CNS Spotlight

Transcranial Magnetic Resonance-Guided Focused Ultrasound Thalamotomy in Essential Tremor: A Comprehensive Lesion Characterization

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BACKGROUND: Transcranial magnetic resonance-guided focused ultrasound (tcMRgFUS) thalamotomy is a novel and effective treatment for controlling tremor in essential tremor patients.

OBJECTIVE: To provide a comprehensive characterization of the radiological, topographical, and volumetric aspects of the tcMRgFUS thalamic lesion, and to quantify how they relate to the clinical outcomes.

METHODS: In this study, clinical and radiological data from forty patients with medically-refractory essential tremor treated with unilateral tcMRgFUS thalamotomy were retrospectively analyzed. Treatment efficacy was assessed with Clinical Rating Scale for Tremor (CRST). Lesions were manually segmented on T1, T2, and susceptibility-weighted images, and 3-dimensional topographical analysis was then carried out. Statistical comparisons were performed using nonparametric statistics.

RESULTS: The greatest clinical improvement was correlated with a more inferior and posterior lesion, a bigger lesion volume, and percentage of the ventral intermediate nucleus covered by the lesion; whereas, the largest lesions accounted for the occurrence of gait imbalance. Furthermore, the volume of the lesion was significantly predicted by the number of sonications surpassing 52°C.

CONCLUSION: Here we provide a comprehensive characterization of the thalamic tcMRgFUS lesion including radiological and topographical analysis. Our results indicate that the location and volume of the lesion were significantly associated with the clinical outcome and that mid-temperatures may be responsible for the lesion size. This could serve ultimately to improve targeting and judgment and to optimize clinical outcome of tcMRgFUS thalamotomy.

KEY WORDS: Essential tremor, Transcranial MR-guided focused ultrasound, Lesion topography

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Essential tremor (ET) is one of the most common movement disorders affecting approximately 1% of the population worldwide.[1] The hallmark motor feature of essential tremor is kinetic tremor affecting upper limbs. A substantial proportion of these patients do not benefit from first-line pharmacotherapy, compromising their daily living ability and quality of life.[2,3] Conventional stereotactic approaches both with deep brain stimulation (DBS) and with radiofrequency ablation targeting at the ventral intermediate nucleus of the thalamus (Vim)[4,5] have been successfully used for the management of medically refractory ET. The development of incisionless transcranial magnetic resonance-guided focused ultrasound (tcMRgFUS)[6-8] has revitalized the field of functional neurosurgery lesioning procedures. Among them, unilateral

ABBREVIATIONS: ANTs, advance normalization tools; **BET,** brain-extraction-tool; **CRST,** clinical rating scale for tremor; **FSL,** FMRIB Software Library; **MR,** magnetic resonance; **MRI,** magnetic resonance imaging; **PC,** posterior commissure; **SWI,** susceptibility-weighted images; **tcMRgFUS,** transcranial magnetic resonance-guided focused ultrasound; **Vim,** ventral intermediate nucleus of the thalamus; **VLpv,** ventrolateral posterior ventral thalamic nucleus

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Supplemental Digital Content 2. Table. Treatment targeting parameters including intercommissural distance (AC-PC), width of the third ventricle (V3), distance of the target to the posterior commissure (dPC), and laterality from the lateral wall of the third ventricle (dV3).

Supplemental Digital Content 3. Table. Treatment sonications summary including total number of sonications, and number of sonications surpassing specific thresholds, sonication, and bed times, accumulated energy.

Supplemental Digital Content 4. Table. Inter-rater accuracies of the lesion segmentations evaluated by means of the DICE coefficient.

Supplemental Digital Content 5. Table. Percentage of the VLpv occupied by the segmented lesion.

Supplemental Digital Content 6. Figure. Relationship between VLpv-lesion overlap and clinical outcomes. Scatterplots showing the relationship between the absolute change in the total CRST between baseline and subsequent follow-ups (3 mo or 1 yr) and the percentage of VLpv voxels that intersected with the lesion boundaries. Patients that presented any adverse events after the treatment in the 3-mo or 1-yr follow-ups are highlighted in different colors, orange for subjective gait imbalance and blue for paresthesias.

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COMMENTS

The authors present a very nice analysis of lesion size and location and their correlation to clinical outcome in a series of 40 patients with essential tremor who underwent unilateral transcranial MRI-guided focused ultrasound (tcMRgFUS) thalamotomy. It is not surprising that better results were achieved with larger lesions and lesions positioned more posterior and inferior in the VL nucleus as this relationship between lesion size and location has been understood for many years from the radiofrequency thalamotomy literature. Complications in this cohort were quite modest in severity. The authors are to be commended for completing such a thorough analysis and describing in great detail their meticulous technique for performing this procedure so that others may learn from them.

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The paper presents an excellent summary and analysis of treatment parameters that were used in a large single-center series of ultrasonic VIM thalamotomy for treatment of essential tremor. Based on their experience, the authors are able to define the size of thalamotomy lesion at different time intervals and then correlate the clinical results with intraoperative thermal effects of focused ultrasonic lesioning.

It would be interesting to see if the same effects are observed in the other busy MRgFUS centers. Even more so, it would be very valuable to find a way to predict the individual patient's reaction to sonication so the procedure can be streamlined, shortened, and simplified.

Finally, the decades of targeting for both lesioning and stimulation taught us not to rely exclusively on anatomical landmarks, particularly when it comes to the thalamus (as opposed to easily defined radiographic targets of subthalamic nucleus and pallidum) - and physiological testing frequently makes us move the target in one or several directions. Therefore, there should be an effort to use functional imaging merged with individual anatomy rather than utilize "one size fits all" atlas coordinates.

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