A quantitative analysis of the very preterm brain at 30 and 40 weeks gestational age; correlation of multi-component T2 relaxation and diffusion tensor anisotropy.

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Introduction: Infants born prematurely are at increased risk of adverse neurodevelopmental outcome. The measurement of white matter tissue composition and structure can help define biomarkers for neurodevelopmental outcome. This work investigates correlations between diffusion MRI and multi-component T_2 relaxation measurements at 3T in a small group of infants born very preterm and scanned at 30 and 40 weeks equivalent gestational age. We show robust differences in tissue composition and diffusion characteristics in four regions of interest at these gestational ages.

Method: Imaging data were acquired for four infants born very preterm on a 3T Phillips Achieva using un-modified sequences; two infants were acquired at 30 weeks and two at 40 weeks equivalent gestational age. Diffusion tensor imaging (DTI) was acquired over 16 directions at a b-value of 750mms^{-2} at resolution 1.75x1.75x2mm^3. Fractional Anisotropy (FA) maps were obtained by linear fitting of the tensor model to the imaging data. 32-echo multi-component quantitative T_2 imaging was acquired at 0.4x0.4x3mm^3 resolution using a GraSE sequence at 12ms TE. T_2 component fitting was carried out using the extended phase graph algorithm (EPG) [1] to extract 20 components at logarithmically spaced T_2 intervals from 15*ms*-2*s*. These are further grouped into a short (<100*ms* which may be used to infer tissue myelin-water content), medium (100-≤1200*ms*) and long component (>1200*ms*). After registration of the FA and mean diffusivity maps to the quantitative T_2 space, four regions of interest for each infant are manually segmented to describe (posterior) cortical grey matter (GM), posterior white matter (WM), the corpus callosum (CC) and the posterior limb of the internal capsule (PLIC). We investigate correlations and variations in the tissue characteristics of each of these regions.

Results: Figure 1 shows differences in the observed T_2 tissue content and diffusion characteristics between 30 and 40 weeks equivalent gestation. FA of the GM is found to be higher than that of WM at 30 weeks equivalent gestational age (A/B) whilst at 40 weeks the situation has changed with WM FA increased and GM FA reduced (C/D) [3]. GM FA at 30 weeks is comparable to that found in both the CC and the PLIC but much lower by term equivalent age. Variations in mid-range T2 component magnitudes likely reflect changes to the tissue water content with larger variation between the 40 week infants. Both FA and mid-range T_2 component strength increase in the CC whilst for the PLIC the FA increase is relatively lower. The number of voxels labelled with large short component magnitude increases markedly between 30 and 40 weeks gestational age representing myelination progressing from the brainstem to the PLIC (E).

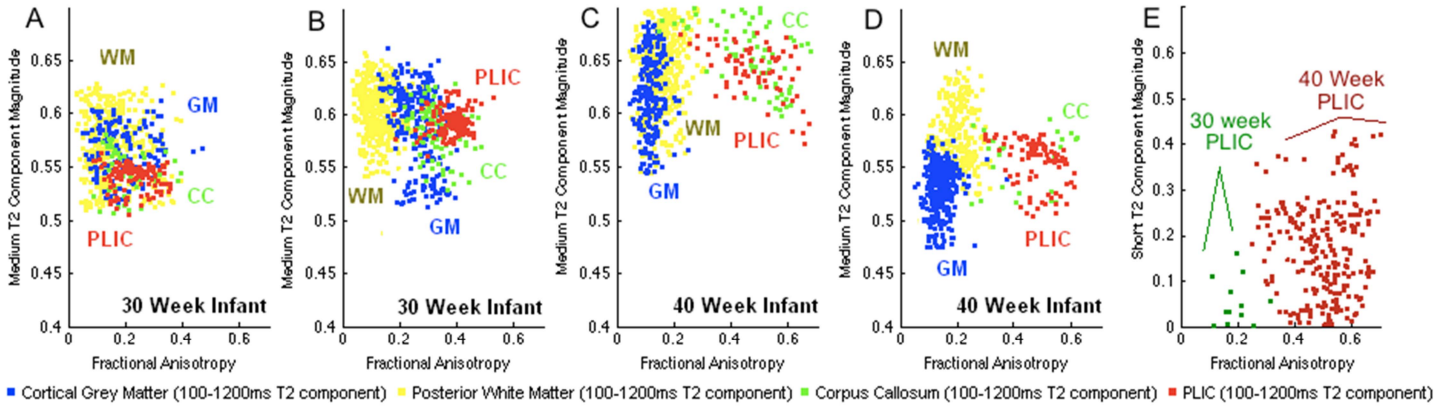

Fig 1) Distribution of FA/mid-range T2 component magnitude for each ROI for 30 week infants A/B and 40 week infants C/D. E) Comparison of voxels with short T2 component magnitude for 30/40 week infant.

Conclusion: The combined technique in this work allows a comparison to be made of tissue composition from multi-echo T_2 with tissue organisation statistics generated from DTI. FA is a function of myelination, tissue water content and an aggregate measure of tissue structural orientation and density, but does not distinguish between these multiple confounding effects. The combination with multi-component T_2 estimation allows the disentangling of some of these factors by quantification of myelin water fraction and free water fraction, thus improving sensitivity to changes in structure, pertinent in this cohort as a result of the dendrite formation in GM and an increase of associative fibres in WM which may manifest as reduced FA in regions close to the cortex. The diffusion tensor model could be improved making use of more advanced diffusion sequences to estimate dispersion and neurite density and although the EPG algorithm allows B_1 inhomogeneity estimation, the method does not implicitly correct for non-uniform re-focussing flip angles through the slice-profile. Future work will investigate to what extent this combination of widely available MR sequences can have on quantitative neurodevelopmental biomarker development in the very-preterm period.

[1] Prasloski *et al* 2012 MRM 67 1803-1814 [2] Mädler *et al* 2008 MRI 26 874-888 [3] McKinstry *et al* 2002 Cerebral Cortex12 1237-1243