NODDI performs better than DTI in brain tumors with vasogenic edema

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TARGET AUDIENCE: Diffusion MRI researchers and clinicians interested in advanced diffusion MRI techniques for imaging brain tumours

PURPOSE: Neurite Orientation Dispersion and Density Imaging (NODDI) [1] is a recent technique that enables detailed characterization of brain tissue microstructure using clinically feasible diffusion MRI (dMRI) protocols. NODDI estimates indices of neurite density (NDI) and orientation dispersion (ODI) that can serve as novel imaging markers for brain disorders [2,3] and improve tractography and structural connectivity mapping [4]. The technique can additionally determine the extent of CSF contamination [3], which has the potential to improve tractography in the presence of brain tumours with vasogenic edema. The present work aims to test this hypothesis. We acquired multi-shell dMRI data in patients with brain tumours and assess the performance of tractography using NODDI relative to diffusion tensor imaging (DTI).

METHODS: *Data:* dMRI data from 22 patients with brain tumours were acquired on a 3T MRI scanner (Siemens Verio, Erlangen, Germany) with the following parameters: TE = 96 ms, TR = 15 s, 8 b = 0 volumes and 60 diffusion-weighted ones in 2 shells (b-values: 700 and 2000 s/mm^2) with 20 and 40 diffusion gradient directions, respectively. 64 axial slices were acquired, with a FOV of 256x256 mm^2 and an isotropic resolution of 2x2x2 mm^3. *Model Fitting:* All the images were corrected for motion and distortions using FSL's FLIRT [5]. The data were fitted to the NODDI model, using the NODDI Matlab Toolbox [6]. The diffusion tensor in each voxel and the derived parameters were calculated with Diffusion Toolkit [7]. *Tractography:* DTI-based and NODDI-based tractography were performed on 12 patients with an Interpolated Streamline algorithm in Trackvis [7] from the directions identified by DTI and NODDI respectively. For DTI we used an FA threshold of 0.2 and angle threshold of 35°. For NODDI, we used the same angle threshold but need to determine a threshold in ODI that is comparable to FA, as explained in the following section. *ODI threshold calibration:* Using data from 10 more patients, having lesions far from the main white matter tracts, we performed tractographic reconstructions from the directions identified by DTI as described above, but using different ODI thresholds between 0.05 and 1 (every 0.01 from 0.25 to 0.7, every 0.05 out of this interval) and using an FA threshold of 0.2 for comparison. The correlation index between the number of tracts reconstructed at each ODI threshold and the number of tracts reconstructed with the FA threshold in each patient's healthy hemisphere was calculated. Inclusive and exclusive regions of interest for the extraction of the corpus callosum (CC) and cortico-spinal tract (CST) were delineated and applied to all the reconstructions and the Dice index was calculated to quantify the overlap between the tract obtained with each ODI threshold and the reference one (FA = 0.2). The optimal ODI threshold was chosen as the one that maximizes this overlap. *Analysis:* The optimal ODI threshold was applied to the 12 patients already mentioned, to assess the differences between NODDI-based and DTI-based tractography. After a visual comparison, a quantitative index of track density, defined as the sum of the number of tracks reconstructed in each voxel inside the lesion areas, was calculated for each method. For comparison, the same index was calculated in the healthy hemisphere of the 10 patients used for calibration.

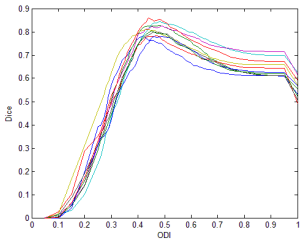

Figure 1. Dice index at each considered ODI threshold for the reconstruction of the CC

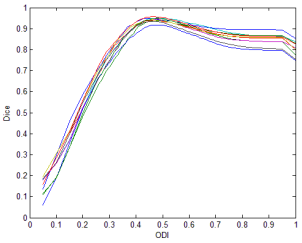

Figure 2. Correlation index between the number of fibers reconstructed with each ODI threshold and those reconstructed with FA=0.2

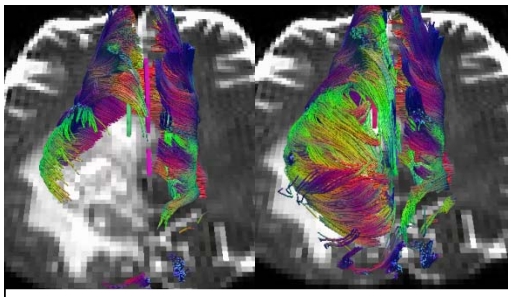

Figure 3. An example of visual comparison between DTI-based (left) and NODDI-based (right) tractography in vasogenic edema

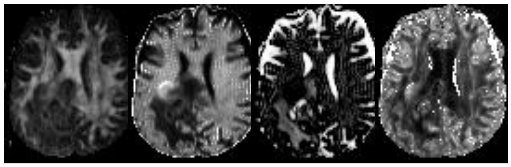

Figure 4. From left to right: maps of FA (from DTI), intracellular fraction, CSF fraction and ODI (from NODDI) in the same lesion shown in fig.3

RESULTS: *Optimal ODI Threshold:* The maximum Dice index for the reconstruction was found with an ODI threshold of 0.463 ± 0.024 for the CC (fig. 1) and 0.477 ± 0.042 for the CST. The maximum correlation between the number of fibers in the healthy hemisphere was found with an ODI threshold of ODI = 0.467 ± 0.0095 (fig. 2). An optimal threshold of ODI = 0.47 was finally chosen. *Tractography Comparison:* Considering the results in the tumour areas, the track density in the lesions was higher with NODDI-based tractography than with DTI-based tractography for all patients. Also in the "calibration group" this index was generally higher in NODDI-based than in DTI-based tractography, but the difference is much smaller: the mean increase in healthy tissue is about 5%, while in lesions the track density from NODDI-based tractography is at least twice the density from DTI-based tractography for all the considered patients. The visual comparison highlighted that differences are found especially in regions with vasogenic edema, which benefits from NODDI's ability to isolate the contribution from CSF contamination. Fig. 3 shows an example, and the maps in fig. 4 show that in the edema FA is low, the intracellular volume fraction is low, the CSF fraction is high, but ODI is low, revealing the presence of ordered structures.

DISCUSSION AND CONCLUSION: This work applies NODDI to improve tractography in patients with brain tumours. We developed a procedure to perform NODDI-based tractography with an ODI threshold equivalent to the commonly used FA = 0.2 in order to fairly compare the results with those from DTI-based tractography. The preliminary results in areas infiltrated by brain tumours showed a higher track density in the lesions with NODDI than with DTI. The advantage of NODDI-based tractography appears to be most evident in areas of vasogenic edema, as we hypothesized. Future work will include a larger cohort to confirm this finding.

REFERENCES [1] Zhang et al., Neuroimage 2012; [2] Winston et al., Epilepsy Research (In Press); [3] Van Bruggen et al., ISMRM 2013; [4] Rowe et al., IPMI 2013; [5] Jenkinson et al., Neuroimage 2002; [6] http://www.nitrc.org/projects/noddi_toolbox; [7] http://www.trackvis.org

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