White-Matter-Nulled MP-RAGE Permits Patient-Specific Tracking of Focused Ultrasound Thalamic Ablation for Essential Tremor

Jason Su[1], Thomas Tourdias[2], Manojkumar Saranathan[3], Casey Halpern[4], Kim Butts-Pauly[3], Jaimie Henderson[4], Pejman Ghanouni[3], and Brian K. Rutt[3]

[1]Electrical Engineering, Stanford University, Stanford, California, United States, [2]Neuroradiology, Bordeaux University Hospital, Bordeaux, France, [3]Neuroradiology, Stanford University, Stanford, California, United States, [4]Neurosurgery, Stanford University, Stanford, California, United States

Target Audience: Scientists interested in MR guided focused ultrasound treatment and visualization of the thalamus.

Purpose: Focused ultrasound (FUS) enables surgical ablation of deep brain structures under MR guidance. The marriage of these technologies promises precise patient-specific and scan-specific treatment targeting. Essential tremor (ET) is a disorder that can be treated with selective FUS ablation of the ventral intermediate nucleus (Vim).[1] Targeting relies on a combination of anatomy and patient tremor response. Recently, the white-matter-nulled MP-RAGE (WMnMPRAGE) contrast at 7T has been shown to allow detailed delineation of thalamic nuclei[2] guided by the Morel atlas[3], which labels the Vim as the ventral portion of the ventral lateral posterior nucleus (VLPv). We present here the first work using pre- and post-FUS WMnMPRAGE images in ET patients to retrospectively correlate treatment location with registered segmentation of the thalamic nuclei. We hypothesized that consistent location of the FUS hotspot with respect to Vim would serve as a functional validation of our WMnMPRAGE imaging and thalamic segmentation procedures.

Methods: After informed consent, a study group of 7 ET patients was first scanned at 7T (Discovery MR950, GE Healthcare) using a 32 channel head coil (Nova Medical) with WMnMPRAGE scan parameters: TS 6s, TI 680ms, TR 10ms, BW 9kHz, flip angle 4°, FOV 18cm, 180x180x200 matrix, slice thickness 1mm, ARC parallel imaging 1.1x1.1 (2D radial fanbeam), scan time 10 min.[4] The patient-specific information from the 7T scan was not used prospectively to plan the procedure in this study as this strategy is not yet validated. On the day of the FUS procedure, usually 2-4 weeks later, the patients were imaged at the 3T scanner, this time with the FUS transducer (ExAblate 4000, InSightec, Israel) in place around the head. Patient positions were adjusted to an initial targeting of the FUS ablation spot in the expected location of the Vim using atlas-based Talairach coordinates and referencing to the AC-PC plane of the individual. Low power FUS was applied and the focal spot was adjusted spatially until reduction of tremor was observed. Higher power FUS was then applied to ablate the target. After completing the ablation, the FUS transducer was replaced by an 8-channel brain coil and post-treatment WMnMPRAGE images were acquired: TS 4.5s, TI 500ms, TR 10ms, BW 9kHz, flip angle 7°, FOV 18cm, 180x180x200 matrix, slice thickness 1mm, no parallel imaging, scan time ~10 min with prospective motion correction. Manual delineation of thalamic nuclei was performed by an expert radiologist using the 7T pre-treatment images blinded to the post-treatment scan. These were then registered to the post-treatment 3T images using FSL's FLIRT to determine the optimal affine transformation with 7 degrees of freedom. The registered VLP nucleus was split into its dorsal and ventral halves, VLPd and VLPv (Vim), by bisecting VLP at its superior-inferior mid-point with a transverse plane. The true boundary was not visible in the images, so this procedure served as a reasonable approximation. From the WMnMPRAGE images, the center of the ablation zone was manually located in each subject, as were the AC-PC plane and the coordinates of the center of mass and inferior edge of the Vim nucleus. The latter was defined as the point on the Vim boundary directly inferior to its center of mass. We then measured the spatial offset between the achieved ablation spot center and these two reference locations within the subject's own Vim.

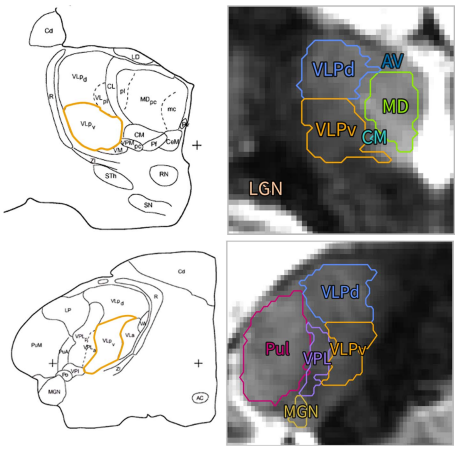

Fig. 1: Coronal (top pair) and sagittal (bottom pair) slices showing the accuracy of the approximation for defining Vim/VLPv and VLPd compared to the Morel atlas.[2]

Results: Fig. 1 shows the manually segmented outlines of thalamic nuclei overlaid on registered 7T WMnMPRAGE images. This figure illustrates that our division of VLP to define VLPv (Vim) is reasonable compared to the Morel atlas delineation in orange. It is noteworthy that these segmentations were only made possible by the 7T WMnMPRAGE images and were not obtainable from any other image contrasts acquired. Fig. 2 displays the 7T-defined thalamic nuclei registered to and overlaid on immediate post-treatment 3T WMnMPRAGE scans of one subject (Patient D). The ablation zone is clearly visible on the WMnMPRAGE images; its center is marked with the red X and the AC-PC plane is indicated by the dashed red line. Table 1 displays the displacements of the treatment spot center from both the center and inferior edge of Vim. In most subjects, the ablation center was closer to the inferior edge, which is near or coincides with the AC-PC plane, than to the center of Vim; subjects F and G were exceptions in this regard in showing the ablation center closer to Vim center than edge.

Discussion/Conclusion: We demonstrate that WMnMPRAGE provides a unique tool, enabling thalamic nuclear segmentation and allowing detailed tracking of selective MRgFUS ablation within the thalamus. This work shows for the first time an ability to track the ablation center to millimeter-scale precision compared to the patient's own thalamic anatomy. We found that the treatment spot, which had been adjusted for maximal tremor-reducing effect in these ET patients, was usually located closer to the inferior edge than to the center of Vim. This may indicate that the portion of Vim responsible for hand/arm tremor is located in this inferior subregion of Vim, as indicated in the Schaltenbrand and Wahren stereotactic atlas.[5] The consistent location of the treatment spot with respect to each subject's image-derived Vim boundary serves as an important functional validation of WMnMPRAGE-based thalamic segmentation and suggests a realistic planning strategy for patient-specific FUS ablation therapy. Ongoing work will continue to test this hypothesis including the use of WMnMPRAGE for prospective targeting and correlation of targeting accuracy to patient outcome.

References: [1 Elias et al. NEJM 2013; 369(7):640-8 [2]Tourdias et al. Neuroimage. 2013; 84C:534-545. [3]Niemann et al. Neuroimage. 2000;12(6):601-16. [4]Saranathan et al. Magn Reson Med. 2014 May 29. [5]Schaltenbrand and Wahren Atlas for stereotaxy of the human brain. 1977.

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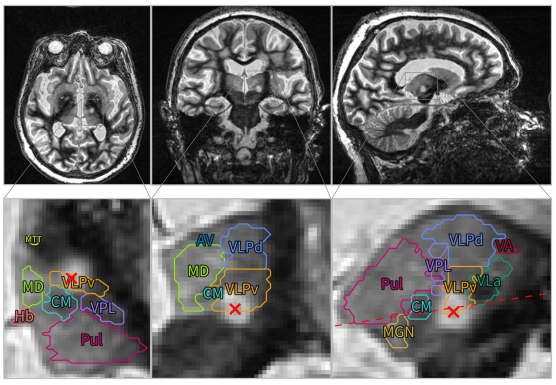

Fig. 2: Images from Patient D showing registered thalamic nuclei on post-treatment 3T images. x marks the center of the ablation zone. The orange ROI is the thalamic nucleus of interest (VLPv or Vim). The red dashed line represents the AC-PC plane.

Patient	Vim Center of Mass – Ablation Center (mm) L-R	A-P	S-I	Δ Distance (mm)
A	0.19	1.80	3.29	3.76
B	-0.38	-0.21	2.18	2.23
C	-1.34	-0.72	3.81	4.1
D	-0.95	0.62	3.45	3.63
E	0.18	-0.74	3.27	3.36
F	0.67	3.59	0.35	3.66
G	0.14	1.05	1.95	2.22
Average	-0.21	0.77	2.61	3.28

Patient	Vim Inferior Edge – Ablation Center (mm) L-R	A-P	S-I	Δ Distance (mm)
A	0.19	1.80	-0.70	1.94
B	-0.38	-0.21	-2.11	2.15
C	-1.34	-0.72	0.00	1.52
D	-0.95	0.62	0.00	1.13
E	0.18	-0.74	-0.70	1.04
F	0.67	3.59	-3.52	5.07
G	0.14	1.05	-2.11	2.36
Average	-0.21	0.77	-1.31	2.17

Table 1: The displacement between the ablation spot center vs. Vim center of mass (left) and inferior edge (right).