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ORIGINAL ARTICLE

The feasibility of using 5D CNS software in obtaining standard fetal head measurements from volumes acquired by three-dimensional ultrasonography: comparison with two-dimensional ultrasound

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Abstract

Objective: To evaluate the performance of a new software (5D CNS) developed to automatically recognize the axial planes of the fetal brain from three-dimensional volumes and to obtain the basic standard biometric measurements. The accuracy, reproducibility, and time required for analysis of 5D CNS were compared with that of two-dimensional (2D) ultrasound.
Methods: This was a prospective study of 120 uncomplicated singleton pregnancies undergoing routine second trimester examination. For every pregnancy standard biometric measurements including biparietal diameter, head circumference, distal lateral ventricle width, transverse cerebellar diameter and cisterna magna width were obtained using 2D ultrasound and three-dimensional (3D) ultrasound with 5D CNS software. Reliability and agreement of the two techniques were evaluated using intraclass correlation coefficients (ICCs) and proportionate Bland–Altman plots were constructed. The time necessary to complete the measurements with either technique was compared and intraobserver and interobserver agreements of measurements calculated.
Results: In 118/120 (98.3%), 5D CNS successfully reconstructed the axial diagnostic planes and calculated all the basic biometric head and brain measurements. The agreement between the two techniques was high for all the measurements considered (all ICCS $>$ 0.920). The time necessary to measure the biometric variables considered was significantly shorter with 5D CNS (54 versus 115 s, $p < 0.0001$) than with 2D ultrasonography. No significant differences were found in 5D CNS repeated measurements obtained either by the same observer or by two independent observers.
Conclusion: 5D CNS software allows us to obtain reliable biometric measurements of the fetal brain and to reduce the examination time. Its application may improve work-flow efficiency in ultrasonographic practices

Keywords

Automatic measurement software, fetal brain, fetal biometry, 3D ultrasound

History

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Introduction

Central nervous system (CNS) malformations are among the most common defects in the human fetus and affect approximately 0.3–1% of live births [1,2]. Prenatal detection and accurate definition of CNS malformations are important since these anomalies frequently have a severe prognosis and in many cases are associated with a genetic syndrome [2].

Transabdominal two-dimensional (2D) ultrasonography is the technique of choice to investigate fetal CNS during the second trimester of gestation in low risk pregnancies. The examination should include the recognition of three axial planes, namely the trans-thalamic, the trans-ventricular, and the trans-cerebellar planes, and the acquisition of several biometric measurements of both the fetal skull and the basic brain structures [3].

The quality and the efficiency of these measurements mainly rely on the skill and experience of the sonographer. For beginners, fetal biometry using real-time 2D ultrasound can take a long time because of the difficulties in obtaining image planes appropriate for the measurements [4–7]. The use of three-dimensional (3D) ultrasound has been suggested to overcome these difficulties [8,9]. Indeed 3D allows examiners to acquire volume datasets of the fetal head and to visualize brain structures of interest using multiplanar displays [10–13]. However, this approach requires the manual ''navigation'' by the operator in the volume acquired, necessitating specific operator experience and skill in 3D orientation and in the subsequent retrieval of the diagnostic planes, thus limiting up to now its clinical use.

To overcome these limitation 5D CNS software (Samsung Electronics Co. Ltd., Suwon, South Korea) has been recently developed. This software analyzes 3D fetal brain volumes

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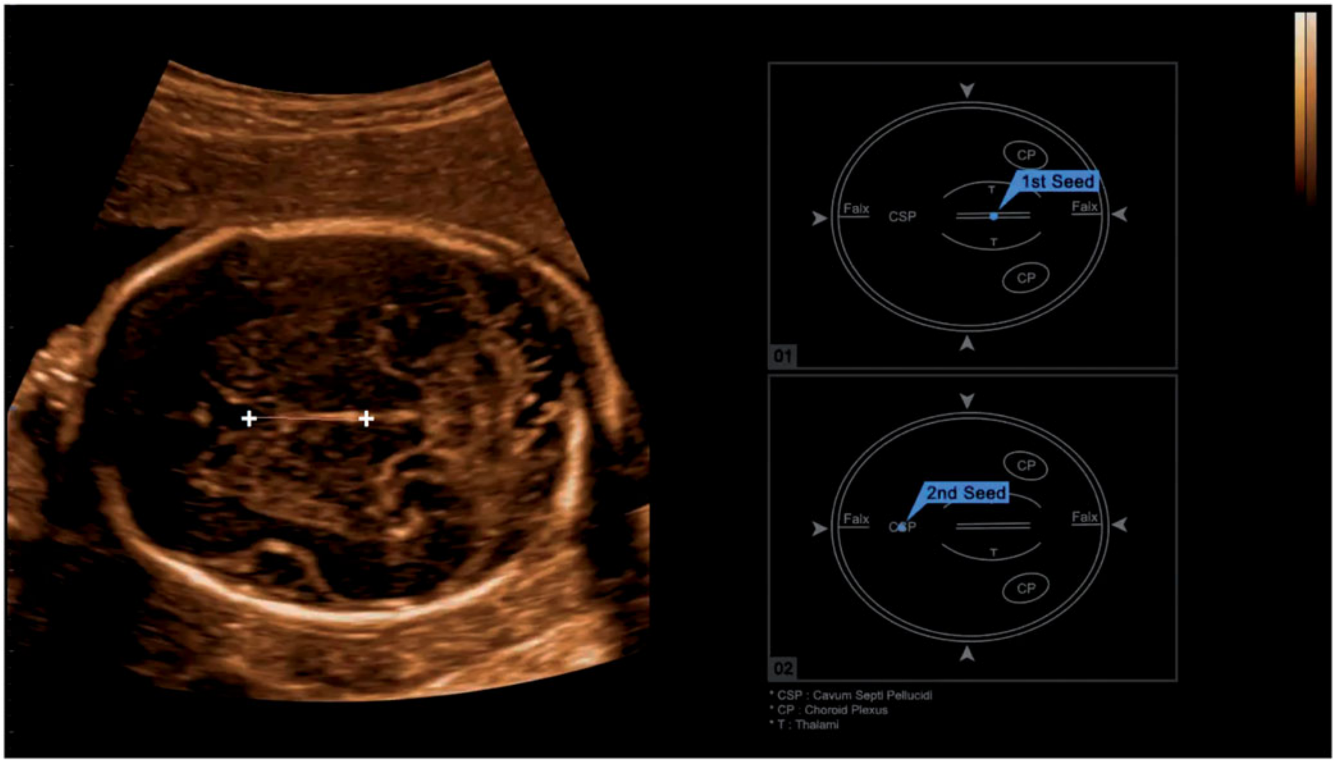

Figure 1. Starting of the 5D CNS software in a fetus at 21 weeks of gestation. Two marker points (+) are placed in the middle of the thalami and in the cavum septi pellucidum.

acquired from a 2D axial trans-thalamic plane and automatically reconstructs the three axial planes of the fetal head and then performs all the measurements required for the routine assessment of CNS during second trimester ultrasound.

The objectives of this study were (1) to evaluate the efficacy of 5D CNS to obtain basic biometric measurements of the fetal brain in a clinical setting; (2) to test the agreements for biometric measurements of the fetal head structures using 2D and 5D CNS, and (3) to compare the time required to complete the CNS measurements using either methods.

Methods

This was a prospective cross-sectional study on 120 consecutive low-risk pregnancies undergoing routine second trimester ultrasonographic examinations. All the pregnancies were singleton, accurately dated by first trimester ultrasonographic examination and all the fetuses were free from structural or chromosomal anomalies. Exclusion criteria were the lack of follow-up on pregnancy outcome and delivery. This research project was approved by our institutional review board and all the women provided written informed consent to participate to the study.

All examinations were performed using the WS80A Elite ultrasound equipment (Samsung Medison Co., Ltd, Seoul, South Korea) with a 1–8 MHz transabdominal volumetric probe.

A single operator (G. R.) performed the examinations of the fetal brain using 2D ultrasound and the three standard diagnostic axial planes were acquired. The biparietal diameter (BPD) and the head circumference (HC) were measured from the trans-thalamic plane. The distal posterior lateral ventricle (VP) width was obtained from the trans-ventricular plane while the transverse cerebellar diameter (TCD) and the cisterna magna (CM) width were assessed from the trans-cerebellar plane following standard techniques [14]. The BPD was measured at the level of the thalami from the outer to the inner edge of the fetal skull. The time elapsing between the acquisition of the first brain plane and the last brain measurement was recorded.

Immediately after the standard 2D brain examination a volume was acquired using a previously reported technique [15] starting with a transverse view of the fetal head at the level of the trans-thalamic axial plane. In order to include the entire fetal brain within the volume, the sweep acquisition angle was set between 45° and 60° according to the gestational age. Volumes were acquired during fetal rest and maternal apnea in an ‘‘extreme’’ quality mode. The 5D CNS function was then activated and two reference points were manually placed, respectively, in the middle of the thalami and in the cavum septi pellucidum (CSP) (Figure 1). The software then automatically reconstructed the three axial planes and performed the same head and brain measurements as those previously done by 2D ultrasound (Figure 2) (Video 1). The time interval elapsing between the end of 2D brain examination and the end of 3D analysis was also noted. Video 1 shows an example of how the software works.

In order to assess the intraobserver variability of 2D and 3D techniques, in 20 fetuses, the brain measurements were obtained twice by repeating the examinations at the end the ultrasound session. Furthermore to assess interobserver variability a second operator, blinded of the measurements

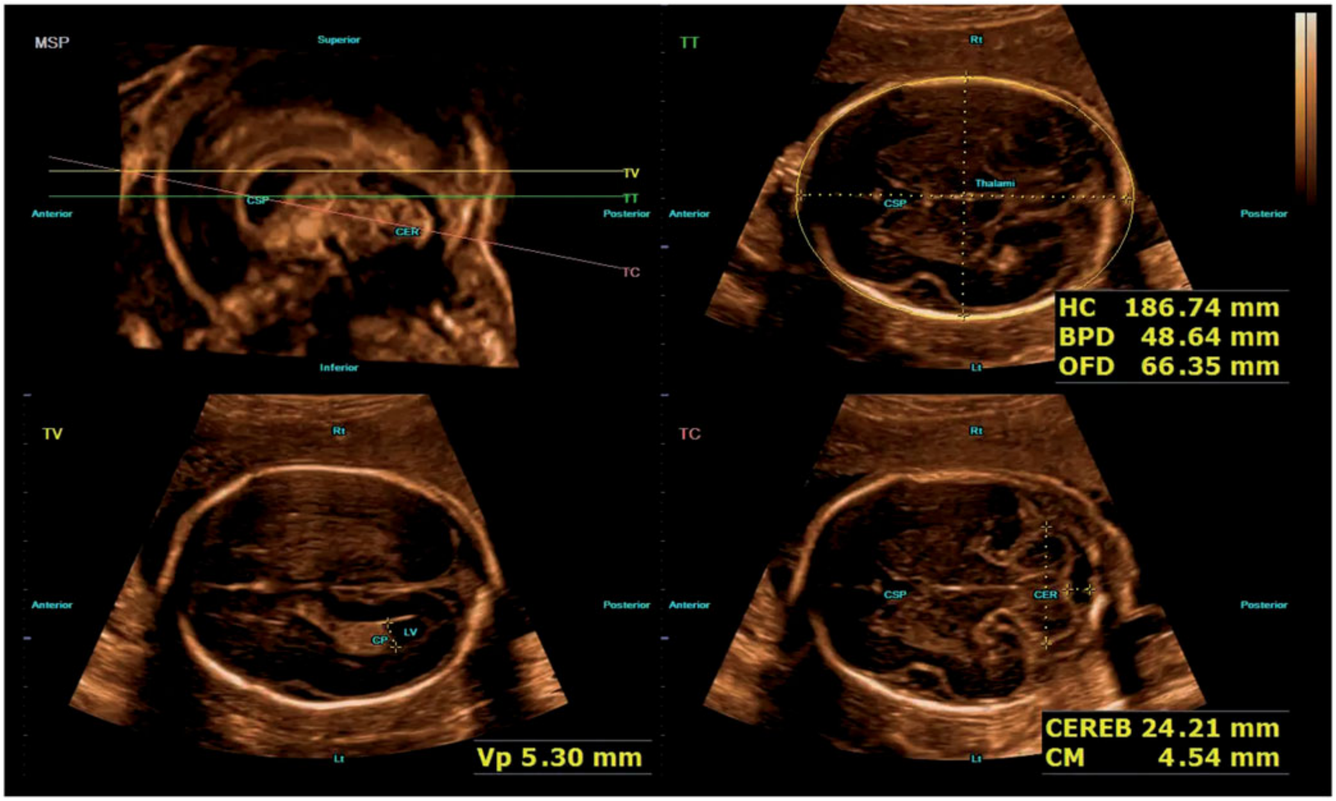

Figure 2. Final output of the 5D CNS software. The three standard diagnostic axial planes are visualized (trans-thalamic, TT; trans-ventricular, TV; trans-cerebellar, TC) and the biometric measurement displayed. The BPD was automatically measured at the level of the trans-thalamic plane from the outer to the inner edge of the fetal skull.

obtained by the first operator, performed the CNS measurements with both techniques on a second set of 20 fetuses.

The agreement between 2D ultrasound and 5D CNS measurements of fetal head was compared using the interclass coefficient of variations (ICCs). The limits of agreement and the under or over estimations of 5D CNS compared with 2D ultrasound were calculated as described by Bland and Altman [16]. The time required to obtain all the brain measurements with the two techniques was evaluated and differences analyzed by the Mann–Whitney *U* test. To quantify the intraobserver and interobserver agreements, the ICCs were assessed and the Bland–Altman plots constructed. A *p* value < 0.05 was considered to be statistically significant.

Results

The general characteristics of the population studied are reported in Table 1. In all the cases, the full set of 2D measurements of the fetal brain and the 3D volumes were obtained. 5D CNS proved to be successful in analyzing the volumes acquired in 118 of 120 pregnancies (98.3%), while in the remaining two cases, the software failed to recognize the axial planes. The reason of these unsuccessful analyses was the low quality of the volumes that did not allow a clear identification of the CSP. Both pregnancies had a body mass index (BMI) > 35 kg/m^2.

A high degree of reliability was observed between 2D and 5D CNS measurements for BPD (ICC 0.974 95% CI 0.946–0.992), HC (ICC 0.981 95% CI 0.973–0.987), VP (ICC 0.926 95% CI 0.895–0.971), TCD (ICC 0.944 95% CI 0.920–0.961), and CM (ICC 0.926 95% CI 0.905–0.983).

Table 1. General characteristic of the study population.

Variable	Mean±SD or median (range)
Maternal age (years)	31 (16–42)
Gestational age at ultrasound examination (weeks)	21.0 ± 1.56
Maternal Body Mass Index (kg/m^2)	24 (16 ± 39)
Gestational age at delivery (weeks)	40.2 ± 1.33
Birthweight (g)	3250 ± 389

Data are expressed as mean±SD or median range according to their distribution.

Figure 3 displays the Bland–Altman plots for the mean difference and the 95% limits of agreement between 2D and 5D CNS measurements. The average time required to analyze the fetal head with 5D CNS was 54 s (range 34–74) which resulted significantly shorter than the 115 s (range 65–180) necessary to obtain the same measurements with 2D ultrasound technique (U 164; *z* 12.96, $p < 0.0001$).

In Tables 2 and 3, the intra- and inter-observer agreements are reported for both 2D and 5D CNS. The standard deviations (SD) of the 2D measurements were slightly larger than those of 5D CNS measurements. Similarly, the ICC resulted higher for 5D CNS than for 2D measurements.

Discussion

Our study demonstrated that automatic measurements of the fetal brain may be obtained in 98% of pregnancies undergoing routine second trimester ultrasonographic examination. The

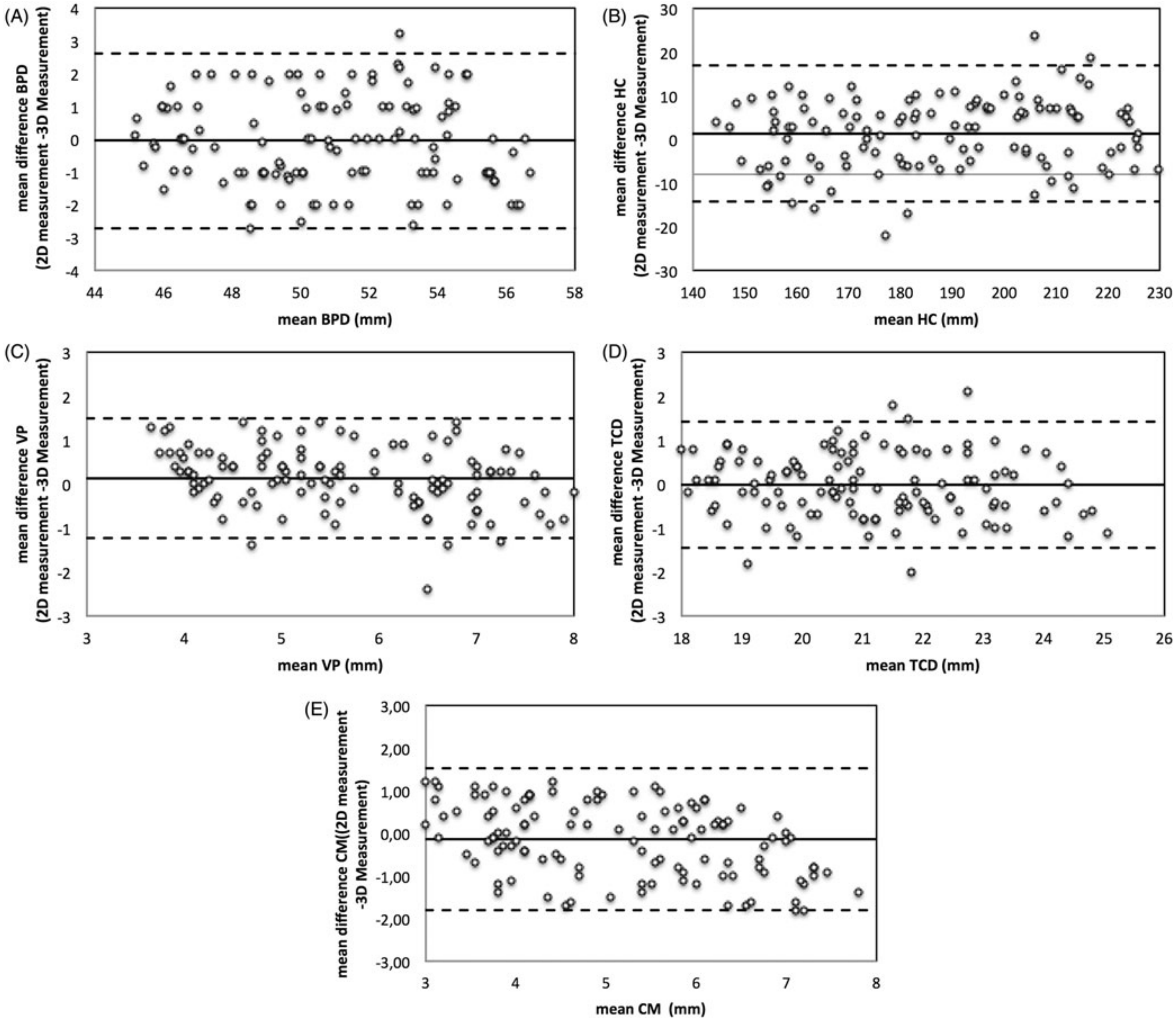

Figure 3. Bland–Altman plots of differences (mm) against mean for measurement of fetal brain obtained by 3D ultransonography (5D CNS software) and 2D ultrasonography with mean and 95% limits of agreement indicated. (A) Biparietal diameter (BPD); (B) head circumference (HC); (C) distal posterior lateral ventricle (VP) width; (D) transverse cerebellar diameter (TCD); (E) cisterna magna (CM) width.

data from this study also evidenced that the measurements automatically obtained by 5D CNS correlated well with those obtained manually by 2D ultrasound. Finally, the head measurements are obtained significantly faster with 5D CNS software than with the conventional 2D manual approach.

The acquisition of accurate biometric measurements of the fetal head is of paramount clinical importance, since we rely on these measurements to confirm gestational age, to evaluate fetal growth and to assess the normal development of the fetal brain. With current 2D ultrasonographic technology the quality of the examination is dependent on two steps: first acquisition of the correct diagnostic plane and second the proper placement the calipers on frozen images. The efficiency of both steps is mainly secondary to the skill and experience of the sonographer.

Softwares that able to automatically assess fetal biometry on frozen 2D images have been developed in the past, and there are evidences that their use may decrease the intra and inter observer variability and reduce the time required to perform the measurements [17,18]. However, the efficiency of these softwares is dependent on the quality of the 2D images acquired. 3D ultrasound has the potential to facilitate the sonographer in obtaining adequate diagnostic planes [8]. Indeed, this technique allows us to acquire volumes containing all the fetal brain and these volumes can subsequently be reviewed offline to recreate the standard planes necessary for a complete study of the fetal brain. Although several algorithms for the 3D reconstruction of the fetal brain have been developed [10–13], these approaches require operator's manual ''navigation'' in the volume acquired, thus necessitating specific experience and skill in 3D orientation and subsequent retrieval of the diagnostic planes.

The 5D CNS software may overcome all these limitations by combining an algorithm that automatically displays the three basic diagnostic brain axial planes with an automatic biometric measurement system. The results obtained in this study support its potential application in a clinical setting.

Table 2. Intraobserver variability for fetal brain biometric measurements by 2D ultrasound and 5D CNS softwareon 3D brain volume assessed using intraclass correlation coefficients and mean differences.

Variable	2D		5 CNS	
	ICC (95% CI)	Mean difference (SD)	ICC (95% CI)	Mean difference (SD)
BPD	0.996 (0.995–0.997)	0.12(1.04)	0.998 (0.996–0.999)	0.2 (0.94)
HC	0.995 (0.994–0.996)	−0.74 (3.24)	0.997 (0.995–0.998)	0.14 (3.13)
LVW	0.993 (0.991–0.995)	0.6 (1.11)	0.994 (0.991–0.996)	−0.34 (0.71)
TCD	0.994 (0.992–0.996)	−0.51 (0.88)	0.995 (0.993–0.995)	0.27 (0.77)
CM	0.990 (0.988–0.994)	0.61 (0.78)	0.991 (0.989-0.993)	−0.29 (0,76)

Table 3. Interobserver variability for fetal brain biometric measurements by 2D ultrasound and 5D CNS software on 3D brain volume assessed using intraclass correlation coefficients and mean differences.

Variable	2D		5 CNS	
	ICC (95% CI)	Mean difference (SD)	ICC (95% CI)	Mean difference (95% SD)
BPD	0.993 (0.989–0.997)	−0.23(1.41)	0.997 (0.995–0.999)	0.2 (0.94)
HC	0.992 (0.987–0.994)	0.94 (4.12)	0.996 (0.9994–0.998)	0.14 (3.13)
LVW	0.990 (0.985–0.993)	−0.8 (123)	0.993 (0.985–0.993)	0.29 (0.82)
TCD	0.992 (0.988–0.995)	−0.73 (0,96)	0.994 (0.992–0.997)	−0.28 (,94)
CM	0.988 (0.985–0.993)	0.73 (0,89)	0.990 (0.988–0.992)	0.33 (0,83)

The limitation of 5D CNS software in obese pregnancies should be acknowledged. Indeed, in two women with BMI > 35, 5D software failed in reconstructing the basic axial planes. These findings suggest that similar to conventional 2D ultrasound imaging 5D is susceptible as to the limitations in scanning windows.

A limitation of this study is that the CNS volume datasets were acquired by an operator with expertise in fetal CNS whose skill may be higher than that of the average sonographer. As a consequence, the success rate in acquiring CNS volumes may be lower in datasets acquired in peripheral centers during routine second trimester ultrasonographic examinations. However, recent data, on volumes obtained from fetal brain by operators performing routine second trimester ultrasound screening, suggest that more than 90% of datasets showed a quality high enough to allow satisfactory basic diagnostic brain views [19]. A further limitation of this software is its inability in the current version to display sagittal and coronal planes thus not allowing us to perform extended brain examination.

In conclusion, 5D CNS reduces the examination time necessary for basic standard measurements of the fetal brain. This approach may improve the work-flow efficiency in second trimester ultrasound examination and may facilitate less experienced operators to perform the basic study of the fetal brain.

Declaration of interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of this article.

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Supplementary material available online