Volumetric and Diffusion Analysis of the Neonatal Brain

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Introduction: With the improvement in neonatal care and increasing survival of infants born prematurely, an increasing number of neuro-developmental deficits at follow-up in survivors such as lower IQ scores, attention deficit hyperactivity disorders, language and learning deficits and even psychiatric problems are exhibited. A body of evidence indicates that infants born prematurely have a significant reduction in brain volume as compared to term infants and that morphologic abnormalities are associated with poorer cognitive outcome.[1] This study reports a semi-automated threshold based volumetric analysis independent of a standard brain template in conjunction with whole brain ADC histogram analysis in preterm infants compared with term infants. Changes in volume and ADC may lead to a better understanding of the origin of deficits observed later in life.

Materials & Methods: A retrospective study of 16 premature infants (13F/3M) with a gestational age of 26 ± 1 weeks were imaged on a 1.5T GE MRI scanner at 39 ± 2 weeks and compared with 9 term infants (5M/4F) imaged at 1 ± 1 weeks after birth. CSF removal was performed by automatically fitting the image intensity histogram from the slice containing the largest ventricular component on the T_2-FLAIR images (10.0s/2.2s/160ms TR/TI/TE, 4/1 mm thickness) with a Gaussian function. Whole brain volumes were validated using the 3D Slicer software package (MIT, Cambridge, MA). Grey (GM) and white matter (WM) segmentation was performed utilizing image subtraction of the T_1 weighted image (T_1W) from the T_2 weighted image (T_2W) as shown in Figures 1A and 1B. WM is hyper-intense on T_2W images and hypo-intense on T_1W images in pre-term infants. The subtraction image resulted in WM appearing maximally brighter than GM. Image masks from the whole brain segmentation were overlaid on the T_2W-T_1W images and a dual Gaussian function was used to fit the histogram. The intersection of the Gaussian functions provided the cutoff for segmentation. Additionally, DWI was performed using a SE-EPI sequence with a b-value of 1000 s/mm^2, 30 slices at 3/0 mm thickness, 18 cm FOV, 128^2 matrix, 12 s/100 ms TR/TE. The whole brain ADC histogram was fit with a dual Gaussian function.[2]

Results: Total brain volumes less CSF were 275.5 ± 45.3 cc and 354.9 ± 38.1 cc for premature and term infants respectively ($p<0.001$). No significant right-left hemispheric volume differences were found ($p=0.7$). Preliminary results (n=12) segmenting GM on the premature infants produced the following linear relation: % GM = 1.6 * Gestational Age (wks) – 1.0 ($R^2=0.62$, $p=0.002$). This yielded %GM as 51.8 ± 5.3% for the premature infants. Whole brain ADC values were 1.280 ± 0.014 x 10^{-3} mm^2/s (SEM) for the premature infants and 1.215 ± 0.009 x 10^{-3} mm^2/s for the term infants ($p=0.0016$). Widths of the ADC histograms were 0.326 ± 0.012 x 10^{-3} mm^2/s (SEM) for the premature infants and 0.240 ± 0.011 x 10^{-3} mm^2/s for the term infants ($p<0.001$). Representative ADC histograms for the populations are shown in Figure 1C.

Discussion: Using a KNN algorithm, Huppi, et.al. reported total brain volumes less CSF of 296.0 cc at 36 weeks and 382.4 cc at 40 weeks derived from their linear regression relation.[3] Zhai, et.al. reported ADC values of 1.15 and 1.35 x 10^{-3} mm^2/s for term infants in WM and GM respectively which are similar to those found in this study.[4] The increased ADC value in premature infants implies greater water content or decreased restriction to water motion in the brain. ADC histograms derived from GM/WM segmentation may provide better characterization of these regions.

Conclusion: In premature infants imaged at a gestational age of 40 weeks, whole brain volume was reduced and whole brain ADC was increased compared with the term population. The increased ADC value in premature infants implies greater water content or decreased restrictions to water motion in the brain usually accounted for by the degree of myelination. Additional serial volumetric analysis of various cerebral structures between populations may localize regions that prove to be the origin of developmental deficits seen later in life.

References: 1) Peterson B, Vohr B. JAMA, 284, 1939-1947., 2) Zhang L, Thomas KM, et.al. AJNR Am J Neuroradiol. 2005 Jan;26(1):45-9. 3) Huppi PS, Warfield S, et.al. Ann Neurol.1998 Feb;43(2):224-35. 4) Zhai G, Lin W, et.al. Radiology. 2003 Dec;229(3):673-81.

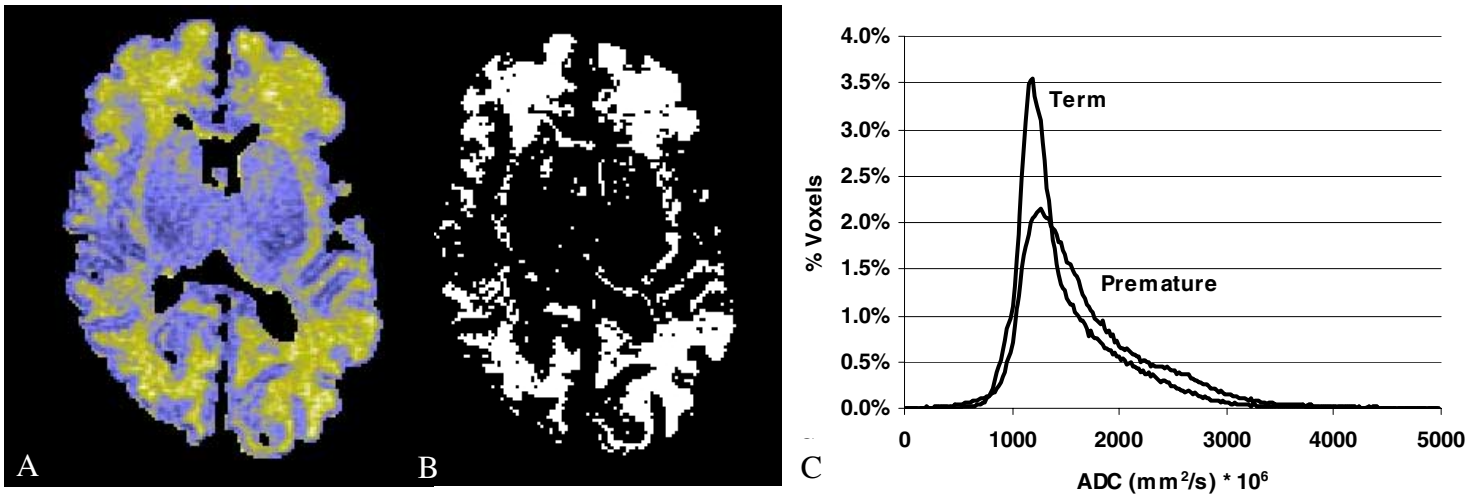

Figure 1: A) T_2W-T_1W subtraction image showing increased contrast between GM and WM and B) the derived WM mask. C) Representative whole brain ADC histograms illustrating differences in the distributions.