Fetal Low Field MRI – the First 150 Cases

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Introduction

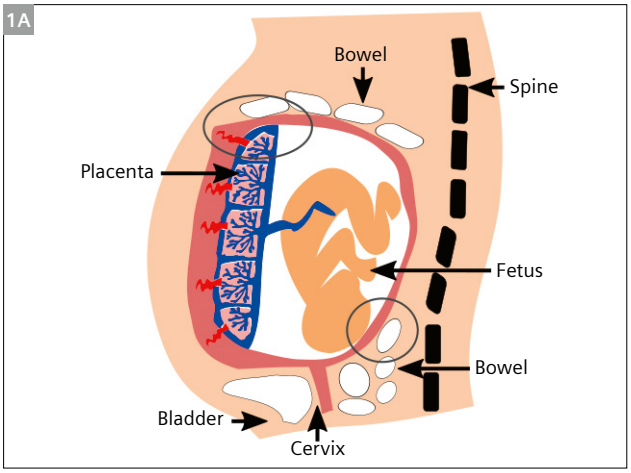
Fetal[1] magnetic resonance imaging (fetal MRI) has continuously increased its prominence in both research and clinical applications. The wide range of available contrasts, the high resolution, the ability to image the entire fetus up until late gestation, and operator-independence make it an essential research tool and an ideal complementary modality to ultrasound for clinical care. Fetal MRI is mainly used to image suspected clinical abnormalities found through ultrasound that require further clarification, such as neurological, spine, thorax, and abdominopelvic malformations or masses. It can also be used for detailed evaluations in cases of abnormal placentation, for antenatal surgical planning of spinal lesion closure in fetuses with spina bifida, and for laser ablations in monochorionic twin pregnancies or fetuses with congenital heart disease.

While anatomical imaging using turbo spin-echo (HASTE) sequences originally dominated, functional contrasts are increasingly being employed for a variety of indications in both research and clinical settings. They are either adapted from other parts of radiology or developed specifically for fetal indications, and include diffusion-weighted MRI [1, 2], T2* relaxometry [3], T1 relaxometry [4], and perfusion MRI [5]. As these complex functional techniques are being developed, they further increase the range of indications and hence applicability of fetal MRI.

While the current trend in MRI is to image at higher field strengths, some of the significant challenges encountered in fetal MRI may be addressed by operating at a lower field strength.

Advanced imaging techniques may be hampered by geometric distortion artifacts arising at air–tissue interfaces. This is made worse by the need to run highly efficient EPI-based read-outs for diffusion MRI, functional MRI, and multi-echo gradient echo sequences for T2* relaxometry, which leads to an increasing need for specialist image-based shimming techniques [6]. This increases examination time and the need for specialized fetal MRI technologists. Further challenges include B_1 inhomogeneity-related artifacts

1A



1B **Localizer**

Clinical protocol		
Anatomical MRI (T2-weighted HASTE)		11 min whole uterus
Diffusion MRI (Diffusion-weighted spin echo single shot EPI)		3 min whole uterus
Dynamic single-slice scan (cine)		1 min 1 slice
T2* Relaxometry (Multi-echo gradient echo single-shot (EPI)	*	4 min whole uterus
Research protocol		
T1 Relaxometry (Multi-echo gradient echo single-shot EPI)	*	3 min whole uterus
Combined T2*-Diffusion MRI (Multi-echo gradient echo single shot EPI)	*	8 min whole uterus
HARDI-Diffusion MRI (Diffusion-weighted spin echo single-shot EPI)	*	4 min placenta
No image-based shimming/calibration		

1 **(1A)** Schematic representation of the area of interest. The black circles signify areas of significant distortion due to air–tissue interfaces. **(1B)** Protocol overview for the clinical 20-minute exam and the research additions. The asterisks indicate custom-made sequences.

[1]*Siemens Healthineers disclaimer: MR scanning has not been established as safe for imaging fetuses and infants less than two years of age. The responsible physician must evaluate the benefits of the MR examination compared to those of other imaging procedures*

enhanced by the presence of amniotic fluid, and specific-absorption-rate (SAR) limitations [7] resulting in inefficiencies in the sequences. Both B_0 and B_1 inhomogeneities increase with higher field strengths. Therefore, lower field strengths reduce both the impact of the aforementioned artifacts and the need for specialist correction tools.

T2* is quickly becoming a widely used functional modality, especially to assess the placenta in major pregnancy complications such as pre-eclampsia and fetal growth restriction. The increase in T2* at lower field strengths provides a clinically beneficial T2* dynamic range that is ideal for these assessments. Similarly, shorter T1 times at low field can potentially increase acquisition speed for T1 relaxometry, facilitating its application in fetal MRI.

While comfort and space are paramount for any patient undergoing an MRI scan, pregnant women in the later weeks of pregnancy present a population where space and comfort is both particularly important and challenging to achieve in a standard-sized MRI bore. In addition, the number of obese pregnant women is rising – with 24% of all pregnant women in the UK and U.S. considered obese as of 2020 [8]. This presents a currently underserved population that could benefit from fetal MRI, as these women often do not receive adequate prenatal imaging due in part to the detrimental effect of increased abdominal fat on ultrasound imaging. Lower-field strength MRI typically allows a homogeneous field even with a wider bore. Increasing the bore size to 80 cm and reducing the required length of the magnet may enable MRI to complement ultrasound in the routine clinical screening of the obese pregnant patient.

Finally, a field strength-independent challenge concerns unpredictable and uncontrollable fetal motion, especially in early-to-mid gestation when fetuses have enough space for large displacements. This can be particularly problematic for fetal functional MRI modalities, which rely on the acquisition of the same slice location multiple times in a time-series format, to then be combined for spatiotemporal analysis. Both post-processing base techniques such as slice-to-volume registration (SVR) [9, 10] and prospective motion-correction techniques based on localization and tracking may be employed at low field strengths.

Main benefits:

- 20-minute efficient and robust clinical imaging workflow at low field
- Improved patient comfort due to wide bore
- Increased magnetic field homogeneity and reduced imaging artifacts
- First evidence proving the efficacy of low-field clinical fetal MRI

Materials and methods

Patient preparation and comfort

Pregnant patients are consented for research by either a research midwife or obstetrician and then prepared for the scan. The weight of the pregnant uterus on the vena cava in supine position can in rare cases lead to vasovagal episodes. To mitigate this and allow early detection, tight blood pressure controls are performed in multiple positions. A first blood pressure reading is taken while the patient is sitting on the scanner table, after which they lie on their left side for a second blood pressure reading, and then slowly the patient is eased onto their back in head first supine position to limit the compression of the vena cava. Padding for the lower back, the head, and the legs is provided as requested. Throughout the scan, blood pressure readings are performed automatically at 10-minute intervals, the maternal heart rate and saturation are continuously monitored, and frequent verbal interaction is maintained.

Clinical protocol

The protocol was crafted to allow assessment of the fetal brain and body, the placenta, and the cervix (see Figure 1A for an overview). It consists of a clinical session (Fig. 1B), which lasts about 20 minutes, and a research session of up to 40 minutes. Both are designed specifically with the advantages and challenges of 0.55T in mind and are therefore modified from our standard fetal imaging at 1.5T and 3T in the following way:

The resolution for the anatomical HASTE scans was reduced, using a slice thickness of 4.5 mm instead of 2.5 mm (in-plane resolution 1.4 × 1.4 mm^2) and 9 stacks (3 uterus stacks, 3 fetal brain stacks, and 3 fetal body stacks) instead of 6 to allow robust SVR.

A multi-echo gradient echo EPI sequence was modified to include multiple echoes, allowing for motion-robust T2* mapping of the entire uterus with 20 dynamics. T2* shortens with advanced gestational age and with most major pathologies. Compared to higher field strengths, the increased T2* at low field allows longer read-outs and the conservation of signal over longer echo times at later gestation and in cases with placental disease. A diffusion MRI scan, allowing both apparent diffusion coefficient (ADC) and intravoxel incoherent motion (IVIM) calculations as typically used for fetal imaging, was acquired covering the entire uterus. Finally, a dynamic (CINE) single-slice HASTE scan was acquired (TR = 4 seconds) to visualize cardiac activity and limb and head motion.

Research protocol

The gradient echo sequence was modified with a global adiabatic inversion pulse and slice-shuffling to reap the benefits of the reduced T1 at this field strength for an efficient quantitative fetal T1 acquisition. A previously

proposed multi-echo diffusion MRI scan [11] was used to sample a large parameter space, combined synergistically with the longer T2* and allowing sampling for a longer time.

Importantly, none of these elements included image-based shimming or any other advanced shimming of the kind required on higher-field scanners, thus saving scanning time.

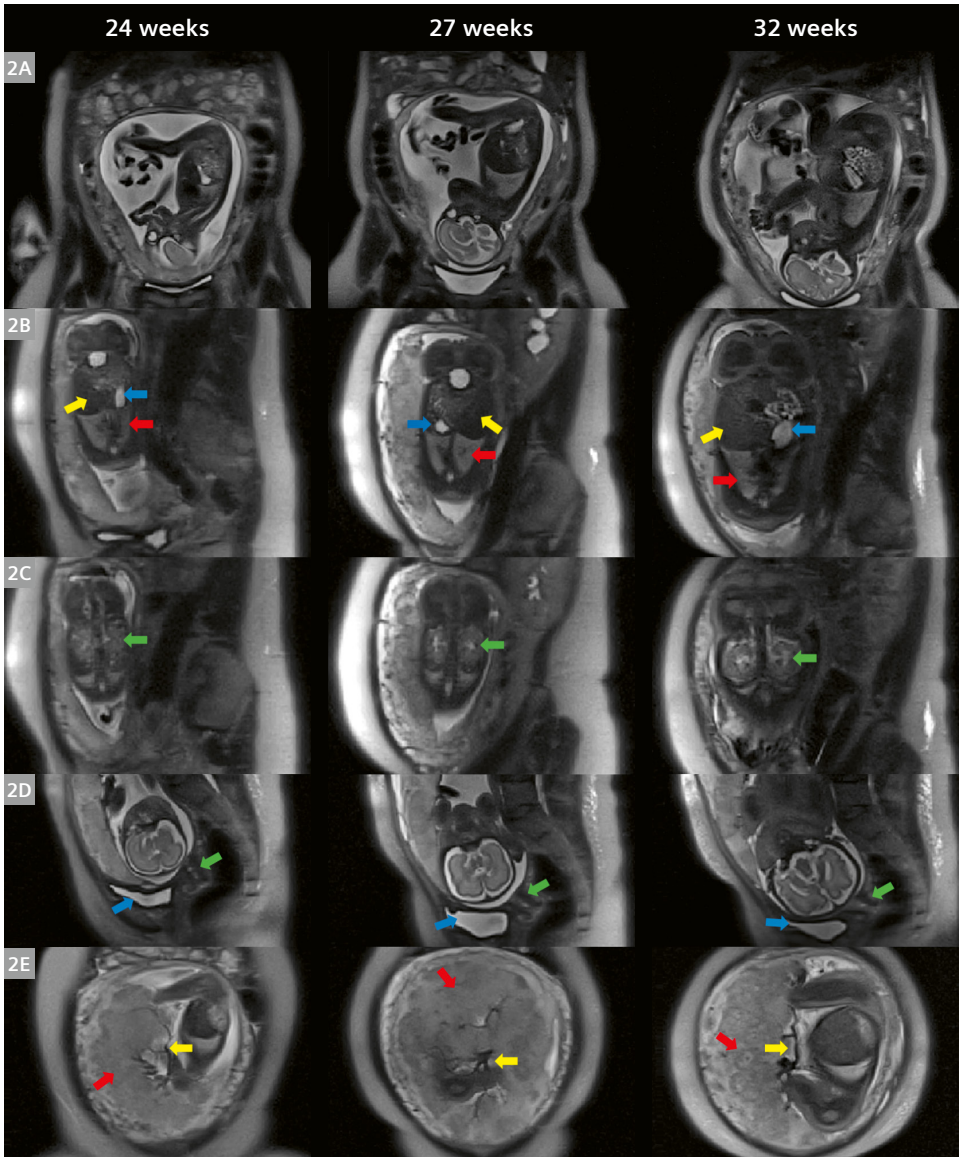
Analysis and quantities obtained

An anatomical brain report is obtained from the HASTE stacks and includes bi-parietal diameter, transcerebellar diameter, ventricular sizes, presence of orbits, ears, and more. The cervical length and the lung are segmented individually to obtain respective quantitative values. The stacks are also reconstructed to 3D volumes using SVR resulting in automatic segmentations and volumes for 16 brain regions. Mono-exponential fitting is performed on the T2* and T1 data to obtain quantitative maps for the brain and placenta. Finally, the dynamic T2* scans are processed using SVR and AI-based localization and segmentation to obtain organ-specific T2* maps and values for 10 organs of interest.

Results

Comfort and success of the examination

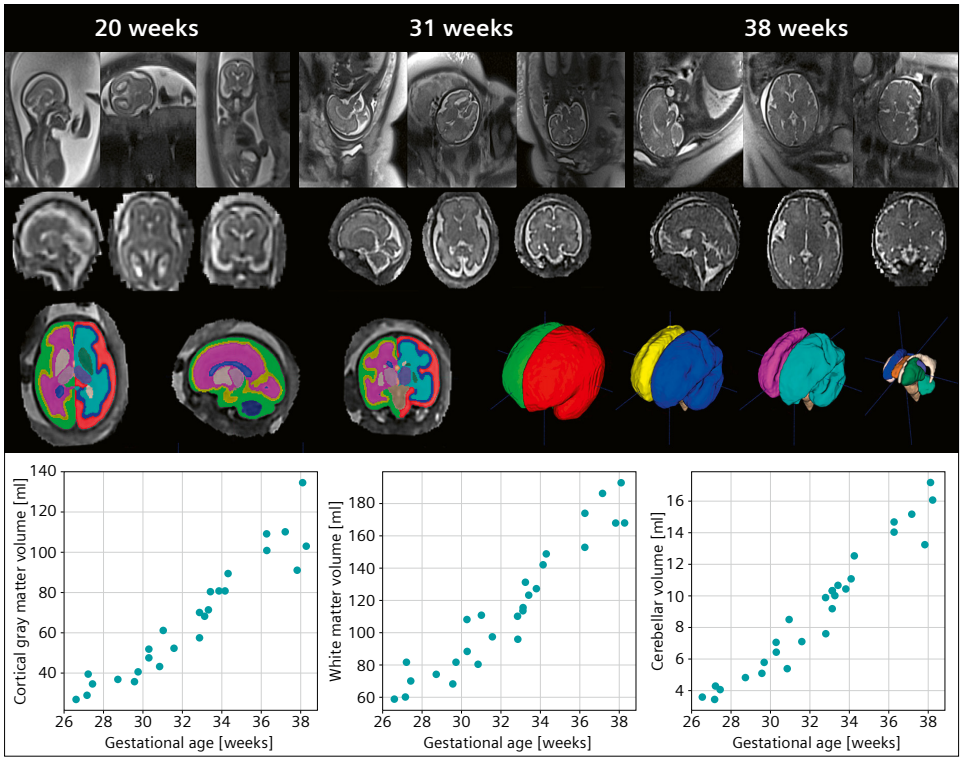
In the first nine months, a total of 150 fetal scans from 16+0 to 40+2 weeks of gestational age were performed on the 0.55T scanner, including 25 patients referred for clinical indications. This cohort includes patients with either significant claustrophobia or a BMI that does not



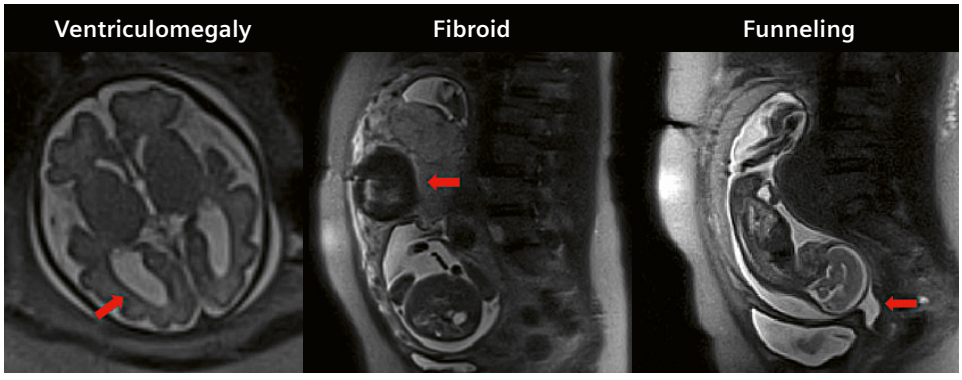
2 Fetal case scanned longitudinally at three time points during pregnancy (24, 27, and 32 weeks) illustrating **(2A)** a coronal whole uterus view; **(2B)** the fetal lung (red), stomach (blue), and liver (yellow); **(2C)** the kidney (green); **(2D)** the cervix (green arrow) and bladder (blue arrow); and **(2E)** a coronal whole uterus view through the placenta showing chorionic vessels connecting the placenta to the umbilical cord (yellow arrows) and the increasing heterogeneity with age within placental lobules (red arrow).

allow comfortable examination on any other available scanner (max BMI = 49.9 kg/m²). The pathologies studied included neurological abnormalities (ventriculomegaly, midline cysts, mega cisterna magna, scalp tumor), fetal body abnormalities (cystic kidney), and big obstetrical syndromes associated with the placenta (pre-eclampsia, fetal growth restriction). They also included findings such as funnels in the cervix, endometrial cysts, and fibroids. Patient feedback from a small cohort of pregnant women who had both a low-field and a high-field MRI scan during the same pregnancy revealed an increase in comfort (from 2.9 to 4.3 on a scale of 1 "not comfortable" to 5 "very comfortable"). This was also reflected in the large number of research patients choosing to come back for up to four scans.

Anatomical data obtained as illustrated in a longitudinal case (the same fetus was scanned at 24, 27, and 32 weeks) shown in Figure 2 clearly depicts all fetal structures (lungs, liver, stomach, and kidney are marked with arrows), the placental vasculature (yellow arrow), heterogeneity (red arrow), and the cervix (green arrow). Figure 3 shows more detailed views of the brain in radiological planes and after SVR at three time points. The results from automatic regional segmentation on these SVR results are shown for 60 healthy control cases in the bottom row, illustrating the ability of the data to accurately assess growth. Finally, Figure 4 shows zoomed images of the described pathologies, illustrating the ability of the low-field data to robustly visualize and quantify these.



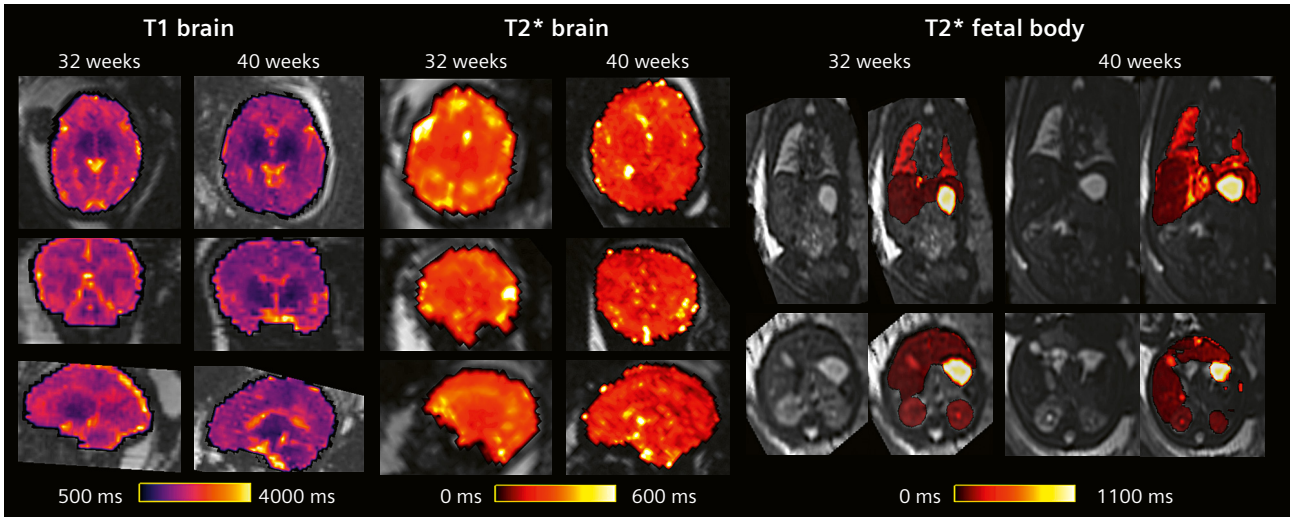
3 Detailed views of the HASTE data from the brain, acquired in radiological planes (top row) and after SVR (second row) at 20, 31, and 38 weeks. Results from the automatic subregion brain segmentation (third row) and volumetric brain assessment over gestational age (bottom row) from left to right: cortical grey matter volume, white matter volume, and cerebellar volume.



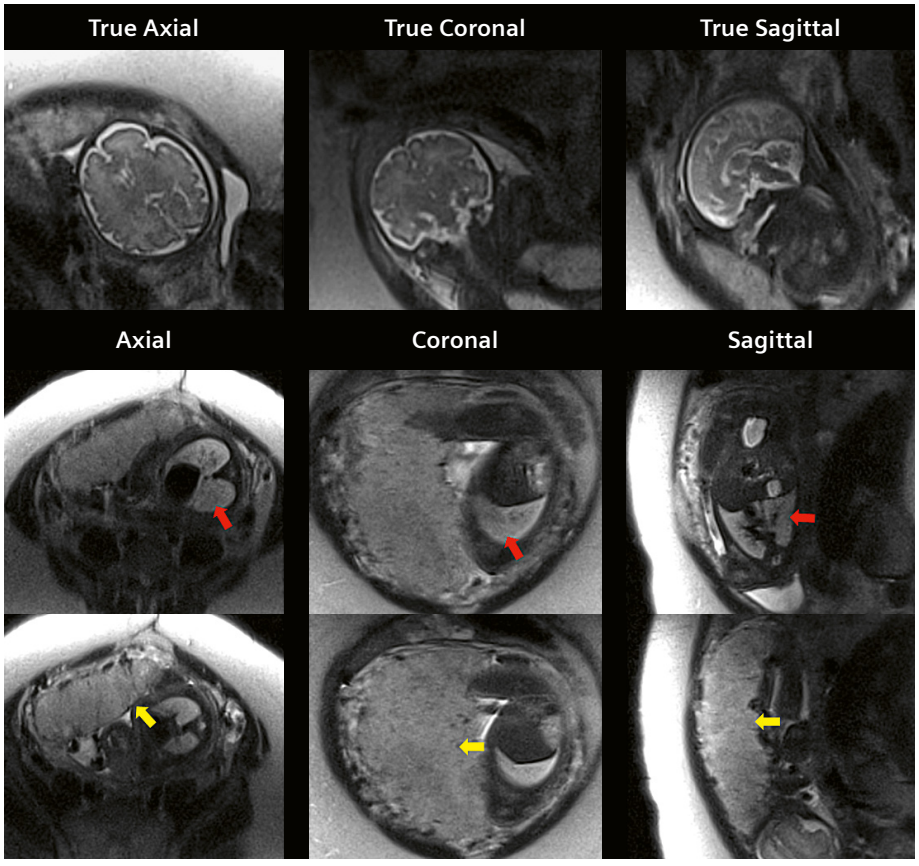
4 Fetal HASTE images of selected pathologies, including ventriculomegaly, an enlarged cisterna magna, a low signal-intensity fibroid, and funneling of the cervix.

Functional data and case study: BMI of 49.9 kg/m²
A total of 128 full sets of functional data were acquired, including T1 and T2* relaxometry and diffusion MRI. Imaging from a longitudinal case (same fetus scanned at 32 and 40 weeks) for T1 and for T2* (Fig. 5) depicts good delineation of major and fine brain structures. Finally, the T2* obtained for each fetal organ shows the ability of the proposed protocol at 0.55T to acquire quantitative information even for small fetal structures throughout gestation.

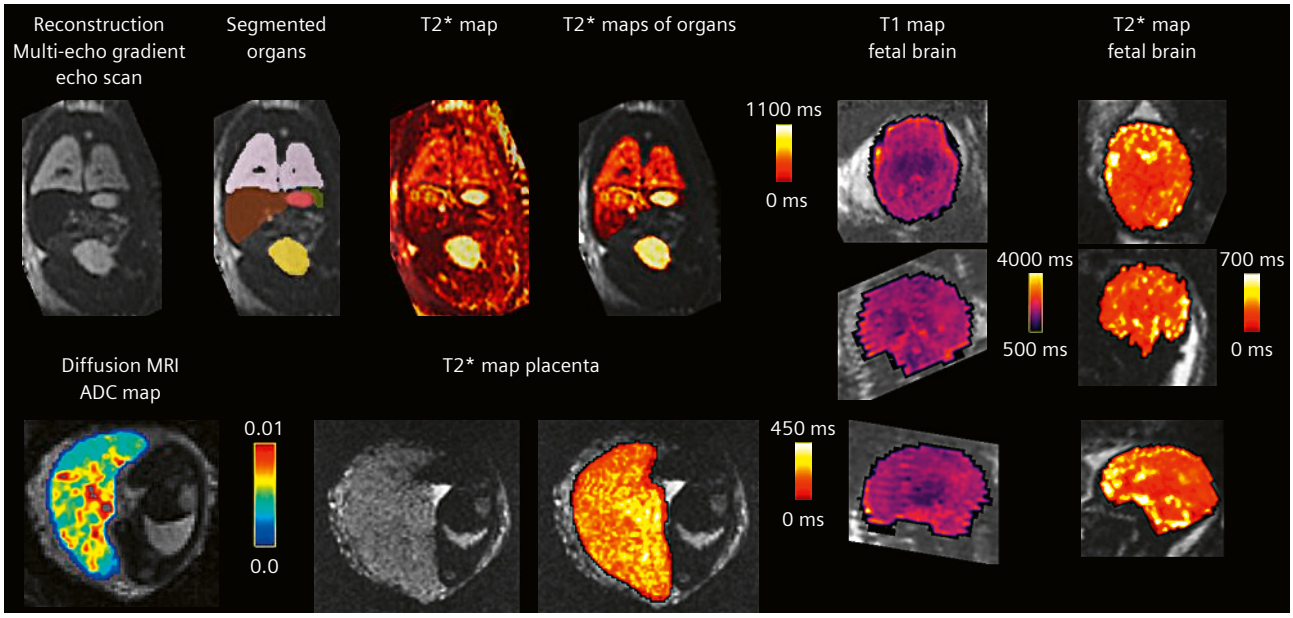
Results in a selected case with BMI = 49.9 kg/m² (Figure 6 for the anatomical and Figure 7 for the functional data) demonstrate the ability to obtain detailed results even in such challenging cases.



5 Longitudinal T1 (left) and T2* (middle) brain maps, and fetal organ T2* maps (right) for a subject scanned at 32 and 40 weeks' gestational age.



6 **Case study of fetal MRI at BMI 49.9 kg/m²: Part I:** Anatomical results for a participant with BMI = 49.9 kg/m² showing the ability to depict the brain structures (top row), the lungs (middle row, red arrows) and the placenta (bottom row, yellow arrows).

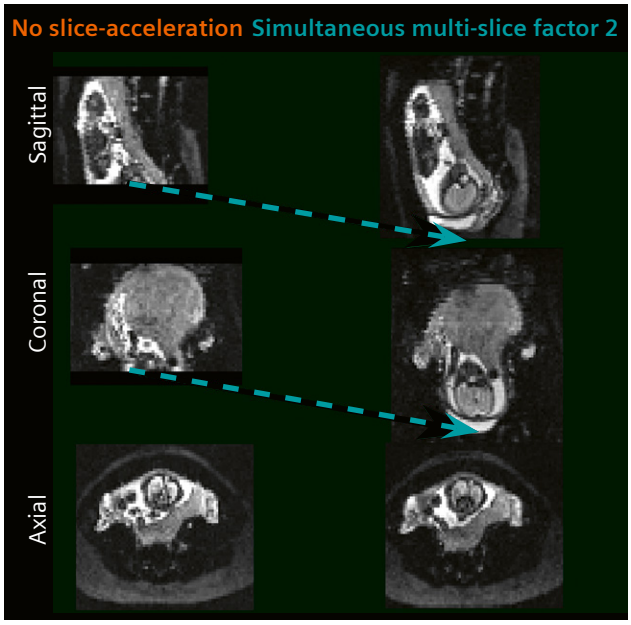


7 **Case study of fetal MRI at BMI 49.9 kg/m²: Part II:** Functional results from the same case for a participant with BMI = 49.9 kg/m² showing the individual organ T2* maps, the T1 and T2* maps of the brain, and the placental ADC and T2* map.

Discussion and conclusion

Fetal MRI at 0.55T is feasible, offers essential benefits, and is thus a promising direction for future antenatal imaging. The proposed short protocol allows anatomical and functional assessment of the fetus within 20 minutes. This is facilitated by foregoing any need for image-based shimming or other special correction tools, and carefully drafted to make use of the longer T2* and shorter T1 at low field. The research sequences allow further insights into desired regions of interest such as placental and lung microstructure and function. The wider bore size and shorter length increases comfort and thus increases access to fetal MRI until late gestation and in patients with higher BMIs. The fact that the scanner is a commercially available system makes it easy to integrate state-of-the-art techniques such as simultaneous multi-slice imaging, illustrated at 0.55T in Figure 8. Next steps will include adding fetal cardiac sequences; scanning further clinical cohorts such as patients with invasive placentation, preeclampsia, and congenital heart disease; and assessing the fetal placental unit prior to labor to assist in birth management. Other routinely used sequences for fetal MRI such as TrueFISP and T1-weighted contrasts will be added in the future.

An important future step is to further increase the availability of fetal MRI by allowing operation in hospitals and imaging centers without fetal MRI specialists. To come closer to this goal, a first step was the development of a prospective motion-correction technique that can detect fetal head translational displacements using deep learning and then feeds this information back to the scanner to continuously update the acquisition geometry in real time. This prospective motion correction shows great potential for applications that would highly benefit from precise correction of motion artifacts and immediate enhancement of the image quality during the scan. This can also be developed to be used to assess the tissue microstructure of the fetal brain through the quantification of the fetal brain's blood-oxygen-level-dependent (BOLD) response to maternal oxygenation and diffusion MRI.



8 Simultaneous multi-slice imaging for T2* imaging at 0.55T illustrating the extension of the field of view by a factor of nearly two in the same scan time.

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