Mapping the myelin g-ratio during neurodevelopment

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Target Audience: Researchers interested in early brain maturation, myelination, white matter imaging and quantitative magnetic resonance imaging (MRI).

Purpose: Myelination is a critical process of white matter development. While several neuroimaging techniques have been used to study white matter development, no prior studies have directly examine the microstructural properties of myelin. The myelin g-ratio, defined as the ratio of the inner axonal diameter to the total outer diameter of the fiber, may provide a novel contrast of the myeloarchitecture[1]. Recently, models relating quantitative magnetization transfer and neurite orientation dispersion and density imaging[2] (NODDI) parameters to the myelin g-ratio have emerged[3,4], thereby providing a method to measure this fundamental property *in vivo*. In this work, we present an alternative approach, combining multicomponent relaxometry and NODDI data, to measure the myelin g-ratio. To highlight this method, we demonstrate myelin g-ratio measurements in typically developing children and, for the first time, provide developmental trajectories of myelin g-ratio.

Methods: *MRI Acquisition:* 19 typically developing infants (102-2713 days, corrected for gestation) were imaged using a 12 channel head RF array on a Siemens Tim Trio scanner during non-sedated sleep. Multi-flip angle SPGR and bSSFP images were acquired and three-pool mcDESPOT post-processing[5] was used to calculate mylin water fraction (VF_M) parameter maps. A two-shell diffusion imaging protocol (b=700 s/mm^2, b=2000 s/mm^2, 30 diffusion encoding directions each) was also acquired and NODDI parameters were calculated using the available MATLAB toolbox[2]. VF_M maps and the volume fractions of the intra-cellular (ν_{icvf}) and isotropic compartments (ν_{iso}) were combined to calculate the myelin g-ratio[3]. Mean VF_M, ν_{ic}, ν_{iso}, and g-ratio across white matter was calculated for each subject and plotted against the subject's gestation-corrected age.

Results: Fig. 1 shows a representative axial slice of VF_M, ν_{icvf}, ν_{iso}, and myelin g-ratio maps from 5 subjects. Fig. 2 shows the trajectory of mean VF_M, ν_{ic}, ν_{iso}, and g-ratio across white matter. VF_M appears to follow a sigmoidal trajectory, ν_{icvf} and ν_{iso} have a linear relationship, while the myelin g-ratio follows a decreasing logarithmic trajectory.

Discussion: The observed changes in VF_M and g-ratio reflect the progressive development of myelinated white matter. Theoretical models suggest that for maximal axonal efficiency, the optimal g-ratio of the developed brain is between 0.6-0.8[1]. Here, calculated g-ratio values are larger, however, values appear to approach these conjectural values as the brain develops over time.

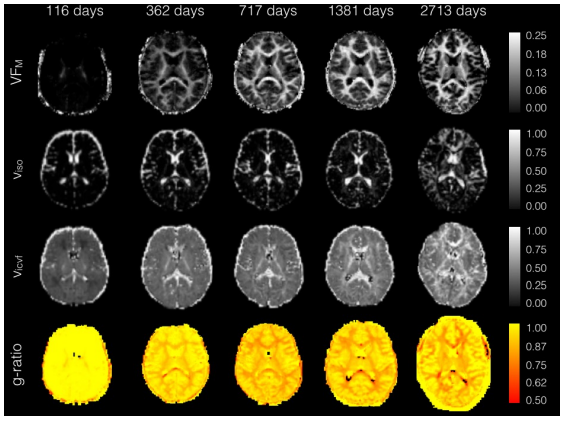

Fig. 1: Fig. 1: Representative axial slices of VF_M, ν_{icvf}, ν_{iso}, and myelin g-ratio maps

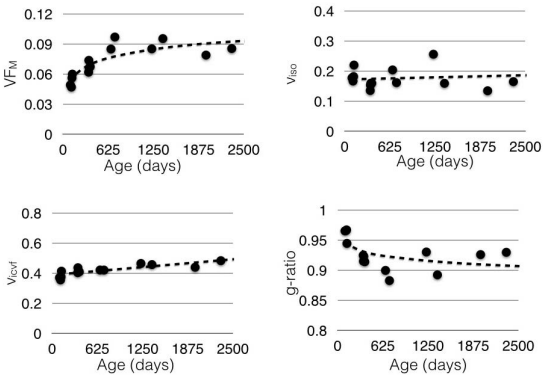

Fig. 2: Developmental trajectories of VF_M, ν_{icvf}, ν_{iso}, and myelin g-ratio.

Conclusion: In this work, we have described an approach to quantifying the myelin g-ratio by combining the mcDESPOT and NODDI imaging techniques and for the first time have presented developmental trajectories of the myelin g-ratio during early childhood. This presented work provides an important step for understanding the developmental patterns of white matter microstructure and the myelin g-ratio. Future research will investigate the utility of the g-ratio as a biomarker of neurodevelopmental and neurological disorders as well explore the relationships between the myelin g-ratio and cognitive/behavioral outcome.

References: [1] Chomiak and Hu. What Is the Optimal Value of the g-Ratio for Myelinated Fibers in the Rat CNS? *A Theoretical Approach.* PLoS ONE 2009;4(11); [2] Zhang et al. NODDI: practical in vivo neurite orientation dispersion and density imaging of the human brain. NeuroImage 2012;61:1000-16; [3] Stikov et al. *In vivo* measurement of the myelin g-ratio with histological validation, In Proc. of the ISMRM 2014, #0102; [4] Campbell et al. Combined NODDI and qMT for full-brain g-ratio mapping with complex subvoxel microstructure, In Proc. of the ISMRM 2014, #0393; [5] Deoni SCL, et al. One Component? Two Components? Three? The effects of including a non-exchanging 'free' water component in mcDESPOT *MRM.* 2012;70:147-154.