View results

Respondent

60 Anonymous

25:34
Time to complete

1. Project Number and Name - (Can be found on email) *

IP1692 MRI-guided focused ultrasound thalamotomy for moderate-to-severe tremor in Parkinson's disease

Your information

2. Name: *

Alexander Laurence Green

3. Job title: *

Professor of Neurosurgery

4. Organisation: *

University of Oxford

5. Email address: *

[redacted]

6. Professional organisation or society membership/affiliation: *

BSSFN, SBNS

7. Nominated/ratified by (if applicable):

Julian Evans

8. Registration number (e.g. GMC, NMC, HCPC) *

GMC 4424585

How NICE will use this information:

The information that you provide on this form will be used to develop guidance on this procedure.

Your advice and views represent your individual opinion and not that of your employer, professional society or a consensus view. Your name, job title, organisation and your responses, along with your declared interests will also be published online on the NICE website as part of public consultation on the draft guidance, except in circumstances but not limited to, where comments are considered voluminous, or publication would be unlawful or inappropriate.

For more information about how we process your data please see our privacy notice: https://www.nice.org.uk/privacy-notice

9. I give my consent for the information in this questionnaire to be used and may be published on the NICE website as outlined above. *

- (●) I agree
- ( ) I disagree

The procedure/technology

Please answer the following questions as fully as possible to provide further inform ation about the procedure/technology and/or your experience.

10. Please describe your level of experience with the procedure/technology, for example:

    Are you familiar with the procedure/technology?

I am familiar with its uses as a rival to Deep Brain Stimulation (which I perform). I do not perform MRgFUS and have no experience of it but I do occasionally refer patients for it. I am familiar with tremor and I have read the papers.

11. Have you used it or are you currently using it?

    - Do you know how widely this procedure/technology is used in the NHS or what is the likely speed of uptake?

    - Is this procedure/technology performed/used by clinicians in specialities other than your own?

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

I do not use it but I do refer patients for it. Most of the clinicians performing it are neurosurgeons or neurologists and I am a neurosurgeon.

12. 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 published this research.
- [x] I have had no involvement in research on this procedure.
- [x] I have not done clinical research in this area but I am running a project looking at low fr

13. Does the title adequately reflect the procedure?

- (•) Yes
- ( ) Other

14. Is the proposed indication appropriate? If not, please explain

Yes

15. How innovative is this procedure/technology, compared to the current standard of care? Is it a minor variation or a novel approach/concept/design?

Lesioning procedures i.e. thalamotomy for tremor in Parkinson's disease already exist in the form of invasive RF lesioning (that I perform) and Gamma knife thalamotomy. This is similar to the latter in that it is 'non-invasive'. All three procedures have the same clinical effect. The stereotactic RF lesioning has the advantage that it is quick and cheap and can be controlled easily intraoperatively but the disadvantage that it has a small risk of stroke and seizures (1:200). MRgFUS has the advantage that it does not have such a large stroke risk but it is still making a lesion i.e. a small hole and therefore there is a small risk of stroke and other side-effects

16. Which of the following best describes the procedure:

- ○ 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.

17. Does this procedure/technology have the potential to replace current standard care or would it be used as an addition to existing standard care?

This is unpredictable but I suspect that it will be used in addition

Current management

18. Please describe the current standard of care that is used in the NHS.

Deep Brain Stimulation is the standard of care for PD tremor and I would argue that lesioning is for a different subset of patients (older, frailer etc with just tremor and minimal other symptoms). For those requiring lesions, the standard now is Stereotactic RF thalamotomy but gamma knife is an alternative

19. Are you aware of any other competing or alternative procedure/technology available to the NHS which have a similar function/mode of action to this?

    If so, how do these differ from the procedure/technology described in the briefing?

As above (RF thalamotomy and gamma knife)

Potential patient benefits and impact on the health system

20. What do you consider to be the potential benefits to patients from using this procedure/technology?

Less invasive

21. Are there any groups of patients who would particularly benefit from using this procedure/technology?

Old, frail patients

22. Does this procedure/technology have the potential to change the current pathway or clinical outcomes to benefit the healthcare system?

    Could it lead, for example, to improved outcomes, fewer hospital visits or less invasive treatment?

Yes it is a one-off procedure with a lower risk

23. What clinical facilities (or changes to existing facilities) are needed to do this procedure/technology safely?

It requires a dedicated MRI scanner (at least for several hours for each procedure). It also requires the dedicated FUS equipment

24. Is any specific training needed in order to use the procedure/technology with respect to efficacy or safety?

Yes - requires a radiologist and neurologist/ neurosurgeon and quite a lot of training would be necessary

Safety and efficacy of the procedure/technology

25. What are the potential harms of the procedure/technology?

    Please list any adverse events and potential risks (even if uncommon) and, if possible, estimate their incidence:

    - Adverse events reported in the literature (if possible, please cite literature)
    - Anecdotal adverse events (known from experience)
    - Theoretical adverse events

    Gait disturbance or ataxia (5-24%), parasthesiae (25%), hemiparesis (3.7-10%), dysgeusia (3-13%),
    See: Neurol Clin Pract. 2021 Aug; 11(4): e497–e503.

26. Please list the key efficacy outcomes for this procedure/technology?

    Many of the papers relate to Essential Tremor and there is not so much on PD tremor. Small case series suggest around 60-70% average reduction in tremor scores

27. Please list any uncertainties or concerns about the efficacy and safety of this procedure/technology?

    There are only small numbers of patients treated for PD tremor so mor trials are needed

28. Is there controversy, or important uncertainty, about any aspect of the procedure/technology?

    As above

29. If it is safe and efficacious, in your opinion, will this procedure be carried out in:

- ( ) 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.

Abstracts and ongoing studies

30. Please list any abstracts or conference proceedings that you are aware of that have been recently presented / published on this procedure/technology (this can include your own work).

    Please note that NICE will do a comprehensive literature search; we are only asking you for any very recent abstracts or conference proceedings which might not be found using standard literature searches. You do not need to supply a comprehensive reference list but it will help us if you list any that you think are particularly important.

    Not aware of them

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

    I do not know

32. Please list any other data (published and/or unpublished) that you would like to share.

Other considerations

33. Approximately how many people each year would be eligible for an intervention with this procedure/technology, (give either as an estimated number, or a proportion of the target population)?

As DBS would be procedure of choice for most patients I would estimate that around 5% of people referred for DBS (which is around 500 per year in the UK but the market is about 10% penetrated). Rough estimate would therefore be around 250 per year max

34. Please suggest potential audit criteria for this procedure/technology. If known, please describe:

Beneficial outcome measures.

These should include short- and long-term clinical outcomes, quality-of-life measures and patient-related outcomes. Please suggest the most appropriate method of measurement for each and the timescales over which these should be measured.

CREST or other tremor score, QOL (e.g. SF36 or ED5D), GIC, pre-op, post-op, 6 months and annually

35. Please suggest potential audit criteria for this procedure/technology. If known, please describe:

Adverse outcome measures.

These should include early and late complications. Please state the post procedure timescales over which these should be measured:

Up to 1 year

Further comments

36. If you have any further comments (e.g. issues with usability or implementation, the need for further research), please describe *

More studies are needed

Declarations of interests

Please state any potential conflicts of interest relevant to the procedure/technology (or competitor technologies) on which you are providing advice, or any involvements in disputes or complaints, in the previous **12 months** or likely to exist in the future. Please use the NICE policy on declaring and managing interests as a guide when declaring any interests. Further advice can be obtained from the NICE team.

37. Type of interest: *

- [ ] Direct: financial
- [x] Non-financial: professional
- [ ] Non-financial: personal
- [ ] Indirect
- [ ] No interests to declare

38. Description of interests, including relevant dates of when the interest arose and ceased. *

I do DBS but not FUS

39. I confirm that the information provided above is complete and correct. I acknowledge that any changes in these declarations during the course of my work with NICE, must be notified to NICE as soon as practicable and no later than 28 days after the interest arises. I am aware that if I do not make full, accurate and timely declarations then my advice may be excluded from being considered by the NICE committee.

    Please note, all declarations of interest will be made publicly available on the NICE website. *

    - (●) I agree
    - ( ) I disagree

Signature

40. Name: *

    Alexander L Green

41. Date: *

    18/01/2024

View results

Respondent

62 Anonymous

46:51
Time to complete

1. Project Number and Name - (Can be found on email) *

IP 1692/2

Your information

2. Name: *

Dipankar Nandi

3. Job title: *

Consultant Neurosurgeon

4. Organisation: *

Imperial College Healthcare NHS Trust

5. Email address: *

[redacted]

6. Professional organisation or society membership/affiliation: *

SBNS

7. Nominated/ratified by (if applicable):

ABN

8. Registration number (e.g. GMC, NMC, HCPC) *

4591845

How NICE will use this information:

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9. I give my consent for the information in this questionnaire to be used and may be published on the NICE website as outlined above. *

- (●) I agree
- ( ) I disagree

The procedure/technology

Please answer the following questions as fully as possible to provide further informa tion about the procedure/technology and/or your experience.

10. Please describe your level of experience with the procedure/technology, for example:

    Are you familiar with the procedure/technology?

    I have been performing MRI-guided Focussed Ultrasound thalamotomy from July 2016. We were among the pioneers in MRgFUS in the world and the first in the UK. I have performed over 110 MRgFUS procedures to date.

11. Have you used it or are you currently using it?

    - Do you know how widely this procedure/technology is used in the NHS or what is the likely speed of uptake?

    - Is this procedure/technology performed/used by clinicians in specialities other than your own?

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

    There are now two NHS centres that perform MRgFUS. Currently it is only used by Functional Neurosurgeons. The MRgFUS thalamotomy pathway is multi-disciplinary. Involves Neurologists (Movement Disorders) and Neuro-radiologists. I have worked closely with colleagues in both these specialties for over 7 years.

12. 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.
- [x] 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.
- [x] I have published this research.
- [ ] I have had no involvement in research on this procedure.
- [ ] Other

13. Does the title adequately reflect the procedure?

- (•) Yes
- ( ) Other

14. Is the proposed indication appropriate? If not, please explain

Yes. Tremor-dominant Parkinson's disease is an appropriate candidate for MRgFUS thalamotomy.

15. How innovative is this procedure/technology, compared to the current standard of care? Is it a minor variation or a novel approach/concept/design?

MRgFUS is a novel approach when compared to standard of care (deep brain stimulation, DBS). It is non-invasive. A one-stop intervention. No maintenance therapy. No hardware.

16. Which of the following best describes the procedure:

- (●) 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.

17. Does this procedure/technology have the potential to replace current standard care or would it be used as an addition to existing standard care?

MRgFUS is applicable in a cohort of Parkinson's disease patients which would generally not be suitable for DBS (standard of care). Thus it would be used in addition.

Current management

18. Please describe the current standard of care that is used in the NHS.

Deep brain stimulation is an invasive procedure that involves insertion of deep-seated brain electrodes and connections to extra-cranial pacemaker.

19. Are you aware of any other competing or alternative procedure/technology available to the NHS which have a similar function/mode of action to this?

    If so, how do these differ from the procedure/technology described in the briefing?

None exist.

Potential patient benefits and impact on the health system

20. What do you consider to be the potential benefits to patients from using this procedure/technology?

MRgFUS offers symptomatic treatment for a debilitating motor condition (tremor) that can be poorly responsive to drug therapy. This leads to functional independence, better quality of life, mental well-being.

21. Are there any groups of patients who would particularly benefit from using this procedure/technology?

Elderly patients with intractable tremor are often not fit for DBS surgery. This cohort would benefit particularly from MRgFUS.

22. Does this procedure/technology have the potential to change the current pathway or clinical outcomes to benefit the healthcare system?

    Could it lead, for example, to improved outcomes, fewer hospital visits or less invasive treatment?

Yes. Significantly fewer Neurologist clinic appointments, less care needs, increased functional independence, return to work (where appropriate).

23. What clinical facilities (or changes to existing facilities) are needed to do this procedure/technology safely?

3-T MRI, MRgFUS machine, modified CRW skull frame.

24. Is any specific training needed in order to use the procedure/technology with respect to efficacy or safety?

Yes. Needs dedicated training in patient assessment, selection, target planning, use of the MRgFUS machine. Experience in other stereotactic neurosurgery techniques (DBS) is essential.

Safety and efficacy of the procedure/technology

25. What are the potential harms of the procedure/technology?

    Please list any adverse events and potential risks (even if uncommon) and, if possible, estimate their incidence:

    - Adverse events reported in the literature (if possible, please cite literature)
    - Anecdotal adverse events (known from experience)
    - Theoretical adverse events

    Very few serious adverse effects, very uncommon. Balance dysfunction, slurred speech. Rarer: chorea, paresthesiae

26. Please list the key efficacy outcomes for this procedure/technology?

    Significant improvement in all validated outcome scales for tremor: CRST, Bain-Findley spirals, QUEST.

27. Please list any uncertainties or concerns about the efficacy and safety of this procedure/technology?

    Most data exists for MRgFUS in Essential Tremor, ET. There are fewer publications and studies of MRgFUS in PD. No concerns about safety.

28. Is there controversy, or important uncertainty, about any aspect of the procedure/technology?

    No

29. If it is safe and efficacious, in your opinion, will this procedure be carried out in:

- ( ) 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.

Abstracts and ongoing studies

30. Please list any abstracts or conference proceedings that you are aware of that have been recently presented / published on this procedure/technology (this can include your own work).

    Please note that NICE will do a comprehensive literature search; we are only asking you for any very recent abstracts or conference proceedings which might not be found using standard literature searches. You do not need to supply a comprehensive reference list but it will help us if you list any that you think are particularly important.

https://pubmed.ncbi.nlm.nih.gov/28298022/
https://pubmed.ncbi.nlm.nih.gov/35791767/
https://pubmed.ncbi.nlm.nih.gov/31993437/
N Engl J Med 2023; 388:683-693
DOI: 10.1056/NEJMoa2202721

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

No

32. Please list any other data (published and/or unpublished) that you would like to share.

There is FDA approval for MRgFUS in PD. Also EMA approval.

Other considerations

33. Approximately how many people each year would be eligible for an intervention with this procedure/technology, (give either as an estimated number, or a proportion of the target population)?

300 patients per year.

34. Please suggest potential audit criteria for this procedure/technology. If known, please describe:

Beneficial outcome measures.

These should include short- and long-term clinical outcomes, quality-of-life measures and patient-related outcomes. Please suggest the most appropriate method of measurement for each and the timescales over which these should be measured.

Standard Parkinson's disease outcome scales. UPDRS, GIC, EuroQuol. Most are done in Neurology Clinic. But the QOL measures can be remote / video questionnaires. One year and 5 years outcomes.

35. Please suggest potential audit criteria for this procedure/technology. If known, please describe:

Adverse outcome measures.

These should include early and late complications. Please state the post procedure timescales over which these should be measured:

Early complications include gait dysfunction, falls, dysarthria. Measured at 3 months and 12 months. Recurrence of tremor is late complcation.

Further comments

36. If you have any further comments (e.g. issues with usability or implementation, the need for further research), please describe *

None.

Declarations of interests

Please state any potential conflicts of interest relevant to the procedure/technology (or competitor technologies) on which you are providing advice, or any involvements in disputes or complaints, in the previous **12 months** or likely to exist in the future. Please use the NICE policy on declaring and managing interests as a guide when declaring any interests. Further advice can be obtained from the NICE team.

37. Type of interest: *

- [x] Direct: financial
- [ ] Non-financial: professional
- [ ] Non-financial: personal
- [ ] Indirect
- [ ] No interests to declare

38. Description of interests, including relevant dates of when the interest arose and ceased. *

I have provided paid consultancy services to the manufacturer Insightec Ltd (small fees, less than £ 500). Also, we have had Clinical Trial part-funded by Insightec. None in last 2 years.

39. I confirm that the information provided above is complete and correct. I acknowledge that any changes in these declarations during the course of my work with NICE, must be notified to NICE as soon as practicable and no later than 28 days after the interest arises. I am aware that if I do not make full, accurate and timely declarations then my advice may be excluded from being considered by the NICE committee.

    Please note, all declarations of interest will be made publicly available on the NICE website. *

    - (●) I agree
    - ( ) I disagree

Signature

40. Name: *

    Dipankar Nandi

41. Date: *

    09/02/2024

NICE National Institute for Health and Care Excellence

Professional Expert Questionnaire

Technology/Procedure name & indication: **IP1692 MRI-guided focused ultrasound thalamotomy for moderate-to-severe tremor in Parkinson's disease**

Your information

Name:	Dr Johannes C Klein
Job title:	Consultant Neurologist and Neurophysiologist
Organisation:	University of Oxford & Oxford University Hospitals NHS Foundation Trust
Email address:	[redacted]
Professional organisation or society membership/affiliation:	British Society for Clinical Neurophysiology (BSCN)
Nominated/ratified by (if applicable):	BSCN
Registration number (e.g. GMC, NMC, HCPC)	6 12 12 52

How NICE will use this information:

The information that you provide on this form will be used to develop guidance on this procedure.

☒ Please tick this box if you would like to receive information about other NICE topics.

Your advice and views represent your individual opinion and not that of your employer, professional society or a consensus view. Your name, job title, organisation and your responses, along with your declared interests will also be published online on the NICE website as part of public

consultation on the draft guidance, except in circumstances but not limited to, where comments are considered voluminous, or publication would be unlawful or inappropriate.

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

☒ I give my consent for the information in this questionnaire to be used and may be published on the NICE website as outlined above. If consent is NOT given, please state reasons below:

Click here to enter text.

Please answer the following questions as fully as possible to provide further information about the procedure/technology and/or your experience.

1	Please describe your level of experience with the procedure/technology, for example: Are you familiar with the procedure/technology? Have you used it or are you currently using it? − Do you know how widely this procedure/technology is used in the NHS or what is the likely speed of uptake? − Is this procedure/technology performed/used by clinicians in specialities other than your own?	I am familiar with the procedure and the technology. I do not have direct experience of performing this intervention, as we do not have a machine in Oxford, but I do have experience with conventional thalamotomy (the direct predecessor technology), gamma knife therapy (used for tumours, on occasion also for thalamotomy, probably to be supplanted by MRgfUS), and deep brain stimulation (DBS) surgery.

	– If your specialty is involved in patient selection or referral to another specialty for this procedure/technology, please indicate your experience with it.	
2	– Please indicate your research experience relating to this procedure (please choose one or more if relevant):	I have done bibliographic research on this procedure. yes I have done research on this procedure in laboratory settings (e.g. device-related research). no I have done clinical research on this procedure involving patients or healthy volunteers. no I have published this research. no I have had no involvement in research on this procedure. yes Other (please comment)
3	Does the title adequately reflect the procedure?	Yes.
	How innovative is this procedure/technology, compared to the current standard of care? Is it a minor variation or a novel approach/concept/design?	This procedure is innovative over standard thalamotomy because of its relative non-invasiveness. Like conventional thalamotomy, this is a single intervention with long-lasting effects. This includes the risk of persistent side-effects, which can however be minimised by using a “stun first” approach (heating to reversible tissue dysfunction rather than necrosis) before applying the definitive lesion. Unlike conventional thalamotomy and DBS, it does not require general anaesthesia. Unlike DBS, no implanted material remains, but this also means the treatment cannot be adjusted.Therefore, this option is suitable for patients who cannot undergo DBS or thalamotomy, for example due to anaesthesia or surgical risks.
	Which of the following best describes the procedure (please choose one):	Established practice and no longer new (in other healthcare systems, like the USA).

4	Does this procedure/technology have the potential to replace current standard care or would it be used as an addition to existing standard care?	It would be an additional option for patients who cannot have (or possibly do not want to have) DBS or conventional thalamotomy. It would likely supplant gamma knife therapy for tremor in patients who cannot have conventional surgery, however this is not an option currently available on the NHS anyway.
5	Have there been any substantial modifications to the procedure technique or, if applicable, to devices involved in the procedure? Has the evidence base on the efficacy and safety of this procedure changed substantially since publication of the guidance?	No Perhaps not substantially, but there is new safety evidence specifically in PD tremor doi: 10.1002/mds.29569

Current management

6	Please describe the current standard of care that is used in the NHS.	Medical management, if not efficacious, then DBS. Thalamotomy in rare cases.
7	Are you aware of any other competing or alternative procedure/technology available to the NHS which have a similar function/mode of action to this? If so, how do these differ from the procedure/technology described in the briefing?	Gamm knife therapy can also provide non-invasive thalamotomy. Unlike MRgfUS, it does not allow for applying a “stun lesion”, arguably the MRgfUS is safer as side-effects (eg. sensory change, dysarthria) can be assessed before the permanent lesion is applied.

Potential patient benefits and impact on the health system

8	What do you consider to be the potential benefits to patients from using this procedure/technology?	No need for craniotomy, no need for general anaesthesia, no implanted material, no cerebral infection risk, can be used with patients on anticoagulants.
9	Are there any groups of patients who would particularly benefit from using this procedure/technology?	Patients with high perioperative risk, elderly patients, patients on anticoagulation, patients who are afraid of anaesthesia or surgery.
10	Does this procedure/technology have the potential to change the current pathway or clinical outcomes to benefit the healthcare system? Could it lead, for example, to improved outcomes, fewer hospital visits or less invasive treatment?	It would enable selected patients to regain hand function which has a major impact on quality of life and care needs. It would also provide less invasive treatment, which widens the circle of patients who could potentially benefit.
11	What clinical facilities (or changes to existing facilities) are needed to do this procedure/technology safely?	MRgfUS requires a dedicated, self-contained system comprising an MRI scanner with an integrated therapy device. It should only be offered in tertiary neuroscience centres that have access to other approaches for tremor management like DBS and/or thalamotomy.
12	Is any specific training needed in order to use the procedure/technology with respect to efficacy or safety?	Yes. The manufacturer provides that training. The team should involve a neurologist, and a neurosurgeon.

Safety and efficacy of the procedure/technology

13	What are the potential harms of the procedure/technology? Please list any adverse events and potential risks (even if uncommon) and, if possible, estimate their incidence:	Haemorrhage – theoretical concern, risk very low, procedure has been safely applied to patients on antiplatelets and anticoagulants Other side-effects – sensory change, dysarthria are similar to conventional thalamotomy but less frequent. In the literature, dysarthria after bilateral thalamotomy (for essential tremor) is reported at 30%, but for MRgfUS this is 5%. In PD tremor, the numbers in the literature are smaller, but a recent study in 48 patients showed side-effects graded as “mild” only: gait

	Adverse events reported in the literature (if possible, please cite literature) Anecdotal adverse events (known from experience) Theoretical adverse events	imbalance (38.24%), sensory deficits (26.47%), motor weakness (17.65%), dysgeusia (5.88%), and dysarthria (5.88%) at 3 months, some of which improve later on.
14	Please list the key efficacy outcomes for this procedure/technology?	Reduction in tremor severity, as assessed by standardised clinical rating scales (eg. Fahn-Tolosa-Marin, UPDRS III), patient disability (eg. UPDRS II, PDQ 39); acclerometry or surface EMG in Neurophysiology are objective measures that are probably more suited to research settings than clinical practice.
15	Please list any uncertainties or concerns about the efficacy and safety of this procedure/?	One concern is the inability to adjust treatment, which means unlike DBS side-effects cannot be addressed after the procedure. Also PD tremor is a progressive condition, and unlike DBS, the intensity of treatment cannot be increased over time, and patients cannot have different stimulation programmes they use for every day use vs fine manual tasks (compromising on dysarthria).
16	Is there controversy, or important uncertainty, about any aspect of the procedure/technology?	Long-term outcomes are not known, but likely comparable to conventional thalamotomy.
17	If it is safe and efficacious, in your opinion, will this procedure be carried out in (please choose one):	Fewer than 10 specialist centres in the UK.

Abstracts and ongoing studies

18	Please list any abstracts or conference proceedings that you are aware of that have been recently presented / published on this procedure/technology (this can include your own work). Please note that NICE will do a comprehensive literature search; we are only asking you for any very recent	n/a

	abstracts or conference proceedings which might not be found using standard literature searches. You do not need to supply a comprehensive reference list but it will help us if you list any that you think are particularly important.	
19	Are there any major trials or registries of this procedure/technology currently in progress? If so, please list.	- MRgFUS Neuro UK-Registry Study (research driven) - Global Registry: ExAblate Neuro MR Guided Focused Ultrasound (MRgFUS) of Neurological Disorders (manufacturer sponsored)
20	Please list any other data (published and/or unpublished) that you would like to share.	n/a

Other considerations

21	Approximately how many people each year would be eligible for an intervention with this procedure/technology, (give either as an estimated number, or a proportion of the target population)?	Worked example: Population in England 44,456,850 x Prevalence of Parkinson's 0.0032 x Proportion of patients with advanced PD 0.34 x Proportion of patients with severe tremor in advanced PD 0.39 x Proportion of patients eligible for device therapy 0.66 x Proportion of patients who cannot have DBS 0.33 = 4,108 patients. (Data used from NICE TA 934 and Parkinsonism and Related Disorders 18S1 (2012) S90–S92)
22	Please suggest potential audit criteria for this procedure/technology. If known, please describe: – Beneficial outcome measures. These should include short- and long-term clinical outcomes, quality-of-life measures and patient-related outcomes. Please suggest the most appropriate method of measurement for each and the timescales over which these should be measured. – Adverse outcome measures. These should include early and late complications. Please state the post	Beneficial outcome measures: Tremor rating scale (Fahn-Tolosa-Marin or similar, full UPDRS) 1) before and 2) after the procedure at 3 and 12 months QoL questionnaires before and after the procedure (as above) Carer impact (PDQ-Carer) before and after the procedure (as above) Consider video of standardised hand tremor examination (postural, kinetic, resting tremor) Adverse outcome measures: Proportion of patients with post-intervention haemorrhage (both clinically apparent, and those seen on MRI only)

	procedure timescales over which these should be measured:	Proportion of patients with typical side-effects after 3 and 12 months: gait imbalance, sensory deficits, motor weakness, dysgeusia, and dysarthria Registry to capture rare, as yet unknown side-effects

Further comments

23	If you have any further comments (e.g. issues with usability or implementation, the need for further research), please describe.	Determining long-term efficacy vs standard approaches would be worthwhile.

NICE National Institute for Health and Care Excellence

Declarations of interests

Please state any potential conflicts of interest relevant to the procedure/technology (or competitor technologies) on which you are providing advice, or any involvements in disputes or complaints, in the previous **12 months** or likely to exist in the future. Please use the NICE policy on declaring and managing interests as a guide when declaring any interests. Further advice can be obtained from the NICE team.

Type of interest *	Description of interest	Relevant dates	
		Interest arose	Interest ceased
Choose an item.	n/a		
Choose an item.			
Choose an item.			

☒ I confirm that the information provided above is complete and correct. I acknowledge that any changes in these declarations during the course of my work with NICE, must be notified to NICE as soon as practicable and no later than 28 days after the interest arises. I am aware that if I do not make full, accurate and timely declarations then my advice may be excluded from being considered by the NICE committee.

Please note, all declarations of interest will be made publicly available on the NICE website.

Print name:	**Dr Johannes C Klein**
Dated:	**25 March 2024**

NICE National Institute for Health and Care Excellence

Professional Expert Questionnaire

Technology/Procedure name & indication: IP1692 MRI-guided focused ultrasound thalamotomy for moderate-to-severe tremor in Parkinson's disease

Your information

Name:	Jibril Osman farah
Job title:	Consultant functional and general neurosurgeon
Organisation:	The Walton centre NHS trust
Email address:	[redacted]
Professional organisation or society membership/affiliation:	RCS(Ed) GMC BSSFN
Nominated/ratified by (if applicable):	BSSFN
Registration number (e.g. GMC, NMC, HCPC)	4287663

How NICE will use this information:

The information that you provide on this form will be used to develop guidance on this procedure.

X Please tick this box if you would like to receive information about other NICE topics.

Your advice and views represent your individual opinion and not that of your employer, professional society or a consensus view. Your name, job title, organisation and your responses, along with your declared interests will also be published online on the NICE website as part of public consultation on the draft guidance, except in circumstances but not limited to, where comments are considered voluminous, or publication would be unlawful or inappropriate.

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

X I give my consent for the information in this questionnaire to be used and may be published on the NICE website as outlined above. If consent is NOT given, please state reasons below:

Click here to enter text.

Please answer the following questions as fully as possible to provide further information about the procedure/technology and/or your experience.

1	Please describe your level of experience with the procedure/technology, for example: Are you familiar with the procedure/technology? Have you used it or are you currently using it? − Do you know how widely this procedure/technology is used in the NHS or what is the likely speed of uptake? − Is this procedure/technology performed/used by clinicians in specialities other than your own? − If your specialty is involved in patient selection or referral to another specialty for this	I am the certified operator for MRI/FUS in the Walton centre NHS trust and I lead the MRI/FUS thalamotomy service for the North of England awarded by NHSEng. I established the MRI/FUS service in 2022 and currently perform 75-85 thalamotomy for Essential tremor per year(3 cases per session). I am familiar with the current indication NICE approved (ET unilateral) both for targeting and treatment delivery with the Insightech MRI/FUS. I am also familiar with other not Nice approved indications such as Parkinson disease (tremor dominant PD), bilateral treatment for ET and chronic neuropathic pain. The treatment delivery (thalamotomy is performed by myself (certified operator) in conjuction with consultant neuroradiologist. Case selection is performed in conjunction with consultant Neurologist (4 neurologist are part of the team and joint clinic are part of the patient pathway)

	procedure/technology, please indicate your experience with it.	
2	– 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 am doing clinical research on this procedure involving patients within a grant application. I have published this research. I looking at new platform for planning the targeting with DTI/anatomy
3	Does the title adequately reflect the procedure? How innovative is this procedure/technology, compared to the current standard of care? Is it a minor variation or a novel approach/concept/design? Which of the following best describes the procedure (please choose one):	Established practice and no longer new for both unilateral and bilateral ET in USA and EU. Not approved for bilateral ET in the UK> A minor variation on an existing procedure, which is unlikely to alter the procedure's safety and efficacy; this apply to use in PD related tremor Other indications such as chronic pain,and dystonia are novel and still require data.

4	Does this procedure/technology have the potential to replace current standard care or would it be used as an addition to existing standard care?	Yes
5	Have there been any substantial modifications to the procedure technique or, if applicable, to devices involved in the procedure? Has the evidence base on the efficacy and safety of this procedure changed substantially since publication of the guidance?	Not that I am aware from the time I utilise the MRI/FUS There are evidence that the use in PD related tremor is safe and tremor control is sustained in time

Current management

6	Please describe the current standard of care that is used in the NHS.	MRI/FUS is only approved for unilateral ET
7	Are you aware of any other competing or alternative procedure/technology available to the NHS which have a similar function/mode of action to this? If so, how do these differ from the procedure/technology described in the briefing?	No

Potential patient benefits and impact on the health system

8	What do you consider to be the potential benefits to patients from using this procedure/technology?	Reduction hardware related complications (if alternative to DBS) Reduction F/U in clinic
9	Are there any groups of patients who would particularly benefit from using this procedure/technology?	Tremor dominat PD
10	Does this procedure/technology have the potential to change the current pathway or clinical outcomes to benefit the healthcare system? Could it lead, for example, to improved outcomes, fewer hospital visits or less invasive treatment?	Yes for both questions
11	What clinical facilities (or changes to existing facilities) are needed to do this procedure/technology safely?	See current workflow in Walton centre; iMRI with MRI/FUS installed ,planning software,dedicated area for day case surgery
12	Is any specific training needed in order to use the procedure/technology with respect to efficacy or safety?	Certification from Insightech

Safety and efficacy of the procedure/technology

13	What are the potential harms of the procedure/technology? Please list any adverse events and potential risks (even if uncommon) and, if possible, estimate their incidence:	Complications related with thalamotomy generally below 1% but depend on experience and familiarity with the hardware/software Motor deficit, sensory deficit, failure to control tremor etc (low incidence)

	Adverse events reported in the literature (if possible, please cite literature) Anecdotal adverse events (known from experience) Theoretical adverse events	
14	Please list the key efficacy outcomes for this procedure/technology?	Tremor control, improvement QOL
15	Please list any uncertainties or concerns about the efficacy and safety of this procedure/?	None currently
16	Is there controversy, or important uncertainty, about any aspect of the procedure/technology?	No
17	If it is safe and efficacious, in your opinion, will this procedure be carried out in (please choose one):	Fewer than 10 specialist centres in the UK, possibly 4-5 centres with yearly case load of 80-100 procedure per year including essential tremor).

Abstracts and ongoing studies

18	Please list any abstracts or conference proceedings that you are aware of that have been recently presented / published on this procedure/technology (this can include your own work). Please note that NICE will do a comprehensive literature search; we are only asking you for any very recent abstracts or conference proceedings which	There are several articles in the literature, I am not aware of any not published material.

	might not be found using standard literature searches. You do not need to supply a comprehensive reference list but it will help us if you list any that you think are particularly important.	
19	Are there any major trials or registries of this procedure/technology currently in progress? If so, please list.	There is a registry with St Mary just started, we applied for a grant recently and we collect prospective outcome measures in all cases treated for ET
20	Please list any other data (published and/or unpublished) that you would like to share.	

Other considerations

21	Approximately how many people each year would be eligible for an intervention with this procedure/technology, (give either as an estimated number, or a proportion of the target population)?	For Tremor dominant PD I suspect the number will be limited to 5-10 cases per year in our centre which has a catchment area of 3.5 mil. Tremor dominant PD need to be done in a centre that does treat ET (number for ET are much higher and make the
22	Please suggest potential audit criteria for this procedure/technology. If known, please describe: − Beneficial outcome measures. These should include short- and long-term clinical outcomes, quality-of-life measures and patient-related outcomes. Please suggest the most appropriate method of measurement for each and the timescales over which these should be measured. − Adverse outcome measures. These should include early and late complications. Please state the post	Beneficial outcome measures: TRS, QOL Adverse outcome measures: Record of complications (this generally is not done with specific scale but record of adverse events.

	procedure timescales over which these should be measured:	

Further comments

23	If you have any further comments (e.g. issues with usability or implementation, the need for further research), please describe.	None

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Declarations of interests

Please state any potential conflicts of interest relevant to the procedure/technology (or competitor technologies) on which you are providing advice, or any involvements in disputes or complaints, in the previous **12 months** or likely to exist in the future. Please use the NICE policy on declaring and managing interests as a guide when declaring any interests. Further advice can be obtained from the NICE team.

Type of interest *	Description of interest	Relevant dates	
		Interest arose	Interest ceased
Choose an item.			
Choose an item.			
Choose an item.			

☐ I confirm that the information provided above is complete and correct. I acknowledge that any changes in these declarations during the course of my work with NICE, must be notified to NICE as soon as practicable and no later than 28 days after the interest arises. I am aware that if I do not make full, accurate and timely declarations then my advice may be excluded from being considered by the NICE committee.

Please note, all declarations of interest will be made publicly available on the NICE website.

Print name:	**Click here to enter text.**
Dated:	**Click here to enter text.**

View results

Respondent

29 Anonymous

159:44
Time to complete

1. Project Number and Name - (Can be found on email) *

IP1692 MRI-guided focused ultrasound thalamotomy for moderate-to-severe tremor in Parkinson's disease

Your information

2. Name: *

Ludvic Zrinzo

3. Job title: *

Professor of Functional Neurosurgery

4. Organisation: *

National Hospital For Neurology and Neurosurgery, UCLH, Queen Square,

5. Email address: *

[redacted]

6. Professional organisation or society membership/affiliation: *

UCLH Foundation Trust

7. Nominated/ratified by (if applicable):

8. Registration number (e.g. GMC, NMC, HCPC) *

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How NICE will use this information:

The information that you provide on this form will be used to develop guidance on this procedure.

Your advice and views represent your individual opinion and not that of your employer, professional society or a consensus view. Your name, job title, organisation and your responses, along with your declared interests will also be published online on the NICE website as part of public consultation on the draft guidance, except in circumstances but not limited to, where comments are considered voluminous, or publication would be unlawful or inappropriate.

For more information about how we process your data please see our privacy notice: https://www.nice.org.uk/privacy-notice

9. I give my consent for the information in this questionnaire to be used and may be published on the NICE website as outlined above. *

- (●) I agree
- ( ) I disagree

The procedure/technology

Please answer the following questions as fully as possible to provide further informa tion about the procedure/technology and/or your experience.

10. Please describe your level of experience with the procedure/technology, for example:

    Are you familiar with the procedure/technology?

Yes
I have 20 year + experience in Functional Neurosurgery (H index 72, >16 000 citations)
I have experience of targeting the subthalamic nucleus during DBS procedures in >2000 patients
I have 18 month experience using Focused Ultrasound (FUS) for essential tremor

11. Have you used it or are you currently using it?

- Do you know how widely this procedure/technology is used in the NHS or what is the likely speed of uptake?

- Is this procedure/technology performed/used by clinicians in specialities other than your own?

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

- FUS for PD is not commissioned by NHS England. Centres commissioned by NHS England are likely to offer this to patients with tremor dominant PD when it becomes available.

FUS is used by neurosurgeons in partnership with neurologists

Functional Neurosurgeons and neurologists specialised in movement disorders select patients for such procedures. I select patients with medically refractory patients for consideration of surgical interventions on a weekly basis.

12. 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 published this research.
- [ ] I have had no involvement in research on this procedure.
- [x] I have published on radiofrequency ablation for PD tremor

13. Does the title adequately reflect the procedure?

- ( ) Yes
- (•) Other

14. Is the proposed indication appropriate? If not, please explain

Focused ultrasound can be used for the treatment of PD tremor but it can ALSO be used to help other motor symptoms of PD, including bradykinesia and rigidity. Targeting the thalamus can help with tremor but targeting the sub thalamus can help with other symptoms as well. NICE should explore the use of FUS of motor symptoms of PD and not simply the use of FUS for PD tremor. Data on the results of subthalamotomy for PD symptoms includes a small RCT and 3 year follow up and the results appear to be better than thalamotomy for PD tremor.

15. How innovative is this procedure/technology, compared to the current standard of care? Is it a minor variation or a novel approach/concept/design?

The use of FUS for motor PD symptoms could represent a significant advance in the management of PD motor symptoms.

16. Which of the following best describes the procedure:

- ( ) 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.

17. Does this procedure/technology have the potential to replace current standard care or would it be used as an addition to existing standard care?

FUS may be used as an addition to existing standard care but is likely to delay the need for deep brain stimulation in a proportion of patients.

18. Have there been any substantial modifications to the procedure technique or, if applicable, to devices involved in the procedure?

Targeting of the subthalamic nucleus requires the use of a different membrane in the FUS instrument that includes an MRI coil, vastly improving the quality of MR images during the procedure.

19. Has the evidence base on the efficacy and safety of this procedure changed substantially since publication of the guidance?

Yes. There are many more publications including a new anatomical target and class I evidence supporting it use.

20. Do you think the guidance needs updating?

Yes. FUS should be approved for essential tremor, including second side surgery in a staged fashion. It should also include the possibility of using FUS for subthalamotomy for PD motor symptoms.

Current management

21. Please describe the current standard of care that is used in the NHS.

FUS is only approved for unilateral thalamotomy in essential tremor.

22. Are you aware of any other competing or alternative procedure/technology available to the NHS which have a similar function/mode of action to this?

    If so, how do these differ from the procedure/technology described in the briefing?

Alternatives include radiofrequency thalamotomy and thalamic DBS for tremor and subthalamic DBS for Parkinson disease.

Potential patient benefits and impact on the health system

23. What do you consider to be the potential benefits to patients from using this procedure/technology?

Patients with asymmetric motor symptoms, particularly but not restricted to tremor, may struggle with medically refractory symptoms. Availability of FUS has the potential to vastly improve the quality of life of a proportion of patients with PD without the need to consider more involved procedures such as deep brain stimulation.

24. Are there any groups of patients who would particularly benefit from using this procedure/technology?

Patients with medically refractory symptoms of PD, especially when symptoms are asymmetrical.

25. Does this procedure/technology have the potential to change the current pathway or clinical outcomes to benefit the healthcare system?

    Could it lead, for example, to improved outcomes, fewer hospital visits or less invasive treatment?

Yes. FUS could delay the need for more involved and expensive procedures such a deep brain stimulation, with a reduction in hospital visits required for programming and medication adjustment.

26. What clinical facilities (or changes to existing facilities) are needed to do this procedure/technology safely?

The National Hospital has a Focused Ultrasound machine that was purchased with charity money. We have applied for NHS commissioning and are awaiting a response. The long waiting list of patients with essential tremor waiting at other NHS commissioned sites is evidence of the need for commissioning of further sites. Additional indications will increase the demand on FUS installations and the need for NHS England to commission further sites. A slight modification of the membrane used during the procedure is required to improve the quality of MR images.

27. Is any specific training needed in order to use the procedure/technology with respect to efficacy or safety?

Most skills are transferrable from the targeting during deep brain stimulation and knowledge of how to use a FUS machine. However, mentorship is essential if these skills are lacking. This is a surgical procedure and neurologists should not perform FUS without a neurosurgeon. Likewise, patient selection requires collaboration between neurologist and neurosurgeon.

Safety and efficacy of the procedure/technology

28. What are the potential harms of the procedure/technology?

Please list any adverse events and potential risks (even if uncommon) and, if possible, estimate their incidence:

- Adverse events reported in the literature (if possible, please cite literature)
- Anecdotal adverse events (known from experience)
- Theoretical adverse events

- dyskinesia, gait ataxia, disinhibition, speech disturbance, weakness - almost always transient but rarely permanent (so far not severe).

Relevant literature:

Martínez-Fernández, R. et al. Focused ultrasound subthalamotomy in patients with asymmetric Parkinson's disease: a pilot study. The Lancet Neurology 17, 54–63 (2018).

Martínez-Fernández, R. et al. Randomized Trial of Focused Ultrasound Subthalamotomy for Parkinson's Disease. New Engl J Med 383, 2501–2513 (2020).

Martínez-Fernández, R. et al. Prospective Long-term Follow-up of Focused Ultrasound Unilateral Subthalamotomy for Parkinson Disease. Neurology 100, e1395–e1405 (2023).

29. Please list the key efficacy outcomes for this procedure/technology?

Improvement in the UPDRS III score in the treated hemibody (OFF and ON medication) is the primary outcome used to evaluate symptom change.
Other relevant scores include: PDQ39 scores and levodopa dose.

30. Please list any uncertainties or concerns about the efficacy and safety of this procedure/technology?

Only one centre has published systematically on FUS subthalamotomy (FUS STN) for PD to date (Madrid) although more centres are planning to publish. The National Hospital is keen to join a multicentre international trial on FUS STN for PD.

31. Is there controversy, or important uncertainty, about any aspect of the procedure/technology?

This is a new technology applied to a well established target. Unilateral interventions are not particularly controversial. However, some clinicians with experience in DBS and without expertise with ablation may feel uncomfortable with the idea of stereotactic ablation.

32. If it is safe and efficacious, in your opinion, will this procedure be carried out in:

- ○ 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.

Abstracts and ongoing studies

33. Please list any abstracts or conference proceedings that you are aware of that have been recently presented / published on this procedure/technology (this can include your own work).

    Please note that NICE will do a comprehensive literature search; we are only asking you for any very recent abstracts or conference proceedings which might not be found using standard literature searches. You do not need to supply a comprehensive reference list but it will help us if you list any that you think are particularly important.

I think it is very important that NICE do NOT combine the results of thalamotomy, subthalamotomy, or pallidotomy for PD symptoms. Section of patients is very different and outcome are also very different. The data available for subthalamotomy in PD are the most encouraging, followed by thalamotomy, and with quite unimpressive results with pallidotomy.

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

Yes.
NCT02912871
NCT01772693
NCT03300193
NCT02692183
NCT02263885
NCT01698450
NCT04593875
NCT05565443
NCT06090292
NCT02246374
NCT05539196
NCT02252380
NCT02003248
NCT04996992
NCT03981055
NCT05008094
NCT04370665
NCT04692116
NCT02347254
NCT03608553
NCT05475340
NCT04002596
NCT03100474
NCT04661241
NCT06232629
NCT05965960
NCT05512299
NCT04250376
NCT04991831

35. Please list any other data (published and/or unpublished) that you would like to share.

N/A

Other considerations

36. Approximately how many people each year would be eligible for an intervention with this procedure/technology, (give either as an estimated number, or a proportion of the target population)?

I estimate that our centre would recruit around 50 patients per year. There is the possibility that this may increase once patient selection criteria have been refined. I suspect <5% of the PD population may be considered for this therapy.

37. Please suggest potential audit criteria for this procedure/technology. If known, please describe:

Beneficial outcome measures.

These should include short- and long-term clinical outcomes, quality-of-life measures and patient-related outcomes. Please suggest the most appropriate method of measurement for each and the timescales over which these should be measured.

UPDRS hemibody scores as well as PDQ-39 and levodopa requirements.

38. Please suggest potential audit criteria for this procedure/technology. If known, please describe:

Adverse outcome measures.

These should include early and late complications. Please state the post procedure timescales over which these should be measured:

Problems with speech, balance, weakness, dyskinesia, behavioural changes. Six and 12 month data as a minimum, preferably also including 3 and 5 year data

Further comments

39. If you have any further comments (e.g. issues with usability or implementation, the need for further research), please describe *

N/A

Declarations of interests

Please state any potential conflicts of interest relevant to the procedure/technology (or competitor technologies) on which you are providing advice, or any involvements in disputes or complaints, in the previous **12 months** or likely to exist in the future. Please use the NICE policy on declaring and managing interests as a guide when declaring any interests. Further advice can be obtained from the NICE team.

40. Type of interest: *

- [x] Direct: financial
- [x] Non financial: professional
- [ ] Non financial: personal
- [ ] Indirect
- [ ] No interests to declare

41. Description of interests, including relevant dates of when the interest arose and ceased. *

I have a professional interest in FUS as I work at an NHS site that has applied for NHS commissioning for FUS.
I have a non personal financial interest as I am a consultant for Insightec, a manufacturer of FUS hardware. Funds are placed in a research account to facilitate activities related to learning and professional development.

42. I confirm that the information provided above is complete and correct. I acknowledge that any changes in these declarations during the course of my work with NICE, must be notified to NICE as soon as practicable and no later than 28 days after the interest arises. I am aware that if I do not make full, accurate and timely declarations then my advice may be excluded from being considered by the NICE committee.

Please note, all declarations of interest will be made publicly available on the NICE website. *

- (●) I agree
- ( ) I disagree

Signature

43. Name: *

Ludvic Zrinzo

44. Date: *

10/02/2024

View results

Respondent

30 Anonymous

97:15
Time to complete

1. Project Number and Name - (Can be found on email) *

IP1692/2 IP1692/2 MRI-guided focused ultrasound thalamotomy for moderate-to-severe tremor in Parkinson's disease

Your information

2. Name: *

WMW Gedroyc

3. Job title: *

Professor

4. Organisation: *

Imperial College Healthcare NHS Trust

5. Email address: *

[redacted]

6. Professional organisation or society membership/affiliation: *

Royal College of Radiologists

7. Nominated/ratified by (if applicable):

8. Registration number (e.g. GMC, NMC, HCPC) *

2443311

How NICE will use this information:

The information that you provide on this form will be used to develop guidance on this procedure.

Your advice and views represent your individual opinion and not that of your employer, professional society or a consensus view. Your name, job title, organisation and your responses, along with your declared interests will also be published online on the NICE website as part of public consultation on the draft guidance, except in circumstances but not limited to, where comments are considered voluminous, or publication would be unlawful or inappropriate.

For more information about how we process your data please see our privacy notice: https://www.nice.org.uk/privacy-notice

9. I give my consent for the information in this questionnaire to be used and may be published on the NICE website as outlined above. *

- (●) I agree
- ( ) I disagree

The procedure/technology

Please answer the following questions as fully as possible to provide further informa tion about the procedure/technology and/or your experience.

10. Please describe your level of experience with the procedure/technology, for example:

    Are you familiar with the procedure/technology?

My unit carries out at least 1 tremor related transcranial brain focussed ultrasound procedure every week and we have been performing these procedures for 5 years.
Very familiar with this procedure and technology as a result.

11. Have you used it or are you currently using it?

- Do you know how widely this procedure/technology is used in the NHS or what is the likely speed of uptake?

- Is this procedure/technology performed/used by clinicians in specialities other than your own?

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

Currently there are three units carrying out brain focused ultrasound for trauma in the UK. There is a unit in Imperial College Saint Mary's London with a further unit at the Wharton hospital in Liverpool and a unit in Dundee Scotland. The units in England are currently funded by NHS England to carry out 150 procedures a year. This is an oval underestimate and is only applicable to essential tremor not to Parkinson's disease.

In our hands the procedure is carried out as a multidisciplinary team process with the involvement of radiologists, neurosurgeons and neurologists all in the same room with all specialties contributing their area of expertise to the procedure so it becomes a true multidisciplinary process .

Patient recruitment for essential tremor procedures is predominantly carried out by a combination of neurologists and neurosurgeons and the same would be true of its application to tremor in Parkinsons disease.

12. 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.
- [x] 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.
- [x] I have published this research.
- [ ] I have had no involvement in research on this procedure.
- [ ] Other

13. Does the title adequately reflect the procedure?

- [x] Yes
- [ ] Other

14. Is the proposed indication appropriate? If not, please explain

It is completely appropriate to utilise transcranial brain focused ultrasound to treat patients with tremor dominant Parkinson's disease. These patients can be treated in very much the same way as our current essential tremor patients are treated and the site of treatment is identical to the patient stream we currently treat in essential tremor. Essential tremor is considered safe and effective by NHS England with very few complications and rapid recovery with no significant operative intervention required Since the procedure is completely noninvasive. A similar approach will be utilised in treating tremor dominant Parkinson's disease and all the acceptable safety aspects already well described are applicable to Parkinson's disease just as much as they are to essential tremor.

15. How innovative is this procedure/technology, compared to the current standard of care? Is it a minor variation or a novel approach/concept/design?

The procedure described in this application is identical to that used in MR guided brain Focused Ultrasound for the treatment of essential tremor. It is therefore completely similar to an already accepted procedure with the same safety aspects and very similar efficacy results. The process is therefore a minor variation to a now existing procedure just utilised in a slightly different disease setting.

16. Which of the following best describes the procedure:

- [ ] 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.

17. Does this procedure/technology have the potential to replace current standard care or would it be used as an addition to existing standard care?

This procedure definitely has the ability to replace more invasive procedures such as deep brain stimulation which is extremely expensive utilised in Parkinson's disease such as deep brain stimulation and to lessen the utilisation of the complex and often problematic drugs that are commonly used in Parkinson's disease.

18. Have there been any substantial modifications to the procedure technique or, if applicable, to devices involved in the procedure?

The procedure would be carried out in a similar manner to the existing process for the treatment of essential tremor using brain focused ultrasound. No extra components or different approaches are required.

19. Has the evidence base on the efficacy and safety of this procedure changed substantially since publication of the guidance?

There are significantly more papers now available describing the efficacy of brain Focused Ultrasound in the treatment of tremor dominant Parkinson's disease. None of these as yet or category one randomized control studies due to the great difficulty of carrying out such studies in the context of medical device applications.

20. Do you think the guidance needs updating?

Yes in the context of the latest literature in this field

Current management

21. Please describe the current standard of care that is used in the NHS.

Current standard of care consists of medication which is often incompletely or poorly effective in severe tremor and occasionally deep brain stimulation. The latter invasive surgical procedure however is more commonly reserved for patients who have bradykinetic and dyskinetic aspects of Parkinson's disease rather than predominantly tremor dominant disease.

22. Are you aware of any other competing or alternative procedure/technology available to the NHS which have a similar function/mode of action to this?

    If so, how do these differ from the procedure/technology described in the briefing?

    No

Potential patient benefits and impact on the health system

23. What do you consider to be the potential benefits to patients from using this procedure/technology?

    Transcranial brain focused ultrasound is a non invasive once only procedure which can massively decrease or completely eliminate tremor. Substantial cost savings can be obtained therefore utilizing this approach in the treatment of patients and also substantial improvements in the quality of life of patients can be rapidly achieved without significant side effects. Patients with PD are frequently elderly with substantial comorbitities and this non invasive procedure can be performed without the frequent severe problems these patients experience after more invasive medical procedures.

24. Are there any groups of patients who would particularly benefit from using this procedure/technology?

    Patients with tremor dominant Parkinsons disease.

25. Does this procedure/technology have the potential to change the current pathway or clinical outcomes to benefit the healthcare system?

    Could it lead, for example, to improved outcomes, fewer hospital visits or less invasive treatment?

    Adopting this procedure for the treatment of tremor dominant Parkinson's disease could significantly decrease the cost of treatment of these patients and allow a rapid return to normal activities. In comparison to deep brain stimulation this procedure is approximately 1/3 of the cost producing similarly effective results. In addition because it is a one off procedure it decreases the amount of hospital visits very substantially also decreases the amount of drug therapy that is required.

26. What clinical facilities (or changes to existing facilities) are needed to do this procedure/technology safely?

    The procedure requires a brain focused ultrasound system to be in place. If the system is already in place then no further technological requirements are necessary to treat patients with tremor dominant Parkinson's disease from the system used for treating patients with essential tremor.

27. Is any specific training needed in order to use the procedure/technology with respect to efficacy or safety?

    Training in the utilization of the machinery is always required from scratch in this situation but if the team is already treating patients with essential tremor using brain Focused Ultrasound no further training would be required

Safety and efficacy of the procedure/technology

28. What are the potential harms of the procedure/technology?

    Please list any adverse events and potential risks (even if uncommon) and, if possible, estimate their incidence:

    - Adverse events reported in the literature (if possible, please cite literature)
    - Anecdotal adverse events (known from experience)
    - Theoretical adverse events

    Sensory parasthesia are reported in the American literature with an incidence of up to 10 - 15%. We have not seen this in our work in this country and this result probably depends on the exact site of therapeutic sonication which differs slightly between individual units. If sonication is carried out too far laterally the possibility of inducing limb weakness is theoretically possible and operators are extremely aware of this and it is an exceptionally rare complication of this procedure. If sonications are carried out too far inferiorly there is a possibility of inducing Chorea which is usually reversible within two to three months . Many patients developed mild transitory unsteadiness after the procedure and this is temporary and resolves within two to three weeks in most cases.

29. Please list the key efficacy outcomes for this procedure/technology?

    Tremor reduction or elimination.
    Improvement in quality of life scores.

30. Please list any uncertainties or concerns about the efficacy and safety of this procedure/technology?

    Repeated descriptions of significant tremor improvement in the short term are available in the literature but the five year post treatment results of this approach in tremor dominant Parkinson's disease are not yet available. Our own results in the treatment of essential tremor show excellent tremor control at five years post procedure but Parkinson's disease is a more progressive neurological disorder and we await five year and longer outcome studies for treatment of tremor dominant PD.

31. Is there controversy, or important uncertainty, about any aspect of the procedure/technology?

    The potential of utilizing brain focused ultrasound to treat tramadol and Parkinson's disease is immense and will become a extremely popular effective method of applying therapy to these patients. Current controversies about this therapeutic modality are predominantly related to clinicians unfamiliarity with this concept and the technology required for this treatment.

32. If it is safe and efficacious, in your opinion, will this procedure be carried out in:

- ( ) 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.

Abstracts and ongoing studies

33. Please list any abstracts or conference proceedings that you are aware of that have been recently presented / published on this procedure/technology (this can include your own work).

    Please note that NICE will do a comprehensive literature search; we are only asking you for any very recent abstracts or conference proceedings which might not be found using standard literature searches. You do not need to supply a comprehensive reference list but it will help us if you list any that you think are particularly important.

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

    No current registries available although we are in the process of setting up a registry for all tremor treatments in the UK but this has only just commenced .

35. Please list any other data (published and/or unpublished) that you would like to share.

Other considerations

36. Approximately how many people each year would be eligible for an intervention with this procedure/technology, (give either as an estimated number, or a proportion of the target population)?

Very difficult to provide an accurate figure. Essential tremor is currently limited to 150 cases a year in England but this is a substantial under estimate of the countrywide requirements. PD tremor dominant treatments would be approximately the same overall numbers starting at 150 but rapidly doubling approximately.

37. Please suggest potential audit criteria for this procedure/technology. If known, please describe:

Beneficial outcome measures.

These should include short- and long-term clinical outcomes, quality-of-life measures and patient-related outcomes. Please suggest the most appropriate method of measurement for each and the timescales over which these should be measured.

Utilisation of tremor measurement repeatable techniques and standardized Parkinson's disability scores such as UPRDS questionnaire. Standardized quality of life scores should also be utilized.

38. Please suggest potential audit criteria for this procedure/technology. If known, please describe:

Adverse outcome measures.

These should include early and late complications. Please state the post procedure timescales over which these should be measured:

Change in severity of tremor.
Incidence of complications to include paresthesia, periods of unsteadiness etcetera.
Number of sonications utilized.
Length of time of procedure.

Further comments

39. If you have any further comments (e.g. issues with usability or implementation, the need for further research), please describe *

As described above longer term follow-up of these patients so that five year results are available for tremor improvement are important in

Declarations of interests

Please state any potential conflicts of interest relevant to the procedure/technology (or competitor technologies) on which you are providing advice, or any involvements in disputes or complaints, in the previous **12 months** or likely to exist in the future. Please use the NICE policy on declaring and managing interests as a guide when declaring any interests. Further advice can be obtained from the NICE team.

40. Type of interest: *

- [ ] Direct: financial
- [ ] Non-financial: professional
- [ ] Non-financial: personal
- [ ] Indirect
- [x] No interests to declare

41. Description of interests, including relevant dates of when the interest arose and ceased. *

I have been involved in the utilization of Focused Ultrasound to treat a variety of body areas over the last 20 years with a variety of different equipment. This includes treatment of uterine fibroids, treatment of facet joint related back pain, early work in noninvasive liver ablation . More recently my Focused Ultrasound work is concentrated on its utilization in the brain and in the treatment of tremor in patients with severe essential tremor and this work is ongoing.

42. I confirm that the information provided above is complete and correct. I acknowledge that any changes in these declarations during the course of my work with NICE, must be notified to NICE as soon as practicable and no later than 28 days after the interest arises. I am aware that if I do not make full, accurate and timely declarations then my advice may be excluded from being considered by the NICE committee.

    Please note, all declarations of interest will be made publicly available on the NICE website. *

    - (●) I agree
    - ( ) I disagree

Signature

43. Name: *

    W.Gedroyc

44. Date: *

    13/02/2024