Vocal tremor presents in 25% of patients with essential tremor (ET).1 Despite its frequency, the vocal component of ET has been proven to be more difficult to treat than limb tremors, underlining the need for novel therapies and further research.2–4 First-line treatment for ET is pharmacotherapy with propranolol and primidone for symptomatic control, but up to 50% of patients with ET experience no therapeutic benefit from these medications.5,6 Case reports have identified bilateral deep brain stimulation (DBS) of the ventral intermediate nucleus of the thalamus (VIM) to treat vocal tremors successfully.1–3,7–10 with improvement in voice tremor noted immediately and assessed objectively in the operating room.11,12 Although bilateral VIM DBS can improve vocal tremors, it is invasive and carries surgical risks including hemorrhage and infection, along with the need for device management.11 Given the risk involved, invasiveness of the procedure, and uncertain benefit, many patients go untreated despite being good surgical candidates.12

Magnetic resonance imaging–guided focused ultrasound (MRgFUS) ablation of the VIM is a minimally invasive intervention that has shown dramatic results in improving upper extremity tremors.13,14 A recent case series of 9 patients (8 with vocal tremor) undergoing bilateral MRgFUS showed a 45% improvement in Clinical Rating Scale for Tremor (CRST) scores related to vocal tremor.15 In comparison with that following DBS, postoperative quality of life for patients with ET after MRgFUS was found to be higher,11 as only one visit is required and there is no risk of device malfunction. Treatment of vocal tremor using MRgFUS is an attractive option; however, concerns remain surrounding the safety of bilateral thalamotomy, as it has been historically associated with an increased risk of dysphagia and dysarthria.16–18 Despite this, early data indicate that the safety and efficacy of bilateral MRgFUS treatments are very similar to those of unilateral focused ultrasound (FUS), without significant added risk.16–21 Thus, further research into this methodology as an option for patients with difficult-to-treat vocal tremor is needed.
The following case report demonstrates the resolution of vocal tremors in a patient with ET who underwent bilateral VIM thalamotomy with MRgFUS.

Illustrative Case

A 69-year-old male presented with an essential vocal tremor, which prevented him from working as a professional opera singer. Seven years after the onset of the vocal tremor, he also developed bilateral hand tremors. Baseline tremor severity was evaluated as 32 at baseline, according to the CRST. The patient received evaluation by otolaryngology and underwent laryngeal videoendoscopy with stroboscopy (Video 1), during which he was diagnosed with muscle tension dysphonia and laryngeal tremor. Severe pathological supraglottic constriction during phonation and tremulousness of pharyngeal and laryngeal structures with sustained phonation were noted. His self-reported Voice Handicap Index (VHI) score, which captures the patient’s perceived handicap from voice impairment, was a 47 (p = 12; F = 14; E = 21), a moderate rating of self-handicap. His voice was rated a level 4 according to the American Speech-Language-Hearing Association (ASHA) National Outcomes Measurement System (NOMS) for voice, meaning the voice is sometimes distracting, and the ability to participate in vocational, avocational, and social activities requiring a voice is occasionally affected in low-vocal demand activities but consistently affected in high-vocal demand activities. He was given severity modifier code CK, meaning at least 40% but less than 60% impaired, limited, or restricted. He described his voice as “severely affected by his disorder.”

VIDEO 1. Clip showing a laryngeal videoendoscopy with stroboscopy conducted by otolaryngology prior to undergoing treatment with MRgFUS thalamotomy. Severe supraglottic constriction and tremulousness of pharyngeal and laryngeal structures with sustained phonation were noted, and the patient was diagnosed with laryngeal tremor. Click here to view.

The patient was trialed on propranolol without benefit to either his vocal tremor or his bilateral hand tremor. After evaluation, the patient was deemed a candidate for VIM thalamotomy with MRgFUS. Given the lack of available data for the treatment of vocal tremor with MRgFUS, extensive counseling was done with the patient, emphasizing that this treatment was intended to improve his bilateral upper extremity tremor with unclear benefit for his vocal tremor. Despite this, the patient elected to proceed with treatment of his upper extremity tremors. He underwent right-sided VIM thalamotomy with MRgFUS. Hand and voice tremors were assessed after each sonication and...
immediately postprocedure. A total of 5 sonications were performed with a maximum average temperature of 58°C and a maximum peak temperature of 64°C. The skull density ratio (SDR) was 0.65. During treatment, 972 transducer elements were available through a 378-cm² skull surface area. The right VIM was targeted with the following coordinates relative to the posterior commissure (PC): 7.4 mm anterior, 13.2 mm medial, 1.0 mm superior. Lesion parameters are depicted in Fig. 1A. Immediate postprocedure magnetic resonance imaging (MRI) is shown in Fig. 2. The patient’s hand tremor resolved. He also reported significant improvement in his vocal tremor, with instantaneous “relaxation of half of the vocal cords.” He experienced mouth/hand paresthesia and gait instability postprocedure, which resolved entirely by the 3-month follow-up. Also, at the 3-month follow-up, his CRST score was a 2, a 94% improvement from baseline. This coincided with the persistence of T2 FLAIR edema (Fig. 2 right). Complete resolution of the voice and hand tremor was observed, although significant muscle tension dysphonia was noted. His self-reported VHI score was a 37 ($p = 5$; $F = 18$; $E = 14$), indicating a mild rating of self-handicap. His voice was rated a level 5 according to the ASHA NOMS for voice, meaning the ability to participate in vocational, avocational, and social activities requiring a voice is rarely affected in low-vocal demand activities but occasionally affected in high-vocal demand activities. He was given severity modifier code CJ, meaning at least 20% but less than 40% impaired, limited, or restricted. Pre- and postprocedural clinical grade scale results are summarized in Table 1. The patient has returned to professional singing since the second thalamotomy and is satisfied with the results.

**Patient Informed Consent**

The necessary patient informed consent was obtained in this study.

**Discussion**

This case report demonstrates a favorable outcome in a patient treated with bilateral VIM MRgFUS thalamotomy for upper extremity ET who also experienced profound improvement of concomitant vocal tremor. The patient’s significant improvement with bilateral lesioning without significant procedural side effects underscores the possible utility of MRgFUS for the treatment of essential vocal tremor.

Diagnosis of essential voice tremor (EVT) suffers from a lack of consensus on the distinct clinical phenotype and anatomy involved. This is compounded by significant overlap in presentations with manifestations of other diseases both neurological and nonneurological in nature. Vocalization is a complex interplay of cerebral processes involving anterior cingulate cortex, periaqueductal gray, basal ganglia, motor cortex, and nucleus ambiguus. This is further complicated by the bilateral innervation of many of these neuronal projections as well as the complex array of pharyngeal and laryngeal musculature involved. Thus, current understanding of the unique pathophysiology of EVT is yet to be determined.

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**TABLE 1. Clinical grading scale assessments**

<table>
<thead>
<tr>
<th>Measure</th>
<th>Baseline</th>
<th>Post-Unilat MRgFUS</th>
<th>Post-Bilat MRgFUS</th>
</tr>
</thead>
<tbody>
<tr>
<td>CRST</td>
<td>32</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>VHI</td>
<td>47</td>
<td>*</td>
<td>37</td>
</tr>
<tr>
<td>NOMS</td>
<td>4</td>
<td>*</td>
<td>5</td>
</tr>
<tr>
<td>Severity modifier</td>
<td>CK</td>
<td>*</td>
<td>CJ</td>
</tr>
</tbody>
</table>

* Denotes values not tested at that time point.
In addition, EVT is a particularly challenging condition to treat because none of the existing treatment options have been proven to improve the quality or intelligibility of the voice.1,4–7,10,28 A meta-analytical review of 11 clinical trials researching EVT therapies reported a lack of sufficient evidence to guide the management of EVT.28 The majority of existing data on the treatment of vocal tremor are from uncontrolled studies and case reports, which offer subjective analyses of patients pre- and posttreatment and present variable treatment responses.29,30 As demonstrated in our patient, the use of laryngoscopy may be a viable option to determine treatment outcome in EVT by providing an objective view of the tremulous vocal cords.

Existing data from the DBS literature illustrate that bilateral implantation is needed for efficacious treatment of vocal tremor.1,4–7,10 Given the bilateral nature of the central neuronal processes involved, bilateral stimulation is needed to modulate these pathways.24,25,30,31 Unfortunately, the use of traditional bilateral thalamotomy has been limited due to significant concerns over irreversible adverse effects including cognitive decline, balance difficulty, and, most notably, speech disruption.32–34 Although current research into bilateral MRgFUS is ongoing, MRgFUS notably benefits from the ability to assess for both tremor reduction and adverse effects in real time with subtherapeutic “temporary” lesions. This may allow the clinician to improve both the safety and efficacy of bilateral thalamotomies.20,21

**Observations**

There has not been a controlled study investigating the use of unilateral or bilateral thalamotomy with MRgFUS in the treatment of EVT, and only a few case reports exist in which vocal tremor was assessed postprocedure. The case report mentioned above demonstrated a moderate improvement in vocal tremor (45% reduction in CRST and 40% improvement in VHI),15 in comparison to the dramatic resolution (100% reduction in CRST and 79% improvement in VHI from baseline) reported here. A notable limitation of our study is the 6-month follow-up of our patient. ET has the potential to worsen over its natural history and may even recur after treatment.2 Thus, further study regarding the durability of this treatment is needed. In the existing literature, thalamotomy has shown no or minimal improvement in axial tremors of the head, neck, or voice.24,30,38 There are no reports or studies presenting the effects of historical methods of VIM thalamotomy (radiofrequency or Gamma Knife ablation) on the ability to reduce vocal tremor. Although the phase 2 results of a clinical trial for bilateral MRgFUS are promising,17 DBS is currently recommended over FUS for the bilateral treatment of ET.

Given the history of bilateral thalamotomy and lack of modern data on MRgFUS, complication avoidance is of the utmost importance to the clinician. Precise targeting of the posterior border of the VIM/ventral caudal thalamic nuclei may prevent adverse events, although further research is required to confirm the optimal lesion location and size.20,21 Benefits of MRgFUS include the ability to perform low-energy sonication, which may detect potential side effects prior to permanent lesioning. The clinician is then able to cease sonication and adjust the target area if these are recognized, providing an extra safety layer to limit adverse effects. Another option to improve lesion targeting may be the use of white matter tractography using diffusion tensor imaging before ablation.39 Although the traditional tremor circuit for ET is well defined, resolution of the optimal white matter tracts involved in EVT is unclear and thus a topic for further research.39 Because vocal tremor may manifest from a variety of pathological disease states, research into optimal identification of ideal candidates most likely to benefit from VIM thalamotomy is needed.23,24

**Lessons**

Bilateral MRgFUS thalamotomy may be a viable treatment modality for vocal tremor, as demonstrated in our case. EVT remains a difficult to treat disease process with a distinct lack of evidence-based treatment options. Further research into larger series is needed to establish reliable efficacy, improve patient selection, and better delineate MRgFUS thalamotomy’s safety profile in the treatment of EVT.

**References**


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Author Contributions
Conception and design: Pearce, Sani. Acquisition of data: all authors. Analysis and interpretation of data: all authors. Drafting the article: Pearce, Thoma, Sani. Critically revising the article: all authors. Reviewed submitted version of manuscript: all authors. Approved the final version of the manuscript on behalf of all authors: Pearce. Study supervision: Sani.

Supplemental Information
Videos

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