Quantitative relationships between brain-water T2 and ADC at term in infants born prematurely

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Introduction. Children born prematurely have a higher risk of later neurodevelopmental impairments than those born at term [1]. It is increasingly recognised that diffuse white matter (WM) injury is the predominant lesion in infants born prematurely and this type of injury has been associated to deep grey matter (DGM) abnormalities [2,3]. Diffuse WM injury has been described as diffuse excessive high signal intensity (DE HSI) on conventional T2 weighted MRI [4] and objectively quantified with abnormal apparent diffusion coefficient (ADC)[5]. Quantitative MRI studies are being used to characterise cerebral development in premature babies since they can objectively reveal subtle tissue abnormalities not apparent on conventional imaging. Whilst many studies have quantified ADC or fractional anisotropy values only few reported cerebral T2 in this population, e.g. [6,7]. Recently early T2 relaxometry was shown to be prognostic in neonatal encephalopathy [8]. We thus decided to perform both T2 relaxometry and ADC measurements in a cohort of preterm infants at term corrected age and to determine their relation in both WM and DGM.

Methods. Twenty one babies (birth gestational age 23-32 wk), had MRI at corrected gestational age 38-42 wk after chloral-hydrate sedation (50 mg/kg). The birthweight was 560-2300 g and none of the subjects had focal pathologies on conventional MR. The study was approved by the local ethics committee and informed parental consent was obtained. MRI used a Siemens (Erlangen, Germany) Avanto 1.5 T scanner with the standard extremity coil. T2 relaxometry used the Siemens EPI spin echo (SE) sequence (23 axial slices; field of view 230 mm x 172.5 mm, data matrix 128 x 96, slice thickness 3 mm with 0.9 mm gap, repetition time (TR) 6.03 s, bandwidth 1260 Hz/pixel) and two echo times (TE; 89 ms and 200 ms; 5 and 10 averages respectively): total acquisition time (AT) was 1 min 42 s. ADC measurement used Siemens double spin echo EPI sequence [9] with 3 orthogonal gradient directions, b 0 and 600 s/mm2, 5 averages, TR 4.2 s, TE 118 ms, and otherwise as for T2 relaxometry (AT 2 min 12 s). ADC maps were generated by the scanner software. After inspection for motion artefacts, T2 maps were automatically generated offline with Matlab 6.0 (Mathworks, USA) software. Thirteen regions of interest (ROI; see Table and Fig. 1) per hemisphere were manually drawn by a single observer on the b 0 s/mm2 images on 3 slices: i) through the 4th ventricle (brain stem and cerebellum); ii) with the basal ganglia displaying anterior and posterior limbs of the internal capsule (frontal, periventricular and posterior WM, as well as several DGM structures); iii) slightly superior to the centrum semiovale (superior (sup) anterior central and posterior WM). T-tests showed ADC and T2 from these ROIs in left and right cerebral hemispheres were similar and, hence, they were averaged. ADC was plotted against T2 and R2 (the relaxation rate = 1/T2).

Results. Representative T2 maps with ROIs are shown in Fig. 1. T2 and ADC (mean ± SD) for each ROI averaged over all subjects are shown in the Table. ADC versus T2 for all infants and all ROIs (291 datapoints) is shown in Fig. 2. There were significant correlations between ADC and T2 for each ROI drawn though these were linear only for anterior and posterior WM at the level of the centrum semiovale and the cerebellar ROI. Pooling together data from all ROIs there was still a significant correlation between ADC and T2 as well as ADC and R2 (data not shown) but the linear regressions did not pass the normality test. Spearman rank order test for ADC vs T2 gave a correlation coefficient 0.9 (p < 0.0001).

Discussion and Conclusions. ADC and T2 were consistent with published values though most of these were obtained at different field strengths. There was a significant but non-linear correlation between T2 and ADC over all ROIs. The correlation extends over both white matter regions where diffuse white matter injury is often observed, as well as deep grey matter areas that may be secondarily affected by axonal injury [2]. The ADC/T2 correlation is consistent with reports on brain maturation of kittens [10] and measurements on term babies with hypoxic-ischemic encephalopathy [11,12] and may be attributable to the dependence of both T2 and ADC on tissue water content. Further studies of healthy babies born at term and detailed neurodevelopment outcome data are necessary to determine regional normal ranges of T2 values at 1.5 T. In conclusion, our study confirms the feasibility of rapid neonatal-brain T2 relaxometry with SE-EPI anatomically matched to ADC measurements. Since most clinical scanners now have EPI, it is important to include T1, T2, and ADC quantitation to provide objective measurements that can complement qualitative radiological assessments.