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Fetal MRI for dummies: what the fetal medicine specialist should know about acquisitions and sequences.

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Conflict of interest

None

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Ethical statement

No ethics approval was obtained as there were no new data acquired for this review. All given data is cited in text and reference list which can be used for more information.

Data availability statement

Data sharing is not applicable to this article as no new data were created or analyzed in this study.

What is already known about this topic?

. Fetal MRI is being used increasingly in current fetal medicine and has proven a complementary tool in the assessment of fetal anomalies and prior to fetal therapy.

. In the last decade conventional anatomical MRI sequences have been supplemented by implementation of advanced sequences providing structural, functional and metabolic information.

What does this study add?

- . Basic knowledge of MRI principles for non-radiologists, including physics, and safety in pregnancy.
- . Insights into the timing, preparation and performance of fetal MRI in order to aid the referring clinician and improve patient counselling prior to arrival in the radiology department.
- . Explanation on basis and clinical implementation of standard and advanced MRI sequences.

Abstract

Fetal MRI is an increasingly used tool in the field of prenatal diagnosis. While US remains the first line screening tool, as an adjuvant imaging tool MRI has been proven to increase diagnostic accuracy and change patient counseling. Further, there are instances when US may not be sufficient for diagnosis. As a multidisciplinary field, it is important that every person involved in the referral, diagnosis, counselling and treatment of the patients is familiar with the basic principles, indications and findings of fetal MRI. The purpose of the current paper is to equip radiologists and non-radiologists with basic MRI principles, essential topics in patient preparation and provide illustrative examples of when fetal MRI may be used. This aims to aid the referring clinician in better selecting and improve patient counselling prior to arrival in the radiology department, and ultimately patient care.

Introduction

Magnetic resonance imaging (MRI) was introduced in the 1970s with the first fetal MR images being published in 1983. (1, 2) For a long time, fetal motion was a major limiting factor to the application of MRI during pregnancy. It was not until the development of faster MR sequences and further technological improvements that fetal MRI could be routinely applied in fetal medicine. (3) As a multidisciplinary field, knowledge of basic physical principles and technical considerations in MR acquisition is crucial for all medical specialties involved in prenatal diagnosis. (4)

The MRI system comprises an operating unit where a technician and radiologist perform the scan, and an examination room where the patient is positioned in the magnet. The main magnet generates a constant magnetic field strength by electric currents through wires that are coiled around the cylindrical magnet core, which are cooled by cryogenic liquid. (5) The direction parallel to this main magnetic field (B_0) is called the longitudinal direction or z-axis. Inside the main magnet are additional gradient coils concentrically placed to identify the three orthogonal directions (x, y, z). Concentric and to the inside of the gradient coils there are radiofrequency (RF) coils, which (1) transmit energy to the tissue, and (2) collect the induced signal back from the tissue. The magnetic field of the RF coils is called the B_1 magnetic field and interacts with B_0 to localize and encode the MR signals to create an MR image.

All tissues in the human body contain hydrogen nuclei or protons, mostly bound to other molecules. These protons are positively charged and constantly spinning causing a magnetic field around them.

When put into an external magnetic field (e.g. MRI system), the protons align with or against the direction of this field. As it is more energy-efficient to align with (parallel) than to align against (antiparallel), more protons will align parallel to the magnetic field causing a net magnetization parallel to B_0 . The proton spinning is also determined by the magnetic field strength which causes the protons to precess at a certain (Larmor) frequency.

RF energy is sent in by the RF coils and flips the protons away from the B_0 in an angle depending on the strength and duration of the RF pulse. This angle is called the *flip angle* (FA). When the RF pulse is turned off, protons will return to their previous state, referred to as the relaxation process (=T1 relaxation). Furthermore, the RF pulse causes the protons to spin simultaneously at a certain precessional frequency (= 'in phase'). Although the main magnetic field is constant, there are magnetic field fluctuations (inhomogeneity) causing the precessional frequency to differ between protons in the same magnetic field. After the RF pulse, protons associated to different tissues will each regain their own precessional frequency (= dephase) based on the local main magnetic field strength. This is called the transverse magnetization (= T2 relaxation).

The process of T1 and T2 relaxation is being measured at different times (milliseconds) by RF receivers and translated into a grey-scale image by the computer. By changing the strength and duration of the RF pulse (= changing the flip angle) and by manipulating the time between two RF pulses (= repetition time (TR)) or the time between the RF pulse and the peak signal in the coil (= echo time (TE)), a variety of sequences and contrasts can be induced. Depending on the region of interest and the pathology, a combination of sequences and contrasts needs to be applied.

Safety

During gestation, both generic and pregnancy-specific safety concerns apply. The main magnetic field, which is never off, attracts ferromagnetic objects that can become dangerous projectiles. Patients should be screened for foreign bodies or implants that can be dislodged or overheat during the examination. (6-8) In addition, the external magnetic field is also exerting a force on biological systems. Although no studies have shown a deleterious effects by short time exposure, there are restrictions on magnetic field strengths of above 4 Tesla (T) for fetal imaging. (9)

The actual number of safety studies remains limited. RF pulses emitted during the MRI-examination deposit energy into the tissues as heat with theoretical risks of causing a temperature increase and even burns. Therefore, regulations worldwide have determined local and global specific absorption rate (SAR) levels (energy that is being deposited within a given mass, expressed as watts per kilogram [W/kg]) that cannot be exceeded during any MRI session. (6, 9) It is very important to understand these SAR principles when supervising a MRI examination. MR systems are self-limiting due to built-in SAR limits to allow safe application of this imaging technique.

To allow imaging of an entire region (e.g. fetus) there is a rapid switching of gradient coils in the MR system, that encode the spatial information. This on and off switching may cause maternal peripheral nerve stimulation resulting in mild tingling or tapping sensations. Further, the switching of gradients produces acoustic noise exceeding patients' comfort levels, causing pain. (10) This is particularly important in the high-speed sequences necessary for fetal MR examinations. (11) Hearing protection is therefore mandatory for the mother. Multiple studies have demonstrated the

protective effect of the gravid uterus which provides sufficient sound attenuation preventing fetal hearing damage. (12) (13-16)

Magnetic field strength (3T vs 1.5T)

Nowadays the most commonly available scanners are 1.5 T and 3.0 T magnets. Both field strengths have been deemed safe for clinical use and are capable of providing quality examinations. While 3 T MRI has the potential to supply more detail, it has also some limitations, mostly pertaining to the higher susceptibility to inhomogeneities and artifacts. (17) Hence, indications such as polyhydramnios may be more easily imaged on 1.5 T scanners. On the other hand, 3.0 T imaging may provide additional information in indications relating to bone anomalies, as higher susceptibility facilitates delineation of small ossified structures or counting of vertebral bodies/ribs, and steady-state free precession (SSFP) sequences detect adequately cartilage. (17)

The decision of which magnetic field to use is often related to which scanner is available in each center. Optimized sequences and operator experience in both using the scanner and interpreting the resulting images are more important than the field strength itself.

MRI supervision

Ideally all fetal MRI examinations should be supervised by a specialist familiar with both MRI physics and fetal anatomy. This will allow to perform ad hoc adaptations to the MRI examination based on unforeseen artefacts, fetal motion or unknown/additional pathology. MRI findings should be integrated with the clinical (obstetrical history, maternal and paternal family history, laboratory tests, etc.) and genetic information, as well as with the sonographic findings, and interpreted in a multidisciplinary approach. (11, 18, 19)

MRI timing

Usually Fetal MRI is not a first-line examination during pregnancy, but a complementary method to previous ultrasound. (20) As such, a recent ultrasound examination providing information on the suspected pathology, relevant history details and the GA should be present. (Table 1) (21)

The timing for MRI is a multifactorial decision. Before 18 GA resolution is overall poor, limiting the additional value of MRI to US. The type of abnormality detected/suspected on US is a major determinant. Meningomyelocele repair is indicated before 26 GA, so fetal MR will be performed prior to 26 weeks GA. In cases of a giant neck masses, fetal MR may be delayed until late pregnancy to allow optimal delivery planning if tracheal patency is compromised. (22) Abdominal and pelvic masses can also be scanned late in pregnancy to allow for higher spatial resolution, optimized perinatal management and avoid early postnatal MRI (and consequent need for sedation). (3)

Besides the pathology and management, timing of MRI can be influenced by the local legislation on termination of pregnancy (TOP) and the confidence of the sonographic diagnosis.

Patient preparation

Expecting mothers undergoing fetal MRI are often anxious concerning the procedure as well as potential findings. Information about the procedure and how the result will be communicated can partially alleviate the stress and be beneficial for the patient and fetal MR examination. (Table 1) (11, 23)

Informed consent should be obtained, verbal or written depending on local regulations, and MRI contraindications should be excluded. Detailed information regarding devices and other contraindications can be found online (i.e. <http://www.mrisafety.com>). When in doubt the radiologist or MR physicist should be contacted.

Ultrafast sequences allow for motion free imaging in the majority of fetal MRI examinations, and routine maternal sedation is unnecessary. (11, 18, 24) Several centers recommend a four-hour fasting period prior to imaging, while others advise only sugar- and/or caffeine avoidance for this time period. (23, 24) Imaging early in the morning may also reduce fetal movement artifacts as fetuses tend to follow a circadian sleep pattern. (21) Emptying the bladder is also recommended prior to the examination to improve maternal comfort. When the mother is claustrophobic and too anxious to enter the MRI suite a mild sedative might be required to relieve the maternal stress and perform the MRI. (11)

In the MR suite, the mother is positioned in a supine or left lateral position, depending on maternal preference and comfort level. (11, 24) Cushions can be used to increase maternal comfort. Ear protection should be provided. A coil is then placed over the abdomen for MRI signal reception. It may be necessary to change coil position during the examination, to optimize signal-to-noise ratio when switching from fetal head to body imaging.

MRI sequences and their applications

Preselection of parameters in order to visualize certain tissue qualities, is an important process in MRI. These so-called sequences are planned and acquired in orthogonal planes (axial, sagittal and coronal; in relation to the brainstem when the brain is being imaged or using the vertebral spine when imaging the body). Due to the continuous fetal movement, it is paramount that the latest acquired images are used for the planning of following sequences. While the aim of this paper is not to provide in depth knowledge of each sequence, it is important to understand basic sequence concepts. Below the reader will find a short description and examples of the most basic and important sequences.

T2

T2-weighted (T2W) contrast is the mainstay of fetal MRI. Good quality acquisitions on three orthogonal planes are essential and should be repeated until satisfactory images are obtained. On T2W images tissues that have a high water content appear white (CSF, amniotic fluid) or brighter than cell rich tissues. Two main T2W sequences are used: single shot fast spin echo (ssFSE) and steady-state free-precession (SSFP). T2W ssFSE provide excellent depiction of fetal anatomy throughout gestation, particularly the brain, fluid filled cavities, lungs, placenta, and the fetal surface including the profile. For fetal body imaging, T2W SSFP allow better depiction of vessels and the fetal heart (Figure 1). (21)

Goal

The main purpose of T2W images is anatomical depiction of fetal structures. T2W images allow for a clear differentiation of the fetus from the surrounding amniotic fluid, most fetal body cavities (Figure 1) but also between different tissues within the fetus. T2W ssFSE images provide the best contrast in fetal brain evaluation, although with adjusted parameters SSFP may be used with equivalent diagnostic accuracy (25). However, T2W contrast has limitations in the identification of fetal brain lamination (particularly the 3rd trimester). Other sequences, such as echo-planar fluid-attenuated inversion recovery (EPI-FLAIR) (Figure 2), which adds an inversion pulse that cancels the signal of

water, or diffusion weighted imaging (DWI), which use water diffusivity in the different layers can be applied for more in depth evaluation. (26, 27) Compared to ssFSE, SSFP sequences provide contrast between the different organs and tissues but also enable better visualization of vessels, particularly intrahepatic vessels, the aorta and the heart chambers. (28).

T1

Several kinds of T1-weighted (T1W) sequences have been used in fetal MRI. At present, fast low angle shot sequence (FLASH, Siemens, Erlangen, Germany) or Fast Field Echo sequences (FFE, Philips, Best, Netherlands) are the most robust ones. They allow quick acquisition of an image pile, but make these sequences prone to movement artifacts. As such, these sequences are acquired in maternal breath-hold of around 15-20 seconds. Free-breathing sequences are available and may facilitate imaging in mothers who are unable to cooperate or when significant fetal movement is present. T1W images should be acquired in at least one plane for the fetal head and the fetal body.

Goal

T1W images are used to identify tissues or lesions with short T1 relaxation time (T1 hyperintense), which comprise normal structures such as the pituitary and thyroid glands, meconium, liver and fat, as well as lesions such as hemorrhage or calcifications. (29) The pituitary and thyroid glands can be identified from 20 GA. (21) This may be of particular importance in cases of septo-optic dysplasia, where the hypothalamic-pituitary dysfunction is an important prognostic factor. (30) T1 hyperintensity of subcutaneous fat can be identified from 26 GA as fetal adipose tissue progressively transforms from brown to white. (31) This can be used to identify lipomas or fat replacement of muscle muscle dystrophies. Meconium can be identified from 20 GA with the functional closure of the anal canal progressive meconium build up. (21) Its identification is useful in suspected anal-rectal malformation, in which sagittal and coronal T1W images of the fetal body should be acquired. (21, 29) Calcifications and blood breakdown products can also be identified on T1W images. It is however worth mentioning that hemorrhage cannot be reliably dated as in postnatal examinations. (32)

Gradient Echo (GE) or Echo Planar Images (EPI)

GE and EPI are imaging techniques that visualize susceptibility artifacts to detect bony structures, blood breakdown products or iron accumulation. These techniques acquire images very fast, hereby overcoming motion artefacts but they have a low spatial resolution and low soft tissue contrast. (21, 33)

Goal

EPI and GE images are extremely useful in detecting regions of hemorrhage (21) While acute hemorrhage can be accurately detected on T1W and T2W, hemosiderin deposits may be difficult to visualize. (32, 34) This becomes particularly important in the cases of ventriculomegaly and hydrocephalus, where the detection of hemosiderin deposits in the ventricular lining is diagnostic of past hemorrhage and helps exclude other pathologies and better counsel the parents.

EPI also allows for demonstration of physiologic changes relating to hepatic hematopoiesis in the fetal liver (35) and show differences between the physiological right and left liver lobes, unlike on T2. (28)

This technique can be applied to evaluate the fetal skeleton, particularly before 27 w of gestation, where bones are depicted as hypointense structures, while the cartilaginous epiphyses as hyperintense structures. (36) (Figure 3) After 27 GA the distinction between bone and surrounding muscles becomes less conspicuous. (21) On higher magnetic fields (≥ 3 T) this sequence may be too sensitive to delineate small bones, leading to so-called susceptibility artifacts, blurring the margins of the bones and should be combined with T2WSSFP images. (17)

Diffusion Weighted Images

DWI is based on the constant random (Brownian) movement of water molecules. Extracellular water molecules will have more freedom and move with equal probability in all directions (= isotropic) while intracellular molecules display a relative “restricted diffusivity” (=anisotropic movement). (37) The biggest technical difficulty of applying DWI to fetal imaging is to overcome the effects of macroscopic motion, while retaining sensitivity to microscopic motion of water molecules. (37, 38) Each tissue has its specific diffusion properties. Pathologic processes alter the relative proportion of the water distribution in the affected tissues, hence will change DWI signal.

Goal

DWI can be used for assessment of normal brain development (39), (39), where it enables depiction of normal brain lamination (Figure 4) (26) (40, 41), lung (42) and kidney assessment. (43) (44)

In the postnatal period, DWI images are used often in the context of acute ischemia or tumor grading, both associated with restricted diffusivity and low ADC. (45, 46) (Figure 5). While the same principles apply prenatally, it is seldom that patients are referred for either of these reasons. Although ADC changes have been described in patients with hydrocephalus or severe IUGR, the clinical value is still unknown on an individual basis. (47-49)

Normal kidney tissue presents high signal intensity (Figure 6) on DWI images. This can be used in pathological cases, particularly in the detection of dysplastic or ectopic kidneys or in the evaluation of remaining functioning tissue in severe cases of multicystic kidney or hydronephrosis. (50)

Other sequences

Other anatomical sequences can be used for specific indication (table 2).

Advanced Sequences

Depending on the indication, further sequences may be applied. Although US and standard MRI sequences grant excellent depiction of anatomical and structural detail, they do not provide functional information. Advanced sequences such as diffusion-tensor imaging (DTI) with tractography, resting state functional imaging (fMRI), and MR spectroscopy (MRS) may provide this information, for both fetal and placental assessment. (51-53)

DTI allows measurement of anisotropic diffusion of water molecules providing insight into the microstructure of tissues by detecting the diffusion direction of water molecules. (26, 54) In utero this technique is applied in white matter development assessment. (55) Besides fractional anisotropy (FA) maps, DTI images can be post-processed in order to identify and reconstruct main projection, commissural, and association fibers (56) by tractography, in a reproducible fashion. (57) Examples of clinical application of this technique include assessment of callosal anomalies, or the cortical spinal tract in space-occupying or destructive lesions, or the crowding in the posterior fossa in open spinal dysraphism. (55, 56, 58)

fMRI, using blood oxygenation level-dependent contrast (BOLD) imaging, allows assessment of brain function, by measuring the increase in local blood flow associated with neuronal activity. (59) Other applications of BOLD imaging in fetal MRI comprise placental assessment (60) and in the evaluation of flow in vascular malformations.

Metabolic profiles of the fetus, amniotic fluid and placenta can be evaluated using magnetic resonance spectroscopy, in both 1.5 T and 3 T magnets. (53, 61, 62) This may be useful in IUGR (63, 64), space occupying lesions (figure 7) or in excluding brain parenchymal involvement in infections such as CMV (62).

Strengths and weaknesses

Since the beginning of fetal MRI applications, its possibilities and uses have increased steadily, with an excellent safety profile. (65) Technical advances have bestowed significant improvements in image quality and allowed for application of advanced techniques without need for sedation. MRI is an adjuvant imaging method to specialized ultrasound and not routinely used as a screening method. (20)

Fetal MRI has been shown to improve diagnostic accuracy and diagnostic confidence for brain anomalies (66), and some body indications (67) leading to management changes in a significant proportion of pregnancies. (66) However, while fetal MR may add clinically relevant information in the second or third trimester of pregnancy, in earlier gestations (first/early second trimesters) its value is limited. Due to fetal size and movement, there is limited spatial resolution, especially when compared to expert sonography. (18, 68, 69)

There are circumstances that can limit US visualization of the fetal structures and for which MRI may be necessary, even in earlier gestations. Fetal MRI can be successfully performed from 18 GA onwards, and even earlier, depending on the indication. On the other end, in late pregnancy anomalies may be difficult to visualize with US due to ossification and fetal position. MRI may be useful in those cases, as a cephalic position is more stable and less prone to maternal breathing movements. Fetal MRI may also be performed in late gestation/term in order to plan for birth, intervention immediately after birth or to avoid the need for postnatal imaging in the unstable neonate.

As fetal MRI is a growing field and being performed in an increasing number of centers, the referring physician should be aware of the expertise and methodology at the different centers. Some centers only image and report on the fetal brain while others scan the placenta and entire fetus. As for the imaging, the expertise in reporting can be different as well. Where in some centers the pediatric radiologist is responsible for the report, in others the fetal brain is reported by a (pediatric) neuroradiologist. For patients and referring physicians, it is most beneficial when US and MRI are being performed on one day, with multidisciplinary discussion of the findings prior to counseling. Recently, the first guidelines on fetal MRI have been published by the International Society of Ultrasound in Gynaecology and Obstetrics. (18) Although these are very broad, they provide information which can be used to setup or improve the fetal MRI service. On the other hand, it can be used by referring physicians to test the fetal MRI to the standard of care principles that are currently available.

In conclusion, fetal MRI is a complimentary imaging method to US in prenatal diagnosis, that can improve lesion detection and exclusion. Its use is highly dependent on availability, the center's

experience (both in MRI and US) and the referring clinicians' and parents' need for further information in terms of diagnosis or prognosis.

Accepted Article

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Figure 1 – 34GA fetus referred for small bowel dilatation. On MRI, dilated intestinal loops can be detected which are meconium filled: high signal intensity on T1 (a, white arrow), and lower SI on T2W SSFP (b, white arrow) and ssFSE (c, white arrow) than "pure" liquids (stomach, light blue arrows, bladder, dashed blue arrows, amniotic fluid). The combination of these findings with hyperperistalsis (dynamic T2W images, not depicted here) suggests lower small intestine atresia. Caudally there are no meconium- or fluid-filled bowel loops are detectable. Notice the differences between T2W sequences; on SSFP, vessels can be readily identified within the liver (b, white dashed arrow), and major vessels such as the umbilical cord (b, c, yellow dashed arrow) and heart (b, c, yellow arrow) appear bright, while vessel walls cannot be distinguished from lumen on T2W ssFSE (c, yellow dashed arrow and c, yellow arrow). Subcutaneous fat can be identified throughout at this gestational age on T1 (a, black arrow).

Figure 2 – 25GA fetus referred for complete callosal agenesis. On MRI, a thin residual part of the body of the corpus callosum (b, black arrow) can be identified. The cortical plate (white arrow), intermediate zone (yellow arrow) and periventricular zone (blue arrow) can be identified on both EPI-FLAIR (c) and DWI (d) images, but not on T2-w ssFSE images (a,b). Identification of cerebral lamination patterns is essential in the assessment of brain development and exclusion of cortical/migration disorders.

Figure 3 - Sagittal sections of three different fetuses; Sagittal (a) and coronal (b) T2W ssFSE images of a 24GA fetus referred for cleft palate. There is a complete absence of soft and hard palate (compare to intact palate: c, yellow arrow), with the oral cavity amply communicating with the nasal cavity (a, b, yellow arrows). MRI is also excellent in the depiction of small structures, such as olfactory nerves (b, dashed blue arrow). Sagittal T2W ssFSE image of a 31GA fetus referred for polyhydramnios (c). A “pouch sign” can be identified denoting the sac-like termination of the esophagus in esophageal atresia (c, white arrow), which is can be identified on dynamic T2-w sequences, mostly after GA28. There is no stomach filling. Sagittal T1w FSE image, depicting normal anatomy of a 25GA fetus (d): meconium filling of the sigmoid and rectum with bright T1 signal intensity (d, dashed white arrow), intermediate T1 hyperintensity of the liver (d, black arrow) and high T1 SI of the hypophysis (d, blue arrow). At this gestational age, no subcutaneous fat can be identified (see Figure 1)

Figure 4 - Acute intraparenchymal hemorrhage in a 23GA fetus referred for normal US (3 days earlier) and previous child with skeletal dysplasia. An acute hemorrhage of the germinal matrix region (black arrows), appearing as an hypointense lesion on T2W ssFSE image (c) and with a “blooming” effect on EPI imaging (a,b), and slight hyperintense signal on T1wi (d). Imaging was repeated 4 weeks later, where a more organized and T1 hyperintense clot can be seen on T1W images. On EPI images, not only the blood products can be identified, but also skeletal structures: radius and cubitus (a, light blue arrows), humerus (a, yellow arrow) and respective epiphysis (a, white arrows), as well as smaller bones such as ribs (a, red arrow) and phalanges (a, dark blue arrow).

Figure 5 - (a) T2W axial image of a fetal brain at 29 GA of gestation with mild bilateral heterogeneous white matter signal intensity in the periventricular white matter. (b) Corresponding b1000 DWI demonstrating bright signal in these areas which appeared dark on the apparent diffusion coefficient (ADC) image (not shown). This is in keeping with ischemia. (c) Follow-up T2-weighted axial image of the fetal brain at 34GA illustrates the evolution into cystic leukomalacia.

Figure 6 - Coronal T2-w ssFSE (a,c,e,g,i) and DWI (b=700, b,d,f,h,j) of 5 different fetuses referred to fetal MRI for kidney anomalies. a,b - 32GA fetus referred for kidney agenesis. There is renal agenesis on the left and renal hypoplasia on the right ((a, white arrow); on DWI, the right kidney shows normal diffusion restriction, confirming the mass seen on T2 is functioning kidney parenchyma. c,d – 23GA fetus with bilateral hydronephrosis with bilaterally dilated kidney pelvis (c, black asterisk) with the remaining kidney parenchyma pushed centrifugally (c, white arrows), while maintaining its normal DWI high signal intensity (d, white arrows). e, f – 25GA with left kidney agenesis. A compensatory hypertrophy of the right kidney can be correctly identified (e, white arrow), with normal signal intensity on T2 and DWI (e,f, white arrow). g, h – 22GA fetus referred for bilateral polycystic kidneys, identified on T2 (g, white arrows), and with high but less bright than usual signal on DWI (h, white arrows). i, j – Hypertrophic dysplastic kidneys at 19GA; there are enlarged multicystic kidneys bilaterally (i, white arrows), without the normal bright signal on DWI (j); the lack of functioning renal parenchyma is confirmed by the oligohydramnios (blue arrow); unlike on the previous cases (blue asterisks), no amniotic fluid can be identified surrounding the fetus.

Figure 7 - 32 GA fetus referred for macrocephaly and hydrocephalus (suspected aqueduct stenosis). Coronal T2W ssFSE image (a) depiction severe bilateral ventriculomegaly, with rupture of the septum pellucidum (blue arrow) and effacement of extracerebral CSF spaces. DWI (b, b value = 700) over the fetal cerebellum depicts increased signal, suggesting a highly cellular tumor. MR spectroscopy (c), TE 135; despite irregular baseline, choline (Cho, green arrow) and lactate/lipid peak (lip, Lac, yellow arrow), without identifiable N-acetyl aspartate (NAA, red arrow) peak.

Table 1 – Steps before referral for fetal MRI

Points	Explanation	Examples
Indication for fetal MRI?	Highly dependent on: availability, experience (MRI and US), legal framework Whenever referring physician/ parents need further information?	Evaluate extent of malformation Confirm diagnosis(18) Help plan fetal intervention Replace postnatal imaging in an unstable neonate
Exclude contra-indications for examination	<ul style="list-style-type: none"> - Claustrophobia - Absolute and relative CI for MRI, such as foreign bodies or implanted devices - Some implanted devices may be safe at 1,5 T but not at 3T - Some devices may have SAR and/or time limitations - Detailed information can be found online (i.e. http://www.mrisafety.com); when in doubt contact radiologist 	<ul style="list-style-type: none"> - Can be reduced by providing as much information as possible or consider mild sedative - Intra-ocular metal foreign bodies, "Triggerfish" Contact Lens, insulin pumps
Determine optimal for imaging	<ul style="list-style-type: none"> - When in doubt after US examination - Reason for MRI (i.e. to decide TOP vs purely diagnostic) - Depending on type of pathology; contact performing radiologist if in doubt 	<ul style="list-style-type: none"> - When the suspected outcome is poor but not bad, to increase the information for counseling - Legal framework of TOP - Severe malformations (i.e. holoprosencephaly, brainstem malformations, etc) can be detected <20GW, and (bad) outcome can be confirmed. - Esophageal atresia might not be visible until 28 GA and may sometimes not even be seen in third trimester - Giant neck masses are preferably scanned in the third trimester for delivery planning
Patient preparation	<ul style="list-style-type: none"> - Parents should be provided information on what to expect - Adjusted food/drink intake to minimize fetal movement 	Claustrophobia Four-hour fasting may be useful Sugar/caffeine avoidance Empty/near empty bladder
Follow-up	<ul style="list-style-type: none"> - Appointment to discuss findings should be made prior to imaging. - Sub-specialty appointments for parent counselling with appropriate experts 	Neuropediatrician appointment to discuss neurological outcome; pediatric surgeon appointment to discuss surgical options, etc

Table 2 – Sequences and applications

	Sequence	Application
Standard Protocol	T2-weighted (T2W) single shot Fast Spin Echo (ssFSE)	Normal anatomy and depiction of structural pathology
	T2W Steady State Free Precession (SSFP)	Normal anatomy with improved depiction of vessels and fetal heart Evaluation of bone and cartilage on 3T
	T1-weighted (T1W), Fast Low Angle SHot (FLASH)	Evaluation of T1 hyperintense tissues: Meconium, Pituitary and thyroid glands, Liver, Fat, Myelin
	Susceptibility imaging (Gradient Echo or Echo planar Imaging)	Depiction of vessels and Hemorrhage Evaluation of Liver and fetal skeleton
	Diffusion Weighted Imaging (DWI)	Evaluation of brain lamination and ischemic lesions Assessment of location and normal development of kidneys Assessment of normal development of the lungs
Additional anatomical sequences	EPI-Fluid Attenuated Inversion Recovery (FLAIR)	Depiction of fetal Brain Lamination Evaluation of intracranial hemorrhage and cystic/Intraventricular lesions
	Dynamic SSFP	Evaluate peristaltic movements and swallowing in suspected esophageal atresia Assess lower limb movement in spinal dysraphism
	Snapshot inversion recovery (SNAPIR)	Better anatomic T1-weighted brain evaluation compared to standard T1 Assessment of myelination
	Thick-slab imaging (slice thickness 30 – 50 mm)	Provide 3D imaging of the fetus Assess limb movement and position
	Cardiotocogram (CTG)/Doppler Ultrasound (DUS) - gated balanced SSFP	Evaluation of heart anatomy
Advanced sequences	Diffusion tensor imaging (DTI)	Fractional Anisotropy (FA) maps for structural brain evaluation Tractography (i.e. Callosal anomalies, assess displacement or involvement of corticospinal tract) for evaluation of fibers
	Resting state Functional MRI (fMRI) Blood oxygenation level-dependent contrast (BOLD)	Assess functional connectivity (research) Blood flow/oxygenation (i.e. arterial-venous fistulas) Placental imaging (i.e. IUGR, infection)
	MR Spectroscopy (MRS)	Evaluate metabolites in function of normal development of brain, amniotic fluid and placenta. TE 35 ms: Myoinositol, NAA, Choline (i.e. Infections, IUGR) TE 140 ms: AA, Choline, Creatine, Lactate (70) (i.e. Space occupying lesions)