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RESEARCH

Laser interstitial thermal therapy versus stereotactic radiosurgery for first-time treatment of recurrent glioblastoma: a retrospective single-center study

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Abstract

Background Despite multimodal therapy, glioblastomas invariably recur. In focal recurrent glioblastoma IDH-wildtype (rGBM), local therapy options include laser interstitial thermal therapy (LITT) and stereotactic radiosurgery (SRS), but their relative utilities are unknown. The goal of this study is to compare the efficacy of these two treatment modalities in a homogeneous rGBM population.

Methods We conducted a retrospective study of patients undergoing surgical procedures for rGBM between 2010 and 2025. All patients underwent either LITT or SRS at first recurrence. Survival outcomes were assessed with univariable log-rank tests and multivariate Cox regression models. A propensity-score matching (PSM) was performed to address confounders.

Results 57 patients were identified; of these, 10 underwent LITT, and 47 underwent SRS. There was no difference in post-recurrence survival (PRS) between groups (11.5 months vs. 13.4 months, $p = 0.824$). There were no surgical complications in the LITT cohort. In the SRS cohort, there were two symptomatic radiation necrosis cases (0% vs. 4.3%, $p = 1.000$). Contrast-enhancing tumor volume at recurrence was larger in the LITT cohort (8.49 cm^3 vs. 1.91 cm^3, $p = 0.007$). To address this difference, we performed a PSM of two cohorts with 7 patients each. This PSM analysis also revealed no significant difference in survival outcomes.

Conclusion Within the limitations of a relatively small sample size, no statistically significant differences in outcomes were observed between LITT and SRS for the treatment of small, focal rGBM. Both modalities remain viable salvage options for small focal rGBM. Larger, multi-institutional studies are warranted.

Keywords Glioblastoma · IDH-WT · LITT · Recurrence treatment · SRS

Introduction

Glioblastoma (GBM) is the most common and aggressive primary malignant brain tumor in adults, accounting for nearly half of all malignant central nervous system neoplasms [1]. It is typically diagnosed in the fifth to sixth decade of life and carries a dismal prognosis, with a 5-year survival rate of only 6.8% [1]. Standard first-line therapy consists of maximal safe surgical resection followed by concurrent chemoradiotherapy with temozolomide [2]. Despite these interventions, recurrence is nearly universal, and median survival after recurrence remains only 9–11 months [3, 4]. Treatment of recurrent GBM (rGBM), therefore, remains a major clinical challenge, with no therapeutic modality proven in randomized trials to significantly prolong overall survival [5].

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Management of rGBM requires balancing local tumor control with preservation of neurological function in a population that has already undergone aggressive therapies. Aggressive interventions such as reoperation are often limited by tumor location, ongoing chemoradiotherapy, and overall patient condition. As a result, minimally invasive local therapies have gained increasing attention as potential salvage strategies. Among these, laser interstitial thermal therapy (LITT) and stereotactic radiosurgery (SRS) represent two distinct yet conceptually similar approaches—each aiming to achieve focal cytoablation or cytotoxicity within a confined target volume while minimizing additional injury to surrounding brain tissue. However, their mechanisms, risks, and durability of effect differ substantially, and the optimal selection between the two remains unclear. Laser interstitial thermal therapy (LITT) is a minimally invasive technique that uses MRI-guided thermal ablation to destroy pathological tissue.6 LITT has typically been used in patients with deep-seated or surgically inaccessible recurrent tumors, although recent reports have demonstrated its efficacy in surgically accessible tumors compared to resection with lower morbidity [7]. Recent studies have demonstrated its safety and feasibility, particularly in the context of recurrent high-grade gliomas [6,8–11]. However, these reports frequently include heterogeneous patient populations and variable definitions of recurrence, limiting the ability to draw firm conclusions about its comparative efficacy. On the other hand, stereotactic radiosurgery (SRS) is another minimally invasive strategy that delivers highly focused radiation to a defined target while sparing surrounding brain tissue [12]. SRS is commonly used for local tumor control in rGBM, and retrospective studies have shown that select patients may achieve meaningful progression-free and overall survival benefits [6, 11–19] Nonetheless, there is a lack of direct comparative evidence to guide clinicians in choosing between LITT and SRS for recurrent disease.

Given the growing clinical adoption of both LITT and SRS for rGBM, a direct comparison of their outcomes is warranted. The goal of this study was to compare the efficacy and safety of LITT and SRS in patients with first recurrence of GBM, aiming to identify clinical factors that may guide optimal treatment selection. Most previous studies lack homogenous cohorts by including patients treated at initial diagnosis and at later recurrences, and likewise failing to account for isocitrate dehydrogenase (IDH) status in their patient cohorts [4, 6, 7, 20]. Unlike these previous studies, our study emphasizes cohort homogeneity by exclusively examining patients diagnosed with GBM (IDH wild-type) treated with LITT or SRS at first recurrence. We incorporated propensity-score matching (PSM) to address potential confounders to further enhance cohort homogeneity, maximize generalizability, and minimize bias of our study.

Methods

Patient selection and data collection

We conducted a retrospective study spanning 2010 to 2025, following Institutional Review Board approval. A consent waiver was obtained from the ethics committee. The study adhered to STROBE reporting guidelines.

The eligibility criteria included patients aged > 18 years with confirmed glioblastoma per the 2021 World Health Organization (WHO) classification of the Central Nervous System (CNS) tumors [21]. All consecutive patients were included if treated for their first recurrence with LITT or single fraction SRS. Recurrence and subsequent treatment were identified and determined by consensus at a local multidisciplinary tumor board meeting using advanced brain tumor imaging (ABTI) modalities.

Exclusion criteria were patients without documented recurrence, those treated with alternative or combination modalities for the first recurrence, those with other diffuse gliomas, or those lacking complete clinical or imaging data.

Data were compiled in a REDCap database [4, 22, 23], including age, sex, anatomic locations, O6-methylguanine-DNA methyltransferase (MGMT) methylation status, extent of resection during primary treatment, and adjuvant and salvage. Karnofsky Performance Score (KPS) at the time of first recurrence was also assessed. Disease progression was monitored through routine follow-up MRIs every 2–3 months. Recurrence was determined according to the Response Assessment in Neuro-Oncology (RANO) criteria [24, 25]. Progression location was categorized as in-field, marginal/out-of-field, as previously described [26]. If patients presented with multifocal disease, they were categorized as out-of-field if any focus was out-of-field.

Laser interstitial thermal therapy

At our institution, LITT was performed using the Visualase™ MRI-guided laser ablation system (Medtronic Inc., Minneapolis, MN, USA). For most patients, a Leksell Stereotactic Frame (model G; Elekta Instruments AB, Stockholm, Sweden) was placed. In three patients within the LITT cohort, catheter placement was performed using robotic assistance with the ROSA One system (Zimmer Biomet, Warsaw, IN, USA). Ablation was performed according to protocols previously described [9, 10, 27–34]. For patients treated with LITT at first recurrence, the following were recorded: "skin to extubation" time, number of trajectories/fibers used, lesion involvement of eloquent areas, lesion depth (from dura to catheter terminus), complications, and hospital length of stay.

Stereotactic radiosurgery

SRS was performed using the Gamma Knife® system (Elekta Instruments AB, Stockholm, Sweden). The procedure was performed on all patients using a Leksell Stereotactic Frame (model G; Elekta Instruments AB, Stockholm, Sweden). Procedures were carried out according to previously described protocols with a target volume based on T1 contrast-enhanced MRI only, without additional margin [4, 13, 14, 35]. For patients undergoing SRS at first recurrence, both the prescribed dose and the isodose line percentage were recorded. Adverse radiation effects were systematically recorded. Radiation necrosis was identified using ABTI protocol or pathology reports from reoperation [36].

Volumetric analysis of recurrent tumors

Volumetric assessment was performed separately for the SRS and LITT cohorts using modality-specific imaging workflows. For patients treated with SRS, MRIs were evaluated in the SRS treatment plans using Syngo.Via® VB20 (Siemens Healthineers, Erlangen, Germany), as previously described [4, 24, 25]. For patients undergoing LITT, semi-automated volumetric segmentation was performed using Vitrea Advanced Visualization software (Olea Medical – Canon Medical Systems, CA, USA). Pre-ablation tumor volume was measured on the immediate pre-LITT postcontrast T1-weighted MRI by delineating the contrast-enhancing tumor. Post-ablation volume was assessed on the immediate post-LITT dynamic contrast-enhanced T1-weighted MRI sequences by delineating the ablation zone [37]. When available, noncontrast T1-weighted sequences were reviewed to help distinguish intrinsic post-ablation signal change from contrast enhancement. Residual enhancing tumor was defined as contrast-enhancing tumor present on the immediate post-LITT MRI outside the ablation zone or incompletely incorporated within the ablated region. Extent of ablation (EOA) was calculated by comparing the pre-ablation contrast-enhancing tumor volume with the residual post-ablation enhancing tumor volume using the following formula: EOA (%) = [(pre-ablation tumor volume − residual post-ablation tumor volume) / pre-ablation tumor volume] × 100.

All volumetric measurements were recorded in cubic centimeters. For multifocal tumors, each enhancing focus was segmented separately, and the total tumor burden was calculated as the sum of all individual foci. When multiple lesions were treated, the extent of ablation was calculated using the aggregate pre-ablation and residual post-ablation enhancing volumes.

Statistical analysis

The date of initial surgery was recorded as the date of diagnosis. The date of first recurrence was defined as the first routine follow-up MRI demonstrating disease progression per the RANO criteria [24, 25]. Post-recurrence survival (PRS), the primary outcome, was defined as the interval between the first recurrence and either death or last follow-up, with a data cutoff of July 25th, 2025. Secondary outcomes included second progression-free survival (PFS2), defined as the interval between first and second recurrence, and the overall survival (OS), defined as the time between initial diagnosis and death or last follow-up.

Statistical analysis was performed using EZR version 1.68 (Saitama Medical Center, Jichi Medical University, Saitama, Japan) and GraphPad Prism version 10.3.0 (GraphPad Software, Boston, Massachusetts, USA). Statistical significance was set at two-tailed $p < 0.05$ with 95% confidence intervals (CI). Nonparametric continuous variables and categorical data were analyzed using the Mann-Whitney U Test and Fisher's Exact Test, respectively. Survival outcomes were assessed with univariable log-rank tests and multivariate Cox regression models. Multivariable Cox regression analyses included variables that were statistically significant in univariable analysis, as well as age, KPS, tumor volume, and MGMT, as these have been shown in the literature to affect survival at recurrence [38, 39] PSM utilizing nearest-neighbor matching without replacement was applied to obtain a balanced 1:1 comparison with a caliper of 0.2 standard deviations of the logit of the PSM. Additionally, a subanalysis including patients with larger tumors in the SRS group ($>4cm^3$ – the 25th percentile of tumor size in the LITT group) was performed to evaluate more comparable tumor sizes. Kaplan-Meier curves were used to graph the survival rates. Missing data were handled using complete-case analysis; patients with unavailable clinical or imaging data for key variables were excluded from the relevant analyses.

Results

Study population

The initial population consisted of 559 patients diagnosed with GBM. After applying eligibility criteria, the final cohort included 57 patients with rGBM, classified according to the 2021 WHO criteria for CNS tumors. Of these, 10 were treated with LITT (Fig. 1A-B) and 47 with SRS (Fig. 1C-D). A flowchart of patient selection is depicted in Fig. 2.

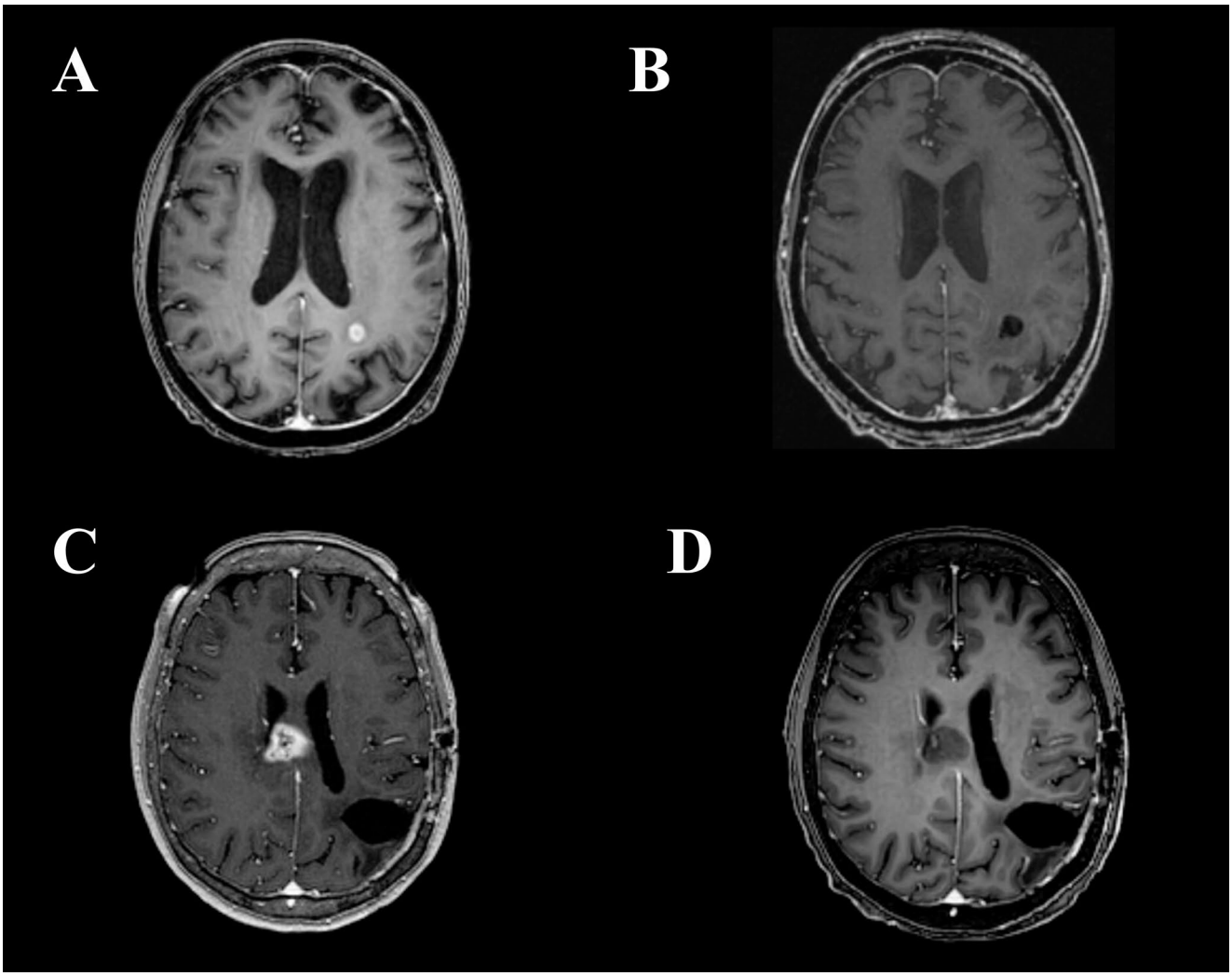

Fig. 1 **A**-**D** Comparable recurrent IDH-WT glioblastoma cases pre- and post-LITT (**A** and **B**) and pre- and post-SRS (**C** and **D**)

The median age was 59.5 years (IQR: 48.5–62.5 years) in the LITT group and 62 years (IQR: 55.5–67 years) in the SRS group. Baseline characteristics were largely comparable between groups (Table 1). However, CE tumor volume at recurrence was significantly larger in the LITT cohort compared to the SRS cohort (8.49 cm^3 vs. 1.91 cm^3, $p = 0.015$). MGMT methylation status was available for all patients in the LITT cohort and for 20 patients in the SRS cohort. Only 1 patient in the LITT group had a methylated MGMT, compared with 10 patients in the SRS group ($p = 0.049$). Progression-free survival (PFS) was identified as the time interval between initial diagnosis and first recurrence. There was no statistically significant difference in PFS between the LITT (6.1 months) and SRS (10.2 months) groups ($p = 0.228$) (Fig. 3A).

In the LITT group, the median surgical time was 216 min (IQR: 167–244), and the median hospital length of stay was 2 days (IQR: 1.25-2), Table 1. The number of trajectories ranged from 1 to 3, with 6 patients being treated with one trajectory, 3 with two trajectories, and 1 patient with three trajectories. The median EOA was 100% (range, 85–100%). Lastly, the median depth to lesion was 5.53 cm (IQR: 4.07–7.54). In the SRS group, the median dose was 18 Gy (IQR: 18–20), and the median isodose line was 53.5% (IQR: 50–60%). Additional salvage therapies at recurrence primarily included temozolomide, bevacizumab, irinotecan, lomustine, and tumor-treating fields (Table 1). Other less-selected options include intense modulated radiotherapy, doxorubicin, TOCA 511, everolimus, and osimertinib.

LITT vs. SRS outcomes for first-line treatment of recurrent GBM

We compared the clinical impact of each treatment modality using primary and secondary outcomes, as well as complication rates following intervention. Median PRS for the

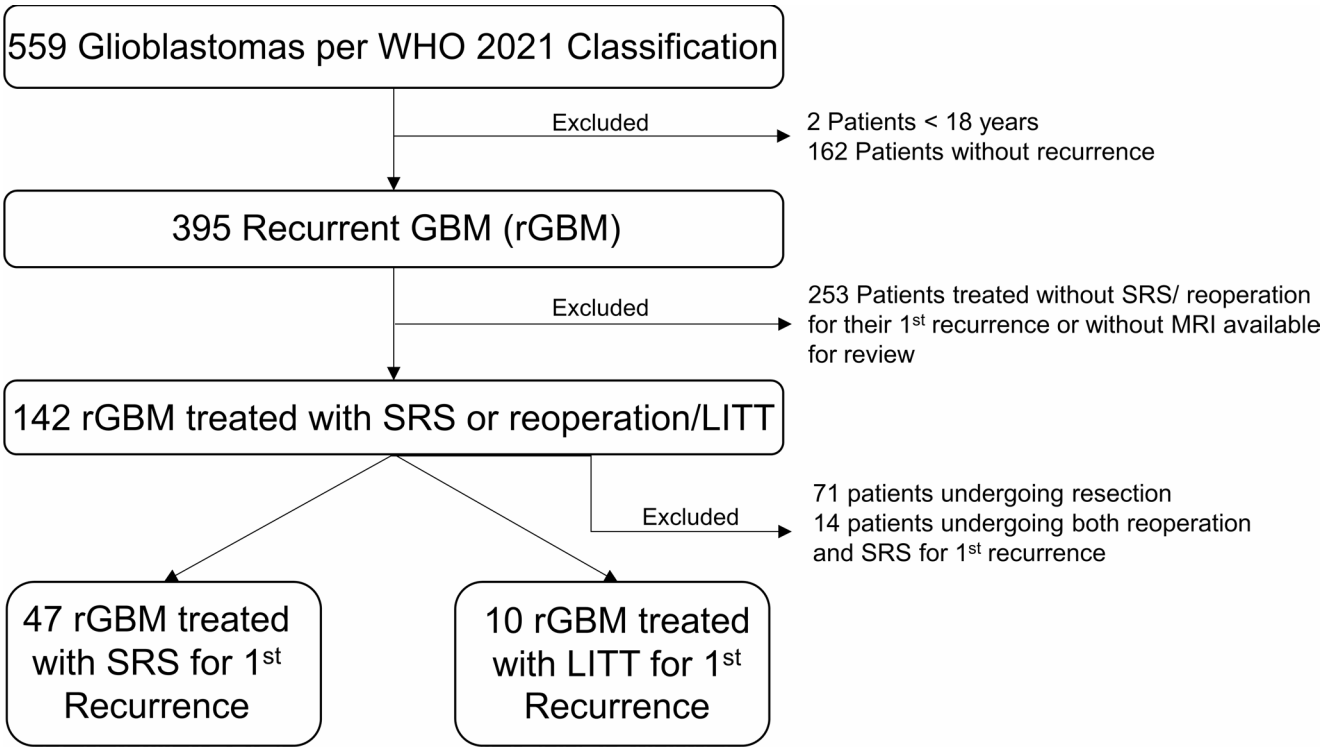

Fig. 2 Flow diagram of eligible patients included in the study

LITT group was 11.5 months (95% CI = 3.7–20) and 13.4 months (95% CI = 9.2–19.2) for the SRS group. Kaplan-Meier curves showed no statistically significant difference in PRS ($p = 0.824$), Fig. 3B. OS was likewise comparable, with median OS of 18.9 months (CI 95% = 10.4–25.7) in the LITT group and 23.0 months (95% CI = 19.8–32.3) in the SRS group ($p = 0.642$), Fig. 3C. Similarly, PFS2 did not differ significantly among groups: 4.8 months (CI 95% = 2.8–8.5) in the LITT group versus 8.5 months (C95% CI = 5-15.5) in the SRS group ($p = 0.195$), Fig. 3D. The LITT group did not have any reported complications; meanwhile, the SRS group had two cases of radiation necrosis that were both managed with corticosteroids (0% vs. 4.3%, $p = 1.000$).

Both univariate (HR = 0.92 [0.43–1.97], $p = 0.824$) and multivariate (HR = 1.34 [0.54–3.29], $p = 0.525$) analyses demonstrated no significant difference in PRS between LITT and SRS as first-line treatment of rGBM (Table 2). In multivariable analysis, patients with unmethylated MGMT status exhibited significantly shorter PRS (HR = 2.93 [1.13–7.59], $p = 0.026$). Higher KPS prior to intervention was associated with a modest but statistically significant increase in PRS (HR = 0.96 [0.94–0.99], $p = 0.021$).

Univariate (HR = 0.83 [0.39–1.79], $p = 0.643$) and multivariate (HR = 1.17 [0.45–3.05], $p = 0.746$) analyses similarly revealed no statistically significant difference in OS treatment modalities (Supplementary Material 1). As with PRS, an unmethylated MGMT status conferred a worse OS in both univariate (HR = 2.45 [1.06–5.67], $p = 0.037$) and multivariate analysis (HR = 2.60 [1.02–6.67], $p = 0.046$).

Lastly, in PFS2, both univariate (HR = 0.59 [0.27–1.29], $p = 0.189$) and multivariate (HR = 0.88 [0.33–2.29], $p = 0.792$) analyses showed no significant difference between treatment groups (Supplementary Material 2). However, larger CE-tumor volume at recurrence was correlated with worse PFS2 in both univariate (HR = 1.05 [1.01–1.09], $p = 0.006$) and multivariate analyses (HR = 1.04 [1.00-1.10], $p = 0.048$).

LITT vs. SRS and outcomes matched by CE-tumor volume

Given the significant difference in CE-tumor volumes between groups, we performed a PSM (nearest-neighbor without replacement with a caliper of 0.2) accounting for this variable. After PSM, 7 patients remained in each group. The matched cohorts were similar in all baseline characteristics (Supplementary Material 3). Most notably, CE-tumor volumes (5.7 cm^3 vs. 5.58 cm^3, $p = 0.902$) and MGMT methylation status ($p = 0.183$) were not significantly different. This analysis showed no significant differences between LITT and SRS in PFS, PRS, and OS (Fig. 4A-C). Although PFS2 showed a significant difference (LITT 4.6 months vs. SRS 18.7 months, $p = 0.007$, Fig. 4D). The sample size limits any firm conclusions. In addition, a subanalysis including

Table 1 Baseline patient demographics and characteristics

Variable, *n* (%)	Stereotactic Radiosurgery *N* = 47	LITT *N* = 10	*p*-value
Age, median (IQR)	62 (55.5–67)	59.5 (48.5–62.5)	0.189
Male	23 (48.9)	6 (60.0)	0.730
Anatomic Primary Tumor Location			0.061
Frontal	19 (40.0)	5 (50.0)	0.727
Parietal	13 (27.7)	4 (40.0)	0.464
Occipital	6 (12.8)	0 (0)	0.577
Temporal	19 (40.4)	6 (60.0)	0.308
Available MGMT status (*n* = 30)	20	10	**0.049**
Methylated	10 (50.0)	1 (10.0)	
Unmethylated MGMT	10 (50.0)	9 (90.0)	
Extent of Resection			0.177
Gross-total resection	19 (40.4)	5 (50.0)	
Near-total resection	12 (25.5)	0 (0)	
Sub-total resection	14 (29.8)	4 (40.0)	
Prior LITT	0 (0)	1 (10.0)	
Primary Adjuvant Therapy			
Chemoradiotherapy with TMZ	47 (100.0)	10 (100.0)	1.000
Bevacizumab	4 (8.5)	1 (10.0)	1.000
Tumor-Treating Fields	9 (19.2)	2 (20.0)	1.000
KPS at recurrence prior to intervention, median (IQR)	80 (80–90)	85 (72.5–90)	0.957
Contrast-enhancing tumor volume at recurrence in cm^3, median (IQR)	1.91 (0.36–6.76)	8.49 (4.37–16.23)	**0.007**
Out-of-field Recurrence	11 (23.5)	3 (30)	0.694
GK-SRS Characteristics			
SRS Gy Dose, median (IQR)	18 (18–20)	N/A	
Isodose Line %, median (IQR)	53.5 (50–60)	N/A	
LITT Characteristics			
Surgical Time, median (IQR)	N/A	216 (167–244)	
Hospital LOS, median (IQR)	N/A	2 (1.25–2)	
Trajectories, median (IQR)	N/A	1 (1–2)	
EOA %, median (range)	N/A	100 (85–100)	
Depth to Lesion in cm, median (IQR)	N/A	5.53 (4.07–7.54)	
Anatomic Recurrent Tumor Location			
Frontal	21 (44.7)	2 (20.0)	0.178
Parietal	11 (23.4)	3 (30.0)	0.694
Occipital	5 (10.6)	0 (0)	0.574
Temporal	15 (31.9)	5 (50.0)	0.298
Multifocality at Recurrence	4 (8.5)	2 (20.0)	0.281
Salvage therapy for recurrence			
TMZ	25 (53.19)	8 (80.0)	0.166
Bevacizumab	31 (66.0)	7 (70.0)	1.000
Irinotecan	16 (34.04)	4 (40.0)	0.728
CCNU	5 (10.64)	1 (10.0)	1.000
Tumor-Treating Fields	11 (23.40)	5 (50.0)	0.124
Other	6 (12.77)	2 (20.0)	0.619
Best supportive care	9 (19.15)	3 (30.0)	0.424
Complications	2 (4.3)	0 (0)	1.000

LITT: laser interstitial thermal therapy; CCNU: lomustine; IQR: Interquartile range; KPS: Karnofsky Performance Scale; MGMT: O(6)-Methylguanine-DNA-methyltransferase, n: number; %: percentage; LOS: length of stay; TMZ: temozolomide; EOA: extent of ablation; N/A: not available. Others include: intense modulated radiotherapy, doxorubicin, TOCA 511, everolimus, and osimertinib

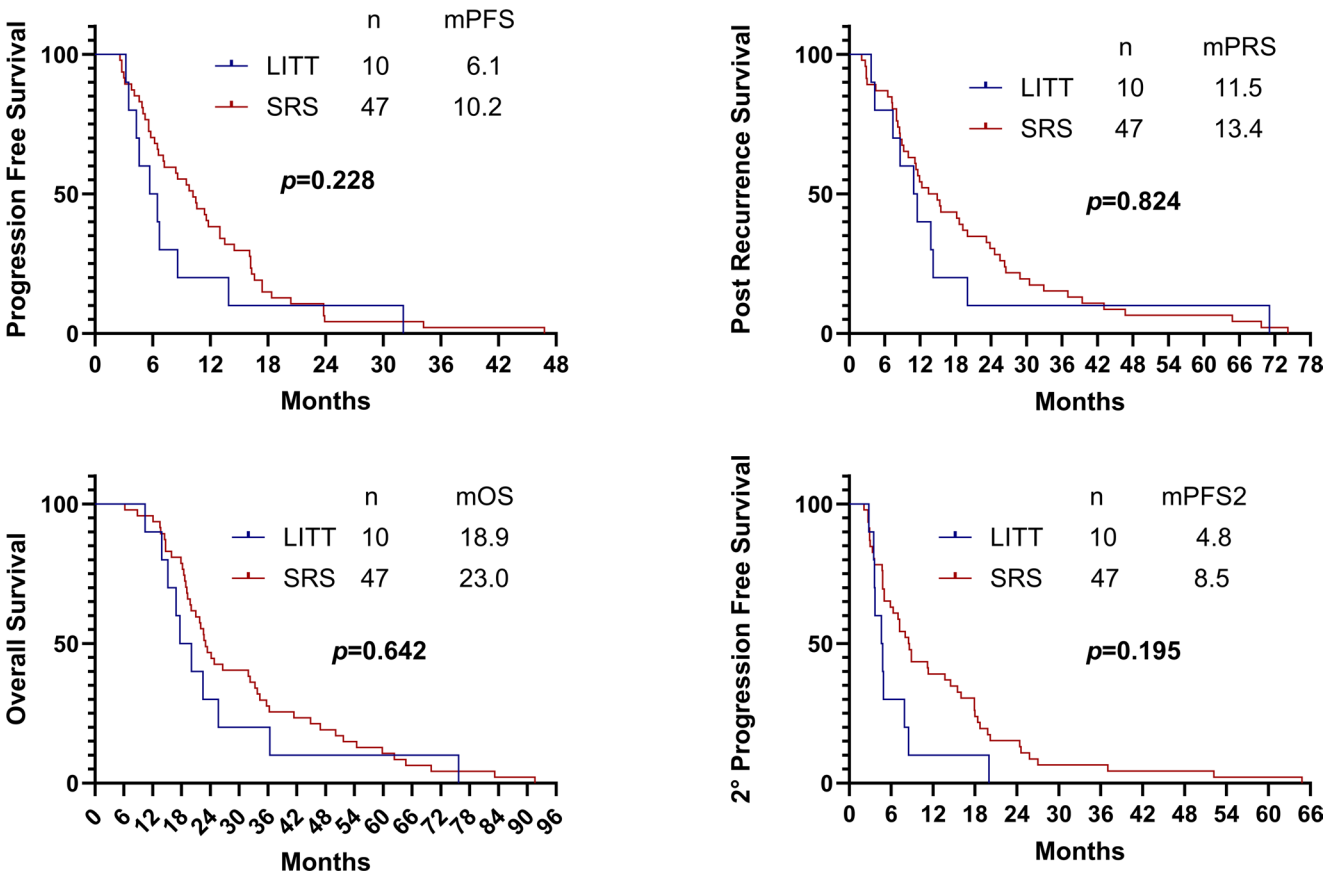

Fig. 3 **A-D.** LITT vs. SRS outcomes in the entire cohort ($n=57$). No statistical difference was observed in (**A**) baseline median progression-free survival (mPFS), $p=0.228$; (**B**) median post recurrence survival (mPRS), $p=0.824$; (**C**) median overall survival (mOS), $p=0.642$; or (**D**) median second PFS (mPFS2), $p=0.195$ among patients undergoing LITT or SRS for their first recurrence

Table 2 Univariable and multivariable cox regression model of post-recurrence survival among patients treated with LITT vs. SRS ($n=57$)

	Univariable HR (95%CI)	*p*-value	Multivariable HR (95%CI)	*p*-value
Stereotactic Radiosurgery (Ref) LITT	0.92 (0.43–1.97)	0.824	1.34 (0.54–3.29)	0.525
Age	0.99 (0.97–1.03)	0.962	1.01 (0.97–1.07)	0.501
MGMT Methylated (Ref) MGMT Unmethylated	2.33 (0.99–5.45)	0.052	2.93 (1.13–7.59)	**0.026**
Contrast-enhancing tumor volume at recurrence in cm^3	1.04 (1.01–1.07)	**0.046**	1.03 (0.99–1.08)	0.083
KPS prior to intervention	0.98 (0.96–1.01)	0.139	0.96 (0.94–0.99)	**0.021**

HR: Hazard ratio; CI: confidence interval; LITT: Laser Interstitial Thermal Therapy; MGMT: O(6)-Methylguanine-DNA-methyltransferase; KPS: Karnofsky Performance Scale. All continuous variables' hazard ratios are per increase of 1 unit (1 cm^3, 1 year of age, or 10 KPS points). P-values <0.05 were considered significant and are bolded

only patients with larger tumors in the SRS group ($>4cm^3$ – the 25th percentile of tumor size in the LITT group) did not reveal significant differences between LITT and SRS in PFS, PRS, OS, and PFS2 (Supplementary Material 4).

Discussion

Both LITT and SRS have historically been reserved as salvage treatment for rGBM in patients for whom surgical resection is suboptimal. To our knowledge, this is the first study that attempts to directly compare these two salvage options in a homogeneous cohort. While we did not observe a clear survival difference between LITT and SRS across PRS, OS, and PFS2, these findings should be interpreted as exploratory and hypothesis-generating rather than definitive. Notably, median CE tumor volume was larger in the LITT group. Prior studies have suggested that higher CE tumor volume predicts poorer PRS, OS, and PFS2 [38]. We also observed that a statistically larger portion of our LITT cohort had unmethylated MGMT methylation status. As with CE tumor volume, prior literature suggests

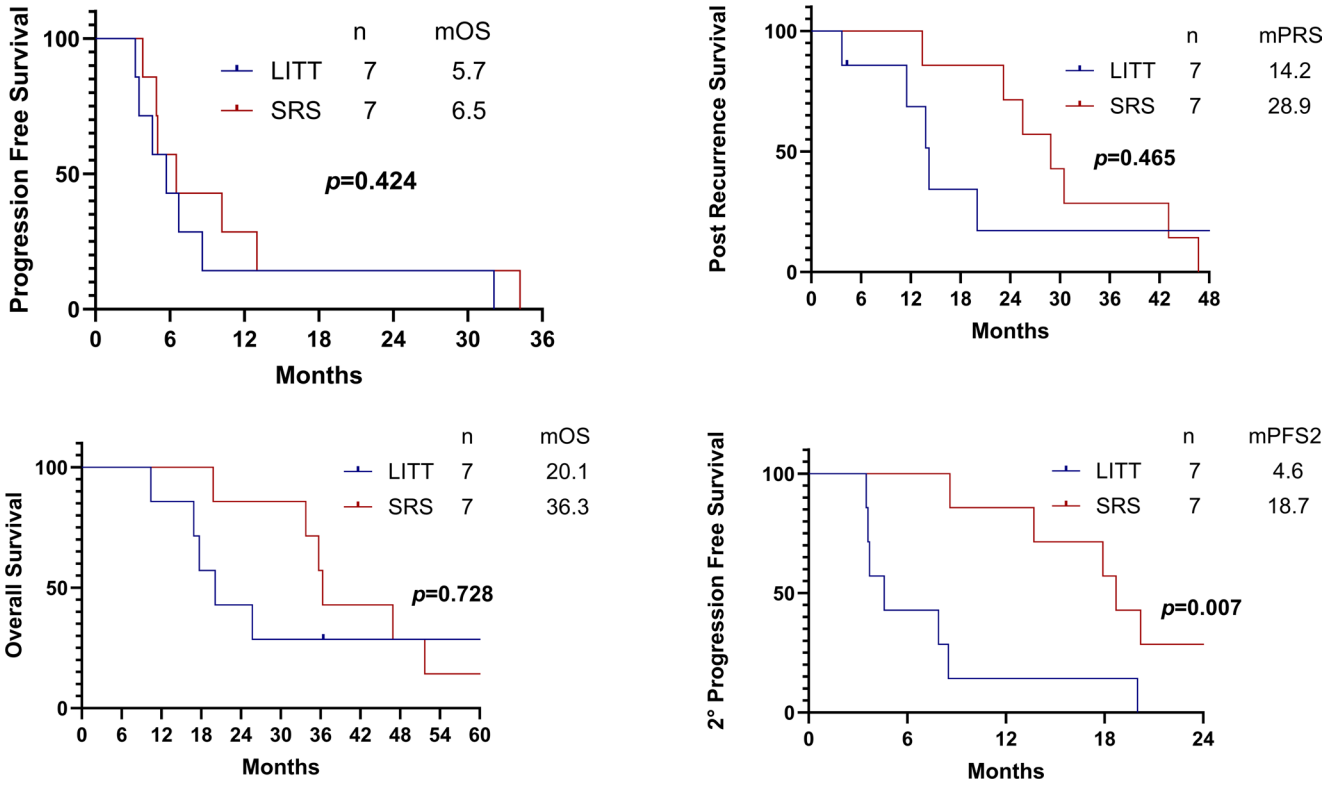

Fig. 4 A-D. LITT ($n=7$) vs. SRS ($n=7$) outcomes in the propensity score-matched cohort. No statistical difference was observed in (**A**) baseline median progression-free survival (mPFS), $p=0.953$; (**B**) median post recurrence survival (mPRS), $p=0.538$; (**C**) median overall survival (mOS), $p=0.559$; or (**D**) median second PFS (mPFS2), $p=0.784$ among patients undergoing LITT or SRS for their first recurrence after matching patients by contrast-enhancing tumor volume

unmethylated MGMT predicts inferior PRS, OS, and PFS2 [40]. To try to account for this, we performed a PSM as well as a subanalysis including only larger tumors in the SRS group, which again revealed no survival advantage for either modality. However, due to the small sample size, we were unable to account for the difference in MGMT status in the PSM. In the PSM based on CE tumor volume, no statistical difference existed in MGMT status between groups. Although this was largely attributable to missing MGMT data in 5 of the 7 SRS patients.

Historically, LITT has been implemented principally for deep-seated tumors – indeed all tumors undergoing LITT in our study were deep, > 2 cm from the surface [30]. No immediate complications were observed in the LITT cohort; however, our sample size was small. Reported complication rates in prior studies range from 0.4% to 22.4%, 41, 42] most commonly due to catheter malposition, hyperthermia, and device cooling malfunctions [42]. The primary complications include hemorrhage, neurologic deficit, and vasogenic or peritumoral edema, though edema is typically transient [6, 42, 43]. The SRS cohort had two instances of radiation necrosis, consistent with prior reports identifying this as the primary complication [44].

Although no statistically significant survival advantage was identified between LITT and SRS, these results should be interpreted within the broader context of clinical relevance and treatment characteristics. SRS offers logistical advantages, typically performed as an outpatient procedure under local anesthesia. In contrast, LITT requires general anesthesia with airway manipulation, ICU monitoring for one to two days, and ultimately is more invasive. Conversely, SRS induces a latency period before tumor cell death, whereas LITT results in immediate cytoreduction [32]. In our practice, both approaches are reserved for carefully selected patients with small, focal rGBM. Accordingly, treatment selection remains highly individualized and is guided by tumor location, prior treatments, patient functional status, and both patient and surgeon preference. In the absence of high-level comparative data demonstrating superiority of one modality over the other, these decisions are best framed within a multidisciplinary tumor board in a patient-centered context.

The blood-brain barrier (BBB) makes delivery of therapeutic agents exceedingly difficult, and it is considered a major limitation in GBM treatment. Emerging evidence suggests that LITT transiently disrupts the BBB, creating a therapeutic window for enhanced local drug delivery [45,

46]. This effect, however, may also lead to peritumoral edema, often necessitating temporary corticosteroid management. To our knowledge, no comparable BBB-modulating benefit exists for SRS. While some studies have reported improved outcomes with concomitant SRS and chemotherapy, others have not [14, 47, 48]. In other tumor types, SRS has been hypothesized to induce an abscopal effect, enhancing systemic immunotherapy efficacy; however, immunotherapy has not demonstrated benefit in rGBM [3, 49]. Finally, LITT supplies access to tumor tissue, conferring additional benefits such as eligibility for window-of-opportunity trials, assessment of glioblastoma longitudinal evolution, and facilitation of clinical trial enrollment at first recurrence [50].

Limitations

Given its retrospective, observational design, this study is inherently susceptible to bias. The primary limitations are the small sample size, the varied volumes, and the lack of methylation status in all patients, which render comparisons statistically underpowered. In addition, we were unable to have a PSM accounting for MGMT, which may harbor residual confounding. This limitation reflects the stringent inclusion criteria applied to ensure homogeneity and minimize confounders. Efforts to control intergroup differences, such as CE tumor volume, reduce the cohort size thereby limiting the power to identify statistical differences. Lack of available tissue from the SRS group makes us unable to exclude radiation necrosis from progression histologically for the evaluation of PFS2; however, the significance of histopathological findings, which are frequently admixed, in survival is unclear [51]. Multi-institutional collaborations are essential to address this, as no individual institution has large enough datasets on its own to overcome these limitations. This study will serve as the initial step of multi-institutional collaborations that are underway. The absence of broader genetic and molecular profiling is another limitation that necessitates further investigation, as particular rGBM subtypes may differentially benefit from LITT or SRS [4].

Conclusion

LITT and SRS are viable salvage options for small rGBM patients in whom surgical resection is not feasible, with LITT offering advantages such as tissue access and potential BBB disruption, and SRS providing logistical benefits as a less invasive outpatient procedure. Larger, multi-institutional studies with molecularly stratified cohorts are warranted to clarify which specific subgroups may derive differential benefits from LITT or SRS, and in which cases there is equipoise.

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Code availability Not applicable.

Declarations

Ethical approval This study was approved by the institutional review board of The University of Texas Health Science Center at Houston and Memorial Hermann Hospital, Houston, TX and it was in accordance with the 1964 Helsinki Declaration and its later amendments.

Consent to participate and publication Not applicable.

Competing interests The authors declare no competing interests.

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