

Diagnostic value of fetal MRI in assessment of congenital anomalies of the central nervous system

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SUMMARY

Introduction. Magnetic resonance imaging is being increasingly utilized in detection of congenital malformations *in utero*, especially when US evaluation encounters significant limitations.

Aim. The aim of this study was to evaluate the diagnostic value of fetal MRI in assessment of congenital anomalies of the central nervous system in comparison to US.

Material and methods. The study was a retrospective review of MRI and US examinations with 35 fetuses from singleton pregnancies at the gestational age of 19–38th weeks. MRI was conducted either to further evaluate anomalies showed by prenatal US examinations or to clarify inconclusive US findings. All MRI exams were compared with previously conducted US examinations.

Results. The data showed that in over 60% of cases fetal MRI provided additional important information, not seen in US images. However, compared with US, MRI showed statistically significant higher identification rate only for the group of corpus callosum abnormalities.

Conclusions. Fetal MRI is a useful modality, complementary to US imaging in the evaluation of congenital malformations and may be an important adjunct to prenatal US in the 2nd and 3rd trimesters, especially when CNS pathology is suspected. MRI increases the accuracy of antenatal diagnoses, provides additional information that are useful in parental counseling, pregnancy management as well as peri- and postnatal care.

Key words: fetus; congenital abnormalities; prenatal diagnosis; magnetic resonance imaging; prenatal ultrasonography

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INTRODUCTION

Congenital abnormalities of the central nervous system (CNS) make up a large and heterogeneous group of congenital anomalies. They encompass brain and spinal cord malformations and are frequently of a complex nature since events that lead to a given anomaly during CNS development usually cause defects in more than one anatomical structure. The prevalence of congenital CNS anomalies in Poland is approximately 16 per 10,000 births [1]. They are a reason for about 40% of all deaths in the first year of life. In the remaining patients, they cause neurological disorders, mental retardation and epilepsy of various degrees [2].

For many years, ultrasound imaging (US) has been the only available method of prenatal imaging of congenital anomalies and still occupies the prime position in prenatal screening. However, as all methods, US has its limitations. Even with a considerable technological progress associated with the use of high-frequency transducers, transvaginal probes, 3D and 4D imaging and accelerated data processing in the most modern US systems, it does not enable detection or sufficient diagnosis of all fetal anomalies [3, 4]. In these cases, it is necessary to use a tool that is free of US limitations and can increase the accuracy of *in utero* diagnosis. That is why magnetic resonance imaging (MRI) is utilized in prenatal imaging.

Since the mid-1990s when fetal MRI stopped being a merely experimental tool and when the development of rapid T2-weighted sequences enabled accurate imaging of CNS structures in a moving fetus, its position and potential role in prenatal imaging has been discussed. The essence of these debates is not whether MRI can

be used to diagnose congenital defects *in utero*, but rather how useful it is in specific clinical situations and to what degree, compared with US, additional information about structural abnormalities of individual fetal organs translate into the modification of diagnosis, change of prognosis and further management.

Based on authors' own experience and collected material, this paper demonstrates that fetal MRI is a highly useful diagnostic tool, feasible to be used in the clinical practice in the case of detection or suspicion of fetal CNS structural abnormalities in prenatal US imaging.

AIM

The aim of this study was to evaluate the diagnostic value of fetal magnetic resonance imaging in assessment of congenital anomalies of the fetal central nervous system in comparison to US.

MATERIAL AND METHODS

In 2008–2013, over 80 fetal MRI scans were conducted in the Magnetic Resonance Laboratory of the Voxel Medical Centers in the Department of Medical Radiology and Radiodiagnosics of the Autonomous Teaching Hospital No 1 of Professor S. Szyszko in Zabrze (Medical University of Silesia in Katowice), Poland. Of these 80 cases, 35 fetuses aged 18–38 weeks (mean 30.68, SD 4.64, median 31) from

singleton pregnancies were included in a retrospective analysis. The mothers, aged from 18 to 41 (mean 27.83, SD 5.39, median 28), were referred for further diagnosis due to US-detected fetal anomalies.

The inclusion criteria were: a referral for a fetal MRI scan, access to a current and complete prenatal US examination, MRI conducted in accordance with the procedure followed in the MRI Laboratory and a sufficiently good MR image. Patients in the first trimester of pregnancy and those without or with an incomplete result of a previous prenatal US scan were excluded from the study.

US scans of fetuses included in the study were conducted by gynecologists and obstetricians specializing in prenatal imaging with the use of GE Voluson 730 Pro or Expert systems in accordance with the guidelines of the Ultrasound Imaging and Fetal Therapy Sections of the Polish Gynecologic Society.

Fetal MRI scans were conducted using an MR 1.5 T Signa Hdx scanner by GE with the use of an 8-channel HD body phased array coil according to personalized imaging protocols. The types and parameters of the applied sequences are presented in Table 1.

Scanning planes were planned in relation to the fetal body, separately for the head and torso. No gadolinium-based contrast agents were used. The MR images were assessed by the authors of this paper. MRI findings were compared with prenatal US results for each fetus.

Tab. 1. Types and parameters of the applied MRI sequences

SEQUENCE PARAMETERS USED SEQUENCES	3 plane localizer	2D FIESTA	SSFSE T2	FSPGR T1	FLAIR
Acquisition type	2D	2D	2D	2D	2D
Imaging planes		ax/cor/sag	ax/cor/sag	ax/cor/sag	cor
TR (ms)	4,7	3,4 - 4,2	4000	110	7000
TE (ms)	1,2	1,5 - 1,8	175 - 185	4,2	125
TI (ms)	0	200	0	0	1750
FA (degree)	30	65	90	85	90
NEX	1	1	0,56	1	1
Number of echoes	1	1	1	1	1
Bandwidth (Hz)	31,3	100	31,2	62,5	64
FOV (mm)	440	400 - 440	380 - 440	400 - 420	400
Matrix	256 x 128	320 x 224	320 x 256	320 x 192	320 x 224
Number of slices	21	13 - 62	12 - 71	12 - 64	40
Thickness of slices	10	8 - 10 / 4 - 5	8 / 2 - 5	2 - 5	4
Interslice gap (mm)	2	0,5 - 1	0 - 1,5	0 - 1	0
Additional scanning options		ASSET	ASSET	ASSET FS	

TR – repetition time, TE – echo time, TI – inversion time, FA – flip angle, NEX – number of excitations, FOV – field of view, FS – fat saturation, ax – axial plane, cor – coronal plane, sag – sagittal plane

Depending on the type of a relationship between the results obtained with the use of these two modalities, a given case was classified into one of three groups:

1. when findings from both examinations were consistent – confirmation of the US diagnosis/ruling out anomalies co-occurring with the US-detected pathology;
2. when MRI delivered new, significant clinical information – additional information;
3. when MRI indicated a different pathology than prenatal US – a change of the diagnosis.

The results of this analysis were presented in absolute and percentage values for each of the groups.

Moreover, the authors compared the frequency with which given CNS anomalies occurred depending on the applied imaging modality. These anomalies included: ventriculomegaly, corpus callosum abnormalities, malformations in the posterior cranial fossa excluding cysts, dysraphism, pathological intracranial fluid collections and malformations of the cerebral cortex (pallium) excluding corpus callosum abnormalities. The results were presented in absolute and percentage values. Statistical significance of the differences was tested using Pearson's chi-squared test with the level of significance at $p < 0.05$. Statistical calculations were conducted in the Statistica 10.0 system (Statsoft Inc.).

RESULTS

In the investigated material, there were 26 fetuses with CNS anomalies. Prenatal ultrasound findings corresponded completely with MRI results in the identification of fetuses with abnormal cerebral images. The prevailing pathologies in this group of fetuses were those manifested by ventriculomegaly (10 cases) and dysraphism (6 cases). In 1 case, a CNS anomaly was concomitant with a urinary tract defect. In 6 cases with a normal CNS image in both US and MRI, developmental defects were detected in other anatomical regions. MRI revealed normal fetal structures in 3 cases, including 2 with cardiac defects detected by echocardiography (Tab. 2).

In the analyzed material, prenatal US findings differed from MRI results in 22 cases (62.86%), 17 of which were fetuses with a CNS anomaly. The group of fetuses (8 cases) with the diagnosis changed by MRI included only fetuses with US-suspected CNS malformations. In the remaining 9 cases, MRI provided new information regarding US-diagnosed pathologies, e.g. it specified the site of changes, determined their nature and/or indicated concomitant defects (Tab. 3).

Table 4 presents the frequency with which given CNS anomalies were diagnosed in the entire investigated population depending on the imaging modality applied. The statistical analy-

Tab. 2. Types of MRI-detected fetal pathologies depending on the anatomical region or system in which they occurred

ANATOMICAL REGION / SYSTEM	PREVAILING TYPE OF PATHOLOGY IN MRI	NUMBER OF CASES IN MRI
CNS	Isolated ventriculomegaly	1
CNS	Defects with predominant ventriculomegaly	9
CNS	Posterior cranial fossa defects	2
CNS	Dysraphism	6
CNS	Pallium and/or midline defects	4
CNS	Other types	3
CNS in total		25
Chest		3
Abdominal cavity and pelvis		3
Normal MR image	Cardiac defect in US	2
Normal MR image	Anhydramnion	1
Beyond CNS in total		9
CNS and abdominal cavity	Defects in 2 systems: ventriculomegaly and urinary tract defect	1

sis demonstrated that both MRI and US detected a similar number of cases in all CNS malformation categories except for corpus callosum abnormalities in the case of which MRI was found superior to US in a statistically significant way.

DISCUSSION

The role of MRI in prenatal imaging is being broadly discussed [5,6] and its potential in solving specific clinical problems is still a subject of various studies [7,8]. According to current reports, CNS pathologies in which MRI can prove superior to US and which can be an indication for a fetal MRI scan include: cere-

bral ventriculomegaly [9,10], corpus callosum abnormalities [11,12], posterior cranial fossa anomalies [13], developmental disorders of the cerebral cortex [2], hemorrhagic changes [14] and other CNS pathologies acquired *in utero* [15] as well as dysraphic defects, particularly meningocele and myelomeningocele, especially in the context of planning *in utero* repair procedures [16,17].

Ventriculomegaly (Fig. 1) is one of the most common causes for extended prenatal diagnosis and inclusion of MRI into the diagnostic work-up. At the same time, it is the most common pathology observed in MRI. In this material, ventriculomegaly was observed in 14 cases,

Tab. 3. Added value of fetal MRI depending on the region of pathology

ADDED VALUE OF MRI	NUMBER (PERCENTAGE) OF SCANS		
	CNS	DIFFERENT ANATOMICAL REGION	TOTAL
Confirmation/ ruling out concurring pathologies	9 (25,71%)	4 (11,43%)	13 (37,14%)
Additional information	9 (25,71%)	5 (14,29%)	14 (40,00%)
Change of diagnosis	8 (22,86%)	0 (0,00%)	8 (22,86%)

Tab. 4. Frequency with which given CNS defects were diagnosed depending on the imaging modality

TYPE OF DEFECT		IMAGING MODALITY				TOTAL	
		MRI		US		N	PERCENTAGE
		N	PERCENTAGE	N	PERCENTAGE		
Ventriculomegaly	present	14	20,00%	13	18,57%	27	38,57%
	absent	21	30,00%	22	31,43%	43	61,43%
	total	35	50,00%	35	50,00%	70	100,00%
Pearson's chi-squared test p= 0,806							
Corpus callosum malformation	present	13	18,57%	4	5,71%	17	24,29%
	absent	22	31,43%	31	44,29%	53	75,71%
	total	35	50,00%	35	50,00%	70	100,00%
Pearson's chi-squared test p= 0,012							
Posterior cranial fossa defects excluding cysts	present	9	12,86%	7	10,00%	16	22,86%
	absent	26	37,14%	28	40,00%	54	77,14%
	total	35	50,00%	35	50,00%	70	100,00%
Pearson's chi-squared test p= 0,569							
Dysraphism	present	6	8,57%	6	8,57%	12	17,14%
	absent	29	41,43%	29	41,43%	58	82,86%
	total	35	50,00%	35	50,00%	70	100,00%
Pearson's chi-squared test p= 1,000							
Pathological intracranial fluid collection	present	6	8,57%	5	7,14%	11	15,71%
	absent	29	41,43%	30	42,86%	59	84,29%
	total	35	50,00%	35	50,00%	70	100,00%
Pearson's chi-squared test p= 0,743							
Cortical (pallium) defects	present	3	4,29%	4	5,71%	7	10,00%
	absent	32	45,71%	31	44,29%	63	90,00%
	total	35	50,00%	35	50,00%	70	100,00%
Pearson's chi-squared test p= 0,690							

i.e. in 40% of fetuses. As other reports in the world literature, the authors' own studies also indicate that MRI is superior to US imaging in terms of visualization of abnormalities accompanying ventriculomegaly. Three of the examined fetuses had MRI due to US-diagnosed isolated ventriculomegaly but the isolated nature of this condition was verified in only one case. In the remaining 2 cases, MRI additionally presented corpus callosum agenesis with the absence of septum pellucidum as well as corpus callosum agenesis with asymmetrical hydrocephalus due to the presence of an intraventricular cyst. In her studies, Girard has demonstrated that, in the case of ventriculomegaly, MRI detects concomitant CNS abnormalities in over a half of cases whilst this rate in US imaging amounts to a dozen or so per cent [18,19]. Similar results have been reported by Morris et al. [20]. They conducted fetal MRI scans in 30 fetuses with US-diagnosed isolated ventriculomegaly and found associated pathologies in 50% of cases. The percentage value reported in a much larger prospective study by Griffiths from 2010, which included 147 fetuses from 8 centers in Great Britain, was 17% [9].

Isolated callosal anomalies are rare. In the investigated material, they account for 15.38% of all corpus callosum malformations. They are much more frequently accompanied by other CNS structural defects (according to literature data: from 50 to 85% of cases) [21]. Tang et al. who reviewed 29 cases of corpus callosum agenesis in MRI found associated brain pathology in 27 cases. These cases mainly involved abnormal development of the cerebral cortex

and/or infratentorial structures [11]. In the group of fetuses analyzed in this study, callosal abnormalities (Fig. 2), apart from being associated with frequently concurrent supratentorial ventriculomegaly (61.54% of cases), were also concomitant with: intracranial cystic structures (3 cases), spinal bifida (2 cases) and other CNS anomalies (4 cases). Callosal agenesis was the only pathology detected by both MRI and US in 2 cases.

While authors agree that MRI is superior to US in detecting *in utero* brain pathologies that accompany callosal defects, there are considerable discrepancies concerning the sensitivity of prenatal ultrasound in diagnosing corpus callosum anomalies [22]. In certain papers, diagnostic accuracy of fetal MRI in the detection of callosal abnormalities is similar to prenatal US [21]. In others, however, MRI is reported to be more sensitive [23]. When conducting a retrospective analysis of 10 fetuses scanned by MRI due to a suspicion of a callosal anomaly, Glenn et al. confirmed the initial diagnosis in 8 cases and detected additional brain defects, invisible in US, in 5 cases [12]. The statistical analysis of the material presented above has provided evidence that callosal malformations were the only group in which MRI was characterized by significantly higher detectability than US imaging. Of 26 fetuses with CNS defects, MRI showed agenesis or other structural defects of the corpus callosum in 13 cases, including 9 fetuses without suspicions of this pathology in US imaging.

There are many publications in the literature that underline the value of fetal MRI in the

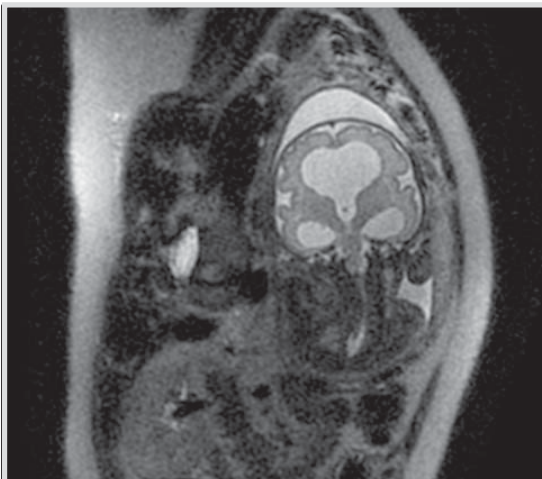


Fig. 1. Ventriculomegaly. Foetal MRI (29 GW), coronal SSFSE T2-weighted image

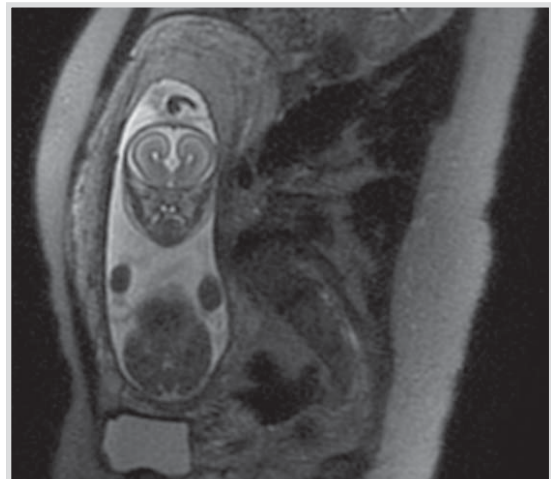


Fig. 2. Corpus callosum agenesis. Foetal MRI (22 GW), coronal SSFSE T2-weighted image

diagnosis of posterior cranial fossa anomalies. Some of them indicate that, compared with transabdominal US, MRI helps visualize additional anomalies of this anatomic region in even 50% of cases and sometimes even changes the primary diagnosis [24]. In the material analyzed above, posterior fossa defects were found in MRI in 11 fetuses (42% of all fetuses scanned with MRI due to CNS defects). Although considerable discrepancies between US and MR assessment of posterior fossa structures concerned 4 cases, fetal MRI did not prove to be significantly superior to prenatal US. Based on MRI, evidence of Dandy-Walker syndrome was found in 1 case (Fig. 3), Joubert syndrome was suspected in 1 fetus, and a malformation of the dural venous sinuses was diagnosed in another case. As for the first case, fetal MRI did not

show the pathology of the posterior cranial fossa found in prenatal US; the fetus with ventriculomegaly did not manifest typical signs of Dandy-Walker syndrome.

Moreover, 4 fetuses were diagnosed with spina bifida (Fig. 4) in both US and MR imaging. All prenatal US results specified the level of the pathology and described features of tightness within the posterior cranial cavity (“banana sign”) which, according to the literature, indicates the Chiari II malformation in nearly 100% of cases. MRI precisely determined the degree of posterior cranial structure herniation according to Sutton [25] and the level of spina bifida. Moreover, MRI showed features of the spinal cord anchoring in the herniations of the lumbar and sacral spine as well as callosal agenesis, which was undetected in US, in 2 cases.

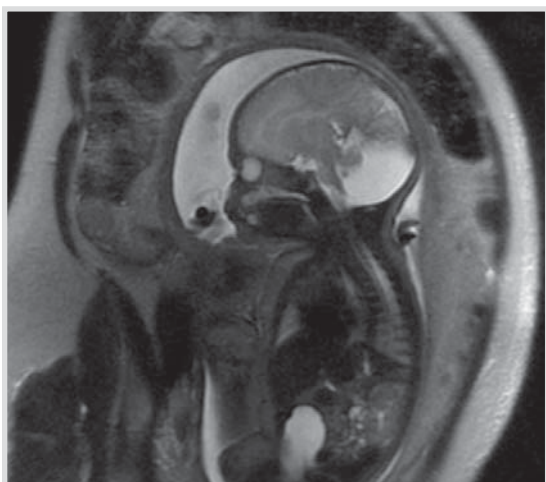


Fig. 3. Dandy-Walker malformation. Foetal MRI (35 GW), sagittal SSFSE T2-weighted image

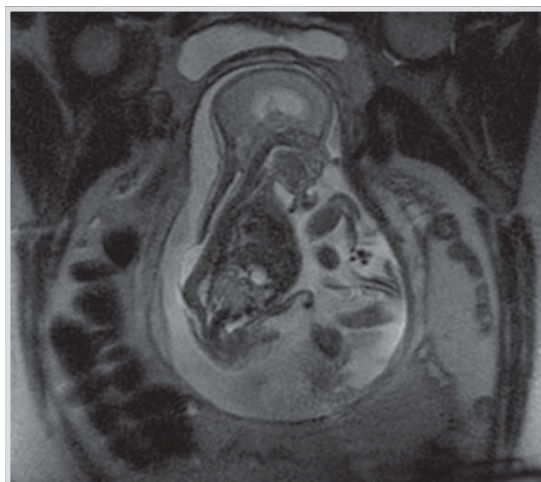


Fig. 4. Spinal myelomeningocele. Foetal MRI (24 GW), sagittal SSFSE T2-weighted image

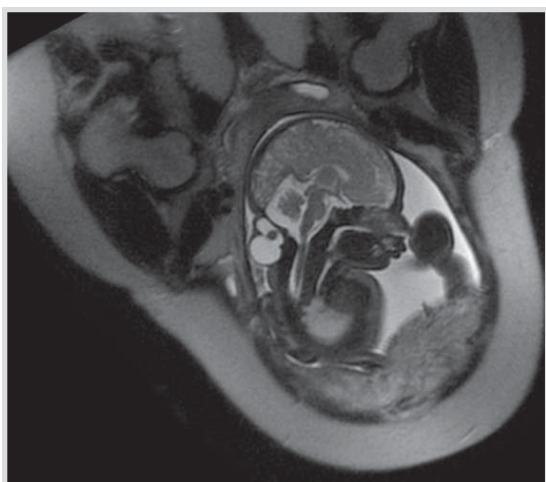


Fig. 5. Occipital meningocele. Foetal MRI (37 GW), sagittal SSSFE T2-weighted image



Fig. 6. Arachnoid cyst. Foetal MRI (38 GW), axial SSFSE T2-weighted image

There is no agreement concerning the superiority of one modality over the other in determining the level of the defect. However, most data indicate that prenatal US is characterized by higher diagnostic efficacy. Nevertheless, Aaronson, who compared the ability of US and MRI to detect the level of myelomeningocele in 61 fetuses, demonstrated the agreement of prenatal methods with postnatal conventional radiography in 79% for US and in 82% for MRI [26]. Similarly, the study by Herman-Sucharska proves that MRI is superior in prenatal determination of the level of spina bifida [27]. Furthermore, fetal MRI is superior in detecting closed dysraphic defects [28]. Saleem et al. analyzed 18 fetuses with neural tube defects (spinal or cranial) and confirmed complete agreement between US and MRI in 58% of cases [29]. In the remaining 42% of cases, MRI delivered additional information and ruled out cephalocele in one case. In a similar study, led by Griffiths, which included 50 fetuses with spinal abnormalities, the agreement amounted to 80%; MRI provided new information in 20% of cases, and ruled out the pathology in 8 cases [30].

In the analyzed material, there were 2 fetuses with US-diagnosed cranial meningocele (Fig. 5). In both cases, the pathology was located in the occipital region. Both fetuses were referred for an MRI scan in order to rule out concomitant pathologies. MRI confirmed the presence of occipital meningocele that did not involve nervous structures in both cases. One fetus had a normal brain image whereas the other presented abnormal brain stem with deep interpeduncular fossa as well as thickened and extended superior cerebellar peduncles and dilated cisterna magna. This was the basis to suspect Joubert syndrome.

Furthermore, 6 fetuses manifested intracranial lesions resembling arachnoid cysts (Fig. 6). They were supratentorial in 4 cases (2 interhemispheric, 1 eccentric at the base of the temporal lobe and 1 intraventricular in the lateral ventricle) and infratentorial in 2 cases. In all cases, the cysts produced the mass effect; the larger the cyst, the larger the mass effect. Two cysts were concomitant with asymmetrical ventriculomegaly. Three supratentorial lesions were accompanied by callosal pathology and one infratentorial cyst occurred together with cisterna magna dilatation. A cyst was an isolated pathology in merely 1 case. Compared with prenatal US, fetal MRI changed the diagnosis in 2 cases and provided additional information in 1 case.

Without a doubt, this study has considerable limitations. It is a retrospective study without a control group. The authors included in the analysis all consecutive fetuses referred for an MRI scan to our Lab provided that the inclusion criteria were met. Consequently, the tested population included only those fetuses that were suspected of having a developmental defect in the CNS based on prenatal US imaging. Fetuses with normal US findings were not considered. Moreover, the investigated group was diverse with a given pathology represented by at most a dozen or so cases. That is why most differences were not statistically significant. Furthermore, the authors did not verify all pathologies detected by MRI with final diagnoses. Such a heterogeneous group would require various verification methods, which would make it impossible to unambiguously evaluate the accuracy of obtained diagnoses. Most authors of similar studies did not determine diagnostic accuracy of prenatal US and MRI, but merely investigated their impact on the change of diagnosis and therapy. This impact occurs even before postnatal verification. The interpretation of MRI images could have been affected by already known US findings, the fact that the interpreting physician focused on already detected pathologies and by the time interval between the two scans. As for the first issue, the authors' goal was always to provide referring physicians with as diagnostically accurate results as possible, which would have been impossible without the knowledge of previous findings. As for the time interval, the authors had no influence on the time point at which both US and MRI examinations were conducted. Finally, a high percentage of MRI outcomes that changed the primary diagnosis or provided additional information might have been increased by a high number of fetuses that presented diagnostic difficulty in US imaging.

The data provided by this study encourage a broader implementation of prenatal MRI in Polish settings and its inclusion into the algorithms of modern prenatal imaging. Although it is poorly accessible and expensive, fetal MRI can be effectively utilized in the clinical practice in the cases of diagnosed or suspected congenital defects. It cannot replace US imaging as the primary fetal imaging modality and should be always complementary to US. Moreover, it should be conducted in reference centers. In difficult cases, fetal MRI can provide additional information, thereby increasing the diagno-

stic accuracy of prenatal diagnosis. This makes it a useful tool in parental counseling, pregnancy management as well as peri- and postnatal care.

CONCLUSIONS

1. Fetal MRI is complementary to US imaging in the evaluation of fetal malformations and may be an important adjunct to prenatal

imaging, particularly when CNS pathology is suspected or detected in US imaging.

2. MRI, being complementary to US imaging, increases the accuracy of prenatal diagnosis. In the case of congenital CNS defects, prenatal MRI can change the US diagnosis or provide new significant information.

3. The superiority of fetal MRI over US mainly concerns the imaging of corpus callosum abnormalities.

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