NPPPRG
(National Public, Patient and Professional Reference Group

NHS National Services Scotland

Stage 1 Application **NPPPRG 2018/79A**

Section 1: Summary information

1.1 Full name of proposed service

Scottish National Neuro MRI-guided Focused Ultrasound for Essential Tremor
at the Clinical Research Imaging Facility (CRIF), University of Dundee

1.2 Short title for proposed service

National Centre for Neuro MRgFUS, Dundee

1.3 Provider & Location

Provider: NHS Tayside - Ninewells Hospital & Medical School University of Dundee
Location: Clinical Research Imaging Facility (CRIF), University of Dundee.
Ninewells Drive, Dundee. DD1 9SY
Contact: 01382 425712 (Mr Hossain-Ibrahim's secretary)

1.4 Contacts and support from NHS Board Management

Prof. Andrew Russell, Medical Director NHS Tayside, is aware of the proposal and formal support is pending.

1.5 Brief description of proposed service *(no more than 100 words)*

MRI-guided focused ultrasound (MRgFUS) technology can be used with the existing research MRI scanning facility to allow neurosurgeons to perform (create) small lesions within the brain using ultrasound beams. MRgFUS has recently gained NICE approval for treatment of patients with essential tremor, targeting an area of the Thalamus; and for Parkinson's disease in a research setting. At present the approval is for unilateral treatment, and NICE does recommend that the patient be advised of alternative interventions that offer bilateral treatment, and that the intervention is delivered under specific local clinical governance oversight.

Section 2: Outline Proposal

2.1 Description of current provision and why there is a need for national commissioning?

The proposal aims to establish a national centre for non-invasive neurosurgery, using MRI-guided focused ultrasound (MRgFUS) for Scottish patients. There is at present only one MRgFUS device in the UK at St Mary's Hospital, London: tremor patients will have to wait until 2022 for this treatment due to the significant waiting list. We wish to provide this service for patients in Scotland in a cost-effective and timely manner.

For the 1 in 25 people who suffer from essential tremor (ET), MRgFUS is potentially a curative procedure. Currently, there is a single MRgFUS facility in the UK which started treating patients with essential tremor in 2016. The waiting list has increased from 25 to 600 patients, as patients have expressed a preference for this non-invasive treatment for tremor, compared to the alternative of deep brain stimulation surgery (DBS). At present there is no MRgFUS service for Scottish patients.

What is MRgFUS?

- Ultrasound is targeted at the brain areas which produce the tremor using MRI. The patients are awake throughout and require no anaesthetic. A small (2-3 millimetre) lesion is created by heating up the brain tissue. The effect on the patient's tremor is both painless and immediate. This is a day case treatment which requires no hospital stay, which is revolutionary.
- This incisionless treatment has the same immediate and long term effect as invasive alternatives (DBS). In contrast, it does not require permanent electrical hardware, or revision operations in the future. MRgFUS is one third of the cost of existing treatments (DBS) Ref: Nandi, 2018.
- DBS is associated with 1/1000 risk of death, 1/100 risk of stroke & 1/30 risk of brain haemorrhage.
- Over 1200 patients have had MRgFUS thalamotomy world-wide without *any* significant comparable complication to date – it is far safer than DBS.

2.2 Number of patients expected to benefit?

Essential tremor (ET)

- No exact incidence or prevalence rates in Scotland. US study estimated incidence at 2.2%. Neurological disorders in Central Spain study found ET prevalence to be 4.8%
- Progressive condition with significant impact on quality of life in an elderly ageing population. By 65 years of age, 45% of these will have moderate to severe symptoms. (25% of population of Scotland is over 60) - conservative estimate **20,000** people with ET in Scotland in total.
- A medication adherence study found that 48% of ET patients were taking daily medication but it is estimated that pharmacological treatments have no effect in 30-50% of ET patients
- Less than 1 in 20 ET patients undergo DBS at present.
- Our estimate is that 1 in 5 of the severely affected are likely to be eligible and receive substantial benefit (**4000** patients in Scotland) from focused ultrasound thalamotomy for essential tremor.

Future option - Parkinson's Disease (PD)

Prevalence of 1 in 375 in Scotland current estimate of **12,000.**

- **600** (5%) are likely to require or are eligible for surgical treatment.

As tremor is one of several symptoms of PD it is unclear at this stage how many patients will be suitable for ultrasound thalamotomy in Scotland but we are not yet at a stage to request funding for this condition. We have included PD in this application as it is a likely *future* intervention given NICE approval for treatment in a research setting (2018).

2.3 Expected benefits/impact in relation to patient experience, quality, outcomes and wider NHS in Scotland?

MRgFUS has Class I evidence demonstrating that it is highly beneficial for the treatment of medication-refractory ET. The real-time MRI monitoring allows for precise targeting of the Vim nucleus of the brain, therefore preventing collateral damage to adjacent healthy tissue. Not having surgery or radiation with MRgFUS contributes to the exceptional safety profile and rapid recovery time. Symptomatic improvement can be observed immediately upon completion of the procedure, and is maintained in the studies conducted over the last 3 years.

Patients with ET may lose the ability to care for themselves since daily tasks such as eating, dressing, writing, holding reading material, and using a computer become increasingly difficult and may therefore become increasingly dependent on others. Tremor-related quality of life (QoL) reflects the physical, emotional and other health effects of tremor and has been found to be significantly reduced in ET patients. The significant psychosocial impact of tremor leads to many patients with ET living reclusively in isolation, with only a small proportion of severely affected patients seeking medical attention (0.5%).

Although ET incidence increases with age, the disease does not shorten life expectancy or predispose patients to other neurological disorders. A treatment that effectively relieves tremor symptoms would therefore greatly improve a patient's disease state and quality of life.

The management of ET imposes a substantial burden on healthcare systems. A study investigating the functional disability of ET in the USA found that three-quarters of community-based cases reported disability. In addition to physical disability, the management of psychosocial aspects of the disease, such as anxiety and depression, further contribute to the healthcare burden. Current pharmacological treatments for ET are not curative and the associated requirement for lifelong treatment leads to accumulation of costs from drugs and neurologists' time. Furthermore, since the available pharmacological treatments are known to only be effective in a small proportion of patients, substantial resources may need to be invested in finding a suitable treatment for each individual patient, with the specific clinical response and side effects necessitating further treatment adjustments.

2.4 What level of evidence is available to support the proposal?

Efficacy:

A growing number of clinical trials have reported the efficacy, safety and value of MRgFUS. The RCT comparing MRgFUS treatment with a sham procedure, reported initially by Elias et al. (2016a), with two-year follow-up results presented by Chang et al. (2017) and supplementary publications from Ondo et al. (2016a), Elias et al. (2016b), Gwinn et al. (2016) and Harary et al. (2018), provide stronger class I evidence of MRgFUS efficacy for Essential Tremor than DBS.

Quality of Life:
102 ET patients were tested with the Short-Form 36-Item Health Survey (SF-36) to determine the impact of their tremor on their Quality of Life. The study demonstrated how the burden of ET on patients results from both physical disability and psychosocial factors, including decreased emotional wellbeing and social withdrawal. **Ref:** Lorenz D, Schwieger D, Moises H and Deuschl G. Quality of life and personality in essential tremor patients. Mov Disord. 2006;21(8):1114-8.

2.5 Is there external support for the development of the service?

Dundee has established a Steering Group for this project with agreement from the **four neurosurgery centres** in Scotland to develop the MRgFUS service. The draft business case was expected to be discussed at the **Neurosurgery MSN Board meeting** on 5/10/18 – subsequent discussion with the MSN Board indicates support for the establishment of a neuro MRgFUS service in Dundee but with close interaction with the existing Glasgow DBS service for essential tremor, so that the most appropriate therapy and choice was offered to patients to patients from all the neurology services in Scotland on an equitable basis.

Establishment of a Scottish Centre for Neuro MRgFUS has been discussed by MSPs in the **Scottish Parliament** in May 2018 (motion put forward by Rhoda Grant, who represents the head of the Scottish Tremor Society). Outcome: There is a need for a Scottish MRgFUS treatment centre of essential tremor for patients for whom DBS was not suitable and research funding for purchase should be requested from the CSO. *However*, since the debate **NICE** has approved MRgFUS for use in the NHS taking this therapy out of the realm of research and into the established treatment domain. As a result, Rhoda Grant is planning to re-debate the need for MRgFUS in the Scottish Parliament again, as the CSO does not fund capital purchase.