Quantification of diffuse white matter abnormalities using T2 relaxometry in preterm infants at term equivalent age

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Introduction: Diffuse non-cystic white matter injury is the predominant lesion in preterm infants (1,2) and has been described on conventional qualitative magnetic resonance imaging (MRI) as white matter signal abnormalities, loss of white matter volume, thinning of corpus callosum and delayed maturation (3, 4). In one series, diffuse excessive high signal intensity (DEHSI) of white matter was observed on conventional T2 weighted images in 75% of preterm infants at term equivalent age (2). However, conventional T2 weighted MRI contrast is dependent on several factors and absolute image intensities are scaled arbitrarily. DEHSI is associated with increased apparent diffusion coefficient (ADC) and axial and radial diffusitivity (5, 6). Quantitative MRI brain-water T2 measurements provide a further opportunity for *in vivo* investigation as T2 relaxometry utilises multiple TEs to yield T2 maps, which are inter-study comparable and independent of intensity scaling and uncontaminated by other contrast mechanisms. Hence, T2 relaxometry may reveal tissue abnormalities unapparent on conventional T2-weighted imaging. We have recently shown the prognostic utility of regional brain-water T2 in the first week of life in infants with neonatal encephalopathy (7).

Aims: To quantify diffuse white matter injury using T2 relaxometry and diffusion weighted imaging at term equivalent age in infants born prematurely. To test the hypothesis that T2 is increased in infants with DEHSI compared with those without white matter signal changes.

Methods: Ethical permission for this study was granted by the UCL/UCLH Research Ethics Committee. 27 preterm infants (15 female) born < 32 weeks were recruited from our neonatal intensive care unit. The median (range) gestational age at birth was 29 (23-42 weeks) and the median birth weight 1098g (500-2030g). The median postmenstrual age at the time of scanning was 39 (38-42 weeks). Infants were sedated with oral chloral hydrate (50mg/kg) and were continuously monitored. All infants were studied within a transparent MR compatible pod and had ear protection comprising earplugs and earmuffs. MRI data was acquired on a Siemens (Erlangen, Germany) Avanto 1.5T scanner using the Siemens CP extremity coil. The brain studies included conventional imaging, T2 relaxometry and diffusion imaging. Conventional imaging: (1) T1 weighted 3D-FLASH (TE/TR=6.06/17ms; 160 1mm slices; field of view (FOV) 200mm x 200mm; data matrix 256 x 200, flip angle 21˚ and bandwidth 100 Hz/pixel) (2) T2-weighted fast spin echo (TR=5.91s, 23 3mm axial slices thickness, FOV 210mm x 157.5mm, data matrix 512 x 192, 11 echoes and an effective echo time TEeff=110ms; bandwidth 65 Hz/pixel). T2 relaxometry: nineteen infants had T2 relaxometry using a spin-echo (SE) sequence (TR/TE = 1.55s / 10, 100 and 300ms; FOV 160mm x 120mm; data matrix 192 x 144; bandwidth 80Hz/pixel; five 5mm axial slices positioned as follows one of which at the level of the centrum semiovale (Fig.1). Eight infants had T2 relaxometry using the manufacturer's EPI SE sequence (TE = 89 and 200ms; 23 axial slices; FOV 210mm x 157.5mm, data matrix 128x96). After inspection for motion artefacts, maps of T2 were calculated offline with software developed in Matlab 6.0 (Mathworks, USA) by fitting a decreasing exponential function to the signal intensity as a function of echo time. Diffusion imaging: images for estimation of the ADC was obtained with the manufacturer's double spin echo EPI sequence [Heid 2000] (TR/TE=4200/118ms , 23 3mm axial slices; FOV 230mm x 172.5mm; data matrix 128 x 96; bandwidth 1260Hz/pixel, 5 averages). 3 orthogonal diffusion encoding directions were used with b values of 0 and 600 s/mm2; ADC maps were calculated online by the scanner). ROIs of predefined size were drawn on the T2w images (fig 1) and transferred to the T2 and ADC maps. Two paediatric neuroradiologists reported the conventional MRIs; DEHSI was defined as white matter high signal intensity of in conventional T2 weighted images (4).

Results: Unpaired t tests showed no significant difference between right and left hemispheric T2, thus mean T2 and ADC across both hemispheres were calculated for each region. The mean T2 and ADC values obtained in the frontal, central and posterior region in preterm infants with and without white matter signal intensity on conventional MRI are shown in Tables 1 and 2. Mean ADC values were significantly higher in the posterior white matter in infants with apparent DEHSI compared to those without apparent DEHSI on conventional MRI. Mean T2 values were significantly higher in the frontal and posterior white matter in infants with apparent DEHSI compared to those without apparent DEHSI on conventional MRI.

Table 1	Mean T2 values (+/-SD) ms		
Region	Normal white matter signal intensity (n=7)	Diffuse excessive high signal intensity (DEHSI) (n=20)	*P value*
Frontal white matter	224 (30)	250 (27)	0.043
Central white matter	227 (45)	240 (45)	0.523
Posterior white matter	221 (48)	288 (51)	0.005

Table 2	Mean ADC values (+/-SD)x10^{-3}mm^2/s		
Region	Normal white matter signal intensity (n=7)	Diffuse excessive high signal intensity (DEHSI) (n=20)	*P value*
Frontal white matter	1.58 (0.19)	1.59 (0.15)	0.81
Central white matter	1.56 (0.19)	1.57 (0.21)	0.963
Posterior white matter	1.51 (0.19)	1.77 (0.19)	0.005

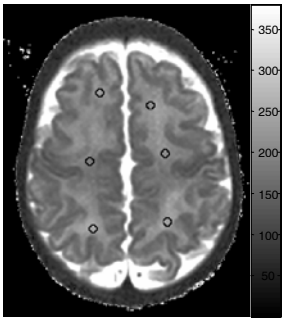

Fig.1. Axial T2 maps generated from 5 slices acquired at TE 11, 100 and 300ms. ROI placed in the frontal, central and posterior white matter at the level of the centrum semiovale

Conclusion:

This study demonstrates that quantitative T2 relaxometry is feasible in preterm infants during a clinical MRI study; such quantitative data has advantages compared to qualitative assessment of white matter signal changes on conventional T2 weighted images; these are prone to inter and intra-observer interpretational variability. In this study, we observed that frontal and posterior white matter T2 values were significantly higher in preterm infants with white matter signal abnormality seen on conventional T2 weighted images whereas ADC values were significantly higher only in the posterior white matter. Hence, quantitative T2 values might be a more precise marker of white matter abnormalities in this population. Increased T2 values could represent loss of tissue integrity (gliosis) resulting in an increase in free water concentration or delayed maturation. T2 values in the central white matter were not significantly different between the two groups. This could be attributed to regional variation in myelination or a regional vulnerability in frontal and posterior white matter.

References:

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