

Laser Interstitial Thermal Therapy for Treating Intracranial Lesions and Epilepsy

A Health Technology Assessment and Policy Analysis

The Health Technology Assessment Unit, University of Calgary

January 27, 2016

Acknowledgements

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We gratefully acknowledge the valuable contributions of the key informants and thank them for their support.

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1 Abbreviations

BC British Columbia

BIA Budget Impact Analysis

CADTH Canadian Agency for Drugs and Technology in Health

CI Confidence Interval

CT Computed Tomography

CTAF California Technology Assessment Forum

eLITT Endometrial Laser Interstitial Thermal Therapy

EQ-5D Euroqol 5D

GBM Glioblastoma multiforme

HIV Human Immunodeficiency Virus

HTA Health Technology Assessment

LITT Laser Interstitial Thermal Therapy

MRgLITT Magnetic Resonance-Guided Laser Interstitial Thermal Therapy

MRI Magnetic Resonance Imaging

MRTI Magnetic Resonance Thermal Imaging

NICE National Institute for Health and Care Excellence

OR Odds Ratio

RCT Randomized Controlled Trial

SF-12 Short Form 12

SLAH Stereotactic laser amygdalohippicampectomy

sLITT Spinal Laser Interstitial Thermal Therapy

TLE Temporal Lobe Epilepsy

TTP Time to Progression

US-LITT Ultrasound Guided Laser Interstitial Thermal Therapy

2 Executive Summary

This report presents the findings and conclusions of a provincial Health Technology Assessment on Laser Interstitial Thermal Therapy for epilepsy and/or intracranial lesions. The primary policy question was:

- Should laser interstitial thermal therapy be publicly provided for patients with intracranial lesions or epilepsy in British Columbia?

The primary research objectives are:

- To determine the safety and effectiveness/efficacy of LITT for the treatment of epilepsy or intracranial lesions
- To understand patient experiences with, quality of life after, or attitudes towards LITT
- To determine the burden of illness, patterns of care and capacity in British Columbia (BC) as it relates to LITT, epilepsy and intracranial lesions
- To determine the budget impact of LITT provision

Introduction

Laser interstitial thermal therapy (LITT), also known as laser-induced interstitial thermotherapy, is a technique of using a laser to heat or ablate a tissue and irreversibly damage cells. Two devices for ablating intracranial lesions or epileptic foci may be used, NeuroBlate and Visualase; currently, only NeuroBlate has been approved by Health Canada. LITT is performed by neurosurgeons, who must be trained on the device prior to using it on patients. The burden and disability for those with intracranial lesions is significant, with cognitive dysfunction and mood disturbance being the most frequent challenges. Although most individuals with epilepsy live an average life span, the burden of illness is high. Those with epilepsy may face challenges including impaired day-to-day living, not being able to drive, stigmatization, finding employment, and difficulties in social relationships.

Approach

The following methodological approaches were used to gather and synthesize the available evidence:

- I. International scan to summarize existing evidence syntheses on LITT for epilepsy and intracranial lesions

- II. Systematic review to determine the safety and effectiveness/efficacy of LITT for the treatment of epilepsy or intracranial lesions
- III. Systematic review to understand patient experiences with quality of life after LITT or attitudes towards LITT
- IV. Clinician interviews and national scan to understand how LITT is being used in Canada and other jurisdictions, and to obtain clinician and patient perspectives on this technology
- V. Budget impact analysis to determine the costs associated with the use of LITT for intracranial lesions and epilepsy

Key Findings

International Scan

- Four technology briefs were identified synthesizing the use of LITT; two on intracranial lesions, one on epilepsy, and one on both intracranial lesions and epilepsy
- These briefs judged the reported complications to be low, and the evidence on LITT to be limited
- No relevant economic evaluations or clinical guidelines were identified
- All four concluded that either: the available evidence was insufficient to make a decision, or the available evidence was insufficient to prove that LITT is a medically necessary procedure

Systematic Review of Effectiveness

- Six studies were included; two on patients with epilepsy and four on patients with intracranial lesions.
- Amongst the two non-randomized controlled studies on epilepsy, one found statistically significant improvements on famous face recognition and common names using LITT compared to surgical resection. The other found that seizure freedom did not significantly differ although length of stay and surgical time were significantly reduced for the LITT patients, compared to those who underwent surgical resection.
- No comparative studies were found on intracranial lesions so it is unknown how LITT compares to the standard of care.
- Four ongoing trials are currently registered on clinicaltrials.gov
- Published literature on the effectiveness of LITT is very limited; published studies have small sample sizes and use weak study designs

Systematic Review of LITT and Quality of Life

- No studies were found evaluating the patient experiences or quality of life of LITT in patients with epilepsy or brain metastases.

Clinician Interviews and National Scan

- LITT has been used at the Vancouver General Hospital since December 2014. The Hospital for Sick Children in Toronto is considering purchasing a Neuroblate system, and is hoping to be able to provide LITT as an option for children with epilepsy by spring of 2016.
- LITT is perceived as an option for patients who do not have other treatment options. This includes patients with malignant brain tumors and patients with certain kinds of epilepsy.

- LITT is a minimally invasive procedure, and outcomes to date (as seen by clinicians in practice) have been promising. Potential complications for LITT are similar to conventional surgery.
- The patient experience with LITT is described as positive by the clinicians, and by the patient interviewed.

Budget Impact Analysis

- Upfront cost of purchasing LITT are \$652,157 including the transportation system, and \$540,390 excluding the transportation system
- A yearly cost for the warranty is \$73,878
- The cost per procedure is \$23,623
- An economic evaluation would be severely limited with the current clinical data; it remains unknown whether LITT is cost-effective.

Proposed Policy Options

Four policy options are proposed, each with advantages, disadvantages and implementation considerations.

- I. Discontinue use of LITT
- II. Access with Evidence Development: support of LITT only within a research context, potentially with limited public funding
- III. Limited support of LITT: maintain current rate of LITT procedures with the provision of public funding to cover ongoing costs. No additional funding to increase capacity.
- IV. Expand public funding of LITT procedures, alongside efforts to increase capacity: expand current rate of LITT procedures with the provision of public funding to increase capacity

3 Purpose of this Health Technology Assessment

The purpose of this health technology assessment (HTA) is to summarize the current evidence on Laser Interstitial Thermal Therapy (LITT) for individuals with epilepsy or intracranial lesions.

The report summarizes evidence on the effectiveness, safety, patient experience and system feasibility of LITT in comparison to available alternatives for both adult and youth/young adult patients with epilepsy or intracranial lesions. Based on the evidence, reasonable policy options are presented with consideration of their respective advantages, disadvantages and feasibility considerations.

3.1 Research Question and Research Objectives

The primary policy question is:

- Should laser interstitial thermal therapy be publicly provided for patients with intracranial lesions or epilepsy in British Columbia?

The primary research objectives are:

- To determine the safety and effectiveness/efficacy of LITT for the treatment of epilepsy or intracranial lesions
- To determine the burden of illness, patterns of care and capacity in British Columbia (BC) as it relates to LITT, epilepsy and intracranial lesions
- To understand patient experiences with, quality of life after, or attitudes towards LITT
- To determine the budget impact of LITT provision

3.2 Background Information

3.3 Laser Interstitial Thermal Therapy

3.3.1 How it works

Laser interstitial thermal therapy (LITT), also known as laser-induced interstitial thermotherapy, is a technique of using a laser to heat or ablate a tissue and irreversibly damage cells¹. LITT for intracranial lesions and epilepsy is considered to be a minimally invasive surgery and is associated with shorter hospital lengths of stay than surgical resection¹. Pre-operatively, patients are given a magnetic resonance imaging (MRI) scan to identify the intracranial lesion and the entry location¹. Then under minimal sedation or general anesthesia a 3 mm incision is made in the skull and a bolt, which later serves as a corridor for the laser probe, is inserted. The patient is moved from the operating room to an MRI suite where the laser is guided to the lesion or epileptic foci (when the facilities exist, an intra-operative MRI suite is used so that the patient does not have to be transferred). MRI is used to ensure that only the intended tissue is ablated; irreversible cell damage occurs between 46°C and 60°C², and coagulation necrosis occurs at higher temperatures³. Note that the technology has improved over time, with earlier uses of LITT being performed without MRI. When used in the brain, LITT may also break down the blood-brain barrier; a property which is being explored to see if it increases chemotherapy success rates⁴.

LITT is performed by neurosurgeons, who must be trained on the device prior to using it on patients. Other professionals that may be involved in the procedure include technicians familiar with the specific LITT technology, a circulating nurse, and a scrub nurse.

3.3.2 Devices

Two devices for ablating intracranial lesions or epileptic foci may be used, NeuroBlate and Visualase. Both NeuroBlate and Visualase have received U.S. Food and Drug Administration approval^{5,6}, but only NeuroBlate has been approved by Health Canada⁷ (Table 1). The NeuroBlate system was approved by Health Canada on September 3, 2014. Several other supplementary devices required to use the system were approved in September 2014⁷. Prior to September 2014, Health Canada had granted a “special access waiver” to allow the device to be used in Vancouver⁸.

Table 1 Devices Used for laser Interstitial Thermal Therapy

Device	Manufacturer	Approved by FDA (US)	Approved by Health Canada
NeuroBlate (previously AutoLITT)	Monteris Medical, Inc.	May 1, 2009 ⁶	September 3, 2014 ⁷
Visualase	Medtronic, Inc. (previously Visualase, Inc. ⁹)	March 1, 2006 ⁵	No ⁷

3.3.3 Indications and contraindications

The Neuroblate system, by Monteris Medical, is indicated for use to “...ablate, necrotize or coagulate soft tissue through interstitial irradiation or thermal therapy in medicine and surgery in the discipline of neurosurgery with 1064 nm lasers.”¹⁰ No contraindications are listed.

3.4 Intracranial Lesions

3.4.1 Overview

Intracranial lesions are abnormalities in the brain observed on an MRI or Computed Tomography (CT) scan¹¹. They can be caused by a number of conditions: brain aneurysms, brain arteriovenous malformations, malignant and benign tumours, encephalitis, hydrocephalus,

multiple sclerosis, and traumatic brain injuries. In the literature, the most common types of intracranial lesions so far treated with LITT have been gliomas and metastatic brain tumours¹.

Brain tumours can be either primary (originating in the brain) or metastatic (spread from another part of the body). Gliomas begin in glial cells, and are a common type of primary brain tumour¹¹.

There are a number of types of glioma, with glioblastoma multiforme (GBM) being the most common. The World Health Organization (WHO) has classified the primary brain tumour types into grades I-IV depending on their aggressiveness, with GBM receiving a grade of IV¹².

3.4.2 Prevalence and Incidence

In 2015, an estimated 3,000 Canadians will be diagnosed with brain or nervous system cancer (age-standardized incidence, 7 per 100,000)¹³. In British Columbia (BC), this number is approximately 350 (age-standardized incidence, 6 per 100,000). The risk factors for primary brain tumours are not well established, but may include: age, male sex, family history, exposure to vinyl chloride, cranial radiation therapy, Epstein-Barr virus infection, Human Immunodeficiency Virus (HIV) infection, and some genetic disorders^{14,15}.

3.4.3 Burden of Illness

Survival rates differ greatly among the gliomas and metastatic brain tumours. One study estimated those with GBM live between 7 and 17 months after diagnosis depending on their age and the severity of the tumour¹⁶. The focus of treatment for GBM is often palliative care to improve survival and quality of life¹. Brain tumours can result in a number of symptoms due to the pressure they exert on surrounding tissue. These can include but are not limited to: fatigue,

headaches, vomiting, nausea, lethargy, balance problems, vision impairment, speech problems, seizures, and other cognitive problems¹⁵. The burden and disability for those with malignant gliomas is significant, with cognitive dysfunction and mood disturbances being the most frequent challenges¹⁷. An estimated 45% of patients who have low-grade gliomas found to have low quality of life, with less than half able to carry out unrestricted normal activities; the symptom most correlated with poor quality of life was fatigue¹⁸.

3.5 Epilepsy

3.5.1 Overview

Epilepsy is a disorder characterized by recurrent seizures¹⁹. Lasting several seconds to several minutes, seizures are a brief change in normal brain activity, and can be classified as generalized or focal seizures. Generalized seizures affect both sides of the brain whereas focal seizures affect a specific part of the brain. For two thirds of people with epilepsy the cause is unknown, however the following conditions are known to cause epilepsy: strokes, brain tumours, brain infections, traumatic brain injury, loss of oxygen to the brain, some genetic disorders (including Down syndrome), and some other neurologic diseases (including Alzheimer's Disease)¹⁹.

3.5.2 Prevalence and Incidence

In 2005 the Canadian Community Health Survey estimated a 0.6%²⁰ point prevalence of epilepsy. However, the lifetime prevalence is estimated to be 2-4%²¹. Earlier estimates have found that the prevalence does not differ significantly by province or territory, with the exception of British Columbia (age-adjusted prevalence, 0.4%; 95% confidence interval [CI] 0.30-0.43%)²². This study also showed that the prevalence is higher among those older than 25

compared to those under 25. Three other socioeconomic factors are associated with a higher prevalence of epilepsy: the lowest income group (odds ratio [OR], 3.3; 95% confidence interval [CI] 2.7–4.1), those without secondary education (OR, 1.6; 95% CI, 1.4–1.8) and those unemployed (OR, 2.5; 95% CI, 2.2–2.9)²². These associations may be because of the impact epilepsy can have on one’s education and/or work.

3.5.3 *Burden of Illness*

Most individuals with epilepsy live an average life span¹⁹. However, severe and frequent seizures can lead to serious accidents, death, or impair day-to-day living. Epileptic seizures can come in a variety of forms, including shaking, collapsing, or staring into space¹⁹. Those with epilepsy can also be affected when they are not having a seizure. This can include challenges finding employment, not being allowed to drive, difficulties in social relationships, or being stigmatized because of having the disorder²³.

4 International Scan

Summary

- Four technology briefs were identified synthesizing the use of LITT; two on intracranial lesions, one on epilepsy, and one on both intracranial lesions and epilepsy
- These briefs judged the reported complications to be low, and the evidence on LITT to be limited
- No relevant economic evaluations or clinical guidelines were identified
- Three of the four concluded that the available evidence was insufficient to make a decision, and the fourth concluded that the available evidence was insufficient to prove that it is a medically necessary procedure

4.1 Purpose

To summarize existing evidence syntheses on LITT for epilepsy and intracranial lesions.

4.2 Methods

A grey literature search was performed. Grey literature, including four large health technology assessment organizations (the National Institute for Health and Care Excellence (NICE), the Canadian Agency for Drugs and Technology in Health (CADTH), the California Technology Assessment Forum (CTAF), and the Blue Cross Blue Shield Technology Evaluation Centre (BCBS TEC)) and Google were searched up until October 8, 2015. Search terms included “Neuroblate,” “Visualase,” and “laser interstitial.” HTAs were also identified from the published literature during the systematic review of clinical effectiveness, both from the HTA Database and other published sources (see section 5.2 for the systematic review methodology). The HTAs identified were subsequently hand-searched for mention of other HTAs.

4.3 Results

Four technology briefs were identified. A fifth report by Hayes, Inc. (November, 2014) was found, but was not accessible as Hayes is a private contractor that does not release their work²⁴. The reports were described as: “technology brief,”²⁵ “clinical policy,”²⁶ “product brief,”²⁷ and “rapid response.”²⁸ It is unclear if the methodology of these reports differed due to vague methodology reporting. A narrative summary of each follows and data from each are synthesized in Table 2.

Table 2 Findings

Organization Year Country	Type of Report	Search Dates	Device(s) Evaluated	Clinical Condition	Evidence	Conclusions
<i>ASERNIPS 2013²⁵ Australia</i>	Technology Brief	Not stated (included studies range from 2005 to 2013)	Neuroblate and Visualase	Intracranial neoplasms	<ul style="list-style-type: none"> • 2 case series 	“At present, the effectiveness of MRT-guided LITT is unknown. Consequently, the small body of evidence cannot be used to make an informed decision regarding the use of MRT-guided LITT.”
<i>Keystone First 2014²⁶ United States</i>	Clinical Policy	Not stated to June 6, 2014 (first study published in 2012)	Not specified	Epilepsy	<ul style="list-style-type: none"> • 1 report • 9 meeting abstracts • 6 studies (no details) 	“Keystone First considers the use of laser thermal ablation for epileptic seizures to be investigational and, therefore, not medically necessary.”
<i>ECRI Institute 2014²⁷ United States</i>	Product brief	January 1, 2009 – August 12, 2014	Visualase	Neurologic tumours and “other focal abnormalities”	<ul style="list-style-type: none"> • 18 case series 	“...the Visualase system can be used to ablate intracranial tumors and seizure foci with minimal complications, but evidence is insufficient to determine whether it works as well as or better than alternatives because no comparative studies are available.”
<i>CADTH 2015²⁸ Canada</i>	Rapid Response	January 1, 2010 – August 31, 2015	Neuroblate and Visualase	Brain tumours and epilepsy	<ul style="list-style-type: none"> • 2 HTAs • 1 systematic review • 2 prospective parallel non- randomized studies • 1 RCT 	Current evidence is “...insufficient to evaluate the efficacy of LITT either for brain tumor or epilepsy treatment.”

4.3.1 ASERNIPS

The 2013 report by ASERNIPS²⁵ examined Neuroblate and Visualase for intracranial neoplasms that are not suitable for treatment by standard surgical resection. This report provided an overview of published literature, cost infrastructure, ethical or religious consideration, and ongoing research.

Two case series were included in the review of the literature. However, inclusion/exclusion criteria, dates, or databases searched were not reported, so the comprehensiveness of this literature search is unknown. The two case series included 20 retrospectively recruited patients²⁹ and 10 prospectively recruited³⁰ participants. Based on these two studies, the report authors interpreted the evidence by stating that LITT “is fairly well tolerated,” but noted that the included studies had significant limitations (e.g. did not report percentage of tumor ablated). The ASERNIPS report stresses the importance of future studies examining: quality of life; appropriate dose, patient, and tumour type; who is at risk for adverse events; and the effectiveness of LITT against a comparator.

The authors report no ethical or religious considerations, and found no economic evaluations. However, they comment that the infrastructure costs would include the purchase of the LITT system, the need for additional specialists, an additional MRI machine (or increased burden on a currently used machine), and ongoing costs related to purchasing laser probes.

The authors of the ASERNIPS report concludes that “At present, the effectiveness of MRT-guided LITT is unknown. Consequently, the small body of evidence cannot be used to make an informed decision regarding the use of MRT-guided LITT.”²⁵

4.3.2 *Keystone First*

Keystone First²⁶ published a clinical policy report in 2014 assessing the evidence-base for using LITT to treat epilepsy. Keystone First is a Pennsylvania Medicaid care plan and part of Independence Blue Cross and Blue Cross Blue Shield of Michigan. The purpose of this report was to assess whether LITT should be covered as a treatment for epilepsy. This report summarized the findings of a systematic review, review of guidelines, and review of economic evaluations.

PubMed, the UK National Health Center for Reviews and Dissemination, and the Centers for Medicare and Medicaid Services were searched up until June 6th, 2014. No systematic reviews, meta-analyses, or economic evaluations were found. Keystone first reports that one summary report (Hayes, Inc.²⁴), nine meeting abstracts, and six peer-reviewed articles were identified by this search; however, no references, author names, titles or discussion of these citations are given. They report that the clinical evidence shows that “...epilepsy foci responded positively to the procedure” and that “Procedure-related complications were infrequent and included hematoma and transient visual deficits.”²⁶

Overall, the report concluded that while the evidence is “...encouraging, larger cohorts of longer duration are needed to assess its safety, efficacy, optimal candidacy and effectiveness compared

with open resection.” In regards to coverage of LITT for epilepsy, the report states: “Keystone First considers the use of laser thermal ablation for epileptic seizures to be investigational and, therefore, not medically necessary.”

4.3.3 ECRI Institute

The 2014 ECRI Institute²⁷ report exclusively examined Visualase. It covered patients with a wide variety of intracranial disorders, but most of the patients in the identified studies had intracranial neoplasms or epilepsy. The only inclusion or exclusion criterion the report provided was that it excluded case series with less than 3 patients. They identified 18 case series with at least three patients, but the authors warn that some patients may have been included in more than one of the studies. No economic evaluations were identified. The opinion of the ECRI Institute based on the evidence they found is: “...the Visualase system can be used to ablate intracranial tumors and seizure foci with minimal complications, but evidence is insufficient to determine whether it works as well as or better than alternatives because no comparative studies are available. This treatment’s effect on patient survival and quality of life is unknown.”

4.3.4 CADTH

The CADTH²⁸ rapid review, published in September 2015, assesses the use of Neuroblate and Visualase for brain tumours and epilepsy. This rapid review includes a literature review on clinical effectiveness, cost-effectiveness, and guidelines. PubMed, The Cochrane Library, the University of York Center for Reviews and Dissemination databases, and ECRI were searched from January 1, 2010 until August 31st, 2015. Additionally, websites of major Canadian and international HTA agencies were hand searched and a focussed internet search was conducted.

Results were limited to: health technology assessments, systematic reviews, randomized controlled trials (RCTs), non-randomized studies, economic evaluations, and evidence-based guidelines. Filters were used to limit to human populations, and English language studies, and studies published prior to 2010 were excluded.

Using this search, five relevant citations included (two HTAs, one systematic review, two prospective parallel non-randomized studies, and one RCT). The two included HTAs were the ASERNIPS report²⁵ and the ECRI report²⁷; both previously described. The included systematic review, by Voigt et al. included 21 case series studies and one RCT on the use of LITT for intracranial lesions. This systematic review concluded that the results of LITT compared favourably to craniotomy procedures. Two prospective non-randomized studies on epilepsy were identified (Waseem et al., 2015,³¹ 14 patients; Drane et al., 2015,³² 58 patients); they both found that LITT had similar outcomes to anterior mesial temporal lobe resection for epilepsy. The included RCT (Sneed et al., 1998,³³ 68 patients), published in 1998, found that “heat” brachytherapy improved survival and increased time to progression for GBM patients. Of note, this RCT was excluded from our work because experts felt that brachytherapy was not comparable to LITT.

In the limitations section, the authors state: “The majority of the evidence included in this report is derived from case series which have inherent limitations and potential for biases.” Based on this evidence, the authors of the CADTH report concluded that the current evidence is “...insufficient to evaluate the efficacy of LITT either for brain tumor or epilepsy treatment.”

4.4 Conclusions

Four synthesis reports on LITT were found; two on intracranial lesions, one on epilepsy, and one on both intracranial lesions and epilepsy. None of the included reports found economic evaluations, or clinical guidelines. They found limited effectiveness literature, primarily case series designs with small numbers of patients. The reports summarized the published literature by judging the reported complications to be low. Three of the reports concluded that the available evidence was insufficient to make a decision, and one concluded that evidence was insufficient to prove that LITT is a medically necessary procedure. None of the reports recommended adoption of this technology.

5 A Systematic Review of Effectiveness of Laser Interstitial Thermal Therapy for Epilepsy or Intracranial Lesions

Summary

- Two non-randomized controlled studies on patients with epilepsy and four case series with patients with intracranial lesions were included (two of which used the same patient population)
- Amongst the two non-randomized controlled studies on epilepsy, one found statistically significant improvements on famous face recognition and common names using LITT, the other found that seizure freedom did not significantly differ although length of stay and surgical time was significantly reduced for the LITT patients.
- No comparative studies were found on intracranial lesions, so it is unknown how LITT compares to the standard of care.
- Four ongoing trials are currently registered on clinicaltrials.gov
- Published literature on the effectiveness of LITT is very limited; published studies have small sample sizes and use weak study designs

5.1 Research Objective

To determine the safety and effectiveness/efficacy of LITT for the treatment of epilepsy or intracranial lesions.

5.2 Methods

A systematic review was completed. MEDLINE, PubMed, Cochrane Database of Systematic Reviews, Cochrane CENTRAL Register of Controlled Trials, EMBASE, and PsycINFO were searched from inception until October 7th, 2015. Terms aimed at capturing the target diagnoses such as “epilepsy,” “epileptic,” “glioblastoma,” and “intracranial lesion” were combined using the Boolean Operator “or.” These terms were then combined, using the Boolean Operator “and” with terms describing the technology, such as “laser interstitial thermal therap*,” “laser thermal therap*,” “stereotactic laser ablation,” “LITT,” and “MRgLITT.” Results were limited to English and French language studies, and animal-model studies were filtered out. No other limitations or filters were applied. Details of this search can be found in Appendix C.

All abstracts were screened in duplicate. Abstracts proceeded to full-text review if: they reported on the effectiveness or efficacy of LITT for epilepsy or intracranial lesions; were English or French; were randomized quasi-randomized, observational cohort, case control or case series design; and if study was a case series it must include twenty or more participants. Abstracts were excluded if they failed to meet any of the above inclusion criteria, or if they: were an animal-model; reported non-original data; or were case reports, editorials, opinions or qualitative studies. Abstracts selected for inclusion by either reviewer proceeded to full-text review. This initial screen was intentionally broad to ensure that all relevant literature was captured.

Studies included after abstract review proceeded to full-text review in duplicate. Studies were included if they met all inclusion criteria and failed to meet any of the criteria for exclusion presented in Table 3. Full-text review was completed in duplicate. Any discrepancy between

reviewers was resolved through discussion and consensus. Published systematic reviews^{34,35} and Health Technology Assessments^{26,36} were hand-searched to ensure all relevant papers were captured in the literature search.

Table 3: Inclusion and Exclusion Criteria for Clinical Effectiveness Systematic Review

Inclusion Criteria	Exclusion Criteria
<ul style="list-style-type: none"> • Report on the effectiveness/efficacy of Laser Interstitial thermal therapy for one of the following: <ul style="list-style-type: none"> ○ epilepsy ○ intracranial lesions • English or French studies only • Human studies • Full-text available • Randomized, quasi-randomized, observational cohort, case control or case series design • If case-series, study must have included twenty or more participants 	<ul style="list-style-type: none"> • Does not assesses the effectiveness/efficacy of Laser Interstitial thermal therapy for either epilepsy or intracranial lesions • Not written in English or French • Animal models • Non-original data • Studies reported only in abstract or as poster presentations • Case reports, editorials, opinions, qualitative studies • Case series, and study included fewer than twenty participants

Included studies were subdivided into patients with epilepsy and patients with intracranial lesions. For all studies, year of publication, country, patient selection, patient characteristics, description of technologies, research methods, outcomes measured, and instruments used were extracted using standardized data extraction forms. Safety outcomes including headaches, nausea, discomfort, and seizures were also extracted. Discrepancies between reviewers during data extraction were resolved through consensus.

During data extraction, quality assessment was completed in duplicate. Non-RCTs were assessed using the previously described Downs and Blacks Checklist³⁷. PRISMA guidelines and reporting standards were used.

5.3 Results

Two hundred and ninety-nine citations were retrieved from MEDLINE (n=67), PubMed (n=62), EMBASE (n=165), PsychINFO (n=5), and hand searching (n=3). After duplicates were removed, 242 citations were reviewed. One hundred and ninety-three were excluded, and forty-nine proceeded to full-text review. Six articles met the final inclusion criteria (Figure 1); however, two of these studies were based on the same population, and therefore will be treated as one here forward. Four of the six included studies were conducted in the United States, and one was conducted in Germany^{38,39}. Two studies included patients with epilepsy^{40,41} and three included patients with intracranial lesions^{29,38,39,42}.

The findings from the five studies are narratively synthesized below. A high level summary is provided in Table 5.

Table 4 Flow chart of included and excluded studies

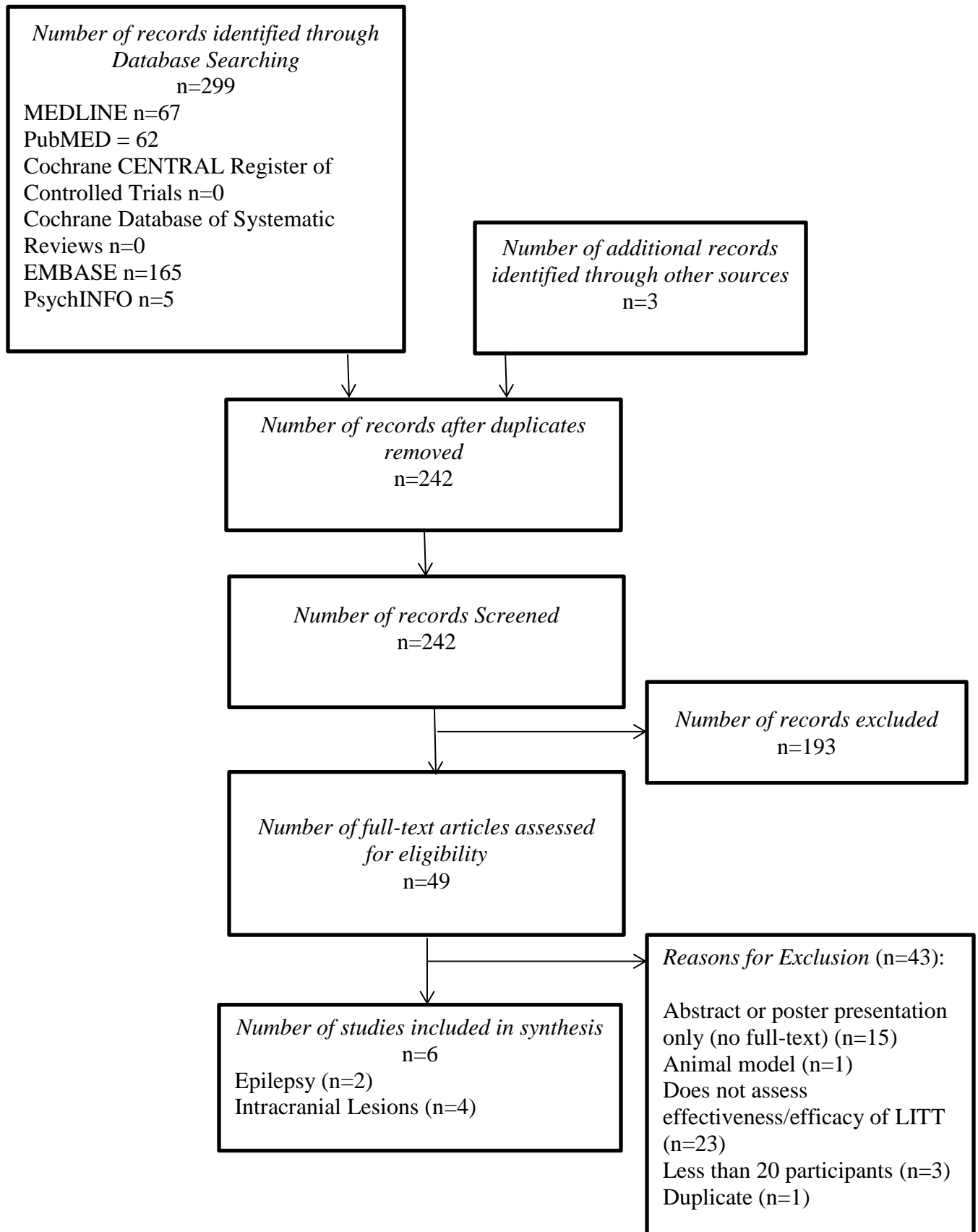


Table 5 Characteristics of Included Studies

Author, Reference, Year of Publication, Country	Patient Selection	Research methods	Key findings	Safety	Reported Conflicts of Interest
<i>Epilepsy</i>					
Drane ⁴⁰ , 2015, United States	<p>Total number of patients: 58</p> <p>Patient Selection: Patients who underwent stereotactic laser amygdalohippocampotomy (SLAH) at Emory University or the University of Washington were eligible for inclusion.</p> <p>Inclusion Criteria: Patients 18 years or older, native English speakers, and patients eligible for surgery (i.e. anteromedial TL resections)</p> <p>Exclusion Criteria: Patients less than 18 years of age and not assessed cognitively (Wada test).</p> <p>Patient Characteristics: Thirty nine patients underwent standard surgical approaches and nineteen underwent SLAH. Patient characteristics are not reported.</p>	<p>Study Design: Non-randomized Controlled study</p> <p>Type of device used: Not specified</p> <p>Comparator: Open resections</p>	<ul style="list-style-type: none"> • Performance declines were significantly greater for patients with dominant temporal lobe epilepsy (TLE) that underwent open resection surgery versus SLAH, for famous face recognition and common names (p<0.0001 and p<0.001) • Performance declines were significantly greater for patients with nondominant temporal lobe epilepsy (TLE) that underwent open resection surgery versus SLAH, for famous face recognition (p<0.02), but not for common names • No SLAH patients experienced any performance declines when examined on an individual basis. 	<p>Adverse events reported:</p> <ul style="list-style-type: none"> • None reported 	<p>One author works for Visualase, and one author works for Wada testing.</p>
Waseem ⁴¹ , 2015, United States	<p>Total number of patients: 14</p> <p>Patient Selection: Patient information was collected through a epilepsy surgery database developed in 1998. The last 14 consecutive patients who met the inclusion criteria were selected.</p> <p>Inclusion Criteria: Over the age of 50, mesial temporal clinical semiology and electrophysiology, underwent anterior mesial temporal lobe resection or magnetic resonance-guided laser interstitial thermal therapy (MRgLITT).</p> <p>Exclusion Criteria: None reported</p> <p>Patient Characteristics: Fourteen participants (10 females and 4 males) with a mean age of 53</p>	<p>Study Design: Non-randomized Controlled Study</p> <p>Type of device used: Visualase</p> <p>Comparator: Anterior mesial temporal lobe resection</p>	<ul style="list-style-type: none"> • At one year postoperative, seizure freedom rates were not significantly different between the anterior mesial temporal lobe resection group and the MRgLITT group (80% for MRgLITT and 100% for AMTL, p>0.05). • Length of stay was significantly shorter in the MRgLITT group (1.3 days compared to 2.6 days for AMTL, p<0.05) • Surgical time was significantly shorter for the MRgLITT 	<p>Adverse events:</p> <ul style="list-style-type: none"> • One participant, who was in the anterior mesial temporal lobe resection group, developed aseptic meningitis that resolved with steroid therapy • One patient in the MRgLITT group had an early postoperative seizure requiring 	<p>The authors report no conflicts of interest</p>

	(range 51-57) were included. Seven (1 male, 6 females, average age of 53 and average years of epilepsy 2537) received anterior mesial temporal lobe resection, and seven (3 males, 4 females, average age 60, and average years of epilepsy 37.9) received MRgLITT.		group (2.9 hours compared to 4.2 hours), p=0.002 <ul style="list-style-type: none"> The need for pain control was significantly reduced in the MRgLITT group (12.9mg/day of morphine compared to 29.6mg/day), p=0.026 	readmission <ul style="list-style-type: none"> Two patients in the MRgLITT group had partial visual field deficits One patient in the MRgLITT group had an extended length of stay due to persistent headaches. 	
<i>Intracranial Lesions</i>					
Jethwa ²⁹ , 2012, United States	Total number of patients: 20 Patient Selection: Patients age 9-85 were recruited between July 1, 2010 and July 1, 2011. All patients had confirmed diagnoses using stereotactic biopsy or resection. Inclusion Criteria: None reported Exclusion Criteria: None reported Patient Characteristics: Twenty patients, ranging from 9-85 years old received LITT. For 17 of the included participants other treatment such as resection or chemotherapy had been attempted prior to the trial.	Study Design: Case Series Type of device used: Visualase Comparator: None	<ul style="list-style-type: none"> The area of thermal damage ranged from 0.95-9.63 cm² Median length of hospitalization was 24 hours, with a range of 24-168 hours 	Adverse events reported: <ul style="list-style-type: none"> Arterial injury requiring operative evacuation Refractory edema requiring hemicraniectomy Inaccurate laser placement, conversion to open resection Development of diabetes insipidus due to acute pituitary injury 	Two authors are full-time employees of Visualase
Leonardi, 2001 ³⁹ and 2002 ³⁸ , Germany	Total number of patients: 24 Patient Selection: Patients with gliomas were recruited from one center between May 1995 and December 1999. Inclusion Criteria: None reported Exclusion Criteria: None reported Patient Characteristics: Twenty-four patients with gliomas, 7 females and 17 males, were included and treated with LITT. All patients had previously been treated with surgery and radiation. Mean age of included participants was 52 years. Mean tumor sizes were: 33.2 mm(low grad gliomas), 21.3 (anaplastic astrocytomas), and 26.3 (glioblastomas)	Study Design: Case series Type of device used: NWL Lasertechnologie Comparator: None	<ul style="list-style-type: none"> The mean energy required per dose was 2979 Joules Response of tumor tissue to ablation was not related to tumor grading The mean total lesion size was 21.2mm² Mean survival times after LITT were 34 months (low grade astrocytomas), 30 months (anaplastic gliomas), 9 months (glioblastomas) Mean time to progression was 16 months (low grade astrocytomas), 10 months (anaplastic gliomas), 4 months 	Adverse events reported: <ul style="list-style-type: none"> None reported 	Conflict of interest not reported

			(glioblastomas)		
Mohammadi ⁴² , 2014, United States	<p>Total number of patients:38</p> <p>Patient Selection: Patients who underwent the NeuroBlate procedure between May 2011 and December 2012 at one of three clinics were considered for inclusion.</p> <p>Inclusion Criteria: 18 years or older, pathology proven high-grade glioma</p> <p>Exclusion Criteria: History of prior GBM including radiation therapy with biopsy showing necrosis and no evidence of recurrent glioma</p> <p>Patient Characteristics: Thirty-eight participants (21 males, 14 females) with a mean age of 56 years (range 19-79) were included. Twenty-four patients had glioblastoma, 6 anaplastic astrocytoma, and 4 anaplastic oligodendroglioma.</p>	<p>Study Design: Case Series</p> <p>Type of device used: Neuroblate system (Monteris Medical Corporation)</p> <p>Comparator: None</p>	<ul style="list-style-type: none"> • During 7 month follow-up, 71% of cases progressed; estimated median progression free survival was 5.1 months • During 7 month follow-up 35% of patients died; 10 patients due to progression and 2 from other causes 	<p>Adverse events reported:</p> <ul style="list-style-type: none"> • None reported 	<p>Four of the authors reported conflicts of interest with Monteris Medical, including paid travel, equity interest, and consulting.</p>

5.3.1 Quality Assessment

Using the Downs and Blacks checklist, the five non-randomized controlled trials studies had total scores of 14⁴⁰, 16²⁹, 17^{38,39}, and 19^{41,42} out of a possible 28 points (Table 6). All five studies were clear in their objectives, outcomes, findings and interventions. None of the included studies blinded outcome assessors, randomized participants, or adjusted for confounding. The full results of the quality assessment can be found in Appendix D.

Table 6 Quality Assessment for non-randomized controlled trials

Study	Quality Assessment Score (Downs and Blacks Checklist)
Drane ⁴⁰	14
Jethwa ²⁹	16
Leonardi ^{38,39}	17
Mohammadi ⁴²	19
Waseem ⁴¹	19

5.3.2 Drane et al.

The study conducted by Drane et al. assessed the effectiveness of stereotactic laser amygdalohippocampectomy (SLAH) for patients with epilepsy. This non-randomized controlled study compared SLAH with open resections in 39 patients (19 had SLAH and 39 had surgery). This study assessed pre- and post-operative performance on famous face recognition and common names. The authors did not specify the type of device used.

This study found that performance declines were significantly greater for patients with dominant temporal lobe epilepsy (TLE) that underwent open resection surgery versus SLAH, for famous face recognition and common names ($p < 0.0001$ and $p < 0.001$). Performance declines were significantly greater for patients with nondominant temporal lobe epilepsy (TLE) that underwent open resection surgery versus SLAH, for famous face recognition ($p < 0.02$), but not for common

names. No SLAH patients experienced any performance declines when examined on an individual basis. No adverse events were reported. The authors concluded that “Preliminary results suggest (1) naming and recognition functions can be spared in TLE patients undergoing SLAH, and (2) the hippocampus does not appear to be an essential component of neural networks underlying name retrieval or recognition of common objects or famous faces.”

5.3.3 Jethwa et al.

Jethwa et al. present their experiences with using LITT for patients who had intracranial lesions²⁹. This study was primarily focused on methodology, however, some outcome data was presented. Twenty patients, ranging from 9-85 years old were included in this case series. All received LITT. A Visualase device was used to perform the LITT procedures.

The area of thermal damage ranged from 0.95-9.63 cm², and the median length of hospitalization was 24 hours, ranging from 24 to 168 hours. Four serious adverse events were reported. One individual experienced an arterial injury which required operative evacuation, one experienced refractory edema after the procedure which required hemicraniectomy, one developed diabetes insipidus after acute pituitary injury, and lately, one patient had inaccurate laser placement which resulted in subsequent standard surgical resection of the tumor. The authors conclude that their “...initial experience demonstrates that this therapy can be both safe and effective in achieving thermal ablation of intracranial tumors and can provide a treatment option in patients with otherwise nonresectable lesions”²⁹.

5.3.4 Leonardi et al

Leonardi et al. published two studies (2001³⁹ and 2002³⁸), based on one patient population. This case series looked at the use of LITT in an open MR to ablate gliomas. Twenty-four patients with

gliomas were recruited from one center between May 1995 and December 1999. The mean age of participants was 52, and mean tumor sizes were: 33.2 mm (low grade gliomas), 21.3 mm (anaplastic astrocytomas), and 26.3 mm (glioblastomas). All patients had been previously treated with surgery and radiation.

This study found that the mean total lesion size was 21.2mm². Mean survival times after LITT were thirty-four months (low grade astrocytomas), thirty months (anaplastic gliomas), nine months (glioblastomas), and mean time to progression was sixteen months (low grade astrocytomas), ten months (anaplastic gliomas), four months (glioblastomas). Based on these findings, these authors conclude that “Due to the minimal invasive technique, the method is a therapy of choice and may be favoured to reoperation. Major indications of this treatment are small tumours, in eloquent regions and deep seated, as well as in older patients or patients in poor function status.”³⁸

5.3.5 Waseem *et al.*

Waseem *et al.* studied the effectiveness of MRgLITT compared to anterior mesial temporal lobe resection for people with epilepsy over the age of 50⁴¹. Patient data was collected through an epilepsy surgery database. Fourteen patients with a mean age of 53 were included, seven of whom received anterior mesial temporal lobe resection, and seven received MRgLITT. A Visualase device was used to perform the MRgLITT procedures.

One year post-surgery, seizure freedom rates were not significantly different between the anterior mesial temporal lobe resection group and the MRgLITT group (80% for MRgLITT and 100% for AMTL, $p > 0.05$). Length of stay was significantly shorter in the MRgLITT group (1.3

days compared to 2.6 days for AMTL, $p < 0.05$) and surgical time was significantly shorter for the MRgLITT group (2.9 hours compared to 4.2 hours, $p = 0.002$). The need for pain control was significantly reduced in the MRgLITT group (12.9mg/day of morphine compared to 29.6mg/day, $p = 0.026$). This paper reported five adverse events, four in the MRgLITT group (two people had partial visual field deficits, one had persistent headaches and one had a post-operative seizure requiring readmission) and one in the anterior mesial temporal lobe resection group (one person developed aseptic meningitis). The authors of this paper conclude that “Short-term follow-up suggests that MRgLITT is safe and provides outcomes comparable to AMTL resection in this population.”⁴¹

5.3.6 *Mohammadi et al.*

This case series assessed the effectiveness of LITT for thirty-eight patients with intracranial lesions; twenty-four patients had glioblastoma, 6 anaplastic astrocytoma, and 4 anaplastic oligodendroglioma.⁴² A Neuroblate (Monteris Medical Corporation) device was used to perform the LITT procedures.

This study found that during 7 month follow-up, 71% of cases progressed; estimated median progression free survival was 5.1 months. During 7 month follow-up 35% of patients died; 10 patients due to progression and 2 from other causes. The authors concluded that “Laser interstitial thermal therapy has been shown to have promising results as a safe and effective treatment modality for high-grade glioma patients in conjunction with standard medical and radiation therapies.”⁴²

5.4 Ongoing Trials

Four ongoing trials on LITT are registered through clinicaltrials.gov (Table 7).

One RCT (NCT02311582), which is currently recruiting participants, aims to assess the ability of MRI-guided laser ablation to disrupt the blood brain barrier. This study intends to recruit 52 adult patients with malignant glioma, with an estimated completion date of December 2019. The primary outcomes to be reported include progression-free survival. The study is being conducted by the Washington University School of Medicine.

As of 2009, a non-randomized pilot study (NCT00787982) was being completed by Visualase, and was recruiting participants. The objective of this study was to assess the effectiveness of Visualase technology for ablating metastatic brain tumors smaller than 3 centimeters. The primary outcome is completion of procedure with no complications, and the secondary outcomes are accuracy of predicting tumor size using Visualase, human resources and costs associated with procedure, patient survival, and post-procedure morbidity. It was estimated that 20 participants would be enrolled. The estimated completion date was September 2010; however, no updates have been submitted since 2009.

In 2002, the Brigham and Women's Hospital has registered a study (NCT00207350) on the use of MRI LITT for ablating brain tumors. The registration shows that this study is currently recruiting participants (estimated enrolment of 24); however, the registration was last updated in 2013. The primary outcome is ablation of tissue, and secondary outcomes include neurological exam, and self-assessment using a Glioma Outcomes Questionnaire. The estimated completion date was December 2014.

A study on the use of LITT for treating pediatric central nervous system tumors (NCT02451215) is being conducted by the Children’s Hospitals and Clinics of Minnesota. This study is recruiting participants; it is anticipated that 18 participants will be enrolled. The primary outcomes of this study are 10-year morbidity, and efficacy (measured as rates of recurrence and progression). The estimated completion date is April 2025.

Table 7: Synthesis of Ongoing Registered Trials

Trial Number	Who is conducting Trial	Objective	Estimated Completion Date	Primary outcomes to be reported	Sample Size	Patient population
NCT02311582	Washington University School of Medicine	To assess the ability of MRI-guided laser ablation to disrupt the blood brain barrier.	December 2019	Progression-free survival	52	Adult patients with malignant glioma
NCT00787982	Visualase	To assess the effectiveness of Visualase technology for ablating metastatic brain tumors smaller than 3 cm	September 2010 (no updates have been submitted since 2009)	Completion of procedure with no complications	20	Adults with metastatic brain tumors smaller than 3 cm.
NCT00207350	Brigham and Women’s Hospital	To assess the effectiveness of using MRI LITT for ablating brain tumors	December 2014	Ablation of tissue	24	Adults with brain tumors that are surgically difficult to access.
NCT02451215	Children’s Hospitals and Clinics of Minnesota	To assess the use of LITT for treating pediatric central nervous system tumors.	April 2025	10-year morbidity, and efficacy (measured as rates of recurrence and progression)	18	Children age 1-22 years old with a difficult to access newly diagnosed low-grade central nervous system tumor.

5.5 Conclusions

Two studies on epilepsy and four on intracranial lesions (two of which assessed the same patient population) were included in this systematic review of LITT. Three studies were case

series^{29,38,39,42}, and two were non-randomized controlled studies^{40,41}. There was substantial heterogeneity among the included studies, in terms of LITT device used, type of LITT, comparator, patient population, and outcomes measured.

Among the two studies on epilepsy, one found that the LITT group experienced significantly less decline in famous face recognition and common names compared to SLAH. The other study found no statistically significant difference between seizure rates for those who had MRgLITT compared to anterior mesial temporal resection. Findings showed that length of stay was significantly shorter as was surgical time for those in the MRgLITT group, and the need for pain control was significantly less. Despite not finding a statistically significant improvement in seizure rates for those in the LITT group, this result suggests that LITT is equally effective at reducing seizures, while resulting in less pain, and shorter length of stay for patients.

Among the studies on intracranial lesions, one found that in the seven months after LITT, 71% of patients had tumor progression with a median progression free survival of 5.1 months. Another found mean time to progression was 16 months for low grade astrocytomas, 10 months for anaplastic gliomas and 4 months for glioblastomas. After LITT, this study found that mean survival times were 34 months for low grade astrocytomas, 30 months for anaplastic gliomas and 9 months for glioblastomas. The last study did not present survival or time to progression, but reported that the area of thermal damage ranged from 0.95-9.63 cm², and the median length of hospitalization was 24 hours.

6 Systematic Review of Patient Experience or Quality of Life and Laser Interstitial Thermal Therapy

Summary

- No studies were found evaluating the patient experiences or quality of life of LITT in patients with epilepsy or brain metastases.
- Three studies were identified in other conditions: eLITT for menorrhagia; sLITT for spinal metastasis; and US-LITT for liver metastases; the findings from these studies may not be generalizable to epilepsy or brain metastases.

6.1 Research Objective

To understand patient experiences with, quality of life after, or attitudes towards LITT.

6.2 Methods

6.2.1 Literature search

A systematic review of the qualitative literature was completed to describe the patient experience with rTMS. MEDLINE, PubMed, and EMBASE were searched from database inception until October 7th, 2015. Terms describing the technology, such as “laser interstitial thermal therapy,” “stereotactic laser ablation,” “LITT” and “MRgLITT” were combined using the Boolean Operator “and.” These terms were then combined using the Boolean Operator “and” with terms such as “quality of life,” “attitudes,” “satisfaction,” and “patient preference.” Results were limited to French and English language, and non-animal studies. Details of this search strategy can be found in Appendix A.

6.2.2 *Selection of Literature*

All abstracts were screened in duplicate. Abstracts proceeded to full-text review if: they reported on patient experiences with, quality of life after, or attitudes towards LITT; were written in English or French; and were original research. Abstracts were excluded if they did not meet the criteria above, or if: they were an animal model; reported physician accounts of patient experiences; or were an editorial or letter. Abstracts selected by either reviewer proceeded to full-text review. This initial screen was intentionally broad to ensure that all relevant literature was captured.

Studies included after abstract review proceeded to full-text review by two reviewers. Studies were included if they met all inclusion criteria and failed to meet any of the exclusion criteria presented in Table 8. Any inclusion or exclusion discrepancy between reviewers was resolved through discussion and consensus. A Kappa Statistic for agreement was calculated.

For all studies, year of publication, country, patient selection, patient population, research methods and key findings were extracted in duplicate using standardized data extraction forms. Discrepancies between reviewers during data extraction were resolved through consensus. During data extraction, quality assessment using the Downs and Blacks checklist³⁷ was completed in duplicate. Using this checklist, each study was assessed based on 27 criteria, widely covering areas reporting quality, external and internal validity, and power³⁷. Studies are assigned a value of “1” if they meet the question criteria, “0” if they do not or if it is not possible to determine whether they meet the criteria; with one exception where one question may be

given “2” points. Any discrepancy between reviewers on quality assessment was resolved through discussion and consensus.

Table 8 Inclusion and Exclusion Criteria for Patient Perspectives Systematic Review

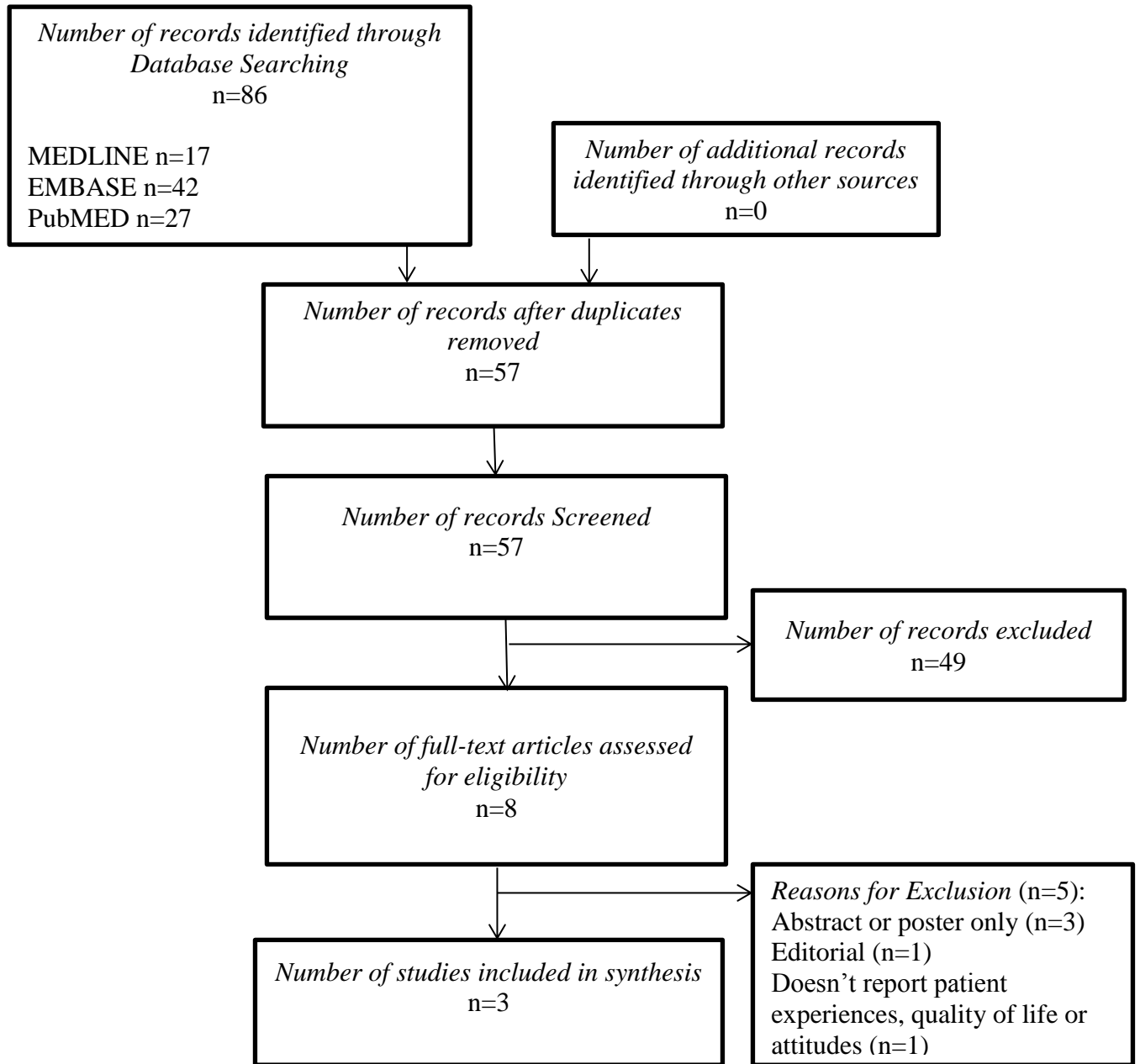
Inclusion Criteria	Exclusion Criteria
<ul style="list-style-type: none"> • Original research • Full-text available • English or French studies only • Human studies • Reports on patient experiences with, quality of life after, or attitudes towards LITT 	<ul style="list-style-type: none"> • Studies written in a language other than English or French • Animal models • Non-original data • Studies reported only in abstract or as poster presentations • Editorials, opinions, reviews • Physician accounts of patient experience

6.3 Results

Eighty-six citations were retrieved from MEDLINE (n=17), EMBASE (n=42), and PubMed (n=27). After duplicates were removed, 57 citations were reviewed. Forty-nine citations were excluded, and eight proceeded to full-text review. No studies were found that looked at quality of life or satisfaction with LITT and epilepsy or intracranial lesions. Three articles reported the use of LITT in other conditions (Figure 1). The Kappa for full-text review was 0.714 (95% CI: 0.212-1.00), or “substantial agreement.”⁴³

The findings from the three studies are narratively synthesized in Appendix E.

Figure 1: PRIMSA Flow chart of included and excluded studies



6.4 Conclusions

Three studies were included in this systematic review of patient experiences and quality of life; these studies looked at eLITT for menorrhagia, sLITT for spinal metastasis, and US-LITT for liver metastases. The findings and conclusions of these studies varied, and there was no clear consensus on whether LITT improved or did not improve quality of life. For quality of life, one

study found statistically significant improvement⁴⁴, and two found no statistically significant differences^{45,46}. The varying results can likely, in part, be attributed to the heterogeneity between the included studies. The types of LITT used (eLITT, US-LITT, and sLITT), diversity of clinical conditions, and range of outcome measurement tools (SF-12, EQ-5D, visual analogue scale and C30 questionnaire) all may have contributed to the differing results.

Based on the included studies, no conclusions can be drawn about quality of life and the use of LITT. Before any conclusions can be drawn about quality of life, and the use of LITT, additional high quality literature is needed.

7 Clinician Interviews and National Scan

Summary

- LITT is new to Canada. LITT has been used at the Vancouver General Hospital since December 2014. The Hospital for Sick Children in Toronto is considering purchasing a Neuroblate system, and is hoping to be able to provide LITT as an option for children with epilepsy by spring of 2016.
- LITT is perceived as an option for patients who do not have other treatment options. This includes patients with malignant brain tumors and patients with certain kinds of epilepsy.
- LITT is a minimally invasive procedure. Based on clinical perception, it usually requires a shorter hospital stay, with no ICU component, follow-up is the same, and outcomes to date have been promising. Potential complications for LITT are similar to conventional surgery.
- The patient experience with LITT is described as positive by the clinicians, and by the patient interviewed.

7.1 Purpose

To develop an understanding of how LITT was being used in Canada and other jurisdictions, and to obtain clinician and patient perspectives on this technology.

7.2 Methods

Two research methods were used. First, an environmental scan was completed. Between October 13th and 15th, thirteen experts in brain lesions and epilepsy (including neurologists and neurosurgeons) were contacted by email. The experts were from the following cities: Vancouver, BC (1); Calgary, Alberta (5); Edmonton, Alberta (1); Saskatoon, Saskatchewan (1); London, Ontario (2); Toronto, Ontario (2); and St. John's, Newfoundland (1). They were asked if they knew of any Canadian centres using LITT to treat epilepsy or intracranial lesions. Those who were using or were intending to use LITT were asked more detailed questions about the technology. All responses were collated and synthesized.

Secondly, interviews with experts (herein described as key informants) in LITT, epilepsy and/or intracranial lesions were conducted. Six key informants from across Canada, with a range of LITT experience, were identified through snowball sampling. Interviews with these six key informants were conducted in November 2015, using a semi-structured interview guide. The interviewees included:

- A patient from British Columbia who had been treated with LITT for a brain tumor;
- A Toronto-based pediatric neurologist with US-based experience with LITT;
- A Montreal-based neurosurgeon specializing in epilepsy with experience in stereotactic techniques and an interest in LITT;
- A Calgary-based neuro-oncologist with an interest in LITT who had referred a patient with a malignant brain tumor to Vancouver for LITT;

- A U.S. based neuro-surgeon with three years of experience using LITT for malignant tumors and epilepsy lesions (completed more than 60 LITT procedures, including 20-30 for epilepsy lesions, and 30-40 for tumors).
- A Vancouver based neuro-surgeon with experience using LITT for malignant brain tumors
- Monteris Medical, manufacturer of NeuroBlate

A semi-structured interview guide was developed to explore areas including: patient populations for which LITT is an option; the Visualase and Neuroblate systems; possible complications and safety concerns; potential benefits for patients and impact on quality of life; capacity for LITT including training and support; patient care pathways; costs of LITT and future comparators for LITT currently under development. These interviews were conducted by phone and ranged in length from 20 to 60 minutes. Detailed notes were taken to capture the interview data. The data was analyzed using constant comparative analysis.

7.3 Results

7.3.1 The Canadian Context

LITT is new to Canada; the Neuroblate system was approved by Health Canada in September 2014. We identified one Vancouver hospital using LITT and one Toronto hospital considering using LITT. This technology is primarily used when patients have no other treatment options.

7.3.1.1 Vancouver General Hospital

Within Canada, LITT is currently only being provided at Vancouver General Hospital by one neurosurgeon. This neurosurgeon first started using LITT in December 2014, and has done nearly twenty procedures to date. He uses LITT primarily for malignant gliomas, and occasionally for Grade 2 tumors. He has supported a colleague in treating one epilepsy case with

LITT. Currently, only evening times are available for LITT, because the MRI's are not being used for diagnostic purposes. Due to barriers, such as MRI and operating room time, the number of procedures done at Vancouver General Hospital is limited; however, without these barriers, the neurosurgeon has estimated that he could do 3-4 LITT procedures per month.

Most referrals have come from colleagues in British Columbia, but referrals have also come from neuro-oncologists in Alberta. Many patients have contacted him directly. The neurosurgeon at the Vancouver General Hospital is well respected by his peers, and he believes that doing LITT in Vancouver has increased interest in the procedure across the country. Neurosurgeons in other parts of the country have expressed interest in observing the procedure.

7.3.1.2 Hospital for Sick Children

The Hospital for Sick Children in Toronto is currently planning on purchasing the Neuroblate system. A pediatric neurologist with experience from the United States has been leading this initiative. Two pediatric neurosurgeons working with the pediatric neurologist have already undergone some training. They are hoping to have the system in place in the spring of 2016, and currently have two children waiting for the procedure.

A few neurologists and neurosurgeons have gone to the Monteris simulation centre in Minneapolis to learn see and learn more about the Neuroblate system. Some have observed and participated in LITT procedures in United States centers. For example, one neurologist has been involved in planning LITT procedures and participated on LITT surgical teams during his fellowship at a United States Children's Hospital. Neurologists and neurosurgeons are interested

in having LITT as an option for their patients, and patients are interested in having this option available to them.

7.3.2 Clinical practice guidelines

LITT is not included in any clinical practice guidelines or incorporated into clinical care pathways for brain tumours or epilepsy. Experts believed that this was due to the lack of clinical trial research completed to date. One clinician noted that because it is a technology approved for clinical use, there are few incentives for the manufacturers to support large critical trials.

7.3.3 Recommended Patient populations

Comparators for LITT include, open surgery (the standard craniotomy) and radiosurgery.

Importantly, for epilepsy and benign tumors, this technology may be curative. However, for patients with malignant gliomas, all of the current treatment options, including LITT, are palliative.

Which patient populations are best suited for LITT is an ongoing question. Clinicians described a number of patient populations for which LITT is an option, based on clinical experience. Key informants described it as a good option for patients with terminal brain cancer. They also described it as a good treatment for patients who are fit and healthy enough to get some benefit, but who do not have any other treatment options (they have had conventional surgery, chemotherapy and radiation). LITT may be a good option for patients who have had numerous surgeries, making additional surgeries increasingly difficult and risky due to scarring. LITT may be used multiple times on a patient due to its less invasive nature. Lastly, if a patient was unable to tolerate a large surgery, they may be more likely to tolerate LITT.

For patients with epilepsy, the following sub-groups were described as being possible good candidates for LITT:

- Patients with small (< 2 centimeter), well-circumscribed, solitary lesions.
- Medial temporal lobe epilepsy
- Highly concordant, drug resistant, lesional epilepsy where access is difficult because the lesion is deep-seated, and where previous craniotomy has failed.
- Patients with epilepsy who have multiple lesions which would require multiple surgeries (e.g., tuberous sclerosis).
- Heterotopia
- Patients that have severe epilepsy but no clear lesion. The first line treatment is to do a Corpus Callosotomy. Now starting to use LITT to cut the corpus callosum with good results.
- Focal Cortical dysplasia (i.e. congenital abnormality of brain development), which is a common cause of treatment-resistant epilepsy in children.
- Hypothalamic hamartoma (i.e. a benign tumour-like malformation that is present at birth). Tends to occur in a very sensitive area of the brain.
- Palliative patients with severe epilepsy who have already had a number of surgeries

There are some patients for which LITT may not be a good option. These include tumours that are very easily reachable using conventional surgery (e.g. a glioblastoma in the right frontal lobe), and tumours or lesions that are larger than 3 centimeters in diameter (due to the increased risk of serious adverse events when ablating tumors of this size, such as swelling).

In adults, epilepsy lesions are more obvious, so it is often simpler to do conventional surgery in adults than in children. LITT has significant potential in treating children with epilepsy. One expert estimated that once the Neuroblate system is in place in Toronto, 10-20% of patients may be good candidates for LITT (rather than conventional surgery), which over time, could increase to 25%. As more experience is gained with LITT, it may become the first line treatment due to its minimally invasive nature.

A clinician based in the United States, who has three years of experience with LITT stated that in their Center it has evolved from an experimental procedure to first line use for some kinds of epilepsy. For example, LITT has become a first line for medial temporal lobe epilepsy – unilateral lesion. This key informant noted that the results have been very promising for these patients, with over 90% of appropriately selected patients being seizure-free following LITT. If LITT is unsuccessful, it is possible to do a craniotomy; craniotomy does not necessarily need to be the first option.

7.3.4 Possible Complications and Safety Concerns

Clinicians were impressed with the software design and the safety features of the Neuroblate system. As one clinician described, you outline your focus areas and the areas that you do not want to treat prior to the procedure. Once the procedure is underway, the software prevents you from treating areas that were identified as areas not to be treated.

One key informant noted that the potential complications for LITT are similar to conventional surgery (i.e. bleeding, swelling, new onset neurological deficits), but in their experience these complications occur less frequently. The principal complications are technical complications such as planning problems and doing the procedure problems (e.g. inaccurate probe placements).

These technical complications will exist at any institution where the technology is new and decrease as experience is gained. The system vendors are interested in preventing these complications, and work closely with the hospitals offering the procedure.

7.3.5 The Visualase and Neuroblate Systems

Both Visualase and Neuroblate were described favorably. These MR guided laser probe systems have only been available for the past three to four years, and Visualase was the first system available for clinical use in the United States. LITT is MR guided, which makes it the procedure directly visible and controllable. MR thermometry measures the temperature to ensure precision.

Key informants with experience using both systems had mixed perspectives. One key informant described Neuroblate as perhaps being a little better for tumours and Visualase a little better for medial lobe epilepsy. Another felt that Neuroblate had learned from Visualize and developed a superior system. Both systems are expected to evolve and improve over time. Both systems can be operated in two ways, using an intra-operative MRI or using a standard operating room with an MRI Suite. All the key informant clinicians with experience using LITT were using the former, as it is not common to have access to an intraoperative MRI. A benefit of LITT is that it is a flexible, modifiable technology. For example, different stereotactic frames, which are used to immobilize the patients head during the procedure, may be used with the machines.

Visualase reports that 1,700 mixed cases have been performed using their technology; all of which have been in the United States. Approximately 1/3 of these have been in pediatrics.

Neuroblate reports that roughly 500 cases have been performed using their technology; only a small number of which were used in pediatrics. Thus far, LITT has been more commonly used for tumors than for lesions.

7.3.6 Capacity, Training, and Support

LITT requires a team. Although it is a reasonably simple surgical procedure, the technology is complex. An important member of this team is the Monteris software specialist, who is in the operating room for every Neuroblate LITT procedure. The role of the Monteris specialist is to run the computer software, help set up the probe in the MRI, and run the MRI to get temperature acquisition. The specialist does not have any role in the operating room procedures. The cost of having the Monteris specialist attend surgeries is covered within the yearly “warranty fee” (more detail in Section 8); this is a fixed cost that does not vary by number of procedures. Monteris has a simulation lab, which allows surgeons to practice the procedure beforehand. Monteris is also able to provide opportunities for interested surgeons to observe the procedure at facilities in the United States. The neurosurgeon in Vancouver has also had interested surgeons observe his procedures.

Training required to conduct the procedure is not extensive. Key informants noted that surgeons who have experience with stereotactic techniques such as stereotactic biopsies, and diagnostic deep brain stimulation, are likely to be comfortable with LITT (e.g. epileptic surgeons, functional neurosurgeons). Prior to doing LITT procedures, the neurosurgeon in Vancouver went to the United States to observe cases. He also trained an epilepsy surgeon colleague, who did LITT on a patient with epilepsy.

Key informants suggested that a major challenge is getting people to be open-minded to changing practice for the benefit of their patients. Clinicians need to be comfortable with the technology. If neuro-surgeons are not exposed to LITT in their training or are uncomfortable with technology, it is unlikely that they will try it, and will rather use conventional treatments.

Additionally, the change in workflow from a conventional surgery may make a team reluctant to try LITT. LITT represents a significant change in practice.

Due to the equipment costs (and the learning curve related to the technology), LITT should remain centralized in a quaternary center. In the future, however, the use of LITT could be opened up to other types of clinical conditions in which case access might become more decentralized. At the Vancouver General Hospital, where LITT is currently being performed, it would be possible to increase the number of procedures performed to three or four per month. More resources, however, would enable a more efficient process. It was suggested that a suite set up beside the MRI suite to do the procedure could alleviate the need to use an operating room. Another option for improving efficiency and patient experience would be to have an intra-operative MRI.

7.3.7 Patient Experience with LITT

Patients have accessed LITT by contacting the neurosurgeon from the Vancouver General Hospital directly by phone or email, or through a referral by their oncologist. Due to significant media coverage, many patients have been aware that this is a new and promising option for some patients with brain tumors, and have contacted the neuro-surgeon directly. When this happens, he asks them to obtain a referral from their oncologist.

Other than travel expenses, there have been no out-of-pocket costs for patients receiving LITT in Vancouver. Currently, the probes are paid for by a private donation which also bought the technology. For out-of-province patients, there are greater travel expenses and there are some costs incurred to get copies of test results and imaging, but no costs are charged for the procedure.

The clinicians' perspective is that patients seek the LITT procedure out because it is minimally invasive, and many do not have any other treatment options. As one clinician stated: *"I can provide a meaningful treatment option to someone who might not have one otherwise."*

Generally, patients are required to be in hospital overnight and there is minimal post-procedure pain. If there are concerns about significant LITT procedures, the patient will go to Neuro Intensive Care Unit otherwise they will go to the general floor overnight, and go home the next day. The follow-up after LITT was described as being be the same as for conventional surgery.

The patient interviewed, who had an inoperable brain tumour, described LITT as a good experience. She had no treatment for her brain tumour prior to LITT. The procedure was uneventful and the hospital stay was short. There was some discomfort during the procedure itself, but it was not unbearable. Follow-up was provided through the Cancer clinic. This patient contacted the neurosurgeon at the Vancouver General Hospital directly after hearing about it through the media. She was able to see him quickly, and had the procedure a few days after seeing him in his office. She described feeling relieved that she was eligible to undergo LITT. She underwent the procedure in December 2014. This was followed by chemotherapy and radiation, and oral chemotherapy. She continues to do well almost a year after the procedure, and to date her tumour has not grown. She has not undergone a second LITT procedure, but her understanding is that should her tumor grow, that option would be available to her. She would highly recommend LITT to other patients in similar circumstances.

7.3.8 *LITT, Now and in the Future*

Many see this type of application, along with robotics, as the future of neurosurgery, “*so the earlier neurosurgeons here in Canada get in and get involved the better off they’ll be*”. The minimally invasive nature of the procedure is of great importance to patients, and to date the outcomes have been very promising.

Some neurologists are reluctant to refer to patients for LITT, because of the lack of trial research to date. One clinician believed that LITT was not really radically different, and that in cases where surgery may not be an option or is very difficult, LITT should be considered. For example, when we know best practice is to do a lobectomy but regular surgery is not possible, this provides another option for doing a lobectomy. Key informants felt that the tool is different, but the goal is the same.

Clinicians who were interested in, or had already referred patients for LITT, were appreciative that someone was trying something new. For example, a neuro-oncologist explained that it was important to keep looking for new options for patients with these aggressive brain tumours. He described himself as being an advocate for conservative, cautious LITT when there are no other options. He believed that his colleagues would also refer patients for LITT, if the patient was a good candidate. Overall, the clinicians interviewed are happy to have this as an option for their patients.

7.3.9 *Other options*

High intensity focused ultrasound (HIFU) is another option that is currently under development that may be useful in treating brain tumours and epilepsy lesions. There are mixed perspectives as to when this option might be clinically available, with some noting that there are many

pragmatic and clinical obstacles to HIFU becoming a standard. In the next few years HIFU may start to be used in brain tumours, but its use in treating epilepsy will likely take longer.

8 Budget Impact Analysis

Summary

- Upfront cost of purchasing one LITT system is \$652,157 when including the transportation system, and \$540,390 when the transportation system is excluded
- A yearly cost for the warranty is \$73,878
- The cost per procedure is \$23,623

8.1 Research Objective

To determine the costs associated with the use of LITT for intracranial lesions and epilepsy.

8.2 Budget Impact Analysis

All included costs are outlined in Table 9. For the purpose of this Budget Impact Analysis (BIA), it has been assumed that the NeuroBlate system will be used, as this is the only machine currently licensed by Health Canada. Fixed one-time costs are required to purchase the machine and necessary accessories, and ongoing costs are associated with each procedure. All estimates are local, and have been provided by either the Vancouver General Hospital, and the manufacturer of NeuroBlate, Monteris Medical. To highlight the difference in one-time capital costs, cost per procedure, and yearly cost estimates are presented below (summarized in Table 9). Of importance, the cost of hospitalization and/or intensive care have not been included in any of the following estimates.

Table 9 Costs Associated with LITT

	Component	Costs (2015 CAN)	Per procedure or Capital Cost	Source Details
<i>Capital Costs (Fixed)</i>	NeuroBlate System	\$524,237	Capital	Monteris Medical
	Transport System (to transport from operating Room to MRI)*	\$111,767	Capital	Monteris Medical
	Axiis CMB Accessory Kit (SET) for brain tumour cases	\$6,578	Capital	Monteris Medical
	Axiis CMB Accessory Kit (SET) for epilepsy cases	\$6,578	Capital	Monteris Medical
	NeuroBlate System Robotic Probe Driver	\$2,997	Capital	Monteris Medical
	Total Capital Costs including Transportation System	\$652,157		
	Total Capital Costs excluding Transportation System	\$540,390		
<i>Yearly Costs (Fixed)</i>	Warranty and support	\$73,878	Per year	Monteris Medical
	Total Yearly Costs	\$73,878		
<i>Per procedure Costs</i>	Mini-Bolt (assuming two per procedure)	\$1,994	Per procedure (variable)	Vancouver General
	Probes (assuming two per procedure)*	\$17,926	Per procedure (variable)	Vancouver General
	Operating Room Time (2.5 hours)	\$805	Per procedure (variable)	Vancouver General
	Anaesthesia	\$1,000	Per procedure (variable)	Vancouver General
	MRI procedure	\$572	Per procedure (variable)	Vancouver General
	Medication	\$150	Per procedure (variable)	Vancouver General
	Neurosurgeon Time	\$472.23	Per procedure (variable)	Vancouver General
	Disposable Instruments and supplies in the operating room	\$704	Per procedure (variable)	Vancouver General
	Total cost per Procedure	\$23,623		
Total annual cost at current utilization (24 procedures/year) at Vancouver General where capital investment has already been made *		\$640,830		
Total annual cost at increased utilization (48 procedures/year) at Vancouver General where capital investment has already been made (no additional capital investment would be required to increase to 48 procedures)*		\$1,207,782		

*excludes all hospitalization costs and intensive care unit costs due to unavailability of data.

*Vancouver General negotiated a discounted price of \$8,963 per probe (current list price \$11,926 per probe)

8.2.1 Capital Costs

Monteris Medical reports that as of November, 2015, a NeuroBlate system is purchased at a one-time cost of \$524,237. Other one-time costs may be required. An accessory kit (Axiis CMB kit) is required for use on brain lesions (\$6,578), and a separate kit is required for epilepsy (\$6,578). A Neuroblate system robotic probe driver is required at a one-time cost of \$2,997. If required, a transportation system, which is used to transport the patient from the operating room to the MRI suite, costs \$111,767. A hospital may choose not to purchase this transportation system, if an adequate system is already in place to transport the patient. Vancouver General Hospital has invested in the NeuroBlate system, mini-bolt accessory kits (2.2mm for epilepsy cases and 3.3 mm for intracranial lesions), and Probe driver; they have not purchased the transportation system. The capital costs, including the machine, probe drivers, transportation system and accessory kits are \$652,157. If the transportation kit is excluded, the capital costs are \$540,390. At the Vancouver General Hospital, these initial costs have been paid for with private funds; however, these costs would need to be considered if expanding LITT outside of the Vancouver General Hospital.

8.2.2 Yearly Costs

A maintenance cost paid to Monteris Medical of \$73,878 per year is required and includes all service calls, both over the phone and in person (if deemed necessary), upgrades, preventative maintenance, and procedural support of an onsite software specialist during LITT procedures.

8.2.3 *Operating Costs*

There are costs associated with each procedure, above and beyond the initial capital costs. For each procedure, at least one mini bolt is required, at a cost of \$1,994. The 3.3mm cranial minibolt is used for lesions and 2.2mm is used for epilepsy cases. Probes must be disposed of after each procedure, and are therefore required for each procedure. Depending on the area to be ablated, between one and four probes will be used per procedure. Monteris Medical incentivizes bulk probe purchasing, by charging \$17,032 for one probe, \$15,327 for twelve to twenty-four probes, \$13,627 for twenty-five to thirty-six probes, and \$11,926 for thirty-seven or more probes. In addition to these costs, the Vancouver General Hospital estimates that disposable supplies in the operating room cost approximately \$704, and medication costs approximately \$150.

Staffing costs are highly dependent on staffing requirements, pay associated with each position, and time spent in the operating room; these costs may vary between procedures and hospitals. Based on clinical experience, the Vancouver General Hospital estimates that the average LITT procedure takes 2.25 hours in the operating room, which costs \$805. Anaesthesia is required, at a cost of approximately \$1,000. The cost associated with MRI use is estimated to be \$572. The neurosurgeon who does the procedure at the Vancouver General Hospital bills using fee 3189; a code used for stereotactic localization during neurosurgery in association with craniotomy. This code is associated with a cost of \$472.23.

At this time the NeuroBlate system can work within existing facilities, although concessions need to be made around timing of procedures in order to not utilize MRI machines when diagnostic imaging needs to be done. No additional facilities are required.

The variable cost per procedure is approximately \$23,623. This cost includes: the cost of the Axiis Cranial Minibolts (assuming two per procedure), the costs for disposable instruments in the operating room, medication costs, laser probe (assuming an average of 2 probes per procedure), the cost of operating room, the cost of anesthesia, the cost of the MRI, and the surgeons time. Importantly, this cost does not include any hospitalization costs, or intensive care unit costs; only the cost of the procedure are presented. A lack of data on hospitalization precluded the inclusion of these costs.

8.2.3.1 Cost of Comparator

Surgery is considered the comparator for LITT. It has been estimated that the cost of surgery for epilepsy, per procedure, is \$35,776⁴⁷. This 2012 estimate is an Ontario based cost from the Ontario Health Technology Assessment Committee, and includes procedure costs, inpatient stay costs and post-surgical follow-up costs. It is important to note that this cost includes post-surgical care; the costs of LITT presented above do not include post-surgical care. In consulting with epilepsy specialists and neurosurgeons, it was determined that for the purpose of this HTA, the cost of surgery for epilepsy would be generalizable to intracranial lesions; it was felt that the cost of surgery would not significantly differ between these two clinical conditions.

8.3 Conclusions

This budget impact analysis estimates that upfront cost of purchasing LITT are \$652,157 with the purchase of a transportation system, or \$540,390 without. Operating costs including the one-use equipment, and operating room time are approximately \$23,623 per procedure. Yearly costs, such as the annual fee for warranty and support are \$73,878.

No economic analyses of LITT compared to surgery have been conducted to date, and therefore, information on cost savings is not available. An economic evaluation would be severely limited with the current clinical data; it remains unknown whether LITT is cost-effective. There is insufficient evidence to determine how many surgeries might be avoided by using LITT.

9 Policy Analysis

Based on the above evidence, policy options were developed. A list of possible options were presented to a group of clinical and policy experts. The options are presented, along with advantages, disadvantages, and implementation considerations in Table 10. Each option is discussed below.

The status quo is not presented as a policy option. The machine used in the Vancouver General Hospital was purchased using private, donated funds and ongoing costs including the cost of the warranty and the probes have also, to date, been covered by this fund. Hospital costs, and costs for the neurosurgeon are currently being covered by public funds. As this fund has finite resources, this method of funding is not a long-term option.

Table 10: Policy Options for LITT

Policy Options	Advantages	Disadvantages	Implementation Considerations
I. Discontinue Use of LITT	<ul style="list-style-type: none"> • Aligned with recommendations from other HTA agencies • Aligns with current weak evidence of clinical effectiveness • Allow for scarce healthcare resources to be reallocated 	<ul style="list-style-type: none"> • Eliminates option for individuals with intracranial lesions who may have no other options and significant disability • Will likely limit possible innovation with LITT in Canada • Eliminates a minimally invasive option that is perceived as a better experience for the patient, compared to a craniotomy • Expertise being developed in LITT will be lost, and no additional expertise developed • Possibility of labelling Canada as 	<ul style="list-style-type: none"> • Neuroblate machine in Vancouver will become obsolete

		unable to adopt or advance innovative technologies	
<p>II. Access with evidence development</p> <ul style="list-style-type: none"> • Support of LITT only within a research context, potentially with limited public funding 	<ul style="list-style-type: none"> • Patients can only access technology within the controlled setting of an organized research study • Encourages the development of a more robust evidence base to evaluate the medical necessity of LITT 	<ul style="list-style-type: none"> • Patients could only access LITT through organized research study • Continued limited capacity to provide procedure • Consuming scarce resources with an intervention of unknown benefit and value • Potentially limits access to a minimally invasive option that is perceived as a better experience for the patient, compared to a craniotomy 	<ul style="list-style-type: none"> • This would require reorganization of current provision • Funding would be required either from a research source or from healthcare • Would require investment in infrastructure to support data collection • the program would be “at-risk” with a possible requirement to obtain research funds on an ongoing basis from competitive funding
<p>III. Limited support of LITT</p> <ul style="list-style-type: none"> • Maintain current rate of LITT procedures with the provision of public funding to cover ongoing costs. No additional funding to increase capacity. 	<ul style="list-style-type: none"> • No requirement to increase capacity • Provides minimally invasive option (although one with uncertain benefit) for individuals with intracranial lesions who may have no other options • Provides a minimally invasive option, although with uncertain benefit, for some individuals with epilepsy • Allows for continued use of what some clinicians perceive to be an intervention that can achieve good clinical outcomes 	<ul style="list-style-type: none"> • Effectiveness literature is very limited; the clinical effectiveness, safety and adverse events remains unknown • Continued limited capacity to provide procedure • Continued limited access to a minimally invasive option that is perceived as a better experience for the patient, compared to a craniotomy • Consuming scarce resources with an intervention of unknown benefit and value 	<ul style="list-style-type: none"> • The current case selection is limited to patients that self-identify and referral from physicians that are aware of the procedure. This may lead to inequitable access and use amongst a patient population that misses ideal candidates. • Once private funds for purchasing probes and yearly fees are used, public funds will be required to cover these costs
<p>IV. Expand support of LITT</p> <p>Expand current rate of LITT procedures with the provision of public funding to increase capacity</p>	<ul style="list-style-type: none"> • Provides a minimally invasive option (although one with uncertain benefit) for individuals with intracranial lesions who may have no other options • Improve access to a minimally invasive option, although with uncertain benefit, for some individuals with epilepsy • Allows for continued use of what some clinicians perceive to be an intervention that can achieve good clinical outcomes • Could establish Vancouver as a center of excellence for LITT in Canada and foster economic and clinical innovation • Improved access to a minimally invasive option that is perceived as a better experience for the patient, compared to craniotomy. 	<ul style="list-style-type: none"> • Effectiveness literature is very limited; the clinical effectiveness, safety and adverse events remains unknown • Not aligned with recommendations from other HTA agencies • Increased consumption of scarce resources with an intervention of unknown benefit and value 	<ul style="list-style-type: none"> • More resources, such as MRI time, and operating room time, will likely be required. Improvements to efficiency could be made with intraoperative MRI. • Additional Neuroblate machines may be required to keep up with demand • Training for additional neurosurgeons may be required

9.1 Discontinue Use of LITT

This policy option is in line with recommendations from other HTA agencies. To date, no HTA agencies have recommended adoption of LITT for epilepsy or intracranial lesions due to lack of evidence. This weak evidence base persists; a limited number of studies (very few with comparative groups) have been published. One advantage of this option is that it would allow for

scarce healthcare resources currently being used by LITT, such as hospital beds, MRIs, and operating rooms, to be reallocated.

This option has disadvantages that need to be considered. Discontinuing LITT will eliminate an option for those who have intracranial lesions, and who may have no other option. These individuals often suffer from significant disability and poor quality of life. Additionally, LITT is a minimally invasive option, and therefore may be a better experience for patients compared to craniotomy. By discontinuing use of this technology, the expertise on LITT will be lost and it is likely that no additional expertise will be developed. Similarly, as British Columbia is currently the only province to have access to LITT, discontinuing use will likely limit other possible innovation within Canada.

An element to consider with this option is that if LITT were to be discontinued in British Columbia, the machine which has been purchased will become obsolete.

9.2 Access with Evidence Development

The access with evidence development policy option would support the use of LITT in a research setting, but would limit its use otherwise.

One advantage of this option is that patients would only be able to access the technology within the setting of an organized research study; a controlled environment, with oversight by an Ethics Board. An organized setting such as this would ensure that the study is stopped if there is evidence of harm, or conversely, if there is overwhelming evidence of benefit. This option would

facilitate the development of a more robust evidence base, which would serve to prove or disprove the necessity of LITT. Contingent on findings, additional funding and expanded capacity may be justified.

A disadvantage of this option is that patients would only be able to access LITT through a research study, and therefore, patients may feel that they have to sign up for the study because it is the only way to receive the treatment. It is unlikely that this option would increase capacity, and therefore, there would still be limited capacity to perform LITT. Although it is presumed that some costs would be covered through research funding (e.g. grants), this option may require limited public funds for expenses not pay for by research funding. If this were to be the case, this option would result in the consumption of be scarce resources by an intervention of unknown benefit and value.

Some consideration would be required when implementing this option. This option would require a reorganization of current provision. It would require an investment in infrastructure to support activities such as data collection. Depending on findings, this option may result in the eventual discontinuation of LITT, or expanded capacity and public funding. If implementing this option, a randomized controlled trial would provide the highest level of evidence with the least potential for bias. Second to a randomized controlled trial, a comparative cohort study would provide the best evidence. This type of study has increased risk of bias, compared to a randomized controlled trial. No randomized controlled trials exist in the literature and only two comparative studies on epilepsy have been published; the addition of either would be a significant contribution to the field.

9.3 Limited Support of LITT

This option is most similar to the current status quo. LITT would continue to be provided at the current rate. There are several advantages and disadvantages of this option.

This option does not require increase capacity. It provides a minimally invasive option, although one with uncertain benefit, for individuals with epilepsy and intracranial lesions. Some individuals with intracranial lesions may have no other options. This would allow for continued use of what some clinicians perceive to be an intervention that can achieve good clinical outcomes.

As discussed, the effectiveness literature on LITT is very limited. As a result, the clinical effectiveness, safety and adverse events remain unknown; funding this technology may or may not result in patient benefit. Resources would be consumed by an intervention that is of unknown value and benefit. Under this option, capacity would not be increased, and therefore, there would still be limited capacity to perform this minimally invasive procedure.

Several implementation considerations merit comment. Private funds are currently being used to cover ongoing costs; however, once these funds are used private funds for purchasing probes and for yearly fees may be required to continue providing LITT at the current rate. Additionally, the current case selection is limited to patients that self-identify and referral from physicians that are aware of the procedure. This may lead to inequitable access and use amongst a patient population that misses ideal candidates.

9.4 Expanded Public Funding

Within this option, additional public funding would be provided for LITT alongside efforts to increase capacity and number of procedures completed per month.

In addition to the benefits outlined in option three, this would provide improved access to a minimally invasive option, although one with uncertain benefit, for individuals with epilepsy and intracranial lesions. This would allow for improved access to some clinicians perceive to be an intervention that can achieve good clinical outcomes. And increasing capacity to provide LITT could establish Vancouver as a center of excellence for LITT in Canada and foster economic and clinical innovation.

This option is not aligned with recommendation from other HTA agencies, who have stated that there is insufficient evidence to recommend adoption of LITT. The effectiveness literature is very limited; this option would result in increased use of a technology where the clinical effectiveness, safety and adverse events remain unknown. It would also result in increased consumption of scarce resources by a technology of unknown benefit and value.

Expanding the capacity to provide LITT would require additional resources, so as MRI time and operating room time. It may be possible to use current resources more efficiently by using an intraoperative MRI, however, funds and space would be required. To keep up with demand, additional Neuroblate machines, and training for neurosurgeons may be required.

10 Conclusions

Through the environmental scan, four technology briefs were identified; none of which recommended the adoption of LITT due to insufficient evidence. However, clinicians report that based on clinical experience, LITT is an effective and minimally invasive option that may be preferred by some patients over a more invasive craniotomy procedure. Published literature on the effectiveness of LITT is very limited; published studies have small sample sizes and use weak study designs. Therefore, effectiveness of LITT is uncertain. No studies were found evaluating the patient experience or quality of life after LITT in patients with epilepsy or intracranial lesions. Based on the available evidence, four policy options were developed: discontinue use of LITT, access with evidence development, limited support of LITT, or expanded public funding.

11 Appendix A: Search Strategy for Patient Perspectives and Quality of Life Systematic Review

MEDLINE (OVID)

1. "laser interstitial thermal therap*".kw,tw.
2. "laser interstitial thermotherap*".kw,tw.
3. "laser induced thermal therap*".kw,tw.
4. "laser induced thermotherap*".kw,tw.
5. "laser thermal therap*".kw,tw.
6. "laser thermotherap*".kw,tw.

7. interstitial laser ablation.kw,tw.
8. "stereotactic laser ablation".kw,tw.
9. "stereotactic laser amygdalohippocampotomy".kw,tw.
10. litt.kw,tw.
11. MRgLITT.kw,tw.
12. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11
13. limit 12 to (english or french)
14. limit 13 to animals
15. limit 13 to (animals and humans)
16. 14 not 15
17. 13 not 16
18. attitude/ or attitude to health/
- 19 "Quality of Life"/
20. "patient acceptance of health care"/ or patient satisfaction/ or patient preference/
21. health behavior/ or patient compliance/ or treatment refusal/
22. (attitudes or behavior* or behaviour* or experiences or perceptions or preference* or "quality of life" or satisfaction).tw.
23. 18 or 19 or 20 or 21 or 22
24. 17 and 23

PubMED

1. (laser interstitial thermal therap* OR laser interstitial thermotherap* OR laser induced thermal therap* OR laser induced thermotherap* OR "laser thermal therap* OR "laser thermotherap* OR interstitial laser ablation OR stereotactic laser ablation OR stereotactic laser amygdalohippocampotomy OR litt OR MRgLITT)[Title/Abstract]
2. (attitude or attitude to health or "Quality of Life" or "patient acceptance of health care" or patient satisfaction or patient preference or health behavior or patient compliance or treatment refusal[MeSH Subjects]
3. (attitudes or behavior* or behaviour* or experiences or perceptions or preference* or "quality of life" or satisfaction)[Title/Abstract]
4. 2 or 3
5. 1 and 4

EMBASE

1. "laser interstitial thermal therap*".kw,tw.
2. "laser interstitial thermotherap*".kw,tw.
3. "laser induced thermal therap*".kw,tw.
4. "laser induced thermotherap*".kw,tw.
5. "laser thermal therap*".kw,tw.
6. "laser thermotherap*".kw,tw.
7. interstitial laser ablation.kw,tw.
8. "stereotactic laser ablation".kw,tw.
9. "stereotactic laser amygdalohippocampotomy".kw,tw.
10. litt.kw,tw.

11. MRgLITT.kw,tw.

12. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11

13. limit 12 to (english or french)

14. limit 13 to animal studies

15. limit 13 to (human and animal studies)

16. 14 not 15

17. 13 not 16

18. exp attitude/ or health behavior/ or exp patient attitude/ or exp "quality of life"/ or

19. (attitudes or behavior* or behaviour* or experiences or perceptions or preference* or "quality of life" or satisfaction).tw.

20. 18 or 19

21. 17 and 20

12 Appendix B: Quality Assessment using Downs and Blacks

<i>Question</i>	Abbott ⁴⁵	Tatsui ⁴⁴	Wietzke-Braun ⁴⁶
<i>1</i>	1	1	1
<i>2</i>	1	1	1
<i>3</i>	1	1	1
<i>4</i>	1	1	1
<i>5</i>	0	0	0
<i>6</i>	1	1	1
<i>7</i>	1	1	1
<i>8</i>	0	1	1
<i>9</i>	1	1	1
<i>10</i>	1	1	0
<i>11</i>	Unclear	1	Unclear
<i>12</i>	Unclear	Unclear	Unclear
<i>13</i>	1	1	1
<i>14</i>	1	0	0
<i>15</i>	0	0	0
<i>16</i>	1	1	1
<i>17</i>	Unclear	1	1

<i>18</i>	1	1	1
<i>19</i>	Unclear	1	1
<i>20</i>	1	1	1
<i>21</i>	Unclear	1	1
<i>22</i>	0	Unclear	1
<i>23</i>	0	0	0
<i>24</i>	0	0	0
<i>25</i>	0	0	0
<i>26</i>	Unclear	Unclear	1
<i>27</i>	1	1	1
<i>Total</i>	14	18	18

13 Appendix C: Search Strategy for Clinical Effectiveness Systematic Review

HTA Calgary LITT Clinical Effectiveness Search Strategy

MEDLINE (OVID)

1. "laser interstitial thermal therap*".kw,tw.
2. "laser interstitial thermotherap*".kw,tw.
3. "laser induced thermal therap*".kw,tw.
4. "laser induced thermotherap*".kw,tw.
5. "laser thermal therap*".kw,tw.
6. "laser thermotherap*".kw,tw.
7. interstitial laser ablation.kw,tw.
8. "stereotactic laser ablation".kw,tw.
9. "stereotactic laser amygdalohippocampotomy".kw,tw.
10. litt.kw,tw.
11. MRgLITT.kw,tw.
12. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11
13. limit 12 to (english or french)
14. limit 13 to animals
15. limit 13 to (animals and humans)
16. 14 not 15
17. 13 not 16
18. exp Epilepsy/
19. (epilepsy or epileptic*).kw,tw.
20. 18 or 19
21. 17 and 20
22. exp Brain Neoplasms/ or exp brain diseases/
23. Glioblastoma/ or glioma/
24. ((intracranial or intra cranial or brain) adj5 (cancer* or carcinoma* or damage or lesion* or metastas* or neoplasm* or tumor* or tumour*)).tw.
25. (glioblastoma* or glioma*).tw.
26. 22 or 23 or 24 or 25
27. 17 and 26

PubMED

1. (laser interstitial thermal therap* OR laser interstitial thermotherap* OR laser induced thermal therap* OR laser induced thermotherap* OR "laser thermal therap* OR "laser thermotherap* OR interstitial laser ablation OR stereotactic laser ablation OR stereotactic laser amygdalohippocampotomy OR litt OR MRgLITT)[Title/Abstract]
2. (epilepsy[MeSH Terms]) OR (epilepsy[Title/Abstract] OR epileptic*[Title/Abstract])
3. ((brain neoplasms OR brain diseases OR Glioblastoma OR glioma[MeSH Terms]))
4. ((intracranial[Title/Abstract] OR intra cranial[Title/Abstract] OR brain)[Title/Abstract] AND (cancer*[Title/Abstract] OR carcinoma*[Title/Abstract] OR damage[Title/Abstract] OR lesion*[Title/Abstract] OR metastas*[Title/Abstract] OR neoplasm*[Title/Abstract] OR tumor*[Title/Abstract] OR tumour*[Title/Abstract]))
5. 2 or 3 or 4
6. 1 and 5
7. Limit 6 to English or French

Cochrane Database of Systematic Reviews

1. "laser interstitial thermal therap*".tw.
2. "laser interstitial thermotherap*".tw.
3. "laser induced thermal therap*".tw.
4. "laser induced thermotherap*".tw.
5. "laser thermal therap*".tw.
6. "laser thermotherap*".tw.
7. interstitial laser ablation.tw.
8. "stereotactic laser ablation".tw.
9. "stereotactic laser amygdalohippocampotomy".tw.
10. litt.tw.
11. MRgLITT.tw.
12. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11
13. (epilepsy or epileptic*).tw.
14. ((intracranial or intra cranial or brain) adj5 (cancer* or carcinoma* or damage or lesion* or metastas* or neoplasm* or tumor* or tumour*)).tw.
15. (glioblastoma* or glioma*).tw.
16. 13 or 14 or 15

17. 12 and 19

Cochrane CENTRAL Register of Controlled Trials

1. "laser interstitial thermal therap*".kw,tw.
2. "laser interstitial thermotherap*".kw,tw.
3. "laser induced thermal therap*".kw,tw.
4. "laser induced thermotherap*".kw,tw.
5. "laser thermal therap*".kw,tw.
6. "laser thermotherap*".kw,tw.
7. interstitial laser ablation.kw,tw.
8. "stereotactic laser ablation".kw,tw.
9. "stereotactic laser amygdalohippocampotomy".kw,tw.
10. litt.kw,tw.
11. MRgLITT.kw,tw.
12. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11
13. exp Epilepsy/
14. (epilepsy or epileptic*).kw,tw.
15. exp Brain Neoplasms/ or exp brain diseases/
16. Glioblastoma/ or glioma/
17. ((intracranial or intra cranial or brain) adj5 (cancer* or carcinoma* or damage or lesion* or metastas* or neoplasm* or tumor* or tumour*)).tw.
18. (glioblastoma* or glioma*).tw.
19. 13 or 14 or 15 or 16 or 17 or 18
20. 12 and 19

EMBASE (OVID)

1. "laser interstitial thermal therap*".kw,tw.
2. "laser interstitial thermotherap*".kw,tw.
3. "laser induced thermal therap*".kw,tw.
4. "laser induced thermotherap*".kw,tw.
5. "laser thermal therap*".kw,tw.
6. "laser thermotherap*".kw,tw.
7. interstitial laser ablation.kw,tw.
8. "stereotactic laser ablation".kw,tw.

9. "stereotactic laser amygdalohippocampotomy".kw,tw.
10. litt.kw,tw.
11. MRgLITT.kw,tw.
12. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11
13. limit 12 to (english or french)
14. limit 13 to animal studies
15. limit 13 to (human and animal studies)
16. 14 not 15
17. 13 not 16
18. exp epilepsy/
19. (epilepsy or epileptic*).kw,tw.
20. 18 or 19
21. 17 and 20
22. exp brain tumor/
23. brain damage/
24. exp glioma/
25. ((intracranial or intra cranial or brain) adj5 (cancer* or carcinoma* or lesion* or metastas* or neoplasm* or tumor* or tumour*)).tw.
26. (glioblastoma* or glioma*).tw.
27. 22 or 23 or 24 or 25 or 26
28. 17 and 27
29. 21 or 28

PsycINFO (OVID)

1. "laser interstitial thermal therap*".kw,tw.
2. "laser interstitial thermotherap*".kw,tw.
3. "laser induced thermal therap*".kw,tw.
4. "laser induced thermotherap*".kw,tw.
5. "laser thermal therap*".kw,tw.
6. "laser thermotherap*".kw,tw.
7. interstitial laser ablation.kw,tw.
8. "stereotactic laser ablation".kw,tw.
9. "stereotactic laser amygdalohippocampotomy".kw,tw.
10. litt.kw,tw.
11. MRgLITT.kw,tw.

12. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11
13. limit 12 to (english or french)
14. exp Epilepsy/
15. (epilepsy or epileptic*).kw,tw.
16. 14 or 15
17. 13 and 16
18. exp Brain Neoplasms/ or exp brain disorders/
19. ((intracranial or intra cranial or brain) adj5 (cancer* or carcinoma* or damage or lesion* or metastas* or neoplasm* or tumor* or tumour*)).tw.
20. glioblastoma*.tw.
21. glioma/
22. glioma*.tw.
23. 18 or 19 or 20 or 21 or 22
24. 13 and 23
25. 17 or 24

14 Appendix D: Downs and Blacks Quality Assessment for Clinical Effectiveness Systematic Review

<i>Question</i>	Drane ⁴⁰	Jethwa ²⁹	Leonardi ^{38,39}	Mohammadi ⁴²	Waseem ⁴¹
1	1	1	1	1	1
2	1	0	1	1	1
3	1	1	1	1	1
4	1	1	1	1	1
5	0	0	0	1	0
6	1	0	1	1	1
7	1	1	1	1	1
8	0	1	0	0	1
9	Unclear	1	1	Unclear	1
10	1	0	0	1	1
11	Unclear	1	1	Unclear	1
12	Unclear	1	1	Unclear	0
13	1	1	1	1	1
14	0	0	0	0	0
15	0	0	0	0	0
16	Unclear	1	1	1	1
17	1	1	1	1	1
18	1	1	1	1	1
19	1	1	1	1	1
20	1	1	1	1	1
21	Unclear	Unclear	Unclear	1	Unclear
22	Unclear	Unclear	Unclear	1	Unclear
23	0	0	0	0	0
24	0	0	0	0	0
25	0	0	0	1	1
26	1	1	1	1	1
27	1	1	1	1	1
<i>Total</i>	14	16	17	19	19

15 Appendix E: Summary of Patient Perspectives Findings

15.1.1 Quality Assessment

Using the Downs and Blacks checklist, the three included studies had total scores of 14⁴⁵, and 18^{44,46} (Table 11). All three studies were clear in their objectives, outcomes, findings and interventions, and all three reported actual p-values, and random variability. None of the included studies blinded outcome assessors, randomized participants, or adjusted for confounding. The full results of the quality assessment can be found in Appendix B.

Table 11: Quality Assessment

Study	Quality Assessment Score (Downs and Blacks Checklist)
Abbott ⁴⁵	14
Tatsui ⁴⁴	18
Wietzke-Braun ⁴⁶	18

15.1.2 Abbott et al.

The study conducted by Abbott et al. assessed the effectiveness of endometrial laser interstitial thermal therapy (eLITT) for women with menorrhagia⁴⁵. This study compared eLITT with three other treatments, cavaterm, endometrial laser ablation, and NovaSure. One-hundred and thirty-nine participants were included in this descriptive cohort study. Outcome of interest, to this systematic review, included Euroqol-5D (EQ-5D) and Short form 12 (SF-12) to assess quality of life before and after treatment across all four treatment modalities.

This study found that using EQ-5D, quality of life after treatment was 0.87 for patients who were treated with eLITT compared to 0.83 for Cavaterm, 0.89 for endometrial laser ablation, and 0.90 for NovaSure⁴⁵. This difference was not statistically significant using a p value of 0.05. Using SF-12 (physical component), quality of life after treatment was 52.57 for patients who were

treated with eLITT, compared to 48.92 for Cavaterm, 51.64 for endometrial laser ablation, and 53.84 for NovaSure. This difference was also not statistically significant. The authors concluded that they “...detected no difference in quality of life measures among the four ablation methods, and using this end point all these second generation procedures seemed equally effective.”⁴⁵

15.1.3 Tatsui et al.

The study conducted by Tatsui et al. assessed the effectiveness of spinal laser interstitial thermotherapy (sLITT) for individuals with malignant compression caused by radioresistant tumors⁴⁴. All patients had documented spinal metastasis from histologies considered to have an unfavourable response to conventional external beam radiation therapy, and patients were excluded if they had acute neurological deficits or a circumferential epidural tumor involving more than 1 vertebral level. Eleven participants (9 males and 2 females) were included in this case series; six had renal cell carcinoma, two had pheochromocytoma, one had melanoma, one had synovial sarcoma, and one had hepatocellular carcinoma. Quality of life was assessed in this study using a visual analogue scale.

This study found that mean preoperative quality of life score was 6.18 (SD 2.27) compared to 4.27 (SD 2.32) 30 days post-operative; a statistically significant improvement, $p=0.035$). Sixty-days after the procedure, quality of life score was 2.8 (SD 1.88, $p=0.01$)⁴⁴. The authors of this study concluded that “Overall, subjective patient satisfaction was very high, and the hospital stay was shorter than that for conventional surgery.”⁴⁴

15.1.4 Wietzke-Braun et al.

The study conducted by Wietzke-Braun et al. assessed the effectiveness of ultrasound guided laser interstitial thermotherapy (US-LITT) for patients with non-resectable liver metastases of colorectal cancer⁴⁶. All patients had primary colorectal cancer with liver metastases; no exclusion criteria were reported. Forty-five participants (30 males and 15 females) were included in this case series. Quality of life was assessed in this study using the Quality of Life Questionnaire C30 from the European Organisation for Research and Treatment of Cancer core questionnaire.

This study found that mean pain was higher one week after LITT, compared to the mean value before ($p < 0.05$), as was mean pain 6 months after initiation compared to the mean value before ($p < 0.05$). However, the authors note these statistically significant differences may not be clinically significant, because there was less than a ten point difference for both; ten points is considered to be the threshold for clinically significant difference using this tool. For physical, emotional, cognitive and social functioning, and global quality of life, the change before and after LITT were not statistically significant. The authors conclude that "...US-LITT procedure is well tolerated and associated with local pain reaction only, which was of short duration."⁴⁶

Table 12 Characteristics of Included Studies

<i>Author, Reference, Year of Publication, Country</i>	<i>Patient Selection</i>	<i>Research methods</i>	<i>Key findings</i>
Abbott, 2003, United Kingdom	<p>Patient Selection: Women with menorrhagia were recruited. Details on recruitment are not reported.</p> <p>Inclusion Criteria: pictorial blood loss assessment chart score above 150, no intrauterine pathology on inpatient or outpatient hysteroscopy, normal endometrial biopsy, uterine length less than 12 cm, premenopausal gonadotropin level, normal Papanicolaou smear, no desire for future childbearing</p> <p>Exclusion Criteria: endometrial hyperplasia and malignancy, active pelvic inflammatory disease, palpable endometriosis, and full-thickness uterine surgery</p> <p>Patient Characteristics: One hundred and thirty-nine participants were included; 55 had Cavaterm, 34 had Endometrial laser ablation, 13 had Endometrial laser interstitial thermal therapy and 37 have NovaSure procedures.</p>	<p>Design: Descriptive cohort study</p> <p>Comparators: Cavaterm, Endometrial laser ablation, NovaSure</p> <p>Outcomes measured: amenorrhea rates, repeat surgery rates, patient satisfaction, and quality of life (EQ-5D, SF-12, sexual activity questionnaire).</p> <p>Follow-up time: 12 months</p>	<ul style="list-style-type: none"> Using EQ-5d, quality of life after treatment was 0.87 for patients who had endometrial laser interstitial thermal therapy, compared to 0.83 for Cavaterm, 0.89 for endometrial laser ablation, and 0.90 for NovaSure. This difference is not statistically significant using a p value of 0.05. Using SF-12 (physical component), quality of life after treatment was 52.57 for patients who had endometrial laser interstitial thermal therapy, compared to 48.92 for Cavaterm, 51.64 for endometrial laser ablation, and 53.84 for NovaSure. This difference is not statistically significant using a p value of 0.05.
Tatsui, 2015, United States	<p>Patient Selection: Participants with spinal metastasis were recruited from the Anderson Cancer Center.</p> <p>Inclusion Criteria: All patients had documented spinal metastasis from histologies considered to have an unfavourable response to conventional external beam radiation therapy</p> <p>Exclusion Criteria: Acute neurological deficits, circumferential epidural tumor involving more than 1 vertebral level.</p> <p>Patient Characteristics: Eleven participants (9 males and 2 females, with a mean age of 56 years (range 33-78) were included. Six had renal cell carcinoma, two had pheochromocytoma, one had melanoma, one had synovial sarcoma, and one had hepatocellular carcinoma. All were treated with spinal laser interstitial thermotherapy.</p>	<p>Design: Case series</p> <p>Comparators: None</p> <p>Outcomes measured: Visual analogue scale for rating quality of life</p> <p>Follow-up time: 12 months</p>	<ul style="list-style-type: none"> Mean preoperative quality of life score was 6.18 (SD:2.27) compared to 4.27 (SD 2.32) 30 days post-operative; a statistically significant improvement, p=0.035). Sixty-days after the procedure, quality of life score was 2.8 (SD 1.88, p=0.01)
Wietzke-Braun, 2003, Germany	<p>Patient Selection: Participants with liver metastases of colorectal cancer were recruited between January 2000 and November 2001.</p> <p>Inclusion Criteria: Primary colorectal cancer with liver metastases, palliative care where patients with progressive disease were undergoing second- or third-line chemotherapies</p> <p>Exclusion Criteria: None reported</p> <p>Patient Characteristics: Forty-five patients (30 males, 15 females), with a mean age of 62 (range 38-79) were included.</p>	<p>Design: Prospective non-randomized study</p> <p>Comparators: None</p> <p>Outcomes measured: The Quality of Life Questionnaire C30 from the European Organisation for Research and Treatment of Cancer core questionnaire</p> <p>Follow-up time: Mean follow-up time of 9.8±0.7 months (range 2-15 months)</p>	<ul style="list-style-type: none"> Mean pain was higher one week after LITT, compared to the mean value before (p<0.05), although the authors note this many not be clinically significant. Mean pain was higher 6 months after initiation compared to the mean value before (p<0.05); however, this difference may not be clinically significant. For physical, emotional, cognitive and social functioning, and global quality of life, the change before and after LITT were not statistically significant.

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