Placental perfusion and permeability assessment by dual echo DCE-MRI in mice using high concentration of gadolinium.

F. Taillieu[1], L. Salomon[1], N. Siauve[1], O. Clément[1], D. Balvay[1], C. Vayssettes[1], Y. Ville[2], C. Cuenod[1]

[1]Laboratoire de Recherche en Imagerie, Université Paris V Descartes, Faculté Necker, Paris, France, France, [2]Gynécologie-Obstétrique, Centre Intercommunal de Poissy, Poissy, France, France

Rationale and objectives: Impaired placental perfusion and permeability are involved in many pathologies like pre-eclampsia and in-utero growth restriction. Dynamic contrast-enhanced T1 weighted MRI is well suited for the measurement of microvascular parameters (2), but the low placenta permeability, yields a low Gd concentration in the fetus and consequently unreliable results (3). The aim of the study is to assess placental perfusion and permeability in mice, with high doses of Gd by using a dual echo sequence to compensate for T2/T2* effects (4, 5).

Materials and methods: 48 pregnant Balb-c mice were examined at 1.5 Tesla. Two protocols were used to inject Gd DOTA (Guerbet, France): a monophasic injection protocol (double clinical dose of 0.25 mmol Gd/kg) and a biphasic injection protocol (quadruple dose).
A 2D fast spoiled gradient-echo (SPGR) monoslice sequence with double echo was used for dynamic MRI (TR 19.5 ms; TE 3.9 and 6.7 ms, α 60°, 256x224, ZIP 512, FOV 14x7 cm, thickness 3 mm) (figure 1) during at least 20 min. The temporal resolution was 1.55 seconds per image. Signal intensities (SI) were measured in the maternal left ventricle (input function), in the placenta and in the fetus. At these high Gd doses a T2* effect correction was used to obtain SI_{T1} dependent only on T1 effect defined as:

$$SI_{T1} = SI_{TE1}.(SI_{TE1}/SI_{TE2})^{\beta} = m_0 . \sin\alpha . \frac{1 - \exp(-TR/T1)}{1 - \cos\alpha.\exp(-TR/T1)}$$

where β = TE1/(TE1-TE2) and SI_{TE1} and SI_{TE2} are the SI measured at the first and second echos respectively. SI were converted to Gd concentrations (6). Twenty two feto-plancental units (FPU) were studied in the monophasic group and 17 FPU in the biphasic group. Quantitative microcirculation parameters were calculated with constant transfer rates obtained by a three-compartmental model (figure 2). Mean arterial, placental and fetal concentrations at 20 minutes were calculated. Final arterial concentrations determined by MRI were compared to those obtained by means of atomic emission spectrophotometry.

Results: The T2/T2* effect correction allowed the restauration of a sharp first peack with the high concentration of gadolinium (figure 3). Transfer rates obtained by monophasic and biphasic injection were not significantly different (table 1). Placenta perfusion and permeability parameters obtained based on the transfer rates are : placental blood flow (Fp) 3.07E-02 (+/-1.53) ml/s/ml, permeability surface coefficient from the maternal placental to the fetal placental compartment ($PS\rho_{mf}$) 10.3 E-04 (+/-6.81 E-04) s^{-1}, from the fetal placental to the maternal placental compartment ($PS\rho_{fm}$) 4.65 E-04 (+/-4.37 E-04) s^{-1} and fractional volume of the maternal vascular placental compartment 36.5% (+/-0.9). The exchanges between the fetal vascular compartment of the placenta and the fetus was represented by the rate of transfert $k_{(4,3)}$: 3.96 E-04 $\pm$2 .69E-04 s-1. Placental Gd concentrations calculated at 20 minutes were higher with the biphasic (146 µmol/L) than with the monophasic protocol (105 µmol/L), and so were fetal concentrations (33.3 vs. 19.1 µmol/L). Arterial Gd concentrations did not differ significantly from the results of spectrophotometry.

Conclusion: In addition to confirm MRI perfusion measurements obtained in our previous study (3) and by Gowland et al. using spin labelling (7), we were able to determine placental permeability. This will be of high importance for placental function assessment.

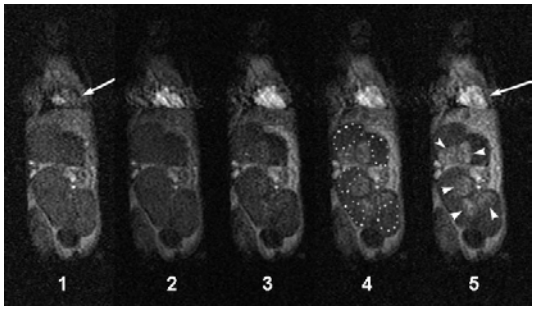

Figure 1: Coronal images obtained during SPGR sequence. One image every 3.1 seconds (images 1 to 5). Before injection of contrast agent (image 1), the maternal left ventricle (arrow) was identified but the placental and fetal areas were not distinguishable. After injection (images 2 to 5), the maternal left ventricle exhibited very strong and rapid enhancement, whereas the placentas (arrowheads) showed slower enhancement and it was not possible to see any enhancement of the fetus (dotted line).

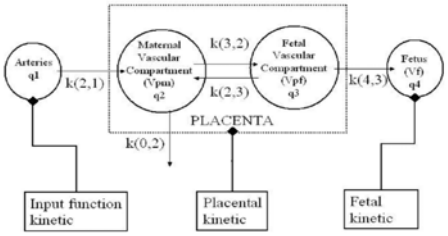

Figure 2: Compartment model of the placenta and the fetus. The placenta consists of a maternal vascular compartment Vpm and a fetal vascular compartment Vpf. Vpm is supplied by an arterial input and drained by a venous output. Vpf may exchange contrast agent with the fetus itself (Vf) through the umbilical cord and with Vpm..

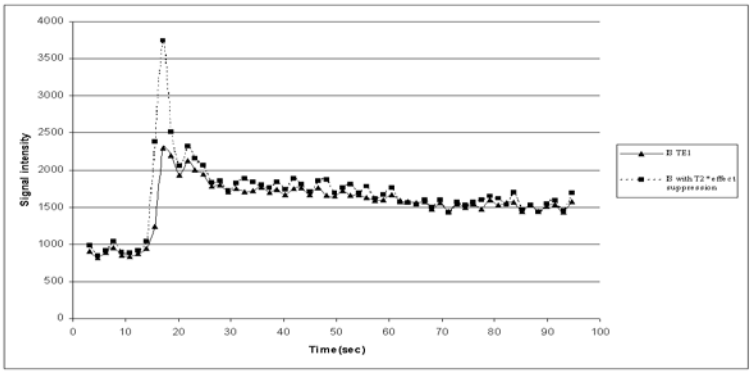

Figure 3: Example of SI curves obtained in the maternal left ventricle during injection of contrast medium with the monophasic protocol (first 100 seconds), at TE1 (TE = 3.9ms) and after T2/T2 effect suppression*

Protocol	Results	$k_{(0,2)}$	$k_{(2,1)}$	$k_{(2,3)}$	$k_{(3,2)}$	$k_{(4,3)}$
Monophasic	**Mean**	$8.48E^{-2}$	$2.76E^{-2}$	$5.59E^{-3}$	$5.22E^{-3}$	$3.55E^{-4}$
	SD	$4.65E^{-2}$	$1.53E^{-2}$	$5.6E^{-3}$	$2.99E^{-3}$	$3.2E^{-4}$
Biphasic	**Mean**	$8.41E^{-2}$	$3.46E^{-2}$	$4.23E^{-3}$	$3.85E^{-3}$	$4.48E^{-4}$
	SD	$2.81E^{-2}$	$1.49E^{-2}$	$3.19E^{-3}$	$2.51E^{-3}$	$1.81E^{-4}$

Table 1: Transfer rates obtained by compartmental modeling

References:

1. Roberts JM, Lain KY. Placenta 2002; 23:359-372.
2. Brasch RC et al. Invest Radiol 1994; 29 Suppl 2:S8-11.
3. Salomon LJ, Siauve N, Balvay D, et al. Radiology 2005; 235:73-80.
4. Zhu XP et al. J Magn Reson Imaging 2000; 11:575-585.
5. Kuperman VY et al. J Magn Reson Imaging 1999; 9:172-176.
6. Pradel C et al. Magn Reson Imaging 2003; 21:845-851.
7. Gowland PA et al. Magn Reson Med 1998; 40:467-473.