

AxCaliber 3D

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Introduction: Diffusion tensor imaging (DTI) provides an opportunity to investigate brain connectivity via fiber-tracking. The major macroscopical pathways in the brain have been demonstrated using this approach¹. Nevertheless, the ability of fiber-tracking to extract structural connectivity is limited due to partial volume effects. These may occur at the boundaries of white matter with surrounding tissue or even within the white matter where several fiber-bundles pass through the same voxel. In this work, we have used the composite and restricted model of diffusion (CHARMED²) and AxCaliber^{3,4} (the measurement of axon diameter distribution (ADD) from diffusion MRI images) frameworks to investigate the micro-structural features of a complex fiber system phantom. So far, the ability to map the ADD along a given pathway was only possible with AxCaliber if the fiber orientation was known and so this precludes any tract-specific assessment. In this work we extended the AxCaliber framework to any arbitrary fiber orientation.

Methods: This work was done on a phantom made from fixed excised porcine spinal cord cut into two segments: one sectioned out from the fasciculus gracilis and the second from the anterior cortico-spinal tract. Those sections were chosen since they are known to have different ADD. The two sections were placed perpendicularly one on top of the other and immersed in proton-free susceptibility fluid (FC-77). The imaging experiments were performed on a 7T Bruker system and comprised multiple CHARMED scans and traditional DTI. CHARMED acquisitions were acquired at 3 different Δ of 35,70,105ms (similar to AxCaliber framework^{3,4}), with the same δ of 5ms, at 6 b-values (linearly increment 1000 to 6000s/mm²) in 16 non-collinear directions. The DTI scan was performed as following: $\Delta/\delta=10/4.5$ ms, b-value=1000s/mm² in 60 non-collinear directions. All the imaging scans were acquired with similar geometric parameters: matrix=96x96, in-plane resolution of 0.325mm² isotropic and slice thickness of 6mm at the axial plane including both spinal cord sections.

Analysis: The CHARMED model² was extended to analyze simultaneously multiple CHARMED data sets at different diffusion times (Δ s). This analysis provided, for each voxel the volume fraction of hindered and restricted diffusion, the fibers orientations (two in each voxel), the hindered and restricted diffusivities and the noise floor. From this data set, a full AxCaliber data set was re-sampled exactly perpendicular to the fitted fiber systems. Finally, AxCaliber model was used to calculate the ADD of each voxel. From the DTI data set, fiber tracking was done with exploreDTI⁵ utilizing the spherical harmonics de-convolution procedure⁶, launching from each spinal cord segment.

Results: Figure 1A demonstrates the variation of the signal strength depending on the diffusion gradient direction at high b values. CHARMED analysis computes the two fiber systems at the crossing region (green frame) (Figure 1B) and single fibers at the non-crossing parts. Figure 1C shows spherical de-convolution analysis of the DTI data set. This analysis allows characterization of the diffusion properties of each of the fiber segment separately. Following re-sampling of the data to create an AxCaliber data set it was possible to calculate, for each image voxel and for each fiber within the ADD as shown for one representative voxel in Figure 2. Figure 3A shows fiber tracking of the DTI data set where the crossing fibers are resolved using the spherical harmonic de-convolution.

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using the spherical harmonic de-convolution. Figure 3B shows the same fibers as in Fig. 3A but colored according to the ADD. Such analysis shows that the spinal cord segments appear to have different ADDs.

Conclusions and Summary

The framework presented in this work shows that the AxCaliber framework can be extended to 3D to achieve a full axon diameter distribution in any voxel of the brain and any fiber orientation. This is done by projecting the data perpendicular to the restricted compartment. In addition, the ability to plot the ADD along a given fiber system allow a new way to look at tractography and connectivity in the brain.

References: (1) Catani M *et al.* (2002) Neuroimage. (2) Assaf Y *et al.* (2005) Neuroimage. (3) Assaf *et al.* (2008) Magn. Reson. Med. 59 (4) Barazany *et al.* (2009), Brain 132. (5) Leemans A *et al.* (2009) Proc. ISMRM 17th Annual Meeting. (6) Tournier JD *et al.* (2004) Neuroimage

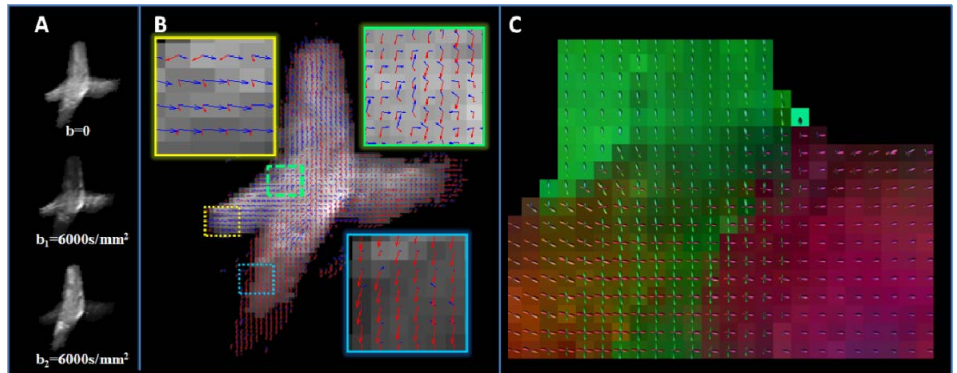


Figure 1: (A) Original diffusion weighted images at different gradient directions. (B) CHARMED analysis reveals two fiber systems at the crossing region similar to (C) the spherical harmonic de-convolution DTI analysis.

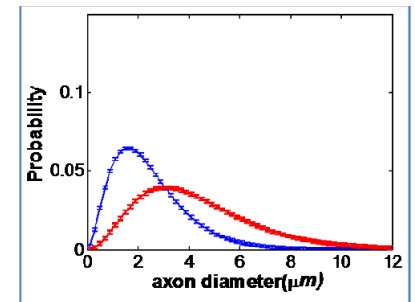


Figure 2: AxCaliber analysis distinguishes between the two fiber system, characterized by different axon diameter distributions.

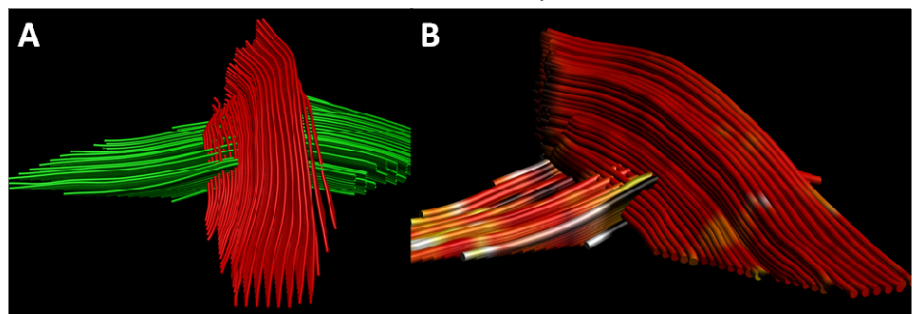


Figure 3: (A) Spherical harmonic de-convolution resolved the two fiber systems, and (B) colored according to their axon diameter distribution.