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: Deonee.Stanislaus@nice.org.uk

Procedure Name:	**Transcranial Magnetic Resonance Image-guided Focused Ultrasound (MRgFUS)**
Name of Specialist Advisor:	Dr David Nicholl
Specialist Society:	Association of British Neurologists

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

☐ Yes.

1.1 Does the title used above describe the procedure adequately?

☐ Yes.

Comments:

2 Your involvement in the procedure

2.1 Is this procedure relevant to your specialty?

☐ Yes.

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.

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.

Comments:

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. (ie literature review as below)

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

Comments:

3 Status of the procedure

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

☐ Definitely novel and of uncertain safety and efficacy.

Comments:

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

Other interventional procedures for tremor (ie Deep Brain Stimulation)

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

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

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)

   sensory and gait disturbances

   gait disturbance in 36% of patients and paresthesias or numbness in 38%; these adverse events persisted at 12 months in 9% and 14% of patients, respectively.

   Deep vein thrombosis (1)

   (see papers below)

2. Anecdotal adverse events (known from experience)

   unknown

3. Theoretical adverse events

   lack of maintenance of effect over a longer time period

4.2 What are the key efficacy outcomes for this procedure?

Clinical Rating Scale for Tremor and the Quality of Life in Essential Tremor Questionnaire are rating scales that have been used in studies to date (eg Elias et al N Engl J Med. 2016)

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

The studies should compare with other existing neurosurgical DBS approaches (eg for essential tremor or Parkinson's disease)

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

Unsure as have not done myself

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

There are only 29 trials listed here
https://clinicaltrials.gov/ct2/results?cond=MRgFUS&term=&cntry1=&state1=&recrs=

Only 2 of these are completed (for breast and prostate cancer- neither of which I feel qualified as a neurologist to comment on), all the neurology trials are in the recruitment phase

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).

I'm only aware of these published studies on Pubmed (14)
https://www.ncbi.nlm.nih.gov/pubmed/?term=Transcranial+Magnetic+Resonance+Image-guided+Focused+Ultrasound
and

Elias et al N Engl J Med. 2016 Aug 25;375(8):730-9. doi: 10.1056/NEJMoa1600159.

5 A Randomized Trial of Focused Ultrasound Thalamotomy for Essential Tremor.

Abstract

BACKGROUND:

Uncontrolled pilot studies have suggested the efficacy of focused ultrasound thalamotomy with magnetic resonance imaging (MRI) guidance for the treatment of essential tremor.

METHODS:

We enrolled patients with moderate-to-severe essential tremor that had not responded to at least two trials of medical therapy and randomly assigned them in a 3:1 ratio to undergo unilateral focused ultrasound thalamotomy or a sham procedure. The Clinical Rating Scale for Tremor and the Quality of Life in Essential Tremor Questionnaire were administered at

baseline and at 1, 3, 6, and 12 months. Tremor assessments were videotaped and rated by an independent group of neurologists who were unaware of the treatment assignments. The primary outcome was the between-group difference in the change from baseline to 3 months in hand tremor, rated on a 32-point scale (with higher scores indicating more severe tremor). After 3 months, patients in the sham-procedure group could cross over to active treatment (the open-label extension cohort).

RESULTS:

Seventy-six patients were included in the analysis. Hand-tremor scores improved more after focused ultrasound thalamotomy (from 18.1 points at baseline to 9.6 at 3 months) than after the sham procedure (from 16.0 to 15.8 points); the between-group difference in the mean change was 8.3 points (95% confidence interval [CI], 5.9 to 10.7; P<0.001). The improvement in the thalamotomy group was maintained at 12 months (change from baseline, 7.2 points; 95% CI, 6.1 to 8.3). Secondary outcome measures assessing disability and quality of life also improved with active treatment (the blinded thalamotomy cohort)as compared with the sham procedure (P<0.001 for both comparisons). Adverse events in the thalamotomy group included gait disturbance in 36% of patients and paresthesias or numbness in 38%; these adverse events persisted at 12 months in 9% and 14% of patients, respectively.

CONCLUSIONS:

MRI-guided focused ultrasound thalamotomy reduced hand tremor in patients with essential tremor. Side effects included sensory and gait disturbances. (Funded by InSightec and others; ClinicalTrials.gov number, NCT01827904.).

Lipsman N et al Lancet Neurol. 2013 May;12(5):462-8. doi: 10.1016/S1474-4422(13)70048-6. Epub 2013 Mar 21.

MR-guided focused ultrasound thalamotomy for essential tremor: a proof-of-concept study.

Abstract

BACKGROUND:

Essential tremor is the most common movement disorder and is often refractory to medical treatment. Surgical therapies, using lesioning and deep brain stimulation in the thalamus, have been used to treat essential tremor that is disabling and resistant to medication. Although often effective, these treatments have risks associated with an open neurosurgical procedure. MR-guided focused ultrasound has been developed as a non-invasive means of generating precisely placed focal lesions. We examined its application to the management of essential tremor.

METHODS:

Our study was done in Toronto, Canada, between May, 2012, and January, 2013. Four patients with chronic and medication-resistant essential tremor were treated with MR-guided focused ultrasound to ablate tremor-mediating areas of the thalamus. Patients underwent tremor evaluation and neuroimaging at baseline and 1 month and 3 months after surgery. Outcome measures included tremor severity in the treated arm, as measured by the clinical rating scale for tremor, and treatment-related adverse events.

FINDINGS:

Patients showed immediate and sustained improvements in tremor in the dominant hand. Mean reduction in tremor score of the treated hand was 89·4% at 1 month and 81·3% at 3 months. This reduction was accompanied by functional benefits and improvements in writing and motor tasks. One patient had postoperative paraesthesias which persisted at 3 months. Another patient developed a deep vein thrombosis, potentially related to the length of the procedure.

INTERPRETATION:

MR-guided focused ultrasound might be a safe and effective approach to generation of focal intracranial lesions for the management of disabling, medication-resistant essential tremor. If larger trials validate the safety and ascertain the efficacy and durability of this new approach, it might change the way that patients with essential tremor and potentially other disorders are treated.

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

All several neurological studies are in recruitment, the results are yet to be published and we do not as yet have the long term follow up data

5 Audit Criteria

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

Needs to be long term follow up

Clinical Rating Scale for Tremor and the Quality of Life in Essential Tremor Questionnaire are rating scales that have been used in studies to date (eg Elias et al N Engl J Med. 2016)

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:

Clinical Rating Scale for Tremor and the Quality of Life in Essential Tremor Questionnaire are rating scales that have been used in studies to date (eg Elias et al N Engl J Med. 2016)

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:

Adverse events in the thalamotomy group included gait disturbance in 36% of patients and paresthesias or numbness in 38%; these adverse events persisted at 12 months in 9% and 14% of patients, respectively.

6 Trajectory of the procedure

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

Totally depends on having more data from published studies later this year.

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

☐ Fewer than 10 specialist centres in the UK. (neuroscience centres)

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:

☐ Minor, whilst limited published data with long term follow-up

Comments:

I appreciate that there has been significant media interest in this technique but the data are unpublished and are not due to publish til later this year.

https://www.imperial.nhs.uk/research/about-our-research/mr-guided-focused-ultrasound-for-essential-tremor

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?

Not that I am aware of

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.

X 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 and in accordance with the Data Protection Act 1998.

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	☐	**NO**
Fee-paid work – any work commissioned by the healthcare industry **– this includes income earned in the course of private practice**	☐	**YES**
	I have performed ~£1500 medicolegal work in the last 12 months (in areas not related to this review)	
Shareholdings – any shareholding, or other beneficial interest, in shares of the healthcare industry	☐	**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	☐	**NO**
Investments – any funds that include investments in the healthcare industry	☐	**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?	☐	**NO**

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

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

Professor Carole Longson, Director, Centre for Health Technology Evaluation.

Jan 2016

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: Deonee.Stanislaus@nice.org.uk

Procedure Name:	**Transcranial Magnetic Resonance Image-guided Focused Ultrasound (MRgFUS)**
Name of Specialist Advisor:	Professor Tom Foltynie
Specialist Society:	**Association of British Neurologists**

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:

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:

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):

☐ 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.

☐ Definitely novel and of uncertain safety and efficacy.

☐ The first in a new class of procedure.

Comments:

MRI guided focussed ultrasound is an established technique for the treatment of other types of patients eg prostate cancer, uterine fibroids.

Thalamotomy performed by radiofrequency ablation or gamma knife is an established technique with known risks and benefits.

MRI guided focussed ultrasound thalamotomy has been adopted in multiple other countries with anecdotal and published evidence of its safety and efficacy.

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

Radiofrequency ablation (thalamotomy) or Deep Brain stimulation.

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)

Transient dysarthric speech, balance impairments, ataxia are described (Elias et al. 2013, Schlesinger 2015) Long term paraesthesia, ataxia and taste disturbance can occur (Zaaroor et al. 2017). Deep Vein thrombosis has been reported in one patient who had prolonged immobilisation as a result of undertaking the procedure (Lipsman 2013). In general the procedure is very safe (Magara et al 2014, Bauer et al 2014, Cheol Na et al. 2015).

2. Anecdotal adverse events (known from experience)

3. Theoretical adverse events

There is a theoretical risk of haemorrhage (due to bubble formation) which is also shared by the comparator procedures- radiofrequency ablation and deep brain stimulation, although this is likely to be extremely rare in experienced hands. This makes the procedure contraindicated in patients on anticoagulant therapy or who have coagulation problems.The previously reported transient adverse events may in theory remain permanent.

4.2 What are the key efficacy outcomes for this procedure?

The key outcome for MRgFUS thalamotomy will be Tremor reduction

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

Application of focussed ultrasound for thalamotomy is likely to be free of major placebo effects and the reported efficacy is likely to be a real and sustained effect. The use of focussed ultrasound in other targets to ameliorate other movement disorder problems is still experimental and should be assessed as part of formal efficacy trials including blinding if logistically feasible.

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

The procedure requires major investment in the appropriate imaging hardware to perform the procedure safely and requires further training of individuals who have prior knowledge and experience of patient selection in the use of functional neurosurgery for movement disorders.

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

Insightec are sponsoring a number of trials in tremor and Parkinson's disease in multiple centres around the world. These can be readily identified on Clinicaltrials.gov under serach term -Exablate

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?

It is well accepted that focussed ultrasound thalamotomy should only be performed as a unilateral procedure in view of well known adverse effects of bilateral thalamotomy (ataxia/ dysarthria).

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:

Essential tremor rating scale or Clinical Rating Scale for tremor (CRST), Questionnaire for Essential Tremor.

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:

All AEs should be recorded for at least 1 month post procedure.

6 Trajectory of the procedure

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

There is only a small number of patients who will require this procedure – After initial enthusiasm (novelty value) wanes, I expect that 3 or 4 specialist centres will suffice for the whole UK.

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?

There is a recent excellent review by Rohani & Fasano 2017.

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 and in accordance with the Data Protection Act 1998.

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).

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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**

[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).

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

Professor Carole Longson, Director, Centre for Health Technology Evaluation.

Jan 2016

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.

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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: Deonee.Stanislaus@nice.org.uk

Procedure Name:	**Transcranial Magnetic Resonance Image-guided Focused Ultrasound (MRgFUS)**
Name of Specialist Advisor:	Professor Dipankar Nandi
Specialist Society:	The Society of British Neurological Surgeons

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:

This is a procedure that should be (and is) performed as part of a multi-disciplinary team approach to the treatment of complex movement disorders. The team should comprise of (at least) a Stereotactic and Functional Neurosurgeon, a Movement Disorders Specialist Neurologist and a Neuro-radiologist.

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 been performing this procedure for the last one year (started July 2016). We do about one case every month.

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:

As with almost all Functional Neurosurgery, patient selection is the key parameter which influences success. This is best done in an MDT setting involving the Neurosurgeon and the Neurologist.

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:

We are currently running an International Prospective Clinical Trial using MGFUS for treatment of Essential Tremor

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:

The most important innovation in MGFUS is the manner in which a deep-seated image-guided brain lesion is achieved. That is, through the use of non-invasive non-ionising ultrasound energy. The actual brain structures being lesioned (most commonly a part of the ventrolateral thalamus) have been standard targets for Functional and Stereotactic Neurosurgeons for over 50 years. There is a wealth of published peer-reviewed literature on the anatomy, radiology and clinical outcomes of these procedures and an equally substantial literature on the safety and efficacy of these interventions.

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

CT / MRI guided radiofrequency brain lesioning (thalamotomy / pallidotomy / sub-thalamic nucleotomy)

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:

The principal reason fewer than 10% of Stereotactic and Functional Neurosurgeons currently use MGFUS is the relatively new technology and the substantial capital cost of the base equipment.

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)

Paresthesiae (8%, mainly transient), gait / balance problems (3%, most transient), headaches (5%, only during procedure), dysarthria (2%, self-limiting within 48 hours).

2. Anecdotal adverse events (known from experience)

Sensation of spinning (only during procedure)

3. Theoretical adverse events

Intracranial bleed, stroke

References:

[1] Martin E, Jeanmonod D, Morel A, Zadicario E, Werner B. High-intensity focused ultrasound for noninvasive functional neurosurgery. Ann Neurol. 2009; 66(6):858–61.

[2] Elias W.J., et al. An International, Randomized, Controlled Trial of Focused Ultrasound Thalamotomy for Essential Tremor. The New England Journal of Medicine, Aug 2016.

[3] Chang WS, Jung HH, Kweon EJ, Zadicario E, Rachmilevitch I, Chang JW. Unilateral magnetic resonance guided focused ultrasound thalamotomy for essential tremor: practices and clinicoradiological outcomes. J Neurol Neurosurg Psychiatry 2015; 86: 257-64.

[4] Lipsman N, Schwartz ML, Huang Y, et al. MR-guided focused ultrasound thalamotomy for essential tremor: a proof-of concept study. Lancet Neurol 2013; 12: 462-8.

4.2 What are the key efficacy outcomes for this procedure?

Depends on clinical indication. 90% of cases done worldwide (> 1000 patients thus far) are for ET. In this cohort control of tremor on standard rating scales and quality of life indices are as good as that achieved by RF lesions and / or DBS. (See references above).

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

Very few bilateral lesions have been done. So not much data exists about efficacy in bilateral tremor control.

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

This procedure should only be performed by Stereotactic and Functional Neurosurgeons with experience in DBS and preferably also in lesioning (a much rarer skill).

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

International Multi-centre Prospective Trial of MGFUS unilateral thalamotomy in ET (ongoing and we are a participating centre).

International Multi-centre Prospective Trial of MGFUS pallidotomy in Parkinson's disease (due to start in Feb 2018).

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?

Not 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:

Tremor rating scales (Internationally standardised and validated rating scales that are very familiar to Movement Disorder Neurologists exist)

Standard QOL scores: e.g. SF36, Euroqol

UPDRS (for Parkinson's disease)

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:

Almost all possible adverse outcomes are early if not immediate (within 48 hours) of the procedure

6 Trajectory of the procedure

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

Given the wealth of background literature and clinical experience with DBS and stereotactic brain lesioning, and the significant numbers of potential patients (especially with ET and PD) I would expect fairly rapid expansion of the use of MGFUS in the UK.

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:

Needs to be performed in an existing DBS centre with additional lesioning experience.

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:
There is a significant cohort of patients with intractable, disabling ET and particular patients with PD who are poorly responsive to medical therapy and are tremor

dominant or have severe on-dyskinesia who are not suitable for DBS / or are not willing to risk the possible adverse effects of DBS (which is considerable). These patients are often also poor candidates for RF lesioning. MGFUS offers an alternative therapeutic option that is cost-effective, is clinically efficacious and has significantly reduced risk of serious adverse events. This procedure is considerably safer than RF lesioning and stereotactic radiotherapy (Gamma knife / Cyberknife).

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?

No

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 and in accordance with the Data Protection Act 1998.

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.

Comments:

Thank you very much for your help.

Dr Tom Clutton-Brock, Interventional Procedures Advisory Committee Chair

Professor Carole Longson, Director, Centre for Health Technology Evaluation.

Jan 2016

[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).

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: Deonee.Stanislaus@nice.org.uk

Procedure Name:	**Transcranial Magnetic Resonance Image-guided Focused Ultrasound (MRgFUS)**
Name of Specialist Advisor:	Dr Leonardo Monzon Rodriquez
Specialist Society:	BSIR - (British Society of Interventional Radiology)

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

☐ Yes.

1.1 Does the title used above describe the procedure adequately?

☐ Yes.

Comments:

The procedure is also known as MRgHIFU (High Intensity Focused Ultrasound)

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?

Comments:

The procedure is currently performed by Interventional Radiologists in collaboration with Neurologists, Neurosurgeons and Neuroradiologists

There is potential inter-specialty controversy with all the above and in addition Interventional Neuroradiologists

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.

Comments:

I have performed MRgFUS and Ultrasound Guided FUS in other contexts (not transcranial)

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.

Comments:

Patients will primarily be derived from neurology and neurosurgery clinics

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

☐ Other (please comment)

Comments:

I have not done any specific Transcranial MRgFUS research (only where it applies to general HIFU reviews)

I have done bibliographic research on HIFU. I have done clinical research on Pelvic Ultrasound Guided HIFU.

3 Status of the procedure

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

☐ Established practice and no longer new.

Comments:

The ExAblate system manufactured by Insightec earned FDA approval to treat essential tremor in July 2016. It is also approved for treating essential tremor in Europe, Korea, Canada, Israel, Japan and Russia.

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

Stereotactic surgery, radiosurgery, deep brain stimulation and neurosurgery

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

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

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)

Elias WJ, Lipsman N, et al

A Randomized Trial of Focused Ultrasound Thalamotomy for Essential Tremor.

N Engl J Med. 2016 Aug 25;375(8):730-9. doi: 10.1056/NEJMoa1600159

Adverse events associated with focused ultrasound thalamotomy included gait disturbance in 36% of patients and paresthesias or numbness in 38%; these adverse events persisted at 12 months in 9% and 14% of patients, respectively

2. Anecdotal adverse events (known from experience)

N/A

3. Theoretical adverse events

Intracranial haemorrhage. Stroke. Increased intracranial pressure.

4.2 What are the key efficacy outcomes for this procedure?

Transcranial MRgFUS is not a homogenous procedure as it is performed for many different conditions and each should be considered separately and in turn

Taking Transcranial MRgFUS for Essential Tremor as an example:
Self-reported Quality of Life in Essential Tremor Questionnaire (QUEST)

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

Not that I am aware

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

Training:
-Neuroradiology
-MRgFUS system specific training

Facilities:
-MRgFUS system in suitable accessible and appropriately designed clinical area
-Neurosurgical centre (in case of complications)

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

Yes – there are ongoing trials

The most prominent centre in the U.K. is St Mary's Hospital, London, Imperial College

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).

N/A

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.

Will depend on the specific procedure being audited. Transcranial MRgFUS has many applications and is a technique rather than a procedure as such.

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:

Transcranial MRgFUS is not a homogenous procedure as it is performed for many different conditions and each should be considered separately and in turn

Taking Transcranial MRgFUS for Essential Tremor as an example:
Self-reported Quality of Life in Essential Tremor Questionnaire (QUEST)

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:

Will depend on the specific procedure being audited. Transcranial MRgFUS has many applications and is a technique rather than a procedure as such.

6 Trajectory of the procedure

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

Over next 10 years due to initial capital outlay to purchase the hardware required

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

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

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.

Comments:
The procedure is already FDA approved for Essential Tremor affecting 3% of the population.

Other transcranial applications include treatment of Parkinson's Disease and certain Brain Tumours (particularly those not possible to reach with conventional surgery and tumour recurrences)

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?

https://www.fusfoundation.org/diseases-and-conditions/neurological

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.

(YES) 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 and in accordance with the Data Protection Act 1998.

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 ☐ **NO**

Fee-paid work – any work commissioned by the healthcare industry **– this includes income earned in the course of private practice** ☐ **NO**

Shareholdings – any shareholding, or other beneficial interest, in shares of the healthcare industry ☐ **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 ☐ **NO**

Investments – any funds that include investments in the healthcare industry ☐ **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? ☐ **NO**

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

Fellowships endowed by the healthcare industry ☐ **NO**

Support by the healthcare industry or NICE that benefits his/her position or department, eg grants, sponsorship of posts ☐ **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

Professor Carole Longson, Director, Centre for Health Technology Evaluation.

[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).

Jan 2016

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.