NICE National Institute for Health and Care Excellence

Professional Expert Questionnaire

Technology/Procedure name & indication: IP2035 MRI guided focused ultrasound subthalamotomy in parkinson's disease

Your information

Name:	Professor Alexander Green
Job title:	Professor of Neurosurgery
Organisation:	University of Oxford/ Oxford University Hospitals NHS FT
Email address:	[redacted]
Professional organisation or society membership/affiliation:	SBNS
Nominated/ratified by (if applicable):	Click here to enter text.
Registration number (e.g. GMC, NMC, HCPC)	4424585

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consultation on the draft guidance, except in circumstances but not limited to, where comments are considered voluminous, or publication would be unlawful or inappropriate.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?	I am not familiar with Focussed Ultrasound technology but am familiar with the concept of lesional procedures for Parkinson's disease
	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?	No.

	− If your specialty is involved in patient selection or referral to another specialty for this procedure/technology, please indicate your experience with it.	I treat patients with Deep Brain Stimulation for PD and so MRgFUS is an alternative
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 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. I have had no involvement in research on this procedure.X Other (please comment)
3	Does the title adequately reflect the procedure? Is the proposed indication appropriate? If not, please explain. 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):	Yes Subthalamotomy is considered an outdated procedure in the Surgical Movement Disorders field. This is because Deep Brain Stimulation is reversible and relatively safe. There are very occasionally patients who may be suitable for a subthalamotomy (which can be performed currently using RF lesioning techniques) but I have seen one patient in 25 years. I would not consider subthalamotomy a suitable alternative to DBS as it is not as efficacious and has high risk of permanent side effects Definitely novel and of uncertain safety and efficacy.

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?	No it will not replace – may be a suitable alternative for a very small number of patients
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 There is no good evidence

Current management

6	Please describe the current standard of care that is used in the NHS.	Deep Brain Stimulation of the STN is the standard of care
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?	Yes – RF lesioning or Gamma knife – very rarely used at this target. RF lesioning is quick and cheap but has risk of stroke and seizures. GK very similar but uses radiation

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?	I think the number of patients would be very small and I am worried that this will be touted as an alternative to DBS which it should not be
9	Are there any groups of patients who would particularly benefit from using this procedure/technology?	Very elderly and unsuitable for DBS but these are the patients who may suffer side-effects
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?	Not substantially in my opinion. MRgFUS means it is a one-off procedure so no follow up which is better for elderly or frail patients and cheaper. However, I am worried about the side-effects as subthalamotomy is rarely better than DBS and any side-effects are permanent. Furthermore it can only be performed unilaterally
11	What clinical facilities (or changes to existing facilities) are needed to do this procedure/technology safely?	It would require dedicated MR scanner and expertise (radiology and neurology)
12	Is any specific training needed in order to use the procedure/technology with respect to efficacy or safety?	As above

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:	Any side-effects may be permanent as it involves a lesion. Specifically, stroke, hemiballism or other dyskinesia, sensory or motor side-effects. Once it has been performed it is unlikely the patient could be rescued using DBS

	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?	UPDRS – especially part 3, QOL
15	Please list any uncertainties or concerns about the efficacy and safety of this procedure/?	As above – very few patients likely to be suitable and I do not consider it to be an alternative to DBS
16	Is there controversy, or important uncertainty, about any aspect of the procedure/technology?	Yes
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 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.	
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)?	10-20
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 procedure timescales over which these should be measured:	Beneficial outcome measures: UPDRS – especially part 3 QOL PDQ39 Adverse outcome measures: Stroke Hemiballsim and other dyskinesias Sensory 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.	

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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
Non-financial professional	I perform DBS which is in competition	**2002**	**n/a**
Choose an item.			
Choose an item.			

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

Print name:	**Professor Alexander L Green**
Dated:	**06/04/2024**

NICE National Institute for Health and Care Excellence

Professional Expert Questionnaire

Technology/Procedure name & indication: IP2035 MRI guided focused ultrasound subthalamotomy in parkinson's disease

Your information

Name:	Dipankar Nandi
Job title:	Consultant Neurosurgeon and Professor
Organisation:	Imperial College Healthcare NHS Trust and Imperial College London
Email address:	[redacted]
Professional organisation or society membership/affiliation:	SBNS and GMC
Nominated/ratified by (if applicable):	Click here to enter text.
Registration number (e.g. GMC, NMC, HCPC)	GMC: 4591845

How NICE will use this information:

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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

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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?	Quite familiar with MRgFUS in brain.
	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 have been using it since July 2016. We in St Mary's Hospital, London have completed over 130 treatments to date. Only other NHS centre is in Liverpool. Only performed by Stereotactic and Functional Specialist Neurosurgeons.

	– If your specialty is involved in patient selection or referral to another specialty for this procedure/technology, please indicate your experience with it.	We are a centre that receives referrals nationally for this procedure.
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 have done clinical research on this procedure involving patients. I have published this research.
3	Does the title adequately reflect the procedure? Is the proposed indication appropriate? If not, please explain. 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. 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.

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?	Current standard of care is Deep Brain Stimulation (DBS). This technology would be used as an addition in most cases (particularly in patients not suitable for DBS or who choose not to have DBS).
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. Yes. There has been a plethora of peer-reviewed publications in the last 5 years with evidence of efficacy and safety of MRgFUS.

Current management

6	Please describe the current standard of care that is used in the NHS.	DBS.
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?	This technology would offer significant symptom relief and enhancement of quality of life to patients who currently have no other alternative therapeutic option.
9	Are there any groups of patients who would particularly benefit from using this procedure/technology?	Elderly patients with intractable Parkinson's disease would particularly benefit from this procedure.
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?	Less carer support. Less Hospital visits, particularly far fewer Neurologist Clinic appointments. Much greater independence for patients in their day to day life. Significantly less invasive than DBS. Significantly safer than DBS. Significantly less expensive than DBS.
11	What clinical facilities (or changes to existing facilities) are needed to do this procedure/technology safely?	3 Tesla MRI machine and the MRgFUS machine. Does not need Anaesthetist. Does not need Operating Theatre. Daycase or overnight admission.
12	Is any specific training needed in order to use the procedure/technology with respect to efficacy or safety?	Yes. Should only be performed by trained specialist Stereotactic and Functional 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:	Intracranial bleed with weakness (very rare ? 1:1000). Permanent paresthesiae (1%). Chorea (2%). Permanent Unsteady gait (3%).

	Adverse events reported in the literature (if possible, please cite literature) Anecdotal adverse events (known from experience) Theoretical adverse events	Permanent dysarthria (2%).
14	Please list the key efficacy outcomes for this procedure/technology?	Significant reduction in tremor. Improved use of hand and arm.
15	Please list any uncertainties or concerns about the efficacy and safety of this procedure/?	Nil.
16	Is there controversy, or important uncertainty, about any aspect of the procedure/technology?	Nil.
17	If it is safe and efficacious, in your opinion, will this procedure be carried out in (please choose one):	A minority of hospitals, but at least 10 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 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.	
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)?	500 per year in the UK.
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 procedure timescales over which these should be measured:	Beneficial outcome measures (all at one year): UPDRS all parts. EuroQuol. Global Index of Improvement. SF-36. Adverse outcome measures (all at one year): Weakness / hemiparesis. Gait ataxia / falls. Speech – dysarthria. Care needs.

Further comments

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

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
Direct - financial	Was paid for a single two hour session for evaluating new version of the planning software by Insightec.	**November 2022.**	**November 2022.**
Choose an item.			
Choose an item.			

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Print name:	**Dipankar Nandi**
Dated:	**18/04/2024**

NICE National Institute for Health and Care Excellence

Professional Expert Questionnaire

Technology/Procedure name & indication: IP2035 MRI guided focused ultrasound subthalamotomy 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:

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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 but only very rarely for subthalamotomy), and deep brain stimulation (DBS) surgery (the current standard of care).

	– 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.
3	Does the title adequately reflect the procedure?	Yes
	Is the proposed indication appropriate? If not, please explain.	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 conventional stereotactic subthalamotomy, which creates a lesion in the subthalamic nucleus (STN) by inserting a probe and heating the target, because of its relative non-invasiveness. Like conventional subthalamotomy, 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 might be 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):	Definitely novel and of uncertain safety and efficacy.
4	Does this procedure/technology have the potential to replace current standard care or	No. It would be an additional option for patients who cannot have (or possibly do not want to have) DBS or conventional subthalamotomy.

	would it be used as an addition to existing standard care?	
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 No

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?	The standard of care is DBS, which is both reversible and adjustable, and programming of the stimulator, for example increasing the stimulation applied, can help control re-emergent symptoms. This is not the case for MRgfUS. On the other hand, like conventional subthalamotomy, MRgfUS does not require implantation of permanent materials, and therefore does not carry the risk of cable breakage or generator dysfunction which would lead to new surgery. The risk of infection is also lower.

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 materials, 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?	Selected 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?	There is the potential to improve Parkinson's symptoms in selected patients who are not well managed with medical management only, and who would otherwise be a candidate for STN stimulation but cannot undergo the procedure. It would provide less invasive treatment, which widens the circle of patients who could potentially benefit. In comparison to DBS, the treatment cannot be adjusted after the procedure (except by applying a new lesion). This means there is less follow-up required, as there will be no appointments to programme a stimulator.
11	What clinical facilities (or changes to existing facilities) are needed to do this procedure/technology safely?	MRgfUS for the brain 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 – the rate is not currently known. The largest study so far published (DOI: 10.1056/NEJMoa2016311) using unilateral MRgfUS subthalamotomy in Parkinson's reports that "27 were assigned to focused ultrasound subthalamotomy (active treatment) and 13 to the sham procedure (control). […] Adverse events in the active-treatment group were dyskinesia in the off-medication state in 6 patients and in the on-medication state in 6, which persisted in 3

	Adverse events reported in the literature (if possible, please cite literature) Anecdotal adverse events (known from experience) Theoretical adverse events	and 1, respectively, at 4 months; weakness on the treated side in 5 patients, which persisted in 2 at 4 months; speech disturbance in 15 patients, which persisted in 3 at 4 months; facial weakness in 3 patients, which persisted in 1 at 4 months; and gait disturbance in 13 patients, which persisted in 2 at 4 months. In 6 patients in the active-treatment group, some of these deficits were present at 12 months." In addition to those listed above, theoretical adverse events can be estimated from those seen in conventional subthalamotomy, and include sensory change, dysarthria, gait disturbance, and ataxia.The risk is likely considerably higher if bilateral subthalamotomy is applied.
14	Please list the key efficacy outcomes for this procedure/technology?	Reduction in PD symptom severity, as assessed by standardised clinical rating scales (eg. UPDRS III, Fahn-Tolosa-Marin, Clinical Tremor Rating Scale), 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 that unlike in DBS, side-effects cannot be reduced after the procedure. PD 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?	The evidence concerning efficacy and safety of subthalamotomy with MRgfUS is still very limited.
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	n/a

	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.	
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 who have advanced (>10 yrs duration) PD that is not tremor-dominant 0.8 x Proportion of patients eligible for device therapy 0.66 x Proportion of patients who cannot have DBS 0.33 = 8,427 patients. The actual number of patients who would, if offered, opt for MRgfUS subthalamotomy is likely considerably lower. (Data used from NICE TA 934 and Parkinsonism and Related Disorders 18S1 (2012) S90–S92 and https://doi.org/10.1016/j.parkreldis.2021.05.016)
22	Please suggest potential audit criteria for this procedure/technology. If known, please describe: – Beneficial outcome measures. These should include short- and long-term	Beneficial outcome measures: Beneficial outcome measures:

	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 procedure timescales over which these should be measured:	Clinical rating scale (Full UPDRS, Fahn-Tolosa-Marin, CTRS or similar) 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: Unified Dyskinesia Rating Scale (UDysRS) 1) before and 2) after the procedure at 3 and 12 months Proportion of patients with post-intervention haemorrhage (both clinically apparent, and those seen on MRI only) Proportion of patients with side-effects after 3 and 12 months: gait imbalance, sensory deficits, motor weakness, ataxia, 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.	This is a new procedure with limited evidence for its efficacy and safety. A robust framework to evaluate efficacy and adverse events will be required.

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Declarations of interests

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

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Print name:	**Dr Johannes C KLEIN**
Dated:	**14/5/2024**

NICE National Institute for Health and Care Excellence

Professional Expert Questionnaire

Technology/Procedure name & indication: IP2035 MRI guided focused ultrasound subthalamotomy in parkinson's disease

Your information

Name:	Ludvic Zrinzo
Job title:	Professor in Neurosurgery
Organisation:	University College London (UCL) & UCLH NHS Foundation Trust
Email address:	[redacted]
Professional organisation or society membership/affiliation:	SBNS / RCS Edinburgh / ESSFN / WSSFN
Nominated/ratified by (if applicable):	Click here to enter text.
Registration number (e.g. GMC, NMC, HCPC)	GMC 5205507

How NICE will use this information:

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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 comfortable using focused ultrasound as a tool to perform stereotactic lesions and have used this to perform thalamotomies in around 20 tremor patients since 2022 I am considered an international expert in targeting the subthalamic nucleus when performing deep brain stimulation for Parkinson disease and have published widely in peer reviewed journals on this topic. I have not used focused ultrasound to perform lesions of the subthalamic nucleus. This is a recently introduced procedure globally and has not been performed in the UK (to the best of my knowledge) If made available on the NHS, I suspect that subthalamotomy for PD would benefit around 100 NHS England patients per annum with the possibility of increasing further as confidence and patient selection improves. As a functional neurosurgeon, I would be involved in both patient selection as well as provision of the procedure.

	– 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. 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. I have had no involvement in research on this procedure. Other (please comment)
3	Does the title adequately reflect the procedure? Is the proposed indication appropriate? If not, please explain. 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):	Yes Yes 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.

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?	Potential to add therapeutic choices to PD patients – may delay more invasive procedures (like Deep Brain Stimulation – DBS) for a some years.
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?	Yes. The membranes used during the procedure have added MR coils to improve visualisation of the subthalamic nucleus (STN) during the procedure, This is the first time guidance will be published on this procedure.

Current management

6	Please describe the current standard of care that is used in the NHS.	Medical management and Deep Brain Stimulation.
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?	Deep brain stimulation Focused ultrasound of the VIM nucleus The first differs by being much more invasive and requiring expensive hardware and time consuming programming. The second targets a different part of the brain and is not so effective for PD tremor.

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?	This has the potential to improve care of patients with asymmetric symptoms, keeping younger patients in employment for longer and preventing or delaying the need for more invasive surgery such as DBS
9	Are there any groups of patients who would particularly benefit from using this procedure/technology?	Yes – patients with asymmetric motor symptoms of Parkinson disease (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 Yes
11	What clinical facilities (or changes to existing facilities) are needed to do this procedure/technology safely?	More focused ultrasounds should be commissioned and upgraded to allow visualisation and targeting of the STN
12	Is any specific training needed in order to use the procedure/technology with respect to efficacy or safety?	Yes. Training in patient selection, imaging and focused ultrasound.

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:	Poor patient selection may cause significant harm. Inaccurate targeting could cause significant neurological deficit. Problems with weakness, hemiballismus, dyskinesia, balance can all occur. Incidence in competent hands should be very low (<1%)

	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?	Change in UPDRS / quality of life scores / change in medication
15	Please list any uncertainties or concerns about the efficacy and safety of this procedure/?	As with any procedure, there is a risk / benefit calculation to be made. Early results from Spain suggest that this may be a powerful tool that will add to the therapeutic possibilities for PD patients. Introduction to the UK should be via experienced centres who have published results on STN DBS and who have experience with focused ultrasound for tremor.
16	Is there controversy, or important uncertainty, about any aspect of the procedure/technology?	The numbers of patients with published results is small. An RCT is in preparation. The UK should collect further data on patients undergoing STN FUS
17	If it is safe and efficacious, in your opinion, will this procedure be carried out in (please 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.

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 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.	**ClinicalTrials.gov ID** NCT02246374
20	Please list any other data (published and/or unpublished) that you would like to share.	Martínez-Fernández, R. *et al.* Prospective Long-term Follow-up of Focused Ultrasound Unilateral Subthalamotomy for Parkinson Disease. *Neurology* **100**, e1395–e1405 (2023). Martínez-Fernández, R. *et al.* Randomized Trial of Focused Ultrasound Subthalamotomy for Parkinson's Disease. *New Engl J Med* **383**, 2501–2513 (2020).

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)?	Difficult to say. Probably 100 but may increase as knowledge expands
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	Beneficial outcome measures: UPDRS scores Quality of life scores (PDQ-39) Levodopa equivalent daily dose (LEDD)

	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 procedure timescales over which these should be measured:	Adverse outcome measures: Comprehensive documentation of adverse events (eg: persistent weakness, dyskinesia, failure to achieve significant benefit)

Further comments

23	If you have any further comments (e.g. issues with usability or implementation, the need for further research), please describe.	This has the potential of changing the surgical management of patients with medically refractory symptoms. Further studies are required to see how big this impact will be. The NHS should lead the way in gathering further data.

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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
Direct - financial	Consultant for companies that produce deep brain stimulation hardware	**2007**	**ongoing**
Direct - financial	Consultant for Insightec, manufacturer of focused ultrasound machine	**2022**	**ongoing**
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:	**Ludvic Zrinzo**
Dated:	**April 24, 2024**