

# Probing white matter microstructure at high spatial resolution combining CHARMED protocol optimization and a high performance gradient set

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## TARGET AUDIENCE

Clinicians and researchers interested in researching white matter microstructure indices in vivo at high resolution and in clinically feasible times.

## PURPOSE

The composite hindered and restricted model of diffusion (CHARMED)<sup>1</sup> describes the diffusion weighted imaging (DWI) signal as a combination of two components which originate from different microstructural compartments: the hindered (extra-axonal) and restricted (intra-axonal) compartment. This requires multiple acquisitions with high b-values and high angular resolution, both of which are difficult to obtain with clinical MRI systems. Recently a protocol optimization pipeline has been proposed which allows CHARMED estimation using a limited number of gradient orientations<sup>2</sup>. In addition, high gradient amplitudes ( $>40\text{mT/m}$ ) allows probing tissue microstructure at higher spatial resolutions. The purpose of this study is to investigate the feasibility of probing white matter microstructure at high spatial resolution in vivo at 3T, combining protocol optimization and a high amplitude, high slew-rate gradient set. This allows probing a maximum resolution of 1.3mm isotropic voxels in ~13 minutes across 6 different b-value shells. Different levels of trade-off between resolution, SNR and diffusion contrast are compared and the results are further compared to a benchmark dataset obtained from the Human Connectome Project (HCP) optimized for white matter orientation estimation.

## METHODS

Exploratory whole-brain data were collected on a Siemens 3T Prisma<sup>3T</sup> MR scanner (80 mT/m, 200T/m gradient, vendor 64Ch Head/Neck RF-coil) at 2mm, 1.5mm and 1.3mm isotropic voxels to evaluate SNR. The maximum b-value was then chosen, for each protocol, to match the maximum signal attenuation to that reported in<sup>2</sup>, which ensures the optimal balance between SNR and the power to resolve compartments and fiber crossings. We then acquired 3 different series of whole brain DWI data sets (PGSE EPI, A->P phase encode direction, GRAPPA 2, PF 6/8, 6 b0s, 45 diffusion directions, 6 shells, 1.3-1.5-2mm cubic voxels, with respectively: max b-values = 4000-5000-6000 s/mm<sup>2</sup>, 90-83-60 axial slices, TE = 80-84-89ms, SNR = 17-26-32 as mean/std-dev of b0 intensity in white matter mask) in two subjects using a protocol optimized for CHARMED estimation<sup>2</sup>. 5 matched b0s with reversed phase encoding direction were acquired after each series. A 3D MPRAGE scan (0.9mm cubic voxels) was acquired for white/grey matter segmentation and coregistration. TOPUP and EDDY tools in fsl 5.0 were applied to correct for motion, eddy currents and off-resonance distortions. The results are further compared to a high SNR and high angular resolution dataset obtained from the HCP which consists of 3 shells acquired in ~55 minutes with a multi-band simultaneous multi-slice sequence, for a total of 270 gradient orientations<sup>3</sup>. The DW signal was fitted to the CHARMED model<sup>1</sup> using an in-house program coded in MATLAB (The Mathworks, Natick, MA) based on the Levenberg–Marquardt algorithm. Maps of the restricted volume fraction (RF), considered a proxy for axonal density, were reconstructed for each subject and each protocol.

## RESULTS

Figure 1 shows the qualitative comparison between RF maps obtained from the human connectome and the acquired datasets upsampled to MNI space at 0.7mm isotropic. Increasing resolution from 2mm (A) to 1.5mm (B) and 1.3mm (C) improves anatomical details in the cerebellum (see insets), despite a decrease in SNR. Three ROIs were selected in the corpus callosum (genu, midbody, splenium) where mean and standard deviation were calculated over voxels and reported in Table 1. This shows that canonical microstructural differences in the different segments of the corpus callosum (high-low-high density) are also maintained. The HCP dataset (Fig. 1D) shows a clear contrast between white matter and gray matter and high SNR, but does not show the same distribution of RF identifiable in the other datasets (see insets and Table 1).

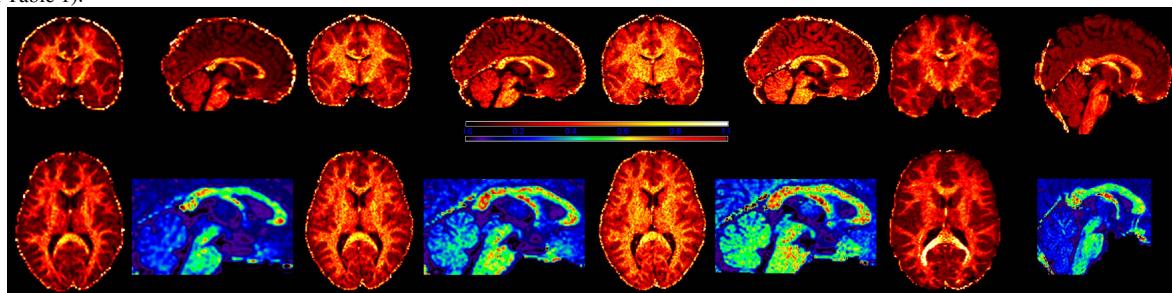


Figure 1 A

B

C

D

DATASET	GENU	MIDBODY	SPLENIUM
HCP 1.25mm	$0.59 \pm 0.10$	$0.62 \pm 0.12$	$0.58 \pm 0.12$
Both Subjects 1.3mm	$0.65 \pm 0.13$	$0.63 \pm 0.15$	$0.73 \pm 0.11$
Both Subjects 1.5mm	$0.68 \pm 0.14$	$0.63 \pm 0.13$	$0.70 \pm 0.14$
Both Subjects 2mm	$0.61 \pm 0.19$	$0.58 \pm 0.12$	$0.63 \pm 0.09$

Table 1

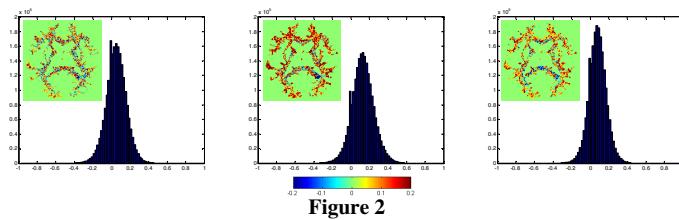


Figure 2

Figure 2 shows the quantitative difference histograms of RF in white matter between the three volumes (1.3 – 1.5mm, 1.3 – 2mm, 1.5 – 2mm) for both subjects together. Differences are normally distributed and their means are  $0.05 \pm 0.11$ ,  $0.13 \pm 0.12$ ,  $0.08 \pm 0.1$ . The insets show an example axial slice for the three difference maps in one subject.

## DISCUSSION & CONCLUSION

Offsets in RF between resolutions (Fig. 2) may be explained by the differences in TE across the acquisitions, since the two compartments have different T2 and a different TE will affect the contribution to total signal loss from the two compartments, which is a topic for future study. The HCP dataset acquired in ~5x the time, but optimized for the purpose of fiber orientation estimation, cannot improve microstructure estimation, showing the importance of specific microstructure protocol optimization. We have shown that protocol optimization and systems equipped with high amplitude gradients allow the robust estimation of microstructural indices at high spatial resolution across the whole brain in clinically feasible times.

## REFERENCES

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