Fetal Magnetic Resonance Imaging: Examination technique for prenatal diagnosis of fetal malformations and placental damage

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KeyWords:
MR (Magnetic Resonance), TI (Reversal Time), placenta, placental pathologies, pregnancy

Abstract

Magnetic resonance imaging is a multi-parametric tomographic imaging method based on the use of magnetic fields and radio frequencies, which provides high spatial resolution images of body structures. It is a third-level imaging technique used to obtain images with high spatial res-olution and excellent tissue differentiation, useful for the detailed study not only of anatomical structures, but especially for the study of possible pathologies and abnormalities of the foetus and/or placenta. This type of method always follows ultrasound imaging: in fact, ultrasound is the elective method for screening for foetal abnormalities because it can provide real-time imag-es with good spatial resolution without presenting harmful aspects to the foetus or mother. The main disadvantage of ultrasound is that it is operator-dependent and in some cases may limit the acquisition of sufficiently diagnostic information for the therapeutic management of the pregnant patient. Although the combination of trans-abdominal and trans-vaginal ultrasound examination is an excellent method for the study of the foetus and placenta and the detection of related pa-thologies, there are situations in which the correct diagnostic framing remains difficult.
Magnetic resonance imaging, on the other hand, provides detailed information that is not opera-tor-dependent. The study protocol includes the acquisition of predominantly T2-weighted se-quences, as they highlight the signal from the amniotic fluid present in the placenta. The basis of fetal imaging with MRI is the possibility of acquiring ultra-fast images that reduce motion arte-facts related to fetal motor activity, in the axial, coronal and sagittal planes of the fetus or or-thogonal to the maternal pelvis, depending on the indications for the examination. MRI exami-nations are recommended from the nineteenth week of gestation. To the best of the current tech-nology available, it is not considered possible to obtain sufficient spatial resolution, as well as contrast, to be able to obtain diagnostic, or at least additional, information from ultrasound be-low 19 weeks' gestation. The fetal MRI study should always take place after a second-level ul-trasound scan. It is considered totally unjustified to perform an MRI examination without an ul-trasound evaluation first, performed by experienced operators. It is not indicated to perform an examination to check doubts arising from the screening ultrasound alone performed at 19-21 weeks' gestation (SIEOG guidelines). Examinations performed in the first trimester are required for pathologies of maternal perinence: they are generally performed when they are deemed in-dispensable and irreplaceable by other methods (ultrasound) or when the MRI examination can provide information that would otherwise require the use of methods with ionising radiation, such as CT.

Introduction

Fetal MRI is a third-level imaging technique used to obtain images with high spatial resolution and excellent tissue differentiation, useful for the detailed study not only of anatomical struc-tures, but especially for the study of possible pathologies and abnormalities of the fetus and/or placenta.

Being a procedure based on the use of magnetic fields and radio frequencies and excluding the use of ionizing radiation, this technique is safe for the mother, but especially for the fetus, as the latter is extremely susceptible to ionizing radiation. It must be remembered, however, that it is an examination performed only and only if ultrasound does not provide sufficient information.

A key role in the successful execution of the examination is played by the radiology technician, who helps to ensure the acquisition of high-quality diagnostic images in a safe and efficient manner. The technologist is involved in all phases of the examination, starting with the prepara-tion of the patient, informing her about the procedure and reassuring her in any doubts or con-cerns about the procedure in order to achieve optimal cooperation, then moving on to the posi-tioning of the patient, which is essential for obtaining good diagnostic images, and finally to the execution of the examination, intervening in the management of the instrumentation

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and optimi-sation of the technical parameters. The paper, which is descriptive in nature, highlights the im-portance of the MRI method in the crucial choices for a correct diagnosis and treatment plan-ning.

Fetal development and placenta: The transition from embryonic to foetal life takes place at the ninth week, with the transformation of the embryo into a foetus, so called until the end of pregnancy (Fig. 1). The main events that characterise foetal development are: rapid growth and differentiation of systems, organs and tissues; the size of the head becomes proportional to the development of the other body elements; the length and weight of the foetus increase very rap-idly.

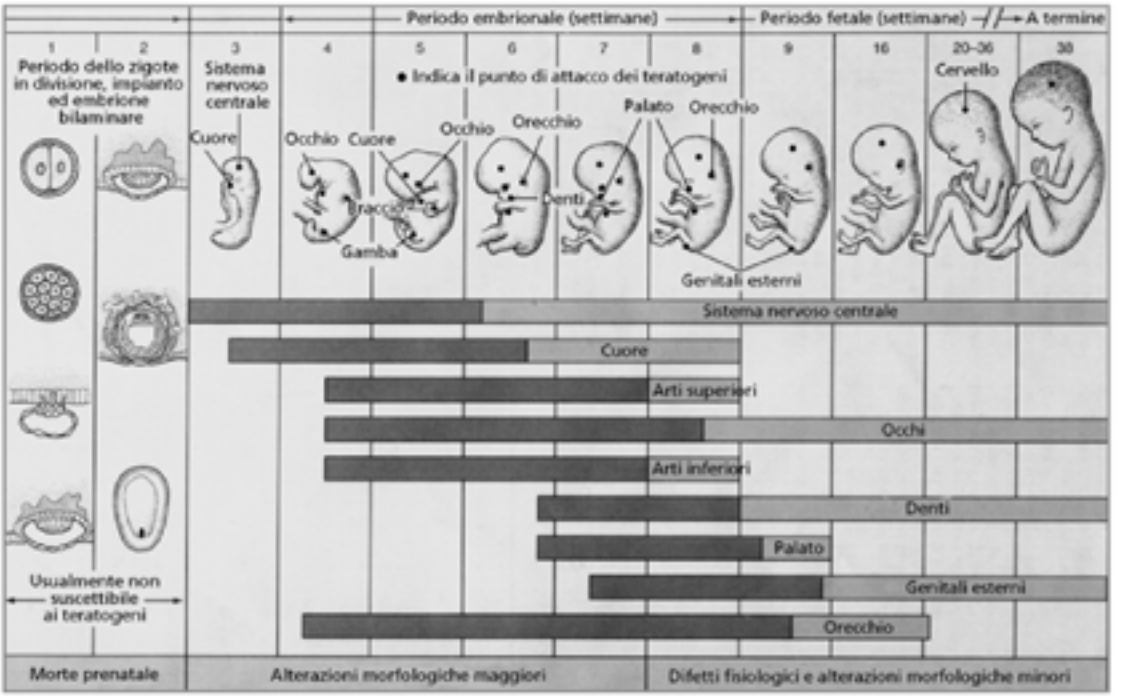

Fig.1 Prenatal development from embryo to fetus

~ From the ninth to the twelfth week: In this period, as well as development in terms of the length of the foetus, the head is always disproportionately large in relation to the rest of the foetus. The face is wide, the eyes are separated, the eyelids are not yet divided, and the ears are set very low. The primary ossification centres of the head and long bones begin to appear; the upper limbs are well developed, while the lower limbs have a more retarded growth. The intestines slowly recede into the abdominal cavity; the liver becomes the erythropoiesis organ, to be replaced around the end by the spleen.

~ From the thirteenth to the sixteenth week: The head becomes more proportionate to the length of the foetus; the lower limbs continue to develop and the ossification of the skeleton begins, which is fundamental for the establishment of the haemopoietic bone marrow. The external genitalia become more distinct and the ovaries already contain some primordial follicles and ovum. Myelinisation of the nerves begins. In the intestines there is meconium, i.e. a greenish material consisting of bile and amniotic fluid, which the newborn will excrete in the first few days after birth.

~ - Seventeenth to twentieth week: There is a slowdown in the development of the foetus, but the final relative proportions of the lower limbs are reached. The skin of the foetus becomes covered with caseous varnish to protect it from the amniotic fluid; hair and eyebrows can be discerned, the fetal body is covered with lanugo and brown fat appears at the level of the neck, retrosternally and perianally. The uterus is completed, the vagina undergoes the process of cavitation, the ovaries multiply and, in the male, the descent of the testicles begins. The mother can feel the first movements of the fetus.

~ Twenty-first to twenty-fifth week: There is a rapid increase in fetal weight. For dila-tion to occur, surfactant production begins in the pulmonary alveoli, although the fetus is not yet alive with autonomic respiration. There is appearance of the celebral cortex. Hand nails are formed.

~ Twenty-sixth to twenty-ninth week: Autonomous breathing of the fetus begins, again due to surfactant production. The pulmonary circulation is more adapted to gas ex-change and the CNS is able to process rhythmic respiratory movements. The spleen los-es its haemopoietic function as it is replaced by bone marrow. The eyes open; hair, fuzz and hair become thicker; toenails are also visible. There is an increase in

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pale fat. Scis-sors and cerebral circumvolutions are formed.

~ Thirtieth to thirty-fourth week: Light fat increases, giving the fetus a smooth and normal appearance. The pupillary reflex to light appears.

~ Thirty-fifth to thirty-eighth week: Fat deposits continue to grow; head circumference equals abdominal circumference; the fetus stops growing in preparation for birth. In the male fetus, the testicles have descended into the scrotum. At birth, the skin is pink and covered with caseous paint, the thorax is prominent, the head is still slightly dispropor-tionate and the umbilical cord is in the centre of the addominal wall.

The placenta is a complex discoidal organ that enables the embryo first and the fetus later to feed, breathe, eliminate waste substances and defend itself against harmful substances and pathogens. It consists mainly of two elements: an embryo-fetal portion formed by the leafy chorion and a maternal portion derived from the basal decidua and presenting swellings called maternal cotyledons. On the embryo-fetal side, the placenta presents the chorionic plate and the attachment point of the umbilical cord from which umbilical arteries and veins distribute. Both the embryo-fetal surface and the umbilical cord are lined by the amnion. In addition, between the basal decidua and the chorionic plate are spaces filled with maternal blood, separated from the embryo-fetal blood by tissue derived from the chorion.

During development, the placenta has two phases:

~ primitive placenta, which forms as early as the end of the second week of embryonic de-velopment and has villi over the entire surface of the chorion;

~ definitive placenta, which begins to form around the third month, as the villi located on the side of the decidua capsularis disappear and the area of the smooth chorion is limited, while the villi near the decidua basalis thicken and limit the area of the leafy chorion. As pregnan-cy continues, the parietal decidua and the capsular decidua fuse into the decidua vera, oblite-rating the uterine cavity. The basal decidua and the frondose chorion form the definitive pla-centa.

The main function of the placenta is to allow the diffusion of nutrients from maternal to foetal blood and the diffusion of excretion products from foetal to maternal blood. For substances such as oxygen, diffusion is simple: the oxygen contained in the maternal blood passes into the foetal blood due to the oxygen pressure gradient established between the two blood types. The same process occurs for carbon dioxide, but passing from fetal to maternal blood. Electrolytes, such as sodium or potassium, also pass through the placenta by simple diffusion. Water uses the mechanism of osmosis. Al- three substances necessary for the metabolism of the foetus usually diffuse by active dif- fusion. Particular elements that manage to cross the placenta, according to the process of transcytosis, are antibodies of the IgG class, providing the foetus with a limited immunity that permeates for a few months after birth.

Another function of the placenta is the production of hormones, which influence the growth of blood vessels, haematopoiesis, the immune response of the foetus, and metabolism, so as to en-sure the appropriate growth of the embryo. Hormones, both steroid and protein hormones, in-clude human chorionic gonadotropin (HCG) for maintenance of the corpus luteum; pro-gesterone, essential for the continuation of pregnancy; and oestrogen, for utero-placental blood flow.

Fetal malformations and placental pathologies: Despite scientific advances, a large number of newborns suffer from significant neurological morbidity that may affect the encephalic dis-trict, abdominal district and/or placenta. The most common brain abnormalities are ventriculo-megalies (enlargement of the lateral ventricles), agenesis of the corpus callosum (absence of the corpus callosum), pathologies of the posterior cranial fossa (Chiari II malformation, vascular and brainstem abnormalities) and ischaemic patholo-gy (deprivation of blood supply to a more or less extensive area of the brain).

Malformations that can affect the thorax and abdomen during fetal development are varied; among the most common are: lung malformations, diaphragmatic hernia, si-tus abnormalities, liver, pancreas and gallbladder abnormalities, kidney abnormalities.

Diseases affecting the placenta, on the other hand, refer to conditions of:

~ Placenta previa: Normally, the placenta is inserted in the upper part of the uterus, far from the cervical canal; however, it may occur that the placenta is inserted in the lower part of the uterus, at the inner orifice of the cervical canal: in this case we speak of pla-centa previa, which in most cases is discovered accidentally during routine ultrasound scans. Placenta previa is subdivided into central when the caudal end of the placental tis-sue completely covers the Internal Uterine Orifice (OUI); partial when it partially covers it; marginal when the placenta inserts itself within a distance of 2 cm from the OUI; and lateral when the placental tissue is located beyond about 2 cm from the OUI. This condi-tion usually manifests itself with vaginal bleeding during pregnancy or bleeding at the time of delivery. For this reason, the patient undergoes a caesarean section.

~ Placenta accreta: refers to the condition in which the placenta is pathologically adher-ent to the uterus due to defect of the basal decidua with invasion of the myometrium by the chorial villi. This condition is classified according to the depth of invasion of the myometrium by the chorionic villi: placenta accreta vera, with the villi adhered to the myometrium without invasion of the muscle; placenta increta, with

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the villi partially invading the myometrium; placenta percreta, with the villi invading the entire myome-trium and passing over the serosa, sometimes even neighbouring organs such as the bladder.

~ Utero-placental insufficiency: Utero-placental insufficiency, or placental dysfunction, is defined as an abnormality of placental growth, a condition attributable to reduced utero-placental blood flow and previous or recent placental infarcts, which in turn causes decreased nutrient supply to the fetus.

Study protocol:

~ Patient preparation: The patient must have seen and filled in the anamnestic que- si-onnaire and must have consented, knowingly and unequivocally, to the informed con-sent form for the MRI examination. The anamnestic questionnaire is intended to ascer-tain the absence of contraindications to the MRI examination and must be carefully completed by each patient or legal guardian, before undergoing the examination, and then signed by the physician in charge of the examination. Affirmative answers to one or more questions may result in contraindication, even absolute, to the performance of the examination. The informed consent form, on the other hand, serves to indicate consent to the performance of the examination, having been made aware of the possible risks.

~ MRI examinations are recommended from the nineteenth week of gestation. To the best of the current technology available, it is not considered possible to obtain sufficient spa-tial resolution, as well as contrast, to be able to obtain diagnostic, or at least additional, information with respect to ultrasound below 19 weeks gestation. Whenever possible it would be preferable to perform the examination in the morning af-ter fasting for at least 4 hours, as hypoglycaemia has been shown to reduce fetal move-ments; alternatively, if it is possible to perform an ultrasound examination prior to the examination, aimed at verifying the sleep or wake phase of the fetus, one can wait for the sleep phase, considering that the regular fetal sleep-wake cycle involves an alterna-tion of these phases every 30 minutes. The removal of corneal contact lenses, spectacles, jewellery, earrings, piercings or other metal objects is obligatory to avoid overheating them or the projectile effect, as well as artefacts that could compromise the quality of the information obtained. The patient, after emptying her bladder, is placed in a comfortable position on the gantry, usually supine or, in cases where this position is not removed, left lateral decubitus, and is rested for a few moments in this position to reduce spontaneous fetal movement. In some cases, to minimise claudrophobic sensation, the patient may be introduced into the gantry breech rather than cephalic. Adequate ventilation within the gantry appears essential; it is helpful to cover the patient as little as possible and only with a light cotton garment. Visual and acoustic contact during the examination should be constant. It may sometimes be necessary to perform the examination in several stages, so that the patient can rest for a few minutes outside the gantry, especially if the supine position makes the procedure burdensome due to uterine compression on the vena cava, with a consequent tendency to hypotension. No sedatives are usually used for either the mother or the foetus, nor contrast medium.

~ The study, in fact, does not require the administration of contrast medium: contrast me-dia containing gadolinium have the ability to cross the placenta and appear at the level of the foetal bladder only a few moments after intravenous administration; from the foetal vein, the contrast medium is excreted into the amniotic fluid and potentially reabsorbed by the foetus. As the actual half-life of gadolinium contrast medium in the foetal circula-tion is not known, its use is not recommended except in cases of absolute necessity, usu-ally implicitly related to maternal health.

~ - Devices: Generally, the fetal MRI study should be performed with equipment with a high magnetic field strength: 1.5 T equipment is used in order to obtain optimal images with fast acquisition times, so that fetal movement is minimally affected. The use of field strengths greater than 1.5 T is currently not yet permitted, although some studies show no harmful effects. Safety issues include the possible biological effects of the static mag-netic field of the magnetic resonance imaging (MRI) system, the risks associated with gradients and radio frequency (RF) and exposure times. For static magnetic fields with an intensity of 1.5 T, only feelings of nausea, metallic taste and dizziness have been de-scribed; more important are the issues of fetal heating, fear and peripheral nerve stimula-tion induced by RF and gradients, although there is no scientific evidence of any dam-age to fetal development. Different types of coils can be used, also depending on gestational age, size of gesta-tional sac and uterus: abdominal phase array coils with 4 to 32 channels are usually used. Chest coils for studying the heart have also proved suitable for fetal studies. It may happen that the coil has to be repositioned after the initial scanogram, due to fetal movement and to ensure optimum SNR.

~ Used sequences: The study protocol includes the acquisition of different sequences, some of which are essential and others optionally added depending on the clinical ques-tion. The basis of fetal MRI imaging is the possibility of acquiring

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ultra-fast images that reduce motion artefacts related to fetal motor activity. Images are acquired in the axial, coronal and sagittal planes of the fetus or orthogonal to the maternal pelvis, depending on the indications of the examination.

The study consists of:

- Survey: centering sequence with respect to the maternal abdomen, therefore with a very wide FOV that must include the entire region. It is acquired with coronal orientation on the patient for the identification of the position of the fetus with respect to the mother in relation to the assessment of the relative position of the fetal head, spine and stomach and for the location of the placenta (anterior/posterior). Being a rapid sequence, the ac-quisition is free-breathing, as it is unaffected by motion artefacts, and is T2-weighted, for optimal contrast between the fetal body and amniotic fluid. From the survey, the other sequences are imposed (Tab.1 and Fig.2).

Tab.1 *Description of Survey sequence acquisition parameters*

Sequenza "Survey T2"	
FOV (mm)	320x320x71
SLICE THICKNESS (mm)	7
DURATA (sec)	36,4
TR (ms)	6066
TE (ms)	250
SAR (W/Kg)	<2

- Single shot T2-weighted fast spin-echo (SSH o HASTE): ultrafast T2-weighted se-quence that acquires all k-space data after a single excitation pulse. Commercially, this sequence is called Half-Fourier Acquisition Turbo Spin Echo (HASTE), as it uses the Half-Fourier technique to fill k-space: slightly more than half of the k-space data is 'physically' acquired; the remaining half is extrapolated by exploiting the k-space's in-trinsic symmetry properties. As a result, the acquisition time is almost halved, the spatial resolution is maintained, paying, however, in terms of reduced SNR. In the complete acquisition, in fact, the two halves of the k-space are identically affected by the noise contribution, with random deviations from the expected values. This makes it possible to limit artefacts related to maternal and foetal movement. The layer must be sufficiently thin (3-4 mm) with as-sial, sagittal and coronal multiplanar orientation orthogonal to the organ/district of interest for detailed assessment of the fetal anatomy. The excellent trade-off between the spatial resolution, contrast and signal-to-noise ratio (SNR) of these se-quences in addition to their speed of execution enable for excellent visualization of the fetal anatomy during all stages of pregnancy and in particular for highlighting static fluids and structures with a predominantly fluidic composition as hyperintense structures (Tab. 2 and Fig. 3).

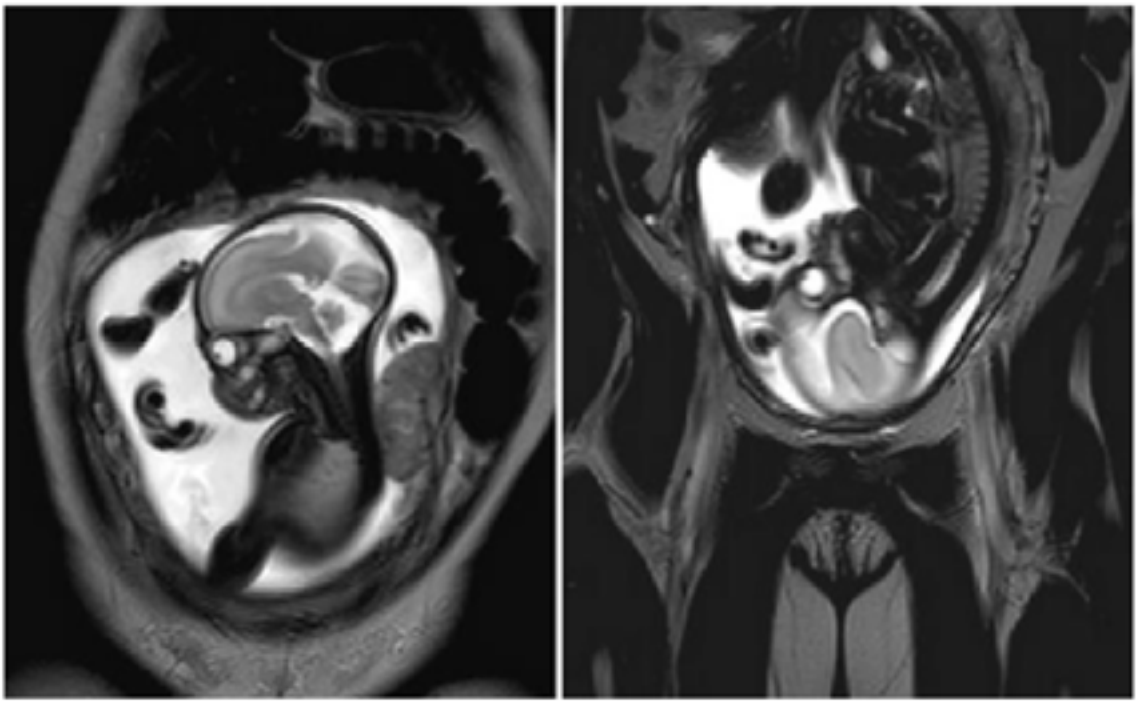

Fig.2 *Survey sequence in T2: Coronal images*

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Tab.2 *Description of SSH sequence acquisition parameters*

Sequenza:	SSH/TSE	SSH/TSE TE 90
FOV (mm)	260x260x63	260x260x63
SLICE THICKNESS (mm)	3	3
DURATA (sec)	18	18
TR (ms)	3000	3000
TE (ms)	180	90
SAR (W/Kg)	<1,7	<1,4

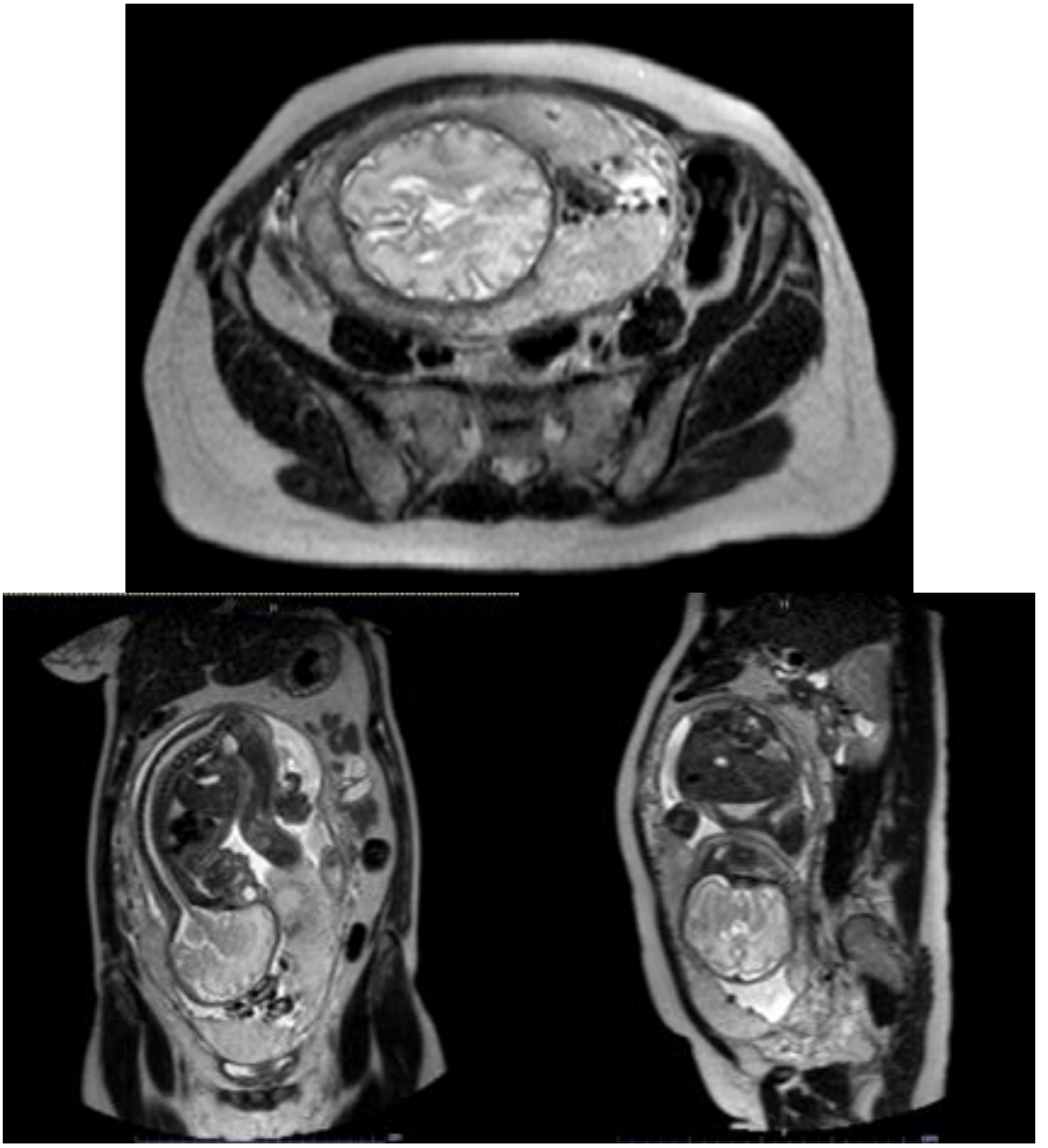

Fig.3 *HASTE sequence: top left coronal image; top right sagittal image; bottom axial image*

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- Balanced Steady-State Free Precession (bS-SFP): Balanced Steady-State Free Preces-sion sequences are unspoiled gradient echo sequences. The Balanced Steady-State Free Precession sequences have an intermediate T1 and T2 contrast determined by the T2/T1 ratio, use an ultra-short TR (<3 ms) and symmetric gradients in the three spatial direc-tions; they are therefore unaffected by motion, offer very good SNR and the fluids are depicted as signal-intensive structures. The study layer can be as thin as 3 mm in cross-sectional thickness with axial, sagittal and coronal multiplanar orientation orthogonal to the organ/district of interest for de-tailed assessment of fetal anatomy (Tab. 3 and Fig. 4).

Tab.3 Description of Balanced Steady State Free Pre-cession sequence acquisition parameters

Sequenza:	BALANCE SAG
FOV (mm)	270x270x38
SLICE THICKNESS (mm)	3
DURATA (sec)	26,3
TR (ms)	7,3
TE (ms)	3,7
SAR (W/Kg)	<0,9

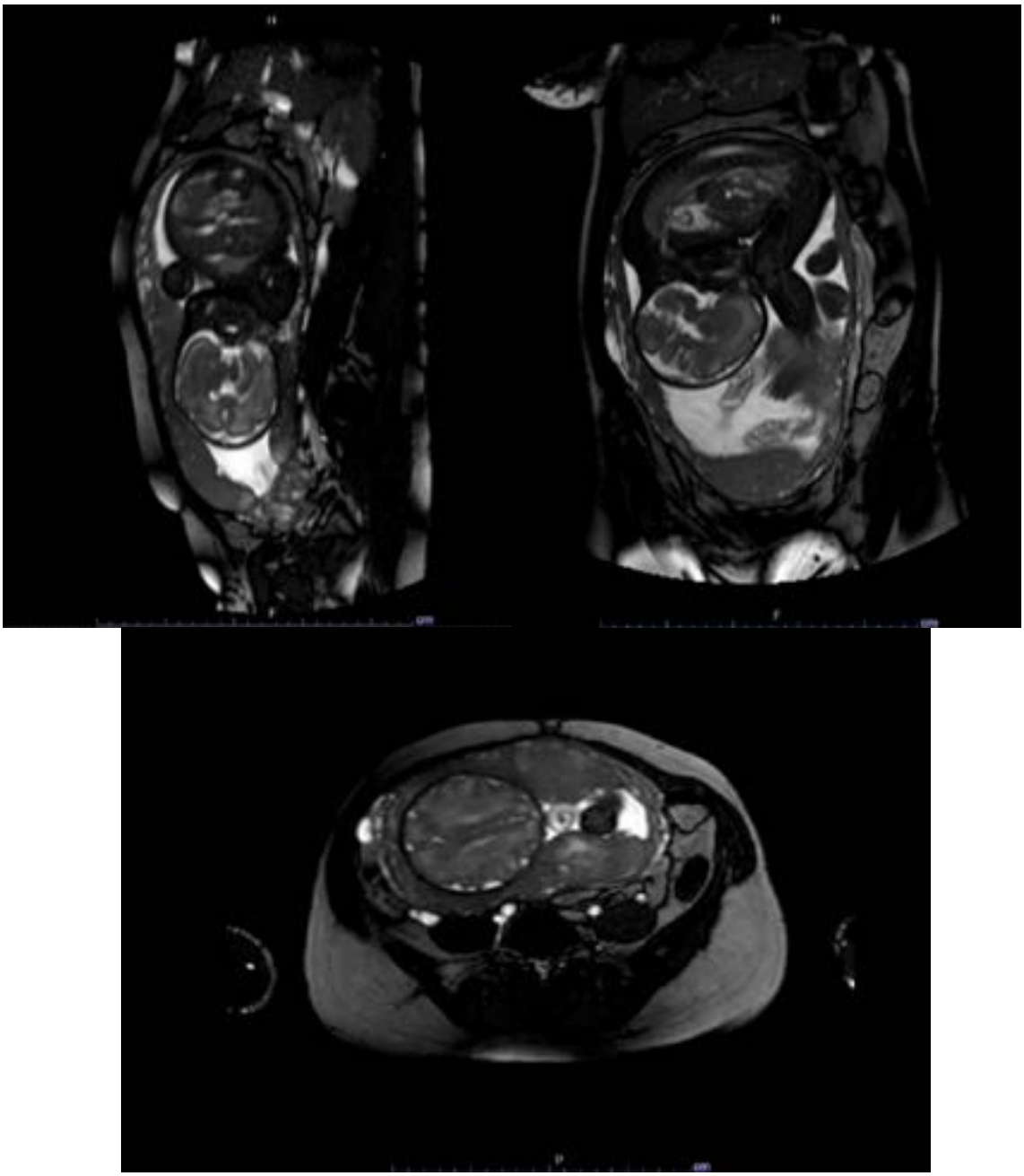

Fig.4 *Balanced sequence: top left coronal image; top right sag-ittal image; bottom axial image*

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- T1-weighted fast spin-echo o gradient-echo (fat-sat): At present, there are no optimal T1 sequences for fetal studies, due to problems with spatial and contrast resolution. Two types of T1-weighted sequences are generally implemented: either gradient-echo, with a repetition time (TR) and short TE or Fast Spin Echo-T1 (FSE-T) sequences. The limita-tions of gradient-echo T1 sequences are their poor contrast resolution and the fact that their acquisition time (usually during maternal apnoea) usually does not fall below 20 seconds; their advantages are their better spatial resolution, with sections even 3 mm thick. The main disadvantage of FSE-T1 sequences is their low spatial resolution (sec-tion thickness around 5-6 mm and in-plane resolution around 2 mm2); however, they offer good contrast resolution (at least in the brain), especially when combined with sat-uration of the fat signal; however, they also require acquisition during maternal apnoea of at least 14 seconds duration. With T1 sequences it is possible to show areas of cere-bral haemorrhagic necrosis, haematomas, meconium, large clots, for example, as hyper-signal. For fat-suppression imaging, SPIRs are used, in which the difference in reso-nance frequency between fat and other tissues is exploited to provide a selective 180° pulse for the protons held in the fat. The magnetisations of the other tissues are therefore not reversed. After a time of about 150 ms, the fat reversal time, the 90° impulse will be given: the signal from the adipose tissue will be poor or nil, but the signal from the other tissues will be preserved. The axial orientation is the most suitable and only one acquisition is performed, unlike the other sequences (Tab. 4 and Fig.5)

Tab.4 *Description of TSE T1 sequence acquisition pa-rameters*

Sequenza:	T1 FETO
FOV (mm)	340x340x53
SLICE THICKNESS (mm)	5,5
DURATA (sec)	14,4
TR (ms)	300
TE (ms)	14
SAR (W/Kg)	<1,2

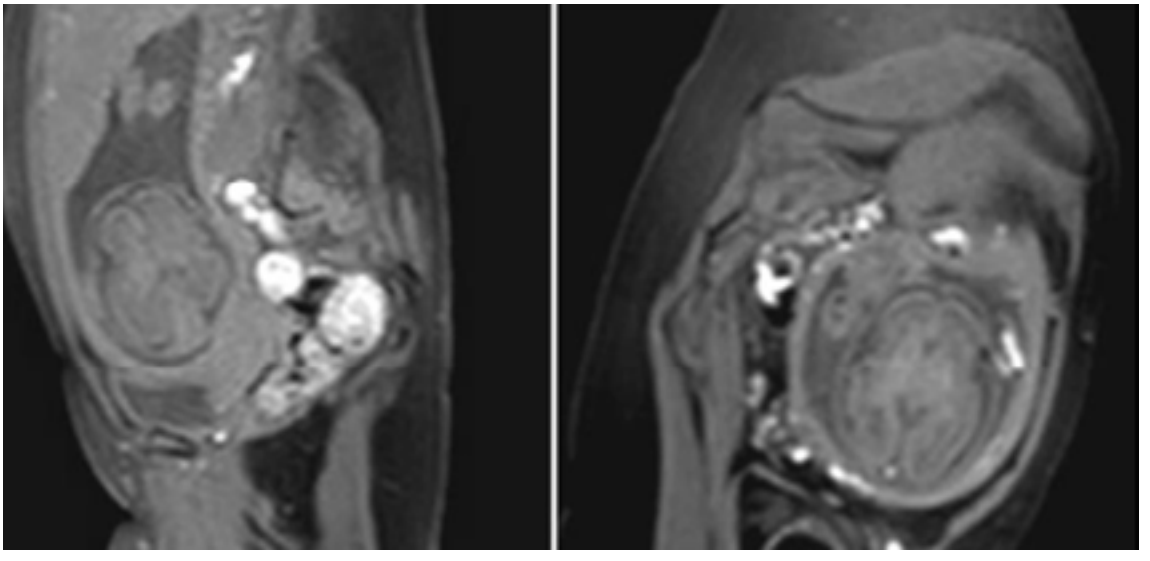

Fig.5 *TSE T1 sequence: axial imaging*

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- FLAIR: FLAIR (Fluid Attenuation Inversion Recovery) sequences are Inversion Re-covery sequences, which result in fluid suppression. In FLAIR the TI is very long, so that the signal of the fluids is cancelled when the RF pulse is applied at 90°. It therefore allows for T2-weighted images, in which signals from the cephalic spinal fluid and other low-viscosity liquids are suppressed. Despite their limited spatial resolution, they can be used, for example, in the analysis of masses or intraventricular cerebral changes in the fetus. In most cases, they are ac-quired with a single-shot technique, so as to make them ultra-fast and minimise fetal movement. The acquisition takes place not too thinly, around 4 mm, with TI 6000 ms and TR assuming values around 2000 ms; an axial and/or coronal orientation follows according to clinical requirements (Tab.5 and Fig.6).

Tab.5 *Description of FLAIR sequence acquisition parameters*

Sequenza:	FLAIR SSH
FOV (mm)	320x320x69
SLICE THICKNESS (mm)	4
DURATA (sec)	24
TR/TI (ms)	6000/2000
TE (ms)	54
SAR (W/Kg)	<1,5

Conclusions

Fetal MRI has revolutionised the landscape of perinatal imaging, offering de-tailed, accurate and non-invasive assessment of the fetus and placenta, especially in cases where conventional diagnostic ultrasound has limitations. As shown in this study, fetal MRI has estab-lished itself as an in-substitutable tool for the diagnosis of fetal pathologies, particularly abnor-malities of the central nervous system, due to its high resolution of soft tissue and ability to ac-quire images in the absence of ionising radiation, as well as for the study of placental patholo-gies. The use of magnetic resonance imaging has made it possible to significantly improve neo-natal prognosis and to plan surgical interventions and postnatal care with greater precision. Re-cent developments in imaging technology and acquisition techniques, such as the use of the SSFSE (Single Shot Fast Spin Echo) sequence, the BALANCE (Balanced Steady Sta-te Free Precession) sequence and the use of fetal movement-specific protocols, have further increased the quality and practicality of the examination, reducing acquisition time and improving image quality even in the presence of fetal movement. However, challenges and limitations remain to be addressed. The fetal MRI study requires specialised equipment and highly qualified person-nel, as well as raising questions about the high costs involved and the need for standardised pro-tocols to ensure reproducibility and comparability of results. In particular, specialised staff train-ing, the development of clear guidelines and interdisciplinary collaboration between radiolo-gists, gynaecologists and TSRMs are crucial to maximise the effectiveness of this technique. In conclusion, fetal MRI represents an advanced frontier in

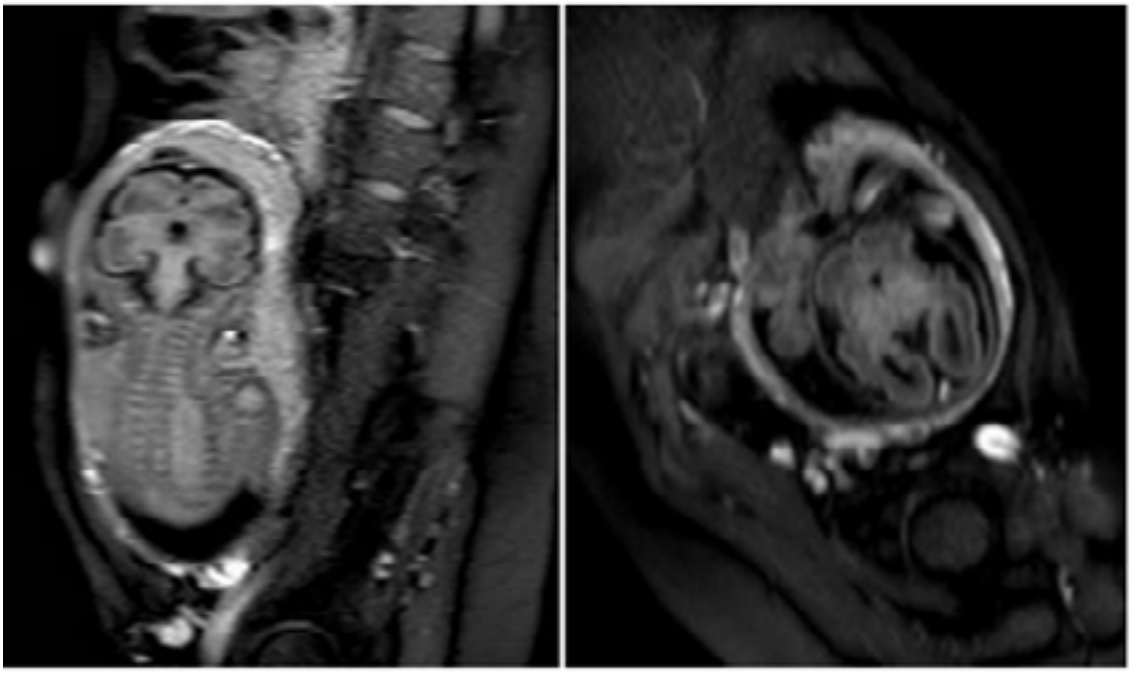

Fig.6 *FLAIR sequence: on the left sagittal image; on the right axial*

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the field of prenatal i-maging and of-fers increasingly promising perspectives for the improvement of early diagnosis of fetal and pla-cental pathologies. As technologies and methodologies continue to evolve, fetal MRI is set to become more and more integrated into clinical practice, offering tangible benefits for maternal and foetal well-being and paving the way for new developments in prenatal medicine.

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