Relaxometry Study of Baboon Fetal Brains at 3T

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INTRODUCTION

A property of brain maturation process accessible to MRI across all fetal ages is the relaxation time values that determine the contrast on images of the brain. Relaxation times are sensitive to brain tissue compositions change because of continuous and rapid change in structural organization and water content of both grey matter and white matter during early life [1]. Sequential *in utero* measurement of T_1 and T_2 can be used in characterization of the earliest stages of longitudinal development of brain tissues.

METHODS

Relaxometry pulse sequences are implemented on GE Signa 3T Excite Scanner (GE Medical System, WI) with a GE quadrature head coil. Pregnant baboon with fetus of up to term of about 185 days of gestation (dg) can comfortably fit in the coil even after being wrapped with a blanket. For scanning, the animal is kept anesthetized and mechanically ventilated. Controlled ventilation minimizes movement artifact from both mother and fetus for scanning of the fetal brain. Heart rate and percent saturation of blood with oxygen are monitored to maintain maternal stability. The baboons are kept warm by swaddling prior to transfer. Ringers lactate (25-50 ml/kg/hr) is given to maintain hydration and blood glucose. With catheterization, maternal urine is monitored and her bladder emptied to avoid inhomogeneity of signal intensity across the fetal brain when the head is in the lower abdominal portion of the uterus.

Fast Spin Echo (FSE) is used for all T_1/ T_2 relaxometry measurements. In brain studies of human newborns [2], FSE provides appropriate tradeoff among resolution, SNR and scan time. The common parameters used in this brain study of fetal baboons are: FOV = 12 cm, matrix size = 128 x 128 (zero-filled to 256 x 256), slice thickness = 3 mm, slice spacing = 0 mm, NEX = 1, echo train length (ETL) = 32. Since the size of the maternal abdomen is usually greater than the selected FOV (12 cm), the no phase wrap (NPW) option is chosen when possible. All the parameters are fixed during the longitudinal scans from the first scan at ~60 dg to last scan just before term gestation (~180 dg). For T_2 relaxometry measurement by FSE, the images are acquired at effective TEs of around 10, 35, 70, 105, 140, 175, 210, and 245 ms, with TR = 3500 ms. For T_1 relaxometry measurement by IR-FSE, the images are acquired at TIs of 60, 300, 750, 1500, and 3000 ms, with TR = 10000 ms and Minimum TE. Curve-fitting these series of images using monoexponential model on pixel-by-pixel basis gives the T_2 and T_1 relaxometry maps.

In a preliminary study, five pregnant baboons have been scanned. The first two pregnancies were used for developing the protocols for animal care and MRI scan. The last three pregnant baboons have been successfully scanned sequentially across pregnancy, with acquisition of MRI images of fetal brains at gestational ages ranging from 64 to 185 dg.

RESULTS AND DISCUSSIONS

Figure 1 shows examples of T_2- and T_1-weighted images obtained using FSE and IR-FSE in a longitudinal study of one pregnancy from 64 to 185 dg. Curves of relaxation times versus gestational ages (Fig.2) show the measured T_1 and T_2 values in selected ROIs (white matter, grey matter, and CSF) of three baboon fetuses at different gestational ages. The curves demonstrate that in early stage of fetus, T_1 and T_2 maps show contrasts opposite to those of adult brains. In early stage of brain development, grey matter has larger T_1 and T_2 values than white matter. As brain develops, the contrast difference gets smaller and might disappear at some point.

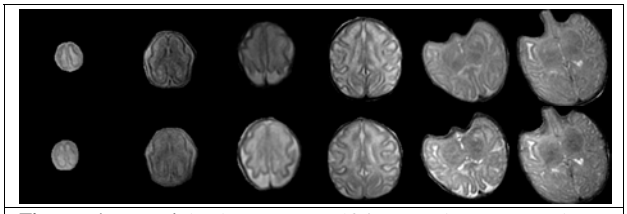

Figure 1 T_2-weighted (upper:TE≈105ms) and IR-prepared T_1-weighted (lower:TI=300ms) images of one baboon fetus (#797), at GA of 64, 92, 114, 141, 162, and 185 days, respectively.

Relaxometry measurements allow us to observe this change of image contrast during fetal brain development. At about 60 dg, white matter is more water-like and relaxation maps show that white matter has T_1 and T_2 values similar to that of CSF. However, the contrast between grey matter and white matter changes as the brain develops. The image contrast is determined by T_1 and T_2 values of different tissues. Around the time of delivery, GM and WM have similar T_1 and T_2 values. Therefore, the contrast is poor at term (~ 175-185 dg) in both T_1-weighted and T_2-weighted images and segmentation is difficult. We have shown that both T_1 and T2 values in GM and WM decrease as the brain develops. This can be explained as the process of myelination, which is a significant feature of brain maturation. Documenting T_1 and T_2 relaxation times along different ages provides a quantitative tool to measure brain maturation. For baboon model, Miot-Noirault *et al* showed that white matter could not be differentiated from the adjacent grey matter on T_2-weighted images at the age of 2 weeks after birth, and T_2 values in GM and WM decrease continuously until 30 months after birth, when the T_2-weighted image of the brain is comparable to that of an adult brain [3]. In our study, we measured the trend of T_1 and T_2 relaxation times in the fetal brain prior to birth and have shown that both T_1 and T_2 in white matter decrease faster than in grey matter. Linked with Miot-Noirault's results, the decaying curves of relaxation times (T_1 or T_2) in both GM and WM imply some crossover point for baboon brains around the time of delivery. At the earlier stages of fetal brain WM has a longer T_1/ T_2 than GM. However, the T_1/ T_2 in WM decreases faster than in GM due to change of water content that accompany myelination. Finally, after a crossover point around the time of delivery, WM has a shorter T_1/ T_2 than GM indicative of mature brain. In this study, we only complete the first half of the curve before the time of delivery with *in utero* measures and use results from Miot-Noirault's study to complete the trend. In subsequent work, we will complete the whole curve by scanning same baboons longitudinally during fetal and postnatal periods.

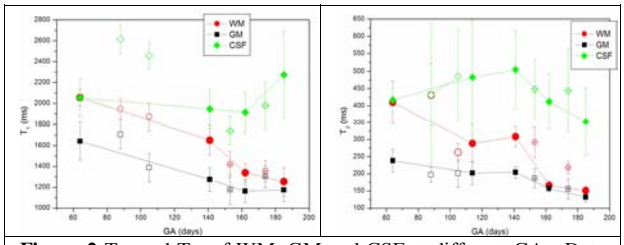

Figure 2 T_1s and T_2s of WM, GM and CSF at different GAs. Data are from three baboon fetuses. The linked data points are from the same baboon #797, and the discrete points are from different baboons (#415 and #434) at different GAs.

REFERENCES

[1] Williams, et al. Radiology 2005;235:595-603. [2] Liu, et al. ISMRM 2006;14:2404. [3] Miot-Noirault, et al. J of Neuro Methods 1997;72:5-14.