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Reduced placental oxygenation during subclinical uterine contractions as assessed by BOLD MRI

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ABSTRACT

Objectives: During placental Blood Oxygen Level Dependent (BOLD) Magnetic Resonance Imaging (MRI), we have observed spontaneous reductions in placental oxygenation lasting 2–4 min. We hypothesize, that these reductions in placental oxygenation are caused by subclinical uterine contractions.
Methods: We evaluated placental oxygenation during a five-minute placental BOLD MRI in 56 normal pregnancies (gestational week 23–40) and observed a spontaneous reduction in eight cases. The 56 BOLD MRIs were systematically analyzed for signs of uterine contractions, i.e. visual changes in uterus shape and reductions in the number of pixels within Regions of interest (ROI) covering the outline of the entire uterus.
Results: The eight reductions in the BOLD signal lasted for 217 ± 51 (mean ± SD) seconds with an average signal loss of 17 ± 5%. They were all associated with a contraction, which started 43 ± 21 s prior to the start of the reduction and ended 71 ± 30 s prior to the end of the reduction. In the remaining 48 MRIs, we observed no contraction.
Conclusion: We suggest that the observed spontaneous reductions in placental oxygenation are caused by uterine contractions. According to our data, subclinical uterine contractions occur regularly and have a markedly impact on placental oxygenation. Therefore, uterine contractions need to be considered in the interpretation of placental MRI as they may interfere with the MRI results.

1. Introduction

In 1872, J. Braxton Hicks described the spontaneous, non-labor uterine contractions in the pregnant woman [1]. These contractions occur throughout pregnancy with increasing frequency as pregnancy advances although they rarely exceed three per hour before term [2]. In the second trimester, most women do not recognize the uterine contraction whereas the amplitude of the contractions increases in the third trimester [3] and even more during labor where the intrauterine pressure exceeds the 30 mmHg limit [4] which compromises the maternal blood supply to the placenta.

In general, it is assumed that non-labor contractions are harmless to the fetus. The scientific background for this assumption is scarce as most studies have focused on labor contractions or induced uterine contractions. In a few studies on spontaneous non-labor contractions in normal pregnancies, Doppler flow examinations have demonstrated increased pulsatility index in the uterine arteries but not in the umbilical arteries and the internal carotic arteries [5–7]. In growth-restricted fetuses, non-labor contractions may induce changes in the fetal heart-rate pattern [8]. To our knowledge, direct assessment of the placental oxygenation during non-labor contractions has never been investigated. However, this can be achieved using dynamic Blood Oxygen Level-Dependent (BOLD) Magnetic Resonance Imaging.

Using the dynamic BOLD-MRI method it is possible to estimate

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changes in tissue oxygenation noninvasively. The BOLD effect is based on the paramagnetic properties of deoxyhemoglobin. The paramagnetic properties of deoxyhemoglobin affect the spin of the neighboring protons thereby creating magnetic field inhomogeneities, which decrease the T2* value and thus the BOLD signal [9]. Thus, reduced tissue oxygenation decreases the BOLD signal.

The BOLD-MRI method has been applied in several human and animal studies of the placenta [10–13] and the fetus [14–24]. In previous placental BOLD-MRI studies, we have observed unexplainable reductions in the BOLD-MRI signal of two to four minutes duration. In this paper, we aim to describe whether these reductions are associated with subclinical uterine contractions.

2. Methods

2.1. Subjects

Fifty-six normal pregnant women (gestational age [GA] 23–40 weeks), were enrolled for placental BOLD MRI as part of another study. In each pregnancy, ultrasound estimated fetal weight (EFW) [25] and Doppler flow measurements in the umbilical artery, the middle cerebral artery and the maternal uterine arteries were normal. The neonatal outcomes including birth weight Z-score [25] and macroscopic placental examinations were normal. Prior to the MRI examination, the women were instructed to report if they felt any uterine contractions during the MRI. The study was approved by the Regional Committees on Biomedical Research Ethics (Journal number M-20090006). Oral and written informed consents were obtained from all participating women.

2.2. MRI

All measurements were performed in a GE Discovery MR450 1.5 T MRI System (GE Healthcare, Milwaukee, USA). During the MRI scan, the pregnant woman was placed in a left lateral position and an eight channel cardiac coil was placed over the abdomen, covering the entire uterus. Initially, a T2 weighted localizer was performed to obtain the anatomic orientation of the placenta. This was followed by a 5-minute dynamic BOLD MRI sequence using a gradient recalled echo sequence with the following parameters: repetition time, 8000 ms; echo time 50 ms; field of view, 360 × 360 mm and matrix 128 × 128. The size of the matrix resulted in an in-plane resolution of 3.6 × 3.6 mm. Six mm slices with a slice gap of 6 mm were placed in transversal orientation covering the entire placenta. During the initial 5-min BOLD scan, each slice-image was repeated every eight seconds leaving approximately 38 frames of each slice. Other MRI sequences were performed during the scan giving a total scan time of 30 min, which was well-tolerated by the women.

2.3. MRI analysis

Images were processed using an in-house developed program written in MATLAB (The MathWorks Inc., Natick, MA, USA).

For investigation of placental oxygenation, placental Regions of interest (ROIs) were drawn on three slices of the central part of the placenta (Fig. 1). In each frame, the ROI covered the entire placenta in the transversal orientation ensuring that the outer placental borders were not crossed, and the ROI was repositioned manually in each frame in order to stay within the placental borders. For each ROI, the BOLD signal during the entire 5- minute scan was recorded and normalized using a steady state period of one minute as a reference level. In each placenta, a normalized BOLD signal (mean of the three separate slices) versus time plot was performed.

In case of spontaneous significant reduction in placental BOLD signal, the duration of the reduction, the speed of the decline and the speed of recovery of the BOLD signal was estimated.

The 56 MRIs were analyzed for any visual signs of uterine contraction. During a contraction, the shape of the uterus shifted from oval-shape to a more circular-shape. Therefore, we assessed changes in the area of the uterus in cross-section. In one central slice, a ROI was drawn covering the entire uterus and the ROI position was adjusted manually in each frame, ensuring that the outer border of the uterus was not crossed (Fig. 1). The number of pixels within the uterus ROI was measured and normalized using a 1-min steady state period. In order to identify subclinical uterine contractions, pixel versus time plot was then performed. Only significant reductions in pixel numbers were considered uterine contractions. Furthermore, we estimated the duration of the contraction and the temporal association between the uterine contraction and the maximum reduction in placenta BOLD signal.

Finally, as a proxy of changes in placental volume during a uterine contraction, we assessed the placental area in three separate slices (one central slice and one slice peripherally on each side, Fig. 1) using placental ROIs covering the entire placenta within the slice. The ROI position was manually adjusted in each frame in order to stay within placental borders. The number of pixels within the placenta ROIs was normalized using a steady state period of one minute and Pixel versus time plot was then performed. We assessed the temporal association between the uterine contraction, the reduction in placental BOLD signal and the changes in placenta volume.

2.4. Statistical analysis

In each case, the reduction in placental BOLD signal was tested against the steady state BOLD signal using a Student's t-test. A p-value < 0.05 was considered statistically significant. The maximum reduction in BOLD signal was defined as the lowest measured signal value within a placental ROI. Furthermore, the change in the number of pixels within each uterus and placental ROI was estimated and tested against steady state pixel-number using a Student's t-test. A p-value < 0.05 was considered statistically significant. The maximum reduction in number of pixels was defined as the smallest pixel number measured within a uterus resp. placental ROI.

3. Results

In eight out of the 56 5-min dynamic scans (GA 23–37 weeks), we observed a spontaneous significant reduction in the placental BOLD signal with an average signal loss of 17 ± 5% (mean ± SD). The mean duration of the reduction in BOLD signal was 217 ± 51 s with the maximum reduction being after 62 ± 36 s. The speed of decline in BOLD signal was 10 ± 6% per minute whereas the speed of recovery was only 3 ± 1% per minute. Thus, loss of BOLD signal occurred faster than recovery of the signal. In the BOLD MR images, the reduction in placental BOLD signal was clearly visible, as the placenta became markedly darker (Fig. 2).

In each of the eight cases, the reduction in placental BOLD signal was preceded by a remarkably change in the uterine shape (video1) and in each case, a uterine contraction could be identified as a significant reduction in the number of uterine pixels. In average, the number of pixels was reduced 8 ± 2%. The mean duration of the contraction was 189 ± 66 s. In the remaining 48 scans, we observed no remarkable change in the uterine shape accompanied by a significant reduction in the number of uterine pixels.

Supplementary video related to this article can be found at http://dx.doi.org/10.1016/j.placenta.2015.12.018.