

# NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

## INTERVENTIONAL PROCEDURES PROGRAMME

### Interventional procedure overview of MRI-guided laser interstitial thermal therapy for drug-resistant epilepsy

Epilepsy causes seizures and other symptoms due to abnormal electrical activity in the brain. Patients whose epilepsy does not respond to medications (drug-resistant epilepsy) have other treatment options to control seizures. In this procedure, a small hole is made in the skull and a laser is inserted into the area of the brain (interstitial) causing the seizures. This laser heats up and destroys this area. MRI scanning is used during the procedure to make sure the laser is put in the correct place and to monitor the treatment. The aim is to destroy the part of the brain that is causing seizures

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## Introduction

The National Institute for Health and Care Excellence (NICE) prepared this interventional procedure overview to help members of the interventional procedures advisory committee (IPAC) make recommendations about the safety and efficacy of an interventional procedure. It is based on a rapid review of the medical literature and specialist opinion. It should not be regarded as a definitive assessment of the procedure.

### ***Date prepared***

This overview was prepared in June 2019.

### ***Procedure name***

- MRI-guided laser interstitial thermal therapy for drug-resistant epilepsy

### ***Specialist societies***

- Society of British Neurological Surgeons (SBNS)
- British Paediatric Neurosurgery Group (BPNG)
- Association of British Neurologists (ABN)
- British Paediatric Neurology Association (BPNA)

## Description of the procedure

### ***Indications and current treatment***

Epilepsy is a neurological condition characterised by episodes of abnormal electrical activity in the brain (recurrent seizures). The seizures can be focal or generalised. The main treatment for epilepsy is anti-epileptic drugs taken to prevent or reduce the occurrence of seizures. However, many people with epilepsy have drug-resistant epilepsy, which is refractory to medical treatment (estimates vary between 20% and 40% of people with epilepsy). They experience frequent seizures and are at risk of status epilepticus and sudden unexpected death in epilepsy. If medical therapy fails to control the epilepsy adequately, surgery may be considered. Surgical options include open surgical resection (such as lesionectomy, anterior temporal lobectomy or hemispherectomy) or disconnection (such as multiple subpial transection or corpus callosotomy), neuroablation (for example, with stereotactic radiosurgery, radiofrequency

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thermocoagulation, or MRI-guided focused ultrasound) or neuromodulation (such as cranial nerve stimulation, deep brain stimulation or closed loop stimulation).

### ***What the procedure involves***

MRI-guided laser interstitial thermal therapy (MRgLITT) is a less invasive treatment than open surgery. Preoperatively, an MRI scan is done to identify the part of the brain causing the seizures and to identify the entry location for the laser catheter. The procedure is usually done under general anaesthesia with the patient lying on an MRI couch. A small burr hole is made in the skull and a fine fibreoptic laser catheter is inserted into the target area under stereotactic guidance. Continuous real-time MRI scanning is done to allow visualisation of the exact target area and the surrounding tissue, and to monitor the temperature in the brain during the procedure. Under computer guidance, laser energy is applied to the target area. The laser is switched off and removed when temperatures have reached levels sufficient to cause coagulation necrosis (usually 46°C to 60°C) and the target tissue has been ablated. After the procedure, an MRI is done to verify lesion location and volume of the tissue ablated. The aim is to precisely ablate the target tissue and to minimise damage to the surrounding area. MRgLITT has most commonly been used for patients with a well-defined epileptogenic focus, especially in the temporal lobe, but can be used elsewhere in the brain.

### **Efficacy summary**

#### **Overall seizure freedom (assessed using Engel epilepsy surgery outcome scale from class I to IV)**

A systematic review and meta-analysis of 19 studies of medically intractable temporal lobe epilepsy (including 415 patients) compared MRgLITT (in 9 studies including 250 patients) with stereotactic radiosurgery (SRS in 10 studies including 165 patients). The rate of overall seizure freedom was comparable between the MRgLITT group (50% [125/250], 95% confidence interval [CI] 44% to 56%) and SRS group (42% [86/165], 95% CI 27% to 59%;  $p=0.39$ ). Excluding a randomised controlled trial from the SRS group did not change the results statistically significantly (44%, 95% CI 37% to 50%).<sup>1</sup>

#### **Seizure freedom in lesional pathological conditions**

The systematic review and meta-analysis of 19 studies reported that the rate of lesional seizure freedom in patients with only lesional pathological conditions was comparable between patients who had MRgLITT (62% [108/188], 95% CI 48% to 74%; 9 studies) and those who had SRS (50% [87/157], 95% CI 37% to 66%,  $p=0.23$ ; 9 studies) at 12 to 36 months of follow up.<sup>1</sup>

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### **Frequency of seizures (assessed using the Engel epilepsy surgery outcome scale from class I to IV)**

A systematic review and meta-analysis of data from 16 studies included 8 studies focused on mesial temporal lobe epilepsy (TLE), 3 on TLE, 3 on focal epilepsy, 1 on insular epilepsy and 1 on mesial temporal sclerosis. A total of 269 patients with drug-resistant epilepsy had MRgLITT. This review reported the frequency of seizures using the Engel epilepsy surgery outcome scale (class I to IV). The pooled rate of patients who had freedom from seizures after ablation (Engel class I, reported in 12 studies with 189 patients) was 61% (95% CI, 0.54 to 0.68;  $p=0.302$ ,  $I^2=14.5\%$ ). Estimates ranged from 41% to 88%. The pooled rate of patients who only rarely had disabling seizures or were almost seizure free after ablation (Engel class II, reported in 7 studies with 134 patients) was 12% (95% CI 0.07 to 0.16,  $p=0.000$ ,  $I^2=86.8\%$ ). Estimates ranged from 3% to 65%. The pooled rate of patients who had worthwhile improvement with reduction in the frequency of seizures after ablation (Engel class III, reported in 6 studies with 135 patients) was 16% (95% CI 0.10 to 0.22,  $p=0.397$ ,  $I^2=3.0\%$ ). Estimates ranged between 9% to 27%. The pooled rate of patients who did not have worthwhile improvement or reduced frequency of seizures (Engel class IV, reported in 5 studies with 109 patients) was 15% (95% CI 0.08 to 0.22,  $p=0.330$ ,  $I^2=13.2\%$ ). Estimates ranged from 9% to 27%.<sup>2</sup>

### **Reoperation rate**

The systematic review and meta-analysis of 19 studies reported that the overall rate of reoperations was comparable between patients who had MRgLITT (15% [29/184], 95% CI 9% to 22%; 7 studies) and those who had SRS (27% [11/39], 95% CI 0.12% to 0.46%;  $p=0.10$ ; 4 studies). In the MRgLITT group ( $n=29$ ), 11 patients had repeated LITT and 17 patients had anterior temporal lobectomy (ATL). Follow up in these patients ranged from 8 months to 5 years. In the SRS group 11 patients had ATL.<sup>1</sup>

### **Neurocognitive outcomes**

A review of 4 case series and 3 case reports (including 119 patients, mostly TLE cases but also 1 hypothalamic hamartoma case and 1 insular epilepsy case) compared neurocognitive outcomes of the MRI-guided stereotactic laser ablation for epilepsy with that of the open resection. None of 19 patients (0%) with TLE that had stereotactic laser amygdalohippocampotomy (SLAH) had cognitive decline in the object recognition and naming outcome. In contrast, 95% (21 of 22) patients with language dominance and open resection had a decline in naming manmade objects or a famous person and 65% (11/17) of patients with non-dominance and open resection had cognitive function decline in the recognising famous person task. In terms of episodic memory outcome, 6 out of 30 patients in the SLAH group declined in the verbal contextual memory task. There were 4

out of 10 patients in the SLAH group who had memory decline on a verbal list-learning task.<sup>4</sup>

## Safety summary

### Overall postoperative complications

The systematic review and meta-analysis of 19 studies reported that the pooled rate of overall complications was lower in the MRgLITT group (20% [42/207], 95% confidence interval [CI] 14% to 26%; 8 studies) compared with the SRS group (32% [49/150], 95% CI 20% to 46%,  $p=0.06$ ; 8 studies).<sup>1</sup>

The systematic review and meta-analysis of data from 16 studies reported 26 complications in 101 patients. The pooled rate (in 6 studies) was 24% (95% CI 0.16 to 0.32;  $p=0.629$ ,  $I^2=0\%$ ) and estimates ranged from 15% to 43%. Complications reported included functional effects (such as visual deficit, hemiparesis and expressive language dysfunction), wound complications (oedema, haemorrhage, infection and pain), psychiatric symptoms (anxiety, insomnia and depression) and complications associated with operating the thermal therapy system (improper machine operation, inaccurate fibre placement and failure of the cooling mechanism around the catheter). In 2 studies, some complications resolved within 6-month follow up, including hemiparesis, language dysfunction, wound pain and psychiatric symptoms.<sup>2</sup>

Severe chronic complications needing intervention were reported in 3% (6/127) of patients in a review of MRgLITT for paediatric epilepsy surgery. These included post-ablation contralateral weakness (in 3 patients), short-term memory deficit by injury to the left mammillary body, diabetes insipidus worsening to vasopressin dependence, right lateral ventricle trapping (because of gadolinium extravasation) resulting in obstructive hydrocephalus and bilateral papilledema in 1 patient each.<sup>3</sup>

### Visual field deficits (quadrantanopia, homonymous hemianopia)

Visual field deficits (quadrantanopia, homonymous hemianopia) were the most common complications reported in the MRgLITT group (in 12 patients from 4 studies) from the systematic review and meta-analysis of 19 studies.<sup>1</sup>

### Cranial nerve and neurological deficit (cranial nerve palsy/injury)

Cranial nerve deficits were reported in 8 patients in the MRgLITT group (in 4 studies) in the systematic review and meta-analysis of 19 studies.<sup>1</sup>

### Intracranial and cerebral haemorrhage (intraparenchymal, epidural, intraventricular)

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Cerebral haemorrhage was reported in 4 patients (in 3 studies) in the MRgLITT group in the systematic review and meta-analysis of 19 studies.<sup>1</sup>

Delayed intraparenchymal and intraventricular haemorrhage (in the MRgLITT catheter placement tract) needing craniotomy and surgical evacuation after treatment to an area of periventricular heterotopia near the right lateral ventricle was reported in a case report of 1 patient. After treatment the patient was seizure free but remained on anti-epileptic drugs.<sup>6</sup>

### **Headache, nausea or gait problems**

Headache, nausea or gait problems were reported in 9 patients (in 3 studies) in the MRgLITT group in the systematic review and meta-analysis of 19 studies.<sup>1</sup>

### **Cognitive deficits or psychosis**

Cognitive deficit or psychosis was reported in 1 patient (in 1 study) in the MRgLITT group in the systematic review and meta-analysis of 19 studies.<sup>1</sup>

### **Disabling amnesic syndrome**

Disabling severe amnesia (persistent memory disorder) was reported in a case report of 1 patient who had stereotactic laser ablation of a hypothalamic hamartoma with previous temporal lobectomy. Severe impairment of memory and attention was seen immediately after laser ablation. Repeat MRI showed damage to the bilateral medial mammillary bodies and significant memory loss. Neuropsychological testing showed a dense anterograde amnesia with impaired attention and processing speed. Cognitive and psychological rehabilitation neuropsychological tests reported improved attention, concentration and immediate recall after 8 months, but there were severe deficits in delayed recall. Authors think that persistent memory disorder resulted from a combination of the right temporal lobectomy and injury to the bilateral medial mammillary bodies.<sup>5</sup>

### **Device and procedure-related complications**

There were 2 procedure-related complications reported in the MRgLITT group in the systematic review and meta-analysis of 19 studies. These include thermal injury and faulty trajectory. Further details were not reported.<sup>1</sup>

Complications associated with operating the thermal therapy system (improper machine operation, inaccurate fibre placement, and failure or technical malfunctioning of the cooling mechanism around the catheter) were also reported in the systematic review and meta-analysis of 16 studies. Further details were not reported.<sup>2</sup>

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Software failure and inaccurate catheter fibre placement (with no consequences for the patients) were reported in 1 patient each in a review on MRgLITT for paediatric epilepsy surgery.<sup>3</sup>

### **Other complications**

Transient complications (needing no intervention) were reported in 19% (34/127) patients in a review of MRgLITT for paediatric epilepsy surgery. These included an increase in gelastic seizures (in 9), hemiparesis (in 7), limb weakness (in 5), delayed wound healing (in 4), hypernatraemia (in 3), asymptomatic sub-arachnoid haemorrhage (in 1), oedema (in 1), Horner's syndrome (in 1), stuttering (in 1), expressive language dysfunction (in 1) and short-term memory dysfunction (in 1).<sup>3</sup>

### ***Anecdotal and theoretical adverse events***

In addition to safety outcomes reported in the literature, specialist advisers are asked about anecdotal adverse events (events which they have heard about) and about theoretical adverse events (events which they think might possibly occur, even if they have never happened). For this procedure, specialist advisers did not list any additional anecdotal adverse events. They considered that the following were theoretical adverse events: thermal injury to the brain tissue, infection, mood disorder and memory problems.

## **The evidence assessed**

### ***Rapid review of literature***

The medical literature was searched to identify studies and reviews relevant to MRgLITT for drug-resistant epilepsy. The following databases were searched, covering the period from their start to 24.04.2019: MEDLINE, PREMEDLINE, EMBASE, Cochrane Library and other databases. Trial registries and the Internet were also searched. No language restriction was applied to the searches (see the [literature search strategy](#)). Relevant published studies identified during consultation or resolution that are published after this date may also be considered for inclusion.

The following selection criteria (table 1) were applied to the abstracts identified by the literature search. Where selection criteria could not be determined from the abstracts the full paper was retrieved.

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**Table 1 Inclusion criteria for identification of relevant studies**

Characteristic	Criteria
Publication type	Clinical studies were included. Emphasis was placed on identifying good quality studies. Abstracts were excluded where no clinical outcomes were reported, or where the paper was a review, editorial, or a laboratory or animal study. Conference abstracts were also excluded because of the difficulty of appraising study methodology, unless they reported specific adverse events that were not available in the published literature.
Patient	Patients with drug-resistant epilepsy
Intervention/test	MRI-guided laser interstitial thermal therapy
Outcome	Articles were retrieved if the abstract contained information relevant to the safety, efficacy or both
Language	Non-English-language articles were excluded unless they were thought to add substantively to the English-language evidence base.

***List of studies included in the IP overview***

This IP overview is based on 984 patients from 2 meta-analyses, 2 reviews and 2 case reports. There was an overlap of patients in some studies.

Other studies that were considered to be relevant to the procedure but were not included in the main extraction table (table 2) are listed in the [appendix](#).



## Table 2 Summary of key efficacy and safety findings on MRgLITT for drug-resistant epilepsy

### Study 1 Grewal SS (2019)

#### Details

Study type	<b>Systematic review and meta-analysis</b>
Country	LITT studies (all in USA), SRS studies in USA, France, China, UK, Japan, Czech Republic.
Search period	Search period: inception to May 2018; databases searched: Ovid, Medline, Embase, Cochrane central register of controlled trials, Cochrane database of systematic reviews and Scopus.
Study population and number	<b>n=19 studies (415 patients with medically intractable TLE)</b> <b>9 studies (n=250) on MRgLITT</b> <b>10 studies (n=165) on SRS</b> <b>All retrospective observational studies</b> except 1 RCT on SRS. <u>Lesional pathological type</u> : mesial temporal sclerosis in most of the studies.
Age and sex	Patients who had MRgLITT were older than those who had SRS (mean age 40.9 years versus 29.5 years, p=0.004). Half of the patients were men.
Patient selection criteria	Inclusion criteria: English language studies reporting only temporal lobe-based seizure pathological conditions, describing either MRgLITT or SRS only without any adjunct therapy, reporting seizure and clinical outcomes and minimum 12 months of follow up. Exclusion criteria: pathological conditions not related to epilepsy, reporting outcomes other than Engel classification or complications, duplicate studies, case reports and conference abstracts.
Technique	MRgLITT- ablation under real time MRI guidance and feedback. Visualase therapy was the most common device used. Technique slightly varied across studies. SRS (technique not described in the study)
Follow up	<b>MRgLITT group: median 22.4 months (range 7-70 months) and</b> <b>SRS group: median 43.12 months (range 24 to 112 months)</b>
Conflict of interest/source of funding	None

#### Analysis

**Follow-up issues:** only 1 patient in 1 MRgLITT study had a follow up of less than 12 months.

**Study design issues:** the review was conducted according to the preferred reporting items for systematic reviews and meta-analysis (PRISMA) guidelines. A comprehensive search strategy was used, 2 independent reviewers systematically reviewed and extracted data and any disagreements were resolved by consensus. Risk of bias was assessed using the modified Newcastle-Ottawa Scale. The quality of evidence was assessed using the grading of recommendations assessment, development and evaluation (GRADE) approach and was low. An indirect meta-analysis of seizure freedom (described by the Engel scale) and clinical outcomes (complication and reoperation rates) between both procedures was done.

**Study population issues.** In half of the patients in both groups, the left side was involved. 75% (188/250) patients in MRgLITT group had a lesional pathological condition of which most had mesial temporal sclerosis or hippocampal atrophy and 2 had low grade glioma. 21% had non-lesional pathological condition. 95% (157/165) patients in the SRS group had lesional pathological condition of which most had mesial temporal sclerosis or hippocampal atrophy.

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**Other issues:** seizure freedom outcomes were assessed at different intervals (12 to 36 months)

### Key efficacy and safety findings

Efficacy	Safety																														
<p>Number of patients analysed: <b>415</b> <b>(MRgLITT n=250; 9 retrospective studies) versus SRS (n=165; 9 retrospective studies and 1 RCT)</b></p> <p><b>Overall seizure freedom (assessed by Engel epilepsy surgery outcome scale - class I to IV)</b></p> <p>The overall seizure freedom rate was comparable between the MRgLITT group (50%, 95% CI 44 to 56%) and SRS group (42%, 95% CI 27 to 59%; p=0.39). Excluding an RCT from the SRS group did not change the results statistically significantly (44%, 95% CI 37 to 50%).</p> <p><b>Seizure freedom among patients with lesional epilepsy (n=18 studies)</b></p> <p>Lesional seizure freedom rates among patients with only lesional pathologies were comparable between patients who had MRgLITT (62%, 95% CI 48 to 74%) and those who had SRS (50%, 95% CI 37 to 66%, p=0.23) at 12 to 36 months of follow up.</p>	<p><b>Complications (n=16 studies)</b> <b>(MRgLITT n=207; 8 retrospective studies) versus SRS (n=150; 7 retrospective studies and 1 RCT)</b></p> <p>The rate of overall complications was lower in the MRgLITT group (20%, 95% CI 14 to 26%) compared with the SRS group (32%, 95% CI 20 to 46%, p=0.06).</p> <table border="1" data-bbox="813 611 1503 957"> <thead> <tr> <th></th> <th>MRgLITT</th> <th>SRS</th> </tr> </thead> <tbody> <tr> <td>Visual deficit</td> <td>12</td> <td>21</td> </tr> <tr> <td>Cranial nerve/neurological deficits</td> <td>8</td> <td>2</td> </tr> <tr> <td>Gait problems</td> <td>9</td> <td>1</td> </tr> <tr> <td>Cerebral haemorrhage</td> <td>4</td> <td>1</td> </tr> <tr> <td>Cerebral oedema</td> <td>0</td> <td>11</td> </tr> <tr> <td>Psychosis/cognitive deficits</td> <td>1</td> <td>7</td> </tr> <tr> <td>Other (fatigue, hippocampus not ablated, site infection, death because of asphyxiation)</td> <td>2</td> <td>2</td> </tr> <tr> <td>Headache/Nausea</td> <td>NR</td> <td>NR</td> </tr> <tr> <td>Total</td> <td>36</td> <td>45</td> </tr> </tbody> </table> <p><b>2 procedure-related complications were reported in MRgLITT group. These include thermal injury and faulty trajectory.</b></p> <p><b>Reoperations (n=11 studies)</b></p> <p>The rate of reoperations was comparable between patients who had MRgLITT (15%, 95% CI 9 to 22%) and those who had SRS (27%, 95% CI 0.12 to 0.46%; p=0.10).</p> <p>In the MRgLITT group (n=29), 11 had repeated LITT, 17 patients had ATL. (follow up in these patients ranged from 8 months to 5 years).</p> <p>In the SRS group, n=11 patients had ATL.</p>		MRgLITT	SRS	Visual deficit	12	21	Cranial nerve/neurological deficits	8	2	Gait problems	9	1	Cerebral haemorrhage	4	1	Cerebral oedema	0	11	Psychosis/cognitive deficits	1	7	Other (fatigue, hippocampus not ablated, site infection, death because of asphyxiation)	2	2	Headache/Nausea	NR	NR	Total	36	45
	MRgLITT	SRS																													
Visual deficit	12	21																													
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Psychosis/cognitive deficits	1	7																													
Other (fatigue, hippocampus not ablated, site infection, death because of asphyxiation)	2	2																													
Headache/Nausea	NR	NR																													
Total	36	45																													
<p>Abbreviations used: ATL, anterior temporal lobectomy; ES, effect size; MRgLITT, MRI-guided laser interstitial thermal therapy; NR, not reported; RCT, randomised controlled trial; SRS, stereotactic radiosurgery; TLE, temporal lobe epilepsy</p>																															

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## Study 2 Xue F (2018)

### Details

Study type	Systematic review and meta-analysis
Country	Review was done in China (studies mainly from USA and 1 from Canada)
Search period	Search period: inception to May 2018; databases searched: PubMed, Medline, Embase Hand searching of journals and screening of reference lists were done.
Study population and number	<b>n=16 observational studies (269 patients with treatment resistant epilepsy)</b> 8 studies on mesial temporal lobe epilepsy (MLTE), 3 studies on temporal lobe epilepsy and 3 on focal epilepsy
Age and sex	Age range 13 to 60 years; sex not reported
Patient selection criteria	Inclusion criteria: English language studies, of patients with epilepsy who were medically resistant with focal onset of seizures, treated with MRgLITT done in a standard manner, with comparable data that evaluated the efficacy of MRgLITT. Exclusion criteria: studies without assessable data, letters, reviews, commentaries.
Technique	MRgLITT- ablation under real time MRI guidance 2 types of devices were used (Visualase and Neuroblate).
Follow up	<b>7 days to 51 months</b>
Conflict of interest/source of funding	None

### Analysis

**Follow-up issues:** short follow-up period

**Study design issues:** the review was conducted according to the preferred reporting items for systematic reviews and meta-analysis (PRISMA) guidelines. A comprehensive search strategy was used, 1 independent reviewer systematically reviewed and extracted data and any disagreements were resolved by consensus with another reviewer. Risk of bias was assessed using the methodological index for non-randomised studies (MINORS) and scores ranged from 13-16 which indicated a low risk. A meta-analysis of postoperative seizure control (assessed by Engel scale) and complications was done.

**Study population issues:** four studies included both adult and juvenile patients.

**Other issues:** studies with small sample size

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**Key efficacy and safety findings**

Efficacy					Safety
Number of patients analysed: <b>269</b>					<p><b>Postoperative complications</b></p> <p>26 complications were reported in 101 patients. The pooled rate in 6 studies was 24% (95% CI 0.16 to 0.32; <math>p=0.629</math>, <math>I^2=0\%</math>) and estimates ranged from 15 to 43%.</p> <p>Complications reported include functional effects (such as visual deficit, hemiparesis, expressive language dysfunction), wound complications (oedema, haemorrhage, infection and pain), psychiatric symptoms (anxiety, insomnia, and depression) and complications associated with operating the thermal therapy system (improper machine operation, inaccurate fibre placement and failure of the cooling mechanism around the catheter). Further details were not reported.</p>
<b>Frequency of seizures (assessed using the Engel epilepsy surgery outcome scale -class I to IV)</b>					
Studies (patients)	Engel classification	Pooled effect size (95% CI)	Range of estimates %	P value	
N=12 (189)	Class I (free from disabling seizures)	61% (95% CI, 0.54–0.68)	41-88%	$I^2=14.5\%$ ; $P=0.302$	
N=12 (135)	Class II (a rare occurrence of disabling seizures or almost seizure free)	12% (95% CI, 0.07–0.16)	3-65%	$I^2=86.8\%$ ; $P=0.000$	
N=6 (135)	Class III (worthwhile improvement with reduction in frequency of seizures)	16% (95% CI, 0.10–0.22)	9-27%	$I^2=3.0\%$ ; $P=0.397$	
N=5 (109)	Class IV (no worthwhile improvement or reduction in frequency of seizures)	15% (95% CI, 0.08–0.22)	9-27%	$I^2=13.2\%$ ; $P=0.330$	
Abbreviations used: MRgLITT, MRI-guided laser interstitial thermal therapy; MLTE, mesial temporal lobe epilepsy.					

### Study 3 Hoppe C (2018)

#### Details

Study type	Systematic review
Country	Germany
Search period	Search period: inception to August 2018; databases searched: PubMed; screening of reference lists done.
Study population and number	<b>n=25 case reports/series (179 paediatric patients with severe epilepsy who had MRgLITT)</b> Underlying aetiologies: hypothalamic hamartomas 64% (115/179), pharmacological intractable structural epilepsies in childhood such as focal cortical dysplasia (n=16), tuberous sclerosis complex (n=11), mesial temporal sclerosis (n=7) or periventricular heterotopia (n=3), anterior 2/3 callosotomy (n=1), non-lesional epilepsies (n=13), frontal lobe epilepsy (n=1), low grade glioma (n=3) and not defined in (n=11).
Age and sex	not reported
Patient selection criteria	Inclusion criteria: paediatric patients with epilepsy (children below 18 years of age [as per European definition of minors]) and reviews on LIIT for therapy-refractory epilepsy in children.
Technique	MRgLITT- ablation under real time MRI guidance 2 types of devices are used (Visualase and Neuroplate).
Follow up	<b>Varied</b>
Conflict of interest/source of funding	None

#### Analysis

**Follow-up issues:** follow-up intervals varied from 1 month to several years.

**Study design issues:** searches were not comprehensive; most studies were retrospective case series or case reports about the feasibility of this treatment, quality assessment of studies was not done, narrative analysis of outcomes was reported. Engel seizure outcome classes were reported in some studies and in some they were reconstructed. No systematic neuropsychological evaluation with standardised psychometric measures was done in any of the studies.

**Study population issues:** small sample size, only 4 studies included more than 10 patients.

**Key efficacy and safety findings**

Efficacy		Safety	
No of patients analysed: <b>179</b>		<b>Complications</b>	
<b>Seizure outcomes</b>			<b>n (%)</b>
	<b>n=127 (%)</b>	None	140 (78.2)
Engel class I	73 (57.5)	<b>Severe chronic complications (needing intervention)</b>	<b>6 (3.4)</b>
Engel class II	9	Post-ablation contralateral weakness	3
Engel class III (including >50% reduction in seizure frequency and reports of worthwhile improvement)	36	Short-term memory deficit (by injury to left mamillary body)	1
Engel class IV	8	Diabetes insipidus worsened to vasopressin dependence	1
None	1	Gadolinium extravasation into right lateral ventricle, 9 months later right lateral ventricle trapped resulting in obstructive hydrocephalus and bilateral papilledema needing intervention	1
<b>Seizure outcome for patients with HH (different seizure types)</b>		<b>Transient (no intervention needed)</b>	<b>34 (19)</b>
Gelastic seizures class 1	72	Increase in gelastic seizures	9
Gelastic seizures class 2	1	Hemiparesis	7
Gelastic seizures class 5	1	Limb weakness	5
Secondary seizures class 1	3	Delayed wound healing	4
Secondary seizures class 5	1	Hyponatremia	3
Several studies reported that therapeutic effect on seizures occurred immediately after the procedure.		Sub-arachnoid haemorrhage (asymptomatic)	1
<b>Cognitive outcomes</b>		Oedema	1
	<b>N (%)</b>	Horner's syndrome (ipsilateral)	1
Not reported	173 (96.6)	Stuttering	1
No cognitive decline	1	Expressive language dysfunction	1
		Short-term memory dysfunction	1
		<b>LITT related complications</b>	<b>2 (1.1)</b>
		Software failure (no consequence for patient)	1
		Inaccurate fibre placement (no consequence for patient)	1
		<b>Total complications</b>	<b>42 (23.5)</b>
Abbreviations used: MRgLITT, MRI-guided laser interstitial thermal therapy.			

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## Study 4 Drane DL (2018)

### Details

Study type	<b>Review</b>
Country	USA
Search period	Search period: 2016-2017; databases searched: PubMed; screening of reference lists done.
Study population and number	<p><b>n=6 studies (4 case series and 3 case reports)</b></p> <p><b>Case series</b>            (Drane DL 2015) prospective study comparing TLE patients having SLAH (n=19) with those having open resection procedures (n=39)            (Waseem 2015) TLE patients having SLAH (n=7) compared with a selective amygdalohippocampectomy procedure (n=7)            (Kang 2016, n=20 SLAH patients; Jermakowicz 2017, n=23 SLAH patients): retrospective studies</p> <p><b>Case reports</b>            Zubkov 2015: 1 patient who had previously had a right ATL had ablation of a hypothalamic hamartoma            Hawasli 2014:1 patient with post-stroke epilepsy had SLAH procedure involving the insular cortex.            Dredla 2016: 2 TLE patients who had SLAH</p>
Age and sex	not reported
Patient selection criteria	Only studies focused on cognitive function outcomes after epilepsy surgery using magnetic resonance-guided stereotactic laser ablation (SLA) were examined (including case studies)
Technique	MRgLITT- ablation under real time MRI guidance 2 types of devices (Visualase or Neuroblate) were used.
Follow up	<b>Varied</b>
Conflict of interest/source of funding	Author received grants from National institute of Health and also from the manufacturer.

### Analysis

**Follow-up issues:** follow-up intervals varied from 1 month to several years.

**Study design issues:** searches were not comprehensive; studies were prospective or retrospective case series or case reports about the feasibility of this treatment, quality assessment of studies was not done, narrative analysis of outcomes was reported. Only one study was reported using own comparative data, the other studies used historical data to compare.

**Study population issues:** The review only covered cognitive outcome in adults. One study in the review only examined cognitive outcome in older patients, some of whom had significant comorbidities.

**Key efficacy and safety findings**

Efficacy	Safety																											
<p>No of patients analysed: <b>119</b></p> <p><b>1. Object Recognition and Naming Outcome</b></p> <p>Drane et al. 2015 reported these cognitive outcomes for select functions which are likely supported by extra-mesial temporal lobe region.</p> <table border="1" data-bbox="110 514 1112 724"> <thead> <tr> <th rowspan="2">Cognitive outcomes</th> <th colspan="2">Number of patients with declined outcomes (%)</th> </tr> <tr> <th>Open resection</th> <th>SLAH</th> </tr> </thead> <tbody> <tr> <td>Naming of manmade objects and/or famous person</td> <td>21/22 (95) *</td> <td>0/10(0)</td> </tr> <tr> <td>Recognising famous person:</td> <td>11/17(65) ^</td> <td>0/9(0)</td> </tr> </tbody> </table> <p>* 22 patients from open resection were TLE patients having language dominant open resection ^17 patients had right(non-dominant) open resection SLAH groups were any dominant.</p> <p><b>2. Episodic Memory Outcome</b></p> <p><b>Verbal contextual memory task (Logical memory substest from the 4<sup>th</sup> edition of the Wechsler Memory Scale)</b></p> <table border="1" data-bbox="110 1012 1112 1186"> <thead> <tr> <th>Studies</th> <th>No. of SLAH patients with declined outcome (%)</th> </tr> </thead> <tbody> <tr> <td>Kang et al. 2016</td> <td>0/6(0)</td> </tr> <tr> <td>Jermakowicz et al. 2017</td> <td>3/20(15)</td> </tr> <tr> <td>Waseem et al. 2015</td> <td>1/4 (25)</td> </tr> <tr> <td>Dredla et al. 2016</td> <td>2/2(100)</td> </tr> </tbody> </table> <p>3 of 20 patients from Jermakowicz et al. declined on the learning portion of the verbal contextual memory task. Similarly, 1 of 4 patients from Waseem et al. studies declined on the learning portion of the task, while none of the four patients declined on delayed recall. All the four patients from Waseem et al. 2015 were older patients with temporal lobe epilepsy.</p> <p>Both patients from Dredla et al. were PET-positive, MRI-negative with adult onset of seizures (higher risk of decline). One patient had history of encephalitis. Both patients had significant declined on verbal and visual memory measures but no decline in naming, verbal fluency and other assessed cognitive functions. Both patients were assessed during early stages of recovery (3 to 4 months) and did not return subsequent follow up.</p> <p>The review compared these results of the contextual learning task of SLAH with historical data from the literature for the open resection procedures for TLE, which was about 30 to 50%.</p> <p><b>Verbal list-learning task (2<sup>nd</sup> edition of the California Verbal Learning test)</b></p> <table border="1" data-bbox="110 1648 1112 1774"> <thead> <tr> <th>Studies</th> <th>No. of SLAH patients with declined outcome (%)</th> </tr> </thead> <tbody> <tr> <td>Kang et al. 2016</td> <td>3/6(50) *</td> </tr> <tr> <td>Waseem et al. 2015</td> <td>1/4 (25) ^</td> </tr> </tbody> </table>	Cognitive outcomes	Number of patients with declined outcomes (%)		Open resection	SLAH	Naming of manmade objects and/or famous person	21/22 (95) *	0/10(0)	Recognising famous person:	11/17(65) ^	0/9(0)	Studies	No. of SLAH patients with declined outcome (%)	Kang et al. 2016	0/6(0)	Jermakowicz et al. 2017	3/20(15)	Waseem et al. 2015	1/4 (25)	Dredla et al. 2016	2/2(100)	Studies	No. of SLAH patients with declined outcome (%)	Kang et al. 2016	3/6(50) *	Waseem et al. 2015	1/4 (25) ^	<p>This review reported only 1 adverse event (severe amnesic syndrome) which is the same case as study 5 below.</p>
Cognitive outcomes		Number of patients with declined outcomes (%)																										
	Open resection	SLAH																										
Naming of manmade objects and/or famous person	21/22 (95) *	0/10(0)																										
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<p>*It was the learning portion of the verbal list-learning task that these 3 patients had decline. The two of these patients also exhibited decline of their subsequent recall of the information.</p> <p>^ 2 of 4 patients actually showed improvement on delayed recall portion of a complex list-learning task (Rey Auditory Verbal Learning Test).</p>	
<p>Abbreviations used: ATL, anterior temporal lobectomy; MRgLITT, MRI-guided laser interstitial thermal therapy; SLAH, stereotactic laser amygdalohippocampectomy; TLE; temporal lobe epilepsy,</p>	

## Study 5 Zubkov S (2015)

### Details

Study type	Case report
Country	USA
Recruitment period	Not reported
Study population and number	n=1 patient with cortical dysplasia and intractable focal seizures who had a right temporal lobectomy subsequently had a hypothalamic hamartoma.
Age and sex	19-year-old man
Patient selection criteria	-
Technique	MRgLITT- ablation under real time MRI guidance
Follow up	<b>8 months</b>
Conflict of interest/source of funding	None

### Key efficacy and safety findings

Efficacy	Safety
<p>No of patients analysed: 1</p> <p><b>Disabling amnesic syndrome</b></p> <p>A severe impairment of memory and attention was observed immediately after laser ablation. Patient reported feeling events happening in a disjointed fashion. Three weeks later, he was hospitalised for agitation and suicidal intention and was diagnosed with a severe amnesic syndrome with confabulation.</p> <p>Video-EEG monitoring captured several complex partial seizures with impaired responsiveness and bilateral ictal discharges. Repeat MRI showed successful ablation of the hamartoma but also persistent right fornix and bilateral medial mammillary body atrophy.</p> <p>Neuropsychological testing revealed a dense anterograde amnesia with impaired attention and processing speed. These findings were attributed to bilateral mammillary body involvement. Patient had intense cognitive and psychological rehabilitation.</p> <p>Neuropsychological testing at 8 months demonstrated improved attention, concentration, and immediate recall but severe deficits in delayed recall (significant memory loss).</p> <p>Clinically, he had a disabling amnesic syndrome so deferred his education and is unable to drive because of ongoing seizures. Authors think that his persistent memory disorder resulted from a combination of the right temporal lobectomy and injury to the bilateral medial mammillary bodies.</p> <p>Abbreviations used: EEG, electroencephalogram; MRgLITT, MRI-guided laser interstitial thermal therapy</p>	

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## Study 6 Barber SM (2017)

### Details

Study type	Case report
Country	USA
Recruitment period	Not reported
Study population and number	n=1 patient with intractable epilepsy.
Age and sex	18-year-old male
Patient selection criteria	-
Technique	MRgLITT- ablation under real time MRI guidance to an area of periventricular heterotopia (3 epileptogenic foci) near the right lateral ventricle with Visualase. After 21 months, because of persistent seizures patient had LITT to the previously untreated area of heterotopia near the right ventricle.
Follow up	<b>Postoperative period</b>
Conflict of interest/source of funding	None

### Key efficacy and safety findings

Efficacy	Safety
No of patients analysed: 1 <b>Delayed intracranial haemorrhage needing evacuation</b>	
<p>Patient was discharged after the procedure on day 1 but returned on day 9 with headache and left hemiparesis. He had an intraparenchymal and intraventricular haemorrhage in the MGgLITT catheter placement tract. CT angiography revealed a small vascular abnormality near the focus of haemorrhage suspicious for pseudoaneurysm formation and trapping of the right lateral ventricle.</p> <p>The patient declined neurologically and had craniotomy and haemorrhage evacuation. Several small vessels along the choroid plexus within the right lateral ventricle bleeding were coagulated but no further source of bleeding identified. He eventually recovered and was discharged to inpatient rehabilitation with persistent left hemiparesis. He was seizure free but remained on anti-epileptic drugs.</p>	
Abbreviations used: MRgLITT, MRI-guided laser interstitial thermal therapy.	

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## Validity and generalisability of the studies

- There are 2 devices (Visualase and Neuroblate) used for this procedure and currently there is no standard method for MRgLITT and it is still evolving.
- There are no prospective randomised comparative studies between MRI-guided LITT and other surgical techniques, minimally invasive techniques (such as radio-surgical techniques,) or non-invasive techniques (such as MRI-guided focused ultrasound surgery) for both adults and children. Only matched historical controls have been used to make comparisons. Most of the studies were small cohort studies.
- Two meta-analyses of MRgLITT mainly focused on drug-resistant or medically intractable mesial temporal lobe epilepsy with curative intent mainly in adult patients. Studies included in the analysis were mainly retrospective case series with small sample size and short-term follow up.
- There is limited evidence on the use of MRgLITT for paediatric epilepsy (including other epileptogenic lesions such as HH, mesial temporal sclerosis, cortical dysplasia). Smaller studies, mainly case series or reports included in a review assessed the use of MRI-guided LITT in varied locations and pathological lesions associated with epilepsy.
- Engel classification (EC) is most commonly used measure to describe seizure outcomes, and usually has been performed at 6-month follow up. rate of seizure freedom at 1–2 years was between 40-60%.
- There is inadequate data on the neuropsychological outcomes.
- There were no studies evaluating quality of life outcomes or patient experiences.

## Existing assessments of this procedure

On 8 November 2018, the FDA issued a [letter](#) to healthcare providers about risk of tissue overheating because of inaccurate magnetic resonance thermometry readings displayed during the use of MRgLITT devices. The new

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recommendations were an update to an April 2018 FDA [warning](#). The agency continued to reiterate their previous safety alert which recommended that providers consider, and discuss with patients, the benefits and risks of these devices, as well as any alternative treatment modalities on a case-by-case basis. They also suggested that healthcare providers to be aware and review the new information from the MRgLITT manufacturers and recommended some precautionary actions to be taken during the procedure, if an MRgLITT device is determined to be the best available treatment. The two manufacturers that market MRgLITT devices, including Medtronic, and Monteris Medical, have also provided updated information with suggested procedural techniques for MRgLITT devices to reduce unintended thermal damage<sup>7</sup>.

The HTA unit at the University of Calgary in Canada, published an HTA and policy analysis report in 2016 on laser interstitial thermal therapy for treating intracranial lesions and epilepsy included 2 non-randomised controlled studies on patients with epilepsy. One study found statistically significant improvements on famous face recognition and common names using LITT compared with surgical resection. The other found that seizure freedom did not statistically significantly differ although length of stay and surgical time were statistically significantly reduced for the LITT patients, compared with those who had surgical resection. The report concluded that published literature on the effectiveness of LITT is very limited and published studies have small sample sizes and used weak study designs<sup>8</sup>.

A rapid review of the clinical effectiveness and cost-effectiveness of MRgLITT for brain tumours and epilepsy published by the Canadian Agency for Drugs and Technologies in Health (CADTH) in 2015 included 2 prospective case series on epilepsy ((Waseem et al., 2015, 14 patients; Drane et al., 2015, 58 patients). The authors concluded that the quantity and quality of the available evidence on clinical efficacy was limited for epilepsy treatment (mainly derived from case series with limitations and biases)<sup>9</sup>. An update of this review in 2019 considered 1 recent systematic review (Grewal et al 2019) on epilepsy that included mainly low-quality retrospective and prospective studies. Evidence suggests that 'LITT proffers no advantage over stereotactic radiosurgery in inducing seizure freedom in patients with drug-resistant, medically-intractable temporal lobe epilepsy. Relative to patients who were treated with stereotactic radiosurgery, patients treated with LITT appeared to experience fewer adverse events and complications. No comparative evidence on disease progression, overall survival, hospitalization, or quality of life was found. None of the studies reported on the incidence of epileptic episodes, post-operative pain, use of medication, or hospital readmissions'<sup>10</sup>.

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## Related NICE guidance

Below is a list of NICE guidance related to this procedure.

### NICE guidelines

- The epilepsies: The diagnosis and management of the epilepsies in adults and children in primary and secondary care. NICE clinical guideline 20 (2004). Available from [www.nice.org.uk/guidance/CG20](http://www.nice.org.uk/guidance/CG20)
- [Epilepsies: diagnosis and management](#) NICE clinical guideline 137 (2012, updated 2018). Available from [www.nice.org.uk/guidance/CG137](http://www.nice.org.uk/guidance/CG137)

## Additional information considered by IPAC

### *Specialist advisers' opinions*

Specialist advice was sought from consultants who have been nominated or ratified by their Specialist Society or Royal College. The advice received is their individual opinion and is not intended to represent the view of the society. The advice provided by specialist advisers, in the form of the completed questionnaires, is normally published in full on the NICE website during public consultation, except in circumstances but not limited to, where comments are considered voluminous, or publication would be unlawful or inappropriate. Six Specialist Adviser Questionnaires for MRgLITT for epilepsy were submitted and can be found on the [NICE website](#).

### *Patient commentators' opinions*

NICE's Public Involvement Programme will send questionnaires to NHS trusts for distribution to patients who had the procedure (or their carers). When NICE has received the completed questionnaires, these will be discussed by the committee.

### *Company engagement*

A structured information request was sent to 1 company who manufacture a potentially relevant device for use in this procedure. NICE received 1 completed

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submission. This was considered by the IP team and any relevant points have been taken into consideration when preparing this overview.

### ***Issues for consideration by IPAC***

- IPAC to note that the FDA has issued a safety alert of issues with MRgLITT devices that could result in tissue overheating and it provided some recommendations for healthcare providers.
- Three ongoing studies are currently registered on clinical trials.gov
  - NCT03489187: Visualase Visualisation database (VIVID-1), a retrospective observational study of clinical images and associated technical files from commercial cases using the Visualase Thermal Therapy System (VTTS), n=210, completion date October 2019, location USA.
  - NCT02844465: The SLATE study: designed to evaluate the safety and efficacy of the Visualase MRI-guided laser ablation system for drug resistant mesial temporal epilepsy (MTLE), single group assignment, n=150, completion date May 2022, location USA, follow up – 12 months, outcomes: freedom from seizures, HRQoL, adverse events and neuropsychological outcomes.
  - NCT02820740: Feasibility Study on Laser Interstitial Thermal Therapy Ablation for the Treatment of Medical Refractory Epilepsy (FLARE), Multicenter, open-label, prospective designed study. N=30, completion date December 2019, Location – USA, follow up – 2 years. Primary outcomes: 1. Adverse events, 2. Changes in neuropsychological functioning. Secondary: changes in seizure frequency, changes in quality of life, surgical outcome classification.

## References

1. Grewal S., Alvi MA, Lu VM et al. (2019) Magnetic resonance-guided laser interstitial thermal therapy versus stereotactic radiosurgery for medically intractable temporal lobe epilepsy: A systematic review and meta-analysis of seizure outcomes and complications. *World Neurosurgery* (122) e32-e47
2. Xue F, Chen T and Sun H (2018) Postoperative outcomes of magnetic resonance imaging (MRI)-guided laser interstitial thermal therapy (LITT) in the treatment of drug-resistant epilepsy: A meta-analysis. *Medical Science Monitor* (24) 9292-9
3. Hoppe C, Witt J-A et al. (2018) Laser interstitial thermotherapy (LiTT) in paediatric epilepsy surgery. *European Journal of Epilepsy* (Article in press) <https://doi.org/10.1016/j.seizure.2018.12.010>
4. Drane DL. (2018) MRI-guided stereotactic laser ablation for epilepsy surgery: promising preliminary results for cognitive outcome. *Epilepsy Res.* 142: 170–5
5. Zubkov S, Del Bene VA et al. (2015) Disabling amnesic syndrome following stereotactic laser ablation of a hypothalamic hamartoma in a patient with a prior temporal lobectomy. *Epilepsy & Behavior Case Reports* (4) 60-2
6. Barber SM, Tomycz L et al. (2017) Delayed intraparenchymal and intraventricular haemorrhage requiring surgical evacuation after MRI guided laser interstitial thermal therapy for lesional epilepsy. *Stereotactic Functional Neurosurgery* 95; 73-8
7. U.S. Food and Drug Administration. (2018) Update regarding risk of tissue overheating due to inaccurate magnetic resonance thermometry. [online] Available at: <https://www.fda.gov/medical-devices/letters-health-care-providers/update-regarding-risk-tissue-overheating-due-inaccurate-magnetic-resonance-thermometry> [Accessed 19 Jul. 2019]
8. Legget LE, Coward S et al. (2016) 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
9. Canadian Agency for Drugs and Technologies in Health. (2015) Laser interstitial thermal therapy for intracranial lesions and epilepsy: a review of the clinical effectiveness, cost-effectiveness and guidelines. (*CADTH Rapid response: summary with critical appraisal*).
10. Williams D, Loshak H. 2019 Laser interstitial thermal therapy for epilepsy and/or brain tumours: a review of the clinical effectiveness and cost-

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effectiveness. Ottawa: CADTH Jun (*Rapid response report: summary with critical appraisal*).

## Literature search strategy

Databases	Date searched	Version/files
Cochrane Database of Systematic Reviews – CDSR (Cochrane)	24/04/2019	Issue 4 of 12, April 2019
Cochrane Central Database of Controlled Trials – CENTRAL (Cochrane)	24/04/2019	Issue 4 of 12, April 2019
HTA database (CRD website)	24/04/2019	n/a
MEDLINE (Ovid)	24/04/2019	1946 to April 23, 2019
MEDLINE In-Process (Ovid)	24/04/2019	1946 to April 23, 2019
MEDLINE Epubs ahead of print (Ovid)	24/04/2019	April 22, 2019
EMBASE (Ovid)	24/04/2019	1974 to 2019 April 23
BLIC (British Library)	24/04/2019	n/a

### MEDLINE search strategy

The following search strategy was used to identify papers in MEDLINE. A similar strategy was used to identify papers in other databases.

- 1 exp Epilepsy/ (106514)
- 2 (epilep\* or aura\*).tw. (132534)
- 3 ((tempor\* or tube\*) adj4 sclerosis).tw. (7880)
- 4 ((focal\* or general\* or gelast\* or dacryst\* or hippocamp\* or (drug-resist\* or "drug resist\*")) adj4 (seizure\* or convuls\*)).tw. (16140)
- 5 Seizures/ (51120)
- 6 Hypothalamic Neoplasms/ (720)
- 7 (hypothal\* adj4 hamartom\*).tw. (655)
- 8 "Malformations of Cortical Development"/ (1200)
- 9 (corti\* adj4 dysplas\*).tw. (2325)
- 10 Periventricular Nodular Heterotopia/ (162)
- 11 (Periventric\* adj4 heterotop\*).tw. (410)
- 12 (solitar\* adj4 lesion\*).tw. (3225)
- 13 (TLE or MTLE or HH or FCD or TSC or PVH).tw. (16690)
- 14 or/1-13 (214502)
- 15 Magnetic Resonance Imaging/ (373234)
- 16 (magnet\* adj4 (resonan\* or (transfer\* adj4 contrast\*))) adj4 (imag\* or tomograph\*).tw. (200612)
- 17 (MRI or MRIs or FMRI or NMR).tw. (335574)
- 18 (proton\* adj4 spin\* tomograph\*).tw. (38)

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- 19 ((spin\* or shift\*) adj4 (echo\* or chemic\*) adj4 imag\*).tw. (5665)
- 20 zeugmatograph\*.tw. (35)
- 21 or/15-20 (594433)
- 22 Laser Therapy/ (36517)
- 23 (laser\* adj4 interstit\* adj4 therm\* adj4 therap\*).tw. (164)
- 24 (((laser\* adj4 induc\*) or "laser\* induc\*" or laser-induc\*) adj4 therm\*).tw. (532)
- 25 (laser adj4 (ablat\* or thermoablat\* or thermo-ablat\*)).tw. (6825)
- 26 LITT.tw. (361)
- 27 or/22-26 (40869)
- 28 14 and 21 and 27 (79)
- 29 MRgLITT.tw. (34)
- 30 ((stereotact\* or stereotax\*) adj4 laser\*).tw. (125)
- 31 (laser\* adj4 (thermocoag\* or thermo-coag\*)).tw. (35)
- 32 SLAH.tw. (18)
- 33 Visualise.tw. (1955)
- 34 or/29-33 (2152)
- 35 14 and 34 (75)
- 36 28 or 35 (119)
- 37 NeuroBlate.tw. (7)
- 38 36 or 37 (123)
- 39 animals/ not humans/ (4540337)
- 40 38 not 39 (120)
- 41 limit 40 to english language (115)

## Appendix

The following table outlines the studies that are considered potentially relevant to the IP overview but were not included in the main data extraction table (table 2). It is by no means an exhaustive list of potentially relevant studies.

Article	Number of patients/follow up	Direction of conclusions	Reasons for non-inclusion in table 2
Alexander H, Cobourn K et al (2019). Magnetic resonance-guided laser interstitial thermal therapy for the treatment of non-lesional insular epilepsy in pediatric patients: thermal dynamic and volumetric factors influencing seizure outcomes. <i>Childs Nervous System</i> (35) 3 453-61	Case series n-5 paediatric patients with insular epilepsy who had sEEG directed MRgLITT. Follow up: 104 days	Four patients had sEEG directed MRgLITT of insular epileptogenic foci. The ablation volume was higher in patients with Engel I outcome (3.93 cm) compared to Engel II-IV outcome (1.02 cm). The proportion of ablation to insula volume was lowest in patients with Engel II-IV outcome (25.09%). The mean energy requirement to create a unit volume of ablation in the insula is 1205.86 J. A linear trend was noted between thermal ablation energy and ablation volume (R= 0.884). Over a mean follow-up period of 104 days, three patients were seizure-free (Engel I), and one patient saw significant improvement in seizure frequency (Engel III).	Larger studies included in table 2.
Atsina KB, Sharan AD, Wu C et al (2017): <i>Journal Club. Longitudinal qualitative characterization of MRI features after laser interstitial thermal therapy in drug-resistant epilepsy. Am J Roentgenol</i> ; 208(1): 48–56	Case series N=23 patients had LITT for drug-resistant epilepsy  Follow up 7 to 51 days	Immediately after LITT, MR images showed a ring-enhancing lesion at the ablation site with minimal surrounding oedema. Seven images showed increased enhancement of the ipsilateral choroid plexus. Images in the subacute phase showed a mild increase in oedema with similar enhancement. Images in the transitional phase showed a decrease in oedema with variable enhancement. Images in the chronic phase showed minimal gliosis with or without cavity formation or cavity formation alone, with either decreased or no enhancement.	Included in systematic review added to table 2.
Ball T, Sharma M et al (2019). Anterior Corpus Callosotomy Using Laser Interstitial Thermal Therapy for Refractory Epilepsy. <i>Stereotactic and Functional Neurosurgery</i> (96) 6 406-11	Case report N=1 patient with refractory epilepsy and frequent drop attacks had MRI guided thermal ablation for an anterior two-Thirds callosotomy. Follow up 1 month.	The frequency had decreased from multiple seizures per day to only 3 over the course of 1 month. In addition, he had not suffered any drop attacks or tonic-clonic movements since the procedure. Five months after surgery, seizures had decreased to 1 per month with no drop attacks or loss of consciousness, consistent with an Engel class II outcome.	Larger studies included in table 2.

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Brown MG, Drees C et al (2018). Curative and palliative MRI-guided laser ablation for drug-resistant epilepsy. <i>Journal of Neurology, Neurosurgery and Psychiatry</i> (89) 4 425-33	Review	Reviews the use of LITT for epileptic indications in the context of its application as a curative (seizure freedom) or palliative (seizure reduction) measure for both lesional and non-lesional forms of epilepsy. The use of LITT for a variety of extratemporal lobe epilepsies discussed. Finally, clinical outcomes, limitations and future applications of LITT for epilepsies discussed.	Review
Curry DJ, Gowda A et al (2012). MR-guided stereotactic laser ablation of epileptogenic foci in children. <i>Epilepsy &amp; Behavior</i> (24) 4 408-14	Case series N=5 paediatric cases with lesional and localised epilepsy who had MRI guided LITT to ablate focal epileptic lesions. Follow up 2-13 months	All 5 patients are seizure free and there were no complications as of 2- to 13-month follow up.	Included in systematic review added to table 2.
Curry DJ, Raskin J et al. (2018). MR-guided laser ablation for the treatment of hypothalamic hamartomas. <i>Epilepsy Research</i> ; 142:131-.	Case series N=71 patients with hypothalamic hamartomas treated with laser ablation.	93% were free of gelastic seizures at one year with 23% of the patients needing more than one ablation. One patient experienced a significant memory deficit and one patient experienced worsening diabetes insipidus.	Included in systematic review added to table 2.
Donos C, Breier J et al (2018). Laser ablation for mesial temporal lobe epilepsy: Surgical and cognitive outcomes with and without mesial temporal sclerosis. <i>Epilepsia</i> (59) 7 1421-1432 07	Retrospective case series N=43 patients had unilateral LITT targeting mesial temporal structures.  Follow up 20.3 months	Engel class I surgical outcome was obtained in 79.5% and 67.4% of the 43 patients at 6 and 20.3 months of follow up respectively. No statistically significant differences in surgical outcomes were found across patient subgroups (hemispheric dominance, hippocampal sclerosis, or need for intracranial evaluation). No statistically significant differences in volumes ablated were found between patients with Engel class IA vs Engel class II-IV outcomes. In patients having LITT in the dominant hemisphere, a decline in verbal and narrative memory, but not in naming function was noted.	Included in systematic review added to table 2.
Drane DL, Loring DW et al (2015). Better object recognition and naming outcome with MRI-guided stereotactic laser amygdalohippocampotomy for temporal lobe epilepsy.	Non-randomised study N=58 19 patients with temporal lobe epilepsy who had stereotactic laser amygdalohippocampotomy (SLAH)	Performance declines were statistically significantly greater for patients with dominant temporal lobe epilepsy (TLE) that had open resection surgery versus SLAH, for famous face recognition and common names (p<0.0001 and p<0.001) Performance declines were statistically significantly greater for patients with non-dominant temporal lobe epilepsy (TLE) that had open resection surgery versus SLAH,	Included in systematic review added to table 2.

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Epilepsia (56) 1 101-13	compared with open resections (n=39). Device: not specified Follow up: 6 months	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.	
Drane, DL (2018). MRI-Guided stereotactic laser ablation for epilepsy surgery: Promising preliminary results for cognitive outcome. Epilepsy Research (142) 170-5	Review	Cognitive outcome data are reviewed with respect to the use of MRI-guided stereotactic laser ablation (SLA) as an epilepsy surgical procedure, with comparisons drawn to traditional open resection procedures. Cognitive outcome with stereotactic laser amygdalohippocampotomy (SLAH) appears better than open resection for several functions dependent on extra-mesial temporal lobe (TL) structures, including category-related naming, verbal fluency, and object/familiar person recognition. Preliminary data suggests episodic, declarative verbal memory can decline following SLAH in the language dominant hemisphere, although early findings suggest comparable or even superior outcomes compared with open resection. The hippocampus has long been considered a central structure supporting episodic, declarative memory, with epilepsy surgical teams attempting to spare it whenever possible. However, ample data from animal and human neuroscience research suggests declarative memory deficits are greater following broader mesial TL lesions that include parahippocampal gyrus and lateral TL inputs. Therefore, employing a neurosurgical technique that restricts the surgical lesion zone holds promise for achieving a better cognitive outcome. Focal SLA lesions outside of the amygdalohippocampal complex may impair select cognitive functions, although few data have been published in such patients to date. SLA is being effectively employed with adults and children with TL or lesional epilepsies across several U.S. epilepsy centres, which may simultaneously optimise cognitive outcome while providing a curative treatment for seizures.	Review
Dredla BK, Lucas JA et al (2016). Neurocognitive outcome following stereotactic laser ablation in two patients with MRI- /PET+ mTLE.	Case report N=2 patients with drug-resistant mTLE had neuropsychologic al assessment pre- and postleft	Both patients demonstrated preserved visual naming ability following surgery. Semantic verbal fluency declined after surgery, but the magnitude of decline did not reach the statistical threshold for reliable change. Both patients demonstrated statistically significant and clinically meaningful declines in memory,	Larger studies included in table 2.

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Epilepsy & Behavior (56) 44-7	temporal MRgLITT.	but abilities across other non-memory neurocognitive domains (that is, visuospatial ability, attention) were preserved.	
Esquenazi Y, Kalamangalam GP et al (2014). Stereotactic laser ablation of epileptogenic periventricular nodular heterotopia. Epilepsy Research (108) 3 547-54	Case report N=2 PVNH epilepsy had MRgLITT	In the first case, seizure medication adjustment coupled with PVNH ablation, and in the second, PVNH ablation in addition to temporal lobectomy rendered the patient seizure free. A transient visual deficit occurred following ablation in the second patient. MRgLITT is a promising minimally invasive technique for ablation of epileptogenic PVNH.	Larger studies included in table 2.
Fayed I, Matthew FS et al . (2018). MR-guided laser interstitial thermal therapy for medically refractory lesional epilepsy in paediatric patients: experience and outcomes. Paediatric neurosurgery; 53:322-9	Retrospective review of patients who had MRgLITT N=12 paediatric patients with 18 lesions (4 hypothalamic hamartomas, 3 periventricular heterotopias, 2 focal cortical dysplasia, 2 tuberous sclerosis and 1 mesial temporal sclerosis. Mean follow up 10 months	Mean length of stay was 1.3 days. After treatment 8 patients were seizure free (Engel class I 66.7%) and 2 patients had worthwhile improvement (class II 16.7%). One patient developed a left superior quadrantanopsia postoperatively.	Included in review added to table 2.
Greenway MRF, Lucas JA et al. (2017). Neuropsychological outcomes following stereotactic laser amygdalohippocampotomy. Epilepsy & Behavior (75) 50-55 10	Retrospective review of 15 patients who had stereotactic laser ablation and also had neuropsychological testing before and after surgery  6-month follow up	all 15 patients experienced at least 1 clinically significant decline in either verbal or visual memory. 10 patients, including 5 with dominant-hemisphere surgery, demonstrated decline in delayed memory for narrative information (Logical Memory II). By contrast, the Boston Naming Test demonstrated more favourable results after surgery. 2/9 patients demonstrated a clinically significant increase in naming ability, and only 1/9 patients demonstrated a clinically significant decline in naming ability, 33% reported seizure freedom.	Larger studies include in systematic reviews added to table 2.
Grewal S, Gupta V et al (2017). Mammillary body changes after laser interstitial thermal therapy of the mesial temporal lobe. Journal of Neurosurgery (126) 4 A1408.	Retrospective case series N=23 patients had LiTT for mesial temporal lobe epilepsy Pre- and post-LiTT ablation MRI was reviewed.	13 were seizure free at 1 year. In the seizure free group, there was an average 34.6% (+/- 13%) decline in ipsilateral mammillary body volume, as opposed to an average decline of 8.4% (+/- 10.9%) in patients with continued seizures (P=0.0026). Our findings show a statistically significant correlation between postoperative volume reduction in ipsilateral mammillary body and seizure outcomes after LiTT.	Included in systematic review added to table 2.

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	Follow up: 32 months (12-70 months)		
Gerwal S, Gorny, KR (2018). Safety of Laser Interstitial Thermal Therapy in Patients With Pacemakers. Operative Neurosurgery (15) 5 E69-E72.	Case report 83-year-old man who had an implanted cardiac pacemaker presented with medically intractable epilepsy and was confirmed to have mesial temporal sclerosis. He had LiTT for ablation of the mesial temporal lobe.	This study reports on a protocol of cardiac and MR SAR to safely perform MR-guided LiTT in the setting of traditional pacemakers in patients who are not pacemaker dependent	Pilot study
Gross RE. and Willie JT (2015). Response to Journal Club: Real-time Magnetic Resonance-Guided Stereotactic Laser Amygdalohippocampotomy for Mesial Temporal Lobe Epilepsy. Neurosurgery (77) 3 E502-4	Case series N=13 patients with MTLE had MRI guided SLAH Follow up 5 to 26 months	. Fifty-four percent of those who had SLAH were seizure-free at 6 months.	Included in systematic review added to table 2.
Gross RE, Willie JT (2016). The Role of Stereotactic Laser Amygdalohippocampotomy in Mesial Temporal Lobe Epilepsy. Neurosurgery Clinics of North America (27) 1 37-50	Review	SLAH may improve access by medication-refractory patients to effective surgical treatments and thereby decrease medical complications, increase productivity, and minimise socioeconomic consequences in patients with chronic epilepsy.	Review
Gross RE, Stern MA et al (2018). Stereotactic laser amygdalohippocampotomy for mesial temporal lobe epilepsy. Annals of Neurology (83) 3 575-87	Retrospective case series N=58 patients with mesial temporal lobe epilepsy had stereotactic laser amygdalohippocampotomy  Follow up 12 months	53.4% of all patients were free of disabling seizures (Engel I). 3/9 patients became seizure-free following repeat ablation. Subgroup analysis showed that 60.5% of patients with mesial temporal sclerosis were free of disabling seizures as compared to 33.3% of patients without mesial temporal sclerosis. Quality of Life in Epilepsy-31 scores statistically significantly improved at the group level, few procedure-related complications were observed, and verbal memory outcome was better than historical open resection data.	Included in systematic reviews added to table 2.

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Hoppe C, Witt JA et al (2017). Laser interstitial thermotherapy (LiTT) in epilepsy surgery. <i>Seizure</i> (48) 45-52	Review	we briefly describe the history and rationale of laser neurosurgery as well as the technical key features of the two currently available systems for MRI-guided LiTT. We also discuss the published clinical experience with LiTT in the field of epilepsy surgery (approximately 200 cases) with regard to complications, LiTT-induced, long-term brain structural alterations, seizure outcome, preliminary neuropsychological findings and first estimates of treatment costs. Overall, the seizure outcome appears to be slightly worse than for resective surgery. Due to insufficient research methods (e.g. non-established measures, lack of a control condition), the expected neuropsychological superiority over resective surgery has not been unambiguously demonstrated thus far. Also, the cost-benefit ratio requires further critical evaluation. Clinical, multicentre and adequately controlled outcome studies of high quality should also accompany the imminent introduction of LiTT into the field of epilepsy surgery and therewith permit critical scientific evaluation and rational, individual, clinical decisions.	Review
Ho AL, Miller KJ et al (2016). Stereotactic laser ablation of the splenium for intractable epilepsy. <i>Epilepsy &amp; Behavior Case Reports</i> (5) 23-6	Case report N=1 patient with a history of prior partial corpus callosotomy who had medically refractory epilepsy had laser ablation of the splenium to achieve full corpus callosotomy four-month follow up	Adequate ablation of the splenial remnant was confirmed by postoperative MRI imaging, the patient's seizure frequency had dropped more than 50%. This is the first reported instance of laser ablation of the splenium to achieve full corpus callosotomy following a previous unsuccessful anterior callosotomy in a patient with intractable generalised epilepsy.	Pilot study
Ho AL, Sussman, Eric S et al. (2018) Improved operative efficiency using a real-time MRI-guided stereotactic platform for laser amygdalohippocampotomy. <i>Journal of Neurosurgery</i> (128) 4 1165-72	Case series N=17 patients had amygdalohippocampal ablation for temporal lobe epilepsy using MRgLITT  Follow up > 3months	There was a learning curve associated with using this real-time MRI-guided system. However, operative times decreased in a linear fashion, as well as total anaesthesia time. In fact, total mean patient time was less in the MRI cohort (362.8 min) than the OR cohort (456.9 min). Mean anaesthesia time was statistically significantly shorter in the MRI cohort (327.2 min) than the OR cohort (435.8 min, p = 0.02).	Included in systematic reviews added to table 2
Ibrahim GM, Weil AG et al. (2018). Presurgical hyperconnectivity of	Exploratory analysis	5 achieved seizure freedom and 12 did not achieve. Greater functional connectivity of the ablation volume to canonical resting-state networks was associated with seizure-	Exploratory analysis.

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<p>the ablation volume is associated with seizure-freedom after magnetic resonance-guided laser interstitial thermal therapy. Seizure-European Journal of Epilepsy; 61:89-93</p>	<p>N=17 children with heterogenous pathologies and epileptogenic lesions had MRgLITT.</p> <p>Insights into associations between MRgLITT ablation zones and large-scale brain networks that portended seizure outcome using resting-state fMRI</p> <p>Follow up 1 year</p>	<p>freedom (<math>p &lt; 0.05</math>, FDR-corrected). The ablated volume in children who subsequently became seizure-free following MRgLITT had significantly greater strength, and eigenvector centrality within the large-scale brain network.</p>	
<p>Jermakowicz WJ, Kanner AM et al (2017). Laser thermal ablation for mesiotemporal epilepsy: Analysis of ablation volumes and trajectories. Epilepsia (58) 5 801-10</p>	<p>Prospective case series</p> <p>n=23 patients having LiTT for the treatment of mTLE.</p> <p>Follow up: 1 year</p>	<p>15 (65%) were free of disabling seizures since the time of their surgery. Sparing of the mesial hippocampal head was statistically significantly correlated with persistent disabling seizures (<math>p = 0.01</math>). A lateral trajectory through the hippocampus showed a trend for poor seizure outcome (<math>p = 0.08</math>). A comparison of baseline and postoperative neurocognitive testing revealed areas of both improvement and worsening, which were not associated with ablation volume or trajectory.</p>	<p>Included in systematic reviews added to table 2.</p>
<p>Kang JY, Wu C et al (2016). Laser interstitial thermal therapy for medically intractable mesial temporal lobe epilepsy. Epilepsia (57) 2 325-34.</p>	<p>Case series</p> <p>N=20 patients with drug-resistant mTLE who had MRI-guided LiTT.</p> <p>Median follow up was 13.4 months</p>	<p>8/15 patients (53%) after 6 months, 4/11 (36.4%) after 1 year, 3/5 (60%) at 2-years were free of seizures. Seizure outcome after LiTT suggests an all or none response. Four patients had anterior temporal lobectomy (ATL) after LiTT; three are seizure-free. Seizure outcome after LiTT suggests an all or none response. Four patients had anterior temporal lobectomy (ATL) after LiTT; three are seizure-free. There were no differences in total ablated volume of the amygdalohippocampus complex or individual volumes of hippocampus, amygdala, entorhinal cortex, parahippocampal gyrus, and fusiform gyrus between seizure-free and non-seizure-free patients. Contextual verbal memory performance was preserved after LiTT, although decline in non-contextual memory task scores were noted.</p>	<p>Included in systematic review added to table 2.</p>
<p>Kang JY and Sperling MR (2017). Magnetic Resonance Imaging-Guided Laser Interstitial</p>	<p>Review</p> <p>This article will review the technical considerations,</p>	<p>Recent advances in imaging, surgical navigation, and real-time thermal monitoring have made LiTT safer and easier to implement, offering an effective and</p>	<p>Review</p>

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Thermal Therapy for Treatment of Drug-Resistant Epilepsy. Neurotherapeutics (14) 1 176-181 01	uses, and potential future directions for LiTT in drug resistant epilepsy.	powerful neurosurgical tool for drug-resistant epilepsy.	
Kang JY and Sperling MR (2018). Epileptologist's view: Laser interstitial thermal ablation for treatment of temporal lobe epilepsy. Epilepsy Research (142) 149-152 05	Review	LITT selectively targets small lesions responsible for seizures, and is far less invasive than open surgery with shorter hospitalisation, less pain, and rapid return to normal activities. Initial results in mesial temporal lobe epilepsy are promising, with perhaps half of patients becoming free of seizures. Neuropsychological deficits appear to be reduced because of the smaller volume of ablated cortex in contrast to large resections. More research must be done to establish optimal targeting of structures for ablation and selection of patients, and to better establish efficacy and adverse effect rates.	Review
Karsy M, Guan J et al (2016). Emerging surgical therapies in the treatment of paediatric epilepsy. Translational Pediatrics (5) 2 67-78	Review In this review, the authors discuss these various technologies, their current applications, and limitations in the treatment of paediatric drug-resistant epilepsy, as well as areas for future research.	The development of minimally invasive diagnostic and ablative surgical techniques together with new paradigms in neurostimulation hold vast potential to improve the efficacy and reduce the morbidity of the surgical management of children with drug-resistant epilepsy.	Review
Le S, Ho AL, Fisher RS et al. (2018). Laser interstitial thermal therapy (LITT): seizure outcomes for refractory mesial temporal lobe epilepsy. Epilepsy & Behaviour 89: 37-41	Prospective case series N=30 patients with mesial temporal lobe epilepsy (MTLE) had selective amygdalohippocampotomy via LITT, MTS was present in 23 patients. Median follow up: 18 months (range 6-44 months).	Most patients had >50% reduction (97%, 28/29) and 76% (22/29) patients had >90% reduction in seizure frequency. Engel class I outcome was achieved in 62% (18/29) patients with complete seizure freedom in 9/29 (31%) patients. 3 (10%) patients have had only focal leisure awareness. Seizure only occurred with medication withdrawal in 21% (6/29) patients. Class I was achieved by 6/29 (21%) and class III by 5/29 (17%) patients. Complications include perioperative seizures in 34% and non-seizure complaints in 21% patients. 3 had neurological deficits including one permanent superior quadrantonopsia, one transient trochlear and one transient oculomotor nerve palsy.	Larger studies added to systematic review in table 2.
Lewis EC, Weil AG et al (2015). MR-guided laser interstitial thermal therapy for pediatric	Retrospective case series N=17 paediatric patients with lesional and	Complications occurred in 4 patients. Average length of hospitalisation post-surgery was 1.56 days. Engel class I outcome was achieved in (7/17; 41%) patients, Engel class II in one (1/17; 6%),	Included in systematic review added to table 2.

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drug-resistant lesional epilepsy. <i>Epilepsia</i> (56) 10 1590-8	localised drug resistant epilepsy had 19 MRgLITT procedures Mean follow up was 16.1 months	Engel class III in three (3/17; 18%), and Engel class IV in six (6/17; 35%). Three patients (3/8; 38%) with class I and II outcomes and five patients (5/9; 56%) with class III and IV outcomes had at least one prior resection.	
Lagman C, Chung Lk et al (2017). <i>Laser neurosurgery: a systematic analysis of magnetic resonance-guided laser interstitial thermal therapies. Journal of clinical neuroscience</i> (36) 20-6	Review systematic analysis of two commercially available MRgLITT systems used in neurosurgery: the Visualase thermal therapy and NeuroBlate Systems	Epilepsy was the most common indication for Visualase therapy (n = 8 studies, 47%). Brain mass was the most common indication for NeuroBlate therapy (n = 3 studies, 60%). There were no statistically significant differences, except in age, wherein the NeuroBlate group was nearly twice as old as the Visualase group (p < 0.001). Frame, total complications, and length-of-stay (LOS) were non-significant when adjusted for age and number of patients. Laser neurosurgery has evolved over recent decades. Clinical indications are currently being defined and will continue to emerge as laser technologies become more sophisticated. Head-to-head comparison of these systems was difficult given the variance in indications (and therefore patient population) and disparate literature.	Review of different indications
Morris SA, Rollo M et al (2017). <i>Prolonged Blood-Brain Barrier Disruption Following Laser Interstitial Ablation in Epilepsy: A Case Series with a Case Report of Postablation Optic Neuritis. World Neurosurgery</i> (104) 467-75	Case series (prospective) N=13 patients having MRI guided laser ablation for focal epilepsy (lesional and localised epilepsy)  Follow up: 5-8 months.	In 12/13 cases, persistent enhancement was seen, consistent with prolonged blood-brain barrier dysfunction. Enhancement was 9%-67% (mean 30%). There was no correlation between the time from surgery and the relative percentage of postoperative enhancement on MRI. The blood-brain barrier remained compromised to gadolinium contrast for up to 8 months after thermal therapy. There were no adverse events from surgical intervention; however, 1 patient developed delayed optic neuritis.	Included in systematic review added to table 2.
McCracken DJ, Willie JT et al (2016). <i>Magnetic Resonance Thermometry-Guided Stereotactic Laser Ablation of Cavernous Malformations in Drug-Resistant Epilepsy: Imaging and Clinical Results. Operative Neurosurgery</i> (12) 1 39-48 03	Case series N=5 patients with cerebral cavernous malformations (CCM) that cause medically refractory epilepsy had real-time magnetic resonance thermography (MRT)-guided stereotactic laser ablation (SLA).	Imaging revealed no evidence of acute haemorrhage following fibre placement within presumed CCM. MRT during treatment and immediate post-procedure imaging confirmed desired extent of ablation. We identified no adverse events or neurological deficits. 4/5 (80%) patients achieved freedom from disabling seizures after SLA alone (Engel class 1 outcome), Reimaging indicated lesion diminution with surrounding liquefactive necrosis, consistent with the surgical goal of extended lesionotomy.	Larger studies included in table 2.

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	Follow up ranging 12-28 months.		
Marashly A, Loman MM (2018). Stereotactic laser ablation for nonlesional cingulate epilepsy: case report. Journal of Neurosurgery Pediatrics (22) 5 481-8	Case report N=1 patient with refractory nocturnal seizures (cingulate epilepsy) had Stereotactic laser ablation	The patient has remained seizure free since immediately after the procedure with no postoperative deficits (follow up of 17 months). This case highlights the utility of SEEG in evaluating difficult-to-localise, focal epilepsy. It also demonstrates that the use of SLA can be extended to non-lesional, extratemporal epilepsies.	Larger studies included in table 2.
North RY, Raskin JS (2017). MRI-Guided Laser Interstitial Thermal Therapy for Epilepsy. Neurosurgery Clinics of North America (28) 4 545-57.	Review Here we present a focused review of technical details and application of LITT to both focal and generalised epilepsy.	MRgLITT for epilepsy has become an established, minimally invasive alternative to traditional epilepsy surgery. MRgLITT is valuable in cases in which open surgery poses unacceptably high morbidity or patient preference precludes craniotomy.	Review
Nour SG, Willie JT and Gross RE (2014). Percutaneous selective laser amygdalohippocampotomy (SLAH) for treatment of mesial temporal lobe epilepsy within an interventional MRI suite. Photonics and Lasers in Medicine (3) 2 117-28	Review	This article reviews the principles of MRI-guided SLAH, procedure set-up and equipment, the detailed phases of intra-procedural MRI guidance and treatment monitoring, and the MRI appearance of the resultant thermal ablation zones and a discussion of experience at Emory University with MRI-guided SLAH.	Review
Perry MS, Donahue DJ et al (2017). Magnetic resonance imaging-guided laser interstitial thermal therapy as treatment for intractable insular epilepsy in children. Journal of Neurosurgery. Pediatrics. (20) 6 575-82	N=20 children having MRI guided LITT for intractable localisation-related epilepsy of insular onset. Follow up: 7-9 months	Engel scale (class I to IV) outcomes: Class I 0.50 (0.28-0.72) Class III 0.25 (0.06-0.44) Class IV 0.20 (0.02-0.38)	Included in systematic review added to table 2.
Pruitt R, Gamble A et al (2017). Complication avoidance in laser interstitial thermal therapy: lessons learned. Journal of	Case series N=46 patients had MRI guided LITT Indications included brain tumours (n = 12), radiation necrosis	Some form of adverse event occurred in 11 (22.4%) of 49 procedures. These included 4 catheter malpositions, 3 intracranial haemorrhages, 3 cases of neurological deficit related to thermal injury, and 1 technical malfunction resulting in an aborted procedure. Of these, direct thermal injury was the only cause of prolonged	Refinements to LITT technique (for different indications) in the context of technical and treatment-

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Neurosurgery (126) 4 1238-45	(n = 2), filum terminale ependymoma (n = 1), mesial temporal lobe epilepsy (n =21), corpus callosotomy for bifrontal epilepsy (n = 3), cavernoma (n = 1), and hypothalamic hamartomas (n = 6).	neurological morbidity and occurred in 3 of 49 procedures. Complications of LITT can result from laser misplacement, laser insertion, and laser treatment. lessons learned include: 1) A stereotactic frame provides optimal laser placement; 2) In patients where a long laser placement is needed, an alignment rod should be inserted before the laser; 3) Preoperative CTA with MR fusion can be used to avoid vascular injury; 4) Critical structures should not be treated with the full hyperthermia dose to minimise the risk of neurological complications; 5) Intraspinal LITT should be used with caution; and 6) Saline coolant flow must remain continuous.	related complications discussed.
Pruitt R, Gamble A et al (2015). Laser interstitial thermal therapy: Lessons learned. Journal of Neurosurgery (123) 2 A533-A534	Case series N=35 patients were treated with MRI guided LITT, 15 with brain tumours, 1 with a filum terminale ependymoma, 15 with mesial temporal lobe epilepsy (MTLE), and 4 with hypothalamic hamartomas (HH). Saline-cooled laser probes (were inserted using intraoperative MRI (5 patients), frameless stereotaxy (FS, in 2), or frame-based in 28.	Laser misplacement occurred in 2 patients; in 1 FS was used for tumour targeting, and in 1 with MTLE, the laser was suboptimally placed when an alignment rod was not inserted beforehand. No other patients with a stereotactic frame sustained laser misplacement. 2 MTLE patients had haemorrhage from laser insertion. 4 patients had complications from the LITT treatment itself. 2 with brain tumours developed deficits from laser hyperthermia, 1 affecting the brainstem, and another the primary motor cortex. The patient with the filum terminale ependymoma developed a paraparesis postoperatively. In one patient with glioblastoma, treatment was aborted when the saline coolant flow ceased, and the laser tip overheated.	Modification of LITT technique (for different indications) in the context of technical and treatment-related complications.
Prince E, Hakimian S et al (2017). Laser Interstitial Thermal Therapy for Epilepsy. Current Neurology & Neuroscience Reports (17) 9 63	Review on MRgLITT	Mesial temporal epilepsy is the most frequently encountered surgically remedial epilepsy suitable for MgLiTT, particularly when there is unilateral hippocampal sclerosis. There is emerging evidence that it can be effective for eliminating seizures in this type of epilepsy, and that it has a lower risk of cognitive deficits than anterior temporal lobectomy.	Review
Shukla ND, Ho AL et al (2017). Laser interstitial thermal therapy for the treatment of epilepsy: evidence to date. Neuropsychiatric	Review	This review summarises the utilisation of MRgLITT for mesial temporal lobe epilepsy and other seizure disorders. Overall, the efficacy of MRgLITT is comparable to that of open surgery and offers a less invasive approach in patients with significantly less morbidity.	Review

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Disease & Treatment (13) 2469-75			
Singh S, Kumar KK et al (2018). Hair sparing does not compromise real-time magnetic resonance imaging guided stereotactic laser fiber placement for temporal lobe epilepsy. Journal of Clinical Neuroscience; 52: 71-3	Case series N=18 patients with mesial temporal epilepsy All had selective amygdalhippocampotomies using MRI guided LITT. No hair was removed during the procedure.	No post-operative wound infections or erosions occurred for any patient. The mean entry point error was 2.87+/-1.3mm and the mean target error was 1.0+/-0.9mm. There have been no other complications associated with this hair-sparing approach. The study's results suggest that hair sparing in MRgLITT surgery for temporal epilepsy does not increase the risk of wound complications.	More relevant studies included in table 2.
Southwell DG, Birk HS (2018). Laser ablative therapy of sessile hypothalamic hamartomas in children using interventional MRI: report of 5 cases. Journal of Neurosurgery. Pediatrics. (21) 5 460-5	Case series N=5 paediatric patients who had laser ablation of sessile hypothalamic hamartomas. MRI-guided laser ablation therapy.	The authors' experiences in these cases substantiate prior work demonstrating the effectiveness of laser therapy for HHs, while elucidating HH complexity as a potentially important factor in laser treatment planning, and in the interpretation of early studies describing this treatment method.	Larger studies included in table 2.
Tao JX, Issa NP et al (2018). Interstitial Stereotactic Laser Anterior Corpus Callosotomy: A Report of 2 Cases with Operative Technique and Effectiveness. Neurosurgery (05) 05	Case report N=2 cases of anterior corpus callosotomy using MRI-guided stereotactic laser interstitial thermal therapy (LITT).	Ablation of 70%-80% of the corpus callosum was confirmed by postoperative MRI diffusion tensor imaging and volumetric analysis. Marked reduction of epileptiform activity was observed in both patients during postoperative video-EEG studies as compared to preoperative video-EEG studies. Freedom from disabling seizures including drop attacks was achieved in 1 patient for 18 months, and more than a 90% reduction of disabling seizures was achieved in the other patient for 7 months with cognitive improvement and without surgical complications.	Early data on 2 patients.
Tatum WO, Thottempudi, N et al. (2019) De novo temporal intermittent rhythmic delta activity after laser interstitial thermal therapy for mesial temporal lobe epilepsy predicts poor seizure outcome. Clinical	Patients were evaluated for TRIDA (EEG pattern to predict focal seizures) after MRgLITT 29 patients had LITT for drug-resistant temporal lobe epilepsy Median follow up 15 months	10 patients had post-LITT ipsilateral TIRDA, another 2 had post-operative TIRDA but they occurred contralateral to the side of ablation. None of the patients with TIRDA on their post-LITT EEG became seizure-free. 6/29 patients (21%) eventually needed anterior temporal lobectomy (ATL), and of those 6 patients, 4 (66%) had evidence of TIRDA on their post-LITT follow-up EEG. The sensitivity and specificity of post-LITT TIRDA in predicting surgical failure was 57.14% and 100% respectively.	EEG abnormalities assessed as a biomarker to predict unsuccessful seizure outcome.

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Neurophysiology (130) 1 122-7			
Thompson SA, Kalamangalam, GP et al (2016). Intracranial evaluation and laser ablation for epilepsy with periventricular nodular heterotopia. Seizure (41) 211-6	Case report and review on chronic invasive EEG recordings in humans and 2 cases of focal epilepsy in the presence of periventricular nodular heterotopia (PVNH).	we review the literature. while inter-ictal spiking from nodules is common, clinical seizures rarely arise solely from nodular tissue. Surgical outcome is more favourable in cases with unilateral PVNH, and when a complete ablation of PVNH is performed. In rare cases, nodular ablation alone may be sufficient, as may be completed by MRI-guided laser interstitial thermal therapy. The mechanism(s) by which PVNH interacts with overlying cortex are not fully understood, but we suggest that PVNH either orchestrates or amplifies local network epileptogenicity. At present, invasive recordings with penetrating depth electrodes are needed before surgical therapy, as illustrated in our cases.	Early data from 2 patients.
Tao JX, Wu SL et al (2018). Stereotactic EEG-guided laser interstitial thermal therapy for mesial temporal lobe epilepsy. Journal of Neurology, Neurosurgery & Psychiatry (89) 5 542-8	Retrospective case series n=21 patients with medically refractory mTLE who had LITT further compared the surgical outcomes in patients with and without mesial temporal sclerosis (MTS).  Follow up (mean 24 months, range 7-43 months)	11 (52%) achieved freedom from disabling seizures. 73% (8/11) patients with MTS achieved freedom from disabling seizures, whereas 30% (3/10) patients without MTS achieved freedom from disabling seizures. Patients with MTS were statistically significantly more likely to become seizure-free, as compared with those without MTS (P=0.002). There was no statistically significant difference in total ablation volume and the percentage of the ablated amygdalohippocampal complex between seizure-free and non-seizure-free patients. There was no group decline in any neuropsychological assessment, a statistically significant postoperative decline in verbal memory and confrontational naming was observed in 10 patients.	Included in systematic review added to table 2.
Tovar-Spinoza Z, Carter D et al (2013). The use of MRI-guided laser-induced thermal ablation for epilepsy. Childs Nervous System (29) 11 2089-94	Case report and overview of the evidence.	Report includes an overview of the development and practice of an MR-guided laser ablation therapy known as MRgLITT. The role of modern image-guided trajectory planning in MRgLITT will also be discussed, with particular emphasis on the treatment of refractory epilepsy.	Review
Vakharia VN, Sparks R et al (2018). Automated trajectory planning for laser interstitial thermal therapy in mesial temporal lobe epilepsy. Epilepsia (59) 4 814-24	Case series (retrospective) N=25 patients who had had LiTT for MTLE.  Follow up: 10.3 to 38.5 months.	Computer assisted planning (CAP) automatically generated feasible trajectories with reduced overall risk metrics (P < .001) and intracerebral length (P = .007). There was a statistically significant correlation between the actual and retrospective CAP-anticipated ablation volumes, supporting a 15 mm diameter ablation zone model (P < .001). CAP trajectories would have provided statistically significantly greater ablation of the amygdala (P = .0004) and AHC (P =	Included in systematic review added to table 2.

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		.008), resulting in less residual unablated mesial hippocampal head (P = .001), and reduced ablation of the parahippocampal gyrus (P = .02).	
Waseem H, Osborn Ke et al (2015). Laser ablation therapy: an alternative treatment for medically resistant mesial temporal lobe epilepsy after age 50. <i>Epilepsy &amp; behavior</i> (51) 152-7	Case series N=7 patients having MRgLITT for MTLE compared with data taken from 7 consecutive patients having AMTL resection. Follow up 1 year	1 AMTL resection patient had a complication of aseptic meningitis. 1 MRgLITT patient experienced an early postoperative seizure, and 2 MRgLITT patients had a partial visual field deficit. Seizure-freedom rates were comparable (80% (MRgLITT) and 100% (AMTL) (p. >. 0.05)) beyond 1-year post-surgery (mean follow-up: 1.0. years (MRgLITT) vs. 1.8. years (AMTL)). Mean LOS was shorter in the MRgLITT group (1.3. days vs. 2.6. days (p. <. 0.05)). Neuropsychological outcomes were comparable.	Included in HTA report
Waseem H, Vivas AC and Vale FL (2017). MRI-guided laser interstitial thermal therapy for treatment of medically refractory non-lesional mesial temporal lobe epilepsy: Outcomes, complications, and current limitations: A review. <i>Journal of Clinical Neuroscience</i> (38) 1-7	Retrospective case series N=38 patients with mesial temporal lobe epilepsy (MTLE) who had MRgLITT were reviewed. 7 with mesial temporal sclerosis (MTS)  Follow up ranged from 6 to 38.5months.	Eighteen (53%) had an Engel class I outcome, 10 patients had repeat procedures/operations, and 12 post-procedural complications occurred. There was a decreased length of procedure time, hospitalisation time, and analgesic requirement when compared to open surgery.	Included in systematic review added to table 2
Wilfong AA. and Curry DJ (2013). Hypothalamic hamartomas: optimal approach to clinical evaluation and diagnosis. <i>Epilepsia</i> (54 Suppl 9) 109-14	Case series N=14 patients with medically refractory gelastic epilepsy epileptogenic (hypothalamic Hamartomas) had MRI-guided stereotactic laser ablation (SLA) procedure	Seizure freedom was obtained in 12 (86%) of 14 cases, with mean follow up of 9 months. There were no permanent surgical complications, neurological deficits or neuroendocrine disturbances. One patient had a minor subarachnoid haemorrhage that was asymptomatic. Most patients were discharged home within 1 day.	Larger studies included in table 2.
Willie JT, Laxpati NG et al (2014). Real-time magnetic resonance-guided stereotactic laser amygdalohippocampotomy for mesial temporal lobe epilepsy. <i>Neurosurgery</i> (74) 6	Case series N=13 adult patients with intractable mesial temporal lobe epilepsy (with and without mesial temporal sclerosis [MTS]) had magnetic resonance-guided	77% (10/13) of patients achieved meaningful seizure reduction, of whom 54% (7/13) were free of disabling seizures. Of patients with preoperative MTS, 67% (6/9) achieved seizure freedom. All recurrences were observed before 6 months. Variances in ablation volume and length did not account for individual clinical outcomes. Although no complications of laser therapy itself were observed, 1 significant complication, a visual field defect, resulted	Included in systematic review added to table 2

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569-84; discussion 584-5	stereotactic laser amygdalohippocampotomy Follow up 5-23 months	from deviated insertion of a stereotactic aligning rod, which was corrected before ablation.	
Willie JT, Malcolm JG et al. (2019) Safety and effectiveness of stereotactic laser ablation for epileptogenic cerebral cavernous malformations. <i>Epilepsia</i> (60) 2 220-32	Retrospective case series N= 19 patients with focal seizures associated with a cerebral cavernous malformations (CCM) had SLA. All but one patient had chronic medically refractory epilepsy (median duration 8 years, range 0.5-52 years). Lesions were located in the temporal (13), frontal (five), and parietal (one) lobes. >12 months of follow up	14/ 17 patients (82%) achieved Engel class I outcomes, of which 10 (59%) were Engel class IA. 2 patients who were not seizure-free from SLA alone became so following intracranial electrode-guided open resection. Delayed postsurgical imaging validated CCM involution (median 83% volume reduction) and ablation of surrounding cortex. Histopathologic examination of 1 previously ablated CCM following open surgery confirmed obliteration. SLA caused no haemorrhages. 2 symptomatic neurological deficits (visual and motor) were predictable, and neither was permanently disabling.	More comprehensive studies added to table 2.
Xu DS, Chen T, Hlubek RJ et al. (2018). Magnetic resonance imaging-guided laser interstitial thermal therapy for the treatment of hypothalamic hamartomas: a retrospective review. <i>Neurosurgery</i> ; 0:1-10	Retrospective review of 18 patients. Mean follow up 17.4 months.	The length of stay was 1 night for 16 (89%) patients. 11 of 18 patients (61%) had full disconnection of the HH, and 12 of 15 (80%) patients with gelastic seizures and 5 (56%) of 9 patients with non-gelastic seizures were seizure free (Class 1). Immediate complications included a 39% (7/18) incidence of neurological deficits, including 1 case of hemiparesis. At the end of follow up, 22% of patients (4/18) had persistent deficits. The hypothyroidism that occurred was delayed in 11% of patients (2/18), as was short-term memory loss (22%, 4/18) and weight gain (22%, 4/18).	Included in systematic review added to table 2.
Youngerman BE, Oh JY et al (2018). Laser ablation is effective for temporal lobe epilepsy with and without mesial temporal sclerosis if hippocampal seizure onsets are localized by stereoelectroencephalography.	Non-randomised study N=30 patients with drug-resistant mesial temporal lobe epilepsy (MTLE)  18 patients with confirmed mesial temporal sclerosis (MTS) had Selective laser	Study reports similar rates of seizure freedom following SLAH in patients with MTS and SEEG-confirmed, non-MTS MTLE. Consistent with early literature, these rates are slightly lower than typically observed with surgical resection (60%-80%). However, SLAH is less invasive than open surgery, with shorter hospital stays and recovery, and severe procedural complications are rare. SLAH may be a reasonable first-line surgical option for patients with both MTS and SEEG confirmed, non-MTS MTLE.	Included in systematic review added to table 2.

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Epilepsia (59) 3 595-606	amygdalohippocampotomy (SLAH) compared with 12 patients with stereoelectroencephalography (SEEG) confirmed MTLE (non-MTS) Follow up: 12-36 months.		
Wright JM, Staudt MD (2018). A novel use of the NeuroBlate SideFire probe for minimally invasive disconnection of a hypothalamic hamartoma in a child with gelastic seizures. Journal of Neurosurgery. Pediatrics. (21) 3 302-7	Case report N=1 boy with primarily intraventricular hypothalamic hamartoma and gelastic seizures had MRI guided stereotactic laser ablation.	There were no perioperative complications, and 2 years postprocedure, the patient remains seizure free with marked behavioural and cognitive improvements.	Larger studies included in table 2.
Zulma TS, Ziechmann R et al (2018). Single and staged laser interstitial thermal therapy ablation for cortical tubers causing refractory epilepsy in pediatric patients. Neurosurgical Focus (45) 3 E9	Case series N=7 paediatric patients with tuberous sclerosis complex (TSC) and medication-refractory epileptogenic cortical tubers had Magnetic resonance-guided laser interstitial thermal therapy (MRgLITT). 2 patients had a single procedure, and 5 patients had staged procedures. Mean follow up was 19.3 months (range 4–49 months).	All of the patients had a meaningful reduction in seizure frequency as reported by Engel and ILAE seizure outcome classifications, and most (71.4%) of the patients experienced a reduction in anti-epileptic drug burden. 3/ 4 patients who presented with neuropsychiatric symptoms had some improvement in these domains after laser ablation. No perioperative complications were noted.	Larger studies included in table 2.