Clinical Commissioning Policy
MR-guided laser interstitial thermal therapy for treatment of epileptogenic zones in children and adults with refractory focal epilepsy (2006) [221009P]

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Commissioning position

Summary

MRgLITT for treatment of epileptogenic zones is recommended to be available as a routine commissioning treatment option for children and adults with refractory focal epilepsy within the criteria set out in this document.

Equality statement

Promoting equality and addressing health inequalities are at the heart of NHS England's values. Throughout the development of the policies and processes cited in this document, we have:

- Given due regard to the need to eliminate discrimination, harassment and victimisation, to advance equality of opportunity, and to foster good relations between people who share a relevant protected characteristic (as cited under the Equality Act 2010) and those who do not share it; and
- Given regard to the need to reduce inequalities between patients in access to, and outcomes from healthcare services and to ensure services are provided in an integrated way where this might reduce health inequalities.

Executive summary

Plain language summary

About refractory focal epilepsy

Epilepsy is a condition in which the electrical signals in the brain misfire, leading to seizures in patients. 'Focal' epilepsy specifically refers to misfiring signals which happen in one specific part of the brain; in some patients the area of misfiring signals can be relatively easily identified. 'Refractory' indicates that two different types of anti-seizure medications (ASMs) have been tried and have failed to control a patient's seizures. Repeated seizures can cause severe harm to patients, through injuries to the body and the brain, prolonged seizures reducing oxygen to the brain, and sudden death. Repeated seizures can also negatively impact the patient and their families or carers psychologically and socially.

About current treatment

Depending on the cause of the refractory focal epilepsy, current standard treatment involves either open neurosurgery, or continuing medications. Unfortunately, open neurosurgery can carry risks such as damaging structures in the brain. Continuing medications alone is often ineffective at controlling seizures in patients who are already resistant to at least two lines of medication.

About the new treatment

MRgLITT, also known as 'laser interstitial thermal therapy' (LITT), is a minimally invasive treatment which can be used in focal refractory epilepsy. Stereotactic neurosurgical technique is used to guide a 3mm diameter fibreoptic laser to the target area of the brain. Under continuous MRI monitoring, laser energy is applied to the target area to destroy the part of the brain causing seizure activity. It is safer than open neurosurgery as there is less risk of collateral damage to other structures in the brain. Open surgery causes damage along the operative pathway to access the part to be removed, which is mitigated by this minimally invasive approach.

What we have decided

NHS England has carefully reviewed the evidence to treat refractory focal epilepsy with MRgLITT. We have concluded that there is enough evidence to make the treatment available at this time.

Links and updates to other policies

NHS England commissions all neurosurgery activity in adult neurosurgery or neurology centres as set out in the neurosurgery service specification (https://www.england.nhs.uk/publication/neurosurgery-adults/). For paediatric patients, The Children's Epilepsy Surgery Service (CESS) centre is commissioned to provide specialist epilepsy pre-surgical evaluation and surgery to children in specialised CESS centres (NHS England, 2018).

NHS England currently commissions vagus nerve stimulation as a non-curative, palliative treatment for patients with medical refractory epilepsy who are not suitable for resective surgery (NHS Commissioning Board Clinical Reference Group for Neurosciences, 2013).

Committee discussion

Clinical Panel members agreed that the evidence base reflected the policy recommendation.

See the committee papers (link) for full details of the evidence.

The condition

Epilepsy is a neurological condition in which abnormal paroxysms of electrical discharges in the brain lead to seizures. These seizures can be focal (meaning arising from one area or zone of the brain) or generalised (those impairing consciousness and involving large areas or the entirety of the brain). Epilepsy is usually managed with ASMs; however, approximately one third of patients will continue to have seizures despite medication. These patients are at risk of recurrent physical and cerebral injury, status epilepticus (prolonged seizures), sudden death in epilepsy, other causes of fatality and psychological, psychiatric, financial and social comorbidities. Drug-resistant or refractory epilepsy is defined as failure to achieve adequate seizure control with adequate trials of two or more appropriate ASMs, taken individually or in combination.

In those who have refractory focal epilepsy and a well-defined epileptogenic zone, open neurosurgical removal or ablation of this part of the brain can be curative. These zones may include structural lesions. However, there may be high risk of adverse events from surgery. Examples of such lesions are:

- Hippocampal sclerosis - Located in the medial temporal lobe, is a common cause of refractory focal epilepsy in which surgical management is currently utilised as an option,

with 60-70% of individuals entering long-lasting remission (Vakharia et al, 2019). Significant impairment of language and memory occurs in 30-50% of resections in the speech-dominant temporal lobe and emerging evidence suggests that these risks are less with MRgLITT (Bermudez et al, 2020; Drane et al, 2015; Kohlhase et al, 2021). An ongoing randomised controlled trial (SLATE) is addressing this issue.

- Other relevant examples include cortical dysplasia, heterotopic nodules and low grade glioneuronal tumours and focal damage caused by previous stroke or infection. These lesions are challenging particularly if they are not located on the surface of the brain and if surgical access to these areas would cause morbidity such as loss of vision, language, sensation or motor control.

For some patients, open neurosurgery is currently relatively contraindicated. An example of this is patients with a lesion called hypothalamic hamartoma (HH). HH is a rare benign lesion in which an abnormal mass of tissue has grown adjacent to the hypothalamus. HH is present from birth and does not grow, though it has a huge effect on quality of life as it may cause drug resistant epilepsy, hormonal disturbance, cognitive decline and neurobehavioural problems (particularly rage attacks). Seizures tend to start as involuntary laughing that then progress to focal seizures with loss of awareness and generalised seizures and which are almost invariably unresponsive to medical treatment. Furthermore, HH lie at the central base of the brain; accessing this area through neurosurgery is associated with a very high risk of severe morbidity.

Current treatments

The current standard treatment for the management of patients with drug-resistant focal epilepsy is open neurosurgery. Patients in whom surgery is contraindicated continue with medical management alone and will hence continue to experience poor seizure control with associated increased morbidity and mortality outlined above and impairment of quality life.

Proposed treatments

MRgLITT involves the identification of the lesion causing abnormal electrical discharges on MRI. A 3.2mm 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 the appropriate volume of tissue has been ablated. After the procedure, an MRI is done to verify lesion location and volume of the tissue ablated. The aim is to precisely ablate the target tissue and to minimise damage to the surrounding area. MRgLITT has most commonly been used for patients with a well-defined epileptogenic focus, especially in the temporal lobe, but it can be used elsewhere in the brain.

The U.S. Food and Drug Administration (FDA) has previously issued a letter to healthcare providers about the risk of tissue overheating due to inaccurate thermometry readings displayed during the use of MRgLITT devices. The advice is that providers consider risks and benefits of MRgLITT on a case-by-case basis and consider any alternate treatment modalities. Specific advice has been issued on temperature controls to minimise the risk of tissue overheating (FDA, 2018).

Patients would normally be discharged home 24-48 hours after the MRgLITT procedure and be expected to resume normal activities and employment in 7 days, compared to a 5-10 day inpatient stay and a 2 month recuperation period after conventional neurosurgery.

Epidemiology and needs assessment

Epilepsy has been estimated to affect between 362,000 and 415,000 people in England (NICE, 2012). As mentioned, one third of this population do not have their epilepsy adequately controlled with ASMs. However, <3% of those who develop epilepsy every year in the UK will be potential candidates for epilepsy surgery.

The prevalence of HH with epilepsy in young people is approximately 1 in 200,000 (Shahar et al, 2007). It is estimated that 10 adult and 10 paediatric patients with HH per year would be suitable for MRgLITT in England.

At this time, it is difficult to estimate the likely number of patients with drug-resistant focal epilepsy due to focal pathologies for whom MRgLITT may be an appropriate therapy, with less morbidity than open neurosurgery. Approximately 250 patients have resections for epilepsy in the UK per year at present. An estimate is that 25-50 patients per year who would be amenable to MRgLITT, by virtue of the location of the epileptogenic zone, surgical access to which would cause new neurological morbidity.

Evidence summary

NHS England has concluded that there is sufficient evidence to support a policy for the routine commissioning of this treatment for the indication. The 2 evidence reviews which inform this commissioning position can be accessed here.

Implementation Criteria

Inclusion criteria

- Patients who have failed to achieve adequate seizure control after treatment with two or more appropriate ASMs at the maximum tolerated doses and have been investigated at an Epilepsy Surgery Centre including video-EEG telemetry, MRI, neuropsychological and neuropsychiatric evaluations.
  AND
- A multi-disciplinary team (MDT)[1] decision has to be reached that makes the recommendation for MRgLITT as opposed to any other treatment option, including resective surgery or a palliative procedure such as vagal nerve stimulation.
  AND
- Patient has:
  - hypothalamic hamartoma OR
  - medial temporal lobe epilepsy OR
  - another focus of epilepsy that would make open neurosurgery higher risk than the proposed treatment. Open neurosurgery would be higher risk if there is a risk of damage to surrounding anatomical structures in the path to resection which would cause unacceptable sequelae to language, memory, vision, motor, or sensory function. This should be decided by the above-mentioned MDT alongside the patient.

This will be a highly selective process, and it is estimated that <3% of those who develop epilepsy every year in England will be potential candidates for epilepsy surgery.

Exclusion criteria

Patients who develop a contraindication for minimally invasive surgery in the interim between MDT evaluation and the procedure.

Follow-up criteria

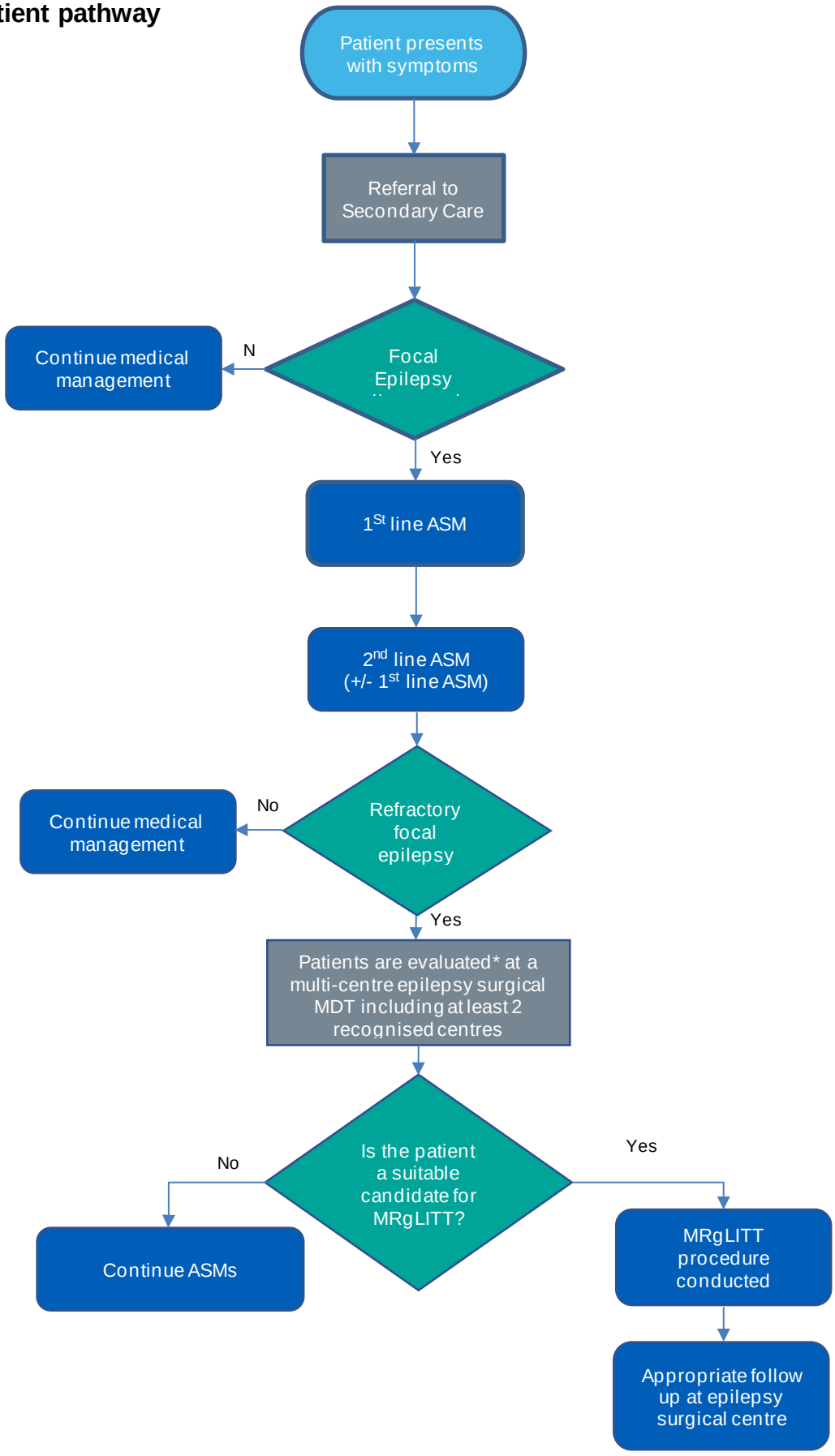
[1] The MDT must include a neurologist, neurophysiologist, neurosurgeon, neuroradiologist, neuropsychologist and psychiatrist; it must be comprised of members from more than one specialist centre.

It is proposed that patients should be reviewed post operatively as follows:

- Neurosurgical and neurology clinic follow-up at 2-3 months
- Neurology clinic, MRI and neuropsychological follow-up at 12 months

Then annual neurology follow-up as the default, for at least 20 years after treatment. Further follow up may be arranged according to clinical need of the individual patient.

Patient pathway



*Evaluation includes consideration of open surgery, MRgLITT and any other appropriate treatment modalities. In paediatric centres, there is a national NHSE children's epilepsy surgery service network.

Governance arrangements

Governance arrangements must be in line with the Service Specifications for Neurosciences: Specialised Neurology (Adult) (NHS England Reference: D04/S/a) or Paediatric Neurosciences (NHS England Reference: E09/S/a).

Mechanism for funding

MR-guided laser interstitial thermal therapy for treatment of epileptogenic zones in children and adults with refractory focal epilepsy will be commissioned and funded by NHS England Specialised Commissioning under existing arrangements for the provision of Specialised Neurology and neurosurgery Adult services and Paediatric Neurosciences services.

Audit Requirements

Provider organisations must register all patients using prior approval software. Specialised centres may use software systems to track and audit use of MRgLITT, in order to demonstrate compliance against the criteria as outlined. Specialised centres will be required to ensure that processes are in place to track decision to treat and evidence of effectiveness through provider level monitoring and data collection. Centres should work collaboratively to ensure that the collected evidence of effectiveness is of an appropriate standard, and in line with the NICE IPG for this service. Providers should aim to collaboratively publish data no later than 3 years from the service being commissioned.

Policy review date

This document will be reviewed when information is received which indicates that the policy requires revision. If a review is needed due to a new evidence base then a new Preliminary Policy Proposal needs to be submitted by contacting england.CET@nhs.net.

Our policies provide access on the basis that the prices of therapies will be at or below the prices and commercial terms submitted for consideration at the time evaluated. NHS England reserves the right to review policies where the supplier of an intervention is no longer willing to supply the treatment to the NHS at or below this price and to review policies where the supplier is unable or unwilling to match price reductions in alternative therapies.

Definitions

MR-guided laser interstitial therapy (MRgLITT)	A minimally invasive treatment which can be used in focal refractory epilepsy.
Identifiable epileptogenic zones	The minimum amount of cortex that must be resected (ablated, inactivated or completely disconnected) to produce seizure freedom (Lüders et al. 2006)
Refractory focal epilepsy	Focal epilepsy specifically refers to misfiring signals which happen in one specific part of the brain; in some patients the area of misfiring signals can be relatively easily identified. 'Refractory' indicates that two different types of anti-seizure medication have been tried and have failed to control a patient's seizures.

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