NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Interventional Procedures Programme

Specialist Adviser questionnaire

Before completing this questionnaire, please read Conflicts of Interest for Specialist Advisers. Certain conflicts exclude you from offering advice, however, please return the questionnaire to us incomplete for our records.

Please respond in the boxes provided.

Please complete and return to: azad.hussain@nice.org.uk and IPSA@nice.org.uk

Procedure Name:	**IP1730 - MRI-guided laser interstitial thermal therapy for epilepsy**
Name of Specialist Advisor:	John Duncan
GMC Number:	2503244
Specialist Society:	

1 Do you have adequate knowledge of this procedure to provide advice

☒ Yes.

☐ No – please return the form/answer no more questions.

1.1 Does the title used above describe the procedure adequately?

☒ Yes.

☐ No. If no, please enter any other titles below.

Comments:

2 Your involvement in the procedure

2.1 Is this procedure relevant to your specialty?

☒ Yes.

☐ Is there any kind of inter-specialty controversy over the procedure?

☐x No. If no, then answer no more questions, but please give any information you can about who is likely to be doing the procedure.

Comments:

This will be carried out by a multidisciplinary team, with a neurologist and neurophysiologist assessing the chances of a good result, and the risks. A neuroradiologist interprets imaging data and oversees the MRI scanning. A Neurosurgeon implants the probe along the planned trajectory.

The next 2 questions are about whether you carry out the procedure, or refer patients for it. If you are in a specialty that normally carries out the procedure please answer question 2.2.1. If you are in a specialty that normally selects or refers patients for the procedure, please answer question 2.2.2.

2.2.1 If you are in a specialty that does this procedure, please indicate your experience with it:

☐x I have never done this procedure.

☐ I have done this procedure at least once.

☐ I do this procedure regularly.

Comments:

As a neurologist, my role is in case selection and treatment strategy. As part of a research project we have evaluated over 100 cases carried out in the USA and determined algorithms for optimizing the calculation of laser probe trajectories.

2.2.2 If your specialty is involved in patient selection or referral to another specialty for this procedure, please indicate your experience with it.

☐ I have never taken part in the selection or referral of a patient for this procedure.

☐x I have taken part in patient selection or referred a patient for this procedure at least once.

☐ I take part in patient selection or refer patients for this procedure regularly.

Comments:

2.3 Please indicate your research experience relating to this procedure (please choose one or more if relevant):

☐x I have done bibliographic research on this procedure.

☐ I have done research on this procedure in laboratory settings (e.g. device-related research).

☐x I have done clinical research on this procedure involving patients or healthy volunteers.

☐ I have had no involvement in research on this procedure.

☐ Other (please comment)

Comments:

As above, we have published on this topic.

3 Status of the procedure

3.1 Which of the following best describes the procedure (choose one):

☐**x** Established practice and no longer new.

☐ A minor variation on an existing procedure, which is unlikely to alter the procedure's safety and efficacy.

☐ Definitely novel and of uncertain safety and efficacy.

☐ The first in a new class of procedure.

Comments:

In the USA, well established

3.2 What would be the comparator (standard practice) to this procedure?

Open surgical resection

3.3 Please estimate the proportion of doctors in your specialty who are doing this procedure (choose one):

☐ More than 50% of specialists engaged in this area of work.

☐**x** 10% to 50% of specialists engaged in this area of work.

☐**x** Fewer than 10% of specialists engaged in this area of work.

☐ Cannot give an estimate.

Comments:

In US Specialist Centres 10-50%, but less than 10% of all neurosurgeons

4 Safety and efficacy

4.1 What is the potential harm of the procedure?

Please list adverse events and major risks (even if uncommon) and, if possible, estimate their incidence, as follows:

1. Adverse events reported in the literature (if possible please cite literature)

This was elaborated in the initial proposal made by myself and Mr Tisdall

2. Anecdotal adverse events (known from experience)

Neurological deficit can occur if laser trajectory is not optimal

3. Theoretical adverse events

Unintended heating of brain tissue causing damage if the placement of the laser probe is not optimal.

4.2 What are the key efficacy outcomes for this procedure?

Freedom from epileptic seizures

4.3 Are there uncertainties or concerns about the *efficacy* of this procedure? If so, what are they?

If the ablation does not encompass the epileptogenic zone, seizures may continue

4.4 What training and facilities are needed to do this procedure safely?

Initial training and input from technical expert employed by the manufacturer.

4.5 Are there any major trials or registries of this procedure currently in progress? If so, please list.

The SLATE trial is in progress, evaluating LITT vs conventional surgery for mesial temporal lobe epilepsy

4.6 Are you aware of any abstracts that have been *recently* presented/ published on this procedure that may not be listed in a standard literature search, for example PUBMED? (This can include your own work). If yes, please list.

Please note that NICE will do a literature search: we are only asking you for any very recent or potentially obscure abstracts and papers. Please do not feel the need to supply a comprehensive reference list (but you may list any that you think are particularly important if you wish).

Wu C, Jermakowicz WJ, Chakravorti S, Cajigas I, Sharan AD, Jagid JR, Matias

CM, Sperling MR, Buckley R, Ko A, Ojemann JG, Miller JW, Youngerman B, Sheth SA, McKhann GM, Laxton AW, Couture DE, Popli GS, Smith A, Mehta AD, Ho AL, Halpern CH, Englot DJ, Neimat JS, Konrad PE, Neal E, Vale FL, Holloway KL, Air EL,Schwalb J, Dawant BM, D'Haese PF. Effects of surgical targeting in laser interstitial thermal therapy for mesial temporal lobe epilepsy: A multicenter study of 234 patients. Epilepsia. 2019 Jun;60(6):1171-1183. doi: 10.1111/epi.15565. Epub 2019 May 21. PubMed PMID: 31112302; PubMed Central PMCID:PMC6551254.

Li K, Vakharia VN, Sparks R, França LGS, Granados A, McEvoy AW, Miserocchi A, Wang M, Ourselin S, Duncan JS. Optimizing Trajectories for Cranial Laser Interstitial Thermal Therapy Using Computer-Assisted Planning: A Machine Learning Approach. Neurotherapeutics. 2019 Jan;16(1):182-191. doi: 10.1007/s13311-018-00693-1. Review. PubMed PMID: 30520003; PubMed Central PMCID: PMC6361073.

4.7 Is there controversy, or important uncertainty, about any aspect of the way in which this procedure is currently being done or disseminated?

Not to my knowledge

5 Audit Criteria

Please suggest a minimum dataset of criteria by which this procedure could be audited.

5.1 Outcome measures of benefit (including commonly used clinical outcomes, both short and long - term; and quality-of-life measures). Please suggest the most appropriate method of measurement for each:

Seizure freedom at 1 year, QOLIE-89

5.2 Adverse outcomes (including potential early and late complications). Please state timescales for measurement e.g. bleeding complications up to 1 month post-procedure:

Persistent neurological deficit at 3 months, changes in language and memory, de novo psychiatric disturbance in the first year after the procedure

6 Trajectory of the procedure

6.1 In your opinion, how quickly do you think use of this procedure will spread?

One centre/year in UK, to max of 5 Centres for epilepsy.

6.2 This procedure, if safe and efficacious, is likely to be carried out in (choose one):

☐ Most or all district general hospitals.

☐ A minority of hospitals, but at least 10 in the UK.

☐x Fewer than 10 specialist centres in the UK.

☐ Cannot predict at present.

Comments:

Max of 5 Centres in UK, specialising in epilepsy surgery. Subsequently, there may be uptake for neuro-oncology in up to the 35 Neurosurgery Centres in the UK

6.3 The potential impact of this procedure on the NHS, in terms of numbers of patients eligible for treatment and use of resources, is:

☐ Major.

☐x Moderate.

☐ Minor.

Comments:
Refractory epilepsy has severe cognitive effects and caries risk of morbidity and fatality. Surgical treatment of epilepsy is appropriate for approx. 1000 patients/year in the UK. The place of this therapy is to treat inaccessible foci and lesions that cannot be safely accessed by open surgery, and to reduce the morbidity caused by surgical access.

7 Other information

7.1 Is there any other information about this procedure that might assist NICE in assessing the possible need to investigate its use?

8 Data protection and conflicts of interest

8. Data protection, freedom of information and conflicts of interest

8.1 Data Protection

The information you submit on this form will be retained and used by the NICE and its advisers for the purpose of developing its guidance and may be passed to other approved third parties. Your name and specialist society will be published in NICE publications and on the NICE website. The specialist advice questionnaire will be published in accordance with our guidance development processes and a copy will be sent to the nominating Specialist Society. Please avoid identifying any individual in your comments.

☑ I have read and understood this statement and accept that personal information sent to us will be retained and used for the purposes and in the manner specified

above. For more information about how we process your personal data please see our privacy notice

8.2 Declarations of interest by Specialist Advisers advising the NICE Interventional Procedures Advisory Committee

Nothing in your submission shall restrict any disclosure of information by NICE that is required by law (including in particular, but without limitation, the Freedom of Information Act 2000).

Please submit a conflicts of interest declaration form listing any potential conflicts of interest including any involvement you may have in disputes or complaints relating to this procedure.

Please use the "Conflicts of Interest for Specialist Advisers" policy as a guide when declaring any conflicts of interest. Specialist Advisers should seek advice if needed from the Associate Director – Interventional Procedures.

Do you or a member of your family[1] have a **personal pecuniary** interest? The main examples are as follows:

Consultancies or directorships attracting regular or occasional payments in cash or kind	☐	**YES**
	x ☐	**NO**
Fee-paid work – any work commissioned by the healthcare industry **– this includes income earned in the course of private practice**	x ☐	**YES**
	☐	**NO**
Shareholdings – any shareholding, or other beneficial interest, in shares of the healthcare industry	☐	**YES**
	x ☐	**NO**
Expenses and hospitality – any expenses provided by a healthcare industry company beyond those reasonably required for accommodation, meals and travel to attend meetings and conferences	x ☐	**YES**
	☐	**NO**
Investments – any funds that include investments in the healthcare industry	☐	**YES**
	x ☐	**NO**
Do you have a **personal non-pecuniary** interest – for example have you made a public statement about the topic or do you hold an office in a professional organisation or advocacy group with a direct interest in the topic?	☐	**YES**
	x	**NO**

Do you have a **non-personal** interest? The main examples are as follows:

Fellowships endowed by the healthcare industry	☐	**YES**

[1] 'Family members' refers to a spouse or partner living in the same residence as the member or employee, children for whom the member or employee is legally responsible, and adults for whom the member or employee is legally responsible (for example, an adult whose full power of attorney is held by the individual).

	x ☐	**NO**
Support by the healthcare industry or NICE that benefits his/her position or department, eg grants, sponsorship of posts	**x**	**YES**
	☐	**NO**

If you have answered YES to any of the above statements, please describe the nature of the conflict(s) below.

Comments:

1. Private practice as a consultant neurologist.
2. Fees paid by Circle Harmony for lecture tour in China, and to explore a UK-China joint venture.
3. Medtronic have loaned my research group a robotic guidance device.

Thank you very much for your help.

Dr Tom Clutton-Brock, Interventional Procedures Advisory Committee Chair

Mark Campbell
Acting Programme Director
Devices and Diagnostics

June 2018

Conflicts of Interest for Specialist Advisers

1 Declarations of interest by Specialist Advisers advising the NICE Interventional Procedures Advisory Committee

1.1 Any conflicts of interest set out below should be declared on the questionnaire the Specialist Adviser completes for the procedure.

1.2 Specialist Advisers should seek advice if required from the Associate Director – Interventional Procedures.

2 Personal pecuniary interests

2.1 A personal pecuniary interest involves a current personal payment to a Specialist Adviser, which may either relate to the manufacturer or owner of a product or service being evaluated, in which case it is regarded as **'specific'** or to the industry or sector from which the product or service comes, in which case it is regarded as **'non-specific'**. The main examples are as follows.

2.1.1 **Consultancies** – any consultancy, directorship, position in or work for the healthcare industry that attracts regular or occasional payments in cash or kind (this includes both those which have been undertaken in the 12 months preceding the point at which the declaration is made and which are planned but have not taken place).

2.1.2 **Fee-paid work** – any work commissioned by the healthcare industry for which the member is paid in cash or in kind (this includes both those which have been undertaken in the 12 months preceding the point at which the declaration is made and which are planned but have not taken place).

2.1.3 **Shareholdings** – any shareholding, or other beneficial interest, in shares of the healthcare industry that are either held by the individual or for which the individual has legal responsibility (for example, children, or relatives whose full Power of Attorney is held by the individual). This does not include shareholdings through unit trusts, pensions funds, or other similar arrangements where the member has no influence on financial management.

2.1.4 **Expenses and hospitality** – any expenses provided by a healthcare industry company beyond that reasonably required for accommodation, meals and travel to attend meetings and conferences (this includes both those which have been undertaken in the 12 months preceding the point at which the declaration is made and which are planned but have not taken place.

2.1.5 **Investments** – any funds which include investments in the healthcare industry that are held in a portfolio over which individuals have the ability to instruct the fund manager as to the composition of the fund.

2.2 No personal interest exists in the case of:

2.2.1 assets over which individuals have no financial control (for example, wide portfolio unit trusts and occupational pension funds) and where the fund manager has full discretion as to its composition (for example, the Universities Superannuation Scheme)

2.2.2 accrued pension rights from earlier employment in the healthcare industry.

3 Personal family interest

3.1 This relates to the personal interests of a family member and involves a **current payment** to the family member of the Specialist Adviser. The interest may relate to the manufacturer or owner of a product or service being evaluated, in which case it is regarded as '**specific**', or to the industry or sector from which the product or service comes, in which case it is regarded as '**non-specific**'. The main examples include the following.

3.1.1 Any consultancy, directorship, position in or work for a healthcare industry that attracts regular or occasional payments in cash or in kind.

3.1.2 Any fee-paid work commissioned by a healthcare industry for which the member is paid in cash or in kind.

3.1.3 Any shareholdings, or other beneficial interests, in a healthcare industry which are either held by the family member or for which an individual covered by this Code has legal responsibility (for example, children, or adults whose full Power of Attorney is held by the individual).

3.1.4 Expenses and hospitality provided by a healthcare industry company (except where they are provided to a general class of people such as attendees at an open conference)

3.1.5 Funds which include investments in the healthcare industry that are held in a portfolio over which individuals have the ability to instruct the fund manager as to the composition of the fund.

3.2 No personal family interest exists in the case of:

3.2.1 assets over which individuals have no financial control (for example, wide portfolio unit trusts and occupational pension funds) and where the fund manager has full discretion as to its composition (for example, the Universities Superannuation Scheme)

3.2.2 accrued pension rights from earlier employment in the healthcare industry.

4 Personal non-pecuniary interests

These might include, but are not limited to:

4.1 a clear opinion, reached as the conclusion of a research project, about the clinical and/or cost effectiveness of an intervention under review

4.2 a public statement in which an individual covered by this Code has expressed a clear opinion about the matter under consideration, which could reasonably be interpreted as prejudicial to an objective interpretation of the evidence

4.3 holding office in a professional organisation or advocacy group with a direct interest in the matter under consideration

4.4 other reputational risks in relation to an intervention under review.

5 Non-personal interests

5.1 A non-personal interest involves payment that benefits a department or organisation for which a Specialist Advisor is responsible, but that is not received by the Specialist Advisor personally. This may either relate to the product or service being evaluated, in which case it is regarded as **'specific,'** or to the manufacturer or owner of the product or service, but is unrelated to the matter under consideration, in which case it is regarded as **'non-specific'**. The main examples are as follows.

5.1.1 **Fellowships** – the holding of a fellowship endowed by the healthcare industry.

5.1.2 **Support by the healthcare industry or NICE** – any payment, or other support by the healthcare industry or by NICE that does not convey any pecuniary or material benefit to a member personally but that does benefit his/her position or department. For example:

- a grant from a company for the running of a unit or department for which a Specialist Advisor is responsible
- a grant, fellowship or other payment to sponsor a post or member of staff in the unit for which a Specialist Adviser is responsible. This does not include financial assistance for students
- the commissioning of research or other work by, or advice from, staff who work in a unit for which the specialist advisor is responsible
- one or more contracts with, or grants from, NICE.

5.2 Specialist Advisers are under no obligation to seek out knowledge of work done for, or on behalf of, the healthcare industry within departments for which they are responsible if they would not normally expect to be informed.

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Interventional Procedures Programme

Specialist Adviser questionnaire

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Please respond in the boxes provided.

Please complete and return to: azad.hussain@nice.org.uk and IPSA@nice.org.uk

Procedure Name:	**MRI-guided laser interstitial thermal therapy for epilepsy**
Name of Specialist Advisor:	**Keyoumars Ashkan**
Specialist Society:	Society of British Neurological Surgeons (SBNS)

1 Do you have adequate knowledge of this procedure to provide advice?

☒ Yes.

☐ No – please return the form/answer no more questions.

1.1 Does the title used above describe the procedure adequately?

☒ Yes.

☐ No. If no, please enter any other titles below.

Comments:

2 Your involvement in the procedure

2.1 Is this procedure relevant to your specialty?

☒ Yes.

☐ Is there any kind of inter-specialty controversy over the procedure?

☐ No. If no, then answer no more questions, but please give any information you can about who is likely to be doing the procedure.

Comments:

The next 2 questions are about whether you carry out the procedure, or refer patients for it. If you are in a specialty that normally carries out the procedure please answer question 2.2.1. If you are in a specialty that normally selects or refers patients for the procedure, please answer question 2.2.2.

2.2.1 If you are in a specialty that does this procedure, please indicate your experience with it:

☐ I have never done this procedure.

☐ I have done this procedure at least once.

☒ I do this procedure regularly.

Comments:

I have had access to this technology since October 2018 when a private hospital I work at, purchased this. I have done the procedure now in several patients, all with brain tumours, some with epilepsy.

2.2.2 If your specialty is involved in patient selection or referral to another specialty for this procedure, please indicate your experience with it.

☐ I have never taken part in the selection or referral of a patient for this procedure.

☐ I have taken part in patient selection or referred a patient for this procedure at least once.

☒ I take part in patient selection or refer patients for this procedure regularly.

Comments:

All patients are selected through a MDT which I am part of.

2.3 Please indicate your research experience relating to this procedure (please choose one or more if relevant):

☒ I have done bibliographic research on this procedure.

☐ I have done research on this procedure in laboratory settings (e.g. device-related research).

☐ I have done clinical research on this procedure involving patients or healthy volunteers.

☐ I have had no involvement in research on this procedure.

☐ Other (please comment)

Comments:

I have published one paper on this.

3 Status of the procedure

3.1 Which of the following best describes the procedure (choose one):

☒ Established practice and no longer new.

☐ A minor variation on an existing procedure, which is unlikely to alter the procedure's safety and efficacy.

☐ Definitely novel and of uncertain safety and efficacy.

☐ The first in a new class of procedure.

Comments:

This procedure has been in routine clinical use in the USA for a decade. However, it only recently obtained CE mark (Spring 2018) with the first machine put in the UK in October 2018 in the Harley Street Clinic and the other in early 2019 at the Great Ormond Street Hospital (only 2 machines in the UK)

3.2 What would be the comparator (standard practice) to this procedure?

Open surgery ie craniotomy.

3.3 Please estimate the proportion of doctors in your specialty who are doing this procedure (choose one):

☐ More than 50% of specialists engaged in this area of work.

☐ 10% to 50% of specialists engaged in this area of work.

☒ Fewer than 10% of specialists engaged in this area of work.

☐ Cannot give an estimate.

Comments:

Only 3-4 surgeons using it with the 2 machines in the UK. Numbers are much greater in the USA

4 Safety and efficacy

4.1 What is the potential harm of the procedure?

Please list adverse events and major risks (even if uncommon) and, if possible, estimate their incidence, as follows:

1. Adverse events reported in the literature (if possible please cite literature)

Compared to the alternative ie open surgery, the risks are far less with a much quicker recovery and shorter length of hospital stay. Nonetheless this is a minimally invasive neurosurgical procedure and therefore does carry some risks including haemorrhage at much less than 1% which if large enough can lead to neurological deficit or even risk to life. Infection risk is rare due to the very small (stab) incision.

2. Anecdotal adverse events (known from experience)

3. Theoretical adverse events

Laser thermal injury to the brain. Given that the procedure is done under real time MRI thermometry, it is possible to put temperature limits to stop the temperature rising in the critical brain structures so this risk is more theoretical.

4.2 What are the key efficacy outcomes for this procedure?

For primary epilepsy: Seizure reduction
For epilepsy secondary to tumours: Tumour ablation

4.3 Are there uncertainties or concerns about the *efficacy* of this procedure? If so, what are they?

Given that this is a new technology, data is still accumulating. The current published literature does not show significant differences in the efficacy between this technique and open surgery.

4.4 What training and facilities are needed to do this procedure safely?

Training: This is a stereotactic technique which should be familiar to stereotactic neurosurgeons. The MRI thermometry component will need training; this is provided through a combination of proctorship and support from the manufacturer.

Facility: Standard neurosurgical theatre; access to a 1.5 T MRI scanner (intra-operative MRI is not necessary). The hardware component consists of a stack located in the MRI control room. It holds the laser generator and 2 computer screens and keyboards. The disposable element consists of the laser catheter and tubings.

4.5 Are there any major trials or registries of this procedure currently in progress? If so, please list.

I believe there is a trial ongoing in the USA.

4.6 Are you aware of any abstracts that have been *recently* presented/ published on this procedure that may not be listed in a standard literature search, for example PUBMED? (This can include your own work). If yes, please list.
Please note that NICE will do a literature search: we are only asking you for any very recent or potentially obscure abstracts and papers. Please do not feel the need to supply a comprehensive reference list (but you may list any that you think are particularly important if you wish).

No I am not.

4.7 Is there controversy, or important uncertainty, about any aspect of the way in which this procedure is currently being done or disseminated?

No

5 Audit Criteria

Please suggest a minimum dataset of criteria by which this procedure could be audited.

5.1 Outcome measures of benefit (including commonly used clinical outcomes, both short and long - term; and quality-of-life measures). Please suggest the most appropriate method of measurement for each:

Primary epilepsy: Seizure freedom (Engel scale); Complication rates: neurological deficits, bleeds; Quality of life: WHO

Secondary epilepsy: Above plus: Tumour control as based on serial MRIs, Progression free survival, overall survival

5.2 Adverse outcomes (including potential early and late complications). Please state timescales for measurement e.g. bleeding complications up to 1 month post-procedure:

Bleeding: 1 week; Neurological deficit: 1, 6 ,12 months; Cognitive deficits: 1, 6, 12 months

6 Trajectory of the procedure

6.1 In your opinion, how quickly do you think use of this procedure will spread?

In the USA this has progressed fast with many units now perform this procedure not only as the first line but also as second line when symptoms recur. UK is likely to follow.

6.2 This procedure, if safe and efficacious, is likely to be carried out in (choose one):

☐ Most or all district general hospitals.

☒ A minority of hospitals, but at least 10 in the UK.

☐ Fewer than 10 specialist centres in the UK.

☐ Cannot predict at present.

Comments:

There are under 20 neurosurgical units in the UK

6.3 The potential impact of this procedure on the NHS, in terms of numbers of patients eligible for treatment and use of resources, is:

☐ Major.

☐ Moderate.

☒ Minor.

Comments:
Overall the number of epilepsy patients needing neurosurgical intervention is very small. In terms of epilepsy related to tumours, again at most brain tumours are less than 2% of all tumours so rare.

7 Other information

7.1 Is there any other information about this procedure that might assist NICE in assessing the possible need to investigate its use?

The current cost of the disposables is high but I suspect this will drop as the use increases. This will then make this procedure very cost effective given that the average length of hospital stay is 1 day compared to around 5 days for the open surgical alternative. Patient choice will also be a major factor given the minimally invasive keyhole nature of this procedure.

8 Data protection and conflicts of interest

8. Data protection, freedom of information and conflicts of interest

8.1 Data Protection

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☑ I have read and understood this statement and accept that personal information sent to us will be retained and used for the purposes and in the manner specified above. For more information about how we process your personal data please see our privacy notice

8.2 Declarations of interest by Specialist Advisers advising the NICE Interventional Procedures Advisory Committee

Nothing in your submission shall restrict any disclosure of information by NICE that is required by law (including in particular, but without limitation, the Freedom of Information Act 2000).

Please submit a conflicts of interest declaration form listing any potential conflicts of interest including any involvement you may have in disputes or complaints relating to this procedure.

Please use the "Conflicts of Interest for Specialist Advisers" policy as a guide when declaring any conflicts of interest. Specialist Advisers should seek advice if needed from the Associate Director – Interventional Procedures.

Do you or a member of your family[1] have a **personal pecuniary** interest? The main examples are as follows:

Consultancies or directorships attracting regular or occasional payments in cash or kind	☒	**YES**
	☐	**NO**
Fee-paid work – any work commissioned by the healthcare industry **– this includes income earned in the course of private practice**	☒	**YES**
	☐	**NO**
Shareholdings – any shareholding, or other beneficial interest, in shares of the healthcare industry	☐	**YES**
	☒	**NO**
Expenses and hospitality – any expenses provided by a healthcare industry company beyond those reasonably required for accommodation, meals and travel to attend meetings and conferences	☐	**YES**
	☒	**NO**

[1] 'Family members' refers to a spouse or partner living in the same residence as the member or employee, children for whom the member or employee is legally responsible, and adults for whom the member or employee is legally responsible (for example, an adult whose full power of attorney is held by the individual).

Investments – any funds that include investments in the healthcare industry	☐	**YES**
	☒	**NO**
Do you have a **personal non-pecuniary** interest – for example have you made a public statement about the topic or do you hold an office in a professional organisation or advocacy group with a direct interest in the topic?	☐	**YES**
	☒	**NO**
Do you have a **non-personal** interest? The main examples are as follows:		
Fellowships endowed by the healthcare industry	☐	**YES**
	☒	**NO**
Support by the healthcare industry or NICE that benefits his/her position or department, eg grants, sponsorship of posts	☐	**YES**
	☒	**NO**

If you have answered YES to any of the above statements, please describe the nature of the conflict(s) below.

Comments:
I have performed consultancy for and also been involved in educational events, attracting payments, organised by the Medtronic company which is the manufacturer of this technology. None of these, however, have been in relation to this particular technology but to do with totally unrelated products.

Thank you very much for your help.

Dr Tom Clutton-Brock, Interventional Procedures Advisory Committee Chair

Mark Campbell
Acting Programme Director
Devices and Diagnostics

June 2018

Conflicts of Interest for Specialist Advisers

1 Declarations of interest by Specialist Advisers advising the NICE Interventional Procedures Advisory Committee

1.1 Any conflicts of interest set out below should be declared on the questionnaire the Specialist Adviser completes for the procedure.

1.2 Specialist Advisers should seek advice if required from the Associate Director – Interventional Procedures.

2 Personal pecuniary interests

2.1 A personal pecuniary interest involves a current personal payment to a Specialist Adviser, which may either relate to the manufacturer or owner of a product or service being evaluated, in which case it is regarded as **'specific'** or to the industry or sector from which the product or service comes, in which case it is regarded as **'non-specific'**. The main examples are as follows.

2.1.1 **Consultancies** – any consultancy, directorship, position in or work for the healthcare industry that attracts regular or occasional payments in cash or kind (this includes both those which have been undertaken in the 12 months preceding the point at which the declaration is made and which are planned but have not taken place).

2.1.2 **Fee-paid work** – any work commissioned by the healthcare industry for which the member is paid in cash or in kind (this includes both those which have been undertaken in the 12 months preceding the point at which the declaration is made and which are planned but have not taken place).

2.1.3 **Shareholdings** – any shareholding, or other beneficial interest, in shares of the healthcare industry that are either held by the individual or for which the individual has legal responsibility (for example, children, or relatives whose full Power of Attorney is held by the individual). This does not include shareholdings through unit trusts, pensions funds, or other similar arrangements where the member has no influence on financial management.

2.1.4 **Expenses and hospitality** – any expenses provided by a healthcare industry company beyond that reasonably required for accommodation, meals and travel to attend meetings and conferences (this includes both those which have been undertaken in the 12 months preceding the point at which the declaration is made and which are planned but have not taken place.

2.1.5 **Investments** – any funds which include investments in the healthcare industry that are held in a portfolio over which individuals have the ability to instruct the fund manager as to the composition of the fund.

2.2 No personal interest exists in the case of:

2.2.1 assets over which individuals have no financial control (for example, wide portfolio unit trusts and occupational pension funds) and where the fund manager has full discretion as to its composition (for example, the Universities Superannuation Scheme)

2.2.2 accrued pension rights from earlier employment in the healthcare industry.

3 Personal family interest

3.1 This relates to the personal interests of a family member and involves a **current payment** to the family member of the Specialist Adviser. The interest may relate to the manufacturer or owner of a product or service being evaluated, in which case it is regarded as '**specific**', or to the industry or sector from which the product or service comes, in which case it is regarded as '**non-specific**'. The main examples include the following.

3.1.1 Any consultancy, directorship, position in or work for a healthcare industry that attracts regular or occasional payments in cash or in kind.

3.1.2 Any fee-paid work commissioned by a healthcare industry for which the member is paid in cash or in kind.

3.1.3 Any shareholdings, or other beneficial interests, in a healthcare industry which are either held by the family member or for which an individual covered by this Code has legal responsibility (for example, children, or adults whose full Power of Attorney is held by the individual).

3.1.4 Expenses and hospitality provided by a healthcare industry company (except where they are provided to a general class of people such as attendees at an open conference)

3.1.5 Funds which include investments in the healthcare industry that are held in a portfolio over which individuals have the ability to instruct the fund manager as to the composition of the fund.

3.2 No personal family interest exists in the case of:

3.2.1 assets over which individuals have no financial control (for example, wide portfolio unit trusts and occupational pension funds) and where the fund manager has full discretion as to its composition (for example, the Universities Superannuation Scheme)

3.2.2 accrued pension rights from earlier employment in the healthcare industry.

4 Personal non-pecuniary interests

These might include, but are not limited to:

4.1 a clear opinion, reached as the conclusion of a research project, about the clinical and/or cost effectiveness of an intervention under review

4.2 a public statement in which an individual covered by this Code has expressed a clear opinion about the matter under consideration, which could reasonably be interpreted as prejudicial to an objective interpretation of the evidence

4.3 holding office in a professional organisation or advocacy group with a direct interest in the matter under consideration

4.4 other reputational risks in relation to an intervention under review.

5 Non-personal interests

5.1 A non-personal interest involves payment that benefits a department or organisation for which a Specialist Advisor is responsible, but that is not received by the Specialist Advisor personally. This may either relate to the product or service being evaluated, in which case it is regarded as **'specific,'** or to the manufacturer or owner of the product or service, but is unrelated to the matter under consideration, in which case it is regarded as **'non-specific'**. The main examples are as follows.

5.1.1 **Fellowships** – the holding of a fellowship endowed by the healthcare industry.

5.1.2 **Support by the healthcare industry or NICE** – any payment, or other support by the healthcare industry or by NICE that does not convey any pecuniary or material benefit to a member personally but that does benefit his/her position or department. For example:

- a grant from a company for the running of a unit or department for which a Specialist Advisor is responsible
- a grant, fellowship or other payment to sponsor a post or member of staff in the unit for which a Specialist Adviser is responsible. This does not include financial assistance for students
- the commissioning of research or other work by, or advice from, staff who work in a unit for which the specialist advisor is responsible
- one or more contracts with, or grants from, NICE.

5.2 Specialist Advisers are under no obligation to seek out knowledge of work done for, or on behalf of, the healthcare industry within departments for which they are responsible if they would not normally expect to be informed.

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Interventional Procedures Programme

Specialist Adviser questionnaire

Please respond in the boxes provided.

Procedure Name:
IP1730 - MRI Guided Laser interstitial thermal therapy (LITT) for treatment of epileptogenic lesions in children and adults
Name of Specialist Advisor:
Martin Tisdall
Specialist Society:
Royal College of Surgeons of England

1 Do you have adequate knowledge of this procedure to provide advice?

x Yes.

☐ No – please return the form/answer no more questions.

1.1 Does the title used above describe the procedure adequately?

x Yes.

☐ No. If no, please enter any other titles below.

Comments:

2 Your involvement in the procedure

2.1 Is this procedure relevant to your specialty?

x Yes.

☐ Is there any kind of inter-specialty controversy over the procedure?

☐ No. If no, then answer no more questions, but please give any information you can about who is likely to be doing the procedure.

Comments: Adult and paediatric neurology also involved in procedure

The next 2 questions are about whether you carry out the procedure, or refer patients for it. If you are in a specialty that normally carries out the procedure please answer question 2.2.1. If you are in a specialty that normally selects or refers patients for the procedure, please answer question 2.2.2.

2.2.1 If you are in a specialty that does this procedure, please indicate your experience with it:

☐ I have never done this procedure.

x I have done this procedure at least once.

☐ I do this procedure regularly.

Comments:

Performed procedure 3 times

2.2.2 If your specialty is involved in patient selection or referral to another specialty for this procedure, please indicate your experience with it.

☐ I have never taken part in the selection or referral of a patient for this procedure.

x I have taken part in patient selection or referred a patient for this procedure at least once.

☐ I take part in patient selection or refer patients for this procedure regularly.

Comments:

Involved in selection in 8 cases

2.3 Please indicate your research experience relating to this procedure (please choose one or more if relevant):

x I have done bibliographic research on this procedure.

☐ I have done research on this procedure in laboratory settings (e.g. device-related research).

☐ I have done clinical research on this procedure involving patients or healthy volunteers.

☐ I have had no involvement in research on this procedure.

☐ Other (please comment)

Comments:

3 Status of the procedure

3.1 Which of the following best describes the procedure (choose one):

x Established practice and no longer new.

☐ A minor variation on an existing procedure, which is unlikely to alter the procedure's safety and efficacy.

☐ Definitely novel and of uncertain safety and efficacy.

☐ The first in a new class of procedure.

Comments:

Well established in USA - approximately 10 yr experience

3.2 What would be the comparator (standard practice) to this procedure?

Open microsurgical neurosurgery resection

3.3 Please estimate the proportion of doctors in your specialty who are doing this procedure (choose one):

☐ More than 50% of specialists engaged in this area of work.

☐ 10% to 50% of specialists engaged in this area of work.

☐ Fewer than 10% of specialists engaged in this area of work.

x Cannot give an estimate.

Comments:

4 Safety and efficacy

4.1 What is the potential harm of the procedure?

Please list adverse events and major risks (even if uncommon) and, if possible, estimate their incidence, as follows:

1. Adverse events reported in the literature (if possible please cite literature)

   Lewis EC, Weil AG, Duchowny M, et al. MR-guided laser interstitial thermal therapy for pediatric drug-resistant lesional epilepsy. Epilepsia 2015;56(10):1590–1598.

MR-guided laser ablation for the treatment of hypothalamic hamartomas.
Curry DJ, Raskin J, Ali I, Wilfong AA.
Epilepsy Res. 2018 May;142:131-134. doi: 10.1016/j.eplepsyres.2018.03.013.
Epub 2018 Apr 7.

2. Anecdotal adverse events (known from experience)

3. Theoretical adverse events

4.2 What are the key efficacy outcomes for this procedure?

Long term seizure freedom and length of stay

4.3 Are there uncertainties or concerns about the *efficacy* of this procedure? If so, what are they?

Multiple peer reviewed publications reporting efficacy

4.4 What training and facilities are needed to do this procedure safely?

Training from equipment suppliers. Cases are supported by equipment supplier technician. Training also available at commercial workshops

4.5 Are there any major trials or registries of this procedure currently in progress? If so, please list.

US based trial of LiTT for hippocampal sclerosis in adults

4.6 Are you aware of any abstracts that have been *recently* presented/ published on this procedure that may not be listed in a standard literature search, for example PUBMED? (This can include your own work). If yes, please list.
Please note that NICE will do a literature search: we are only asking you for any very recent or potentially obscure abstracts and papers. Please do not feel the need to supply a comprehensive reference list (but you may list any that you think are particularly important if you wish).

No

4.7 Is there controversy, or important uncertainty, about any aspect of the way in which this procedure is currently being done or disseminated?

Uncertainty around further patient groups such as neuro oncology patients who may benefit from this procedure.

5 Audit Criteria

Please suggest a minimum dataset of criteria by which this procedure could be audited.

Demographics, indication, presumed pathology, number of catheters used, post-procedure complications, length of stay, seizure outcome, endocrine outcome (where appropriate)

5.1 Outcome measures of benefit (including commonly used clinical outcomes, both short and long - term; and quality-of-life measures). Please suggest the most appropriate method of measurement for each:

Seizure outcome - Engel score

5.2 Adverse outcomes (including potential early and late complications). Please state timescales for measurement e.g. bleeding complications up to 1 month post-procedure:

Peri-operative neurological deficit - immediate and 30 days post op
Infection - 30 days
Endocrine outcome - 6 months
Opthalmology outcome - 6 months

6 Trajectory of the procedure

6.1 In your opinion, how quickly do you think use of this procedure will spread?

Infrastructure within England and Wales Children's Epilepsy Surgery Service would allow adoption of this technique for treatment of epilepsy in children within short timescale. We already have a national virtual MDT at which these cases can be discussed.

6.2 This procedure, if safe and efficacious, is likely to be carried out in (choose one):

☐ Most or all district general hospitals.

☐ A minority of hospitals, but at least 10 in the UK.

x Fewer than 10 specialist centres in the UK.

☐ Cannot predict at present.

Comments:

6.3 The potential impact of this procedure on the NHS, in terms of numbers of patients eligible for treatment and use of resources, is:

☐ Major.

☐ Moderate.

x Minor.

Comments:

7 Other information

7.1 Is there any other information about this procedure that might assist NICE in assessing the possible need to investigate its use?

8 Data protection and conflicts of interest

8. Data protection, freedom of information and conflicts of interest

8.1 Data Protection

The information you submit on this form will be retained and used by the NICE and its advisers for the purpose of developing its guidance and may be passed to other approved third parties. Your name and specialist society will be published in NICE publications and on the NICE website. The specialist advice questionnaire will be published in accordance with our guidance development processes and a copy will be sent to the nominating Specialist Society. Please avoid identifying any individual in your comments.

xI have read and understood this statement and accept that personal information sent to us will be retained and used for the purposes and in the manner specified above. For more information about how we process your personal data please see our privacy notice

8.2 Declarations of interest by Specialist Advisers advising the NICE Interventional Procedures Advisory Committee

Nothing in your submission shall restrict any disclosure of information by NICE that is required by law (including in particular, but without limitation, the Freedom of Information Act 2000).

Please submit a conflicts of interest declaration form listing any potential conflicts of interest including any involvement you may have in disputes or complaints relating to this procedure.

Please use the "Conflicts of Interest for Specialist Advisers" policy as a guide when declaring any conflicts of interest. Specialist Advisers should seek advice if needed from the Associate Director – Interventional Procedures.

Do you or a member of your family[1] have a **personal pecuniary** interest? The main examples are as follows:

Consultancies or directorships attracting regular or occasional payments in cash or kind	☐	**YES**
	x	**NO**
Fee-paid work – any work commissioned by the healthcare industry **– this includes income earned in the course of private practice**	☐	**YES**
	x	**NO**
Shareholdings – any shareholding, or other beneficial interest, in shares of the healthcare industry	☐	**YES**
	x	**NO**
Expenses and hospitality – any expenses provided by a healthcare industry company beyond those reasonably required for accommodation, meals and travel to attend meetings and conferences	☐	**YES**
	x	**NO**
Investments – any funds that include investments in the healthcare industry	☐	**YES**
	x	**NO**
Do you have a **personal non-pecuniary** interest – for example have you made a public statement about the topic or do you hold an office in a professional organisation or advocacy group with a direct interest in the topic?	☐	**YES**
	x	**NO**

Do you have a **non-personal** interest? The main examples are as follows:

Fellowships endowed by the healthcare industry	☐	**YES**
	x	**NO**
Support by the healthcare industry or NICE that benefits his/her position or department, eg grants, sponsorship of posts	☐	**YES**
	x	**NO**

If you have answered YES to any of the above statements, please describe the nature of the conflict(s) below.

Comments:

Thank you very much for your help.

Dr Tom Clutton-Brock, Interventional Procedures Advisory Committee Chair

Mirella Marlow Programme Director

[1] 'Family members' refers to a spouse or partner living in the same residence as the member or employee, children for whom the member or employee is legally responsible, and adults for whom the member or employee is legally responsible (for example, an adult whose full power of attorney is held by the individual).

July 2019

Conflicts of Interest for Specialist Advisers

1 Declarations of interest by Specialist Advisers advising the NICE Interventional Procedures Advisory Committee

1.1 Any conflicts of interest set out below should be declared on the questionnaire the Specialist Adviser completes for the procedure.

1.2 Specialist Advisers should seek advice if required from the Associate Director – Interventional Procedures.

2 Personal pecuniary interests

2.1 A personal pecuniary interest involves a current personal payment to a Specialist Adviser, which may either relate to the manufacturer or owner of a product or service being evaluated, in which case it is regarded as **'specific'** or to the industry or sector from which the product or service comes, in which case it is regarded as **'non-specific'**. The main examples are as follows.

2.1.1 **Consultancies** – any consultancy, directorship, position in or work for the healthcare industry that attracts regular or occasional payments in cash or kind (this includes both those which have been undertaken in the 12 months preceding the point at which the declaration is made and which are planned but have not taken place).

2.1.2 **Fee-paid work** – any work commissioned by the healthcare industry for which the member is paid in cash or in kind (this includes both those which have been undertaken in the 12 months preceding the point at which the declaration is made and which are planned but have not taken place).

2.1.3 **Shareholdings** – any shareholding, or other beneficial interest, in shares of the healthcare industry that are either held by the individual or for which the individual has legal responsibility (for example, children, or relatives whose full Power of Attorney is held by the individual). This does not include shareholdings through unit trusts, pensions funds, or other similar arrangements where the member has no influence on financial management.

2.1.4 **Expenses and hospitality** – any expenses provided by a healthcare industry company beyond that reasonably required for accommodation, meals and travel to attend meetings and conferences (this includes both those which have been undertaken in the 12 months preceding the point at which the declaration is made and which are planned but have not taken place.

2.1.5 **Investments** – any funds which include investments in the healthcare industry that are held in a portfolio over which individuals have the ability to instruct the fund manager as to the composition of the fund.

2.2 No personal interest exists in the case of:

2.2.1 assets over which individuals have no financial control (for example, wide portfolio unit trusts and occupational pension funds) and where the fund manager has full discretion as to its composition (for example, the Universities Superannuation Scheme)

2.2.2 accrued pension rights from earlier employment in the healthcare industry.

3 Personal family interest

3.1 This relates to the personal interests of a family member and involves a **current payment** to the family member of the Specialist Adviser. The interest may relate to the manufacturer or owner of a product or service being evaluated, in which case it is regarded as '**specific**', or to the industry or sector from which the product or service comes, in which case it is regarded as '**non-specific**'. The main examples include the following.

3.1.1 Any consultancy, directorship, position in or work for a healthcare industry that attracts regular or occasional payments in cash or in kind.

3.1.2 Any fee-paid work commissioned by a healthcare industry for which the member is paid in cash or in kind.

3.1.3 Any shareholdings, or other beneficial interests, in a healthcare industry which are either held by the family member or for which an individual covered by this Code has legal responsibility (for example, children, or adults whose full Power of Attorney is held by the individual).

3.1.4 Expenses and hospitality provided by a healthcare industry company (except where they are provided to a general class of people such as attendees at an open conference)

3.1.5 Funds which include investments in the healthcare industry that are held in a portfolio over which individuals have the ability to instruct the fund manager as to the composition of the fund.

3.2 No personal family interest exists in the case of:

3.2.1 assets over which individuals have no financial control (for example, wide portfolio unit trusts and occupational pension funds) and where the fund manager has full discretion as to its composition (for example, the Universities Superannuation Scheme)

3.2.2 accrued pension rights from earlier employment in the healthcare industry.

4 Personal non-pecuniary interests

These might include, but are not limited to:

4.1 a clear opinion, reached as the conclusion of a research project, about the clinical and/or cost effectiveness of an intervention under review

4.2 a public statement in which an individual covered by this Code has expressed a clear opinion about the matter under consideration, which could reasonably be interpreted as prejudicial to an objective interpretation of the evidence

4.3 holding office in a professional organisation or advocacy group with a direct interest in the matter under consideration

4.4 other reputational risks in relation to an intervention under review.

5 Non-personal interests

5.1 A non-personal interest involves payment that benefits a department or organisation for which a Specialist Advisor is responsible, but that is not received by the Specialist Advisor personally. This may either relate to the product or service being evaluated, in which case it is regarded as **'specific,'** or to the manufacturer or owner of the product or service, but is unrelated to the matter under consideration, in which case it is regarded as **'non-specific'**. The main examples are as follows.

5.1.1 **Fellowships** – the holding of a fellowship endowed by the healthcare industry.

5.1.2 **Support by the healthcare industry or NICE** – any payment, or other support by the healthcare industry or by NICE that does not convey any pecuniary or material benefit to a member personally but that does benefit his/her position or department. For example:

- a grant from a company for the running of a unit or department for which a Specialist Advisor is responsible
- a grant, fellowship or other payment to sponsor a post or member of staff in the unit for which a Specialist Adviser is responsible. This does not include financial assistance for students
- the commissioning of research or other work by, or advice from, staff who work in a unit for which the specialist advisor is responsible
- one or more contracts with, or grants from, NICE.

5.2 Specialist Advisers are under no obligation to seek out knowledge of work done for, or on behalf of, the healthcare industry within departments for which they are responsible if they would not normally expect to be informed.

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Interventional Procedures Programme

Specialist Adviser questionnaire

Before completing this questionnaire, please read Conflicts of Interest for Specialist Advisers. Certain conflicts exclude you from offering advice, however, please return the questionnaire to us incomplete for our records.

Please respond in the boxes provided.

Please complete and return to: azad.hussain@nice.org.uk and IPSA@nice.org.uk

Procedure Name:	**MRI-guided laser interstitial thermal therapy for epilepsy**
Name of Specialist Advisor:	Rajiv Mohanraj
Specialist Society:	Association of British Neurologists (ABN)

1 Do you have adequate knowledge of this procedure to provide advice?

☒ Yes.

☐ No – please return the form/answer no more questions.

1.1 Does the title used above describe the procedure adequately?

☒ Yes.

☐ No. If no, please enter any other titles below.

Comments:

2 Your involvement in the procedure

2.1 Is this procedure relevant to your specialty?

☒ Yes.

☐ Is there any kind of inter-specialty controversy over the procedure?

☐ No. If no, then answer no more questions, but please give any information you can about who is likely to be doing the procedure.

Comments:

Neurologists would be involved in the selection of patients for the procedure, but the procedure itself will be done by neurosurgeons. Patients under the age of 16 would be evaluated by paediatric neurologists with interest in epilepsy.

The next 2 questions are about whether you carry out the procedure, or refer patients for it. If you are in a specialty that normally carries out the procedure please answer question 2.2.1. If you are in a specialty that normally selects or refers patients for the procedure, please answer question 2.2.2.

2.2.1 If you are in a specialty that does this procedure, please indicate your experience with it:

☒ I have never done this procedure.

☐ I have done this procedure at least once.

☐ I do this procedure regularly.

Comments:

I am not aware of any centres in the UK where this procedure is perofrmed

2.2.2 If your specialty is involved in patient selection or referral to another specialty for this procedure, please indicate your experience with it.

☐ I have never taken part in the selection or referral of a patient for this procedure.

☒ I have taken part in patient selection or referred a patient for this procedure at least once.

☐ I take part in patient selection or refer patients for this procedure regularly.

Comments:

However, it was not possible for the patient to receive this treatment in the UK

2.3 Please indicate your research experience relating to this procedure (please choose one or more if relevant):

☒ I have done bibliographic research on this procedure.

☐ I have done research on this procedure in laboratory settings (e.g. device-related research).

☐ I have done clinical research on this procedure involving patients or healthy volunteers.

☐ I have had no involvement in research on this procedure.

☐ Other (please comment)

Comments:

I have attended international conferences where experience of LITT in other countries was discussed, and read peer reviewed publications

3 Status of the procedure

3.1 Which of the following best describes the procedure (choose one):

☐ Established practice and no longer new.

☐ A minor variation on an existing procedure, which is unlikely to alter the procedure's safety and efficacy.

☒ Definitely novel and of uncertain safety and efficacy.

☐ The first in a new class of procedure.

Comments:

LITT was first reported as treatment for epilepsy was first published in 2012, seven groups have published their results to date, involving 175 patients with epilepsy

3.2 What would be the comparator (standard practice) to this procedure?

Standard treatment would be resection (removal) area of the brain causing seizures (the epileptogenic zone). For patients with temporal lobe epilepsy (which is the indication LITT is being used for most widely) the standard treatment would be anterior temporal lobectomy

3.3 Please estimate the proportion of doctors in your specialty who are doing this procedure (choose one):

☐ More than 50% of specialists engaged in this area of work.

☐ 10% to 50% of specialists engaged in this area of work.

☒ Fewer than 10% of specialists engaged in this area of work.

☐ Cannot give an estimate.

Comments:

I am not aware of anyone in the UK currently providing LITT for epilepsy

4 Safety and efficacy

4.1 What is the potential harm of the procedure?

Please list adverse events and major risks (even if uncommon) and, if possible, estimate their incidence, as follows:

1. Adverse events reported in the literature (if possible please cite literature)

Visual field defects, hyponatraemia and cognitive (memory) impairment have been reported, but the rates are generally lower than with standard treatment (temporal lobectomy)

2. Anecdotal adverse events (known from experience)

none

3. Theoretical adverse events

The main proposed advantage of LITT over temporal lobectomy is lower likelihood of cognitive adverse effects. This remains to be fully established

4.2 What are the key efficacy outcomes for this procedure?

Seizure freedom rates, as measured on the Engel scoring system at 12 months follow up, longer term (2-5 year) seizure freedom rates, post operative neuropsychological (cognitive) scores and quality of life measures (eg QOLIE31)

4.3 Are there uncertainties or concerns about the *efficacy* of this procedure? If so, what are they?

The efficacy of LITT in producing seizure freedom may be inferior to that of temporal lobectomy, but only relatively small numbers of patients have been treated by this modality, and follow up has been short.

4.4 What training and facilities are needed to do this procedure safely?

I am unable to comment on this. Mr Martin Tisdale, Consultant Neurosurgeon has treated some patients at Great Ormond Street hospital, and may be best placed to comment. I believe the procedure is also performed in the private sector by Prof Ashkan, Consultant Neurosurgeon at Kings College Hospital

4.5 Are there any major trials or registries of this procedure currently in progress? If so, please list.

None that I am aware of

4.6 Are you aware of any abstracts that have been *recently* presented/ published on this procedure that may not be listed in a standard literature search, for example PUBMED? (This can include your own work). If yes, please list.
Please note that NICE will do a literature search: we are only asking you for any very recent or potentially obscure abstracts and papers. Please

do not feel the need to supply a comprehensive reference list (but you may list any that you think are particularly important if you wish).

This is a good review of published evidence to date
https://journals.sagepub.com/doi/full/10.5698/1535-7597.18.6.382#focusIdbibr1-1535-7597.18.6.382

4.7 Is there controversy, or important uncertainty, about any aspect of the way in which this procedure is currently being done or disseminated?

Many aspects of the use of LITT remain to be clarified. In temporal lobe epilepsy – presence or absence of hippocampal sclerosis, need for stereo EEG implantation before performing LITT, impact of volume of tissue ablated on outcomes, planning of trajectories to name a few.

5 Audit Criteria

Please suggest a minimum dataset of criteria by which this procedure could be audited.

5.1 Outcome measures of benefit (including commonly used clinical outcomes, both short and long - term; and quality-of-life measures). Please suggest the most appropriate method of measurement for each:

Seizure freedom at 12 months (Engel classification)
Quality of life scores (QOLIE 31)
Neuropsychological outcomes

5.2 Adverse outcomes (including potential early and late complications). Please state timescales for measurement e.g. bleeding complications up to 1 month post-procedure:

Length of stay
Cognitive impairment

6 Trajectory of the procedure

6.1 In your opinion, how quickly do you think use of this procedure will spread?

In patients with temporal lobe epilepsy who have high cognitive scores, where temporal lobectomy may be associated with a risk of cognitive decline, LITT could be a useful option. I estimate 2-3 cases per centre in the UK per year, which would equate to about 25-30 cases per year initially.

6.2 This procedure, if safe and efficacious, is likely to be carried out in (choose one):

☐ Most or all district general hospitals.

☐ A minority of hospitals, but at least 10 in the UK.

☒ Fewer than 10 specialist centres in the UK.

☐ Cannot predict at present.

Comments:

6.3 The potential impact of this procedure on the NHS, in terms of numbers of patients eligible for treatment and use of resources, is:

☐ Major.

☐ Moderate.

☒ Minor.

Comments:
I am uncertain about the resource implications, as I do not know much the hardware costs

7 Other information

7.1 Is there any other information about this procedure that might assist NICE in assessing the possible need to investigate its use?

8 Data protection and conflicts of interest

8. Data protection, freedom of information and conflicts of interest

8.1 Data Protection

The information you submit on this form will be retained and used by the NICE and its advisers for the purpose of developing its guidance and may be passed to other approved third parties. Your name and specialist society will be published in NICE publications and on the NICE website. The specialist advice questionnaire will be published in accordance with our guidance development processes and a copy will be sent to the nominating Specialist Society. Please avoid identifying any individual in your comments.

☑ I have read and understood this statement and accept that personal information sent to us will be retained and used for the purposes and in the manner specified above. For more information about how we process your personal data please see our privacy notice

8.2 Declarations of interest by Specialist Advisers advising the NICE Interventional Procedures Advisory Committee

Nothing in your submission shall restrict any disclosure of information by NICE that is required by law (including in particular, but without limitation, the Freedom of Information Act 2000).

Please submit a conflicts of interest declaration form listing any potential conflicts of interest including any involvement you may have in disputes or complaints relating to this procedure.

Please use the "Conflicts of Interest for Specialist Advisers" policy as a guide when declaring any conflicts of interest. Specialist Advisers should seek advice if needed from the Associate Director – Interventional Procedures.

Do you or a member of your family[1] have a **personal pecuniary** interest? The main examples are as follows:

Consultancies or directorships attracting regular or occasional payments in cash or kind	☒	**YES**
	☐	**NO**
Fee-paid work – any work commissioned by the healthcare industry **– this includes income earned in the course of private practice**	☐	**YES**
	☒	**NO**
Shareholdings – any shareholding, or other beneficial interest, in shares of the healthcare industry	☐	**YES**
	☒	**NO**
Expenses and hospitality – any expenses provided by a healthcare industry company beyond those reasonably required for accommodation, meals and travel to attend meetings and conferences	☐	**YES**
	☒	**NO**
Investments – any funds that include investments in the healthcare industry	☐	**YES**
	☒	**NO**
Do you have a **personal non-pecuniary** interest – for example have you made a public statement about the topic or do you hold an office in a professional organisation or advocacy group with a direct interest in the topic?	☐	**YES**
	☒	**NO**

Do you have a **non-personal** interest? The main examples are as follows:

Fellowships endowed by the healthcare industry	☐	**YES**
	☒	**NO**
Support by the healthcare industry or NICE that benefits his/her position or department, eg grants, sponsorship of posts	☐	**YES**
	☒	**NO**

If you have answered YES to any of the above statements, please describe the nature of the conflict(s) below.

[1] 'Family members' refers to a spouse or partner living in the same residence as the member or employee, children for whom the member or employee is legally responsible, and adults for whom the member or employee is legally responsible (for example, an adult whose full power of attorney is held by the individual).

Comments:
I have acted as paid consultant for UCB pharma and Eisai UK, manufacturers of antiepileptic medications. This is not relevant to mode of treatment reviewed in this document

Thank you very much for your help.

Dr Tom Clutton-Brock, Interventional Procedures Advisory Committee Chair

Mark Campbell
Acting Programme Director
Devices and Diagnostics

June 2018

Conflicts of Interest for Specialist Advisers

1 Declarations of interest by Specialist Advisers advising the NICE Interventional Procedures Advisory Committee

1.1 Any conflicts of interest set out below should be declared on the questionnaire the Specialist Adviser completes for the procedure.

1.2 Specialist Advisers should seek advice if required from the Associate Director – Interventional Procedures.

2 Personal pecuniary interests

2.1 A personal pecuniary interest involves a current personal payment to a Specialist Adviser, which may either relate to the manufacturer or owner of a product or service being evaluated, in which case it is regarded as **'specific'** or to the industry or sector from which the product or service comes, in which case it is regarded as **'non-specific'**. The main examples are as follows.

2.1.1 **Consultancies** – any consultancy, directorship, position in or work for the healthcare industry that attracts regular or occasional payments in cash or kind (this includes both those which have been undertaken in the 12 months preceding the point at which the declaration is made and which are planned but have not taken place).

2.1.2 **Fee-paid work** – any work commissioned by the healthcare industry for which the member is paid in cash or in kind (this includes both those which have been undertaken in the 12 months preceding the point at which the declaration is made and which are planned but have not taken place).

2.1.3 **Shareholdings** – any shareholding, or other beneficial interest, in shares of the healthcare industry that are either held by the individual or for which the individual has legal responsibility (for example, children, or relatives whose full Power of Attorney is held by the individual). This does not include shareholdings through unit trusts, pensions funds, or other similar arrangements where the member has no influence on financial management.

2.1.4 **Expenses and hospitality** – any expenses provided by a healthcare industry company beyond that reasonably required for accommodation, meals and travel to attend meetings and conferences (this includes both those which have been undertaken in the 12 months preceding the point at which the declaration is made and which are planned but have not taken place.

2.1.5 **Investments** – any funds which include investments in the healthcare industry that are held in a portfolio over which individuals have the ability to instruct the fund manager as to the composition of the fund.

2.2 No personal interest exists in the case of:

2.2.1 assets over which individuals have no financial control (for example, wide portfolio unit trusts and occupational pension funds) and where the fund manager has full discretion as to its composition (for example, the Universities Superannuation Scheme)

2.2.2 accrued pension rights from earlier employment in the healthcare industry.

3 **Personal family interest**

3.1 This relates to the personal interests of a family member and involves a **current payment** to the family member of the Specialist Adviser. The interest may relate to the manufacturer or owner of a product or service being evaluated, in which case it is regarded as '**specific**', or to the industry or sector from which the product or service comes, in which case it is regarded as '**non-specific**'. The main examples include the following.

3.1.1 Any consultancy, directorship, position in or work for a healthcare industry that attracts regular or occasional payments in cash or in kind.

3.1.2 Any fee-paid work commissioned by a healthcare industry for which the member is paid in cash or in kind.

3.1.3 Any shareholdings, or other beneficial interests, in a healthcare industry which are either held by the family member or for which an individual covered by this Code has legal responsibility (for example, children, or adults whose full Power of Attorney is held by the individual).

3.1.4 Expenses and hospitality provided by a healthcare industry company (except where they are provided to a general class of people such as attendees at an open conference)

3.1.5 Funds which include investments in the healthcare industry that are held in a portfolio over which individuals have the ability to instruct the fund manager as to the composition of the fund.

3.2 No personal family interest exists in the case of:

3.2.1 assets over which individuals have no financial control (for example, wide portfolio unit trusts and occupational pension funds) and where the fund manager has full discretion as to its composition (for example, the Universities Superannuation Scheme)

3.2.2 accrued pension rights from earlier employment in the healthcare industry.

4 **Personal non-pecuniary interests**

These might include, but are not limited to:

4.1 a clear opinion, reached as the conclusion of a research project, about the clinical and/or cost effectiveness of an intervention under review

4.2 a public statement in which an individual covered by this Code has expressed a clear opinion about the matter under consideration, which could reasonably be interpreted as prejudicial to an objective interpretation of the evidence

4.3 holding office in a professional organisation or advocacy group with a direct interest in the matter under consideration

4.4 other reputational risks in relation to an intervention under review.

5 Non-personal interests

5.1 A non-personal interest involves payment that benefits a department or organisation for which a Specialist Advisor is responsible, but that is not received by the Specialist Advisor personally. This may either relate to the product or service being evaluated, in which case it is regarded as **'specific,'** or to the manufacturer or owner of the product or service, but is unrelated to the matter under consideration, in which case it is regarded as **'non-specific'**. The main examples are as follows.

5.1.1 **Fellowships** – the holding of a fellowship endowed by the healthcare industry.

5.1.2 **Support by the healthcare industry or NICE** – any payment, or other support by the healthcare industry or by NICE that does not convey any pecuniary or material benefit to a member personally but that does benefit his/her position or department. For example:

- a grant from a company for the running of a unit or department for which a Specialist Advisor is responsible
- a grant, fellowship or other payment to sponsor a post or member of staff in the unit for which a Specialist Adviser is responsible. This does not include financial assistance for students
- the commissioning of research or other work by, or advice from, staff who work in a unit for which the specialist advisor is responsible
- one or more contracts with, or grants from, NICE.

5.2 Specialist Advisers are under no obligation to seek out knowledge of work done for, or on behalf of, the healthcare industry within departments for which they are responsible if they would not normally expect to be informed.

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Interventional Procedures Programme

Specialist Adviser questionnaire

Before completing this questionnaire, please read Conflicts of Interest for Specialist Advisers. Certain conflicts exclude you from offering advice, however, please return the questionnaire to us incomplete for our records.

Please respond in the boxes provided.

Please complete and return to: azad.hussain@nice.org.uk and IPSA@nice.org.uk

Procedure Name:	**MRI-guided laser interstitial thermal therapy for epilepsy**
Name of Specialist Advisor:	Rachel Thornton
Specialist Society:	British Paediatric Neurology Association (BPNA)

1 Do you have adequate knowledge of this procedure to provide advice?

x Yes, with some limitations: please see below.

☐ No – please return the form/answer no more questions.

I have been involved in the care of the first three patients to undergo LiTT for focal epilepsy in the UK, as well as a number of other patients who travelled to the USA for the procedure. The numbers are necessarily small as the procedure has not been available at all until recently in this country. My role is as part of the decision making team.

1.1 Does the title used above describe the procedure adequately?

x Yes.

☐ No. If no, please enter any other titles below.

Comments:

2 Your involvement in the procedure

2.1 Is this procedure relevant to your specialty?

x Yes.

☐ Is there any kind of inter-specialty controversy over the procedure?

x No. If no, then answer no more questions, but please give any information you can about who is likely to be doing the procedure.

Comments:

The next 2 questions are about whether you carry out the procedure, or refer patients for it. If you are in a specialty that normally carries out the procedure please answer question 2.2.1. If you are in a specialty that normally selects or refers patients for the procedure, please answer question 2.2.2.

2.2.1 If you are in a specialty that does this procedure, please indicate your experience with it:

x I have never done this procedure.

☐ I have done this procedure at least once.

☐ I do this procedure regularly.

Comments:

2.2.2 If your specialty is involved in patient selection or referral to another specialty for this procedure, please indicate your experience with it.

☐ I have never taken part in the selection or referral of a patient for this procedure.

x I have taken part in patient selection or referred a patient for this procedure at least once.

☐ I take part in patient selection or refer patients for this procedure regularly.

Comments:

The numbers of patients for whom the procedure is considered are currently small, owing to fact that the procedure has not been available in this country.

2.3 Please indicate your research experience relating to this procedure (please choose one or more if relevant):

☐ I have done bibliographic research on this procedure.

☐ I have done research on this procedure in laboratory settings (e.g. device-related research).

☐ I have done clinical research on this procedure involving patients or healthy volunteers.

☐ I have had no involvement in research on this procedure.

x Other (please comment)

Comments:

I have no formal involvement in research programmes, but a knowledge of the literature relevant to the selection of patients for the procedure.

3 Status of the procedure

3.1 Which of the following best describes the procedure (choose one):

☐ Established practice and no longer new.

x A minor variation on an existing procedure, which is unlikely to alter the procedure's safety and efficacy (see below for clarification).

x Definitely novel and of uncertain safety and efficacy (see below)

☐ The first in a new class of procedure.

Comments:

LiTT is an established treatment for a number of intracranial pathologies with MRI guidance (Ammar 2013), and laser therapy for many other indications has been in use for many years. The application of LiTT in focal epilepsy was initially reported in 2012, but larger series of outcomes have only been published in the last 2 years.

This means that the longer term efficacy data is limited because it is generally accepted that the meaningful follow up period for assessment of epilepsy surgery outcomes should be at least 12 months. However there is good safety data for a number of different indications, particularly hypothalamic hamartoma and the efficacy in the short to medium term has been demonstrated. Thus the status of the procedure sits somewhere between 'variation on established practice' and 'definitely novel' at present – relatively novel for this indication, but with a growing field of literature supporting its safety and efficacy in the short to medium term.

3.2 What would be the comparator (standard practice) to this procedure?

Standard: Open or endoscopic resection.
Other comparators: Stereotactic radiosurgery (gamma knife) or radiofrequency thermoablation for a limited number of indications (very limited availability)..

3.3 Please estimate the proportion of doctors in your specialty who are doing this procedure (choose one):

☐ More than 50% of specialists engaged in this area of work.

☐ 10% to 50% of specialists engaged in this area of work.

x Fewer than 10% of specialists engaged in this area of work.

☐ Cannot give an estimate.

Comments:

4 Safety and efficacy

4.1 What is the potential harm of the procedure?

Please list adverse events and major risks (even if uncommon) and, if possible, estimate their incidence, as follows:

1. Adverse events reported in the literature (if possible please cite literature)

Permanent/ long term adverse effects:

General related to LiTT:

- Intracranial haemorrhage, (as in any intracranial procedure), significant effect reported in 1/179 cases in major paediatric series (Du 2017, Hoppe 2019). Timescale: immediate.
- Software failure leading to inaccuracy in estimate of tissue damage and excess or inaccurate thermal injury (reported in 1 case early in the evolution of the method): the risk which would likely be mitigated by appropriate procedural training and improvements already made to software.
- Misplacement of catheter owing to error in registration (led to intraventricular bleeding in one case) (Lewis et al 2015, Hoppe et al 2017)
- New neurological deficit including hemiparesis (permanent in 3/179 cases overall in the paediatric literature (Hoppe 2018), two of whom had insular epilepsy in which the risk of neurological deficit associated with any surgical intervention is high, regardless of the approach used. Amnesia in a single adult patient (see below). A recent study comparing the open resection and LiTT treatment in children with insular epilepsy reported similar rates of temporary deficit (Hale 2019).
- Reduction in CSF flow related to ablated tissue entrapment at the ventricle leading to hydrocephalus (Curry 2018)

Dependent on indication (in addition to general complications listed):

Ablation for mesial temporal lobe epilepsy

• Decline in verbal memory (Gross 2018 Donos et al 2018, Kang et al 2016).8-15%.

• Visual field defects 1.7% clinically significant in the largest series, 8.6% in total (Gross 2018):

Ablation for Hypothalamic Hamartoma

- Risk of cognitive decline reported as 1.5% in the largest series, amnesia reported in 1/71 (Curry 2018).
- Endocrine complications including diabetes insipidus (rare: 1/71 patients in the largest case series) (Curry 2018). Other endocrine complications (hypothyroidism, weight gain) are reported in very small numbers (2/18 patients in one series Xu et al 2018, none of 71 patients Curry 2018). Of note these are much lower than those reported in open procedures for this condition.

Ablation for Focal Cortical Dysplasia

- Risk depends on the location of the FCD, but greatest experience in the insular cortex in common with open resection – see above.

Temporary adverse effects (<6 months):

New neurological deficit (dependent on location of ablation, highest risk in the insula).

Transient endocrine disturbance

Delayed wound healing

Intracranial haemorrhage without significant clinical impact

Transient increase in seizures

Transient hyponatraemia in hypothalamic hamartoma (4%)

2. Anecdotal adverse events (known from experience)

None in addition to those in the literature.

3. Theoretical adverse events (in addition to the above)

Infection

4.2 What are the key efficacy outcomes for this procedure?

Seizure freedom (primary) or reduction in seizure frequency (secondary). Some of the published outcomes in larger studies for seizure freedom are as follows.

- Mesial temporal lobe epilepsy (53% -67% at one year, Gross et al 2018, Donos et al 2018)
- Insular epilepsy (c. 50% in a number of small studies, Perry et al 2018, Hale et al 2019)
- Hypothalamic hamartoma (80-90% for gelastic seizures, Xu et al 2018, Curry et al)

4.3 Are there uncertainties or concerns about the *efficacy* of this procedure? If so, what are they?

The short to medium term efficacy is established for hypothalamic hamartoma and is superior to open resection (particularly for gelastic seizures, the predominant seizure type in this condition, there is still some uncertainty around other seizure types). Efficacy is overall reported as *slightly* lower than the equivalent open procedure for mTLE and comparable for cortical dysplasia in the insula although series in this condition are not large.

The long term efficacy is still uncertain. This is a problem shared with any interventional procedure for epilepsy as it is recognised that long term seizure freedom rates (>10 years) are not as good as the short to medium outcomes, particularly in the context of reduction of pharmacological therapy (De Tisi et al 2011). In addition, although larger studies are emerging, numbers are still modest.

4.4 What training and facilities are needed to do this procedure safely?

Procedure

- Image guided laser ablation system (e.g. Medtronic Visualase, Neuroblate or similar)
- Associated MRI compatible consumables
- Operating theatre with capability for laser equipment and appropriate image guidance (interventional MRI suite not required)
- Image guided navigation system for insertion of catheter
- MRI suite capable of imaging patients under general anaesthetic
- Neurosurgeon with experience in epilepsy surgery trained in the procedure
- Training in laser safety and procedure for operating team

Planning, peri-operative care and follow up

- Epilepsy surgery multi-disciplinary team (including neurologist or paediatric neurologist with expertise in managing patients undergoing surgery for epilepsy, epilepsy nurse specialist, neuroradiologist, neurophysiologist, neuropsychologist and neuropsychiatrist).
- Capacity for invasive EEG monitoring, if therapy for MRI negative or those in whom seizures are hard to localise are included (particularly relevant to the treatment of insular epilepsy).
- Access to appropriate pre-operative imaging and functional studies (MRI, PET, ictal SPECT, fMRI etc)
- Endocrine team for management of complications related to the treatment of hypothalamic hamartoma in particular.
- Capacity for short and medium term follow up at the centre where the procedure is performed.

4.5 Are there any major trials or registries of this procedure currently in progress? If so, please list.

Not in the UK

4.6 Are you aware of any abstracts that have been *recently* presented/ published on this procedure that may not be listed in a standard literature search, for example PUBMED? (This can include your own work). If yes, please list.

Please note that NICE will do a literature search: we are only asking you

for any very recent or potentially obscure abstracts and papers. Please do not feel the need to supply a comprehensive reference list (but you may list any that you think are particularly important if you wish).

Not to my knowledge

4.7 Is there controversy, or important uncertainty, about any aspect of the way in which this procedure is currently being done or disseminated?

No

5 Audit Criteria

Please suggest a minimum dataset of criteria by which this procedure could be audited.

Demographic information

REFERRAL

Indication for referral for LiTT

- Aetiology of epilepsy
- Duration of seizures at time of referral and at time of treatment
- Number of seizure types
- MRI findings
- Functional imaging findings if performed (PET, ictal SPECT etc)
- Video EEG telemetry findings (seizure type, interictal and ictal scalp and invasive EEG (if relevant))
- Neuropsychological or neurodevelopmental assessment as appropriate
- Other clinical investigations undertaken

Treatment offered: yes/no (if no, state reason)

Patient or family (for paediatric patients) consent to proceed (if no, state reason)

PROCEDURE

Planned procedure

Accuracy of treatment volume compared with planned procedure (trajectory and extent of tissue ablation)

- MRI post treatment (serial)

Complications at the time of procedure

FINANCIAL AND PATIENT PATHWAYS

Total cost of procedure

Duration of inpatient stay

Time to treatment from onset of seizures and decision to treat

Location of referral sources and distance from patient location to treatment centre

SAFETY AND EFFICACY

Immediate adverse effects (<1 month)

Persistent adverse effects including

- new neurological deficit (and whether this was expected or not)
- endocrine complications for hypothalamic harmatoma
- neuropsychological outcome

Efficacy of treatment

- Seizure outcome

- Quality of life measures (see below)

5.1 Outcome measures of benefit (including commonly used clinical outcomes, both short and long - term; and quality-of-life measures). Please suggest the most appropriate method of measurement for each:

- Rates of seizure freedom or improvement in seizure frequency (ILAE or Engel outcome score)
- Cognitive function (neuropsychological or formal neurodevelopmental assessment using standardised tests of language and memory appropriate to each centre and the age/ developmental stage of the patient)
- Length of hospital stay
- Quality of life score (for example QULIE-31 +/- Hospital Anxiety and Depression Scale in adults or Impact of paediatric epilepsy scale (IEPS) in children).

5.2 Adverse outcomes (including potential early and late complications). Please state timescales for measurement e.g. bleeding complications up to 1 month post-procedure:

- Intracranial haemorrhage (early):
    - Post procedure imaging (immediate)
    - Clinical assessment for new neurological deficit
- New neurological deficit (early, but ongoing): clinical assessment, assessed at intervals up to 12 months to quantify whether temporary or permanent
- Endocrine complications (hypothalamic hamartoma): clinical assessment pre and post operative, ongoing.
- Neuropsychological assessment (up to 1 year initially, but may require longer term evaluation)

6 Trajectory of the procedure

6.1 In your opinion, how quickly do you think use of this procedure will spread?

This is difficult to quantify precisely at present. There has been a large increase in the number of patients with MRI negative or complex focal epilepsy undergoing pre-surgical evaluation in the last 5 years in the UK and techniques for the evaluation of these patients have spread quickly, partly owing to the establishment of well integrated inter-centre networks sharing practice (for example the expansion of paediatric epilepsy surgery since the advent of the Children's Epilepsy Surgery Service or CESS).

These networks, together with the increased numbers of complex patients being evaluated and the benefits in terms of duration of stay mean that the use of (or referral for) LiTT is likely to disseminate fairly rapidly among the centres who already evaluate complex patients (as stated above, this is not the majority of hospitals) similar to other novel techniques in this field (examples include RF thermoablation and sEEG in which there has been at least a 5 fold increase in 4 years across the CESS network).

For other indications, where the data for open resection has been established over many years (e.g. mesial temporal lobe epilepsy), the uptake may be slower pending longer term outcome data although the benefits in terms of duration of stay are also relevant.

6.2 This procedure, if safe and efficacious, is likely to be carried out in (choose one):

☐ Most or all district general hospitals.

☐ A minority of hospitals, but at least 10 in the UK.

x Fewer than 10 specialist centres in the UK **(at present).**

x Cannot predict at present **(longer term: please see below).**

Comments:

It is most likely that LiTT will be used for a limited number of indications (indications would include hypothalamic hamartoma and focal cortical dysplasia in brain regions at high risk from an open procedure) in the first instance. At present, the number of centres treating this patient group is limited to those who have established complex epilepsy surgery programmes (7 hospitals for children (6 in England, 1 in Scotland), but of these 4 work as combined centres and a similar number of adult centres, some of which are co-located with paediatric facilities).

In the longer term, it may become an alternative to amygdalo-hippocampectomy for mesial temporal sclerosis. Published series suggest that the outcomes with regard to seizure freedom are slightly lower for LiTT compared to open resection, but the length of stay is significantly lower.

6.3 The potential impact of this procedure on the NHS, in terms of numbers of patients eligible for treatment and use of resources, is:

☐ Major.

x Moderate.

☐ Minor.

Comments:
The impact on patient numbers is dependent on the indication:

- If taken up for solely for hypothalamic hamartoma, this condition is rare and the impact on absolute numbers of patients treated with epilepsy, therefore, minor (although highly significant for those who have the condition, as LiTT is now the 1st line treatment of choice for this condition in centres where the technique is established)
- For FCD and mesial temporal lobe epilepsy, numbers are likely to be higher as these comprise the commonest aetiology in refractory focal epilepsy.

The cost of the hospital stay and peri-operative care is lower for LiTT compared with open resection for the procedure in all procedures meaning there is a significant impact on the resources required (hospital stays of 24-48 hours are typical for most patients undergoing LiTT). Other resources required for pre-surgical evaluation and long term follow up are similar to other interventional modalities.

If successful, in common with other interventional treatment for epilepsy, there is a major impact on resource as there is a signficant reduction in the need for long term pharmacotherapy and medical management.

7 Other information

7.1 Is there any other information about this procedure that might assist NICE in assessing the possible need to investigate its use?

This procedure is very new in the UK, but there is significant experience in the USA. It may be appropriate to approach one or more of the centres in whom the procedure is established for further information.

An expert in neuropsychology would be able to provide more specific information around the expected cognitive outcomes for each procedure type and the most appropriate tests for measuring these outcomes.

8 Data protection and conflicts of interest

8. Data protection, freedom of information and conflicts of interest

8.1 Data Protection

The information you submit on this form will be retained and used by the NICE and its advisers for the purpose of developing its guidance and may be passed to other approved third parties. Your name and specialist society will be published in NICE publications and on the NICE website. The specialist advice questionnaire will be published in accordance with our guidance development processes and a copy will be sent to the nominating Specialist Society. Please avoid identifying any individual in your comments.

☑ I have read and understood this statement and accept that personal information sent to us will be retained and used for the purposes and in the manner specified above. For more information about how we process your personal data please see our privacy notice

8.2 Declarations of interest by Specialist Advisers advising the NICE Interventional Procedures Advisory Committee

Nothing in your submission shall restrict any disclosure of information by NICE that is required by law (including in particular, but without limitation, the Freedom of Information Act 2000).

Please submit a conflicts of interest declaration form listing any potential conflicts of interest including any involvement you may have in disputes or complaints relating to this procedure.

Please use the "Conflicts of Interest for Specialist Advisers" policy as a guide when declaring any conflicts of interest. Specialist Advisers should seek advice if needed from the Associate Director – Interventional Procedures.

Do you or a member of your family[1] have a **personal pecuniary** interest? The main examples are as follows:

Consultancies or directorships attracting regular or occasional payments in cash or kind	☐	**YES**
	x	**NO**
Fee-paid work – any work commissioned by the healthcare industry **– this includes income earned in the course of private practice**	x	**YES**
	☐	**NO**
Shareholdings – any shareholding, or other beneficial interest, in shares of the healthcare industry	☐	**YES**
	x	**NO**
Expenses and hospitality – any expenses provided by a healthcare industry company beyond those reasonably required for accommodation, meals and travel to attend meetings and conferences	☐	**YES**
	x	**NO**
Investments – any funds that include investments in the healthcare industry	☐	**YES**
	x	**NO**
Do you have a **personal non-pecuniary** interest – for example have you made a public statement about the topic or do you hold an office in a professional organisation or advocacy group with a direct interest in the topic?	☐	**YES**
	x	**NO**

Do you have a **non-personal** interest? The main examples are as follows:

Fellowships endowed by the healthcare industry	☐	**YES**
	x	**NO**
Support by the healthcare industry or NICE that benefits his/her position or department, eg grants, sponsorship of posts	x	**YES**
		NO

If you have answered YES to any of the above statements, please describe the nature of the conflict(s) below.

Comments:
I am involved in research for which a studentship has been sponsored by the Oakgrove Foundation (a personal charitable foundation for one of the directors of Renishaw PLC). This is not industrial sponsorship per se however. The research is related to the analysis of sEEG signals rather than directly relate to LiTT.

Thank you very much for your help.

Dr Tom Clutton-Brock, Interventional **Mark Campbell**

[1] 'Family members' refers to a spouse or partner living in the same residence as the member or employee, children for whom the member or employee is legally responsible, and adults for whom the member or employee is legally responsible (for example, an adult whose full power of attorney is held by the individual).

Procedures Advisory Committee Chair **Acting Programme Director Devices and Diagnostics**

June 2018

References

Ammar H. Hawasli, MD, PhD, Swapnil Bagade, MD, Joshua S. Shimony, MD, PhD, Michelle Miller-Thomas, MD, Eric C. Leuthardt, MD. Magnetic Resonance Imaging-Guided Focused Laser Interstitial Thermal Therapy for Intracranial Lesions: Single-Institution Series. Neurosurgery, Volume 73, Issue 6, December 2013, Pages 1007–1017,

Curry DJ, Raskin J, Ali I, Wilfong AA. MR-guided laser ablation for the treatment of hypothalamic hamartomas. Epilepsy Res. 2018 May;142:131-134.

de Tisi J, Bell GS, Peacock JL, McEvoy AW, Harkness WF, Sander JW, Duncan JS. The long-term outcome of adult epilepsy surgery, patterns of seizure remission, and relapse: a cohort study.Lancet. 2011 Oct 15;378(9800):1388-95.

Donos C, Breier J, Friedman E, Rollo P, Johnson J, Moss L, Thompson S, Thomas M, Hope O, Slater J, Tandon N.. Laser ablation for mesial temporal lobe epilepsy: Surgical and cognitive outcomes with and without mesial temporal sclerosis. Epilepsia. 2018 Jul;59(7):1421-1432.

Hale AT, Sen S, Haider AS, Perkins FF, Clarke DF, Lee MR, Tomycz LD. Open Resection vs Laser Interstitial Thermal Therapy for the Treatment of Pediatric Insular Epilepsy. Neurosurgery. 2019 Mar 19. pii: nyz094.

Hoppe C, Helmstaedter C. Laser interstitial thermotherapy (LiTT) in pediatric epilepsy surgery. Seizure. 2018 Dec 18. pii: S1059-1311(18)30575-2..

Hoppe C, Witt JA, Helmstaedter C, Gasser T, Vatter H, Elger CE. Laser interstitial thermotherapy (LiTT) in epilepsy surgery. Seizure. 2017 May;48:45-52

Kang JY Wu C, Tracy J, Lorenzo M, Evans J, Nei M, Skidmore C, Mintzer S, Sharan AD, Sperling MR. Laser interstitial thermal therapy for medically intractable mesial temporal lobe epilepsy Epilepsia. 2016 Feb;57(2):325-34...

E.C. Lewis, A.G. Weil, M. Duchowny, S. Bhatia, J. Ragheb, I. Miller
MR-guided laser interstitial thermal therapy for pediatric drug-resistant lesional epilepsy. Epilepsia, 56 (2015), pp. 1590-159

Perry MS, Donahue DJ, Malik SI, Keator CG, Hernandez A, Reddy RK, Perkins FF, Lee MR, Clarke DF. Magnetic resonance imaging-guided laser interstitial thermal therapy as treatment for intractable insular epilepsy in children. J Neurosurg Pediatr. 2017 Dec;20(6):575-582.

Robert E. Gross, Matthew A. Stern, BS, Jon T. Willie, Rebecca E. Fasano, Amit M. Saindane, Bruno P. Soares, Nigel P. Pedersen, and Daniel L. Drane, Stereotactic Laser Amygdalohippocampotomy for Mesial Temporal Lobe Epilepsy. Ann Neurol. 2018 March ; 83(3): 575–587.

Waseem H, Osborn KE, Schoenberg MR, et al. Laser ablation therapy: An alternative treatment for medically resistant mesial temporal lobe epilepsy after age 50. Epilepsy & Behavior. 2015 Oct.51:152–7]

Xu DS, Chen T, Hlubek RJ, Bristol RE, Smith KA, Ponce FA, Kerrigan JF, Nakaji P. Magnetic Resonance Imaging-Guided Laser Interstitial Thermal Therapy for the Treatment of Hypothalamic Hamartomas: A Retrospective Review. Neurosurgery. 2018 Dec 1;83(6):1183-1192

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These might include, but are not limited to:

4.1 a clear opinion, reached as the conclusion of a research project, about the clinical and/or cost effectiveness of an intervention under review

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- a grant from a company for the running of a unit or department for which a Specialist Advisor is responsible
- a grant, fellowship or other payment to sponsor a post or member of staff in the unit for which a Specialist Adviser is responsible. This does not include financial assistance for students
- the commissioning of research or other work by, or advice from, staff who work in a unit for which the specialist advisor is responsible
- one or more contracts with, or grants from, NICE.

5.2 Specialist Advisers are under no obligation to seek out knowledge of work done for, or on behalf of, the healthcare industry within departments for which they are responsible if they would not normally expect to be informed.

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Interventional Procedures Programme

Specialist Adviser questionnaire

Before completing this questionnaire, please read Conflicts of Interest for Specialist Advisers. Certain conflicts exclude you from offering advice, however, please return the questionnaire to us incomplete for our records.

Please respond in the boxes provided.

Please complete and return to: azad.hussain@nice.org.uk and IPSA@nice.org.uk

Procedure Name:	**MRI-guided laser interstitial thermal therapy for epilepsy**
Name of Specialist Advisor:	Sofia Eriksson
Specialist Society:	Association of British Neurologists (ABN)

1 Do you have adequate knowledge of this procedure to provide advice?

☒ Yes.

☐ No – please return the form/answer no more questions.

1.1 Does the title used above describe the procedure adequately?

☒ Yes.

☐ No. If no, please enter any other titles below.

Comments:

2 Your involvement in the procedure

2.1 Is this procedure relevant to your specialty?

☒ Yes.

☐ Is there any kind of inter-specialty controversy over the procedure?

☒ No. If no, then answer no more questions, but please give any information you can about who is likely to be doing the procedure.

Comments:

The next 2 questions are about whether you carry out the procedure, or refer patients for it. If you are in a specialty that normally carries out the procedure please answer question 2.2.1. If you are in a specialty that normally selects or refers patients for the procedure, please answer question 2.2.2.

2.2.1 If you are in a specialty that does this procedure, please indicate your experience with it:

☒ I have never done this procedure.

☐ I have done this procedure at least once.

☐ I do this procedure regularly.

Comments:

2.2.2 If your specialty is involved in patient selection or referral to another specialty for this procedure, please indicate your experience with it.

☒ I have never taken part in the selection or referral of a patient for this procedure.

☐ I have taken part in patient selection or referred a patient for this procedure at least once.

☐ I take part in patient selection or refer patients for this procedure regularly.

Comments:

I regularly refer patients for resective epilepsy surgery, but as laser therapy is not yet available in the UK, I have not referred anyone for the procedure. However, on a number of occasions, it is clear that had the therapy been available, patients would have been referred for this procedure.

2.3 Please indicate your research experience relating to this procedure (please choose one or more if relevant):

☐ I have done bibliographic research on this procedure.

☐ I have done research on this procedure in laboratory settings (e.g. device-related research).

☐ I have done clinical research on this procedure involving patients or healthy volunteers.

☒ I have had no involvement in research on this procedure.

☐ Other (please comment)

Comments:

3 Status of the procedure

3.1 Which of the following best describes the procedure (choose one):

☒ Established practice and no longer new.

☐ A minor variation on an existing procedure, which is unlikely to alter the procedure's safety and efficacy.

☐ Definitely novel and of uncertain safety and efficacy.

☒ The first in a new class of procedure.

Comments:

None of the options above are suitable. This is a new procedure but has been use in other parts of the world for some time with published data on outcome (efficacy and safety).

3.2 What would be the comparator (standard practice) to this procedure?

Resective epilepsy surgery. Possibly gamma knife (for hypothalamic hamartoma)

3.3 Please estimate the proportion of doctors in your specialty who are doing this procedure (choose one):

☐ More than 50% of specialists engaged in this area of work.

☐ 10% to 50% of specialists engaged in this area of work.

☐ Fewer than 10% of specialists engaged in this area of work.

☒ Cannot give an estimate.

Comments:

Also not entirely applicable as the procedure is not available. Epilepsy surgery is done in a small number of specialist centres only.

4 Safety and efficacy

4.1 What is the potential harm of the procedure?

Please list adverse events and major risks (even if uncommon) and, if possible, estimate their incidence, as follows:

1. Adverse events reported in the literature (if possible please cite literature)

Haemorrhage, transient neurological symptoms, visual loss, mood disorder, memory problems

- Wu *et al.* Effects of surgical targeting in laser interstitial thermal therapy for mesial temporal lobe epilepsy: A multicenter study of 234 patients. Epilepsia. 2019 Jun;60(6):1171-1183. doi: 10.1111/epi.15565.
- Hale AT *et al.* Open Resection vs Laser Interstitial Thermal Therapy for the Treatment of Pediatric Insular Epilepsy. Neurosurgery. 2019 Mar 19. pii: nyz094. doi: 10.1093/neuros/nyz094.
- Cajigas I *et al.* Magnetic Resonance-Guided Laser Interstitial Thermal Therapy for Mesial Temporal Epilepsy: A Case Series Analysis of Outcomes and Complications at 2-Year Follow-Up. World Neurosurg. 2019 Mar 15. pii: S1878-8750(19)30694-1. doi: 10.1016/j.wneu.2019.03.057.

For a review including additional references - Shimamoto S, Wu C, Sperling MR. Laser interstitial thermal therapy in drug-resistant epilepsy. Curr Opin Neurol. 2019 Apr;32(2):237-245. doi: 10.1097/WCO.0000000000000662.

2. Anecdotal adverse events (known from experience)

N/A

3. Theoretical adverse events

As outlined above. Theoretically the risk of complications will be greater the greater areas ablated and will also depend on the area of the brain treated.

4.2 What are the key efficacy outcomes for this procedure?

Seizure outcome, proportion seizure free, seizure reduction, most commonly using Engel or ILAE scores/scales.

4.3 Are there uncertainties or concerns about the *efficacy* of this procedure? If so, what are they?

Literature suggests that the procedure is effective with fairly similar results to open surgery. Larger series and longer follow up are needed to ensure this is correct.

4.4 What training and facilities are needed to do this procedure safely?

Surgeons need training on this. I can unfortunately not comment on the type, duration or what facilities are needed – suggest discussion with the surgeons. I am not certain if someone from the company also need to attend during the procedures.

4.5 Are there any major trials or registries of this procedure currently in progress? If so, please list.

The procedure is currently undertaken at several sites in US who should be collecting data. I am not aware of any central registries for this.

4.6 Are you aware of any abstracts that have been *recently* presented/ published on this procedure that may not be listed in a standard literature search, for example PUBMED? (This can include your own work). If yes, please list.
Please note that NICE will do a literature search: we are only asking you for any very recent or potentially obscure abstracts and papers. Please do not feel the need to supply a comprehensive reference list (but you may list any that you think are particularly important if you wish).

No. It is likely that there were abstracts/posters at the recent 33rd International Epilepsy Congress but I did not attend and do not have access to the abstracts.

4.7 Is there controversy, or important uncertainty, about any aspect of the way in which this procedure is currently being done or disseminated?

Not that I am aware

5 Audit Criteria

Please suggest a minimum dataset of criteria by which this procedure could be audited.

5.1 Outcome measures of benefit (including commonly used clinical outcomes, both short and long - term; and quality-of-life measures). Please suggest the most appropriate method of measurement for each:

Seizure frequency following procedure using ILAE scale or Engel classification reviewed at 3, 6, 12 months and yearly after this.
QoL - QOLIE-89 and QOLIE-31 seems to be most commonly used in epilepsy patients.

5.2 Adverse outcomes (including potential early and late complications). Please state timescales for measurement e.g. bleeding complications up to 1 month post-procedure:

Complications to be assessed immediately following the procedure, such as bleeding.
Neurological symptoms (motor, visual etc) to be assessed immediately and also reviewed at 3, 6, 12 months.

Neuropsychological assessment (to review for example potential memory decline) 3 and 12 months and possibly at 2 years.

6 Trajectory of the procedure

6.1 In your opinion, how quickly do you think use of this procedure will spread?

Rapidly

6.2 This procedure, if safe and efficacious, is likely to be carried out in (choose one):

☐ Most or all district general hospitals.

☒ A minority of hospitals, but at least 10 in the UK.

☐ Fewer than 10 specialist centres in the UK.

☐ Cannot predict at present.

Comments:

6.3 The potential impact of this procedure on the NHS, in terms of numbers of patients eligible for treatment and use of resources, is:

☐ Major.

☐ Moderate.

☒ Minor.

Comments:
Only a small number of patients undergo epilepsy surgery every year. Of these, the majority may still have the conventional open resective surgery and the numbers eligible for this treatment for epilepsy is unlikely to be large.

7 Other information

7.1 Is there any other information about this procedure that might assist NICE in assessing the possible need to investigate its use?

8 Data protection and conflicts of interest

8. Data protection, freedom of information and conflicts of interest

8.1 Data Protection

The information you submit on this form will be retained and used by the NICE and its advisers for the purpose of developing its guidance and may be passed to other approved third parties. Your name and specialist society will be published in NICE publications and on the NICE website. The specialist advice questionnaire will be published in accordance with our guidance development processes and a copy will be sent to the nominating Specialist Society. Please avoid identifying any individual in your comments.

☑ I have read and understood this statement and accept that personal information sent to us will be retained and used for the purposes and in the manner specified above. For more information about how we process your personal data please see our privacy notice

8.2 Declarations of interest by Specialist Advisers advising the NICE Interventional Procedures Advisory Committee

Nothing in your submission shall restrict any disclosure of information by NICE that is required by law (including in particular, but without limitation, the Freedom of Information Act 2000).

Please submit a conflicts of interest declaration form listing any potential conflicts of interest including any involvement you may have in disputes or complaints relating to this procedure.

Please use the "Conflicts of Interest for Specialist Advisers" policy as a guide when declaring any conflicts of interest. Specialist Advisers should seek advice if needed from the Associate Director – Interventional Procedures.

Do you or a member of your family[1] have a **personal pecuniary** interest? The main examples are as follows:

Consultancies or directorships attracting regular or occasional payments in cash or kind	☐ **YES** ☒ **NO**
Fee-paid work – any work commissioned by the healthcare industry **– this includes income earned in the course of private practice**	☐ **YES** ☒ **NO**
Shareholdings – any shareholding, or other beneficial interest, in shares of the healthcare industry	☐ **YES** ☒ **NO**

[1] 'Family members' refers to a spouse or partner living in the same residence as the member or employee, children for whom the member or employee is legally responsible, and adults for whom the member or employee is legally responsible (for example, an adult whose full power of attorney is held by the individual).

Expenses and hospitality – any expenses provided by a healthcare industry company beyond those reasonably required for accommodation, meals and travel to attend meetings and conferences	☐	**YES**
	☒	**NO**
Investments – any funds that include investments in the healthcare industry	☐	**YES**
	☒	**NO**
Do you have a **personal non-pecuniary** interest – for example have you made a public statement about the topic or do you hold an office in a professional organisation or advocacy group with a direct interest in the topic?	☐	**YES**
	☒	**NO**

Do you have a **non-personal** interest? The main examples are as follows:

Fellowships endowed by the healthcare industry	☐	**YES**
	☒	**NO**
Support by the healthcare industry or NICE that benefits his/her position or department, eg grants, sponsorship of posts	☐	**YES**
	☒	**NO**

If you have answered YES to any of the above statements, please describe the nature of the conflict(s) below.

Comments:

Thank you very much for your help.

Dr Tom Clutton-Brock, Interventional Procedures Advisory Committee Chair

Mark Campbell
Acting Programme Director
Devices and Diagnostics

June 2018

Conflicts of Interest for Specialist Advisers

1 Declarations of interest by Specialist Advisers advising the NICE Interventional Procedures Advisory Committee

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