Functional imaging of the human placenta with magnetic resonance

Nathalie Siauve, MD, PhD; Gihad E. Chalouhi, MD; Benjamin Deloison, MD, PhD; Marianne Alison, MD, PhD; Olivier Clement, MD, PhD; Yves Ville, MD; Laurent J. Salomon, MD, PhD

Abnormal placentation is responsible for most failures in pregnancy; however, an understanding of placental functions remains largely concealed from noninvasive, in vivo investigations. Magnetic resonance imaging (MRI) is safe in pregnancy for magnetic fields of up to 3 Tesla and is being used increasingly to improve the accuracy of prenatal imaging. Functional MRI (fMRI) of the placenta has not yet been validated in a clinical setting, and most data are derived from animal studies. FMRI could be used to further explore placental functions that are related to vascularization, oxygenation, and metabolism in human pregnancies by the use of various enhancement processes. Dynamic contrast-enhanced MRI is best able to quantify placental perfusion, permeability, and blood volume fractions. However, the transplacental passage of Gadolinium-based contrast agents represents a significant safety concern for this procedure in humans. There are alternative contrast agents that may be safer in pregnancy or that do not cross the placenta. Arterial spin labeling MRI relies on magnetically labeled water to quantify the blood flows within the placenta. A disadvantage of this technique is a poorer signal-to-noise ratio. Based on arterial spin labeling, placental perfusion in normal pregnancy is 176 ± 91 mL $\times$ min^{-1} $\times$ 100 g^{-1} and decreases in cases with intrauterine growth restriction. Blood oxygen level–dependent and oxygen-enhanced MRIs do not assess perfusion but measure the response of the placenta to changes in oxygen levels with the use of hemoglobin as an endogenous contrast agent. Diffusion-weighted imaging and intravoxel incoherent motion MRI do not require exogenous contrast agents, instead they use the movement of water molecules within tissues. The apparent diffusion coefficient and perfusion fraction are significantly lower in placentas of growth-restricted fetuses when compared with normal pregnancies. Magnetic resonance spectroscopy has the ability to extract information regarding metabolites from the placenta noninvasively and in vivo. There are marked differences in all 3 metabolites N-acetyl aspartate/choline levels, inositol/choline ratio between small, and adequately grown fetuses. Current research is focused on the ability of each fMRI technique to make a timely diagnosis of abnormal placentation that would allow for appropriate planning of follow-up examinations and optimal scheduling of delivery. These research programs will benefit from the use of well-defined sequences, standardized imaging protocols, and robust computational methods.

Key words: ASL, BOLD, DCE, IUGR, IVIM, MRI, pregnancy, spectroscopy

The placenta is a regulatory organ that has involvement far beyond nutritive and respiratory functions to encompass endocrine and immune system regulation.[1] As a signaling organ, the placenta produces a myriad of bioactive molecules that affect both maternal and fetal metabolism and physiologic condition. Advances in imaging technology and animal studies have led the way in noninvasive in vivo study of the placenta. Placental perfusion and permeability have been explored extensively, because abnormal placentation is responsible for most failures in pregnancy, from early losses through to severe growth restriction and preeclampsia and preterm birth and late intrauterine death.[2-4] Ultrasound is the most commonly used imaging modality in pregnancy. It is safe, relatively inexpensive, and widely available. Ultrasound examination provides accurate information on the location, size, and anatomy of the placenta.[5] Although ultrasound examination can been used to identify growth-restricted fetuses at a higher risk of perinatal complications, based on umbilical artery Doppler,[6,7] ultrasound examination is limited for the assessment of placental function, which usually is suspected to be abnormal only late in pregnancy, when related complications such as preeclampsia and/or intrauterine growth restriction (IUGR) have already developed.

Magnetic resonance imaging (MRI) has been performed in pregnancy for >30 years,[8] mainly as a second-line imaging modality of the fetus used in combination with ultrasound examination.[9,10] This technique is more expensive and not as widely available as ultrasound examination but benefits from a larger field of view and from multiplanar capabilities and acceptable spatial and temporal resolutions of high-contrast images. MRI is now being used increasingly often in pregnancy, especially at advanced gestational age or in obese women.[11] MRI of the placenta has developed primarily to improve the diagnosis of placenta accreta.[12-14] The safety of MRI in pregnancy has been established for magnetic

From INSERM, U970, Sorbonne Paris Cite, Paris Cardiovascular Research Center—PARCC (Drs Siauve, Chalouhi, Deloison, Alison, Clement, and Salomon); EA FETUS and LUMIERE Unit, Université Paris-Descartes (Drs Siauve, Chalouhi, Deloison, Ville, and Salomon); and Assistance Publique-Hôpitaux de Paris, Hôpital Necker-Enfants Malades (Drs Chalouhi, Deloison, Ville, and Salomon) and Hôpital Européen Georges Pompidou, (Drs Siauve and Clement), Paris, France.

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Corresponding author: Laurent J. Salomon, MD, PhD. laurentsalomon@gmail.com

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TABLE 1
Functional magnetic resonance imaging techniques and their functional parameters

Magnetic resonance imaging technique	Imaging technique	Parameters	Units
Dynamic contrast-enhanced (DCE)	Imaging sequence: T1-weighted gradient echo (GE) imaging sequence, with high temporal resolution	Perfusion (F) or blood flow (BF)	$mL \times min^{-1} \times mL^{-1}$
	Imaging data: signal intensity (SI) curve over time	Fractional blood volume	%
	Data analysis: compartmental modeling	Extracellular volume fraction	%
		Permeability surface area (PS)	$mL \times min^{-1} \times g^{-1}$
Arterial spin labeling (ASL)	Imaging sequence: single shot spin echo EPI flow sensitive alternating inversion recovery (FAIR) images	Delta SI	Arbitrary units (AU)
	Imaging data: SI measurement		
	Imaging sequence: T1-weighted imaging sequence	Perfusion (F)	$mL \times min^{-1} \times g^{-1}$
	Imaging data: SI curve according to inversion time		
	Data analysis: modeling or deconvolution		
Blood oxygen level–dependent (BOLD)	Imaging sequence: T2-weighted gradient echo planar imaging (EPI) sequence	Delta SI	%
	Imaging data: SI measurements		
	Imaging sequence: T2-weighted gradient echo (GE) imaging sequence repeated at different echo times SI curve over time	Delta T2	%
	Data analysis: monoexponential fit to compute T2 (msec)		
	Imaging sequence: T2* weighted multi-echo gradient-echo (GE) imaging sequence	Delta T2*	%
	Imaging data: SI curve according to echo time		
	Data analysis: monoexponential fit to compute T2* (msec)		
Diffusion weighted imaging (DWI) intravoxel incoherent motion (IVIM)	Imaging sequence: diffusion weighted imaging with multiple (3) values of b	Apparent diffusion coefficient (ADC)	$10^{-3}\ mm^2 \times s^{-1}$
	Imaging data: SI curve according to b	Perfusion fraction (f)	%
	Data analysis: monoexponential fit	Pseudo diffusion coefficient (D*)	$10^{-3}\ mm^2 \times s^{-1}$
	Imaging sequence: diffusion weighted imaging with multiple (>8) values of b	Diffusion coefficient (D) or (Dr)	$10^{-3}\ mm^2 \times s^{-1}$
	Imaging data: SI curve according to b		
	Data analysis: Bi exponential fit		
Magnetic resonance spectroscopy	Imaging sequence: chemical shift imaging (CSI)	Adenosine triphosphate (ATP)	%
	Imaging data: ^{31}P spectrum	Phosphocreatine (Pcr)	%
	Data analysis: fraction of total phosphorus signal	Phosphodiesters (PDE)	%
		Phosphomonoesters (PME)	%
		PDE/PME	No units

For each magnetic resonance imaging technique, the type of sequence, the data required for postprocessing, and the analysis are given in column 2. The functional parameters are summarized in column 3, and their units are given in column 4.

Siauve. Functional MRI (fMRI) of the human placenta. Am J Obstet Gynecol 2015.