

# VISUALIZATION OF INTRA-THALAMIC ANATOMY WITH WHITE-MATTER-NULLED MPRAGE AT 7T

Thomas Tourdias<sup>1,2</sup>, Manojkumar Saranathan<sup>2</sup>, Ives R Levesque<sup>2</sup>, Jason Su<sup>2</sup>, and Brian K Rutt<sup>2</sup>

<sup>1</sup>Service de NeuroImagerie Diagnostique et Thérapeutique, CHU Pellegrin - Université de Bordeaux, Bordeaux, France, <sup>2</sup>Department of Radiology, Stanford University, Stanford, California, United States

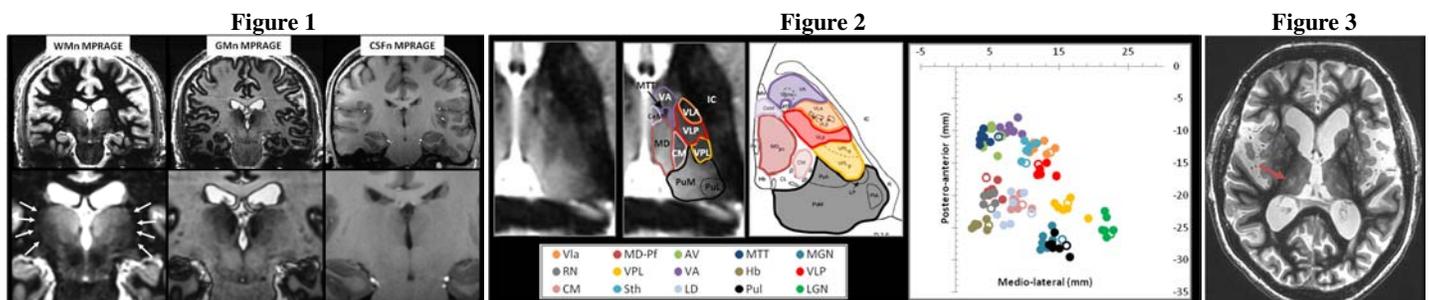
**Target audience:** People interested in promoting clinical applications for new ultra high field (UHF) methods.

**Background and purpose:** The thalamus is a heterogeneous structure, composed of several nuclei interlocked in a complex anatomy.<sup>1</sup> Direct visualization of thalamic nuclei by MRI remains a challenge because of their small size and low contrast between adjacent nuclei. We hypothesized that the combination of ultra-high-field (UHF) and a T<sub>1</sub>-weighted MPRAGE pulse sequence could help visualize thalamic anatomy by virtue of higher intrinsic SNR and increased T<sub>1</sub> dispersion between adjacent structures at higher field strength. We present the development, optimization and application of a 3D white-matter-nulled MPRAGE pulse sequence at 7T, and show that it reliably visualized 15 different intra-thalamic nuclei in 6 human subjects in clinically relevant scan times.

**Methods:** We first measured T<sub>1</sub> values within different nuclei of the thalamus at 7T in 5 individuals using a standard IR-FSE method. We used T<sub>1</sub> values of adjacent nuclei to simulate the MPRAGE signal behavior, and used these theoretical results to guide empirical optimization of scan parameters to achieve the best trade-off between signal, contrast, and resolution for visualization of the thalamic nuclei in healthy volunteers (n=17 experiments). The optimal set of parameters defined from the above steps (TS=6000ms, TI=670ms, N=200, BW=20KHz, TR/TE=6.9ms/3.0ms;  $\alpha=4^\circ$ , 1x1x1 mm<sup>3</sup> acquisition resolution, 0.7x0.7x0.5 mm<sup>3</sup> reconstructed voxel size) was used to collect high-quality 7T MPRAGE data in a subsequent group of 6 volunteers. Delineation of thalamic nuclei by manual tracing was performed twice by one trained reader, after which MR-defined nuclei were compared to the classic Morel histological atlas.<sup>1</sup>

**Results:** Within the thalamus a large range of T<sub>1</sub> values was observed (1250ms to 1800ms). The next step of simulation was conducted to maximize the signal and the contrast between a nucleus with 1800ms T<sub>1</sub> (e.g. pulvinar (Pul) and mediodorsal (MD) nuclei), and an adjacent nucleus with 1400ms T<sub>1</sub> values (e.g. center median (CM) and ventral posterior lateral (VPL) nuclei). Using these values for theoretical evaluations combined with *in vivo* measurements, we showed that a short inversion time (TI=670ms) close to the white matter nulled (WMn) regime enhanced both the contrast between the thalamus and the surrounding tissues, as well as intra-thalamic nuclear contrast, and furthermore revealed thin hypointense boundaries believed to be attenuated WM lamellae separating adjacent nuclei. Theoretical and experimental data showed that these features were specific to the WMn regime, which therefore showed better delineation of thalamic nuclei than gray matter (GM) or a cerebro-spinal fluid (CSF) nulled regimes (Figure 1)<sup>2</sup>. In this nulling regime, setting the time between successive inversion pulses at TS=6000ms provided the best thalamic SNR efficiency and increased intra-thalamic contrast; and lengthening the  $\alpha$  pulse train time (N\*TR; i.e. higher N and higher TR) further increased thalamic SNR efficiency. Finally, a low flip angle ( $\alpha=4^\circ$ ) was found to best mitigate the blur induced by the signal modulation along the  $\alpha$  pulse train. This optimized set of parameters enabled the 3D delineation of 15 thalamic substructures in all 6 healthy individuals; these substructures corresponded well with the known anatomical structures of the thalamus based on the classical Morel atlas (Figure 2). The mean Euclidean distance between the centers of mass of MR- and Morel atlas-defined nuclei was 2.67mm ( $\pm 1.02$ mm). The reproducibility of the MR-defined nuclei was excellent with intraclass correlation coefficient measured at 0.997 and a mean Euclidean distance between corresponding centers of mass found at first versus second readings of 0.69mm ( $\pm 0.38$ mm).

**Discussion:** This novel 7T imaging strategy provided a detailed anatomical visualization of internal thalamic anatomy that is usually not clearly discriminated. This method could have a strong impact on managing patients with tremor (Figure 3) and on planning deep brain stimulation procedures. It could further pave the way toward investigation of regional thalamic changes in several neurological disorders involving the thalamus.



**Figure 1.** Delineation of the thalamus and its internal anatomy in the WMn regime. Thalamic nuclei were uniquely identified in WMn due to enhanced intrinsic contrast between adjacent structures and thin hypointense boundaries. These MR-defined nuclei corresponded well with known anatomical structures observed on the corresponding histological plates.<sup>1</sup> **Figure 2.** Axial reconstruction and the scatter plots which illustrates the axial projection of the center of mass of the 15 identified nuclei in the 6 volunteers together with the atlas-based center of mass coordinates (open icons). **Figure 3.** An old stroke was found in the right VPL-VLP nuclei (arrow) to be responsible for tremor in a 75 years old patient. Nuclei abbreviations: VLa: ventral lateral anterior; MD-Pf: mediodorsal; AV: anterior ventral; MTT: mamillothalamic tract; MGN: medial geniculate nucleus; RN: red nucleus; VPL: ventral posterior lateral; VA: ventral anterior; Hb: habenular; VLP: ventral lateral posterior; CM: center median; Sth: subthalamic; LD: lateral dorsal; Pul: pulvinar; LGN: lateral geniculate nucleus.

## References:

1. Morel A, Magnin M, Jeanmonod D. Multiarchitectonic and stereotactic atlas of the human thalamus. *J Comp Neurol* 1997;387:588-630.
2. Tourdias T, Saranathan M, Levesque IR, Su J, Rutt BK. Visualization of intra-thalamic nuclei with optimized white-matter-nulled MPRAGE at 7T. *Neuroimage* 2013;84C:534-545.

**Acknowledgement:** Research support from NIH P41 EB015891, GE Healthcare and the Richard M. Lucas Foundation. TT received financial support from ARSEP foundation, CHU de Bordeaux, Fondation Université de Bordeaux, TRAIL, Institut Servier and France/Stanford Center for Interdisciplinary studies.