

Interventional procedure overview of MRI-guided focused ultrasound thalamotomy for treating moderate to severe tremor in Parkinson's

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Table 1 Abbreviations

Abbreviation	Definition
BAI	Beck Anxiety Inventory
BDI-II	Beck Depression Inventory-II
CRST	Clinical Rating Scale for Tremor
DBS	Deep brain stimulation
ET	Essential Tremor
FTM	Fahn-Tolosa-Marin
IQR	Interquartile range
LED	Levodopa
MOCA	Montreal Cognitive Assessment
MRgFUS	Magnetic Resonance Image guided Focused Ultrasound
PD	Parkinson's
PDQ-8	Parkinson's disease Questionnaire-8
QoL	Quality of Life
RT	Radiofrequency thalamotomy
SD	Standard deviation
TDPD	Tremor-dominant Parkinson's
UPDRS	Unified Parkinson Disease Rating Scale
US	Ultrasound
VIM	Ventral Intermediate

Indications and current treatment

Parkinson's is a progressive neurodegenerative condition that damages the brain over many years. It is caused by a loss of the cells in the brain that produce dopamine, which helps to control and coordinate body movements. People with

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Parkinson's classically present with the symptoms and signs described as 'parkinsonism' these include: bradykinesia (slow movements), rigidity, rest tremor (shaking) and postural instability (loss of balance). In later stages of Parkinson's, other symptoms sometimes described as the 'non-motor' manifestations of Parkinson's such as depression, cognitive impairment, dementia and autonomic disturbances) may be prominent. The condition may progress to cause significant impairments, adversely affecting quality of life and, indirectly, the quality of life of family and carers.

For people with early Parkinson's, drug treatments such as levodopa, other dopamine agonists and monoamine oxidase B inhibitors may be considered. In the later stages, other drugs may be used with levodopa (as adjuvants) to reduce the motor complications associated with prolonged levodopa use. Non-pharmacological management such as, physiotherapy, occupational therapy and speech and language therapy may be considered. Invasive surgical procedures may be considered for people with Parkinson's that is refractory to medical and supportive therapies. These include deep brain stimulation and less commonly radiofrequency thalamotomy. Treatments for non-motor symptoms such as sleep disturbance and depression may also be considered.

Unmet need

MRI-guided focused ultrasound thalamotomy is a minimally invasive procedure that may benefit a subgroup of people who do not want the risks of more invasive brain surgery (that is, DBS or RT), or when brain surgery is not an option, especially in older and more frail people.

What the procedure involves

This outpatient procedure is done with the patient lying supine inside an MRI scanner for several hours. The person's head is shaved, and a stereotactic head frame is attached. The person is usually kept awake during the procedure so they

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can be regularly assessed by the treating physician to evaluate the clinical response (report any improvement of symptoms or adverse events). Some people may be offered light sedation.

Real time MRI guidance and thermal mapping are used to identify the target area of the brain (the thalamic nucleus) precisely, and monitor treatment. Low power ultrasound is delivered to confirm the chosen location. Then, several high-power focused ultrasound pulses are delivered to ablate target tissue in the thalamus. The energy released and the location of the ultrasound focus are monitored in real time during the procedure by MRI thermometry, and adjusted to reach above the definitive ablation temperature (of 55°C) according to clinical response. Chilled water is circulated around the head during the treatment to prevent thermal damage to the scalp caused by the increase in bone temperature. The procedure is considered finished when there is sufficient clinical improvement, and considering the total amount of energy delivered and the number of sonications. The procedure takes about 2 hours and symptom relief should be immediate.

Outcome measures

The main outcomes include quality of life, tremor, use of antiparkinsonian medicine, neuropsychological outcomes and recurrence of tremor.

The measures used are detailed in the following paragraphs:

Quality of life

This is measured by the Parkinson's Disease Questionnaire, the score of which ranges from 0 to 156. The UPDRS is also used to assess quality of life in people with Parkinson's disease. It consists of: mentation, behaviour and mood (part 1); activities of daily living (part 2); motor examination (part 3); complications of therapy (part 4); modified Hoehn and Yahr staging (part 5); and the Schwab and

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England scale (part 6). The questions can be answered in the on or off state. Lower scores are better.

Tremor

Tremor score can be derived from the Clinical Rating Scale, which ranges from 0 to 32 for tremor in the hand. The CRST part A rates tremor severity from 0 to 4, with 0 being no tremor and 4 being severe tremor. Tremor can also be derived from the UPDRS, which ranges from 0 to 8 for action and rest tremor in the hand. The FTM tremor rating scale is composed of head, voice, rest, postural, and intention tremor of the affected limb. It is graded from 0 to 4 (0 representing no tremor and 4 representing highest tremor severity).

Use of antiparkinsonian medicine

Levodopa is a common first-line drug for managing Parkinson's motor symptoms.

Neuropsychological outcomes:

The following tests were included as neuropsychological outcome measures:

- Montreal Cognitive Assessment test
- Categorical Verbal Fluency test
- Raven's Progressive Matrices
- Hamilton Anxiety rating scale
- Beck Anxiety Inventory (BAI)
- Beck Depression Inventory-II
- Parkinson's disease Questionnaire-8.

MOCA

Some of the cognitive domains examined in this brief screening tool are attention and concentration, executive functions, memory, language, visuo-constructional skills, conceptual thinking, calculations, and orientation. The MOCA can differentiate healthy cognitive aging from mild cognitive impairment.

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Categorical Verbal Fluency test

This test explores lexical retrieval and production by asking people to say as many words as possible belonging to the 'colours', 'animals' and 'fruits' categories in 3 different trials, which last 60 seconds each. The final score corresponds to the total number of words produced.

RPM test

This test provides a non-verbal estimate of fluid intelligence and reasoning. It measures the problem-solving ability of a person to think logically and solve problems in novel situations, using logical reasoning and regardless of previous knowledge.

BAI and BDI-II

These tests investigate the presence of anxiety and depressive feelings.

PDQ-8

This 8-item version of the Parkinson's disease questionnaire (PDQ-8) is a shortened version of the 39-item Parkinson's disease questionnaire (PDQ-39) for quality of life.

Evidence summary

Population and studies description

This interventional procedures overview is based on 261 people from 6 case series, 1 RCT (reported in 2 papers) and 1 systematic review. This is a rapid review of the literature, and a flow chart of the complete selection process is shown in [figure 1](#). This overview presents 9 studies as the key evidence in [table 2](#) and [table 3](#), and lists 21 other relevant studies in [table 5](#).

One systematic review (Lin 2021) did a network metanalysis based on a Bayesian framework to compare the efficacy of DBS and MRgFUS in

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parkinsonian tremor. Twenty four studies were included in the analysis, comprising data from 784 people, 77 of whom had treatment with MRgFUS thalamotomy.

One RCT, which was reported in 2 articles (Bond 2017 and Sperling 2018) assessed safety and efficacy at 12-month follow up of unilateral FUS thalamotomy for people with TDPD, accounting for placebo response. Assessments were double-blinded through the primary outcome and the placebo group was offered open-label treatment after unblinding.

One prospective study (Zur 2020) of 56 people (17 with PD and 39 with ET) looked at tremor relief and structural integrity after MRgFUS thalamotomy in tremor disorders. People with ET or PD having thalamotomy were prospectively recruited between March 2016 and October 2018. Tremor and quality of life were assessed before, 1 month after, and 6 months after thalamotomy.

A prospective study of 18 people with PD investigated cognitive outcomes after focused ultrasound thalamotomy for tremor (Saporito 2023).

Three prospective studies (Yamatoto 2021, Sinai 2022 and Chua 2023) studied the long-term results of focused ultrasound thalamotomy in TDPD. In Sinai 2022, the primary aim of treatment was to relieve arm tremor. For people with other tremors such as leg, chin, and head tremor, the aim was to relieve those tremors as well.

One retrospective study (Lak 2022) was a single centre study with 160 procedures of MRgFUS thalamotomy (10 procedures for people with PD, Lak 2022).

[Table 2](#) presents study details.

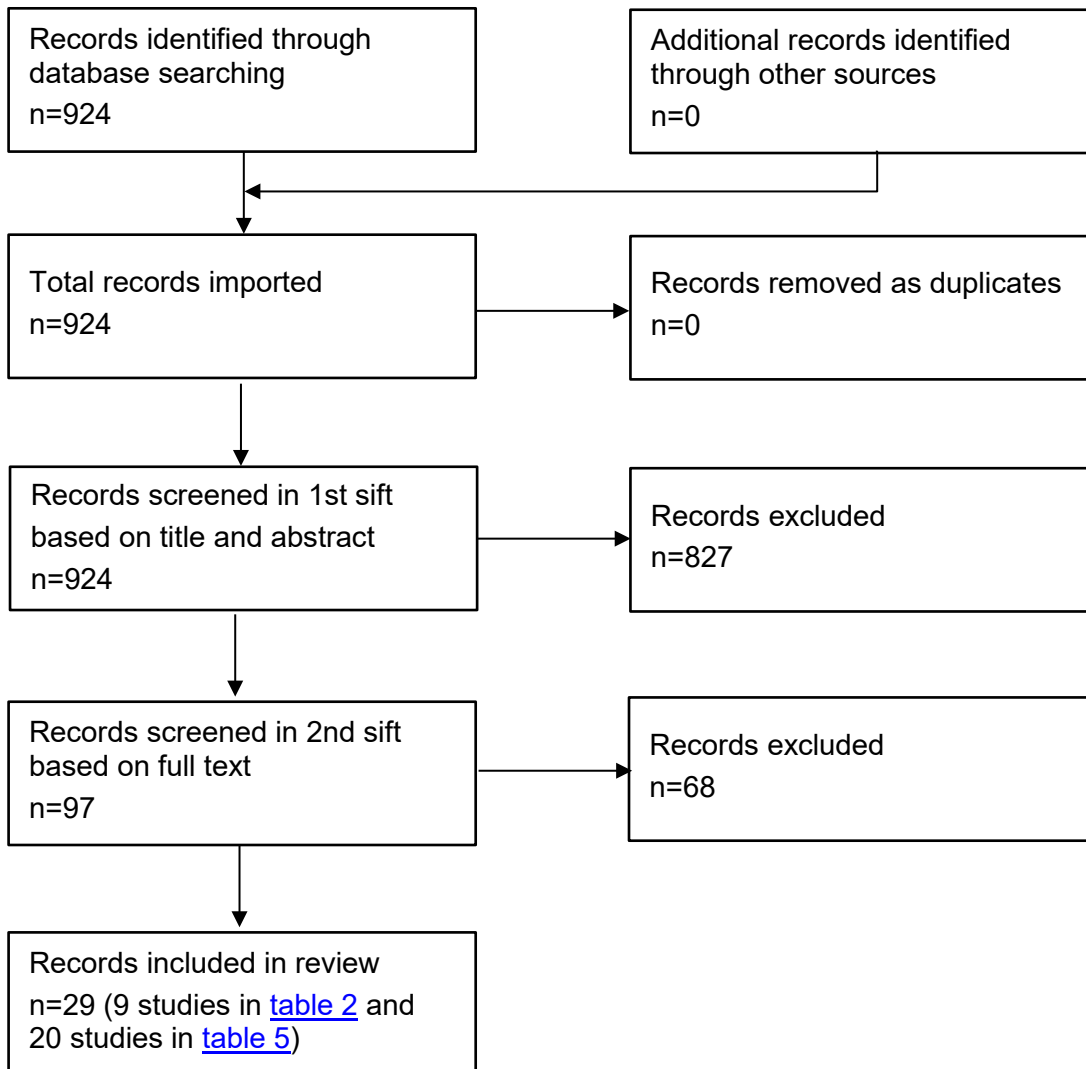
Figure 1 Flow chart of study selection

Table 2 Study details

Study no.	First author, date country	Patients (male: female)	Age	Study design	Inclusion criteria	Intervention	Follow up
1	Lin 2021	N= 784 (77 for MRgFUS thalamus)	NA	Systematic review and network meta-analysis of 24 studies	People with clinical diagnosis of PD	MRgFUS	Follow-up ranging from 1 month to 48 months
2 and 3	Bond 2017, US Sperling 2018, US	N=27 (20 intervention and 7 placebo) (26:1)	Median age = 67.8 years (IQR, 62.1-73.8 years)	Randomised controlled trial	People with tremor dominant Parkinson's disease	Unilateral FUS thalamotomy	12 months
4	Zur 2020 Israel and US	N=56 (17 PD and 39 ET) (13:4)	Mean age (SD) for those with PD: 65 (8) years	Prospective case series	Individuals undergoing MRI-guided focused US thalamotomy with disabling tremor despite at least two full-dose therapeutic medication trials	MRI-guided focused US thalamotomy	6 months
5	Lak 2022	N=160 (Laterality of Thalamotomy, Left, n = 128; Right, n = 32) (109:51)	Mean age (SD)= 75.0 (7.50) Years (range: 48 to 93)	Case series	People who underwent unilateral MRgFUS thalamotomy for medically	MRgFUS thalamotomy	Mean= 14 months (range: 1 to 48 months)

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Study no.	First author, date country	Patients (male: female)	Age	Study design	Inclusion criteria	Intervention	Follow up
		N=150 (medically refractory essential Tremor) N=10 (tremor predominant Parkinson's disease)			refractory ET or tremor predominant Parkinson's disease from March 2016 to January 2021		
6	Saporito 2023, Italy	N=40 (22 ET and 18 PD) (38:2)	Mean age (SD)= 67.7 (10.7)	Prospective case series	Adults who underwent unilateral MRgFUS thalamotomy	MRgFUS thalamotomy	2 years
7	Sinai 2022, Israel	N=26 (20:6)	Median age = 60 years (range 46 to 79)	Prospective case series	People with tremor dominant Parkinson's disease	MRgFUS VIM-thalamotomy	Median follow-up= 36 months, range 12 to 60 months
8	Chua 2023, US	N=48 (38:10)	Mean age (SD, range) = 73.27 (7.31, 56–90)	Case series	People with tremor dominant Parkinson's disease	MRgFUS VIM-thalamotomy	3 years
9	Yamatoto 2021 Japan	N=11 (5:6)	Mean age= 71.6 years	Prospective case series	People with medication-	VIM thalamotomy	1 year

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Study no.	First author, date country	Patients (male: female)	Age	Study design	Inclusion criteria	Intervention	Follow up
					refractory TDPD (TDPD was defined as tremor-dominant with tremor dominant/postural instability and gait difficulty ratio >1.15. This was calculated from the UPDRS in the "on" state)	with Transcranial MR-guided FUS	

Table 3 Study outcomes

First author, date	Efficacy outcomes	Safety outcomes
Lin 2021	<u>UPDRS III-Tremor (medication-off):</u> Mean difference compared to baseline: <ul style="list-style-type: none"> MRgFUS (internal globus pallidus)=4.90 (95% CI 0.81 to 9,06) MRgFUS (ventral intermediate nucleus) =5.62 (95% CI 1.41 to 9.57) DBS (internal globus pallidus)=3.06 (95% CI 1.05 to 5.25) 	<u>GPi-MRIgFUS:</u> Mild headache =10 Back pain =4 Dysarthria and grade III right motor hemiparesis =1 scalp hypoesthesia =1 speech difficulties =7 <u>VIM-MRIgFUS:</u>

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First author, date	Efficacy outcomes	Safety outcomes
	<ul style="list-style-type: none"> • DBS (ventral intermediate nucleus)=6.64 (95% CI 4.49 to 8.93) • DBS (combined subthalamic nucleus and caudal zona incerta) =6.92 (95% CI 1.72 to 12.09) <p>Pedunculopontine nucleus was the only DBS site that did not show a statistically significant change from baseline.</p> <p><u>UPDRS III-Tremor (medication-on):</u></p> <p>Mean difference compared to baseline:</p> <ul style="list-style-type: none"> • MRgFUS (internal globus pallidus)=3.54 (95% CI 1.54 to 5.74) • MRgFUS (ventral intermediate nucleus) =2.54 (95% CI 1.11 to 4.18) • DBS (internal globus pallidus)=1.64 (95% CI 0.06 to 3.32) • DBS (combined pedunculopontine nucleus and caudal zona incerta)=2.95 (95% CI 0.31 to 5.80) • DBS (caudal zona incerta)=3.34 (95% CI 1.66 to 4.78) <p><u>UPDRS III-Total (medication-off):</u></p> <p>Mean difference compared to baseline:</p> <ul style="list-style-type: none"> • MRgFUS (internal globus pallidus)=13.46 (95% CI 2.46 to 25.10) • MRgFUS (ventral intermediate nucleus) =18.62 (95% CI -2.09 to 38.79) 	<p>During sonications:</p> <p>headache =3 dizziness =2 vertigo =4 lip paraesthesia =1</p> <p>Lasted from procedures:</p> <p>hypogeusia =1 subjective unsteady feeling when walking =1 disturbance when walking tandem =1</p> <p>Thalamotomy Related:</p> <p>Finger paraesthesia:</p> <p>Transient =7 Persistent =1</p> <p>Orofacial paraesthesia:</p> <p>Transient =1 Persistent =4</p> <p>Ataxia:</p> <p>Transient =8 Persistent =1</p> <p>Hemiparesis:</p> <p>Transient =2 Persistent =2</p>

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First author, date	Efficacy outcomes	Safety outcomes
	<ul style="list-style-type: none"> • DBS (internal globus pallidus)=15.24 (95% CI 5.79 to 24.82) • DBS (ventral intermediate nucleus)=5.42 (95% CI -9.52 to 20.61) • DBS (combined subthalamic nucleus and caudal zona incerta)=12.76 (95% CI -12.73 to 38.22) <p><u>UPDRS III-Total (medication-on):</u></p> <p>Mean difference compared to baseline:</p> <ul style="list-style-type: none"> • MRgFUS (internal globus pallidus)=11.47 (95% CI 5.90 to 17.01) • MRgFUS (ventral intermediate nucleus) =11.63 (95% CI 3.67 to 19.06) • DBS (internal globus pallidus)=2.24 (95% CI -2.34 to 6.60) • DBS (combined pedunclopontine nucleus and caudal zona incerta)=11.65 (95% CI 0.73 to 22.39) • DBS (caudal zona incerta)=7.62 (95% CI 0.42 to 14.71) <p>In the network meta-analysis, DBS and MRgFUS showed similar efficacy for tremor suppression (assessed using UPDRS)</p>	<p>Dysmetria, transient =1 Mild vocal change, persistent =1</p> <p>MRI or Ultrasonography Related, All Transient: Scalp numbness =1 Headache =12 Dizziness or vertigo =8 Head pain or heat sensation =3 Stomach pain or nausea or emesis =4 Periorbital swelling =2 Neck or back or shoulder pain =4 Decline in mental status =1 Pin site pain =1 Anxiety =1</p>
Bond 2017 and Sperling 2018	<u>Median scores (IQR) for CRST, UPDRS, quality of life, neuropsychological and LEDD</u>	Thalamotomy related adverse events n (%): <u>Finger paraesthesia:</u>

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First author, date	Efficacy outcomes	Safety outcomes
	<p>CRST: <u>Tremor subscore (CRST A+B), treated hand (FUS group):</u> Baseline = 17 (10.5 to 27.5) 1 month = 4 (1.5 to 11.5) 3 months = 4.5 (3.0 to 16.0) 1 Year = 5.0 (2.0 to 14.0) <u>Total CRST (FUS group):</u> Baseline = 41.5 (28.0 to 65.0) 1 month = 14.5 (7.0 to 43.5) 3 months = 18.0 (8.0 to 52.0) 1 Year = 18.0 (7.0 to 42.0) <u>Tremor subscore (CRST A+B), treated hand (sham group):</u> Baseline = 23 (14 to 27) 1 month = 15 (12 to 17) 3 months = 17 (12 to 21) <u>Total CRST (sham group):</u> Baseline = 48 (43 to 62) 1 month = 39 (27 to 54) 3 months = 37 (29 to 53) UPDRS: <u>Total UPDRS (FUS group):</u> Baseline = 37.5 (32.5 to 44.5)</p>	<p>Transient 2 (33) Persistent 0 (0) <u>Orofacial paraesthesia:</u> Transient 2 (33) Persistent 0 (0) <u>There were no reports of thalamotomy-related ataxia, hemiparesis or dysmetria.</u></p> <p>Transient adverse events resolved during the 1year study. Persistent adverse events were still present at 1 year.</p>

First author, date	Efficacy outcomes	Safety outcomes
	<p>1 month = N/A 3 months = 27.0 (11.5 to 41.0) 1 Year = 19.5 (9.0 to 36.0) <u>Total UPDRS (sham group):</u> Baseline = 39 (25 to 53) 1 month = N/A 3 months = 24 (21 to 50) Quality of life: <u>PDQ-39 (FUS group):</u> Baseline = 21.2 (12.6 to 32.0) 1 month = N/A 3 months = 7.9 (4.8 to 23.5) 1 Year = 7.5 (3.4 to 22.2) <u>CRST disability (part C) (FUS group):</u> Baseline = 13.0 (10.0 to 18.5) 1 month = 2.0 (0.5 to 8.0) 3 months = 3.5 (1.0 to 10.0) 1 Year = 2.5 (0 to 11.0) <u>PDQ-39 (sham group):</u> Baseline = 25.0 (14.8 to 27.7) 1 month = N/A 3 months = 17.4 (1.8 to 20.6) <u>CRST disability (part C) (sham group):</u> Baseline = 17 (13 to 20)</p>	

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First author, date	Efficacy outcomes	Safety outcomes
	<p>1 month = 16 (11 to 18) 3 months = 16 (13 to 18)</p> <p>Neuropsychological:</p> <p><u>MoCA (FUS group):</u> Baseline = 25.5 (23.0 to 28.0) 1 month = N/A 3 months = 25.5 (23.5 to 26.5) 1 Year = 25.0 (24.0 to 26.0)</p> <p><u>BDI-II (FUS group):</u> Baseline = 5.0 (2.5 to 9.0) 1 month = N/A 3 months = 6.0 (1.5 to 9.0) 1 Year = 5.0 (3.0 to 8.0)</p> <p><u>MoCA (sham group):</u> Baseline = 27.0 (23.0 to 28.0) 1 month = N/A 3 months = 26.0 (23.0 to 28.0)</p> <p><u>BDI-II (sham group):</u> Baseline = 5.0 (4.0 to 8.0) 1 month = N/A 3 months = 8.0 (2.0 to 9.0)</p> <p>LEDD (mg):</p> <p><u>FUS group:</u> Baseline = 751 (450 to 950)</p>	

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First author, date	Efficacy outcomes	Safety outcomes
	<p>1 month = 573 (400 to 950) 3 months = 500 (400 to 836) 1 Year = 550 (400 to 800)</p> <p><u>Sham group:</u> Baseline = 640 (550 to 1250) 1 month = 640 (550 to 1250) 3 months = 840 (550 to 1250)</p> <p>Results for FUS group at baseline, 1 month and 3 months n=20 and trial is blinded. At 1 year n=14 and trial is unblinded. Results for sham group at baseline, 1 month and 3 months n=7 and trial is blinded.</p> <p><u>Results from Sperling 2018</u></p> <p><u>Data are presented as median (IQR)</u></p> <p>Cognitive MoCA Test</p> <p>Baseline: Active=25.5 (23 to 27.5), Sham=27 (23 to 28), p=0.766</p> <p>3 months:</p>	

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First author, date	Efficacy outcomes	Safety outcomes
	<p>Active=25.5 (23.3 to 26.8), Sham=26 (23 to 28), p=0.498</p> <p>Mood (High scores on all mood and behavioural measures indicate worse symptoms):</p> <p>BAI baseline:</p> <p>Active=6.5 (5 to 10), Sham=10 (5 to 14), p=0.4</p> <p>BAI 3 months:</p> <p>Active= 6 (3.3 to 11.8), Sham=12 (8 to 15), p=0.219</p> <p>BDI-II Baseline:</p> <p>Active=5 (2.5 to 9), Sham=5 (4 to 8), p=0.935</p> <p>BDI-II 3 months:</p> <p>Active=6 (1.25 to 9), Sham=8 (2 to 9), p=0.893</p>	

First author, date	Efficacy outcomes	Safety outcomes
	<p>Changes in quality of life after active treatment, PDQ-39 domains:</p> <p>Mobility:</p> <p>Baseline=17.5 (10 to 35), 3 months=10 (5 to 22.5), p=0.012, 12 months=15 (2.5 to 22.5), p=0.507, omnibus p value=0.093, MCID=9.13</p> <p>ADL:</p> <p>Baseline=37.5 (25 to 50), 3 months=20.83 (4.2 to 51), p<0.001, 12 months=12.5 (4.2 to 29.2), p<0.001, omnibus p value<0.001, MCID=12.12</p> <p>Emotion Wellness:</p> <p>Baseline=20.83 (8.3 to 29.2), 3 months=8.3 (0 to 24), p=0.035, 12 months=8.3 (0 to 16.7), p=0.023, omnibus p value=0.004, MCID= 9.89</p> <p>Stigma:</p> <p>Baseline=18.75 (12.5 to 43.8), 3 months= 2.5 (0 to 26.6), p=0.01, 12 months=6.25 (0 to 18.8), p=0.01, omnibus p value=0.005, MCID=15.51</p> <p>Social Support:</p>	

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First author, date	Efficacy outcomes	Safety outcomes
	<p>Baseline=0 (0 to 8.33), 3 months=0 (0 to 0), p=0.301, 12 months=0 (0 to 0), p=0.496, omnibus p value=0.069, MCID=13.31</p> <p>Cognitive Impairment:</p> <p>Baseline=12.5 (6.3 to 37.5), 3 months=6.25 (0 to 20.3), p=0.005, 12 months=12.5 (6.3 to 31.3), p=0.197, omnibus p value=0.021, MCID=15.79</p> <p>Communication:</p> <p>Baseline=16.67 (0 to 26.7), 3 months=0 (0 to 27.1), p=0.381, 12 months=0 (0 to 16.7), p=0.048, omnibus p value=0.081, MCID=14.91</p> <p>Bodily Discomfort:</p> <p>Baseline=25 (8.3 to 33.3), 3 months= 6.67 (0 to 25), p=0.258, 12 months=16.67 (8.3 to 27.1), p=0.732, omnibus p value=0.064, MCID=17.13</p> <p>Total:</p> <p>Baseline=21.35 (12.9 to 28.6), 3 months=9.16 (3.9 to 31.9), p=0.003, 12 months=11.2 (4.23 to 23), p=0.018, omnibus p value=0.004, MCID=5.31</p>	

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First author, date	Efficacy outcomes	Safety outcomes
	<p>Associations with quality of life:</p> <p>CRST A: 3 months τ_b (Kendall tau-b)=0.266, $p=0.06$, change $\tau_b=0.12$, $p=0.4$</p> <p>CRST B: 3 months $\tau_b = 0.125$, $p=0.385$, change $\tau_b=0.233$, $p=0.105$</p> <p>CRST A&B: 3 months $\tau_b=0.057$, $p=0.690$, change $\tau_b=0.151$, $p=0.288$</p> <p>UPDRS-III: 3 months $\tau_b=0.374$, $p=0.008$, change $\tau_b= -0.279$, $p=0.049$</p> <p>UPDRS-II: 3 months $\tau_b=0.609$, $p<0.001$, change $\tau_b= -0.382$, $p=0.008$</p>	

First author, date	Efficacy outcomes	Safety outcomes
Zur 2020	<p>Tremor score for n=17 people with PD, mean (SD) Before ablation: 5.4 (1.6) 1 month after ablation: 1.5 (2.1) 6 months after ablation: 0.8 (2.2)</p> <p>QoL score for n=17 people with PD, mean (SD) Before ablation: 43.8 (20.9) 1 month after ablation: 27.1 (20.4) 6 months after ablation: 25 (24)</p>	No safety outcomes measured
Lak 2022	<p>Mean Tremor Score at rest (measured using CRST Part A) for people with PD 1 year follow up (n = 4) = 0.75 2 year follow up (n = 2) = 1.00</p> <p>Loss of treatment benefit or recurrence 1 year: n=9 lost more than 50% of their treatment benefit 2 years: n=5 patients with recurrence</p> <p><u>Mean tremor scores at baseline in tremor predominant PD</u> rest: 3.5 SD 0.52 posture: 2.8 SD 0.78</p>	<p>Adverse events</p> <p>Motor weakness:</p> <ul style="list-style-type: none"> • 1-day post-op= 14 (8.75%), • 3-months post-op= 6 (5.17%), • 1-year post-op= 3 (2.85%), • 2-years post-op= 1 (2.0%) <p>Dysarthria:</p> <ul style="list-style-type: none"> • 1-day post-op= 30 (18.75%), • 3-months post-op= 9 (7.75%), • 1-year post-op= 6 (5.71%), • 2-years post-op= 1 (2.0%) <p>Sensory deficits (Paraesthesia/Numbness):</p> <ul style="list-style-type: none"> • 1-day post-op= 40 (25.0%), • 3-months post-op= 28 (24.15%), • 1-year post-op= 17 (16.2%), • 2-years post-op= 5 (10.0%)

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First author, date	Efficacy outcomes	Safety outcomes
	<p>intention: 1.5 SD 1.18.</p> <p><u>Mean tremor scores after the procedure in tremor predominant PD</u></p> <p>1 day: 0.29 SD 0.48 (n=148)</p> <p>3 months: 0.50 SD 0.95 (n=110)</p> <p>1 year: 0.66 SD 1.08 (n=101)</p> <p>2 years: 0.87 SD 0.90 (n=49)</p> <p>3 years: 1.25 SD 0.57 (n=8)</p> <p>4 years: 1 SD 0.63 (n=6)</p>	<p>Gait imbalance:</p> <ul style="list-style-type: none"> • 1-day post-op= 91 (56.87%), • 3-months post-op= 30 (25.8%), • 1-year post-op= 15 (14.28%), • 2-years post-op= 9 (17.5%) <p>Dysgeusia:</p> <ul style="list-style-type: none"> • 1-day post-op= 1 (0.62%), • 3-months post-op= 9 (7.75%), • 1-year post-op= 3 (2.85%), • 2-years post-op= 2 (4.0%) <p>Dysmetria:</p> <ul style="list-style-type: none"> • 1-day post-op= 18 (11.25%), • 3-months post-op= 12 (10.34%), • 1-year post-op= 7 (6.66%), • 2-years post-op= 4 (8.0%) <p>Headache:</p> <ul style="list-style-type: none"> • 1-day post-op= 5 (3.12%) <p>Others (hypotension/ light-headedness, somnolence, new onset LE tremor):</p> <ul style="list-style-type: none"> • 1-day post-op= 4 (2.5%)
Saporito 2023	<p><u>Neuropsychological tests</u></p> <p>Mini Mental State Examination:</p> <ul style="list-style-type: none"> • Baseline 25.70 ± 3.78, • 6-month follow-up 27.31 ± 2.44 (p=0.072) <p>Montreal Cognitive Assessment:</p> <ul style="list-style-type: none"> • Baseline 22.56 ± 4.10, • 6-month follow-up 23.94 ± 3.65 (p=0.003) 	<p>Adverse events</p> <p>Dizziness: n=21.52%</p> <p>Scalp burning: n=16.40%</p> <p>Nausea: n=8.42%</p> <p>Headache: n=6.15%</p> <p>Vagal reaction: n=2.5%</p> <p>Thalamotomy-related complications</p>

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First author, date	Efficacy outcomes	Safety outcomes
	<p>Frontal Assessment Battery:</p> <ul style="list-style-type: none"> Baseline 13.83 ± 3.31, 6-month follow-up 14.33 ± 3.80 ($p=0.189$) <p>Single letter-cued (phonemic) fluency test:</p> <ul style="list-style-type: none"> Baseline 26.04 ± 12.68, 6-month follow-up 26.98 ± 13.67 ($p=0.628$) <p>Single letter-cued (semantic) fluency test:</p> <ul style="list-style-type: none"> Baseline 9.04 ± 2.46, 6-month follow-up 9.97 ± 3.27 ($p=0.333$) <p>Rey Auditory Verbal Learning Test R.I:</p> <ul style="list-style-type: none"> Baseline 30.56 ± 8.36, 6-month follow-up 32.94 ± 9.57 ($p=0.093$) <p>Rey Auditory Verbal Learning Test R.D:</p> <ul style="list-style-type: none"> Baseline 4.73 ± 3.74, 6-month follow-up 32.94 ± 9.57 ($p=0.324$) <p>Raven's Progressive Matrices:</p> <ul style="list-style-type: none"> Baseline 28.23 ± 4.66, 6-month follow-up 28.19 ± 4.09 ($p=0.959$) <p>Hamilton Anxiety rating scale:</p> <ul style="list-style-type: none"> Baseline 5.50 ± 4.07, 6-month follow-up 2.33 ± 1.94 ($p=0.004$) <p>Beck Depression Inventory-II:</p> <ul style="list-style-type: none"> Baseline 2.78 ± 2.75, 	<p>Contralateral weakness: $n=3$, 7.5%</p> <p>Dysgeusia: $n=1$, 2.5%</p> <p>Gait instability: $n=1$, 2.5%</p>

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First author, date	Efficacy outcomes	Safety outcomes
	<ul style="list-style-type: none"> 6-month follow-up 1.61 ± 1.94 ($p=0.156$) Parkinson's disease Questionnaire-8 (PDQ-8): <ul style="list-style-type: none"> Baseline 5.61 ± 4.65, 6-month follow-up 1.39 ± 2.33 ($p=0.001$) <u>Recurrence</u> N=1, at 12 months postoperatively	
Sinai 2022	<u>Median change of tremor and motor scores before and after FUS</u> n=26 at baseline and 1 month, 22 at 6 months, 23 at 12 months, 15 at 24 and 36 months, 12 at 48 months and 7 at 60 months. <u>UPDRS:</u> Baseline (raw score), 22.5 (9 to 43) 1 month, -10 (-34 to 6) $p<0.0001$ 6 months, -16 (-34 to 16) $p<0.0001$ 12 months, -18 (-31 to 47) $p<0.0001$ 24 months, -15 (-33 to -1) $p<0.0001$ 36 months, -16 (-29 to 0) $p=0.0002$ 48 months, -10 (-30 to -4) $p=0.0005$ 60 months, -19 (-31 to -5) $p=0.016$ <u>Hemi-UPDRS:</u> Baseline (raw score), 15 (5 to 24) 1 month, -9 (-19 to 4) $p<0.0001$ 6 months, -12 (-18 to 2) $p<0.0001$ 12 months, -12 (-20 to 6) $p<0.0001$	Adverse events <u>Week 1, mild level 1 events (resolved within 3 months):</u> headache n=9, vertigo n=8, dizziness n=3, hand/scalp heat n=3, lip/tongue paraesthesia n=2 hand paraesthesia n=1 <u>Adverse events after the procedure (resolved):</u> objective unsteadiness on tandem gait (n=5, for 1–4 weeks), subjective unsteadiness of gait (n=1, for 7 days), arm ataxia (n=2, for 1–4 weeks), asthenia (n=2, for 1–4 weeks), mild right hemiparesis (for 3 months),

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First author, date	Efficacy outcomes	Safety outcomes
	<p>24 months, -12 (-17 to 2) p<0.0001 36 months, -10 (-17 to 2) p=0.0002 48 months, -8 (-16 to -3) p=0.0005 60 months, -8 (-17 to -4) p=0.016</p> <p><u>CRST:</u> Baseline (raw score), 20 (9 to 70) 1 month, -15 (-66 to -5) p<0.0001 6 months, -17.5 (-64 to -5) p<0.0001 12 months, -17 (-63 to -5) p<0.0001 24 months, -20 (-69 to -6) p<0.0001 36 months, -14 (-70 to 6) p=0.015 48 months, -15 (-54 to 6) p=0.013 60 months, -14 (-54 to 3) p=0.031</p> <p><u>Hemi- CRST:</u> Baseline (raw score), 13 (5 to 28) 1 month, -12 (-28 to -4) p<0.0001 6 months, -13 (-28 to 2) p<0.0001 12 months, -13 (-28 to 2) p<0.0001 24 months, -14 (-28 to 1) p<0.0001 36 months, -13 (-28 to 1) p=0.0002 48 months, -14.5 (-28 to 0) p=0.0010 60 months, -8 (-28 to 1) p=0.031</p> <p><u>PDQ39:</u> Baseline (raw score), 32 (17 to 79)</p>	<p>hypogeusia (n=1, for 3 months) and scalp numbness (n=1, for one week).</p>

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First author, date	Efficacy outcomes	Safety outcomes
	<p>1 month, -18* (-42 to 27) p<0.0001 6 months, -19 (-61 to 9) p<0.0001 12 months, -15 (-66 to 11) p<0.0001 24 months, -7 (-43 to 15) not significant 36 months, -8 (-46 to 24) not significant 48 months, -6 (-48 to 29) not significant 60 months, -11 (-47 to 24) not significant</p> <p><u>Levodopa equivalent:</u> Baseline (raw score), 300 (0 to 1050) 1 month, 0 (-200 to 141) not significant 6 months, 0 (-200 to 582) not significant 12 months, 0 (-200 to 985) not significant 24 months, 66 (-250 to 1676) not significant 36 months, 199 (-250 to 1076) p=0.0049 48 months, 122.5 (-250 to 1676) p=0.037 60 months, 151 (0 to 1476) p=0.031</p> <p>Negative values indicate improvement on all scales. p values are based on Wilcoxon signed rank test of changes (follow-up – baseline). *N = 25 for this item.</p> <p>Note: there appear to be some discrepancies between the table and text of the paper regarding the labelling of outcomes.</p> <p><u>PD related outcomes</u></p>	

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First author, date	Efficacy outcomes	Safety outcomes
	<p>Before FUS: Receiving levodopa: n=11 Receiving symptomatic therapy but not levodopa: n=11 Not receiving antiparkinsonian medication: n=4</p> <p>During follow-up: Started taking levodopa: n=6, 5 people for rigidity (6 months n=2, 12 months n=1, 24 months n=1, 60 months n=1) and 1 person for tremor (24 months) Motor fluctuations: n= 3</p> <p>At the last follow up: Not using levodopa: n=9 Not taking any antiparkinsonian medication: n=3 people (12 months n=2, 36 months n=1) Not taking any antiparkinsonian medication: n=6 people (12 months n=1, 24 months n=1, 36 months n=1, 48 months n=3)</p> <p><u>Tremor suppression</u></p> <p>6 months, n = 22, p < 0.0001 1 year, n = 23, p < 0.0001</p>	

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First author, date	Efficacy outcomes	Safety outcomes
	2 years, n = 15, p < 0.0001 3 years, n = 15, p = 0.023 4 years, n = 12, p = 0.012 5 years, n = 7, p = 0.031	
Chua 2023	Total FTM score (SD, range): Baseline (n=49) = 6.31 (2.48, 2 to 13) 1 day (n=49) = 0 1 month (n=44) = 0.16 (0.52, 0 to 3) 3 months (n=34) = 0.59 (1.24, 0 to 6) 1 year (n=23) = 1.35 (2.41, 0 to 9) 2 years (n=5) = 0.20 (0.40, 0 to 1) 3 years (n=2) = 0.50 (0.50, 0 to 1)	Adverse events: <u>Motor weakness:</u> 1 day = 3 (6%) 1 month = 9 (20%) 3 months = 6 (18%) 1 year = 3 (14%) 2 years = 1 (20%) Upper extremity 1 day = 1 (2%) Lower extremity: 1 day = 3 (6%) 1 month = 9 (20%) 3 months = 6 (18%) 1 year = 3 (14%) 2 years = 1 (20%) <u>Sensory deficit (paraesthesia/ numbness):</u> 1 day = 7 (14%) 1 month = 12 (27%) 3 months = 9 (26%) 1 year = 3 (14%)

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First author, date	Efficacy outcomes	Safety outcomes
		<p>Lips:</p> <p>1 day = 6 (12%)</p> <p>1 month = 6 (14%)</p> <p>3 months = 6 (18%)</p> <p>1 year = 2 (9%)</p> <p>Tongue:</p> <p>1 day = 1 (2%)</p> <p>1 month = 2 (5%)</p> <p>3 months = 1 (3%)</p> <p>Orofacial (lips and tongue):</p> <p>1 month = 3 (7%)</p> <p>3 months = 2 (6%)</p> <p>1 year = 1 (5%)</p> <p>Fingers:</p> <p>1 day = 2 (4%)</p> <p>1 month = 3 (7%)</p> <p>3 months = 1 (3%)</p> <p><u>Gait imbalance:</u></p> <p>1 day = 29 (59%)</p> <p>1 month = 28 (64%)</p> <p>3 months = 13 (38%)</p> <p>1 year = 6 (27%)</p> <p>2 years = 1 (20%)</p> <p><u>Dysarthria:</u></p>

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First author, date	Efficacy outcomes	Safety outcomes
		1 day = 8 (16%) 1 month = 6 (14%) 3 months = 2 (6%) <u>Dysgeusia:</u> 1 day = 3 (6%) 1 month = 7 (16%) 3 months = 2 (6%) 1 year = 1 (5%) At 1 day (n=49), 1 month (n=44), 3 months (n=34), 1 year (n=22), 2 years (n=5) and 3 years (n=2)
Yamatoto 2021	<u>Tremor</u> UPDRS Part III score at baseline: Median (interquartile range) = 25 (18–34) UPDRS Part III score at 1 year: Median (interquartile range) = 9 (5–13) <u>Median improvement in CRST scores (interquartile range)</u> 12 months postoperatively = 87.9% (70.5–100.0) Median improvement of functional disability in Part C on the CRST = 66.7% (15.5–85.1) Median improvement in total tremor scores from baseline to 12 months = 65.3% (55.7–87.7) Treated upper extremity: Resting tremor: 66.7% (50.0–100.0)	Adverse events related to thalamotomy Headache: During procedure=9 Floating sensation: During procedure=3 Gait disturbance: During procedure=1, 1 day=3, 1 months=1 Exacerbation of bradykinesia: 1 day=3 Dysesthesia: During procedure=1, 1 day=1, 1 month=1, 3 months=1, 12 months=1 Hemiparesis: During procedure=1, 1 day=1 Hypoesthesia: 1 day=1, 1 month=1, 3 months=1 Ageusia: 1 day=1, 1 month=1 Hypotonia: 1 day=1 Bradypragia: 1 day=1 Dysphagia: 1 day=1 Dysarthria: 1 day=1, 1 month=1, 3 months=1

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First author, date	Efficacy outcomes	Safety outcomes
	<p>Postural tremor: 100.0% (100.0–100.0) Action tremor: 100.0% (100.0–100.0)</p> <p><u>Levodopa equivalent dose in individual cases</u> Of the 11 people treated, the levodopa equivalent dose remained the same or decreased in 6 and increased in 3 at 12 months, when compared to baseline. One person refused to take medications because of lack of efficacy and one other individual did not have a recorded dose at 12 months but their dose remained constant at baseline, 1 week, 1 month and 3 months.</p> <p><u>Recurrence</u> N=1, at 12 months postoperatively (maximum temperature was 49°C, and the lesion volume was 46.2 mm³, the lowest and smallest of all the patients)</p>	<p>Adverse events related to stereotactic frame Eyelid oedema: Eyelid oedema=2</p>

Procedure technique

Of the 9 studies, 6 studies detailed the focused ultrasound procedure technique and devices used as being a Neuro ExAblate machine (NeuroAblate 4000, InSightec; Bond 2017, Sperling 2018, Yamatoto 2021, Sinai 2022, Chua 2023 and Saporito 2023). One study did MRI examinations on a 3.0-T system (Discovery MR750; GE Healthcare, Milwaukee, Wisconsin; Zur 2020). One study described the procedure technique but gave no details about specific devices (Lak 2022). Eight studies targeted the ventral intermediate nucleus of the thalamus (Bond 2017, Sperling 2018, Lin 2021, Yamatoto 2021, Sinai 2022, Lak 2022, Chua 2023 and Saporito 2023).

Efficacy

Quality of life

In the RCT of 27 people comparing MRgFUS with a sham procedure, the quality-of-life rating, assessed by PDQ39 score improved to 7.5 (IQR, 3.4 to 22.2) at 1 year from 21.2 (IQR, 12.6 to 32.0) at baseline, in the MRgFUS group. In the sham group the PDQ39 was 25.0 (IQR, 14.8 to 27.7) at baseline and 17.4 (IQR, 1.8 to 20.6) at 3 months. The CRST disability (part C) score improved to 2.5 (IQR, 0 to 11.0) at 1 year from 13.0 (IQR, 10.0 to 18.5) at baseline, in the MRgFUS group. In the sham group the CRST disability (part C) score was 17 (IQR, 13 to 20) at baseline and 16 (IQR, 13 to 18) at 1 year (Bond 2017).

In the prospective study of 56 people (17 with PD) looking at tremor relief and structural integrity after MRI-guided focused US thalamotomy in tremor disorders, the quality of life increased after ablation (mean 43.82, SD 20.94 at baseline compared with 27.07, SD 20.37 at 1 month, $p < 0.001$; Zur 2020).

In the prospective study of 18 people with PD investigating cognitive outcomes after MRgFUS thalamotomy for tremor, there were statistically significant improvements in quality of life at 6-month follow up (PDQ-8: 5.61, SD 4.65

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compared with 1.39, SD 2.33, $p=0.001$), and the overall cognitive status (MOCA 22.56, SD 4.10 compared with 23.94, SD 3.65, $p=0.003$; Saporito 2023).

The prospective study of 26 people studied the long-term results of MRgFUS thalamotomy in TDPD. The quality-of-life rating, assessed by PDQ39 score, showed a statistically significant improvement after MRgFUS. The raw baseline score before treatment was 32 (range 17 to 79). At 1 month after treatment the change in median score was -18 (range -42 to 27, $p<0.0001$). At 6 months the change in median score was -19 (range -61 to 9, $p<0.0001$) and at a year it was -15 (range -66 to 11, $p<0.0001$). When compared with the baseline, the improvement in PDQ39 score was not statistically significant at the 24-month, 36-month or 48-month follow up (Sinai 2022).

Tremor

In the RCT of 27 people comparing MRgFUS with a sham procedure, in the MRgFUS group, the tremor sub-score (CRST A+B) of the treated hand improved to 5.0 (2.0 to 14.0) at 1 year from 17 (10.5 to 27.5) at baseline. In the sham group, the tremor sub-score (CRST A+B) of the treated hand improved to 17 (12 to 21) at 3 months from 23 (14 to 27) at baseline. In the MRgFUS group, the total CRST score improved to 18.0 (7.0 to 42.0) at 1 year from 41.5 (28.0 to 65.0) at baseline. In the sham group, the total CRST score improved to 37 (29 to 53) at 3 months from 48 (43 to 62) at baseline. In the MRgFUS group, the total UPDRS score improved to 19.5 (9.0 to 36.0) at 1 year from 37.5 (32.5 to 44.5) at baseline. In the sham group, the total UPDRS score improved to 24 (21 to 50) at 3 months from 39 (25 to 53) at baseline (Bond 2017).

In the prospective study of 56 people (17 with PD), tremor decreased in those with PD from 5.4 (SD 1.6) at baseline to 1.5 (SD 2.1) at the 1-month follow up ($p<0.001$; Zur 2020).

In the prospective study of 11 people with PD, the median scores on the UPDRS part 3 were 25 (IQR 18 to 34) at baseline and 9 (IQR 5 to 13) at 12 months after surgery. During this procedure, tremor significantly improved for everyone. Also, from baseline to 12 months, the median improvement in total tremor scores on the CRST was 65.3% (IQR 55.7 to 87.7; Yamatoto 2021).

In the retrospective study in a single centre with 160 procedures of MRgFUS thalamotomy (10 procedures for people with PD), the mean tremor component scores at baseline in tremor-predominant PD were 3.5 (SD 0.52; rest), 2.8 (SD 0.78; posture) and 1.5 (SD 1.18; intention). Intention tremor scores after the procedure were 0.29 (SD 0.48) at 1 day (n=148), 0.50 (SD 0.95) at 3 months (n=110), 0.66 (SD 1.08) at 1 year (n=101), 0.87 (SD 0.90) at 2 years (n=49), 1.25 (SD 0.57) at 3 years (n=8) and 1 (SD 0.63) at 4 years (n=6) (Lak 2022).

In the prospective study of 26 people with PD, the median CRST score decreased by 15 points from baseline 1 month after treatment ($p < 0.0001$). Tremor suppression continued during follow-up visits up to 5 years and remained statistically significant (6 months, n=22, $p < 0.0001$; 1 year, n=23, $p < 0.0001$; 2 years, n=15, $p < 0.0001$; 3 years, n=15, $p = 0.023$; 4 years, n=12, $p = 0.012$; 5 years, n=7, $p = 0.031$). Likewise, the median hemi-CRST dropped by 12 points (range -28 to -4, $p < 0.0001$) after 1 month. Over time, the hemi-CRST score remained statistically significantly decreased. The median hemi-UPDRS score fell by 9 points at 1 month (range: -19 to 4 points; $p < 0.0001$). Similar notable changes were also shown in part 3 of the total UPDRS. Over a period of up to 5 years, the median UPDRS part 3 and hemi-UPDRS remained statistically significantly decreased (Sinai 2022).

In the retrospective study of 48 people, the FTM score was 6.31 (SD 2.48, range 2 to 13) at baseline, 0 at day 1 and 0.50 (SD 0.50, range 0 to 1) after 3 years (Chua 2023).

In the systematic review of 77 people with PD, the network meta-analysis comparisons for UPDRS III-Tremor (medication-off) showed that the mean difference for MRgFUS (internal globus pallidus and ventral intermediate nucleus) compared with baseline was significant (4.90, 95% CI 0.81 to 9.06, and 5.62, 95% CI 1.41 to 9.57, respectively). For UPDRS III-Tremor (medication-on), the mean difference for MRgFUS (internal globus pallidus and ventral intermediate nucleus) compared with baseline was significant (3.54, 95% CI 1.54 to 5.74, and 2.54, 95% CI 1.11 to 4.18, respectively). The UPDRS III-Total (medication-off) showed that the mean difference for MRgFUS (internal globus pallidus and ventral intermediate nucleus) compared with baseline was significant (13.46, 95% CI 2.46 to 25.10, and 18.62, 95% CI -2.09 to 38.79, respectively). The UPDRS III-Total (medication-on) showed that the mean difference for MRgFUS (internal globus pallidus and ventral intermediate nucleus) compared with baseline was significant (11.47, 95% CI 5.90 to 17.01, and 11.63, 95% CI 3.67 to 19.06, respectively; Lin 2021).

Use of antiparkinsonian medication

In the RCT of 27 people comparing MRgFUS with a sham procedure, the LEDD (mg) was 550 (400 to 800) at 1 year and 751 (450 to 950) at baseline in the MRgFUS group. In the sham group the LEDD (mg) was 840 (550 to 1250) at 3 months and 640 (550 to 1250) at baseline (Bond 2017).

In the prospective study of 11 people with PD, the levodopa equivalent dose remained the same or decreased in 6 people and increased in 3 people at 12 months, when compared with baseline. One person refused to take medications because of lack of efficacy and one other individual did not have a recorded dose at 12 months but their dose remained constant at baseline, 1 week, 1 month and 3 months (Yamatoto 2021).

In the prospective study of 26 people with PD, before the procedure 11 people had levodopa, 11 people had symptomatic therapy but not levodopa, and

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4 people did not have any antiparkinsonian medicine. Six people started taking levodopa during follow up, 5 people for rigidity (6 months n=2, 12 months n=1, 24 months n=1, 60 months n=1) and 1 person for tremor (24 months). Motor fluctuations occurred in 3 of these people. At the last follow up, 9 people were not using levodopa, and 3 people were not taking any antiparkinsonian medications and 6 people were not taking any other antiparkinsonian medications (Sinai 2022).

Neuropsychological outcomes

In the RCT of 27 people comparing MRgFUS with a sham procedure, in the MRgFUS group, the MOCA score was 25.0 (IQR 24.0 to 26.0) at 1 year and 25.5 (IQR 23.0 to 28.0) at baseline. In the sham group, the MOCA score was 27.0 (IQR 23.0 to 28.0) at 3 months and 26.0 (IQR 23.0 to 28.0) at baseline. In the MRgFUS group, the BDI-II score was 5.0 (IQR 3.0 to 8.0) at 1 year and 5.0 (IQR 2.5 to 9.0) at baseline. In the sham group, the BDI-II score was 8.0 (IQR 2.0 to 9.0) at 3 months and 5.0 (IQR 4.0 to 8.0) at baseline (Bond 2017).

In the same RCT, the MoCA score change in the active group was 0 (IQR -1.5 to 2.5) and in the sham group was -1 (IQR -1 to 2; p=0.725). The change in BAI score, measuring mood, was -0.5 (IQR -4 to 2.8) in the active group and 3 (IQR -3 to 6) in the sham group (p=0.533). The change in BDI-II score, measuring mood, was 0 (IQR -3 to 2.0) in the active group and 1 (IQR -2 to 2) in the sham group (p=0.646; Sperling 2018).

In the prospective study of 18 people with PD there was a statistically significant improvement in the overall cognitive status at 6-month follow up (MOCA 22.56, SD 4.10 compared with 23.94, SD 3.65, p=0.003). All the other cognitive and behavioural domains remained unchanged (Saporito 2023).

Recurrence of tremor

In the prospective study of 11 people with PD, 1 person had a tremor recurrence 12 months after surgery. The lesion volume in this person was 46.2 mm³, and the maximal temperature was 49°C. These were the lowest and smallest values among everyone in the study (Yamatoto 2021).

In the retrospective study in a single centre with 160 procedures of MRgFUS thalamotomy (10 procedures for people with PD), 9 people had lost more than half of their treatment benefit at the 1-year follow up, and 5 more people experienced tremor recurrences at the 2-year follow up (Lak 2022).

Safety

Head discomfort or pain

In the prospective study of 11 people with PD, 9 people experienced headache related to thalamotomy during the procedure (Yamatoto 2021).

In the prospective study of 18 people with PD, 16% experienced scalp burning, 8% experienced nausea, 6% experienced headache and 3% experienced a vagal reaction (Saporito 2023).

In the prospective study of 26 people with PD, 9 people experienced headache and 3 experienced hand or scalp heat during the first week, which was resolved within 3 months. One person experienced scalp numbness for 1 week after the procedure (Sinai 2022).

In the systematic review of 77 people with PD, 3 people experienced headache during the sonications (MRgFUS targeting the VIM). During the MRI ultrasonography procedure, 1 person experienced scalp numbness, 12 people experienced headache and 3 people experienced head pain or heat sensation (all of these were transient and for MRgFUS targeting the VIM; Lin 2021).

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Vestibular symptoms (dizziness or vertigo)

In the retrospective study of a single centre experience with 160 procedures of MRgFUS thalamotomy (10 procedures for people with PD), 1 day after surgery (n=160), 25% of people experienced sensory deficits. At the 3-month follow up (n=116), 24% of people experienced sensory deficits. At the 1-year follow up (n=105), 16% of people experienced sensory deficits. At the 2-year follow up (n=51), 10% of people experienced sensory deficits (Lak 2022).

In the prospective study of 18 people with PD, 22% experienced dizziness (Saporito 2023).

In the prospective study of 26 people with PD studying the long-term results of focused ultrasound thalamotomy in TDPD, 8 patients experienced vertigo and 3 experienced dizziness during the first week, which was resolved within 3 months (Sinai 2022).

In the systematic review, 2 people experienced dizziness and 4 people experienced vertigo during sonication, 1 person experienced a subjective unsteady feeling when walking and 1 person experienced disturbance when walking tandem (from Schlesinger 2015 in the Lin 2021 review).

During the MRI ultrasonography procedure, 8 people experienced dizziness or vertigo (all of these were transient and for MRgFUS targeting the VIM; Lin 2021).

Paraesthesia or numbness

In the RCT of 27 people comparing MRgFUS with a sham procedure, 33% of people (n=2) experienced transient finger paraesthesia (which was resolved within 1 year) and orofacial paraesthesia related to the thalamotomy (Bond 2017).

In the prospective study of 26 people with PD, 2 patients experienced lip or tongue paraesthesia and 1 experienced hand paraesthesia during the first week, which was resolved within 3 months (Sinai 2022).

In the systematic review of 77 people with PD, 1 person experienced lip paraesthesia during sonication (MRgFUS targeting the VIM). Seven people experienced transient finger paraesthesia and 1 person experienced persistent finger paraesthesia (MRgFUS targeting the VIM). One person experienced transient orofacial paraesthesia and 4 people experienced persistent orofacial paraesthesia (MRgFUS targeting the VIM; Lin 2021).

Taste

In the prospective study of 11 people with PD, 1 person experienced ageusia at 1 day and another 1 at 1 month (Yamatoto 2021).

In the prospective study of 18 people with PD, thalamotomy-related complications were reported in 5 people with 1 person experiencing dysgeusia (n=1, 3%) with a gradual improvement in the 3 months after MRgFUS thalamotomy (Saporito 2023).

In the prospective study of 26 people with PD, 1 person experienced hypogeusia for 3 months after the procedure (Sinai 2022).

In the systematic review of 77 people with PD, 1 person experienced hypogeusia (MRgFUS targeting the VIM; Lin 2021).

Gait disturbance

In the prospective study of 11 people with PD, 1 person experienced gait disturbance related to thalamotomy during the procedure, 3 person experienced disturbance at 1 day, and 1 person experienced disturbance at 1 month (Yamatoto 2021).

In the retrospective study of a single centre experience with 160 procedures of MRgFUS thalamotomy (10 procedures for people with PD), 1 day after surgery (n=160), the most common adverse event was gait imbalance (57%). At the 3-month follow up (n=116), gait imbalance was seen in 26% of people. At the 1 year follow up (n=105), the second most common adverse event was gait imbalance (14%). At the 2-year follow up (n=51), the most common adverse event was gait imbalance (18%; Lak 2022).

In the prospective study of 18 people with PD, thalamotomy-related complications were reported in 5 people, including contralateral weakness (n=3, 8%) and gait instability (n=1, 3%) with a gradual improvement in the 3 months after MRgFUS thalamotomy (Saporito 2023).

In the prospective study of 26 people with PD, 5 people experienced objective unsteadiness on tandem gait for 1 to 4 weeks after the procedure and 1 experienced subjective unsteadiness of gait for 7 days after the procedure (Sinai 2022).

In the retrospective study of 48 people, the most common adverse event at all follow-up time points was gait imbalance, with 59% (29/49) of people affected at day 1. This increased to 64% (28/44) by 1 month, then decreased over time (3 months 38% [13/34], 1 year 27% [6/22], 2 years 20% [1/5]; Chua 2023).

In the systematic review of 77 people with PD, 1 person experienced hypogeusia, 1 person experienced a subjective unsteady feeling when walking and 1 person experienced disturbance when walking tandem, during sonication (MRgFUS targeting the VIM; Lin 2021).

Hand ataxia

In the prospective study of 11 people with PD, 3 people experienced exacerbation of bradykinesia at 1 day (Yamatoto 2021).

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In the prospective study of 26 people with PD, 2 people experienced arm ataxia for 1 to 4 weeks after the procedure, which did not persist (Sinai 2022).

In the systematic review of 77 people with PD, 8 people experienced transient ataxia and 1 person experienced persistent ataxia (MRgFUS targeting the VIM; Lin 2021).

Dysarthria

In the prospective study of 11 people with PD, 1 person experienced dysarthria at 1 day, 1 month and 3 months (Yamatoto 2021).

In the retrospective study of 160 procedures of MRgFUS thalamotomy (10 procedures for people with PD), 1 day after surgery (n=160), the third most common adverse event was dysarthria (19%). At the 1-year follow up (n=105), the fourth most common adverse event was dysarthria (6%; Lak 2022).

In the retrospective study of 48 people, the least common adverse event was dysarthria (16% [8/49] at day 1, 14% [6/44] at 1 month, 6% [2/34] at 3 months; Chua 2023).

Asthenia

In the prospective study of 26 people with PD, 2 people experienced asthenia after the procedure for 1 to 4 weeks, which did not persist (Sinai 2022).

Vocal change

In the systematic review of 77 people with PD, 1 person experienced persistent mild vocal change (MRgFUS targeting the VIM; Lin 2021).

Anecdotal and theoretical adverse events

Expert advice was sought from consultants who have been nominated or ratified by their professional society or royal college. They were asked if they knew of any other adverse events for this procedure that they had heard about

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(anecdotal), which were not reported in the literature. They were also asked if they thought there were other adverse events that might possibly occur, even if they had never happened (theoretical).

They listed the following theoretical adverse events:

- sonications that are done too far laterally have a possibility of inducing limb weakness
- sonications that are done too far inferiorly have a possibility of inducing chorea, which is usually reversible within 2 to 3 months.

Five professional expert questionnaires for this procedure were submitted. Find full details of what the professional experts said about the procedure in the [specialist advice questionnaires for this procedure](#).

Validity and generalisability

- Follow up ranged from 3 months to 60 months.
- Studies were conducted in Israel, Japan, and the US.
- There was no major variability in the procedure technique, and 5 of the 10 studies stated that the ExAblate Neuro device was used.
- Some of the evidence included people with ET rather than PD, and safety outcomes have been included from both.
- The manufacturer, Insightec, was involved in the funding and clinical research support in 6 of the 10 studies.
- All studies concluded that MRgFUS ventral intermediate nucleus thalamotomy is a safe efficacious intervention in improving moderate to severe tremor in Parkinson's.

Existing assessments of this procedure

The treatment guidelines on Parkinson's disease (invasive therapies) by the European Academy of Neurology and the European section of the Movement IP overview: MRI-guided focused ultrasound thalamotomy for moderate to severe tremor in Parkinson's

Disorder Society recommend 'unilateral thalamotomy with MRgFUS only within clinical studies or registries because of the lack of appropriate data'.

The guidelines task force considered that 'there are no sufficient RCTs available for unilateral or bilateral MRgFUS thalamotomy for medically resistant tremor in PD. Although there is promising preliminary data, this treatment should only be applied within clinical studies or registries' (Deuschl 2022).

Related NICE guidance

Interventional procedures

- [Overview | Subthalamotomy for Parkinson's disease | Guidance | NICE](#) IPG65 (June 2004)
- [Overview | Deep brain stimulation for Parkinson's disease | Guidance | NICE](#) IPG19 (November 2003)

NICE guidelines

- Parkinson's disease in adults NICE guideline NG71 (July 2017)

Professional societies

- British Society for Stereotactic and Functional Neurosurgery (BSSFN)
- British Society of Interventional Radiology (BSIR)
- British Society of Neurological Surgeons (BSNS)
- Association of British Neurologists (ABN)

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Evidence from patients and patient organisations

NICE received 1 [submission from a patient organisation](#) about MRI-guided focused ultrasound thalamotomy for moderate to severe tremor in Parkinson's. NICE received **no** questionnaires from patients who had the procedure (or their carers).

Company engagement

NICE asked companies who manufacture a device potentially relevant to this procedure for information on it. NICE received 1 completed submission. This was considered by the IP team and any relevant points have been taken into consideration when preparing this overview.

References

1. Sinai A, Nassar M, Sprecher E (2022). Focused ultrasound thalamotomy in tremor dominant Parkinson's disease: long-term results. *Journal of Parkinson's disease*, 12(1): 199-206
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6. Bond A E, Shah B B, Huss D S (2017). Safety and efficacy of focused ultrasound thalamotomy for patients with medication-refractory, tremor-dominant Parkinson disease: a randomized clinical trial. *JAMA neurology* 74(12): 1412-1418.

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7. Chua M M, Blitz S E, Patrick Ng P R (2023). Focused ultrasound thalamotomy for tremor in Parkinson's disease: outcomes in a large, prospective cohort. *Movement Disorders* 38(10): 1962-1967.
8. Lin F, Wu D, Yu J (2021). Comparison of efficacy of deep brain stimulation and focused ultrasound in parkinsonian tremor: a systematic review and network meta-analysis. *Journal of Neurology, Neurosurgery & Psychiatry* 92(4): 434-443
9. Sperling, SA, Shah BB, Barrett MJ (2018). Focused ultrasound thalamotomy in Parkinson disease: nonmotor outcomes and quality of life. *Neurology*, 91(14): pp. e1275-e1284.
10. Deuschl G, Antonini A, Costa J et al. (2022). European Academy of Neurology/Movement Disorder Society-European Section Guideline on the Treatment of Parkinson's Disease: I. Invasive Therapies. *Mov Disord.* 37(7):1360-1374.

Methods

NICE identified studies and reviews relevant to MRI-guided focused ultrasound thalamotomy for moderate to severe tremor in Parkinson's from the medical literature. The following databases were searched between the date they started to 23 January 2024: MEDLINE, EMBASE, Cochrane Library and other databases. Trial registries and the internet were also searched (see the [literature search strategy](#)). Relevant published studies identified during consultation or resolution that are published after this date may also be considered for inclusion.

The following inclusion criteria were applied to the abstracts identified by the literature search.

- Publication type: clinical studies were included with emphasis on identifying good quality studies. Abstracts were excluded if they did not report clinical outcomes. Reviews, editorials, and laboratory or animal studies, were also excluded and so were conference abstracts, because of the difficulty of appraising study methodology, unless they reported specific adverse events that not available in the published literature.
- Patients with Parkinson's and tremor.

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- Intervention or test: MRgFUS thalamotomy.
- Outcome: articles were retrieved if the abstract contained information relevant to the safety, efficacy, or both.

If selection criteria could not be determined from the abstracts the full paper was retrieved.

Potentially relevant studies not included in the main evidence summary are listed in the section on [other relevant studies](#).

Find out more about [how NICE selects the evidence for the committee](#).

Table 4 literature search strategy

Databases	Date searched	Version/files
MEDLINE ALL (Ovid)	23/01/2024	1946 to January 22, 2024
EMBASE (Ovid)	23/01/2024	1974 to January 22 2024
Cochrane Database of Systematic Reviews – CDSR (Cochrane Library)	23/01/2024	Issue 1 of 12, January 2024
Cochrane Central Database of Controlled Trials – CENTRAL (Cochrane Library)	23/01/2024	Issue 1 of 12 January 2024
International HTA database (INAHTA)	23/01/2024	-

The following search strategy was used to identify papers in MEDLINE. A similar strategy was used to identify papers in other databases.

MEDLINE search strategy

- 1 Parkinson Disease/ 84286
- 2 Parkinsonian Disorders/ 9451
- 3 PD.tw. 193005
- 4 parkinson*.tw. 147490
- 5 Tremor/ or Essential Tremor/ 13254
- 6 Tremor*.tw. 26936
- 7 Movement Disorders/ 16990
- 8 ((movement* or motor) adj4 (disord* or diseas* or dysfunct*)).tw. 57655

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9 (shaking palsy or shaking palsies).tw. 83
10 (Paralysis adj4 agitans).tw. 204
11 or/1-10 355249
12 Magnetic Resonance Imaging/ 482375
13 Magnetic Resonance Imaging, Interventional/ 1871
14 MRI.tw. 317937
15 ((MR or magnet*) adj4 (guid* or imag* or resonanc*)).tw. 470159
16 or/12-15 800244
17 exp Ultrasonic Therapy/ 14094
18 Ultrasonography, Interventional/ 28603
19 High-Intensity Focused Ultrasound Ablation/ 2254
20 ((ultraso* or ultra-so*) adj4 (therap* or surg* or ablat* or thalamotom*)).tw. 17476
21 ((High-intensity or focus*) adj4 (ultraso* or ultra-so* or thalamotom*)).tw. 10839
22 (focus* adj4 acoustic* adj4 energy*).tw. 65
23 (ultrasonograph* adj4 intervention*).tw. 463
24 HIFU.tw. 3007
25 thermoablat*.tw. 542
26 (therm* adj4 ablat*).tw. 5970
27 or/17-26 66218
28 11 and 16 and 27 457
29 (MRgFUS or MRgHIFU).tw. 711
30 28 or 29 969
31 exablate.tw. 69
32 30 or 31 992
33 animals/ not humans/ 5155377
34 32 not 33 897
35 limit 34 to ed=20230118-20240131 73
36 limit 34 to dt=20230118-20240131 102
37 35 or 36 116

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Other relevant studies

Other potentially relevant studies to the IP overview that were not included in the main evidence summary (tables 2 and 3) are listed in table 5.

Table 5 additional studies identified

Article	Number of patients and follow up	Direction of conclusions	Reason study was not included in main evidence summary
Dahmani, L., Bai, Y., Li, M., et al. (2023). Focused ultrasound thalamotomy for tremor treatment impacts the cerebello-thalamo-cortical network. <i>npj Parkinson's Disease</i> , 9(1), 90.	Non-randomised controlled trial N=13	MRgFUS is a highly efficient treatment for tremor, and that lesioning the VIM may result in the reorganization of the cerebello-thalamo-cortical tremor network.	More comprehensive studies added to evidence summary. Not all patients had PD, some had ET.
Fasano, A., Llinas, M., Munhoz, et al. (2017). MRI-guided focused ultrasound thalamotomy in non-ET tremor syndromes. <i>Neurology</i> , 89(8), 771-775.	Case series N=6 (3 PD, 2 dystonic tremor and 1 dystonia gene-associated tremor)	Vim MRgFUS is a promising, incision-free, but invasive technique to effectively treat tremors but further future studies on larger samples and longer follow-up are necessary to assess effectiveness and safety.	More comprehensive studies added to evidence summary. Not all patients had PD.
Golfrè Andreasi, N., Cilia, R., Romito, et al. (2022). Magnetic resonance-guided focused ultrasound thalamotomy may spare dopaminergic therapy in early-stage tremor-dominant Parkinson's disease: a pilot study. <i>Movement</i>	Prospective case series N=10	In early-stage tremor-dominant PD, MRgFUS thalamotomy may be useful to reduce tremor and avoid the need to increase dopaminergic medications.	More comprehensive studies added to evidence summary. Results were based on patients receiving FUS and oral dopaminergic therapy.

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<i>Disorders</i> , 37(11), 2289-2295.			
Iacopino, D. G., Gagliardo, C., Giugno, A., Giammalva, G. R., Napoli, A., Maugeri, R., ... & Lagalla, R. (2018). Preliminary experience with a transcranial magnetic resonance-guided focused ultrasound surgery system integrated with a 1.5-T MRI unit in a series of patients with essential tremor and Parkinson's disease. <i>Neurosurgical Focus</i> , 44(2), E7.	Case series N=26	The transcranial MRgFUS procedure using a 1.5-T MRI unit resulted in a safe and effective treatment option for motor symptoms in patients with ET and PD.	More comprehensive studies added to evidence summary. Not all patients had PD, some had ET.
Jung, N. Y., & Chang, J. W. (2018). Magnetic resonance-guided focused ultrasound in neurosurgery: taking lessons from the past to inform the future. <i>Journal of Korean medical science</i> , 33(44).	Review article	MRgFUS is an important first step for the ideal neurosurgery for neurological disorders due to its non-invasive nature and safety. Larger scaled data from phase II and III trials are necessary to confirm the efficacy.	More comprehensive studies added to evidence summary.
Ko, T. H., Lee, Y. H., Chan, L., et al. (2023). Magnetic Resonance-Guided focused ultrasound surgery for Parkinson's disease: A mini-review and comparison between deep brain stimulation. <i>Parkinsonism & Related Disorders</i> , 105431.	Literature review of 20 studies N=258	MRgFUS offers an effective and relatively safe treatment option for patients with drug-resistant PD-related tremor.	More comprehensive studies added to evidence summary. This systematic review contains data from papers with ablation targets other than the thalamus.

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Lennon, J.C. and Hassan, I., 2021. Magnetic resonance-guided focused ultrasound for Parkinson's disease since ExAblate, 2016–2019: a systematic review. <i>Neurological Sciences</i> , 42, pp.553-563.	Systematic review of 2 studies N= 37 Follow-up of 12 months	This systematic review demonstrates a substantial gap in the literature that must be addressed.	More comprehensive studies added to evidence summary.
Lu, H., Wang, X., & Lou, X. (2023). Current applications for magnetic resonance-guided focused ultrasound in the treatment of Parkinson's disease. <i>Chinese Medical Journal</i> , 136(07), 780-787.	Systematic review of 8 studies N=128 12 months follow up	MRgFUS is an effective therapy for the treatment of PD . However, further clinical trials are required to assess the long-term efficacy and potential risks of MRgFUS.	More comprehensive studies added to evidence summary. This systematic review contains data from papers with ablation targets other than the thalamus.
Magara, A., Bühler, R., Moser, D et al. (2014). First experience with MR-guided focused ultrasound in the treatment of Parkinson's disease. <i>Journal of Therapeutic Ultrasound</i> , 2, 1-8.	Case series N=13	This study demonstrated the feasibility, safety, and accuracy of the MRgFUS pallidothalamic tractotomy.	More comprehensive studies added to evidence summary.
Maragkos, G.A., Kosyakovskiy, J., Zhao, P., et al. (2022) Patient-Reported Outcomes After Focused Ultrasound Thalamotomy for Tremor-Predominant Parkinson's Disease. <i>Neurosurgery</i> , pp.10-1227.	Retrospective study N=29 16 months follow up	Patient satisfaction with FUS thalamotomy for tremor-predominant PD was very high, even at longer term.	More comprehensive studies added to evidence summary.
Ogrodnik R, Sepulveda MC, Fernandez E (2022) Magnetic resonance-guided	Conference abstract	MRgFUS thalamotomy has shown good results in the	More comprehensive studies added to

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<p>focused ultrasound thalamotomy for tremor: First experience in Latin America. MOVEMENT DISORDERS CLINICAL PRACTICE (S1): S8–S73</p>	<p>N=20 (10 ET and 10 PD)</p>	<p>treatment of Parkinson's. The procedure is well tolerated, and adverse events were found to be generally mild and/or transient. However, longer follow-up is needed to confirm results.</p>	<p>evidence summary.</p>
<p>Rodríguez Oroz M C, Parras O, Gorospe A (2020) Efficacy of unilateral thalamotomy by MRgFUS in essential tremor and Parkinson's disease in a large cohort of patients. <i>Movement Disorders</i> (Vol. 35, Suppl. S1)</p>	<p>Conference abstract N=135 (88 ET and 47 PD)</p>	<p>MRgFUS thalamotomy for Parkinson's is associated with a great improvement in tremor at 3-month follow-up. Although side effects are frequent, the vast majority are mild without any clinical relevance.</p>	<p>More comprehensive studies added to evidence summary.</p>
<p>Rohani, M., & Fasano, A. (2017). Focused ultrasound for essential tremor: review of the evidence and discussion of current hurdles. <i>Tremor and Other Hyperkinetic Movements</i>, 7.</p>	<p>Narrative review</p>	<p>Studies have shown the safety and effectiveness of unilateral MRgFUS thalamotomy in the treatment of ET. It has been successfully used in a few patients with Parkinson's disease-related tremor, and in fewer patients with fragile X-associated tremor/ataxia syndrome. The safety and long-term effects of the procedure are still unclear, as temporary and</p>	<p>More comprehensive studies added to evidence summary.</p>

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		permanent adverse events have been reported as well as recurrence of tremor.	
Schlesinger, I., Eran, A., Sinai, A., al. (2015). MRI guided focused ultrasound thalamotomy for moderate-to-severe tremor in Parkinson's disease. <i>Parkinson's disease</i> , 2015.	Case series N=7	Thalamotomy using MRgFUS is safe and effective in PD patients. Large randomized studies are needed to assess prolonged efficacy and safety.	More comprehensive studies added to evidence summary.
Stanziano, M., Golfrè Andreasi, et al. (2022). Resting state functional connectivity signatures of MRgFUS vim Thalamotomy in Parkinson's disease: a preliminary study. <i>Frontiers in Neurology</i> , 12, 786734.	Prospective case series N=20	MRgFUS can effectively modulate brain functional connectivity within the tremor network and related changes are associated with clinical outcome.	More comprehensive studies added to evidence summary.
Tian, X., Hu, R., He, P. and Ye, J., (2023) Efficacy and safety of magnetic resonance-guided focused ultrasound for Parkinson's disease: a systematic review and meta-analysis. <i>Frontiers in Neurology</i> , 14, p.1301240.	Systematic review and meta-analysis of 20 studies N=258	MRgFUS offers an effective and relatively safe treatment option for patients with drug-resistant PD-related tremor	More comprehensive studies added to evidence summary. This systematic review contains data from papers with ablation targets other than the thalamus.
Wang, X., Wang, S., Lin, J., et al.. (2023). Gray matter alterations in tremor-dominant Parkinson's disease after MRgFUS thalamotomy are correlated with tremor improvement: a pilot study. <i>Quantitative</i>	Prospective case series N=9	Grey matter volume can be used to reflect tremor improvement after MRgFUS thalamotomy.	More comprehensive studies added to evidence summary.

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<i>Imaging in Medicine and Surgery</i> , 13(7), 4415.			
Xu, Y., He, Q., Wang, et al. (2021) Safety and efficacy of magnetic resonance imaging-guided focused ultrasound neurosurgery for Parkinson's disease: a systematic review. <i>Neurosurgical Review</i> , 44, pp.115-127.	Systematic review of 11 studies N=147 Follow-up ranging from 3 weeks to 30 months	Most adverse events were mild and transient. MRgFUS is a potential treatment for PD with satisfying efficacy and safety.	More comprehensive studies added to evidence summary.
Yongqin Xiong, Dongshan Han, Jianfeng He et al. (2022) Correlation of visual area with tremor improvement after MRgFUS thalamotomy in Parkinson's disease. <i>Journal of neurosurgery</i> , 136(3), pp.681-688.	Prospective study N=9 PD participants treated with MRgFUS, 12-month follow-up	The present study investigated the impact of MRgFUS ventral intermediate nucleus thalamotomy on spontaneous neural activity in medication-refractory tremor-dominant PD. The visual area is relevant to tremor improvement in PD after MRgFUS thalamotomy, suggesting a distant effect of MRgFUS thalamotomy and the involvement of specific visuomotor networks in tremor control in PD.	More comprehensive studies added to evidence summary.
Zaaroor, M., Sinai, A., Goldsher, et al. (2017). Magnetic resonance-guided focused ultrasound thalamotomy for tremor: a report of 30	Case series N=30 (18 ET, 9 PD and 3 ET-PD)	MRgFUS VIM thalamotomy to relieve medication-resistant tremor was safe and effective in	More comprehensive studies added to evidence summary. Not all

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Parkinson's disease and essential tremor cases. <i>Journal of neurosurgery</i> , 128(1), 202-210.		patients with ET, PD, and ET-PD but large randomised controlled trials are needed to assess longer term efficacy and safety.	patients had PD, some had ET.
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