Prenatal imaging – role of fetal MRI

Pränatale Bildgebung – Rolle der fetalen MRT

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ABSTRACT

Background Congenital abnormalities occur in about 3 in 100 fetuses. Prenatal ultrasound is the standard technique to detect these fetal abnormalities. In Germany, three ultrasound examinations are provided in the first, second, and third trimesters, respectively. Fetal magnetic resonance imaging (MRI) can be used as an adjunct technique to provide further information in cases of congenital abnormalities.

Method A literature search was performed on PubMed focusing on publications that used fetal MRI as a secondary approach after prenatal ultrasound. **Results** MRI is a safe imaging method that does not harm the fetus when used during pregnancy. Some publications with experts in radiology show a very clear diagnostic advantage with respect to performing MRI on fetuses with brain abnormalities, while other publications with experts in neurosonography do not find the advantage to be that evident. Both techniques are clearly user-dependent.

Conclusion Fetal MRI can supplement the information obtained by fetal ultrasound and can provide additional information or exclude others. Diagnosis made by an interdisciplinary cooperation based on all available ultrasound and MRI findings is the key to optimal imaging and advice for expectant parents.

Key Points

- Fetal MRI poses no risk for the fetus.
- MRI aids prenatal ultrasound in the evaluation of prenatal findings.

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ZUSAMMENFASSUNG

Hintergrund Fast 3 von 100 Feten zeigen eine Organfehlbildung auf. Der pränatale Ultraschall ist das etablierte Standardverfahren zur Detektion dieser fetalen Erkrankungen und wird in Deutschland im ersten, zweiten und dritten Trimenon eingesetzt. Die fetale Magnetresonanztomografie (MRT) wird bei Auffälligkeiten im Ultraschall als zusätzliche Modalität in der pränatalen Bildgebung genutzt.

Methode Die Literaturrecherche zur Rolle der fetalen MRT wurde in PubMed durchgeführt und fokussierte sich auf Studien, die die fetale MRT als sekundäres Verfahren nach einem Ultraschall einsetzten.

Ergebnisse Die fetale MRT ist sicher in der Schwangerschaft anwendbar und zeigt keine assoziierten fetalen Entwicklungsstörungen. Studien mit radiologischem Schwerpunkt attestieren der fetalen MRT bei fetalen Hirnauffälligkeiten eine deutliche Überlegenheit gegenüber der Neurosonografie. Im Vergleich zeigen allerdings andere Studien mit neurosonografischem Schwerpunkt, dass die Überlegenheit der MRT deutlich geringer ausfällt. Diese Studien zeigen, dass beide Verfahren von der Expertise der durchführenden Person abhängig sind. **Schlussfolgerung** Bei einer Auffälligkeit im pränatalen Ultraschall kann die fetale MRT eine ergänzende Methode darstellen, die zu einer Bestätigung oder zu einem Ausschluss der Diagnose führt oder neue Befunde erhebt. Eine interdisziplinäre Kooperation zur gemeinsamen Diagnosefindung anhand aller verfügbaren Befunde aus Ultraschall und MRT ist der Schlüssel für eine optimale Bildgebung und Beratung der werdenden Eltern.

Kernaussagen

- Das fetale MRT ist in der Schwangerschaft sicher anwendbar.
- Das fetale MRT ergänzt den Ultraschall in der pränatalen Bildgebung.

Introduction

A fetal organ abnormality is present in 2.8% of all pregnancies [1]. Details regarding the various organ systems that are affected are provided in **Table 1**. Prenatal imaging is used for the early diagnosis of these fetal diseases and to classify them with respect to prognosis and possible therapeutic options with the goal of improving the child's outcome. Therefore, the place of birth and mode of birth can be selected based on the relevant pediatric/surgical focus [2]. The indication for prenatal interventions is sometimes already determined based on imaging.

Ultrasound is the basis of diagnostic prenatal imaging [3]. Transabdominal and vaginal ultrasound access is established due to the good availability and diagnostic quality. With high spatial and temporal resolution, ultrasound can visualize the smallest structures without movement artifacts, and the cost is minimal [3].

While some abnormalities can already be seen in the first trimester, others can only be visualized in the second to third trimesters (**> Fig. 1**) [4]. Accordingly, the German Maternity Care Guidelines recommend three basic ultrasound examinations in the first, second, and third trimesters [5]. The standard examina-

tion for detecting fetal anomalies is performed in the second trimester in the 19th–22nd gestational week. In addition to determining the number of fetuses and the position of the placenta, there are two options for detecting anomalies: basic ultrasound (measurement of the head and abdominal circumference and one thigh) and an expanded basic ultrasound examination (with additional examination of the neck and back, chest, and torso). This examination is not equivalent to a systematic ultrasound examination performed by an examiner with level II or III certification by the German Society of Gynecology and Obstetrics. In this ultrasound examination, all organ systems are systematically examined and documented [6].

Studies regarding detection rates of fetal anomalies show that there is a positive correlation between examiner qualifications, equipment quality, and detection rates [7]. The timing of the examination also plays a role. The ability to evaluate ultrasound is increasingly limited at the end of pregnancy due to ossification of the skeletal system and the dorsoanterior position of the fetus. However, oligohydramnios and the composition of the maternal abdominal wall, e.g., in the case of obesity, can limit the quality of an ultrasound examination [8].

Table 1 Prevalence of congenital organic and chromosomal abnormalities per 10 000 births based on the EURCAT data. According to the underlying abnormality, data (n, %) are given on continuation of pregnancy (lifebirths and stillbirths after 20 weeks of gestation) and termination of pregnancy.

	Prevalence per 10 000 births	Continued pregnancies in %	Terminated pregnancies in %
Central nervous system including spina bifida	26.7	49.3	50.7
Face, eyes, mouth and jaw region	20.9	89.1	10.9
Heart	81.1	89.5	10.5
Lung	3.9	82.8	17.2
GI tract	18.0	86.2	13.8
Abdominal wall	6.9	55.7	44.3
Kidneys and urinary tract	34.6	86.1	13.9
Genitals	21.7	96.5	3.5
Extremities	37.9	88.5	11.5
Other more rarely affected organ systems	14.7	68.1	31.9
Chromosomal abnormalities	54.9	49.4	50.6



► Fig. 1 Detection rates of fetal anomalies depending on the timing of the ultrasound examination based on Sygelaki et al. 27.6% of abnormalities can be detected during first-trimester screening (light gray), another 53.8% during second-trimester screening (gray), while another 18.6% (black) can only be detected during thirdtrimester screening. Individual abnormalities of the central nervous system are shown as examples.

Fetal magnetic resonance imaging (MRI) has become established as a complementary imaging method to ultrasound. It is used to confirm or rule out previously acquired suspected diagnoses, to characterize individual findings more precisely, and to identify possible associated abnormalities [3]. The advantages of MRI compared to ultrasound are the ability to plan the image planes regardless of fetal position, superposition-free imaging, and a large field of view [9]. MRI is also characterized by excellent soft-tissue contrast. As a result of the development of fast sequence techniques, it is now possible to achieve high image quality in spite of fetal movement [10].

Safety aspects of fetal MRI

Fetal MRI is performed without (maternal) intravenous contrast administration and without sedation. Since the introduction of MRI, possible teratogenic effects have been the subject of numerous studies, with a teratogenic effect not being able to be shown in numerous experimental and clinical studies. This is valid for field strengths of 1.5 and 3 Tesla [11]. Hearing damage due to the generation of acoustic signals in the gradient fields also could not be shown [12]. If the specific absorption rate (SAR) limits defined for fetal MRI of <2 W/kg are maintained, a critical temperature increase for the fetus due to the energy produced by the radiofrequency pulses is not to be expected [11]. Therefore, the method is considered safe [13]. However, every indication should be thoroughly examined [3].

General implementation of fetal MRI

Fetal MRI is based on T1- and T2-weighted sequences during free maternal respiration and is acquired with the mother in a supine position or, in the case of impaired circulation due to vena cava compression syndrome, with the mother lying on her left side (45°) [3]. As a rule, the entire fetus is first visualized before the examination focuses on an organ system. Classic standard planes (transverse, coronal, and sagittal with respect to the fetus) are used with a slice thickness of 2-5 mm. Additional sequences can be added depending on the particular issue. T1-weighted turbo spin echo (TSE) sequences generally require a longer acquisition time and are consequently more susceptible to motion artifacts but are suitable for visualizing meconium, bleeding, and stages of myelinization (T1-shortened) [14]. Diffusion-weighted imaging is the standard for CNS issues and in the case of focal thoracoabdominal changes. MRI-specific, gestational age-specific standard curves are used to evaluate measurements [15]. Fetal MRI examinations should be kept short (usually 20-30 minutes depending on the particular issue). Cardiovascular MRI, e.g., flow-sensitive quantitative techniques and cardiac cine MRI, require the recording of fetal cardiac function for synchronization with MRI data acquisition (cardiac gating). Innovative techniques can be used for this purpose [16, 17, 18].

Indications for fetal MRI

Fetal MRI can provide information in addition to ultrasound with respect to detailed organ imaging and pathological characterization primarily between the 26th and 32nd weeks of gestation [3]. In the first trimester and up to the 18th gestational week, ultrasound is greatly superior so that there is no indication for fetal MRI during this time period. The main indications for performing MRI are the presence of a ventriculomegaly, structural abnormalities of the corpus callosum or septum pellucidum, suspicion of cortical malformations, and anomalies of the posterior cranial fossa. However, fetal MRI can also be used in the case of issues regarding other organ systems and placenta anomalies [3].

It should be emphasized that both ultrasound and MRI are affected by the expertise of the examiner. Several studies with a focus on radiology find that fetal MRI is greatly superior to neurosonography. Examples are provided in the following section. The interdisciplinary authors of this article do not see the methods as competing in the case of a suitable indication but rather as complementary and see interdisciplinary cooperation for joint determination of the diagnosis based on all available findings as key for optimal imaging and counseling of expectant parents.

Central nervous system

Ventriculomegaly. Depending on the diameter of the atrium of the lateral ventricle, ventriculomegaly (VMG) is classified as mild (10–11.9 mm), moderate (12–14.9 mm), and severe (>15 mm) over the course of the entire pregnancy [19]. One study showed that, given the presence of VMG on ultrasound, MRI examination showed causative or associated findings in a substantial number of fetuses, resulting in a change of prognosis in 25% of cases [19].



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Other work groups examining the added value of MRI after a detailed neurosonography examination performed by an expert showed additional findings on MRI in the case of mild or moderate VMG on ultrasound in only 5.4% of cases [20]. These additional findings include cerebral hemorrhage (27%), polymicrogyria (20%), lissencephaly (13%), corpus callosum anomalies (10%), and other individual findings that cannot be grouped (30%). In the case of suspicion of VMG due to cerebral hemorrhage on ultrasound, MRI can help to clarify the cause by detecting and characterizing blood degradation products and is therefore important particularly in the case of mild VMG (**> Fig.2**).

In the case of severe VMG, the cause could only be identified on MRI in 18.1% of cases [21]. The identified causes included disrupted cortical development (32%), midline defects (27%), and hemorrhage (15%). Aqueduct stenosis is an example of severe VMG and involves enlargement of the third ventricle and the two lateral ventricles (known as triventricular hydrocephalus), while the fourth ventricle is normal (**> Fig. 3**). The third ventricular recess is typically enlarged [22]. However, there are different dysge-



▶ Fig. 3 Fetus at 25+0 and 28+5 gestational weeks as well as postnatal scans. Transabdominal ultrasound (**a**-**c**) shows triventricular ventriculomegaly and the aqueduct cannot be visualized. Fetal MRI shows an abnormal head shape with a flat forehead and relatively small head circumference (second percentile). Triventricular ventriculomegay with significant enlargement of the lateral ventricles (star) and the third ventricle. The width of the fourth ventricle is normal. The outer CSF spaces are narrow. The tectum is enlarged (**d**: sagittal; arrow) and the aqueduct cannot be detected which is consistent with aqueduct stenosis. Nodular subependymal heterotopia on the left (**f**: T2 hyperintense; **i**: T1 hypointense; arrowheads). Postnatal MRI confirms the findings (**g**: T2 drive sagittal; h: dual echo stir, axial; arrowheads).



Fig. 4 Fetus at 31 + 1 weeks of gestation. Fetal MRI shows complete agenesis of the corpus callosum with steer horn configuration of the anterior horns of the lateral ventricles (a: coronal; arrows; c: sagittal) and atypical configuration of the anterior horns of the lateral ventricles (e.g., axial; colpocephaly or teardrop configuration). There are no further abnormalities. Transabdominal ultrasound examination (b, d, f, h) performed on the same planes yields similar findings.

netic causes that can be associated with complex changes (including *x*-linked aqueductal stenosis).

Corpus callosum anomalies. Absence of the corpus callosum can be best evaluated on sagittal and coronal images (**> Fig. 4**). Indirect signs include the absence of the cavum septi pellucidi, ventriculomegaly with teardrop configuration of the lateral ventricles (colpocephaly), ascension of the third ventricle, and gyri extending in a radial pattern due to the absence of the cingulate gyrus (sunrise phenomenon). This abnormality can be isolated but is more common in combination with other malformations inside and outside the CNS [23].

To evaluate neurological development in the case of agenesis of the corpus callosum, a point system based on seven categories (gyration, opercularization, temporal lobe symmetry, lamination, hippocampal position, basal ganglia, and ventricular size) was developed for MRI [24]. There was a significant correlation between the severity of the MRI findings and a negative outcome related to cognitive, motor, and language development [24].

Griffiths et al. showed that in the case of an isolated corpus callosum anomaly on ultrasound, MRI examination is more precisely correlated with the postnatal diagnosis in 61% of cases [25]. The diagnostic gain achieved as a result of performing MRI was more significant in the case of hypoplasia or partial agenesis of the corpus callosum than in complete agenesis (correct diagnosis with ultrasound vs. MRI 8% vs. 87%). This study was performed by radiologists. Neurosonography was not performed by experts. The influence of neurosonography expertise on the ability to identify additional findings was examined in a review article [26]. The article showed that MRI detected additional findings after a detailed neurosonography examination in only 5.7% of cases, while additional information, primarily cortical malformations and anomalies of the posterior cranial fossa, was found in 18.5% of cases after a standard ultrasound examination.

Malformations of cortical development. Malformations of cortical development include various cerebral malformations due to abnormal neuronal proliferation, neuronal migration, and postmigration development [27, 28]. Prenatal detection of malformations of cortical development is very challenging. These changes are often first seen late based on the gyration that is present in the later stages of pregnancy, and therefore at a time when the increasing ossification of the skull greatly limits ultrasound. MRI does not have this limitation regarding ossification thus allowing complete visualization of the CNS with good differentiation of white and gray matter to the periphery of the brain [29]. MRI, therefore, plays an important role in the diagnosis of malformations of cortical development. A concomitant phenomenon in migration disorders is Z shape of the brain stem (kinked brain stem) which can be effectively diagnosed with fetal MRI (> Fig. 5). This is associated with Walker-Warburg syndrome, tubulinopathies, and L1CAM mutations and entails severe neurological limitations.

Pathologies of the posterior cranial fossa. The subgroup analysis of the MERIDIAN study, a prospective cohort study for evaluating the role of fetal MRI compared to ultrasound, showed that



▶ Fig. 5 Fetus at 29+0 weeks of gestation. Fetal MRI shows pronounced triventricular hydrocephalus with asymmetrical enlargement of the lateral ventricles and the third ventricle. The gyri are flattened and the region of the insula is ill-defined (**a**, **g**: arrows). The cortex does not have a clear margin with respect to the white matter. Frontal polymicrogyria is present (**e**: arrowhead). Signs of retinal detachment (**e**: dashed arrow), pontomesencephalic kink with cobra or Z-shaped configuration (**b**, **c**: dotted line), hyperplasia of the tectum with aqueduct stenosis (**c**, **f**: filled-in arrowhead), and pronounced vermis hypoplasia (**c**, **e**: arrowhead). The finding is typical for Walker-Warburg syndrome (type 2 lissencephaly). On transabdominal ultrasound, the posterior cranial fossa is difficult to visualize (**d**). The asymmetrical ventriculomegaly can be effectively visualized (**g**, **h**: star).

the initial diagnosis of ultrasound was changed by MRI in 44% of cases [30]. A retrospective analysis in which the diagnosis changed in 60% of cases yielded similar results [31]. The posterior cranial fossa is also difficult to evaluate postnatally on ultrasound and often requires supplementary MRI [32]. MRI can effectively visualize the vermis and additionally quantify the lobules of the vermis [33]. The tegmentovermian angle can also be examined, allowing the further differentiation of Dandy-Walker malformation, vermis hypoplasia, and Blake's pouch cyst in the case of an abnormal fourth ventricle.

If the Blake's pouch persists past the second trimester (Blake's pouch cyst), apical displacement of the cerebellum and the vermis can occur. A vermis with apical rotation can be a normal variant [34]. However, the differential diagnosis of vermis hypoplasia is sometimes difficult. Associated malformations of the CNS are common and occur in up to 56% of cases [35]. A hypoplastic vermis with cranial rotation in addition to an elevated tentorium, torcula, and transverse sinus indicates a Dandy-Walker malformation [32]. In a meta-analysis, MRI detected further anomalies of the CNS not seen in a detailed ultrasound examination in 13.7% of fetuses with Dandy-Walker malformation [36]. Additional anomalies were first seen on postnatal imaging in almost 18% of cases and were not diagnosed prenatally on ultrasound or MRI.

Cerebellar hypoplasia is often first detected in the third trimester since the significant increase in the size of the cerebellum and the ability to perform precise measurements are often only present at the end of pregnancy [36]. A reduced cerebellar volume can be caused by acquired atrophy or congenital hypoplasia. It can be unilateral or bilateral and can be primary congenital or secondary acquired. A particular strength of MRI is the detection and differentiation of infarctions and hemorrhage of the posterior cranial fossa using a combination of T1-weighted, T2-weighed, and diffusion-weighted sequences.

Rhombencephalosynapsis (RES) is a rare malformation of the cerebellum in which the vermis is partially or completely absent and the hemispheres of the cerebellum are fused [37]. Foliation from right to left can be shown, and the typical dumbbell shape of the cerebellum is not visible (▶ Fig.6). An abnormal diamond-shaped fourth ventricle is seen [38]. This data shows how difficult prenatal evaluation of the posterior cranial fossa is even with MRI. It can be very difficult to determine the prognosis. Interdisciplinary care has a clear advantage here.

The cisterna magna should be between 2 and 10 mm after the 20th gestational week. It can be barely measurable in the case of spina bifida aperta with a Chiari type II malformation due to the caudal displacement of the cerebellum (**> Fig. 7**). In addition, cor-



Fig. 6 Fetus at 28+0 weeks of gestation. Midsagittal plane (**a**) on fetal MRI shows an atypical vermis configuration with an abnormally rounded fourth ventricle (**a**, **c**: arrows). Particularly on transverse slices of the posterior cranial fossa, the typical dumbbell shape of the cerebellum is absent. Consistent foliation of the hemispheres of the cerebellum is seen on ultrasound (**d**) and MRI (**e**, **f**) (arrowheads). The finding is characteristic of rhombencephalosynapsis.

pus callosum anomalies can be seen in 69% of spina bifida cases, hypoplasia of the pons in 50%, and hypoplastic mesencephalon in 20%. These changes can be detected primarily on MRI [39]. The height and extent of the spinal lesion can be evaluated with both techniques with only limited reliability as they both seemed to slightly overestimate the lesion [40]. Periventricular heterotopia (**> Fig. 7**) can be detected on ultrasound based on the irregular border to the lateral ventricular wall but is very difficult to diagnose. On T1- and T2-weighted MRI, periventricular heterotopia appears isointense with respect to the cortex.

Organ changes outside the CNS

MRI examinations are increasingly requested and performed for further characterization of fetal abnormalities on ultrasound outside the CNS. The indications include changes in the face and neck region, the chest, and the abdomen. The following describes thoracic indications as an example.

Heart. Visualization of the fetal heart on MRI was not possible for a long time due to the small size of the heart (2–4 cm) and the movement at high heart rates of 110–160 beats/min. As a result of the development of fast sequences and cardiac gating techniques (= synchronization of cardiac motion with data acquisition), it is now possible to image the fetal heart. Various work groups have shown the possibility of including fetal cardiovascular MRI in diagnostic prenatal imaging [16, 17, 18]. An example of an atrioventricular septal defect is shown in **Fig.8**. The role and value of MRI will be further defined in the coming years since an added value of MRI being performed in addition to ultrasound currently cannot be shown.

Diaphragmatic hernia. The mortality rate for a diaphragmatic is between 10% in mild cases and 90% in severe cases and depends on the extent of the elevation of the organs and the achieved lung volume [41]. MRI is important for the prenatal diagnostic workup of diaphragmatic hernias since the abdominal organs emit different signals and thus can be effectively differentiated (> Fig.9). The stomach and proximal small intestine have strong signal intensity on T2-weighted sequences, while the meconium-filled distal small intestine and the colon are hyperintense on the T1-weighted sequences. The position of the liver can be better evaluated on MRI than ultrasound. For further differentiation of the severity of a diaphragmatic hernia, the calculated total lung volume is used as an indirect indication of pulmonary hypoplasia [42]. The planimetric determination of lung size (by tracing both halves of the lung on every slice, known as the tracing method) is suitable for calculating the total lung volume, allowing conclusions about prognosis with high reliability.



▶ Fig. 7 Fetus at 32 + 1 weeks of gestation. Coronal plane (a) on fetal MRI shows lumbosacral meningomyelocele (arrow). Note the low-lying tonsils indicative of Arnold Chiari type 2 (d: arrowhead). Impaired CSF circulation with enlargement of the lateral ventricles (a) is present. Isolated sube-pendymal nodular heterotopia is also seen (e, f: dashed arrows). On transabdominal ultrasound the defect in the region of L2/3 is seen in the saqittal plane (b). Ventriculomegaly (c) can also be seen. The heterotopia was not visible on ultrasound.

Placental abnormalities. The term placenta accreta spectrum (PAS) has become established for an abnormally invasive placenta in terms of placenta accreta, increta, and percreta [43]. Whether and in which form MRI examination can be helpful is still the subject of numerous studies. As in the case of fetal malformations, comparison of the two techniques is complicated by the fact that MRI is only used as a secondary method after the diagnosis has been determined based on ultrasound. Review articles indicate that MRI allows good differentiation of PAS [44].

In summary, fetal MRI examination as a supplementary method to ultrasound is an increasingly important part of diagnostic prenatal imaging in the last trimester. Particularly between the 26th and 32nd weeks of gestation, isolated abnormalities in various organ systems can be characterized more precisely on MRI. At this stage of pregnancy, diagnostic ultrasound imaging is increasingly limited by the ossification of the skeletal system and skull as well as by superposition of maternal structures. An interdisciplinary approach to the evaluation of prenatal imaging is needed to acquire complementary information from ultrasound and MRI, to better evaluate the dynamics of the findings, and to avoid contradictory and incomplete information transfer, thus making it possible to counsel expectant parents in an effective and targeted manner.



▶ Fig. 8 Fetus at 32 + 1 weeks of gestation. Doppler ultrasound gated cine SSFP image of an endosystolic cine-SSFP image in the 4-chamber view. The cine-SSFP sequence was performed with cardiac gating (direct, external Doppler ultrasound gating), thus allowing high temporal and spatial resolution. An AVSD can be seen (arrow at the level of the ventricular defect and star at the level of the atrial defect).



Fig.9 Fetus at 27 + 0 weeks of gestation. Coronal planes (**a**, **d**), sagittal planes (**b**, **c**) and axial planes (**e**) on fetal MRI show a left-sided diaphragmatic hernia. Observe the normal diaphragmatic position on the right (C: lung circumscribed; H: heart; T: thymus). Segments of the bowel (arrows, dashed) and stomach are displaced to the right side of the chest with subsequent shift of the mediastinum to the right. Meconium can be detected based on the shortened T1 effect in T1 weighting (d: dashed arrows). The right half of the lung is clearly hypoplastic (**b**: circumscribed). The total lung volume measured via planimetry was 21.5 ml (age-specific normal range 23–66 ml, mean 37 ml).

Conflict of Interest

Manuela Tavares de Sousa and Björn Schönnagel are Co-founder and stakeholder of northh medical

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