



Clinical Commissioning Policy Proposition:

**Stereotactic Radiosurgery (SRS) for
adults with Parkinson's tremor and
Familial Essential Tremor**

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Clinical Commissioning Policy Proposition: Stereotactic Radiosurgery (SRS) for adults with Parkinson's tremor and Familial Essential Tremor

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Equality Statement

NHS England has a duty to have regard to the need to reduce health inequalities in access to health services and health outcomes achieved as enshrined in the Health and Social Care Act 2012. NHS England is committed to fulfilling this duty as to equality of access and to avoiding unlawful discrimination on the grounds of age, gender, disability (including learning disability), gender reassignment, marriage and civil partnership, pregnancy and maternity, race, religion or belief, gender or sexual orientation. In carrying out its functions, NHS England will have due regard to the different needs of protected equality groups, in line with the Equality Act 2010. This document is compliant with the NHS Constitution and the Human Rights Act 1998. This applies to all activities for which NHS England is responsible, including policy development, review and implementation.

Plain Language Summary

Movement disorders including Parkinson's disease and familial essential tremor (FET) can severely affect the ability of a patient to undertake activities of daily living (eating, shopping, brushing teeth etc.). Whilst medications can be used to control unwanted movements, sometimes these are ineffective or the side effects prevent the medication being used and so further interventions need to be considered. Lesional surgery, the process of destroying the brain tissue causing the uncontrolled movements, has mostly been replaced with the use of deep brain stimulation (DBS) which can be adjusted in response to a patient's symptoms.

SRS is another method by which the area of the brain causing the uncontrolled movements can be destroyed.

NHS England has concluded that there is not sufficient evidence to routinely commission SRS for drug-resistant movement disorders.

1. Introduction

This document describes the evidence that this has been considered by NHS England in formulating a proposal to not routinely commission stereotactic radiosurgery (SRS) for Parkinson's tremor and familial essential tremor.

For the purpose of consultation NHS England invites views on the evidence and other information that has been taken into account as described in this policy proposition.

A final decision as to whether SRS for drug-resistant movement disorders will be routinely commissioned is planned to be made by NHS England by June 2016 following a recommendation from the Clinical Priorities Advisory Group.

2. The proposed intervention and clinical indication

The basic principle of stereotactic radiosurgery (SRS) is the elimination of a functional disorder, or destruction of abnormal tissues, by administration of a strong and highly focused dose of radiation. The procedure allows radiation to be limited to the targeted area and thus helps spare the surrounding tissues as much as possible.

SRS is routinely used in the treatment of a number of different brain and central nervous system pathologies as defined by a number of clinical commissioning pathways. Here, we consider the use of SRS as the final treatment option for patients with drug resistant tremor associated with Parkinson's disease and familial essential tremor (FET).

3. Definitions

For the purpose of this policy the term SRS is used to mean treatment given as a single fraction. SRS is a highly conformal radiotherapy treatment to a precisely delineated target volume, delivered using stereotactic localisation techniques. A multidisciplinary team of neurosurgeons, neuro-oncologists and neuro-radiologists are involved in SRS case selection, treatment planning and delivery.

Parkinson's disease is a chronic disease of the brain which may occur when the brain does not produce enough dopamine, a chemical it needs to perform certain functions. This affects the brain's ability to control movement and other muscle functions and is characterised by gradually worsening tremor, muscle rigidity and difficulties with starting and stopping movements. The condition is usually treated with drugs. Surgery can be considered in people who have responded poorly to drugs, who have severe side-effects from medication, or who have severe fluctuations in response to drugs (on-off syndrome).

Essential tremor is a progressive neurological condition that causes a trembling of the hands, head, voice, legs, or trunk. It is not caused by loss of dopamine. Essential tremor has familial tendency, people with familial essential tremor (FET) may get it earlier in life than those with non-familial or sporadic essential tremor. Severe tremor can be disabling because it affects fine-movement coordination. Tremor can be treated by rehabilitation and drug therapy, and early appropriate treatment may minimise functional disability. Anti-tremor drugs reduce the amplitude but not the frequency of tremor, and this does not always translate into functional improvement. Due to the side-effect profile of anti-tremor

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medications, there are some cases where the dose required to effectively control the tremor causes unacceptable side effects, worsening the patient's quality of life. Lesional surgery, which often involves ablation of the thalamic nucleus, is reserved for patients with severe disabling tremor and functional disability that interferes with activities of daily living, and for tremor that is refractory to the highest tolerated doses of medication. Surgery of this nature is currently routinely commissioned and has a significant evidence base. Due to the degenerative nature of Parkinson's disease, the anticipated benefits acquired by undergoing SRS can relapse, in contrast to essential tremor where SRS outcomes remain permanent.

Usual surgical care of drug-resistant Parkinson's disease and FET will continue to be deep brain stimulation and thalamotomy. SRS represents a different tool by which to make a lesion in the area of the brain responsible for the uncontrolled movements.

4. Aim and objectives

The policy aims to define NHS England's commissioning position on stereotactic radiosurgery for the treatment of patients with movement disorders associated with Parkinson's disease and familial essential tremor.

The objective is to ensure evidence based commissioning with a view to improving outcomes for patients with movement disorders.

5. Epidemiology and needs assessment

Parkinson's disease affects 0.5% of the population aged 65-74 and 1-2% of the population over 75. Of this patient cohort, 90-99% of patients will respond to medications, leaving a small group of patients suitable for brain surgery. Deep brain stimulation will remain the preferred choice of brain surgery for these patients.

Estimations of the incidence and prevalence of tremor vary widely as a mild degree of tremor is a very common finding affecting between 2-4% of the population. More unusual is to have a tremor severe enough to interfere with activities of daily living, necessitating surgical intervention. One functional neurosurgery practice estimates that tremor surgery (deep brain stimulation) is being offered to one patient in 400,000 - 500,000. The majority of interventions for tremor will continue to be deep brain stimulation, due to the flexibility that this device offers, or alternatively thalamotomy. The remaining patients that would be eligible to receive stereotactic radiosurgery is estimated at less than 10 patients per year nationwide.

6. Evidence base

NHS England has concluded that there is not sufficient evidence to support a proposal for the routine commissioning of SRS for drug-resistant Parkinson's tremor and familial essential tremor.

We conclude there is low level evidence (level 3) to support the use of stereotactic radiosurgery in the treatment for movement disorders. In conclusion there is insufficient evidence for efficacy, safety, impact on quality of life and cost effectiveness.

To date there has been no randomised trial comparing stereotactic radiosurgery with any other treatment modality such as deep brain stimulating and/or radiofrequency ablation. Stereotactic radiosurgery has been reserved for patients with intractable tremor, where more invasive surgical therapies are contraindicated.

Two recent prospective studies (level 3) have reported a significant improvement in activities of daily living (ADL). Witjas et al (2015) reported a 72.2% improvement (0-100%) in ADL and Ohye et al (2012) reported 81.1% patients rating a tremor score as 'excellent' or 'good' post stereotactic radiosurgery. The largest case series (level 3) within the last five years by Kooshkabadhi et al, 2013 (n=88) showed at least 81% improvement in at least one of the three tremor scores.

These two prospective studies have also evaluated the size of the thalamic lesion pre and post radiation with brain MRI scans, with an overall expected lesion response in the majority of patients. However, authors have noted the thalamic site can fluctuate and warrants further investigation. Witjas et al (2015), described one patient (n=50) with an extensive thalamic response that spontaneously resolved.

The results of these three cases series are consistent with a recent systematic review by Campbell et al, 2015 (level -2). The review evaluated 29 papers of which were primarily case reports and patient case series. Sixteen studies evaluated tremor scores pre and post stereotactic radiosurgery, patient numbers in the studies varied from 172 to 8. All studies except one study showed an improvement in tremor score, range of improvement from 50-100%. Overall the systematic review concluded approximately 80% of patients with intractable tremor had some clinical benefit following the procedure. The review identified the largest case series, conducted by Young et al 2010 (n=172) which showed an improvement in both drawing and writing scores ($P < 0.001$), at 6 month follow-up.

The three recent cases series (Witjas et al (2015), Ohye et al (2012) and Kooshkabadhi (2013)) describe at least one patient developing transient contralateral weakness following SRS therapy, which resolved spontaneously. No other significant side effects were reported. In the systematic review (Campbell et al, 2015) complication rate reported varied between 0% -16 %, predominately motor symptoms. In the review, one group reported a thalamic haemorrhage at treatment site, although the patient was on anticoagulant treatment. In addition three groups in the review reported patient deaths attributed to the therapy. One patient developed aspiration pneumonia secondary to dysphagia, one died of radiation necrosis (bilateral lesions), one died of haemorrhagic stroke at site of lesion 7.5 years after procedure. One group described a correlation between lesion size and dose in Gy. The authors concluded on the basis of the systematic review unilateral gamma knife thalamotomy using doses from 130-150 Gy is well tolerated and safe. However to date

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there has not been a long term follow-up study and requires further investigation.

We found no specific evidence relating to the model of care post-SRS that may impact on the long term duration of response, for example input from other specialities such as occupational health, physiotherapy.

7. Documents which have informed this policy proposition

Publications Gateway Reference 02469 / Stereotactic Radiosurgery and Radiotherapy Services - Needs assessment and Service Review, NHS England / November 2014

8. Date of review

This document will lapse upon publication by NHS England of a clinical commissioning policy for the proposed intervention that confirms whether it is routinely or non-routinely commissioned (expected by June 2016)