Longitudinal imaging of the preterm brain: white matter multi-component T2 relaxometry and MR spectroscopy
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Introduction: Infants born prematurely are at increased risk of white matter injury and subsequent neurodevelopmental impairment. In such infants white matter injury at term is believed to be related to disrupted maturation and long-term myelination impairment. The posterior periventricular white matter (PWM) is thought to be a vulnerable area and MR measurements here may elucidate the causes and nature of white matter injury and recovery. In this work we investigate the use of multi-component MRI T2 relaxometry in infants born very preterm but scanned between 30 and 40 weeks equivalent gestational age (EGA) and correlate white-matter T2 with proton MRS metabolite ratios. White-matter T2 may have greater specificity than metabolite ratio changes [5,6].

Method: Spectroscopy data were acquired from 22 infants born very preterm (mean birth gestational 25.7±1.6 weeks) using a 3T Philips Achieva with unmodified pulse sequences. Four infants had data acquired at 2 timepoints: the remainder were studied once only. For 17 of the 22 infants, 32-echo multi-component quantitative T2 imaging was performed at 0.4x0.4x3mm³ resolution using a GraSE sequence (TE 12ms). Multi-component T2 fitting used the extended phase graph algorithm [2] to extract 20 components at logarithmically spaced T2 intervals from 15ms-800ms. In addition to calculating a single T2, these components were further grouped into a short (<60ms: used to infer myelin-water content), medium (≤500ms: non-myelin tissue) and long T2 component (>500ms, fluid specific). Proton MRS used water suppressed Point Resolved Spectroscopy (PRESS; TR 2288 ms,TE 288 ms) with a 14x13x11mm³ voxel in the left PWM. Spectra were analysed using the AMARES algorithm in the jMRUI spectroscopy package. After head movement and scanner magnetic-field decay correction, peak-area ratios choline (Cho)/total creatine (Cr), N-acetylaspartate (NAA)/Cho, and NAA/Cr were calculated. Spherical PWM regions of interest in the T2 images were selected according to the MRS-voxel position and size (Fig. 1e). PWM T2 and metabolite-ratio EGA dependences and correlation statistics were investigated.

Results: Fig. 1a plots the single-component T2 showing a strong correlation with EGA (r=-0.91, p<0.001, rate=-13.5ms/week). The non-myelin tissue average T2 (medium component) was uncorrelated with EGA (r=0.34 p=0.14, Fig. 1b). NAA/Cho and Cho/Cr correlated with EGA respectively positively (r=0.81, p<0.001, rate=0.039/week) and negatively (r=-0.60 p=0.001 rate=-0.059/week) (Fig. 1c/d). After corrections for gestational age at scan, single-component T2 did not correlate with either Naa/Cho or Cho/Cr. Naa/Cho did correlate with Cho/Cr (r=0.74, p<0.001). In addition we did not detect a short T2 component in the PWM (expected due to absence of PWM myelination in our EGA range [7]).

Conclusion: The results suggest that apparent T2 change with EGA in this population is predominantly due to altered long T2-component (attributable to a cerebrospinal or other fluid fraction). Previous MRS studies have demonstrated changes in white-matter metabolism with brain development including apparently increasing NAA and decreasing Cho [3,6]. NAA and Cho are involved in myelination, metabolism of brain fatty acids and neuro-modulation. In normal myelin development choline moities incorporate into macromolecules and become MRS-invisible resulting in falling Cho/Cr. However, our results showed Cho/Cr falls even when T2 relaxometry detects no myelin. Future work will investigate the potential of this combination of widely-available MR pulse sequences for the development of quantitative neurodevelopmental biomarkers in infants born very preterm.