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Beyond Tremor Reduction: Embarrassment, Functional Disability, and Quality of Life after MRgFUS Thalamotomy in Essential Tremor

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Abstract

Background

Essential tremor (ET) is a multidimensional disorder impairing quality of life (QoL) through motor and non-motor manifestations. Magnetic Resonance-guided Focused Ultrasound (MRgFUS) thalamotomy reduces tremor, but clinical dimensions associated with patient-perceived benefit remain unclear.

Objective

To characterize 1-year multidimensional outcomes post-unilateral MRgFUS thalamotomy in ET and examine how changes in treated-hand tremor, functional disability, and tremor-related embarrassment relate to QoL.

Methods

From a consecutive institutional cohort undergoing unilateral MRgFUS thalamotomy, 1-year outcome data from 33 ET patients were retrospectively analyzed. Pre/post-MRgFUS changes in motor tremor (CRST), functional disability (CRST Part C), tremor-related embarrassment (ETEA), QoL (QUEST), cognitive and neuropsychiatric domains were evaluated using FDR-corrected paired Wilcoxon tests. Exploratory postoperative QoL associations (n = 26) were evaluated using Spearman correlations (Δ-scores) and an ANCOVA including baseline QUEST, ΔETEA, ΔCRST Part C, and Δtreated-hand tremor.

Results

At 11 ± 2 months post-MRgFUS, treated-hand tremor, functional disability, tremor-related embarrassment, and QoL improved by 69%, 56%, 39%, and 41%, respectively, compared with pre-MRgFUS baseline. Other neuropsychiatric measures and cognition showed no significant change after FDR correction. In a common sample (n = 26), QoL improvement correlated with improvements in embarrassment ($r = 0.67$, $pFDR < 0.001$) and functional disability ($r = 0.60$, $pFDR = 0.002$), but not treated-hand tremor ($r = 0.30$, $pFDR = 0.143$). In the adjusted model, embarrassment ($\beta = 0.43$, $p = 0.019$) and functional disability ($\beta = 0.54$, $p = 0.010$) remained independently associated with post-MRgFUS QoL, treated-hand tremor did not ($\beta = 0.21$, $p = 0.253$).

Conclusion

Improvements in embarrassment and functional disability, but not treated-hand tremor, were independently associated with postoperative QoL. Tremor-related embarrassment, alongside tremor severity and functional disability, should be systematically evaluated in MRgFUS candidates.

Introduction

Essential tremor (ET) affects millions of individuals worldwide [1]. Although traditionally considered a motor condition characterized by action tremor, ET is now recognized as a multidimensional disorder with cognitive, emotional, and social manifestations [1–9]. Non-motor features including depression, anxiety, embarrassment, alexithymia, and impaired social abilities [2, 5, 6, 10, 11], can contribute substantially to quality of life (QoL) impairment, sometimes exceeding the burden of motor symptoms alone [7, 8]. This multidimensional clinical profile highlights the need for comprehensive outcome assessment when evaluating therapeutic interventions in ET.

Among these non-motor manifestations, tremor-related embarrassment is one of the most frequent and clinically meaningful contributors to reduced QoL, yet remains considerably less investigated than motor symptoms. Nearly half of patients with mild tremor report significant embarrassment, which may influence treatment seeking and willingness to consider invasive therapies more strongly than tremor severity alone [3, 12].

Ventral intermediate nucleus (VIM) Magnetic Resonance-guided Focused Ultrasound (MRgFUS) thalamotomy is an effective incisionless treatment for ET, improving tremor severity, disability and QoL [13, 14]. Its efficacy in reducing tremor severity, upper-limb disability and improving QoL has been consistently demonstrated [13, 15]. However, functional disability in ET reflects complex interactions between objective tremor severity and patient-perceived task limitation in daily life [16], suggesting that motor reduction and functional gain do not necessarily align. Current evidence also indicates that MRgFUS thalamotomy does not adversely affect global cognition or most cognitive domains [17–22]. By contrast, neuropsychiatric outcomes remain less well characterized. Prior studies assessing apathy, depression and anxiety have reported heterogeneous findings with some showing significant improvements in depression and/or anxiety after treatment [14, 23], others reporting no meaningful change [24–26], and others suggesting domain-specific or transient effects over time [17, 18].

To date, only one prospective study (n = 53) specifically assessed tremor-related embarrassment after MRgFUS and reported improvement at 4 months post-procedure [27]. However, the relative contributions of tremor severity, functional disability, and tremor-related embarrassment to postoperative QoL after MRgFUS remain unclear. Indeed, beyond documenting tremor reduction, comprehensive assessment of postoperative motor, functional, neuropsychiatric and cognitive outcomes may provide a better understanding of patient-perceived benefit after MRgFUS.

To address these knowledge gaps, we retrospectively analyzed data from the standardized multidisciplinary MRgFUS program established at Geneva University Hospital. We characterized motor, functional, neuropsychiatric, cognitive, and QoL outcomes approximately one year after unilateral VIM-MRgFUS thalamotomy and explored the associations of changes in tremor severity, functional disability, and tremor-related embarrassment with postoperative QoL.

Methods

Study design and participants

This study is a retrospective analysis of systematically collected data from the institutional MRgFUS program at Geneva University Hospitals. The program was established in 2021 together with a standardized multidisciplinary clinical pathway for patients undergoing unilateral VIM-MRgFUS thalamotomy. At the time of its implementation, a multidisciplinary working group developed a predefined assessment battery to comprehensively characterize motor, neuropsychiatric, cognitive and quality-of-life outcomes following VIM-MRgFUS thalamotomy. As part of routine clinical care, all patients selected for unilateral VIM-MRgFUS thalamotomy for ET undergo this standardized assessment battery before treatment and approximately 12 months after the procedure. The assessment protocol remained identical throughout the study period.

The present study includes all consecutive patients with medication-refractory or medication-intolerant ET who underwent unilateral VIM-MRgFUS thalamotomy within the institutional program between June 2021 and December 2025. Patients completed the standardized baseline and approximately 12-month follow-up assessments. Patients undergoing second-side VIM-MRgFUS thalamotomy or without standardized postoperative follow-up were excluded from the present analysis. Most patients without standardized follow-up resided outside the Geneva catchment area, precluding the planned in-person assessment.

All eligible patients were included. No formal sample-size calculation was performed. The clinical assessment pathway was predefined, whereas the association analyses reported here were exploratory and were not specified in a prospective statistical analysis plan. The study is reported in accordance with the STROBE recommendations for observational studies.

The study was approved by the Geneva Ethics Committee (CCER 2025 – 00828). All participants provided written informed consent in accordance with the Declaration of Helsinki.

Unilateral MRgFUS thalamotomy

Patients were considered eligible for unilateral VIM-MRgFUS thalamotomy if they had disabling medication-refractory or medication-intolerant ET according to international consensus recommendations and following multidisciplinary evaluation [28]. MRgFUS thalamotomy was performed using the ExAblate Neuro 4000 system, version 1.1 (Insightec, Haifa, Israel). The VIM was targeted using standard stereotactic coordinates refined by preoperative MRI and intraoperative clinical testing as previously described [29]. All procedures were performed according to the institutional clinical protocol by the same multidisciplinary MRgFUS team (neurologist, neurosurgeon, MRI physicist, neuroradiologist, nurse, and neuropsychologist). The treated hemisphere corresponded to the side contralateral to the most disabling upper-limb tremor. The energy delivered during sonications was progressively increased

until an optimal clinical effect was achieved while minimizing adverse effects, according to routine clinical practice.

Assessments

All assessments were performed by trained members of the multidisciplinary MRgFUS team using standardized institutional procedures. The assessment comprised four predefined domains: (1) motor outcomes, including tremor severity using the Clinical Rating Scale for Tremor (CRST) [30, 31] and gait and balance assessed with the Tinetti Performance-Oriented Mobility Assessment (POMA) [32]; (2) QoL, assessed with the Quality of Life in Essential Tremor Questionnaire (QUEST) [33] ; (3) neuropsychiatric outcomes, including tremor-related embarrassment (ETEA) [33], alexithymia (TAS-20) [34, 35], apathy (SAS) [36], depression (HADS-D) [37], and anxiety (HADS-A) [37]); and (4) cognition, including global cognition, attention, episodic and working memory, executive functions, social cognition, language, visuospatial abilities, and praxis. The complete neuropsychological assessment battery and corresponding references are provided in Supplementary Material (SM) (SM2 and SM10).

For the present analyses, total CRST was used as a measure of overall tremor severity, while CRST Part C was analyzed separately as a measure of tremor-related functional disability. To specifically assess tremor severity in the upper limb contralateral to the treated VIM, we used a side-specific hand tremor score ranging from 0 to 32, with higher scores indicating greater tremor severity. This score was derived from CRST Part A (rest, postural, and kinetic tremor of the hand) and Part B (five tasks involving handwriting, drawing, and pouring) for the hand contralateral to the thalamotomy [13]. Treated-arm kinetic and postural tremor scores were also analyzed separately.

Lower CRST, hand tremor, CRST Part C, ETEA, and QUEST scores indicate less impairment, whereas higher Tinetti scores indicate better mobility.

Statistical analysis

Analyses were conducted in R (version 4.4.2). The primary statistical objective was to characterize postoperative changes across the predefined multidimensional assessment battery. Pre- and post-VIM-MRgFUS changes were assessed using paired Wilcoxon signed-rank tests. Benjamini–Hochberg false discovery rate (FDR) correction was applied separately within each predefined clinical domain. Results are reported as median (interquartile range [IQR]) unless otherwise specified. For key clinical outcomes, paired improvement was additionally quantified using Hodges–Lehmann estimators and 95% confidence intervals, with permutation and leave-one-out analyses used to assess robustness; full results and interval methods are detailed in SM1 and SM3.

Change scores were defined as postoperative minus baseline values. To compare the relationships of tremor-related embarrassment, functional disability, and treated-hand tremor severity with QoL in an identical sample, correlations between ΔETEA, ΔCRST Part C, Δhand tremor score, and ΔQUEST were

restricted to common complete cases (n = 26). Spearman correlations were accompanied by BCa 95% confidence intervals and permutation-based p values; Benjamini–Hochberg FDR correction was applied across the three QoL correlations displayed in Fig. 3.

Independent associations with postoperative QoL were examined using an ANCOVA model with postoperative QUEST as the dependent variable and baseline QUEST, ΔETEA, ΔCRST Part C, and Δhand tremor score as predictors. Postoperative QUEST and all continuous predictors were z-standardized before model fitting to obtain standardized β coefficients. Predictor-specific contributions were summarized using partial R^2. Permutation inference used the Freedman–Lane approach, with BCa bootstrap confidence intervals for coefficients. Variance inflation factors were inspected for multicollinearity.

Sensitivity analyses evaluated total CRST using a change-score model (postoperative QUEST ~ baseline QUEST + ΔETEA + ΔCRST total) and a postoperative-value model (postoperative QUEST ~ baseline QUEST + postoperative ETEA + postoperative CRST total). Exploratory relative-importance analyses partitioned the incremental clinical R^2 using Shapley values. Differences between partial R^2 estimates were summarized with BCa bootstrap confidence intervals, and dependent correlations sharing ΔQUEST were compared using Williams tests. These secondary analyses were considered descriptive and hypothesis-generating.

Missing data were not imputed. Paired pre-post analyses used all available pairs for each measure; multivariable and common-sample association analyses used complete cases for all variables entering the respective model.

Results

Participants and baseline characteristics

Between June 2021 and December 2025, 45 consecutive patients with ET underwent unilateral VIM-MRgFUS thalamotomy within the institutional program. At data lock, eight had not yet reached the approximately 12-month follow-up time point. Of the 37 patients eligible for follow-up, four did not complete the standardized postoperative assessment, leaving 33 patients (21 men) included in the analysis (Fig. 1).

Mean age was 67.4 ± 14.4 years and mean disease duration was 28.9 ± 19.1 years. Twenty-nine patients underwent left-sided and four right-sided VIM-MRgFUS thalamotomy, and mean follow-up was 11 ± 2 months. At baseline, median total CRST was 42 (IQR 18), median QUEST was 45 (IQR 21), and median MoCA was 26 (IQR 2). Baseline demographic and clinical characteristics are summarized in Table 1.

Data completeness varied across assessments, with 15–33 paired observations depending on the measure. Analyses were performed using all available paired observations without imputation. The

common complete-case sample used for the primary QoL association analyses comprised 26 participants.

Flowchart showing the selection of patients from the institutional MRgFUS program for inclusion in the present retrospective analysis.

Table 1
Baseline Demographic and Clinical Characteristics

Demographics	
Number of participants (men)	33 (21)
Mean age in years (SD)	67.4 (14.4)
Mean ET duration in years (SD)	28.9 (19.1)
Hand dominance (left, right) (N)	2, 31
MRgFUS thalamotomy (left, right) (N)	29, 4
Skull density ratio, mean (SD)	0.45 (0.1)
Clinical measures	
QUEST score (/100), median, IQR	45 (21)
CRST total score (/156), median, IQR	42 (18)
MoCA score (/30), median, IQR	26 (2)

CRST, Clinical Rating Scale for Tremor; ET, essential tremor; IQR, Interquartile Range, MoCA, Montreal Cognitive Assessment; MRgFUS, magnetic resonance-guided focused ultrasound; N, number of patients, QUEST, Quality of Life in Essential Tremor Questionnaire, SD, standard deviation.

Clinical outcomes after unilateral VIM-MRgFUS thalamotomy

Significant improvements were observed in tremor severity, functional disability, tremor-related embarrassment, and QoL approximately one year after unilateral VIM-MRgFUS thalamotomy (Table 2; Fig. 2). Total CRST significantly decreased after treatment (pFDR < 0.001). Treated-hand tremor showed a marked improvement, with the median score decreasing from 15 (IQR 7.25) to 4 (IQR 5; pFDR < 0.001), corresponding to an approximately 69% mean improvement relative to baseline. Treated-arm kinetic and postural tremor also significantly improved (both pFDR < 0.001).

Tremor-related functional disability also improved substantially, with median CRST Part C decreasing from 13 (IQR 7.5) to 5 (IQR 6.5; pFDR < 0.001), corresponding to an approximately 56% mean improvement. Mobility, as assessed by the Tinetti score, did not significantly change.

Among neuropsychiatric outcomes, tremor-related embarrassment was the only measure showing significant improvement after FDR correction. Median ETEA decreased from 40 (IQR 16.5) to 18 (IQR 29; pFDR = 0.001), corresponding to an approximately 39% mean improvement relative to baseline. Depression, anxiety, apathy, and alexithymia did not significantly change after correction for multiple comparisons. No significant postoperative decline was detected across the cognitive battery after FDR correction (SM2).

QoL improved substantially, with median QUEST decreasing from 45 (IQR 21) to 22 (IQR 21; pFDR < 0.001), corresponding to an approximately 41% mean improvement relative to baseline (Fig. 2A).

Table 2
Clinical outcomes before and approximately 1 year after unilateral VIM-MRgFUS thalamotomy

Domain	Measure	n	Baseline	1 year	pFDR
Motor	CRST total score (/156)	33	42 (18)	27 (15)	< 0.001
	Hand tremor score (/32)	28	15 (7.25)	4 (5)	< 0.001
	Kinetic tremor score (/4) (treated upper limb)	27	2 (1)	1 (1)	< 0.001
	Postural tremor score (/4) (treated upper limb)	27	3 (1)	0 (0)	< 0.001
	CRST Part C (/32) (disability score)	27	13 (7.5)	5 (6.5)	< 0.001
	Tinetti score (/28)	30	28 (1)	28 (1)	0.374
Neuropsychiatric	ETEA (/70)	31	40 (16.5)	18 (29)	0.001
Quality of life	QUEST (/100)	33	45 (21)	22 (21)	< 0.001

Values are median (IQR). pFDR values are Benjamini-Hochberg-adjusted paired Wilcoxon signed-rank p values within the relevant clinical domain.

Baseline and approximately 1-year scores for treated-hand tremor, total CRST, tremor-related embarrassment assessed with the ETEA, CRST Part C disability, and quality of life assessed with the QUEST. Half-violin plots show score distributions, boxes indicate medians and IQR, and points represent individual participants. Paired observations are connected within participants. Trajectories indicating worsening are highlighted in amber, whereas all other trajectories are shown in light grey. Δ% represents percentage improvement based on group means, calculated as 100 × (baseline mean − 1-year mean) / baseline mean; positive values indicate improvement. Asterisks indicate significance of paired Wilcoxon signed-rank tests after Benjamini–Hochberg false discovery rate (FDR) correction within predefined clinical domains (*pFDR < 0.05; **pFDR < 0.01; ***pFDR < 0.001).

Adverse events

No serious procedure-related adverse events occurred. At approximately 12-month follow-up, 19 of 33 patients reported at least one adverse event, with some patients reporting more than one. All adverse events recorded at this time point were mild, with no moderate or severe events. The most frequent were balance disturbances (n = 10), dysmetria (n = 7), sensory disturbances (n = 7), dysarthria (n = 4), and dysgeusia (n = 3) (Table 3). No clinically significant cognitive or neuropsychiatric adverse events attributable to the procedure were observed.

Table 3
Adverse events at 12-month follow-up after unilateral VIM-MRgFUS thalamotomy

Adverse event	Number
Sensory disturbances	7
Balance disturbances	10
Dysmetria	7
Paresis	0
Dysgeusia	3
Dystonia	0
Dysarthria	4
Dysphagia	0
Headache (> 1 day post-FUS)	0
Fatigue	0
Tinnitus	0
Hypophonia	0
Memory disturbances	0

Patients could be counted in more than one adverse event category.

Clinical factors associated with postoperative QoL

In the common complete-case sample (n = 26), greater reductions in ETEA and CRST Part C were significantly associated with greater improvement in QUEST, whereas the association between treated-hand tremor reduction and improvement in QUEST was not statistically significant (Fig. 3). Spearman correlations with ΔQUEST were $r = 0.67$ for ΔETEA (95% BCa CI 0.39–0.83; pFDR < 0.001), $r = 0.60$ for ΔCRST Part C (95% BCa CI 0.22–0.83; pFDR = 0.002), and $r = 0.30$ for Δhand tremor score (95% BCa CI −

0.15 to 0.64; *p*FDR = 0.143). Formal comparisons between dependent correlations did not demonstrate significant differences between predictor pairs (all $p > 0.11$; Table SM9).

The mutually adjusted ANCOVA, including baseline QUEST, ΔETEA, ΔCRST Part C, and Δhand tremor score, explained 64% of the variance in postoperative QUEST (adjusted $R^2 = 0.57$). After mutual adjustment, both ΔETEA (standardized β = 0.43, 95% BCa CI 0.13–0.68; partial $R^2 = 0.24$; permutation $p = 0.019$) and ΔCRST Part C (β = 0.54, 95% BCa CI 0.09–1.06; partial $R^2 = 0.26$; $p = 0.010$) remained independently associated with postoperative QUEST. In contrast, Δhand tremor score was not independently associated with postoperative QUEST (β = 0.21, 95% BCa CI − 0.31 to 0.57; partial $R^2 = 0.06$; $p = 0.253$). Variance inflation factors ranged from 1.48 to 2.22.

Sensitivity analyses using total CRST were broadly consistent with the primary findings (Table SM6). In the change-score model, both ΔETEA and ΔCRST total were associated with postoperative QUEST after adjustment for baseline QUEST, although the BCa confidence interval for the CRST coefficient included zero. In the postoperative-value model, postoperative ETEA remained associated with postoperative QUEST, whereas postoperative CRST total did not. Exploratory relative-importance analyses attributed 51.8% of the clinical increment in R^2 to CRST Part C, 34.2% to ETEA, and 14.0% to treated-hand tremor (Table SM7); however, pairwise differences in partial R^2 were not statistically supported (Table SM8).

(A) Spearman correlations between changes in ETEA, CRST Part C, and treated-hand tremor scores and change in QUEST were calculated in the common complete-case sample (n = 26). Δ denotes 1-year minus baseline score. Points represent Spearman correlation coefficients (r), horizontal bars represent 95% bias-corrected and accelerated (BCa) bootstrap confidence intervals, and displayed p values are FDR-adjusted permutation p values. **(B)** Independent associations with postoperative QUEST were examined using a single ANCOVA model including baseline QUEST, ΔETEA, ΔCRST Part C, and Δhand tremor score. Each clinical coefficient is adjusted for baseline QUEST and the other two clinical changes. Points represent standardized regression coefficients (β), horizontal bars represent 95% BCa bootstrap confidence intervals, and labels report partial R^2 and Freedman–Lane permutation p values

Discussion

In this retrospective analysis of a standardized institutional MRgFUS program, unilateral VIM-MRgFUS was associated with marked improvements in tremor severity, functional disability, tremor-related embarrassment, and QoL at 1-year follow-up, without detectable cognitive decline. Despite an approximately 69% mean improvement in treated-hand tremor, change in hand tremor was not significantly associated with change in QoL. In contrast, improvements in both tremor-related embarrassment and functional disability were strongly associated with QoL improvement and remained independently associated with postoperative QUEST in the mutually adjusted model. Formal comparisons did not demonstrate significant differences between these associations, providing no evidence that the contribution of embarrassment differed from that of functional disability.

These results are consistent with the growing recognition that the burden of ET extends beyond motor symptoms to important emotional and social consequences. Tremor-related embarrassment is particularly common. More than three-quarters of patients in one clinical cohort reported at least occasional embarrassment, and more than one-third reported it daily [38]. Importantly, embarrassment is not restricted to patients with severe tremor [39]. Louis and Rios found that nearly half of patients with mild arm tremor and no head tremor reported embarrassment, and that embarrassment was associated with greater use of tremor medication independently of tremor severity [3]. The clinical relevance of these dimensions is further supported by patients themselves. In a large survey of more than 1,400 individuals with ET, psychological support, management of embarrassment, and the social effects of tremor were among the most frequently identified unmet treatment needs [40].

Our findings extend the limited literature on non-motor outcomes after MRgFUS thalamotomy. Sit et al. recently reported significant improvements in tremor-related embarrassment, subjective cognition, functional abilities, and QoL approximately four months after unilateral MRgFUS thalamotomy [27]. Our study builds on these observations by showing that improvement in tremor-related embarrassment remains evident at approximately 1 year after treatment and by examining its relationship with QoL alongside motor and functional changes. Within our standardized multidimensional assessment, tremor-related embarrassment was the only neuropsychiatric measure showing significant postoperative improvement after correction for multiple comparisons, while other neuropsychiatric measures did not significantly change and no significant cognitive decline was detected. Most importantly, whereas Sit et al. demonstrated parallel postoperative improvements in embarrassment, functional disability, and QoL, our analyses directly examined the relationships between these changes. Improvements in both tremor-related embarrassment and functional disability were independently associated with postoperative QoL, whereas improvement in treated-hand tremor was not. Thus, although treated-hand tremor showed the largest proportional improvement after MRgFUS, tremor reduction alone may not fully capture patient-perceived benefit.

Clinically, these findings may have implications for how treatment burden and benefit are assessed in patients considered for MRgFUS. Current patient selection for VIM-MRgFUS appropriately prioritizes medication-refractory, functionally disabling tremor, and treatment efficacy is primarily evaluated through motor outcomes. Our results suggest that tremor-related embarrassment should also be systematically assessed, as part of a comprehensive evaluation of disease burden and treatment benefit. Indeed, patients with relatively moderate tremor severity may nevertheless experience substantial embarrassment and associated social avoidance, loss of confidence, and QoL impairment. This does not imply that embarrassment alone should constitute an indication for lesional therapy, particularly given the potential adverse effects of MRgFUS [15, 41]. Rather, validated patient-reported measures of tremor-related embarrassment, alongside motor and functional assessments, may provide a more comprehensive evaluation of disease burden, particularly in patients with substantial embarrassment that persists despite appropriate psychological, occupational, or other supportive interventions.

The principal strengths of this study include the standardized multidisciplinary assessment pathway, which was established before implementation of the institutional MRgFUS program and applied consistently to consecutive patients throughout the study period. This enabled systematic longitudinal assessment of motor, functional, neuropsychiatric, cognitive, and quality-of-life outcomes under routine clinical conditions. An additional strength was the ability to distinguish treated-hand tremor severity from tremor-related functional disability and embarrassment and to examine their relationships with QoL within the same complete-case sample and in a mutually adjusted model. Finally, the use of permutation-based inference, bootstrap confidence intervals, and sensitivity analyses provided additional robustness to the findings despite the relatively modest sample size.

Several limitations should be acknowledged. First, although the clinical assessment pathway and outcome battery were predefined and applied systematically, the association analyses were not specified in a prospective statistical analysis plan and should therefore be considered exploratory and hypothesis-generating. Second, the relatively modest sample size, missing follow-up data, and the use of complete-case analyses (reducing the primary analysis sample to 26 participants) may have introduced selection bias while limiting statistical power, precision, and generalizability of the estimates. Accordingly, although improvements in both tremor-related embarrassment and functional disability were independently associated with postoperative QoL, formal comparisons did not establish differences in the strength or independent contribution of these factors, and some bootstrap confidence intervals indicated substantial uncertainty around predictor-specific estimates. Furthermore, the stronger associations of ETEA and CRST Part C with QUEST may partly reflect conceptual overlap and, for ETEA, shared patient-reported method variance. Third, the observational design precludes causal inference: the observed associations cannot establish that reductions in embarrassment or disability directly caused improvements in QoL. Finally, postoperative QoL and tremor-related embarrassment may be influenced by factors not specifically assessed in this study, including treatment expectations, psychosocial adaptation, coping strategies, and patients' subjective appraisal of tremor in everyday life. Larger prospective studies are needed to confirm these findings and further clarify the respective contributions of motor, functional, and embarrassment-related improvements to patient-perceived benefit after MRgFUS.

In conclusion, unilateral VIM-MRgFUS thalamotomy was associated with substantial improvements in tremor severity, functional disability, tremor-related embarrassment, and QoL at 1-year follow-up. Importantly, improvements in both tremor-related embarrassment and functional disability were independently associated with postoperative QoL, whereas treated-hand tremor reduction was not independently associated with QoL in the mutually adjusted model. These findings highlight dimensions of patient-perceived benefit beyond tremor reduction and support the systematic assessment of tremor-related embarrassment alongside conventional motor and functional measures as part of the multidimensional evaluation of patients with ET before and after MRgFUS.

Declarations

Authors' Roles:

SCC, PRB, SM, and VF contributed to study conception. SCC, PRB, SM and VF contributed to study organization. SCC, CM, ET, AAB, CB, BW, EA, PO, SD, JFB, OL, PRB, SM, and VF contributed to study execution. TC contributed to the retrospective study implementation, initial statistical analysis design and ethics-related procedures. CM reproduced and updated the initial statistical analyses on the expanded dataset and contributed to the revised analyses. AAB developed the revised statistical analysis framework and performed the analyses presented in the current manuscript, with contributions from CM. SCC, TC, ET, CB, BW, EA, PO, JH, SD, JFB, RS, OL, PRB, SM, and VF contributed to statistical analysis review and critique. SCC contributed to writing the first draft. SCC, TC, CM, ET, AAB, CB, BW, EA, PO, JH, SD, JFB, RS, OL, PRB, SM, and VF contributed to manuscript review and critique.

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Financial Disclosures/Conflict of Interest concerning the research related to the manuscript

The authors declare no conflicts of interest relevant to this work.

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Figures

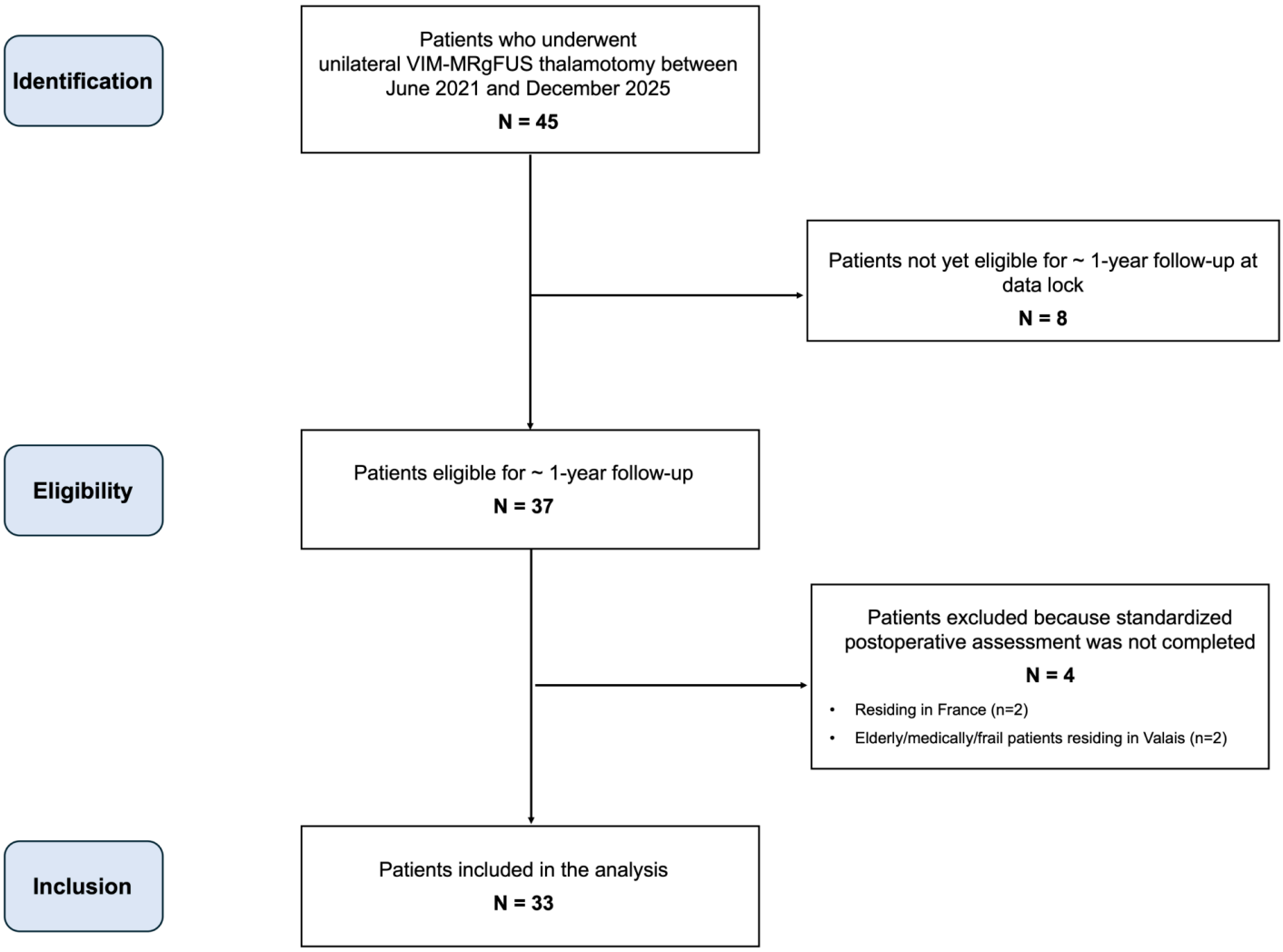


Figure 1

the Flowchart of AdaHet-Clust algorithm.

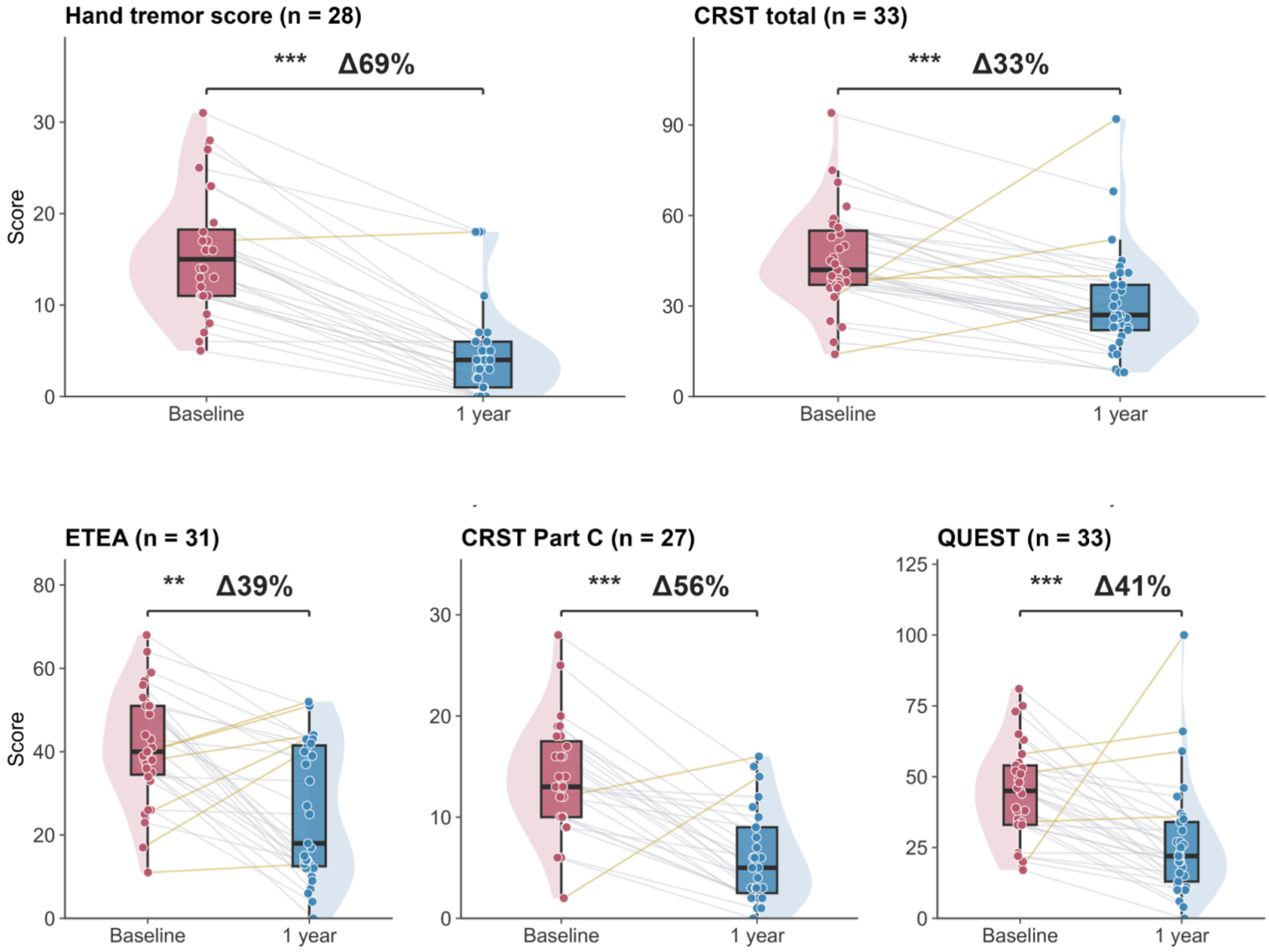


Figure 2

Network lifetime comparison (FND, HND, LND) with error bars showing plus or minus one standard deviation

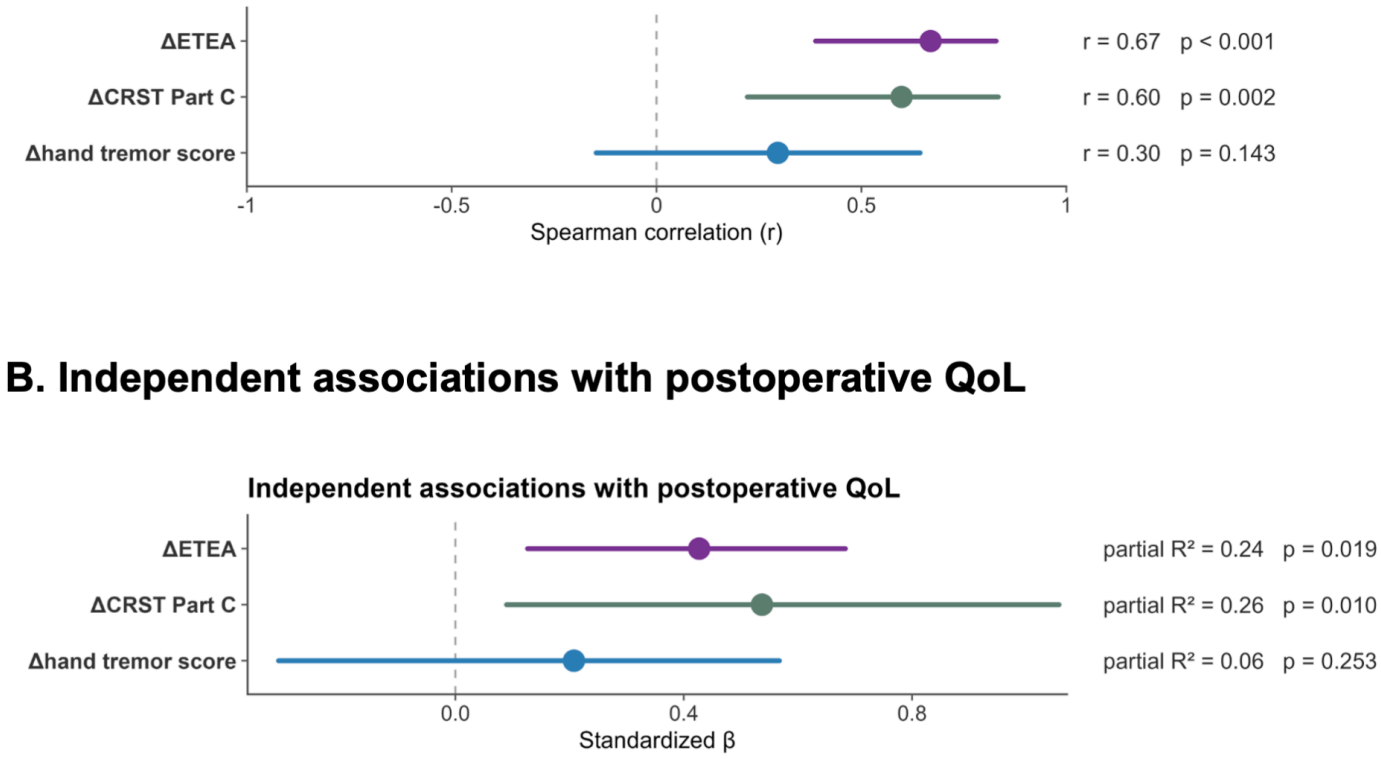


Figure 3

Energy uniformity comparison at Half Node Death.