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Use of intravoxel incoherent motion MR imaging to assess placental perfusion in patients with placental adhesion disorder on their third trimester

Tao Lu[a], Hong Pu[a,*], Wei Cui[a], Jie Mei[b], Meng-wei Huang[b], Shao-yu Wang[c]

[a] Department of Radiology, Sichuan Academy of Medical Science & Sichuan Provincial People's Hospital, 32 West Second Section, First Ring Road, Chengdu 610072, Sichuan, China
[b] Department of Obstetrics, Sichuan Academy of Medical Science & Sichuan Provincial People's Hospital, 32 West Second Section, First Ring Road, Chengdu 610072, Sichuan, China
[c] Siemens Healthineer, No.278, Zhouzhu Road, Pudong New Area District, 201318 Shanghai, China

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ABSTRACT

Objective: Our primary aim was to investigate if women with placenta accreta can be differentiated with women without using IVIM quantitative assessment of the placental perfusion. A second aim was to investigate if IVIM parameters could be used to differentiate placenta accreta from increta.

Methods: The study population included 17 patients with placenta accreta, 29 patients with placenta increta and 16 patients without placenta accreta between 28 + 0 to 41 + 6 weeks. All women underwent a MRI examination including an IVIM sequence at 1.5 T. The perfusion fraction (f), pseudodiffusion coefficient (D*) and standard diffusion coefficient (D) were calculated. Results Women with placenta accreta and increta had a smaller placenta perfusion fraction ($P < 0.05$) than patients without placenta accreta, placental perfusion fraction didn't differ between placenta accreta and increta ($p > 0.05$). Differences of D and D* in three groups showed no statistical significance ($p > 0.05$).

Conclusion: Placenta accreta and increta differ in placental perfusion fraction from women without the disease. The perfusion fraction can be used as a feasible index to evaluate placenta perfusion.

1. Introduction

Placental adhesion disorder (PAD) is classified on the basis of the depth of myometrial invasion and encompasses placenta accreta, increta and percreta, which occur when a defect of the decidua basalis allows the invasion of chorionic villi into the myometrium [1,2]. Clinically, placenta accreta is a critical and tough problem during delivery because it is difficult for the placenta completely separating from the uterus. This can cause massive intrapartum or postpartum hemorrhage, disseminated intravascular coagulopathy, damage to the uterus, sepsis, deep venous thrombosis, and even death.

The rate of placenta accreta increased dramatically in recent years worldwide. The incidence was not clear in China, but may be higher due to the adjustment of fertility policy in recent years. In recent years, MRI has been frequently used in the diagnosis of placenta invasion, particularly when results from ultrasonography are equivocal in patients clinically suspected of having this disease. Ultrasonography is also limited for the assessment of placental function, which usually is suspected to be abnormal in certain conditions such as preeclampsia and fetal growth restriction (FGR). Functional MRI is surely to aid in the analysis of placental vascular physiology and function, which may improve the diagnosis of pregnancy complications, and potentially assist in decisions on the timing of delivery and on perinatal outcome. IVIM is a derivative DW MRI that aims to distinguish between diffusion and perfusion of fluids. It is appropriate for highly vascularized organs containing both high blood fraction and a large perfusion component, especially the placenta [3].

IVIM has been applied in several studies involving the placenta with some findings [4–8]. But the these studies have several limitations, they included only a small number of patients or were performed on a scanner with low strength field, or they just used a mono-exponential rather than bi-exponential fitting. On the second hand, it has not been studied with placental adhesion disorders using IVIM. So the aim of the study was to compare the placental perfusion fraction in patients with placental adhesion disorders with patients without the disease and the second aim was to compare the placental perfusion fraction between

* Corresponding author.
E-mail address: ph1726148853@qq.com (H. Pu).

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Table 1
Physical and sociodemographic features of patients studied.

	Patients without placenta accreta	Patients with placenta accreta	Patients with placenta increta	*P* value
Number	16 (25.81%)	17 (27.42%)	29 (46.77%)	
Age (years)				
< 35	13 (20.97%)	12 (19.35%)	20 (32.26%)	
35 or older	3 (4.84%)	5 (8.06%)	9 (14.525%)	0.424
Gestational age At examination (weeks)	34.25 ± 3.28	33.82 ± 3.57	33.26 ± 3.81	> 0.05
Gestational age At the time of delivery (weeks)	38.87 ± 1.08	38.59 ± 1.28	36.21 ± 0.77	0.000
Number of previous cesarean section				
0	7 (11.29%)	6 (9.68%)	12 (19.35%)	
1	9 (14.52%)	11 (17.74%)	14 (22.58%)	
2 or more	0	0	3 (4.84%)	0.275
Previous uterine Dilation and Curettage				
No	5 (8.06%)	8 (12.90%)	13 (20.97%)	
Yes	11 (17.74%)	9 (14.52)	16 (25.81%)	0.632
Placenta previa				
No	7 (11.29%)	5 (8.06%)	5 (8.06%)	
Yes	9 (14.52%)	12 (19.35%)	24 (30.70%)	0.158
Amount of bleeding (ml)	337.5 ± 162.79	420.59 ± 199.26	948.27 ± 524.83	0.025

patients with placenta accreta and increta using IVIM analysis.

2. Materials and methods

2.1. Patients

The ethical review aboard of Sichuan Academy of Medical Science & Sichuan Provincial People's Hospital approved the study and reformed consent was obtained from each women participating in the study. We searched the radiological records of our department from between May 2015 and December 2016 to extract all patients who had undergone MRI examination for screening for suspect of placental invasion. Only single pregnancies with a living fetus had a gestation length between 28 + 0 and 41 + 6 weeks were included. All the pregnancies were dated by ultrasound scan in the first trimester. Women with chronic hypertension, pre-existing renal disease, diabetes mellitus or severe claustrophobia were excluded. The final degree of placental invasion and its specific tomography were established in the operating room according to clinical and anatomical criterion. Placenta accreta was defined as the placenta adhere firmly to the endometrium and showed non-self-controlled bleeding when detached, placenta increta was defined as the placenta deeply implanted in the myometrium and required curettage to remove invasive tissue.

2.2. IVIM techniques and biexponential fitting

MR imaging was performed on a 1.5 T scanner (Magnetom Area, Siemens, Erlangen, Germany) using the integrated whole-body transmit-receive coil. The MRI protocol included examination from the diaphragm to the symphysis pubis. Echoplanar DWI derived IVIM sequence with 8 different b-values (0, 50, 100, 150, 200, 250, 500, 800 s/mm^2) was obtained perpendicular to the placenta. The average was 1 for each b value below 800 s/mm^2 and was 3 for 800 s/mm^2 0.40 slices, each of 5.5 mm thickness were collected. The matrix was 192 × 120, and the FOV was 390 × 304 mm. Acquisition time for this sequence was typically 8 min and 37 s. On the basis of the IVIM concept, we assumed that movement of water molecules within a voxel can be separated into 2 components by using a biexponential fit of the signal intensity (SI) decay curve according to the multiple b values [9].

2.3. IVIM analysis

2.3.1. Region of interest

Evaluation of the perfusion fraction was performed with research software (MITK diffusion). ROI were placed including as large parts of the placenta as possible in patients without placental adhesion, and the ROI were placed in the regions of placental adhesion according to the maternity record after surgery and secondly at the site where placenta separated from uterine wall normally in the same patient, but excluding areas with infarcts, hemorrhage or other artifactual signal loss. To avoid the flow artifacts in large vessels, ROIs should locate at least 2 cm from the insertion of the umbilical cord. The same ROIs were drawn on the slice above and below the middle slice. Values of D, D* and f were then calculated by averaging over 3 ROIs totally.

2.4. Statistics

Physical and sociodemographic factors for placental adhesions were investigated by using Chi-square test for comparing patients with placenta accreta and increta to those without. Three groups of IVIM parameters were compared by LSD-test of one-way ANOVA. *P*-values < 0.05 were considered statistically significant. All analyses were performed using IBM SPSS Statistics 20.

3. Results

Of the 67 pregnant women originally included in the study, 5 were excluded because of severe artifacts prohibiting perfusion fraction calculations. Thus, 62 pregnant women with satisfied raw images remained in the analyses. The mean maternal age was 20.95 ± 4.68 years (range 19–40 years), the mean gestational age at examination was 33.81 ± 3.04 weeks (range 28–41 weeks). All medical records were received postpartum, 17 patients were clinically diagnosed as placenta accreta when the placenta attaches to the myometrium, 29 patients were diagnosed as placenta increta when the placenta penetrates into the myometrium and 16 patients were without placenta adhesion. The methods of delivery included 41 cases of cesarean section, 16 cases of prophylactic distal abdominal aorta balloon occlusion and cesarean section, 3 cases of natural birth, 1 case of total hysterectomy and 1 cases of partial hysterectomy.10 out of 62 patients (16.13%) received blood transfusion.

Table 1 presents the maternal characteristics of the study participants. There was no significant difference between physical and sociodemographic factors of the patients with and without placenta adhesion. The f value was 31.30 ± 10.39%, D value was 1.74 ± 0.19 (10^{-3} mm^2/s) and D* value was 25.83 ± 14.59 (10^{-3} mm^2/s) at the site where placenta separated from uterine wall normally in the patient with placenta accreta. The results showed no significant difference compared with these parameters in patients without placenta accreta ($p > 0.05$). When compared with regions of placenta accreta, f value was significantly higher at the site where placenta separated from uterine wall normally ($p < 0.05$), while D and D* values showed no

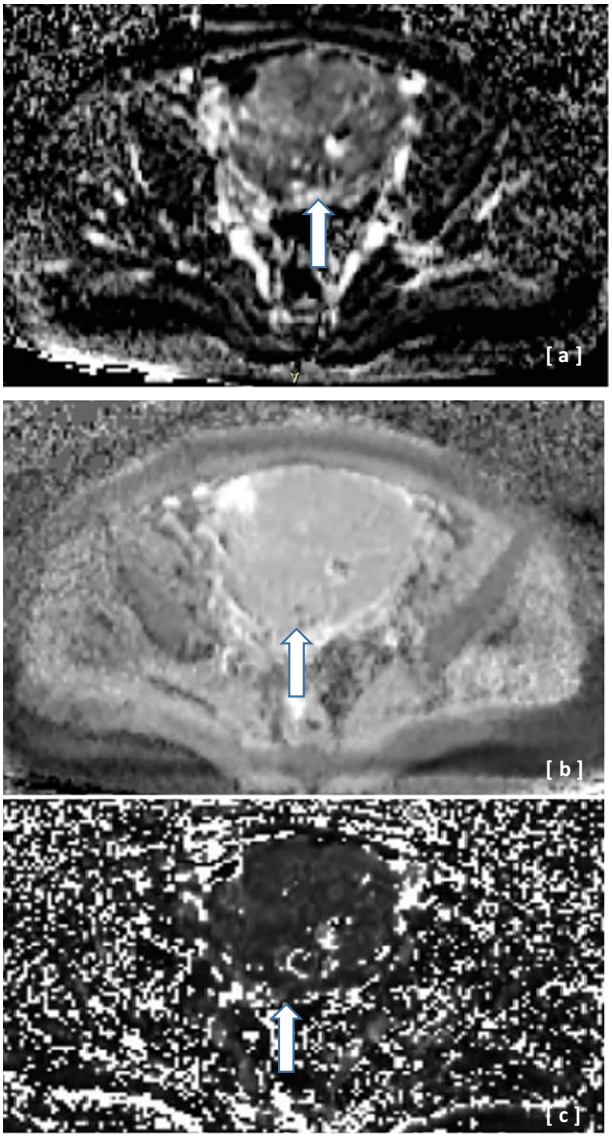

Fig. 1. a–c are IVIM images of a 30-year-old woman, GA 33 weeks, with 1 previous cesarean section and placenta increta. A: map of perfusion fraction (f) with f value of 26.07%, B: map of diffusion coefficient (D), which reflects tissue diffusivity, with D value of $1.67 \times 10^{-3}\,mm^2/s$, C: map of pseudo-diffusion coefficient (D*), which reflects microcapillary perfusion, with D* value of $31.8210^{-3}\,mm^2/s$. Arrows indicated the placenta.

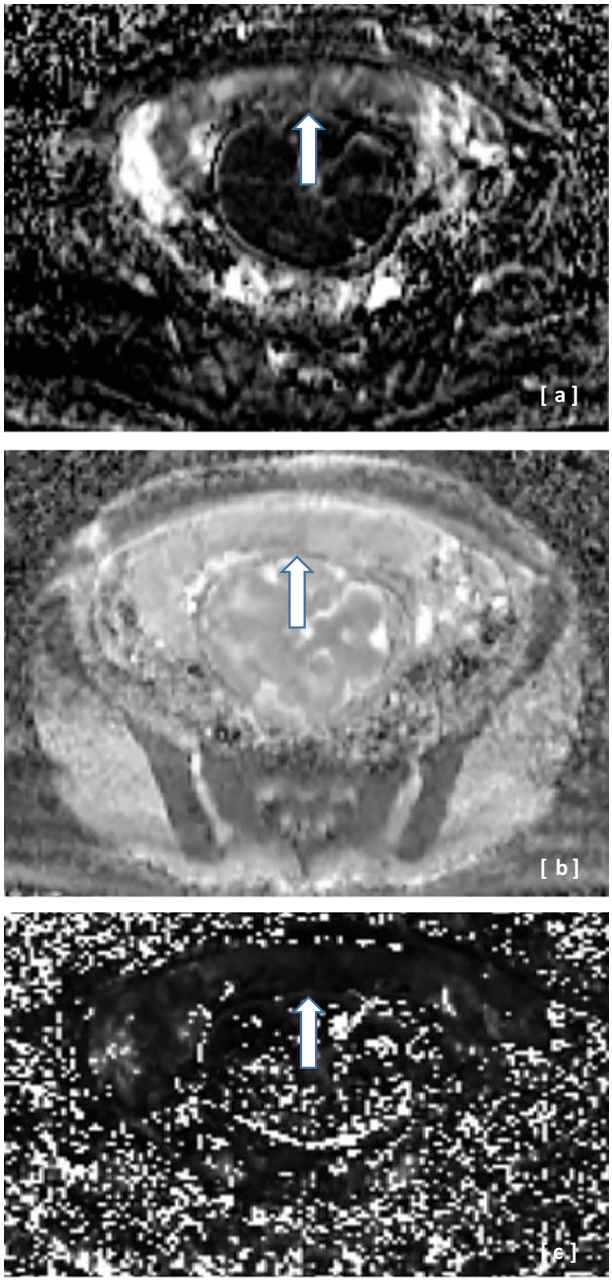

Fig. 2. a–c are images of a 33-year-old woman, GA 36 weeks, with 1 previous cesarean section, 2 induced abortions and placenta increta. A: map of perfusion fraction (f) with f value of 29.43%, B: map of diffusion coefficient (D), which reflects tissue diffusivity, with D value of $1.73 \times 10^{-3}\,mm^2/s$, C: map of pseudo-diffusion coefficient (D*), which reflects microcapillary perfusion, with D* value of $21.86 \times 10^{-3}\,mm^2/s$. Arrows indicated the placenta.

statistical significance between the 2 regions ($p > 0.05$). Difference of parameters (D, D*, f) between three groups were compared by LSD test of one-way ANOVA analysis. The results demonstrated that f values among three groups had significant difference. Multiple comparisons showed f values in patients with placenta accreta and increta were significantly lower than in patients without placenta accreta, meanwhile f values in patients with placenta accreta were not significantly different from patients with placenta increta (Figs. 1, 2). Difference from three groups in D and D* values were not statistically significant (Table 2).

4. Discussion

The most important risk factors of placenta accreta were previous cesarean delivery, previa and advanced maternal age [10]. A World Health Organization (WHO) survey from 2004 to 2008 reported a 25.7% average cesarean section rate, with 27.3% in Asia, 19.05 in Europe and 29.2% in Latin America [11,12]. China had the highest overall cesarean section rate (46.2%) of the 24 countries in the survey [11]. When it came to 2011, the situation became more serious, the overall cesarean section rate was 54.5% according to Wang's report [5].The cesarean section rate in China is well above accepted target, and with the implementation of the second child policy, more families are allowed to have a second child, so more women will begin the second child-bearing in older age with a history of cesarean section. So the situation of placenta accreta will become more and more serious in China. In our study of 62 patients who were suspected of having placenta accreta, > 1/4 of the patients were after 35 years old, > 1/3 had previous cesarean section and > 1/2 had placenta previa.

Table 2
One-way ANOVA analysis between different groups of three parameters (n = 62)

Group	n	f (%)	D (10^{-3} mm^2/s)	D* (10^{-3} mm^2/s)
Patients without placenta accreta	16	33.20 ± 5.99	1.71 ± 0.21	20.37 ± 6.20
Patients with placenta accreta	17	22.47 ± 7.93	1.64 ± 0.22	17.46 ± 10.30
Patients with placenta increta	19	22.55 ± 8.80	1.65 ± 0.33	22.86 ± 14.67
F value	62	10.74	0.341	1.124
P value		0.000	0.713	0.332

Ultrasound remains the primary diagnostic tool for the diagnosis of abnormal placentation. However, when ultrasound findings are suspicious or inconclusive, MRI is recommended as an adjunct imaging technique according to several guidelines from the UK, the United States and China. The typical MRI features of abnormal placenta invasion include dark intra-placenta bands, disorganized abnormal intra-placenta vascularity, abnormal uterine bulging, heterogeneous placenta, abnormal uterine myometrial thinning and focal disruption of myometrium, invasion of adjacent organ and tenting of the bladder [13–16]. However, these criteria are subjective and require both experience and expertise. It is also difficult to differentiate placenta accreta from increta using the above MRI features.

Meanwhile, the placenta contains two dependent blood transport systems, fetal and maternal. The fetal placenta is composed of a vascular bed, in tree-like network with different vessel sizes emanating from the umbilical cord. The maternal placenta is different from the classical plan of a vascular bed. Maternal blood flows directly round the fetal villi, within the intervillous spaces (IVS) rather than within maternal vessels. The IVS are randomly distributed with both size and shape changing with the gestational weeks. In this sense, IVIM measuring blood movement in placenta is more suitable than in other tissue where blood is confined to a vascular bed [6]. Recent advances in IVIM studies of placenta function, in both animal models and humans, have led a way to our understanding of placental perfusion. So we tried to assess placenta perfusion in patients with placenta invasion using IVIM.

In our study, we found a reduction in perfusion fraction in patients with placenta accreta and increta compared to patients without placenta accreta. Pathologically, placenta accreta is defined as the deficiency of decidualisation or an overinvasiveness of the trophoblast. The volume of the IVS which is filled with maternal blood may decline in this situation, leading the decrease of the perfusion fraction. In placenta accreta vera, placental villi embed directly onto myometrium in the absence of decidua, and in placenta increta, placental villi are found deeper into the myometrium, so maybe the perfusion fraction is different between placenta accreta and increta. However, in our study, we have not found the statistical difference of f value between patients with placenta accreta and increta yet.

The diffusion coefficient reflects cellular and interstitial characteristics of the tissue [5]. The D value in patients with placenta accreta and increta were slightly lower than patients without placenta accreta, but were not statistically significant. Whether the passive Brownian motion of water molecules in the interstitial space would decrease in patients with placenta accreta and increta, it still needs further investigation with more sample size. The pseudodiffusion coefficient would reflect the movement of blood in the intervillous spaces and in the fetal capillaries within the villi [6]. The difference of D* value also showed no statistically significant change between patients with and without placenta accreta, this may due to its poor signal-to-noise ratio. Another reason may be this parameter is more sensitive to velocity of blood flow, as shown in the study of Federan [17], in which the value of D* was found to be changed closely with pulse pressure.

This study has several limitations. First, it is not a prospective study but a retrospective clinical note. Therefore, there likely is an observer bias of image interpretation. Second, the number of patients in this study is small, it is possible to underestimate the difference of D and D* value, and it is also not able to differentiate placenta accreta form increta depending on f value in this study. Third, we lack the data from patients with placenta percreta, so further studies with more cases of placenta percreta are required. Fourth, we used 8 b-value including 5 b-values in the low range, more low b-values would be needed to properly sample the first part of the SI decay curve corresponding to the perfusion component.

5. Conclusion

To the best our knowledge, our study seems to be the first study to explore the difference between patients with placenta accreta and patients without in the third trimester using IVIM. We tried to quantitatively assess the placenta perfusion with the method of IVIM. We found a decrease in the placental perfusion fraction in patients with placenta accreta and increta compared to patients without placenta accreta. So the perfusion fraction can be used to quantitatively evaluate placenta perfusion in patients with placenta accreta. We also found the D values were slightly lower in patients with placenta accreta and increta than in patients without the disease, but the difference was no statistically significant. Meanwhile, we also could not detect the difference between accreta and increta using this IVIM parameter. Since the number of the participants in this study is small, further study with larger sample size and including more cases of placental adhesion disorders are required, so that their predictive value may be detected, and we can further evaluate placental perfusion in patients with different degree of placental accreta using such quantitative index.

List of abbreviations

IVIM	intravoxel incoherent motion
PAD	placental adhesion disorder
WHO	World Health Organization
IUGR	intrauterine growth restriction
MRI	magnetic resonance imaging
DWI	diffusion weighted imaging
PE	preeclampsia
HASTE	half-Fourier acquisition single shot turbo spin echo
TRUFISP	half-Fourier acquisition single shot turbo spin echo
FOV	field of view
ROI	region of interest
IVS	intervillous spaces

Disclosure of potential conflicts of interest

There is no conflict of interests of this article.

Research involving human participants and/or animals

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent

Informed consent was obtained from all individual participants

included in the study.

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