Texture Analysis of Myometrium-Derived T2WI in the Evaluation of Placenta Increta: An Observational Retrospective Study

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Research Article

Keywords: Placenta increta, Texture analysis, Myometrium-derived T2WI

Posted Date: July 23rd, 2021

DOI: https://doi.org/10.21203/rs.3.rs-645695/v1

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Abstract

Background: To develop an objective and quantitative measurement based on texture analysis of myometrium-derived T2WI to differentiate placenta accreta from increta.

Methods: Participants with MRI and clinical or histopathological diagnosis of placenta increta were included. Texture analysis of T2WI was implemented on normal myometrium and placenta increta by MaZda software. Parameter selection and reduction was automatically done with Fisher discriminant method. Multivariate analysis was used for the comparison of response variables between two groups. Profile analysis was used to compare the contours of multivariable average vectors. Two-step clustering was performed to evaluate the importance of parameters.

Results: Multivariate analysis showed that nine second-order parameters between normal myometrium and placenta increta were statistically significant ($P < 0.05$). The $t$-test showed that there were two parameters (Skew and Kurtosis) that had no statistical significance. Profile analysis showed that the profiles of seven parameters were neither parallel ($P > 0.05$) nor coincident ($P > 0.05$). The results of two-step cluster indicated that Mean, Percentile 90% and Percentile 99% were important (predictor importance ≥ 0.8).

Conclusion: The study showed statistically significant differences for Mean, Percentile 90% and Percentile 99% between normal myometrium and placenta increta. Texture analysis of myometrium-derived T2WI may be a useful add-on to MRI in diagnosing placenta increta.

Trial registration: Registration number: ChiCTR2000038604 and name of registry: Evaluation of diagnostic accuracy of MRI multi-parameter imaging combined with texture analysis for placenta accreta spectrum disorders (PAD).

Background

Placenta increta refers to a form of placenta accreta spectrum disorders (PAS disorders), which include placenta accreta, increta and percreta[1]. Several concepts have been proposed to explain how PAS disorders occur. The current prevailing hypothesis is that a secondary defect of the endometrium-myometrial interface leads to a failure of normal decidualization in the area of a uterine scar, allowing abnormally deep placental anchoring villi and trophoblast infiltration[2, 3]. The potential outcomes can be devastating, including severe maternal hemorrhage, death and other complications at delivery[4].

It is therefore crucial for radiologists to be involved in the multidisciplinary team and to provide standardized diagnostic assessment of PAS disorders[5]. Ultrasonography (US) had a lower diagnostic accuracy in detecting PAS disorders than MRI, which had a sensitivity 66%, specificity 71% and accuracy 68%[6, 7]. Even though US is the frontline imaging modality for the evaluation of PAS disorders due to its large availability and lower costs [8], MRI is typically recommended for equivocal sonographic findings or suspicion of posterior/lateral placental extension[9–11]. No matter what kind of imaging modality is
used, prenatal diagnosis of PAS disorders remains subjective, with accuracy depending on the experience of the operator, which has been limited by the lack of training programs similar to that existing for the screening of fetal congenital defects[12, 13].

The visual qualitative analysis of MRI may not be completely accurate to extract the corresponding diagnostic information. Texture analysis can be applied to MRI through the analysis of quantitative parameters which reflect heterogeneity of region-of-interest (ROI) and other features beyond what is visible to the eye[14]. Placenta percreta is relatively easy to be diagnosed because the chorionic villi penetrate the myometrium and may extend into adjacent pelvic organs, and whether the myometrium is invaded by the chorionic villi is the premise to distinguish placenta accreta from increta. There is architectural distortion of the myometrium in the setting of placenta increta. Our hypothesis was that texture analysis may reflect histological abnormalities underlying placenta increta [15], thus helping in assessing the presence/absence of placenta increta. The objective of the study was to develop an objective and quantitative measurement based on texture analysis of myometrium-derived T2WI to differentiate placenta accreta from increta.

**Materials And Methods**

**Study design**

All procedures performed in the study 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. The Institutional Review Boards (IRBs) approved the observational study of MRI examinations performed for the evaluation of PAS disorders at our institution over the previous 5 years. The IRBs granted a waiver of written informed consent since this study used existing MRI data. The authors had control of the data and information submitted for publication. The retrospective study represented a substudy from Magnetic Resonance Imaging in PAS disorders trial. The study was registered at [http://www.chictr.org.cn](http://www.chictr.org.cn) (registration no.ChiCTR2000038604). The full study protocol could be accessed from the corresponding author by request.

**Study participants**

The study was conducted at the Radiology Department of a university-affiliated hospital. All participants were evaluated and screened for study eligibility by the authors prior to the study entry. Of all participants consecutively retrieved from our database spanning from September 2016 through April 2021, only participants with MRI examinations and clinical or histopathological diagnosis of placenta increta were included. Participants eligible for inclusion were: ≥ consecutive adults (≥18 years) with placenta increta; who performed an MRI examination at our institution; for whom clinical or histopathological diagnosis was available. Exclusion criteria were: they had no complete images; they were examined by different MRI devices; due to extreme fetal movements resulting in MRI artifacts.

**Standard of reference**
The clinical history of placenta increta is considered as an efficient reference standard to be used in both research and clinical settings, that is, difficult manual, piecemeal removal of the placenta, absence of spontaneous placental separation 20 to 30 minutes after birth despite active management including bimanual massage of the uterus, use of oxytocin and controlled traction of the umbilical cord, retained placental fragment requiring curettage after vaginal birth and heavy bleeding from the placentation site after removal of the placenta during cesarean delivery\cite{16, 17}. It has good reliability and validity rates compared with other diagnostic standards, such as histopathology. Diagnosis of placenta increta using histopathology findings as the reference standard may not always be reliable since the entire placenta is not able to be sampled and sampling errors can occur\cite{4, 9, 18, 19}.

**MRI protocol**

All MRI examinations were performed on a 1.5 Tesla MRI scanner (Siemens Healthcare, System Type: Avanto, Software Version: Syngo MR B19) with a body array coil that covered the entire pelvis for signal acquisition\cite{9}. Pregnant women were positioned in the supine or left lateral decubitus position in order to comfort and decrease the risk of impaired venous return from caval compression by the uterus\cite{20}. MRI was obtained with a partially filled bladder because an appropriate amount of urine in the urinary bladder aided optimal evaluation of the bladder-serosal interface \cite{19-21}. Multi-breathholding was utilized to minimize respiratory motion artifacts\cite{4, 19}.

The short MRI protocol (20-25 min) was designed with respect to the safety of pregnant woman and fetus. All participants received T1-gradient sequence for detection of intraplacental hemorrhage and T2-haste sequence to limit artifacts caused by fetal motion. The parameters for T1WI were: repetition time (TR) / echo time (TE), 169/4.76 msec; resolution matrix, 256×173; flip angle (FA), 70°; slice thickness, 5mm and for T2WI they were: TR/TE, 1350/94 msec; resolution matrix, 256×205; FA, 170°; slice thickness, 5mm\cite{22}. The field-of-view (FOV) read of 400-480 mm and FOV phase of 75-100% were used. The MRI examinations of some participants also included T2-truFI sequence in the coronal and sagittal planes without fat suppression using TR/TE of 3.87/1.68 msec and FA of 60°; T1-vibe in-phase and out-of-phase sequences in the transversal plane without fat suppression with TR/TE of 7.6/2.4 msec and FA of 10°\cite{23}. To maximize signal, a multi-channel surface coil was used whenever possible. No sedative or gadolinium contrast agent was administered\cite{20, 24}.

**Image interpretation**

MRI of placenta increta was archived to the LandWind Picture Archiving and Communication System (PACS) and then retrieved in Digital Imaging and Communications in Medicine (DICOM) format for image analysis. All images of participants were anonymized. MRI of placenta increta was independently evaluated by two obstetric fellowship-trained radiologists with 13 and 9 years of experience respectively, who were blinded to all clinical history, including the final histopathological diagnosis.

**Texture analysis**
Texture analysis of T2WI was implemented on normal myometrium and placenta increta by MaZda software (Version 4.6.2.0; Institute of Electronics, Technical University of Lodz, Lodz, Poland) in BMP format[12, 14, 25]. At first, raw-MRI options consisted of image dimensions with 256×256 and pixels intensity encoded with 8 bits[14]. The ROIs were manually drawn on sagittal and coronal T2WI with MaZda ROI editor by one radiologist and supervised by a board-certified radiologist for consistency. Four first-order texture parameters were extracted with MaZda options, which were run-length matrix (RLM); co-occurrence matrix (COM); gradient and wavelet[14]. The images were normalized before analysis using the “±3 sigma” technique to minimize the effect of brightness and contrast variation on texture analysis[14]. Parameter selection and reduction was automatically done with Fisher discriminant method in MaZda software.

The two steps of parameter selection and reduction led to a decrease of the parameter space dimensionality in order to those that contributed most to accurate differentiation between normal myometrium and placenta increta [14]. ROI depiction was repeated twice in a subgroup of 13 participants after a pause of 6 weeks by the same radiologist for intraobserver agreement (intra-class correlation coefficients, ICC=0.90, 95% CI 0.71,0.97) and by another radiologist for interobserver agreement (ICC=0.86, 95% CI 0.61,0.96). Data of the study were blinded for both radiologists. Additionally, two radiologists reviewed the results of texture analysis to render an impression of placenta increta based on the culmination of findings.

**Statistical analysis**

Statistical analyses were carried out by NCSS statistical software (PASS, Version 11), IBM SPSS software (SPSS, Version 23) and MEDCALC statistical software (MedCalc, Version 19.5). Data generated or analyzed during the study were available from the corresponding author by request. Normal variables were expressed as mean ± standard deviation, while variables with skewed distribution were expressed as median (interquartile range). A two-sided $P$ value of less than 0.05 was regarded as indicative of statistical significance. Indeterminate results were considered false-positive or false-negative and incorporated into the final analysis. Missing data were handled by exclusion as well as by the worst-case imputation. The interobserver agreement was tested by the Kappa value ($\kappa=0.78$).

The intended sample size was calculated according to power 0.90, alpha 0.05, prevalence 0.19%, sensitivity 0.78, specificity 0.71 in PASS 11. Multivariate analysis was used when multivariate normal distribution and equal covariance matrix was satisfied for the comparison of response variables between two groups. Profile analysis was used to compare the contours of multivariable average vectors. Due to multicollinearity among texture parameters, two-step clustering was performed to evaluate the importance of parameters[26].

**Results**

**Study participants**
The study flow was illustrated in Fig.1. Participants who were excluded (and reasons for this) were noted. The characteristics of participants were shown in Table 1. The median age of participants was 29 years (range 22-43 years). The mean time interval between MRI and delivery was 3 days (range 1-9 days). The predominant clinical history was placenta previa and scar pregnancy, partly followed by pelvic adhesions and anemia, whereas uterine weakness and oligohydramnios were less frequent.

**Results of texture analysis**

After the multistep processes for participants, MaZda allowed computation of a variety of second-order parameters that were derived from first-order parameter histogram. There were nine second-order parameters, i.e. Mean, Variance, Skew, Kurtosis, Percentile1%, Percentile10%, Percentile50%, Percentile90% and Percentile99% selected for further statistical analysis. Exemplary T2W images of placenta increta were shown in Fig.2. Two histograms obtained from normal myometrium and placenta increta showed a narrow and a wider distribution of pixel intensity, respectively (Fig.3). The values of nine second-order parameters were displayed in the database (Table 2). Multivariate analysis showed that nine second-order parameters between normal myometrium and placenta increta were statistically significant ($F=294.61, P<0.05$, Table 2). The $t$-test showed that there were two parameters (Skew and Kurtosis) that had no statistical significance. Profile analysis showed that the profiles of seven second-order parameters were neither parallel ($F=8.08, P<0.05$) nor coincident ($F=45.36, P<0.05$). The mean value of second-order parameters of placenta increta was higher than that of normal myometrium (Fig.4). The results of two-step cluster indicated that three second-order parameters, i.e. Mean, Percentile 90% and Percentile 99% were important (predictor importance $>0.8$) (Fig.5). Multivariate analysis of three second-order parameters further showed that Mean, Percentile 90% and Percentile 99% between normal myometrium and placenta increta were different (Fig.6). No significant adverse events occurred as a result of MRI. Texture analysis as post hoc analysis, performed after looking at the data, did not carry a risk. The application of texture analysis in clinical practice was feasible and safe.

**Discussion**

**Main findings**

This study had two main findings. Firstly, seven second-order parameters of histogram derived from normal myometrium and placenta increta were statistically significant differences. Secondly, three of the seven parameters mentioned above, i.e. Mean, Percentile 90% and Percentile 99% were important.

**Strengths and weaknesses**

The advantage of texture analysis over US and MRI was its ability to overcome subjective characteristics of interpretation and provide quantitative analysis. In the study, texture parameters were extracted according to a standardization procedure in order to promote transparency and reproducibility. Another advantage of this study was the establishment of a control of normal myometrium remote from placenta increta as an acknowledgement of increased heterogeneity of the placenta[20]. The findings of texture
analysis should be evaluated in the context of the placental aging process which occurs throughout gestation.

The study also had several limitations. Firstly, there was a relative lack of placenta increta cases for texture analysis. Secondly, the flaw of the study was reference standard bias. Placenta increta was defined by clinical history and histopathological diagnosis. If histopathological findings were not available, then placenta increta was defined by clinical history alone. It was recognized that the use of such clinical history rather than final histopathology may result in misdiagnosis of placenta increta. A statistical concern was that the evaluated texture parameters were correlated with one another and thus may tend to be redundant. Future studies should explore redundant texture parameters to fine-tune the best fit in larger cohort[12]. Finally, it was acknowledged that this was a preliminary study. The study may not be generalized outside our cohort in part due to the minor differences in design and procedure. In addition, application of the study to a prospective cohort will allow validation testing.

**Interpretation**

It was reported that placenta increta remained undiagnosed before delivery in half to two-thirds of cases[27, 28]. Current prenatal diagnosis mainly rests on subjective interpretation of US and MRI findings[13]. US is the first-level imaging modality to assess placenta increta due to convenience and lower cost[9, 20]. However, it suffers from high operator-dependence and low reproducibility. MRI is relatively operator-independent and can be subjected to re-evaluations[4]. MRI has yet to clearly demonstrate a significant improvement in the diagnosis of placenta increta though it is widely employed[29]. The radiologists not only assess the image qualitatively but also interpret the image quantitatively to obtain objective diagnostic information. Texture analysis will become an important adjunctive index test when the assessment of placenta increta is inconclusive or incomplete in US and MRI.

Texture analysis characterizes the internal structure of tissues and organs[14]. The quantitative and objective texture analysis of placenta increta may remove the subjectivity and serve as its predictor. Placenta increta was associated with histogram which was consistent with underlying tissue heterogeneity. A wider range of histogram indicated increased heterogeneity(Fig.3)[30]. Mean, Percentile 90% and Percentile 99% were three important texture parameters derived from histogram. It will be shown that texture analysis can aid in the diagnosis of placenta increta through quantification of texture parameters in MRI. Optimizing quantitative analysis of heterogeneity and controlling for confounding variables will further help to reduce the subjectivity that is associated with evaluating the heterogeneity of placenta increta. Nevertheless, despite our attempts to overcome the limitations, future studies, preferably prospective and conducted on a larger cohort of participants are mandatory to confirm study results and further assess the role of texture analysis in the diagnosis of placenta increta.

The study supported the hypothesis that texture analysis could reflect underlying heterogeneity of placenta increta and help radiologists to differentiate placenta accreta from increta. We felt that the introduction of texture analysis as a routine examination in cases of suspected placenta increta would
reduce the obstetrician's concern of an accurate diagnosis in order to organize the most appropriate and safest surgical procedure.

**Conclusion**

In conclusion, our study showed statistically significant differences for Mean, Percentile 90% and Percentile 99% between normal myometrium and placenta increta, which suggested a potential role of texture analysis in helping to diagnose placenta increta. Texture analysis that was derived from histogram may be a useful add-on to MRI in diagnosing placenta increta.

**Abbreviations**

PAS disorders: placenta accreta spectrum disorders; US: ultrasonography; ROI: region-of-interest; IRBs: Institutional Review Boards; TR: repetition time; TE: echo time; FA: flip angle; FOV: field-of-view; RLM: run-length matrix; COM: co-occurrence matrix;

ICC: intra-class correlation coefficients

**Declarations**

**Conflicts of interest and sources of funding:** The authors declare no conflicts of interest. This work was mainly supported by the National Natural Science Foundation of China (grant number 81671743), the Clinical Key diseases diagnosis and therapy Special project of Health and Family Planning Commission of Suzhou (LCZX201801), the High-level Health Personnel “six-one” Project of Jiangsu Province (LGY2016035) and Program for Advanced Talents within Six Industries of Jiangsu Province (WSW-057).

**Ethics approval and consent to participate**

This study was approved by the Institutional Review Boards of Shanghai Concord Medical Diagnostic Imaging Center (No.2020-22). Written informed consent was waived since this study used existing MRI data. We confirmed that all methods were carried out in accordance with relevant guidelines and regulations.

**Consent for publication**

Not applicable.

**Availability of data and materials**

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

**Competing interests**
The authors declare that they have no competing interests.

**Funding**

Not applicable.

**Authors’ contributions**

This article involved 5 authors and each played an essential part, as follows: LD, initiation and design of the study, collection of samples, analysis, interpretation of data, writing and submission. ZL, JZ, ZS, data collection, image analysis, statistical analysis. YL, supervisor, analysis and revision. All authors read and approved the final manuscript.

**Acknowledgements**

Not applicable.

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Tables

Due to technical limitations, table 1-2 is only available as a download in the Supplemental Files section.
Figures

**Potentially eligible participants n=192**

Excluded n=46
- Due to extreme fetal movements resulting in MRI artifacts (n=9)
- Missing part of images (n=11)
- Images produced by different MRI devices (n=6)
- Different MRI sequences (n=10)
- Unqualified positions (n=6)
- Other causes (n=4)

**Eligible participants n=146**

No texture analysis n=123
- Placenta accreta and percreta (n=89)
- Inconclusive clinical diagnosis (n=34)

**Texture analysis of placenta increta n=23**

Figure 1

Flow diagram of the study. The number of participants and corresponding test results at each stage of the study were provided, as well as detailed reasons for excluded participants.
Figure 2

Representative sagittal and coronal T2W images of placenta increta (a-b 26 years old; c-d 31 years old and e-f 29 years old) with their respective ROIs in green boxes for texture analysis.

Figure 3
The histogram from texture analysis obtained from normal myometrium showed a relatively narrow distribution of pixel intensity indicating homogeneity (a) and the other from placenta increta showed a wider distribution of pixel intensity indicating heterogeneity (b).

![Estimated Marginal Means of MEASURE_1](image)

Figure 4

The values of seven second-order parameters of placenta increta and normal myometrium. The mean value of placenta increta was higher than that of normal myometrium.
Figure 5

Results of two-step cluster. The texture parameters were divided into two categories (a), the prediction of importance was shown (b, d) and the clustering model was of excellent quality (c)
Figure 6

The bubble plot of three second-order parameters. The mean value of placenta increta was different from that of normal myometrium

Supplementary Files

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