



MAGNETIC RESONANCE–GUIDED FOCUSED ULTRASOUND THALAMOTOMY FOR MEDICATION-REFRACTORY ESSENTIAL TREMOR: A PROSPECTIVE COHORT STUDY AT SAMARKAND STATE MEDICAL UNIVERSITY

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Abstract. Essential tremor (ET) is one of the most prevalent movement disorders, affecting up to 4–5% of the elderly population. Pharmacological therapy remains first-line treatment; however, a substantial proportion of patients develop medically refractory tremor requiring surgical intervention. Magnetic resonance–guided focused ultrasound (MRgFUS) thalamotomy has emerged as a minimally invasive ablative technique targeting the ventral intermediate nucleus of the thalamus without craniotomy or general anesthesia.

This prospective cohort study conducted at the Neurosurgery Department of Samarkand State Medical University between 2022 and 2025 evaluated the safety and efficacy of MRgFUS thalamotomy in 42 patients with severe medication-refractory ET. Clinical outcomes were assessed using the Clinical Rating Scale for Tremor (CRST) preoperatively and during follow-up up to 24 months.

Significant contralateral tremor reduction was observed, with a mean improvement of approximately 65–70% in limb tremor severity and nearly 40% reduction in total CRST scores ($p < 0.001$). Adverse events were generally transient and mild, including paresthesia and gait imbalance. No permanent neurological deficits or intracranial hemorrhage were recorded.

MRgFUS thalamotomy demonstrated high clinical efficacy and favorable safety profile, supporting its integration into functional neurosurgical practice in tertiary academic centers.

Keywords: Essential tremor; MRgFUS; focused ultrasound; thalamotomy; ventral intermediate nucleus; functional neurosurgery; CRST; minimally invasive neurosurgery.

ТАЛАМОТОМИЯ МЕТОДОМ МАГНИТНО-РЕЗОНАНСНО-КОНТРОЛИРУЕМОГО СФОКУСИРОВАННОГО УЛЬТРАЗВУКА ПРИ МЕДИКАМЕНТОЗНО- РЕФРАКТЕРНОМ ЭССЕНЦИАЛЬНОМ ТРЕМОРЕ: ПРОСПЕКТИВНОЕ КОГОРТНОЕ ИССЛЕДОВАНИЕ САМАРКАНДСКОГО ГОСУДАРСТВЕННОГО МЕДИЦИНСКОГО УНИВЕРСИТЕТА

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Аннотация. Эссенциальный тремор (ЭТ) является одним из наиболее распространённых двигательных расстройств, достигая 4–5% среди лиц пожилого возраста. Медикаментозная терапия остаётся методом первой линии, однако значительная часть пациентов формирует рефрактерность к лечению и нуждается в хирургической коррекции.

Магнитно-резонансно-контролируемый сфокусированный ультразвук (MRgFUS) представляет собой малоинвазивную абляционную технологию, направленную на вентральное промежуточное ядро таламуса без трепанации черепа и общей анестезии. В проспективное когортное исследование, выполненное в нейрохирургическом отделении Самаркандского государственного медицинского университета в 2022–2025 гг., включено 42 пациента с тяжёлым медикаментозно-рефрактерным ЭТ. Эффективность оценивалась по шкале клинической оценки тремора (CRST) в динамике до 24 месяцев. Отмечено статистически значимое снижение контралатерального тремора на 65–70% и общего балла CRST примерно на 40% ($p < 0,001$). Осложнения носили транзиторный характер и включали парестезии и нарушение равновесия. Персистирующих неврологических дефицитов не зарегистрировано. Метод MRgFUS-таламотомии продемонстрировал высокую эффективность и безопасность, что подтверждает целесообразность его внедрения в практику функциональной нейрохирургии.

Ключевые слова: эссенциальный тремор; MRgFUS; сфокусированный ультразвук; таламотомия; вентральное промежуточное ядро; функциональная нейрохирургия; CRST; малоинвазивная хирургия.

**DORI VOSITALARIGA REZISTENT ESSENSIAL TREMORDA MRT NAZORATI
OSTIDA YO'NALTIRILGAN FOKUSLANGAN ULTRATOVUSH YORDAMIDA
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Samarqand davlat tibbiyot universiteti huzuridagi
Ixtisoslashtirilgan ilmiy-amaliy neyroxirurgiya va neyroreabilitatsiya markazi

Annotatsiya. Essensial tremor (ET) eng keng tarqalgan harakat buzilishlaridan biri bo'lib, keksa yoshdagi aholida 4–5% gacha uchraydi. Farmakologik davolash birinchi bosqich hisoblanadi, biroq bemorlarning sezilarli qismida dori vositalariga rezistentlik rivojlanadi va jarrohlik muolajasi talab etiladi. MRT nazorati ostida fokuslangan ultratovush (MRgFUS) talamotomiyasi bosh suyak trepanatsiyasiz va umumiy anesteziyasiz ventral oraliq yadro (VIM)ni selektiv ablyatsiya qilish imkonini beradi. 2022–2025 yillarda Samarqand davlat tibbiyot universiteti neyroxirurgiya bo'limida o'tkazilgan prospektiv kohort tadqiqotiga og'ir, dori vositalariga rezistent ET bilan 42 bemor kiritildi. Klinik samaradorlik CRST shkalasi bo'yicha 24 oygacha kuzatuvda baholandi. Natijada qarama-qarshi tomondagi tremor 65–70% ga kamaydi, umumiy CRST ko'rsatkichi esa taxminan 40% ga pasaydi ($p < 0,001$). Asoratlari vaqtinchalik bo'lib, paresteziya va muvozanat buzilishlari bilan cheklangan. Doimiy nevrologik nuqsonlar aniqlanmadi. MRgFUS talamotomiyasi yuqori samaradorlik va xavfsizlik ko'rsatkichlarini namoyon etdi hamda funksional neyroxirurgiya amaliyotida qo'llash uchun istiqbolli usul ekanligini tasdiqladi.

Kalit so'zlar: essensial tremor; MRgFUS; fokuslangan ultratovush; talamotomiya; ventral oraliq yadro; funksional neyroxirurgiya; CRST; minimal invaziv jarrohlik.

Introduction. Essential tremor (ET) represents one of the most prevalent movement disorders worldwide and constitutes a significant source of disability, particularly in the elderly population. Epidemiological data indicate a prevalence of approximately 0.9% among individuals younger than 65 years and up to 4.6% in older age groups [1]. The disorder is traditionally characterized by bilateral, largely symmetric postural and kinetic tremor of the upper extremities; however, cranial and axial involvement—including tremor of the head, voice, mandible, and lower

extremities—occurs in a substantial subset of patients [2]. Although ET has historically been considered a benign condition, contemporary neurobiological models increasingly conceptualize it as a progressive cerebellothalamocortical network disorder with structural and functional alterations involving the dentate nucleus, red nucleus, and thalamic ventral intermediate nucleus (VIM) [3].

Pharmacological therapy remains the first-line treatment for ET, with beta-adrenergic antagonists (e.g., propranolol) and anticonvulsants (e.g., primidone) forming the mainstay of medical management. Nevertheless, approximately 30–50% of patients exhibit insufficient response or intolerance to medication [4]. For this cohort of medically refractory individuals, neurosurgical interventions such as radiofrequency thalamotomy and deep brain stimulation (DBS) targeting the VIM nucleus have historically provided symptomatic relief [5]. However, these approaches are associated with invasiveness, surgical morbidity, hardware-related complications (in DBS), and resource-intensive perioperative management.

Magnetic resonance-guided focused ultrasound (MRgFUS) thalamotomy has emerged over the last decade as a non-invasive ablative alternative that combines high-intensity focused ultrasound (HIFU) energy delivery with real-time magnetic resonance imaging (MRI) thermometry to create a precisely localized lesion in the VIM nucleus [6]. In 2017, MRgFUS was approved by Roszdravnadzor for the treatment of essential tremor. The kinetic energy of converging ultrasound waves results in rapid thermal elevation at the focal point, inducing coagulative necrosis while sparing surrounding neural structures [7]. The integration of MRI-based stereotaxy and real-time thermometry significantly enhances targeting accuracy and safety, obviating the need for craniotomy, scalp incision, or general anesthesia.

Since June 2022, the Neurosurgery Department of Samarkand State Medical University has implemented MRgFUS thalamotomy for patients with severe, medication-refractory ET. This study presents a comprehensive prospective cohort analysis conducted between 2022 and 2025, evaluating clinical outcomes, safety profile, and quality-of-life measures following unilateral and bilateral MRgFUS thalamotomy.

Materials and Methods. This investigation was designed as a prospective observational cohort study conducted at the Neurosurgery Department of Samarkand State Medical University between June 2022 and January 2025. Ethical approval was obtained from the institutional review board, and informed consent was secured from all participants.

A total of 42 patients diagnosed with severe, medication-refractory essential tremor were enrolled during the study period. The cohort comprised 26 males and 16 females, with a mean age of 64.8 ± 8.9 years (range 49–78 years). Inclusion criteria encompassed a confirmed diagnosis of ET according to Movement Disorder Society criteria, inadequate response or intolerance to at least two pharmacological agents, and significant functional impairment as assessed by the Clinical Rating Scale for Tremor (CRST). Exclusion criteria included severe cognitive impairment, unstable cardiovascular conditions, and contraindications to MRI.

All procedures were performed using an MRgFUS system integrated with a 3T MRI scanner. Patients underwent stereotactic frame placement under local anesthesia. The VIM nucleus was targeted using indirect stereotactic coordinates relative to the anterior and posterior commissures, supplemented by tractography-based visualization of cerebellothalamic pathways when feasible. Low-power sonications were initially administered to verify target localization and assess clinical response. Incremental increases in acoustic energy were delivered until focal temperatures of 55–60°C were achieved, producing a permanent lesion. Real-time MRI thermometry enabled continuous monitoring of temperature gradients and spatial confinement of thermal effects [6].

Intervention Groups. Of the 42 patients, 34 underwent unilateral MRgFUS thalamotomy targeting the hemisphere contralateral to the dominant tremor. Four patients underwent staged bilateral procedures with a minimum interval of six months between interventions. Four patients underwent same-session bilateral procedures following multidisciplinary evaluation.

Primary efficacy endpoints included changes in the Clinical Rating Scale for Tremor (CRST), encompassing Part A (tremor severity), Part B (specific motor tasks), and Part C (functional disability). Assessments were conducted preoperatively, intraoperatively, immediately postoperatively, and at 1, 6, 12, and 24 months post-procedure. Secondary endpoints included

adverse events, neurocognitive changes, and patient-reported quality-of-life metrics. Data were analyzed using non-parametric Wilcoxon signed-rank tests due to non-normal distribution of CRST scores. Statistical significance was established at $p < 0.05$.

Results

Table 1 summarizes demographic and clinical characteristics of the cohort.

Parameter	Value
Number of patients	42
Mean age (years)	64.8 ± 8.9
Male/Female	26/16
Mean disease duration (years)	11.2 ± 4.7
Baseline total CRST score	56.4 ± 9.3

A statistically significant reduction in contralateral tremor severity was observed immediately following sonication. The median reduction in contralateral limb tremor, measured by CRST, reached 68.9% ($V = 512$, $p < 0.001$). Total tremor score improved by 41.7% ($V = 498$, $p < 0.001$). At 12 months, sustained improvement was maintained at 64.2% for contralateral limb tremor and 37.8% for overall tremor burden. Patients undergoing staged bilateral procedures demonstrated additive benefit without significant increase in adverse effects. However, transient gait imbalance was more frequently observed in the bilateral cohort. Adverse events were generally mild and transient. These included paresthesia (19%), transient ataxia (14%), mild dysarthria (7%), and headache (12%). No intracranial hemorrhage, infection, or persistent neurological deficits were observed.

Table 2 outlines complication rates.

Complication	Incidence (%)
Transient paresthesia	19
Transient gait instability	14
Mild dysarthria	7
Persistent deficit	0

Patient-reported outcomes demonstrated significant improvement in functional autonomy and psychosocial well-being. Activities such as writing, eating, and self-care were substantially enhanced post-treatment.

Discussion. Our findings corroborate international data indicating that MRgFUS VIM thalamotomy provides robust tremor suppression in medication-refractory ET [6][8]. The magnitude of tremor reduction observed in our cohort aligns with multicenter randomized controlled trials reporting 47–68% improvement at one year [9]. The absence of hardware-related complications distinguishes MRgFUS from DBS. Additionally, elimination of general anesthesia reduces perioperative risk, particularly in elderly patients with comorbidities. Neurophysiologically, ablation of the VIM nucleus interrupts pathological oscillatory circuits linking the cerebellum and motor cortex, thereby attenuating tremor amplitude [3]. MRI thermometry enhances spatial precision, minimizing collateral damage to adjacent thalamic nuclei and internal capsule fibers. Our study contributes novel data from Central Asia, reflecting successful integration of advanced functional neurosurgical technologies within the Uzbek healthcare system. Limitations include non-randomized design and limited long-term follow-up beyond two years. Further comparative analyses with DBS are warranted.

Conclusion. MRgFUS thalamotomy at the Neurosurgery Department of Samarkand State Medical University between 2022 and 2025 demonstrated significant and sustained reduction in contralateral and overall tremor severity in patients with medication-refractory essential tremor. The procedure exhibited a favorable safety profile and contributed to marked improvements in quality of life. MRgFUS represents an effective, minimally invasive neurosurgical modality that can be successfully implemented in tertiary academic centers in Uzbekistan.

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