Multiexponential T_2 and Quantitative Magnetization Transfer in Rodent Brain Models of Hypomyelination

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Target Audience:

Researchers interested in myelin imaging of rodent models and underlying changes in microstructure.

Purpose:

Myelin water imaging (MWI) by multi-exponential transverse relaxation (MET_2) and quantitative Magnetization Transfer (qMT) provide information about myelin content and microstructure in white matter[1,2]. Recently developed tuberous sclerosis complex (TSC) and Rictor conditional knockout (CKO) mouse models display significant decreases in myelin[3,4]. With development of 3D MWI for rodent brain[5], these high-resolution quantitative imaging methods provide an opportunity to analyze the myelin across whole brain in these and other rodent models. With the addition of histology, comparison of quantitative measures can be used to unravel the discord between MWI and qMT measures to better understand the relationship between white matter microstructure and MRI contrast.

Methods:

Mouse brains from control and knockout (TSC and Rictor CKO) were perfusion-fixed and loaded with 1mM of Gadolinium (Magnevist) in preparation for high resolution MRI studies at 15.2 T. A 3D Extended Phase Graph (EPG)-compliant multi-spin echo sequences was used to acquire images for MET_2 analysis[5,6], and an inversion-recovery prepared 3D fast spin echo sequence was used to acquire images for qMT analysis. Both image sets were acquired at 150 µm isotropic resolutions, requiring a total of ≈ 9.5 hr. An EPG-signal model was used for B_1-insensitive fitting of T_2-spectra[7] on a voxel-wise basis from the multiple spin echo images. From each spectrum, the myelin water fraction (MWF) was extracted as signal with T_2<17 ms. Macromolecular pool size ratio (PSR) was extracted from the qMT as previously described[8].

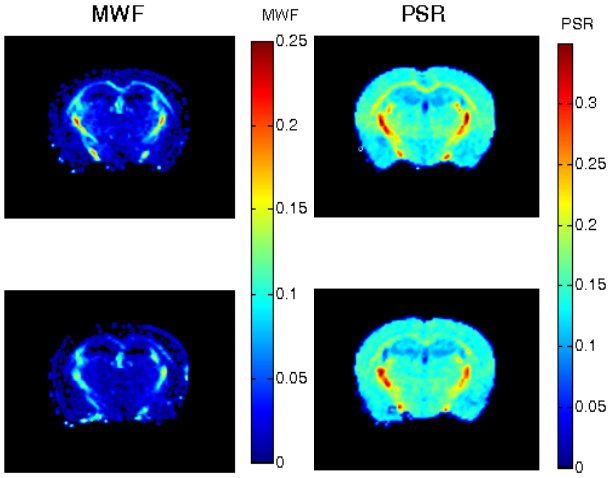

Figure 1. (Left) Myelin Water Fraction maps and (Right) Pool Size Ratio Maps at 15.2T of (top) control and (bottom) Rictor CKO mice.

Results and Discussion:

Both MWF and PSR maps from a Rictor CKO brain (Fig 1) demonstrate widespread reductions in myelin, in agreement with prior histological analysis[4]. Figure 2 shows MWF and PSR values broken down across three white matter tracts. The TSC CKO model, known to result in more pronounced myelin loss likewise showed greater reductions in MRI based measures (not shown). In both cases, MWF values declined between control and knockout to a much greater extent than did PSR values. This discordance is partially due to the fact that PSR does not drop to 0 in non-myelinated tissues, but may also reflect an increased effect of inter-compartmental water exchange on MWF measurements[2] due to thinner myelin in the knockout models. In addition, the long-lived T_2 values (not shown) increased for both CKO mouse models, consistent with a model in which long T_2 in fully myelinated white matter is significantly reduced due to myelin and less affected when the volume of myelin is less (despite a greater inter-compartmental exchange rate). Pending histology will be used to test this hypothesis and unravel the microstructural basis for the discord known between MWF and PSR.

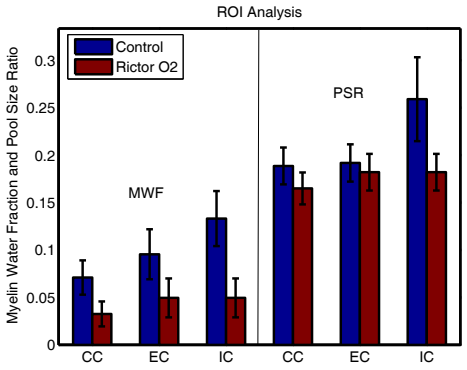

Figure 2. Mean MWF and PSR of white matter ROIs (corpus collosum (CC), external capsule (EC) and internal capsule (IC) between control (blue) and Rictor CKO (red) mice.

Conclusion:

MWI and qMT provide an efficient means of whole brain evaluation of abnormal myelination, and comparing these measures to each other and histology in well-controlled models of hypomyelination provides a means to better understand the relationship between white matter microstructure and water proton relaxation.

References:

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