NHS ENGLAND SPECIALISED SERVICES
CLINICAL PANEL REPORT

Date: July 2021

Intervention: MR-guided laser interstitial thermal therapy (MRgLITT)

Indication: treatment of epileptogenic lesions in children and adults with refractory focal epilepsy

URN: 2006

Gateway: 2, Round 1

Programme: Trauma
CRG: Neuroscience

Information provided to the Panel
Policy Proposition
Two evidence reviews completed by Solutions for Public Health – unsuitable for neurosurgery and high risk neurosurgery.
Equality and Health Inequalities Assessment (EHIA) Report
Clinical Priorities Advisory Group (CPAG) Summary Report
Patient Impact Form
Policy Working Group Appendix
Change of Policy Title Report

Key elements discussed
This policy proposition recommends the routine commissioning of MR-guided laser interstitial thermal therapy (MRgLITT) as first line management in adults and children with refractory focal epilepsy and a well-defined epileptogenic zone. Refractory focal epilepsy refers to epileptic seizure activity which originates from one area of the brain, which is resistant to at least 2 lines of anti-epileptic drugs (AEDs). Open neurosurgical treatment can be effective in experienced centres. However, some patients are at risk of neurological deficits if they undergo open neurosurgical access due to the location of the lesion and pre-existing co-morbidities, and in certain patients the risk of the procedure result in it being contraindicated.

Two evidence reviews were presented. The review for MRgLITT when open neurosurgery carries a high risk of serious adverse effects included eight studies – three were systematic review and meta-analyses (SRMA), one cohort study, two retrospective case series. The certainty of the evidence for all critical and important outcomes was very low. Panel noted an improvement in seizure control was reported with MRgLITT. Some adverse events such as neuropsychological outcomes were reported in the surgical cases.

The second review for those unsuitable for neurosurgical resection included three non-comparative studies – one SRMA and two retrospective cases series. The certainty of the evidence for all critical and important outcomes was very low. Again, an improvement in seizure control was reported with MRgLITT.

It was raised that there are existing not for routine commissioning policies for other treatments relating to this subject area. Work needs to be undertaken to ensure no conflict with this proposition and those in terms of levels of evidence.

It was noted that the Policy Working Group consist of members from the same centre which caused Panel a lot of concern regarding the risk of bias.

A clinical trial is currently underway in America and it was uncertain regarding the progress of this.

EHIA – no additional comments received.

Patient Impact Form – no additional comments received.

Recommendation
Clinical Panel recommends that this proposition returns to a future meeting as no decision could be made.

Why the panel made these recommendations
The Panel requested several actions to be undertaken which would need to be considered by members, including a revision of the Policy Working Group membership.

Documentation amendments required
Policy Working Group:

- Revision of membership to gain a broader involvement across the range of epilepsy surgery centres. Documentation and proposition to then be re-reviewed by the extended PWG.
- More detail required on the research that is currently underway – SLATE trial.
- Check the levels of evidence and our position regarding two other policies relating to Deep Brain Stimulation and Stereotactic Radiosurgery currently published as not for routine commissioning, so not to introduce conflicting positions.

Policy Proposition:

- Define more clearly what it means by those people in high risk surgery
- Inclusion criteria – state the Multidisciplinary team need to include members from more than one centre

Declarations of Interest of Panel Members: One member declared this is within their specialty area but they have never undertaken such a procedure and not likely to. Another member has previously had interaction with the manufacturer of the equipment.
Panel Chair: James Palmer, Medical Director Specialised Services

PWG Post Panel Comments

Policy Working Group:

- Revision of membership to gain a broader involvement across the range of epilepsy surgery centres. *Dr Udo Wieshmann (Consultant Neurologist at Kingston Hospital) and Dr Paul Cooper (Consultant Neurologist at The Greater Manchester Neurosciences Centre) have been added to the PWG by way of extension.*
- More detail required on the research that is currently underway – SLATE trial – *see below.*
- Check the levels of evidence and our position regarding two other policies relating to Deep Brain Stimulation and Stereotactic Radiosurgery currently published as not for routine commissioning, so not to introduce conflicting positions – *see cover paper.*

Policy Proposition:

- Define more clearly what it means by those people in high risk surgery – *see policy proposition updates.*
- Inclusion criteria – state the Multidisciplinary team need to include members from more than one centre – *see policy proposition updates.*

Level of Evidence Check – Deep Brain Stimulation and Stereotactic Radiosurgery

Please see cover paper for further information.

This comparison of evidence was undertaken by the Clinical Policy Team and then shared with the PWG. The PWG stated that as they were not party to the discussions that led to the commissioning decisions for these therapies it is difficult to pass comment.
In conclusion, it is challenging to directly compare the evidence bases for DBS and VNS with MRgLITT. For DBS, the main source of evidence is an RCT of 109 patients comparing DBS turned on and turned off over a 3 month period. The evidence base for MRgLITT is multiple case series analyses with one comparative cohort study.

The population for DBS was refractory partial (also known as focal) epilepsy in non-resectable disease; the two identified populations for MRgLITT are those with refractory focal epilepsy in those with HH unsuitable for neurosurgery OR those with refractory focal epilepsy where the risk of neurosurgery is deemed too high. The populations can therefore be deemed comparable. The population for VNS is refractory epilepsy of focal and generalized onset and is therefore not easily comparable.

The DBS evidence showed a reduction in seizures with only 16% being seizure free with a duration of at least 6 months and the MRgLITT evidence reports a range of between 20-71% being seizure free depending on the aetiology and duration of follow-up. In the HH patient group between 92-100% of patients with drug-resistant focal epilepsy were not having disabling seizures more than 6 months after MRgLITT. The evidence however is difficult to directly compare as the studies are of such different quality and quantity. A comparison of outcomes assessed in each review can be seen in annex A in tabular format.

Comments were sought from the clinical lead who reported that 'DBS is not commissioned for epilepsy treatment in the UK, being largely palliative, with 5% becoming seizure free. Stereotactic Radiosurgery is not commissioned for epilepsy treatment in the UK and is not in clinical favour, as the side-effects are significant, including possible late consequences of irradiation, and that at best, benefit takes 1-2 years to develop.'

Current Research Check

- **The SLATE Trial**

Due to complete May 2022 – results expected 2023.

The purpose of the study is to evaluate the safety and efficacy of the Visualase MRI-guided laser ablation system for necrotization or coagulation of epileptogenic foci in patients with intractable mesial temporal lobe epilepsy (MTLE).

The study will include approximately 150 adult patients with drug resistant MTLE treated at selected epilepsy centers across the United States. After the Visualase procedure, patients will be followed for 12 months and evaluated for freedom from seizures, quality of life, adverse events, and neuropsychological outcomes. Currently there are 102 patients enrolled, with 85 patients having completed a 1 year follow up. The results for these patients are not available as they are not yet validated (information supplied by Medtronic).

The clinical lead commented that '*This study is ongoing, recruitment is slower than anticipated, in large part because patients do not feel equipoise and choose LITT.'*

- **Recently Published Evidence**

Kanner AM, Irving LT, Cajigas I, et al. Long-term seizure and psychiatric outcomes following laser ablation of mesial temporal structures [published online ahead of print, 2022 Feb 9]. *Epilepsia*. 2022;10.1111/epi.17183. doi:10.1111/epi.17183

This recently published paper is a retrospective review of seizure outcome following LiTT, demonstrating it to be a safe and effective option for treatment resistant mesial temporal lobe epilepsy.

Comments from Clinical Experts

Professor Helen Cross was asked to comment on the policy. In summary, the notes received were editorial in nature and did not oppose the policy.

Professor Finbar O'Callaghan was also approached to comment but did not respond.

Conflicts of Interest

All PWG members have completed updated conflict of interest forms and these have been reviewed by the Clinical Policy Team.

Shared Decision Making Tool

The Clinical Policy Team have discussed the option of creating a shared decision making tool for this policy and would like to present this as an option to clinical panel. This would include MRgLITT, resective surgery, vagal nerve stimulation, palliative care or ongoing medication use.