Comparative Effectiveness of Focused Ultrasound Therapy for Movement Disorders

July 2025

U.S. Department of Veterans Affairs
Veterans Health Administration
Health Systems Research

Recommended citation: Rieke K, Rudolph J, Mai HJ, et al. Comparative Effectiveness of Focused Ultrasound Therapy for Movement Disorders: A Systematic Review. Washington, DC: Evidence Synthesis Program, Health Systems Research, Office of Research and Development, Department of Veterans Affairs. VA ESP Project #22-116; 2025.

AUTHORS

Author roles, affiliations, and contributions (using the CRediT taxonomy) are listed below.

Author	Role and Affiliation	Report Contribution
Katherine Rieke, PhD, MPH	Lead Investigator, Providence Evidence Synthesis Program (ESP) Center Providence, RI	Conceptualization, Methodology, Investigation, Data curation, Visualization, Writing – original draft, Writing – review & editing, Project administration
James Rudolph, MD	Co-Director, Providence ESP Center Director, THRIVE Professor of Medicine, Brown University School of Public Health Providence, RI	Conceptualization, Methodology, Investigation, Data curation, Visualization, Writing – original draft, Writing – review & editing
Htun Ja Mai, MBBS, MPH	Senior Research Associate, Providence ESP Center Brown University School of Public Health Providence, RI	Conceptualization, Methodology, Investigation, Data curation, Investigation, Writing – review & editing
Eduardo Lucia Caputo, PhD	Research Associate, Providence ESP Center Brown University School of Public Health Providence, RI	Conceptualization, Methodology, Investigation, Data curation, Investigation, Writing – review & editing
Victoria Chang, MD	Subject Matter Expert, Providence ESP Center Neurologist, Providence VA Medical Center Providence, RI	Conceptualization, Methodology, Investigation, Data curation, Writing – review & editing
Taylor Rickard, MS	Project Manager, Providence ESP Center Providence, RI	Project administration, Visualization, Investigation, Data curation
Ethan Balk, MD, MPH	Co-Investigator, Providence ESP Center Professor, Brown University School of Public Health Providence, RI	Conceptualization, Methodology, Investigation, Visualization, Writing – original draft, Writing – review & editing
Eric Jutkowitz, PhD	Director, Providence ESP Center Associate Professor, Brown University School of Public Health Providence, RI	Conceptualization, Methodology, Investigation, Funding acquisition, Visualization, Writing – original draft, Writing – review & editing

PREFACE

The VA Evidence Synthesis Program (ESP) was established in 2007 to conduct timely, rigorous, and independent systematic reviews to support VA clinicians, program leadership, and policymakers improve the health of Veterans. ESP reviews have been used to develop evidence-informed clinical policies, practice guidelines, and performance measures; to guide implementation of programs and services that improve Veterans' health and well-being; and to set the direction of research to close important evidence gaps. Four ESP Centers are located across the US. Centers are led by recognized experts in evidence synthesis, often with roles as practicing VA clinicians. The Coordinating Center, located in Portland, Oregon, manages program operations, ensures methodological consistency and quality of products, engages with stakeholders, and addresses urgent evidence synthesis needs.

Nominations of review topics are solicited several times each year and submitted via the ESP website. Topics are selected based on the availability of relevant evidence and the likelihood that a review on the topic would be feasible and have broad utility across the VA system. If selected, topics are refined with input from Operational Partners (below), ESP staff, and additional subject matter experts. Draft ESP reviews undergo external peer review to ensure they are methodologically sound, unbiased, and include all important evidence on the topic. Peer reviewers must disclose any relevant financial or non-financial conflicts of interest. In seeking broad expertise and perspectives during review development, conflicting viewpoints are common and often result in productive scientific discourse that improves the relevance and rigor of the review. The ESP works to balance divergent views and to manage or mitigate potential conflicts of interest.

ACKNOWLEDGMENTS

The authors are grateful to Becky Baltich Nelson, MLS, MS, Gaelen Adam, MLIS, PhD, and Cheryl Banick, MLIS for literature searching and retrieval, external peer reviewers, and the following individuals for their contributions to this project:

Operational Partners

Operational partners are system-level stakeholders who help ensure relevance of the review topic to the VA, contribute to the development of and approve final project scope and timeframe for completion, provide feedback on the draft report, and provide consultation on strategies for dissemination of the report to the field and relevant groups.

Dawn McHale
Program Specialist
Philadelphia PADRECC
National Coordinator
National VA Parkinson's Disease Consortium

Pavan Vaswani, MD, PhD
Attending Neurologist
Philadelphia PADRECC

Technical Expert Panel

To ensure robust, scientifically relevant work, the technical expert panel (TEP) guides topic refinement; provides input on key questions and eligibility criteria, advising on substantive issues or possibly overlooked areas of research; assures VA relevance; and provides feedback on work in progress. TEP members included:

Wael Asaad, MD, PhD
Neurosurgeon
Brown- Rhode Island Hospital

Amie Hiller, MD
Neurologist
Portland PADRECC

Roshni Patel, MD
Neurology Attending Physician
Jesse Brown VAMC

DISCLOSURES

This report was prepared by the ESP Center located at the **VA Providence Health Care System,** directed by Eric Jutkowitz, PhD and James Rudolph, MD and funded by the Department of Veterans Affairs, Veterans Health Administration, Health Systems Research.

The findings and conclusions in this document are those of the author(s) who are responsible for its contents and do not necessarily represent the views of the Department of Veterans Affairs or the United States government. Therefore, no statement in this article should be construed as an official position of the Department of Veterans Affairs. The final research questions, methodology, and/or conclusions may not necessarily represent the views of contributing operational and content experts. No investigators have affiliations or financial involvement (eg, employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties) that conflict with material presented in the report.

Executive Summary

KEY FINDINGS

Essential Tremor (ET):

Magnetic Resonance-Guided Focused Ultrasound (MRgFUS) versus Other Treatments (3 Comparative Studies)

- Bilateral deep brain stimulation (DBS) compared to unilateral MRgFUS may provide better improvement of tremor-related outcomes and quality of life (low confidence).
- There was insufficient evidence to assess adverse events or other outcomes for studies that compared treatments (no conclusions), and no studies reported on functional outcomes.

Unilateral versus Bilateral MRgFUS (3 Comparative Studies)

- Bilateral treatment compared to unilateral treatment may provide better improvement of tremor-related outcomes (moderate confidence).
- There were no differences in functional outcomes between unilateral and bilateral treatments (low confidence).
- There is insufficient evidence for quality of life, adverse events, and other outcomes (no conclusions).

Target Location (2 Comparative Studies)

- MRgFUS targeting the PSA or targets with PSA compared to VIM alone may provide better improvement of tremor-related outcomes (low confidence).
- There is insufficient evidence for adverse events between target locations (no conclusion).
- No other outcomes were reported for this comparison.

Left versus Right Side Treatment (1 Comparative Study)

- Evidence was insufficient to make any conclusions about the effect of treatment side on tremor-related outcomes (no conclusion).
- No other outcomes were reported.

Results from the Systematic Reviews (7 Studies)

- MRgFUS for ET improves tremor-related symptoms, quality of life, and functional outcomes (single group and comparative data), but overall it was not clear how MRgFUS compared to other treatments for these outcomes (certainty of evidence not assessed).
- Results (single group and comparative data) were mixed for the effects of MRgFUS on adverse events for ET (certainty of evidence not assessed).

Parkinson's Disease (PD):

- Only 1 comparative study reported comparative data for PD. There was insufficient evidence to make any conclusions about the use of MRgFUS in these patients.

Results from the Systematic Reviews (7 Studies)

- MRgFUS for PD improved tremor-related outcomes (single group and comparative data), but results were mixed when compared to other treatments (certainty of evidence not assessed).
- Results (single group and comparative data) were mixed for the effects of MRgFUS for PD on quality of life and adverse events (certainty of evidence not assessed).

Other Movement Disorders (4 Single Group Studies):

- Single group studies showed improvements in several outcomes of interest, but there was insufficient evidence to make any conclusions about the use of MRgFUS in patients with dystonia conditions.

Results from the Systematic Reviews (8 studies)

- MRgFUS improved tremor-related outcomes in cohorts of people with mixed conditions (single group and comparative data), but no differences were seen when compared to other treatments (certainty of evidence not assessed).
- For mixed condition studies, reviews favored MRgFUS over other treatments for quality of life, but adverse event outcomes were mixed (certainty of evidence not assessed).

Movement disorders are a group of neurological conditions that cause problems with movement, including changes in movement frequency, speed, or control. The most common movement disorders include Parkinson's disease (PD) and essential tremor (ET), which affect approximately 11.8 and 24.9 million people globally, respectively. Other common movement disorders include dystonia, chorea, and tic disorders.

Treatment options for movement disorders include medications, neurorehabilitation therapy, surgical therapies such as deep brain stimulation (DBS), and more research-based interventions such as stem cell replacement or gene therapies. More aggressive methods, such as invasive lesioning or stimulation therapies, are generally used as second- or third-line treatments after best medical management; however, aggressive therapies are associated with risks of serious adverse events. More recently, high intensity focused ultrasound (FUS) therapy, a noninvasive technique for targeted tissue ablation, has been shown to be effective for treating a variety of health issues including pain, certain cancers, fibroids, and movement disorders. Magnetic resonance-guided focused ultrasound (MRgFUS) combines magnetic resonance imaging (MRI) to target and destroy tissue without damaging surrounding structures or requiring an open surgical approach. MRgFUS has been approved by the US Food and Drug Administration (FDA) for the treatment of ET and PD; however, there is limited information about the comparative effectiveness of MRgFUS relative to other available treatments (*eg*, MRgFUS vs DBS) and minimal evidence about other comparative factors such as anatomical target or unilateral versus bilateral treatments. Additionally, while MRgFUS is being explored for use in other movement-related conditions, such as dystonia, its efficacy to treat these conditions is still uncertain.

CURRENT REVIEW

To help inform decisions about the use of MRgFUS within the VHA, the VA Parkinson's Disease Research, Education, and Clinical Centers (PADRECCs) requested a review of the available evidence

on the efficacy and safety of MRgFUS for movement disorders. The following key questions (KQs) were developed in collaboration with VA partners:

- *Key Question 1a (KQ1a)*: What is the comparative effectiveness of high-intensity focused ultrasound therapy versus other surgical treatments (*eg*, deep brain stimulation, stereotactic radiosurgery and other ablative treatments) applied to specific anatomic targets for the treatment of essential tremor or Parkinson's disease?
    - *Key Question 1b (KQ1b):* Does the comparative effectiveness vary by patient characteristics (including treatment history) and anatomic targets?
- *Key Question 2a (KQ2a)*: What are the benefits and harms of high-intensity focused ultrasound therapy applied to specific anatomic targets for the treatment of other neurological conditions?
    - *Key Question 2b (KQ2b)*: Do benefits and harms vary by patient characteristics (including treatment history) and anatomic targets?

We searched for peer-reviewed articles in PubMed, EMBASE, Cochrane, and ClinicalTrials.gov from inception to August 26, 2024. We used medical subject headings and free text terms specific to FUS, MRgFUS, and movement disorders. We ensured that known relevant publications were captured by our searches. Additional citations were sought from hand-searching reference lists of relevant systematic and non-systematic reviews and consultation with content experts.

We focused on comparative studies only for ET and PD and included single group study designs for other movement disorders. For KQ1, we focused on individuals with ET or PD who were treated with MRgFUS (with or without magnetic resonance guidance) ablation of brain tissue. Studies included randomized controlled trials (RCTs) and nonrandomized comparative studies (NRCS). Comparisons of interest included unilateral versus bilateral treatment, side of treatment, different treatment procedures, and comparisons of anatomical targets. For KQ2, we focused on other neurological conditions that involved movement disorders (such as dystonia). Study designs included RCTs, NRCSs, and single group studies since the overall benefits and harms of MRgFUS for these conditions are unknown.

RESULTS

Of 3,856 records screened, 422 records underwent full-text screening. Upon reviewing the full text of records, 14 studies were eligible and were included for KQ1 and/or KQ2. Additionally, we identified 22 systematic reviews or meta-analyses that were related to our KQs.

The 14 included studies were conducted between 1995 to 2024 and included 497 patients. Nine studies focused on patients with ET, 1 study focused on patients with PD, and 4 studies focused on patients with dystonia conditions. Four studies used a crossover NRCS design (*eg*, patients received a first treatment and were assessed, then received a second treatment and were assessed), 6 NRCS compared 2 or more groups of patients, and 4 studies used a single group design.

We also summarized results from existing systematic reviews that included single group and comparative study designs. Importantly, there was an overlap in the studies included across the existing systematic reviews, as well as overlap with the primary studies included in our current review.

Essential Tremor

Comparative of Effects of MRgFUS from Primary Studies

Nine studies (4 crossover NRCS and 5 NRCS) conducted between 1995 and 2022 reported results for 407 patients with ET. The studies were conducted in the US (*N* = 4), Canada (*N* = 3), Korea (*N* = 1), and the UK (*N* = 1) between 1995 and 2022. The 4 crossover NRCS were low risk of bias. The 5 other NRCS were high risk of bias due to the following concerns: use of crude analyses (*N* = 5), lack of or unclear blinding of the assessor (*N* = 4), concerns about comparator representativeness (*N* = 3), unclear representativeness of the cohort (*N* = 2), and concerns about adequacy of description of the intervention lack of clear eligibility criteria and lack of clear reporting (*N* = 1).

Comparative Effectiveness of Unilateral versus Bilateral

Three crossover NRCS compared unilateral to bilateral MRgFUS treatment. In summary, bilateral treatment compared to unilateral treatment was associated with improved tremor-related outcomes (3 studies; moderate confidence). There were no differences in functional outcomes between unilateral and bilateral treatments (2 studies; low confidence). Evidence is insufficient for quality of life, adverse events, and other outcomes (no conclusion).

Comparative Effectiveness of Treatment Sides

Only 1 NRCS of 98 patients compared outcomes by treatment side. Evidence is insufficient to make any conclusions. No other outcomes were reported for this study.

Comparative Effectiveness of Target Locations

Two NRCS compared target locations for MRgFUS in ET. In summary, there was greater improvement in tremor-related outcomes for MRgFUS targeting the posterior subthalamic area (PSA) or targets with PSA compared to ventral intermedius (VIM) (2 studies; low confidence). Evidence is insufficient for difference in adverse events between target locations (no conclusion). No other outcomes were reported for this comparison.

Comparative Effectiveness of Treatments

Three NRCS reported outcomes comparing MRgFUS for ET. In summary, tremor-related outcomes and quality of life improved for patients who received bilateral DBS compared to unilateral MRgFUS (2 studies; low confidence). Evidence is insufficient for adverse events between MRgFUS and other treatments (no conclusion), and no studies reported on functional outcomes.

Results from Systematic Reviews

Across systematic reviews for ET (*N* = 7 systematic reviews), MRgFUS appears to improve tremor-related symptoms, quality of life outcomes, and functional outcomes, but comparative effectiveness results were mixed, particularly when compared to DBS. Adverse event outcomes also showed mixed results. However, cost outcomes favored MRgFUS over DBS and radiofrequency (RF).

Parkinson's Disease

Comparative of Effects of MRgFUS from Primary Studies

One NRCS compared MRgFUS targeted at either the VIM or the pallidothalamic tract (PTT) in people with PD (*ie*, comparison of anatomical targets). The 40-person study was conducted between 2020–

2022 in Russia. The study was high risk of bias due to concerns about comparator representativeness, use of crude analyses, lack of clarity for blinding of an outcome assessor, and representativeness of the cohort

In summary, evidence is insufficient for recurrence of tremor based on MRgFUS targeted at the VIM or PTT in people with PD (no conclusion). The study did not report tremor-related outcomes, quality of life, function, or adverse events.

Results from Systematic Reviews

Overall for PD ($N = 7$ systematic reviews), MRgFUS appeared to show benefit from before to after treatment for tremor-related outcomes. However, results were mixed when compared to RF or DBS. Results were mixed for quality of life, but 1 review showed improvement in function compared to sham. Results for adverse events compared with sham, RF, or no comparator were mixed.

Other Conditions

Effects of MRgFUS for Dystonia Conditions from Primary Studies

Four single group studies reported results for 50 patients with dystonia conditions that were treated with MRgFUS. The treated conditions included dystonic tremor ($N = 2$), focal hand dystonia (FHD; $N = 1$), and X-linked dystonia-parkinsonism (XDP) ($N = 1$). Three single group studies were moderate risk of bias for having unclear or high risk of blinding of the outcome assessor, high risk of incomplete outcome data, or unclear representativeness of the cohort. One single group study had no concerns (low risk of bias).

In summary, evidence was insufficient on the effect of MRgFUS for people with dystonia conditions on tremor-related outcomes, quality of life, function, or adverse events (no conclusion).

Results from Systematic Reviews for Mixed or Other Conditions

For mixed conditions ($N = 8$ systematic reviews), MRgFUS generally showed improvements in tremor-related outcomes, but no differences were seen when compared to RF, gamma knife, DBS, or other lesioning surgeries based on 2 reviews, and 1 review reported favorable results for MRgFUS compared to stereotactic radiosurgery (SR). Two reviews reported that quality of life results favored MRgFUS over DBS, sham, or without a comparator group. One review reported no difference in function after MRgFUS. Overall adverse event outcomes were mixed.

DISCUSSION

Overall, bilateral compared to unilateral MRgFUS and targeting the PSA versus VIM alone appears to improve tremor-related outcomes for people with ET. There were sparse data on the effect of MRgFUS compared to other active treatment for people with ET. One meta-analysis of single group studies indirectly compared bilateral DBS to unilateral MRgFUS and concluded that bilateral DBS may be more beneficial for tremor control, though less so for postoperative quality of life. However, this was an indirect comparison and there were important baseline differences between patient groups.

For PD, there is limited information on comparisons of MRgFUS to other treatments, use of different treatment targets, or other similar comparisons. Only 1 study of people with PD compared target locations and found a lower recurrence in individuals who received treatment of the PTT target compared to VIM. For other movement disorders, it appears that MRgFUS improves tremor-related

outcomes, quality of life, and function, and that adverse effects generally dissipate by 12 months post procedure. However, we could not draw definitive conclusions about these effects because studies were small, did not include comparison groups, and included a variety of conditions.

Future studies should address several gaps in the evidence base. First, there is a need for more comparative studies (either RCTs or NRCS) that compare target locations, laterality, sides, and different treatments. In addition, future NRCS should adjust for confounders such as patient characteristics and availability of treatment options and infrastructure. Second, many studies noted that slight target adjustments were made during procedures to ensure lesioning was effective. Future studies should document when and how treatment adjustments are made and consider approaches to control for adjustments in the analysis. Third, future studies should aim to compare treatment outcomes based on patient characteristics that might be important for treatment, such as skull density ratio.

There are several strengths and limitations to this systematic review. We employed standard systematic review methodology to capture studies that aligned with the key questions. MRgFUS has already been proven to be effective for ET and PD, so for these conditions we focused only on studies that provided comparative results based on treatment, target location, or laterality. Because of this, the literature base for these conditions was small and did not include several pivotal trials that compared MRgFUS to sham or best medical management. By focusing on comparative studies for ET and PD, we excluded single group studies that may have offered insight into potential adverse effects that may occur from MRgFUS. Furthermore, we chose to only include studies that intentionally and prospectively targeted different treatment locations in the brain. We excluded several studies that conducted post hoc retrospective analyses of people who received treatments in different locations due to concerns of unobserved confounding. While this helped to ensure intentionality in differing treatment targets, the omitted studies that examined lesion location post hoc may offer further insight into the outcome differences based on lesion location. Finally, for conditions other than ET and PD, we included single group studies, which do not provide information on how treatment compares to other treatments including usual medical management.

CONCLUSIONS

MRgFUS has emerged within the last decade as a viable and less invasive alternative for the treatment of movement disorders. For ET, bilateral DBS compared to unilateral MRgFUS may provide better improvement of tremor-related outcomes and quality of life; however, we cannot rule out that these differences are not based on unobserved patient characteristics since comparative studies did not conduct adjusted analyses. We were unable to assess differences between other treatments and MRgFUS for tremor-related outcomes. Staged bilateral MRgFUS compared to unilateral treatment may improve tremor-related outcomes. MRgFUS treatments that target or include the PSA compared to VIM alone may improve tremor-related outcomes. There was insufficient evidence to assess adverse events or other outcomes for the above comparisons. Systematic reviews of single group studies and comparative data indicate that MRgFUS improves tremor-related symptoms, quality of life, and functional outcomes, but it was not clear how these outcomes compare to other treatments.

For PD, the single comparative study found insufficient evidence to make any conclusions regarding the use of MRgFUS when the VIM and/or PTT were targets. There were no direct head-to-head comparisons of MRgFUS targeting the subthalamus nuclear versus the globus pallidus internus for PD. However, systematic reviews of single group and comparative data indicate improved tremor-related

outcomes but with mixed results when compared to other treatments for effects on quality of life, and adverse events.

For other movement disorders—mainly dystonic conditions—single group studies showed improvements in several outcomes of interest, but there was insufficient evidence to make any conclusions about use of MRgFUS in patients with dystonia conditions. Systematic reviews of single group and comparative data indicate improved tremor-related outcomes in those with mixed conditions, but no differences were seen when compared to other treatments. MRgFUS was favored over other treatments for quality of life, but adverse event outcomes were mixed.

Future NRCS should adjust for baseline patient characteristics such as skull density ratios and tremor laterality and distribution. Adverse events have been reported in the larger literature of single group studies of MRgFUS and those of MRgFUS compared to sham. Evidence on adverse events from the comparative studies for the specific diseases discussed was insufficient to draw definitive conclusions. There is a need for well-designed RCTs that compare MRgFUS to other treatments and to understand the effect of different anatomical targets as well as longer-term outcomes of unilateral and bilateral procedures. As the MRgFUS establishes itself in the treatment of movement disorders, these suggestions may allow for more robust studies to better guide patient care and improve outcomes.