Laser Interstitial Thermal Therapy (LITT)

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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. 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 however other areas being

studied include but are not limited to; breast tumors, prostate cancer, osteoid osteoma (bone tumor), lung cancer, and liver cancer.

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 MRI are also applicable to the administration of LITT.

Note: Other terms for LITT include, but may not be limited to, focal laser therapy, interstitial laser ablation, interstitial laser coagulation, interstitial laser photocoagulation, laser induced thermal therapy, MRI-guided laser interstitial thermal therapy (MRgLITT) (e.g., Neuroablate, Visulase) and photothermal therapy.

Primary or Metastatic Brain Tumors
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 patients 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 patients 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 patients with cancer, particularly in those with cancer of the lung, breast, colon, kidney, and melanoma.

Interventions
The therapy being considered is LITT as an alternative to open craniotomy with resection or stereotactic radiosurgery (SRS). LITT is performed under real-time magnetic resonance imaging (MRI) guidance.

Comparators
The following therapies are currently being used to treat primary and metastatic brain tumors: surgical resection, SRS, radiotherapy, 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. 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.

Laser Interstitial Thermal Therapy for the Treatment of Nonglioblastomas and Glioblastomas
Brain cancer is a clinical term that encompasses a wide variety of malignant tumors originating in brain tissue and its adnexa, as well as metastases from distant tumors. About 60% of the estimated 17,000 primary brain tumors diagnosed yearly are gliomas, which arise from the central nervous system’s non-neuron cells. Most gliomas are high-grade (World Health Organization grade II and I) and feature poorly differentiated cells, an aggressive course, and a poor prognosis. Patients typically survive 12 to 16 months after diagnosis. Low-grade tumors have well-differentiated cells and better prognosis, with patients surviving a median 10 years. Nongliomas vary greatly in origin and evolution; common tumors include meningiomas (benign tumors arising from the meninges), oligodendrogliomas (slow-growing neuronal tumors), and medulloblastomas (malignant tumors arising from immature neurons and occurring almost exclusively in children). Metastases from other sites account for about 60% of all intracranial tumors, and most have a poor prognosis typically associated with advanced cancers. Common origins include breast, bone, lung, urogenital, and skin cancers.

Many factors influence clinician and patient decisions regarding brain cancer treatment, including tumor type and prognosis, treatment goals (curative versus palliative), comorbidities, symptoms, and patient physiologic status and life expectancy. Treatment may consist of surgical resection with or without interstitial chemotherapy (i.e., Gliadel®

nitrosourea wafers), external beam radiation therapy, brachytherapy, chemotherapy, and immunotherapy. Laser interstitial thermal therapy (LITT) is a minimally invasive tissue ablation technique that uses continuous or pulsed lasers to achieve thermal coagulation of tumor cells while minimizing damage to the surrounding tissues. Because laser energy is delivered with a fiberoptic catheter through a burr hole in the skull, LITT may constitute an alternative to conventional craniotomy, in particular for patients at high risk of surgical complications, with tumors in hard-to-reach brain areas or undergoing palliative debulking and who wish to avoid surgery.

Glioblastoma (GBM) is the most common and aggressive type of glioma (i.e., a tumor arising from the central nervous system's non-neuron cells). Gliomas compose 60% of the estimated 17,000 primary brain tumors diagnosed yearly in the United States: GBM accounts for 55% of all gliomas. GBM may occur in individuals of any age but are rare in children and are more prevalent in people between 45 and 70 years of age. GBM is also more common in men than women (3:2 ratio) and in Caucasians. Other risk factors include exposure to radiation and a family history of brain tumors. Clinicians classify gliomas according to their cell of origin and histopathologic features, which correlate with prognosis. Low-grade tumors (World Health Organization [WHO] grade II and I) have well-differentiated cells and better prognosis, with patients surviving a median 10 years. HGGs are poorly differentiated ("anaplastic") astrocytomas with WHO grade III or IV and have a dire prognosis. Patients with grade IV gliomas (i.e., GBM) typically live for 12 to 16 months; fewer than 5% live beyond 5 years.

GBM is often resistant to standard chemotherapy. At the time of diagnosis, patients typically undergo biopsy or debulking surgery to remove as much of the tumor as possible. Many factors influence clinician and patient decisions regarding surgical intervention. Adjuvant therapy may include radiation, chemotherapy, or both, possibly followed by maintenance therapy with temozolomide. Virtually all GBMs recur. Second-line options depend on prior treatments, the extent and location of recurrence, and the patient's condition. Options may include a second debulking surgery with or without interstitial chemotherapy (i.e., Gliadel® nitrosourea wafers), radiation therapy, and salvage chemotherapy. LITT is a minimally invasive tissue ablation technique that uses continuous or pulsed lasers to achieve thermal coagulation of tumor cells while minimizing damage to the surrounding tissues. Because laser energy is delivered with a fiberoptic catheter through a burr hole in the skull, LITT may constitute an alternative to conventional craniotomy, in particular for patients at high risk of surgical complications, patients with tumors in hard-to-reach brain areas, or patients undergoing palliative debulking and who wish to avoid surgery.

(2019) Based on an ECRI systematic review the available evidence on laser interstitial thermal therapy (LITT) is inconclusive as a minimally invasive alternative to surgical resection or as alternative to stereotactic radiation therapy for the treatment of glioblastoma multiforme (GBM) and other high-grade gliomas (HGGs). The available evidence on LITT ablation of Glioblastomas is inconclusive due to too few and low-quality data. ECRI concluded very-low-quality evidence from three systematic reviews

(SRs) (two with meta-analyses) suggests LITT is feasible and relatively safe for treating new or recurrent GBM, and outcomes may favor LITT over surgery; however, available studies have a high risk of bias, few patients, and heterogeneity, which prevents drawing more definitive conclusions on safety and efficacy. The evidence base lacks moderate- and high-quality comparative studies. The great majority of studies are small, single-center case series; findings may not generalize to other centers. Combining data from case series for meta-analytic purposes is limited because several factors may confound the data (e.g., patient selection, patient condition, treatment setting). Many studies in the SRs were published more than 10 years ago and may not represent current practice. Two of the meta-analyses had an overlap of 51 patients in 5 studies; we include both because they reported on different outcomes.

The available evidence on LITT ablation of HGGs is limited to small case series at high risk of bias. Published meta-analyses suggest that LITT may work as well as surgery, but findings need validation in prospective, multicenter studies with parallel control groups. Studies that assess LITT in conjunction with, or as an alternative to, stereotactic radiation therapy are also needed to define LITT's optimal place in the HGG treatment pathway.

Systematic Review and Evidence -Based Guideline by the Congress of Neurological Surgeons

In 2019, the Congress of Neurological Surgeons completed a systematic review and evidence-based guideline on the role of emerging and investigational therapies for the treatment of adults with metastatic brain tumors. Brain metastases associated with systemic cancer remain challenging to treat. Current standard treatment modalities, including surgery and radiation, cannot be applied to all patients and are not uniformly successful when applied. Therefore, novel treatment strategies are necessary. The objective of this paper is to review the available clinical research regarding non-standard or "emerging" therapies (high intensity focus ultrasound [HIFU], laser interstitial thermal therapy (LITT), radiation sensitizers, local therapy [radiation (intraoperative) or chemotherapy (carmustine wafer)], immune modulators [ipilimumab, nivolumab, vaccine], molecular targeted agents. Therapies considered "emerging" are in the investigational stage and generally are not currently in use aside from clinical trials. Electronic databases including MEDLINE and Cochrane were searched from September 2008 (the end date of previous search) through December 2015. Overall, 74 new studies met eligibility criteria. (*Accessed November 2022*)

Brain Tumors: Systematic Reviews

Brain Tumors: Systematic Reviews	
Author/Year	Viozzi (2021)
Purpose	Laser interstitial thermal therapy (LITT) is a minimal invasive neurosurgical technique for the treatment of brain tumors. Results of LITT have been reported in a case series of patients with deep seated and/or recurrent glioblastoma or cerebral metastases. With this review we aim to summarize

	the currently available evidence regarding safety and effectiveness of LITT in patients with newly diagnosed glioblastoma (nGBM).
Searched Resources/ Inclusion Criteria	A literature search was performed using electronic databases (PubMed and Embase). Papers were assessed for the methodological quality using the Risk of Bias in Non- randomized Studies - of Interventions (ROBINS-I) tool, and the Grading of Recommendations Assessment, Development and Evaluation (GRADE) was used to assess the quality of the evidence.
Findings Reported by Authors	Identified 835 papers of which only 11 articles were eligible for review. All papers suffered from serious or critical risk of bias, and the quality of evidence was graded as very low according to the GRADE criteria. None of the studies were randomized and reporting of confounders and other parameters was poor. Median overall survival (OS) ranged from 4.1 to 32 months and progression free survival (PFS) from 2 to 31 months. The mean complication rate was 33.7%. No quality of life or cost-effectiveness data were reported.
Authors' Conclusions	Due to the low quality of the studies, it is not possible to draw firm conclusions regarding the (cost) effectiveness of LITT in patients with newly diagnosed glioblastoma. The low quality of evidence shows the need for a well-designed prospective multicenter randomized controlled trial.

Brain Tumors: Systematic Reviews	
Author/Year	de Franca et al. (2020)
Purpose	Minimally invasive procedures are gaining widespread acceptance in difficult-to-access brain tumor treatment. Stereotactic radiosurgery (SRS) is the preferred choice; however, laser interstitial thermal therapy (LITT) has emerged as a tumor cytoreduction technique. The present meta-analysis compared current SRS therapy with LITT in brain tumors.
Searched Resources/ Inclusion Criteria	A search was performed in Lilacs, PubMed, and Cochrane database. Patient's demographics, tumor location, therapy used, Karnofsky performance status score before treatment, and patient's outcome (median overall survival, progression-free survival, and adverse events) data were extracted from studies. The risk of bias was assessed by Cochrane collaboration tool.
Findings Reported by Authors	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 mo; $p<.02$) and was associated with a 15% reduction in risk of adverse events overall.
Authors' Conclusions	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 adverse events. 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 adverse events observed in this group.

Brain Tumors: Systematic Reviews	
Author/Year	Hong et al. (2020)
Purpose	Laser interstitial thermal therapy (LITT) remains a promising advance in the treatment of primary central nervous system malignancies. As indications for its use continue to expand, there has been growing interest in its ability to induce prolonged blood brain barrier (BBB) permeability through hyperthermia, potentially increasing the effectiveness of current therapeutics including BBB-impermeant agents and immunotherapy platforms.
Searched Resources/ Inclusion Criteria	The PubMed database was searched for studies in the English literature on LITT for the treatment of primary and metastatic brain tumors, meningiomas, as well as for radiation necrosis (RN) in previously irradiated brain tumors.
Findings Reported by Authors	There is evidence to suggest a highly immunogenic response to laser interstitial thermal therapy through activation of both the innate and adaptive immune response. These mechanisms have been shown to potentiate standard methods of oncologic care. There are only a limited number of clinical trials are ongoing to evaluate the utility of LITT in combination with immunotherapy. This review provides an update of the relevant literature regarding application of LITT in neurosurgical oncology for the treatment of de novo and recurrent primary gliomas and brain metastases radiographically regrowing after previous irradiation as recurrent tumor or RN. In addition, this review details the limited experience of LITT with meningiomas and symptomatic peritumoral edema after radiosurgery. The advantages and disadvantages, indications, and comparisons to standard of care treatments such as craniotomy for open surgical resection are discussed for each pathology. Finally, the literature on cost-benefit analyses for LITT are reviewed.
Authors' Conclusions	LITT continues to be studied as a possible technique to bridge the gap between exciting preclinical results and the limited successes seen in the field of neuro-oncology. Preliminary data suggests a substantial benefit for use of LITT as a combination therapy in several clinical trials. Further investigation is required to determine whether or not this treatment paradigm can translate into long-term durable results for primary intracranial malignancies.

Brain Tumors: Systematic Reviews	
Author/Year	Barnett et al. (2016)
Purpose	To identify studies which examined extent of resection (EOR) or extent of ablation (EOA) and major complications (defined as neurocognitive or functional complications which last >3 months duration after surgery) associated with either brain laser interstitial thermal therapy (LITT) or open craniotomy in high-grade tumors in or near areas of eloquence.
Searched Resources/ Inclusion Criteria	A systematic review and meta-analysis were undertaken of the peer reviewed literature

Findings Reported by Authors	Eight studies on brain LITT (n = 79 patients) and 12 craniotomy studies (n = 1,036 patients) were identified which examined either/both EOR/EOA and complications. Meta-analysis demonstrated an EOA/EOR of 85.4 ± 10.6% with brain LITT versus 77.0 ± 40% with craniotomy (mean difference: 8%; 95% CI: 2-15; p = 0.01; inverse variance, random effects model). Meta-analysis of proportions of major complications for each individual therapy demonstrated major complications of 5.7% (95% CI: 1.8-11.6) and 13.8% (95% CI: 10.3-17.9) for LITT and craniotomy, respectively.
Authors' Conclusions	In patients presenting with high-grade gliomas in or near areas of eloquence, early results demonstrate that brain LITT may be a viable surgical alternative

Brain Tumors: Systematic Reviews	
Author/Year	Ivan et al. (2016)
Purpose	Investigate initial data on the use of magnetic resonance-guided laser-interstitial thermotherapy (MR-LITT) in the treatment of newly diagnosed high-grade gliomas
Searched Resources/ Inclusion Criteria	The use of the PubMed, OVID, and Google-scholar database systems, a comprehensive search of the literature was performed, and eighty-five articles were identified plus 1 that is pending publication. Four articles were accounted for in this review, including 25 patients with newly diagnosed high-grade gliomas who underwent MR-LITT treatment. We evaluated safety, progression-free survival, and overall survival
Findings Reported by Authors	Twenty-five patients with a mean age of 53.8 years underwent LITT treatments. On average, 82.9% of the pretreatment lesion volume was ablated. The average tumor volume treated was 16.5 cm. The mean follow-up time was 7.6 months. Median overall survival was found to be 14.2 months (range 0.1-23 months). The median progression-free survival was 5.1 months (range 2.4-23 months); however, these data are limited by the relatively short follow-up of the patients reviewed and small sample size of only 25 patients. There was 1 (3.4%) major perioperative complication, which was a central nervous system infection.
Authors' Conclusions	MR-LITT is a promising technology for the treatment of small, yet difficult-to-treat newly diagnosed high-grade gliomas. This study demonstrates that MR-LITT is safe, and future randomized studies are needed to evaluate its role as a treatment adjunct for newly diagnosed high-grade gliomas.

Brain Tumors: Systematic Reviews	
Author/Year	Banerjee et al. (2015)
Purpose	The use of magnetic resonance-guided laser-induced thermal therapy (MR-LITT) as a minimally invasive method of treating intra-cranial pathology is a rapidly growing field. The use of MR-LITT in neurooncology has shown promising results; however, there has been no review to date of the current literature
Searched Resources/	A review of the published literature regarding MR-LITT in neurooncology was performed. Studies on PubMed were included if at least one patient with

Inclusion Criteria	a cerebral tumor or radiation necrosis was treated using quantitative MR thermography guided LITT, as well as if either safety or outcomes were discussed.
Findings Reported by Authors	In treating recurrent Grade-III and IV gliomas, we found improved median overall survival of 20.9 months from diagnosis of recurrence, which is comparable with that of 18.9 months for high-dose-rate brachytherapy and 24.4 months for repeated open surgery. Median progression-free survival (PFS) of recurrent glioma is noted to be 4.5 months. For metastatic lesions, we found a median overall survival (OS) to vary between 9.0 and 19.8 months with a PFS between 3.8 and 8.5 months. Current literature reports median OS in similar patients to lie between 7.0 and 28.6 months. Severe complication rates (with permanent deficits) are found to be between 12 and 16.7%, comparable with 11% found in literature for open surgery
Authors' Conclusions	The current literature shows that MR-LITT is safe and shows promising local tumor control rates. Larger randomized studies are warranted to further investigate this adjuvant therapy in the treatment of recurrent high-grade gliomas and metastases.

Brain Tumors: Clinical Trials

Brain Tumors: Clinical Trials	
Author/Year	Shin et al (2021)
Study Type Patients, Intervention	Retrospective review to highlight the mechanism of hyperthermic BBB disruption and LITT-induced immunogenic cell death in preclinical models and humans. Summarized ongoing clinical trials evaluating a combination approach of LITT and immunotherapy, which will likely serve as the basis for future neuro-oncologic treatment paradigms.
Findings Reported by Authors	There is evidence to suggest a highly immunogenic response to laser interstitial thermal therapy through activation of both the innate and adaptive immune response. These mechanisms have been shown to potentiate standard methods of oncologic care. There are only a limited number of clinical trials are ongoing to evaluate the utility of LITT in combination with immunotherapy.
Authors' Conclusions	LITT continues to be studied as a possible technique to bridge the gap between exciting preclinical results and the limited successes seen in the field of neuro-oncology. Preliminary data suggests a substantial benefit for use of LITT as a combination therapy in several clinical trials. Further investigation is required to determine whether or not this treatment paradigm can translate into long-term durable results for primary intracranial malignancies.

Brain Tumors: Clinical Trials	
Author/Year	de Almeida Bastos (2020a)
Study Type & Patients	Retrospective review with consecutive patients with brain metastases treated with LITT. Based on radiological aspects, lesions were divided into progressive disease after SRS (recurrence or radiation necrosis) and new lesions. Primary endpoint was time to local recurrence.

Intervention	Laser Interstitial Thermal Therapy (LITT) used to treat recurrent brain metastasis after stereotactic radiosurgery (SRS).
Findings Reported by Authors	A total of 61 consecutive patients with 82 lesions (5 newly diagnosed, 46 recurrences, and 31 radiation necrosis). Freedom from local recurrence at 6 mo was 69.6%, 59.4% at 12, and 54.7% at 18 and 24 mo. Incompletely ablated lesions had a shorter median time for local recurrence (P < .001). Larger lesions (>6 cc) had shorter time for local recurrence (P = .03). Dural-based lesions showed a shorter time to local recurrence (P = .01). Tumor recurrence/newly diagnosed had shorter time to local recurrence when compared to RN lesions (P = .01). Patients receiving systemic therapy after LITT had longer time to local recurrence (P = .01). In multivariate Cox-regression model, the HR for incomplete ablated lesions was 4.88 (P < .001), 3.12 (P = .03) for recurrent tumors, and 2.56 (P = .02) for patients not receiving systemic therapy after LITT. Complication rate was 26.2%.
Authors' Conclusions	Incompletely ablated and recurrent tumoral lesions were associated with higher risk of treatment failure and were the major predicting factors for local recurrence. Systemic therapy after LITT was a protective factor regarding local recurrence.

Brain Tumors: Clinical Trials	
Author/Year	Kim et al. (2020)
Study Type & Patients	A review to compare 12-mo outcomes from all subjects undergoing LITT for intracranial tumors/neoplasms.
Intervention	Real-time MRI-guided stereotactic laser interstitial thermal therapy (LITT) with the Visualase system
Findings Reported by Authors	A total of 14 centers enrolled 223 subjects; the median follow-up was 223 d. There were 119 (53.4%) females and 104 (46.6%) males. The median age was 54.3 yr (range 3-86) and 72.6% had at least 1 baseline comorbidity. The median baseline Karnofsky Performance Score (KPS) was 90. Of the ablated tumors, 131 were primary and 92 were metastatic. Most patients with primary tumors had high-grade gliomas (80.9%). Patients with metastatic cancer had recurrence (50.6%) or radiation necrosis (40%). The median post procedure hospital stay was 33.4 h (12.7-733.4). The 1-yr estimated survival rate was 73%, and this was not impacted by disease etiology. Patient-reported QoL as assessed by the Functional Assessment of Cancer Therapy-Brain was stabilized post procedure. KPS declined by an average of 5.7 to 10.5 points post procedure; however, 50.5% had stabilized/improved KPS at 6 mo. There were no significant differences in KPS or QoL between patients with metastatic vs primary tumors.
Authors' Conclusions	The authors concluded that the findings from the ongoing LAANTERN registry demonstrated that LITT stabilized and improved QOL from baseline levels in a malignant brain tumor patient population with high rates of co-morbidities. Overall survival was better than anticipated for a real-world registry and comparative to published literature. Moreover, these researchers stated that enrollment is ongoing, and further sub-analyses of these data are

	planned and are likely to yield additional learning regarding patient selection and management. The authors stated that because LAANTERN is a standard of care (SOC) registry, data are not available for all time-points or patients. This is a limitation of the registry and something all SOC studies are impacted by; however, the demographics and attrition are representatives of patients and experiences described in other publications.

Brain Tumors: Clinical Trials	
Author/Year	Mohammadi et al. (2019)
Study Type & Patients	A case series review utilizing LITT on patients with thalamic tumors.
Objective / Intervention	Analyzed 13 consecutive patients treated with LITT for thalamic tumors from 2012 to 2017. Radiographic, clinical characteristics, and outcome data were collected via review of electronic medical records.
Findings Reported by Authors	Thirteen patients with thalamic tumors were treated with LITT. Most had high-grade gliomas, including glioblastoma (n = 9) and anaplastic astrocytoma (n = 2). The average tumor volume was 12.0 cc and shrank by 42.9% at 3 mo. The average hospital stay was 3.0 d. Median ablation coverage as calculated by thermal damage threshold (TDT) lines was 98% and 95% for yellow (>43° C for >2 min) or blue (>10 min), respectively. Median disease-specific progression-free survival calculated for 8 patients in our cohort was 6.1 mo (range: 1.1-15.1 mo). There were 6 patients with perioperative morbidity and 2 perioperative deaths because of intracerebral hematoma.
Authors' Conclusions	LITT is a feasible treatment for patients with thalamic tumors. LITT offers a cytoreduction option in this challenging population. Patient selection is key. Close attention should be paid to lesion size to minimize morbidity. More studies comparing treatment modalities of thalamic tumors need to be performed.

Brain Tumors: Clinical Trials	
Author/Year	Ahluwalia et al. (2018)
Study Type & Patients	Laser Ablation After Stereotactic Radiosurgery (LAASR) is a multicenter prospective study of laser interstitial thermal (LITT) ablation in patients with radiographic progression after stereotactic radiosurgery for brain metastases.
Objective / Intervention	Patients with a Karnofsky Performance Scale (KPS) score ≥ 60, an age > 18 years, and surgical eligibility were included in this study. The primary outcome was local progression-free survival (PFS) assessed using the Response Assessment in Neuro-Oncology Brain Metastases (RANO-BM) criteria. Secondary outcomes were overall survival (OS), procedure safety, neurocognitive function, and quality of life.

Findings Reported by Authors	reported results from the multicenter, prospective Laser Ablation After Stereotactic Radiosurgery (LAASR) study, which assessed the efficacy and safety of LITT as salvage treatment in patients with radiographic progression after SRS for brain metastasis. Forty-two patients were enrolled, including 20 patients with recurrent brain tumors, 19 patients with biopsy-proven radiation necrosis, and 3 patients with no diagnosis. Progression-free survival rates for patients with recurrent tumors was 54% at 12 weeks and 62% at 26 weeks. Corresponding OS rates were 71% at 12 weeks and 64.5% at 26 weeks. Of 4 tumor lesions that received total ablation, 3/4 achieved a complete response, compared to 0/8 that received subtotal ablation. Patient Karnofsky performance, quality of life, and neurocognitive scores did not change significantly over the duration of survival. Overall, 35/42 (83%) patients developed adverse events, including 5 cases of immediate LITT-related neurological complications and 14 surgery-related adverse events.
Authors' Conclusions	In this study, in which enrolled patients had few alternative options for salvage treatment, LITT ablation stabilized the KPS score, preserved quality of life and cognition, had a steroid-sparing effect, and was performed safely in the majority of cases.

Brain Tumors: Clinical Trials	
Author/Year	Sharma et al. (2016) *Authors were paid consultants for the manufacturer (Monteris)*
Study Type & Patients	Retrospective, single-center case series of 80 patients with lesions located near corticospinal tracts (CSTs), including high-grade gliomas (n = 46), low-grade gliomas (n = 16), other tumors (n = 14), and radiation necrosis (n = 4)
Intervention	Stereotactic laser interstitial thermal therapy (LITT) guided by real-time MRI using NeuroBlate
Findings Reported by Authors	High-grade glioma (n = 46) was the most common indication for LITT. Postoperative motor deficits (PMDs) (partial or complete) were seen in 14 patients (11 with permanent and 3 with temporary PMDs). The median overlap volumes between CSTs with yellow, blue, and white thermal - damage-threshold (TDT) lines in patients with any PMD (temporary or permanent) were 1.15, 0.68, and 0.41 $cm^{3,}$ respectively. The overlap volumes and surface areas revealed significant differences in those with PMDs and those with no deficits (p = 0.0019 and 0.003, 0.012 and 0.0012, and 0.001 and 0.005 for the yellow, blue, and white TDT lines, respectively). The receiver operating characteristic was used to select the optimal cutoff point of the overlapped volumes and areas. Cutoff points for overlap volumes and areas based on optimal sensitivity (92%-100%) and specificity (80%-90%) were 0.103, 0.068, and 0.046 cm^3 and 0.15, 0.07, and 0.11 mm^2 for the yellow, blue, and white TDT lines, respectively.
Authors' Conclusions	Even a minimal overlap between the TDT lines and CSTs can cause a PMD after LITT. Precise planning and avoidance of critical structures and important white matter fibers should be considered when treating deep-seated tumors.

Brain Tumors: Clinical Trials	
Author/Year	Patel et al. (2016)
Study Type & Patients	Retrospective, single-center case series of 80 patients with lesions located near corticospinal tracts (CSTs), including high-grade gliomas (n = 46), low-grade gliomas (n = 16), other tumors (n = 14), and radiation necrosis (n = 4)
Intervention	Real-time MRI-guided stereotactic laser interstitial thermal therapy (LITT) with the Visualase system
Findings Reported by Authors	A total of 133 lasers were placed in 102 patients who required intervention for intracranial tumors (87 patients), chronic pain syndrome (cingulotomy, 5 patients), or epilepsy (10 patients). The procedure was completed in 98% (100) of these patients. Ninety-two patients (90.2%) had undergone previous treatment for their intracranial tumors. The average (± SD) total procedural time was 170.5 ± 34.4 minutes, and the mean laser-on time was 8.7 ± 6.8 minutes. The average intensive care unit (ICU) and hospital stays were 1.8 and 3.6 days, respectively, and the median length of stay for both the ICU and the hospital was 1 day. By postoperative Day 1, 54% of the patients (n = 55) were neurologically stable for discharge. There were 27 cases of morbidity, including new-onset neurological deficits, and 2 perioperative deaths. Fourteen patients (13.7%) developed new deficits after the MRgLITT procedure, and of those 14 patients, 64.3% (n = 9) had complete resolution of deficits within 1 month, 7.1% (n = 1) had partial resolution of symptoms within 1 month, 14.3% (n = 2) had not had resolution of symptoms at the most recent follow-up, and 14.3% (n = 2) died without resolution of symptoms. The 30-day readmission rate was 5.6%.
Authors' Conclusions	MRgLITT, although minimally invasive, must be used with caution. Thermal damage to critical and eloquent structures can occur despite MRI guidance. Once the learning curve is overcome, the overall procedural complication rate is low, and most patients can be discharged within 24 hours, with a relatively low readmission rate. In cases in which they occurred; most neurological deficits were temporary. The therapeutic role of MRgLITT in various intracranial diseases will require larger and more rigorous studies.

Brain Tumors: Clinical Trials	
Author/Year	Kamath et al. (2017) *Authors were paid consultants for the manufacturer (Medtronic)*
Study Type & Patients	Retrospective, single-center case series of 80 patients with lesions located near corticospinal tracts (CSTs), including high-grade gliomas (n = 46), low-grade gliomas (n = 16), other tumors (n = 14), and radiation necrosis (n = 4)
Intervention	Real-time MRI-guided stereotactic laser interstitial thermal therapy (LITT) with the Visualase system
Findings Reported by Authors	A total of 133 lasers were placed in 102 patients who required intervention for intracranial tumors (87 patients), chronic pain syndrome (cingulotomy, 5 patients), or epilepsy (10 patients). The procedure was completed in 98% (100) of these patients. Ninety-two patients (90.2%) had undergone previous treatment for their intracranial tumors. The average (± SD) total procedural

	time was 170.5 ± 34.4 minutes, and the mean laser-on time was 8.7 ± 6.8 minutes. The average intensive care unit (ICU) and hospital stays were 1.8 and 3.6 days, respectively, and the median length of stay for both the ICU and the hospital was 1 day. By postoperative Day 1, 54% of the patients (n = 55) were neurologically stable for discharge. There were 27 cases of morbidity, including new-onset neurological deficits, and 2 perioperative deaths. Fourteen patients (13.7%) developed new deficits after the MRgLITT procedure, and of those 14 patients, 64.3% (n = 9) had complete resolution of deficits within 1 month, 7.1% (n = 1) had partial resolution of symptoms within 1 month, 14.3% (n = 2) had not had resolution of symptoms at the most recent follow-up, and 14.3% (n = 2) died without resolution of symptoms. The 30-day readmission rate was 5.6%.
Authors' Conclusions	MRgLITT, although minimally invasive, must be used with caution. Thermal damage to critical and eloquent structures can occur despite MRI guidance. Once the learning curve is overcome, the overall procedural complication rate is low, and most patients can be discharged within 24 hours, with a relatively low readmission rate. In cases in which they occurred; most neurological deficits were temporary. The therapeutic role of MRgLITT in various intracranial diseases will require larger and more rigorous studies.

Laser Interstitial Thermal Therapy (LITT) in the Treatment for Brain Metastases

Brain Metastasis: Systemic Reviews	
Author/Year	Chen et al. (2021)
Study Type & Patients	Systemic review and meta-analysis in patients with brain metastasis with in-field recurrence following SRS
Systematic Review Purpose	To study the efficacy of LITT for BM patients experiencing in-field recurrence following SRS.
Searched Resources & Inclusion Criteria	A literature search was conducted to identify studies investigating local control (LC) rate and overall survival (OS) of LITT for BMs with IFR following SRS.
Findings	Identified 63 studies including 1608 patients whose breast tumors were treated with radiofrequency (RFA), high intensity focused ultrasound (HIFU), cryo-, laser or microwave ablation. Fifty studies reported on the number of patients with complete ablation as found on histopathology and the highest rate of complete ablation was achieved with RFA (87.1%, 491/564) and microwave ablation (83.2%, 89/107). Short-term complications were most often reported with microwave ablation (14.6%, 21/144). Recurrence was reported in 24 patients (4.2%, 24/570) and most often with laser ablation (10.7%, 11/103). The shortest treatment times were observed with RFA (15.6 ± 5.6 min) and the longest with HIFU (101.5 ± 46.6 min).

Authors' Conclusions	LITT is an effective treatment for BM patients experiencing IFR following SRS. For different pathological entities, LITT showed more satisfactory local control efficacy on RN than BM recurrence (LC-6: 87.4% vs. 67.9%, p =0.009; LC-12: 76.3% vs. 59.9%, p = 0.041).

Brain Tumors: Clinical Trials	
Author/Year	Murayi et al. (2020)
Study Type & Patients	Retrospective, single-center case series of 80 patients with lesions located near corticospinal tracts (CSTs), including high-grade gliomas (n = 46), low-grade gliomas (n = 16), other tumors (n = 14), and radiation necrosis (n = 4)
Intervention	Real-time MRI-guided stereotactic laser interstitial thermal therapy (LITT) with the Visualase system
Findings Reported by Authors	A total of 133 lasers were placed in 102 patients who required intervention for intracranial tumors (87 patients), chronic pain syndrome (cingulotomy, 5 patients), or epilepsy (10 patients). The procedure was completed in 98% (100) of these patients. Ninety-two patients (90.2%) had undergone previous treatment for their intracranial tumors. The average (± SD) total procedural time was 170.5 ± 34.4 minutes, and the mean laser-on time was 8.7 ± 6.8 minutes. The average intensive care unit (ICU) and hospital stays were 1.8 and 3.6 days, respectively, and the median length of stay for both the ICU and the hospital was 1 day. By postoperative Day 1, 54% of the patients (n = 55) were neurologically stable for discharge. There were 27 cases of morbidity, including new-onset neurological deficits, and 2 perioperative deaths. Fourteen patients (13.7%) developed new deficits after the MRgLITT procedure, and of those 14 patients, 64.3% (n = 9) had complete resolution of deficits within 1 month, 7.1% (n = 1) had partial resolution of symptoms within 1 month, 14.3% (n = 2) had not had resolution of symptoms at the most recent follow-up, and 14.3% (n = 2) died without resolution of symptoms. The 30-day readmission rate was 5.6%.
Authors' Conclusions	MRgLITT, although minimally invasive, must be used with caution. Thermal damage to critical and eloquent structures can occur despite MRI guidance. Once the learning curve is overcome, the overall procedural complication rate is low, and most patients can be discharged within 24 hours, with a relatively low readmission rate. In cases in which they occurred; most neurological deficits were temporary. The therapeutic role of MRgLITT in various intracranial diseases will require larger and more rigorous studies.

Brain Metastases	
Author/Year	Chaves de Almeida Bastos et al. (2020)
Purpose of the Review	To investigate the use of LITT in the treatment of BM.

Rationale for LITT Reported by Authors	The main advantage of LITT, in comparison to other salvage treatments for patients with BM recurrence after SRS, is the ability to treat lesions not amenable to surgical resection due to its difficult location. The minimal invasiveness of the procedures renders minimal injury to structures superficial to the tumor when compared to open surgery, it also translates in shorter hospital stays, less systemic response to surgical trauma, and faster transition to adjuvant treatments like chemotherapy and radiation. This benefits patients with compromised performance scores. LITT can also be repeated if progression is found after the procedure with no concern of accumulated ionizing radiation damage, also it does not preclude a future open surgery in the case of treatment failure. Lastly, the potential disruption of the BBB making it permeable to cytotoxic drugs open the possibility of better local control with the use of combined chemotherapy in selected cases, although this still pends confirmation by further studies.
Authors' Conclusions	LITT has been employed to treat BM after SRS failure for over a decade now and has demonstrated to be a safe minimally invasive procedure, with improved outcomes. Predictors for success include ablation extension of the lesion, particularly in the cases of tumor recurrence, where complete ablation is fundamental to achieve longer PFS. At the present time, complete ablation is determined by whether the enhancing portion of the mass is encompassed entirely by the blue TDT line. This amounts to a complete ablation using the Monteris system. However, most tumors can be irregular, and the margins can be hard to treat. Hence improved imaging during treatments may better assist in maximizing coverage off the treated lesions. DCE/AUC imaging was used as a predictor of recurrence especially at the margins. Future studies with new imaging modalities will likely provide a better estimation of lesion coverage improving outcomes. Also, heat sink in tumors that are adjacent to the dura-mater large venous lakes and adjacent to large caliber blood vessels makes these tumors difficult to completely ablate. Advancing probe designs might be able to overcome this challenge in the future. The use of chemotherapy within the first two weeks after the procedure has been demonstrated to decrease local recurrence rate, but this needs to be further evaluated in larger series. Optimizing the use of chemotherapeutic agents and immunotherapeutic agents while the blood-brain barrier remains disrupted has shown in our studies to help local control. Additional work in this field needs to be done to optimize the timing, dosing and responses of different types of agents. Future studies are also necessary to better understand the role of different tumor histopathology in the outcomes for patients treated with this modality. The main advantage of LITT lies in its capacity to treat deep

	seated lesions in difficult to access areas, minimally disrupting surrounding tissues and proving good local control in patients that otherwise wouldn't be considered surgical candidates.

Brain Metastases	
Author/Year	Beecher et al (2018)
Study Type & Patients	Retrospectively reviewed and analyzed volumetric response of metastatic brain tumors that progressed despite treatment with stereotactic radiosurgery (SRS) after treatment with laser interstitial thermal therapy (LITT).
Intervention	Patients treated from 1/2012 to 10/2015 with LITT for metastatic brain tumors demonstrating progression after SRS. Volumes were quantified using MRI with contrast-enhanced T1-weighted (T1W) and fluid-attenuated inversion recovery (FLAIR).
Findings Reported by Authors	Fifty lesions from 36 patients were studied. Lesions were assessed prior to LITT, immediately after LITT, 0–90 days after LITT, 90–180 days after LITT, 180–270 days after LITT, and 270–360 days after LITT. The median T1W volume was 5.05 cc (range-0.54 to 23.31 cc) before LITT treatment (n=50), 7.70 cc (range-1.72 to 38.76 cc) 0–90 days after LITT (n=47), and 3.68 cc (range-1.282 to 48.31 cc) 180–270 days after LITT(n=21). The median FLAIR volume was 43.36 cc (range-3.09 to 233.01 cc) before LITT treatment (n=50), 37.13 cc (range- 3.48 to 244.23 cc) 0–90 days after LITT (n=43), 31.68 cc (range 1.6 to 248.75 cc) 180–270 days after LITT (n=18). The 6-month FLAIR volume showed a statistically significant reduction compared to pretreatment (p=0.04). After selecting for cases where patients had two or more post-operative MRIs, we found that 24 lesions (63%) demonstrated an overall downward trend, and 14 lesions (37%) demonstrated an upward trend. The median pre-treatment T1W volume for the patients whose lesions demonstrated volumetric reduction after LITT was 3.54 cc (range 0.539 cc to 10.06 cc) and for those who did not demonstrate volumetric reduction after LITT it was 8.81 cc (range 0.926 cc to 23.313 cc).
Authors' Conclusions	The pre-treatment tumor volume plays a significant role in determining response to LITT with smaller tumor volumes responding better to LITT than tumors with larger volumes. A weakness of the study is that at the 6-month post-treatment time point, only 20 of the original 50 lesions were available for analysis. Patients were either deceased or lost to follow up. This is however an inherent difficulty when studying metastatic disease given the poor prognosis. One possible avenue for future studies would be to examine the difference between the estimated ablation zone and the actual lesion. One possible explanation for the increase seen in 14 lesions lies in the fact that total ablation of the entire lesion may not have been achieved.

	Each lesion has a unique shape and size while the laser ablation probe creates an ablative field that is cylindrical in shape. Directional probes may help to better contour the thermal ablation to match the lesion geometry.

Brain Metastases: Study Selection and Characteristics

Among 5 manuscripts screened met the criteria for inclusion in the guidelines. All studies were case series without control patients in a small number of patients. The largest study described 15 patients who received laser interstitial thermal therapy (LITT) for previously treated brain metastases (BMs) with post-radiosurgery progression or radiation necrosis. Laser interstitial thermal therapy is a minimally invasive surgical procedure in which a laser applicator is placed stereotactically and used to perform thermal ablation under magnetic resonance imaging (MRI) guidance. The other 3 studies described <10 patients each.

Brain Metastases: Results of Individual Studies

Each study demonstrated limitations inherent in small case series without a control population. Three studies used prospective data collection. In each study, LITT was demonstrated to be safe and well-tolerated. Efficacy was assessed using MRI to evaluate for local control and analysis of overall survival. Three of the studies addressed brain metastases only, while one included patient with other pathologies, such as glioma. In the largest case series, 15 patients were followed prospectively after receiving LITT for progressive BM or radiation necrosis after prior radiation treatment for BM. At a median 24 -weeks follow-up, 13 of 15 patients demonstrated local control, and the median PFS was 37 weeks. The remaining 3 manuscripts described 18 patients total with BM treated with LITT. Another prospective trial evaluated 17 patients, 5 of whom had progressive BM after prior radiation. The median PFS among these 5 patients was 5.8 months. The third prospective study was a pilot trial in which 7 patients with 15 BM refractory to chemotherapy and radiation were treated with LITT. In this study, local control was noted for all treated lesions at up to 30 months of follow-up, and median OS was 19.8 months

Brain Metastases: Synthesis of Results

In multiple small case series, LITT appears to be a safe treatment option for patients with BM. For patients with progressive disease after prior radiation, LITT may have value as a treatment option. In each study reviewed, the authors acknowledged the emerging nature of LITT as a treatment option for BM.

Summary of Evidence: Brain Tumors

The main advantage of LITT, in comparison to other salvage treatments for patients with BM recurrence after SRS, is the ability to treat lesions not amenable to surgical resection due to its difficult location. The minimal invasiveness of the procedures renders minimal injury to structures superficial to the tumor when compared to open surgery, it also translates to shorter hospital stays, less systemic response to surgical trauma, and faster transition to adjuvant treatments like chemotherapy and radiation. This benefits patients

with compromised performance scores. LITT can also be repeated if progression is found after the procedure with no concern of accumulated ionizing radiation damage, also it does not preclude a future open surgery in the case of treatment failure. Lastly, the potential disruption of the BBB making it permeable to cytotoxic drugs open the possibility of better local control with the use of combined chemotherapy in selected cases, although this still pends confirmation by further studies.

A review of the current NCCN guideline Central Nervous System Cancers Version 2.2022 recommends MRI-guided laser interstitial thermal therapy (LITT) may be considered for patients who are not surgical candidates (craniotomy or resection). Potential indications include relapsed brain metastases and radiation necrosis. (Category 2B)

A review of American Association of Neurological Surgeons (AANS) 2021 position statement on MR-guided laser interstitial thermal therapy (LITT) for brain tumors and radiation necrosis states 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 nGBM, rGBM, and Mets/rMets. 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.*
- *A multidisciplinary approach remains the cornerstone in the treatment of patients with brain tumors or radiation necrosis. It is important that physicians have discretion to exercise their clinical judgement when evaluating the most appropriate option for their patients' individual treatment plan. There is consensus that intracranial LITT should be considered as a potential option for patients with recurrent or progressive malignant tumor (primary or metastatic), lesion(s) inaccessible to surgical resection, or when the patient is unable to tolerate surgical resection due to medical comorbidities. (Accessed November 2022)*

The available evidence on laser interstitial thermal therapy (LITT) is somewhat favorable for the treatment of primary and metastatic brain cancer. Based on case series, randomized control trials, and systemic reviews the safety as a treatment for recurrent or progressive malignant brain tumor(s) (primary or metastatic) or brain lesion(s) which are inaccessible to surgical resection suggests effectiveness similar to that of surgical resection. Based on the above the American Association of Neurological Surgeons position statement and NCCN guidelines support the use of LITT in this subpopulation of patients. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcomes.

Laser Interstitial Thermal Therapy for the Treatment of Breast Cancer

Breast cancer is the most common malignancy in women and a leading cause of cancer mortality. Risk factors for developing breast cancer include family history, presence of known predisposing mutations, age, and low or late exposure to pregnancy hormones (e.g., nulliparity). Conventional treatment of early-stage breast cancer involves mastectomy or lumpectomy typically followed by five to seven weeks of daily external beam radiation therapy of the whole breast. Some women with early-stage breast cancer who undergo lumpectomy are candidates for accelerated partial-breast irradiation, which permits delivery of high doses of radiation directly to the lumpectomy site over one week. Surgical resection can cure many cases of early-stage breast cancer but involves surgical risks and may result in significant disfigurement and a heavy psychosocial burden for the patient. Several energy-based, minimally invasive ablative techniques have emerged as potential alternatives to surgical resection of early-stage tumors, but experts disagree on their effectiveness, safety, and optimal utilization. Laser interstitial thermal therapy (LITT) is a minimally invasive thermal ablation technique used to treat multiple tumor types. In patients with small, early-stage breast tumors, LITT is intended as an alternative to lumpectomy or mastectomy in patient's ineligible for surgical resection.

(2019) Based on an ECRI systematic review the available evidence on laser interstitial thermal therapy (LITT) is inconclusive as a minimally invasive alternative treatment for the treatment of breast cancer. Available evidence on LITT for early-stage breast cancer consists of small case series, some of which are synthesized in systematic reviews (SRs). Findings are at high risk of bias and are of unclear significance because of low statistical precision and because most patients underwent sequential LITT and resection, so the contribution LITT made to the outcomes cannot be discerned. Prospective studies with a parallel control group are needed to validate LITT as an alternative to surgery and to compare LITT with other minimally invasive techniques.

Breast Cancer: Systematic Reviews

Breast Cancer: Systematic Reviews	
Author/Year	Peek et al (2016)
Study Type & Patients	To assess the current evidence for clinical outcomes with minimally invasive ablative techniques in the non-surgical treatment of breast cancer.
Systematic Review Purpose	Each group comprised 36 cases according to the method of treatment. Compare and analyze the difference between minimally invasive percutaneous laser ablation and open surgery in our center to provide reference for clinical treatment.
Searched Resources & Inclusion Criteria	A systematic search of the literature was performed using PubMed and Medline library databases to identify all studies published between 1994 and May 2016. Studies were considered eligible for inclusion if they evaluated the role of ablative techniques in the treatment of breast cancer and included ten patients or more. Studies that failed to fulfil the inclusion criteria were excluded
Findings	Identified 63 studies including 1608 patients whose breast tumors were treated with radiofrequency (RFA), high intensity focused ultrasound

	(HIFU), cryo-, laser or microwave ablation. Fifty studies reported on the number of patients with complete ablation as found on histopathology and the highest rate of complete ablation was achieved with RFA (87.1%, 491/564) and microwave ablation (83.2%, 89/107). Short-term complications were most often reported with microwave ablation (14.6%, 21/144). Recurrence was reported in 24 patients (4.2%, 24/570) and most often with laser ablation (10.7%, 11/103). The shortest treatment times were observed with RFA (15.6 ± 5.6 min) and the longest with HIFU (101.5 ± 46.6 min).
Authors' Conclusions	Minimally invasive ablative techniques are able to successfully induce coagulative necrosis in breast cancer with a low side effect profile. Adequately powered and prospectively conducted cohort trials are required to confirm complete pathological ablation in all patients.

Breast Cancer: Clinical Trials

Breast Cancer: Clinical Trials	
Author/Year	Nori et al (2018)
Study Type & Patients	Single-center retrospective study; 12 consecutive patients underwent percutaneous US-guided laser ablation as radical treatment of primary inoperable unifocal BC.
Intervention	Each group comprised 36 cases according to the method of treatment. Compare and analyze the difference between minimally invasive percutaneous laser ablation and open surgery in our center to provide reference for clinical treatment.
Findings Reported by Authors	At median follow-up of 28.5 months (range 6-51), no residual disease or progression occurred; the overall success rate for complete tumor ablation was therefore 100%. No significant operative side effects were observed, with only 2 (13.3%) experiencing slight to mild pain during the procedure, and all patients complained of a mild dull aching pain in the first week after procedure.
Authors' Conclusions	Laser ablation is a feasible, minimally invasive, and cost-effective alternative for a subset of patients affected by small lesions, who are not eligible to the standard surgical approach, as well as for patients who refuse surgery. However, further larger prospective studies are strongly needed in order to confirm our preliminary results

Breast Cancer: Clinical Trials	
Author/Year	Schwartzberg et al (2018)
Study Type & Patients	Open-label, phase 2 institutional review board (IRB)-approved, multicenter clinical trial; 61 women 18 to 80 years of age with a single focus of percutaneous biopsy-proven IDC measuring 20 mm or smaller were eligible for enrollment in the study. The cancer had to be visible by mammography, ultrasound, or both as a mass 20 mm or smaller or as a single cluster of microcalcifications 10 mm or smaller. The lesion

	had to be 5 mm or further from the skin and chest wall. Any intraductal component could not exceed 25%.
Intervention	The primary goal of this research study was to evaluate the performance of a newly improved percutaneous laser ablation device in achieving complete pathologic tumor ablation in a multicenter study. A secondary aim was to measure the performance of imaging in evaluation of complete tumor ablation. Tissue pathology at surgical excision was used as the gold standard.
Findings Reported by Authors	In this study, 61 patients were reported as the intention-to-treat cohort for determination of PLA efficacy. Of these 61 patients, 51 (84%) had complete tumor ablation confirmed by pathology analysis. One subject's MRI imaging was not performed per protocol, which left 60 subjects evaluable for MRI pathology correlation. Five patients (8.3%) had residual IDC shown by both MRI and pathology. Post-ablation discordance was noted between MRI and pathology, with four patients (6.7%) false-positive and four patients (6.7%) false-negative. The negative predictive value (NPV) of MRI for all the patients was 92.2% (95% confidence interval [CI], 71.9–91.9%). Of the 47 patients (97.9%) with tumors 15 mm or smaller, 46 were completely ablated, with an MRI NPV of 97.7% (95% CI, 86.2–99.9%).
Authors' Conclusions	Percutaneous laser therapy, which works by focal destruction, is a potential alternative to traditional breast cancer conservation surgery for treatment of early-stage IDC. Strong correlations exist between post-ablation MRI findings and pathologic alterations in CK8/18, ER, and Ki67 staining. Clinical trials that evaluate PLA efficacy and outcome in the absence of subsequent surgical resection are necessary to further determine the potential of this breast cancer therapy.

Summary of Evidence: Breast Cancer

Case series individually reviewed or synthetized in a systematic review provide only low-quality evidence on laser interstitial thermal therapy (LITT) safety and effectiveness for early-stage breast cancer. Because the studies were all small and lacked control groups, reported findings are at high risk of bias. Moreover, long-term survival and freedom from recurrence rates reported may not be attributed to LITT alone because patients underwent subsequent surgical resection. Control groups that include surgery-only controls are needed to provide this data and to validate perioperative LITT outcomes reported in available studies. Similarly, direct comparison of LITT and other minimally invasive techniques in prospective studies with parallel treatment groups is needed. Independent studies synthetized in the review by Peek et al. suggest that LITT may not perform as well as RFA, MWA, or HIFU; thus, additional prospective studies to identify the optimal approach for patients with unresectable early-stage cancer are warranted. *In 2018, the American Society of Breast Surgeons issued a consensus guideline on the use of transcutaneous and percutaneous ablation for the treatment of benign or malignant tumors of the breast that included the following: "At the present time, cryoablation is approved for treatment of soft tissue malignancies.* However, there is emerging data from

clinical trials utilizing percutaneous ablative therapies for patients with early-stage breast cancer without surgical excision. Techniques being evaluated include ablation by focused ultrasound, laser, cryotherapy, microwave, and radiofrequency. Participation in registries and clinical trials evaluating the use of these technologies with and without surgical excision of a breast malignancy is advised as early data emerges on their efficacy.*" A review of the current NCCN guideline Breast Cancer Version 1.2022 does not address laser thermal therapy or laser ablation as treatment for breast cancer.*

Laser Interstitial Thermal Therapy for the Treatment of Epilepsy
Epilepsy is a neurologic disorder characterized by recurrent, unprovoked, excessive electrical discharges from the central nervous system that result in recurring seizures. The seizure characteristics depend on the location of the epileptic discharges in the cerebral cortex but are generally sudden and violent in onset and short in duration. Neurologists characterize seizures as generalized if they originate in both brain hemispheres (typically leads to major motor seizures) and as partial if they originate in discrete foci (with local or generalized spread). Epilepsy's etiology is complex and may be classified as idiopathic (spontaneous, often generalized seizures in patients with or without family history), symptomatic (seizures caused by specific brain lesions), or syndromic (seizures that follow a predictable course, often with a known genetic component and associated features).

The majority of patients with epilepsy can use medication to adequately control their condition. However, about 20% to 30% of patients have medically refractory epilepsy, defined as recurrent seizures despite optimal treatment for two to three years. Many patients with medically refractory epilepsy may benefit from surgery, provided their seizure focal points can be located and resected without causing harm to critical areas of the brain. Surgical decisions are based on magnetic resonance imaging and electroencephalography evaluations with noninvasive scalp electrodes used to locate the focal area responsible for the seizures. Despite advances, surgical resection still involves significant risks of complications and neurological sequelae, and some locations remain out of reach to surgical resection. Major emerging approaches intended to address these limitations include stereotactic ablative radiosurgery (e.g., Gamma Knife), neurostimulation with deep or cortical brain electrodes, magnetic resonance-guided focused ultrasound ablation, stereotactic radiofrequency ablation, and laser interstitial thermal therapy (LITT).

Laser interstitial thermal therapy (LITT) uses fiberoptic tools to achieve minimally invasive tissue ablation in various neurologic and oncologic applications. In patients with epilepsy that does not respond to medication (i.e., medically refractory), surgeons may use LITT to discreetly destroy brain foci where seizures originate, as a minimally invasive alternative to surgical resection and in patients with foci inaccessible with conventional surgery tools.

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 patients 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, 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 mesial temporal lobe epilepsy 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.
Patients with an identifiable seizure focus that can be targeted to achieve seizure freedom are primary candidates for epilepsy surgery, but patients 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 the Table below.

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: • 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. Follow-up durations of 2 to 3 years are appropriate when compared to SRS, due its known latency for seizure reduction or remission. 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.

(2019) Based on an ECRI systematic review the available evidence on laser interstitial thermal therapy (LITT) is somewhat favorable for the treatment of medically refractory epilepsy. Systematic reviews (SRs) with meta-analysis of low-quality, before-and-after cohort studies shows that LITT results in freedom from seizures up to 2 years in about 60% of treated patients with medically refractory epilepsy; complications were reported in about one-fourth to one-fifth of LITT patients. LITT appears to be as safe and effective as stereotactic radiosurgery (e.g., Gamma Knife®). Nonrandomized studies suggest LITT may be safer than open surgery, but larger studies are needed to validate these data. Studies comparing LITT and neurostimulation techniques would also be useful. Epilepsy management guidelines have yet to address LITT.

(2018) Kang et al. published an epileptologist's view on laser interstitial thermal ablation treatment of temporal lobe epilepsy. A procedure called laser interstitial thermal ablation has been utilized to treat drug resistant epilepsy. With this technique, a probe is stereotactically inserted into a target structure responsible for seizures, such as mesial temporal lobe, hypothalamic hamartoma, or a small malformation of cortical development, and the tip is then heated by application of laser energy to ablate structures adjacent to the probe tip. This procedure has the advantage of selectively targeting small lesions responsible for seizures and is far less invasive than open surgery with shorter hospitalization, less pain, and rapid return to normal activities. Initial results in mesial temporal lobe epilepsy are promising, with perhaps half of patients becoming free of seizures after the procedure. Neuropsychological deficits appear to be reduced because of the smaller volume of ablated cortex in contrast to large resections. More research must be done to establish optimal targeting of structures for ablation and selection of candidates for surgery, and more patients must be studied to better establish efficacy and adverse effect rates.

Epilepsy: Clinical Trials

Clinical Trials	
Author/Year	Landazuri et al. (2021)
Study Type & Patients	Retrospective, multicenter study of laser ablation for drug resistant epilepsy – one-year outcomes.
Intervention	LITT (laser interstitial thermal therapy). Data from an ongoing prospective, multi-center registry were assessed. Procedural information, Engel seizure outcomes, and quality of life (QoL) scores were analyzed. A responder analysis was performed to better understand potential clinical characteristics that could influence seizure outcome.
Findings Reported by Authors	Sixty patients have been enrolled into LAANTERN (Laser Ablation of Abnormal Neurological Tissue Using Robotic NeuroBlate System) specifically for epilepsy treatment, of which 42 reached one year follow up. Engel I outcome was achieved in 64.3 % at one year follow up. Patients with mesial temporal lobe epilepsy (MTLE) comprised 56.7 % of this cohort of multiple epilepsy types. Other significant etiologies included focal cortical dysplasia, hypothalamic hamartoma,

	cavernoma, heterotopias, and tuberous sclerosis. Median length of stay was 32.7 h. At discharge, head pain score averaged 1.4 ± 2.1 on a scale from 1 to 10. Five adverse events were reported, one categorized as serious. Seizure worry and social functioning scores improved significantly in quality-of-life measures.
Authors' Conclusions	Surgical treatment with LITT for epileptic foci is a safe and effective treatment option for people with drug resistant epilepsy. Our multicenter prospective seizure outcomes continue to expand published LITT experience in MTLE as well as non-MTLE epilepsies. The minimally invasive nature allows for short hospitalizations with minimal reported pain and discomfort.

Clinical Trials: Case Series	
Author/Year	Brotis et al. (2021)
Study Type & Patients	A meta-analysis to estimate the efficacy of LITT for TLE (Q1). We also examined the effect of the patient's age (Q2), the total ablation volume (TAV) (Q3), the strength of the MRI unit (Q4), the type of the utilized stereotactic platform (Q5), and the follow up period (Q6) on the patient's outcome. Fixed- and random-effects model meta-analysis was conducted to assess the proportion estimate for each parameter individually. Kaplan-Meier survival-analysis was performed on the available individual patient time-to-first seizure data.
Intervention	Laser interstitial thermal therapy (LITT) in mesial temporal lobe epilepsy (MTLE)
Findings Reported by Authors	Sixteen studies with 575 patients fulfilled our eligibility criteria. The efficacy of LITT was 0.547 (95%CI: 0.506-0.588). Our statistical analysis had robust results after stratification according to the study population (Q2; $p = 0.3418$), and the type of the utilized stereotactic platform (Q5; $p = 0.286$), whereas the role of the TAV (Q3; $p = 0.058$) and strength of the magnetic field (Q4; $p = 0.062$) in seizure control remained unclear. The median seizure-free period (Q6) was 0.643 (0.569-0.726) and 0.467 (0.385-0.566) for the one- and the two-year follow up.
Authors' Conclusions	LITT seems to offer a viable alternative to resective surgery, with a moderate efficacy and enduring results. Higher ablation volumes may be associated with improved seizure control, although our current study provided no statistically significant data. More high-quality studies are required to highlight the role of LITT in epilepsy surgery, particularly in the pediatric population.

Clinical Trials	
Author/Year	Grewal et al. (2019)
Study Type & Patients	Systematic Reviews and Meta-Analysis (PRISMA) guidelines were followed to perform an indirect meta-analysis of seizure and clinical

	outcomes between MRgLITT and SRS. Only studies reporting outcomes for patients with TLE were included in the current review.
Intervention	LITT (laser interstitial thermal therapy) for medically intractable temporal lobe epilepsy (TLE)
Findings Reported by Authors	A total of 19 studies were included in the final analysis, giving a total of 415 TLE patients. Of those studies, 9 were on MRgLITT, with a total of 250 patients (60%), and 10 were on SRS, with a total of 165 patients (40%). We found that the overall seizure freedom rate was comparable between the 2 procedures (MRgLITT 50%, 95% confidence interval [CI] 44% to 56%, vs. SRS 42%, 95% CI 27% to 59%, P = 0.39). Similarly, among patients with lesional pathologic conditions only, the seizure freedom rate was comparable between the 2 procedures (MRgLITT 62%, 95% CI 48% to 74%, vs. SRS 50%, 95% CI 37% to 64%, P = 0.23). Compared with SRS, MRgLITT was associated with lower complication rates (MRgLITT 20%, 95% CI 14% to 26% vs. SRS 32%, 95% CI 20% to 46%, P = 0.06) but similar reoperation rates (15%, 95% CI 9% to 22% vs. 27%, 95% CI 12% to 46%, P = 0.31).
Authors' Conclusions	As minimally invasive procedures continue to gain popularity for use in surgery for epilepsy, it is imperative to evaluate their efficacy and safety outcomes. In this study we pooled the data from existing studies to compare the seizure and clinical outcomes in patients with TLE undergoing MRgLITT and SRS. We found similar outcomes and complications between the two procedures.

Clinical Trials: Case Series	
Author/Year	Wu et al. (2019)
Study Type & Patients	Retrospective, multicenter study of 234 patients with medically temporal lobe epilepsy (mTLE)
Intervention	LITT (laser interstitial thermal therapy)
Findings Reported by Authors	Ablations including more anterior, medial, and inferior temporal lobe structures, which involved greater amygdalar volume, were more likely to be associated with Engel class I outcomes. At both 1 and 2 years after LITT, 58.0% achieved Engel I outcomes.
Authors' Conclusions	LITT is a viable treatment for mTLE in patients who have been properly evaluated at a comprehensive epilepsy center. Consideration of surgical factors is imperative to the complete assessment of LITT.

Epilepsy: Clinical Trials: Nonrandomized Comparison Studies	
Author/Year	Hale et al. (2019)
Study Type & Patients	Retrospective study of 26 pediatric patients with insular cortex epilepsy
Intervention	Laser interstitial thermal therapy (LITT) (n = 14) or open surgical resection (n = 12)

Findings Reported by Authors	The average age in our cohort was 10.3 yr, 58% were male, and the average length of follow-up was 2.43 ± 0.20 (SEM) yr. Complications in patients undergoing either LITT or open resection were mostly minimal and generally transient. Forty-three percent of patients who underwent LITT were Engel Class I, compared to 50% of patients who underwent open insular resection.
Authors' Conclusions	Both surgical resection and LITT are valid management options in the treatment of medically refractory insular/opercular epilepsy in children. Although LITT may be a less invasive alternative to craniotomy, further studies are needed to determine its noninferiority in terms of complication rates and seizure freedom.

Epilepsy: Clinical Trials: Nonrandomized Comparison Studies	
Author/Year	Petito et al. (2018)
Study Type & Patients	Retrospective, single-center study of 54 patients with medically refractory epilepsy.
Intervention	LITT (n = 33) or open surgical resection (n = 21)
Findings Reported by Authors	A discrete lesion was present on brain magnetic resonance imaging (MRI) in 27/32 (84.4%) of SLA [stereotactic laser ablation, i.e., LITT] patients compared with 7/20 (35%) of resection patients with a normal MRI. Overall, 55-60% of patients became seizure-free (SF). Four of five patients with initial failure to SLA became SF with subsequent resection surgery. Complications were more frequent with resection although SF outcomes did not differ (Chi square; p=0.79). Stereotactic laser ablation patients were older than those with resections (47.0 years vs. 35.4 years, p=0.001). The mean length of hospitalization prior to discharge was shorter for SLA (1.18days) compared with open resection (3.43 days; SD: 3.16 days) (p=0.0002).
Authors' Conclusions	We now use SLA as a first line therapy at our center in patients with lesional temporal lobe epilepsy (TLE) before resection. Seizure-free outcome with SLA and resection was similar but with a shorter length of stay. Long-term follow-up is recommended to determine sustained SF status from SLA.

Epilepsy: Clinical Trials: Nonrandomized Comparison Studies	
Author/Year	Lam et al. (2017)
Study Type & Patients	Retrospective, multicenter study of 58 children with medically refractory epilepsy secondary to hypothalamic hamartoma.
Intervention	LITT (n = 16) or open surgical resection (n = 42)
Findings Reported by Authors	The TCH [Texas Children's Hospital, LITT group] cohort had an average hospital LOS [length of stay] of 2.1 days, with a range of 1 to 8 days. The KID [Kids' Inpatient Database, surgery group] cohort had an average LOS of 8.4 days (range: 3–32 days). The average hospitalization charges for the TCH group were $65,525, with a standard deviation (SD) of $19,390). All values are reported in

	2013 U.S. dollars. The KID group average charges were more than double that of the TCH group at $145,760 (SD: $84,252). Based on cost-to charge ratios, the average cost per stay in KID ($42,450 ± $23,115) was also double the cost at TCH ($23,589 ± $6,981).
Authors' Conclusions	Our study has shown that children undergoing SLA for [hypothalamic hamartoma] have a shorter length of stay and lower cost of hospitalization compared with those who underwent craniotomy and resection for the same diagnosis. Together with previous findings from our institution regarding the safety and efficacy of SLA, our findings suggest that SLA may represent an attractive alternative to craniotomy for the treatment of refractory epilepsy secondary to [hypothalamic hamartoma]."

Epilepsy: Clinical Trials: Nonrandomized Comparison Studies	
Author/Year	Drane et al. (2015)
Study Type & Patients	Prospective, single-center study of 58 adult patients with anteromedial TLE
Intervention	LITT (n = 19) or open surgical resection (n = 39)
Findings Reported by Authors	[Boston Naming Test] performance declines were significantly greater for the dominant TLE patients undergoing open resection versus SLAH [stereotactic laser amygdalohippocampotomy; i.e., LITT] for naming famous faces and common nouns ($F=24.3$, $p<.0001$, $\eta2=.57$, & $F=11.2$, $p<.001$, $\eta2=.39$, respectively), and for the nondominant TLE patients undergoing open resection versus SLAH for recognizing famous faces ($F=3.9$, $p<.02$, $\eta2=.19$). When examined on an individual subject basis, no SLAH patients experienced any performance declines on these measures. In contrast, 32 of the 39 undergoing standard surgical approaches declined on one or more measures for both object types ($p<.001$, Fisher's exact test).
Authors' Conclusions	Initial experience with SLAH suggests that it is a promising surgical approach that appears to minimize aspects of the cognitive morbidity associated with open surgical resection.

Epilepsy: Systematic Reviews

Epilepsy: Systematic Reviews	
Author/Year	Brotis et al. (2021)
Purpose	Conducted a meta-analysis to estimate the efficacy of LITT for mTLE
Searched Resources/ Inclusion Criteria	Sixteen retrospective case series published between 2012 and 2019 representing 575 patients (range, 1 to 231) were identified.
Findings Reported by Authors	Overall, seizure freedom was achieved in 54.7% (95% CI, 50.6% to 58.8%: I2=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.
Authors' Conclusions	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.

Epilepsy: Systematic Reviews	
Author/Year	Kohlhase et al. (2021)
Purpose	To complete systematic review and meta-analysis to compare outcomes and complications from MR-guided LITT, radiofrequency ablation (RFA), and conventional open surgery (ie, anterior temporal lobe resection [ATL] or selective amygdalohippocampectomy [sAHE]) in patients with drug-refractory mesial temporal lobe epilepsy (mTLE).
Searched Resources/ Inclusion Criteria	Forty-three studies were identified (13 LITT; 6 RFA; 24 conventional surgery) between 1995 and 2018.
Findings Reported by Authors	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.
Authors' Conclusions	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.

Epilepsy: Systematic Reviews	
Author/Year	Grewal et al. (2019)
Purpose	To systematically review the current literature summarizing the effects of MRgLITT [magnetic resonance-guided laser interstitial thermotherapy] and SRS [stereotactic radiosurgery] in the management of [mesial temporal lobe epilepsy] and to compare, by meta-analysis, the seizure freedom, complications, and reoperation outcomes
Searched Resources/ Inclusion Criteria	MEDLINE, EMBASE, Cochrane Central, and Scopus in May 2018 for clinical studies reporting on 1-year or longer outcomes in patients who underwent LITT or SRS for medically refractory mesial lobe epilepsy. Included 17 studies (n = 404), of which 9 addressed LITT (n = 239)
Findings Reported by Authors	The overall seizure freedom rate was comparable between the 2 procedures (MRgLITT 50%, 95% confidence interval [CI] 44% to 56%, vs. SRS 42%, 95% CI 27% to 59%, P = 0.39). Similarly, among patients with lesional pathologic conditions only, the seizure freedom rate was comparable between the 2 procedures (MRgLITT 62%, 95% CI 48% to 74%, vs. SRS 50%, 95% CI 37% to 64%, P = 0.23). Compared with SRS, MRgLITT was associated with lower complication rates (MRgLITT 20%, 95% CI 14% to 26% vs. SRS 32%, 95% CI 20% to 46%, P = 0.06) but similar reoperation rates (15%, 95% CI 9% to 22% vs. 27%, 95% CI 12% to 46%, P = 0.31)." "We found the overall quality of evidence for most outcomes obtained through this indirect meta-analysis to be low as per the GRADE [Grading of Recommendations Assessment, Development and Evaluation] assessment.
Authors' Conclusions	Found similar outcomes and complications between the two procedures.

Epilepsy: Systematic Reviews	
Author/Year	Xue et al. (2019)
Purpose	To undertake a systematic review of the literature with meta-analysis of the data from published studies to assess the effectiveness of [MRgLITT]) in treatment-resistant epilepsy.
Searched Resources/ Inclusion Criteria	PubMed, MEDLINE, and EMBASE in May 2018 for clinical studies reporting outcomes of LITT in patients with medically refractory epilepsy. Included 16 studies (n = 269) [overlap 200]
Findings Reported by Authors	The studies included postoperative follow-up of between 7 days to 51 months… Eight publications focused on mesial temporal lobe epilepsy (MTLE), three on temporal lobe epilepsy (TLE), and another three publications on focal epilepsy." "The prevalence of Engel Class I (free from disabling seizures) after ablation were reported in 12 studies that included a total of 189 individuals. The pooled prevalence of patients who achieved postoperative freedom from epileptic seizures was 61% (95% CI, 0.54–0.68). Estimates ranged from 41–88% and low study

	heterogeneity were found (I2=14.5%; P=0.302) Seven studies reported postoperative complications, with a total of 26 complications in 101 patients with drug-resistant epilepsy. The pooled prevalence was 24% (95% CI, 0.16–0.32) and estimates ranged from 15–43%. Low study heterogeneity was detected (I2=0%; P=0.629).
Authors' Conclusions	Meta-analysis of data from 16 studies that included 269 patients with treatment-resistant epilepsy showed that MRI-guided LITT significantly reduced the frequency of seizures and reduced postoperative complications, supporting the safety and effectiveness of MRI-guided LITT in the treatment of drug-resistant epilepsy.

Epilepsy: Systematic Reviews	
Author/Year	Hoppe and Helmstaedter (2018)
Purpose	The review extends the former more general review on LiTT for epilepsy surgery with a special focus on children aged below 18 years.
Searched Resources/ Inclusion Criteria	PubMed in August 2018 for clinical studies of LITT in pediatric patients with epilepsy. Included 25 case series and case reports (n = 179) [overlap 62].
Findings Reported by Authors	Hypothalamic hamartomas (HH) represented the most frequent indication (64.2%) while therapeutic evidence for other more frequent etiologies underlying severe focal childhood epilepsies (e.g., focal cortical dysplasia, mesiotemporal sclerosis) is still scarce (n<20). For the published cases, the rate of severe complications was 3.4% and the overall complication rate was 23.5%. The seizure freedom rate (Engel class 1) was 57.5% (including patients with early follow-up and repeat thermoablations). None of the studies included the systematic evaluation of the cognitive outcome.
Authors' Conclusions	Only limited evidence for the therapeutic outcome of LiTT in this population is available so far. This concerns both the quantity of published studies and reported patients as well as the scientific quality of these publications (as these are uncontrolled case series reports).

Summary of Evidence: Epilepsy

The available evidence on laser interstitial thermal therapy (LITT) is somewhat favorable for the treatment of medically refractory epilepsy. Systematic reviews (SRs) with meta-analysis are of low-quality, however, before-and-after cohort studies shows that LITT results in freedom from seizures up to 2 years in about 60% of treated patients with medically refractory epilepsy; complications were reported in about 20% to 25% of LITT patients. LITT appears to be as safe and effective as stereotactic radiosurgery (e.g., Gamma Knife®) and nonrandomized studies suggest LITT may be safer than open surgery. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcomes. *In addition, the American Society for Stereotactic and Functional Neurosurgery (ASSFN) released a position statement in February 2022 related to laser interstitial thermal therapy for the treatment of Drug-*

Resistant Epilepsy noting indications for use as a treatment option for patients with DRE as follows:

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

They identified contraindication to use of LITT as follows:

1. *Inability to identify the epileptogenic focus (or foci) or critical pathways within epileptogenic networks.*
2. *Inability to undergo magnetic resonance imaging (MRI) because of medical reasons.*
3. *Medical contraindications to surgery, e.g., unstable cardiac or respiratory conditions, anticoagulants that cannot be stopped, bleeding diatheses.*

They also report their recommendations are based on the following:

1. *Safety and efficacy demonstrated in multiple peer-reviewed large case series demonstrating the safety and efficacy of MRgLITT in reducing seizure frequency in patients with DRE that is nearly comparable with data obtained from case series of open surgical procedures.*

2. *Published literature demonstrates that MRgLITT is a less invasive option for many types of focal DREs that involves a shorter hospital stay and less surgical and neurological morbidity as compared to open surgical resection for such common epilepsy etiologies as mesial temporal epilepsy, hypothalamic hamartomas, and focal cortical dysplasia/periventricular nodular heterotopia.*

3. *Some published studies indicate that MRgLITT may better preserve cognitive functions as compared to open epilepsy surgery.*

4. *When offered a choice between open surgery and MRgLITT, patients increasingly prefer LITT to open surgery, and many will otherwise refuse surgical treatment at all. Moreover, MRgLITT has also become the first-choice procedure of many epilepsy teams for treatment of many focal epilepsies and has essentially completely supplanted open surgery for epilepsy because of hypothalamic hamartomas. These trends make it unlikely that any randomized trials between MRgLITT and open surgery will be performed.*

Laser Interstitial Thermal Therapy for the Treatment of Liver Cancer

Metastatic liver cancer is a cancer that originated in a different part of the body and has spread to the liver. More common than primary liver cancer (cancer that originated in the liver), liver metastases often originate from colorectal, lung, breast, pancreatic, stomach,

melanoma, and neuroendocrine tumors. Patients may remain asymptomatic or develop symptoms depending on the number and location of the tumors in the liver. Symptoms may include fatigue, loss of appetite, weight loss, fever jaundice, itchy skin, discomfort and swelling of the abdomen, and swelling of the ankles. Diagnosis includes the use of blood tests to assess liver function and MRI or CT imaging to visualize the tumors.

The goal of treating liver metastases is to control or slow tumor growth and spread. Complete removal of metastases typically requires surgery. The main treatment for liver metastases is chemotherapy; oncologists typically recommend surgery (liver resection) only if one or few tumors are found. In many cases, surgery is not possible because of the location of the tumors or the patient's surgical risk. Alternative methods for removing liver metastases include ablative techniques, such as radiofrequency ablation, microwave ablation, ethanol ablation, cryosurgery, and arterial embolization. Laser interstitial thermal therapy (LITT) is a minimally invasive thermal ablation technique used to treat multiple tumor types. In patients with metastatic liver tumors, LITT is intended as an alternative to surgical resection or radiofrequency needle ablation and as adjunct to transarterial chemoembolization (TACE).

Based on an ECRI systemic review (2019), the available evidence on laser interstitial thermal therapy (LITT) is inconclusive as a minimally invasive alternative treatment for the treatment of liver metastases. Only low-quality nonrandomized studies address LITT for liver metastases. Findings are at high risk of bias and are of unclear significance because some studies involved patients with different etiologies and prognoses. Randomized controlled trials focusing on each tumor type are needed to compare LITT with other methods (e.g., surgery, microwave, radiofrequency).

Liver Cancer: Case Series

Liver Cancer: Case Series	
Author/Year	Pacella et al. (2016)
Study Type & Patients	Ten patients (mean age: 53.6 years ± 14.1; range: 24–79) with neuroendocrine tumors (NETs) and 13 liver metastases (mean diameter: 4.3 ± 2.8 cm; range: 1.5–12) underwent LA alone (n = 9) or LA followed by selective transarterial chemoembolization (n = 3)
Intervention	Evaluate the effectiveness of laser ablation (LA) with or without selective transarterial chemoembolization in patients with large, isolated or oligonodular unresectable neuroendocrine liver metastases.
Findings Reported by Authors	Complete response was obtained in six patients with LA alone and in two patients with combined treatment. The 5-year overall survival rates from the initial diagnosis and post-treatment were 80 and 50%, respectively.
Authors' Conclusions	This treatment modality may provide effective control of tumor burden and general symptoms improvement in patients with limited but unresectable disease.

Liver Cancer: Clinical Trials: Nonrandomized Comparative Studies

Liver Cancer: Clinical Trials: Nonrandomized Comparative Studies	
Author/Year	Vogel et al. (2014)
Study Type & Patients	110 patients with unresectable non-colorectal non-breast cancer liver metastases with progression under systemic chemotherapy. Excluded were patients with Karnofsky score ≤ 70, respiratory, renal and cardiovascular failure, and general TACE contraindications.
Intervention	Evaluate safety, feasibility, and overall survival rates for transarterial chemoembolization (TACE) alone or combined with MR-guided laser-induced-thermotherapy (LITT) in liver metastases of non-colorectal and non-breast cancer origin.
Findings Reported by Authors	TACE using Mitomycin alone, Mitomycin-Gemcitabine or Mitomycin-Gemcitabine-Cisplatin was performed to all patients. After TACE 146 metastases were ablated with MR-guided LITT. To be eligible for LITT metastases should be < 5 cm in size and ≤ 5 in number. Tumor response was evaluated using MRI according to RECIST. Survival was evaluated using Kaplan-Meier analysis. A total of 110 patients (mean age 59.2 years) with 371 metastases received TACE (mean 5.4 sessions/patient, n=110) with 76 (69%) receiving LITT (mean 1.6 session/patient) afterwards. TACE resulted in a mean decrease of mean maximum diameter of 52% ± 26.6 and volume change of -68.5% ± 22.9 in the 25 patients (23%) with partial response. Stable disease (n=59, 54%). Progressive disease (n=26, 23%). The RECIST outcome after LITT showed complete response (n=13, 17%), partial response (n=1, 1%), stable situation (n=41, 54%) and progressive disease (n=21, 28%). The mean time to progression (TTP) was 8.6 months. Median survival of all patients was 21.1 months.
Authors' Conclusions	TACE with different protocols alone and in combination with LITT is a feasible palliative treatment option resulting in a median survival of 21.1 months for unresectable liver metastases of non-colorectal and non-breast cancer origin.

Liver Cancer: Clinical Trials: Nonrandomized Comparative Studies	
Author/Year	Linchun et al. (2016)
Study Type & Patients	Eighty-five cases colorectal cancer liver metastases were assigned to the treatment group (43 cases) and to the control group (42 cases). The treatment group patients received LTA combined with FOLFIRI regimen chemotherapy, and the control group patients only received FOLFIRI regimen chemotherapy. The curative effects, the survival rate and adverse reaction of the two groups were observed and evaluated.
Intervention	Study to evaluate the efficacy and adverse reaction of a combination therapy of chemotherapy and laser thermal ablation (LTA) on liver metastases from colorectal cancer.

Findings Reported by Authors	Response rate was 53.4% in the treatment group and 38.1% in the control group (P>0.05); disease control rate in the treatment group was 79.1%, higher than 64.3% in control group with significant difference (P<0.01); median progression free survival was 11.8 months in treatment group and 6.8 months in control group (P<0.01); The median overall survival time was 19.1 months in treatment group and 14.9 months in control group (P<0.05). Among the 113 lesions receiving LTA, 104 lesions (92%) were completely destroyed. The main complications of LTA were fever and local pain. The adverse effects between both groups showed no difference.
Authors' Conclusions	LTA in combination with chemotherapy of colorectal carcinoma liver metastases is effective and well-tolerated.

Summary of Evidence: Liver Cancer
Evidence from available studies suggests that laser interstitial thermal therapy (LITT) may be safe for liver metastases, 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. *A review of the current NCCN guideline for Hepatobiliary Cancers Version 3.2022 does not address laser thermal therapy or laser ablation as treatment in hepatobiliary cancers. The evidence is insufficient to determine the effects of the technology on health outcomes.*

Laser Interstitial Thermal Therapy for the Treatment of Lung Cancer
Metastatic lung cancer is a malignancy that originates from a primary tumor in a different part of the body and has spread to the lung. Lung metastases are identified in up to 55% of all patients with cancer, and their prevalence varies depending on the primary cancer type. Lungs are the second most common site for all metastases. Primary tumors that most commonly spread to the lungs include those in the bladder, thyroid, head and neck, colon, breast, prostate, connective tissue, kidney, and adrenal gland. Patients are typically asymptomatic but may also experience cough, shortness of breath, frequent chest infections, coughing up blood, pain or discomfort in the chest, and weight loss. Diagnosis includes blood tests to assess lung function; serum screening for cancer-specific genetic markers; chest radiography or advanced imaging techniques, such as computed tomography (CT) and positron emission tomography to visualize tumors; bronchoscopy; and transthoracic/transbronchial needle aspiration biopsy.

The goal of treating lung metastases is to control or slow tumor growth and spread. The main treatment for lung metastases is chemotherapy; oncologists typically recommend surgery (metastasectomy) only if a significant likelihood exists that it will be curative. Alternative methods for removing lung metastases include bronchoscopic or thoracoscopic interventions, such as electrocauterization, argon plasma coagulation, cryotherapy, brachytherapy, rigid bronchoscopy, endoluminal stent placement, RFA, and external beam radiotherapy. Laser interstitial thermal therapy (LITT) is a minimally invasive ablation technique used to treat multiple tumor types. LITT is intended as an alternative to surgical resection and energy-based ablation techniques, such as microwave ablation (MWA) or radiofrequency ablation (RFA).

(2019) Based on an ECRI systematic review the available evidence on laser interstitial thermal therapy (LITT) is inconclusive as a minimally invasive alternative treatment for the treatment of lung metastases. Only low-quality, small, nonrandomized studies and case series address LITT for lung metastases. Findings are at high risk of bias and are of unclear significance because some studies pooled patients with different etiologies and prognoses. Randomized controlled trials focusing on each primary tumor type are needed to compare LITT with alternative treatments. (*Accessed December 2021*)

Lung Cancers: Clinical Trials: Nonrandomized Comparative Studies

Lung Cancer: Clinical Trials: Nonrandomized Comparative Studies	
Author/Year	Nour -Eldin et al. (2017)
Study Type & Patients	Retrospective analysis comparing local tumor control, time to progression and survival rates in patients with pulmonary metastases from non-colorectal cancer origin; 109 patients (43 males and 66 females)
Intervention	Microwave ablation (MWA), radiofrequency ablation (RFA) and laser-induced thermotherapy (LITT)
Findings Reported by Authors	The overall- survival rates at 1, 2, 3 and 4 years were 93.8, 56.3, 50.0 and 31.3% for patients treated with LITT; 81.5, 50.0, 45.5, and 24.2% for patients treated with RFA and 97.6, 79.9, 62.3 and 45.4% for patients treated with MWA respectively. The man survival time was 34.14 months for MWA, 34.79 months for RFA and 35.32 months for LITT. In paired comparison a significant difference could be detected between MWA versus RFA (p=0.032. The progression free survival showed a median of 23.49 + 0.62 months for MWA, 19.88 + 2.17 months for LITT and 16.66 + 0.66 months for RFA (p=0.048). The lowest recurrence rate was detected in lesions ablated with MWA (7.7%; 8 of 104 lesions) followed by RFA (20.4%; 10 of 49 lesions) and LITT (27.3%; 6 of 22 lesions) (p=0.012). Pneumothorax was detected in 22.16% of MWA ablations, 22.73% of LITT ablations and 14.23% of RFA ablations.
Authors' Conclusions	LITT, RFA and MWA may provide an effective therapeutic option for non-colorectal cancer lung metastases with an advantage for MWA regarding local tumour control and progression-free survival rate.

	This study was limited by a number of factors including the non-randomized non-controlled retrospective design, the relatively short imaging follow-up of 24 months, the element of selection bias of the modality of ablation and the absence of histopathologic correlation after ablation. The selection of method was driven by breakthroughs in the field of pulmonary ablation therapy. Another factor is the difference in number of lesions treated by each modality.

Lung Cancer: Clinical Trials: Nonrandomized Comparative Studies	
Author/Year	Vogl et al. (2016)
Study Type & Patients	Retrospective evaluation of local tumor control, time to tumor progression, and survival rates among patients with lung metastatic colorectal cancer; 109 patients (71 men and 38 women)
Intervention	Ablation performed using laser-induced thermotherapy (LITT), radiofrequency ablation (RFA) or microwave ablation (MWA)
Findings Reported by Authors	Local tumor control was achieved in 17 of 25 lesions (68.0%) treated with LITT, 45 of 65 lesions (69.2%) treated with RFA, and 91 of 103 lesions (88.3%) treated with MWA. Statistically significant differences were noted when MWA was compared with LITT at 18 months after ablation ($p = 0.01$) and when MWA was compared with RFA at 6 months ($p = 0.004$) and 18 months ($p = 0.01$) after ablation. The overall median time to local tumor progression was 7.6 months. The median time to local tumor progression was 10.4 months for lesions treated with LITT, 7.2 months for lesions treated with RFA, and 7.5 months for lesions treated with MWA, with no statistically significant difference noted. New pulmonary metastases developed in 47.6% of patients treated with LITT, in 51.2% of patients treated with RFA, and in 53.2% of patients treated with MWA. According to the Kaplan-Meier test, median survival was 22.1 months for patients who underwent LITT, 24.2 months for those receiving RFA, and 32.8 months for those who underwent MWA. The overall survival rate at 1, 2, and 4 years was 95.2%, 47.6%, and 23.8%, respectively, for patients treated with LITT; 76.9%, 50.8%, and 8.0%, respectively, for patients treated with RFA; and 82.7%, 67.5%, and 16.6%, respectively, for patients treated with MWA. The log-rank test revealed no statistically significant difference among LITT, RFA, and MWA. The progression-free survival rate at 1, 2, 3, and 4 years was 96.8%, 52.7%, 24.0%, and 19.1%, respectively, for patients who underwent LITT; 77.3%, 50.2%, 30.8%, and 16.4%, respectively, for patients who underwent RFA; and 54.6%, 29.1%, 10.0%, and 1.0%, respectively, for patients who underwent MWA, with no statistically significant difference noted among the three ablation methods.
Authors' Conclusions	LITT, RFA, and MWA can be used as therapeutic options for lung metastases resulting from colorectal cancer. Statistically significant differences in local tumor control revealed a potential advantage in using MWA. No differences in time to tumor progression or survival rates were detected when the three different ablation methods were compared

Summary of Evidence: Lung Cancer
Evidence from available studies suggests laser interstitial thermal therapy (LITT) may be safe for lung metastases, 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 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 intervention or chemotherapy. Randomized controlled trials focusing on each primary tumor type are needed to compare LITT with alternative treatments. The evidence is insufficient to determine the effects of the technology on health outcomes.

Laser Interstitial Thermal Therapy for the Treatment of Osteoid Osteoma
Osteoid osteomas are benign tumors composed of cells that produce bone matrix (osteoblasts), a nidus (origin site), and very loose vascular connective tissue. The tumors are typically smaller than 1.5 to 2.0 cm in size, can occur anywhere in the skeletal system, and may involve single or multiple bones. The most common sites for primary osteoid osteomas include the intercapsular regions of the hip and the diaphyseal parts of the tibia and humerus. The principal symptoms in initial and recurrent disease are pain, described as continuous, deep, aching, and intense; these symptoms may vary in severity. The pain is localized to the site of the tumors.

Osteomas are often initially misdiagnosed as osteomyelitis, Brodie abscesses, eosinophilic granulomas, or other benign cysts due to the disease's atypical presentation. Diagnosis of osteoid osteoma may take years (11.8 to 36.0 months on average) due to the disease's similarities to other bone diseases based on radiographic evidence. Other diagnostic methods, including radionuclide scanning, arteriography, CT, and MRI, can be used when radiographic findings are not informative. Pathologic examination is the only way to confirm a diagnosis of osteoid osteoma. To do this, a pathologist identifies a discrete central nidus, cherry-red in color, and smaller than 1 cm in diameter that can be extracted from the surrounding dense reactive bone.

Physicians initially recommend nonsurgical interventions for pain management, including the use of aspirin or nonsteroidal anti-inflammatory drugs, for primary osteomas. Surgery is typically reserved for patients whose disease does not respond to conservative treatment. Complete excision of the nidus provides complete pain relief and is curative in most cases; however, treatment success highly depends on the surgeon's ability to identify the exact location of the nidus. If the surgeon is unable to locate the nidus before surgery using advanced imaging techniques, the nidus may not be located intraoperatively, resulting in tissue removal larger than the tumor itself. Removing excessive bone during surgery may lead to the need for internal fixation, bone grafting, or disability if weight-bearing bones are affected. Surgical procedures for nidus removal

include en-bloc resection, unroofing and curettage, prophylactic internal fixation, and spinal fusion. Surgeons may not recommend surgical intervention in patients in whom the nidus is difficult to reach or for whom surgery may cause increased morbidity or disability. Laser interstitial thermal therapy (LITT) is a minimally invasive tissue ablation technique used to treat multiple tumor types, including osteoid osteomas.

LITT is intended as an alternative to conventional surgical osteoid osteoma resection in patients with symptoms (e.g., pain, disability) not controlled with medical therapy.

(2019) Based on an ECRI systematic review the available evidence on laser interstitial thermal therapy (LITT) is inconclusive as a minimally invasive alternative treatment for the treatment of osteoid osteomas. Limited evidence from case series at high risk of bias suggests that LITT is safe and that symptoms were reduced in most patients at 1-month to 1-year follow-up; however, these studies are at too high a risk of bias to be conclusive. A single nonrandomized comparative study reports on perioperative outcomes, and only small case series report on long-term (≥1 year) patient outcomes. Validation is needed in long-term trials comparing LITT to other treatments, such as surgical removal of the nidus and radiofrequency thermal ablation.

Osteoid Osteoma: Case Series

Osteoid Osteoma: Case Series	
Author/Year	Tsoumakidou et al. (2016)
Study Type & Patients	Retrospective; 57 patients (40 men and 17 women) with spinal osteoid osteoma (OO)
Intervention	Evaluate the safety and efficacy of percutaneous image-guided laser photocoagulation for the treatment of spinal osteoid osteoma (OO) in proximity to neural structures
Findings Reported by Authors	OO was in the vertebral body for 18 of 57 patients, the neural arch for 21 of 57 patients, and the articular process for 18 of 57 patients. Mean nidal diameter was 8 mm, and the mean distance from the closest neural structure was 6.6 mm (minimum distance, ≤5 mm in 35 of 57 patients). In 35 of 57 patients, no cortical coverage was present between the nidus and neural structure in danger. Mean total energy delivered was 1271 J (2-watt continuous power mode). Thermal insulation (carbon dioxide and/or hydrodissection), temperature monitoring, and electrostimulation were used in 42, 24, and one patient, respectively. Primary clinical success at 1 month was 98.2%. Total recurrence rate was 5.3%. All recurrences were addressed percutaneously. Secondary success rate was 100%. One-year follow-up is available in 54 of 57 patients. No major complications were noted.
Authors' Conclusions	Spinal OO can be safely and effectively treated with percutaneous laser photocoagulation. In cases that are less than 8 mm to 10 mm distance and in the absence of cortical coverage, thermal protection techniques of the neural structures should be used.

Osteoid Osteoma: Case Series	
Author/Year	Kachare et al. (2016)
Study Type & Patients	Study of 30 cases of osteoid osteomas in various bone diagnosed on various modalities (age not stated)
Intervention	CT-guided laser interstitial thermal therapy
Findings Reported by Authors	Over the period of 5 years 30 cases of osteoid osteomas in various bones diagnosed on various modalities were treated by CT guided LASER ablation. Bone wise distribution of cases was spine (3), upper end of femur (11), lower end of femur (6), upper end of tibia (4), upper end of humerus (3), lower end of radius (2) and calcaneum (1). 22 patients were treated under spinal and regional anesthesia and 8 patients were treated under short general anesthesia. All the patients were treated on day care basis. The LASER fiber was inserted in the nidus under CT guidance through bone biopsy needle and 1800 joules energy delivered in the lesion continuous mode. (96%) patients have complete relief of pain in twenty-four hours after LASER ablation, one week after treatment all 30 patients were pain free. No neurologic complication was observed in any of our patients with spinal osteoid osteomas.
Authors' Conclusions	CT guided laser ablation is a safe, simple and effective method of treatment for osteoid osteoma

Osteoid Osteoma: Clinical Trials: Nonrandomized Controlled/Comparative Studies

Osteoid Osteoma: Clinical Trials: Nonrandomized Controlled/Comparative Studies	
Author/Year	Wu et al. (2017)
Study Type & Patients	A total of 72 cases of children with osteoid osteoma. Selected patients were then divided into a control group and an observational group. The control group comprised 24 cases of boys and 13 cases of girls. The children were aged 3–16 years (average, 10.5±4.6 years), with a disease duration of 1–5 months (average, 2.2±1.3 months), and a maximum lesion diameter of 0.4–1.3 cm (average, 0.8±0.3 cm). The observational group included 22 boys and 14 girls, aged 3.5–15 years (average, 10.2±4.5 years), with a duration of 1.5–5 months (average, 2.6±1.5 months), and a maximum lesion diameter of 0.5–1.4 cm (average, 0.7±0.4 cm).
Intervention	Each group comprised 36 cases according to the method of treatment. Compare and analyze the difference between minimally invasive percutaneous laser ablation and open surgery in our center to provide reference for clinical treatment.
Findings Reported by Authors	The control group underwent conventional open surgery while the observational group underwent minimally invasive CT guided percutaneous laser ablation. Effects of both operations were compared. The operation duration, blood loss and plaster fixation duration of the observational group were significantly less than those of the control

	group. The postoperative pain score (VAS) at 1 day and 7 days were significantly lower than that of the control group, the differences were statistically significant (P<0.05). The lesion resection rate, effective rate of bone hyperplasia, effective rate of swelling and effusion and total effective rate of the observational group were significantly higher than those of the control group, the differences were statistically significant (P<0.05). Incidence of adverse reactions of observational group was significantly lower (P<0.05) than that of the control group.
Authors' Conclusions	The difference was not significant when comparing 1-year recurrence rate for the two groups. The minimally invasive percutaneous laser ablation has better surgery effects compared with open surgery in the treatment of children with osteoid osteoma. Additional large number of samples, randomized controlled clinical trial should still be conducted to further discuss the safety, effectiveness, indications of osteoid osteoma with minimally invasive operation.

Summary of Evidence: 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). Only one study compared laser interstitial thermal therapy (LITT) with conventional surgery and had heterogeneity among patients 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. *A review of the current NCCN guideline Bone Cancer Version 2.2022 the guideline does not address laser thermal therapy or laser ablation treatment in bone cancers. The evidence is insufficient to determine the effects of the technology on health outcomes.*

Laser Interstitial Thermal Therapy for the Treatment of Prostate Cancer
Prostate cancer is the most common noncutaneous cancer affecting men. Prostate cancer often develops when the rate of cell division and cell death is no longer equal in the prostate tissue, leading to uncontrolled tumor growth. The majority of prostate cancers (95%) are adenocarcinomas, while 4% are transitional cell carcinomas arising from the urothelial lining of the prostatic urethra. Less common cases of prostate cancer (1%) are squamous cell carcinomas that typically arise after radiation or hormone treatment. In the United States, prostate cancer affects an estimated one in six Caucasian men and one in five African American men, with the likelihood of developing the cancer increasing with age. Globally, the rate of prostate cancer is highest in men of sub-Saharan African ancestry and lowest in those of Asian ancestry. Other factors associated with the

development of prostate cancer include familial predisposition, diet, hormones, genetics, and environmental factors.

Patients with prostate cancer may present with symptoms that include urinary retention, hematuria (blood in urine), or back pain, although the presence of symptoms more often indicates other underlying disease. Patients with advanced stages of prostate cancer will often present with skeletal manifestations due to the cancer's tendency to metastasize to the bone. A physician is more likely to diagnose the disease in asymptomatic patients during a routine cancer screening, such as a prostate-specific antigen (PSA) level screening or digital rectal examination (DRE). A urologist may also diagnose prostate cancer incidentally while treating a patient for benign prostate hyperplasia (prostate enlargement) using the transurethral resection procedure, which involves removing prostate tissue. Patients with an elevated PSA or abnormal DRE will require a needle biopsy to confirm the diagnosis of cancer. Pathology of the dissected prostate tissue will provide the Gleason score which urologists use to determine prognosis.

Treatment for prostate cancer is based on the patient's prostate cancer risk profile, age, health, and life expectancy. Laser interstitial thermal therapy (LITT) is being researched as a minimally invasive focal therapy option for treating localized prostate cancer. LITT uses continuous or pulsed thermal energy that enables thermal coagulation of tumor cells locally within the prostate gland while theoretically preserving the surrounding tissues, including the neurovascular and sphincter structures responsible for potency and urinary continence.

(2019) Based on an ECRI systematic review the available evidence on laser interstitial thermal therapy (LITT) is inconclusive as a minimally invasive alternative treatment for the treatment of localized prostate cancer. Limited evidence from very small case series and systematic reviews (SRs) of other small case series suggests that LITT may be safe and without negative effects on sexual and urinary function in the short term (≤1 year) when used for localized prostate cancer; however, clinical trials have not yet demonstrated efficacy because studies have not assessed or reported on patient-oriented outcomes, such as 5-year overall survival or progression-free survival. Available studies are at high risk of bias, and results need confirmation in prospective controlled trials that compare LITT to other treatments for localized prostate cancer, such as radical prostatectomy, cryotherapy, and radiation therapy (external or radioactive seed implants).

Prostate Cancer: Clinical Trials

Prostate Cancer: Clinical Trials	
Author/Year	Eggener et al. (2016)
Study Type & Patients	Phase II evaluation in 27 men with stage T1c-T2a prostate cancer. Inclusion criteria included prostate specific antigen (PSA) < 15 ng/ml or PSA density < 0.15 ng/ml3, Gleason score of 7 or less in 25% or less of biopsies, and MRI with 1 or 2 lesions concordant with biopsy-detected cancer.
Intervention	MRI-guided focal laser ablation

Findings Reported by Authors	In the 27 men median age was 62 years and mean prostate specific antigen was 4.4 ng/ml. Biopsy Gleason score was 6 in 23 patients (85%) and Gleason 7 in 4 (15%). Seven men (26%) had low volume Gleason 6 disease outside the intended ablation zone(s). At 3 months 26 patients (96%) had no evidence of cancer on magnetic resonance imaging guided biopsy of the ablation zone. No significant I-PSS changes were observed (each p >0.05). SHIM was lower at 1 month (p = 0.03), marginally lower at 3 months (p = 0.05) and without a significant difference at 12 months (p = 0.38). At 12-month biopsy cancer was identified in 10 patients (37%), including in the ablation zone(s) in 3 (11%) and outside the ablation zone(s) in 8 (30%) with cancer in and outside the ablation zone in 1.
Authors' Conclusions	The authors concluded that in select individuals with localized prostate cancer and visible MRI lesions, focal laser ablation has an acceptable morbidity profile and is associated with encouraging short-term oncologic outcomes. Significantly longer follow-up is mandatory to fully assess this treatment. Furthermore, the study was limited by lack of comparison group.

Prostate Cancer: Clinical Trials	
Author/Year	Natarajan et al. (2017)
Study Type & Patients	Prospective institutional review board approved pilot study. Patients (n = 10) with intermediate- risk prostate cancer
Intervention	Focal laser ablation using MRI -ultrasound fusion guidance
Findings Reported by Authors	Mean procedure time was 95 minutes (range 71 to 105). Posttreatment magnetic resonance imaging revealed a confined zone of nonperfusion in all 10 men. Mean zone volume was 4.3 cc (range 2.1 to 6.0). No CTCAE [Common Terminology Criteria for Adverse Events] grade 3 or greater adverse events developed, and no changes were observed in urinary or sexual function. At 6 months magnetic resonance imaging-ultrasound fusion biopsy of the treatment site showed no cancer in 3 patients, microfocal Gleason 3 + 3 in another 3 and persistent intermediate risk prostate cancer in 4.
Authors' Conclusions	Focal laser ablation of prostate cancer appears safe and feasible with the patient under local anesthesia in a urology clinic using magnetic resonance imaging-ultrasound fusion for guidance and thermal probes for monitoring. Further development is necessary to refine out of bore focal laser ablation and additional studies are needed to determine appropriate treatment margins and oncologic efficacy.

Prostate Cancer: Systematic Reviews

Prostate Cancer: Systematic Reviews	
Author/Year	Walker et al. (2018)

Purpose of Systematic Review	"To systematically review erectile function (EF) outcomes following primary whole gland (WG) and focal ablative therapies for localized prostate cancer to ascertain whether the treatment modality or intended treatment volume affects the time taken to recover baseline EF."
Searched Resources & Inclusion Criteria	Cochrane library, Scopus, and PubMed was performed from inception to February 2017 for studies that reported on men with localized prostate cancer treated with primary, ablative therapy. Included 17 studies reporting on 1,297 patients. Of those, 4 case series reported on 35 unique patients undergoing focal photothermal (FP) therapy.
Findings Reported by Authors	"WG cryotherapy was associated with a significant decline in EF at 6 months with minimal improvement at 36 months. Baseline IIEF-15 [International Index of Erectile Function] of patients undergoing focal HIFU [high-intensity focused ultrasound] fell 30 points at 1 month but returned to baseline by 6 months. The remaining focal therapies demonstrated minimal or no effect on EF, but the men in these studies had small foci of disease. The review is limited by lack of randomized studies and heterogeneous outcome measures." "[FP], VTP [vascular targeted photothermal therapy], and IRE [irreversible electroporation] appeared to cause very little change from baseline though the men in these studies tended to have low volume lesions."
Authors' Conclusions	"Most studies assessing the outcomes of focal therapy on sexual function were not of high quality, used heterogeneous outcomes, and had relatively short follow up, highlighting the need for more robustly designed studies using validated patient reported outcome measures for comparison. However, FT in general resulted in less effect on EF than WG ablation."

Prostate Cancer: Systemic Reviews	
Author/Year	Valerio et al. (2017)
Purpose of Systematic Review	To complete systematic review & meta-analysis to summarize the evidence regarding sources of energy employed in focal therapy of prostate cancer has been proposed as an alternative to whole-gland treatments.
Searched Resources & Inclusion Criteria	Thirty-seven articles reporting on 3230 patients undergoing focal therapy were selected, with one of the focal therapies being laser interstitial thermal therapy (LITT). Four prospective Stage 1 to 2a studies evaluating LITT in 50 patients have been reported in literature. One study only included men with low-risk disease, whereas the other studies also included Gleason score ≤ 4+3, although risk stratification was not clearly reported. The median age was 63.5 yrs.; median PSA was 5.4 ng/ml; median follow-up was 4.5 months with all series including mandatory sampling after treatment. In the Stage 1 study, participants underwent radical prostatectomy, whereas in the other 3 studies participants underwent MR-transrectal ultrasound (TRUS) standard and/or targeted biopsy.

Findings Reported by Authors	Overall, the presence of significant and insignificant tumors was 4.8% and 22.2%, respectively. The probability of transition to secondary local treatment was 0%; overall and disease-specific survival, pad-free continence and potency preservation were 100% and 100%, respectively. No adverse events were reported in any study. The authors concluded that focal therapy seems safe and appears to offer good preservation of genito-urinary function.
Authors' Conclusions	Seven sources of energy have been employed to selectively ablate discrete areas of prostate cancer. There is high evidence that focal therapy is safe and has low detrimental impact on continence and potency. The oncological outcome has yet to be evaluated against standard of care. Tumor control in studies with intention to treat is encouraging, although this needs to be verified against standard of care in high quality comparative effectiveness trials.

Summary of Evidence: 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. *A review of the current NCCN guideline for Prostate Cancer Version 1.2023 mentions laser ablation as an emerging local therapy, however, the NCCN Panel does not include this as local therapy option for the treatment of localized prostate cancer in initial disease or recurrent settings. The evidence is insufficient to determine the effects of the technology on 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 patients 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 patients 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 patients 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 patients.

Interventions
The therapy being considered is LITT as an alternative to open craniotomy with resection 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 progression-free survival. 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.

Laser Interstitial Thermal Therapy for the Treatment of Radiation Necrosis
Cranial irradiation (brain irradiation) is used to treat patients with primary or metastatic brain tumors and as prophylaxis for selected patients at high risk of neoplastic involvement of the nervous system. Tissue necrosis is a distinct syndrome of radiation toxicity, thought to be the consequence of vascular endothelial cell damage, resulting in fibrinoid necrosis of small vessels and direct brain parenchymal necrosis.

Treatment-induced brain tissue necrosis (also referred to as radiation necrosis) is a serious complication that typically develops one to three years after radiation, although the range is quite broad, and cases have been reported more than 10 years after radiation. The dose that causes a higher than 5 percent risk of focal radiation necrosis using conventional 2 gray (Gy) fractionation is usually estimated to be 72 Gy, but this may be an oversimplification, and the dose that causes necrosis may vary by region of the brain as well. Tissue necrosis is more likely to occur when high doses per fraction are administered and perhaps with concurrent chemotherapy or radiosensitizers. The risk of tissue necrosis after stereotactic radiosurgery (SRS) has been reported to be higher, with a steep dose-response relationship. Tissue necrosis typically develops at or adjacent to the original site of tumor, the location that received the highest radiation dose. Tissue necrosis can also develop in part of the normal brain parenchyma that was included in the treatment field of a tumor outside the brain, such as temporal lobe necrosis that develops in some patients treated for nasopharyngeal cancer or clival chordoma. In this setting, brain tissue necrosis typically results in new focal neurologic signs, and imaging studies such as computed tomography (CT) or magnetic resonance imaging (MRI) may show an enhancing mass lesion with edema.

The clinical course of brain tissue necrosis is highly variable. No causal therapies have been established, and management is primarily symptomatic. The treatment decisions require a balance between the often-competing goals of symptom control and avoidance of side effects. In some cases, tissue necrosis is an asymptomatic, self-limited process that can be managed conservatively without intervention. In patients who are symptomatic, initial treatment includes a moderate dose of glucocorticoid (e.g., 4 to 8 mg of oral dexamethasone daily), which usually produces prompt symptomatic improvement by reducing cerebral edema. Once symptoms are controlled, glucocorticoids can then be gradually tapered over the course of several weeks. Follow-up imaging after one to two months is generally recommended. In patients who do not achieve symptomatic response to glucocorticoids, or when glucocorticoids cannot be tapered without return of symptoms, surgical resection of the necrotic tissue is sometimes required particularly in cases where there is diagnostic uncertainty as to whether the radiographic changes are indicative of tumor progression or treatment – induced tissue necrosis, or in patients with severe necrosis who have contraindications to bevacizumab. Surgery can provide palliative benefit by reducing mass effect and decreasing steroid requirements postoperatively. Minimally invasive laser interstitial thermal therapy (LITT) has been explored as therapeutic intervention in the treatment of radiation necrosis.

Radiation Necrosis: Retrospective Review	
Author/Year	Sujijantarat et al. (2020)
Purpose of the Review	Both laser interstitial thermal therapy (LITT) and bevacizumab have been used successfully to treat radiation necrosis (RN) after radiation for brain metastases. Our purpose is to compare pre-treatment patient characteristics and outcomes between the two treatment options.
Inclusion Criteria	Single-institution retrospective chart review identified brain metastasis patients who developed RN between 2011 and 2018. Pre-treatment factors and treatment responses were compared between those treated with LITT versus bevacizumab.
Findings Reported by Authors	Twenty-five patients underwent LITT and 13 patients were treated with bevacizumab. The LITT cohort had a longer overall survival (median 24.8 vs. 15.2 months for bevacizumab, $p = 0.003$) and trended to have a longer time to local recurrence (median 12.1 months vs. 2.0 for bevacizumab), although the latter failed to achieve statistical significance ($p = 0.091$). LITT resulted in an initial increase in lesional volume compared to bevacizumab ($p < 0.001$). However, this trend reversed in the long term follow-up, with LITT resulting in a median volume decrease at 1 year post-treatment of – 64.7% (range – 96.0% to + > 100%), while bevacizumab patients saw a median volume increase of + > 100% (range – 63.0% to + > 100%), $p = 0.010$.
Authors' Conclusions	The study suggests that patients undergoing LITT for RN have longer overall survival and better long-term lesional volume reduction than those treated with bevacizumab. However, it remains unclear whether our findings are due only to a difference in efficacy of the treatments or the implications of selection bias.

Radiation Necrosis: Retrospective Review	
Author/Year	Hong et al. (2019)
Purpose of the Review	Many publications report laser-interstitial thermal therapy (LITT) as a viable alternative treatment to craniotomy for radiation necrosis (RN) and re-growing tumor occurring after stereotactic radiosurgery (SRS) for brain metastases. No studies to-date have compared the two options. The aim of this study was to retrospectively compare outcomes after LITT versus craniotomy for regrowing lesions in patients previously treated with SRS for brain metastases.
Inclusion Criteria	Data were collected from a single-institution chart review of patients treated with LITT or craniotomy for previously irradiated brain metastasis.

Findings Reported by Authors	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 progression-free survival 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.
Authors' Conclusions	LITT was as efficacious as craniotomy in achieving local control of recurrent irradiated brain metastases and facilitating steroid taper, regardless of pathology. Craniotomy appears to be more advantageous for providing symptom relief in those with pre-operative symptoms.

Radiation Necrosis	
Author/Year	Rammo et al. (2018)
Purpose of the Review	This study seeks to determine the safety of laser interstitial thermal therapy (LITT) for CRN and identify the pattern of post-ablation volume change over time.
Inclusion Criteria	Patients undergoing LITT for tumor treatment at Henry Ford Hospital between November 2013 and January 2016 with biopsy-confirmed CRN were prospectively collected and retrospectively reviewed with attention to ablation volume, survival, demographic data, steroid dose, and complications. Imaging occurred at set intervals beginning pre-ablation. Ten patients with 11 ablations were evaluated. Four patients had a primary diagnosis of high-grade glioma, while six had metastatic lesions. An average of 86% of CRN volume was ablated. Ablation volume increased to 430% of initial CRN volume at 1-2 weeks before decreasing to 69% after 6 months.
Findings Reported by Authors	No patient had a decline in baseline neurological examination while in the hospital. Four patients developed delayed neurological deficits likely due to post-operative edema, of which three improved back to baseline. The 6-month survival was 77.8% and the 1-year survival was 64.8% based on Kaplan-Meier curve estimates.
Authors' Conclusions	In this study, LITT was a relatively safe treatment for CRN, providing both a diagnostic and therapeutic solution for refractory patients. Significant increase in ablation volume was noted at 1-2 months, gradually decreasing in size to less than the original volume by 6 months. Further studies are needed to better define the role of LITT in the treatment of CRN.

Radiation Necrosis	
Author/Year	Rao et al. (2014)
Purpose of the Review	To report the largest series to date of local control with LITT for the treatment of recurrent enhancing lesions after stereotactic radiosurgery for brain metastases.
Inclusion Criteria	Patients with recurrent metastatic intracranial tumors or radiation necrosis who had previously undergone radiosurgery and had a Karnofsky performance status of >70 were eligible for LITT. Sixteen patients underwent a total of 17 procedures. The primary end point was local control using magnetic resonance imaging scans at intervals of >4 weeks. Radiographic outcomes were followed up prospectively until death or local recurrence (defined as >25% increase in volume compared with the 24-hour postprocedural scan).
Findings Reported by Authors	Fifteen patients (age, 46-82 years) were available for follow-up. Primary tumor histology was non-small-cell lung cancer (n = 12) and adenocarcinoma (n = 3). On average, the lesion size measured 3.66 cm (range, 0.46-25.45 cm); there were 3.3 ablations per treatment (range, 2-6), with 7.73-cm depth to target (range, 5.5-14.1 cm), ablation dose of 9.85 W (range, 8.2-12.0 W), and total ablation time of 7.43 minutes (range, 2-15 minutes). At a median follow-up of 24 weeks (range, 4-84 weeks), local control was 75.8% (13 of 15 lesions), median progression-free survival was 37 weeks, and overall survival was 57% (8 of 14 patients). Two patients experience recurrence at 6 and 18 weeks after the procedure. Five patients died of extracranial disease progression; 1 patient died of neurological progression elsewhere in the brain.
Authors' Conclusions	Magnetic resonance imaging guided LITT is a well-tolerated procedure and may be effective in treating tumor recurrence/radiation necrosis. This was a small, single-arm, non-randomized study. Moreover, the authors stated that "larger studies with longer follow-up that include patient quality of life, decreased steroid dependence and neurological symptoms as end-points are necessary to confirm these findings and better define the appropriate patient for this therapy".

Summary of Evidence: Radiation Necrosis

In addition to the literature information above, related to primary brain tumors and brain metastasis which also addresses radiation necrosis in previously irradiated primary and metastasized brain cancers, an advantage of LITT, in comparison to other salvage treatments for patients is the ability to treat lesions not amenable to surgical resection due to its difficult location. The minimal invasiveness of the procedures renders minimal injury to structures superficial to the tumor when compared to open surgery, it also translates to shorter hospital stays, less systemic response to surgical trauma, and faster transition to adjuvant treatments like chemotherapy. This benefits patients with compromised performance scores. LITT can also be repeated if progression is found after the procedure with no concern of accumulated ionizing radiation damage, also it does not

preclude a future open surgery in the case of treatment failure. Lastly, the potential disruption of the BBB making it permeable to cytotoxic drugs open the possibility of better local control with the use of combined chemotherapy in selected cases, although this still pends confirmation by further studies.

A review of the current NCCN guideline Central Nervous System Cancers Version 2.2022 recommends MRI-guided laser interstitial thermal therapy (LITT) may be considered for patients who are not surgical candidates (craniotomy or resection). Potential indications include relapsed brain metastases and radiation necrosis. (Category 2B)

The AANS released a position statement in 2021 on MR-guided laser interstitial thermal therapy (LITT) for brain tumors and radiation necrosis stating the following:

- *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 nGBM, rGBM, and Mets/rMets. 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. A multidisciplinary approach remains the cornerstone in the treatment of patients with brain tumors or radiation necrosis. It is important that physicians have discretion to exercise their clinical judgement when evaluating the most appropriate option for their patients' individual treatment plan.*
- *There is consensus that intracranial LITT should be considered as a potential option for patients with recurrent or progressive malignant tumor (primary or metastatic), lesion(s) inaccessible to surgical resection, or when the patient is unable to tolerate surgical resection due to medical comorbidities. (Accessed November 2022)*

The available evidence on laser interstitial thermal therapy (LITT) is somewhat favorable for the treatment of radiation necrosis previously irradiated primary and metastasized brain cancers based on case series, randomized control trials, and systemic reviews. Based on the above the American Association of Neurological Surgeons position statement and NCCN guidelines support the use of LITT in this subpopulation of patients. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcomes.

Practice Guidelines and Position Statements

American Association of Neurological Surgeons (AANS) et al.
(2021) The AANS released a position statement on MR-guided laser interstitial thermal therapy (LITT) for brain tumors and radiation necrosis stating the following:

- 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 nGBM, rGBM, and Mets/rMets. 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. A multidisciplinary approach remains the cornerstone in the treatment of patients with brain tumors or radiation necrosis. It is important that physicians have discretion to exercise their clinical judgement when evaluating the most appropriate option for their patients' individual treatment plan.
- There is consensus that intracranial LITT should be considered as a potential option for patients with recurrent or progressive malignant tumor (primary or metastatic), lesion(s) inaccessible to surgical resection, or when the patient is unable to tolerate surgical resection due to medical comorbidities. (*Accessed November 2022*)

American Society of Breast Surgeons (ASBrS)
(2018) The American Society of Breast Surgeons issued a consensus guideline on the use of transcutaneous and percutaneous ablation for the treatment of benign and malignant tumors of the breast that included the following:

- **Indications for percutaneous or transcutaneous ablative treatment of malignant tumors of the breast:** At this time, there are no FDA approved percutaneous or transcutaneous ablative treatments for breast cancer. At the present time, cryoablation is approved for treatment of soft tissue malignancies. However, there is emerging data from clinical trials utilizing percutaneous ablative therapies for patients with early-stage breast cancer without surgical excision. Techniques being evaluated include ablation by focused ultrasound, laser, cryotherapy, microwave, and radiofrequency. Percutaneous excision by vacuum-assistance is also being investigated

Recommendation:

- Cryoablation is currently approved for treatment of benign and malignant soft tissue tumors by the FDA. Currently, there are no specific technologies that have FDA approval for breast tumors. Participation in registries and clinical trials evaluating the use of these technologies with and without surgical excision of a breast malignancy is advised as early data emerges on their efficacy. (*Accessed November 2022*)

American Society of Clinical Oncology (ASCO)
The ASCO clinical guidelines do not address laser thermal therapy as treatment in tumors of the genitourinary system, head and neck, breast, bone, or in neurooncology. (*Accessed December 2021*)

American Society for Radiation Oncology
The American Society for Radiation Oncology (ASTRO) clinical practice guideline on radiotherapeutic and surgical management for newly diagnosed brain metastases (2012) does not address the use of LITT.

American Society for Stereotactic and Functional Neurosurgery (ASSFN)
(February 2022) The AASFN released a position statement on laser interstitial thermal therapy for the treatment of Drug-Resistant Epilepsy:

Indications for the Use of MRgLITT as a Treatment Option for Patients with DRE include all of the following

Criteria:

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

Contraindication to Use of MRgLITT:

1. Inability to identify the epileptogenic focus (or foci) or critical pathways within epileptogenic networks.
2. Inability to undergo magnetic resonance imaging (MRI) because of medical reasons.
3. Medical contraindications to surgery, e.g., unstable cardiac or respiratory conditions, anticoagulants that cannot be stopped, bleeding diatheses.

They also report their recommendations are based on the following:

1. Safety and efficacy demonstrated in multiple peer-reviewed large case series demonstrating the safety and efficacy of MRgLITT in reducing seizure frequency in patients with DRE that is nearly comparable with data obtained from case series of open surgical procedures.
2. Published literature demonstrates that MRgLITT is a less invasive option for many types of focal DREs that involves a shorter hospital stay and less surgical and neurological morbidity as compared to open surgical resection for such common epilepsy etiologies as mesial temporal epilepsy, hypothalamic hamartomas, and focal cortical dysplasia/periventricular nodular heterotopia.
3. Some published studies indicate that MRgLITT may better preserve cognitive functions as compared to open epilepsy surgery.
4. When offered a choice between open surgery and MRgLITT, patients increasingly prefer LITT to open surgery, and many will otherwise refuse surgical treatment at all. Moreover, MRgLITT has also become the first-choice procedure of many epilepsy teams for treatment of many focal epilepsies and has essentially completely supplanted open surgery for epilepsy because of hypothalamic hamartomas. These trends make it unlikely that any randomized trials between MRgLITT and open surgery will be performed.

(*Accessed November 2022*)

Congress of Neurological Surgeons
In 2019, the Congress of Neurological Surgeons issued a systematic review and evidence-based guideline on the role of emerging and investigational therapies for the treatment of adults with metastatic brain tumors that included the following recommendation:

- **Laser Interstitial Thermal Therapy**
  - 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. (*Accessed November 2022*)

National Comprehensive Cancer Network (NCCN)

- **Breast Cancer Version 4.2022**
  - The NCCN Guideline does not address laser thermal therapy or laser ablation as treatment in breast cancer.
- **Bone Cancer Version 2.2023**
  - The NCCN Guideline does not address laser thermal therapy or laser ablation as treatment in bone cancers.
- **Central Nervous System Cancers Version 2.2022**
  - MRI-guided laser interstitial thermal therapy (LITT) may be considered for patients who are not surgical candidates (craniotomy or resection). Potential indications include relapsed brain metastases and radiation necrosis. (Category 2B)
- **Hepatobiliary Cancers Version 3.2022**
  - The NCCN Guideline does not address laser thermal therapy or laser ablation as treatment in hepatobiliary cancers.
- **Non-Small Cell Lung Cancer Version 5.2022**
  - The NCCN Guideline does not address laser thermal therapy as treatment for lung cancer.
- **Prostate Cancer Version 1.2023**
  - **Other Local Therapies**
    - Many therapies have been investigated for the treatment of localized prostate cancer in the initial disease and recurrent settings, with the goals of reducing side effects and matching the cancer control of other therapies. Cryotherapy or other local therapies are not recommended as routine primary therapy for localized prostate cancer due to lack of long-term data comparing these treatments in radiation or radical prostatectomy. At this time, the panel recommends only cryosurgery and high-intensity focused ultrasound (HIFU; category 2B) as local therapy options for RT recurrence in the absence of metastatic disease.
  - Other emerging local therapies, such as focal laser ablation and vascular targeted photodynamic (VTP) therapy have also been studied. The multicenter, open-label, phase 3, randomized controlled CLIN1001 PCM301 trial compared VTP therapy (IV padeliporfin, optical fibers inserted into the prostate, and

subsequent laser activation) to active surveillance in 413 patients with low-risk prostate cancer.545 After a median follow-up of 24 months, 28% of participants in the VTP arm had disease progression compared with 58% in the active surveillance arm (adjusted HR, 0.34; 95% CI, 0.24–0.46; P < .0001). Negative prostate biopsy results were more prevalent in the VTP group (49% vs. 14%; adjusted RR, 3.67; 95% CI, 2.53–5.33; P < .0001). The most common serious adverse event in the VTP group was urinary retention (3 of 206 patients), which resolved within 2 months in all cases
    - The NCCN Guideline mentions laser ablation as an emerging local therapy but currently does not recommend as treatment for prostate cancer.
- **Small Cell Lung Cancer Version 2.2023**
    - The NCCN Guideline does not address laser thermal therapy as treatment for lung cancer.

(*Accessed December November 2022*)

National Institute for Health and Care Excellence (NICE)

In 2020, the National Institute for Health and Care Excellence (NICE) published an interventional procedures guidance on the use of MRI-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. (*Accessed November 2022*)

Regulatory Status

In August 2007, the Visualase™ Thermal Therapy System (Medtronic; formerly Biotex, Inc.) received initial marketing clearance by the FDA through the 510(k) pathway (K071328). As of March 2019, the system is indicated for use "to necrotize or coagulate soft tissue through interstitial irradiation or thermal therapy under magnetic resonance imaging (MRI) guidance in medicine and surgery in cardiovascular thoracic surgery (excluding the heart and vessels in the pericardial sac), dermatology, ear-nose-throat surgery, gastroenterology, general surgery, gynecology, head and neck surgery, neurosurgery, plastic surgery, orthopedics, pulmonology, radiology, and urology, for wavelengths 800 nm through 1064 nm" (K181859). Data from compatible MRI sequences can be processed via proton resonance-frequency shift analysis and image subtraction 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.

On April 25, 2018, the FDA issued a safety alert on MR-guided LITT (MRgLITT) devices with a letter to healthcare providers stating that the FDA is currently evaluating data suggesting that potentially inaccurate MR thermometry information can be displayed during treatment, which may contribute to a risk of tissue overheating and potentially associated adverse events, including neurological deficits, increased intracerebral edema or pressure, intracranial bleeding, and/or visual changes. Several risk mitigation strategies were recommended. In an updated letter released on November 8, 2018, risk mitigation recommendations specific to the Visualase™ and NeuroBlate® systems were issued

PRIOR APPROVAL

Not required

POLICY

See Related Medical Policies

- 02.01.53 High Intensity Focused Ultrasound (HIFU)
- 04.01.09 MRI-Guided High-Intensity Focused Ultrasound (MRGFUS) Ablation
- 07.01.69 Treatments for Benign Prostatic Hyperplasia (BPH)

Brain Tumor(s)/Radiation Necrosis

Treatment of *brain tumor(s)* 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 recurrent or progressive malignant tumor(s) (primary or metastatic); **or**
- A lesion(s) which is inaccessible to surgical resection.

Refractory Epilepsy

The treatment of *medically 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 regiments; **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 is because the evidence is insufficient to determine the effects of the technology on the net health outcomes:

- Brain tumors (primary and metastatic, except as indicated above)
- Breast cancer (benign or malignant)

- Epilepsy (except as indicated above)
- Liver cancer (primary and metastatic)
- Lung cancer (primary and metastatic)
- Osteoid osteoma
- Prostate cancer
- Radiation necrosis (except as indicated above)

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.

PROCEDURE CODES AND BILLING GUIDELINES

To report provider services, use appropriate CPT* codes, Alpha Numeric (HCPCS level 2) codes, Revenue codes, and/or ICD diagnosis codes.

- 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)

SELECTED REFERENCES

- Grewal, SS, Alvi, MA, Lu, VM, Wahood, W, Worrell, GA, Tatum, W, Wharen, RE, Jr., and Van Gompel, JJ. Magnetic Resonance-Guided Laser Interstitial Thermal Therapy Versus Stereotactic Radiosurgery for Medically Intractable Temporal Lobe Epilepsy: A Systematic Review and Meta-Analysis of Seizure Outcomes and Complications. World Neurosurg. 2019;122:e32-e47
- Hoppe, C, and Helmstaedter, C. Laser interstitial thermotherapy (LiTT) in pediatric epilepsy surgery. Seizure. 2018
- Xue, F, Chen, T, and Sun, H. Postoperative Outcomes of Magnetic Resonance Imaging (MRI)-Guided Laser Interstitial Thermal Therapy (LITT) in the Treatment of Drug-Resistant Epilepsy: A Meta-Analysis. Med Sci Monit. 2018;24:9292-9299
- Petito, GT, Wharen, RE, Feyissa, AM, Grewal, SS, Lucas, JA, and Tatum, WO. The impact of stereotactic laser ablation at a typical epilepsy center. Epilepsy Behav. Jan 2018; 78: 37-44. PMID 29172137

- Lam, S, Hadley, C, Curry, DJ, and Pan, IW. Comparison of Perioperative Costs between Stereotactic Laser Ablation and Craniotomy for Hypothalamic Hamartoma. Journal of Pediatric Epilepsy. 2017;6(2):97-102
- Drane, DL, Loring, DW, Voets, NL, Price, M, Ojemann, JG, Willie, JT, Saindane, AM, Phatak, V, et al. Better object recognition and naming outcome with MRI-guided stereotactic laser amygdalohippocampotomy for temporal lobe epilepsy. Epilepsia. 2015;56(1):101-113
- Wu, C, Jermakowicz, WJ, Chakravorti, S, Cajigas, I, Sharan, AD, Jagid, JR, Matias, CM, Sperling, MR, et al. Effects of surgical targeting in laser interstitial thermal therapy for mesial temporal lobe epilepsy: A multicenter study of 234 patients. Epilepsia. 2019;60(6):1171-1183
- Boerwinkle, VL, Foldes, ST, Torrisi, SJ, Temkit, H, Gaillard, WD, Kerrigan, JF, Desai, VR, Raskin, JS, et al. Subcentimeter epilepsy surgery targets by resting state functional magnetic resonance imaging can improve outcomes in hypothalamic hamartoma. Epilepsia. 2018;59(12):2284-2295
- Rennert, RC, Khan, U, Bartek, J, Jr., Tatter, SB, Field, M, Toyota, B, Fecci, PE, Judy, K, et al. Laser Ablation of Abnormal Neurological Tissue Using Robotic Neuroblate System (LAANTERN): Procedural Safety and Hospitalization. Neurosurgery. Apr 01 2020; 86(4): 538-547. PMID 31076762
- Lagman, C, Chung, LK, Pelargos, PE, Ung, N, Bui, TT, Lee, SJ, Voth, BL, and Yang, I. Laser neurosurgery: A systematic analysis of magnetic resonance-guided laser interstitial thermal therapies. J Clin Neurosci. 2017;36:20-26
- Kang JY and Sperling MR. Epileptologist's view: Laser interstitial thermal ablation for treatment of temporal lobe epilepsy. Epilepsy Res. 2018 Nat; 142:149-152
- American Academy of Orthopaedic Surgeons (AAOS) website. OrthoInfo, Osteoid Osteoma. https://orthoinfo.aaos.org/en/diseases--conditions/osteoid-osteoma
- American Society of Breast Surgeons (ASBrS). Consensus Guideline on the Use of Transcutaneous and Percutaneous Ablation for the Treatment of Benign and Malignant Tumors of the Breast. October 2018. https://www.breastsurgeons.org/docs/statements/Consensus-Guideline-on-the-Use-of-Transcutaneous-and-Percutaneous-Methods-for-the-Treatment-of-Benign-and-Malignant-Tumors-of-the-Breast.pd
- American Society of Clinical Oncology (ASCO) website. Guidelines, Tools, and Resources. https://www.asco.org/research-guidelines/quality-guidelines/guidelines
- National Comprehensive Cancer Network (NCCN) Prostate Cancer Version 1.2023. Also available at https://www.nccn.org
- National Comprehensive Cancer Network (NCCN) Central Nervous System Cancers Version 2.2022. Also available at https://www.nccn.org
- National Comprehensive Cancer Network (NCCN) Bone Cancer Version 2.2023. Also available at https://www.nccn.org
- National Comprehensive Cancer Network (NCCN) Non-Small Cell Lung Cancer Version 5.2022. Also available at https://www.nccn.org

- National Comprehensive Cancer Network (NCCN) Small Cell Lung Cancer Version 2.2023. Also available at https://www.nccn.org
- National Comprehensive Cancer Network (NCCN) Hepatobiliary Cancers Version 3.2022. Also available at https://www.nccn.org
  National Comprehensive Cancer Network (NCCN) Breast Cancer Version 4.2022. Also available at https://www.nccn.org
- ECRI Institute. Laser Interstitial Thermal Therapy for Breast Cancer. Plymouth Meeting (PA): ECRI Institute; 2019 Jan 14. (Custom Rapid Responses)
- ECRI Institute. Laser Interstitial Thermal Therapy for Nonglioblastoma Brain Cancers. Plymouth Meeting (PA): ECRI Institute; 2019 Jan 14. (Custom Rapid Responses)
- ECRI Institute. Laser Interstitial Thermal Therapy for Epilepsy. Plymouth Meeting (PA): ECRI Institute; 2019 Sept 10. (Custom Rapid Responses)
- ECRI Institute. Laser Interstitial Thermal Therapy for Osteoid Osteoma. Plymouth Meeting (PA): ECRI Institute; 2019 Jan 11. (Custom Rapid Responses)
- ECRI Institute. Laser Interstitial Thermal Therapy for Treating Glioblastoma. Plymouth Meeting (PA): ECRI Institute; 2019 Jan 08. (Custom Rapid Responses)
- ECRI Institute. Laser Interstitial Thermal Therapy for Localized Prostate Cancer. Plymouth Meeting (PA): ECRI Institute; 2019 Jan 07. (Custom Rapid Responses)
  ECRI Institute. Laser Interstitial Thermal Therapy for Lung Cancer Published January 14, 2019 (Custom Rapid Responses)
- ECRI Institute. Laser Interstitial Thermal Therapy for Metastases to the Liver Published January 14, 2019 (Custom Rapid Responses)
- UpToDate. Overview of the Treatment of Brain Metastases. Jay S. Loeffler M.D., Topic last updated October 15, 2020. Also available at https://www.uptodate.com
- UpToDate. Management of Recurrent High-Grade Gliomas. Tracy Batchelor M.D., MPH, Helen A. Shih M.D., MS, MPH, Bob S. Carter M.D. PhD. Topic last updated June 25, 2020. Also available at https://www.uptodate.com
- UpToDate. Nonsurgical Therapies for Localized Hepatocellular Carcinoma: Radiofrequency Ablation, Laser and Microwave Thermal Ablation, Percutaneous Injection Therapies, Cyroablation, High-Intensity Focused Ultrasound and Irreversible Electroporation. Steve A. Curley M.D., FACs, Keith E. Stuart M.D., Jonathan M. Schwartz M.D., Robert L. Carithers Jr, M.D., Topic last updated March 26, 2020. Also available at https://www.uptodate.com
- UpToDate. Delayed Complications of Cranial Irradiation. Jorg Dietrich M.D., PhD, Viani Gondi M.D., Minesh Mehta M.D., Topic last updated September 11, 2020. Also available at https://www.uptodate.com
- UpToDate. Image-Guided Ablation of Skeletal Metastases. Anil Nicholas Kurup M.D., Matthew R. Callstrom M.D., PhD. Topic last updated May 19, 2020. Also available at https://www.uptodate.com
- UpToDate. Nonmalignant Bone Lesions in Children and Adolescents. John E. Tis M.D., Topic last updated March 26, 2020. Also available at https://www.uptodate.com

- Faure Walker, NA, Norris, JM, Shah, TT, Yap, T, Cathcart, P, Moore, CM, Ahmed, HU, Emberton, M, et al. A comparison of time taken to return to baseline erectile function following focal and whole gland ablative therapies for localized prostate cancer: A systematic review. Urol Oncol. 2018;36(2):67-76
- Valerio, M, Cerantola, Y, Eggener, SE, Lepor, H, Polascik, TJ, Villers, A, and Emberton, M. New and established technology in focal ablation of the prostate: a systematic review. Eur Urol. 2017;71(1):17-34
- Natarajan, S, Jones, TA, Priester, AM, Geoghegan, R, Lieu, P, Delfin, M, Felker, E, Margolis, DJA, et al. Focal laser ablation of prostate cancer: Feasibility of magnetic resonance imaging-ultrasound fusion for guidance. J Urol. 2017;198(4):839-847
- Westin, C, Chatterjee, A, Ku, E, Yousuf, A, Wang, S, Thomas, S, Fan, X, Eggener, S, et al. MRI findings after MRI-guided focal laser ablation of prostate cancer. AJR Am J Roentgenol. 2018;211(3):595-604.
- Wang, S, Fan, X, Yousuf, A, Eggener, SE, Karczmar, G, and Oto, A. Evaluation of focal laser ablation of prostate cancer using high spectral and spatial resolution imaging: a pilot study. J Magn Reson Imaging. 2018
- Knull, E, Oto, A, Eggener, S, Tessier, D, Guneyli, S, Chatterjee, A, and Fenster, A. Evaluation of tumor coverage after MR-guided prostate focal laser ablation therapy. Med Phys. 2018
- Nour-Eldin, NA, Exner, S, Al-Subhi, M, Naguib, NNN, Kaltenbach, B, Roman, A, and Vogl, TJ. Ablation therapy of non-colorectal cancer lung metastases: retrospective analysis of tumour response post-laser-induced interstitial thermotherapy (LITT), radiofrequency ablation (RFA) and microwave ablation (MWA). Int J Hyperthermia. 2017;33(7):820-829
- Vogl, TJ, Eckert, R, Naguib, NN, Beeres, M, Gruber-Rouh, T, and Nour-Eldin, NA. Thermal Ablation of Colorectal Lung Metastases: Retrospective Comparison Among Laser-Induced Thermotherapy, Radiofrequency Ablation, and Microwave Ablation. AJR Am J Roentgenol. 2016;207(6):1340-1349
- Wu, H, Lu, C, and Chen, M. Evaluation of minimally invasive laser ablation in children with osteoid osteoma. Oncol Lett. 2017;13(1):155-158
- Tsoumakidou, G, Thenint, MA, Garnon, J, Buy, X, Steib, JP, and Gangi, A. Percutaneous image-guided laser photocoagulation of spinal osteoid osteoma: A single-institution series. Radiology. 2016;278(3):936-943
- Kachare, MB, Kulkarni, SB, and Patil, SA. Computed tomography guided laser ablation of osteoid osteoma: a study of 30 cases. Int J of Res in Med Sci. 2016;4(11):4
- Fuchs, S, Gebauer, B, Stelter, L, Schafer, ML, Renz, DM, Melcher, I, Schaser, K, Hamm, B, et al. Postinterventional MRI findings following MRI-guided laser ablation of osteoid osteoma. Eur J Radiol. 2014;83(4):696-702
- Etienne, A, Waynberger, E, and Druon, J. Interstitial laser photocoagulation for the treatment of osteoid osteoma: retrospective study on 35 cases. Diagn Interv Imaging. 2013;94(3):300-310
- Lanza, E, Thouvenin, Y, Viala, P, Sconfienza, LM, Poretti, D, Cornalba, G, Sardanelli, F, and Cyteval, C. Osteoid osteoma treated by percutaneous thermal

ablation: when do we fail? A systematic review and guidelines for future reporting. Cardiovasc Intervent Radiol. 2014;37(6):1530-1539
- Pottecher, P, Sibileau, E, Aho, S, Hamze, B, Parlier, C, Laredo, JD, and Bousson, V. Dynamic contrast-enhanced MR imaging in osteoid osteoma: relationships with clinical and CT characteristics. Skeletal Radiol. 2017;46(7):935-948
- Peek, MC, Ahmed, M, Napoli, A, Usiskin, S, Baker, R, and Douek, M. Minimally invasive ablative techniques in the treatment of breast cancer: a systematic review and meta-analysis. Int J Hyperthermia. 2016:1-12
- Nori, J, Gill, MK, Meattini, I, Delli Paoli, C, Abdulcadir, D, Vanzi, E, Boeri, C, Gabbrielli, S, et al. The evolving role of ultrasound guided percutaneous laser ablation in elderly unresectable breast cancer patients: a feasibility pilot study. Biomed Res Int. 2018;2018:9141746
- Schwartzberg, B, Lewin, J, Abdelatif, O, Bernard, J, Bu-Ali, H, Cawthorn, S, Chen-Seetoo, M, Feldman, S, et al. Phase 2 open-label trial investigating percutaneous laser ablation for treatment of early-stage breast cancer: MRI, pathology, and outcome correlations. Ann Surg Oncol. 2018;25(10):2958-2964
- Haraldsdottir, KH, Ingvar, C, Stenram, U, and Tranberg, KG. Long-term follow-up after interstitial laser thermotherapy of breast cancer. Anticancer Res. 2015;35(11):6147-6152
- Barnett, GH, Voigt, JD, and Alhuwalia, MS. A systematic review and meta-analysis of studies examining the use of brain laser interstitial thermal therapy versus craniotomy for the treatment of high-grade tumors in or near areas of eloquence: an examination of the extent of resection and major complication rates associated with each type of surgery. Stereotact Funct Neurosurg. 2016;94(3):164-173
- Ivan, ME, Mohammadi, AM, De Deugd, N, Reyes, J, Rodriguez, G, Shah, A, Barnett, GH, and Komotar, RJ. Laser ablation of newly diagnosed malignant gliomas: a meta-analysis. Neurosurgery. 2016;79 Suppl 1:S17-s23
- Banerjee, C, Snelling, B, Berger, MH, Shah, A, Ivan, ME, and Komotar, RJ. The role of magnetic resonance-guided laser ablation in neurooncology. Br J Neurosurg. 2015;29(2):192-196
- Kamath, AA, Friedman, DD, Hacker, CD, Smyth, MD, Limbrick, DD, Jr., Kim, AH, Hawasli, AH, and Leuthardt, EC. MRI-guided interstitial laser ablation for intracranial lesions: A large single-institution experience of 133 cases. Stereotact Funct Neurosurg. 2017;95(6):417-428
- Sharma, M, Habboub, G, Behbahani, M, Silva, D, Barnett, GH, and Mohammadi, AM. Thermal injury to corticospinal tracts and postoperative motor deficits after laser interstitial thermal therapy. *Neurosurg Focus*. 2016;41(4):E6
- Voigt, JD, and Barnett, G. The value of using a brain laser interstitial thermal therapy (LITT) system in patients presenting with high grade gliomas where maximal safe resection may not be feasible. Cost Eff Resour Alloc. 2016;14:6
- Lee, I, Kalkanis, S, and Hadjipanayis, CG. Stereotactic laser interstitial thermal therapy for recurrent high-grade gliomas. Neurosurgery. 2016;79 Suppl 1:S24-s34
- Rao MS, Hargreaves EL, Khan AJ, et al. Magnetic resonance-guided laser ablation improves local control for postradiosurgery recurrence and/or radiation necrosis. Neurosurgery. 2014;74(6):658-667

- Rammo R, Scarpace L, Nagaraja T, Lee I. MR-guided laser interstitial thermal therapy in the treatment of recurrent intracranial meningiomas. Lasers Surg Med. 2019;51(3):245-250
- Beechar, V. B., Prabhu, S. S., Bastos, D., Weinberg, J. S., Stafford, R. J., Fuentes, D., Hess, K. R., & Rao, G. (2018). Volumetric response of progressing post-SRS lesions treated with laser interstitial thermal therapy. Journal of neuro-oncology, 137(1), 57–65. https://doi.org/10.1007/s11060-017-2694-3
- Mohammadi AM, Sharma M, Beaumont TL, et al. Upfront magnetic resonance imaging-guided stereotactic laser-ablation in newly diagnosed glioblastoma: A multicenter review of survival outcomes compared to a matched cohort of biopsy-only patients. Neurosurgery. 2019;85(6):762-772. PMID 30476325
- Murayi, Roger et al. “Laser Interstitial Thermal Therapy in the Treatment of Thalamic Brain Tumors: A Case Series.” Operative neurosurgery (Hagerstown, Md.) vol. 19,6 (2020): 641-650. doi:10.1093/ons/opaa206
- Kim, Albert H et al. “Laser Ablation of Abnormal Neurological Tissue Using Robotic NeuroBlate System (LAANTERN): 12-Month Outcomes and Quality of Life After Brain Tumor Ablation.” Neurosurgery vol. 87,3 (2020): E338-E346. doi:10.1093/neuros/nyaa071
- de Almeida Bastos DC, Rao G, Oliva ICG, et al. Predictors of local control of brain metastasis treated with laser interstitial thermal therapy. Neurosurgery. 2020a;87(1):112-122.
- de Almeida Bastos DC, Weinberg J, Kumar AA, et al. Laser interstitial thermal therapy in the treatment of brain metastases and radiation necrosis. Cancer Lett. 2020b;489:9-18.
- Hong CS, Kundishora AJ, Elsamadicy AA, Chiang VL. Laser interstitial thermal therapy in neuro-oncology applications. Surg Neurol Int. 2020;11:23
- Landazuri P, Shih J, Leuthardt E, et al. A prospective multicenter study of laser ablation for drug resistant epilepsy -One-year outcomes. Epilepsy Res. 2020 Nov;167:106473. (LAANTERN [Laser Ablation of Abnormal Neurological Tissue Using Robotic NeuroBlate System] trial) PMID 33045664
- Viozzi, Ilaria et al. “Laser Interstitial Thermal Therapy in Patients with Newly Diagnosed Glioblastoma: A Systematic Review.” Journal of clinical medicine vol. 10,2 355. 19 Jan. 2021, doi:10.3390/jcm10020355
- Chen, Chao et al. “The efficacy of laser interstitial thermal therapy for brain metastases with in-field recurrence following SRS: systemic review and meta-analysis.” International journal of hyperthermia : the official journal of European Society for Hyperthermic Oncology, North American Hyperthermia Group vol. 38,1 (2021): 273-281. doi:10.1080/02656736.2021.1889696
- Sujijantarat, N., Hong, C.S., Owusu, K.A. et al. Laser interstitial thermal therapy (LITT) vs. bevacizumab for radiation necrosis in previously irradiated brain metastases. J Neurooncol July 2020. 148(3): 641-649. PMID 32602021. https://doi.org/10.1007/s11060-020-03570-0
- Grewal, Sanjeet S et al. “Magnetic Resonance-Guided Laser Interstitial Thermal Therapy Versus Stereotactic Radiosurgery for Medically Intractable Temporal Lobe Epilepsy: A Systematic Review and Meta-Analysis of Seizure Outcomes and

Complications." World neurosurgery vol. 122 (2019): e32-e47. doi:10.1016/j.wneu.2018.08.227

- Hoppe, C., and Helmstaedter, C. "Laser interstitial thermotherapy (LiTT) in pediatric epilepsy surgery." Seizure vol. 77 (2020): 69-75. doi:10.1016/j.seizure.2018.12.010
- Chaves de Almeida Bastos D., Weinberg J., A. Kumar v., D., et al. Laser Interstitial Thermal Therapy in the Treatment of Brain Metastases and Radiation Necrosis, Cancer Letters, Volume 489, 2020, Pages 9-18, ISSN 0304-3835, https://doi.org/10.1016/j.canlet.2020.05.014. (https://www.sciencedirect.com/science/article/pii/S0304383520302688)
- The American Association of Neurologival Surgeons. Position statement on MR-guided Laser Interstitial Thermal Therapy (LITT) for Brain Tumors and Radiation Necrosis. 7-Sept-2021. Accessed December 7, 2021.
- American Society for Stereotactic and Functional Neurosurgery Position Statement on Laser Interstitial Thermal Therapy for the Treatment of Drug-Resistant Epilepsy. September 2021. https://www.aans.org/-/media/Files/AANS/Advocacy/PDFS/ASSFN_Position_Statement_on_LITT_for_the_Treatment_of_Drug_Resistant_Epilepsy_091321
- Wu, C., Schwalb, J., Rosenow, J., McKhann, G., et al. on behalf of the American Society for Stereotactic and Functional Neurosurgeons. The American Society for Stereotactic and Functional Neurosurgery Position Statement on Laser Interstitial Thermal Therapy for the Treatment of Drug-Resistant Epilepsy. Neurosurgery: February 2022 - Volume 90 - Issue 2 - p 155-160 doi: 10.1227/NEU.0000000000001799
- Lagman C, Chung LK, Pelargos PE, et al. Laser neurosurgery: A systematic analysis of magnetic resonance-guided laser interstitial thermal therapies. J Clin Neurosci. Feb 2017; 36: 20-26. PMID 27838155
- Medvid R, Ruiz A, Komotar RJ, et al. Current Applications of MRI-Guided Laser Interstitial Thermal Therapy in the Treatment of Brain Neoplasms and Epilepsy: A Radiologic and Neurosurgical Overview. AJNR Am J Neuroradiol. Nov 2015; 36(11): 1998-2006. PMID 26113069
- Holste KG, Orringer DA. Laser interstitial thermal therapy. Neurooncol Adv. Jan-Dec 2020; 2(1): vdz035. PMID 32793888
- US Food and Drug Administration (FDA). Risk of Tissue Overheating Due to Inaccurate Magnetic Resonance Thermometry: Letter to Health Care Providers. 2018;https://www.fda.gov/medical-devices/letters-health-care-providers/risk-tissue-overheating-due-inaccurate-magnetic-resonance-thermometry-letter-health-care-providers.
- US Food and Drug Administration (FDA). Update Regarding Risk of Tissue Overheating Due to Inaccurate Magnetic Resonance Thermometry: Letter to Health Care Providers. 2018; https://www.fda.gov/medical-devices/letters-health-care-providers/update-regarding-risk-tissue-overheating-due-inaccurate-magnetic-resonance-thermometry.

- de Franca SA, Tavares WM, Salinet ASM, et al. Laser interstitial thermal therapy as an adjunct therapy in brain tumors: A meta-analysis and comparison with stereotactic radiotherapy. Surg Neurol Int. 2020; 11: 360. PMID 33194293
- Barnett GH, Voigt JD, Alhuwalia MS. A Systematic Review and Meta-Analysis of Studies Examining the Use of Brain Laser Interstitial Thermal Therapy versus Craniotomy for the Treatment of High-Grade Tumors in or near Areas of Eloquence: An Examination of the Extent of Resection and Major Complication Rates Associated with Each Type of Surgery. Stereotact Funct Neurosurg. 2016; 94(3): 164-73. PMID 27322392
- Kim AH, Tatter S, Rao G, et al. Laser Ablation of Abnormal Neurological Tissue Using Robotic NeuroBlate System (LAANTERN): 12-Month Outcomes and Quality of Life After Brain Tumor Ablation. Neurosurgery. Sep 01 2020; 87(3): E338-E346. PMID 32315434
- Ahluwalia M, Barnett GH, Deng D, et al. Laser ablation after stereotactic radiosurgery: a multicenter prospective study in patients with metastatic brain tumors and radiation necrosis. J Neurosurg. May 04 2018; 130(3): 804-811. PMID 29726782
- Patel P, Patel NV, Danish SF. Intracranial MR-guided laser-induced thermal therapy: single-center experience with the Visualase thermal therapy system. J Neurosurg. Oct 2016; 125(4): 853-860. PMID 26722845
- Hong CS, Deng D, Vera A, et al. Laser-interstitial thermal therapy compared to craniotomy for treatment of radiation necrosis or recurrent tumor in brain metastases failing radiosurgery. J Neurooncol. Apr 2019; 142(2): 309-317. PMID 30656529
- Kwan P, Arzimanoglou A, Berg AT, et al. Definition of drug resistant epilepsy: consensus proposal by the ad hoc Task Force of the ILAE Commission on Therapeutic Strategies. Epilepsia. Jun 2010; 51(6): 1069-77. PMID 19889013
- Wieser HG, Blume WT, Fish D, et al. ILAE Commission Report. Proposal for a new classification of outcome with respect to epileptic seizures following epilepsy surgery. Epilepsia. Feb 2001; 42(2): 282-6. PMID 11240604
- Kohlhase K, Zollner JP, Tandon N, et al. Comparison of minimally invasive and traditional surgical approaches for refractory mesial temporal lobe epilepsy: A systematic review and meta-analysis of outcomes. Epilepsia. Apr 2021; 62(4): 831-845. PMID 33656182
- Brotis AG, Giannis T, Paschalis T, et al. A meta-analysis on potential modifiers of LITT efficacy for mesial temporal lobe epilepsy: Seizure-freedom seems to fade with time. Clin Neurol Neurosurg. Apr 20 2021; 205: 106644. PMID 33962146
- Grewal SS, Alvi MA, Lu VM, et al. Magnetic Resonance-Guided Laser Interstitial Thermal Therapy Versus Stereotactic Radiosurgery for Medically Intractable Temporal Lobe Epilepsy: A Systematic Review and Meta-Analysis of Seizure Outcomes and Complications. World Neurosurg. Feb 2019; 122: e32-e47. PMID 30244184
- Xue F, Chen T, Sun H. Postoperative Outcomes of Magnetic Resonance Imaging (MRI)-Guided Laser Interstitial Thermal Therapy (LITT) in the Treatment of Drug-

Resistant Epilepsy: A Meta-Analysis. Med Sci Monit. Dec 21 2018; 24: 9292-9299. PMID 30573725
- Hoppe C, Helmstaedter C. Laser interstitial thermotherapy (LiTT) in pediatric epilepsy surgery. Seizure. Apr 2020; 77: 69-75. PMID 30591281
- Hale AT, Sen S, Haider AS, et al. Open Resection versus Laser Interstitial Thermal Therapy for the Treatment of Pediatric Insular Epilepsy. Neurosurgery. Oct 01 2019; 85(4): E730-E736. PMID 30888028
- Petito GT, Wharen RE, Feyissa AM, et al. The impact of stereotactic laser ablation at a typical epilepsy center. Epilepsy Behav. Jan 2018; 78: 37-44. PMID 29172137
- Wu C, Jermakowicz WJ, Chakravorti S, et al. Effects of surgical targeting in laser interstitial thermal therapy for mesial temporal lobe epilepsy: A multicenter study of 234 patients. Epilepsia. Jun 2019; 60(6): 1171-1183. PMID 31112302
- Barnett G, Leuthardt E, Rao G, et al. American Association of Neurological Surgeons and Congress of Neurological Surgeons (AANS-CNS) Position Statement on MR-guided Laser Interstitial Thermal Therapy (LITT) for Brain Tumors and Radiation Necrosis. September 2021; https://www.aans.org/-/media/Files/AANS/Advocacy/PDFS/AANS-CNS_Position_Statement_Paper_LITT_Tumor-Oncology_090721.ashx.
- Tsao MN, Rades D, Wirth A, et al. Radiotherapeutic and surgical management for newly diagnosed brain metastasis(es): An American Society for Radiation Oncology evidence-based guideline. Pract Radiat Oncol. Jul-Sep 2012; 2(3): 210-225. PMID 25925626
- Wu C, Schwalb JM, Rosenow J, et al. American Society for Stereotactic and Functional Neurosurgery Position Statement on Laser Interstitial Thermal Therapy for the Treatment of Drug-Resistant Epilepsy. September 2021; https://www.aans.org/-/media/Files/AANS/Advocacy/PDFS/ASSFN_Position_Statement_on_LITT_for_the_Treatment_of_Drug_Resistant_Epilepsy_091321.ashx.
- Elder JB, Nahed BV, Linskey ME, et al. Congress of Neurological Surgeons Systematic Review and Evidence-Based Guidelines on the Role of Emerging and Investigational Therapties for the Treatment of Adults With Metastatic Brain Tumors. Neurosurgery. Mar 01 2019; 84(3): E201-E203. PMID 30629215
- National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Central Nervous System Cancers. Version 2.2021; https://www.nccn.org/professionals/physician_gls/pdf/cns.pdf.
- National Institute for Health and Care Excellence (NICE). Interventional procedures guidance: MRI-guided laser interstitial thermal therapy for drug-resistant epilepsy [IPG671]. March 4, 2020; https://www.nice.org.uk/guidance/ipg671.
- Centers for Medicare and Medicaid Services (CMS). National Coverage Determination: Laser Procedures (140.5). 1997; https://www.cms.gov/medicare-coverage-database/view/ncd.aspx?NCDId=69&ncdver=1&DocID=140.5.
- Hayes, Inc. Evidence Analysis Research Brief. Laser Interstitial Thermal Therapy for Brain Radiation Necrosis. Hayes, Inc.; Aug 11, 2022.

- Hayes, Inc. Health Technology Assessment. Laser Interstitial Thermal Therapy (LITT) for Treatment of Glioblastoma in Adults. Hayes, Inc. Oct 31, 2022.

POLICY HISTORY		
Date	**Reason**	**Action**
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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