

# Transcranial Focused Ultrasound in Functional Neurosurgery for Essential Tremor and Parkinson's Disease: A Review Article

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## ABSTRACT

**Purpose:** Transcranial magnetic resonance guided focused ultrasound (MRgFUS) is a new development in the field of functional neurosurgery. A comprehensive review of the current literature was performed to evaluate of transcranial MRgFUS in treatment of essential tremor (ET) and Parkinson's disease.

**Methods:** Articles available in electronic databases of PubMed, and Web of Science, as of July 2016 were reviewed. The strategy included a combination of key words 'MRgFUS', 'tremor', 'Parkinson', 'brain', 'head', 'tumor', 'transcranial' and 'focused ultrasound' in the title and abstract of the manuscripts. In addition transcranial MRgFUS systems and cost-effectiveness of treatment were assessed. Finally, the major findings are summarized.

**Results:** Fifty-eight articles met the inclusion criteria for review. Among these, 15 studies eligible for inclusion in this review. The synthesis of the data demonstrated that, transcranial MRgFUS have been successfully used for treatment of essential tremor and Parkinson's disease. Lesions were created under real-time MRI guidance, with peak temperatures of between 52° C and 63° C. Adverse events during transcranial MRgFUS reported such as headache, dizziness, vertigo, lip paresthesia, and hypogeusia. However, there were no significant treatment-related complications or side effects. At present, one of the limitations of transcranial MRgFUS is high price of treatment. However, continued advances in technology can be expected to further refine the high price market of transcranial MRgFUS.

**Conclusion:** The findings showed that essential tremor and Parkinson's disease can be effectively treated with transcranial MRgFUS method. Long-term clinical data are forthcoming.

**Keywords:** Transcranial Focused Ultrasound; Essential Tremor; Parkinson's Disease

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## INTRODUCTION

Essential tremor (ET) is the most common movement disorder; its cause is unknown. It naturally involves a tremor of the arms, hands or fingers but sometimes involving the head, vocal cords or other body parts during voluntary movements such as eating and writing<sup>1</sup>. On the other hand, Parkinson's disease (PD) is a disorder of the central nervous system that mainly affects the motor system<sup>2</sup>. Early in the disease, the most symptoms are

shaking, rigidity, slowness of movement, and difficulty with walking<sup>2</sup>. Thinking, and behavioral problems, and dementia may also occur. Depression and anxiety are also common occurring in more than a third of people with PD<sup>3</sup>. Up to 20% of patients with ET may develop PD, and 10% report a family history of PD. However, whether ET is a risk factor for PD remains an unresolved and somewhat controversial issue<sup>4</sup>.

Several options exist for treatment of essential tremor,

including radiofrequency lesioning, deep brain stimulation (DBS) and Gamma knife radiosurgery of the ventralis intermedius nucleus of the thalamus. However, it is vital that optimum treatment strategy for ET and PD remains uncertain<sup>5</sup>. Although, for over 50 years researchers have been trying to perform noninvasive thermal ablation for brain treatments<sup>6-7</sup>. However, high-intensity focused ultrasound (HIFU) or magnetic resonance guided focused ultrasound (MRgFUS) is a novel technique and has been developed as a surgical tool to precisely create focal thermal lesions in the body<sup>5</sup>. MRgFUS is involving minimally-invasive or non-invasive methods to deliver highly focused acoustic energy into the body with a potential role to treat a range of disorders<sup>8-9</sup>, such as targeted drug delivery<sup>10</sup>, neurostimulation<sup>11</sup>, and several other diseases<sup>12</sup>. Transcranial MRgFUS, have been used to direct acoustic energy, without the need for craniotomy or implanted hardware to precisely generate focal thermal lesions in the brain for the treatment of patients with neuropathic pain, essential tremor or Parkinson's disease<sup>5,9,13-14</sup>, ablation of tumors,<sup>15</sup> blood-brain barrier disruption<sup>10</sup>, and psychiatric diseases<sup>16</sup>. It also will eventually change the future management of many patients<sup>14</sup>.

Transcranial MRgFUS provides numerous unique properties for scientific and practical medicine<sup>17</sup>. It's a method of targeted tissue thermal ablation in the field of functional neurosurgery<sup>17</sup>. In recent years, some clinical studies have demonstrated that transcranial MRgFUS could be used for the treatment of patients with essential tremor or Parkinson's disease<sup>8,13,17</sup>. Recently, the transcranial MRgFUS is approved for treatment of ET in patients who have not responded to medication<sup>18-19</sup>. Hence, this manuscript provides a review of updated recommendations to evaluate of transcranial MRgFUS in functional neurosurgery for essential tremor and Parkinson's disease in the critical care.

## MATERIAL AND METHODS

### Physics of transcranial MRgFUS

When an ultrasound wave propagates through biological tissue, thermal and mechanical, or non-thermal, effects occur. Ultrasound can be focused, either via a lens, a curved transducer, or a phased array or any combination of the three methods into a small focal zone. As an acoustic wave propagates through the tissue, part of it is absorbed and converted to heat. A thermal mechanism of focused ultrasound creates a rapid temperature rise at the focus and can be utilized to treat many diseases. In MRgFUS therapy, ultrasound beams

are focused on diseased tissue and due to the significant energy deposition at the focus, temperature within the tissue can rise to levels from 65° to 85° C, destroying the diseased tissue by coagulation necrosis. Higher temperature levels are typically avoided to avoid boiling of liquids inside the tissue.<sup>19</sup> In transcranial MRgFUS, ultrasound energy is delivered across the skull, without an incision or craniotomy, heating the targeted tissue above the protein denaturation threshold at temperatures near 60° C. Prior to the delivery of high temperatures, destructive sonication delivery of lower energy focused ultrasound allows for proper anatomic localization, as well as physiologic evaluation of symptom relief and/or any unwanted side effects. This process allows for adjustments before making a permanent lesion. Treatment effects are immediate and the several hour treatment is generally well tolerated with mild sedatives<sup>19</sup>. In patients with ET or PD, the effect of transcranial MRgFUS is according to tissue destruction within the Vim nucleus of the thalamus which enables a highly accurate and controlled thermal effect.

### Transcranial MRgFUS (Intervention) procedure

The commercially available MRgFUS system (InSightec LTD, Carmel-Tirat, Israel) combines a clinical 3 Tesla MRI system with a transcranial hemispheric array transducer (650 kHz) that has 1024 ultrasound elements. It also consists of a radiofrequency driving electronics, water cooling and degassing system, electronic interfaces to remote control the MR scanner and access the scanner's image database, and a workstation next to the scanner console to operate and control the focused ultrasound procedure. Patient's anisotropic skull bone requires CT-based analysis and modeling of ultrasound beam aberration to set phase and amplitude for each transducer element individually allowing for electronic steering of the focus<sup>9</sup>. The patient's head is shaved and is fixed to the system in a stereotactic frame and the transducer is filled with degassed water to allow ultrasound waves to propagate toward the patient's head. A diaphragm placed around the patient's scalp keeps the water in place. Treatment planning is based on MRI, and MR thermometry is used for target verification during the sonication process. Each sonication typically lasts 10–25 seconds and is monitored by MRI and MR thermometry until the ablative peak temperature between 56° C and 62° C is reached. Transcranial MRgFUS allows shaping of any desired lesion volume by electronically repositioning the thermal hotspot. There are no trajectory restrictions. During the cooling periods of several minutes duration

between each treatment sonication, the awake patients are interviewed and neurologically examined for desired therapeutic or undesired adverse somatosensory and motor effects.<sup>9</sup> All steps of transcranial MRgFUS are shown in Figure 1.

### Advantages of transcranial MRgFUS

Advantages of MRgFUS neurosurgery are (a) Physician & Clinical value; completely non-invasive; no penetrating trajectories, no ionizing radiation, real time MRI for targeting, real time thermal feedback, intra-operative physiologic feedback, and sharp, accurate, lesions as small as 2 mm. (b) Patient value, no craniotomy, no implanted hardware, immediate results, minimal risk of infection, bleeding or other surgical complications, single session treatment with no anesthesia, short recovery time, with minimal hospitalization. (c) Economic value; little to no hospitalization period, attract and treat additional patient groups, strengthen hospital/clinic leadership in innovation and advanced care<sup>19</sup>. In addition, since no device is implanted into the brain, there is no restriction to future diagnostic work-up with MR-imaging<sup>9,19</sup>.

### Search strategy

A comprehensive literature search was performed to assess all relevant citations found in PubMed, and Web of Science, for the following key words individually or in combination in the English language: ‘MRgFUS’, ‘tremor’, ‘Parkinson’, ‘brain’, ‘head’, ‘tumor’, ‘transcranial’, ‘cost-effectiveness’ and ‘focused ultrasound’ in the title and abstract of the manuscripts. Since the first study of proton therapy in neurosurgery was published in 2013, time interval was set from 2013 to present (2016). The date of the last search was 1 August 2016.

### Inclusion and exclusion criteria

All research articles using the transcranial MRgFUS in treatment patients with ET and PD were included. Papers were excluded if the topic was about other disease conditions or the manuscript dealt with human cadaver studies.

### Data synthesis

The data obtained from each study were synthesized by providing descriptive tables reporting authors’ names, publication year, study setting, study sample, disease

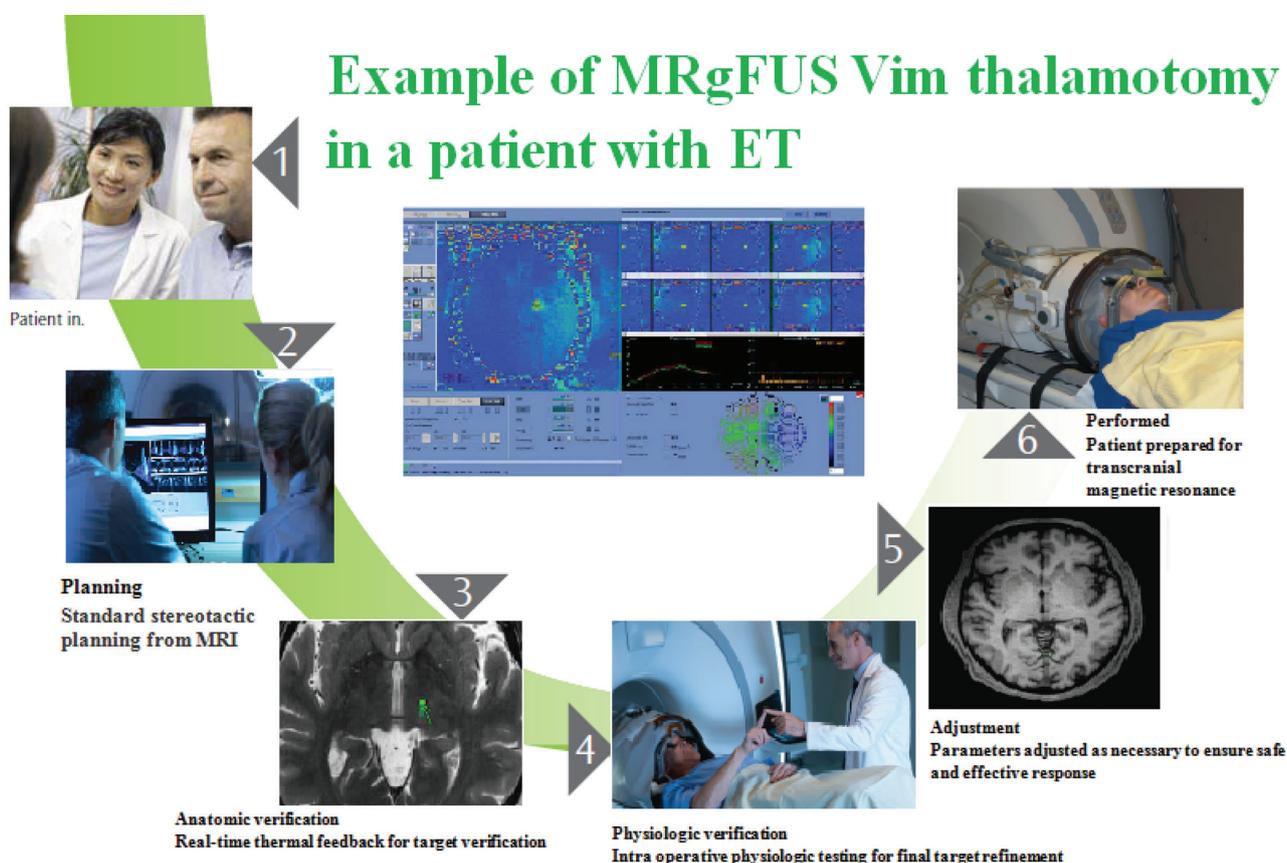


Figure 1. All steps of transcranial MRgFUS.

conditions (where relevant data were available), and the main findings or conclusions. The findings were then sorted and presented chronologically.

## RESULTS

### Statistics

Fifty-eight articles met the inclusion criteria for review. Among these, 15 studies involved humans. Overall, 43 papers were found irrelevant. Thus, 15 were included in this review (Figure 2). Factor of “Cost-effectiveness of transcranial MRgFUS” was assessed. In addition the application of transcranial MRgFUS in patients with essential tremor and Parkinson’s disease were assessed. The major findings are summarized and presented under the following headings.

### Cost-effectiveness of treatment of transcranial MRgFUS

One of the limitations of transcranial MRgFUS is high price of treatment. Current MRgFUS systems are expensive, and there are no regulatory-approved clinical applications for brain disorders. The setup cost for such a system involves the purchase of a 3-T clinical-grade MRI scanner as well as the MRI-compatible ultrasound

transducer for brain targeting <sup>12</sup>.

### Transcranial focused ultrasound for Essential Tremor

To date, transcranial MRgFUS has been used in human clinical trials to create thermal lesions for treatment of essential tremor (ET) <sup>5,9,13-14,18,20-30</sup>. A number of studies have in relation to reviewed paper <sup>25-26</sup>, or neurophysiologic effects <sup>27</sup>. In the other hand, some studies have also assessed the targeting accuracy in transcranial MRgFUS <sup>23</sup>, and different MRI patterns in patients with essential tremor after transcranial MRgFUS <sup>24,28</sup>. One study after treatment with transcranial MRgFUS showed that one patient experienced persistent finger paresthesias and another developed a deep venous thrombosis requiring anticoagulation <sup>20</sup>. However, there were no significant treatment-related complications or side effects. All of patients underwent thalamotomy. Lesions were created under real-time MRI guidance, with peak temperatures of between 54° C and 63° C <sup>14</sup>, as measured by real-time MRI thermometry. A list of papers on transcranial MRgFUS used in the essential tremor is shown in Table 1. At present, transcranial MRgFUS for ET were approved in countries as European CE Mark and South Korea, Canada and USA <sup>19</sup>.

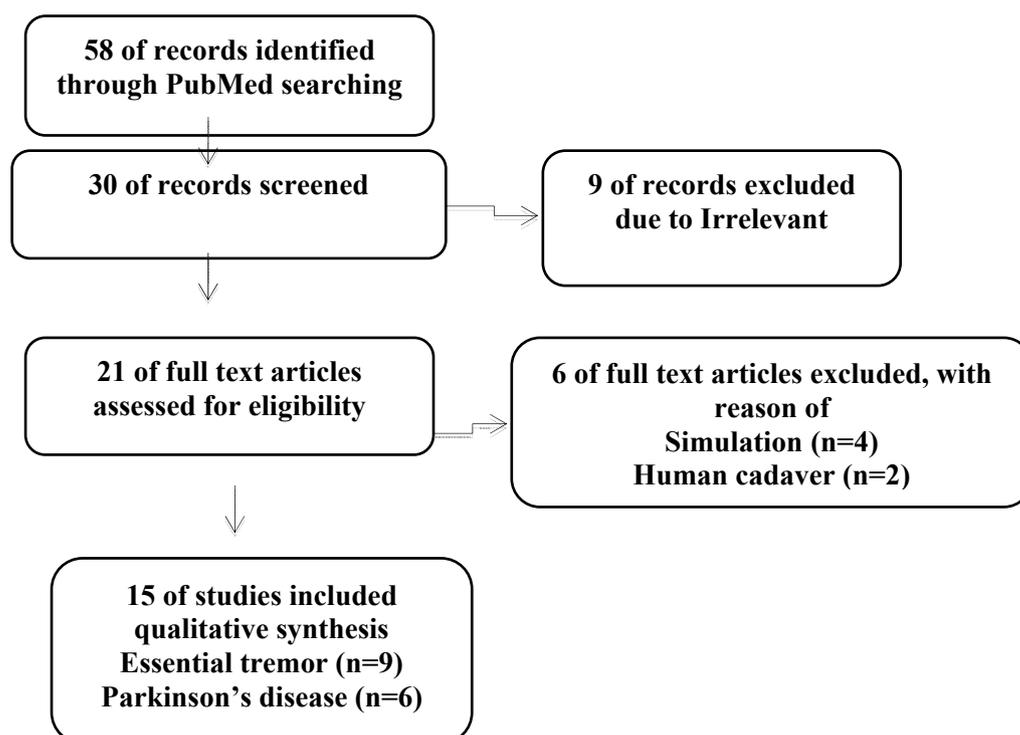


Figure 2. Relevant manuscript selection process.

**Table 1.** A list of papers on transcranial focused ultrasound used in essential tremor

Author(s) Ref	Year	Country	Institution	Sample size	Main focus	Comparison with other treatment	Results/Conclusion(s)
Lipsman et al. <sup>20</sup>	2013	Canada	Toronto Western Hospital, University of Toronto	4	To assess transcranial MRgFUS approach in ET	NR	Patients showed immediate and sustained improvements in tremor in the dominant hand. Mean reduction in tremor score of the treated hand was 89.4% at 1 month and 81.3% at 3 months. One patient had postoperative paraesthesias which persisted at 3 months. Another patient developed a deep vein thrombosis, potentially related to the length of the procedure. MR-guided focused ultrasound might be a safe and effective approach to generation of focal intracranial lesions for the management of disabling, medication-resistant essential tremor.
Moser et al. <sup>23</sup>	2013	Switzerland	Center of Ultrasound Functional Neurosurgery, Leopoldstrasse	2: 1 in the centrum medianum thalamic nucleus and 1 on the cerebello-thalamic tract	To describe targeting accuracy in transcranial MRgFUS in ET	NR	This study showed that a high accuracy of the MR-guided focused ultrasound technique.
Elias et al. <sup>14</sup>	2013	USA	University of Virginia Health Sciences Center, Charlottesville	15	Effectiveness of tremor suppression using the Clinical Rating Scale for Tremor, hand subscore, and disability subscore were assessed. Patients' perceptions of treatment efficacy with the Quality of Life in Essential Tremor Questionnaire were also evaluated.	NR	Thermal ablation of the thalamic target occurred in all patients. Adverse effects of the procedure included transient sensory, cerebellar, motor, and speech abnormalities, with persistent paresthesias in four patients. Scores for hand tremor improved from 20.4 at baseline to 5.2 at 12 months (P=0.001). Total tremor scores improved from 54.9 to 24.3 (P=0.001). Disability scores improved from 18.2 to 2.8 (P=0.001). Quality-of-life scores improved from 37% to 11% (P=0.001). In this pilot study, essential tremor improved in 15 patients treated with MRI-guided focused ultrasound thalamotomy.
Wintermark et al. <sup>13</sup>	2014	Switzerland	University of Virginia	15	To identify the structural connectivity of the ventralis intermedialis nucleus of the thalamus and determine how DT imaging changes correlated with tremor changes after lesion inducement	NR	Diffusion-tensor (DT) MR imaging after MR imaging-guided focused ultrasound thalamotomy showed changes in specific brain structures. The magnitude of the DT imaging changes after thalamic lesion inducement correlated with the degree of clinical improvement in essential tremor

Table 1. Continued

Author(s) Ref	Year	Country	Institution	Sample size	Main focus	Comparison with other treatment	Results/Conclusion(s)
Wintermark et al. <sup>24</sup>	2014	USA	Charlottesville, Virginia	15	To describe MR imaging findings pre- and post-ventralis intermedius nucleus lesioning by MRgFUS	NR	Transcranial MRgFUS in ET could accurately ablate a precisely delineated target, with typical imaging findings seen in the days, weeks, and months following the treatment
Chang et al. <sup>5</sup>	2015	Korea	Yonsei University College of Medicine, Seoul	11	Tremor severity and functional impairment were assessed at baseline and then at 1 week, 1 month, 3 months and 6 months after treatment. Adverse effects were also sought	NR	All patients showed immediate and sustained improvements in tremors lasting for the 6-month follow-up period. No patient developed significant postsurgical complications; about half of the patients had bouts of dizziness during the MRgFUS. The results showed that MRgFUS thalamotomy was a safe, effective and less- invasive surgical method for treating medication-refractory ET.
Huss et al. <sup>21</sup>	2015	USA	University of Virginia Health System	Bilateral Vim DBS (n=57), unilateral Vim DBS (n=13), or unilateral focused ultrasound Vim thalamotomy (n=15).	Functional outcomes and quality of life in essential tremor patients treated	To compare functional outcomes and quality of life in essential tremor patients treated with either bilateral Vim DBS or unilateral procedures (focused ultrasound or DBS).	Patients underwent bilateral DBS treatment had more baseline tremor and worse quality of life scores. Patients had significant improvements in tremor symptoms and quality of life with all three treatments. Both DBS procedures improved axial tremor. No difference was seen in the degree of improvement in upper extremity tremor score, disability, or overall quality of life between bilateral and either unilateral procedure. Bilateral thalamic DBS improved overall tremor more than unilateral DBS or focused ultrasound treatment; however, unilateral treatments were equally effective in treating contralateral hand tremor. Despite the greater overall tremor reduction with bilateral DBS, there was no difference in disability or quality of life comparing bilateral versus unilateral treatments.
Jung et al. <sup>28</sup>	2015	Korea	Yonsei University College of Medicine, Seoul	11	To report different MRI patterns in patients with essential tremor (ET) after transcranial MR- guided focused ultrasound (MRgFUS)	NR	Successful and failed patient groups showed differences in their ratio of cortical-to-bone marrow thickness (i.e., skull density). The finding showed skull characteristics, such as low skull density, should be evaluated prior to MRgFUS to successfully achieve thermal rise.
Gallay et al. <sup>30</sup>	2016	Switzerland	Center of Ultrasound Functional Neurosurgery, Leopoldstrasse	21	To describe the first results of the MRgFUS cerebellothalamic tractotomy (CTT).	NR	The mean patient estimation of global tremor relief after CTT was 92 % at 2 days and 77 % at 1-year follow-up. The CTT with MRgFUS was shown to be an effective and safe approach for patients with therapy-refractory essential tremor, combining neurological function sparing with precise targeting and the possibility to treat patients bilaterally.

### Transcranial focused ultrasound for Parkinson’s disease

Transcranial MRgFUS has been successfully used for treatment of Parkinson’s disease (PD)<sup>9,17,18,23,29,31-32</sup>. Adverse events during MRgFUS reported such as headache, dizziness, vertigo, lip paresthesia, and hypogeusia<sup>17</sup>. In the other hand, final temperatures at target for treatment of PD were reported between 52° C and 59° C<sup>31</sup>. A list of papers on transcranial MRgFUS used in the PD is shown in Table 2. At present, transcranial MRgFUS for PD were approved in countries as European CE Mark and South Korea.<sup>19</sup>

### DISCUSSION

This literature review on the clinical results of transcranial MRgFUS for essential tremor and Parkinson’s disease demonstrates the precision and efficacy of this

surgical approach and confirms the short-term results. Moreover, the treatment is free of ionizing radiation and is repeatable. However, the evidence on clinical efficacy of transcranial MRgFUS in these patients relies to a large extent on non-controlled studies, and thus is associated with a low level of evidence. Randomized controlled trials to determine the optimal approach for patients with essential tremor and Parkinson’s disease would be beneficial, however, these studies are difficult to complete. Long-term clinical data are forthcoming.

Fifteen patients suffering from severe medication-refractory essential tremor underwent a unilateral VIM thalamotomy with transcranial MRgFUS. Elias et al. were reported after 12 months, a 75% improvement in the tremor on the treated side and 85% improvement in disability. They were also reported that 80% of patients have an improvement between baseline and follow-up.

**Table 2.** A list of papers on Transcranial focused ultrasound used in Parkinson’s disease.

Author(s) Ref	Year	Country	Institution	Sample size	Main focus	Comparison with other radiotherapy	Results/Conclusion(s)
Moser et al. <sup>23</sup>	2013	Switzerland	Center of Ultrasound Functional Neurosurgery, Leopoldstrasse	10: on the pallido-thalamic tract	To describe targeting accuracy in transcranial MRgFUS in ET	NR	This study showed that a high accuracy of the MR-guided focused ultrasound technique.
Bauer et al. <sup>9</sup>	2014	Switzerland	Department of Neurosurgery, Kantonsspital St. Gallen	1	Idiopathic Parkinson’s syndrome with predominant resting tremor. The tremor was not responsive to levodopa treatment. The presynaptic dopaminergic deficit could be confirmed using 123I-FP CIT (DATSCAN) SPECT.	On the basis of the patient’s history as a polytoxicomaniac person with recurrent infections, deep brain stimulation (DBS) was not a therapeutic option and the patient was evaluated for and treated with transcranial MRgFUS	The tremor stopped almost completely immediately after the intervention. During the follow-up period of 6 months no adverse events were reported, especially no psychiatric side effects. The tremor disappeared completely. The score on the Unified Parkinson’s Disease Rating Scale UPDRS part III was 32 points before intervention, and dropped to 24 points (out of 108 possible points) at three and six months control after intervention.
Magara et al. <sup>31</sup>	2014	Switzerland	Praxis für Neurologie, Monbijoustrasse 73, 3007 Bern,	13	To assess initial results of the MRgFUS pallidothalamic tractotomy (PTT),	NR	These patients enjoyed a mean UPDRS reduction of 60.9% and a GSR of 56.7%, very close to the results obtained with radiofrequency lesioning. The targeting accuracy for the whole patient group was 0.5, 0.5, and 0.6 mm for the anteroposterior (AP), mediolateral (ML), and dorsoventral (DV) dimensions, respectively. This study demonstrated the feasibility, safety, and accuracy of the MRgFUS PTT.

Table 2. Continued

Author(s) Ref	Year	Country	Institution	Sample size	Main focus	Comparison with other radiotherapy	Results/Conclusion(s)
Schlesinger et al. <sup>17</sup>	2015	Israel	Rambam Health Care Campus, Haifa, Israel	7	To assess treatment of PD with transcranial MRgFUS	NR	Tremor stopped in the contralateral upper extremity in all patients immediately following treatment. Total UPDRS decreased from 37.4± 12.2 to 18.8± 11.1 (p = 0.007) and PDQ-39 decreased from 42.3± 16.4 to 21.6± 10.8 (p = 0.008) following MRgFUS. These effects were sustained (mean follow-up 7.3 months). Adverse events during MRgFUS included headache (n = 3), dizziness (n = 2), vertigo (n = 4), and lip paresthesia (n = 1) and following MRgFUS were hypogeusia (n = 1), unsteady feeling when walking (n = 1, resolved), and disturbance when walking tandem (n = 1, resolved). Thalamotomy using MRgFUS was safe and effective in PD patients.
Na et al. <sup>32</sup>	2015	Korea	Yonsei University College of Medicine, Seoul	1	To assess the first GPI MRgFUS pallidotomy	NR	At 6-months follow-up, this patient achieved a 60% reduction in UPDRS part III score on medication and 55% reduction off medication without changes in L-dopa equivalent daily dosage.
Bond et al. <sup>29</sup>	2016	USA	University of Virginia Health Sciences Center, Charlottesville	27	To designed a double-blinded, randomized controlled trial to investigate the effectiveness of MRgFUS thalamotomy in tremor-dominant PD. Patients with medication- refractory, tremor- dominant PD were enrolled in the 2-center study and randomly assigned 1:2 to receive either a sham procedure or treatment.	NR	For the primary outcome assessment, there was a mean 50% improvement in hand tremor from MRgFUS thalamotomy at 3 months compared with a 22% improvement from the sham procedures. The 1-year tremor scores for all 19 patients treated with 1-year follow-up data (blinded and unblinded) showed a reduction in tremor scores of 40.6% and a mean reduction in medicated UPDRS motor scores of 3.7 (32%, P = .033). Sham patients had a notable placebo effect with a mean 21.5% improvement in tremor scores at 3 months. Overall, transcranial MRgFUS demonstrated a trend toward improvement in hand tremor, and a clinically significant reduction in mean UPDRS.

Four patients had persistent paresthesias at 12 months with 3 mild and one moderate. Mean peak voxel temperature at the target was 58.5°C (range, 54–63), whereas tremor suppression was usually first noted at about 50°C<sup>14</sup>. On the other study by Lipsman et al. four patients that suffered from severe, medication-refractory essential tremor were treated with transcranial

MRgFUS. Patients showed immediate and sustained improvements in tremor in the dominant hand. Mean reduction in tremor score of the treated hand was 89.4% at 1 month and 81.3% at 3 months. One patient experienced persistent finger paresthesias and another developed a deep venous thrombosis requiring anticoagulation<sup>20</sup>. Similarly, Chang and colleagues treated 11 patients

with refractory ET with Vim transcranial MRgFUS and confirmed similar improvement in contralateral hand tremor of 78% at 6 months in most patients, but 3 of 11 patients were not successfully treated because of inability to achieve sufficient target temperatures.<sup>5</sup> This difficulty with transcranial sonication was found to be correlated with increased skull thickness. More recent study by Gallay et al., reported 21 cases treated with MRgFUS cerebellothalamic tractotomy (CTT)<sup>30</sup>. The mean Essential Tremor Rating Scale (Fahn, Tolosa, and Marin) (ETRS) score for all patients was 57.6±13.2 at baseline and 25.8±17.6 at 1 year (n = 10). The mean patient estimation of global tremor relief after CTT was 92 % at 2 days and 77 % at 1-year follow-up. CTT with MRgFUS was shown to be an effective and safe approach for patients with therapy-refractory essential tremor, combining neurological function sparing with precise targeting and the possibility to treat patients bilaterally<sup>30</sup>. Recently, an international, multicenter, randomized, controlled trial (n=76) has been performed. Patients were randomized to MRgFUS thalamotomy or sham treatment in a blinded fashion. Patients have been followed for 1 year, however, results from this trial was not reported<sup>33</sup>.

In early studies, Magara et al. showed the effects of transcranial MRgFUS to a thalamotomy (pallidothalamic tractotomy, PTT) for 13 patients with medication refractory Parkinson's disease<sup>31</sup>. They were reported that after 3 months patients showed a 61% mean unified Parkinson's disease rating scale (UPDRS) improvement and a mean global symptom relief of 57%. They were also reported that, their PTT lesions were clearly visible on 3 month MRI. Mean maximum target temperature was 56°C from mean maximum energy of 20,400 J. The mean absolute targeting accuracy was 0.5 mm for the mediolateral, 0.5 mm for the anteroposterior and 0.6 mm for the dorsoventral dimension<sup>31</sup>. Schlesinger et al. treated 7 patients with tremor-dominant PD with unilateral Vim MRgFUS and reported outcomes with mean follow-up of 8 months<sup>17</sup>. They reported that tremor ceased in all patients post-treatment and recurred in a mild form in 3 of 7 by 6 months. Mean UPDRS score decreased from 37.4 to 18.8 (50% improvement). Recently, Na and colleague reported the first GPi MRgFUS pallidotomy in a patient with PD and L-dopa-induced dyskinesias. At 6-months follow-up, this patient achieved a 60% reduction in UPDRS part III score on medication and 55% reduction off medication without changes in L-dopa equivalent daily dosage<sup>32</sup>. In addition, ongoing clinical trials such as MRgFUS pallidotomy for L-dopa-induced dyskinesia, MRgFUS

Vim thalamotomy for tremor-dominant symptoms and staged lesioning of the subthalamus for asymmetrical motor impairments are in process to assessment of additional MRgFUS targets for PD<sup>34-38</sup>.

The studies above mentioned showed that transcranial MRgFUS is safe for with essential tremor and Parkinson's disease. However, several issues must be resolved before clinical application of transcranial MRgFUS, including optimal patient selection and management of patients during treatment<sup>5</sup>.

This study has several limitations. First, the range and volume of intracranial treatments are variable. It is not currently possible to focus the ultrasound beams adjacent to the convexity because of physical limitations imposed by the skull; so, central targets are more favorable. Due to the need for ongoing MRI during the procedure, treatment times may be lengthy; especially for the ablation of a large target volume<sup>12</sup>. Continued advances in technology can be expected to further refine our current ability and also the high price market of transcranial MRgFUS. Second, yet no clinical trials have been performed to reveal that transcranial MRgFUS is superior to traditional treatment as DBS. So, large-scale research is required prior to the widespread clinical application. But, we can already state that application of this system will significantly enhance therapeutic potential of functional neurosurgery.

## CONCLUSION

The findings showed that transcranial MRgFUS is effective way to improve essential tremor and Parkinson's disease. However, large, randomized, controlled trials will be needed to assess the procedure's safety and efficacy. It is also clear need for developing transcranial MRgFUS services in the Iran

## Competing interests

The authors declare that they have no competing interests.

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