Untangling a fiber bundle knot - Preliminary results on STN connectivity using DTI and HARDI on rat brains

E. BRUNENBERG[1], V. PRCKOVSKA[1], B. PLATEL[2], G. STRIJKERS[1], AND B. TER HAAR ROMENY[1]

[1]BIOMEDICAL ENGINEERING, EINDHOVEN UNIVERSITY OF TECHNOLOGY, EINDHOVEN, NETHERLANDS, [2]BIOMEDICAL ENGINEERING, UNIVERSITY HOSPITAL MAASTRICHT, MAASTRICHT, NETHERLANDS

INTRODUCTION - Deep Brain Stimulation (DBS) of the subthalamic nucleus (STN) for Parkinson's Disease alleviates the motor symptoms, but causes cognitive and emotional side effects in half of the cases [1]. We strive to locate the STN motor part more precisely by analyzing the connections of the STN subterritories with other brain areas. This study compares DTI and HARDI glyphs around the rat STN, which has two parts, namely a motor and a cognitive/emotional territory [2]. The post-mortem rat measurements enable very high-resolution imaging.

METHODS - Wistar rat brains were perfused and fixed using 4% paraformaldehyde, stored for 14 weeks and subsequently rinsed and put in PBS for 48 hours. Before imaging, they were immersed in Fomblin (Fens Chemicals). Imaging was done on a 9.4T Bruker Biospec AVANCE-III system. Anatomical images were made using a RARE sequence, measuring 15 coronal slices with matrix 384^2. The FOV was 25.6^2 mm^2, leading to a pixel dimension of 67 µm. Slice thickness was 500 µm (gap 50 µm). HARDI was done using a diffusion-weighted spin-echo sequence with two unipolar gradients symmetrically around the 180 degree pulse (TE 27 ms, TR 4000 ms, NA 1). Number of slices, slice thickness, and FOV were identical, the matrix was 128^2, zero-filled to 256^2, leading to a pixel dimension of 100 µm. We measured 132 different gradient directions with b-value 3000 s/mm^2, together with an unweighted image. We implemented Q-ball imaging [3] and Diffusion Orientation Transform (DOT) [4]. The order of the Spherical Harmonics l was varied between 4 and 8. Crossings in the STN area could be observed even at $l = 4$. We included Laplace-Beltrami smoothing, with smoothing parameter $\lambda = 0.00005$ as an empirical optimum for our data. For DOT, the effective diffusion time was determined to be $t = \Delta - \delta/3 = 12$ ms. The radius of a shell R_0 was varied in order to reconstruct the correct probability profile, validated using the corpus callosum, as in [4]. We assume that the fiber directions are given by the local maxima of the normalized [0,1] probability profile.

RESULTS - The anatomical image is shown in Figure 1 (left). The STN can be seen along the internal capsule. The FA map, colored according to MEV direction, is presented as inlay. To the right, this is overlaid with the corresponding slice from the Paxinos rat brain atlas. We rendered three types of diffusion glyphs for the red ROI. For a better view, this ROI is rotated about 50° clockwise. In Figure 2 (top), superquadrics based on the second order diffusion tensor, as derived from the HARDI, can be seen. The middle and bottom images show Q-ball and DOT glyphs. It is clear that superquadrics are unable to resolve the diffusion in the ROI. They show linear diffusion in the internal capsule, but oblate tensors elsewhere. The Q-ball and DOT glyphs are more heterogeneous. We clearly observe crossings in the lateral part of the STN and the ventral zona incerta. A more linear configuration can again be seen in the upper left corner of the ROI, which corresponds with the medial part of the STN and the nigrostriatal bundle. We may distinguish the two subterritories of the rat STN, the lateral motor part (to the right) and the medial cognitive/emotional part (to the left) [2].

DISCUSSION - HARDI definitely provides more information on the STN region neuroanatomy than DTI. Many crossings can be seen, indicating an entangled fiber network. We know that this network comprises the internal capsule, the ansa lenticularis, the thalamic fasciculus, and the lenticular fasciculus, amongst others [5]. If we can visualize these and assess the connections of the STN with other brain areas, we could locate the STN motor part with more certainty. Avoidance of the cognitive and emotional side effects due to DBS then becomes feasible. Therefore, it is certainly necessary to investigate advanced tractography methods using HARDI information. These methods should be validated with histological data.

ACKNOWLEDGMENTS - Supported by the Netherlands Organization for Scientific Research (NWO). **REFERENCES** - [1] Temel et al. *Parkinsonism Relat D*, 12: 265-272, 2006. [2] Temel et al. *Prog Neurobiol*, 76:393-413, 2005. [3] Descoteaux et al. *Magn Reson Med*, 58:497-510, 2007. [4] Özarslan et al. *Neuroimage*, 36:1086-1103, 2006. [5] Hamani et al. *Brain*, 127:4-20, 2004.

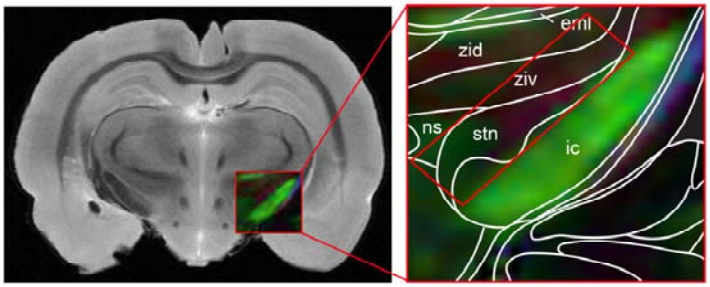

Figure 1: Left: RARE image of a rat brain slice, with as inlay a weighted FA-map around the STN. Right: Enlarged region with part of the Paxinos rat atlas as overlay (eml = external medullary lamina, ic = internal capsule, ns = nigrostriatal bundle, stn = subthalamic nucleus, zid = dorsal zona incerta, ziv = ventral zona incerta).

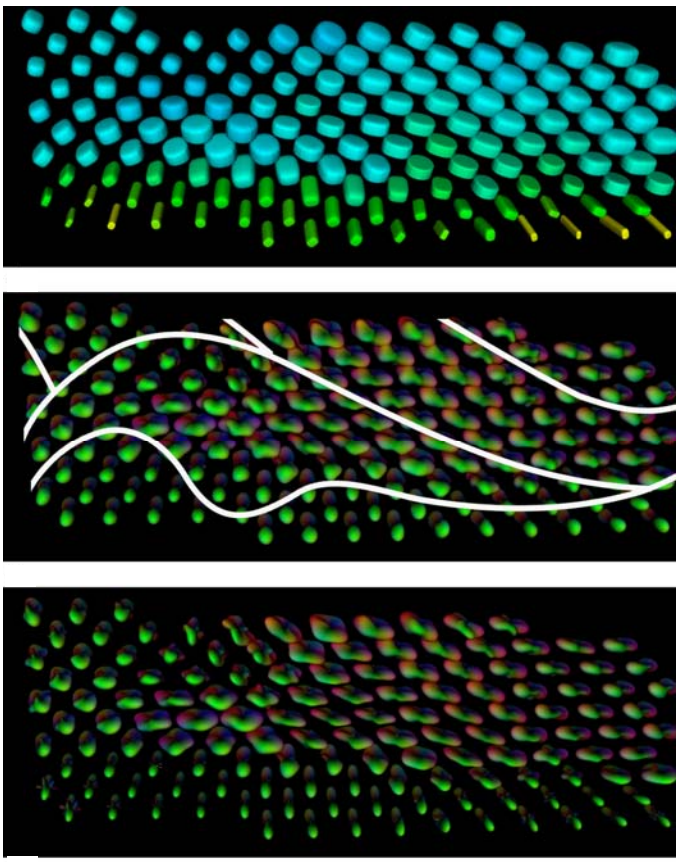

Figure 2: Top: Second order diffusion tensor superquadrics, color-coded according to FA (blue: FA ~0.25, yellow: FA ~0.75). Middle: Q-ball normalized glyphs with rat atlas overlay (sixth order Spherical Harmonics). Bottom: DOT glyphs (sixth order Spherical Harmonics).