Texture analysis of dark intraplacental bands on T2WI in the evaluation of placenta accreta spectrum disorders: a feasibility study

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Research Article

Keywords: Placenta accreta spectrum disorders, Texture analysis, Dark intraplacental bands on T2WI, Prenatal diagnosis

Posted Date: June 22nd, 2021

DOI: https://doi.org/10.21203/rs.3.rs-569430/v1

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Abstract

Background: To evaluate whether texture analysis of dark intraplacental bands on T2WI can provide a novel methodological viewpoint valuable in assessing the classification of placenta accreta spectrum disorders (PAS disorders).

Methods: 174 participants with suspected PAS disorders were consecutively included in the study. Texture analysis was implemented on dark intraplacental bands on T2WI by MaZda software. The two steps of parameter selection and reduction led to a decrease of the parameter space dimensionality. The logistics regression models were constructed with texture parameters to evaluate the classification of PAS disorders.

Results: Both run length nonuniformity (RLN) and grey level nonuniformity (Gle) of four directions showed significant differences between participants with placenta accreta, increta and percreta ($P<0.05$). The AUC and cut-off for logistic regression model of accreta vs increta were 0.75 (95% CI: 0.54, 0.90) and 6.72, respectively; corresponding values for logistic regression model of increta vs percreta were 0.81 (95% CI: 0.61, 0.93) and 10.92. The sensitivity and specificity for cut-off of 6.72 were 88.46% and 84.62%, respectively; corresponding values for cut-off of 10.92 were 92.59% and 85.71%.

Conclusion: Texture analysis offered promise for more quantitative and objective assessment of PAS disorders than other image modalities. It may be a useful add-on to MRI in evaluating the classification of PAS disorders.

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 accreta spectrum disorders (PAS disorders) refer to a form of abnormal placentation resulting in partial or complete retention of placenta at the time of delivery, including placenta accreta, increta and percreta. Placenta accreta, the least severe entity, means the attachment of the chorionic villi to the myometrium without invasion, unlike in placenta increta that is defined by partial myometrial invasion. In placenta percreta, the most severe form, the chorionic villi penetrate the uterine serosa and may extend into adjacent pelvic organs[1]. The recent systematic review indicated that placenta accreta represented about 69.5% of PAS disorders, whereas placenta increta and placenta percreta accounted for 23.7% and 6.8% of PAS disorders, respectively[2]. Several concepts have been proposed to explain why and 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[3, 4]. This life-threatening obstetric condition is generally diagnosed at the time of delivery, often resulting in emergency treatment with a
A greater risk of morbidity[5]. In this regard, prenatal diagnosis of PAS disorders and correct identification of topography of invasion is crucial in minimizing morbidity and planning safer obstetric surgery [1, 5-7].

It is therefore crucial for radiologists to be involved in the multidisciplinary team and to provide standardized diagnostic assessment of PAS disorders[8]. Ultrasonography (US) had a lower diagnostic accuracy in detecting PAS disorders than MRI, which had a sensitivity 66%, specificity 71% and accuracy 68%[9, 10]. Even though US is the frontline imaging modality for the evaluation of PAS disorders[11], MRI is used as a problem-solving tool for equivocal sonographic findings or suspicion of posterior/lateral placental extension[12-14]. 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[15, 16].

However, the visual qualitative analysis of images may not be completely accurate to extract the corresponding diagnostic information. Texture analysis can be applied to medical images through the analysis of quantitative parameters which reflect region-of-interest (ROI) heterogeneity[17]. The quantitative, objective texture analysis of PAS disorders may remove the subjectivity and serve as predictors of three subtypes. Our hypothesis was that texture analysis may reflect heterogeneity underlying PAS disorders[18], thus helping in assessing the classification of PAS disorders. The objective of the study was to evaluate whether texture analysis of dark intraplacental bands on T2WI can provide a novel methodological viewpoint valuable in differentiating between placenta accreta, increta and percreta.

**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 Board (IRB) approved the observational study of MRI examinations performed for the evaluation of PAS disorders at our institution over the previous 4 years. The IRB granted a waiver of written informed consent since this study used existing MRI data. Funding was provided in the form of the extra diagnostic equipment needed for the study. The funders had no role in the initiation or design of the study, collection of samples, analysis, interpretation of data, writing of the paper, or the submission for publication. The study and researchers were independent of the funders. 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 (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 patients were evaluated and screened for study eligibility by the author prior to study entry. Of all participants consecutively retrieved from our database spanning from September 2016 through October 2020, only participants with MRI examinations and clinical or histopathological diagnosis of PAS disorders were included. Participants eligible for inclusion were consecutive adults (≥18 years) with suspected PAS disorders, based on the presence of the following: who performed an MRI examination at our institution and for whom clinical or histopathological diagnosis was available. We excluded participants if they had no clinical history and complete images, they were examined by different MRI devices, they received incomplete MRI examinations due to extreme fetal movements resulting in MRI artifacts, or follow-up was not possible.

**Standard of reference**

The clinical history of PAS disorders 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 placental site after removal of the placenta during cesarean delivery[19, 20]. It has good reliability and validity rates compared with other diagnostic standards, such as histopathology[5, 12, 21, 22].

**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[12]. 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[23]. 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[22-24]. Multi-breathholding was utilized to minimize respiratory motion artifacts[5, 22]. 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[25]. 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
To maximize signal, a multi-channel surface coil was used whenever possible. No sedative or gadolinium contrast agent was administered[23, 27].

**Image interpretation**

MRI of PAS disorders 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 PAS disorders 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 PAS disorders was implemented on dark intraplacental bands on T2WI by MaZda software (Version 4.6.2.0; Institute of Electronics, Technical University of Lodz, Lodz, Poland) in BMP format[17, 28, 29]. The flowchart illustrating typical steps of texture analysis was shown in Fig. 1. At first, raw-MRI options consisted of image dimensions with 256×256 and pixels intensity encoded with 8 bits[17]. 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. A total of 328 ROIs were positioned, of which 136 on the sagittal plane and 192 on the coronal plane. Four first-order texture parameters were extracted with MaZda options, which were run-length matrix (RLM); co-occurrence matrix (COM); gradient and wavelet[17]. The images were normalized before analysis using the “±3 sigma” technique to minimize the effect of brightness and contrast variation on texture analysis[17]. 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 classification of PAS disorders[17]. 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 texture analysis results to render an impression of the degree of invasion 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-tailed $P$ 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 of PAS disorders 0.19%, sensitivity 0.78, specificity 0.71 in PASS 11. Analysis of covariance was used by prespecifying gestation age as the covariate when variance homogeneity and parallelism assumption was satisfied for the comparison of data between three groups. Two-step clustering was performed to predict the importance of parameters. Logistic regression models were fitted by carrying out ordinal logistic regression for important parameters. The receiver operating characteristic curves (ROC curve) were derived by calculated sensitivity-specificity pairs for all possible cut-offs. The cut-off of the index test was performed by the maximum Yuden index. The diagnostic accuracy of index test was evaluated from the contingency table.

**Results**

**Study participants**

The study flow was illustrated in Fig. 2. Participants who were excluded (and reasons for this) were noted. The participant characteristics 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, the run length matrix-based parameters were computed 4 times for each ROI (in horizontal, vertical, $45^0$ and $135^0$ direction). Exemplary T2W images differentiating between placenta accreta, increta and percreta were shown in Fig. 3. Two second-order parameters were selected for further statistical analysis: one was run length nonuniformity (RLN) and the other was grey level nonuniformity (Gle)[17]. The values of two second-order parameters were displayed in the dataset (Table 2). Two second-order parameters of four directions showed significant differences between participants with placenta accreta, increta and percreta ($P<0.05$, Table 2). The results of two-step cluster predicted that two second-order parameters of four directions were important (predictor importance $0.8$) and the clustering model was of excellent quality (Fig. 4).

The logistic regression models were formed by two second-order parameters of four directions.

Logit(accreta vs increta) = $3.38 - 0.01 \times \text{HRLN} - 1.89 \times \text{HGLe} - 0.05 \times \text{VRLN} - 1.23 \times \text{VGLe} - 0.02 \times 45\text{RLN} - 0.59 \times 45\text{GLe} - 0.07 \times 135\text{RLN} - 1.72 \times 135\text{GLe}$ and Logit (increta vs percreta) had the same regression coefficients and independent variables except that the intercept of 5.49 was different. The area under the receiver operating characteristic curve (AUC), Yuden index and cut-off for the logistic regression model of accreta vs increta were 0.75 (95% CI: 0.54, 0.90), 0.46 and 6.72, respectively; corresponding values for the logistic regression model of increta vs percreta were 0.81 (95% CI: 0.61, 0.93), 0.62 and 10.92 (Table 3, Fig. 5).
Table 4-A, 4-B showed the cut-offs in relation to diagnosis of gold standard. The sensitivity and specificity for cut-off of 6.72 were 88.46% and 84.62%, respectively; corresponding values for cut-off of 10.92 were 92.59% and 85.71%. 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, the interobserver agreement of texture analysis for the diagnosis of PAS disorders was substantial, which was a little higher than that of MRI[9]. Secondly, although interobserver agreement of texture analysis and MRI for the diagnosis of PAS disorders was similar, the AUC, sensitivity and specificity of texture analysis were perfect and higher than previously reported MRI findings[9, 10].

**Strengths and weaknesses**

In this retrospective study, we directly compared the accuracy of MRI with that of texture analysis in the same group of participants. Therefore, the study provided real-world information about the diagnostic accuracy of texture analysis in a group of participants suspected of having PAS disorders[30]. The gestational age is the confounding variable for any type of analysis in PAS disorders. The degree of placental heterogeneity generally increases with gestational age[23]. The importance of this study was to determine baseline texture changes in PAS disorders when gestational age was taken as the covariate. 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. The first flaw of the study was reference test bias. PAS disorders were defined by clinical history and histopathological diagnosis. If histopathological findings were not available, then PAS disorders were defined by clinical history alone. It was recognized that the use of such clinical history rather than final histopathology may result in the misclassification of PAS disorders. Secondly, patients underwent MRI because they were thought to be at high risk for PAS disorders on the basis of their clinical history or US findings in our hospital. Thus, the probability for PAS disorders was generally high in patients referred for texture analysis. Given the retrospective nature of this study, unfortunately this bias was unavoidable. 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[15]. Finally, the study may not be generalized because of minor differences in design and procedure.

**Interpretation**
It was reported that PAS disorders remained undiagnosed before delivery in half to two-thirds of cases\cite{16,31}. Current prenatal diagnosis mainly rests on subjective interpretation of US and MRI findings\cite{16}. US is the first-level imaging modality to assess PAS disorders due to its convenience and lower cost\cite{12,23}. However, it suffers from high operator-dependence and low reproducibility. MRI is relatively operator-independent and can be subjected to re-evaluations\cite{5}. MRI has yet to clearly demonstrate a significant improvement in the diagnosis of PAS disorders though it is widely employed\cite{32}. Texture analysis will become an important adjunctive index test when the assessment of PAS disorders is inconclusive or incomplete in US and MRI. Even when US and MRI findings are convincing for the diagnosis of PAS disorders, texture analysis can be beneficial in planning subsequent management by quantifying the extent of PAS disorders.

Dark intraplacental bands on T2WI are the most sensitive predictor for the diagnosis of PAS disorders\cite{1,5,12,33}, which are thicker than septa and extend within the placenta from the placenta-myometrium interface\cite{23}. They appear as nodular or linear areas and may represent overlapping features of flow void, sinusoids, aberrant septa and fibrin deposition\cite{1,4,22,23,34}.

The radiologists not only assess the image qualitatively but also interpret the image quantitatively to obtain objective diagnostic information. The texture characterizes the internal structure of tissues and organs\cite{17}. RLN and Gle are two important texture parameters derived from RLM, which holds counts of pixel runs with the specified gray-scale level and length\cite{17}. RLN and Gle may reflect the underlying tissue heterogeneity in the setting of PAS disorders so that the cut-offs in logistic regression models were different between participants with accrete vs increta and increta vs percreta. It will be shown that texture analysis can aid in the diagnosis of PAS disorders through quantification of texture parameters within an image. In this perspective, texture analysis represented a novel methodological viewpoint that can benefit less experienced radiologists in the detection of PAS disorders or aid experienced ones when facing doubtful cases. As an additional result, we found that texture analysis had a good interobserver agreement that can allow a repeated evaluation of PAS disorders.

There have been no studies showing that radiological techniques can accurately determine the extent of PAS disorders\cite{23,35}. The study supported the hypothesis that texture analysis could play a role as an adjunctive tool in clinical practice and aid radiologists in differentiating PAS disorders. Based on these findings, we resort to texture analysis not only to optimize the MRI diagnostic accuracy in cases of suspicious PAS disorders but also to use it as a classification technique. We feel that the introduction of texture analysis as a routine examination in cases of suspected PAS disorders will reduce the obstetrician’s concern of an accurate diagnosis in order to organize the most appropriate and safest surgical procedure.

**Conclusion**

Texture analysis offered promise for more quantitative and objective assessment of PAS disorders than other image modalities. It may be a useful add-on to MRI in evaluating the classification of PAS disorders.
Abbreviations

PAS disorders: Placenta accreta spectrum disorders; US: Ultrasonography; ROI: region-of-interest; IRB: Institutional Review Board; TR: repetition time; TE: echo time; FA: flip angle; FOV: field-of-view; PACS: Picture Archiving and Communication System; DICOM: Digital Imaging and Communications in Medicine; RLM: run-length matrix; COM: co-occurrence matrix; ICC: intra-class correlation coefficients; ROC curve: receiver operating characteristic curves; RLN: run length nonuniformity; Gle: grey level nonuniformity; AUC: area under the receiver operating characteristic curve

Declarations

Ethics approval and consent to participate

This study was approved by the Institutional Review Board of our hospital (approval No.2020-22). Written informed consent was waived since this study used existing MRI data (approval No.2020-13).

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

Funding was provided in the form of the extra diagnostic equipment needed for the study. The funders had no role in the initiation or design of the study, collection of samples, analysis, interpretation of data, writing of the paper, or the submission for publication. The study and researchers were independent of the funders.

Authors’ contributions

This article involved 8 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. HS,YL, supervisor, analysis and writing; JZ, data collection; SW, ZL, ZS, image analysis; YT, statistical analysis. All authors read and approved the final manuscript.

Acknowledgements
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).

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References


Tables

**Table 1** Participant characteristics of the study

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<th>Participant characteristics</th>
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Remark: Unless stated otherwise, data were the number of participants. Data in parentheses were percentages.
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*Texture parameters were dimensionless.

**Remark:** HRLN=Horzl-RLNonUni, HGLe=Horzl-GlevNonU, VRLN=Vertl-RLNonUni, VGLe=Vertl-GlevNonU, 45RLN=45-RLNonUni, 45GLe=45-GlevNonU, 135RLN=135-RLNonUni, 135GLe=135-GlevNonU

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Table 3 Diagnostic performance of logistic regression models

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<th>PAS</th>
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<th>Accreta vs Increta</th>
<th>Increta vs Percreta</th>
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Remark: Data in parentheses were 95% CI

Table 4-A Contingency table of cut-off (6.72)

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Table 4-B Contingency table of cut-off (10.92)

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Remark: Data in parentheses were percentages, i.e., sensitivity, specificity, false positive and false negative

Figures

Figure 1
Flowchart illustrating typical steps of MRI texture analysis in MaZda software

Potential eligible participants n=174
- Excluded n=50
  - No clinical history (n=13)
  - Due to extreme fetal movements resulting in MRI artifacts (n=7)
  - Unable to follow-up (n=4)
  - Missing part of images (n=11)
  - Images produced by different MRI devices (n=5)
  - Different MRI sequences (n=10)

Eligible participants n=124
- No texture analysis n=12
  - Uncertain gestational age (n=7)
  - Inconclusive clinical diagnosis (n=5)

Texture analysis n=112
- Negative result n=11
  - No clinical history n=5
    - Drop-out (n=3)
    - Referral (n=2)
- Positive result n=92
  - No clinical history n=23
    - Drop-out (n=7)
    - Referral (n=11)
    - Death (n=2)
    - Unknown cause (n=3)
- Inconclusive result n=9
  - No clinical history n=4
    - Drop-out (n=2)
    - Referral (n=1)
    - Unknown cause (n=1)

Referred for the clinical history n=6
- PAS disorders
  - Present (n=3)
  - Absent (n=2)
  - Inconclusive (n=1)

Referred for the clinical history n=69
- PAS disorders
  - Present (n=63)
  - Absent (n=4)
  - Inconclusive (n=2)

Referred for the clinical history n=5
- PAS disorders
  - Present (n=2)
  - Absent (n=1)
  - Inconclusive (n=2)

Equilibration between the groups for analysis of covariance n=29
- Placenta accreta (n=13); placenta increta (n=13); placenta percreta (n=13)

Figure 2

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 3

Representative placental sagittal and coronal T2W images of placenta accreta (28 years old, a,b), placenta increta (28 years old, c,d) and placenta percreta (25 years old, e,f) with their respective ROIs in the green boxes for texture analysis.
Figure 4

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 5

The ROC curves indicated the accuracy of logistic regression models. The left ROC (a) curve represented the logistic regression model of accreta vs increta and AUC was 0.75, as well as the right (b) indicated the logistic regression model of increta vs percreta and AUC was 0.81. The diagnostic values of both were moderate.