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. The 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.

Contents

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 drug treatment (estimates vary between 20% and 40% of people with epilepsy). They have frequent seizures and are at risk of status epilepticus and sudden unexpected death in epilepsy. If drug treatment 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

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

What the procedure involves

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 46^0C to 60^0C) 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. MRI-guided laser interstitial thermal therapy (MRgLITT) has most commonly been used for patients with a well-defined epileptogenic focus, especially in the temporal lobe, but it 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%).[1]

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.[1]

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 from 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, I2=13.2%). Estimates ranged from 9% to 27%.[2]

A retrospective case series of 234 patients who had MRgLITT for mesial TLE reported that 58% patients had Engel class I outcomes at both 1 (134/231) and 2 years (96/167) follow up. Around 77% (178/231) and 80% (134/178) of patients had either Engel class I or II outcomes at 1- and 2-year follow up. At last follow up (mean 30±14 months), 58% (134/234) patients had Engel class I outcomes and 77% (180/234) of patients had either Engel class I or II outcomes. Patients with a history of focal to bilateral tonic-clonic seizures were less likely to have Engel class I outcomes at last follow up (odds ratio [OR] 0.52, 95% CI 0.27 to 0.98, p<0.042) and either Engel class I or II outcomes at 6, 12 months and last follow up (OR 0.31 to 0.38, 95% CI 0.14 to 0.83; p<0.014). There were no significant differences in rates of Engel class I outcome between the radiographic hippocampal sclerosis (rHS) and non-rHS subgroups after 6-month follow up. Ablation of mesial, anterior, and inferior structures of the temporal lobe including the amygdala, hippocampal head, para-hippocampal gyrus, entorhinal cortex and perirhinal cortex were associated with higher Engel class I outcomes.[4]

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.[1]

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 of22) 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.[5]

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).[1]

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.[2]

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.[3]

Mortality

Mortality (attributed to sudden unexplained death in epilepsy) at 12-month follow up was reported in 1 patient in the case series of 234 patients.[4]

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.[1]

Visual disturbances were reported in 5% (12/234) of patients in the case series of 234 patients. Further details were not available.[4]

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.[1]

Neurological deficits (n=42) were reported in 15% (35/234) of patients in the case series of 234 patients; 8 of these were transient deficits and 34 persisted at last follow up.[4]

Intracranial and cerebral haemorrhage (intraparenchymal, epidural, intraventricular)

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

Postoperative haemorrhage was reported in 1% (3/234) of patients in the retrospective case series of 234 patients. One was associated with transient double vision.[4]

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.[7]

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.[1]

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.[1]

Disabling amnestic 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.[6]

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.[1]

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.[2]

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.[3]

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).[3]

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.

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 1,218 patients from 2 meta-analyses, 2 reviews, 1 retrospective case series 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	**Systematic review and meta-analysis**
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	**n=19 studies** (**415 patients with medically intractable TLE)** **9 studies (n=250) on MRgLITT** **10 studies (n=165) on SRS** **All retrospective observational studies** except 1 RCT on SRS. Lesional pathological type: 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	**MRgLITT group: median 22.4 months (range 7-70 months) and** **SRS group: median 43.12 months (range 24 to 112 months)**
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 conditions. 95% (157/165) patients in the SRS group had lesional pathological conditions of which most were mesial temporal sclerosis or hippocampal atrophy.

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

Key efficacy and safety findings

<table>
<tr><th>Efficacy</th><th>Safety</th></tr>
<tr><td>Number of patients analysed: 415
MRgLITT (n=250; 9 retrospective studies) versus SRS (n=165; 9 retrospective studies and 1 RCT)

Overall seizure freedom (assessed by Engel epilepsy surgery outcome scale - class I to IV)
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%).

Seizure freedom among patients with lesional epilepsy (n=18 studies)
Lesional seziure 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.</td><td>Complications (n=16 studies)
MRgLITT (n=207; 8 retrospective studies) versus SRS (n=150; 7 retrospective studies and 1 RCT)

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).

<table>
<tr><th></th><th>MRgLITT</th><th>SRS</th></tr>
<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>
</table>

2 procedure-related complications were reported in MRgLITT group. These include thermal injury and faulty trajectory.

Reoperations (n=11 studies)

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).

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).
In the SRS group, n=11 patients had ATL.</td></tr>
<tr><td colspan="2">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</td></tr>
</table>

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	**n=16 observational studies (269 patients with treatment resistant epilepsy)** 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	**7 days to 51 months**
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 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

Key efficacy and safety findings

Efficacy

Number of patients analysed: **269**

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

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 seziures 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 imporvement with reduction in frequency of seziures)	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 redution in frequency of seizures)	15% (95% CI, 0.08–0.22)	9-27%	I^2=13.2%; P=0.330

Safety

Postoperative complications

26 complications were reported 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 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.

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	**n=25 case reports/series (179 paediatric patients with severe epilepsy who had MRgLITT)** 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 callostomy (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 Neuroblate).
Follow up	**Varied**
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

No of patients analysed: **179**

Seizure outcomes

	n=127 (%)
Engel class I	73 (57.5)
Engel class II	9
Engel class III (including> 50% reduction in seizure frequency and reports of worthwhile improvement)	36
Engel class IV	8
None	1
Seizure outcome for patients with hypothalamic hamartoma (different seizure types)	
Gelastic seizures class 1	72
Gelastic seizures class 2	1
Gelastic seizures class 5	1
Secondary seizures class 1	3
Secondary seizures class 5	1

Several studies reported that therapeutic effect on seizures occurred immediately after the procedure.

Cognitive outcomes

	N (%)
Not reported	173 (96.6)
No cognitive decline	1

Safety

Complications

	n (%)
None	140 (78.2)
Severe chronic complications (needing intervention)	**6 (3.4)**
Post-ablation contralateral weakness	3
Short-term memory deficit (by injury to left mamillary body)	1
Diabetes insipidus worsened to vasopressin dependence	1
Gadolinium extravasation into right lateral ventricle,9 months later right lateral ventricle trapped resulting in obstructive hydrocephalus and bilateral papilledema needing intervention	1
Transient (no intervention needed)	**34 (19)**
Increase in gelastic seizures	9
Hemiparesis	7
Limb weakness	5
Delayed wound healing	4
Hyponatremia	3
Sub-arachnoid haemorrhage (asymptomatic)	1
Oedema	1
Horner's syndrome (ipsilateral)	1
Stuttering	1
Expressive language dysfunction	1
Short-term memory dysfunction	1
LITT related complications	**2 (1.1)**
Software failure (no consequence for patient)	1
Inaccurate fibre placement (no consequence for patient)	1
Total complications	42 (23.5)

Abbreviations used: MRgLITT, MRI-guided laser interstitial thermal therapy.

Study 4 Wu C (2019)

Details

Study type	Retrospective case series
Country	USA (11 centres)
Recruitment period	December 2011 to August 2017
Study population and number	**n=234** patients who had amygdalohippocampal complex (AHC) LITT for treatment of mesial temporal lobe epilepsy (mTLE).
Age and sex	mean 42 years, 53% (124/234) women
Patient selection criteria	Inclusion criteria: patients who had LITT for mTLE with at least 1-year follow up.
Technique	MRgLITT ablation under real-time MRI guidance Each centre did the procedure according to its own practices, with no effort to standardise across centres.
Follow up	**Mean 30±14 months (range 12-75 months)**
Conflict of interest/source of funding	The study was funded by National Institute of Health. Most authors received grants and consulting fees from a number of companies. 2 authors are co-founders of Neurotargeting LLC.

Analysis

Follow-up issues: Limited follow up in some patients because seizure outcomes were not available for all at each follow-up point.

Study design issues: large multicentre retrospective cohort study. Data were obtained through chart review of medical records. Study assessed the effect of surgical targeting on seizure outcomes. To assess ablation cavity location, all ablation locations were manually traced on postoperative MRI by an investigator blinded to seizure outcomes. These images were subsequently non-linearly normalised to a common atlas space. Using multivariate regression analysis and statistical models, the association of clinical variables and ablation location to seizure outcomes was calculated.

Key efficacy and safety findings

Efficacy

No of patients analysed: **234**

Seizure outcomes

	6 months (n=226)	12 months (n=231)	18 months (n=161)	24 months (n=167)	Last follow up* (n=234)
Engel class I	NR	58 (134/231)	50.9 (82/161)	57.5 (96/167)	58 (134/234)
Engel class I or II	NR	77.1 (178/231)	73.3 (118/161)	80.2 (134/167)	76.9 (180/234)

*of at least 1 year (mean 30±14 months, range 12-75 months)

There were no significant differences in rates of Engel class I outcome between the radiographic hippocampal sclerosis (rHS) and non-rHS subgroups after 6-month follow up. After excluding patients with dual pathology on MRI, no significant difference was seen at any time point. Implementation of iEEG was not associated with seizure outcome (p>0.475).

Patients with a history of FTC were less likely to demonstrate Engel class I outcomes at last follow up (OR 0.52, 95% CI 0.27 to 0.98, p<0.042) and either Engel class I or II outcomes at 6, 12 months and last follow up (OR 0.31 to 0.38, 95% CI 0.14 to 0.83; p<0.014).

Volume of ablation for mesial structures

Multivariate regression analyses showed that more extensive amygdalar ablation was associated with greater chances of Engel class I outcomes at 6, 12 and 18 months (OR 1.60 to 1.77 per additional percent ablation, p<0.040) and extensive hippocampal ablation was associated a decreased chance of Engel class I outcomes at 6, 12 and 24 months (OR 0.04 per additional percent ablated, p<0.040).

Ablation location

Ablation of mesial, anterior, and inferior structures of the temporal lobe including the amygdala, hippocampal head, parahippocampal gyrus, entorhinal cortex and perirhinal cortex were associated with higher Engel class I outcomes. Ablations extending posteriorly beyond the coronal plane in line with the lateral mesencephalic sulcus were less likely to be associated with Engel class I outcomes.

Safety

Complications

	% (n)
Postoperative haemorrhage (1 had transient double vision)	1.3 (3/234)
Transient neurological deficits	n=8
Persistent neurological deficits	n=34
Visual disturbances	5.1 (12/234)
Worsening of a pre-existing affective disorder	4.3 (10/234)
Death (due to sudden unexplained death in epilepsy [SUDEP] at 12 months)	1

Postoperative complications were associated with lower chance of Engel class I outcomes at 24 months and at last follow up (OR 0.18 to 0.26, 95% CI 0.04 to 0.86, p<0.026).

Abbreviations used: CI, confidence interval; FTC, focal to bilateral tonic-clonic seizures; iEEG, intracranial electroencephalography; MRgLITT, MRI-guided laser interstitial thermal therapy; NR, not reported; OR, odds ratio; rHS, radiographic hippocampal sclerosis.

Study 5 Drane DL (2018)

Details

Study type	**Review**
Country	USA
Search period	Search period: 2016-2017; databases searched: PubMed; screening of reference lists done.
Study population and number	**n=6 studies (4 case series and 3 case reports)** **Case series** (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 **Case reports** 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
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	**Varied**
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

<table>
<tr><th>Efficacy</th><th>Safety</th></tr>
<tr><td>
No of patients analysed: 119

<u>1. Object Recognition and Naming Outcome</u>

Drane et al. 2015 reported these cognitive outcomes for select functions which are likely supported by extra-mesial temporal lobe region.

<table>
<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>
<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>
</table>
* 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.

<u>2. Episodic Memory Outcome</u>

Verbal contextual memory task (Logical memory subtest from the 4th edition of the Wechsler Memory Scale)

<table>
<tr><th>Studies</th><th>No. of SLAH patients with declined outcome (%)</th></tr>
<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>
</table>
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 4 patients declined on delayed recall. All the 4 patients from Waseem et al. 2015 were older patients with temporal lobe epilepsy.

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.

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%.

Verbal list-learning task (2nd edition of the California Verbal Learning test)

<table>
<tr><th>Studies</th><th>No. of SLAH patients with declined outcome (%)</th></tr>
<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>
</table>
</td><td>This review reported only 1 adverse event (severe amnestic syndrome) which is the same case as study 5 below.</td></tr>
</table>

*It was on the learning portion of the verbal list-learning task that these 3 patients had decline. Two of these patients also exhibited decline of their subsequent recall of the information. ^ 2 of 4 patients actually showed improvement on the delayed recall portion of a complex list-learning task (Rey Auditory Verbal Learning Test).	
Abbreviations used: ATL, anterior temporal lobectomy; MRgLITT, MRI-guided laser interstitial thermal therapy; SLAH, stereotactic laser amygdalohippocampectomy; TLE; temporal lobe epilepsy.	

Study 6 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	**8 months**
Conflict of interest/source of funding	None

Key efficacy and safety findings

Safety
No of patients analysed: **1** **Disabling amnestic syndrome** 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 amnestic syndrome with confabulation. 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. 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. Neuropsychological testing at 8 months demonstrated improved attention, concentration, and immediate recall but severe deficits in delayed recall (significant memory loss). Clinically, he had a disabling amnestic 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.
Abbreviations used: EEG, electroencephalogram; MRgLITT, MRI-guided laser interstitial thermal therapy

Study 7 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	**Postoperative period**
Conflict of interest/source of funding	None

Key efficacy and safety findings

Safety
No of patients analysed: **1** **Delayed intracranial haemorrhage needing evacuation** 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. 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.
Abbreviations used: MRgLITT, MRI-guided laser interstitial thermal therapy.

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 MRIgLITT 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 hypothalamic hamartoma, 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 the 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% and 60%.
- There are 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

recommendations were an update to an April 2018 FDA warning. The agency continued to reiterate its 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. It also suggested that healthcare providers 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 2 manufacturers that market MRgLITT devices, Medtronic and Monteris Medical, have provided updated information with suggested procedural techniques for MRgLITT devices to reduce unintended thermal damage.[8]

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. This included 2 non-randomised controlled studies of patients with epilepsy. One study found statistically significant improvements on famous-face recognition and common-names recognition using LITT compared with surgical resection. The other study found that seizure freedom did not statistically significantly differ but length of hospital stay and surgical time were statistically significantly reduced for patients who had LITT compared with 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.[9]

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 and was mainly derived from case series with limitations and biases.[10] 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. It concluded that 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'.[11]

Related NICE guidance

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

NICE guidelines

- Epilepsies: diagnosis and management NICE clinical guideline 137 (2012, updated 2019). Available from 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 was unable to gather patient commentary for this procedure.

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 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 January 2020, 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, health-related quality of life, adverse events and neuropsychological outcomes.
  - NCT02392078: Laser Ablation of Abnormal Neurological Tissue using Robotic NeuroBlate System (LAANTERN; Monteris Medical); prospective registry, n=1,000 patients from 50 sites; conditions: metastatic brain tumor, primary brain tumor, epileptic seizure foci; evaluate procedural success, local control failure rate, and quality of life; location USA; estimated completion September 2020; status: recruiting.

References

1. Grewal S., Alvi MA, Lu VM et al. (2019) Magnetic resonance-guided laser tnterstitial 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. Wu C, Jermakowicz WJ, Chakravorti S et al. (2019) Effects of surgical targeting in laser interstitial thermal therapy for mesial temporal lobe epilepsy. A multicentre study of 234 patients. Epilepsia 60:1171-1183.
5. Drane DL. (2018) MRI-guided stereotactic laser ablation for epilepsy surgery: promising preliminary results for cognitive outcome. Epilepsy Res. 142: 170–5
6. Zubkov S, Del Bene VA et al. (2015) Disabling amnestic syndrome following stereotactic laser ablation of a hypothalamic hamartoma in a patient with a prior temporal lobectomy. Epilepsy & Behavior Case Reports (4) 60-2
7. 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
8. 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]
9. 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
10. 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)*.

11. Williams D, Loshak H. 2019 Laser interstitial thermal therapy for epilepsy and/or brain tumours: a review of the clinical effectiveness and cost-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 Library)	11/10/2019	Issue 10 of 12, October 2019
Cochrane Central Database of Controlled Trials – CENTRAL (Cochrane Library)	11/10/2019	Issue 10 of 12, October 2019
HTA database (CRD website)	11/10/2019	n/a
MEDLINE (Ovid) & MEDLINE In-Process (Ovid)	11/10/2019	1946 to October 10, 2019
Medline ePub ahead (Ovid)	11/10/2019	October 10, 2019
EMBASE (Ovid)	11/10/2019	1974 to 2019 October 10

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 generali* 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)
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)
42 limit 41 to ed=20190401-20191031 (21)

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. Childs Nervous System (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): Journal Club. Longitudinal qualitative characterization of MRI features after laser interstitial thermal therapy in drug-resistant epilepsy. Am J Roentgenol; 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.
Arocho-Quinones E. and Lew S (2019). Magnetic resonance-guided stereotactic laser ablation therapy for the treatment of pediatric epilepsy: A multi-institutional retrospective study. Journal of Neurosurgery (131) 1 38-39.	Retrospective case series N=195 paediatric patients (ages 12.8yr +/- 5.9yr) treated with SLA (visualase 171 cases, neuroblate 24 cases) for a diagnosis of refractory epilepsy Treatment locations included cortical (51%), subcortical (11%), mesiotemporal	Engel classification was reported for 71.3% patients. Of these patients, 91 (65.5%) had Engel Class I or II, and 48 (34.5%) had Engel Class III or IV at latest follow up. Improvement in targeted seizure type was reported for 82% patients. Subsequent surgery after SLA treatment was not required in 81.5% patients. None of the patients with epilepsy secondary to brain tumors required subsequent surgery after SLA therapy. Complications included: malpositioned catheters (3), intracranial hemorrhage (1), transient neurological deficits (16), permanent neurological deficits (3), worsened neuropsychological testing (1), symptomatic perilesional edema	Abstract only.

	(25%), and hypothalamic (13%). Median follow-up time was 23.7months (range 3-71months).	(4), and hydrocephalus (1). Neither the number of laser trajectories or number of lesions created resulted in a significantly increased risk of complications, however, there was an association between higher volumes of the lesion created and the incidence of complications.	
Ball T, Sharma M et al (2019). Anterior Corpus Callosotomy Using Laser Interstitial Thermal Therapy for Refractory Epilepsy. Stereotactic and Functional Neurosurgery (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.
Bermudez CI, Jermakowicz WJ, Kolcun JPG et al. (2019) Cognitive outcomes following laser interstitial therapy for mesiotemporal epilepsies. Neurology: Clinical Practice 10.1212/CPJ.0000000000000728 (2019) doi:10.1212/CPJ.0000000000000728.	Case series (retrospective) N=26 patients who had LiTT for mTLE	Case-by-case review comparing presurgical to postsurgical scores revealed clinically significant improvement in both dominant and nondominant patients in learning and memory and other aspects of cognition such as processing speed and executive functioning. Of the few patients who did experience clinically significant decline following LiTT, a greater proportion had undergone dominant hemisphere procedures.	Larger studies included in table 2.
Brown MG, Drees C et al (2018). Curative and palliative MRI-guided laser ablation for drug-resistant epilepsy. Journal of Neurology, Neurosurgery and Psychiatry (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
Cajigas I, Kanner AM, Ribot R et al. Magnetic Resonance–Guided Laser Interstitial Thermal Therapy for Mesial Temporal Epilepsy: A Case Series Analysis of Outcomes and	Retrospective case series LITT for drug-resistant mesial temporal epilepsy [MTE] N=26	After a mean follow-up time of 42.9 months (range, 24.3–58.8 months), 61.5% (16/26) were free of disabling seizures, and 26.9% (7/26) had only rare disabling seizures. Whereas seizure-freedom rates between patients with and without mesial temporal sclerosis (MTS) were not statistically different (68% vs. 43%, P = 0.23), NSF patients without MTS had a shorter median time to first seizure than did NSF patients	Larger and more comprehensive studies added to table 2.

Complications at 2-Year Follow-Up. World Neurosurgery. Jun2019, Vol. 126, pe1121-e1129. 9p. DOI: 10.1016	Follow-up-minimum 2 years	with MTS (0.55 month vs. 10 months, log-rank test P = 0.007). Postoperative complications occurred in 2 patients (7.7%), consisting of 1 permanent and 1 transient homonymous hemianopia.	
Curry DJ, Gowda A et al (2012). MR-guided stereotactic laser ablation of epileptogenic foci in children. Epilepsy & Behavior (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. Epilepsy Research; 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. Epilepsia (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. Epilepsia (56) 1 101-13	Non-randomised study N=58 19 patients with temporal lobe epilepsy who had stereotactic laser amygdalohippocampotomy (SLAH) compared with open resections (n=39).	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, 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.	Included in systematic review added to table 2.

	Device: not specified Follow up: 6 months		
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. Epilepsy & Behavior (56) 44-7	Case report N=2 patients with drug-resistant mTLE had neuropsychological assessment pre- and postleft temporal MRgLITT.	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, but abilities across other non-memory neurocognitive domains (that is,	Larger studies included in table 2.

		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 1 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.
Gadgil N, Lam S, Pan IW et al (2019) Staged MR-guided laser interstitial thermal therapy for hypothalamic hamartoma: Analysis of ablation volumes and morphological considerations. Journal of Neurosurgery (131) 1 92.	Retrospective review N=58 pediatric patients who had MRgLITT for hypothalamic hamartoma Follow-up 6 months	Eighty-one percent of patients were completely free of gelastic seizures at last follow-up; of 22 patients with secondary non-gelastic epilepsy, 15 were free of additional seizures. Post-operative complication rate was low. There was no significant difference in gelastic seizure outcome related to pre- or post-operative hamartoma size. Residual hamartoma percentage in those free of gelastic seizures was 43% compared to 71% in those with continued seizures (p=0.021). Larger hamartomas required multiple ablations to achieve seizure freedom.	Abstract only.
Greenway MRF, Lucas JA et al. (2017). Neuropsychological outcomes following stereotactic laser amygdalohippocampectomy. Epilepsy	Retrospective review of 15 patients who had stereotactic laser ablation and also had neuropsychological testing before and after surgery	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	Larger studies include in systematic reviews added to table 2.

& Behavior (75) 50-55 10	6-month follow up	clinically significant increase in naming ability, and only 1/9 patients demonstrated a clinically significant decline in naming ability, 33% reported seizure freedom.	
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. Follow up: 32 months (12-70 months)	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.
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	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

America (27) 1 37-50			
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.
Hoppe C, Witt JA et al (2017). Laser interstitial thermotherapy (LiTT) in epilepsy surgery. Seizure (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. Epilepsy & Behavior Case Reports (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. Journal of Neurosurgery (128) 4 1165-72	Case series N=17 patents 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 the ablation volume is associated with seizure-freedom after magnetic resonance-guided laser interstitial thermal therapy. Seizure-European Journal of Epilepsy; 61:89-93	Exploratory analysis N=17 children with heterogenous pathologies and epileptogenic lesions had MRgLITT. Insights into associations between MRgLITT ablation zones and large-scale brain networks that portended seizure outcome using resting-state fMRI Follow up 1 year	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-freedom ($p < 0.05$, 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.	Exploratory analysis.
Jermakowicz WJ, Kanner AM et al (2017). Laser thermal ablation for mesiotemporal epilepsy: Analysis of ablation volumes and trajectories. Epilepsia (58) 5 801-10	Prospective case series n=23 patients having LiTT for the treatment of mTLE. Follow up: 1 year	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 (p = 0.01). A lateral trajectory through the hippocampus showed a trend for poor seizure outcome (p = 0.08). A comparison of baseline and postoperative neurocognitive testing revealed areas of both improvement and worsening, which were not associated with ablation volume or trajectory.	Included in systematic reviews added to table 2.
Kang JY, Wu C et al (2016). Laser interstitial thermal therapy for medically intractable mesial temporal lobe epilepsy. Epilepsia (57) 2 325-34.	Case series N=20 patients with drug-resistant mTLE who had MRI-guided LiTT. Median follow up was 13.4 months	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	Included in systematic review added to table 2.

		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.	
Kang JY and Sperling MR (2017). Magnetic Resonance Imaging-Guided Laser Interstitial Thermal Therapy for Treatment of Drug-Resistant Epilepsy. Neurotherapeutics (14) 1 176-181 01	Review This article will review the technical considerations, uses, and potential future directions for LiTT in drug resistant epilepsy.	Recent advances in imaging, surgical navigation, and real-time thermal monitoring have made LiTT safer and easier to implement, offering an effective and powerful neurosurgical tool for drug-resistant epilepsy.	Review
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	Prospective case series N=30 patients with mesial temporal lobe epilepsy (MTLE) had selective	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. 3 910%) patients have had only focal leisure awareness. Seizure	Larger studies added to systematic review in table 2.

temporal lobe epilepsy. Epilepsy & Behaviour 89: 37-41	amygdalohippocampotomy via LITT, MTS was present in 23 patients. Median follow up: 18 months (range 6-44 months).	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.	
Lewis EC, Weil AG et al (2015). MR-guided laser interstitial thermal therapy for pediatric drug-resistant lesional epilepsy. Epilepsia (56) 10 1590-8	Retrospective case series N=17 paediatric patients with lesional and localised drug resistant epilepsy had 19 MRgLITT procedures Mean follow up was 16.1 months	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%), 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.	Included in systematic review added to table 2.
Lagman C, Chung Lk et al (2017). Laser neurosurgery: a systematic analysis of magnetic resonance-guided laser interstitial thermal therapies. Journal of clinical neuroscience (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). Prolonged Blood-Brain Barrier Disruption Following Laser Interstitial Ablation in Epilepsy: A Case Series with a Case Report of Postablation Optic Neuritis. World Neurosurgery (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). Magnetic	Case series	Imaging revealed no evidence of acute haemorrhage following fibre placement within presumed CCM. MRT during	Larger studies included in table 2.

Resonance Thermometry-Guided Stereotactic Laser Ablation of Cavernous Malformations in Drug-Resistant Epilepsy: Imaging and Clinical Results. Operative Neurosurgery (12) 1 39-48 03	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). Follow up ranging 12-28 months.	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.	
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	N=20 children having MRI guided LITT for intractable localisation-	Engel scale (class I to IV) outcomes: Class I0.50 (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.

thermal therapy as treatment for intractable insular epilepsy in children. Journal of Neurosurgery. Pediatrics. (20) 6 575-82	related epilepsy of insular onset. Follow up: 7-9 months		
Pruitt R, Gamble A et al (2017). Complication avoidance in laser interstitial thermal therapy: lessons learned. Journal of Neurosurgery (126) 4 1238-45	Case series N=46 patients had MRI guided LITT Indications included brain tumours (n = 12), radiation necrosis (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).	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 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.	Refinements to LITT technique (for different indications) in the context of technical and treatment-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
Rennert, RC, Khan U, Bartek J et al (2019). Laser Ablation of Abnormal Neurological Tissue Using Robotic Neuroblate System (LAANTERN): Procedural Safety and Hospitalization. Neurosurgery (2019) doi:10.1093/neuros/nyz141	Prospective registry N=100 patients with intracranial lesions had SLA	There were 5 adverse events (AEs) attributable to SLA (5/100; 5%). After the procedure, 84.8% of patients were discharged home. There was 1 mortality within 30 d of the procedure (1/100; 1%), which was not attributable to SLA. The main safety outcomes reported in this registry study were: hypoxia (related to sedation), wide-complex tachycardia (related to prior cardiac history), wound dehiscence, subdural hematoma, bacteremia, intraventricular hemorrhage (all related to surgical manipulation), abnormal gait, hemi-body weakness, sensory changes and post-operative seizures (all related to laser ablation-neurological deficits).	Very few patients with epilepsy
Shimamoto S, Wu C, Sperling MR. (2019) Laser interstitial thermal therapy in drug-resistant epilepsy. Curr Opin Neurol. 32(2):237-245	Review	LiTT may offer benefit when treating drug-resistant epilepsy because of mesial temporal sclerosis, hypothalamic hamartoma, cavernous hemangioma, and small cortical dysplasias and malformations. It is now offered in place of anterior temporal lobectomy, and a prospective study is underway to compare it with historical temporal lobectomy reports.	Review
Shukla ND, Ho AL et al (2017). Laser interstitial thermal therapy for the treatment of epilepsy: evidence to date. Neuropsychiatric Disease & Treatment (13) 2469-75	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
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	Case series N=18 patients with mesial temporal epilepsy All had selective amygdalhippocampotomies using MRI guided LITT.	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.

Clinical Neuroscience; 52: 71-3	No hair was removed during the procedure.		
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 Neurophysiology (130) 1 122-7	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.
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 PNVH interacts with overlying cortex are not fully understood, but we suggest that PVNH	Early data from 2 patients.

		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.	
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 = .008), resulting in less residual unablated mesial hippocampal head (P = .001), and reduced ablation of the parahippocampal gyrus (P = .02).	Included in systematic review added to table 2.
Waseem H, Osborn Ke et al (2015). Laser ablation therapy: an alternative treatment for medically resistant mesial temporal lobe epilepsy after	Case series N=7 patients having MRgLITT for MTLE compared with data taken from 7 consecutive patients having AMTL resection.	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	Included in HTA report

age 50. Epilepsy & behavior (51) 152-7	Follow up 1 year	the MRgLITT group (1.3. days vs. 2.6. days (p. <. 0.05)). Neuropsychological outcomes were comparable.	
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. Journal of Clinical Neuroscience (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. Epilepsia (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 in12 (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. Neurosurgery (74) 6 569-84; discussion 584-5	Case series N=13 adult patients with intractable mesial temporal lobe epilepsy (with and without mesial temporal sclerosis [MTS]) had magnetic resonance-guided stereotactic laser amygdalohippocampotomy Follow up 5-23 months	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 from deviated insertion of a stereotactic aligning rod, which was corrected before ablation.	Included in systematic review added to table 2
Willie JT, Malcolm JG et al. (2019) Safety and effectiveness of stereotactic laser ablation for epileptogenic cerebral cavernous	Retrospective case series N= 19 patients with focal seizures associated with a cerebral cavernous	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	More comprehensive studies added to table 2.

malformations. Epilepsia (60) 2 220-32	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	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.	
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. Neurosurgery; 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. Epilepsia (59) 3 595-606	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 amygdalohippocampotomy (SLAH) compared with 12 patients with stereoelectroencephalography (SEEG) confirmed MTLE (non-MTS) Follow up: 12-36 months.	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.

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.