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ORIGINAL RESEARCH ARTICLE

# Placental volume in gestational week 27 measured by three-dimensional ultrasound and magnetic resonance imaging

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## Abstract

**Introduction:** Ultrasound is the diagnostic tool of choice in pregnancy. We lack valid ultrasound methods for placental size measurements. Our aim was therefore to compare three-dimensional (3D) ultrasound with magnetic resonance imaging (MRI) for measurements of placental volume.

**Material and methods:** We measured placental volume by 3D ultrasound and MRI in 100 unselected pregnancies at 27 weeks of gestation ($25^{+4}$–$28^{+4}$ weeks). The 3D ultrasound acquisitions were analyzed offline, and the placental outline was manually traced using the virtual organ computer-aided analysis (VOCAL) 30° rotational technique. The MRI examinations included a T2-weighted gradient echo sequence in the sagittal plane, with 5-mm slices through the entire uterus. The placental outline was manually traced in each slice. The correlation between 3D ultrasound and MRI placental volumes was estimated by intraclass correlation coefficients. Bland-Altman analysis was applied to visualize systematic bias and limits of agreement, in which the ratio MRI placental volume/3D ultrasound placental volume was plotted against the average of the two methods.

**Results:** The intraclass correlation coefficient between 3D ultrasound and MRI measurements was 0.49 (95% confidence interval 0.33-0.63). In general, 3D ultrasound measured smaller placental volumes (median 373 $cm^3$, interquartile range 309-434 $cm^3$) than MRI (median 507 $cm^3$, interquartile range 429-595 $cm^3$) and the systematic bias was 1.44. The 95% limits of agreement between the two methods were wide (0.68-2.21).

**Conclusions:** We found poor to moderate correlation between 3D ultrasound and MRI placental volume measurements. Generally, 3D ultrasound measured smaller placental volumes than MRI, suggesting that 3D ultrasound failed to visualize the entire placenta. Our findings may hopefully contribute to the improvement of ultrasound methods for placental measurements.

**Abbreviations:** 95% CI, 95% confidence intervals; ICC, intraclass correlation coefficient; LoA, limits of agreement.

**KEYWORDS**
magnetic resonance imaging, placenta, placental volume, pregnancy, ultrasound

## 1 | INTRODUCTION

In previous studies of births, disproportional weight of the placenta relative to birthweight has been associated with adverse outcomes for the infant, such as fetal death, neonatal death and cerebral palsy.[1-3] Both low and high absolute placental weight for gestation seems to increase the risk of adverse outcomes for the child.[1,3,4] These findings were independent of the absolute birthweight. In fact, a large proportion of newborns with an adverse outcome have appropriate size for gestation at birth.[1,3,5] Pregnancies with normal fetal weight are not easily identified as being at high risk. Thus, information about placental size while the pregnancy is still ongoing, may possibly improve the identification of pregnancies with increased risk of adverse outcomes.[1-4] However, we lack valid and easily available tools for measurement of placental size in ongoing pregnancies.

Ultrasound is the diagnostic tool of choice in pregnancy. 3D ultrasound has previously been used to measure placental volume,[6,7] and low placental volumes measured by 3D ultrasound early in pregnancy has been associated with unfavorable pregnancy outcomes.[8-11] However, we do not know whether ultrasound is a valid tool for placental size measurements. One study compared placental volume measured by 3D ultrasound late in pregnancy with placental weight and volume after the delivery.[7] Comparisons of ultrasound with other imaging modalities for placental size measurements in ongoing pregnancies have, to our knowledge, not been performed.

Non-contrast MRI provides excellent soft tissue contras, and may be safely used in pregnant women.[12,13] MRI images of the uterus provide a good overview of the entire placenta and several previous studies have estimated placental volumes using MRI.[14-19] MRI has been shown to measure organ volumes accurately.[20] Hence, we believe that MRI is the best tool available for measuring placental volume in ongoing pregnancies.

In this study, we measured placental volume by 3D ultrasound and by MRI, and estimated the correlation and the agreement between the two methods.

**Key message**

We compared placental volume measured by 3D ultrasound and MRI, and found poor to moderate correlation between the two methods. 3D ultrasound measured smaller placental volumes than MRI, suggesting that 3D ultrasound failed to visualize the entire placenta.

## 2 | MATERIAL AND METHODS

Our study took place at the Department of Obstetrics, Akershus University Hospital in Norway. During the study inclusion period from April 2017 to May 2018, approximately 5000 pregnant women were scheduled for routine fetal ultrasound examinations at 17-19 weeks after their last menstrual period.[21] Among these women, 350 were invited to participate in a prospective study of fetal and placental growth. Women who had their scheduled hospital appointment when we had facilities available for the study, were invited to participate. The women were invited by a postal letter and received additional oral information at the study site.

The gestational age of the pregnancy was determined at the routine fetal ultrasound.[22] Women with a multiple pregnancy and women who did not understand any Scandinavian language or English were not eligible. There were no other exclusion criteria. A total of 255 women fulfilled the inclusion criteria, agreed to participate, and gave their written consent to participate.

Of the 255 eligible women, we selected 116 women to be examined by both 3D ultrasound and MRI in gestational week 27. For the MRI examination, we selected the women who would be in gestational week 27 at the time of available MRI facilities for our study (four examinations per week). For 12 of the 116 selected women, the MRI examination was either not performed or not completed, due to claustrophobia (n = 3), low back pain (n = 1), anxiety (n = 2), migraine (n = 1), failure to attend the appointment (n = 2) or MRI technical problems (n = 3). Additionally, four women were not included in our data analyses due to very poor quality of the 3D ultrasound images (evaluated during offline analysis, without knowledge of MRI measurements). Thus, 100 women could be included in our data analyses.

### 2.1 | Placental measurements by ultrasound

To obtain placental volume measurements by 3D ultrasound, a single operator (S.S.) used a Voluson E8 machine (GE Healthcare) equipped with a transabdominal 3D curved-array probe (RAB 4-8-D). The 3D volume angle was set to the maximum (85°) and the sector angle was 90°. The ultrasound probe was placed on the woman's abdomen in the position where the placenta was best visualized. The women were asked to hold their breath during the 3D volume acquisition. The 3D volume acquisition was rejected and reacquired if major artifacts were present. For each placenta, three, 3D volume acquisitions were stored for offline analysis.

Each 3D placental volume acquisition was traced offline by one investigator (K.S.) using the virtual organ computer-aided analysis (VOCAL) 30° rotational technique, a feature of the commercially

available 4DVIEW software version 18 (GE Healthcare). The 3D volume was rotated stepwise by 30° around a central fixed axis, generating a 2D image for each rotation, a total of six images. In each of those six images, the borders of the placenta were traced manually. We did not include the decidual layers as parts of the placenta. Based on the manual tracing of the six images of each placenta (Figure S1), the 4DVIEW software rendered a 3D model and calculated the placental volume. Of the three 3D acquisitions of each placenta, we used the largest estimated placental volume for comparison with MRI.

Twenty of the placentas were retraced by two investigators (K.S. and V.H.) for intra- and interrater reliability analyses. The investigators were blinded to the previously estimated volumes.

### 2.2 | Placental measurements by MRI

All MRI examinations were performed using the same 1.5 T MRI scanner (Ingenia; Philips Healthcare). The vast majority of the women tolerated the MRI scan being performed in a supine position. If not, they were placed in a slightly tilted left decubital position. An anterior abdominal coil allowed the entire uterus to be imaged without repositioning the coil.

The volumetric acquisitions of the placenta included a steady-state free-precession (balanced fast field echo: bFFE) sequence through the uterus (slice thickness 5 mm, no slice gap, echo time [TE] 1.7 ms, repetition time [TR] 3.3 ms, field of view [FOV] 300-350 mm). This sequence was acquired within 20 seconds of maternal breath holding. We performed one scan of each placenta, unless technical problems occurred.

The placental borders were manually traced in each slice through the uterus, and the placental volume was calculated based on the area of interest in each slice ($mm^2$) and the slice thickness (5 mm), using the commercially available software ITK-SNAP (ITK-SNAP version 3.6.0).[23] The decidual layers were not included as a part of the placenta. An example of tracing of MRI images is provided in Figure S1. All tracings were performed by one investigator (V.H.). In addition, 20 of the placentas were retraced both by V.H. and a second investigator (A.B.) for intra- and interrater reliability analyses.

The tracing of the placentas was performed without knowledge of previous tracing results.

### 2.3 | Statistical analyses

We used the Sign test to compare median placental volume measured by 3D and by MRI. The strength of the correlation between the 3D ultrasound and the MRI placental volume was estimated by the intraclass correlation coefficient (ICC) with 95% confidence intervals (95% CI), using the consistency definition of ICC.[24]

The agreement between 3D ultrasound and MRI measurements of placental volume was assessed with Bland-Altman analyses. In the Bland-Altman plots, the y-axis presents the ratio of the two volumes (MRI volume/3D ultrasound volume) for each placenta, and the x-axis presents the average volume (MRI volume + 3D ultrasound volume/2) for each placenta. We calculated the mean ratio of all the placentas (the systematic bias) and the 95% limits of agreement (LoA) (mean ratio ± 1.96 SD) between the methods.[25,26]

To explore whether the correlation between 3D ultrasound and MRI measurements increased with the investigators' increasing experience, we divided our study sample into five subgroups of 20 placentas by the order of placental examinations (3D ultrasound placental volume acquisition and offline tracing). We also performed separate analyses of the placentas located on the anterior and on the posterior uterine wall.

The intra- and interrater reliability of placental volume was tested using the ICC with absolute agreement definition, and we calculated the systematic bias and the 95% LoA.

All statistical analyses were performed using the IBM SPSS Statistics for Windows, version 25 (IBM Corp.).

### 2.4 | Ethical approval

Our study was approved by the Regional Committee for Medical and Health Research Ethics, Norway (REK south-east A, Reference no. 2016/1185, 21 September 2016) and recommended by the Data Protection Officer at Akershus University Hospital (Reference no. 16-179, 15 November 2016).

## 3 | RESULTS

Maternal and pregnancy characteristics of the study sample are presented in Table 1. For 93 of the women (93%), the MRI examination took place within 2 days of the ultrasound examination.

### 3.1 | Placental volume measurements

In general, 3D ultrasound measured smaller placental volumes (median 373 $cm^3$, interquartile range 309-434 $cm^3$) than MRI (median 507 $cm^3$, interquartile range 429-595 $cm^3$) ($P < .001$). Only seven placentas were measured to be larger by 3D ultrasound than by MRI, and the difference was never >5%.

Overall, the 3D ultrasound measurements showed poor to moderate correlation with the MRI measurements (ICC 0.49, 95% CI 0.33-0.63; Figure 1A). The Bland-Altman analysis showed a systematic bias (mean ratio) of 1.44, meaning that placental volume was estimated to be on average 44% larger by MRI than by 3D ultrasound (Figure 1B). The limits of agreement between the two methods were wide (95% LoA 0.68-2.21). For eight placentas, the MRI volume was more than twice as large as the 3D ultrasound volume.

For the first 20 placentas that we examined, we found no correlation between the 3D ultrasound and the MRI measurements

**TABLE 1** Maternal and pregnancies characteristics of the study sample (n = 100)

| Maternal and pregnancy characteristics | n (%) | Median (IQR) |
|---|---|---|
| Prior deliveries | | |
| 0 | 45 (45) | |
| 1 | 44 (44) | |
| 2 | 8 (8) | |
| >3 | 3 (3) | |
| Location of the placenta and MRI placental volume ($cm^3$) | | |
| Anterior | 51 (51) | 533 (432-618) |
| Posterior | 41 (41) | 501 (426-578) |
| Fundus | 8 (8) | 448 (409-937) |
| Daily smoking | | |
| Yes | 1 (1) | |
| No | 99 (99) | |
| Pre-pregnancy body mass index ($kg/m^2$) | | 23.6 (21.5-26.9) |
| Maternal age (years) | | 30.6 (27.7-34.8) |
| Gestational week at 3D ultrasound examination (weeks+days) | | $26^{+6}$ ($26^{+4}$-$27^{+2}$) |
| Gestational week at MRI examination (weeks+days) | | $27^{+0}$ ($26^{+4}$–$27^{+3}$) |

Abbreviations: 3D, three-dimensional; IQR, interquartile range; MRI, magnetic resonance imaging.

(ICC 0.15, 95% CI −0.31 to 0.55, $P$ = .26). Within each of the subsequent four groups of 20 placentas, the correlation was stronger than in the first group (Figure S2). After exclusion of the 20 placentas first examined, the ICC was 0.59 (95% CI 0.43-0.72; Figure 1C) and the Bland-Altman analyses showed a systematic bias of 1.40 (95% LoA 0.77-2.04) (Figure 1D).

We excluded the 20 placentas that we first examined, and we performed separate analysis of placentas on the anterior and placentas on the posterior uterine wall. The correlation between 3D ultrasound and MRI measurements was stronger for placentas on the posterior uterine wall (n = 34) (ICC 0.79, 95% CI 0.62-0.89) than for those on the anterior uterine wall (n = 40) (ICC 0.41, 95% CI 0.12-0.63) (Figure 2A,C). The Bland-Altman plots suggest a stronger agreement between 3D ultrasound and MRI for placentas on the posterior uterine wall (systematic bias of 1.3, 95% LoA 0.86-1.80) compared with placentas on the anterior uterine wall (systematic bias 1.5, 95% LoA 0.72-2.20) (Figure 2B,D).

## 3.2 | Intrarater and interrater reliability

When retracing the same 3D ultrasound volume acquisition, both the intrarater and the interrater reliability were high, and higher than when comparing two different volume acquisitions of the same placenta (Table 2). Retracing of the MRI placental volume acquisition also showed very high intrarater and interrater reliability (Table 2).

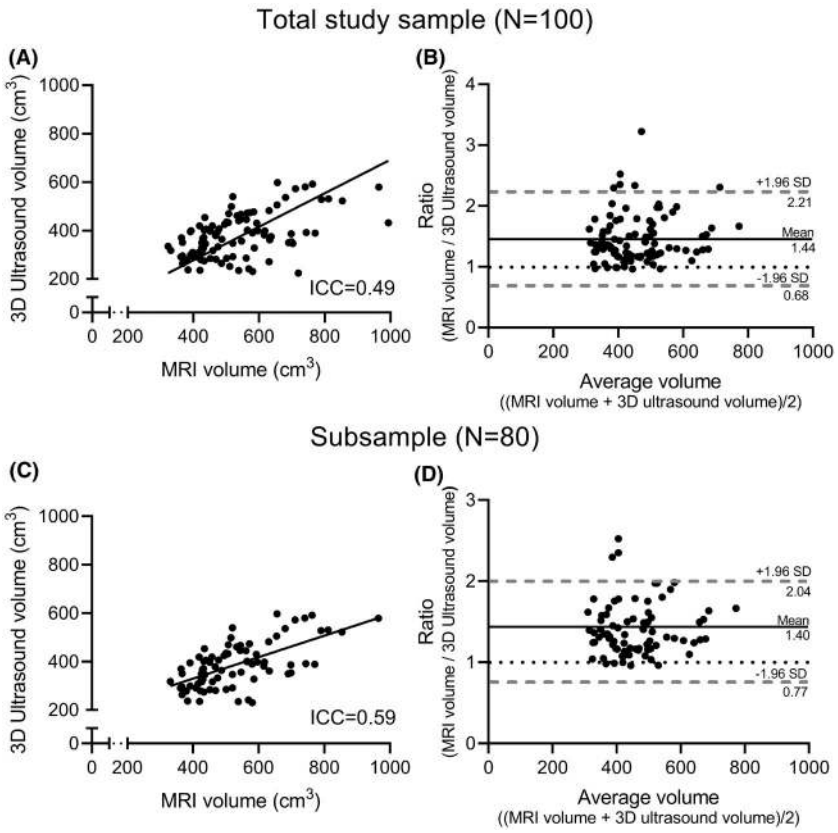


**FIGURE 1** Correlation (A, C) and agreement (B, D) between MRI and three-dimensional (3D) ultrasound measurements of placental volume. The subsample of 80 placentas (C, D) was obtained by excluding from the total study sample (n = 100) the 20 placentas first examined. ICC, intraclass correlation coefficient

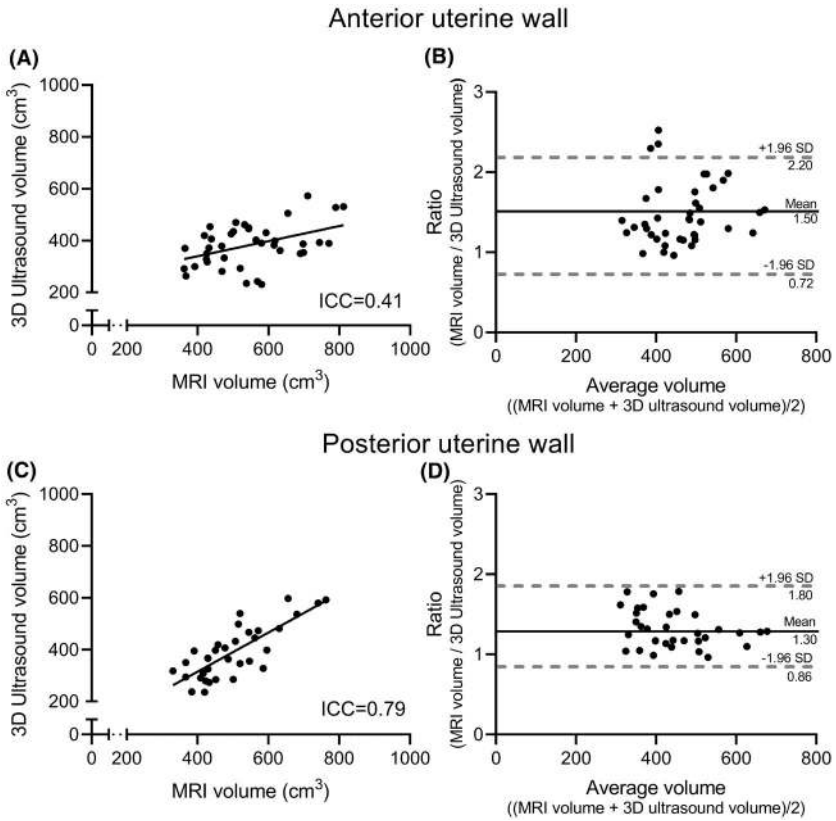


**FIGURE 2** Correlations (A, C) and agreement (B, D) between MRI and three-dimensional (3D) ultrasound measurements of placental volume among placentas on the anterior uterine wall (n = 40, A and B) and placentas on the posterior uterine wall (n = 34, C and D). ICC, intraclass correlation coefficient

## 4 | DISCUSSION

In this study, we found poor to moderate correlation between 3D ultrasound and MRI measurements of placental volume. Generally, 3D ultrasound measured smaller placental volumes than MRI.

To our knowledge, this is the first study to compare 3D ultrasound and MRI measurements of placental volume in ongoing pregnancies. Previously, one study measured the placental volume shortly before delivery using six different 2D or 3D ultrasound methods, and the measurements were compared with the placental volume and weight immediately after delivery.[7] The correlations were moderate. In that study, the strongest correlation with the delivered placenta was achieved using 3D ultrasound in the ongoing pregnancy combined with the virtual organ computer-aided analysis (VOCAL) 30° rotational technique for offline tracing (Spearman rank coefficient, $R_s$ = 0.4). Therefore, we chose this method for placental measurement in our study.

MRI has previously been used to measure placental volume, and the volumes in those studies ranged from 409 to 580 $cm^3$ in the interval between gestational weeks 26-30.[14-19] The median placental volumes in gestational week 27 was around 500 $cm^3$, and this finding is in agreement with the median MRI estimated volume in our study.[16,18,19]

Our MRI images provided a good overview of the placentas, as well as good soft tissue contrast. Thus, the smaller placental volumes measured by 3D ultrasound compared with MRI, suggest that 3D ultrasound fails to visualize the entire placenta. While recording the 3D ultrasound acquisitions, our overall impression was that the field of view was sufficient to capture the entire placenta. However, missing placental tissue in the 3D ultrasound acquisition could possibly explain the relatively weak correlation between the 3D ultrasound and the MRI measurements. The angle of the ultrasound probe that we used (sector angle 90°, volume angle 85°) may have been too narrow to capture the entire placenta. Such an assumption is supported by the stronger agreement between 3D ultrasound and MRI on the posterior uterine wall than on the anterior uterine wall, which is closer to the probe.

Acoustic shadows on the 3D ultrasound images may have caused inaccurate placental volume estimates. In many of the images that we traced offline, placental tissue was hidden behind acoustic shadows from the fetus, and the edges of these placentas were therefore difficult to identify. Additionally, the 30° rotational technique for placental volume estimation is based on interpolation between the six images of the placenta that were traced. Interpolation may have generated inaccurate volumes. A narrower rotational angle with smaller rotational steps could possibly have improved the accuracy. However, in a previous study comparing 15° and 30° rotation for offline tracing of 3D ultrasound acquisition, the 30° rotational technique showed a stronger correlation with the delivered placenta.[7]

The 3D ultrasound and the MRI examinations were performed within a 2-day interval for almost all pregnancies. Placental growth between the two examinations is therefore likely to be minimal,[17] and cannot explain the discrepancies between 3D ultrasound and MRI measurements in our study. We found a stronger correlation and agreements between 3D ultrasound and MRI when we excluded from the data analyses the 20 placentas that we first examined. The

**TABLE 2** Intrarater and interrater reliability of 3D ultrasound and MRI measurements of placental volume

| | Intrarater | | | | Interrater | | | |
|---|---|---|---|---|---|---|---|---|
| | Investigator: KS (*n* = 20) | | | | Investigator: KS + VH (*n* = 20) | | | |
| 3D ultrasound | ICC | 95% CI | Bias | LoA | ICC | 95% CI | Bias | LoA |
| Retracing of same acquisition | | | | | | | | |
| Acquisition 1 vs acquisition 1 | 0.90 | 0.75-0.96 | 0.96 | 0.82-1.18 | 0.84 | 0.64-0.93 | 1.03 | 0.69-1.31 |
| Acquisition 2 vs acquisition 2 | 0.84 | 0.64-0.93 | 0.95 | 0.77-1.23 | 0.88 | 0.72-0.95 | 0.98 | 0.78-1.22 |
| Acquisition 3 vs acquisition 3 | 0.95 | 0.86-0.98 | 0.96 | 0.84-1.16 | 0.92 | 0.80-0.97 | 1.01 | 0.73-1.27 |
| Tracing of different acquisitions | | | | | | | | |
| Acquisition 1 vs acquisition 2 | 0.70 | 0.37-0.87 | 1.01 | 0.57-1.43 | | | | |
| Acquisition 1 vs acquisition 3 | 0.79 | 0.54-0.91 | 1.11 | 0.70-1.52 | | | | |
| Acquisition 2 vs acquisition 3 | 0.70 | 0.39-0.87 | 1.13 | 0.66-1.61 | | | | |
| | Investigator: VH (*n* = 20) | | | | Investigator: VH + AB (n = 20) | | | |
| MRI | ICC | CI | Bias | LoA | ICC | CI | Bias | LoA |
| Retracing of same acquisition | 0.98 | 0.95-0.99 | 0.99 | 0.90-1.07 | 0.96 | 0.90-0.99 | 1.00 | 0.89-1.12 |

Abbreviations: 3D, three-dimensional; CI, confidence interval; ICC, intraclass correlation coefficient; LoA, limits of agreement; MRI, magnetic resonance imaging.

stronger correlation is likely to be explained by a learning effect. Nevertheless, the 3D ultrasound method that we have used is, in our opinion, not good enough for placental size measurements in clinical practice.

In our study, placental size was measured in gestational week 27. The main reason for this choice was that the safety of MRI examinations in early pregnancy was uncertain when we planned our study. An additional reason was that in very preterm deliveries, the risk of adverse outcome for the infant has been estimated to be particularly high if the placental to infant ratio is disproportional.[1,2,27]

Several studies of births strongly suggest that a disproportional growth of the placenta relative to the fetus increases the risk of adverse outcomes for the infant.[1-3,9,27] Also, in pregnancies with preeclampsia, pregnancies after in vitro fertilization or maternal diabetes, the placenta is disproportional relative to the infant.[28,29] Thus, a valid tool for measurement of placental size in ongoing pregnancies could possibly improve the identification of high-risk pregnancies. Previously, low placental volume in gestational week 11-13, as measured by ultrasound, has been associated with preeclampsia and delivery of an infant small for gestational age.[8-11] An MRI study suggested that a fetus with normal size in gestational week 24-29, but a small placenta, increased the risk of being small for gestational age at birth.[15] MRI is an accurate tool for soft tissue measurements; however, it is an expensive and inconvenient tool for examination of a large number of pregnancies. Ultrasound is the diagnostic tool of choice in pregnancy[30] and has potentials for placental size measurements.

## 5 | CONCLUSION

In this study, we found a poor to moderate correlation between 3D ultrasound and MRI placental volume measurements. Generally, 3D ultrasound measured smaller placental volumes than MRI did. We have identified and discussed possible limitations of the ultrasound method that we have used and, hopefully, our findings will encourage improvements of ultrasound techniques for placental volume measurements.

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### CONFLICT OF INTEREST

The authors have stated explicitly that there are no conflicts of interest in connection with this article.

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## SUPPORTING INFORMATION

Additional Supporting Information may be found online in the Supporting Information section.

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