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# Fully Automated 5D CNS+™:

## Anatomical Knowledge Based Tool for Standardized Plane Detection in Fetal Neurosonography

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## Introduction

Although the first detailed description of fetal CNS anomalies dates back more than 100 years, and despite the fact that brain abnormalities are being increasingly recognized, a comprehensive prenatal workup of the entire CNS anatomy in its complexity remains challenging. Moreover, structural disorders of the CNS might occur at various embryonic or fetal stages and are the result of the impairment of a complex and well-orchestrated process. Their overall prevalence has recently been estimated to be 9.8 per 10,000 live births[1].

According to the recently updated ISUOG guidelines for both screening and targeted sonographic examination of the fetal CNS, the diagnostic value of the three axial planes (transthalamic, transventricular, and transcerebellar) alone is limited[2,3]. Any suspicion of an abnormal anatomic arrangement and/or an increased a priori risk should encourage a more detailed diagnostic approach as the three-dimensional architecture of the brain clearly emphasizes the need for additional coronal and sagittal planes to establish a complete fetal neurosonogram. However, one has to bear in mind that the latter fundamentally requires a high level of expertise in this field. Strategies to overcome these limitations include volumetric approaches as numerous studies impressively highlighted[4–7]. The main benefit of 3D ultrasound encompasses the possibility of performing multiplanar imaging correlation (Figure 1).

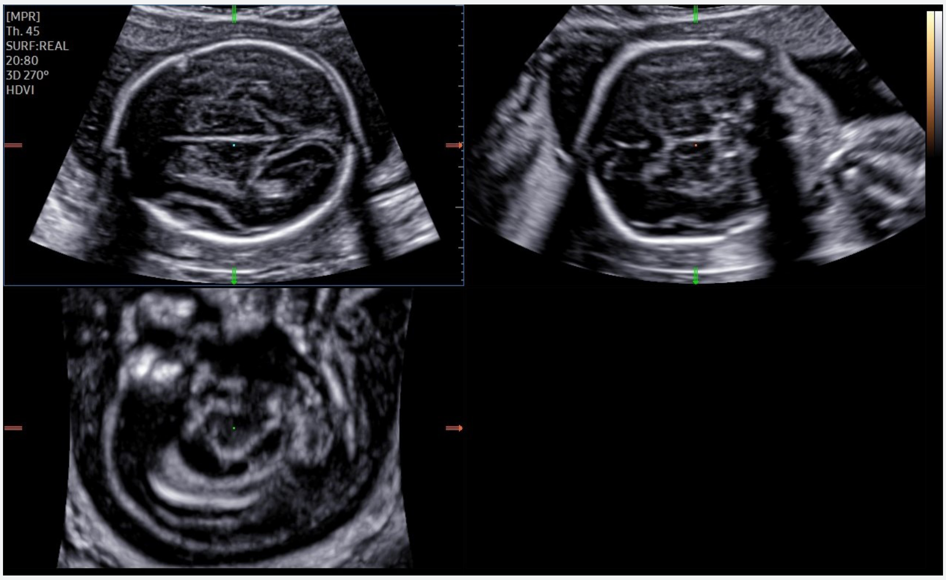


**Figure 1.** Triplanar display of a single 3D volume acquired in an axial (transverse) position of the fetal head corresponding to the transthalamic diagnostic plane (recommended for biparietal diameter quantification).

A recent prospective study emphasized that the application of an evidence-based guideline for the acquisition of brain volumes significantly improves the quality of these by increasing the number of evaluable structures within the 3D volume[4]. It has further been shown that with the advance of a workflow-based volumetric software solution, a standardized and less operator-dependent approach to the entire fetal brain became not only feasible, but could also be implemented in clinical routine[6] (Figure 2).

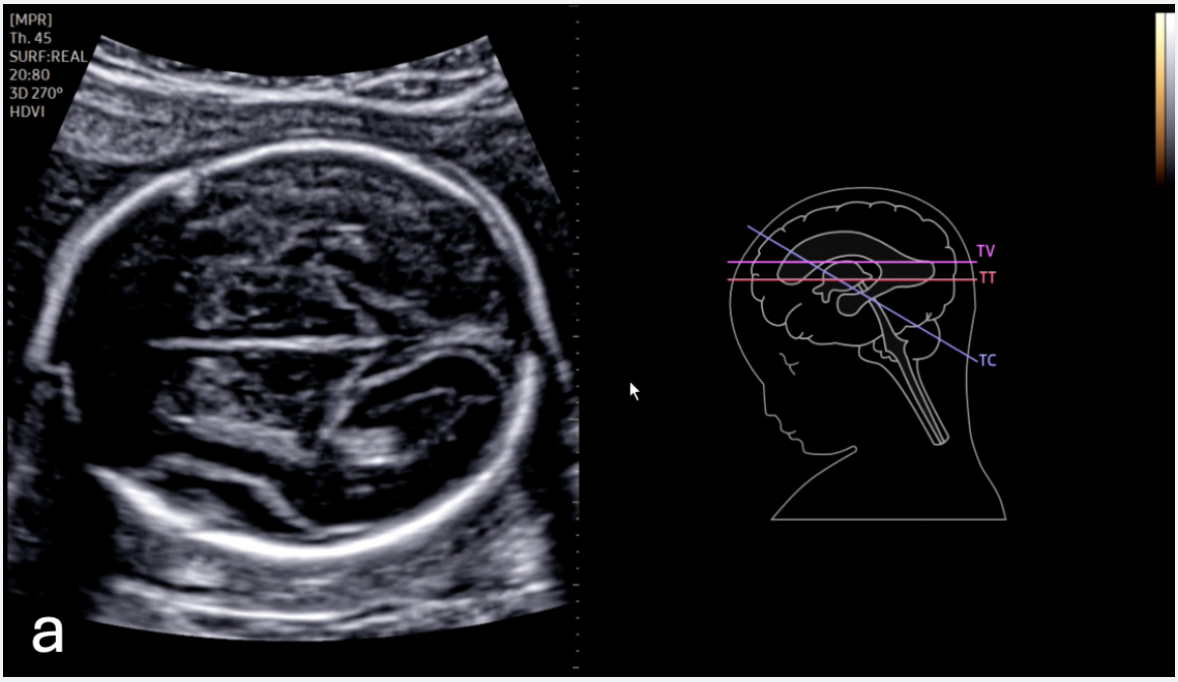


**Figure 2a.** Image of an axial plane taken during fully automated volume postprocessing

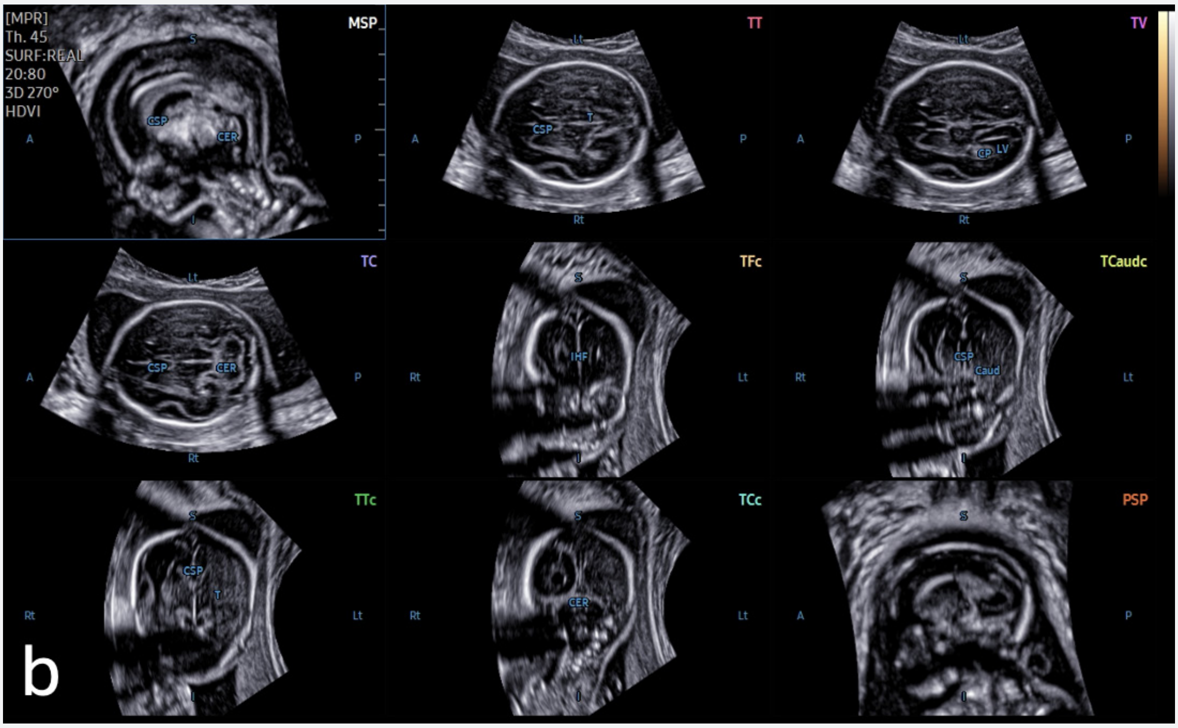


**Figure 2b.** Resulting diagnostic nine-view template showing axial, coronal and sagittal planes of the fetal brain after completion of volume re-slicing

In this work, we aimed to evaluate the performance of a novel fully automated 5D CNS+™ (Fully-automated 5D CNS+™) for assessment of the fetal CNS architecture compared to a semi-automated software tool 5D CNS+™ (Semi-automated 5D CNS+™). Both versions are built-in, commercially available software installed on the high-end ultrasound system HERA W10 (SAMSUNG MEDISON Co., Ltd. Korea).

## Methods

A total of 51 stored 3D volumes of the brain of unselected, structurally normal second- and third-trimester fetuses were examined. All volumes were acquired in the transthalamic plane needed for biometric assessment of biparietal diameter (BPD) and head circumference (HC), resulting in a triplanar orthogonal reconstruction of fetal central nervous structures.

Two operators with different levels of expertise (level I and level III - the former certifying familiarity with the basics of ultrasound diagnostics, the latter characterizing a proven expert far beyond basic knowledge) independently applied both Semi-automated 5D CNS+™ and Fully-automated 5D CNS+™ separately for detailed assessment of the fetal CNS.

To run the Semi-automated 5D CNS+™ tool, a horizontal alignment of the falx in the acquisition plane (a plane) and ± depth adjustment of the cutting section was required. During the following step, two seeds between the anterior most third of the thalami and the cavum septi pellucidi were placed and all nine diagnostic planes were displayed. The novel algorithm of Fully-automated 5D CNS+™ does not require any further operator intervention after volume acquisition, since it automatically finds CNS standard planes and measures its key diagnostic elements by using automatic segmentation and plane-navigation (Figure 3).

The procession time from the initiation of the volume reconstruction to the initial display of the nine-image template was measured for each operator and for both program versions. In addition, the number of correctly calibrated planes were evaluated and the requirement for manual adjustment of the planes was registered as well as the time span until the final result with adequately reconstructed planes has been achieved.

Descriptive statistics, paired t-test and Wilcoxon matched-pairs signed rank test were performed. A statistical level of $p < 0.05$ was assumed to be significant. The intraclass correlation coefficient (ICC) was calculated for interoperator reproducibility. ICC values were calculated using a two-way mixed effects model for absolute agreement. The data were compared between Semi-automated 5D CNS+™ and Fully-automated 5D CNS+™ application for both operators using a Bland-Altman plot (average between the planes to be corrected manually after processing with Semi-automatic and Fully-automatic 5D CNS+™ of both operators against the difference between these two) to test the agreement between both software algorithms.

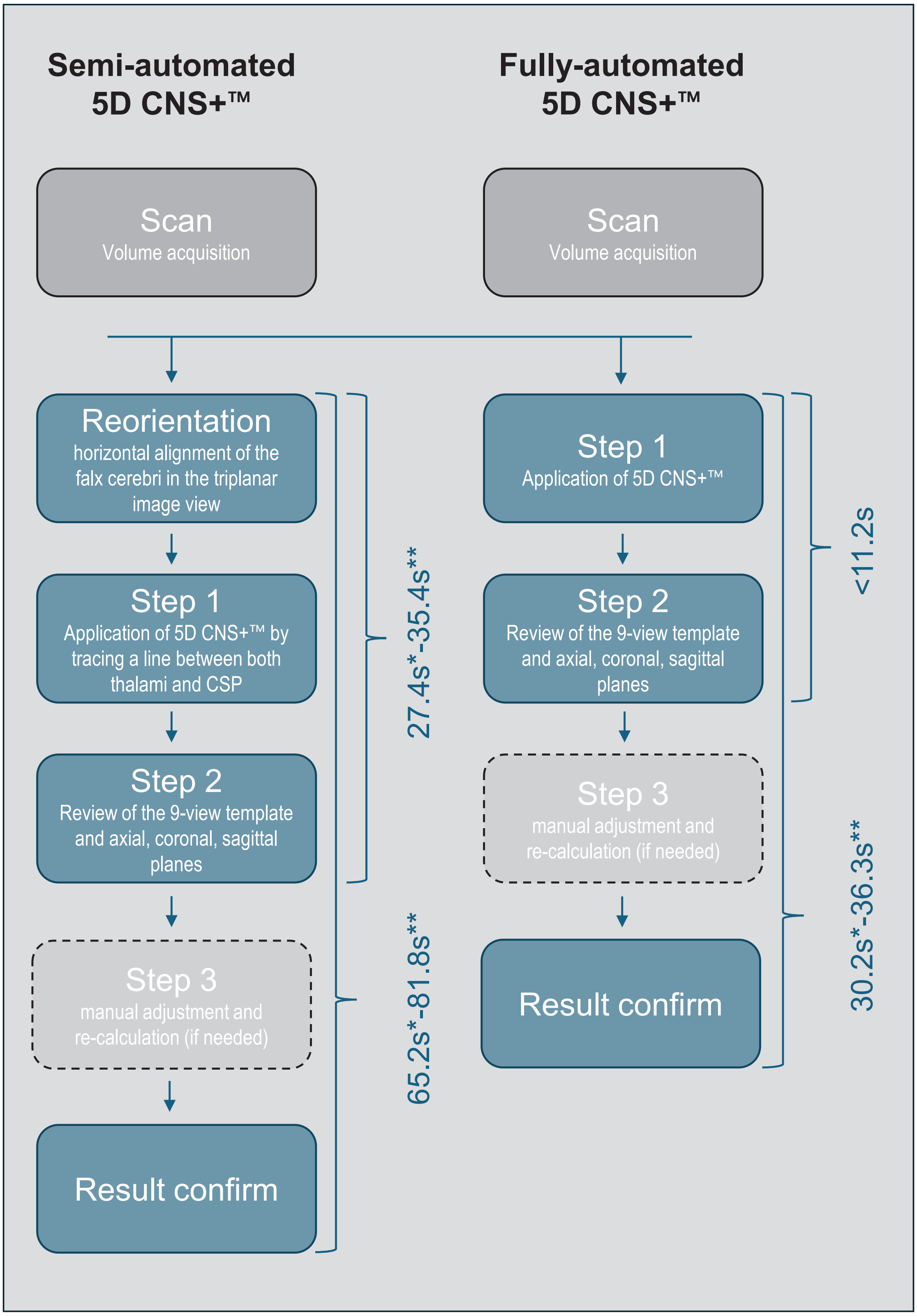


**Figure 3.** Workflow scheme of both programs demonstrating illustrating reduced steps/workload when applying Fully-automated 5D CNS+™ on stored 3D volumes compared to Semi-automated 5D CNS+™. Most strikingly, volume reconstruction was accomplished in less than 12 seconds compared to Semi-automated 5D CNS+™ irrespective of the operator's expertise and with a significantly reduced necessity of manual plane adjustment (* - operator 1; ** - operator 2).

## Results

The mean maternal age was 32 years (ranging from 23 to 43 years), and the mean maternal body mass index prior to pregnancy was 23.44 $kg/m^2$ (16.90 to 44.05 $kg/m^2$). The gestational age ranged from 17.7 to 27.7 (average 22.5 weeks). The ICC between both operators of correctly depicted planes after application of both software algorithms without requirement for manual correction was 0.614 (0.321 – 0.780) for Semi-automated 5D CNS+™ and 0.818 (0.677 – 0.897) for Fully-automated 5D CNS+™. The acquisition time of application of both software algorithms until all nine planes are obtained without manually correction for Semi-automated 5D CNS+™ was 27.41 s ± 4.86 s for operator 1 and 35.45 s ± 10.50 s for operator 2 ($p < 0.0001$), for Fully-automated 5D CNS+™ 11.09 s ± 0.65 s for operator 1 and 11.13 s ± 0.47 s for operator 2 ($p = 0.744$) (Figure 4).

For operator 1 (level III expert), planes to be corrected manually after volume processing with both software algorithms were 1.61/9 planes ± 0.90/9 planes for Semi-automated 5D CNS+™ and 0.16/9 planes ± 0.42/9 planes for Fully-automated 5D CNS+™, for operator 2 (level I examiner) 1.63/9 planes ± 0.85/9 planes for Semi-automated 5D CNS+™ and 0.28/9 planes ± 0.57/9 planes for Fully-automated 5D CNS+™ (Figure 5). The statistical analysis for manually corrected planes by both operators between software algorithms showed a Bland-Altman-Bias of 1.45/9 planes (95% Limits of Agreement (LoA) from -0.41 (LoA-) to 3.30 (LoA+)) for operator 1 and 1.35/9 planes (95% LoAs from -0.60 (LoA-) to 3.31 (LoA+)) for operator 2. In other words, on average, operator 1 had to correct 1.45/9 planes less with Fully-automated 5D CNS+™ than with Semi-automated 5D CNS+™, operator 2 had to correct 1.35/9 planes less on average with Fully-automated 5D CNS+™ compared to Semi-automated 5D CNS+™, which in turn further exemplifies the superior accuracy of a fully-automated approach.

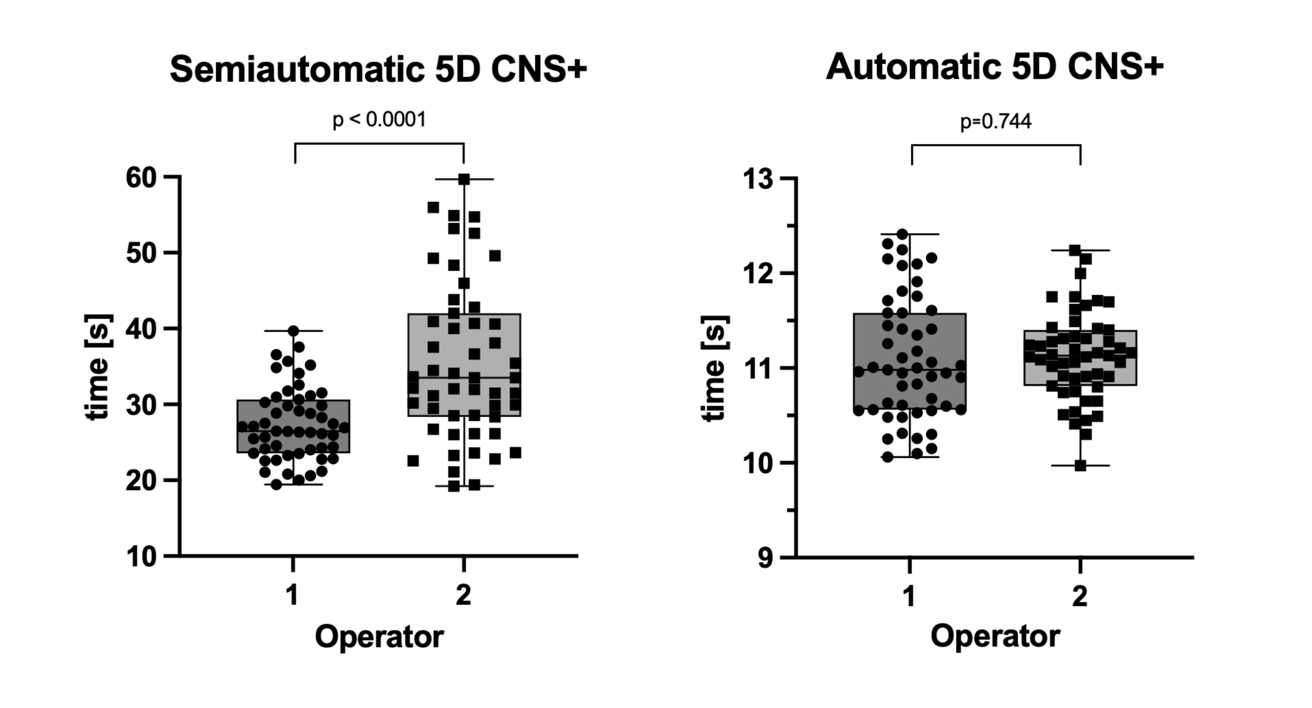


**Figure 4.** Acquisition time of application of Semi-automatic 5D CNS+™ and Fully-automated 5D CNS+™ until all nine planes are obtained prior to manually correction (if necessary) for both operators.

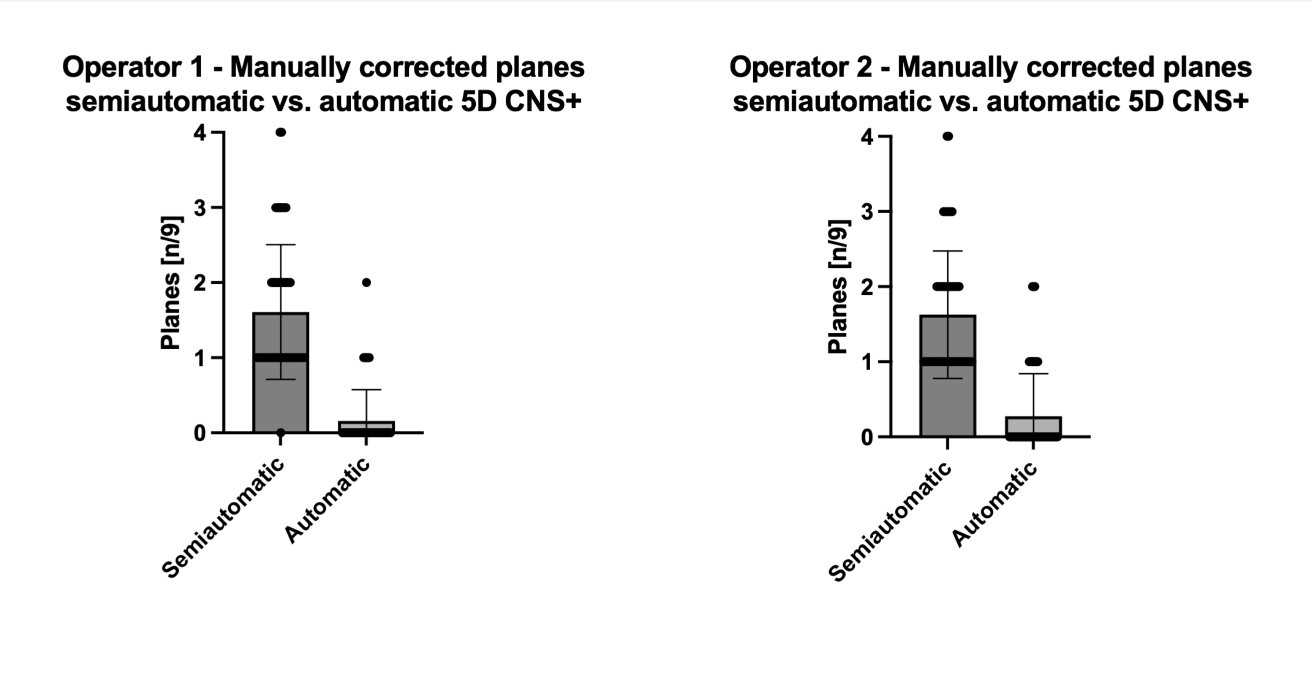


**Figure 5.** Planes to be corrected manually after application (processing) with Semi-automated and Fully-automated 5D CNS+™ algorithms for operator 1 and 2 [number of planes, mean with SD].

## Discussion

The clinical applicability of the 5D CNS+™ algorithm has been clearly demonstrated in previous studies[8-9]. This workflow-based volumetric approach reportedly aids in a thorough evaluation of the fetal brain as it enables reconstruction of all diagnostic planes needed for a complete neurosonogram based on a single 3D volume acquired with the fetus' head in an axial position (BPD plane). By being able to simultaneously assess axial and additional coronal and sagittal diagnostic planes in a single template, both the normal and abnormal CNS anatomy can be reproducibly analyzed and tracked in a step-by-step manner (Figure 6 and 7)[9]. However, to run the Semi-automatic 5D CNS+™ properly, a few initial steps following volume acquisition are needed (as discussed above). With the introduction of the novel 5D CNS+™, a refined algorithm is now available and allows a rapid 3D auto-segmentation of all standard views of the fetal brain with impressive efficiency and reliability underpinning the superior clinical value.

Based on our data, application of Fully-automated 5D CNS+™ provided a nine-view template in less than 12 seconds on average following volume acquisition irrespective of the operator's expertise as fewer crucial steps (e.g. reorientation of the triplanar image, placing the seeds between the thalami and the cavum septi pellucidi and the need for repeated confirmational steps throughout the examination) are needed to achieve an entire neurosonogram. It is of note that on average, both examiners had fewer planes to correct manually using the Fully-automated 5D CNS+™ software compared to Semi-automatic 5D CNS+™. This has a direct effect on both the accuracy and the efficiency of each examination in daily clinical routine. Both tools reliably calculated six biometric measurements (BPD-biparietal diameter; OFD-occipitofrontal diameter; HC-head circumference; Vp-atrial with of the lateral ventricle; CEREB-diameter of the cerebellum; CM-width of the cisterna magna) retrieved from three axial views without significant differences (Figure 6).

## Conclusion

Both versions of 5D CNS+™ are able to provide reliable in-depth information of the fetal cerebral anatomy deploying all standard views for fetal neurosonography as recommended by national and international guidelines[2-3]. With the advance of 5D CNS+™, a fully automated ready for use algorithm ('on the fly') became available, further increasing reproducibility and simplifying clinical workflow with a maximum reduction of both examination time and operator dependency. Furthermore, intelligent navigation enables the algorithm to exactly locate diagnostic planes resulting in a marked refinement of accuracy in quantification of cerebral structures.

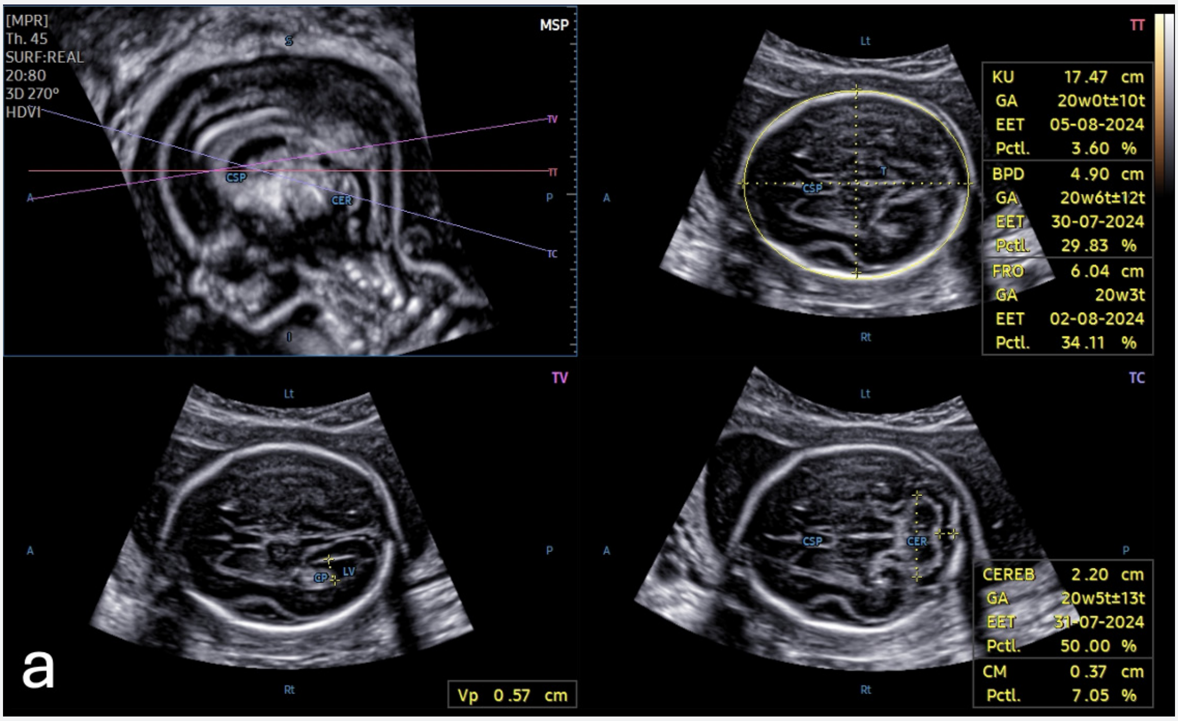


**Figure 6a.** Differently sliced images for proper display of all axial planes including automatic quantification of six CNS measures

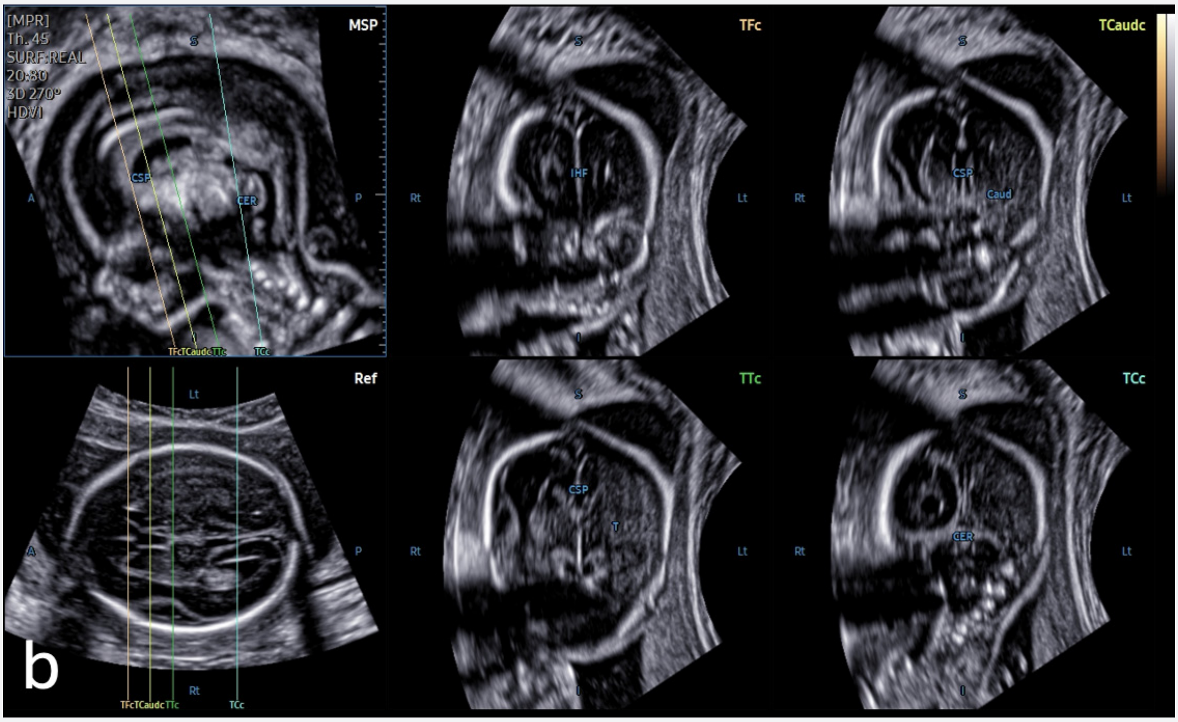


**Figure 6b.** Four additional coronal cutting sections that give information on CNS anatomy (e.g. progress of operculization of the Sylvian fissure)

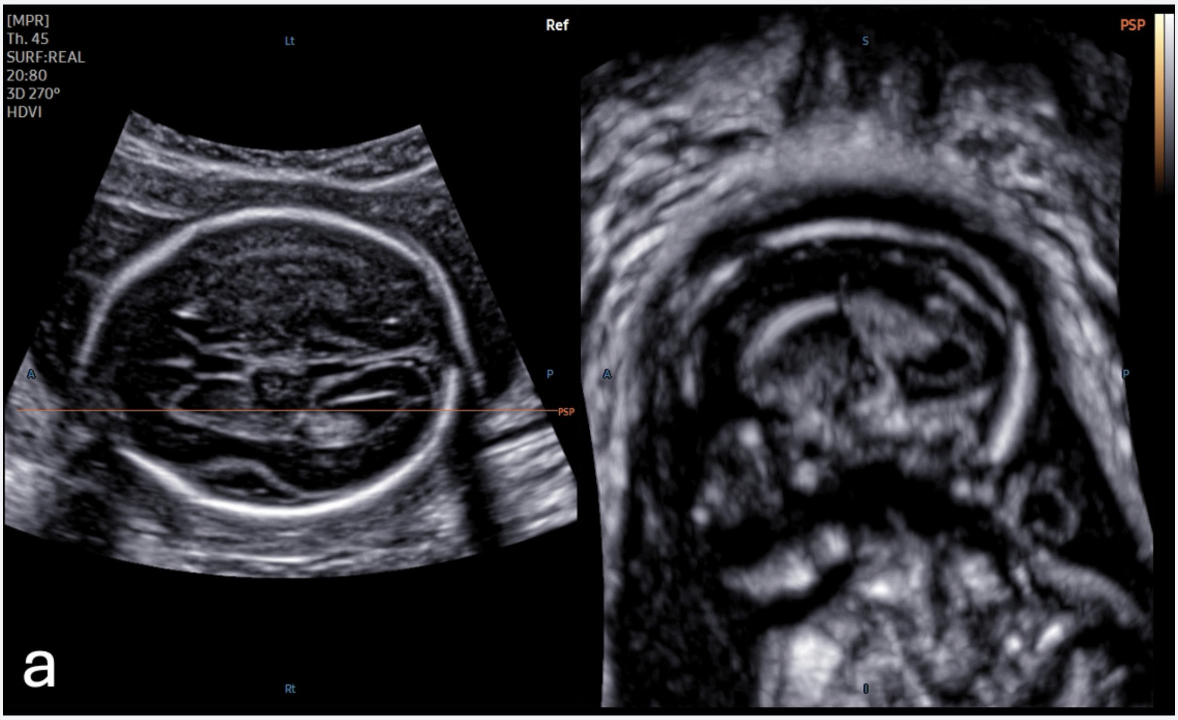


**Figure 7a.** Display of (para)sagittal planes - note the correct placement of the cutting line within the lateral ventricle

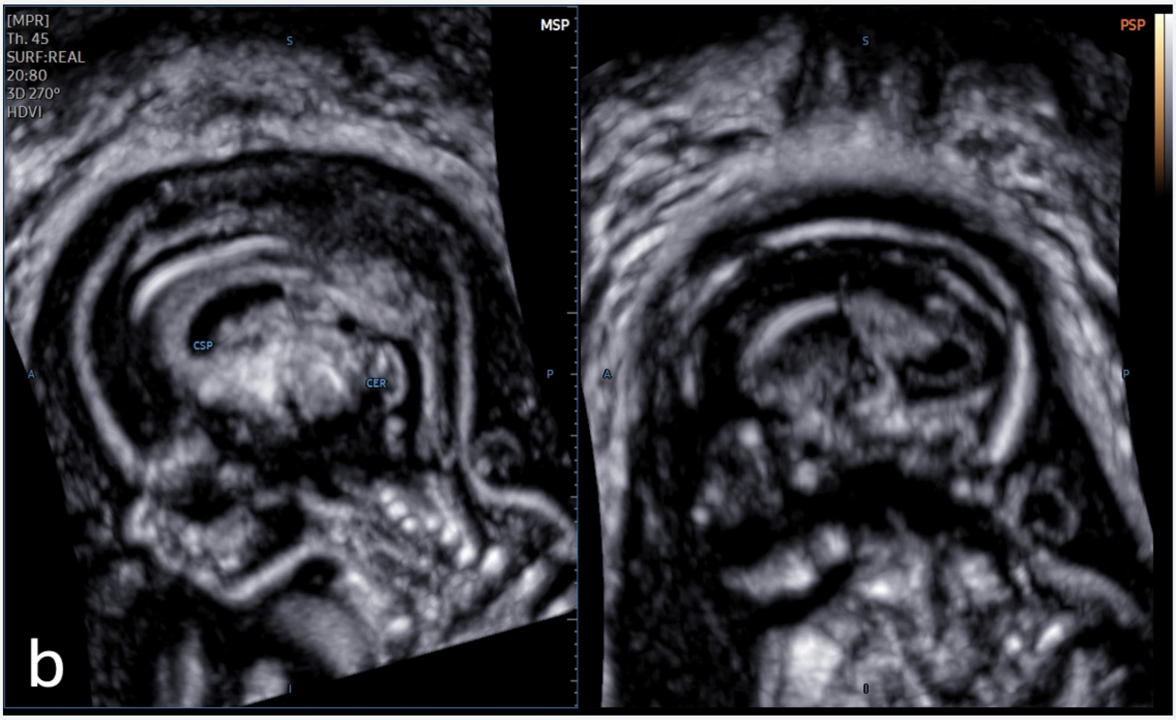


**Figure 7b.** Sagittal plane nicely depicting both the cavum septi pellucidi and the spatial relationship of the vermis cerebelli with the brain stem (left image of Figure 7b) and the normally shaped plexus choroideus within the lateral ventricle (right image of Figure 7b)

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