Higher order diffusion MRI acquired in clinical setting: white matter microstructure mapping across the lifespan

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INTRODUCTION

- Diffusion MRI (dMRI) has the ability to probe tissue microstructure noninvasively by measuring diffusion of water molecules in-vivo.
- Diffusion tensor imaging (DTI) [1], used in clinic and clinical research, probes directionality and Gaussian properties of water diffusion in tissue for diffusion weighting *b* up to 1000 s/mm^2.
- Diffusional kurtosis imaging (DKI) [2] additionally measures non-gaussian diffusion properties for slightly larger *b* ~2000 s/mm^2.
- In brain, we can use biophysical models such as standard model imaging (SMI) [3] which allows us to be specific to cellular changes.
- DKI and SMI require higher order dMRI, which are not yet routinely acquired in the clinical setting, as it requires longer acquisition time, leading to poor image and data quality [4].
- Here we evaluate feasibility of higher order dMRI in clinic. We added a higher order dMRI protocol to routine clinical brain scans in an outpatient center between 2014 and 2020 and scanned approx. 8000 patients.
- We extracted and retrospectively analyzed a subgroup of normal subjects to map changes during aging in white matter regions of interest (ROIs) using DKI and SMI.

METHODS

Data acquisition (~7min)

Protocol (# of direction measurements x *b*-values (s/mm^2))	5 x *b*=0, 20 x *b*=1000, 4 x *b*=250, 60 x *b*=2000 **b-value (deg. of diffusion weighting)*
TE	70-96ms (Prisma 3T), 95-100ms (Skyra 3T)
TR	3.2-4s (Prisma 3T), 3.5-4.3s (Skyra 3T)
Resolution mm^3	1.7x1.7x3, 50 slices
Partial Fourier	6/8

Subjects (N=589)

M/F	182/407
Age	Range: 7-75 yo, Average: 43.6±15 yo

Image processing: dMRI datasets were preprocessed to remove noise and image artefacts using DESIGNER pipeline [5] (noise removal [6-8], Gibbs correction [8], distortion correction [10], eddy current & motion correction [11], b0 normalization, and Rician bias correction [12]). Then, DKI (MD, FA, MK) and SMI (f, D_a, $D_e^{\perp}$, $D_e^{\parallel}$, p_2) metrics were derived [3,13].

Last, JHU white matter atlas [14] was warped to each patient's FA map to extract mean values from genu of corpus collosum (GCC), splenium of corpus collosum (SCC), and cingulum.

RESULTS

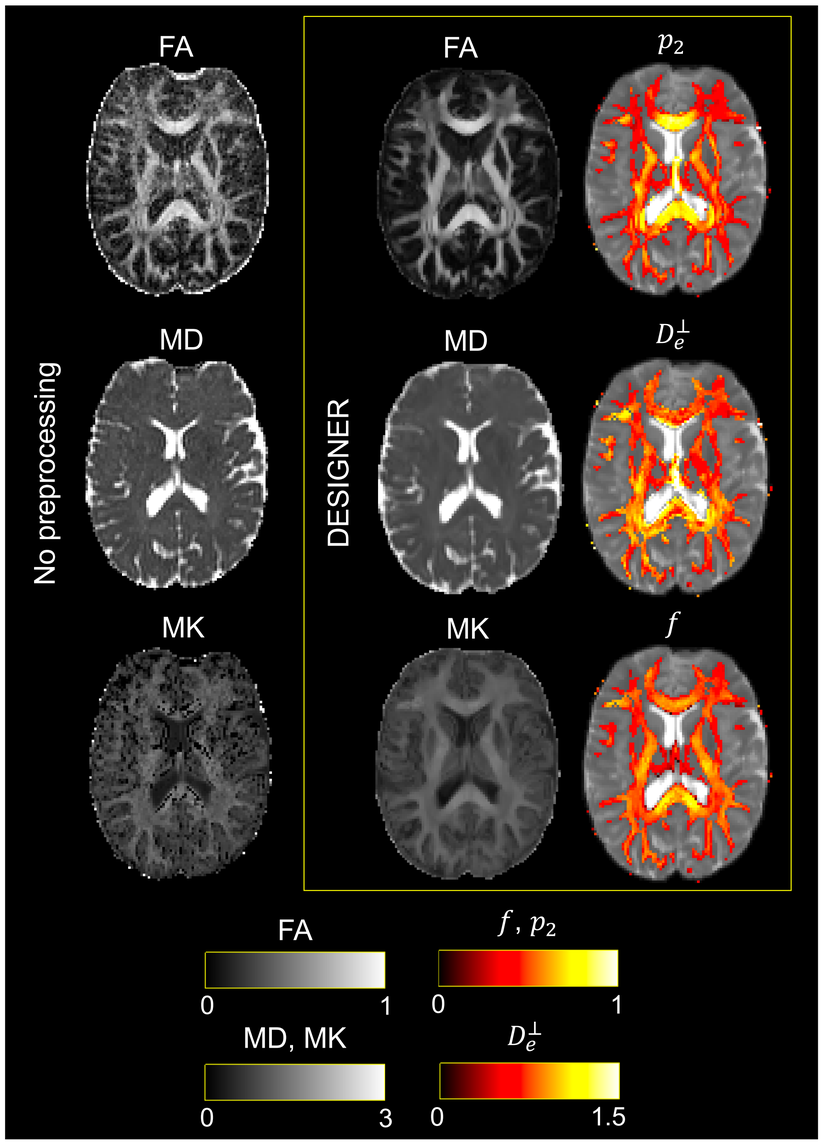

Figure 2. Parameter maps (FA, MD, MK; $p_2, D_e^{\perp}, \& f$ overlay on *b*=0 image) from dMRI of a 60-year-old female after preprocessing with DESIGNER pipeline. Image quality appears good with little to no apparent outliers from noise and image artefacts.

DISCUSSION AND CONCLUSION

- Higher order dMRI can feasibly be acquired in the clinical setting with reliable image quality.
- MD, MK, and $D_e^{\perp}$ age associations imply myelination hindering diffusion during development followed by demyelination after peak age.
- FA and f age associations suggest axonal growth leading to increased f and tighter fiber packing during development followed by possibly axonal shrinkage after peak age
- By acquiring higher order dMRI, we can obtain more informative and accurate representation of tissue microstructure.

Mean diffusivity (MD, $\mu m^2/ms$): describes magnitude of diffusion in brain tissue

Fractional anisotropy (FA): degree of anisotropy of water movement scaled from 0 (isotropic) to 1 (anisotropic)

Mean kurtosis (MK): degree of non-gaussian or restricted diffusion

Fiber orientation anisotropy (p_2): anisotropy of orientation distribution fxn (ODF)

Radial diffusivity ($D_e^{\perp}$, $\mu m^2/ms$): diffusion ⊥ to axon in extra-axonal space

Axonal water fraction (f): ratio of intra-axonal to total (intra- & extra-) water

Intra-axonal diffusivity (D_a, $\mu m^2/ms$): diffusion of water inside & along axon

Axial diffusivity ($D_e^{\parallel}$, $\mu m^2/ms$): diffusion ∥ to axon in extra-axonal space

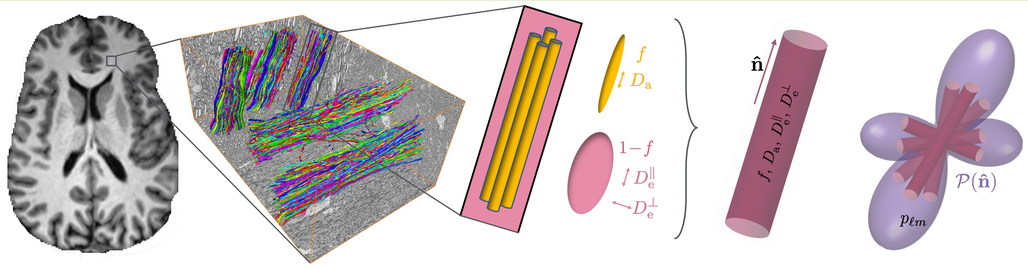

Figure 1. Standard model of diffusion in white matter. Elementary fiber fascicle is represented as multiple diffusion compartments described by f, D_a, $D_e^{\perp}$, $D_e^{\parallel}$. A voxel contains a cluster of fascicles oriented in an arbitrary ODF.

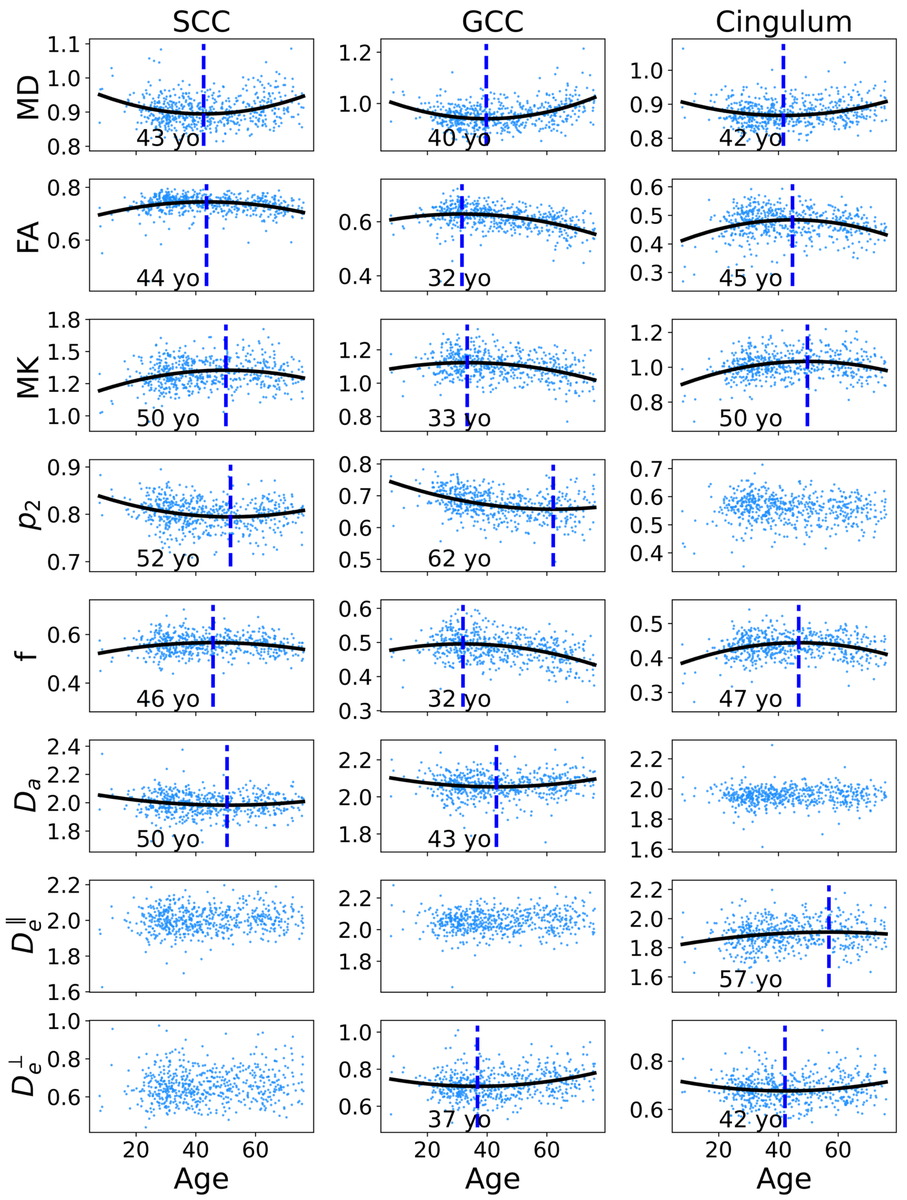

Figure 3. Age correlation plots with DKI and SMI metrics in genu of corpus collosum, splenium of corpus collosum, and cingulum. Quadratic fits were plotted for statistically significant age associations (p-value<0.05). Peak age is indicated if it is within 7-75 yo range. Plots show MD and $D_e^{\perp}$ (except in SCC) decrease during development before increasing while FA, MK, and f increase during development before decreasing.

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