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Detailed laminar characteristics of the human neocortex revealed by NODDI

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Introduction Over the past two decades, diffusion weighted imaging (DWI) enabled detailed investigation of white matter (WM) microstructure. More recently, progress in advanced DWI methods (e.g. high-field DWI) is now allowing the *cortical* structure to be studied noninvasively [1]. This is a particularly exciting development, because DWI has the potential to provide the richest *in vivo* description of cortical cytoarchitecture. Previous work has shown that the diffusion properties of the primary visual cortex (V1) are layer-specific [2]. In particular, the stria of Gennari displays low diffusivity and anisotropy. Here, we extend these findings by fitting the recent NODDI tissue model [3] to multi-shell DWI data to support a much more fine-grained division of the V1 cortical layers.

Methods DWI measurements were performed on human V1 samples (1x1x1 cm). Prior to imaging, samples were soaked in phosphate buffered saline (>72h) and mounted in a syringe with proton-free liquid under low pressure to release air bubbles from the sample (~24h). MRI was performed on a Bruker Biospec 94/20 USR system with BGA12S HP gradient set (660 mT/m; 4570 T/m/s) equipped with a Bruker CryoProbe 1x2 coil array cooled to 20-30K. DWI was acquired with 0.2 mm isotropic resolution (read-out segmented SE-EPI with 4 segments; matrix=128x128; FOV=25.6x25.6 mm; Sample A: 45 slices; TR/TE=6750/23.8 ms; b=[0,12000,4000,12000] mm^2s^{-1} in 768 directions; δ=7 ms; Δ=11.3 ms; TA=24h; Sample B: 40 slices; TR/TE=6000/26.7 ms; b=[0,800,3000,4000, 8000, 12000,16000,20000] mm^2s^{-1} in 48 directions; δ=8.4 ms; Δ=12.8 ms; TA=3h). Standard DWI processing included coregistration and diffusion tensor estimation from the b=4000 shell using FSLv5.0. The datasets were fitted using NODDI, a recent multi-compartment tissue model of diffusion suitable for modeling both gray and white matter [3]. NODDI distinguishes tissue into space bounded by axons and dendrites (intra-cellular compartment) and the space surrounding neurites (extra-cellular compartment). The neurite density and orientation distribution are then quantified by the intra-cellular volume fraction and a Watson distribution (providing estimates of the dominant direction $\boldsymbol{\mu}$ and the concentration of the orientations around $\boldsymbol{\mu}$, κ). NODDI includes a CSF compartment to capture CSF contamination. Here, following [4], we include an isotropic restriction compartment required for ex vivo samples. The model fit was achieved using the NODDI Matlab Toolbox.

Results and Discussion In the mean diffusivity (MD), three cortical layers could be distinguished (Figs.a). These coincide with the superficial layers, the stria of Gennari (low diffusivity) and the deep layers. The neurite density (Figs.d) was found to be high in WM. In the cortex, the neurite density (Figs.d) is distinct in at least four layers: the deep layers subdivide in a inner and outer layer; the stria of Gennari is characterized by high neurite density (overlapping the hypointense layer in the MD) and the superficial layers have a very low neurite density. This reflects fiber architecture as the WM, deep layers and stria of Gennari are rich in myelinated fibers, while in the superficial cortical layers these are more sparse. These superficial layers show a more prominent isotropic fraction (Figs.f) unaffected by dense cylindrical structure. The isotropic restriction compartment (Figs.e) varies slowly over the cortex. It features a hyperintense layer at the superficial boundary of the stria of Gennari, putatively layer IVA that is rich in closely packed cells. The dispersion parameter κ (Figs.c) correlates well with fractional anisotropy (Figs.b), but κ appears to be a more sensitive measure of fiber coherence because more contrast is observed in WM as well as GM.

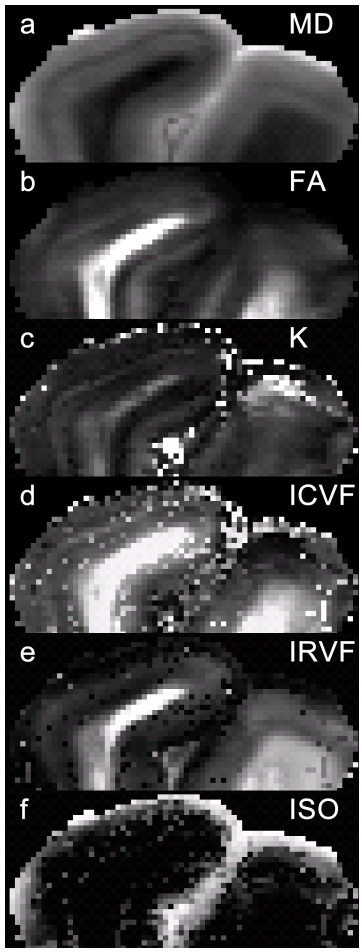

Figure 1. Sample A (2-shell data).

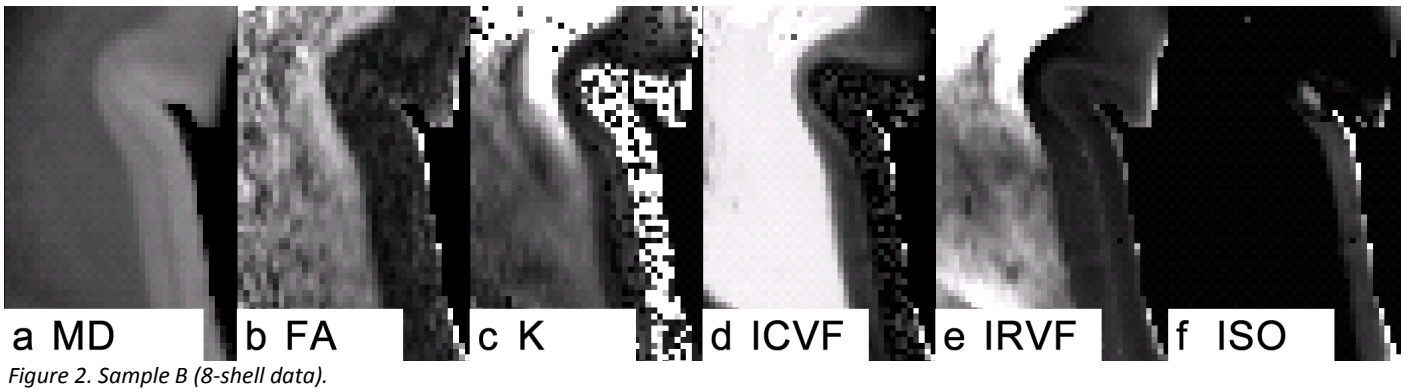

Figure 2. Sample B (8-shell data).

Conclusion Additional detail on cortical architecture is obtained by fitting the NODDI multi-compartment model to multi-shell data when compared to diffusion-tensor metrics. Additional layers were identified not visible in the MD or FA maps. Furthermore, whereas the deep and superficial layers have comparable properties in the MD, the volume fractions from the NODDI model distinguish between these as a neurite-dense deep layer and a superficial layer sparser in neurites. The dispersion parameter κ is more sensitive than FA. As NODDI does not require extreme b-values and scan times *in vivo* [3], these results suggest that NODDI has more potential for capturing cortical microstructure than compared to diffusion tensor metrics.

References [1] Heidemann et al. NeuroImage 2012; [2] Kleinnijenhuis et al. ISMRM 2011; [3] Zhang et al. NeuroImage 2012; [4] Alexander et al. NeuroImage 2010