LITTing up Gliomas—Is the Future Bright?

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■ BACKGROUND: **Laser interstitial thermal therapy (LITT) represents an attractive therapeutic strategy for several intracranial pathologies; however, there is a paucity of literature regarding its efficacy for the treatment of gliomas.**

■ METHODS: **MEDLINE, EMBASE, Scopus, and Web of Science were searched from inception until March 19, 2021. Studies specifically relating to the use of LITT in treatment of glioma were eligible for inclusion. A meta-analysis of means was performed to assess the progression-free survival (PFS) and overall survival (OS) following LITT and descriptive statistics relating to patients undergoing LITT were collated and a meta-analysis of proportions was also performed to assess the rate of complications.**

■ RESULTS: **In total, 17 studies were included for the meta-analysis, comprising 401 patients with 408 gliomas of which 88 of 306 (28.8%) were grade 1 or 2 and 218 of 306 (71.2%) were grade 3 or 4. Of these, 256 of 408 (62.8%) were primary presentation and 152 of 408 (37.2%) were recurrent. The pooled mean OS was 13.58 months (95% confidence interval [CI] 9.77—17.39) and the PFS was 4.96 months (95% CI 4.19—5.72). The OS and PFS of recurrent glioblastoma were 12.4 months (95% CI 9.61—16.18) and 4.84 months (95% CI 0.23—9.45), respectively. Complications occurred in 114 of 411 (24%; 95% CI 14—41), of which 44 (11%) were transient deficits.**

■ CONCLUSIONS: **There is an increasing body of evidence demonstrating the use of LITT in the surgical management of deep-seated gliomas in patients of poor performance status. However, further studies are required to interrogate the clinical effectiveness of LITT in the setting of gliomas as well as assessing the survival benefit versus standard treatment alone.**

INTRODUCTION

Gliomas account for 28% of all primary central nervous system tumors, of which glioblastoma (grade IV) is the most common primary malignant brain tumor.[1] Despite significant advancements in the understanding of key molecular pathways as well as the microenvironment, the survival of patients with glioblastoma remains poor. Current evidence supports the role of safe maximum resection along with adjuvant chemo/radiation strategies as part of the standard therapeutic approach in both a primary[2-4] and recurrent setting of gliomas.[5] However, there are many confounding factors in achieving this goal, such as age, anatomical considerations, and neurologic functional limitations of the surgery, as well as patients with a poor performance status. Such restrictions may preclude a cohort of patients from the inherent survival and quality of life benefit of cytoreductive therapy.

Since the inception of laser interstitial thermal therapy (LITT) in 1983 by Bown,[6] the therapeutic effects of tissue hyperthermia have grown in popularity. The neodymium-doped yttrium aluminum garnet laser initially described targeted deep abnormalities with a flexible fiberoptic cable, albeit without real-time treatment monitoring. The advent of proton resonance frequency as a surrogate marker of thermal damage allows surgeons to circumvent this limitation and allows for magnetic resonance thermography based on temperature variations. The effectiveness of LITT is

Key words
- Glioma
- Laser ablation
- Laser interstitial thermocoagulation therapy
- LITT

Abbreviations and Acronyms
CI: Confidence interval
LITT: Laser interstitial thermal therapy
OS: Overall survival
PFS: Progression-free survival

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based on the delicate balance of absorption and scatter of the heat, in addition to the tissue properties.[7]

At present, 2 systems are approved by the Food and Drug Administration for intracranial use: NeuroBlate (Monteris, Minnetonka, Minnesota, USA) and Visualase (Medtronic, Minneapolis, Minnesota, USA). Although the 2 LITT systems differ, the same primary outcome of thermocoagulation-mediated cell death is achieved. The fiberoptic wires are covered by a catheter sheath that facilitates cooling, equal energy dispersal for optimum temperature control, and avoids charring of adjacent tumor tissue.[8] Temperature homeostasis is integral to cellular metabolism, and consequently deviation from within normal limits leads to DNA and protein denaturation and cell death.[9] Temperatures ranging from 46°C to 60°C cause irreversible cellular damage via apoptosis,[10] with temperatures >60°C resulting in instantaneous coagulative necrosis. The zone of irreversible cell death is quantified via the Arrhenius equation, color coded, and subsequently overlayed on the reference image. The Arrhenius model takes into consideration time and temperature as variables.

In recent years, numerous studies have demonstrated the potential role of LITT in intracranial tumors,[11] specifically relating to metastatic disease,[12] radiation necrosis,[12] and epilepsy.[13] However, the role of LITT in the treatment regime of gliomas in an upfront or recurrent setting remains unclear. This manuscript aims to review existing literature and describe the indications and complications of LITT in glioma management.

METHODS

A systematic review and meta-analysis was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines.[14]

Eligibility Criteria

Research papers relating to the use of LITT for the treatment of gliomas were eligible for inclusion. Studies were excluded if they did not relate specifically to gliomas, or if the tumor grade was not specified. Only studies published in English were eligible for inclusion.

Information Sources, Search Strategies, and Study Selection

MEDLINE, Scopus, EMBASE, and Web of Science were searched from inception until March 3, 2021, for terms relating to LITT and glioma. The full search strategy is provided in **Appendix 1**. Abstracts were deduplicated using *revtools*[15] for R, version 4.0.2 (R Foundation for Statistical Computing, Vienna, Austria), and then screened using Rayyan QCRI.[16] Screened citations were collated in Microsoft Excel (Microsoft, Redmond, Washington, USA) and full texts assessed for eligibility, with data extracted from eligible full texts via predetermined proforma, as described in data items.

Data Items

Data items extracted included sample size, study design, glioma grade and location, LITT system used, pre-LITT tumor size, study outcomes as reported including overall (OS) and progression-free (PFS) survival, and the amount and nature of any complications observed.

Risk of Bias in Individual Studies

Risk of bias in individual studies was assessed using a modified Newcastle–Ottawa Scale[17] for single-arm studies, wherein comparability was omitted from consideration (**Appendix 2**). As such, quality was assessed on a scale of 1–6 as opposed to 1–9 in the standard Newcastle–Ottawa Scale.

Summary Measures

A pooled proportion was estimated for complication rate, along with a pooled mean estimate for PFS and OS.

Synthesis of Results

All statistical analysis was performed using meta[18] in R, version 4.0.2. Visual plots were generated using ggplot2.[19] Proportion of complications in each study was transformed using the Freeman-Tukey double arcsine transformation to account for variance induced by studies with zero complications, and then pooled in a random effects model with inverse variance weighting to derive a pooled estimate for complication rate. Pooled estimates for mean OS and PFS were also derived from a random-effects model with inverse variance weighting. Where studies did not report OS or PFS in the form of mean ± standard deviation, these values were imputed from reported data including medians, ranges and interquartile ranges. Heterogeneity was quantified via calculation of I^2 for each analysis, using the DerSimonian-Laird estimator for tau.[15] Median pre-LITT tumor size and length of stay were calculated using a simple weighted median.

Risk of Bias Across Studies

Risk of bias across studies was assessed qualitatively using funnel plots.

RESULTS

In total, 2731 citations were identified in total, of which 1417 abstracts were screened. 17 studies were included (**Figure 1**), comprising a total of 401 patients with 408 gliomas (**Table 1**). The median pre-LITT tumor size was reported by all studies (**Table 1**), contributing to a weighted median of 13.95 cm^3. Sufficient detail breakdown regarding tumor grade was available for 306 of 408 gliomas (75.0%), of which 88 of 306 (28.8%) were grade 1 or 2 and 218 of 306 (71.2%) were grade 3 or 4 (**Figure 2A**). Of the gliomas, 256 of 408 (62.8%) were primary and 152 of 408 (37.2%) were recurrent (**Figure 2B**). Tumor location was reported in sufficient detail for 248 gliomas, of which the majority (80/248, 32.3%) were frontal (**Table 2**). The locations of tumors are shown in **Figure 2C**. The most common complication reported was transient deficit (**Figure 2D**). Length of stay was reported in sufficient detail in 10 studies (**Table 2**), and the weighted median length of stay was 3.7 days.

Complications

All 17 studies reported the rate of complications, of which 1 case report was excluded from meta-analysis. In total, 114 complications were reported across 411 procedures (24%, 95% confidence interval [CI] 14–35) (**Figure 3A**). Of these, there were 44 transient deficits, 17 were permanent deficits, 11 were seizures, 7 were infections, 6 were intracranial hemorrhage, and 1 cerebrospinal

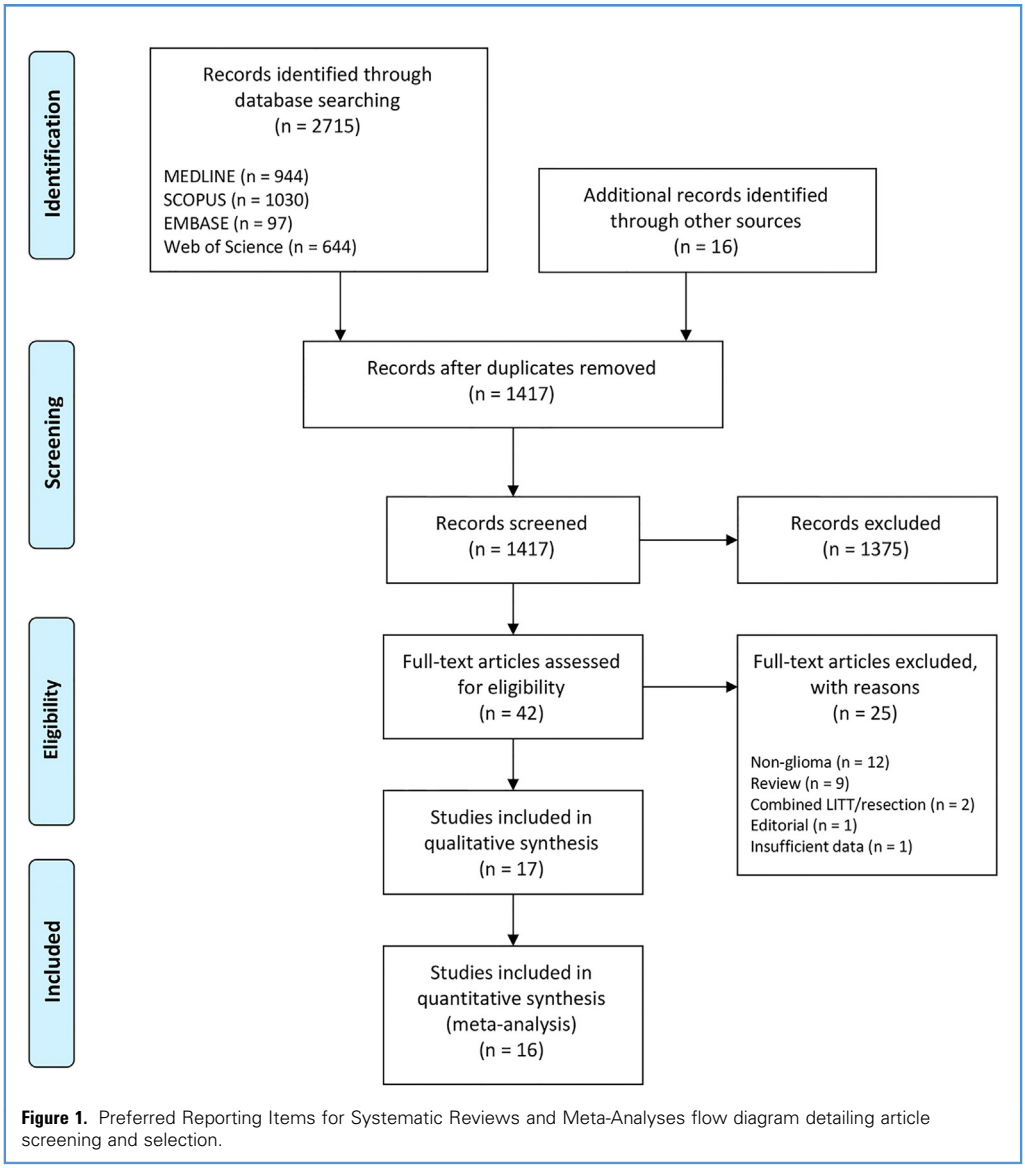

Figure 1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses flow diagram detailing article screening and selection.

fluid leak (Figure 2D). There was significant heterogeneity in this analysis (I^2 = 75%, $P < 0.01$), which is likely due to a heterogenous patient cohort, varying definitions of complications and institutional effects.

Survival

Sufficient detail regarding OS was reported by 8 studies, and the pooled mean OS was 13.58 months (95% CI 9.77–17.39) (Figure 3B). One study was a particular outlier, which is likely explained by the fact that 50% of the study population consisted of low-grade tumors. There was significant heterogeneity (I^2 = 94%, $P < 0.01$). Sufficient detail regarding PFS was reported by 7 studies and the pooled mean PFS was 4.96 months (95% CI 4.19–5.72), with significant heterogeneity (I^2 = 93%, $P < 0.01$) (Figure 3C).

In the subgroup analysis assessing recurrent glioblastoma, sufficient detail regarding OS was reported by 6 studies, for which the pooled mean OS was 12.4 months (95% CI 9.61–16.18) (Figure 4A). Three studies reported sufficient detail regarding PFS, for which the pooled PFS was 4.84 months (95% CI 0.23–9.45) (Figure 4B).

Risk of Bias Across Studies

Funnel plots are presented for each analysis (Figure 5), demonstrating no significant evidence of publication bias.

DISCUSSION

The present analysis assessed 411 LITT procedures performed for both primary and recurrent gliomas of various grades,

Table 1. Chronological Summary of Series LITT in Gliomas

Author	Design	No. of Patients	Pathology	Treatment	Pre-LITT Tumor Size	Outcome	mNOS
Reimer et al., 1998[20]	Prospective Single center	4	1 rGBM 3 rG3 AA	Nd: YAG laser	6.125 cm^3	NR	4
Leonardi and Lumenta, 2002[21]	Prospective Single center	24	9 rGBM 12 G3 9 G2	Nd: YAG laser	NR	rGBM: 9 months G3: 30 months G2: 34 months	5
Schwarzmaier et al., 2005[22]	Prospective Single center	2	rGBM	Nd: YAG laser	20 cm^3	OS Patient 1: 13 months Patient 2: 15 months	4
Schwarzmaier et al., 2006[23]	Prospective Single center	16	rGBM	Nd: YAG laser	21.6 ± 18.6 cm^3	OS: 6.9 months	5
Carpentier et al., 2012[24]	Prospective Single center	4	rGBM	Visualase	3.83–8.86 cm^3	PFS: 30 days OS: 10 months	5
Sloan et al., 2013[25]	Prospective Single center	10	rGBM	NeuroBlate	2.6–19 cm^3	OS: 10.5 months	6
Mohammadi et al., 2014[26]	Retrospective Multicenter	34	24 GBM 6 G3 AA 4 G3 AO	NeuroBlate	0.7–49.9 cm^3	PFS: 5.1 months OS: 1-year estimate 68 ± 9%	6
Thomas et al., 2016[27]	Retrospective Single center	21	8 GBM 13 rGBM	Visualase and NeuroBlate	14.6–22.4 cm^3	Primary GBM: PFS: 2 months OS: 8 months rGBM: PFS: 5 months OS: >7 months	6
Leuthardt et al., 2016[28]	Prospective Single center	20	15 GBM 3 G3 AA 1 G2 Astro 1 G2 OA	NeuroBlate + Doxorubicin	<3 cm^3	BBB disruption 1–2 weeks post-LITT BBB resolution 4–6 weeks post-LITT	4
Beaumont et al., 2018[29]	Retrospective Multicenter	15	9 GBM 6 rGBM	NeuroBlate	1.1–62.7 cm^3	Primary GBM: PFS: 3.1 months OS: 7 months rGBM: PFS: 3.6 months OS: 20 months	6
Mohammadi et al., 2019[30]	Prospective Mutticenter	24	24 GBM	NeuroBlate	1.31–62.7 cm^3	PFS: 4.3 months OS: 14.4 months	5
Shah et al., 2018[31]	Retrospective Single center	6	GBM	Visualase	4.2–52 cm^3	PFS: 14.3 months Mean follow-up 19.7 months	6
Hafez et al., 2020[32]	Prospective Single center	1	G2 Oligo 1p/19q codeleted IDH1 mutated	NeuroBlate	40 cm^3	Follow-up: 2 years Alive 88% reduction in tumor size	N/A
Kamath et al., 2019[33]	Retrospective Single center	54	17 GBM 41 rGBM	NeuroBlate	12.5 ± 13.4 cm^3	Primary GBM: PFS: 3.6 months OS: 9.1months rGBM: PFS: 7.3 months OS: 11 months	6
Arocho-Quinones et al., 2020[34]	Retrospective Multicenter	86 (Pediatrics)	10 G3/G4 76 G1/G2	NeuroBlate + Visualase	8.0 ± 14.0 cm	PFS: 92% @ 72 months	6

Continues

Table 1. Continued

Author	Design	No. of Patients	Pathology	Treatment	Pre-LITT Tumor Size	Outcome	mNOS
Murayi et al., 2020[35]	Retrospective Single center	11	2 G3 1 rGBM 8 GBM	NeuroBlate	12 cm^3 (range 1.67—30.3)	OS: 18.1 months PFS: 6.1 months	6
Traylor et al., 2021[36]	Retrospective Single center	69	20 GBM 49 rGBM	NeuroBlate + Visualase	10.4 cm^3 (range 1.0—64.0)	OS: 12 months PFS: 4 months	6

LITT, laser interstitial thermal therapy; mNOS, modified Newcastle—Ottawa Scale; rGBM, recurrent glioblastoma; rG, recurrent grade; AA, anaplastic astrocytoma; Nd: YAG, neodymium-doped yttrium aluminum garnet; GBM, glioblastoma; NR, not recorded; G, grade; OS, overall survival; PFS, progression-free survival; AO, anaplastic oligodendroglioma; OA, oligoastrocytoma; BBB, blood—brain barrier; Oligo, oligodendroglioma; N/A, not available.

demonstrating a complication rate of approximately 23%, pooled mean OS of 13.6 months, and PFS of 5 months. Since the advent of the Stupp protocol in 2005,[37] maximal safe resection with concomitant temozolomide chemotherapy and radiotherapy has been the gold standard of care in high-grade glioma. In low-grade glioma, treatment is driven by individualized consideration of local anatomy, histologic subtype, gene profiling, patient factors and patient preferences but still relies on the principle of maximal safe resection. Achieving this goal can be challenged, however, by the involvement of eloquent structures. Deep-seated lesions suffer poorer surgical outcomes and greater rates of postoperative deficits.[38,39] In addition, survival may be indirectly impaired as extent of resection is restricted.[40] LITT has been successfully applied to a wide range of pathologies across functional neurosurgery, metastases, and radiation necrosis and may offer precise access to deep-seated tumors unsuitable for conventional resection. In our analysis, 9 gliomas were insular and 37 were thalamic. In 2 included studies, deep-seated tumors appeared to have poorer survival,[36,30] due to anatomical location. In contrast, one study demonstrated equivalent survival in tumors grouped as lobar, cerebellar, or deep.[34] Notably, complications were also equally distributed between the groups in this paper, whereas the relationship between complications and locations was unreported in others.[34] Many of these lesions

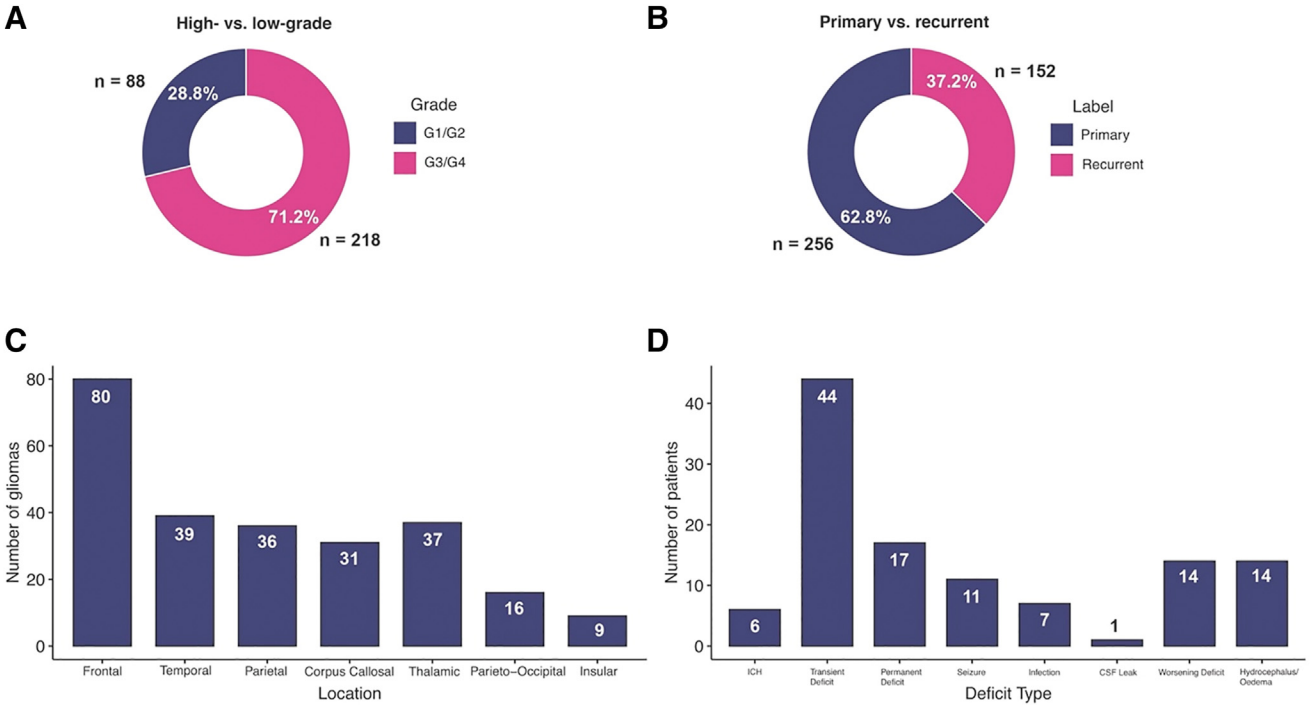

Figure 2. (**A**) Donut chart detailing the number of high-grade (grade 3 or 4) versus low-grade (grade 1 or 2) gliomas included. (**B**) Donut chart detailing the number of primary versus secondary gliomas included. (**C**) Bar chart detailing the locations of included gliomas. (**D**) Bar chart detailing the types and number of complications of laser interstitial thermal therapy observed.

Table 2. Chronological Summary of Series LITT Therapy in Gliomas

Author	Location	Laser Tx Time	LOS, days	Complications
Reimer et al., 1998[20]	Frontal (3), temporal (1)	3—10 minutes	NR	Transient aphasia (1), intracranial hemorrhage (1)
Leonardi and Lumenta, 2002[21]	Frontal (7), frontotemporal (2), frontoparietal (2), temporal (1), parietal (5), parietooccipital (6), thalamic (1)	2.1—27.2 minutes	NR	Transient hemiparesis (2), brain abscess (1), SSI (2), seizure (1)
Schwarzmaier et al., 2005[22]	Temporal (1) parietooccipital (1)	NR	NR	None
Schwarzmaier et al., 2006[23]	Temporal (1), frontal (3), frontoparietal (1), frontotemporal (2), temporoparietal (2), parietal (2), genu of CC (1), occipital (1), parietooccipital (3)	NR	12.0 ± 4.2	Transient monoparesis (1), neutropenia (3), thrombocytopenia (1), elevated transaminases (1)
Carpentier et al., 2012[24]	Temporal (2), CC (1), frontal (1)	30—180 seconds	1	Seizure (1), dysphasia (1)—resolved day 7, CSF leak (1)
Sloan et al., 2013[25]	Temporal (2), frontal (3), parietal (3), temporoparietal (1), temporooccipital (1)	7.5—50.2 minutes	2—7	Transient monoparesis/dysphasia (1) Transient hemiparesis/homonymous hemianopia (1) ICH secondary to pseudoaneurysm 6 weeks post LITT (1)—coiled Hemiplegia (1)—function regained @ 8 weeks
Mohammadi et al., 2014[26]	Frontal (15), thalamus (7), temporal (5), parietal (5), insular (2), CC (1)	NR	1—29	Transient hemiparesis (5) Permanent hemiparesis (2) Seizure (1) Hyponatremia (1) Bilateral DVT (1) Infection (2)
Thomas et al., 2016[27]	Butterfly (5), insular (2), thalamus (1), motor (3), speech (3), temporal (1), splenium of CC (2), cingulate (1), insular (2)	NR	NR	Seizure (1), worsening functional status (2)
Leuthardt et al., 2016[28]	Frontal (7), temporal (4), parietal (6), parietooccipital (1), thalamic (1)	NR	1—5	None
Beaumont et al., 2018[29]	Frontal CC (7), parietal CC (2), callosal (6)	3.7 ± 2.2 vs. 0.6 ± 0.4 minutes	1—11	Transient hemiparesis (2), permanent hemiplegia (2), edema (1), ventriculitis (1), hydrocephalus (1), visual field defect (1)
Mohammadi et al., 2019[30]	lobar (13), thalamus (7), callosum (2), insula (2)	2—10 minutes	1—26	Transient hemiparesis (2) Permanent hemiplegia (4) DVT (1) Moderate/severe ICH—treated conservatively (2)
Shah et al., 2018[31]	Splenium (1), frontal (1), parietooccipital (1), postcingulate (1), precuneus (1), genu (1)	NR	NR	None
Hafez et al., 2020[32]	Insular (1)	NR	1	None
Kamath et al., 2019[33]	Frontal (14), temporal (8), parietal (9), occipital (1), parieto-occipital (4), temporo-occipital (4), CC (8), insular (2), thalamic (8)	2—10 minutes	3.2 ± 4.6	Edema (3), seizure (3), death (2), hydrocephalus (1), hyponatremia (1), infection (1)
Arocho-Quinones et al., 2020[34]	Frontal (11), temporal (13), parietal (6), occipital (3), thalamus (10), hypothalamus (6), basal ganglia (6), periventricular (17), cerebellar (14)	NR	NR	ICH (2), transient deficits (11), permanent deficits (5), death (2), malposition of laser probe (3), edema (2), hydrocephalus (4)
Murayi et al., 2020[35]	Thalamic (11)	NR	3	Transient deficit (4), hydrocephalus (2)
Traylor et al., 2021[36]	Deep-seated (35), non-deep seated (34)	NR	NR	Seizure (4), transient dysphasia (11), new persistent motor deficit (4), worsened pre-existing motor deficit (13)

LITT, laser interstitial thermal therapy; LOS, length of stay; NR, not recorded; SSI, surgical-site infection; CC, corpus callosum; CSF, cerebrospinal fluid; ICH, intracranial hemorrhage; DVT, deep-vein thrombosis.

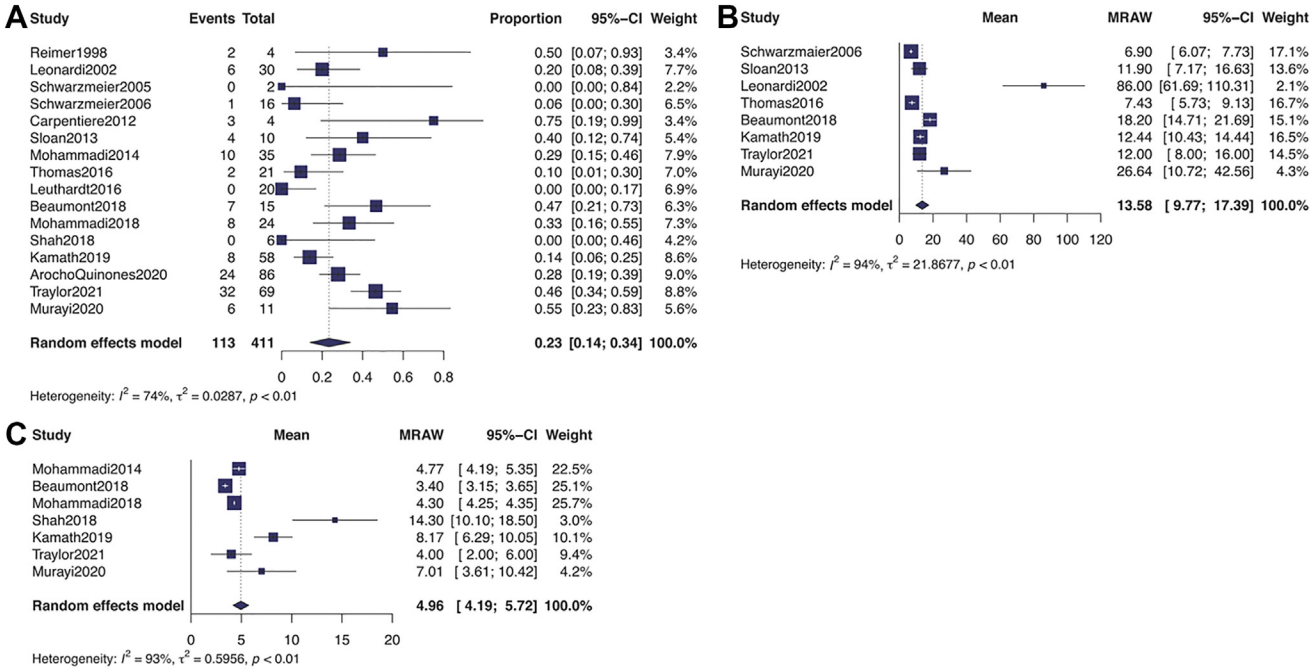

Figure 3. Forest plots for each analysis. (**A**) Complication rate, (**B**) overall survival, and (**C**) progression-free survival.

are considered unsuitable for resection and are conventionally managed with biopsy and chemoradiation alone.[41]

In our analysis, complications occurred in 23%, but a substantial proportion of these complications (44/411, 10.7%) were transient deficits. Transient deficits were typically defined as those that resolved within the immediate postoperative period, which varied among included studies. In the entire analysis, only 17 of 411 (4.1%) were permanent deficits. Seizure (occurring in 11 of 411 [2.7%]) and infection (7/411, 1.7%) were relatively rare following LITT and can both be managed in the same manner as following conventional therapy.

New deficits post-LITT are managed conservatively, after ruling out contributing ischemia, hemorrhage, or edema. Our findings show that a majority of these deficits are transient and likely to improve. Many comparable patients would normally undergo stereotactic biopsy only, which is diagnostic but postoperative deficits still occur in a comparable 6%–8%.[42,43] This is an encouraging finding for LITT, which may have an additional therapeutic benefit. This is exemplified in the study by Mohammadi et al.,[30] wherein patients undergoing LITT were matched with comparable controls undergoing stereotactic biopsy alone. The patients who received LITT appeared to have improved survival without significantly increased complications or treatment-related morbidity.

This may be particularly true in the setting of recurrent glioma. In our analysis, 152 of 408 (37.3%) were recurrent gliomas with an OS and PFS in recurrent glioblastoma of 12.4 months and 4.84 months, respectively. Recurrent gliomas have manifestly poor prognosis,[44,45]

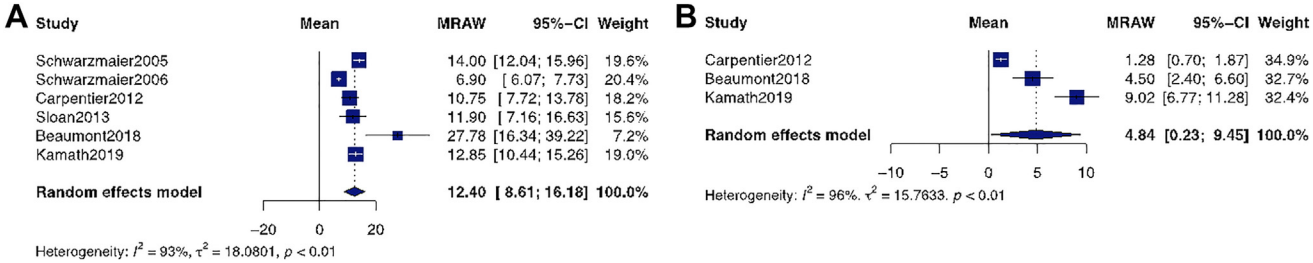

Figure 4. Forest plots showing the results of a subgroup analysis assessing recurrent glioblastomas (rGBMs). (**A**) Overall survival (OS) and (**B**) progression-free survival (PFS).

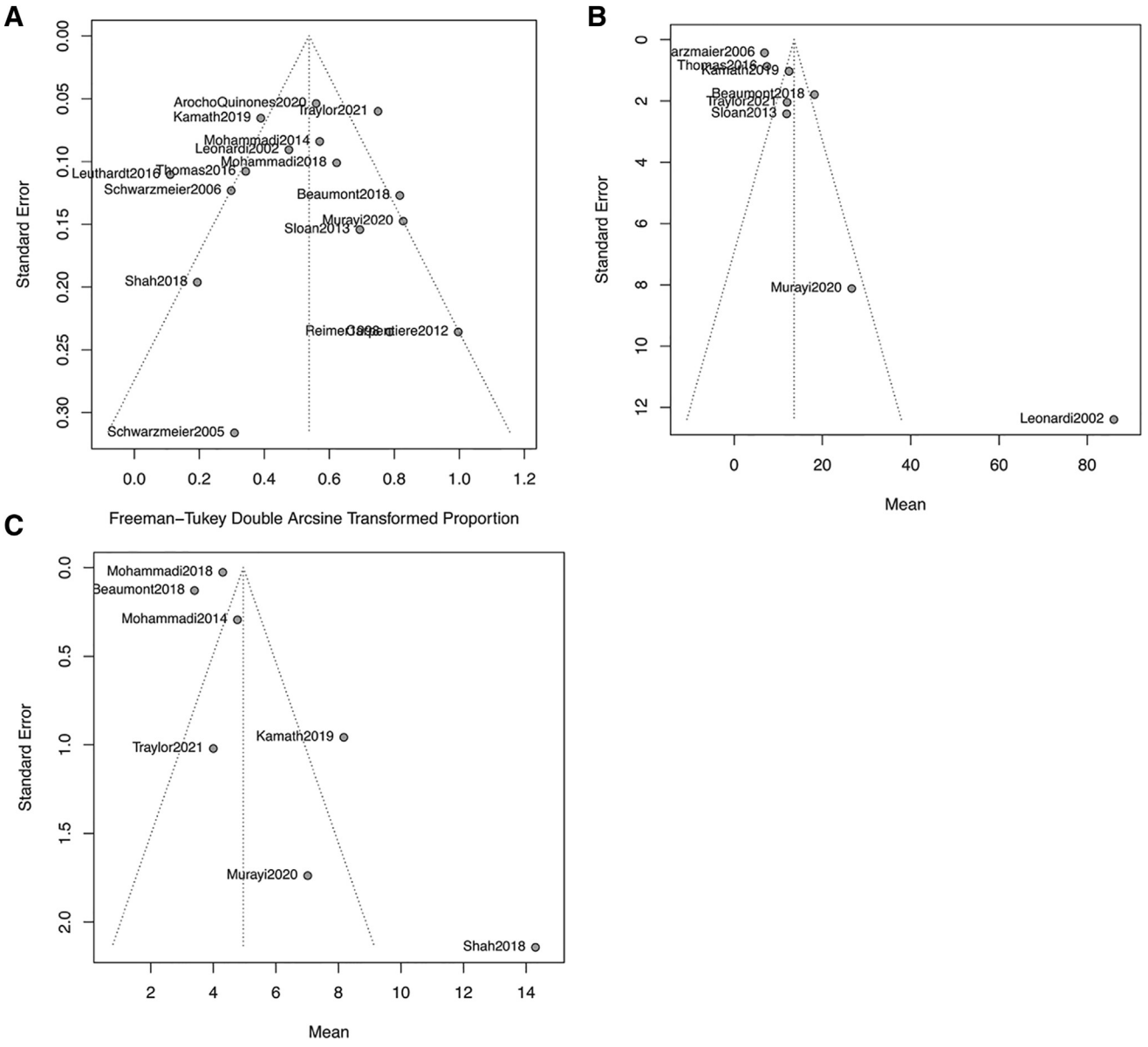

Figure 5. Funnel plots for each analysis. (**A**) Complications, (**B**) overall survival, and (**C**) progression-free survival.

and there are few effective treatments currently available.[46] Repeated resection of gliomas carries several challenges, including technical difficulties with multiple reoperations of previous sites, decreased intervals to further recurrences following re-resection, leptomeningeal or intraventricular metastasis, and deterioration in functional status.[41] Treatment options are further limited by a reduction in sensitivity to chemoradiation.[47] LITT may provide a further treatment option in cases in which the aforementioned are unfeasible or suboptimal, having been successfully applied for recurrent glioblastoma in many of the series in our analysis.[22,24-27,29,33]

Operative duration is an important consideration in LITT. Care must be taken to avoid extension of the thermal radius into healthy brain, which requires careful monitoring via magnetic resonance imaging or thermometry. Duration is potentially shortened in newer systems using real-time magnetic resonance thermometry, which allows real-time visualization of thermal lesions.[48] Before this feature, lesions required visualization on magnetic resonance imaging, which take up to 15 minutes to appear in addition to acquisition time.[48] However, operative duration can still be protracted, given the application time, particularly in the case of multiple and/or large lesions. Mean

operative duration ranged from 1.5 to more than 12 hours, with medians of 3.7[33] and 7.7 hours.[29] Like any novel methodology, there is also a learning curve associated with LITT, which also may contribute to operative duration. However, a decrease in operative time as familiarity with LITT improves has been described,[49,50] with a decrease in complications also observed over time.[49] Operative duration is also naturally related to tumor size, which ranged from 0.7 cm^3 to more than 10 cm^3 in our analysis (**Table 1**).

The majority of gliomas (71.2%) in our analysis were high grade. Five-year survival following conventional therapy for high-grade glioma is estimated at only 4%,[51] with median survival in the Stupp trial only 14.6 months overall.[52] However, patients undergoing biopsy alone had a median survival of less than 10 months[52] and are likely more comparable with patients undergoing LITT. OS following LITT was estimated at 13.6 months in our analysis, which represents a significant period of time in the glioma disease course. It is also important to note that significant heterogeneity was observed in our analyses, which is likely the result of substantial variations in tumor size, grades and primacy across all analyses. When more data are available, future analyses should consider synthesizing pooled survival curves and accounting for the time-to-event component, as pooling of mean survival times is likely to be less informative and result in data loss. One particular outlying study was observed with a substantial proportion of low-grade gliomas, which likely explains this finding.[21] Further evaluation of LITT in comparison to primary management in prospective designs will be required.

Cost-effectiveness is an important consideration when evaluating any new therapeutic modality, which was unexplored in our review. To our knowledge, no studies have directly assessed the cost-effectiveness of LITT in comparison with current best practice or stereotactic biopsy alone. Future studies should consider a cost–benefit analysis to inform the implementation of LITT in patients with glioma, which should additionally include functional indices to infer a patient-centered cost–benefit.

Limitations

Our study has several limitations reflecting the deficits of the existing literature. Sample sizes for each study included were small and patient populations were heterogenous in terms of demographics, molecular information, prognosis, tumor locations and previous treatment. LITT was not compared directly to standard care, so no inferences can be made regarding its efficacy. Future studies should consider matching schemes or other comparative methodologies, or ideally prospectively randomized designs to facilitate comparison with standard treatment. Furthermore, pooling of OS and PFS, as well as grouping grade 1/2 and grade 3/4, provides limited insight into survival and serves as descriptive analysis only, so future studies should consider making full data regarding patient survival as well as the molecular characteristics available so that pooled survival curves can be synthesized. Future studies should also consider standardized reporting of complications, as we observed substantial heterogeneity in the description and rate of complications reported.

CONCLUSIONS

Maximal resection with adjuvant chemoradiation remains the gold standard for treatment of high-grade glioma where feasible. However, LITT offers a minimally invasive therapeutic strategy that may potentially be efficacious in the treatment of deep-seated or recurrent gliomas and should be further investigated in randomized control trials.

CRediT AUTHORSHIP CONTRIBUTION STATEMENT

Philip J. O'Halloran: Conceptualization, Investigation, Literature review, Formal analysis, Data curation, Writing – original draft, Writing – review & editing, Read and approved the final version of the manuscript, Agree with the order of presentation of the authors. **Jack Henry:** Investigation, Literature review, Formal analysis, Data curation, Edited and made corrections to the manuscript, Read and approved the final version of the manuscript, Agree with the order of presentation of the authors. **Michael Amoo:** Investigation, Literature review, Formal analysis, Data curation, Edited and made corrections to the manuscript, Read and approved the final version of the manuscript, Agree with the order of presentation of the authors. **Aristotelis Kalyvas:** Investigation, Literature review, Edited and made corrections to the manuscript, Read and approved the final version of the manuscript, Agree with the order of presentation of the authors. **Nilesh Mohan:** Investigation, Literature review, Edited and made corrections to the manuscript, Read and approved the final version of the manuscript, Agree with the order of presentation of the authors. **Gelareh Zadeh:** Edited and made corrections to the manuscript, Read and approved the final version of the manuscript, Agree with the order of presentation of the authors. **Suneil K. Kalia:** Edited and made corrections to the manuscript, Read and approved the final version of the manuscript, Agree with the order of presentation of the authors. **Paul N. Kongkham:** Conceptualization, Edited and made corrections to the manuscript, Read and approved the final version of the manuscript, Agree with the order of presentation of the authors.

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