

# Intra-Uterine Sub-Structure Evaluation of the Developing Neuro-Anatomical Fiber Tracts in Fetuses Using DTI

Travis S. Scharr<sup>1</sup>, Katherine L. Ragland<sup>2</sup>, Majid A. Khan<sup>2</sup>, Kenneth Liechty<sup>3</sup>, James A. Bofill<sup>3</sup>, Razvan Buciu<sup>2</sup>, and Judy R. James<sup>2</sup>

<sup>1</sup>School of Medicine, University of Mississippi Medical Center, Jackson, Mississippi, United States, <sup>2</sup>Department of Radiology, University of Mississippi Medical Center, Jackson, Mississippi, <sup>3</sup>University Center for Fetal Medicine, University of Mississippi Medical Center, Jackson, Mississippi

## INTRODUCTION:

Diffusion Tensor Magnetic Resonance imaging (DTI) holds a great potential for identifying cellular-scale structural properties and white matter development in the brain non-invasively. Understanding water diffusion properties during cerebral white matter micro structural development is a key issue in interpreting the patho-physiology of brain abnormalities in fetuses and infants. Though DTI is a promising tool for evaluating fetal brain micro-architectural development in-utero, it is highly sensitive to fetal motion and other physiological movements which often lead to image quality degradation and deliver inaccurate results. Our objectives for this study are to optimize this highly sensitive technique for performing in-utero fetal imaging and to explore the utility of DTI to assess the in-utero maturation-dependent micro structural changes of the fetal cerebral matter.

## MATERIALS AND METHODS:

15 normal fetal brain images (30 - 36 weeks of gestation age (GA)), with no structural brain abnormality found on ultrasound or correlative fetal MRI, were examined using an optimized DTI technique. The fetuses were scanned on 1.5T ESPREE MRI scanner (Siemens, Germany) using echo-planar SE at  $b = 0,800 \text{ s/mm}^2$  along 12 non co-linear directions with an imaging time of 2-3 min. DTI images were processed and analyzed with DTI-studio (S. Mori, John Hopkins) to extract tensor measurements, such as fractional anisotropy (FA), magnitudes and direction of the existing tracts and apparent diffusion coefficient (ADC) of water molecules. Fiber tractography was also performed on these fetal DTI images. Mathematical tensor measurements obtained from DTI processing were then correlated with gestational age to examine trends in brain maturation. The emerging white matter tracts were analyzed and described according to gestational age.

ROIs were drawn on the DTI images encompassing the cerebral hemispheres at the level of centrum semi-ovale and few specific fiber tracts from the main three brain white matter tracts namely: projection tracts (P-fibers), commissural tracts (C-fibers) and association tracts (A-fibers). ROIs encompassed the a) Bilateral brain hemispheres (BH); A-fibers: b) Cortico-spinal tract (Posterior limbs of the internal capsule, (PLIC) and Crus cerebri (Crus)); P-fibers: c) Corpus callosum (genu, body and splenium); C-fibers: d) Bilateral Centrum semiovale (CSO), and e) Optic radiations (OR) for the fetal brain MR. This was done to examine the effectiveness of using DTI to observe the development of specific white matter tracts that could be different due to fiber compaction and myelination within the fetal brain. DTI parameters that were extracted from each ROI were: 1) fiber count, 2) density, 3) number of voxels/ fiber, 4) fiber length, 5) fractional anisotropy (FA), 6) relative anisotropy (RA), 7) volume ratio (VR) 8) ADC, 9) trace, 10) mean diffusivity (MD), and 11) radial diffusivity (RD). To reduce any intra-rater and intra-slice variability, multiple ROIs were placed on various sub-structures of the brain to obtain mean  $\pm$  S.D trivial DTI parameters from brain slices. Scatter plots and a linear regression model were used to evaluate relationship between GA and DTI parameters.

## RESULTS:

Figure 1 (top panel) shows representative fetal MR slices with significant difference in the quality of DW images, ADC and FA maps acquired at 31 and 36 weeks of GA. The structure of the tracked fibers is more symmetrical and developed at 36 weeks compared to 31 weeks. The anterior colossal fibers are visualized at 31 weeks of GA with body and splenial fibers easily appreciated at 36 weeks. Optic radiations along with a better visualization of uncinate fasciculus and superior fronto-parieto-occipital fascicle are also observed posterior at 36 weeks of GA.

A positive correlation was observed between most of the DTI indices with increasing GA as shown in Figure 1 (bottom panel). Among all the DTI parameters, fiber count showed a rapid increase with brain development in the BH, CSO, OR and PLIC structures (slopes ( $R^2$ ) = 1175 (0.84), 410 (0.68); 193.5 (0.84) and 93.52 (0.70)), followed by fiber length in BH, PLIC, OR structures (slopes ( $R^2$ ) = 13.3 (0.71); 6.9 (0.87) and 5.4 (0.78)). A strong linear increase was observed in fiber density with GA in BH, PLIC and CSO structures (slopes ( $R^2$ ) = 1.3 (0.78), 2.6 (0.82) and 3.6 (0.69)). It was also interesting to note that as the brain matured the number of voxels the fibers passed through also increased at an alarming rate in BH, PLIC, CSO, OR and Crus with strong correlations (slopes ( $R^2$ ) = 3012 (0.83), 670 (0.65); 1200 (0.91), 382 (0.97) and 423 (0.74)). Changes in FA, RA and VR were increasing with GA but was minimal in structures such as PLIC, BH, CSO, Crus (mean slope =  $0.034 \pm 0.008$ ;  $R^2 = 0.66 \pm 0.18$ ). All the other attributes (MD, RD, ADC or trace) showed a minimal positive or no trend with GA.

The strongest correlations in the DTI parameters obtained for the fetal brain at various GA were in the BH and the P-fibers and the A-fibers. The initial data suggests that this technique could be especially helpful for assessment of early developing white matter tracts involved in motor function, such as the cortico-spinal tract. This finding correlates with the current knowledge that motor function is more fully developed at birth than cognitive functions.

## CONCLUSION:

The study has helped reveal the utility of diffusion tensor MR imaging for evaluating intra-uterine conditions and to describe functional development of the in-utero fetus in a qualitative and quantitative manner. The data is highly suggestive that DTI can capture microscopic changes in water diffusion properties occurring with brain maturation. The optimized DTI technique should serve as a promising tool for the evaluation of fetal brain abnormalities in-utero and could be used widely in numerous at-risk obstetric situations. Technical improvements as well as a larger study population are still needed to assess the reliability of DTI in evaluating fetal white matter anisotropy development.

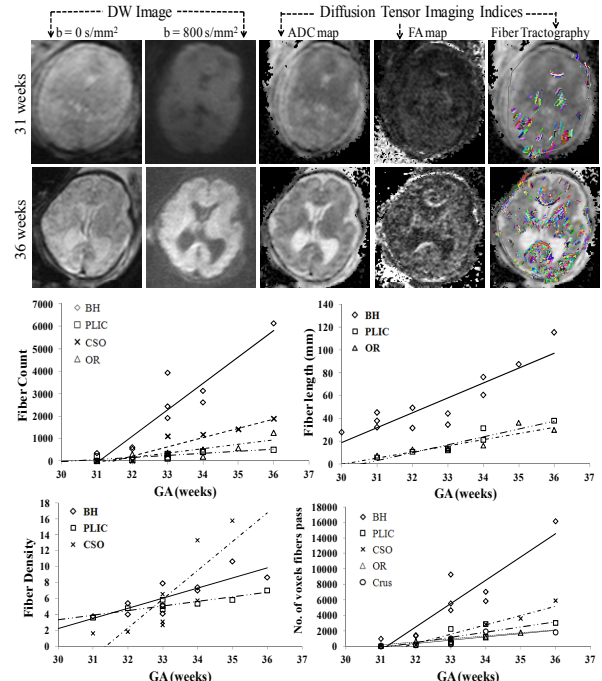


Figure 1: Top panel - Diffusion Weighted (DW) MRI and Diffusion Tensor (DTI) indices of fetal brains acquired at 31 and 36 weeks of gestation. Bottom panel - Relationship between some DTI parameters (fiber count, length, density and voxels fibers pass) with increasing GA shown for various brain structures.