Can Artificial Intelligence Outperform Neurosurgeons in Targeting During Focused Ultrasound Thalamotomy for Essential Tremor?

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Background

- Magnetic Resonance-guided Focused Ultrasound (FUS) thalamotomy treats essential tremor by ablating the thalamic ventral intermediate nucleus (VIM)
- Accurate targeting of the VIM is challenging for multiple reasons
  - Small size (0.15-0.25cm^3)
  - Radiologically occult on MRI (Figure 1)
  - Neuroanatomical variability between patients
- Thus, neurosurgeons use 2 stereotactic landmarks to map the VIM
  - Midline
  - Anterior-posterior commissural (AC-PC) plane
- Neighboring ventral posteromedial (VPM) and ventral posterolateral (VPL) are sensory nuclei posterior to the VIM (Figure 1)
  - Misplaced lesion → VPM/VPL damage → Chronic sensory deficits from FUS in 10% of patients (numbness, paresthesia, regional dysgeusia)
- OptimMRI (Artificial Intelligence targeting software, ReBrain) uses 18 stereotactic landmarks to identify the VIM
- The accuracy of OptimMRI (18 landmarks) compared to neurosurgeon planning (3 landmarks) is unknown

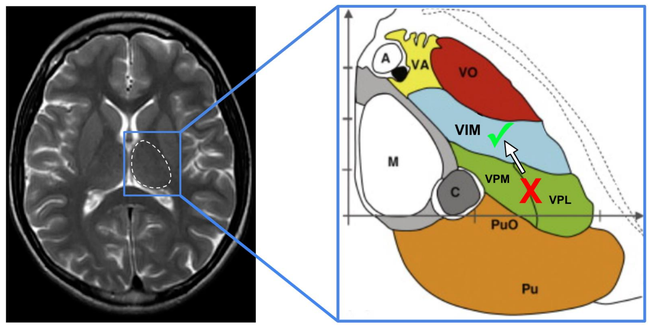

Figure 1. Axial T2 MRI of the left thalamus (left) with corresponding nuclei (right). The VIM (blue) is located anterior to the VPM and VPL (green). The VIM is the intended target in FUS for ET ("✓"), while the VPM and VPL are avoided ("X"). *Adapted from Mai JK, Forutan F. Thalamus. In: Mai JK, Paxinos G, eds.* ***The Human Nervous System.*** *Academic Press; 2012:618–677.*

Methods

- 36 ET patients treated with FUS thalamotomy at a single institution, 2011-2025
- 18 patients who developed chronic sensory deficits were matched to 18 patients without deficits (med. follow-up 11.5mo; IQR 10-14mo)
- Lesion metrics analyzed by OptimMRI: volume, coordinates, roundness, principal components, and bounding boxes
- Targeting accuracy determined by the difference between actual vs OptimMRI-predicted lesion coordinate along each axis
- Tremor outcomes given as reported by patient/neurosurgeon at follow-up
- Group differences analyzed using appropriate statistical tests
- Outliers in lesion volume (4 per group) removed for secondary analyses

Results

Difference in AI-predicted Target vs Lesion Location Along Anatomical Axes

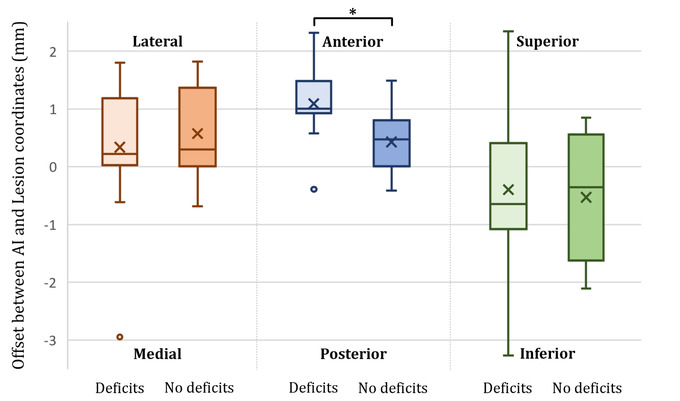

Figure 2. Box plot comparing the difference between AI-predicted and actual lesion coordinates ("AI-lesion offset") along each axis between patients with and without sensory deficits. The asterisk represents a significant difference in the magnitude of AI-lesion offset between patients with and without sensory deficits along a given axis

AI: More Accurate along Anteroposterior Axis (Figure 2)

- AI predicted that lesions in sensory deficit patients should have been placed significantly more anterior, but not in those without deficits (p = 0.007)
- No group differences in AI-lesion offset along mediolateral (ML) or superoinferior (SI) planes

Lateral Lesion Placement

- Sensory deficit patients had more lateral lesions (14.7mm vs 13.9mm from midline, p = 0.005), but lateral AI-lesion offset did not differ between groups.

Less Tremor Improvement and More Recurrence

- Sensory deficit patients had less tremor improvement (58 ± 46% vs 85 ± 29%, p = 0.035) and trended toward more frequent total recurrence (5/14 vs 1/14, p = 0.16)

Larger Lesions

- Sensory deficit patients had larger lesions than those without deficits (278 ± 119mm^3 vs 184 ± 77mm^3, p = 0.01), but this difference disappeared after removing outliers (253 ± 71mm^3 vs 206 ± 60mm^3, p = 0.07)

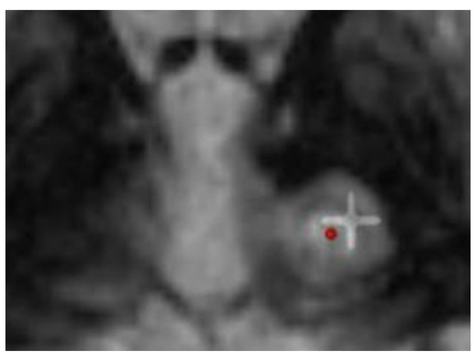

Figure 3. Axial Fast Gray Matter Acquisition T1 Inversion Recovery (FGATIR) MRI showing the AI-predicted target (plus sign) anterolateral to thalamotomy lesion (center at red dot) in a patient with persistent dysgeusia one year after surgery

Discussion

- Posterior mistargeting would reduce tremor benefit and increase sensory side effects as the lesion moves away from the VIM and toward the VPM/VPL
  - AI suggested that lesions were placed significantly more posterior in patients with sensory deficits vs. those without deficits
  - Sensory deficit patients experienced less tremor improvement and trended toward more frequent total recurrence
- Therefore, OptimMRI was likely more accurate than conventional 2-landmark targeting in predicting VIM location
- ML and SI coordinates play less of a role in VIM targeting
  - More lateral lesions did not appear symptom-relevant given no lateral AI–lesion offset difference between groups
  - The proposed widened shape of the VIM (Figure 1) may explain the insignificance of these coordinates
- Sensory deficits are likely not attributed to a larger lesion volume
  - AI-lesion AP offset remained significant after removing outliers and adjusting for lesion volume using linear regression analyses of both the 14 and 18-patient cohorts.

Conclusions

Chronic sensory deficits, most commonly paresthesia, numbness, or dysgeusia, are among the more common side effects in FUS for ET, occurring in roughly 10% of patients. The present study provides evidence that this may be due to an inappropriately posterior lesion placement. These findings suggest that AI targeting may enable more precise lesion placement, allowing for smaller lesions that optimize tremor suppression while minimizing chronic side effects.

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