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Research Article

Real-Time Virtual Sonography Using MRI And Ultrasound Fusion in the Evaluation of CNS Anomalies

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Abstract

Purpose: Prenatal detection of structural brain lesions mainly relies on mid-trimester ultrasound. Complementary MRI techniques may enrich the detailed sonographic exploration of the fetal brain. Merging prenatal ultrasound and MRI may combine the best of both worlds.

The study aims to explore the added value of real-time virtual sonography in CNS anomalies after initial diagnosis by a fetal medicine expert and further investigation by a fetal MRI specialist to detect additional brain abnormalities.

Methods: This retrospective study over 4 months in a tertiary referral center looked into all pregnant women in the second and third trimester referred for congenital CNS anomalies diagnosed by prenatal ultrasound and subsequent fetal MRI. Fourteen MR-US fusion examinations were performed for evaluation of the fetal brain in case of suspected CNS malformation. Imaging on fusion images of the congenital CNS lesions was done by an independent specialist. Discussion between the 3 different specialists assessed the feasibility of fusion, and additional findings of US, MRI and fusion.

Results: Real-time virtual sonography was technically possible in all patients. The axial plane was obtained in all cases. The coronal and the sagittal planes were more difficult to obtain, in 28,5 % and 42,8 % of the cases respectively.

Overall, the real-time ultrasound fusion technique did not enhance the final diagnosis of the CNS anomaly.

Conclusions: Fusion imaging may be useful as an educational tool in the assessment of fetuses with CNS anomalies from the second trimester onward. However, so far this technique does not add to diagnose other CNS findings already revealed by MRI or US experts individually and separately.

Keywords: Central nervous system anomalies; Prenatal ultrasound; Fetal MRI; Real-time virtual sonography

Abbreviations: CNS: Central Nervous System; US: Ultrasound; ISUOG: International Society of Ultrasound in Obstetrics and Gynecology; MRI: Magnetic Resonance Imaging; MR: Magnetic Resonance; CMV: Cytomegalovirus; PCR: Polymerase Chain Reaction; AF: amniotic Fluid; TOP: Termination of Pregnancy; C/S: Caesarean section; IVH: Intraventricular hemorrhage; TTTS: Twin-to-twin transfusion syndrome; MMC: Myelomeningocele; IOL: induction of labor

Introduction

Congenital anomalies of the central nervous system (CNS) account for 10.2% of all registered congenital anomalies with a prevalence of 25.81 per 10,000 births. In contrast with the leading causes of congenital anomalies, the number of live births is only

43,6% because of the high number of terminations of pregnancy (53.2%) or fetal deaths (3.2%) [1].

Prenatal detection of structural brain lesions mainly relies on mid-trimester ultrasound (US) trans-thalamic, ventricular, and posterior fossa planes [2].

Extended fetal neurosonography performed in fetuses suspicious of brain anomalies performed by dedicated fetal medicine specialists includes however additional evaluation in multiple orthogonal planes, both transabdominal and transvaginal whenever possible. Additional imaging by 3D ultrasound may enhance detailed fetal brain exploration.

Complementary magnetic resonance imaging (MRI) techniques may enrich the detailed sonographic exploration of the fetal brain in several conditions after 24 weeks of gestation [3], particularly when assessing the corpus callosum, the posterior fossa, brain stem and the development of the cortex [4]. Recently the International Society of Ultrasound in Obstetrics and Gynecology (ISUOG) published practice guidelines for fetal MRI [5].

Due to the complementarity of both modalities, merging prenatal ultrasound and MRI images may combine the best of both worlds demonstrating the information of each modality simultaneously next to each other.

The MRI/US fusion technology has been introduced successfully into medicine to diagnose and treat tumors. [6-8].

To date, five papers have addressed the potential of this technique in fetal medicine addressing its feasibility for prenatal diagnosis of structural defects [2] and stressing its educational potential in difficult pathological situations [9-12].

The study aims to explore the added value of real-time virtual sonography in the presence of central nervous system anomalies diagnosed by neurosonogram and explored with fetal MRI.

Materials and Methods

This retrospective study over 4 months in a tertiary referral center investigated all pregnant women in the second and third trimester referred for congenital CNS anomalies diagnosed by prenatal ultrasound and subsequent fetal MRI. In this period 14 patients were eligible for the study. Although the study had no impact on clinical management, all patients consented to participate. Fourteen MR-US fusion examinations were performed for evaluation of the fetal brain in case of suspected CNS malformation.

After the initial sonographic diagnosis and workup, a fetal MRI was scheduled on a 1.5 Tesla system (Siemens, Erlangen, Germany) using a six-channel phased-array body coil. Patients were positioned supine or in a left lateral position. T2-weighted imaging of the brain was done with a half-Fourier acquired single-shot turbo spin-echo sequence in a transverse, coronal and sagittal plane (according to the fetal head orientation). Geometric parameters of T2 weighted images were as follows: repetition time 1000 ms, echo time 133 ms, slice thickness 3mm, field of view 380 x 380 mm (with an in-plane resolution of 1,5 mm x 1,5 mm). Additional scanning was performed as part of the routine protocol, including gradient echo sequences, T1-weighted imaging and diffusion-weighted imaging of the fetal head and body. The mean examination time of the entire clinical protocol was 25-30 minutes. The routine MRI protocol did not include three-dimensional acquisitions.

Real-time ultrasound-fusion procedures were performed abdominally with a second-generation Logic E9 ultrasound system (GE Healthcare, GE Medical System Europe, Zipf, Austria) and two-dimensional probes (3,5-5 MHz curvilinear abdominal or 6-9 MHz vaginal transducer) by experienced sonographers.

The fusion system contains a position-sensing unit mounted on the ultrasound unit, a magnetic field transmitter and a sensor fixed to the probe. The magnetic field transmitter was placed near the area of scanning. The magnetic tracking system detects the movements of the sensor fixed on the probe during scanning. The probe remained 30-40 cm from the magnetic field transmitter to obtain maximal field strength.

Real-time US/MRI fusion was started within 2 hours following the MRI scan.

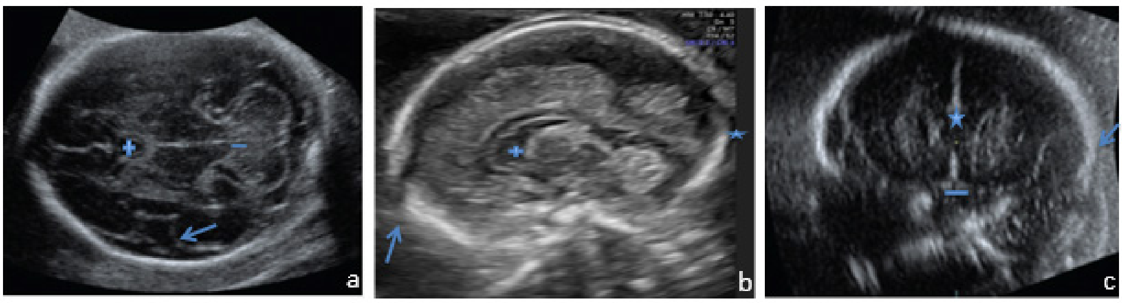

Figure 1
a: Axial plane: landmarks cavum septi pellucidi (+), 4th ventricle (-), posterior side insula (arrow)
b: Sgital plane: landmarks : nose (arrow), CSP (+), occiput (*)
c: Coronal plane: landmarks corpus callosum (*), 4th ventricle (-), lateral wall skull (arrow)

First, the MRI acquisition dataset needed to be loaded into the US system Subsequently, spatial synchronization between the MRI imager and the corresponding US image was performed on a split screen using 3 anatomical reference points carefully chosen to the landmarks of each orthogonal plane (Figure 1).

Once the images are aligned, the MRI dataset can be explored simultaneously with the real-time ultrasound examination of the fetal brain in that particular orthogonal plane (V-Nav). The display screen allowed for side-by-side comparison and evaluation of US and MRI images. The fusion images of the congenital CNS lesions whereas compared to B-mode by a specialist, independent of the one who made the US or MRI images.

A systematically evaluated discussion between the 3 different specialists assessed the feasibility of fusion, the influence of time between the MRI and US, the approach on the impact of fetal positioning, and the additional findings of US, MRI and fusion compared to the other imaging techniques. The added value of real-time fusion in the multidisciplinary discussion was assessed.

Although Institutional Review Board approval was not required because this study had no impact on routine management, information was given to patients and oral consent was sought before all examinations.

Results

Over 4 months 14 MR-US fusion examinations were performed for evaluation of the fetal brain in case of suspected CNS malformation.

Five patients were referred for CMV seroconversion in the first trimester of pregnancy. They had a positive PCR CMV on amniocentesis. Two patients were referred for ventriculomegaly and one for discordant ventricles within the normal limits. Two patients with spina bifida and one patient with meningomyelocele were included. One patient had a subdural bleeding; another patient had a grade 1 intraventricular hemorrhage. In the last patient, a subependymal cyst was diagnosed.

The general characteristics of mothers and fetuses are discussed in Table 1.

Table 1: General Characteristics of mothers and fetuses.

CASE	GA	Ultrasound Finding	Additional findings on MRI + /-	Additional findings on fusion +/-	Additional value in multi-disciplinary discussion	GP	Outcome
1	DCDA twin 22 2/7 wks	CMV AF PCR pos Broad peri-ventricular halo Cyst posterior horn lateral ventricle	none	none	none	G1P0	selective TOP @30 2/7 wks
2	24 6/7 wks	CMV AF PCR pos Broad peri-ventricular lining, cyst formation in germinative matrix	none	none	none	G1P0	TOP @27 5/7 wks
3	26 2/7 wks	CMV AF PCR pos Broad periventricular halo, bilateral adhesions in lateral horn	delayed gyration?	none	Positive	G2P1	TOP @28 wk
4	28 4/7 wks	CMV AF PCR pos Cyst posterior horn, broad lining lateral ventricles, calcification subependymal region	none	none	none	G3P2	Delivery @ term boy. Neuromotoric delay delay @ 5 y
5	DCDA twin 35 wks	CMV AF PCR pos Broad echogenic lining , VM , LSV	Polymicrogyria, hyper-intense PV white matter sign	none	Positive	G1P0	C/S @35 wks Unilateral deafness in Child 1, Both children neuromotoric delay @ 5y
6	32 5/7 wks	Subdural bleeding (tempo parietal region) White matter compression Contralateral VM	none	none	none	G1P0	TOP @ 35 3/7 wks Mutation in F 5 gen
7	MCDA twin TTTS 1 laser @ 20 wks	IVH Gr 1 in caudothalamic region (ex donor)	none	none	none	G2P1	C/S 29 3/7 wks PPROM
8	DCDA twin 27 2/7 wks	Multiple Subependymal cysts bilaterally metabolic	septations	none	Positive	G2P0	selective TOP @ 31 2/7 wks
9	22 1/7 wks	MMC L4, cheilognato-palatoschizis	none	none	none	G8P7	C/S @ 36 wks
10	DCDA 22 1/7 wks	Rachischizis, VMtalipes, anglation of spine > 30°	none	none	none	G1P0	selective TOP @ 32 wks
11	22 5/7 wks	MMC L2-S3, microcephaly	none	none	none	G1P0	IUFD @ 24 4/7 wks
12	24 2/7 wks	VM 18 mm hypoplastic gyration	none	none	none	G11P4	TOP @ 26 wks

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13	26 wks	VM 13 mm, hypoplastic cerebellum, vermis normal	Normal Cerebellum	none	Positive	G1P0	IOL @40 wks , 3995g Nl outcome
14	26 1/7 wks	discordant ventricles 12mm-8 mm	none	none	none	G1P0	Delivery @term Nl outcome

9/14 patients were primipara. The median age of fusion was 25 weeks 4 days (SD 3wk 5 days). Real-time virtual sonography was technically possible in all patients. The axial plane was most easily obtained in all cases and obtained in all cases. The coronal and the sagittal planes were more difficult to obtain in ultrasound, in 28,5 % and 42,8 % of the cases respectively, due to the advanced gestational age and the fetal position.

Overall, the fusion technique did not provide additional information to the final diagnosis. Although in 2/5 cases of CMV-related abnormalities, it enhanced the multidisciplinary discussion between the different experts. Polymicrogyria in one patient and a cyst in the posterior horn of the lateral ventricle in another patient were picked up by MRI. In a fetus with the subependymal cyst, ultrasound demonstrated septa in the cyst unable to pick up by MRI/fusion. In the case of ventriculomegaly the cerebellum was assessed differently by US and MRI experts and a new ultrasound was performed 2 weeks later. The fusion only contributed to the discussion between the specialists in 4/14 cases (28.5 %). In all of these cases, the images led to multidisciplinary discussion and were a great teaching tool for juniors and fellows (Figures 2-6).

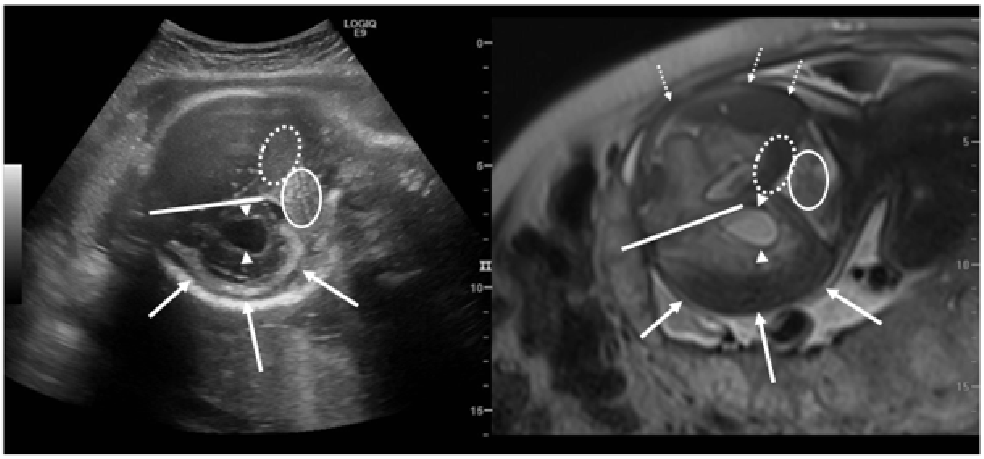

Figure 2: Fusion image of a fetus as a gestational age of 32 weeks in the coronal plane. On ultrasound the large subdural in the deeper half of the skull (white arrows) as well as the subdural hematoma on the superficial part of the tentorium (dashed circle) are clearly seen. The cerebellum is also depicted (white circle), In addition MRI demonstrates the hematoma in the superficial half of the skull (dashed arrows).

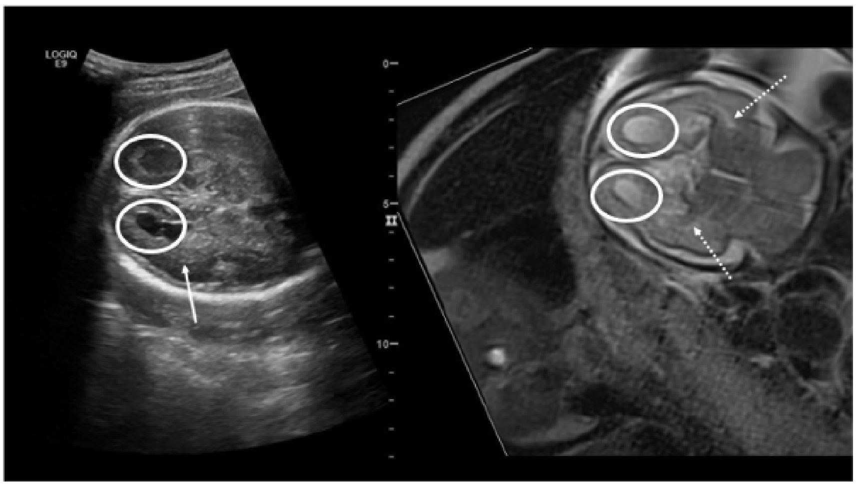

Figure 3: Fusion image of sonographic and MR image in the axial plane of a fetus at a gestational age of 22 weeks with proven CMV infection. Bilateral occipital cysts are seen (white circles). On the sonographic image, there is a discrete hyperechoic zoom around the ventricular wall (white arrow). On MR, increased signal intensity is noted at the periventricular crossroads (dashed white arrow).

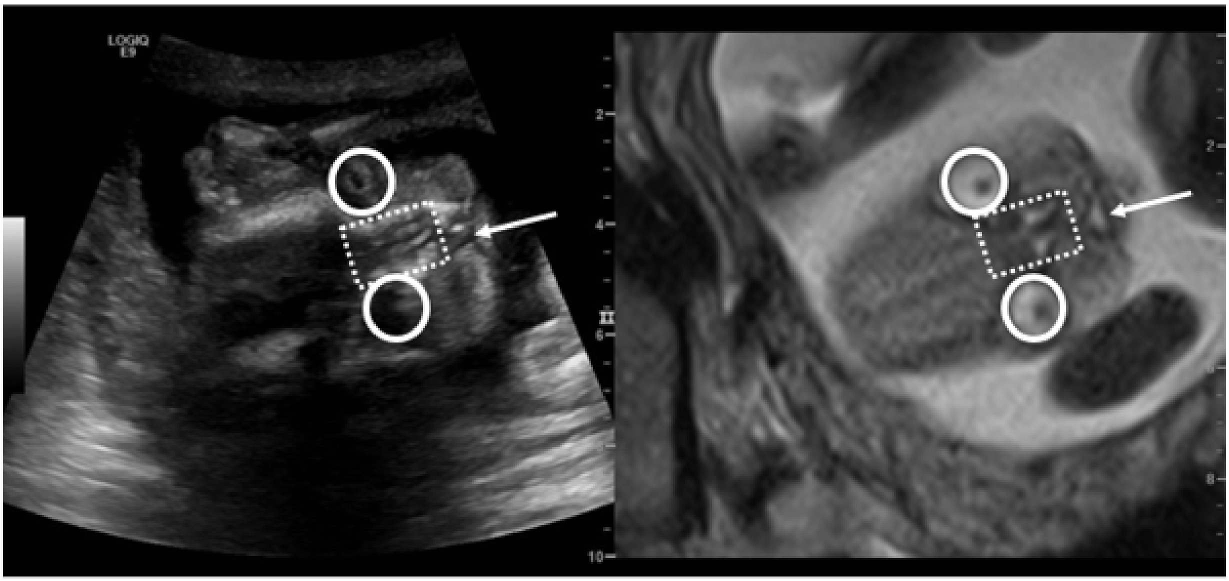

Figure 4: Fusion image of a sonographic and MR image in the coronal plane of a fetus at 22 weeks of gestation. In this image, the face with the eyes (white circles) and nasal cavity (white cubicle) are seen with a unilateral cleft lip (white arrow).

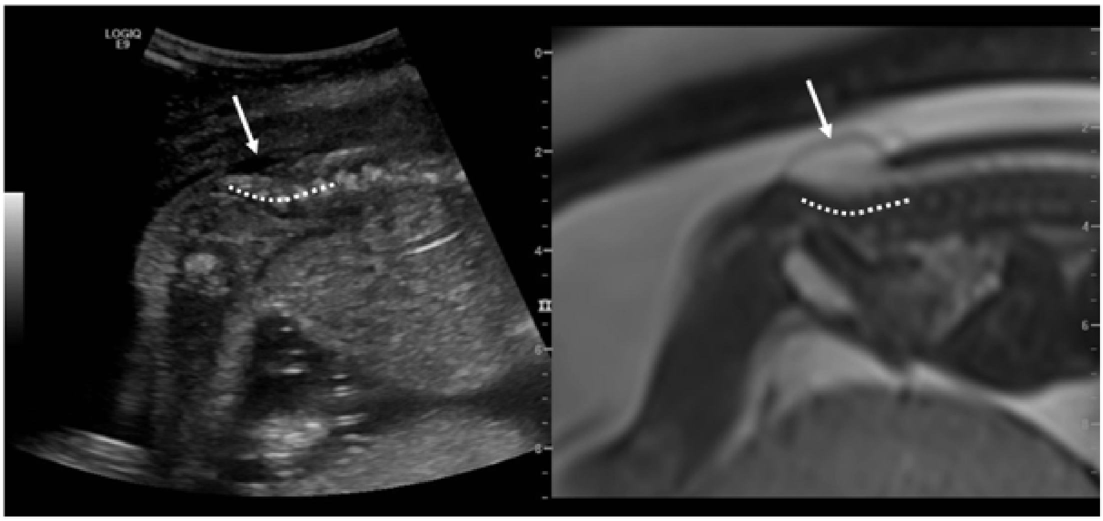

Figure 5: Fusion image of a sonographic and MR image in the sagittal plane of a fetus at 22 weeks of gestation at the level of the lower spine demonstrating a neural tube defect. Fusion image of a sonographic and MR image in the sagittal plane of a fetus at 22 weeks of gestation at the level of the lower spine demonstrating a neural tube defect. The cele (white arrow) is seen at the lumbosacral junction (dashed line).

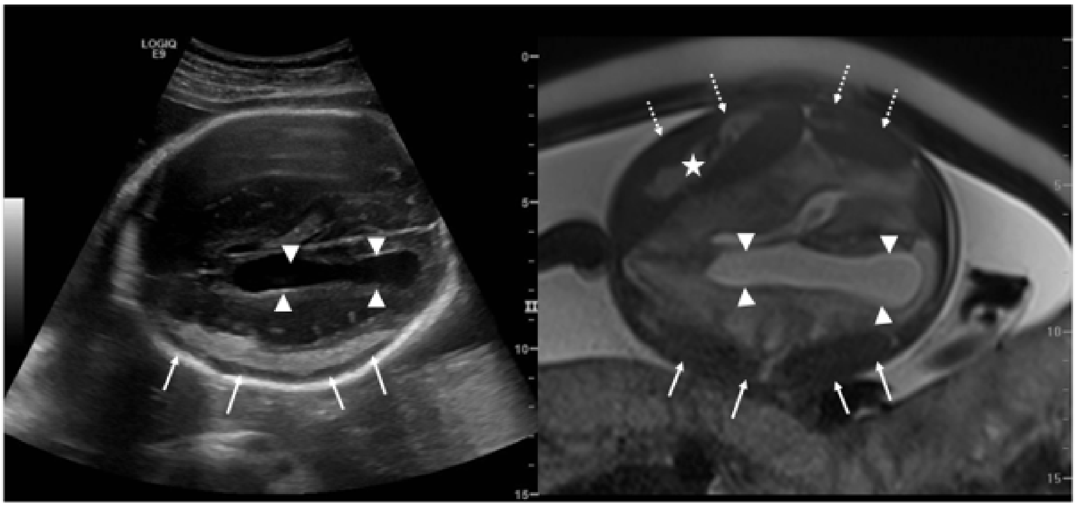

Figure 6: Fusion image of a fetus at a gestational age of 32 weeks. On ultrasound, the bilateral subdural bleeding is seen most clearly in the deeper hemisphere with a large hyperechoic sickle-shaped structure (small white arrows) compressing the hemisphere with enlargement of the lateral ventricle, (white arrowhead). The superficial half of the skull is not easily seen on ultrasound. On MR, the same findings are seen in the deeper half of the skull. In the superficial half, the subdural hematoma is even larger (dashed arrows) and contains a large clot (white star), again compressing the brain parenchyma. cubicle) is seen with a unilateral cleft lip (white arrow).

Discussion

Dedicated neurosonograply by an experienced feto-maternal specialist is an effective diagnostic method in the majority of severe prenatal CNS abnormalities in the first and second trimesters of pregnancy [13].

Furthermore, ultrasound is a widely available cheap and clinically powerful tool providing high-resolution imaging of fetal development. Surely the higher contrast images of MRI and its ability to overcome maternal and fetal constraints during US examination enriches the sonographic diagnosis [14]. Although fetal MRI has a higher intra- and inter-observer agreement, it is less widely spread, more expensive and lacks blood flow analysis [15,16].

In the last years, the fusion of MRI and ultrasound data has grown in popularity, particularly in prostate and intestinal medicine [7,8,17]. This technique is rather underdeveloped in the field of obstetrics and Gynaecology. Preliminary studies underlined the value of Caesarean section scars and deep pelvic endometriosis [18,19]. In prenatal imaging, MR and US fusion imaging are still in the experimental phase since this technique relies on accurate spatial resolution. The accuracy of the registration in prenatal medicine depends on the movements and the fetal growth [9]. The early papers on the fusion technique report on anatomical structures independent of movements and growth.

The longer the time interval between the 2 examinations the more significant changes in the fetal position may occur as well as significant developmental evolutions in the brain. We experienced the same findings in our study where one baby turned into a breech position between the MRI and ultrasound examination.

Several reports suggest a benefit of the fusion by improving the recognition of anatomical structures and therefore it has great teaching potential by allowing easier recognition of cerebral structures [9-12].

Limitations of the fusion technique are related to fetal movements. Therefore, vigilance is needed to verify that the ultrasound and MRI planes are identical and properly aligned. This is quite time-consuming since fusion was easily performed in an axial view, but it was more difficult to re-align coronal and sagittal sections in real-time ultrasound in advanced gestational age. Knowledge of the fetal cerebral anatomy in the different imaging techniques is mandatory.

Another important limitation results from the spatial divergence during the acquisition of ultrasound and MRI images. Acquisition of a 3D MR volume would solve this problem; however, currently, the acquisition of a 3D MRI volume is only possible with loss of either spatial or contrast resolution, rendering the diagnostic information of MR inferior to the standard image quality [15].

Overall, access to this fusion technique is still limited seeing the limited expertise of MRI by fetal specialists which is usually performed in a radiology unit rather than an obstetrical unit. Therefore, this technique is not applicable in routine practice unless there is a routine and quick interaction between both units. Limitations of our study are first of all the small number of cases.

Second, the fusion of ultrasound and MRI images does not show anatomical details that would not be seen by MRI or US separately. Thirdly, our study was not designed to demonstrate improvement in prenatal diagnosis or pregnancy outcome since there was no control group where both modalities were used separately. We only aimed to demonstrate the feasibility and added value of this new technique rather than an improvement in detection by one or both modalities. The multidisciplinary integration of both modalities improves prognostic appraisal and prenatal counselling. Finally, it is difficult to score the additional value of the fusion technique.

Conclusion

Fusion imaging is feasible in the assessment of fetuses with affected CNS anomalies from the second trimester onwards. It has a potential educational tool for both MR and US specialists to improve their knowledge and skills in the demonstration of anatomical details but does not add to the findings already seen by MRI or US separately and it is time-consuming. This technique improves the multidisciplinary assessment of the condition.

Acknowledgement

None.

Conflict of Interest

Authors declare no conflict of interest.

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