Oxygen-Enhanced MRI and BOLD in the human placenta
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Background: Preeclampsia and Fetal Growth Restriction are common pregnancy complications which cause maternal and fetal morbidity and mortality. Theories suggest that both are caused by a compromised placentral phenotype[1, 2] which could affect placental oxygen delivery. Previously obtained data on the placental oxygen environment is restricted to dissolved oxygen and is measured non-invasively in the first trimester only [3]. MRI allows us to non-invasively obtain new information informing us about the oxygen environment. In this study we apply two MRI techniques under hyperoxia challenge to obtain complementary data on placental oxygen delivery: Oxygen-Enhanced MRI (OE-MRI) and BOLD. OE-MRI is sensitive to changes in PO2 via T1 quantification. Dissolved molecular oxygen causes T1 shortening, with an increase in ∆R1 (R1 = 1/T1). BOLD is sensitive to changes in hemoglobin saturation (SO2) via T2* quantification, with a decrease in ∆R2* (R2* = T1/T*) indicative of an increase in SO2 in the absence of blood flow changes. Increases in SO2 also have an effect of decreasing ∆R1. We report preliminary placental OE-MRI and BOLD data acquired during normal pregnancy under hyperoxia challenge. Methods: MR imaging was carried out with a 1.5T Philips Intera system (Philips Medical Systems, Best, NL) in 10 subjects during the 3rd trimester of normal pregnancy. To investigate possible differences in oxygenation along the maternal-fetal axis of the placenta, each patient was acquired in either an in-plane view parallel to the placental plane (4 subjects), or a through-plane view perpendicular to it (6 subjects). Static T1 maps were acquired in a single coronal slice through the placenta during periods of breathing medical air (21% oxygen) and 100% oxygen using a respiratory-triggered inversion recovery-HASTE (IR-HASTE) sequence with 4 inversion times (TI=50, 300, 1100, 2000 ms) combined with a respiratory-triggered HASTE sequence (with no inversion pulse) to provide an estimate of T1. TR=TI+8000 ms, TE=5.4 ms. Each TI was acquired with at least 2 repeats to improve SNR. Static T2* maps were acquired using a breathhold multiple gradient-recalled echo (mGRE) sequence with 10 equally spaced echo times (TE = 5-50 ms). For both sequences Matrix=128 x 128; FOV=450x450 mm; slice thickness = 10mm. T1 maps for air and oxygen breathing were obtained by fitting the inversion recovery sequence to magnitude-reconstructed signal, using a fixed inversion efficiency derived from an initial three-parameter fit to magnitude-reconstructed signal. T2* maps were obtained by fitting the free induction decay equation to magnitude-reconstructed signal. Static parameter changes were then recorded as the median change between air and oxygen maps on a region of interest (ROI). Between the two static T1 mapping acquisitions, a dynamic sequence of IR-HASTE scans was acquired for a total of 8 minutes at TI=1100ms to record the evolution of R1 against time. Triggering was introduced to remove through-plane motion. Using the air T1 map as a baseline, ∆R1 against time was calculated from each dynamic’s mean signal in a ROI of placental tissue present through dynamic acquisition. The gas supply was switched at image 10. Gases were delivered throughout scanning at 15l/min with a non-rebreathing face-mask (Intersurgical, Wokingham, UK).

Results: Median ∆R1 and ∆R2* across a placental ROI are presented in Figure 1 for all subjects. Mean R1 and R2* changes were both statistically significant across the group. Mean ∆R1 was 0.0196 ± 0.0199 s−1 (p = 0.015) while mean ∆R2* was -3.65 ± 2.21s (p = 0.003). No correlation was found between ∆R1 and ∆R2*. Placental ∆R1 and ∆R2* maps for a through-plane view are presented in Figures 2 & 3 respectively. Mainly positive R1 changes and mainly negative R2* changes were observed here. The dynamic ∆R1 curve (Figure 4) shows an increase coincident with gas switchover. Discussion: We have presented results in 10 subjects demonstrating the feasibility of combining OE-MRI and BOLD measurements in the placenta to obtain information relating to placental oxygen delivery noninvasively. Significant mean increases in R1 and mean decreases in R2* were observed. Increases in R1 suggest increases in dissolved molecular oxygen concentration, while decreases in R2* suggest increases in hemoglobin saturation. These two results are consistent with observing uptake of oxygen in placental tissue. There was no correlation between the changes in R1 and R2* and further studies are required to understand the relationship between these parameters in the placenta. Use of these techniques in compromised pregnancies may allow a comparison of the oxygenation state between normal and compromised pregnancy. Hence, the technique offers the possibility to investigate alterations in oxygen delivery in the placenta in preeclampsia and FGR.

Figure 1. ∆R1 and ∆R2* between air and oxygen.

Figure 2. Placental R1 changes in through-plane subject between air and 100% O2, Median ∆R1* = 0.0173s.

Figure 3. Placental R2* changes in through-plane subject between air and 100% O2, Median ∆R2* = -3.36s.

Figure 4. Placental dynamic R1 changes in through-plane subject. Switch from medical air to 100% O2 occurred at dynamic number 10 (line).