes in patients with large, deep-seated nGBM, defined as tumor volumes ≥ 10 $cm^3$,[23] with those with smaller deep-seated nGBM (< 10 $cm^3$).

## Methods

### Patient Selection

After Institutional Review Board approval, a retrospective chart review was conducted of all patients treated with LITT at our institution from February 2013 to August 2023. LITT was offered to patients deemed high-risk surgical candidates due to age, comorbidities, or tumor locations posing higher risks of postoperative neurological morbidity, as evaluated by the primary neurosurgeons (R.J.K., M.E.I., and A.H.S.). Detailed information regarding our LITT protocol has been previously reported.[24]

### Inclusion Criteria

We included patients with 1) age ≥ 18 years, 2) histopathological diagnosis of GBM, 3) preoperative Karnofsky Performance Scale (KPS) score > 50, 4) life expectancy of at least 3 months, and 5) no contraindications to MRI. Patients with recurrent GBM were excluded from this study. Patients lacking postoperative follow-up were excluded from the analysis. At our institution, patients who undergo LITT for nGBM include those with deep-seated lesions or lesions in eloquent brain that do not come to the surface, and therefore only these locations were included. Deep-seated tumors were defined as those located in regions of the brain that are not easily accessible via traditional surgical approaches, specifically those in areas such as the basal ganglia, thalamus, hypothalamus, corpus callosum, internal capsule, hippocampus, and insular cortex. Patients with tumor volume ≥ 10 $cm^3$ were categorized under the study group, while those with tumor volume < 10 $cm^3$ were categorized under the control group.

### Data Collection

Patient demographic and preoperative data, including age at surgery, sex, preoperative KPS score, preoperative deficits, and modified 11-item frailty index (mFI-11) score, were collected. MR images were reviewed to obtain preoperative lesion characteristics, including location, laterality, and volume. The Philips PACS image system's freehand tool was used to measure lesion volume, as previously described.[24] Intraoperative data collected included operative time, ablation time, number of trajectories and passes, and extent of ablation (EOA). EOA was calculated as follows: EOA = postoperative ablation volume/preoperative tumor volume × 100.

Data on outcomes included postoperative deficits, KPS score, 30-day readmission, and postoperative complication. Postoperative complications were grouped as occurring either within 30 days postoperatively or 30 days to 3 months postoperatively and encompassed new-onset neurological deficits, complications, or other clinical occurrences. Information about adjuvant treatment (radiation therapy and/or chemotherapy) was collected. Data on OS, defined as the time from treatment to the date of death or last follow-up, were also obtained.

### Statistical Analysis

Comparison of the categorical variables between the study and control cohorts was performed using the chi-square and Fisher exact tests, as appropriate. Continuous variables were compared using either the Student t-test or Welch's t-test depending on the equality of variance tested using Levene's test. Mean and standard deviation were reported for all continuous variables, except for KPS and mFI-11 scores, for which median and IQR (25th–75th percentile) were used due to nonnormal distributions.

Kaplan-Meier survival curves were constructed to assess OS from the date of the LITT procedure. Univariable and multivariable Cox regression analyses were conducted to identify predictors of OS. Prior to finalization of the multivariate Cox model, exploratory interaction term analysis was performed to assess changes in the effects of the covariates based on the volume group variable.

In the final multivariable model, continuous variables were scaled, and the model was bootstrapped (n = 1000) with a penalizer of 0.1. The final variables included in the multivariate model were age at surgery, tumor volume > 10 $cm^3$, EOA, and 30-day readmission. Statistical significance was set at a p value < 0.05 for all analyses. Statistical analyses were performed using Python version 3.11.5 for MacOS and GraphPad Prism software version 10.1.2 (GraphPad Software Inc.).

## Results

### Patient Characteristics

During the study period, 313 patients underwent the LITT procedure at our institution. Of these, 56 patients met the inclusion criteria and had nGBM with tumors located deep in the cortex or underneath eloquent structures. These included 33 patients with tumor volume ≥ 10 $cm^3$ categorized as the study group and 23 patients with tumor volumes < 10 $cm^3$ categorized as the control group. The mean ± SD (range) preoperative tumor volume in the study group was 36.0 ± 21.6 (11.34–91.73) $cm^3$ compared to 5.2 ± 2.7 (0.36–9.63) $cm^3$ in the control group (p < 0.001). Figure 1 shows representative MRI slices of the patients with tumors ≥ 10 $cm^3$ categorized under the study group.

Patient demographic, clinical, and radiological characteristics are detailed in Table 1. There were no significant differences in age, sex, tumor location, mFI-11, or preoperative deficits between the two groups. Although the median (IQR) KPS scores were similar in both groups, the difference was statistically significant (80 [70–80] for the study group vs 80 [80–80] for the control group, p = 0.009).

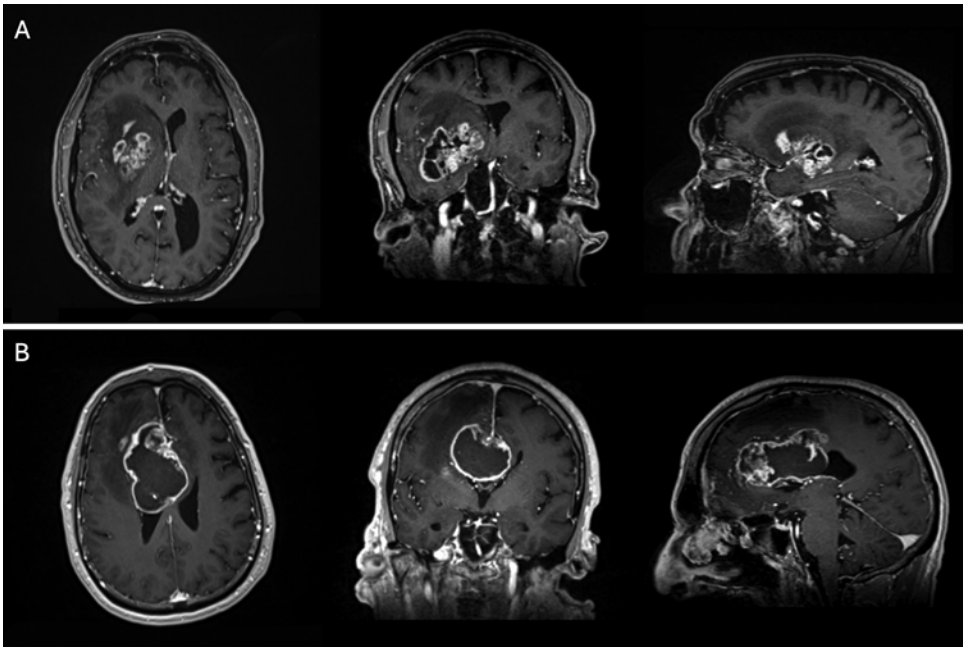


**FIG. 1.** Preoperative T1-weighted MR images with contrast of sample cases in the study group (≥ 10 $cm^3$) showing patients with nGBM with a 45.86-$cm^3$ lesion involving the basal ganglia (**A**) and a 79.56-$cm^3$ lesion involving the bilateral frontal lobe and anterior corpus callosum (**B**).

### Operative Data

Regarding operative data, the mean procedure duration, ablation time, and number of pullbacks were greater in the study group, and the differences were statistically significant (Table 2). There was no significant difference in the number of trajectories between the two groups (p = 0.113). Moreover, EOA was significantly lower in the study group compared to the control group (121.2% ± 47.9% vs 195.2% ± 127.1%, p = 0.013).

### Outcomes

There were no significant differences in the mean length of hospital stay and rates of temporary neurological deficits within 30 days and 30-day readmission (Table 3). Although 1 patient in the study group compared to 0 patients in the control group had cerebral edema within 30 days, the difference was not statistically significant (p > 0.999). Similarly, while 7 patients (21.21%) in the study group compared to 6 patients (32.58%) in the control group had complications within 30 days, the difference was not statistically significant. Complications within 30 days in the study group included altered mental status (n = 2), cerebral edema (n = 1), hydrocephalus (n = 1), intracranial hemorrhage (n = 1), seizure (n = 1), and urinary tract infection (n = 1). In comparison, 30-day complications in the control group included aphasia (n = 1), anaphylactic cardiac arrest (n = 1), hyperglycemia (n = 1), right-sided hemiparesis (n = 1), and seizure (n = 2) (p = 0.918). Moreover, there were no significant differences between the study and control groups in terms of the incidence of complications from 30 days to 3 months postsurgery (28% vs 22%, p = 0.903). These complications in the study group included altered mental status (n = 2), cerebral edema (n = 1), deep vein thrombosis (n = 1), impaired balance (n = 1), noncommunicating hydrocephalus (n = 1), and sinus bradycardia (n = 1). In contrast, complications within 30 days to 3 months in the control group included altered mental status (n = 1), anaphylaxis (n = 1), aphasia (n = 1), and dysphagia (n = 1) (p = 0.903). Finally, there were no significant differences in the development of new motor and speech deficits within 3 months of surgery.

### Survival Outcomes and Predictors of Survival

The mean OS was longer in the control group (392 days vs 282 days). However, Kaplan-Meier analysis (Fig. 2) showed no statistically significant difference in OS between the two groups (p = 0.227).

Univariate Cox regression revealed that older age at surgery (HR 1.04, 95% CI 1.01–1.08, p = 0.007) and 30-day readmission rate (HR 6.26, 95% CI 2.24–17.50, p < 0.001) were factors predictive of reduced OS. EOA and preoperative tumor volume were nonsignificant on univariate analysis (Table 4).

In fitting the Cox model, interaction terms showed no significant disproportionate effects of the covariates based on the volume group. Thus, no interaction terms were included in the final model. In the final multivariate Cox analysis (Fig. 3, Table 4), older age at surgery was associated with a significant increase in the hazard ratio for the entire cohort (HR 1.73, 95% CI 1.19–2.51, p < 0.005). Similarly, 30-day readmission increased the hazard ratio (HR 4.92, 95% CI 1.74–13.92, p < 0.005). EOA did not significantly alter the hazard ratio in the sample (p = 0.690). Importantly, patients with large-volume tumors also did not show a significantly increased hazard ratio (p = 0.150).

**TABLE 1. Patient demographic and tumor characteristics**

| Variable | Study Group (n = 33) | Control Group (n = 23) | p Value |
|---|---|---|---|
| Demographic | | | |
| Age, yrs | 65.7 ± 10.2 | 67.0 ± 12.5 | 0.663 |
| Male sex | 19 (58) | 14 (61) | >0.999 |
| Preop KPS score | 80 (70–80) | 80 (80–80) | **0.009** |
| Preop mFI-11 score | 18 (9–18) | 18 (9–18) | 0.600 |
| Preop neurological deficit | 30 (91) | 20 (87) | 0.976 |
| Preop seizure | 7 (21) | 9 (39) | 0.246 |
| Tumor characteristics | | | |
| Preop tumor vol, $cm^3$ | 36.0 ± 21.6 | 5.2 ± 2.7 | **<0.001** |
| Max tumor diameter, cm | 4.95 ± 1.14 | 2.72 ± 0.94 | **<0.001** |
| Supratentorial | 33 (100) | 22 (96) | 0.855 |
| Infratentorial | 0 (0) | 1 (4) | 0.855 |
| Side | | | |
| Rt | 16 (48.48) | 5 (21.74) | **0.024** |
| Lt | 10 (30.30) | 15 (65.22) | **0.009** |
| Bilat | 7 (21.21) | 3 (13.04) | 0.500 |
| Location* | | | |
| Frontal | 10 (30.30) | 7 (30.43) | 0.779 |
| Temporal | 11(33.33) | 9 (39.13) | >0.999 |
| Parietal | 12 (36.36) | 6 (26.09) | 0.270 |
| Cerebellum | 0 (0.00) | 1 (4.35) | 0.450 |
| Involvement of deep-seated structures | | | |
| Corpus callosum | 11 (33.33) | 6 (26.09) | 0.768 |
| Hippocampus | 6 (18.18) | 6 (26.09) | 0.522 |
| Basal ganglia | 5 (15.15) | 2 (8.69) | 0.688 |
| Insula | 4 (12.12) | 2 (8.69) | >0.999 |
| Thalamus | 4 (12.12) | 4 (4.35) | 0.704 |
| Amygdala | 3 ( 9.09) | 2 (8.69) | >0.999 |
| Cerebellum | 0 (0) | 1 (4.35) | >0.999 |

Values are shown as number (%), mean ± SD, and median (IQR) unless indicated otherwise. Boldface type signifies statistical significance ($p < 0.05$).
* Predominant locations had extension into the deep-seated structures listed.

**TABLE 2. Operative characteristics**

| Variable | Study Group (n = 33) | Control Group (n = 23) | p Value |
|---|---|---|---|
| Op time, mins* | 256 ± 70.7 | 212 ± 84 | **0.045** |
| Ablation time, mins* | 11.5 ± 4.6 | 7.1 ± 3.1 | **<0.001** |
| No. of trajectories | | | |
| 1 | 27 (82) | 22 (96) | 0.113 |
| 2 | 6 (18) | 1 (4) | 0.113 |
| No. of pullbacks | 4 (3–4) | 2 (1–3.5) | **<0.001** |
| EOA, % | 121.2 ± 47.9 | 195.2 ± 127.1 | **0.013** |

Values are shown as number (%), mean ± SD, and median (IQR) unless indicated otherwise. Boldface type signifies statistical significance ($p < 0.05$).
* Data were unavailable for all patients.

**TABLE 3. Treatment outcomes**

| Variable | Study Group (n = 33) | Control Group (n = 23) | p Value |
|---|---|---|---|
| Hospital LOS, days | 3.9 ± 3.5 | 3.3 ± 2.1 | 0.494 |
| New temporary neurological deficit <30 days* | 1 (3) | 2 (10) | 0.705 |
| Complications <30 days* | 7 (21.21) | 6 (32.58) | 0.918 |
| Postop edema <30 days* | 1 (4) | 0 (0) | >0.999 |
| 30-day readmission | 5 (15) | 0 (0) | 0.139 |
| Complications 30 days to 3 mos* | 9 (28) | 4 (22) | 0.903 |
| New motor deficit <3 mos* | 2 (8) | 2 (38) | 0.883 |
| New speech deficit <3 mos* | 3 (10) | 2 (15) | >0.999 |
| Postop radiation therapy* | 24 (92) | 16 (100) | 0.696 |
| Postop chemotherapy* | 26 (100) | 14 (93) | 0.778 |
| OS, days | 282 ± 291 | 392 ± 361 | 0.213 |
| Death | 25 (76) | 16 (70) | 0.835 |

LOS = length of stay.
Values are shown as number (%) or mean ± SD unless indicated otherwise.
* Data were unavailable for all patients.

No variables violated the Cox proportional hazards assumption, and multicollinearity was not observed (variance inflation factor < 1.5).

## Discussion

Since its first description by Sugiyama et al. in 1990,[25] LITT has emerged as an effective treatment modality for direct cytoreduction of GBM.[26] Its minimally invasive nature has led to a recent increase in its adoption for the surgical management of GBM.[17,26] Initially, concerns were raised regarding the efficacy of LITT for large (≥ 10 $cm^3$) or nonspherical tumors,[15,27] but subsequent studies demonstrated that multiple catheters and trajectories could achieve complete ablation despite their tumor size or morphology.[15] Many authors have raised concerns about increased perioperative and postoperative complications, particularly pertaining to cerebral edema and mass effect.[26,28]

### Study Overview

In this study, we investigated whether LITT increased complications or affected survival in patients with large nGBM ≥ 10 $cm^3$ compared to controls. We found no significant differences in postoperative complications or survival outcomes between the study and control groups.

### Operative Data

It is intuitive to expect greater mean procedure duration, ablation time, and number of pullbacks while treating large-volume nGBM. Our findings of statistically significant differences between the study and control groups in terms of these operative parameters align with those of other authors.[23,29] Despite this, our study found no significant difference in postoperative outcomes between the study and control groups.

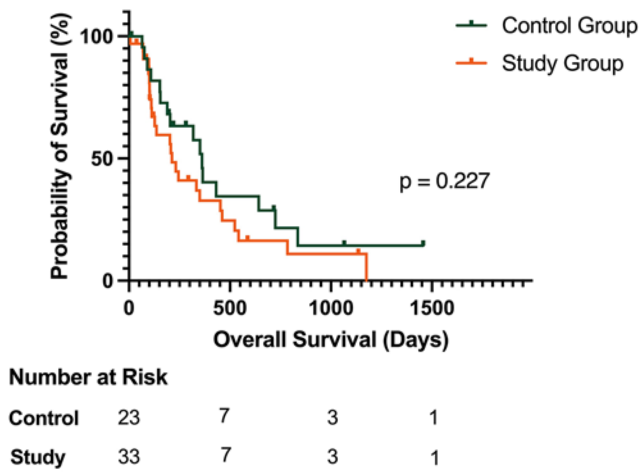


**FIG. 2.** Kaplan-Meier plot comparing OS between the study and control groups. No significant difference was observed between groups.

### Cerebral Edema Risk

LITT for large GBM in our study did not increase malignant cerebral edema risk. There was no associated significant overall perioperative or postprocedural morbidity related to cerebral edema or resultant mass effect. Contrastingly, the systematic review of Alattar et al. on LITT noted edema risk in brain metastases, wherein patients with lesion volumes ranging from 29 to 70 $cm^3$ developed postablation malignant edema, thereby suggesting caution for lesions ≥ 10 $cm^3$.[23] Our study had 1 patient in the study group develop cerebral edema within 30 days of surgery; however, none had malignant edema. Therefore, our study challenges the notion of avoiding LITT solely based on lesion size.

### Extent of Ablation

Our findings of a lower EOA within our study group, as compared to the control group, align with the findings of other authors who demonstrated a negative linear relationship between preoperative lesion size and EOA.[5] EOA has been likened to EOR for predicting PFS and OS in patients with GBM.[12,30] Our institution previously reported the association between greater EOA and survival in patients with nGBM,[12] showing an EOA threshold of 70% yielding the most significant differences in PFS and OS. Despite the study group having a lower EOA, both the study and control groups in our study had a mean EOA greater than 70%. Because of this, it is understandable that there was no significant difference in OS between groups. Our hypothesis is that in addition to ablation of the surrounding tumor, LITT likely also causes a local immune response that assists in providing a treating effect toward the tumor.[29,31] This finding supports the use of LITT for large-volume GBM and challenges the narrative that one cannot achieve sufficient ablation to yield a benefit in this difficult-to-treat patient population.

### Survival and Prognostic Factors

Age at surgery and 30-day readmission significantly impacted OS in our cohort. Our findings align with those of other authors who similarly noted that age negatively impacted OS.[19] Although age is a significant negative prognostic factor for GBM,[32,33] some studies did not show it to influence either PFS or OS after LITT.[34] Variability in the impact of age on post-LITT survival warrants further exploration, yet we believe that older age is associated with decreased intracranial compliance, increased frailty, and brain elastance,[35–38] thereby negatively affecting OS after LITT.

Our findings regarding the significant impact of 30-day readmission on OS are consistent with those of other studies in the literature.[39–41] Botros et al. found that even after adjusting for age, mFI-5 score, KPS score, tumor EOR, and total number of surgical procedures, 30-day readmis-

**TABLE 4. Univariate and multivariate Cox regression analyses of factors affecting OS**

| Covariates | Univariate Analysis | | | | Multivariate Analysis | | | |
|---|---|---|---|---|---|---|---|---|
| | HR | Lower 95% CI Limit | Upper 95% CI Limit | p Value | HR | Lower 95% CI Limit | Upper 95% CI Limit | p Value |
| Age (yrs) | 1.04 | 1.01 | 1.08 | **0.007** | 1.73 | 1.19 | 2.51 | **<0.005** |
| Male sex | 1.24 | 0.65 | 2.37 | 0.507 | | | | |
| Preop KPS score | 1.01 | 0.96 | 1.06 | 0.608 | | | | |
| Preop mFI-11 score | 4.33 | 0.34 | 55.33 | 0.259 | | | | |
| Preop neurological deficit | 2.42 | 0.73 | 8.03 | 0.147 | | | | |
| Preop seizure | 0.88 | 0.45 | 1.74 | 0.720 | | | | |
| Preop tumor vol >10 $cm^3$ | 1.47 | 0.78 | 2.77 | 0.230 | 1.66 | 0.83 | 3.29 | 0.150 |
| No. of pullbacks | 1.00 | 0.81 | 1.25 | 0.981 | | | | |
| EOA | 1.00 | 0.99 | 1.00 | 0.259 | 1.08 | 0.75 | 1.54 | 0.690 |
| Hospital LOS (days) | 0.95 | 0.86 | 1.06 | 0.344 | | | | |
| New temporary neurological deficit <30 days | 1.37 | 0.33 | 5.78 | 0.665 | | | | |
| 30-day readmission | 6.26 | 2.24 | 17.50 | **<0.001** | 4.92 | 1.74 | 13.92 | **<0.005** |
| Complications 30 days to 3 mos | 1.21 | 0.59 | 2.49 | 0.742 | | | | |

Boldface type signifies statistical significance ($p < 0.05$).

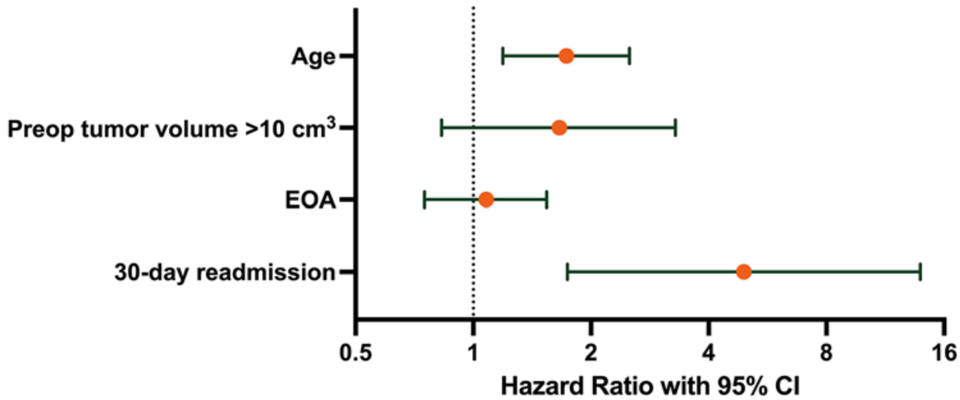


**FIG. 3.** Multivariate Cox proportional hazards model. Older age at surgery and 30-day readmission were associated with higher risk of death. Patients with larger tumor volumes were not at significantly increased risk of death.

sion remained associated with increased risk of death.[39] Our study reinforces the need to closely monitor patients readmitted within 30 days, keeping these negative prognostic outcomes in mind.

### Institutional Experience and Evolution

Our institution's LITT experience over the past decade (2013–2023) suggests that we are offering LITT to patients with larger tumor volumes as compared to the past.[24,42] We believe that in parallel with technological advancements, as brain tumor centers continue to perform LITT and as neurosurgeons gain experience, the criteria for what tumor volume is considered amenable to ablation should expand.

### Strengths and Limitations

Our study was inherently limited by its retrospective nature and small patient size. To overcome these limitations, we included only patients with complete records available. Additionally, this was a single-institution study, but it involved patients managed under three neurosurgeons. Because our study was not powered to detect small differences in OS outcomes, these data cannot be interpreted as indicative of a trend, and any observed differences should be interpreted with caution. Future studies and validation in larger cohorts and multi-institutional collaborations are crucial to provide the statistical power needed.

Despite these limitations, to the best of our knowledge, we report the first and the largest series to specifically evaluate the use of LITT for deep-seated, large-volume nGBM. Our study assessed its viability as a safe and efficacious treatment option in this vulnerable patient population, with the largest patient cohort compared to those of any existing volumetric subgroup analyses. We believe our results would help counsel patients regarding management options for treating deep-seated, large-volume nGBM.

## Conclusions

Our study indicates that LITT is safe for large, deep-seated nGBM. There was no increase in postoperative morbidity for patients with large nGBM. Age at surgery and readmission significantly impacted survival, irrespective of tumor size. Further research is warranted to validate our findings and optimize patient outcomes in this challenging patient population.

## References

1. Bikfalvi A, da Costa CA, Avril T, et al. Challenges in glioblastoma research: focus on the tumor microenvironment. *Trends Cancer*. 2023;9(1):9-27.
2. Liau LM, Ashkan K, Brem S, et al. Association of autologous tumor lysate-loaded dendritic cell vaccination with extension of survival among patients with newly diagnosed and recurrent glioblastoma: a phase 3 prospective externally controlled cohort trial. *JAMA Oncol*. 2023;9(1):112-121.
3. von Mehren M, Kane JM, Bui MM, et al. NCCN Guidelines Insights: Soft Tissue Sarcoma, Version 1.2021. *J Natl Compr Canc Netw*. 2020;18(12):1604-1612.
4. Stupp R, Mason WP, van den Bent MJ, et al. Radiotherapy plus concomitant and adjuvant temozolomide for glioblastoma. *N Engl J Med*. 2005;352(10):987-996.
5. Shah AH, Burks JD, Buttrick SS, Debs L, Ivan ME, Komotar RJ. Laser interstitial thermal therapy as a primary treatment for deep inaccessible gliomas. *Neurosurgery*. 2019;84(3):768-777.
6. Wright J, Chugh J, Wright CH, et al. Laser interstitial thermal therapy followed by minimal-access transsulcal resection for the treatment of large and difficult to access brain tumors. *Neurosurg Focus*. 2016;41(4):E14.
7. Awad AW, Karsy M, Sanai N, et al. Impact of removed tumor volume and location on patient outcome in glioblastoma. *J Neurooncol*. 2017;135(1):161-171.
8. Barnholtz-Sloan JS, Williams VL, Maldonado JL, et al. Patterns of care and outcomes among elderly individuals with primary malignant astrocytoma. *J Neurosurg*. 2008;108(4):642-648.
9. McGirt MJ, Mukherjee D, Chaichana KL, Than KD, Weingart JD, Quinones-Hinojosa A. Association of surgically acquired motor and language deficits on overall survival after resection of glioblastoma multiforme. *Neurosurgery*. 2009;65(3):463-470.
10. Thomas JG, Rao G, Kew Y, Prabhu SS. Laser interstitial thermal therapy for newly diagnosed and recurrent glioblastoma. *Neurosurg Focus*. 2016;41(4):E12.
11. de Groot JF, Kim AH, Prabhu S, et al. Efficacy of laser interstitial thermal therapy (LITT) for newly diagnosed and recurrent *IDH* wild-type glioblastoma. *Neurooncol Adv*. 2022;4(1):vdac040.

12. Di L, Wang CP, Shah AH, et al. A cohort study on prognostic factors for laser interstitial thermal therapy success in newly diagnosed glioblastoma. *Neurosurgery*. 2021;89(3):496-503.
13. Daggubati LC, Ramos-Fresnedo A, Merenzon MA, et al. Bilateral laser interstitial thermal therapy for butterfly gliomas compared with needle biopsy: a preliminary survival study. *Oper Neurosurg (Hagerstown)*. 2023;25(5):435-440.
14. Jubran JH, Scherschinski L, Dholaria N, et al. Magnetic resonance-guided laser interstitial thermal therapy for recurrent glioblastoma and radiation necrosis: a single-surgeon case series. *World Neurosurg*. 2024;182:e453-e462.
15. Ashraf O, Patel NV, Hanft S, Danish SF. Laser-induced thermal therapy in neuro-oncology: a review. *World Neurosurg*. 2018;112:166-177.
16. Bartlett S, Nagaraja TN, Griffith B, et al. Persistent periablation blood-brain barrier opening after laser interstitial thermal therapy for brain tumors. *Cureus*. 2023;15(4):e37397.
17. Muir M, Patel R, Traylor JI, et al. Laser interstitial thermal therapy for newly diagnosed glioblastoma. *Lasers Med Sci*. 2022;37(3):1811-1820.
18. Muir M, Traylor JI, Gadot R, Patel R, Prabhu SS. Repeat laser interstitial thermal therapy for recurrent primary and metastatic intracranial tumors. *Surg Neurol Int*. 2022;13:311.
19. Traylor JI, Patel R, Muir M, et al. Laser interstitial thermal therapy for glioblastoma: a single-center experience. *World Neurosurg*. 2021;149:e244-e252.
20. Fadel HA, Haider S, Pawloski JA, et al. Laser interstitial thermal therapy for first-line treatment of surgically accessible recurrent glioblastoma: outcomes compared with a surgical cohort. *Neurosurgery*. 2022;91(5):701-709.
21. Beechar VB, Prabhu SS, Bastos D, et al. Volumetric response of progressing post-SRS lesions treated with laser interstitial thermal therapy. *J Neurooncol*. 2018;137(1):57-65.
22. Sanvito F, Telesca D, Cho NS, et al. Small pretreatment lesion size and high sphericity as favorable prognostic factors after laser interstitial thermal therapy in brain metastases. *J Neurosurg*. 2023;140(2):338-349.
23. Alattar AA, Bartek J Jr, Chiang VL, et al. Stereotactic laser ablation as treatment of brain metastases recurring after stereotactic radiosurgery: a systematic literature review. *World Neurosurg*. 2019;128:134-142.
24. Gurses ME, Lu VM, Gecici NN, et al. Laser interstitial thermal therapy in neurosurgery: a single-surgeon experience of 313 patients. *J Neurosurg*. Published online May 31, 2024. doi:10.3171/2024.3.JNS245
25. Sugiyama K, Sakai T, Fujishima I, Ryu H, Uemura K, Yokoyama T. Stereotactic interstitial laser-hyperthermia using Nd-YAG laser. *Stereotact Funct Neurosurg*. 1990;54-55:501-505.
26. Kamath AA, Friedman DD, Akbari SHA, et al. Glioblastoma treated with magnetic resonance imaging-guided laser interstitial thermal therapy: safety, efficacy, and outcomes. *Neurosurgery*. 2019;84(4):836-843.
27. Xie R, Wu Z, Zeng F, et al. Retro-enantio isomer of angiopep-2 assists nanoprobes across the blood-brain barrier for targeted magnetic resonance/fluorescence imaging of glioblastoma. *Signal Transduct Target Ther*. 2021;6(1):309.
28. Pisipati S, Smith KA, Shah K, Ebersole K, Chamoun RB, Camarata PJ. Intracerebral laser interstitial thermal therapy followed by tumor resection to minimize cerebral edema. *Neurosurg Focus*. 2016;41(4):E13.
29. Chandar JS, Bhatia S, Ingle S, et al. Laser interstitial thermal therapy induces robust local immune response for newly diagnosed glioblastoma with long-term survival and disease control. *J Immunother*.2023;46(9):351-354.
30. Shah AH, Semonche A, Eichberg DG, et al. The role of laser interstitial thermal therapy in surgical neuro-oncology: series of 100 consecutive patients. *Neurosurgery*. 2020;87(2):266-275.
31. Figueroa JM, Semonche A, Magoon S, et al. The role of neutrophil-to-lymphocyte ratio in predicting overall survival in patients undergoing laser interstitial thermal therapy for glioblastoma. *J Clin Neurosci*. 2020;72:108-113.
32. Laigle-Donadey F, Greffard S. Management of glioblastomas in the elderly population. *Rev Neurol (Paris)*. 2020;176(9):724-732.
33. Blakstad H, Brekke J, Rahman MA, et al. Survival in a consecutive series of 467 glioblastoma patients: association with prognostic factors and treatment at recurrence at two independent institutions. *PLoS One*. 2023;18(2):e0281166.
34. Kaisman-Elbaz T, Xiao T, Grabowski MM, Barnett GH, Mohammadi AM. The impact of extent of ablation on survival of patients with newly diagnosed glioblastoma treated with laser interstitial thermal therapy: a large single-institutional cohort. *Neurosurgery*. 2023;93(2):427-435.
35. Cherain LGG, Barbosa MGS, Francisco GGOA, Cherain LMG, Frigieri G, Rabelo NN. Age as a predictive factor for reduced intracranial compliance in patients with headache. *Arq Neuropsiquiatr*. 2024;82(2):1-6.
36. Kiening KL, Schoening W, Unterberg AW, et al. Assessment of the relationship between age and continuous intracranial compliance. *Acta Neurochir Suppl (Wien)*. 2005;95:293-297.
37. Boraschi A, Hafner M, Spiegelberg A, Kurtcuoglu V. Influence of age on the relation between body position and non-invasively acquired intracranial pulse waves. *Sci Rep*. 2024;14(1):5493.
38. Czosnyka M, Czosnyka ZH, Whitfield PC, Donovan T, Pickard JD. Age dependence of cerebrospinal pressure-volume compensation in patients with hydrocephalus. *J Neurosurg*. 2001;94(3):482-486.
39. Botros D, Khalafallah AM, Huq S, et al. Predictors and impact of postoperative 30-day readmission in glioblastoma. *Neurosurgery*. 2022;91(3):477-484.
40. Nuño M, Ly D, Ortega A, et al. Does 30-day readmission affect long-term outcome among glioblastoma patients? *Neurosurgery*. 2014;74(2):196-205.
41. Dickinson H, Carico C, Nuño M, et al. Unplanned readmissions and survival following brain tumor surgery. *J Neurosurg*. 2015;122(1):61-68.
42. Merenzon MA, Bhatia S, Levy A, et al. The learning curve and clinical outcomes with 250 laser ablations for brain tumors: a pathway to experience. *Oper Neurosurg (Hagerstown)*. 2024;27(2):205-212.

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## Author Contributions

Conception and design: Khalafallah, K Shah, Knott, Berke, Komotar, Ivan. Acquisition of data: K Shah, Knott, Berke, Ivan. Analysis and interpretation of data: Khalafallah, K Shah, Knott, Berke, Ivan. Drafting the article: Khalafallah, K Shah, Knott, Berke, Komotar, Ivan. Critically revising the article: Khalafallah, K Shah, Knott, Berke, Ivan. Reviewed submitted version of manuscript: all authors. Approved the final version of the manuscript on behalf of all authors: Khalafallah. Statistical analysis: Khalafallah, Ivan. Administrative/technical/material support: Khalafallah, Knott, Berke. Study supervision: Khalafallah, Knott, Komotar, Ivan.

## Correspondence

Adham M. Khalafallah: University of Miami Miller School of Medicine, Miami, FL. adham.khalafallah@jhsmiami.org.