Oxygen-Enhanced MRI in the human placenta: preliminary results

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Background: Preeclampsia and Fetal Growth Restriction (FGR) are common pregnancy complications which cause maternal and fetal morbidity and mortality. Theories suggest that both are caused by an insufficiency in oxygen supply to the placenta[1]. There is a lack of data about the placental oxygen environment; one of the few studies in this area quantified partial oxygen pressure (PO_2) invasively in the first trimester only [2]. MRI offers the possibility to obtain information related to placental function non-invasively during pregnancy to inform understanding of aetiology. Oxygen-Enhanced MRI (OE-MRI) quantifies changes in PO_2 through T_1 quantification. Dissolved molecular oxygen causes T_1 shortening, with ΔR_1 ($R_1 = 1/T_1$) proportional to ΔPO_2[3] by a constant[4], allowing quantification of tissue ΔPO_2 under a change in administered oxygen concentration. We present preliminary placental OE-MRI data acquired during normal pregnancy, demonstrating the feasibility of the approach and the potential for non-invasive investigation of pregnancies affected by preeclampsia and FGR in the future.

Methods: MR imaging was carried out using a 1.5T Philips Intera system (Philips Medical Systems, Best, NL) in two subjects, each during the third trimester of a normal pregnancy. Static T_1 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, 2000ms) combined with a respiratory-triggered HASTE sequence (with no inversion pulse) to provide an estimate of M_0. For both sequences TR/TE=6000/5.4ms; Matrix=128 x 128; FOV=450x450mm; slice thickness = 10mm. Each TI was acquired with 5 repeats to improve SNR. This triggering scheme was chosen in order to minimize artifacts due to respiratory motion while maintaining a reasonably short trigger delay, since a long delay which would be necessary for a long TI acquisition would lead to a reduction in the effectiveness of the respiratory gating. This short-delay triggering was first evaluated in 3 non-pregnant volunteers by comparison to both a free-breathing and a respiratory triggered IR-HASTE sequence (long-delay triggering) with 5 inversion times (TI=50, 300, 1100, 2000, 5000ms) using the spleen as a surrogate organ. T_1 maps for air and oxygen breathing were obtained by fitting the inversion recovery equation to the magnitude-reconstructed images (the non-inversion HASTE image was included in the fitting as a TI=0 data point). These were converted to ΔPO_2 maps using a relaxivity constant of 2.49×10^{-4} $mmHg^{-1}$ s^{-1}[4]. Between the two static T_1 mapping acquisitions, a dynamic sequence of IR-HASTE scans was acquired with a temporal resolution of 6 seconds for a total of 8 minutes at TI=1100ms to record the evolution of ΔPO_2 over time. The gas supply was switched from medical air to 100% oxygen at image number 10. Gases were delivered throughout the scanning protocol at 15l/min using a non-rebreathing face-mask (Intersurgical, Wokingham, UK).

Results: A comparison of reproducibility (coefficient of variation between repeats) and T_1 fit quality (norm of residuals) is presented in Table 1 for the normal volunteer spleen data for the free-breathing, short-delay and long-delay respiratory triggering regimes. Short-delay triggering produced the best reproducibility in every case. The best fit quality (lowest norm of residuals) for each subject was achieved with triggering methods, with short-delay triggering best in 2 of 3 subjects. It was therefore decided to use short-delay triggering for static scan acquisition in the pregnant subjects.

	Coefficient of variation			Norm of residuals		
Method	Subject A	Subject B	Subject C	Subject A	Subject B	Subject C
Free-breathing	0.0418±0.0581	0.0733±0.0953	0.0555±0.108	1.15±3.10	0.280±0.411	0.653±2.52
Long-delay triggering	0.105±0.151	0.0843±0.0418	0.0260±0.0419	2.62±5.64	0.230±0.152	0.0608±0.0513
Short-delay triggering	0.0198±0.0198	0.0392±0.0434	0.0207±0.025	0.0987±0.0611	0.168±0.150	0.111±0.123

Table 1. Comparison of reproducibility (coefficient of variation) and fit quality (norm of residuals) between different triggering regimes.

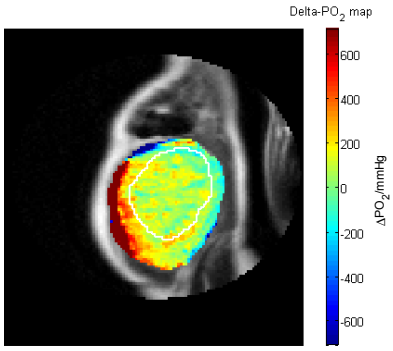

Figure 1. Placental PO_2 changes in subject 1 between air and 100% O_2. ROI (white border) mean ΔPO_2: +81 mmHg. Mean $\Delta T1$: -0.0446s.

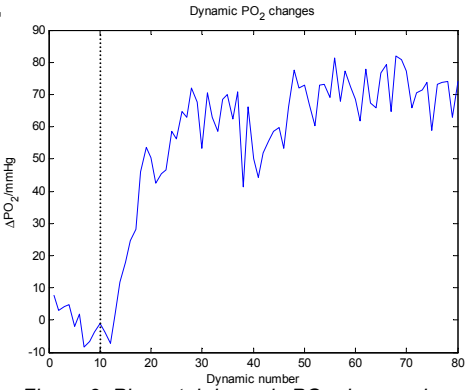

Figure 3. Placental dynamic PO_2 changes in subject 1. Switch from medical air to 100% O_2 occurred at dynamic number 10 (line).

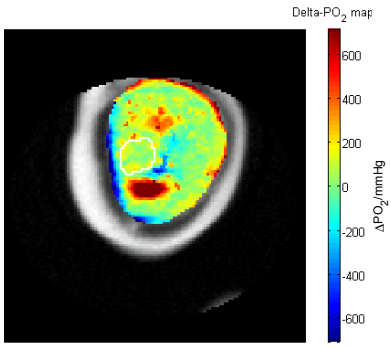

Figure 2. Placental PO_2 changes in subject 2 between air and 100% O_2. ROI (white border) mean ΔPO_2: +73 mmHg. Mean $\Delta T1$: –0.0353s.

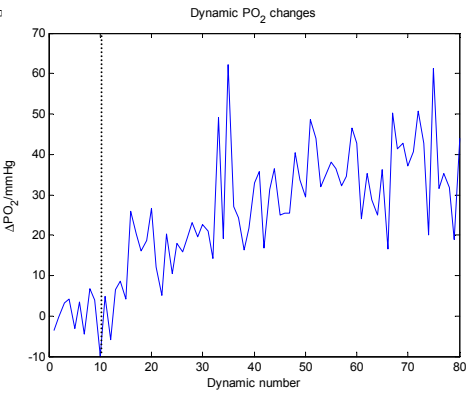

Figure 4. Placental dynamic PO_2 changes in subject 2. Switch from medical air to 100% O_2 occurred at dynamic number 10 (line).

Placental ΔPO_2 maps for pregnant subjects 1 & 2 are presented in Figures 1 & 2 respectively. ROIs were selected in areas least affected by partial volume effects in order to calculate dynamics and average changes. We observed considerable fetal motion in subject 2 (which cannot be accounted for by respiratory triggering) and as a result chose a small ROI unaffected by fetal intrusion. In both subjects, mainly positive PO_2 changes were observed across the placenta. The average ΔPO_2 in the ROIs indicated was 81mmHg for subject 1 and 73mmHg for subject 2. This compares with an average ΔPO_2 in the spleen of the three non-pregnant volunteers of 229±88.5mmHg. The dynamic ΔPO_2 for subject 1 (Figure 3) shows a clear increase coincident with gas switchover. The dynamic ΔPO_2 for subject 2 (Figure 4) contains more noise, though a trend can still be observed. **Discussion:** We have presented preliminary results demonstrating the feasibility of using OE-MRI in the placenta to obtain information relating to placental oxygen delivery noninvasively for the first time. PO_2 changes in placenta were successfully observed between air and 100% oxygen breathing, derived from both static T_1 maps and dynamic signal curves. In both subjects, an apparent heterogeneity can also be seen in ΔPO_2 maps, possibly reflecting placental structure. The technique offers the possibility to investigate alterations in oxygen delivery in the placenta in preeclampsia and FGR. **Acknowledgements:** This work was supported by The University of Manchester Biomedical Imaging Institute, The University of Manchester Magnetic Resonance Imaging Facility and the Manchester Wellcome Trust Clinical Research Facility. **References:** 1. Kanasaki, K. et al. Kidney Int, 2009. **76**(8): p. 831-7. 2. Jauniaux, E. et al. American Journal of Obstetrics and Gynecology, 2001. **184**(5): p. 998-1003. 3. Ohno, Y. et al. European Journal of Radiology, 2007. **64**(3): p. 320-328. 4. Zaharchuk, G. et al. Academic Radiology, 2006. **13**(8): p. 1016-1024.