## Direct visualization of thalamic structures: comparison of super-resolution track-density imaging to conventional MRI at 7T

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Introduction: Accurate identification of sub-thalamic nuclei is of great importance for many clinical applications, particularly those involving deep brain stimulation such as in Parkinson's disease, dystonia, chronic pain, and depression. Direct visualisation of thalamic structures with high spatial resolution is not easily achieved with clinical MRI scanners (1-4). Improvements in ultra-high field MRI (7T and above) have opened up the possibility of addressing this issue (5), but access to this technology remains limited. The technique of *super-resolution track-density imaging* (TDI) has been recently proposed as a means to create images with very high resolution and anatomical contrast, based on the results from whole-brain fibre-tracking (6). This method was shown to produce enhanced anatomical detail within the thalamus (6), suggesting its possible role in thalamic mapping. In this study, we assess the role of TDI for direct visualisation of sub-thalamic nuclei and compare the results to those obtained using T1-weighted MRI at 7T.

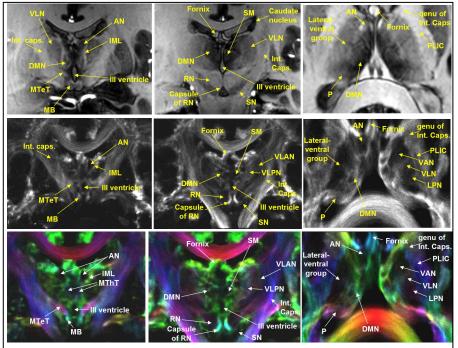
Methods: Data from 4 healthy volunteers were obtained on a 7T scanner (Siemens); for each subject, the diffusion MRI (DWI) and 3D T1-weighted images (MPRAGE) were acquired on separate sessions. DWI sequence: single-shot DW-EPI (TE/TR=83/6000ms, 1.8mm isotropic resolution, 64 DW-directions, b=2000s/mm², 3 repeats). MPRAGE sequence: TR/TE/TI=400/5.26/900ms, 0.375×0.375×1.5mm³ resolution. DWI data were corrected for geometric distortions using a combined two dimensional PSF mapping method (7), which takes into account both the distortion and non-distortion dimensional PSF correction schemes, in contrast to previous methods where only either non-distortion (8) or distortion dimensional (9) correction were used.

<u>Fibre-tracking</u>: Whole-brain fibre-tracking was done using in-house software based on MRtrix (10), which includes CSD (11) to calculate the fibre orientation distributions (FOD) to model multiple fibre-orientations, and probabilistic streamlines using the  $2^{nd}$  order integration over fibre orientation distributions (iFOD2) algorithm (12): 1mm step-size, maximum angle between steps = 45°, 3 FOD samples/step, termination criteria: exit the brain or when the FOD amplitude was < 0.4. Four million tracks were generated for each data-set. <u>Track-density imaging</u>: TDI maps were generated by calculating the number of tracks in each element of a grid – Note that the grid element can be much smaller than the acquired voxel size (6). For this study, a 200μm isotropic grid-size was used. Directionally-encoded colour (DEC) TDI maps (the super-resolution equivalent (6) of the DEC map in diffusion tensor imaging (13)) were also generated for each data-set. The resulting TDI and DEC-TDI maps were registered to the corresponding MPRAGE images, and the various sub-thalamic structures manually labelled in each of the images (14).

Results: Several brain structures in the thalamic and surrounding areas were easily identified based on the anatomical content of the TDI map (middle row in figure) and the directional-information contained on the superresolution DEC-TDI maps (bottom row). Many of these structures have a correlate with the structures identified from the more conventional T1-weighted contrast (top row). In particular, these structures include the anterior (AN), dorsomedial (DMN) and lateral posterior (LPN) nuclei, the ventrolateral anterior (VLAN) and posterior (VLPN) nuclei, pulvinar (P), internal medullary lamina (IML), stria mudullaris (SM), the mammillary body (MB), mammillotegmental (MTeT) and mammillo-thalamic (MThT) tracts, substantia nigra (SN) and red nucleus (RN). The results shown in the figures are typical for the subjects included in this study.

Discussion: The results from our study suggest that the DEC-TDI maps are particularly useful in helping the visualisation of structures in the thalamic area. The combination of the local directional-information and the very high-resolution achieved by the super-resolution method (200μm isotropic in our examples) provide high contrast and resolution to delineate many structures. Note also that, since the TDI contrast originates from the fibre-tracking results, some structures appear hypointense in the TDI maps (e.g. anterior nucleus) and their edges are defined by the surrounding hyperintense structures (e.g. internal medullary lamina).

Conventional MRI at 7T provides high resolution and tissue contrast not achievable at lower field strength, which has



**Figure**: Example results from one subject. (Top) MPRAGE images; (middle) super-resolution TDI maps; (bottom) super-resolution DEC-TDI maps. First 2 columns show coronal slices; the last column shows axial slices. See Results section for anatomical notation. The colours represent the main local orientation (red: left-right, green: anterior-posterior, blue: inferior-superior).

been useful for the delineation of brain structures (5,14,15). The similarity between many of the structures identified in this study in the TDI maps to those in the T1-weighted images suggests the super-resolution TDI method can provide a useful imaging modality for mapping of thalamic and surrounding structures. Importantly, since the diffusion contrast mechanism is  $B_0$ -independent, the TDI technique has been shown to still produce high-quality images at more commonly used magnetic field strength such as 3T scanners (6). Therefore, the super-resolution TDI technique should play a very important role in the direct visualisation of sub-thalamic structures for studies in clinical scanners, where the role of conventional MRI is limited.

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