Intra Voxel Incoherent Motion in the Human Placenta using the Akaike Information Criterion

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Background – The placenta is important in fetal development for supplying nutrients and removing waste. Therefore, functional disruptions can lead to Fetal Growth Restriction (FGR) with increased perinatal mortality and morbidity [1]. Placental perfusion as determined by contrast enhanced MRI, is regionally compromised in FGR in the human placenta [2]. Intra Voxel Incoherent Motion (IVIM) can non-invasively determine flow characteristics using the diffusion of water as an intrinsic contrast agent and has been used in the placenta [3]. Applying the bi-exponential IVIM model to diffusion data over the simple mono-exponential model is flawed when the data do not support the fitting of the more complex model. The Akaike Information Criterion (AIC) [4] has been applied to provide an objective assessment of those voxels where IVIM values can be assessed.

Methods – After obtaining informed consent, 16 normal pregnancies, mean gestational age 32.6 weeks, were scanned. Women were scanned with a 1.5 T Achieva Scanner (Philips Medical Systems, Best, Netherlands) using an interleaved EPI sequence TE/TR 70 ms/5000 ms, matrix 128x128 with three slices, resolution 3x3x8 mm^3 and a rectangular view 0.8. Images were acquired with diffusion weighting (b) of 0, 1, 2, 5, 10, 15, 25, 50, 100, 200 and 400 s/mm^2. Scans were not breath held because of poor patient compliance while respiratory gating was discounted due to time constraints. The SAR was limited, gradient speeds restricted and women introduced feet first into the scanner at a left lateral tilt for comfort and safety. Regions for analysis were defined on the middle slice to include all placental tissue free from partial volume effects and motion artefacts, mean size 920 voxels. Voxels where the noise levels prevented the convergence of the least squares fitting routine (Matlab 2008a, The Mathworks, Inc. Massachusetts, U.S.A) were excluded. The signal attenuation may be expressed in the case of mono-exponential decay by:

$$S(b) = S(0)e^{-bD} \qquad \textbf{Equ. 1}$$

Here S is the signal intensity and D is the apparent diffusion coefficient. Alternatively, bi-exponential decay, where D* is a fast apparent diffusion coefficient observed at low b values attributed to flowing blood and f is the fraction of the tissue in which this is occurring, may be used:

$$S(b) = S(0)[(1-f)e^{-bD} + fe^{-bD^*}] \qquad \textbf{Equ. 2}$$

Both models are fitted and the AIC calculated to determine the model that best describes the data. The AIC penalises the greater number of free parameters required to determine f and D* and includes a correction for the low number of data points available [4,5]:

$$AIC = N \times \ln(SS/N) + 2K + 2K(K+1)/N-K-1 \qquad \textbf{Equ. 3}$$

Here N is the number of data points used for model fitting, K is the number of free parameters and SS is the sum of squares difference of the fitted model from the data. The difference between the AIC of Equ.1 or 2 (AICequ.1/2) is used to calculate the probability (Prob) of the more complex model over the simpler:

$$Prob = e^{-(AICequ.2-AICequ.1)}/(1+ e^{-(AICequ.2-AICequ.1)}) \qquad \textbf{Equ. 4}$$

The median of the IVIM parameters (f, D & D*) was calculated for the whole region regardless of probability and separately for those volexs where Prob. ≥ 0.5 and those voxels where Prob < 0.5 to allow for comparison.

Results – For each of the volunteers the median of the voxel values within the region of interest was calculated for the IVIM parameters (Table 1). Using a paired T test, significant differences (P = 0.019, 0.034 & 0.002) were observed between the median values of f, D and D* for the region with and without those voxels with Prob < 0.5 removed. Figure 1 shows a sample of these distributions, for f, D and D* in one individual. Also a paired T test indicated that the voxels removed, Prob <0.5, had f, D and D* values significantly different to the remainder, Prob ≥ 0.5., (P = 0.001, 0.015 & < 0.001). The regions of similar probability are spatially coherent and follow placental structure as shown in Figure 2 for the same individual as Fig. 1.

	Mean f (%)	Mean D ($mm^2/s \times 10^{-3}$)	Mean D* ($mm^2/s \times 10^{-3}$)
All voxels in ROI	29.9 ± 11.3	1.72 ± 0.65	111 ± 104
Voxels with Prob. ≥ 0.5	34.2 ± 6.2	1.85 ± 0.64	236 ± 147
Voxels with Prob. < 0.5	20.0 ± 16.0	1.51 ± 0.74	22.2 ± 19.2

Table 1 Mean and standard deviation of the f & D and D* IVIM values for 16 subjects

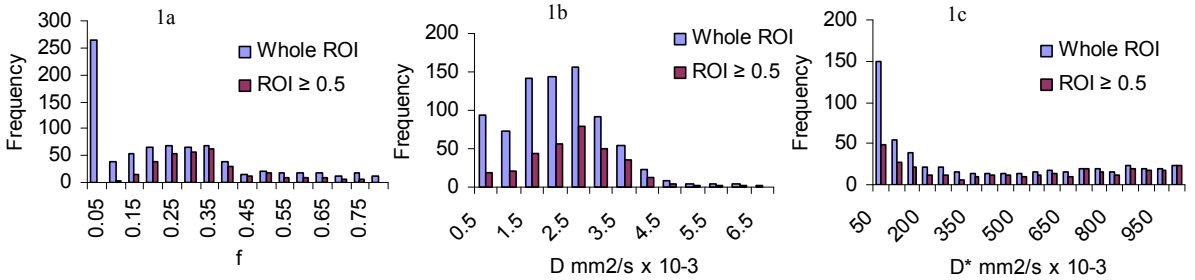

Figure 1: Histogram plots of f(a), D(b) and D*(c) whole region (Blue) and Prob ≥ 0.5 (Red)

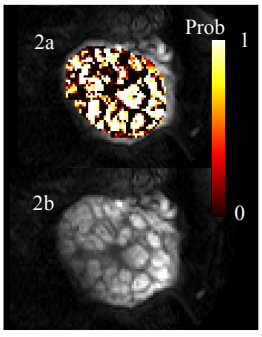

Figure 2: Probability map (a) overlaid on a B = 0 image (b)

Conclusions – The Akaike Information Criterion has been applied to IVIM data obtained in the human placenta. The use of the AIC removes voxels where IVIM flow parameters are unreliable. If those voxels where the bi-exponential model is inappropriate are included f, D and D* estimates are significantly lowered. The placenta is not homogenous when estimating flow parameters and the increased accuracy from determining f and D* only where they are supported by the data may aid in the identification of fetuses at risk of FGR.

References – [1] Sibley et al *Paed. Res.* 58: 827 2005 [2] Brunelli et al Placenta doi:10.1016/j.placenta 2010.09.004 2010 [3] Moore et al *Placenta* 21: 726-733 2000 [4] Akaike *IEEE Trans. Auto. Cont.* 19 (6): 716–723 1974 [5] Sugiura *Comm. Statist.* A7: 13-26 1978.

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