Regional Diffusion and Volumetric MR alterations in premature infants

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Introduction: Prematurity is the most prevalent cause of perinatal mortality and long-term cognitive and motor disabilities. The occurrence of these disabilities in preterm infants suggests that premature birth disrupts one or more components of cerebral development. However, the specific mechanisms by which the developing brain is affected by preterm birth are not well understood. While conventional magnetic resonance imaging provides an excellent tool for the study of anatomical changes in the developing brain, it cannot detect more subtle changes such as direction and integrity of the cerebral white matter microstructure. Previous studies have shown that diffusion weighted MR imaging reveals white matter abnormalities, enabling the assessment of the integrity and organization of white matter tracts in the developing brain.

Aim: The aim of this study was to determine the regional variation in cerebral tissue between term and preterm infants using conventional quantitative volumetric and diffusion tensor magnetic (DTI) imaging in order to provide a better understanding of normal brain development and the impact of prematurity on cerebral development.

Method: The study population consisted of 52 preterm infants and 9 controls. MRI scans were taken with a 1.5 T GE scanner utilizing 1.5 mm SPGR 3D sequence and coronal T2 sequences for primary acquisition. These images were used for volumetric analysis. The image processing algorithms used are designed to reduce imaging system noise, align T1 and T2 images, and segment imaged volumes. The image segmentation method applied is a spatially varying statistical classification in which the anatomical template is used to modify the result of tissue classification. Comparison of total and regional brain volumes of different tissue classes was performed by dividing the brain into hemispheres and further subdividing each hemisphere into 8 anatomical sectors. Diffusion tensor images were also acquired fro each subject using line scan protocol (5-6 mm axial slices, 0.5-1 mm gap; TE = 78 msec; TR = 2139 msec; FOV = 22 cm; matrix=256 x2 56; diffusion sensitivity: 2 baselines of b = 5 and six of b = 700 with diffusion gradients oriented in six non-collinear directions). Quantitative measures of the water apparent diffusion coefficient (ADC) and fractional anisotropy (FA) were calculated from axial images positioned above the lateral ventricles for 6 circular regions of interest (ROI) (area=15 mm^2). In addition, 3 ROI's were placed on the axial image passing through basal ganglia and posterior limb of the internal capsule. The data analysis was performed using SPSS 12.0 ANOVA correcting for factors including the presence of sepsis, white and gray matter injury, and birth weight.

Results: ***Volumetric results***: The regions that were most affected by prematurity with reductions in brain tissue volumes included the dorsal, orbitofrontal, premotor, sensorimotor and parieto-occipital areas. For dorsal and premotor regions, tissue loss was most prominent in un-myelinated white matter, while in sensorimotor and parietooccipital region this was most prominent in cortical grey matter. ***Diffusion results, inferior slice analysis:*** Premature infants displayed a significant elevation in ADC and reduction in FA in comparison to term born infants in the occipital region. No statistically-significant relationship of volumes to occipital diffusion measures was present. The anisotropy values from the posterior limb of internal capsule were not altered in the premature infants, but were correlated with basal ganglia volumes. ***For the superior slice analysis***, the frontal region displayed an elevation in ADC in premature infants compared to term born infants which was correlated with a reduction in dorsofrontal grey matter volume. Although in frontal region CSF volume increases dramatically with gestation age, interestingly, the ADC values are not correlated with CSF volumes. The strongest perinatal predictor of alterations in frontal volumes and ADC was immature gestational age. The central area displayed an elevation in ADC and reduction in FA in premature infants, which was correlated with CSF volume in the sensorimotor region. No changes in diffusion parameters were observed in the superior slice, posterior ROI positions.

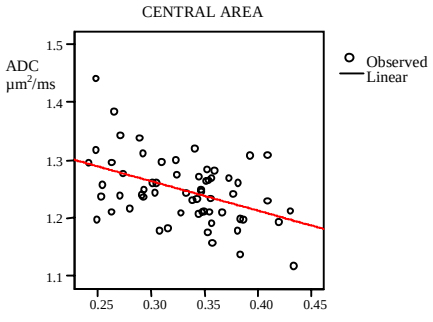

Figure 1Pearson Correlation Coefficient = -0.446 red, PLIC; and light green ,occipital WM

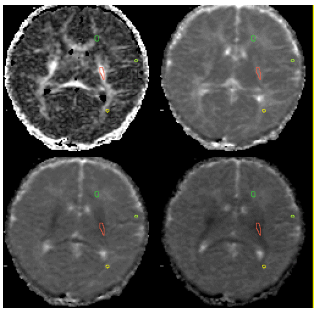

Figure 2 Inferior Slice ROI's: green, dorsal WM;

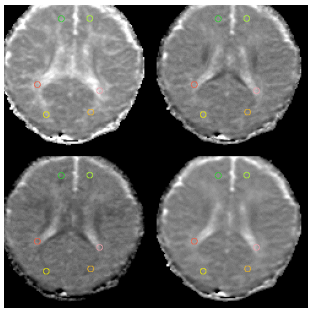

Figure 3 ROI's (anterior, central and posterior)

Volumes and Diffusion measures (mean ± SD)

	CORTICAL GM (%)	CSF (%)	MYELINATED WM (%)	BASAL GANGLIA (%)	UN-M WM (%)	ADC (μm^2/ms)	FA
PREMATURE	0.39±0.04	O.08 ±0.03	0.04 ±0.01	0.11 ±0.02	0.39 ±0.05	1.585 ±0.262	18.7 ±5.2
TERM	0.40 ±0.03	0.04 ±0.01	0.04 ±0.01	0.10 ±0.04	0.43 ±0.02	1.346 ±0.226	26.2 ±11.7
p value	0.823	**0.004**	0.937	0.314	**0.035**	**0.014**	**0.002**

Conclusion: Premature infants display alterations in volumetric and diffusion measures at term equivalent in comparison to term born infants. These alterations vary with regional analysis. There are clear relationships between regional brain volumes and cerebral white matter diffusion measures. The regional variability of diffusion parameters can be explained by differences in cerebral white matter maturation with myelination. The relationship of white matter microstructural integrity to cortical gray matter and basal ganglia volumes provide further evidence of the importance of consideration of the neuro-axonal unit in the premature infant. A combination of volumetric and diffusion techniques provides unique insight into the nature of the structural alterations associated with premature birth.