Population-averaged high resolution human fetal brain DTI atlas

Hao Huang[1,2], Tina Jeon[1], Linda Richards[3], Paul Yarowsky[4], Horst R Zielke[5], and Susumu Mori[6]

[1]*Advanced Imaging Research Center, University of Texas Southwestern Medical Center, Dallas, Texas, United States,* [2]*Department of Radiology, University of Texas Southwestern Medical Center, Dallas, Texas, United States,* [3]*Queensland Brain Institute, The University of Queensland, St Lucia, Queensland, Australia,* [4]*Pharmacology and Experimental Therapeutics, University of Maryland, Baltimore, Maryland, United States,* [5]*Pediatrics, University of Maryland, Baltimore, Maryland, United States,* [6]*Department of Radiology, Johns Hopkins University, Baltimore, Maryland, United States*

Introduction

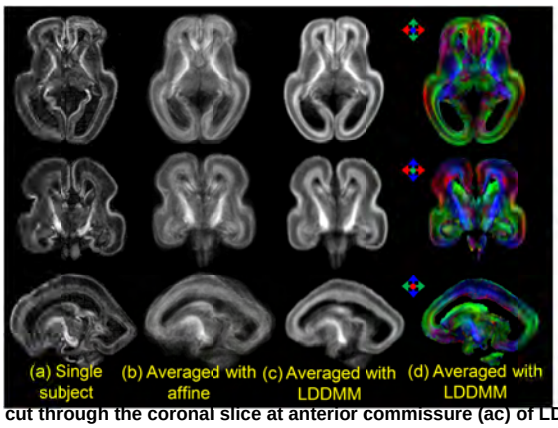
Anatomical abnormality of human brains at the fetal stage is highly related to neurodevelopmental disorders at infancy and childhood. With the recent advances in medicine, extremely preterm baby as early as 22 weeks of gestation (wg) can survive (1). A population-averaged high resolution atlas at 20 wg, around the middle point of prenatal development, is essential for fetal evaluation which may lead to life-saving diagnosis and therapy for the extremely preterm babies. Compared to state-of-the-art in-utero DTI (e.g. 2) implemented recently, high resolution, high SNR and high contrasts of *ex vivo* DTI have made it more suitable for atlas making (3) for its capability of delineating detailed anatomy of human fetal brain. Talairach coordinates (4), widely used in adult human brain MRI, has greatly enhanced data sharing and report of the experimental findings. Due to dramatic differences between adult and fetal brain, Talairach coordinates cannot be applied to fetal brain. In this study, we acquired high resolution DTI data with isotropic resolution 0.29 mm from 10 postmortem fetal brain samples at around 20wg. By applying linear affine and large deformation diffeomorphic metric mapping (LDDMM) (5) transformation, we established a population-averaged human fetal brain DTI atlas. Major white matter tracts, including cerebral peduncle (CP), were also traced through DTI tractography. The same transformation was applied to establish the population-averaged atlas of these tracts. A coordinate system unique to the fetal brain was also built up with population-averaged atlas.

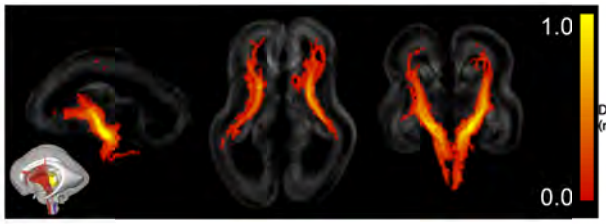
Methods

Fetal brain samples: 10 postmortem fetal brain samples at around 20 wg were borrowed from the University of Maryland Brain and Tissue Bank for Developmental Disorders (NICHD contract no. N01-HD-4-3368 and N01-HD-4-3383). The normality of the borrowed tissue was ensured and guaranteed by tissue bank. *High resolution and high SNR DTI data acquisition:* 3D multiple spin echo diffusion tensor imaging was performed in 4.7T Bruker scanner. Multiple echo (number of echoes = 8) sequence was adopted to improve the SNR. A set of diffusion weighted images (DWI) with b value 1000s/mm^2 were acquired in seven linearly independent directions. DWI parameters were effective TE=67ms, TR=0.8s, FOV=38-45mm/38-45mm/38-45mm, imaging matrix=128×80×80 (zero filled to data matrix=128×128×128). The imaging resolution was isotropic 0.29 mm. *DTI tractography:* FACT (6) was used for tractography of major fetal white matter tracts including CP. *Establishing the population-averaged DTI atlas:* A symmetric fetal brain at 20wg with median brain size was chosen as the template. Following the protocol of establishing population-averaged DTI atlas of adult human brain (7), the linear affine and LDDMM transformations were applied to individual DTI data. Tensor reorientation follows the methods in the literature (8). Same transformation matrices were also applied to traced white matter tracts.

Results

Population-averaged DTI atlas with affine and LDDMM transformation: Fig. 1 shows the averaged FA maps with affine linear (Fig. 1b) and LDDMM (Fig. 1c) transformations and averaged DTI colormaps with LDDMM transformations (Fig. 1d) from DTI of 10 *ex vivo* fetal brains at around 20wg. Note that the template of LDDMM transformation is the averaged FA map after affine linear transformation (Fig. 1b) which is less biased than the FA map of a single subject (Fig. 1a) and represents averaged shape of the population. In this way, the resultant population-averaged atlas with LDDMM transformation (Fig. 1c and 1d) has sharp boundary while keeping the averaged shape It is also clear that neural structures with higher FA in all 10 *ex vivo* fetal brains, such as internal capsule and cortical plate, stay prominent in the population-averaged FA map with LDDMM (Fig. 1c). The isotropic resolution of all images shown in Fig. 1 is 0.29x0.29x0.29mm. The sharp contrasts of the colors encoding the orientations of microstructures in Fig. 1d are due to 1) consistent orientations of ordered neural structures among the 10 fetal brains and 2) very elastic registration with LDDMM. *Population-averaged white matter tract atlas:* The probability map of a major fetal white matter tract, CP, is overlaid on the affine-averaged FA map in Fig. 2. Despite its apparent appearance at 20wg, most of this tract only projects to the frontal area. *Coordinate system of fetal brain at 20wg:* Fig. 3 shows the established coordinates for the fetal brain. The relationship of anatomical orientation and X, Y, Z is that X indicates left-right (LR) direction, Y indicates anterior-posterior direction and Z indicates dorsoventral (DV) direction.





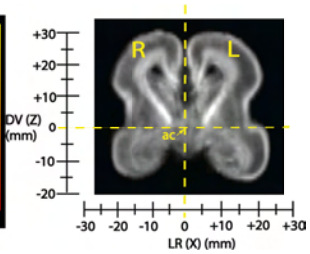


Fig. 1 (left): Population-averaged FA maps. Axial (upper), coronal (middle) and sagittal (lower) views of template single subject FA map (a), population-averaged FA maps with affine (b) and LDDMM (c) transformation and population-averaged DTI colormap (d) with LDDMM transformation are shown.

Fig. 2 (middle): Population-average atlas of CP in sagittal (left), axial (middle) and coronal (right) view overlaid on affine-averaged FA map. Color bar encodes the probability of CP. The 3D reconstructed CP (red fibers) is shown at the lower left corner as an anatomical guidance.

Fig. 3 (right): Zero horizontal and zero sagittal planes (yellow horizontal and vertical dashed lines) cut through the coronal slice at anterior commissure (ac) of LDDMM-averaged FA map of 20wg fetal brain. The scales are real physical scales in millimeters.

Conclusion and discussion

Population-averaged atlas minimizes the structural bias from individual subjects. To the best of our knowledge, this abstract presents the first population-averaged DTI atlas of human fetal brain. It can be used as clinical reference for early detection of fetal brain abnormality such as ventriculomegaly and eventually will allow early intervention to minimize the negative outcomes of developmental disorders for postnatal children. DTI data from more postmortem fetal brain samples are acquired so that our atlas can represent a larger population. This atlas will also be integrated with in-utero MRI to obtain a population-averaged DTI atlas with in-utero brain shape.

References: [1] http://www.preemiesurvival.org/info. [2] Kasprian, G et al (2008) Neuroimage 43:213. [3] Huang, H et al (2009) J Neurosci 29: 4263. [4] Talairach, J and Tournoux, P, 1988, Thieme. [5] Miller, MI et al (2002) Annu Rev Biomed Eng 4: 375. [6] Mori, S et al (1999) Annual Neurol 45: 265. [7] Mori, S et al., (2008) Neuroimage 40: 570. [8] Xu, D et al (2003) MRM 50: 175. **Acknowledgement:** This study is sponsored by NIH MH092535 and NIH EB009545.