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# Reproducibility of Placental Volume and Vasculature Indices Obtained by 3-Dimensional Power Doppler Sonography

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**Objective.** The purpose of this study was to evaluate the reproducibility of 3-dimensional (3D) power Doppler assessment of placental volumes and vascularization before adopting these in routine evaluation of normal and complicated pregnancies. **Methods.** A prospective study was performed on 30 normal singleton pregnancies from 11 to 14 weeks. To evaluate placental vascularization, 3D power Doppler sonography was applied to obtain a placental volume, and the volume acquired was analyzed using virtual organ computer-aided analysis. Two consecutive measurements were taken from each patient by two observers blinded to each other's and the individual's previous measurement. This yielded a total of 60 data set pairs. The placental volume, vascularization index, flow index, and vascularization-flow index (VFI) were calculated. Normal distribution of the data was confirmed with the Kolmogorov-Smirnov test. Intraobserver and interobserver correlations were evaluated. Bland-Altman plots and statistics were used to compare the 95% limits of agreement between measurements. **Results.** All 3D power Doppler placental volumes and vascular indices showed intraobserver correlations of 0.80 or higher. Similar excellent interobserver correlations were seen for all indices with the exception of the VFI, which showed a lower but acceptable correlation. The Bland-Altman analyses indicated good reproducibility of the evaluated placental indices. **Conclusions.** Our findings provide validation of the technique, showing good reproducibility of the 3D power Doppler parameters when applied to studies of the placental volume and vascular tree. **Key words:** flow index; placenta; placental volume; 3-dimensional sonography; vascularization indices.

## Abbreviations

CC, correlation coefficient; FI, flow index; 3D, 3-dimensional; VFI, vascularization-flow index; VI, vascularization index

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The placenta plays a central role in the pathogenesis of most adverse pregnancy outcomes. With improved 3-dimensional (3D) sonographic technology, it is now possible to evaluate the placental volume as well as vascularization status using power Doppler sonography.<sup>1–6</sup> The Doppler parameters derived from 3D interrogation are different from those using conventional sonography and include the vascularization index (VI), flow index (FI), and vascularization-flow index (VFI).<sup>2–4</sup> These indices have been reliably measured in the placenta and other gynecologic organs.

Given the important role of the placenta and the potential to use these assessments in predicting women at risk for adverse outcomes in pregnancy, the reliability of the measurements is of paramount importance. Very few studies have addressed the reproducibility of 3D evalua-

tion of placental volume and the vascularization indices derived therefrom in detail.<sup>7-9</sup> These studies varied in their design and inclusion criteria and may not be generalizable to all study populations because they were performed by pioneers in the area of study using earlier techniques for 3D volume acquisition. More current and detailed evaluation is needed before adopting these in routine assessment of normal and complicated pregnancies.

The aim of the study was to evaluate the reproducibility of 3D power Doppler assessment of placental volumes and vascularization.

### Materials and Methods

This was a prospective cohort study including women with singleton pregnancies seen between 11 and 14 weeks as part of a screening program for aneuploidy. The study was approved by the Institutional Review Board at Washington University, and each patient participating in the study gave a signed and approved informed consent form.

The methods used in acquiring the placental volume and vascularization indices have previously been described.<sup>10,11</sup> Briefly, all images were acquired using Voluson 730 Expert ultrasound machines (GE Healthcare, Milwaukee, WI) equipped with a 4- to 8-MHz transducer. The same pre-established instrument power settings (angio mode, cent; smooth, 4/5; frequency, low;

quality, 16; density, 6; enhance, 16; balance, GO150; filter, 2; actual power, 2 dB; and pulse repetition frequency, 0.9) were used in all cases. The entire view of the placenta was identified by 2-dimensional sonography, and the volume box was adjusted to scan the entire placenta. The angle of volume acquisition varied from 45° to 90°, and the duration was 10 to 15 seconds. For posteriorly and laterally located placentas, a slight lateral inclination of the transducer was used to acquire the images. After the entire volume was scanned, the sonograms were stored on a removable hard disk for subsequent analysis. The 3D scans used for the analysis were performed by experienced sonographers.

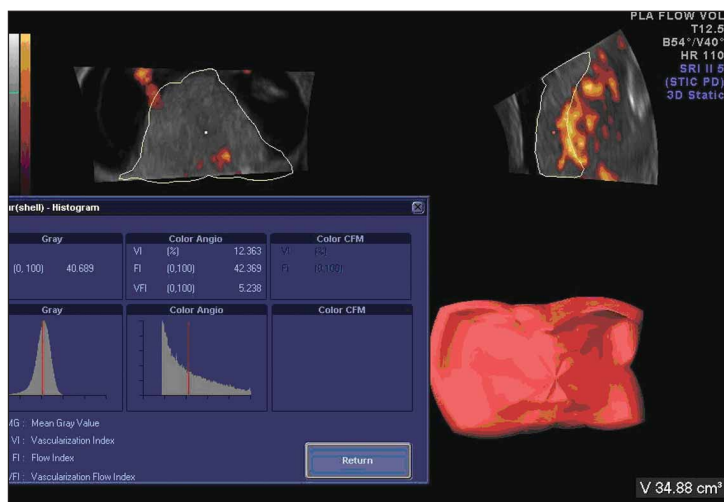
Each image was recovered in succession for processing. Evaluation of the entire placenta was performed using the rotational technique in the virtual organ computer-aided analysis program included in the GE 4D View computer software. This involved rotating the image at 30° intervals and outlining the contour of the placenta 6 times. When completed, the program automatically calculated the vascular indices from computer algorithms (Figure 1). Placental volumes and vascularization indices were acquired twice by the first evaluator (K.M.H.) and similarly by the second operator (A.O.O.). Each operator was blinded to their first and the other's placental volume and vascularization index measurements.

Normal distribution of the data was confirmed with the Kolmogorov-Smirnov test and log transformed when necessary. The intraobserver and interobserver variability expressed as an intraclass correlation coefficient (CC) and interclass CC were assessed. A value of greater than 0.75 was considered as reflecting good consensus for the intraclass and interclass CCs. Systematic bias between the first and second observations was determined by calculating the difference between the means.

We constructed Bland-Altman plots to assess the systematic bias between the two operators and the relationship between the difference between the two measurements and the magnitude of the measurements.<sup>12</sup> The mean of all measurements was used as an estimate for the magnitude of the measurements.

Statistical analyses were performed using Stata version 10.0 software (StataCorp, College Station, TX) and Prism version 5.0 software (GraphPad

Figure 1. Rendered 3D placental volume and vascularization indices.



Software, Inc, La Jolla, CA). Tests with  $P < .05$  were considered significant.

## Results

The placental volume and vascularization indices were calculated by each observer in 30 women. The mean maternal age  $\pm$  SD was  $31.9 \pm 6.0$  years, and the median gestational age was 12.1 weeks (range, 11.4–13.8 weeks). Most of the patients (18 of 30 [60%]) were multiparous, and most were white (62%) or Hispanic (23%). The placental locations were anterior in 53% (16 of 30), posterior in 44% (13 of 30), and lateral or fundal in 3% (1 of 30) of cases. The placental volumes and vascularization indices were all normally distributed by the Kolmogorov-Smirnov test; therefore, log transformation was not necessary for any of the values.

The mean placental volumes and vascular indices by each observer are shown in Tables 1 and 2. The intraobserver differences, bias, 95% limits of agreement, and intraobserver CC are shown in Table 1. The limits of agreement for measurements of the placental volume and VI

for observer B were higher than for observer A, but no significant systematic bias was observed between each paired set of intraobserver measurements. Examples of the Bland-Altman plots for intraobserver measurements of the placental volumes and FI for both observers are shown in Figures 2 and 3. With the exception of a few outliers, the delta for most measurements was within 2 SDs of their pairs.

The interobserver differences, bias, 95% limits of agreement, and interobserver CC are shown in Table 2. With the exception of measurements of the VFI, which showed an acceptable CC, the interobserver CC for all other indices was excellent. There was no significant systematic bias in the measurements, and the 95% limits of agreement were generally excellent. The limit of agreement was wide only for placental volume measurements between the observers.

Bland-Altman plots for the interobserver measurements of the placental volumes and vascular indices are shown in Figures 4–7. Similar to the intraobserver plots, there were few outliers, but the delta for most measurements was within 2 SDs of the measurements of the other observer.

**Table 1.** Intraobserver Differences Between First and Second Measurements of Placental Volume and Vascular Indices

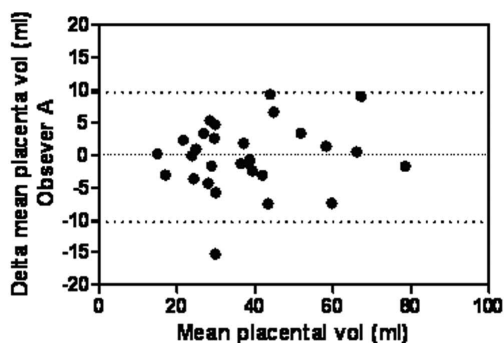
Placental Index	Mean of First Measurement	Mean of Second Measurement	Bias	95% Limits of Agreement	Intraobserver CC (95% CI)
Placental volume, cm <sup>3</sup>					
Observer A	38.2	37.9	-0.3	-10.3 to 9.6	0.95 (0.89–0.98)
Observer B	39.2	37.9	-1.3	-21.9 to 19	0.84 (0.68–0.92)
VI, %					
Observer A	12.9	11.4	-1.4	-9.1 to 6.3	0.90 (0.80–0.95)
Observer B	14.3	12.1	-2.1	-16.4 to 12.2	0.88 (0.77–0.94)
FI					
Observer A	43.3	42.5	-0.8	-6.7 to 5.1	0.94 (0.87–0.97)
Observer B	44.4	41.8	-2.6	-13.7 to 8.4	0.92 (0.84–0.96)
VFI					
Observer A	5.9	5.0	-0.9	-5.6 to 3.8	0.88 (0.76–0.94)
Observer B	6.7	5.2	-1.5	-10.5 to 7.4	0.80 (0.62–0.90)

CI indicates confidence interval.

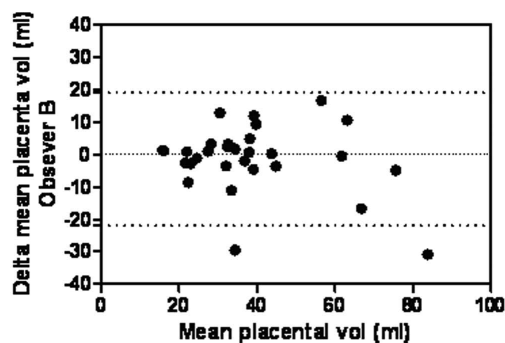
**Table 2.** Interobserver CCs of Placental Indices

Placental Index	Mean for Observer A	Mean for Observer B	Bias	95% Limits of Agreement	Intraobserver CC (95% CI)
Placental volume, cm <sup>3</sup>	38.0	38.6	-0.6	-15.7 to 16.8	0.88 (0.75–0.94)
VI, %	12.2	13.2	-1.0	-8.6 to 10.6	0.80 (0.61–0.90)
FI	42.9	43.1	-0.2	-8.2 to 8.6	0.85 (0.70–0.92)
VFI	5.5	6.0	-0.5	-5.2 to 6.1	0.72 (0.48–0.86)

CI indicates confidence interval.



A



B

Figure 2. **A**, Bland-Altman plot of intraobserver differences for placental volumes of observer A. **B**, Bland-Altman plot of intraobserver differences for placental volumes of observer B.

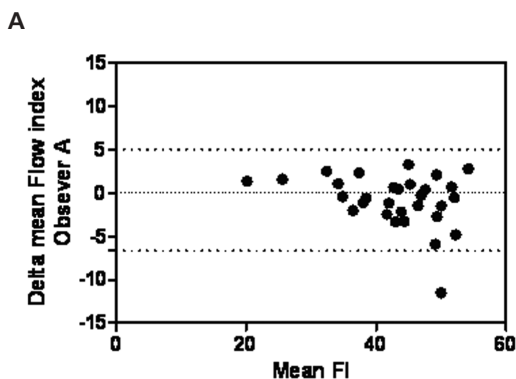
Discussion

The use of 3D sonographic measurements of placental volume and vascular indices has been proposed as a screening tool for adverse pregnancy outcomes fetal growth restriction and preeclampsia.<sup>13</sup> In a small study comparing the VI, FI, and VFI in 10 growth-restricted fetuses and 79 healthy controls, Noguchi et al<sup>10</sup> showed these indices to be significantly lower in the growth-restricted fetuses. Another study also showed altered placental vascular indices in pregnancies with low levels of pregnancy-associated plasma protein-A that resulted in adverse outcomes, including gestational hypertension, preeclampsia, and growth restriction.<sup>14</sup> Our study confirms that the measurements are highly reproducible. The intraobserver and interobserver CCs were

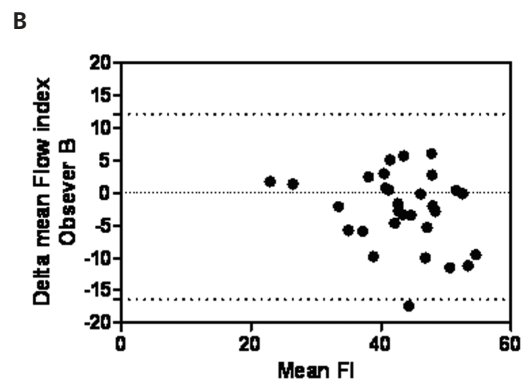
greater than 0.75 for most indices, with the exception of the VFI, which had a lower but acceptable interobserver CC. Despite some relatively wide limits of agreement in the intraobserver measurements for observer B, there was no significant systematic bias in any of the measurements because the biases were close to 0 (-0.3 to -2.6). The findings from this study are consistent with reports by other investigators validating the reproducibility of 3D sonographic measurements of placental volumes and vascular indices.<sup>1,8,9,15</sup>

The calculations of placental volumes by both observers showed the widest variability or limits of agreement. This was probably due to less-than-optimal distinction of the placental margins from the uterine walls. A similar finding was observed by Deurloo et al<sup>9</sup> in a study of the repro-

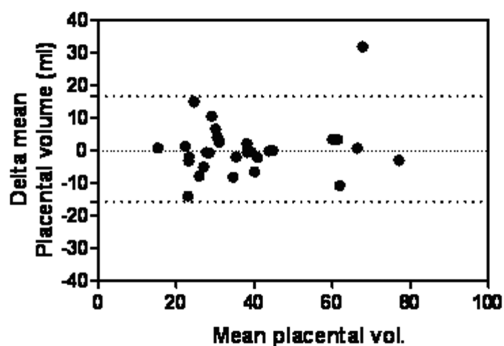
Figure 3. **A**, Bland-Altman plot of intraobserver differences for the FI of observer A. **B**, Bland-Altman plot of intraobserver differences for the FI of observer B.



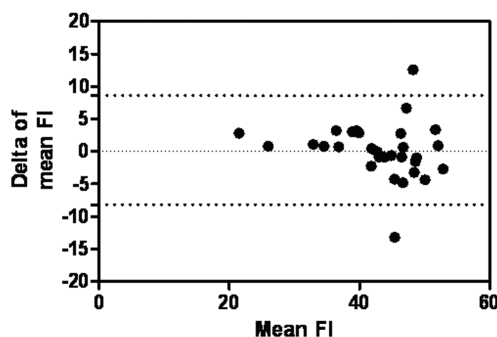
A



B



**Figure 4.** Bland-Altman plot of interobserver differences for placental volumes.



**Figure 6.** Bland-Altman plot of interobserver differences for the FI.

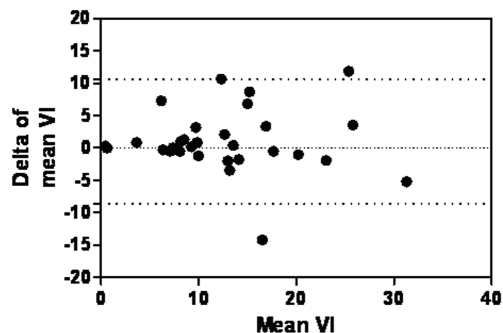
ducibility of placental volume measurements. The variability in measurements observed did not appear to be related to the level of experience of the sonographer/sonologist because observer B, who had longer experience (2 years) with these measurements, had wider limits of agreement compared with the 1 year of experience of observer A. This finding suggests a need for obtaining higher image quality with clearer margins of the placenta.

Our study was limited to the first trimester, during which the whole placental volume can be obtained. However, reports from other investigators also suggest that evaluation of sonographic biopsies of the placenta at other gestational age ranges is reproducible.<sup>7,9</sup> We limited our evaluation to the first trimester because this study was performed as a prelude to an ongoing study using

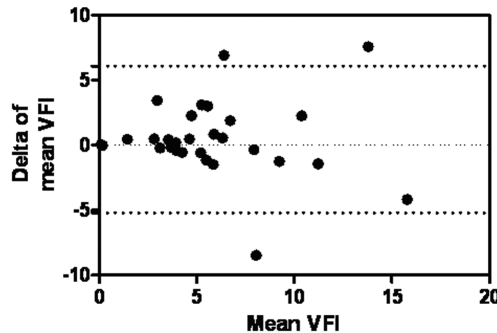
first-trimester placental volume and vasculature indices to predict adverse outcomes in the latter half of pregnancy. Another limitation of this study was in restricting the analysis to the reproducibility of the tracing and calculations of the volumes and vascular indices and not to the actual acquisition of the volumes. A previous study, however, showed that volumes acquired by different operators are reproducible.<sup>9</sup>

Our study findings provide validation of the technique, showing good reproducibility of the 3D power Doppler parameters when applied to the study of the placental volume and vascular tree. Future studies should address the reproducibility of these measurements using different ultrasound equipment across the same study population.

**Figure 5.** Bland-Altman plot of interobserver differences for the VI.



**Figure 7.** Bland-Altman plot of interobserver differences for the VFI.



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