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# Reproducibility of transvaginal three-dimensional endometrial volume measurements with virtual organ computer-aided analysis (VOCAL) during ovarian stimulation

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**KEYWORDS:** Endometrial volume, IVF, Reproducibility, Three-dimensional ultrasound, VOCAL

## ABSTRACT

***Objective*** *To calculate inter- and intraobserver reliabilities for three-dimensional endometrial volume measurements during* in vitro *fertilization using virtual organ computer-aided analysis (VOCAL™).*

***Patients and methods*** *Three-dimensional ultrasound measurements of the endometrium using VOCAL software were performed on the day of oocyte retrieval in each of 79 consecutive patients undergoing* in vitro *fertilization or intracytoplasmic sperm injection. Endometrial volume was calculated every 15° and every 30° by two different observers in order to determine the reproducibility of the technique.*

***Results*** *Intraobserver reliability for the 15° measurements was 0.97 for both observers; for the 30° measurements, it was 0.93 for one observer and 0.96 for the other. Interobserver reliability was 0.80 for the endometrial volumes calculated every 15° and 0.83 for the volumes calculated every 30°. The intra- and interobserver measurement agreement showed good reproducibility. However, the volumes calculated every 15° were more accurate because the means of differences were close to zero.*

***Conclusion*** *VOCAL provides a reproducible method for the estimation of the endometrial volume.*

## INTRODUCTION

Several investigators have suggested that endometrial thickness is a useful criterion in predicting embryo implantation success and pregnancy rate in patients undergoing *in vitro* fertilization (IVF)[1]. However, the relationship between endometrial thickness diagnosed by two-dimensional ultrasound and pregnancy rate is not universally accepted. In the meta-analysis reported by Friedler *et al.*[2] including 3558 cycles following ovarian stimulation for IVF and embryo transfer and 411 cycles with hormone replacement therapy for oocyte donation, sonographic parameters of the endometrium had a high negative predictive value and sensitivity but a limited positive predictive value and specificity. The conclusion of Friedler *et al.* was that the value of measuring the endometrium with ultrasound in assisted reproductive medicine as a prognostic indicator for implantation following embryo transfer has yet to be proved[2]. Calculation of the endometrial volume does not yet play an important role in infertility treatments. Three-dimensional (3D) ultrasound may, however, be a useful tool in reproductive medicine[3,4].

Before evaluating the clinical role of a measurement method, its reliability must be checked. Few studies describe the clinical implications of volume measurements with 3D ultrasound[5,6]. Only two studies have reported on calculating endometrium volumes, based on transvaginal 3D ultrasound in stimulated cycles[6,7]. None of these studies used virtual organ computer aided analysis (VOCAL™) PC-3D View (Kretz Technik AG, Zipf, Austria).

The aim of this study was to document the reliability of 3D ultrasound endometrial volume measurements using VOCAL.

## MATERIALS AND METHODS

One 3D endometrial measurement was performed on each of 79 consecutive infertile patients undergoing ovarian stimulation for IVF or intracytoplasmic sperm injection. In all cases the stimulation was carried out with the long protocol using a gonadotrophin releasing hormone agonist in association with recombinant follicle stimulating hormone (FSH). The 3D ultrasound measurements were performed on the day of oocyte retrieval. Each operator performed two measurements of surface geometry twice every 15° and every 30°. Each endometrial volume was calculated twice by each of the

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two observers. Endometrial volumes were measured on Plane B (which we assigned as the sagittal view of the uterus, Figure 1). The decision to take measurements every 15° and 30° was arbitrary.

To ensure statistical reliability, each operator worked separately and each measurement was taken in a series of planes. In all, surface geometry was measured 12 times for the measurements taken every 15° and six times for the measurements taken every 30°. Since ultrasound examinations were performed routinely, the study was not subject to institutional review board approval.

All 3D scans were obtained using the Voluson 530 D (Kretz Technik AG, Zipf, Austria) ultrasound machine with a transvaginal 5–7.5-MHz volume transducer. After ultrasonic investigation of uterine morphology, the uterus was visualized in B mode. Plane B was chosen in preference to Planes A and C for volume acquisition. The system was then switched into volume mode. After targeting the endometrium in a vertical plane by the volume box, the slow volume acquisition setting was activated. Volume data were captured by holding the transducer stationary while the crystal electronically swept through 95° for 2–3 s. All scanned volumes were stored on a 540MB hard disk with an integrated magnetic optical drive for later analysis and measurements. All volume measurements were calculated with the VOCAL software.

The basic principle of VOCAL is the combination of 3D ultrasound tissue presented as voxels and the geometric information of surfaces in a 3D dataset. The main advantage of VOCAL is the surface characterization. Calculation of the surface geometry is the first step of VOCAL. It is defined by rotating an image plane around a fixed axis (the main contour axis) and defining 2D contours on each plane. The 2D contours can be defined automatically (for prostate or breast lesions), manually, or by a sphere. For endometrial volume, the manual mode must be chosen because the automatic mode is unable to correctly perform a series of 2D contours. The rotation step for each contour plane is selectable in the range from 6 to 30°. Surface geometry is defined by 3D triangularization of the 2D contours, meaning that each point of the 2D contour in Plane X is connected via a triangle mesh to corresponding points in plane X – 1 and plane X + 1. The second step is the definition of a shell contour (geometry). This involves defining the thickness of the reference surface geometry. The parallel contours define surface geometries (describing the shell). The parallel contours are either defined symmetrically to the reference contour or limited to one direction, inside or outside. All measurements are performed using pixel resolution on the screen. All distances are calculated in screen coordinates. The accuracy of the method depends on the resolution of the Cartesian dataset and the magnification of the image on the screen. This means that highly magnified datasets lead to a finer resolution than less magnified datasets; a highly magnified image on the screen leads to more accurate measurements than a less magnified image.

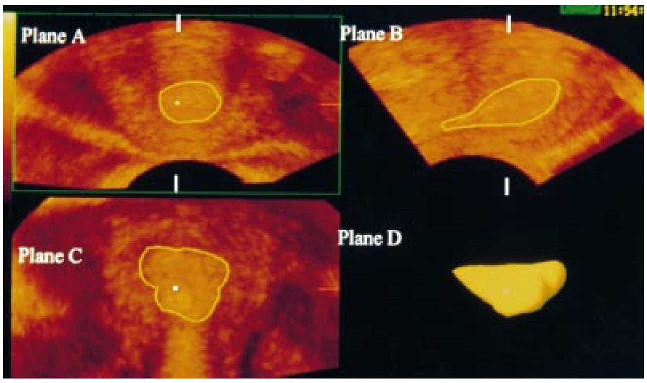


**Figure 1** Endometrial volume calculated with VOCAL. The resulting volume is shown in Plane D.

The overall accuracy depends on the accuracy of the ultrasound machine, the type of magnification of the volume dataset, and the type of magnification of the image on the screen. For distance and circumference measurements, the distance of screen points is calculated and converted to mm ultrasound units. For area measurements the area of the marked polygon points on the screen is calculated. The result is converted to $cm^2$ ultrasound units. Volume measurements are performed by integrating polygon areas marked in parallel planes. The result is converted to mL or $cm^3$ ultrasound units. VOCAL measurements are performed by integration of polygon areas generated by rotation via a fixed axis (rotation axis of contours). The method used for the integration of the polygon areas is given by:

$$\text{Volume} = \tfrac{1}{2}\left[\textstyle\sum_{i=2}^{n}(A_{i-1} + A_i) \cdot d_{i-1,i}\right],$$

where N is the number of marked polygon areas, $A_i$ is the polygon area in Plane I and $d_{i-1,i}$ is the distance between Planes i and j. The result is converted to mL or $cm^3$ ultrasound units.

The intraclass correlation method was used to express the inter- and intraobserver reliability index. The intraclass correlation coefficient is defined as the correlation between any two measurements on the same subject. Its values lie between 0 and 1, where 1 indicates total reliability. In this study it is a measure of correlation between the endometrial volume measurements obtained by any two randomly chosen observers on the same individual. To determine the extent of inter- and intraobserver measurement agreement we used the procedure proposed by Bland and Altman in 1986[8]. We calculated the limits of measurement agreement and plotted the difference against the mean of the measurements in order to visualize their accuracy.

## RESULTS

The patients' average (standard deviation (SD)) age was 35.06 ± 6.43 years. The average number (SD) of 75-IU ampoules of human menopausal gonadotrophin (hMG) administered was 28.6 ± 10.53. The average (SD) duration of stimulation was 11.2 ± 1.23 days. Figures 2–4 present the statistical data used to calculate the intraclass correlation coefficients. These data gave an intraobserver reliability index of 0.9754 for Observer 1 (Figure 2a), and 0.9683 for Observer 2 (Figure 3a) for the volume measurements made every 15°. For those made every 30°, the intraobserver reliability index was 0.9303 for Observer 1 (Figure 2b) and 0.9602 for Observer 2 (Figure 3b).

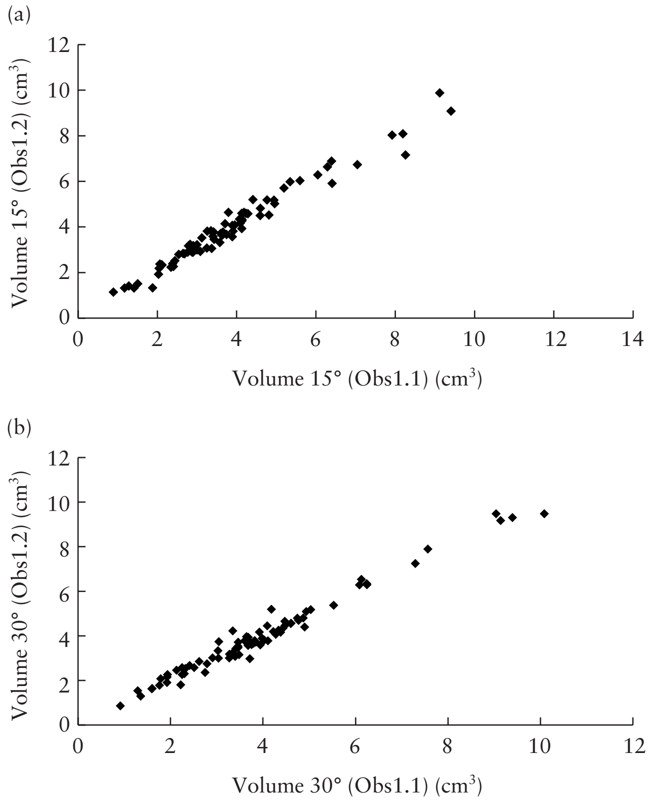


**Figure 2** Intraobserver reliability for Observer 1 at 15° ($y = 0.9869x + 0.1759$; $r^2 = 0.9754$) (a) and at 30° ($y = 0.1638x - 0.1627$; $r^2 = 0.9303$) (b).

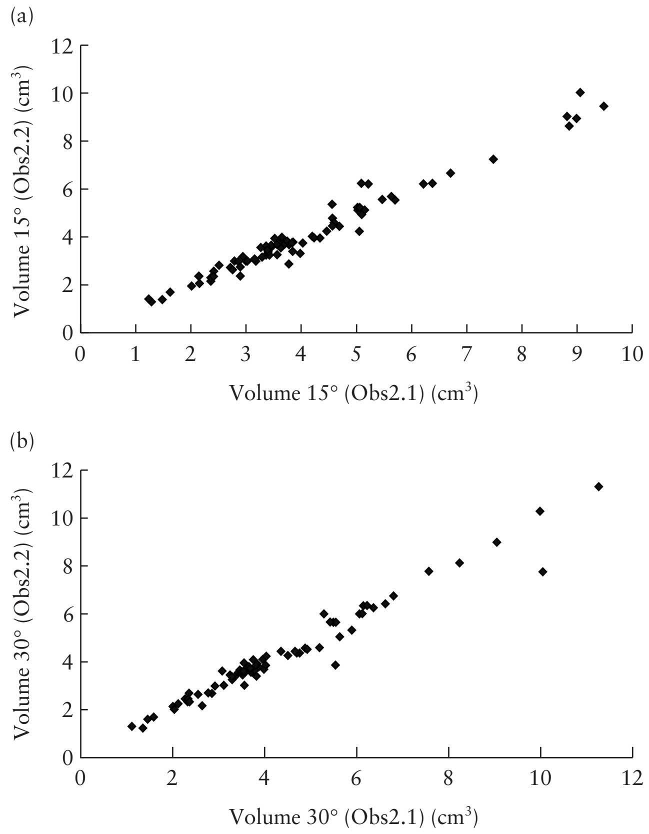


**Figure 3** Intraobserver reliability for Observer 2 at 15° ($y = 1.016x - 0.0606$; $r^2 = 0.9683$) (a) and at 30° ($y = 0.9391x + 0.1972$; $r^2 = 0.9602$) (b).

Table 1 shows the intraobserver measurement agreement calculated every 15° and 30°. The measurements agreed almost exactly. The difference in mean measurements was approximately 0 in all cases as the limits of agreements were small enough to demonstrate good reproducibility.

The interobserver reliability index between the two observers was 0.8008 for the endometrial volumes calculated every 15° and 0.8345 for the volumes calculated every 30° (Figure 4). Table 2 shows the interobserver agreement. The interobserver measurements agreed almost exactly. However, the measurements obtained with the 15° procedure seemed to be more accurate because the mean of difference was closer to zero (Figure 5).

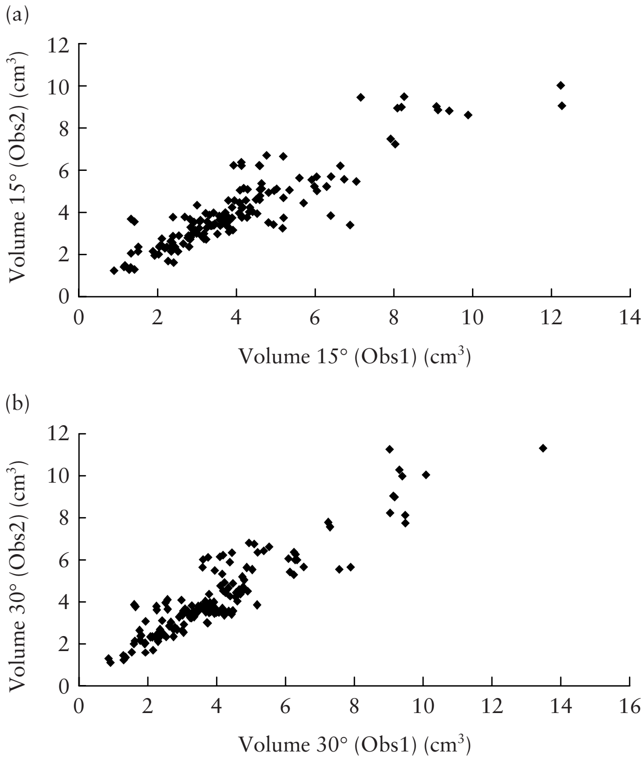


**Figure 4** Interobserver reliability at 15° ($y = 1.8146x + 0.791$; $r^2 = 0.8008$) (a) and at 30° ($y = 0.8761x + 0.6872$; $r^2 = 0.8345$) (b).

**Table 1** Intraobserver repeatability of the measurements

| | *Mean* | *SD* | *SEM* | *95% CI* |
|---|---|---|---|---|
| 15° measurement | | | | |
| Diff: Observer 1 | −0.12 | 0.31 | 0.04 | −0.05 to −0.19 |
| Mean + 2SD | 0.5 | | 0.06 | 0.62 to 0.38 |
| Mean − 2SD | −0.75 | | 0.06 | −0.63 to −0.87 |
| Diff: Observer 2 | −0.09 | 0.57 | 0.06 | 0.04 to −0.22 |
| Mean + 2SD | 1.06 | | 0.11 | 1.28 to 0.84 |
| Mean − 2SD | −1.24 | | 0.11 | −1.02 to −1.46 |
| 30° measurement | | | | |
| Diff: Observer 1 | 0.00 | 0.33 | 0.04 | 0.07 to −0.08 |
| Mean + 2SD | 0.65 | | 0.06 | 0.78 to 0.53 |
| Mean − 2SD | −0.66 | | 0.06 | −0.54 to −0.79 |
| Diff: Observer 2 | 0.06 | 0.40 | 0.04 | 0.15 to −0.03 |
| Mean + 2SD | 0.86 | | 0.08 | 1.01 to 0.71 |
| Mean − 2SD | −0.73 | | 0.08 | −0.58 to −0.89 |

SD, standard deviation; SEM, standard error of mean; CI, confidence interval; Diff, difference between measurements.

## DISCUSSION

The use of 3D ultrasound remains limited in gynecology. Lee *et al.* measured changes of the endometrial volume in the menstrual cycle[9]. The changes of the uterus–endometrium volume ratio showed a good correlation with the day of the menstrual cycle. However, Lee *et al.* did not give information on the clinical impact of endometrium volume estimation[10]. Three-dimensional ultrasound has been reported to be accurate for an irregularly shaped object and ovarian volume[11,12]. This method spontaneously measures a third plane (the frontal plane, i.e. the depth or diameter from right to left). The frontal plane identifies, for example, uterine malformations with greater precision.

The full planar method is the best method for 3D ultrasound volume measurement, as previously described by Yaman *et al.*[12]. In their experience, the full planar method had high inter- and intraobserver reliability. Kretz Technik's VOCAL software automates volume measurements of structures such as the endometrium. Intraobserver reliability was satisfactory for measurements calculated every 15° and every 30°. However, the better observer agreement was observed for the measurements obtained every 15°. Our statistical analysis supports the work of Yaman *et al.*[12]. The average number of parallel sections for the full planar measurements in their study was 11.04 ± 2.4 for the first observer and 8.87 ± 3.2 for the second observer[12]. The VOCAL system, for the measurements every 30°, needs only six measurements to be made, while 12 parallel cross sections are necessary for a measurement every 15°. The diminution of interobserver statistical correlation at 30° may be explained by the insufficient number of measurements.

With VOCAL, calculating the volume of asymmetric endometria with a poorly contrasted myometrium posed no problems. The software allowed for varying the contrast between the myometrium and the endometrium to permit identification of the contour of the endometrium (Figure 1). The software also allowed the visualization of the calculated volume to ensure that the tracing was correctly performed (Figure 1). In all cases, it was possible to identify the internal

**Table 2** Interobserver measurement agreement

| | *Mean* | *SD* | *SEM* | *95% CI* |
|---|---|---|---|---|
| 15° measurement | | | | |
| *Study 1* | | | | |
| Observer 1 − Observer 2 | 0.01 | 0.87 | 0.10 | 0.20 to −0.18 |
| Mean + 2SD | 1.75 | | 0.17 | 2.09 to 1.42 |
| Mean − 2SD | −1.73 | | 0.17 | −1.40 to −2.07 |
| *Study 2* | | | | |
| Observer 1 − Observer 2 | −0.02 | 0.90 | 0.10 | 0.18 to −0.21 |
| Mean + 2SD | 1.79 | | 0.18 | 2.13 to 1.44 |
| Mean − 2SD | −1.82 | | 0.18 | −1.47 to −2.16 |
| 30° measurement | | | | |
| *Study 1* | | | | |
| Observer 1 − Observer 2 | 0.26 | 0.80 | 0.09 | 0.44 to 0.09 |
| Mean + 2SD | 1.86 | | 0.16 | 2.16 to 1.56 |
| Mean − 2SD | −1.33 | | 0.16 | −1.03 to −1.64 |
| *Study 2* | | | | |
| Observer 1 − Observer 2 | 0.11 | 0.85 | 0.10 | 0.30 to −0.08 |
| Mean + 2SD | 1.82 | | 0.17 | 2.15 to 1.49 |
| Mean − 2SD | −1.60 | | 0.17 | −1.27 to −1.92 |

SD, standard deviation; SEM, standard error of mean; CI, confidence interval.

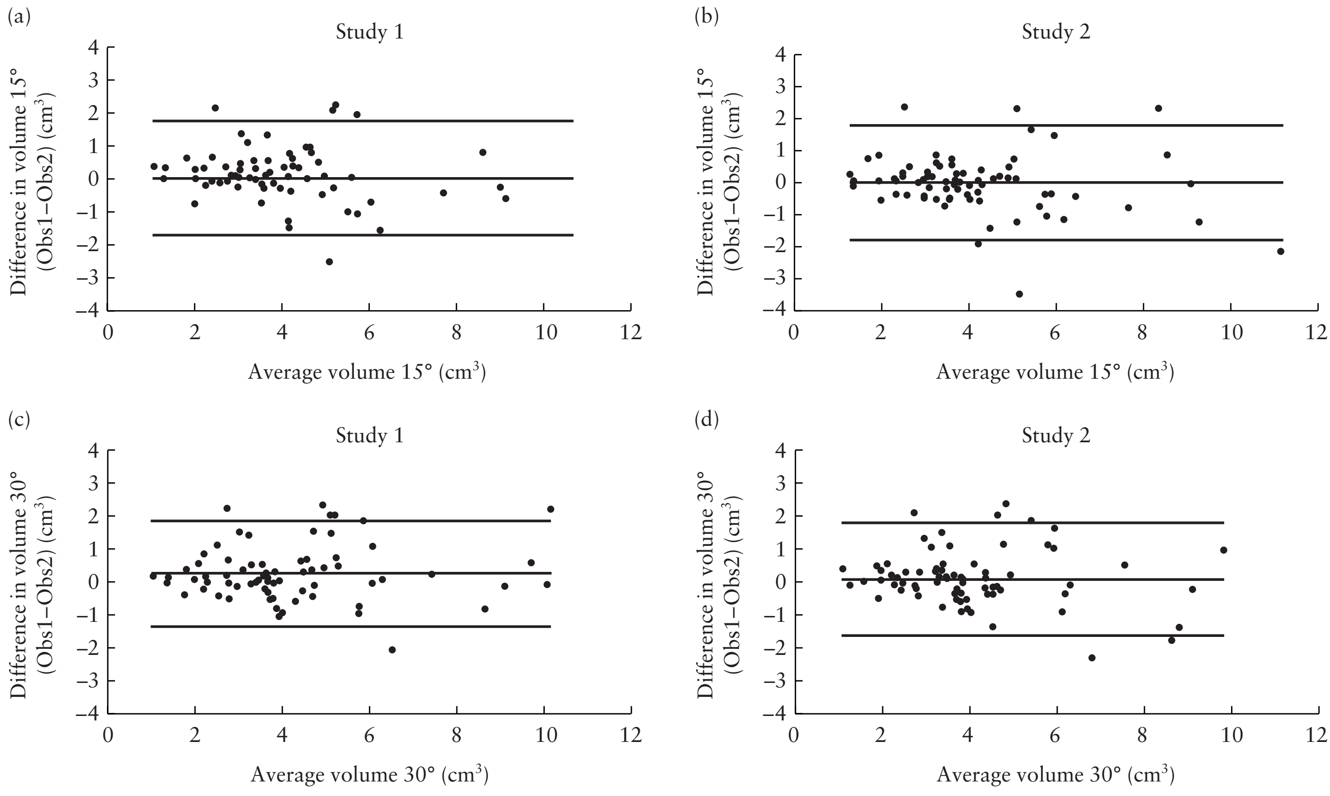


**Figure 5** Difference against the mean for each observer and volume: 15° for Study 1 (a) and Study 2 (b) and 30° for Study 1 (c) and Study 2 (d).

os for the measurements of endometrial length on the vertical plane. Yaman *et al.* reported how important it was to identify the internal os to obtain reliable volume measurements. In their experience, the full planar method was more reliable, because first of all, several parallel sections could be measured consecutively, and secondly, the internal os could be identified on several sections, limiting the risk of error. However, they found that the full planar method took three times as long to perform, the greatest drawback of this method in their view.

The VOCAL software offers several advantages with regards to the manual method described by Yaman *et al.*[12]. Volume measurements are rapid with the VOCAL software, even when taking a measurement every 15°. The calculation of endometrial volume takes only a few minutes. After defining the contour of the images on all planes, VOCAL shows the volume results calculated in the lower right-hand portion of the image. The contour is drawn on all three planes; combined with the result this verifies the quality of the image obtained and thus the value for endometrial volume obtained.

Uterine receptivity to the embryo is vital for implantation. Several ultrasound parameters to determine receptivity such as the thickness and the aspect of the endometrium and the uterine pulsatility index have been suggested[6,7]. Calculation of the endometrial volume has until now been difficult with two-dimensional ultrasound. It is still too early to come to decisive conclusions as to the place endometrial volume could take in evaluating uterine receptivity. Publications on endometrial volume in IVF are as yet too few and contradictory. However, the ability of the VOCAL software to quantify the endometrial volume using 3D ultrasound could improve the prediction of pregnancy in assisted reproduction treatment.

The VOCAL system estimates the volume of the endometrium during ovarian stimulation, with good reliability and rapidity. Determining the importance of estimating endometrial volume with transvaginal 3D ultrasound requires future clinical studies in IVF.

## REFERENCES


1 Imoedemhe DA, Shaw RW, Kirkland A, Chan R. Ultrasound measurement of endometrial thickness on different ovarian stimulation regimens during in-vitro fertilization. *Hum Reprod* 1987; 2: 545–7
2 Friedler S, Schenker JG, Herman A, Lewin A. The role of ultrasonography in the evaluation of endometrial receptivity following assisted reproductive treatments: a critical review. *Hum Reprod Update* 1996; 2: 323–35
3 Tan SL. Clinical applications of Doppler and three-dimensional ultrasound in assisted reproductive technology. *Ultrasound Obstet Gynecol* 1999; 13: 153–6
4 Kupesic S. The present and future role of three-dimensional ultrasound in assisted conception. *Ultrasound Obstet Gynecol* 2001; 18: 191–4
5 Brunner M, Obruca A, Bauer P, Feichtinger W. Clinical application of volume estimation based on three-dimensional ultrasonography. *Ultrasound Obstet Gynecol* 1995; 6: 358–61
6 Schild RL, Indefrei D, Eschweiler S, Van der Ven H, Fimmers R, Hansmann M. Three-dimensional endometrial volume calculation and pregnancy rate in an in-vitro fertilization programme. *Hum Reprod* 1999; 14: 1255–8
7 Raga F, Bonilla-Musoles F, Casan EM, Klein O, Bonilla F. Assessment of endometrial volume by three-dimensional ultrasound prior to embryo transfer: clues to endometrial receptivity. *Hum Reprod* 1999; 14: 2851–4
8 Bland JM, Altman DG. Statistical methods for assessing agreement between two methods of clinical measurement. *Lancet* 1986; 1: 307–10
9 Lee A, Sator M, Kratochwil A, Deutinger J, Vytiska-Binsdorfer E, Bernaschek G. Endometrial volume change during spontaneous menstrual cycles: volumetry by transvaginal three-dimensional ultrasound. *Fertil Steril* 1997; 68: 831–5
10 Riccabona M, Nelson TR, Pretorius DH. Three-dimensional ultrasound: accuracy of distance and volume measurements. *Ultrasound Obstet Gynecol* 1996; 7: 429–34
11 Kyei-Mensah A, Maconochie N, Zaidi J, Pittrof R, Campbell S, Tan SL. Transvaginal three-dimensional ultrasound: reproducibility of ovarian and endometrial volume measurements. *Fertil Steril* 1996; 66: 718–22
12 Yaman C, Sommergruber M, Ebner T, Polz W, Moser M, Tews G. Reproducibility of transvaginal three-dimensional endometrial volume measurements during ovarian stimulation. *Hum Reprod* 1999; 14: 2604–8