Non-invasive average axon diameter mapping using double pulsed field gradient (d-PFG) filtered MRI.

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Abstract:
The diameter of myelinated axons is a critical neurophysiological parameter that scales with nerve conduction velocity. In the spinal cord, axons are somatotopically organized into distinct anatomical regions performing specific functions, and characterized by different diameters and diameter distributions. Measuring axon diameters can shed light on nerve function and pathology. In this study we use double pulsed-field gradient (d-PFG) MRI, which measures correlations between displacements of water molecules, to measure and map the apparent mean diameters within different regions of spinal cord white matter. Double-PFG MRI images were acquired on a formalin-fixed pig spinal cord and diameter maps were obtained using a recently introduced theoretical framework. A pixel-by-pixel analysis was performed to create an axon diameter map within white matter regions of the spinal cord. K-means segmentation was performed on these diameter maps to identify distinct clusters. The MRI data compare favorably with histology results obtained using toluidine blue stained sections of the same spinal cord specimens. Axon diameter estimates ranged between 3 and 5 µm, which is in the expected range for such specimen. The distinct clusters obtained by d-PFG MRI showed good homology with histological staining and known somatotopic organization. This work demonstrates that d-PFG filtered MRI is a powerful non-invasive tool for mapping axon diameter. Double PFG MRI also has the potential for measuring other important microstructural characteristics and features of cells, including cell shape and eccentricity, and their macroscopic ordering or alignment.
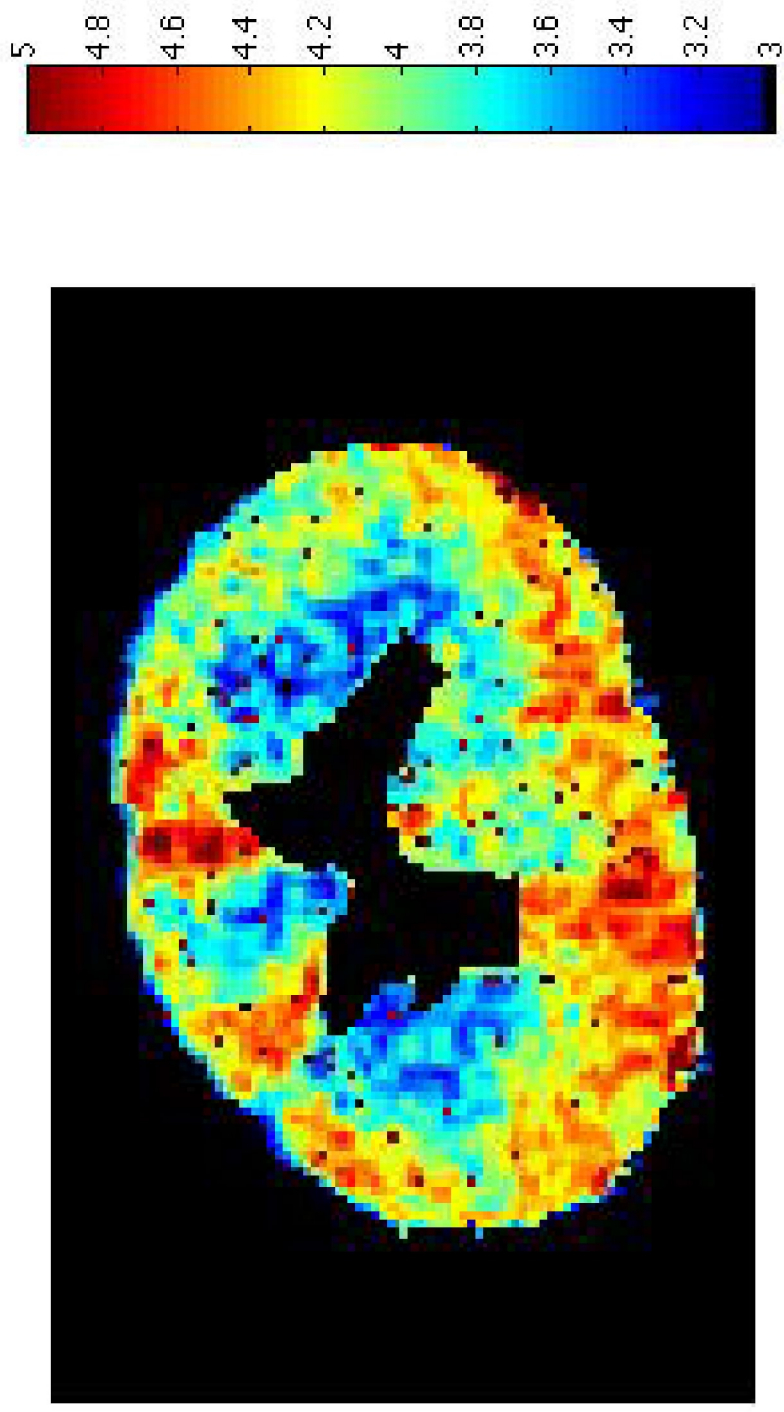
Map of average axon diameter of pig spinal cord (μm)