dPFG MRI assessment of axonal beading in an injury model

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Introduction: Central Nervous System (CNS) neurites exhibit a beaded axonal morphology following mechanical, chemical, or metabolic insults. Recently, this mechanism of axonal beading was advanced to explain both the reduction in the mean ADC during traumatic brain injury (TBI) and ischemia, and its re-elevation observed during recovery. The ADC parallel and perpendicular to nerve fibers obtained by DTI showed demonstrable macroscopic changes associated with these injuries. While sensitive, these DTI-derived parameters do not provide specific microstructural or anatomical information about the origin of these changes in axonal dimensions. Here we use double Pulsed-Field Gradient (dPFG) MRI to provide important new microstructural information that can help to characterize the beading process in axons. In a model of beading axons, we show that dPFG MRI furnishes estimates of the aspect ratio (shape) of axonal "beads" following injury. This unique information cannot be obtained by single PFG macroscopic diffusion MRI methods.

Materials and Methods: Rat sciatic nerves were excised and subjected to axial tension sufficient to induce beading or minimal tension to straighten the injured nerve diameter ranged between 4.12

Results: Figure 1 a and b show confocal microscope images of the injured and control nerves. The long axis of the beads in the injured nerves ranged between 17.2–35.6 µm with an average diameter, d, of 25.7 µm while the short axis ranged between 2.57–7.18 µm with d = 4.26 µm. The control nerve diameter ranged between 4.12–6.86 µm with d = 5.67 µm. Figure 2 a-c show the angular dependence of the signal in the dPFG experiments for the injured, control, the GCA (symbols) and their corresponding model fits (lines), respectively. Model fitting shows an average long axis of 7.91 µm, with d = 4.7 µm for the beaded nerve and d = 4.1 µm for the control nerve. For the GCA, d = 9.7 µm, which is very close to its nominal value.

Discussion: This study shows a significant change in the angular dependence of the dPFG MR signal between the injured and control nerves. The average long axis appears larger than the one obtained by optical microscopy. This discrepancy may be due to the fact that the model assumes the individual beads are capped while it is apparent in the optical microscopy images that they are connected. Alternatively, the dPFG signal is obtained from the entire nerve, whereas the small field-of-view (FOV) optical measurements reflect only a portion of the sample. Nonetheless, the estimated mean diameters of all samples however are resolvable.

Conclusion: dPFG MRI shows potential for characterizing microstructural changes and their time-course in injured or ischemic white matter. The development of a more complex theoretical framework to represent other features of beaded axonal morphology is in progress.