5D CNS+ Software for Automatically Imaging Axial, Sagittal, and Coronal Planes of Normal and Abnormal Second-Trimester Fetal Brains

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The purpose of this study was to test new 5D CNS+ software (Samsung Medison Co, Ltd, Seoul, Korea), which is designed to image axial, sagittal, and coronal planes of the fetal brain from volumes obtained by 3-dimensional sonography. The study consisted of 2 different steps. First in a prospective study, 3-dimensional fetal brain volumes were acquired in 183 normal consecutive singleton pregnancies undergoing routine sonographic examinations at 18 to 24 weeks' gestation. The 5D CNS+ software was applied, and the percentage of adequate visualization of brain diagnostic planes was evaluated by 2 independent observers. In the second step, the software was also tested in 22 fetuses with cerebral anomalies. In 180 of 183 fetuses (98.4%), 5D CNS+ successfully reconstructed all of the diagnostic planes. Using the software on healthy fetuses, the observers acknowledged the presence of diagnostic images with visualization rates ranging from 97.7% to 99.4% for axial planes, 94.4% to 97.7% for sagittal planes, and 92.2% to 97.2% for coronal planes. The Cohen κ coefficient was analyzed to evaluate the agreement rates between the observers and resulted in values of 0.96 or greater for axial planes, 0.90 or greater for sagittal planes, and 0.89 or greater for coronal planes. All 22 fetuses with brain anomalies were identified among a series that also included healthy fetuses, and in 21 of the 22 cases, a correct diagnosis was made. 5D CNS+ was efficient in successfully imaging standard axial, sagittal, and coronal planes of the fetal brain. This approach may simplify the examination of the fetal central nervous system and reduce operator dependency.

Key Words—automatic software; central nervous system defects; fetal brain; obstetric ultrasound; prenatal diagnosis; 3-dimensional sonography

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Abbreviations

CNS, central nervous system; 3D, 3-dimensional; 2D, 2-dimensional

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Approximately 0.3% to 1% of neonates are affected by central nervous system (CNS) malformations.[1,2] Their prenatal diagnosis is of clinical interest, since these anomalies frequently have a severe prognosis and are often associated with an abnormal karyotype, genetic syndromes, and disabilities.[2]

Despite the relatively high prevalence of CNS anomalies and the importance of their prenatal diagnosis, the efficacy of screening programs is still far from reaching satisfactory results, especially when the investigation of the fetal brain is limited to the axial planes.[3] An extended study of fetal brain anatomy that also considers sagittal and coronal planes of the fetal brain is likely to improve the diagnostic efficacy.[4,5] However, an experienced operator is necessary to obtain sagittal and coronal imaging of the fetal CNS, thus limiting routine application of this approach.[5]

Three-dimensional (3D) sonography has recently been suggested as a tool that is able to reduce operator dependency.[6,7] Indeed, this technique allows acquisition of volumes containing most of the anatomic information, and these volumes can subsequently be reviewed offline to recreate the planes necessary for an extended study of the fetal CNS.[8,9]

Several algorithms have been developed to allow 3D reconstruction of the fetal brain.[10–16] Indeed, using an algorithm based on OmniView technology (GE Healthcare, Kretztechnik, Zipf, Austria), we demonstrated how it is possible to reconstruct coronal and sagittal images from brain volumes acquired from an axial plane.[12] However, this approach requires the operator's manual "navigation" in the volume acquired, thus requiring experience and skill in 3D orientation to allow the retrieval of the diagnostic planes.

To overcome these limitations, 5D CNS+ software (Samsung Medison Co, Ltd, Seoul, Korea) has been recently developed. This software analyzes 3D fetal brain volumes acquired from a 2-dimensional (2D) axial transthalamic plane and automatically reconstructs the axial, sagittal, and coronal planes of the fetal head. The objective of this study was test the efficacy of 5D CNS+ software in reconstructing brain diagnostic planes in healthy second-trimester fetuses and fetuses with CNS defects.

Materials and Methods

This study was designed in 2 different steps. In the first step, we considered 183 consecutive normal singleton pregnancies undergoing routine second-trimester examinations from October 2014 to March 2015. In the second step, we selected second-trimester brain volumes of 22 fetuses with CNS defects (8 with posterior fossa anomalies, 4 with isolated ventriculomegaly, 8 with agenesis of the corpus callosum, and 2 with complex disease No 2) from our database and the databases of the Fetal Medicine Units of the Universities of Milan, Naples, and Bologna, which were recorded from October 2014 to June 2015. All of the CNS defects were confirmed either at autopsy or by prenatal or postnatal magnetic resonance imaging. This research project was approved by the Institutional Review Boards, and all the women provided written informed consent to participate to the study.

All examinations were performed with WS80A Elite ultrasound equipment (Samsung Medison Co, Ltd) equipped with a 1–8-MHz transabdominal volumetric transducer. Brain volumes were acquired transabdominally by a previously reported technique,[12] starting with an axial view of the fetal head at the level of the axial transventricular plane. 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.

Volumes were stored and later analyzed independently by 2 authors with experience in 3D CNS analysis (G.R. and A.C.). Brain volumes were retrieved, and the 5D CNS+ function was activated. Two reference points were manually placed, respectively, in the middle of the thalami and in cavum septi pellucidi, and the software automatically reconstructed the axial coronal and sagittal planes of the brain (Figure 1 and Video 1). Finally, the software allowed review of the diagnostic planes individually or in groups (axial, sagittal, and coronal planes; Figure 2)

The diagnostic planes obtained were then independently classified by the reviewers as either satisfactory or not satisfactory for providing diagnostic-quality images according to the criteria reported in Table 1. The time spent for the analysis by the reviewers was recorded.

The 22 cases with CNS anomalies were anonymized and randomly included in a series of 68 brain volume data sets from healthy fetuses. One of the reviewers, who was blinded to the sequence and type of CNS defect, analyzed this series of 90 brain volumes with the help of this software. When the cavum septi pellucidi was not evident, the second point was placed on the midline in a position equidistant from the first point and the fetal skull. The reviewer was asked to differentiate normal from abnormal volumes and to provide possible diagnoses for the anomalies.

The Cohen κ coefficient was used to evaluate the agreement rates between the reviewers.[17] The differences in time required for the analysis by the reviewers were analyzed by the Mann-Whitney *U* test. The percentage of volumes in which a manual adjustment after the initial display provided by the software was necessary was evaluated, and differences between normal and abnormal cases were analyzed by the Fisher exact test. $P < .05$ was considered as significant. The SPSS version 20.0 statistical software package (IBM Corporation, Armonk, NY) was used for data analyses.

Results

The characteristics of the population studied are reported in Table 2. Brain volumes were recorded in all of the pregnancies. 5D CNS+ proved to be successful in analyzing the volumes acquired in 180 of 183 pregnancies (98.4%), whereas in the remaining 3 cases, the software failed to reconstruct the diagnostic planes. The reason for these

Figure 1. **A**, Example of the processing of a fetal brain volume acquired from an axial view of the fetal head at the level of the transventricular axial plane in a fetus at 20 weeks' gestation. After the volume was obtained, the 5D CNS+ software function was activated, and 2 marker points (calipers) were placed in the middle of the thalami and the cavum septi pellucidi. **B**, Final output of the 5D CNS+ software. The standard diagnostic axial coronal and sagittal planes are shown. Caud indicates caudate; CER, cerebellum; CP, choroid plexus; CSP, cavum septi pellucidi; IHF, interhemispheric fissure; LV, lateral ventricle; MSP, midsagittal plane; PSP, parasagittal plane; TC, transcerebellar plane; TCaudc, coronal transcaudate plane; TCc, coronal transcerebellar plane; TFc, coronal transfrontal plane; TT, transthalamic plane; TTc, coronal transthalamic plane; TV, transventricular plane.

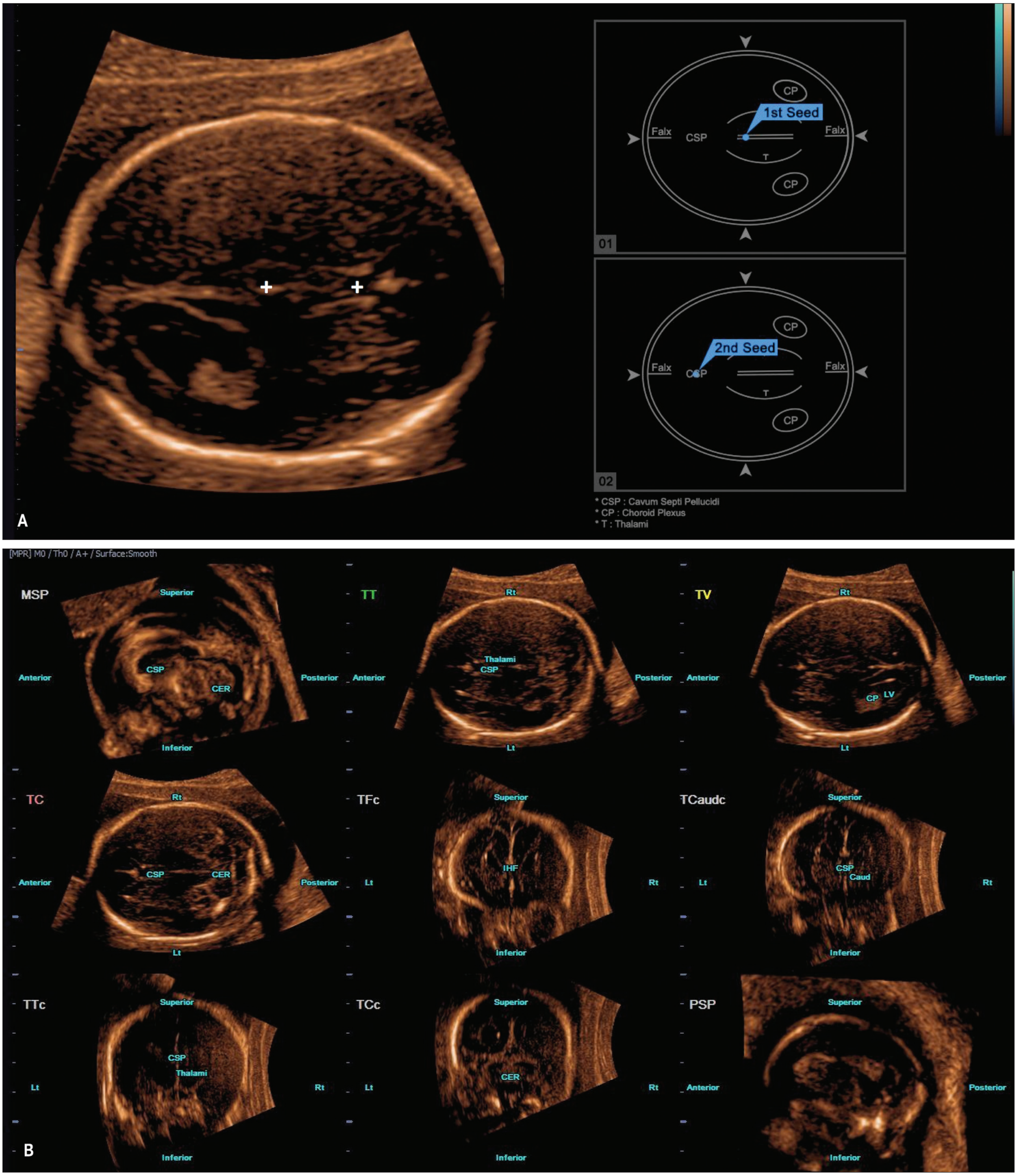


Figure 2. Details of diagnostic planes. **A**, Axial planes (transthalamic, transventricular, and transcerebellar planes) with the standard automatically performed biometric measurements superimposed. **B**, Coronal planes (transfrontal, transcaudate, transthalamic, and transcerebellar planes) (continued).

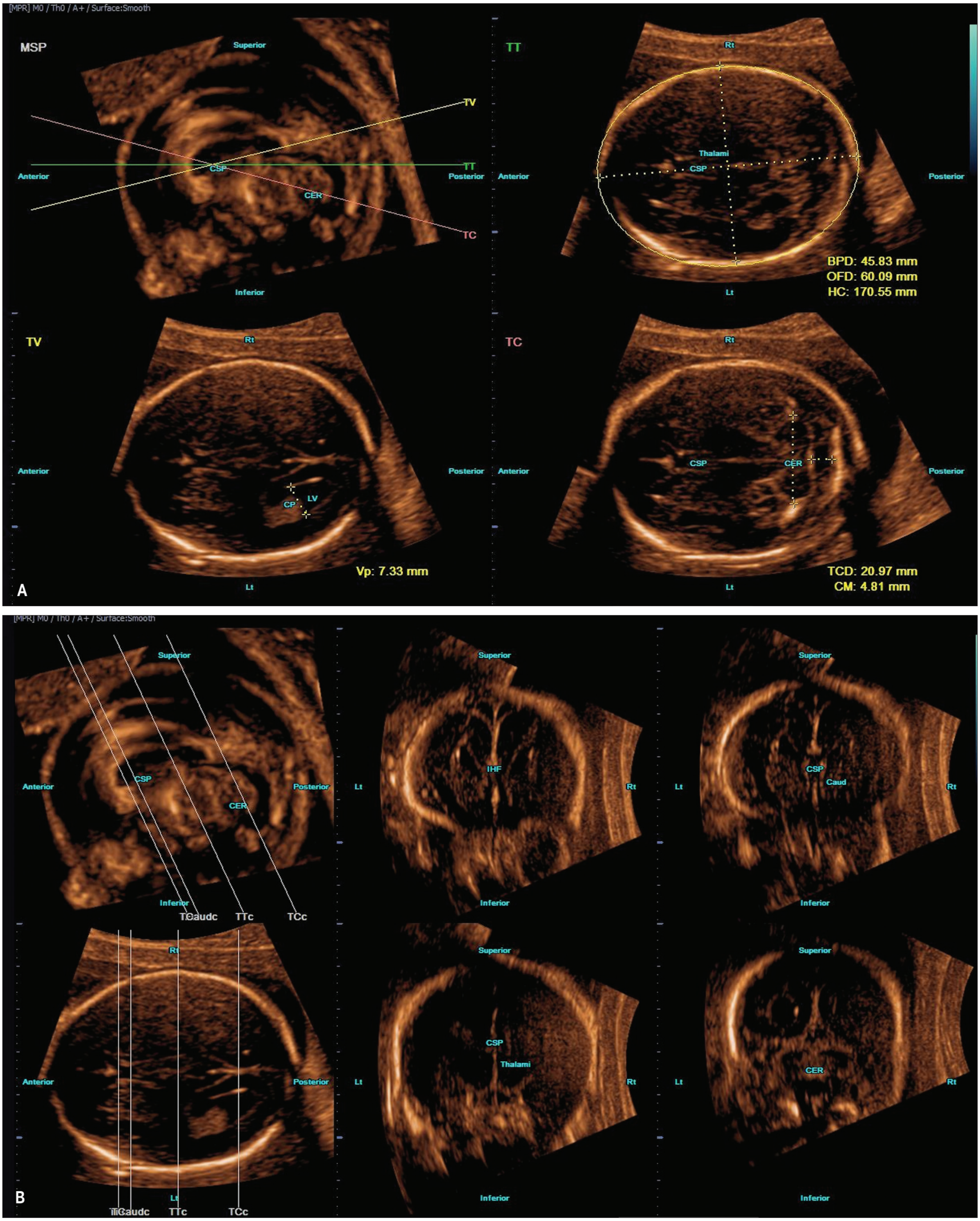
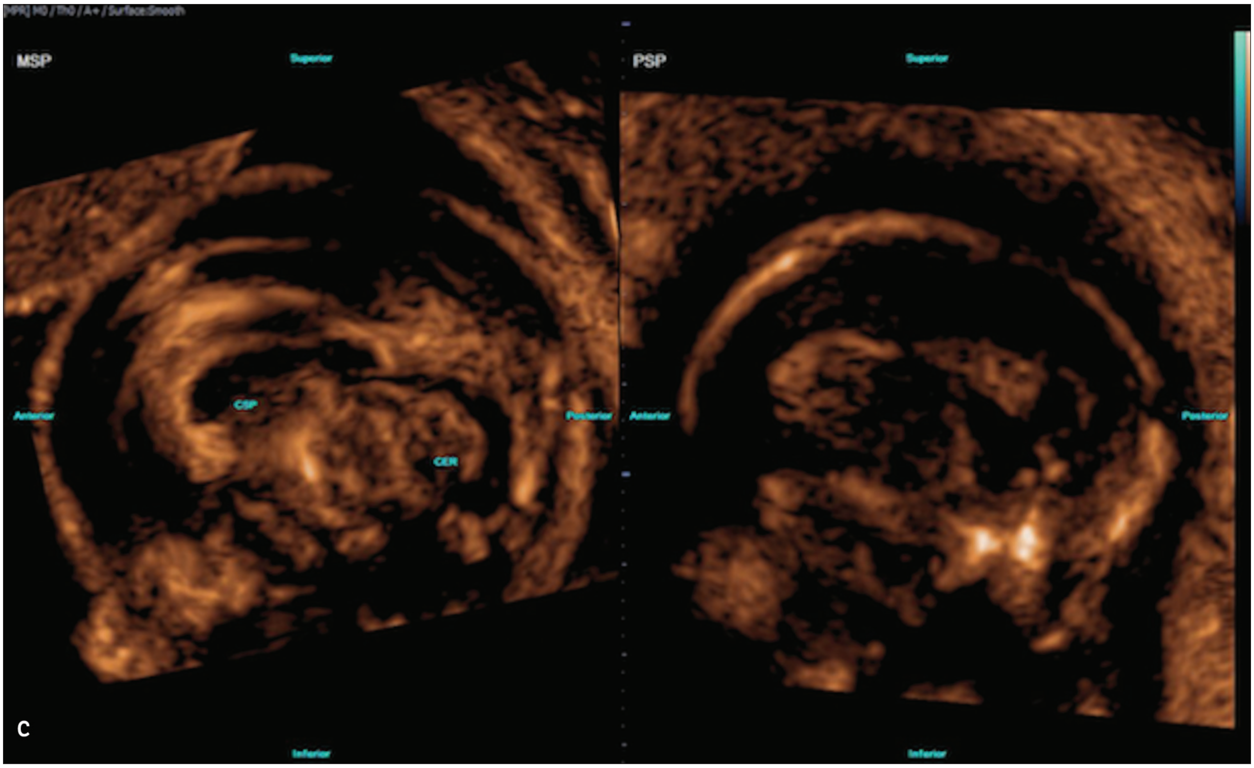


Figure 2. (continued) **C**, Sagittal planes (midsagittal and parasagittal planes). BPD indicates biparietal diameter; CM, cisterna magna; HC, head circumference; OFD, occipitofrontal diameter; TCD, transverse cerebellar diameter; and Vp posterior ventricle; other abbreviations are as in Figure 1.



unsuccessful analyses was the low quality of the volumes. All 3 of these pregnancies had a body mass index of greater than 35 kg/m^2.

Table 3 reports the frequencies at which each type of CNS view was judged satisfactory by the reviewers. For all of the diagnostic planes considered, Cohen κ values were greater than 0.81, suggesting very good agreement between the observers.[17] The time required to analyze all of the diagnostic planes was similar for both reviewers (median, 50 seconds [range, 32–68 seconds] versus 53 seconds [range, 30–71 seconds]; $P = .399$). Manual adjustment to obtain diagnostic planes after the application of the 5D CNS+ software was necessary in 14 of 180 (7.77%) normal cases and 4 of 22 (18.18%) abnormal cases ($P = .11$).

Concerning the series including normal and abnormal data sets, the reviewer correctly identified all 22 pathologic CNS volumes and made the correct diagnosis in 21 of 22 cases (95.4%). None of the normal volumes was incorrectly identified as abnormal. Examples of fetuses with borderline ventriculomegaly, complete agenesis of the corpus callosum, and a posterior fossa anomaly are shown in Figures 3–5.

Discussion

In this study, we tested new software developed to automatically visualize axial, coronal, and sagittal fetal brain planes from 3D volumes. We have recently demonstrated how it is possible to automatically obtain reproducible biometric measurements of the fetal head and brain from 3D brain volumes acquired from axial transthalamic diagnostic planes in a shorter time than with the conventional 2D sonographic approach.[18] We hereby tested the evolution of this software by studying a subsequent group of pregnancies in which brain volumes were acquired starting from the axial transventricular plane. These data demonstrate that automatic reconstruction of the sagittal and coronal planes may be obtained in 98% of pregnancies undergoing routine second-trimester sonographic examinations.

Guidelines for the screening of fetal brain anomalies suggest limiting the study of the fetal head to the axial planes on which the falx, cavum septi pellucidi, thalami, lateral ventricles with the choroid plexus, cerebellum, and cisterna magna can be studied.[4,17,19,20] The axial planes, however, do not allow visualization of the corpus callosum, cerebellar vermis, and other midline brain structures. As a consequence, anomalies concerning these structures are usually not evident in screening programs.[5] Missing these diagnoses is clinically relevant, since these anomalies are usually severe and frequently associated with other chromosomal or genetic diseases and structural malformations.[2]

The implementation of fetal brain visualization by the addition of sagittal and coronal planes has been suggested as an essential integration in the study of the fetal CNS.[4,5] However, visualization of these additional planes requires either a transvaginal approach in fetuses with a head presentation or a transabdominal approach by a transfrontal view through the metopic suture. With both approaches, the success rate for obtaining correct plane views is greatly dependent on the operator's experience and fetal position and furthermore may be time-consuming. As a consequence, up to now, their visualization has been limited to referral cases in specialized centers with expertise in fetal neurosonography.

The advantage of the 3D over the 2D approach in visualizing coronal and sagittal planes must be pointed out. Three-dimensional sonography allows one to acquire a volume of the fetal head and then, by subsequently reconstructing the image in a multiplanar approach, to obtain the diagnostic sagittal and coronal views, thus reducing the difficulties of the 2D approach. The actual limitation of 3D sonography is the complex anatomy of the fetal brain, which requires operator expertise in 3D orientation and subsequent reconstruction of the diagnostic planes from the acquired volumes.[5,9,10,12–16] Indeed, our data show how it is possible to obtain all of the diagnostic sagittal and coronal planes by applying the 5D CNS+ software to the volumes acquired from the standard axial transventricular plane, which is a view that is routinely obtained in screening sonographic examinations.

Of interest is the rate of agreement found between the reviewers in analyzing brain volumes. This finding supports clinically acceptable repeatability of fetal brain examinations by using the 5D CNS+ software. Furthermore, the rapid time for the analysis (median, 50 seconds) necessary to

Table 1. Criteria Followed by the Reviewers to Classify Fetal Brain Axial, Sagittal, and Coronal Planes as Satisfactory or Not Satisfactory

Plane	Criteria
Axial	
Transthalamic	Visualization of the cavum septi pellucidi and midline thalami; cerebellum not visible
Transventricular	Visualization of the cavum septi pellucidi, lateral ventricle, and choroid plexus
Transcerebellar	Visualization of the cavum septi pellucidi, cerebellum, and cisterna magna
Sagittal	
Midsagittal	Visualization of the cavum septi pellucidi–corpus callosum complex, cerebellar vermis, and posterior fossa
Parasagittal	Visualization of the entire lateral ventricle and choroid plexus
Coronal	
Transfrontal	Visualization of the midline interhemispheric fissure and anterior horns of the lateral ventricles on each side
Transcaudate	Visualization of the cavum septi pellucidi and corpus callosum; the lateral ventricles are found at each side
Transthalamic	Visualization of both thalami, the cavum septi pellucidi–corpus callosum complex, and the atria of the lateral ventricles with the choroid plexus on each side
Transcerebellar	Visualization of the occipital horns of the lateral ventricles, cerebellar hemispheres, and vermis

Table 2. General Characteristics of the Uncomplicated Pregnancies Considered

Characteristic	Value
Maternal age, y	33 (17–48)
Parity	1 (0–3)
Gestational age at sonography, wk	21.2 (18.1–23.8)
Body mass index, kg/m^2	24.9 (17.4–41.8)
Gestational age at delivery, wk	40.1 ± 1.24
Birth weight, g	3250 ± 387

Data are presented as median (range) and mean ± SD.

Table 3. Frequency of Satisfactory Views Obtained Stratified by Reviewer and CNS Plane

Plane	Reviewer 1 (G.R.), %	Reviewer 2 (A.C.), %	κ (95% CI)
Axial			
Transthalamic	98.8	99.4	0.98 (0.96–1.00)
Transventricular	97.7	98.3	0.96 (0.93–0.99)
Transcerebellar	98.8	98.3	0.97 (0.95–0.99)
Sagittal			
Midsagittal	97.7	97.2	0.95 (0.91–0.98)
Distal parasagittal	95.5	94.4	0.90 (0.85–0.94)
Coronal			
Transfrontal	94.4	96.1	0.90 (0.86–0.96)
Transcaudate	95.0	93.8	0.89 (0.84–0.94)
Transthalamic	92.2	93.3	0.92 (0.87–0.96)
Transcerebellar	96.6	97.2	0.94 (0.90–0.97)

CI indicates confidence interval.

Figure 3. Example of application of 5D CNS+ software to a fetus with isolated ventriculomegaly. **A**, Standard diagnostic planes. Asterisks indicate the dilated ventricles in the axial transventricular plane, coronal transcerebellar plane, and parasagittal plane. **B**, Details of the transventricular and parasagittal planes.

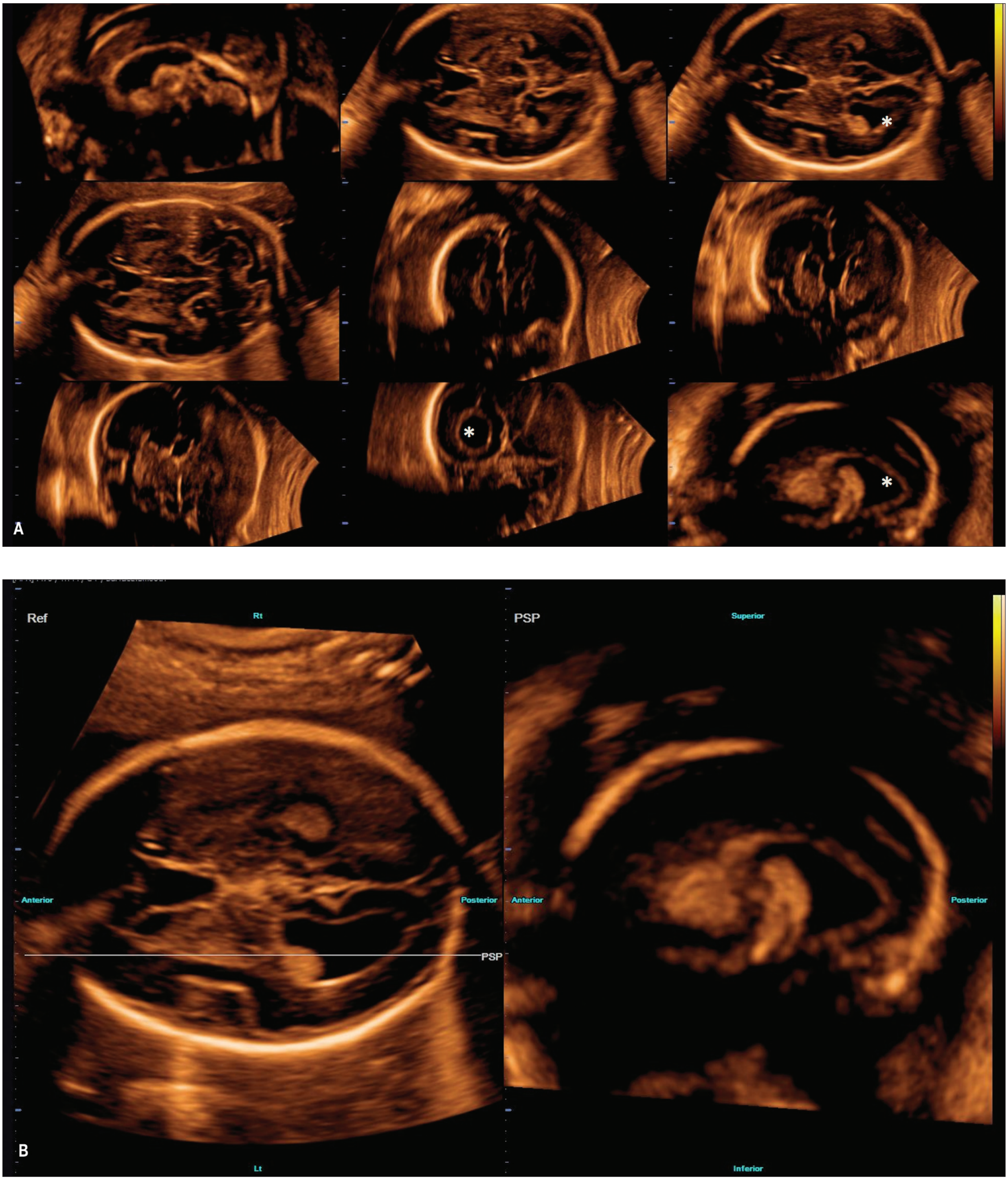


Figure 4. Example of application of 5D CNS+ software to a fetus with complete agenesis of the corpus callosum. Arrows indicate the absence of the cavum septi pellucidi and corpus callosum complex; and asterisks, concomitant mild ventriculomegaly.

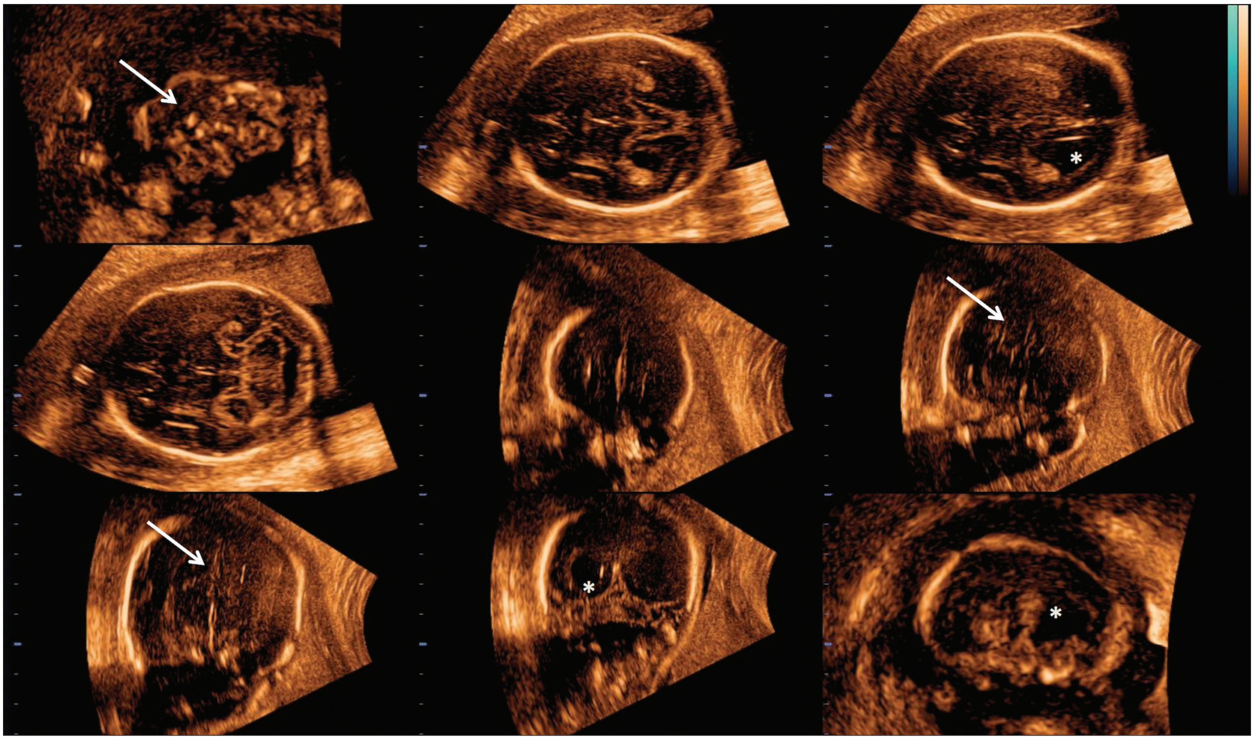
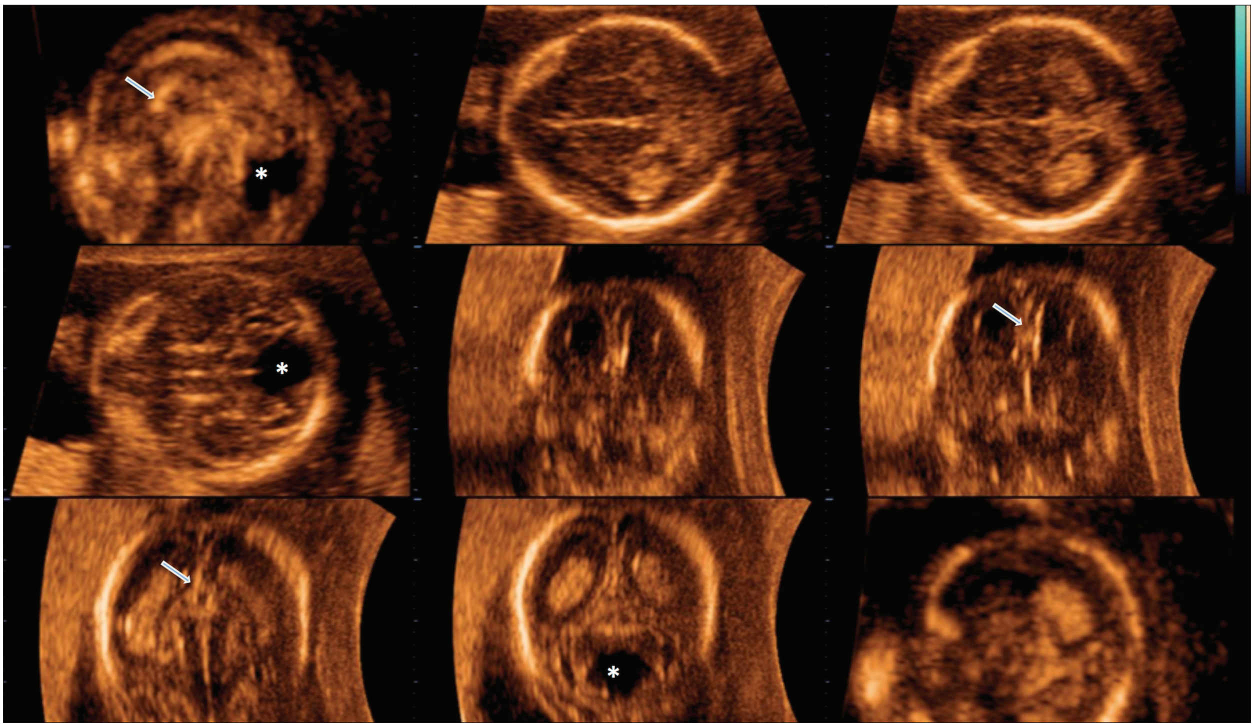


Figure 5. Example of application of 5D CNS+ software to a fetus with Dandy-Walker malformation and complete agenesis of the corpus callosum. Arrows indicate the absence of the cavum septi pellucidi and corpus callosum complex; and asterisks, dilated posterior fossa due to agenesis of the cerebellar vermis.



analyze the diagnostic planes suggests easy clinical applicability. Another compelling advantage of using this software is the possibility to simultaneously obtain all of the standard biometric measurements of the fetal head and brain, thus improving efficiency in the study of the fetal CNS.

In abnormal cases, the software displayed views that deviated from the norm, thus allowing the reviewer to distinguish CNS defects and to make the correct diagnosis in 21 of the 22 cases studied. Moreover, in cases without a visible cavum septi pellucidi, such as in the presence of agenesis of the corpus callosum, the software succeeded in showing the abnormal planes and allowing the reviewer to make the correct diagnosis. Although these results are encouraging, caution is necessary before applying this method to clinical practice.[21] Indeed, in this study, the software was tested on a small number of brain anomalies, and future studies on larger numbers of CNS defects are required to evaluate its diagnostic efficacy. However, its ability to show views deviating from what is expected in examinations of normal brains is promising and suggests its potential role for identification of fetal brains that are suspicious for structural anomalies.

A limitation of 5D CNS+ is the impossibility of analyzing the proximal parasagittal plane. This same limitation also occurs frequently with 2D sonography, and it is secondary to the difficulties of obtaining proper visualization of the proximal atria because of ossification of head bones and their subsequent shadowing effect, which hampers complete visualization of proximal brain structures. This factor suggests that, as with conventional 2D sonography, 3D sonography is also susceptible to the same intrinsic limitations in scanning windows.

A second limitation of this study was the choice of recording volumes transabdominally, thus obtaining data sets with lower resolution then when acquired transvaginally. Nonetheless, we believe that this disadvantage is outweighed by the possibility of also obtaining volumes from fetuses in a breech presentation and by the higher familiarity with the transabdominal approach of operators performing routine second-trimester fetal sonographic studies.

A further limitation of this study was that the operators acquiring the CNS volumes had expertise in fetal CNS imaging, and their skills were probably higher than those of the average sonographers. As a consequence, it is possible that the success rate for postprocessing examinations of CNS volumes may be lower when data sets are obtained by less-experienced operators. However recent data on volumes obtained from the fetal brain by operators working in peripheral centers and performing routine second-trimester sonographic screenings showed that more than 90% of their data sets had quality that was high enough to allow satisfactory views of all diagnostic planes.[22]

In conclusion, the 5D CNS+ software allows visualization of all of the diagnostic fetal brain planes. This software may improve work flow efficiency in second-trimester sonographic examinations and may allow less-experienced operators to perform extended studies of the fetal brain.

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