5857

Axon Diameter Distribution (ADD) MRI

Raisa Freidlin[1], Evren Ozarslan[2], Sinisa Pajevic[1], Michal E Komlosh[3], and Peter J Basser[3]

[1]NIH/CIT/DCB, Bethesda, MD, United States, [2]Radiology, BWH, Harvard Medical School, Boston, MA, United States, [3]NIH/NICHD/PPITS, Bethesda, MD, United States

Introduction: Myelinated axons transmit signals at a speed proportional to their diameter. The axon diameter distribution (ADD) provides information about how much information can be transmitted along a fascicle. Here we present an integrated and general experimental and theoretical framework for using diffusion MRI data to measure the ADD in brain white matter throughout the entire Central Nervous System (CNS).

3D DWI (q-space) Data Analysis: We obtain estimates of the ADD for fascicles in *any* orientation, *anywhere* within a brain volume, unlike AxCaliber MRI and other inherently 1-D ADD MRI measurement methods, which require the axon's orientation to be known *a priori*. We first estimate an average propagator in each voxel using a 3-D generalization of the framework in [1]. With it we determine the direction of maximum diffusivity and then estimate the DW signal attenuation profile, $E(q_\perp)$ vs. $q_\perp$, perpendicular to the fascicle's main axis. This data is then used with models of diffusion in impermeable tubes [2,3] to estimate the $E(q_\perp)$ that would be produced by a pack of axons with a particular ADD. The estimated ADD is obtained by minimizing the residual errors between the predicted signals and measured $E(q_\perp)$ vs. $q_\perp$ data. Our calculation of $E(q_\perp)$ also corrects for the motional narrowing artifact caused by using finite-width diffusion gradient pulses without which, the ADD would be artifactually skewed towards having smaller diameter axons.

ADD Models: We use two novel statistical models to fit ADD data. One is a parametric probability density function (pdf) developed by maximizing the information transmitted along fascicles subject to anatomical and energetic constraints. This pdf was found to be more robust than the lognormal, γ, and other parametric pdfs previously used to fit histological and MRI ADD data. The second is a non-parametric modeling framework that empirically determines the form of the ADD by using non-uniform b-splines (NUBS).

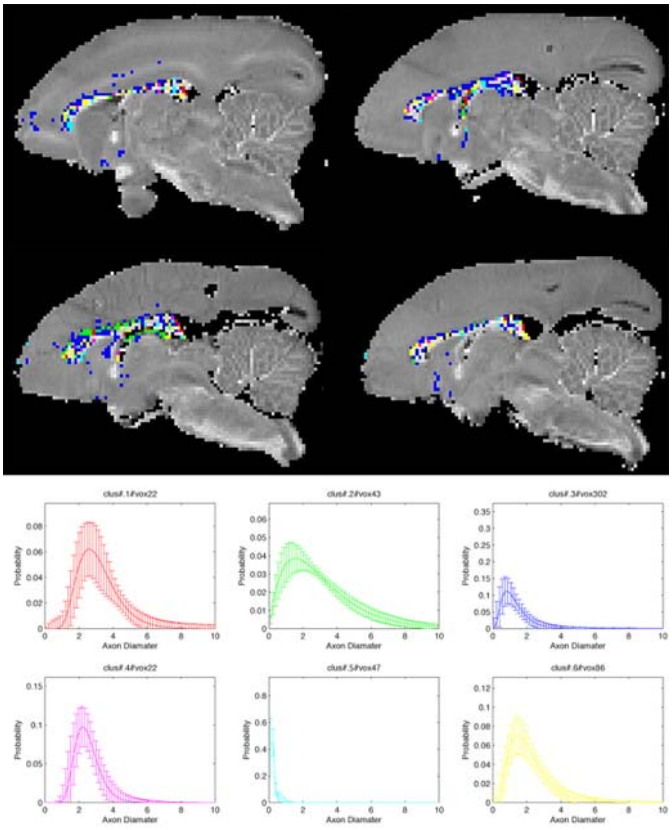

Fig 1. White matter pathways identified in sagittal slices of marmoset brain with corresponding ADDs (μm)

Materials and Methods: Marmoset brains obtained after necropsy were fixed in 4% formaldahyde, then rehydrated and packed in Fomblin. They were scanned with a Bruker 7T (Avance III) microimager. The q-space MRI protocol consisted of 496 DWI acquisitions on 7 shells (q-values between 13 and 93 mm^{-1}) with δ=2.85 ms with diffusion times (Δ) of 20 and 40 ms.

Results: Multivariate k-means clustering was performed using a set consisting of the hindered compartment fractions, diffusion coefficients, and two parameters of the estimated ADD in each voxel within white matter pathways. Fig. 1 shows six clusters within white matter pathways in four consecutive sagittal slices with a corresponding color-coded ADD plots. 3D visualization of ADD clusters in 40 slices is shown in Fig. 2.

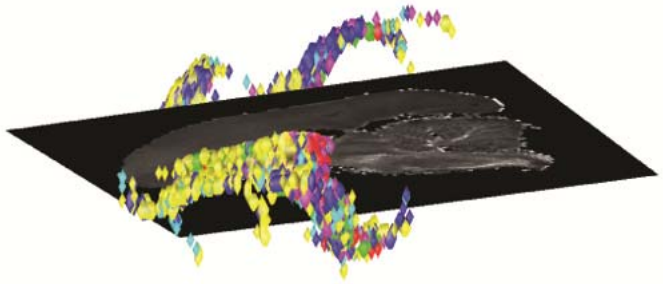

Fig 2. 3D visualization of white matter pathways

Discussion and Conclusion: The ADD is a high-value histological feature that is now accessible in all brain white matter pathways. The need for a non-parametric ADD model is acute in both developmental biology and in pathological applications where one has no *a priori* knowledge about how skewed or heavy tailed the ADD is or even whether it is mono or multi-modal.

Because of the relatively low overhead of estimating average propagators in each voxel now, this new MRI approach has the potential to be translated *in vivo* to both animal and humans with current DWI hardware. Next generation MRI scanners equipped with stronger and faster gradient systems should enable both parametric and non-parametric ADD MRI measurements like these for routine assessments in the clinic.

References: [1] Ozarslan et al., Proc Intl Soc Mag Reson Med, 16, p. 35, 2008; [2] Grebenkov, Rev Mod Phys, 79, p. 1077, 2007; [3] Ozarslan et al., J Chem Phys, 130, 104702, 2009;