



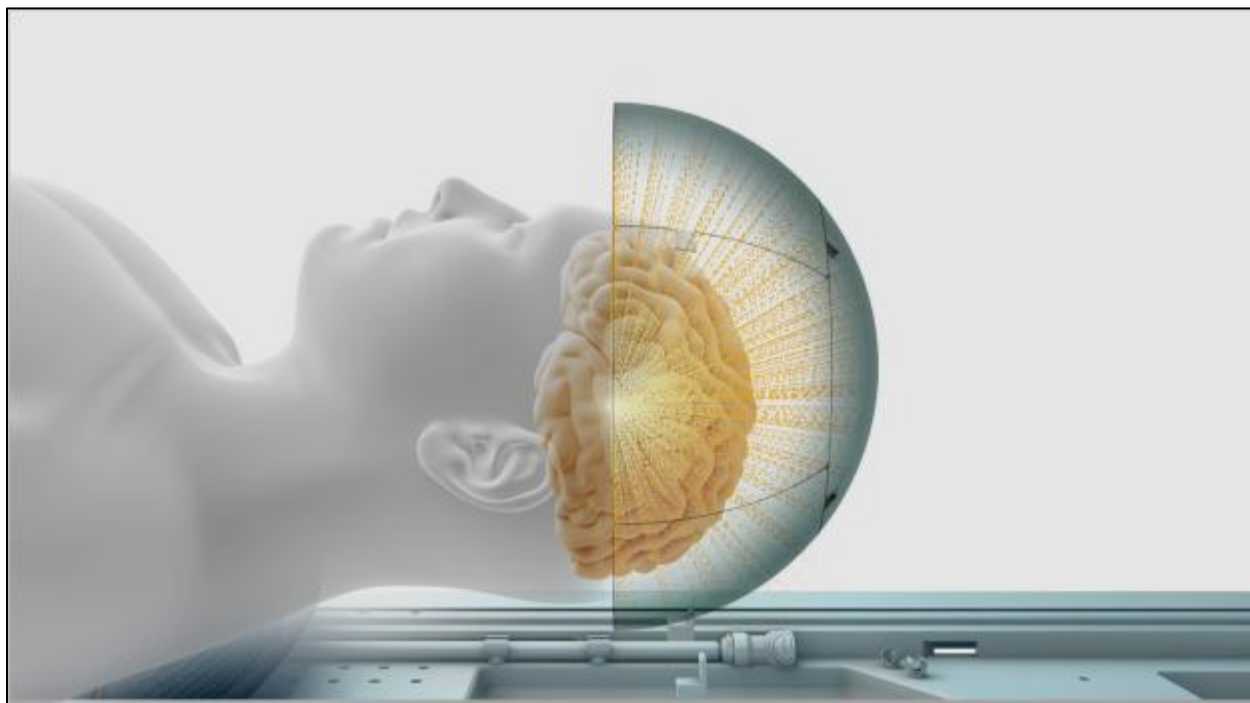
School of Medicine
University of Dundee

Funding Application

Prepared for:

Project Title: Establishment of the Scottish MRI-guided Focused Ultrasound centre for research and treatment of neurological conditions

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Project Summary

A cure for Parkinson's and its associated conditions may be many years away, but here at Dundee we have the ability to transform patients' lives today. Building on our world-leading research into Parkinson's disease, we aim to broaden our research into the clinical sphere by establishing the Scottish Centre for MRI-guided Focused Ultrasound. This pioneering treatment for Essential Tremor is proving to be transformational by returning patients to an almost pre-tremor state, thus allowing them to function fully again in their lives and communities. This treatment is currently not available in Scotland.

We want to urgently address this situation by purchasing a Focused Ultrasound machine to conduct clinical trials exploring the use of focused ultrasound neurosurgery, which will lead to an improvement in the standard and accessibility of treatment in Scotland. Specifically, our immediate goal is to initiate trials in the treatment of Multiple Sclerosis tremor, advanced Parkinson's disease and brain tumours deemed too deep and dangerous to operate on by conventional neurosurgery.

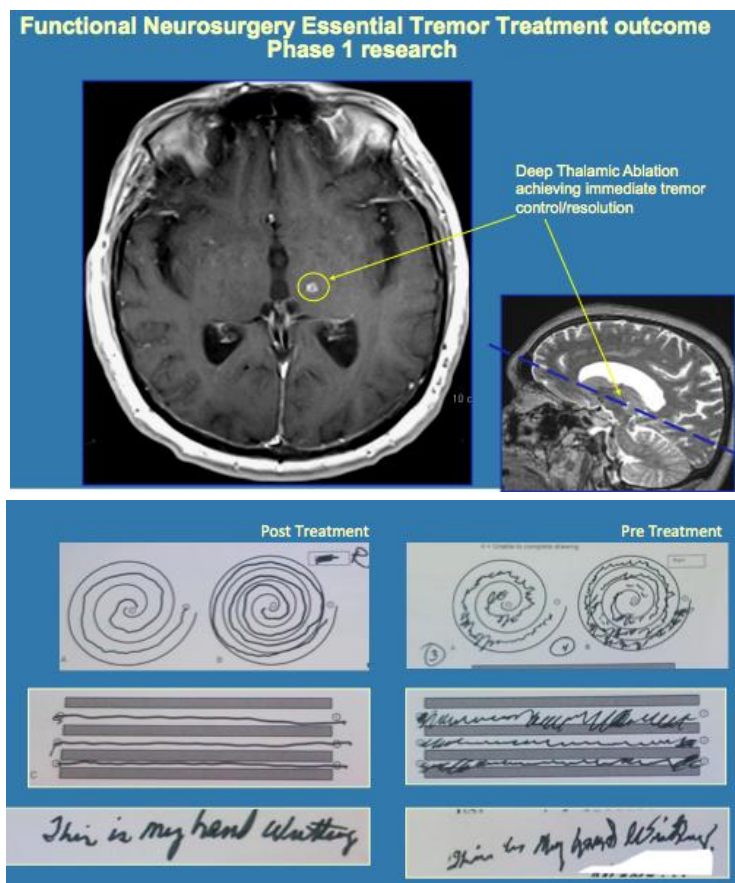
There are an estimated 20,000 patients with neurological conditions that are untreatable by the medicine currently available in Scotland. They lead lives debilitated by tremors that cause great difficulty with performing everyday tasks, resulting in deep psychological and social consequences.



Project Aims

Our project has two key aims. Firstly, to establish a national MRI-guided Focused Ultrasound (MRgFUS) centre for non-invasive neurosurgery for Scottish patients, involving a multi-disciplinary team incorporating clinicians and scientists across the fields of neuroscience, imaging and psychiatry. Secondly, to become part of a unique group of international centres participating in ongoing clinical trials applying MRgFUS to the treatment of Parkinson's disease, Multiple Sclerosis tremor and brain tumours.

In order to achieve these goals and to start treating patients in Scotland, we need to raise £1.2 million to purchase a High Frequency machine for tremor treatment, £800,000 for a low frequency machine to treat brain tumours, and a further £300,000 for running costs over the first three years. This proposal outlines in more detail what we are fundraising for and how non-invasive surgery on neurological conditions will change lives and end suffering for thousands of people. We would respectfully like to ask the Scottish Government to consider a grant of £500,000.



Example of pre and post-treatment results achieved with MRI Focused Ultrasound
 Courtesy of: Jeff Elias, MD; University of Virginia, Department of Neurosurgery

Why is access to Focused Ultrasound treatment so important?

About 50% of severely affected Essential Tremor patients have symptoms that are resistant or intolerant to medication, meaning that invasive deep brain stimulation is the only treatment option. Surgical intervention in Essential Tremor has been used for over 50 years, and is used for patients who have particularly severe or disabling tremors that have not responded to medication. Many patients choose to opt against brain surgery, especially as complications can result in further surgery, infections, haemorrhage, stroke, cognitive impairment, speech disorder, depression, suicide and even death. For the 1 in 25 people in Scotland who suffer from Essential Tremor, MRgFUS treatment is a potential non-invasive, cost effective and curative procedure.

Focused Ultrasound surgery destroys target tissue, whilst sparing adjacent tissues and organs using real time image guidance and control. These painless operations can even be performed on an outpatient basis. The treatment is illustrated in this BBC article from December 2016, <http://www.bbc.co.uk/news/health-38157770> .

Early studies on MRgFUS for treatment of breast cancer, prostate cancer, liver tumours and pancreatic cancer have demonstrated encouraging results, leading to a global appetite and curiosity for the development of MRgFUS for neurological conditions.



Focused Ultrasound is currently offered in 34 centres worldwide, with 1,000 recorded treatments to date and ***no adverse effects yet recorded***. There is a single Focused Ultrasound facility serving the population in England (MR Therapy Centre, St Mary's Hospital, London), which started treating patients with Essential Tremor in 2016. As patients have expressed a preference for non-invasive treatment for tremor, compared to the alternative of deep brain stimulation surgery, their waiting list has subsequently increased from 25 to over 600 patients. If we were to refer a patient to St Mary's, they would have to wait until 2022 just to be assessed. Moreover, St Mary's is unable to develop Focused Ultrasound for the treatment of brain tumour patients. The interdisciplinary team at Dundee is well positioned to perform the preclinical and clinical research needed to repurpose the technique to treat brain tumours.

Patients in Scotland who may benefit immediately from MRgFUS suffer from:

- Essential Tremor, which affects at least 30,000 people. It is estimated that around 30 patients per year may benefit from this treatment.

- Parkinson's disease, which affects over 12,000 people in Scotland. Across the UK, that number is expected to double in the next 50 years as the population grows and people live longer. MRgFUS could be used to treat around 50 patients per year.
- Dystonia. 10-15 patients per year may be candidates for MRgFUS.

The Essential Tremor Society Scotland have had expressions of interest in treatment from a further 500 sufferers (none of whom want the alternative treatment of deep brain stimulation, because of the risks posed by a neurosurgical operation), thus highlighting the 'hidden' clinical need of this under-served population of patients.



What is being proposed?

If we can purchase a focused ultrasound machine for Scotland, we can run trials to demonstrate safety and efficacy for a number of neurological conditions. We want to place Dundee – and Scotland – at the forefront of this emerging technological revolution in non-invasive neurosurgery by purchasing the first focused ultrasound machine in Scotland (second in the UK). By housing the focused ultrasound machine within Dundee's state-of-the-art Clinical Research Centre (CRC), we will have the necessary expertise and research skills to conduct clinical and pre-clinical research exploring the use of focused ultrasound surgery in other neurological and neurosurgical conditions.

Initially, our aim is to initiate trials focusing on treating tremors in patients with Multiple Sclerosis and advanced Parkinson's Disease, and treating brain tumours that are too risky to remove through conventional neurosurgical methods. This technology provides a personalised treatment, adjusted to the individual patient anatomy and treatment results. With the addition of these ultrasound machines, the CRC will house the MRI-guided Focused Ultrasound Centre, offering treatment and hope to thousands of Scottish patients with Essential Tremor, symptoms associated with Parkinson's disease, Multiple Sclerosis and inoperable brain tumours.

Why Dundee?

Through the strong links formed between the University of Dundee's Clinical Research Imaging Facility (CRIF), Clinical Research Centre (CRC), Division of Neuroscience and Institute for Medical Science and Technology (IMSaT), Dundee has an international level of expertise required for the use and further development of MRgFUS. Dundee has a history of leading the field of functional neurosurgery in Scotland, having been the first centre in Scotland to perform Deep Brain Stimulation in 1993. Here at Dundee we have the expertise and resources to deliver world-class research and potential for an ongoing NHS clinical service. We have established a collaborative platform for research and development of the MRgFUS for destroying brain tumours and the safe treatment and follow-up of NHS tremor patients.

Ongoing Research

This project is being led by consultant neurosurgeon, Mr Kismet Hossain-Ibrahim, consultant neurologist, Dr Thomas Gilbertson, and consultant psychiatrist, Professor Douglas Steele. They are developing a dynamic research programme to apply this revolutionary technique to patients with Parkinson's disease, Multiple Sclerosis and brain tumours, and eventually epilepsy and dementia. This effort is supported by biomolecular and bioengineering research at the University of Dundee, led by Professors Tim Hales (Neuroscience) and Zhihong Huang (Engineering). A multidisciplinary programme of research in Dundee will develop the focused ultrasound approach for the non-invasive destruction of brain tumours. The goal is to specifically target brain cancer cells by sensitizing them to ultrasound using reagents administered orally that preferentially accumulate in malignant brain tissue. These sonosensitizers reduce the intensity of ultrasound required to kill cancer cells while sparing neighbouring non-malignant brain tissue, thereby increasing the likelihood of normal brain function following successful tumour destruction. Preclinical studies have begun to optimise the approach and establish its effect on malignant and normal brain tissues.

With the purchase of a Focused Ultrasound machine, we have a unique opportunity to develop a state-of-the-art research environment allowing us to investigate novel treatments for a range of distressing and debilitating neurological conditions and symptoms.

Full Project Budget

A full budget is available on request, detailing the equipment specifications and the projected running costs. Maintenance costs will be covered by the supplier for the first two years. Years 3 and onwards will be covered by the University and by income generated from treating NHS patients thereafter.

Fundraising Plan

Project Cost	Equipment	Running Costs	Totals
MRI Guided Focus Ultrasound Scanner			
• Phase One*	1,200,000		
• Phase Two**	802,000		
Running costs over 3 years		300,000	
Total Cost	2,002,000	300,000	2,302,000
Income Secured			
• Towards Equipment	500,000		
• Towards Running Costs		400,000	
Total Income			900,000
Funding Gap			
Equipment			
• Phase 1	700,000		
• Phase 2	802,000		
Total Funding Gap	£1,502,000		

*£1.2 million to purchase a High Frequency machine for tremor treatment

**£0.8 million for a low frequency machine to treat brain tumours

Income Secured	Equipment	Running Costs
InsightTec		400,000
Northwood Charitable Trust	300,000	
Stagecoach Plc	100,000	
NHS Endowment Fund	50,000	
Brain Tumour Action	20,000	
Community Fundraising	20,000	
Stagecoach	10,000	
Total Income	£500,000	£400,000

We have made some good initial progress in our fundraising campaign to complete the £2.3M project costs. We have secured over £500k, and have a robust fundraising plan in place for raising the remaining funds from UK wide Trust and Foundations. A donation from the Scottish Government will show prospective donors that prestigious grant-makers have faith in our project and commend the unique quality of training and education it provides to the healthcare system. It paves the way for further donations from our alumni community, corporate donors and philanthropic individuals, which will allow us to close the funding gap in a timely manner.

Ongoing Research Costs

We have letters of intent to fund research from Parkinson's UK and the Brain Tumour Charity, and aim to fund ongoing research costs through peer-reviewed competitive grants awarded by charities relevant to the neurological condition being studied.

Sustainability

The first 2 years' maintenance is free. After that, maintenance costs will be covered by research grants and a long-term fundraising campaign. InsightTec have offered research income at approximately £10,000 per patient enrolled in our clinical trials. It is envisaged that NHS England will allow treatment of Essential Tremor if NICE recommends MRgFUS for use in this condition later in 2018. We would then apply for our project to be recognized by NHS Scotland for National Service designation with funding centrally from the Scottish government to treat these patients. Our long-term aim is for our clinical trials to allow similar National Service designation for other neurological conditions that we will research over the coming years.

Summary

Thousands of patients in Scotland suffer from disabling tremor as a consequence of Parkinson's disease or Multiple Sclerosis. Currently, the only effective treatment available is invasive neurosurgical surgery. Furthermore, only a proportion of sufferers are fit enough for surgery, leaving the majority to just live with their disability and essentially diminished lives. For this group of patients, MRgFUS is a life-changing treatment with no need for surgical incisions. We hope to bring this highly innovative and exciting research and treatment opportunity to Scotland.

If we can establish the first MRI-guided Focused Ultrasound Centre for treatment of neurological symptoms of disease at the University of Dundee, we will be able to deliver world-class research with the potential for ongoing NHS clinical service to patients. We believe that this non-invasive procedure represents the future of neurosurgery, where operations can be performed painlessly in an outpatient setting.