# 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 $T_2$ relaxometry in infants born very preterm but scanned between 30 and 40 weeks equivalent gestational age (EGA) and correlate white-matter $T_2$ with proton MRS metabolite ratios. White-matter $T_2$ 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 $T_2$ imaging was performed at 0.4x0.4x3mm$^3$ resolution using a GraSE sequence (TE 12ms). Multi-component $T_2$ fitting used the extended phase graph algorithm [2] to extract 20 components at logarithmically spaced $T_2$ intervals from 15ms-800ms. In addition to calculating a single $T_2$, these components were further grouped into a short (<60ms: used to infer myelin-water content), medium (≤500ms: non-myelin tissue) and long $T_2$ component (>500ms, fluid specific). Proton MRS used water suppressed Point Resolved Spectroscopy (PRESS; TR 2288 ms,TE 288 ms) with a 14x13x11mm$^3$ 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 $T_2$ images were selected according to the MRS-voxel position and size (Fig. 1e). PWM $T_2$ and metabolite-ratio EGA dependences and correlation statistics were investigated.

**Results:** Fig. 1a plots the single-component $T_2$ showing a strong correlation with EGA (r=-0.91, p<0.001, rate=-13.5ms/week). The non-myelin tissue average $T_2$ (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 $T_2$ 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 $\mathbf{T_2}$ component in the PWM (expected due to absence of PWM myelination in our EGA range [7]).

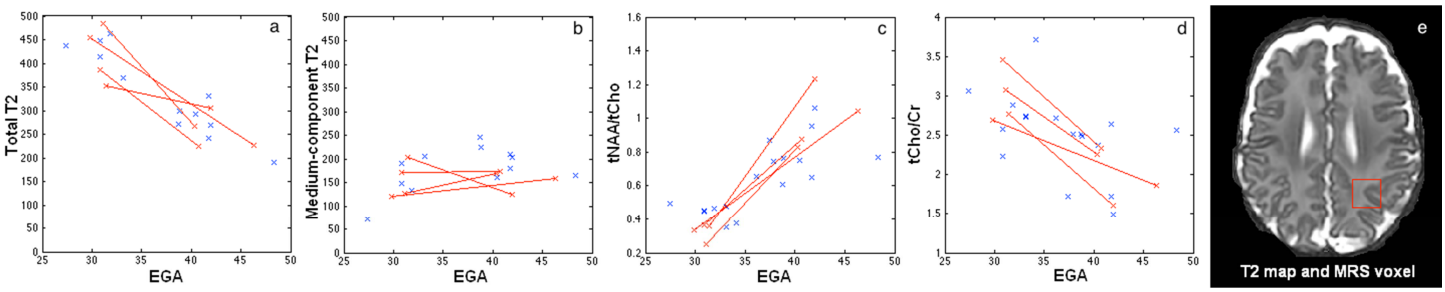


Figure 1: Quantitative posterior PWM MRI $T_2$ and MRS metabolite ratios with increasing EGA (weeks): a) single-component fit $T_2$, b) non-myelin, non-fluid tissue $T_2$ , c) NAA/Cho, d) Cho/Cr, and e) PWM region of interest and MRS voxel location on T2 map for a 40 week gestation infant. Data from the infants studied twice are joined by red lines.

**Conclusion: Conclusion:**The results suggest that apparent $T_2$ change with EGA in this population is predominantly due to altered long $T_2$-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 $T_2$ 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.

[1] Volpe JJ. Et al. 2009 Lancet Neurol 8 110-124 [2] Prasloski *et al* 2012 MRM 67 1803-1814 [3] Kreis *et al* 2002 MRM 48 949-958 [4] Bartha *et al* 2007 AJNR 28 1015-1021 [5] Vanhamme et al 1997 129 35-43 [6] Card et al Ped. Res. 74 75-81 [7] Brody et al 1987 J Neuropathol Exp Neurol 46 283–301