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Association of placental perfusion, as assessed by magnetic resonance imaging and uterine artery Doppler ultrasound, and its relationship to pregnancy outcome

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ABSTRACT

Purpose: To investigate (a) if placental perfusion in the second trimester of pregnancy, measured by two non-invasive magnetic resonance imaging (MRI) techniques, is related to impedance to flow in the uterine arteries, as assessed by Doppler ultrasound; and (b) if these measures are associated with future gestational outcome.
Methods: In 37 singleton pregnancies at 24–29 weeks' gestation, uterine artery pulsatility index (PI) was measured by Doppler ultrasound and placental perfusion was measured by Arterial Spin Labelling (flow-sensitive alternating inversion recovery (FAIR)) and intravoxel incoherent motion (IVIM) echo-planar imaging at 1.5 T in basal, central and placental regions of interest. The values were compared between those delivering small for gestational age (SGA) and appropriate for gestational age (AGA) neonates.
Results: In 23 pregnancies that resulted in delivery of SGA neonates, compared to the 14 with AGA neonates, the median basal FAIR measure was significantly lower (923.0 vs. 2359.0 arbitrary units; $p = 0.003$) as were IVIM measures of perfusing fraction (f) in basal, central and whole-placental regions (37.8 vs. 40.7%; $p = 0.046$; 24.3 vs. 35.1%; $p = 0.014$ and 27.9% vs. 36.2%; $p = 0.001$, respectively). In the SGA group, the median uterine artery PI was increased (1.96 vs. 1.03; $p = 0.001$). There were significant associations between uterine artery PI and placental perfusion assessed by both FAIR and IVIM.
Conclusion: Pregnancies that result in SGA neonates exhibited reduced placental perfusion as assessed by MRI during the second trimester. This measurement was found to be strongly associated with impedance to flow in the uterine arteries. We suggest that FAIR or IVIM MRI examinations may be used to directly and non-invasively determine placental perfusion, and that the measured values are strong indicators of future gestational outcome.

1. Introduction

Small for gestational age (SGA) neonates have increased risk of perinatal death and handicap. The condition includes neonates who are both constitutionally small and who are growth restricted due to impaired placentation, genetic disease or environmental damage. Abnormal placentation [1–4] leads to increased impedance to flow measured by the uterine artery pulsatility index (PI) on Doppler ultrasound [5] at 22–24 weeks gestational age (GA) in pregnancies that subsequently develop preeclampsia and, to a lesser extent, in those delivering SGA neonates without preeclampsia [6,7].

Power Doppler ultrasound measurements of placental perfusion have limited depth, reliability and reproducibility, and quantification remains unclear [8,9]. In contrast, magnetic resonance imaging (MRI) can clearly image the placenta, independent of GA or location [10] Ultrafast MRI sequences, such as echo-planar imaging (EPI) and single shot fast spin echo imaging (SS-FSE), can overcome the

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effects of fetal motion [11,12]. Fetal MRI is considered to be safe, and follow-up studies have found no adverse effects [13–15] and non-invasive MR perfusion measurements have been employed in several studies of the placenta [16–21]: the flow-sensitive alternating inversion recovery (FAIR) sequence [22] Arterial Spin Labelling (ASL; [23,24]) and intravoxel incoherent motion (IVIM; [25]) sequences.

In FAIR, arterial blood flowing into the imaged region is labelled non-invasively using radio-frequency pulses. In IVIM, a pulsed field gradient is used to impose diffusion dependent contrast, with the degree of contrast being summarised by the '*b*-factor' [25]. In tissue the MR signal decays bi-exponentially with *b*-factor; the first component of the signal decay is dominated by blood motion and the second by diffusion, so that the relative size (f) of the first component can be interpreted as the fractional perfusing blood volume. Two previous studies related FAIR measures of placental perfusion to birth weight; the first found no differences in pregnancies that delivered SGA neonates [16], but the second found a difference in the distribution of perfusion values across the placenta between the SGA and AGA groups [17]. Two other studies found changes in pregnancies that delivered SGA neonates and those with preeclampsia using IVIM [21].

The aim of this study was to compare placental perfusion measured using FAIR and IVIM in SGA fetuses, to relate results to uterine artery PI and to determine whether detected changes in perfusion precede the clinical onset of SGA.

2. Methods

The study was carried out at the Harris Birthright Research Centre (HBRC), London, between February 2006 and May 2008. It was approved by the local NHS Research Committee and all participants provided written, informed consent. Consecutive women with singleton pregnancies attending for scan at 22–24 weeks, and those referred with a known SGA fetus or a minor congenital abnormality were invited to participate. Many of the women who participated in this study also participated in our study on placental T_2 relaxation [26]. All the pregnancies were dated by ultrasound scan in the first trimester.

All participants had an ultrasound scan on the same day as the MRI exam, to measure fetal weight (estimated from measurements of head circumference, abdominal circumference and femur length [27]) and amniotic fluid volume; and pulsatility indices (PIs) assessing impedance to flow in the maternal uterine arteries (averaged over left and right sides), umbilical arteries, fetal cerebral vessels and ductus venosus. Uterine artery blood flow is routinely assessed by transvaginal sonography to determine the women's risk of developing preeclampsia and/or a SGA fetus [6]. The fetal weight percentile was determined from the mother's height and weight, ethnicity and parity, the GA and sex of the fetus and the estimated fetal weight using the GROW centile calculator v5.15_UK [28].

Data on pregnancy outcome were obtained from maternity records or the women's general medical practitioners. The outcome measures were preeclampsia, as defined by the International Society for the Study of Hypertension in Pregnancy [29], and SGA if the birth weight was <10th percentile for GA at delivery, using the GROW centile calculator.

Three groups of subjects were defined. Group 1: estimated fetal weight >10th percentile of the reference range and uterine artery PI <95th percentile of the reference range ($n = 9$). These fetuses were complicated by isolated minor congenital abnormalities. Group 2: estimated fetal weight >10th percentile but uterine artery PI >95th percentile ($n = 21$). These women had structurally normal fetuses but were at risk of preeclampsia or an SGA fetus. Group 3: estimated fetal weight <10th percentile and uterine artery PI >95th percentile ($n = 10$). These fetuses were known SGA at the time of the MRI, with seven having abnormal fetal Doppler measurements and four also having reduced amniotic fluid volume.

MRI was performed on a 1.5 T GE Signa HDx scanner (General Electric, Waukesha, USA), with a body coil for RF transmission and a torso array coil for signal reception. The mother was placed supine in the scanner feet first to minimise claustrophobia, but angled 20° onto her left hand side with pads to reduce aorto-caval compression.

Localiser images were obtained to determine the overall position of the uterus and placenta. Oblique sagittal (sequence 1 – see Table 1) and axial (sequence 2) T_2-weighted single shot fast spin echo (SS-FSE) images were acquired across the whole uterus, to visualise the placenta in detail. The axial images were used to determine where to examine placental blood flow. Three contiguous true axial slices were acquired in an additional axial SS-FSE scan whose field of view (FOV) was matched to those to be used for the FAIR and IVIM scans (sequence 3). If these images demonstrated good placental and basal plate coverage (Fig. 1), these slices were used for the FAIR and IVIM scans; if not, sequence 3 was repeated with different slice positions until good visualisation was achieved.

Table 1
Summary of scanning parameters for the different sequences used.

Sequences	Scanning parameters
1	TE 140 ms, TR 4000 ms; Sagittal; slice thickness 6 mm, slice gap 1 mm, 28 slices, FOV 28 × 28 cm, matrix 256 × 224, scan time 3 min
2	TE 140 ms, TR 4000 ms; Axial; slice thickness 4 mm, slice gap 1 mm, 46 slices, FOV 40 × 40 cm, matrix 320 × 224, scan time 5 min
3	TE 140 ms, TR 4000 ms; Axial; slice thickness 4 mm, slice gap 0 mm, three slices, FOV 24 × 24 cm, matrix 192 × 192, scan time 15 s
4	TE 35 ms, TR 2500 ms; Axial; slice thickness 4 mm, slice gap 0 mm, three slices, FOV 24 × 24 cm, matrix 64 × 64, reconstructed resolution 1.875 mm, scan time 5 min
5	TE 69 ms, TR 2000 ms; Axial; slice thickness 4 mm, slice gap 0 mm, three slices FOV 24 × 24 cm, matrix 64 × 64, scan time 8 min

TE = echo time, TR = repetition time, FOV = field of view.

Single shot spin echo EPI FAIR images (sequence 4) were acquired labelled (after inverting the magnetisation within the image volume) and non-labelled (after inverting a region 1.35 times wider than the image volume). A post-labelling delay (T_i) of 1.2 s between the inversions and readouts allowed the labelled blood to move into the image volume. Twenty-five pairs of labelled and non-labelled images were collected to increase signal-to-noise ratio (SNR), and the average difference image ('non-label' – 'label') was calculated. This perfusion weighted image (arbitrary units) showed signal attenuation proportional to the amount of inverted blood that perfused into the image volume during the post-labelling delay. Whilst the raw values of the tagged and un-tagged images may have differed slightly between subjects due to small differences in the transmitter and receiver settings, the values of the *difference* images are comparable between subjects. We therefore employed these as a measure of tissue perfusion. It was not possible to convert these to physiological units of ml of blood per 100 g of tissue per minute, as there is no suitable model to perform this conversion in the placenta. IVIM data were acquired using spin echo EPI (sequence 5) with pulsed magnetic field gradients applied in the through-slice direction with 11 logarithmically spaced *b*-values (0, 0.7, 3, 9, 18, 32, 54, 88, 147, 252, 500 s/mm^2).

The FAIR time series of one slice was displayed as a movie, and images in which the placenta was displaced by more than two pixels in-plane were excluded from

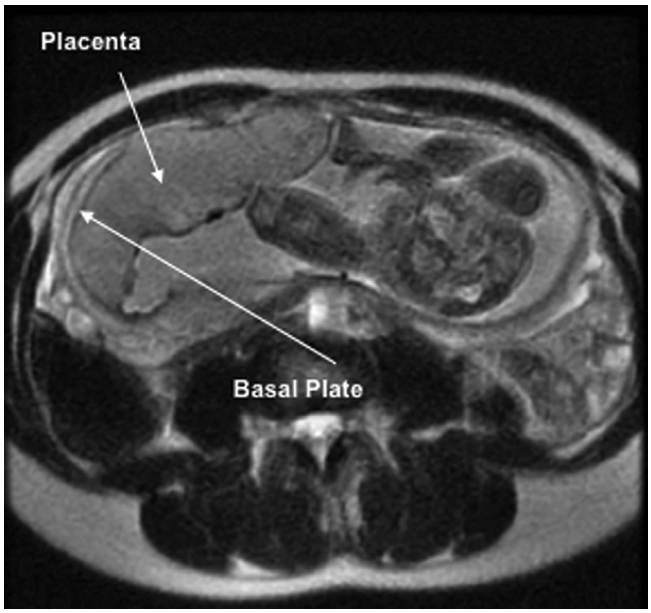

Fig. 1. T_2-weighted magnetic resonance image demonstrating the placental anatomy and basal plate.

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