Clinical Commissioning Policy
Transcranial magnetic resonance guided focused ultrasound thalamotomy for treatment of medication-refractory essential tremor (adults) [200803P] (URN 1904)

Publication date: November 2020 **Version number:** 1.0

Commissioning position

Summary

Transcranial magnetic resonance guided focused ultrasound (TcMRgFUS) thalamotomy is recommended to be available as a treatment option through routine commissioning for the treatment of medication refractory essential tremor, in patients that are not eligible for deep brain stimulation, within the criteria set out in this document.

The policy is restricted to adults (aged 18 years and over) as there is insufficient evidence to confirm safety in those age groups not included in the policy.

Executive summary

Equality statement

Promoting equality and addressing health inequalities are at the heart of NHS England's values. Throughout the development of the policies and processes cited in this document, we have:

- Given due regard to the need to eliminate discrimination, harassment and victimisation, to advance equality of opportunity, and to foster good relations between people who share a relevant protected characteristic (as cited under the Equality Act 2010) and those who do not share it; and
- Given regard to the need to reduce inequalities between patients in access to, and outcomes from healthcare services and to ensure services are provided in an integrated way where this might reduce health inequalities

Plain language summary

About essential tremor

Essential tremor (ET) is the most common movement disorder. It causes parts of the body to move in an uncontrolled and repetitive manner, most commonly affecting the arms and hands. The cause of ET is not known, although approximately 50% of people affected have a family history of the condition. ET can have a profound impact on people by impacting on their quality of life, social life and employment.

About current treatments

Drug treatment is the first line therapy for ET. Drug treatment will stop working for between a quarter and half of patients and this is known as medication-refractory ET. Surgical intervention in ET is offered to patients whose symptoms are significant and severe and have not responded to medication.

Deep brain stimulation (DBS) is a well-established surgical procedure that is currently commissioned for patients with medication-refractory ET. Electrodes are inserted into a specific area of the brain that is responsible for modifying movements. In ET, the area of the brain most commonly targeted to improve tremor is the ventral intermediate [VIM] nucleus of the thalamus. DBS is effective at improving people's symptoms, but the benefits of DBS tend to diminish over

time. This is an invasive procedure and the main risks are bleeding within the skull, stroke and infection.

Surgical thalamotomy is another procedure that is commissioned for patients with ET. This involves the surgical destruction of the specific area of the brain responsible for modifying movements. Although surgical thalamotomy is still performed today, it is used less than DBS.

About the Treatment

TcMRgFUS thalamotomy is a new procedure for the treatment of ET. This procedure uses focused ultrasound waves generated externally to the body that are directed to, and alter the function of, the VIM nucleus to improve tremor. This is done under magnetic resonance imaging (MRI) guidance.

This is a non-invasive procedure that does not require the introduction or maintenance of hardware into the brain, avoiding the maintenance of the inserted hardware (i.e. battery replacement) and minimising the risk of bleeding within the skull, stroke and infection. This can be done as a day-case procedure.

What we have decided

NHS England has carefully reviewed the evidence to treat medication refractory essential tremor with TcMRgFUS thalamotomy. We have concluded that there is enough evidence to make the treatment available at this time.

Committee discussion

The Clinical Panel considered that the evidence base supported the policy as written.

The Clinical Priorities Advisory Group considered the policy proposition and supporting documentation. See the committee papers (link) for full details of the evidence.

The condition

ET is the most common movement disorder. The cause of ET is not known, although approximately 50% of cases are familial. ET is characterised by uncontrolled oscillatory bilateral movements.

The distinctive postural and intention tremor typically affects the arms more than the legs, trunk, head or voice. The tremor usually begins in one arm or hand. Within one or two years, the other arm is likely to be affected. Initially the tremor may not be present all the time and may be mild. The tremor becomes worse and may eventually be present all the time when the affected body part is held in a position or with certain movements. It may be worse with stress, tiredness, hunger, heightened emotions, or extremes in temperature. As the tremor increases in severity, it can become disabling in the home and workplace, interfering significantly with quality of life, functional activities (dressing, eating, drinking, using a phone), mood and socialisation and often leaving the patient reclusive.

Current treatments

Pharmacotherapy is the first line treatment of ET. Once people with ET become medication-refractory, they may be considered for non-pharmacological techniques, such as deep brain stimulation (DBS), surgical thalamotomy or stereotactic radiosurgery (SRS).

<u>Pharmacotherapy</u>
Tremor can be controlled satisfactorily with medication in most patients. Pharmacotherapy (derived from guidelines published by American Academy of Neurology, Zesiewicz *et al.* 2011) consists of:

- First line drugs: Propranolol and Primidone

- Second line drugs: Topiramate, Gabapentin and benzodiazepines (Clonazepam and Alprazolam)

However, it is estimated that between 25% and 55% of patients with ET are refractory to medication (Louis E.D., 2011). ET is defined as medication-refractory once 2 or more trials of appropriate medical therapy (which includes at least one first line agent: propranolol or primidone) have failed (Elias *et al.* 2016). Medications have poor benefit to adverse effect profiles for patients with ET. Over time, many patients develop resistance to pharmacological treatments after which side-effects become more prominent rather than providing useful symptomatic benefit.

DBS

DBS is a well-established surgical procedure performed by neurosurgeons that can be considered for patients with severe medication-refractory ET. Using image guidance, thin electrodes are passed through burr holes in the skull and placed into the VIM nucleus of the thalamus. The VIM nucleus is a specific area of the brain responsible for modifying movements of the body. The electrodes are then connected to a wire running under the skin to a battery and implanted pulse generator (IPG) in the chest. The application of electrical current to the VIM nucleus alters its function and improves the tremor. Local and / or general anaesthesia may be used in the procedure.

The effects of DBS tend to diminish over time. Adverse events of DBS include: pain, intracranial haemorrhage, infection, stroke, balance disturbances, hardware malfunction, speech and visual problems as well as a small operative mortality. DBS for a variety of movement disorders is currently commissioned by NHS England in accordance with the clinical commissioning policy of DBS in Movement Disorders (NHS England, 2013). The role of DBS for tremor and dystonia is discussed in the National Institute for Health and Care Excellence (NICE) IPG 188 (NICE, 2006).

Surgical thalamotomy

Surgical thalamotomy is a surgical procedure using stereotactic technology to identify the area of the brain to target using CT or MRI. The patient is awake during the procedure and various methods can be used to destroy the target cells; liquid nitrogen or heat. The success rate is similar to that of DBS, however, the post-operative complication rate is higher (Schuuman *et al.* 2008).

Stereotactic radiosurgery

SRS is a historical non-invasive technique using highly conformal radiotherapy delivered to the VIM nucleus. NHS England has concluded there is insufficient evidence to support the routine commissioning of SRS for familial ET (NHS England, 2016).

About the new treatment

TcMRgFUS is a non-invasive thermal ablation technique. A stereotactic head frame is fixed to the patient's head under local anaesthetic and then the patient lies down in an MRI scanner. Focused ultrasound waves are precisely delivered under image guidance to the VIM nucleus, disrupting its function. TcMRgFUS is directed unilaterally at the VIM nucleus to improve tremor on the other (contralateral) side of the body. Throughout the procedure, the patient is continuously monitored for changes in tremor. This can be performed as a day-case procedure and does not require the use of general anaesthesia. The technique does not require the introduction of hardware into the brain, eliminating the risk of hardware malfunction and battery replacement, while reducing the risk of infection. There is still an associated risk of intracranial haemorrhage.

The NICE IPG 617 states that the evidence for TcMRgFUS thalamotomy for ET raises no major safety concerns; however, current evidence on efficacy is limited in quantity and recommends that the procedure should not be used unless there are special arrangements for clinical governance, consent, and audit or research (NICE, 2018).

Epidemiology and needs assessment

There are no estimates for the prevalence of ET specific to England. ET has an estimated world pooled prevalence of 0.9% (all ages) that increases markedly with age (≥65 years old = 4.6%, ≥95 years old = 21.7%) (Louis & Ferreira 2010). A recent estimate for the prevalence of ET in the US population is 2.2% (Louis & Ottman 2014). However, it is hard to accurately estimate the prevalence of ET because it can often be mis- or under-diagnosed. The age of onset of ET is bimodal with two peaks, one at age 15 and a second peak at 50 to 70 years of age (Brin & Koller 1998). Some studies have also shown a higher prevalence of ET in men (Louis & Ferreira 2010). There have been even fewer estimates of ET incidence. One study in Spain estimated the annual incidence of ET at 616 per 100,000 person-years, in people aged ≥65 years (Romero *et al.* 2012).

In England, there are 40-50 DBS surgeries commissioned each year (taken from commissioning data). It is estimated that there are 50-150 patients per year that would meet the eligibility criteria for TcMRgFUS thalamotomy. This range is derived from the policy working group's experience and clinical commissioning data for patients that are referred to movement disorder clinics for further treatment, but are not eligible for DBS.

Evidence summary

NHS England has concluded that there is sufficient evidence to support a policy for the routine commissioning of this treatment for the indication.

- This rapid evidence review identified six studies which met the inclusion criteria. Four were comparisons of TcMRgFUS thalamotomy and DBS: two retrospective unrandomised controlled studies (Kim et al 2017 and Huss et al 2015) and two cost utility modelling studies (Li et al 2019 and Ravikumar et al 2017). Li et al (2019) also reported results of cost utility modelling for TcMRgFUS thalamotomy versus no treatment. There was also a randomised trial of TcMRgFUS thalamotomy versus sham treatment (Elias et al 2016) and an uncontrolled study reporting later results for this study, after nearly all participants had received TcMRgFUS thalamotomy (Chang et al 2018).

- The studies reported a number of outcomes including the effects of treatment on tremor and quality of life, and the cost-effectiveness and adverse effects of treatment. Studies selected for inclusion in this review did not report results for any subgroups that may benefit from TcMRgFUS more than the wider population of interest.

Clinical effectiveness

TcMRgFUS thalamotomy for essential tremor compared with DBS

- **Successful treatment at one month (one study, n=59):** Kim et al (2017) reported rates of successful treatment[1] at one month after TcMRgFUS thalamotomy of 21/23 (91%) and after DBS of 17/19 (89%). No p-values were reported.

- **Complete remission at one month (one study, n=59):** Kim et al (2017) reported rates of complete remission at one month after TcMRgFUS thalamotomy of 10/23 (43%) and after DBS of 6/19 (32%). No p-values were reported.

- **Successful treatment at twelve months (one study, n=59):** Kim et al (2017) reported rates of successful treatment at twelve months after TcMRgFUS thalamotomy of 18/23 (78%) and after DBS of 16/19 (84%). No p-values were reported.

[1] Defined as absent tremor (complete remission) or occasional tremor (greater than 90% improvement) on the Fahn-Tolosa-Marin scale. This scale contains sections for assessing rest, postural and kinetic/intention tremor amplitude in specific anatomic locations (Part A), tremor in writing, drawing, and pouring (Part B), activities of daily living (Part C) and global assessments by the patient and examiner (Part D), with each item rated on a scale from 0 to 4. Higher scores indicate worse tremor.

- **Complete remission at twelve months (one study, n=59):** Kim et al (2017) reported rates of complete remission at twelve months after TcMRgFUS thalamotomy of 8/23 (35%) and after DBS of 9/19 (47%). No p-values were reported.

- **Proportion of participants with CRST tremor score of 2 to 4 in dominant hand pre-procedure who had a score of 0 to 1 post-procedure (one study, n=85):** Huss et al (2015) reported the following results for this outcome: bilateral DBS 46/55 (83.6%), unilateral DBS 11/13 (84.6%), TcMRgFUS thalamotomy 12/15 (80%) ($p>0.05$ for comparison between treatments).

- **Proportion of participants with CRST handwriting score of 3 to 4 pre-procedure who had a score of 0 to 2 post-procedure (one study, n=85):** Huss et al (2015) reported the following results for this outcome: bilateral DBS 20/26 (76.9%), unilateral DBS 7/8 (87.5%), TcMRgFUS thalamotomy 6/7 (86.7%) ($p>0.05$ for comparison between treatments).

- **QUEST summary score[2] (one study, n=85:)** Huss et al (2015) reported mean pre- and post-procedure scores as follows: bilateral DBS 52.1, 72.0; unilateral DBS not reported; TcMRgFUS thalamotomy 37.5, 68.0. Although scores for both procedures rose, indicating poorer quality of life, both post-procedure scores were reported as showing "significant improvements" versus baseline ($p<0.05$), but not showing different improvement between procedures. SPH contacted the authors about this apparent error but received no reply.

- **Change in Clinical Rating Scale for Tremor (CRST) total score[3]: (one study, n=85)** Huss et al (2015) reported post-procedure CRST scores as follows: bilateral DBS 13.2 (79.5% improvement from baseline), unilateral DBS 15.8 (62.8% improvement from baseline) and TcMRgFUS thalamotomy 17.7 (55.7% improvement from baseline). All three procedures were reported as improved versus baseline ($p<0.05$), and the second two procedures were reported as different from bilateral DBS ($p<0.05$). Pre-treatment scores were not reported, nor were there reported comparisons of unilateral DBS with TcMRgFUS thalamotomy.

TcMRgFUS thalamotomy for essential tremor compared with sham treatment

- **Change in mean CRST hand tremor score[4] at three months (one study, n=76):** Elias et al (2016) reported the following mean CRST hand tremor scores for TcMRgFUS thalamotomy: pre-treatment 18.1, three months post-treatment 9.6. For sham treatment, the results were pre-treatment 16.0 and three months post-treatment 15.8. The difference was 8.3 points (95% confidence interval (CI) 5.9 to 10.7, $p<0.001$).

- **Change in mean CRST hand tremor score at 12 months (one study, n=76):** Elias et al (2016) reported the following mean CRST hand tremor scores for TcMRgFUS thalamotomy: pre-treatment 18.1 and three months post-treatment 10.9. Results for sham treatment were not reported. The difference between the two treatments was reported as 7.2 points (95% CI 6.1 to 8.3, $p<0.001$).

[2] The Quality of Life in Essential Tremor Questionnaire (QUEST) includes 30 items in five domains (physical, psychosocial, communication, leisure and work/finance). Higher scores indicate lower quality of life.

[3] The CRST is used to assess the severity of tremor. It has three parts: Part A (observed tremor), Part B (tasks) and Part C (disability), each scored from 0 to 4; higher scores indicate more severe tremor. Part A separately scores resting, postural, and action or intention components of hand tremor. Higher scores indicate worse tremor.

[4] This hand tremor score (on a scale ranging from 0 to 32, with higher scores indicating more severe tremor) was derived from the CRST, Part A (three items: resting, postural, and action or intention components of hand tremor), and the CRST, Part B (five tasks involving handwriting, drawing, and pouring), in the hand contralateral to the thalamotomy.

- **Change in mean CRST disability score at three months (one study, n=76):** Elias et al (2016) reported the following mean CRST disability scores for TcMRgFUS thalamotomy: pre-treatment 16.5 and three months post-treatment 6.2. For sham treatment, the results were pre-treatment 16.0 and three months post-treatment 15.6. The difference was 9.9 points (p<0.001).

- **Change in mean QUEST score at three months (one study, n=76):** Elias et al (2016) reported the following mean QUEST scores for TcMRgFUS thalamotomy: pre-treatment 42.6 and three months post-treatment 23.1. For sham treatment, the results were pre-treatment 42.8 and three months post-treatment 41.1. The difference between the two treatments was 17.8 points (p<0.001).

No other results were reported.

TcMRgFUS thalamotomy for essential tremor (no comparator)

- **Change in mean CRST hand tremor score at 24 months (one study, n=67):** Chang et al (2018) reported the following mean CRST hand tremor scores for TcMRgFUS thalamotomy: pre-treatment 19.8 and 24 months after treatment 8.8. The difference was 11 points (95% CI 7.6 to 10.0, p<0.001).

- **Change in mean CRST disability score at 24 months (one study, n=67):** Chang et al (2018) reported the following mean CRST disability scores for TcMRgFUS thalamotomy: pre-treatment 16.4 and 24 months after treatment 6.5. The difference was 9.9 points (95% CI 5.3 to 7.7, p<0.001).

Safety

The safety outcome reported was adverse effects of treatment. No study reported tests of the significance of any differences in rates of adverse effects.

TcMRgFUS thalamotomy for essential tremor compared with DBS

- **Adverse effects (two studies, n=59 and n=85):** Kim et al (2017) reported the following adverse effects of TcMRgFUS thalamotomy: mild facial paresis for first month after procedure 1/23 (4%); balance problems due to brain oedema for first month after procedure, controlled with oral steroid therapy plus mild facial paresis still present at 12 month 1/23 (4%). For DBS, the reported adverse effects were mild facial paresis for first month after procedure 1/19 (5%); balance problems relieved with stimulation adjustment 3/19 (16%); and muscle twitching in the contralateral forearm 1/19 (5%). Huss et al (2015) reported a paraesthesia rate of 3/15 (20%) after TcMRgFUS thalamotomy. For bilateral DBS, the reported adverse effects were paraesthesia 1/57 (1.8%), dysarthria 6/57 (11%), weakness 1/57 (1.8%), mental state change 3/57 (5.3%), hardware infection 1/57 (1.8%) and lead erosion 2/57 (3.5%). For unilateral DBS, the reported adverse effects were paraesthesia in 2/13 (15%).

TcMRgFUS thalamotomy for essential tremor compared with sham treatment

- **Adverse effects (one study, n=76):** Elias et al (2016) reported the following adverse effects after TcMRgFUS thalamotomy: gait disturbance in 36% and paraesthesias or numbness in 38%, persisting for 12 months in 9% and 14% of patients respectively. One patient had dense and permanent hypaesthesia of the dominant thumb and index finger, categorised as a serious adverse event. One patient had a transient ischaemic attack six weeks after undergoing thalamotomy. Among the patients treated with sham treatment, one (5%) reported paraesthesia, one (5%) reported subjective unsteadiness or imbalance, four (20%) reported headache for more than a day and one (5%) reported fatigue.

TcMRgFUS thalamotomy for essential tremor (no comparator)

- **Adverse effects (one study, n=67):** Chang et al (2018) reported that none of the adverse events reported in Elias et al (2016) worsened at two years follow-up and that two of these events resolved (dysergia and paraesthesia). There were no new adverse events in the participants reported during the second year of follow-up.

Cost effectiveness

The cost effectiveness outcome reported was the incremental cost effectiveness ratio.

TcMRgFUS thalamotomy for essential tremor compared with DBS

Incremental cost effectiveness ratio (two modelling studies): Li et al (2019) reported an estimated incremental cost of DBS vs TcMRgFUS thalamotomy of Canadian$34,026 (£20,200)[5], an estimated incremental utility of 0.26 QALYs over five years and an estimated incremental cost effectiveness ratio (ICER) of C$130,850 (£77,700) per QALY. Ravikumar et al (2017) reported that TcMRgFUS thalamotomy cost an estimated US$20,593 (£16,140)[6] and yielded an estimated 0.194 QALYs. DBS without staging cost an estimated US$27,906 (£21,900) and yielded an estimated 0.134 QALYs.

TcMRgFUS thalamotomy for essential tremor compared with no treatment

- Incremental cost effectiveness ratio (one modelling study): Li et al (2019) reported an estimated incremental cost of TcMRgFUS thalamotomy vs no surgery of C$21,438 (£12,700), an estimated incremental utility of 0.47 QALYs over five years and an estimated incremental cost utility $45,817 (£27,200) per QALY.

Subgroups that may benefit from TcMRgFUS more

Studies selected for inclusion in this review did not report results for any subgroups that may benefit from TcMRgFUS more than the wider population of interest.

Definitions of essential tremor, treatment-refractory tremor and severity scores of essential tremor

Elias et al (2016) defined essential tremor as “characterized by a distinctive postural and intention tremor typically affecting the hands more than the legs, trunk, head, or voice.” The other included studies which included a definition were consistent with this.

Elias et al (2016) defined treatment-refractory tremor as “tremor that was refractory to at least two trials of medical therapy, including at least one first-line agent (propranolol or primidone).” The other five studies included in this review did not report a definition of the term.

Conclusions

Elias et al (2016) is a reliable randomised trial indicating that TcMRgFUS thalamotomy is more effective than sham treatment, but is associated with a risk of gait disturbance, paraesthesia and numbness. Chang et al (2018) indicates effects of treatment reported by Elias et al (2015) are still present two years later and suggests that some adverse effects may improve while others do not emerge within this period of follow-up. However, discrepancies in Chang et al (2018)’s reporting cast doubt on the accuracy of the data reported in this study.

TcMRgFUS thalamotomy may have advantages over DBS because it is less invasive. However, these are not reported in the two low quality studies (Kim et al 2017 and Huss et al 2015) comparing DBS with TcMRgFUS thalamotomy; these indicate that the treatment outcomes are similar. Both studies are of low quality, with a number of serious methodological weaknesses, and neither is reliable. Similarly, both the cost effectiveness studies are unsuitable for decision-making: Li et al (2019)’s conclusions rest on insecure assumptions and use Canadian

[5] Currency conversion carried out by SPH
[6] Currency conversion carried out by SPH

healthcare costs, making them of little relevance to the NHS, while Ravikumar et al (2017) is affected by serious methodological weaknesses and is unreliable.

This evidence is consistent with NICE's recommendation that TcMRgFUS thalamotomy "should not be used unless there are special arrangements for clinical governance, consent, and audit or research."

Implementation

Before treatment starts the following factors must be taken into account:

- If patients are taking anticoagulants (warfarin, apixaban, rivaroxaban, dabigatran) or antiplatelets (aspirin, clopidogrel, ticagrelor) they need to stop these for a period of time before the procedure as set out by local guidelines in order to minimise the risk of TcMRgFUS causing a haemorrhage in the brain.
- Patients with MRI compatible cardiac pacemakers can be treated providing that a cardiac technician is available, and the pacemaker is in safe mode.
- Unilateral treatment of patients with bilateral tremor can be safely treated with TcMRgFUS thalamotomy.

Criteria

Inclusion criteria

Patients meeting all the following (relevant) criteria should be considered for TcMRgFUS thalamotomy for treatment of medication refractory ET:

- Patients with medication-refractory tremor
- Patients who are not eligible for DBS (see Clinical Commissioning Policy: Deep Brain Stimulation (DBS) in Movement Disorders, April 2013) https://www.england.nhs.uk/wp-content/uploads/2013/04/d03-p-b.pdf
- Patients with either a postural tremor or an intention tremor of grade 3 or 4 in the target upper limb (scored using the CRST part A, see Appendix)
- A score of 2 or above in any one of its items in the CRST Part C (items 16-23).

Tremor sufficient to significantly impair activities of daily living to an extent that it impairs quality of life supported by a clinical tremor rating score. All other medical and surgical interventions have been considered and exhausted or are not felt to be applicable post assessment by a movement disorder consultant neurologist in a functional neurosurgery for movement disorders team.

Exclusion criteria

Patients who meet any of the following criteria are not suitable for TcMRgFUS thalamotomy for treatment of essential tremor:

- Patients who are receiving or are currently eligible to receive DBS
- Patients with a diagnosis of Parkinson's disease
- Unable to undergo an MRI scan.

Absolute contra-indications

- A low Skull Density Ratio (<0.3) preventing enough power being deposited at target site

Relative contra-indications

- Significant speech impairments.
- Unsteadiness when walking or turning.
- Significant cognitive impairments (Mini Mental State Examination less than 25/30) or dementia.
- A high level of frailty.
- Significant other medical co-morbidities (co-existent medical problems), which would increase the risk and diminish the benefits of the procedure (including terminal conditions).

- Abnormalities on a cerebral MRI scan that would negatively affect the outcome of TcMRgFUS.

Patient pathway

Patients with unilateral medication-refractory tremor are referred into neurology outpatients department where they are seen by a movement disorder specialist neurologist and a functional neurosurgeon. Patients may also be considered with bilateral medication-refractory essential tremor, provided that treatment is only considered on one side. They have routine (simple) blood tests, along with a CT head and MRI head. They are discussed at MDT level (with movement disorder neurologist, neuroradiologist, functional neurosurgeon and appropriate specialist nursing, neuropsychological and neuropsychiatric input). If agreed to have medication-refractory tremor, baseline tremor severity is assessed with a CRST score. Patients with either a postural tremor or an intention tremor of grade 3 or 4 in the target upper limb (scored using the CRST part A score), and a score of 2 or above in any of the items in the CRST part C can be considered for the procedure. If the patient meets the eligibility criteria and does not meet any of the exclusion criteria they are consented and booked in for the procedure, which is completed as day case. The procedures are booked as a morning or afternoon session and last up to 4-5 hours. The procedure requires a stereotactic head frame affixed to their shaved head with the use of local anaesthetic. The procedure is performed in an MRI-guided focused ultrasound system. The patients are then followed up routinely by the movement disorder specialist neurologist.

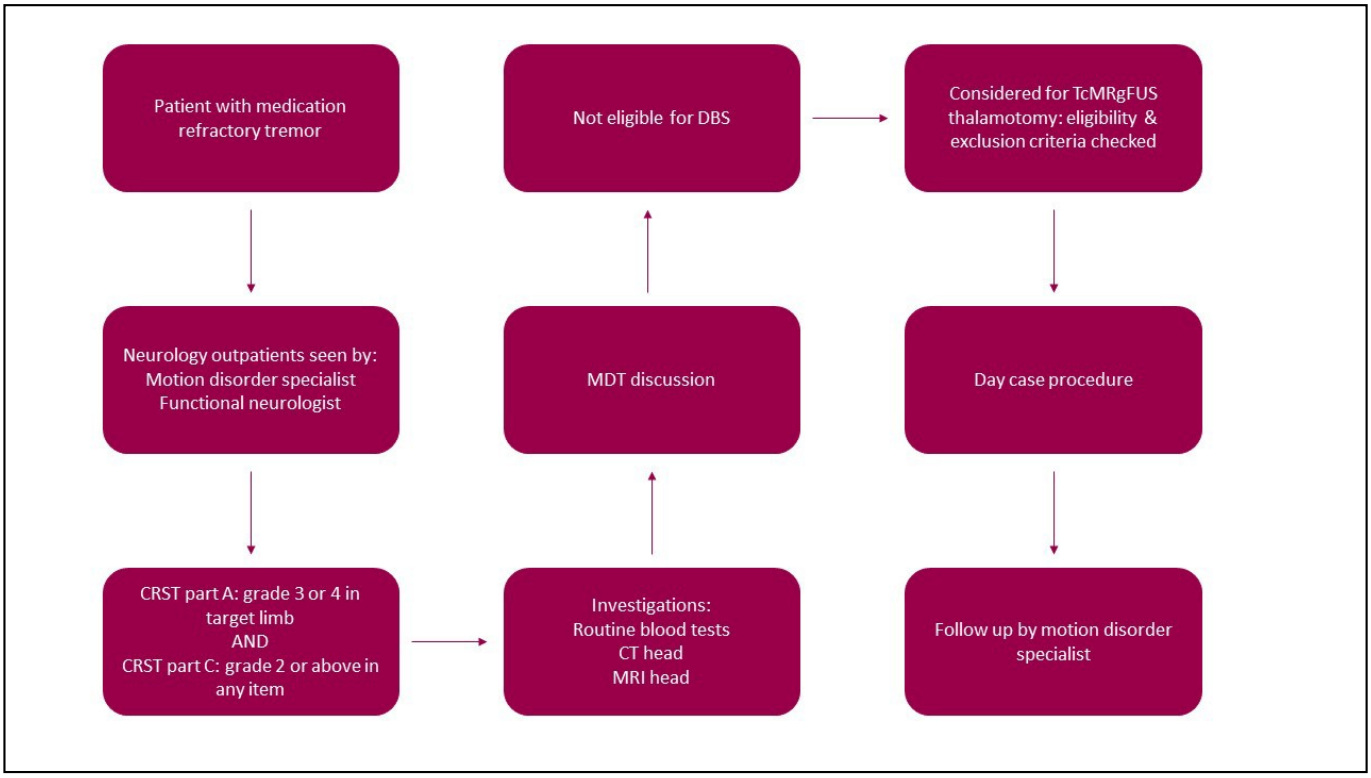

Figure 1. Patient pathway. CRST; clinical rating scale for tremor, DBS; deep brain stimulation, MDT; multidisciplinary team.

Governance arrangements

The Service Specifications for Neurosciences: Specialised Neurology (Adult) (NHS England Reference: D04/S/a) and Neurosurgery (Adults) (NHS England Reference: 170109S) describe the governance arrangements for this service for adults. This policy should be read in conjunction with Clinical Commissioning Policy: Deep Brain Stimulation (DBS) In Movement Disorders (NHS England Reference: NHSCB/D03/P/b)

Mechanism for Funding

TcMRgFUS thalamotomy for essential tremor will be commissioned and funded by NHS England Specialised Commissioning under existing arrangements for the provision of Specialised Neurology and Neurosurgery Adult services.

It is estimated that there will be up to 150 patients that meet the inclusion criteria per annum. The actual patient numbers will be reviewed on a regular basis.

Audit requirements

Patients are currently followed up with CRST scores at 1, 3, 6 & 12 months and the results are kept locally.

There are currently no national patient databases or clinical registries available.

Policy review date

This document will be reviewed when information is received which indicates that the policy requires revision. If a review is needed due to a new evidence base then a new Preliminary Policy Proposal needs to be submitted by contacting england.CET@nhs.net.

Our policies provide access on the basis that the prices of therapies will be at or below the prices and commercial terms submitted for consideration at the time evaluated. NHS England reserves the right to review policies where the supplier of an intervention is no longer willing to supply the treatment to the NHS at or below this price and to review policies where the supplier is unable or unwilling to match price reductions in alternative therapies.

Definitions

Essential tremor	A common neurological disorder that causes involuntary, repetitive movements of body parts, often the arms or hands.
Focused ultrasound	Non-invasive intervention using ultrasonic energy to target tissue deep in the body without incisions or radiation.
Magnetic resonance imaging	Medical imaging technique using strong magnetic fields and radio waves to generate images of the body.
Medication refractory	Has not responded to two medications (one of which is first line treatment – propranolol or primidone).
Thalamotomy	The precise destruction of a tiny area of the brain called the thalamus.

References

Brin, M.F. & Koller W. (1998) Epidemiology and genetics of essential tremor. Mov Disord. 13(3): 55-63.

Elias, W.J., Lipsman, N., Ondo, W.G., Ghanouni, P., Kim, Y.G., Lee, W., Schwartz, M., Hynynen, K., Lozano, A.M., Shah, B.B., Huss, D., Dallapiazza, R.F., Gwinn, R., Witt, J., Ro, S., Eisenberg, H.M., Fishman, P.S., Gandhi, D., Halpern, C.H., Chuang, R. Pauly, K.B., Tierney, T.S., Hayes, M.T., Cosgrove, G.R., Yamaguchi, T., Abe, K., Taira, T., Chang, J.W. (2016) A randomized trial of focused ultrasound thalamotomy for essential tremor. NEJM. 375 (8): 730-739.

Louis, E.D. (2011) Treatment of Essential Tremor: Are there Issues We are Overlooking? Front Neurol. 2: 91.

Louis, E.D. & Ferreira J.J. (2010) How common is the most common adult movement disorder? Update on the worldwide prevalence of essential tremor. Mov. Disord. 25(5): 534-41.

Louis, E.D., Ottman, R., Hauser W.A. (1998) How common is the most common adult movement disorder? estimates of the prevalence of essential tremor throughout the world. Mov Disord. 13(1): 5-10.

Health Quality Ontario (2018) Magnetic resonance-guided focused ultrasound neurosurgery for essential tremor: a health technology assessment. Ontario Health Technology Assess Series. May;18(4):1–141. Available from: http://www.hqontario.ca/evidence-to-improve-care/journal-ontario-health-technology-assessment-series.

Koller, W.C., K. Busenbark, K. Miner (1994) The relationship of essential tremor to other movement disorders: report on 678 patients. Essential Tremor Study Group. Ann Neurol. 35(6): 717-23.

NHS England. Deep Brain Stimulation (DBS) in Movement Disorders. Clinical Commissioning Policy. Reference: NHSCB/D03/P/b. NHS England 2013. Available from: https://www.england.nhs.uk/wp-content/uploads/2018/07/DBS-for-MD.pdf.

NHS England. Stereotactic Radiosurgery (SRS) for adults with Parkinson's Tremor and Familial Essential Tremor. Reference: 16007/P. NHS England 2016. Available from: https://www.england.nhs.uk/wp-content/uploads/2018/07/Stereotactic-radiosurgery-for-adults-with-Parkinsons-tremor-and-familial-essential-tremor.pdf.

National Institute for Health and Care Excellence (NICE). Deep brain stimulation for tremor and dystonia (excluding Parkinson's disease). NICE interventional procedure guidance 188 (2006). Available from http://www.nice.org.uk/guidance/IPG188.

National Institute for Health and Care Excellence (NICE). Unilateral MRI-guided focussed ultrasound thalamotomy for treatment-resistant essential tremor. NICE Interventional Procedures Guidance 617. Published: June 2018. URL available at: https://www.nice.org.uk/guidance/ipg617/evidence.

Office for National Statistics. Estimates of the population for the UK, England and Wales, Scotland and Northern Ireland. Accessed 19th September 2019. URL available at: https://www.ons.gov.uk/peoplepopulationandcommunity/populationandmigration/populationestimates/datasets/populationestimatesforukenglandandwalesscotlandandnorthernireland

Romero, J.P., Benito-Leon, J., Bermejo-Pareja, F. (2012) The NEDICES study: recent advances in the understanding of the epidemiology of essential tremor. Tremor Other Hyperkinet Mov (NY). 2: tre-02-70-356-2. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3570054/.

Schuumann, P.R., Bosch, D.A., Merkus, M.P., Speelman, J.D. (2008) Long-term follow-up of thalamic stimulation versus thalamotomy for tremor suppression. Mov. Disorder. 23(8): 1146-1153.

Sur, H., Ilhan, S., Erdogan, H., Ozturk, E., Tasdemir, M., Boru, U.T. (2009) Prevalence of essential tremor: a door-to-door survey in Sile, Istanbul, Turkey. Parkinsonism Relat. Disord. 15(2): 101-4.

Zesiewicz, T.A., Chari, A., Jahan, I., Miller, A.M., Sullivan, K.L. (2010) Overview of essential tremor. Neuropsychiatr. Dis. Treat. 6(1): 401-408.

Zesiewicz, T.A. *et al.* (2011) Evidence-based guideline update: treatment of essential tremor: report of the Quality Standards subcommittee of the American Academy of Neurology. Neurology. 77(19): 1752-5.

Appendix

1. Clinical Rating Scale for Tremor (CRST)

Part A: Tremor location / severity rating (1-10)

1-10. Tremor: rate tremor

a. At rest (in repose). For head and trunk, when lying down.
b. ***With posture*** holding (upper extremity – arms outstretched, wrists mildly extended, fingers spread apart; lower extremity – legs flexed at hips and knees, foot dorsiflexed; tongue – when protruded; head and trunk – when sitting or standing).
c. ***With*** helium ***and intention*** (upper extremity – finger to nose and other actions; lower extremity – toe to finger in a flexed posture)
   0 – None
   1 – Slight; barely perceivable. May be intermittent.
   2 – Moderate; amplitude <2cm. May be intermittent.
   3 – Marked; amplitude 2-4cm.
   4 – Severe; amplitude >4cm.

		Rest	Posture	Action/Intention	Total
1.	Face tremor	□0 □1 □2 □3 □4			
2.	Tongue tremor	□0 □1 □2 □3 □4	□0 □1 □2 □3 □4		
3.	Voice tremor			□0 □1 □2 □3 □4	
4.	Head tremor		□0 □1 □2 □3 □4		
5.	RUE tremor	□0 □1 □2 □3 □4	□0 □1 □2 □3 □4	□0 □1 □2 □3 □4	
6.	LUE tremor	□0 □1 □2 □3 □4	□0 □1 □2 □3 □4	□0 □1 □2 □3 □4	
7.	Trunk tremor		□0 □1 □2 □3 □4		
8.	RLE tremor	□0 □1 □2 □3 □4	□0 □1 □2 □3 □4	□0 □1 □2 □3 □4	
9.	LLE tremor	□0 □1 □2 □3 □4	□0 □1 □2 □3 □4	□0 □1 □2 □3 □4	
10.	Orthostatic (trunk/legs when standing)		□0 □1 □2 □3 □4		

Table 1: CRST part A scoring. RUE – right upper extremity, LUE – left upper extremity, RLE – right lower extremity, LLE – left lower extremity.

Part B: Specific motor tasks / functional rating (11-15)

11. Handwriting: have patient write the standard sentence "This is a sample of my best handwriting," sign their name, and write the date.
   0 – Normal
   1 – Mildly abnormal. Legible, but with considerable tremor.
   2 – Moderately abnormal. Legible, but with considerable tremor.
   3 – Markedly abnormal. Illegible.
   4 – Severely abnormal. Unable to keep pencil or pen on paper without holding hand down with the other hand.

12-14. Drawings: (See parts A, B and C): ask the patient to join both points of the various drawings without crossing the lines. Test each hand, beginning with the lesser involved, without leaning the hand or arm on the table.
   0 – Normal
   1 – Slightly tremulous. May cross lines occasionally.
   2 – Moderately tremulous or crosses lines frequently.
   3 – Accomplishes the task with great difficulty. Many errors.
   4 – Unable to complete drawing.

15. Pouring: Use firm plastic cups (8cm tall), filled with water to 1cm from top. Ask patient to pour water from one cup to another. Test each hand separately.
   0 – Normal
   1 – More careful than a person without tremor, but no water is spilled.
   2 – Spills a small amount of water (up to 10% of total amount).

3 – Spills a considerable amount of water (10-50%).
4 – Unable to pour without spilling most of the water.

		Right	Left	Total
11.	Handwriting (Dominant only)	□0 □1 □2 □3 □4	□0 □1 □2 □3 □4	
12.	Drawing A	□0 □1 □2 □3 □4	□0 □1 □2 □3 □4	
13.	Drawing B	□0 □1 □2 □3 □4	□0 □1 □2 □3 □4	
14.	Drawing C	□0 □1 □2 □3 □4	□0 □1 □2 □3 □4	
15.	Pouring	□0 □1 □2 □3 □4	□0 □1 □2 □3 □4	

Table 2: CRST part B scoring.

Part C: Functional disabilities resulting from (16-23)

16. Speaking: This includes spastic dysphonia if present.
    0 – Normal
    1 – Mild voice tremulousness when nervous only.
    2 – Mild voice tremor, constant.
    3 – Moderate voice tremor.
    4 – Severe voice tremor. Some words difficult to understand.

17. Feeding (other than liquids):
    0 – Normal
    1 – Mildly abnormal. Can bring all solids to mouth, spilling only rarely.
    2 – Moderately abnormal. Frequent spills of peas and similar foods. May bring head at least halfway to meet food.
    3 – Markedly abnormal. Unable to cut or uses two hands to feed.
    4 – Severely abnormal. Needs help to feed.

18. Bringing liquids to mouth:
    0 – Normal
    1 – Mildly abnormal. Can still use a spoon, but not if it is completely full.
    2 – Moderately abnormal. Unable to use a spoon. Uses cup or glass.
    3 – Markedly abnormal. Can drink from cup or glass but needs two hands.
    4 – Severely abnormal. Must use a straw.

19. Hygiene:
    0 – Normal
    1 – Mildly abnormal. Able to do everything but is more careful than the average person.
    2 – Moderately abnormal. Able to do everything, but with errors; uses electric razor because of tremor.
    3 – Markedly abnormal. Unable to do most fine tasks, such as putting on lipstick or shaving (even with electric shaver), unless using two hands.
    4 – Severely abnormal. Unable to do any fine-movement tasks.

20. Dressing:
    0 – Normal
    1 – Mildly abnormal. Able to do everything but is more careful than the average person.
    2 – Moderately abnormal. Able to do everything, but with errors.
    3 – Markedly abnormal. Needs some assistance with buttoning or other activities, such as tying shoelaces.
    4 – Severely abnormal. Requires assistance even for gross motor activities.

21. Writing:
    0 – Normal
    1 – Mildly abnormal. Legible. Continues to write letters.

2 – Moderately abnormal. Legible, but no longer writes letters.
3 – Markedly abnormal. Illegible.
4 – Severely abnormal. Unable to sign checks or other documents requiring signature.

22. Working:
0 – Tremor does not interfere with the job.
1 – Able to work but needs to be more careful than the average person.
2 – Able to do everything, but with errors. Poorer than usual performance because of tremor.
3 – Unable to do regular job. May have changed to a different job because of tremor. Tremor limits housework, such as ironing.
4 – Unable to do any outside job; housework very limited.

23. Social activities:
0 – No changes
1 – Minimal change in social activities, still socialises.
2 – Moderate change in social activities, avoids encounters with strangers.
3 – Marked change in social activities, avoids encounters with friends.
4 – Severe change in social activities, avoids any public encounters.

16. Speaking	□0 □1 □2 □3 □4
17. Eating	□0 □1 □2 □3 □4
18. Drinking	□0 □1 □2 □3 □4
19. Hygiene	□0 □1 □2 □3 □4
20. Dressing	□0 □1 □2 □3 □4
21. Writing	□0 □1 □2 □3 □4
22. Working	□0 □1 □2 □3 □4
23. Social activities	□0 □1 □2 □3 □4

Table 3: CRST part C scoring.