The Effect of Maternal Diabetes on Placental Blood Flow Assessed Using IVIM

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Introduction: The placenta is a complex organ and is vital for successful fetal development. High volume, low resistance blood flow in the placenta is thought to be essential for optimal materno-fetal nutrient exchange. Intrauterine Growth Restriction and maternal diabetes are often related to abnormal placental perfusion[1]. In maternal diabetes the placenta is often large with abnormal vascular development and increased villous volume on histology[2]. Hence, antenatal assessment of placental vascular function will assist in assessing fetal well-being. Intravoxel incoherent motion (IVIM) has been shown to be a sensitive method of measuring moving blood fraction (*f*) in the placenta[3].

Aim: To study placental blood flow in normal and diabetic pregnancies.

Methods: Scanning: With ethics committee approval, 4 normal women and 6 women with Type 1 diabetes were recruited from Queen's Medical Centre Nottingham during the first trimester of pregnancy and gave informed consent to participate in the study involving two scans at 24–26 weeks and 34–36 weeks gestational age (GA). Scanning was performed on a 1.5 T Philips Achieva MRI scanner with 5-element SENSE cardiac coil or 4-element SENSE torso coil, depending on the woman's size. Women lay on their right side in the decubitus position to avoid vena cava compression and all these scans were conducted with a specific absorption rate of < 2.0 W kg^{-1}. The IVIM sequence used was respiratory gated, standard diffusion pulsed spin echo sequence acquired with 5 transverse slices encompassing the placenta in 108 seconds (TR = 3000 ms, TE = 95 ms, FOV = 350×350×107 mm^3, resolution = 1.46×1.46×7 mm^3, slice gap = 18 mm, 12 b values = 0, 1, 3, 15, 47, 80, 115, 206, 246, 346, 468 and 800 s mm^{-2}, repeated 5 times. Analysis: A region of interest was drawn around the whole placenta in a central slice for an intermediate b value. Each pixel in the ROI was fitted to the IVIM equation in Box 1[3] for *f*, D, D* and S_o in Matlab (R2010a). *f* is interpreted as the moving blood volume in the placenta. Data points corrupted by excessive motion identified as lying > 2 standard deviations from the fitted line were excluded and the data were refitted. The histogram of *f* in the ROI was found, and the mean, mode and fraction of pixels with $f > 0.8$ in the histogram were found.

Results: So far only 4 controls and 6 diabetics have completed the study and have been analysed for visit 1. Figure 2 shows maps of *f* for a control and diabetic subject and Figure 3 shows the related histograms. Considering all subjects, the mean value of *f* in the normal placenta (0.37 ± 0.01) was higher than in the diabetic placenta (0.34 ± 0.03), although this was not statistically significant. The mode of the distribution was higher in the normal placenta (0.32 ± 0.3) than in the diabetic placenta (0.26 ± 0.05) ($p = 0.04$). However the fraction of the voxels with high perfusion ($f > 0.8$) tended to be higher in diabetics (4.1 %) than controls (2.5 %) ($p = 0.06$). (Data shown in Figure 4)

Discussion: This is the first report of a difference in the distribution of placental blood flow in diabetic placentae. In the normal placenta *f* was fairly uniformly distributed, whilst in the diabetic placenta the *f* distribution was generally shifted to lower *f* but with small areas of higher *f*. Figure 2 demonstrates a negative correlation ($R^2 = 0.108$, all subjects grouped) between the fraction of pixels with high *f* and the mode of the histogram, suggesting that areas of particularly high flow are associated with a general depression in flow across the rest of the placenta. It has been suggested that abnormal spiral artery remodeling causes increased intravascular resistance leading to high velocity blood flow in the intervillous spaces. This abnormal intervillous circulation causes damage to villous architecture affecting the materno-fetal nutrient transfer[4]. This may be related to the abnormal fetal development associated with diabetic pregnancies.

BOX 1: The signal attenuation due to the pulsed gradient:

$$S = S_0 [(1 - f)\exp(-bD) + f\exp(-bD^*)]$$

where S_o = equilibrium signal intensity, f = moving blood volume, D = diffusion coefficient, D* = pseudo diffusion coefficient and b = diffusion parameter

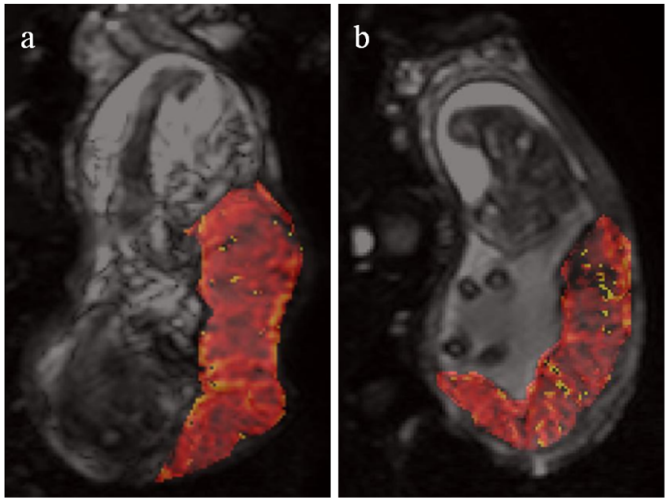

Figure 2: Map of *f* for a (a) control and (b) diabetic subject

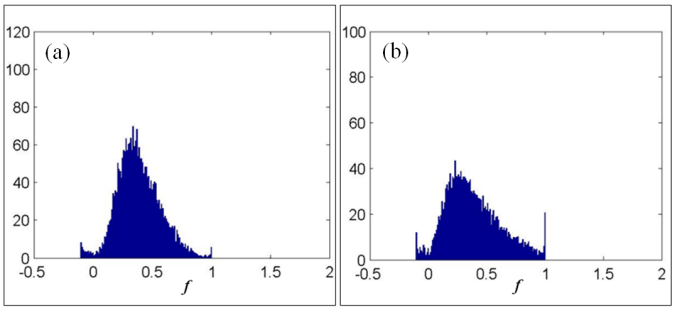

Figure 3: Histogram of *f* for a (a) control and (b) diabetic subject

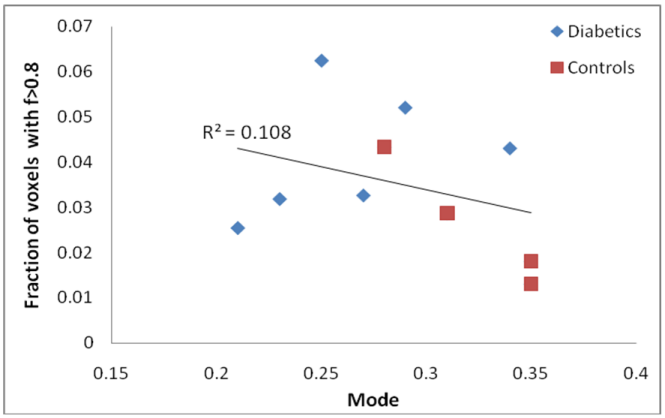

Figure 4: Correlation between fraction of pixels with $f > 0.8$ and mode of *f* distribution across the placenta.

References: [1] Pregnancy in women with Type 1 and Type 2 diabetes. Confidential Enquiry into Maternal and Child Health Report. (2005). [2] T. Mayhew. (2002), Diabetologia, **45** 1434-1439. [3] R.J.Moore. (2000), Placenta, **21** 726-732. [4] G.J. Burton et al. (2009), Placenta **30(6)** 473-82. **FUNDED BY DIABETES UK.**