SUPPLEMENTAL MATERIAL

Data S1.

Numerical Simulations on the Effect of Echo Time Length

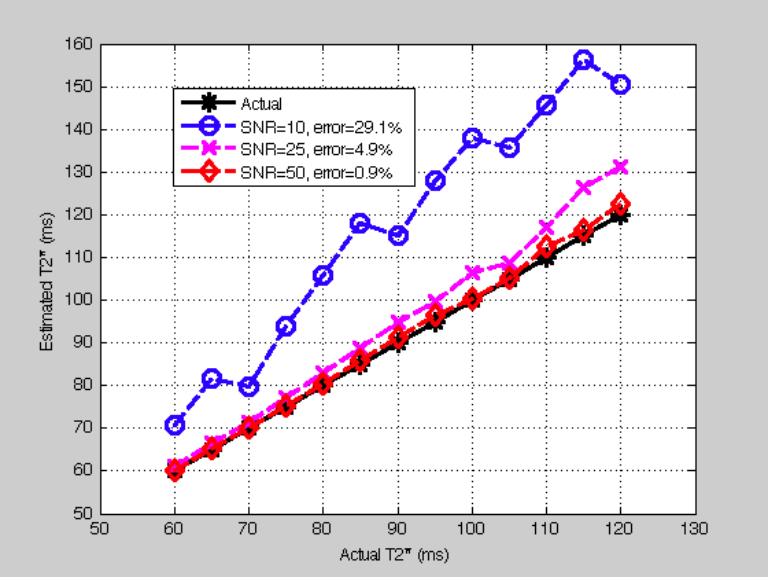
The MRI scans were performed at 3T, targeting fetuses at 32-34 weeks gestational age. T2* decay values were in the range of 60-120 msec as reported in previous studies[14]. There is a tradeoff between scan time efficiency and fitting accuracy (such as using longer TE for better estimated T2* value). We acquired data at 8 echo times ranging from 2 ms to 22 ms. Given the echo times and the range of T2* decay (60-120 msec), the numerical simulations showed that the accuracy of the derived T2* values depend on the signal-to-noise ratio (SNR) of the images. As shown in Figure S1, with a high SNR of 50, the error of the estimation is very low (<1%); and with a reasonable/common SNR of 25 (the range in our study), the error is within 5%.

Semi-Automatic Segmentation on Fetal Brain

Segmentation of the fetal brain was performed using a semi-automatic segmentation tool that we developed for this study. The main steps include the following:

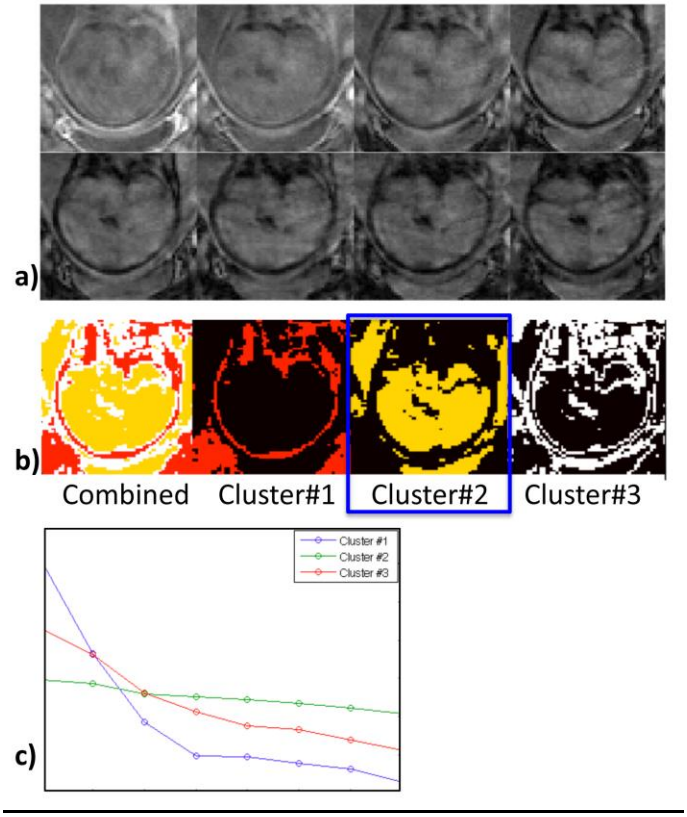
- Cropping. The center of the fetal brain (three axis locations) was manually detected for cropping the images to a region of interest (corresponding to 12x12x12 mm^3 volume), which mainly covers the fetal brain;
- Clustering. A modified k-means clustering algorithm based on the T2* signal decay was applied to initially detect the cluster that includes the brain tissue, on baseline and maternal hyperoxia images separately.
- Level Set segmentation. An initial circle shaped contour iteratively deformed to the final contour by catching the edges of the fetal brain, using a Level Set method with annular shape constraint[40].
- Registration. The fetal brain segmentations at baseline and maternal hyperoxia were registered to each other for all echo times. The overlapped brain region between the registered baseline and maternal hyperoxia images was used as the final segmentation for data analysis.

Figure S1. Numerical simulations on assessing the accuracy of fitted T2* values with varied signal-to-noise (SNR) of the images.



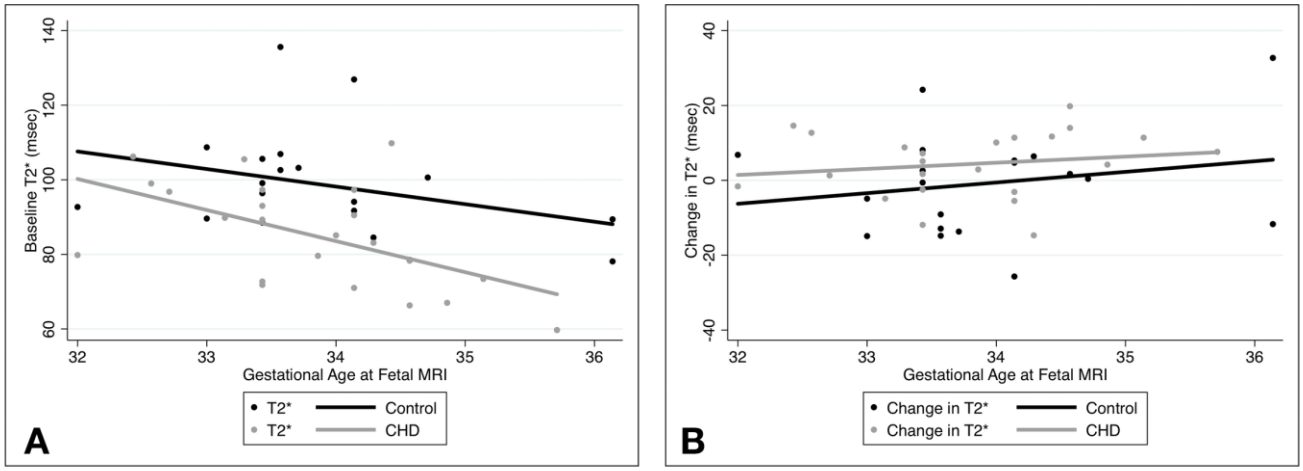
With a SNR of 25 (similar to images in the current study), the error is 4.9%.

Figure S2. A) cropped images centered at the fetal brain; B) three image clusters generated using modified k-means clustering algorithm (first subimage combines the three clusters, which are displayed in different colors as subimages #1-3); C) plots of the averages signal from each of the three clusters throughout 8 echo times.



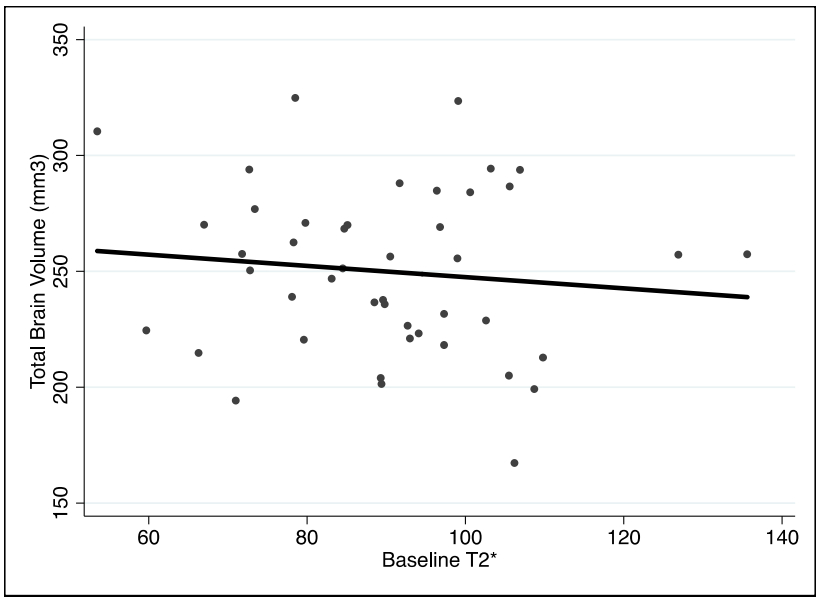
Cluster #2 was automatically identified with the most non-zero voxels for segmentation.

Figure S3. Relationships between T2* values with Gestational Age & Brain Volume.



A) The relationship between T2* values at baseline with gestational age at scan in the control and CHD groups. In both groups, T2* declines with advancing gestational age at the same rate. In control subjects, for every one week increase in gestational age, T2* declines by 7.1 msec (95% CI: -14.8, 0.72, p= 0.07). In CHD subjects, for every one week increase in gestational age, T2* declines by 8.2 msec (95% CI: -14.5, -1.8, p= 0.01). The rate of change is similar between both groups (no interaction noted between study group and gestational age). For every one week increase in gestational age, T2* declines by 1 msec more in the CHD group compared with the control group (Coeff: -1.1, 95% CI: -9.9, 7.7, p= 0.81). **B)** The change in T2* with maternal hyperoxia is not associated with GA at scan for either group. Overall, the change in T2* with maternal hyperoxia is 5.3 msec faster in the CHD group compared with control group (95% CI:-1.4, 12.0, p=0.1).

Figure S4. The relationship between T2* values at baseline with total brain volume (TBV mm^3).



No correlation was noted between the variables (r= -0.11, p= 0.47).