Validation of NODDI estimation of dispersion anisotropy in V1 of the human neocortex

Maira Tariq[1], Michiel Kleinnijenhuis[2], Anne-Marie van Cappellen van Walsum[3,4], and Hui Zhang[1]

[1]Department of Computer Science & Centre for Medical Image Computing, University College London, London, England, United Kingdom, [2]FMRIB Centre, University of Oxford, Oxford, United Kingdom, [3]Department of Anatomy, Radbound University, Nijmegen Medical Centre, Nijmegen, Netherlands, [4]MIRA Institute for Biomedical Technology and Technical Medicine, Enschede, Netherlands

Purpose: This work presents a validation of estimating dispersion anisotropy of neurites, using Bingham-NODDI [1]. Bingham-NODDI is a recent development of the diffusion MRI (d-MRI) technique called NODDI (neurite orientation dispersion and density imaging) [2]. NODDI enables mapping of the morphology of neurites (axons and dendrites) in the brain with indices that are sensitive and specific to the microstructural changes, resulting in a rapid uptake of NODDI in the field of neuroimaging [3,4]. But the original NODDI technique, Watson-NODDI, is limited, as it constrains the orientation dispersion of neurites to be isotropic. Bingham-NODDI was developed to address this limitation and enables estimation of dispersion anisotropy and the primary dispersion orientation, along with the standard NODDI indices, without imposing any additional acquisition requirements compared to the Watson-NODDI. Dispersion anisotropy is widespread in the human brain [5]; its estimation is a potential biomarker [6] and can enhance the accuracy of tractography algorithms [7]. The in vivo feasibility of the Bingham-NODDI metrics has been evaluated in [1], but the estimates obtained need to be validated. Here we conduct such a validation study using high-resolution ex-vivo imaging data, acquired on post-mortem samples of the human primary visual cortex (V1). V1 is a very well characterised region of the neocortex, with a diverse cytoarchitecture including fibres fanning/bending into the cortical layers, making it attractive for validating the measures from Bingham-NODDI. We hypothesise that using Bingham-NODDI will enable a more detailed differentiation of these characteristics and explain the data better compared to Watson-NODDI.

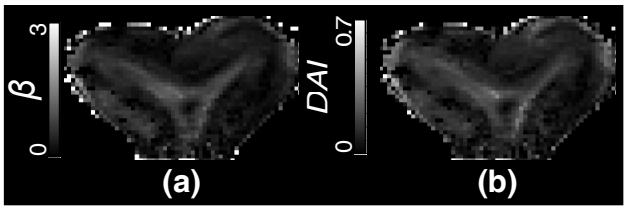

Fig. 1 Maps of the novel Bingham-NODDI parameters, (a) **β** and (b) DAI, for a slice in sample A

Methods: Data: Two fixed ex-vivo samples of the human V1 (as used in [8]) were imaged using a $9.4\mathrm{T}$ small animal MR scanner. Diffusion weighted images were acquired for $\mathrm{b} = [0,1000,4000,8000,12000,16000,20000]\mathrm{s/mm}^2$ and $\delta = 8.4\mathrm{ms}$, $\Delta = 12.8\mathrm{ms}$, $\mathrm{TE} = 27\mathrm{ms}$, with 60 and 432 equally spaced gradient directions for Sample A and Sample B, respectively. The resulting images were of $0.2\mathrm{mm}$ isotropic resolution with $\mathrm{FOV} = 28.8\mathrm{x}28.8\mathrm{mm}$, covering the cortex and the underlying (white matter) WM. NODDI model: NODDI is a two-level multi-compartment model, which separates the signal from the tissue and non-tissue components of the brain at the first level, while the second level models the signal from tissue compartment as a sum of the signal originating from inside and the space outside the neurites. The tissue compartments include an orientation density function (ODF) to account for the dispersion of neurites. Watson-NODDI uses the Watson distribution [9] as ODF, while Bingham-NODDI uses the Bingham distribution [10].

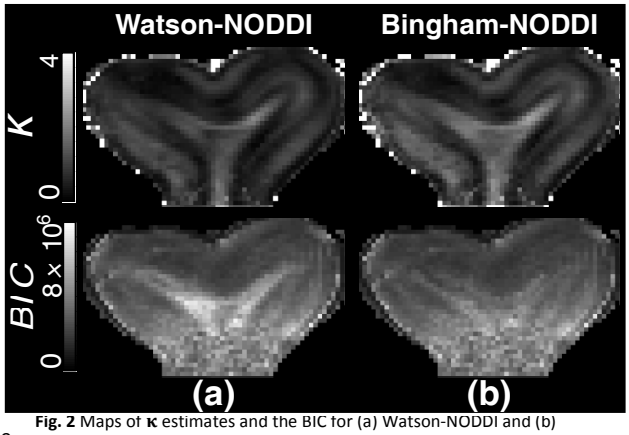

Fig. 2 Maps of **κ** estimates and the BIC for (a) Watson-NODDI and (b) Bingham-NODDI, for a slice of sample A

The neurite parameters estimated included their density (υ_{in}), dominant orientation ($\hat{\mu}_1$) and the coherence (κ) about $\hat{\mu}_1$. Bingham-NODDI also includes an estimate of the primary dispersion orientation ($\hat{\mu}_2$) and the associated coherence parameter (β). The relative coherence about $\hat{\mu}_1$ *and* $\hat{\mu}_2$ in Bingham-NODDI is represented in terms of the eigenvalues of the orientation tensor (OT), τ_1 and τ_2, respectively, as described in [1]. The dispersion anisotropy index, is defined as $\mathrm{DAI} = (\tau_2 - \tau_3)/\tau_1$. An isotropic restriction compartment (with volume fraction υ_{ir}) is added to the models to account for ex-vivo imaging as proposed in [11]. Model fitting: The models were fitted to the data using the NODDI Matlab Toolbox. Watson-NODDI parameters were obtained using the optimisation procedure described in [2], with the intrinsic diffusivity also fitted. To make the Bingham-NODDI fitting more stable and faster, the maximum-likelihood parameters from the Watson-NODDI fit were used to initialise the fitting. Model comparison: The parameters from the two models were evaluated using a standard model comparison metric, the Bayesian Information Criterion (BIC).

Results and discussion: Estimation of dispersion anisotropy: Fig.1 shows the maps of the novel parameters β and DAI estimated from Bingham-NODDI for one of the samples. The DAI maps show highest values in WM, which gradually get lower as the WM fibres disperse into the cortical grey matter (GM) areas, signifying the presence of fanning and bending fibres in the cortical areas. The β plot has a contrast very similar to the DAI, but the higher values are limited to the WM regions, unlike the higher DAI values, signifying that the WM fibres can be traced extending all the way to the cortical GM, from the DAI estimate. Model comparison: Fig.2 (2nd row) shows the BIC plots for the two models and demonstrates that Bingham-NODDI explains the data better than Watson-NODDI. Watson-NODDI fits the data particularly poorly in the WM regions, especially near the WM/GM boundary, the areas where dispersion anisotropy is expected due to the fanning and bending of the WM fibres towards the cortical GM regions. Fig.2 also shows the maps obtained for κ for the two NODDI models and it is clear that the values obtained from Bingham-NODDI have a higher intensity in WM, as well as the various cortical layers. This increased intensity and contrast in the κ map from Bingham-NODDI is more closely aligned with histology, as it is found in [12] that Watson-NODDI underestimates the actual neurite coherence (derived directly from histology), although this needs to be confirmed by a direct comparison. The comparison of the parameters obtained, confirm the results from the in vivo assessment of the two models in [1]; the volume fraction and τ_1 estimates are very similar, while τ_2 is significantly different between the two models. The Bingham-NODDI maps, particularly for sample B (results not shown), seem noisier, but a quality of fit assessment in those areas revealed that a) Watson-NODDI performs worse than Bingham-NODDI and b) even Bingham-NODDI is not fitting the data very well. This highlights the need for further work to be done to enable more stable fitting of the coherence parameters of Bingham-NODDI.

Conclusion: The results demonstrate that Bingham-NODDI is able to capture the fibres projecting deep into the cortex, by accounting for fanning/bending fibres. This has implications not only to enable better understanding of the organisation of the human brain microstructure, but also to enable fibres obtained from tractography to extend all the way into the cortical regions. Future work will involve a direct comparison of the Bingham-NODDI indices and the histological measurements from these samples.

References: 1. Tariq et.al. MICCAI, 2014; 2. Zhang et.al. Neuroimage, 2012; 3. Winston et al, Epilepsy Research, 2014; 4. Kunz et al, Neuroimage, 2013; 5. Sotiropoulos et.al. Neuroimage, 2012; 6. Jespersen et.al. IEEE, 2012; 7. Rowe et.al. IPMI, 2013; 8. Kleinnijenhuis et.al. ISMRM, 2013; 9. Mardia and Jupp, Wiley ser. in probability and statistics, 1990; 10. Bingham, Annals of Statistics, 1974; 11. Alexander et.al, Neuroimage, 2010; 12. Kleinnijenhuis et.al. OHBM, 2013;