

07.01.81 Laser Interstitial Thermal Therapy (LITT)

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Related Policies:

- [06.01.15 Stereotactic Radiosurgery \(SRS\) and Stereotactic Body Radiation Therapy \(SBRT\)](#)
- [07.01.71 Responsive Neurostimulation for the Treatment of Refractory Focal Epilepsy](#)
- [07.01.60 Vagus Nerve Stimulation \(VNS\) and Vagal Nerve Blocking Therapy](#)

Summary

Description

Laser interstitial thermal therapy (LITT) involves the introduction of a laser fiber probe to deliver thermal energy for the targeted ablation of diseased tissue. The goal of therapy is selective thermal injury through the maintenance of a sharp thermal border, as monitored via the parallel use of real-time magnetic resonance (MR) thermography and controlled with the use of actively cooled applicators. In neurological applications, LITT involves the creation of a transcranial burr hole for the placement of the laser probe at the target brain tissue. Probe position, ablation time, and intensity are controlled under magnetic resonance imaging (MRI) guidance. LITT has been proposed as a less invasive treatment option for

individuals with neurological conditions compared to surgery. Two LITT systems, Visualase and NeuroBlate, have received marketing clearance from the U.S. Food and Drug Administration (FDA).

Summary of Evidence

For individuals who have primary or metastatic brain tumors who receive MR-guided LITT, the evidence includes systematic reviews and meta-analyses and several nonrandomized comparative and single-arm studies. Relevant outcomes are overall survival (OS), disease-specific survival, symptoms, change in disease status, functional outcomes, quality of life, and treatment-related morbidity. Overall survival estimates have ranged from 9.0 to 14.4 months in new or recurrent glioblastoma. Among patients with metastatic tumors receiving LITT following prior SRS, OS rates have ranged between 72% to 76% at 6 months and 63% to 65% at 12 months. In a more heterogeneous population of patients with primary and metastatic brain tumors who received LITT, 12-month OS rates were slightly lower in individuals with brain metastases (56.3%) and high-grade glioma (43.0%) than other analyses. Systematic reviews comparing LITT to open craniotomy with resection or stereotactic radiosurgery (SRS) suggest a reduced incidence of adverse events with LITT; however, neurological deficits attributable to LITT-induced thermal damage have been observed despite concurrent MRI guidance. Studies are limited by predominantly retrospective designs, small sample sizes, and population heterogeneity, with study subjects varying by performance status, lesion volume and location, extent of prior therapies, and extent of ablation. Prospective comparative studies in well-defined and -controlled patient populations are lacking. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome. However, even though there is a paucity of data in the peer-reviewed scientific literature, relevant society guidelines (see [Practice Guidelines and Position Statements](#) below) support LITT use in identified individuals who have primary or metastatic brain tumors. Therefore, LITT will be considered medically necessary for individuals with a primary brain tumor or metastatic disease when the [policy criteria](#) below have been met.

For individuals who have symptomatic cranial radiation necrosis who receive MR-guided LITT, the evidence includes meta-analyses, nonrandomized comparative studies, and a single-arm study. Relevant outcomes are OS, disease-specific survival, symptoms, change in disease status, functional outcomes, quality of life, and treatment-related morbidity. Studies have reported improved local control and survival outcomes in individuals with radiation necrosis compared to those with brain metastases. One study comparing LITT to bevacizumab suggested that LITT treatment may be more successful among patients before radiation necrosis lesions become symptomatic. One study comparing LITT to craniotomy and one study comparing LITT to medical management did not report significant survival differences between groups. Studies are limited by retrospective designs, small sample sizes, population heterogeneity, and unclear relevance, as symptomatic status and steroid-related morbidity were not consistently reported. Prospective comparative studies in well-defined and -controlled patient populations are lacking. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome. However, even though there is a paucity of data in the peer-reviewed scientific literature, relevant society guidelines (see [Practice Guidelines and Position Statements](#) below) support LITT use in identified individuals who have symptomatic cranial radiation necrosis. Therefore, LITT will be considered medically necessary for individuals with symptomatic cranial radiation necrosis when the [policy criteria](#) below have been met.

For individuals who have drug-resistant epilepsy who receive MR-guided LITT, the evidence includes systematic reviews and meta-analyses, nonrandomized comparative studies, and single-arm studies. Relevant outcomes are disease-specific survival, symptoms, change in disease status, functional outcomes, quality of life, and treatment-related morbidity. Meta-analyses have reported seizure freedom rates ranging from 50% to 61% but are limited by heterogeneous study populations and follow-up durations. Studies comparing LITT to open resection have reported comparable outcomes in patients with

pediatric insular epilepsy and adult temporal lobe epilepsy (TLE). In one meta-analysis comparing LITT to radiofrequency ablation (RFA) and conventional surgery, superior outcomes were noted with conventional surgery among individuals with mesial TLE (mTLE). A subsequent meta-analysis concluded that while there is no evidence to suggest that LITT is less effective than open surgical resection in the short term, long-term data are lacking. Total quality of life scores reported in the ongoing LAANTERN registry increased by 72.4%, but this change was not considered statistically significant. Prospective comparative studies in well-defined and - controlled patient populations are required to assess a net health outcome and to identify patients most likely to benefit from LITT. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome. However, even though there is a paucity of data in the peer-reviewed scientific literature, relevant society guidelines (see [Practice Guidelines and Position Statements](#) below) support LITT use in identified individuals who have drug-resistant epilepsy. Therefore, LITT will be considered medically necessary for individuals with drug-resistant epilepsy when the [policy criteria](#) below have been met.

For individuals who have other miscellaneous cancers who receive LITT, the evidence includes systematic reviews, small single-arm case series studies, comparative observational studies. Relevant outcomes are overall survival (OS), disease-specific survival, symptoms, change in disease status, functional outcomes, quality of life (QoL), and treatment-related morbidity. The evidence is highly heterogeneous and inconsistently reports health outcomes. Further prospective randomized studies are needed that evaluate health outcomes in larger patient populations with longer follow-up. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome. However, even though there is a paucity of data in the peer-reviewed scientific literature, relevant society guidelines (see [Practice Guidelines and Position Statements](#) below) support LITT use in identified individuals who have other gliomas. Therefore, LITT will be considered medically necessary for individuals with other gliomas when the [policy criteria](#) below have been met.

Additional Information

None

OBJECTIVE

The objective of this evidence review is to determine whether the use of MR-guided laser interstitial thermal therapy (LITT) improves the net health outcome in individuals with cancer, radiation necrosis or refractory epilepsy.

PRIOR APPROVAL

Not applicable

POLICY

Tumor(s)/Radiation Necrosis

Treatment of glioblastomas and other gliomas or radiation necrosis of the brain using laser interstitial thermal therapy (LITT) may be considered **medically necessary** when it is being used to treat **one of the following**:

- A progressive (primary or metastatic) or recurrent malignant glioblastoma or other glioma(s) **or**
- A lesion(s) inaccessible to surgical resection.

Refractory Epilepsy

The treatment of drug refractory epilepsy using laser interstitial thermal therapy is considered **medically necessary** when **all of the following** criteria are met:

- Documented disabling seizures despite the use of two or more tolerated antiepileptic drug regimens; **and**
- Documented (i.e., imaging or EEG) presence of well-defined epileptogenic foci accessible by laser interstitial thermal therapy (LITT).

Investigational

Laser interstitial thermal therapy (LITT) is considered **investigational** when the above criteria is not met and for all other indications, including but not limited to the following because the evidence is insufficient to determine the effects of the technology on the net health outcomes:

- Liver cancer
- Lung cancer
- Osteoid osteoma
- Prostate cancer

POLICY GUIDELINES

- **Epileptogenic lesion:** Is the structural abnormality that is presumed be the basis of the seizure(s).
- **Medically refractory epilepsy:** Occurs when an individual has failed to become seizure free with adequate trials of two seizure medications (called AEDs). These seizure medications must have been chosen appropriately for the individual's seizure type, tolerated by the individual, and tried alone or together with other seizure medications.

Coding

See the [Codes](#) table for details.

BACKGROUND

Laser Interstitial Thermal Therapy

Laser interstitial thermal therapy (LITT) involves the introduction of a laser fiber probe to deliver thermal energy for the targeted ablation of diseased tissue. Thermal destruction of tissue is mediated via DNA damage, necrosis, protein denaturation, membrane dissolution, vessel sclerosis, and coagulative necrosis. The goal of therapy is selective thermal injury through the maintenance of a sharp thermal border, as monitored via the parallel use of real-time magnetic resonance (MR) thermography and controlled with the use of actively cooled applicators. In neurological applications, LITT involves the creation of a transcranial burr hole for the placement of the laser probe at the target brain tissue. Probe position, ablation time, and intensity are controlled under MRI guidance.

The majority of neurological LITT indications described in the literature involve the ablation of primary and metastatic brain tumors, epileptogenic foci, and radiation necrosis in surgically inaccessible or eloquent brain areas. LITT may offer a minimally invasive treatment option for patients with a high risk of morbidity with traditional surgical approaches. The most common complications following LITT are transient and permanent weakness, cerebral edema, hemorrhage, seizures, and hyponatremia. Delayed neurological deficits due to brain edema are temporary and typically resolve after corticosteroid therapy.

Contraindications to magnetic resonance imaging (MRI) are also applicable to the administration of LITT.

Regulatory Status

In August 2007, the Visualase™ MRI-Guided Laser Ablation System (Medtronic; formerly Biotex, Inc.) received initial marketing clearance by the U.S. Food and Drug Administration (FDA) through the 510(k) pathway (K071328). In January 2022 (K211269), the system (software version 3.4) was classified as a neurosurgical tool with narrowed indications for use, including "to ablate, necrotize or coagulate intracranial soft tissue including brain structures (for example, brain tumor, radiation necrosis and epileptic foci as identified by non-invasive and invasive neurodiagnostic testing, including imaging) through interstitial irradiation or thermal therapy in medicine and surgery in the discipline of neurosurgery with 800 nm through 1064 nm lasers." The device is contraindicated for patients with medical conditions or implanted medical devices contraindicated for MRI and for patients whose physician determines that LITT or invasive surgical procedures in the brain are not acceptable. Data from compatible MRI sequences can be processed to relate imaging changes to relative changes in tissue temperature during therapy. The Visualase™ cooling applicator utilizes saline.

In April 2013, the NeuroBlate® System (Monteris Medical) received initial clearance for marketing by the FDA through the 510(k) pathway (K120561). As of August 2020, the system is indicated for use "to ablate, necrotize, or coagulate intracranial soft tissue, including brain structures (e.g., brain tumor and epileptic foci as identified by non-invasive and invasive neurodiagnostic testing, including imaging), through interstitial irradiation or thermal therapy in medicine and surgery in the discipline of neurosurgery with 1064 nm lasers" (K201056). The device is intended for planning and monitoring of thermal therapy under MRI guidance, providing real-time thermographic analysis of selected MRI images. The NeuroBlate® system utilizes a laser probe with a sapphire capsule to promote prolonged, pulsed laser firing and a controlled cooling applicator employing pressurized CO₂.

RATIONALE

This evidence review was created in December 2020 and has been updated regularly with searches of the PubMed database. The most recent literature update was performed through January 2026.

Evidence reviews assess the clinical evidence to determine whether the use of a technology improves the net health outcome. Broadly defined, health outcomes are length of life, quality of life, and ability to function, including benefits and harms. Every clinical condition has specific outcomes that are important to patients and to managing the course of that condition. Validated outcome measures are necessary to ascertain whether a condition improves or worsens; and whether the magnitude of that change is clinically significant. The net health outcome is a balance of benefits and harms.

To assess whether the evidence is sufficient to draw conclusions about the net health outcome of a technology, 2 domains are examined: the relevance and the quality and credibility. To be relevant, studies must represent 1 or more intended clinical use of the technology in the intended population and compare an effective and appropriate alternative at a comparable intensity. For some conditions, the alternative will be supportive care or surveillance. The quality and credibility of the evidence depend on study design and conduct, minimizing bias and confounding that can generate incorrect findings. The randomized controlled trial (RCT) is preferred to assess efficacy; however, in some circumstances, nonrandomized studies may be adequate. Randomized controlled trials are rarely large enough or long enough to capture less common adverse events and long-term effects. Other types of studies can be used for these purposes and to assess generalizability to broader clinical populations and settings of clinical practice.

Primary or Metastatic Brain Tumors

Clinical Context and Therapy Purpose

The purpose of magnetic resonance (MR)-guided laser interstitial thermal therapy (LITT) is to use a focused thermal therapy technique to ablate primary or metastatic brain tumors and to avoid potential complications associated with alternative surgical interventions.

The following PICO was used to select literature to inform this review.

Populations

The population of interest is individuals with primary or metastatic brain tumors that are inaccessible surgically or located in proximity to eloquent or radiosensitive areas. LITT is typically used when surgery is contraindicated due to a high risk of procedural morbidity and/or presence of comorbidities that preclude candidacy for open surgery. LITT may be preferred by individuals desiring a less invasive surgical alternative and its use has been explored in first-line, adjunct, and salvage settings.

Primary intracranial malignant tumors include gliomas, astrocytomas, malignant meningiomas, and primitive neuroectodermal tumors (i.e., medulloblastoma, pineoblastoma). Treatment of primary brain tumors such as gliomas is more challenging, due to their generally larger size and infiltrative borders.

Intracranial metastases tend to have a smaller spherical size and noninfiltrative borders. Brain metastases occur frequently, seen in 25% to 30% of all individuals with cancer, particularly in those with cancer of the lung, breast, colon, kidney, and melanoma.

Interventions

The therapy being considered is laser interstitial thermal therapy (LITT), also known as stereotactic laser ablation. LITT is performed under real-time magnetic resonance imaging (MRI) guidance.

Comparators

The following therapies are currently being used to treat primary and/or metastatic brain tumors in select treatment settings: open surgical resection (e.g., craniotomy), stereotactic radiosurgery (SRS), radiotherapy (including whole-brain radiotherapy [WBRT]), and systemic therapies (e.g., chemotherapy).

Outcomes

Primary outcomes of interest are overall survival (OS) and progression-free survival (PFS). Additional outcomes include local disease control, symptom improvement, functional outcomes, change in disease status, quality of life, and treatment-related morbidity. Follow-up duration of at least 2 to 3 years is of interest for survival outcomes in individuals with low-grade tumors. For patients with tumors associated with a poor prognosis (e.g., recurrent glioblastoma), shorter follow-up durations may be appropriate.

Study Selection Criteria

Methodologically credible studies were selected using the following principles:

- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.
- To assess long-term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.
- Consistent with the 'best available evidence approach', within each category of study design, studies with larger sample sizes and longer durations were sought.
- Studies with duplicative or overlapping populations were excluded.

Review of Evidence

Systematic Reviews

Systematic review characteristics and survival outcomes are summarized in Table 1.

Pandey et al (2024) conducted a meta-analysis of 22 studies (N=206) that reported use of LITT for primary brain tumors (glioblastoma [n=185] and IDH-mutated astrocytoma [n=21]). Among patients with glioblastoma, OS was 9.3 months (range, 7.1 to 11.4 months) and PFS was 4.8 months (range, 2.0 to 7.9 months). Neurologic complications occurred in 10.3% and non-neurologic complications occurred in 4.8% of patients with glioblastoma. Among patients with astrocytoma, OS and PFS could not be determined due to a lack of data. Neurologic complications occurred in 33% and non-neurologic complications occurred in 8.3% of patients with astrocytoma.

Zhao et al (2024) performed a systematic review and meta-analysis of 8 studies (N=128) in patients with recurrent glioblastoma multiforme (rGBM). At 6 months, PFS was 25% (95% CI, 15% to 37%; I²=53%) and OS was 92% (95% CI, 83% to 100%; I²=0%). At 12 months, PFS was 9% (95% CI, 4% to 15%; I²=24%) and OS was 42% (95% CI, 13% to 73%; I²=67%). Complication rates were low overall, and most complications were mild to moderate in severity.

Alkazemi et al (2023) published a systematic review of comparative and descriptive studies (excluding case reports) assessing the evidence for LITT in primary and metastatic brain tumors. A total of 45 studies (N=826) were included. Lesions were categorized as high-grade gliomas (n=361), low-grade gliomas (n=116), metastatic brain tumors (n=337), or nonglial tumors (n=15). The majority of studies offered LITT in patients with inaccessible or deep tumors (n=12), after failed radiosurgery (n=9), or were nonspecific (n=12). One-year PFS was 19.6% (95% confidence interval [CI], 11.3% to 29.0%; I²=0%) in high-grade gliomas, 16.9% (95% CI, 11.6% to 24.0%; I²=0%) in grade 4 astrocytomas, and 51.2% (95% CI, 36.7% to 65.5%; I²=0%) in brain metastases. One-year OS was 43.0% (95% CI, 36.0% to 50.0%; I²=7.6%) in high-grade glioma, 45.9% (95% CI, 37.9% to 54%; I²=0%) in grade 4 astrocytomas, 93.0% (95% CI, 42.3% to 100%; I²=not applicable) in low-grade gliomas, and 56.3% (95% CI, 47.0% to 65.3%; I²=not applicable) in brain metastases. Major procedure-related adverse events (AEs) were 30% (95% CI, 27% to 40%) with a 16% incidence (95% CI, 12% to 22%) of major or minor neurological deficits. This study is limited by lack of comparator data.

Chen et al (2021) published a systematic review and meta-analysis of retrospective studies and case series investigating the efficacy of LITT for brain metastases with in-field recurrence or radiation necrosis following treatment with SRS. A meta-analysis of 14 studies (470 patients with 542 lesions) was performed. The overall 12-month local control rate ranged between 56.0% and 84.7% with a pooled rate of 69.0% (95% CI, 60.0% to 76.7%; I²=50.584%; p=.048) and pooled OS of 17.15 months (95% CI, 13.27 to 24.8). Among 153 recurrent brain metastatic lesions across 5 studies, the 12-month local control rate was 59.9% (95% CI, 47.9% to 70.9%). Among 75 radiation necrosis lesions across 4 studies, the 12-month local control rate was 76.3% (95% CI, 65.0% to 84.8%). Thus, LITT provided more favorable local control efficacy in patients with radiation necrosis compared to those with brain metastasis recurrence. No significant difference in median OS at 1 year was determined between the radiation necrosis and brain metastasis groups (66.5% vs. 66.8%; p=.978). Survival outcomes were not stratified by pathology and safety outcomes were not reported. Compared to previously reported estimates for surgical resection with a local control rate ranging from 62% to 93% and a median OS of 8.7 months, the authors concluded that LITT demonstrates comparable local control but a more satisfactory survival benefit. The analysis is limited by study heterogeneity, small sample sizes, and the lack of a standardized definition for local disease control.

de Franca et al (2020) published a systematic review and meta-analysis of LITT as a therapy for brain tumors compared to SRS based on 25 studies. Patient populations included patients with brain metastasis and rGBM. A significant improvement in median OS was observed in patients treated with LITT compared to SRS among patients with brain metastasis (12.8 vs. 9.8 months; $p < .02$) and was associated with a 15% reduction in risk of AEs overall. The authors concluded that "there is no evidence that LITT can be used as a treatment of choice when compared to SRS," but use of LITT may have a role in lowering the risk of AEs. The analysis was limited by inclusion of heterogeneous populations, the small number of patients treated with LITT ($n=39$), and a lack of reporting on prior treatments. In particular, patients treated with SRS varied in their degree of radiosensitivity and prior radiation exposure, which may have influenced the higher rate of AEs observed in this group.

Barnett et al (2016) conducted a systematic review and meta-analysis comparing LITT (8 studies; 77 patients) to open craniotomy (12 studies; 1036 patients) for the treatment of high-grade gliomas in or near areas of eloquence, with a focus on AEs. Proportions of major complications occurred in 5.7% (95% CI, 1.8% to 11.6%) and 13.8% (95% CI, 10.3% to 17.9%) of patients treated via LITT and craniotomy, respectively. Studies were rated at high risk of bias due to lack of randomization and blinding. The analysis was also limited by heterogeneous patient populations (e.g., age, Karnofsky score, recurrent vs. primary disease) and lack of reporting on health outcomes.

Table 1. Systematic Review and Meta-Analysis Characteristics and Results

Study	Dates	Studies	Participants	N (Range)	Design	Duration	Survival Outcomes
Pandey et al (2024)	To 2023	22	Patients with primary brain tumors (glioblastoma or IDH-mutated astrocytoma)	206 (2 to 29)	Noncomparative studies	NR	OS: Glioblastoma: 9.3 months (range, 7.1 to 11.4 months) Astrocytoma: NR
Zhao et al (2024)	2001-2022	8	Patients with rGBM treated with LITT	128 (3 to 60)	Noncomparative studies	At least 6 to 12 mo	OS at 6 mo: 92% (95% CI, 83% to 100%; $I^2=0\%$) OS at 12 mo: 42% (95% CI, 13% to 73%; $I^2=67\%$)
Alkaze mi et al (2023)	To Oct 2021	45	Patients with primary or metastatic brain tumors undergoing LITT	826 (2 to 91)	RCTs; retrospective and prospective observational studies; case series	NR	OS at 1 year: 43.0% (95% CI, 36.0% to 50.0%; $I^2=7.6\%$; $p=.37$; 12 studies) for

Study	Dates	Studies	Participants	N (Range)	Design	Duration	Survival Outcomes
							high-grade glioma; 56.3% (95% CI, 47.0% to 65.3%; I ² =NA; p=.7; 5 studies) for metastatic brain tumors
Chen et al (2021)	2011-2020	14	Patients treated with LITT for brain metastases with in-field recurrence or radiation necrosis following treatment with SRS <ul style="list-style-type: none"> • Median age, 59.6 y (range, 23 to 90) • Male, 34.5% • Median KPS, 85 (range, 50 to 100) • Median pre-operative lesion volume, 4.6 cm³ (range, 0.2 to 38.9) • Radiation necrosis, 168/470 (35.7%) 	470 (7 to 92)	Phase I-II nonrandomized; Prospective registry; Retrospective case-control; Retrospective case series	At least 6 to 12 mo	OS at 6 mo: 76.0% (95% CI, 71.4% to 80.0%; I ² =43.81%; p=.059) OS at 12 mo: 63.4% (95% CI, 52.9% to 72.7%; I ² =68.2%; p=.001)

Study	Dates	Studies	Participants	N (Range)	Design	Duration	Survival Outcomes
de Franca et al (2020)	2007-2017	25	Patients with brain metastasis or recurrent glioblastoma multiforme treated with LITT or SRS <ul style="list-style-type: none"> • Mean age, 55.8 to 59.4 • Median Karnofsky score, 70 to 87.5 • Mean tumor volume, 6.8 to 20.1 cm³ 	BM: 12 (LITT); 1555 (SRS) rGBM: 27 (LITT); 232 (SRS)	Randomized controlled study (SRS); Prospective cohort studies; Retrospective studies	NR	Median OS: LITT: <ul style="list-style-type: none"> • BM: 12.8 mo (range, 9.3 to 16.3) • rGBM: 10.5 mo (NA)¹ SRS: <ul style="list-style-type: none"> • BM: 9.8 mo (range, 8.3 to 9.9) • rGBM: 10.5 mo (range, 9.9 to 11.4)
Barnett et al (2016)	1992-2014	20	Patients with recurrent or primary high-grade gliomas (WHO grade III or IV) in or near areas of eloquence treated with LITT or craniotomy, respectively <ul style="list-style-type: none"> • Mean age, 54.3 vs. 45.6 (p<.00001) • Male, 64.2% vs. 58.8% (p=.37) • Karnofsky score, 73.4 vs. 78.4 (p=.0006) • Recurrent glioma, 68% vs. 22% (p<.00001) 	LITT: 67 Craniotomy: 522	Prospective cohort studies; Retrospective studies	NR	NR

BM: brain metastasis; CI: confidence interval; KPS: Karnofsky Performance Status; LITT: laser interstitial thermal therapy; NA: not available; NR: not reported; OS: overall survival; rGBM: recurrent glioblastoma multiforme; SRS: stereotactic radiosurgery; WHO: World Health Organization.

¹ Only 1 study result reported.

Comparative Observational Studies

Grabowski et al (2022) published a multicenter, retrospective study of patients undergoing treatment for biopsy-proven brain metastasis recurrence after stereotactic radiotherapy (SRT). Patients were stratified

into three groups: planned LITT plus SRT (n=21), LITT alone (n=25), or repeat SRT alone (n=9). Mean patient age was 60 years (range, 37 to 86) and median follow-up duration was 7.3 months (range, 1.0 to 30.5). No patients in the LITT plus SRT group received prior surgery or WBRT, compared to 20% and 28% treated with LITT alone and 11% and 56% treated with SRT alone (p=.05 and .01, respectively). Median time to index lesion progression for LITT plus SRT, LITT alone, and repeat SRT alone was 29.8, 7.5, and 3.7 months, respectively (p=.022). A univariate analysis found a significantly increased risk of tumor progression among patients receiving prior surgery (hazard ratio [HR], 5.33; 95% CI, 1.41 to 16.93; p=.007). The authors noted that future prospective studies are required to validate these findings.

Fadel et al (2022) retrospectively reviewed an institutional database to identify patients with unifocal, lobar, surgically accessible recurrent glioblastoma who were treated with LITT or resection between 2013 and 2020. Of 744 patients identified, a LITT cohort of 17 patients was compared with 23 surgical patients. Baseline characteristics were similar between groups except for average lesion size, which was smaller in patients treated with LITT (4.37 cm³ vs. 7.54 cm³; p=.017). Overall survival (14.1 vs. 13.8 months; p=.578) and PFS (3.7 vs. 3.3 months; p=.004) were not significantly different between groups. Significantly shorter hospital stays were observed in patients treated with LITT (2.2 vs. 3.0 days; p=.004).

Mohammadi et al (2019) conducted a multicenter retrospective review of survival outcomes in patients with deep seated newly diagnosed glioblastoma treated with upfront MR-guided LITT prior to chemo/radiotherapy (n=24; median age, 54 years; 50% male; 71% <70 years) compared to a matched cohort of biopsy-only patients (n=24; median age, 64 years; 58% male; 75% <70 years). Patients were matched based on age, gender, tumor location (deep vs. lobar), and tumor volume. Median follow-up was 9.3 months (range, 2 to 43 months) and 14.7 months (range, 2 to 41 months) in LITT and biopsy-only cohorts, respectively. Overall median estimates of OS and PFS in the LITT cohort was 14.4 and 4.3 months compared to 15.8 and 5.9 months for the biopsy-only cohort. Age <70 years and tumor volume <11 cm³ were identified as favorable prognostic factors for OS. The study was limited by its retrospective design, lack of randomization, small sample size, and short follow-up durations. Additionally, concurrent chemotherapy and radiotherapy regimens were not specified.

Single-Arm Studies

The Laser Ablation of Abnormal Neurological Tissue Using Robotic NeuroBlate System (LAANTERN) registry is an ongoing industry-sponsored, multicenter, multinational prospective registry of the NeuroBlate device enrolling patients with primary and metastatic brain tumors, epileptic foci, and movement disorders (NCT02392078). Rennert et al (2019) reported procedural safety outcomes for the first 100 patients enrolled in the LAANTERN. Kim et al (2020) reported 12-month survival and quality of life outcomes among 223 patients enrolled in the LAANTERN registry with primary (n=131) or metastatic (n=92) brain tumors who received treatment with the NeuroBlate device. The majority of patients with primary tumors had high-grade glioma (n=90) and patients with metastatic disease had recurrent tumors (n=43) or radionecrosis (n=34). The 1-yr estimated OS rate was 73% (95% CI, 65.3% to 79.2%), which was not found to be significantly different between primary or metastatic tumors (74.6% vs. 70.7%, respectively). Quality of life assessments with the Functional Assessment of Cancer Therapy - Brain (FACT-Br) questionnaire did not meet the criteria for a clinically meaningful change (>10%) and EQ-5D questionnaires indicated an overall decline of 0.1 points from baseline. In 2022, de Groot and coworkers published a subgroup analysis of LAANTERN registry data focusing on new (n=29) and recurrent (n=60) cases of IDH wild-type glioblastoma. Median OS was 9.73 months (95% CI, 5.16 to 15.91) for newly diagnosed patients and 8.97 months (95% CI, 6.94 to 12.36) for recurrent patients. Median OS in newly diagnosed patients receiving post-LITT chemo/radiation was 16.14 months (95% CI, 6.11 to not reached).

Section Summary: Primary or Metastatic Brain Tumors

Evidence for the use of LITT in primary or metastatic brain tumors includes systematic reviews and meta-analyses and several nonrandomized comparative and single-arm studies. Overall survival estimates have ranged from 9.0 to 14.4 months in new or recurrent glioblastoma. Among patients with metastatic tumors receiving LITT following prior SRS, OS rates have ranged between 72% to 76% at 6 months and 63% to 65% at 12 months. In a more heterogeneous population of patients with primary and metastatic brain tumors who received LITT, 12-month OS rates were slightly lower in patients with brain metastases (56.3%) and high-grade glioma (43.0%) than other analyses. Systematic reviews comparing LITT to open craniotomy with resection or SRS suggest a reduced incidence of adverse events with LITT; however, neurological deficits attributable to LITT-induced thermal damage have been observed despite concurrent MRI guidance. Studies are limited by predominantly retrospective designs, small sample sizes, and population heterogeneity, with study subjects varying by performance status, lesion volume and location, extent of prior therapies, and extent of ablation. Prospective comparative studies in well-defined and -controlled patient populations are required to assess net health outcomes.

Radiation Necrosis

Clinical Context and Therapy Purpose

The purpose of LITT is to use a focused thermal therapy technique to ablate regions of cerebral radiation necrosis in symptomatic individuals with an insufficient or intolerable response to medications, and to potentially avoid complications associated with alternative surgical interventions.

The following PICO was used to select literature to inform this review.

Populations

The population of interest is individuals with symptomatic cranial radiation necrosis with insufficient response or intolerance to medication management. LITT is typically used when open surgery is contraindicated due to high risk of procedural morbidity and/or presence of comorbidities that precludes candidacy for open surgery.

Treatment-induced brain tissue necrosis (also referred to as cranial radiation necrosis or radionecrosis) is a serious delayed complication of cranial irradiation that typically develops after 1 to 3 years. Radiation necrosis is more likely to occur with high-dose fractionation and potentially with concurrent chemotherapy or use of radiosensitizers. The risk of radiation necrosis following SRS has been reported to be higher, with a steep dose-response relationship. Differentiating radiation necrosis from recurrent brain tumors via imaging can be difficult, as conventional structural MRI may reveal features that overlap with the typical radiographic appearance of high-grade primary or metastatic brain tumors. Biopsy may be required for a definitive diagnosis of radiation necrosis, particularly among individuals who are symptomatic or with worsening radiographic findings over time.

Symptoms of radiation necrosis are dependent on the location of the lesion and may include focal neurologic deficits or more generalized signs and symptoms of increased intracranial pressure. Seizures are observed in approximately 20% of individuals.

Interventions

The therapy being considered is LITT as an alternative to open craniotomy with resection and/or medication management. LITT is performed under real-time MRI guidance.

Comparators

The following therapies are currently being used to treat primary and metastatic brain tumors: surgical resection and medication management. Medications used in the management of radiation necrosis include corticosteroids and bevacizumab, a vascular endothelial growth factor (VEGF) inhibitor.

Outcomes

Outcomes of interest are symptom improvement, medication use, quality of life, treatment-related morbidity, OS, and PFS. Follow-up duration of at least 2 to 3 years is of interest for survival outcomes.

Study Selection Criteria

Methodologically credible studies were selected using the following principles:

- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.
- To assess long-term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.
- Studies with duplicative or overlapping populations were excluded.

Review of Evidence

Systematic Reviews

Gecici et al (2024) conducted a systematic review and meta-analysis of 24 studies (N=547) that compared bevacizumab and LITT in patients with radiation necrosis. Most of the included studies were retrospective. Symptomatic improvement or stability occurred in 87.7% and 71.2% of patients, respectively (p=.02). Radiologic improvement or stability occurred in 86.2% and 64.7%, respectively (p=.27). Steroid discontinuation occurred in 45% and 62.4%, respectively (p=.90). Heterogeneity for all comparisons was high ($I^2>70\%$). Adverse event rates were similar between groups (11.2% vs. 14.9%; p=.66).

Vellayappan et al (2024) conducted a systematic review of treatments for radiation necrosis in patients who had previously undergone SRS. The review was conducted on behalf of the International Stereotactic Radiosurgery Society. Of the 21 included studies, only 5 included LITT (n=151); one LITT study was prospective, and the rest were retrospective. The pooled radiologic improvement/stability rate was 88% (95% CI, 82% to 93%) with LITT compared to 94% with bevacizumab. Symptom improvement was only reported in 2 studies and could not be pooled for analysis. Toxicity results were not consistently reported, and no conclusions could be made. The authors concluded that the role of LITT is evolving and that prospective comparative studies are needed.

The meta-analysis published by Chen and coworkers (2021), described previously in Table 1, included 168 (35.7%) patients with radiation necrosis who received LITT following prior treatment with SRS. The local control rate for patients with radiation necrosis at 6 and 12 months was 83.1% (95% CI, 68.4% to 91.8%) and 66.8% (95% CI, 49.1% to 80.8%), respectively, and was more satisfactory compared to patients with recurrent brain metastasis. Overall survival was 83.1% versus 69.2% at 6 months and 66.8% versus 66.5% at 12 months for radiation necrosis and recurrent brain metastasis groups, respectively. Pre-ablation biopsy, which can accurately diagnose radiation necrosis, was not routinely performed in all analyzed studies, highlighting a major limitation of this meta-analysis given that it can be quite challenging to accurately distinguish radiation necrosis from brain metastases based on radiographic evidence alone.

Palmisciano et al (2021) published a systematic review and meta-analysis of bevacizumab versus LITT for the treatment of radiation necrosis in patients with brain metastases previously treated with radiotherapy. Eighteen studies were included for analysis, including 143 patients treated with bevacizumab and 148 treated with LITT. Compared to LITT, a higher proportion of patients treated with bevacizumab experienced symptomatic improvement (73.3% vs. 60.8%) and ability to wean off steroids (66.7% vs. 44.1%), but these differences were not significantly different between groups ($p=.187$; $I^2=54.8\%$ and $p=.614$; $I^2=25.5\%$, respectively). At 18 months, median OS was significantly higher for patients treated with LITT (46.4% vs. 25%; $p=.038$; $I^2=73.7\%$). Rates of AEs were similar between bevacizumab (14.7%) and LITT (12.2%) cohorts. This analysis is limited by inclusion of primarily retrospective studies, heterogeneous study populations and treatment centers, and limited patient-level data.

Comparative Observational Studies

Sankey et al (2022) published a multicenter, retrospective study of SRS-treated patients with brain metastases who developed biopsy-proven radiation necrosis who were treated with LITT ($n=57$) or medical management ($n=15$). Median follow-up was 10.0 months (range, 4.2 to 25.1 months). There was no significant difference in median OS (15.2 vs. 11.6 months; $p=.60$) or freedom from local progression (13.6 vs. 7.06 months; $p=.40$) in LITT or medical management cohorts, respectively. Patients were able to discontinue steroid therapy earlier in the LITT cohort at a median of 37 versus 245 days ($p<.001$). The authors note that prospective trials should be designed to validate the utility of LITT for radiation necrosis, including its impact on steroid-induced morbidity.

Sujjantarat et al (2020) conducted a retrospective chart review comparing outcomes for patients with biopsy-confirmed radiation necrosis treated with LITT ($n=25$) or bevacizumab ($n=13$) at a single center between 2011 and 2018. The LITT group had a significantly longer OS compared to bevacizumab (median, 24.8 vs. 15.2 months; $p=.003$). Time to local recurrence was not statistically significant between groups ($p=.091$) but trended longer in the LITT cohort. Among 13 patients with pre-treatment symptoms in the LITT group, 9 (69%) achieved symptom relief. Among 11 patients with pre-treatment symptoms in the bevacizumab group, 4 (36%) achieved symptom relief. No significant difference was noted between groups for the ability to wean off concurrent steroids. Given that only 50% of lesions treated with LITT were symptomatic compared to 80% of lesions treated with bevacizumab, the authors suggest that LITT treatment may be more successful before radiation necrosis lesions become symptomatic. The study is limited by its retrospective design, small samples size, and population heterogeneity.

Hong et al (2019) conducted a single-center retrospective chart review of patients treated with LITT or craniotomy for previously irradiated brain metastasis, including 42 patients with recurrent brain tumors and 33 patients with radiation necrosis. Among the 33 radiation necrosis patients, 15 received craniotomy and 18 received LITT, of which 20% and 38.9% received adjuvant post-operative bevacizumab, respectively. No significant differences for mean length of hospital stay, symptom improvement, ability to wean off steroids, or rate of perioperative complications were observed between LITT and craniotomy groups. Overall PFS for patients with radiation necrosis was 73.2% and 86.7% at 24 months for patients treated with LITT and craniotomy, respectively. Overall survival for patients with radiation necrosis at 24 months was 64.6% for those receiving craniotomy and 63.2% for those receiving LITT. Study interpretation is limited by its retrospective nature and heterogeneity of prior and adjuvant treatments.

Single-Arm Studies

The LAASR study, described previously [Ahluwalia et al (2018)], included 19 patients with biopsy-confirmed radiation necrosis who received LITT following prior treatment with SRS for brain tumors. Progression-free survival and OS were 100% and 91%, respectively, at 12 weeks, and 100% and 82.1%, respectively, at 26 weeks. Progression-free survival was significantly higher at 12 weeks for patients with

radiation necrosis compared to patients with recurrent tumors ($p=.016$) but was not significantly different at 12 weeks ($p=.166$). Similar trends were seen for OS in patients with radiation necrosis at 12 weeks ($p=.02$) and 26 weeks ($p=.09$). Thirty percent of subjects were able to stop or reduce steroid usage by 12 weeks after surgery. For patients with radiation necrosis, regardless of whether a lesion was totally or subtotally ablated, LITT resulted in close to 100% lesion control and >80% survival at 6 months. No significant differences in Karnofsky performance status, quality of life, or neurocognitive scores were detected between subgroups.

Section Summary: Radiation Necrosis

Evidence on the use of LITT in patients with radiation necrosis includes meta-analyses, nonrandomized comparative studies, and single-arm study. Studies have reported improved local control and survival outcomes in individuals with radiation necrosis compared to those with brain metastases. One study comparing LITT to bevacizumab suggested that LITT treatment may be more successful among individuals before radiation necrosis lesions become symptomatic. One study comparing LITT to craniotomy did not report significant survival differences between groups. One retrospective study of patients treated with LITT, or medical management reported earlier steroid discontinuation with LITT but no significant differences in median OS or freedom from local progression. Studies are limited by retrospective designs, small sample sizes, population heterogeneity, and unclear relevance, as symptomatic status was not consistently reported. Prospective comparative studies in well-defined and -controlled patient populations are required to assess a net health outcome.

Drug-Resistant Epilepsy

Clinical Context and Therapy Purpose

The purpose of LITT is to use a focused thermal therapy technique to ablate epileptogenic foci when seizures have become drug-resistant or medication-related adverse events are intolerable, and to potentially avoid complications associated with alternative surgical interventions.

The following PICO was used to select literature to inform this review.

Populations

The population of interest is individuals with drug-resistant or medication-intolerant epilepsy, defined as failure to achieve sustained seizure freedom despite adequate trials of 2 or more appropriately chosen and tolerated antiseizure medications, as specified by the International League Against Epilepsy (ILAE) Commission on Therapeutic Strategies consensus definition for drug resistant epilepsy.

Epilepsy is diagnosed when an individual has unprovoked seizures. Primary seizure disorders include multiple subtypes that are recognizable by the degree and type of impairment of consciousness and motor capacity. Seizure disorders may be secondary to brain tumors or other space-occupying intracranial lesions such as congenital malformations, stroke, genetic syndromes, brain trauma, and cerebral infections. Mesial temporal lobe epilepsy (mTLE), also known as complex partial seizures, is a focal epilepsy syndrome. The epileptogenic foci may present in the hippocampus, amygdala, or parahippocampal gyrus. The most common non-traumatic or non-infectious etiology of mTLE is hippocampal sclerosis. The associated neuronal loss is a partial explanation for the difficulties in achieving satisfactory seizure control with antiepileptic medication. Approximately one-third of patients with epilepsy do not achieve adequate seizure control with antiepileptic drugs.

Individuals with an identifiable seizure focus that can be targeted to achieve seizure freedom are primary candidates for epilepsy surgery, but individuals with multifocal or generalized epilepsy may also be considered.

Interventions

The therapy being considered is LITT as an alternative to open craniotomy with resection, SRS, or neurostimulation. LITT is performed under real-time MRI guidance.

Comparators

The following therapies are currently being used to treat medication-refractory epilepsy: open craniotomy with resection, SRS, vagus nerve stimulation, and responsive cortical neurostimulation. Surgical treatment may be considered in instances where seizures have proven refractory to medical management and when the frequency and severity of the seizures significantly diminish quality of life.

Outcomes

Outcomes of interest are symptom improvement, change in disease status, quality of life, hospitalizations, medication use, treatment-related morbidity, and disease-specific survival. Key outcome measures are summarized in Table 2.

Table 2. Epilepsy Outcome Measures

Outcome Domain	Outcome Measures
Symptom Improvement	Change in seizure frequency (> 50% reduction considered clinically meaningful)
Change in Disease Status	Time to cessation of seizures; Postoperative outcome status, as measured by the Engel classification: <ul style="list-style-type: none">• Class I: Free of disabling seizures• Class IA: Completely seizure free since surgery• Class II: Rare disabling seizures• Class III: Worthwhile improvement• Class IV: No worthwhile improvement
Quality of Life	QOLIE-89 or QOLIE-31 multi-scale questionnaires (higher scores indicate improved health outcomes); eligibility to drive
Treatment-related Morbidity	Neuropsychological and neurocognitive testing
Disease-specific Survival	Incidence of SUDEP

QOLIE: Quality of Life in Epilepsy questionnaire; SUDEP: sudden unexpected death in epilepsy.

Follow-up duration of at least 2 years is of interest to evaluate the effect of the procedure when compared to resection or neurostimulation. Rarely, a transient increase in seizure frequency and severity may be observed following surgical interventions. Therefore, time to cessation of seizures and proportion of patients with increased seizure frequency represent additional outcomes of interest.

Study Selection Criteria

Methodologically credible studies were selected using the following principles:

- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.

- To assess long-term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.
- Studies with duplicative or overlapping populations were excluded.

Systematic Reviews

Larcipretti et al (2024) performed a systematic review and meta-analysis on MR-guided LITT compared to open surgical corpus callosotomy in pediatric patients with drug-resistant epilepsy. Five nonrandomized studies were included (N=240). There were no statistically significant differences between MR-guided LITT and open surgery in favorable Engel outcome (class I, II, and III) (relative risk [RR]: 0.89; 95% CI: 0.70 to 1.14; $p=.36$). Secondary outcomes showed that MR-guided LITT was associated with a shorter hospital stay, reduced blood loss, and lower perioperative morbidity compared to open surgery. The authors note several limitations of the meta-analysis including the inclusion of mostly retrospective studies, the heterogeneity of certain endpoints among studies, and the overall limited number of available studies comparing MR-guided LITT to open surgery in pediatric patients.

Ekman et al (2024) performed a systematic review and meta-analysis of MR-guided LITT compared to temporal lobe resection in patients with drug-resistant mTLE. Only cohort studies with a follow-up of at least 24 months were considered for inclusion (randomized trials were excluded). Of the 55 studies in the review, 14 studies assessed MR-guided LITT (n=534) and 41 studies assessed temporal lobe resection (n=4606). The primary outcome (seizure freedom, defined as the proportion of patients achieving Engel I status) was reported in 6 of the MR-guided LITT studies. A random effects model found that the proportion of patients with seizure freedom after MR-guided LITT was 57.1% (95% CI, 51.2% to 62.7%) versus 72.5% (95% CI, 65.6% to 78.5%) after temporal lobe resection ($p<.01$). The overall rate of complications was 6.5% (95% CI, 3.3% to 12.3%) after MR-guided LITT and 11.4% (95% CI, 7.4% to 17.2%) after temporal lobe resection ($p=.15$). There was no difference in major complications (2.7% vs. 2.0%, respectively; $p=.54$) but minor complications were more common with temporal lobe resection (9.9%) than with MR-guided LITT (4.1%; $p=.04$).

Hect et al (2023) conducted a systematic review of MR-guided LITT corpus callosum ablation for drug-resistant epilepsy. Sixteen observational reports were included (N=85 patients). Seizure freedom at 6 months was evaluable in 53 patients and occurred at a rate of 18.87%. The rate of freedom from atonic seizures postoperatively was 46.28%. Overall, the rate in average number of seizures per day decreased by 80.12%. The complication rate was 12.94% and permanent neurologic deficits occurred in 4.71% of patients. The authors concluded that most patients experienced a meaningful decrease in seizure frequency and that LITT with an acceptable rate of complications.

Barot et al (2022) published a systematic review and meta-analysis of LITT treatment outcomes among patients with drug-resistant epilepsy of varying etiologies. Twenty-eight studies representing 559 patients were identified. The overall prevalence of Engel class I outcomes was 56% (95% CI, 52% to 60%). Highest seizure freedom rates were observed among patients with hypothalamic hamartomas (67%; 95% CI, 57% to 76%). Comparable seizure freedom rates were observed between patients with mTLE (56%; 95% CI, 50% to 61%) and extratemporal epilepsy (50%; 95% CI, 40% to 59%). The overall rate of AEs was 19% (95% CI, 0.14% to 25%), of which visual field defects were most common.

Marathe et al (2021) conducted a systematic review and meta-analysis comparing open surgical resection, SRS, LITT, and radiofrequency ablation in drug-resistant mTLE. Forty-one publications were included in the analysis, including 19 studies on open surgery, 11 on LITT, 4 on radiofrequency, and 7 on radiosurgery. The pooled seizure-free rate per person-year was 0.72 (95% CI, 0.66 to 0.79) with transylvian selective amygdalohippocampectomy (sAHE), 0.70 (95% CI, 0.64 to 0.77) with anterior temporal lobe resection (ATL), 0.60 (95% CI, 0.49 to 0.73) with transcortical sAHE, 0.59 (95% CI, 0.53 to 0.65) with LITT, 0.50 (95% CI, 0.34 to 0.73) with SRS, and 0.38 (95% CI, 0.14 to 1.00) with radiofrequency ablation

(RFA). The authors concluded that while there is no evidence to suggest that LITT is less effective than open surgical resection in the short term, long-term data are lacking and an RCT comparing LITT to open surgical methods is needed. Additionally, reporting of secondary neuropsychological and treatment-related morbidity outcomes is inconsistent and lacks standardization.

Kohlhase et al (2021) performed a systematic review and meta-analysis to compare outcomes and complications from MR-guided LITT, RFA, and conventional open surgery (i.e., ATL or sAHE) in patients with drug-refractory mTLE. Forty-three studies were identified (13 LITT; 6 RFA; 24 conventional surgery) between 1995 and 2018. Meta-analytic estimates for the proportion of patients achieving Engel I outcomes were 34% (95% CI, 15% to 61%), 57% (95% CI, 53% to 61%), 65% (95% CI, 58% to 72%) and 69% (95% CI, 62% to 75%) for RFA, LITT, sAHE, and ATL, respectively. No significant difference in outcome was noted between LITT and RFA ($p=.098$), whereas significantly better outcomes were observed following conventional surgery with both sAHE ($p=.0247$) and ATL ($p=.0113$) compared to LITT. In a subgroup analysis of patients with follow-up duration ≥ 60 months, both ATL ($p=.009$) and sAHE ($p=.043$) resulted in significantly higher rates of Engel I outcomes compared to LITT. Among patients treated with LITT, significantly better outcomes were observed in patients with mTLE and hippocampal sclerosis ($p=.0035$). Overall complication rates were 14.1%, 17.5%, 31.3%, and 18.2% for LITT, RFA, ATL, and sAHE, respectively, with corresponding major complication rates of 3.8%, 3.7%, 10.9%, and 7.4%. However, meta-analysis revealed no significant differences concerning overall and major complication rates between procedures. The authors concluded that overall, patients treated with MR-guided LITT had a lower chance of achieving an Engel I outcome compared to those who received conventional surgery and that the presence of mesial hippocampal sclerosis might be a prognostic factor for a more favorable outcome with LITT.

Brotis et al (2021) conducted a meta-analysis to estimate the efficacy of LITT for mTLE. Sixteen retrospective case series published between 2012 and 2019 representing 575 patients (range, 1 to 231) were identified. Overall, seizure freedom was achieved in 54.7% (95% CI, 50.6% to 58.8%; $I^2=18.7\%$) of patients undergoing LITT with a median follow-up duration of 18 months (interquartile range [IQR], 12 to 26 months). Sensitivity analyses yielded similar results. Four studies representing 150 patients indicated that the prevalence of Engel Class IA outcomes decreased with time, estimated at 64.2%, 46.9%, and 42.4% at 12-, 24-, and 36-month follow-up, respectively. The overall quality of evidence was regarded as 'very low' according to GRADE recommendations, with only 4 studies including more than 20 patients. The authors concluded that while mTLE resective surgeries are invasive and irreversible, they offer better seizure control rates, with previously reported seizure-free rates ranging from ranging from 60% to 90% for mTLE.

Grewal et al (2019) published a systematic review and meta-analysis comparing MR-guided LITT versus SRS for medically intractable temporal lobe epilepsy (TLE). A total of 19 studies published between 2008 and 2018 representing 404 patients (range, 5 to 58) were identified, including 9 retrospective studies on LITT ($n=239$). The overall seizure freedom rate was not found to be significantly different between LITT (50%; 95% CI, 44% to 56%) and SRS (42%; 95% CI, 27% to 59%; $p=.39$), nor was it significantly different for patients with lesional conditions (62% [95% CI, 48% to 74%] vs. 50% [95% CI, 37% to 64%]; $p=.23$). While LITT was associated with a significantly lower procedural complication rate (20% vs. 26%; $p=.06$), reoperation rates were not significantly different (15% vs. 27%; $p=.31$). The authors noted that the quality of evidence was low and that large-scale studies directly comparing LITT and SRS are required to validate findings.

Xue et al (2018) reported postoperative outcomes for MR-guided LITT in the treatment of drug-resistant epilepsy. Sixteen nonrandomized studies published between 2014 and 2018 representing 269 patients (range, 5 to 30) were included in the meta-analysis. The prevalence of Engel Class I, II, III, and IV outcomes was 61%, 12%, 16%, and 15%, respectively. The prevalence of postoperative complications

was 24% (95% CI, 16% to 32%). Interpretation of outcomes is limited by small study size and short follow-up durations (range, 7 days to 51 months).

Hoppe and Helmstaedter (2018) reported postoperative outcomes for pediatric patients aged < 18 years treated with LITT for drug-resistant epilepsy. Twenty-five case series representing 179 patients were included in the review, with the majority of cases attributed to hypothalamic hamartomas (64.2%). Among published cases, the overall complication rate was 23.5% with a 3.4% rate of severe complications. Engel I seizure-free outcomes were achieved by 57.5% of patients across studies, including individuals with short follow-up (e.g., 1 month) and repeat treatments. No studies reported on cognitive outcomes on the basis of standardized psychometric measures. Overall, the authors concluded that the published evidence does not yet allow a scientific or clinical judgement on the utility of LITT for pediatric epilepsy surgery.

Comparative Observational Studies

Hale et al (2019) reported postsurgical outcomes in 26 pediatric patients with insular epilepsy treated with LITT (n=14) or open resection (n=12). Mean follow-up was 2.43 years. Engel Class I outcomes were achieved in 43% of patients treated with LITT compared to 50% who underwent open insular resection at 1-year post-surgery. Postoperative complications occurred in 6 patients treated with LITT and 7 patients treated with resection, all of which resolved within 3 to 4 months. The authors concluded that further studies are needed to determine the noninferiority of LITT with respect to resection in terms of complication rates and seizure freedom, especially in cases of cortical dysplasia that may involve extensive regions of the brain.

Petito et al (2018) published a retrospective, single center analysis of 100 consecutive neurosurgeries performed between 2013 and 2015 in patients with drug-resistant epilepsy, representing 33 LITT procedures and 21 open resections with mean follow-up durations of 21.7 and 21.3 months, respectively. A discrete lesion was radiographically identified in 85% of patients treated with LITT and 65% of patients treated with resection. The mean post-operative hospital length of stay was significantly shorter for LITT compared to resection (1.18 vs. 3.43 days; p=.0002). Patients treated with resection were significantly younger, with a mean age of 35.4 years (p=.001). At 12 months, seizure freedom was achieved in 56.3% (95% CI, 39.3% to 71.8%) and 60% (95% CI, 38.7% to 78.12%) of patients treated with LITT and resection, respectively (p=0.79). Among patients with focal lesions, the seizure freedom outcomes were not significantly different between groups (p=.21). For nonlesional patients, LITT treatment trended towards a better outcome, but did not achieve statistical significance (p=.05). Study interpretation is limited by the small sample size, retrospective analysis, and population heterogeneity.

Single-Arm Studies

Landazuri et al (2025) reported follow-up results from the LAANTERN registry. This multicenter prospective cohort study evaluated LITT for drug-resistant mTLE in 145 patients (including 14 pediatric cases) with up to 5 years of follow-up. At 2 years, 58.4% (45/77) achieved seizure freedom (Engel 1), and 57.2% (44/77) achieved ILAE 1/2 outcomes. Quality of life (QOL) scores improved at nearly all time points, with notable gains in seizure worry, medication effects, and social functioning. One-third of patients stopped or reduced antiseizure medications by 2 years. Adverse events occurred in 16.5% (24/145), and were mostly mild or transient, with permanent deficits in 5.5%. The procedure had a median hospital stay of 1.3 days and low pain scores at discharge. Pediatric outcomes were similar to adults.

Esmaeili et al (2023) conducted a prospective observational study of consecutive LITT-treated patients with drug-resistant epilepsy from 2013 to 2021. The primary outcome was sudden unexpected death in epilepsy (SUDEP). There were 4 SUDEP cases among 135 patients over a median duration of 3.5 years (range, 0.1 to 9.0) for an estimated SUDEP incidence of 8 per 1000 person-years. Among a historical

control group, the incidence of SUDEP was estimated to be 2 per 1000 person-years in patients who underwent resection surgery and 6.1 per 1000 years in patients who did not receive surgical intervention but were candidates. Thus, LITT-treated patients had significantly higher SUDEP incidence compared with surgery ($p=.02$) but similar rates compared with those without intervention ($p=.55$)

Kanner et al (2022) conducted a retrospective review of long-term seizure and psychiatric outcomes among patients who underwent LITT for drug-resistant mTLE between 2013 and 2019 at a single academic center. Forty-eight patients (mean age, 43 years) were identified with a mean follow-up duration of 50 ± 20.7 months (range, 18 to 81). Engel class I outcomes were achieved in 29 (60.4%) subjects and 11 (22.9%) reported 1 to 3 seizures per year. The seizure-freedom rate was 77.8% among patients with 24-month follow-up which decreased to 50% among patients with >61-month follow-up data. Seizure freedom was associated with mesial temporal sclerosis, no pre-treatment focal to bilateral tonic-clonic seizures, and no psychopathology in the last follow-up year. Mood and/or anxiety disorders were identified in 30 (62.5%) of patient's pre-surgery, of which 19 (62%) remitted following LITT.

Landazuri et al (2020) reported 1-year outcomes following LITT of epileptogenic foci with the NeuroBlate system in patients with drug resistant epilepsy enrolled in the previously described LAANTERN registry (see Rennert et al [2019]). Engel Class I outcomes were achieved in 27/42 (64.3%; 95% CI, 48.0% to 78.5%) patients at 1 year. No significant difference was observed in patients with mTLE (70.8%) versus other etiologies. Five AEs were reported, with 1 categorized as serious. Median baseline Quality of Life in Epilepsy questionnaire (QOLIE-31) score was 51.7 (range, 8.7 to 77.3). Median scores increased by 14.1 points reflecting a 72.4% improvement (95% CI, 52.8% to 87.3%) in quality-of-life measures. However, the total score change was not statistically significant ($p=.2173$). Seizure worry and social functioning subscores were considered statistically significant ($p=.0219$ and $p=.0175$, respectively). The authors noted that the primary success of LITT remains in well localized lesions/localizations, such as those seen in mTLE/mesial temporal sclerosis (MTS), cortical dysplasia, and hypothalamic hamartoma.

Wu et al (2019) published the results of a multicenter, retrospective cohort study of 234 patients with drug-resistant mTLE who underwent LITT between 2011 and 2017. At both 1 and 2 years after LITT, 58% of patients achieved Engel I outcomes. Engel I outcomes were associated with ablations involving more anterior, medial, and inferior temporal lobe structures, which tended to involve greater amygdalar volume. Presence or absence of hippocampal sclerosis did not have a significant effect on seizure outcomes. Overall, Engel I or II outcomes were achieved by 76.9% of patients at the time of last follow-up. A total of 42 complications were observed in 35 patients, of which 34 persisted at last follow-up.

Section Summary: Drug-Resistant Epilepsy

The evidence for the use of LITT in drug-resistant epilepsy includes systematic reviews and meta-analyses, 2 nonrandomized comparative studies, and 3 single-arm studies. Meta-analyses have reported seizure freedom rates ranging from 46% to 61% but are limited by heterogeneous study populations and follow-up durations. Nonrandomized studies comparing LITT to open resection have reported comparable outcomes in patients with pediatric insular epilepsy and adult TLE. In one meta-analysis comparing LITT to RFA and conventional surgery, superior outcomes were noted with conventional surgery among patients with mTLE. A subsequent meta-analysis concluded that while there is no evidence to suggest LITT is less effective than open surgical resection in the short term, long-term data are lacking. Total quality of life scores reported in the ongoing LAANTERN registry increased by 72.4%, but this change was not considered statistically significant ($p=.2173$). Prospective comparative studies in well-defined and -controlled patient populations are required to assess a net health outcome and to identify patients most likely to benefit from LITT.

Miscellaneous Cancers

Clinical Context and Therapy Purpose

The purpose of magnetic resonance (MR)-guided laser interstitial thermal therapy (LITT) is to use a focused thermal therapy technique to ablate primary or metastatic tumors (for brain tumors see [above](#)) and to avoid potential complications associated with alternative surgical interventions.

The following PICO was used to select literature to inform this review.

Populations

The population of interest is individuals with primary or metastatic tumors (for brain tumors see [above](#)) that are inaccessible surgically or located in proximity to eloquent or radiosensitive areas. LITT is typically used when surgery is contraindicated due to a high risk of procedural morbidity and/or presence of comorbidities that preclude candidacy for open surgery. LITT may be preferred by individuals desiring a less invasive surgical alternative and its use has been explored in first-line, adjunct, and salvage settings.

Interventions

The therapy being considered is laser interstitial thermal therapy (LITT), also known as stereotactic laser ablation. LITT is performed under real-time magnetic resonance imaging (MRI) guidance.

Comparators

The following therapies are currently being used to treat primary and/or metastatic tumors in select treatment settings: surgical resection, stereotactic radiosurgery (SRS), radiotherapy, and systemic therapies (e.g., chemotherapy).

Outcomes

Outcomes of interest are symptom improvement, medication use, quality of life, treatment-related morbidity, OS, and PFS. Follow-up duration of at least 2 to 3 years is of interest for survival outcomes.

Study Selection Criteria

Methodologically credible studies were selected using the following principles:

- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.
- To assess long-term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.
- Studies with duplicative or overlapping populations were excluded.

Miscellaneous Cancers: Liver Cancer

Evidence from available studies (i.e., case series and nonrandomized comparative studies) suggests that laser interstitial thermal therapy (LITT) may be safe for liver cancer, but the studies are too limited in quality and scope to support conclusions. Comparative studies are at risk of bias due to retrospective design and lack of randomization. Case series are at risk of bias due to single center focus and lack of control groups. None of these studies reported on how LITT may improve symptoms (e.g., jaundice or pain from biliary obstruction) or quality of life. The studies provide data on patient survival but included patient groups with different tumor etiologies. Because tumor origin is a critical factor in metastatic disease prognosis, the studies do not validate each other and may not generalize to other types of

metastatic disease. Furthermore, no studies provide data to assess LITT as an alternative to surgical resection or other ablative techniques. Prospective, multicenter studies that focus on specific etiologies and that include relevant control groups are needed to address these large evidence gaps.

Miscellaneous Cancers: Lung Cancer

Evidence from available studies (i.e., nonrandomized comparative studies) suggest laser interstitial thermal therapy (LITT) may be safe for lung cancer, but the studies are too limited in size, quality, and scope to support conclusions. Comparative studies are at risk of bias due to lack of randomization. No studies reported on how LITT may improve symptoms (e.g., pain, difficulty breathing) or quality of life. The studies provide data on patient survival but included patient groups with different tumor etiologies.

Because tumor origin is a critical factor in disease prognosis, the studies do not validate each other and may not generalize to other types of metastatic disease. Furthermore, no studies provide data to assess LITT as an alternative to surgical intervention or chemotherapy. Randomized controlled trials focusing on each primary tumor type are needed to compare LITT with alternative treatments.

Miscellaneous Cancers: Osteoid Osteoma

Limited evidence from case series and a single nonrandomized comparative study are at high risk of bias for one or more of the following reasons: small sample size, lack of control groups and randomization, single-center focus, and/or heterogeneous patient populations (ages and tumor sites varied widely). Studies also reported relatively short follow-up (1 to 13.6 months). One study compared laser interstitial thermal therapy (LITT) with conventional surgery and had heterogeneity among individuals regarding tumor location, which may affect pain levels and physical function. Studies comparing LITT to conventional surgical procedures for removing osteoid osteomas (en-bloc resection, unroofing and curettage, prophylactic internal fixation, and spinal fusion) as well as other thermal ablative techniques (radiofrequency thermal ablation) are needed to assess longer-term patient-oriented LITT outcomes, including pain level, physical function, and quality of life.

Miscellaneous Cancers: Prostate Cancer

The evidence is limited from very small series and systematic reviews, no published studies compare the use of laser interstitial thermal therapy (LITT) for localized prostate cancer with any other treatment for localized prostate cancer. Included studies had much heterogeneity in terms of patient selection and disease severity. Prospective controlled trials comparing LITT to standard treatments for localized prostate cancer (e.g., prostatectomy, radiation therapy, cryotherapy) and reporting on long-term (> 5 year) patient-oriented outcomes, including overall survival, progression-free survival, urinary function, sexual function, and quality of life, are needed. Studies should report results separately for each risk category of diagnosed prostate cancer.

Section Summary: Miscellaneous Cancers

A number of small, single-arm case series studies, systematic reviews, and comparative observational studies have explored LITT as a therapeutic intervention in the treatment of a range of miscellaneous other cancer - conditions, including, but not limited to liver cancer, lung cancer, osteoid osteoma, and prostate cancer. Although findings from these studies suggest that LITT may reduce symptoms in the short-term, these findings are difficult to interpret due to notable heterogeneity in their patient populations and outcomes assessed. Additionally, to date, no randomized study has examined the effects of LITT on health outcomes.

SUPPLEMENTAL INFORMATION

The purpose of the following information is to provide reference material. Inclusion does not imply endorsement or alignment with the evidence review conclusions.

Practice Guidelines and Position Statements

Guidelines or position statements will be considered for inclusion in 'Supplemental Information' if they were issued by, or jointly by, a US professional society, an international society with US representation, or National Institute for Health and Care Excellence (NICE). Priority will be given to guidelines that are informed by a systematic review, include strength of evidence ratings, and include a description of management of conflict of interest.

American Association of Neurological Surgeons et al

In September 2021, the American Association of Neurological Surgeons (AANS) and Congress of Neurological Surgeons (CNS) Joint Section on Tumors issued a position statement regarding the use of laser interstitial thermal therapy (LITT) for brain tumors and radiation necrosis. The statement concludes that "LITT is an appealing option because it offers a method of minimally invasive, targeted thermal ablation of a lesion with minimal damage to healthy tissue. There is a growing body of evidence to demonstrate that LITT is an effective and well tolerated cytoreductive option for treatment of [newly diagnosed glioblastoma multiforme (GBM), recurrent GBM, and primary or recurrent brain metastases.] Intracranial LITT is also an effective option for addressing radiation necrosis with an overall reduction in steroid dependence for these patients. Especially in instances where the therapeutic window is narrowed such that craniotomy is not a viable option, LITT can play an important role in treatment for glioma or metastatic brain cancer."

American Society of Clinical Oncology et al

In 2021, the American Society of Clinical Oncology (ASCO) issued a joint evidence-based guideline on the treatment of brain metastases with the Society for Neuro-Oncology (SNO) and the American Society for Radiation Oncology (ASTRO). The guideline stated that "no recommendation can be made for or against laser interstitial thermal therapy (Type: informal consensus; Evidence quality: low; Strength of recommendation: none)."

American Society for Stereotactic and Functional Neurosurgery

In September 2021, the American Society for Stereotactic and Functional Neurosurgery (ASSFN) issued a position statement on the use of LITT in drug-resistant epilepsy. The statement recommends consideration of MR-guided LITT (MRgLITT) as a treatment option when all of the following criteria are met:

- "Failure to respond to, or intolerance of, at least 2 appropriately chosen medications at appropriate doses for disabling, localization-related epilepsy AND
- Well-defined epileptogenic foci or critical pathways of seizure propagation accessible by MRgLITT."

Congress of Neurological Surgeons

The Congress of Neurological Surgeons (CNS) guidelines for the treatment of adults with metastatic brain tumors (2019) state that "there is insufficient evidence to make a recommendation regarding the routine use of laser interstitial thermal therapy (LITT), aside from use as part of approved clinical trials.

International Stereotactic Radiosurgery Society

In 2024, the International Stereotactic Radiosurgery Society published recommendations for managing radiation necrosis after stereotactic radiosurgery. Patients with corticosteroid-refractory symptoms can be considered for LITT based on low quality evidence (weak recommendation). The suggested management flowchart includes LITT as a treatment option for patients with refractory symptoms after noninvasive therapy such as bevacizumab or hyperbaric oxygen therapy, and as first-line or second-line therapy for patients with more severe symptoms who require invasive treatment.

National Comprehensive Cancer Network

Bone Cancer

The National Comprehensive Cancer Network (NCCN) clinical practice guidelines for bone cancer (v2.2026) does not include LITT as a recommendation for bone cancer.

Breast Cancer

The National Comprehensive Cancer Network (NCCN) clinical practice guidelines for breast cancer (v1.2026) does not include LITT as a recommendation for breast cancer.

Central Nervous System Cancers

The National Comprehensive Cancer Network (NCCN) clinical practice guidelines for central nervous system cancers (v.3.2025) states that magnetic resonance (MR) - guided LITT "may be considered for patients who are poor surgical candidates (craniotomy or resection). Potential indications include relapsed brain metastases, radiation necrosis, glioblastoma, and other gliomas." (Category 2B). The guidelines additionally state that LITT "can be considered on a case-by-case basis for treatment of radiation necrosis in patients with a history of RT [radiation therapy] for primary brain tumor or metastatic disease. Consultation with neurosurgeons trained in LITT should be done when the procedure is considered."

Hepatocellular Carcinoma

The National Comprehensive Cancer Network (NCCN) clinical practice guidelines for hepatocellular carcinoma (v2.2025) does not include LITT as a recommendation for hepatocellular carcinoma.

Non-Small Cell Lung Cancer

The National Comprehensive Cancer Network (NCCN) clinical practice guidelines for non-small cell lung cancer (v3.2026) does not include LITT as a recommendation for non-small cell lung cancer.

Prostate

The National Comprehensive Cancer Network (NCCN) clinical practice guidelines for prostate cancer (v4.2026) does not include LITT as a recommendation for prostate cancer.

Small Cell Lung Cancer

The National Comprehensive Cancer Network (NCCN) clinical practice guidelines for small cell lung cancer (v2.2026) does not include LITT as a recommendation for small cell lung cancer.

National Institute for Health and Care Excellence

In 2020, NICE published an interventional procedures guidance on the use of MR-guided LITT for drug-resistant epilepsy. The NICE recommends that LITT should only be used with special arrangements, given serious but well-recognized safety concerns and low-quality evidence for efficacy.

Ongoing and Unpublished Clinical Trials

Some currently ongoing and unpublished trials that might influence this review can be located at clinicaltrials.gov.

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CODES

To report provider services, use appropriate CPT codes, HCPCS codes, Revenue codes, and/or ICD diagnosis codes.

Codes	Number	Description
CPT		
	61736	Laser interstitial thermal therapy (LITT) of lesion, intracranial, including burr hole(s), with magnetic resonance imaging guidance, when performed; single trajectory for 1 simple lesion
	61737	Laser interstitial thermal therapy (LITT) of lesion, intracranial, including burr hole(s), with magnetic resonance imaging guidance, when performed; multiple trajectories for multiple or complex lesion(s)
HCPCS		
	No code(s)	
Type of Service	Surgery	
Place of Service	Inpatient	

POLICY HISTORY

Date	Reason	Action
February 2026	Annual Review	Policy Renewed
February 2025	Annual Review	Policy Revised
February 2024	Annual Review	Policy Renewed
December 2023	Annual Review	Policy Revised
December 2022	Annual Review	Policy Revised
December 2021	Annual Review	Revision
December 2020		New Medical Policy Created

New information or technology that would be relevant for Wellmark to consider when this policy is next reviewed may be submitted to:

Wellmark Blue Cross and Blue Shield
 Medical Policy Analyst
 PO Box 9232
 Des Moines, IA 50306-9232

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