A Fast Anatomical and Quantitative MRI Fetal Exam at Low Field

Jordina Aviles[1,2(✉)], Kathleen Colford[1], Megan Hall[1,3], Massimo Marenzana[1], Alena Uus[1,2], Sharon Giles[2], Philippa Bridgen[2], Mary A. Rutherford[1], Shaihan J. Malik[1,2], Joseph V. Hajnal[1,2], Raphael Tomi-Tricot[2,4], and Jana Hutter[1,2]

[1] Centre for the Developing Brain, School of Biomedical Engineering and Imaging Sciences, King's College London, London, UK
jordina.aviles_verdera@kcl.ac.uk
[2] Department of Biomedical Engineering, School of Biomedical Engineering and Imaging Sciences, King's College London, London, UK
[3] Department of Women and Children's Health, King's College London, London, UK
[4] MR Research Collaborations, Siemens Healthcare Limited, Camberley, UK

Abstract. Fetal Magnetic Resonance Imaging (Fetal MRI) allows insights into human development before birth, complementing conventional Ultrasound imaging with its high resolution and available numerous contrast options. Significant challenges still exist including geometric distortion caused by maternal bowel gas in echo-planar imaging, and restrictions in bore size limiting access to MRI in the obese and or claustrophobic population. Recent developments of clinical low-field scanners can meet these challenges and thus render fetal MRI more accessible. This study shows anatomical imaging and quantitative T2* mapping on a 0.55T system with an analysis pipeline for both placenta and fetal brain. Results show an expected increased overall T2* compared to higher fields, with values decreasing over gestation as shown at higher field. Future work will be directed towards exploring additional types of relaxometry and the use of the presented techniques in subjects with higher Body Mass Index. Included data and analysis code are publicly available.

Keywords: Fetal and Placental MRI · Low field

1 Introduction

Fetal Magnetic Resonance Imaging (MRI) is increasingly used for both research and clinical fetal examinations. Its ability to offer high resolution, and both anatomical and functional information allows fetal MRI to play a growing role in perinatal management and early detection of pathologies complementing widely used Ultrasound (US) screening. Multiple recent studies show an increasing range of uses in fetal neurological applications [16], congenital heart disease, placental

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pathologies such as placenta accreta, percreta and increta and in the prediction of pregnancy complications such as pre-eclampsia, fetal growth restriction and preterm birth. Thereby, two techniques have found particularly widespread use: First, T2-weighted anatomical imaging, often performed using single-shot 2D Turbo-Spin-Echo techniques to freeze fetal motion within each slice, is the standard for anatomical imaging due to its excellent soft tissue contrast and achievable high resolution. Typical assessments, which usually require motion correction, include fetal volumetric quantification of the fetal brain growth, the fetal body and the placenta. Second, more recently T2* relaxometry, sensitive to the concentration of deoxygenated haemoglobin via the blood-oxygen level dependency effect, has been more widely employed in a research capacity, especially to assess placental function [18].

A decreasing trend in placental mean T2* over gestational age has consistently been observed. Reduction in T2* has been shown in pregnancies associated with pre-eclampsia [10], fetal growth restriction and reduced birth weight [17] as well as congenital heart disease [19]. T2* data is typically acquired using a single shot gradient-echo Echo Planar Imaging (EPI) sequence acquired at different echo times (TE), either using repeated single-echo or multi-echo sequences.

Fetal MRI data is currently almost exclusively acquired at 1.5T and to a lesser extent 3T, with the move to ever higher field strength driven by the available higher signal-to-noise ratio (SNR) [15] allowing, for example, higher b-values for diffusion-weighted MRI, and thus the ability to probe smaller structures, as well as higher resolution anatomical scans. However, another recent emerging push in the opposite direction, towards lower field strengths, most notably for interventional applications, cardiac MRI and lung MRI, can be observed. The advantages of low field, such as reduced susceptibility to tissue-air interfaces, and thus reduced geometric distortions, often reduced bore length and wider diameter as well as longer T2* times, meet some of the requirements and challenges for fetal MRI: Reduced susceptibility lowers the requirements for shimming, typically required at high field targeted to the organ of interest [5] to reduce geometric distortions especially for functional EPI-based sequences. The increased comfort of the larger bore fits the requirements of an increasingly obese pregnant population and increases comfort for claustrophobic women of all sizes. Finally, the longer T2* times allow longer read-out trains to be employed in single-shot sequences and thus higher resolution.

First quantitative studies at 0.5T were presented in the late 90s by Gowland et al. in a purpose-built scanner, providing quantification of T1 and T2 in the human placenta from 20 weeks gestational age to term in both normal and compromised pregnancies [6]. Significant decay in T1 and T2 relaxation times with gestational age were shown for the first time in low-field. Furthermore, in compromised pregnancies with intra-uterine growth restriction and pre-eclampsia, T1 values were significant lower than in control group, this trend persisted for T2 but did not reach significance. These findings motivate the further exploration of low-field for pregnancy assessment and diagnostics.

Contributions

This work introduces a fast, 15 min fetal examination at 0.55T including full uterus anatomical and quantitative T2* imaging together with an analysis pipeline. It provides the first evidence of the feasibility of this approach at low field and initial data over gestation. Benefits and possible avenues to generate new information to be obtained at low field are discussed.

2 Methods

Pregnant women were scanned on a contemporary clinical 0.55T scanner (MAGNETOM Free.Max, Siemens Healthcare, Erlangen, Germany) after informed consent was obtained as part of the MEERKAT study (REC 21/LO/0742). The acquisitions were performed with a 6-element flexible coil (BioMatrix Contour Coil, Siemens Healthcare, Erlangen, Germany) and a 9-element spine coil built in the patient table. Women were scanned in head first supine position fully supported with head and leg rests with continuous life monitoring including heart rate and blood pressure measurements as well as frequent verbal interaction. A mid examination break was offered but declined in all cases described here. Exclusion criteria were maintained from the high field studies and include maternal age < 16 years, lack of ability to consent, contraindications for MRI such as metal implants, claustrophobia, multiple pregnancies and a maximal weight of 200 kg.

Structural T2-weighted Turbo Spin Echo (TSE) acquisitions using the clinically available sequence was employed. For the T2* relaxometry, a clinical gradient echo single-shot EPI sequence was modified to include up to 5 back-to-back readout trains defining as many echoes.

The T2-weighted data sets were acquired in five different orientations, the parameters include resolution $= 1.48 \times 1.48 \times 4.5\,\text{mm}^3$, FOV $= 449 \times 499\,\text{mm}^2$ TE $= 105$–106 ms, TR $= 1460$–2500 ms and total acquisition time (TA) $= 2$ min–3 min. T2* acquisitions were performed in transverse orientation for the fetal brain and both transverse and coronal for the placenta. The quantitative T2* datasets were acquired with a resolution of $4\,\text{mm}^3$ isotropic and a FOV $= 400 \times 400\,\text{mm}^2$, TEs $= 80$ ms, 222.62 ms and 365.24 ms, TR $= 9670$ ms, TA $= 39$ s. Parallel imaging for T2* was applied with same resolution and FOV, TEs $=$ 44 ms, 117.92 ms and 191.84 ms, TR $= 5120$ ms and TA $= 31$ s. A 5 echoes image with parallel imaging with an acceleration factor of 2 was acquired for one of the patients. The T2 and T2* acquisitions were performed in a sequential order without global changes to the maternal position with a total acquisition time of 15 min.

In addition, to demonstrate the field-strength dependent differences, data sets with placental and brain T2* data acquired as part of another ethically approved study (REC 16/LO/1573) using a similar protocol on a clinical 3T scanner (Philips Achieva, 104 data sets) and on a clinical 1.5T scanner (Philips Ingenia, 50 data sets) were considered. This data was acquired following the

same selection process as the present study, including only healthy volunteers with gestational age ranging from 16 to 40 weeks.

2.1 Evaluation

The included cohort consists of a total of eight datasets with gestational ages ranging from 21 to 37 weeks. Two of these subjects were diagnosed with high risk pregnancies. This included one with chronic hypertension and fetal growth restriction and another with threatened preterm labour and ruptured membranes. The remaining four were considered low risk controls, two of these were scanned twice during pregnancy, characteristics are given in Table 1.

Table 1. Studied cohort characteristics. cHTN: Chronic Hypertension; FGR: Fetal Growth Restriction; PPROM: Prolonged preterm rupture of the membranes. For the acquired data, a X in the third and/or fourth column indicates Turbo Spin Echo (TSE) data and/or gradient echo single-shot Echo-plannar Imaging (EPI) data was acquired.

Study ID	gestational age [weeks] at scan	Cohort	TSE data	EPI data
Participant 1	31.43	control	X	
Participant 2	30.28	control	X	
Participant 4	28.01	cHTN + FGR	X	
Participant 5	21.01	control		X
Participant 6	32.01	PPROM	X	X
Participant 1, scan 2	37.01	control	X	X
Participant 2, scan 2	33.85	control	X	X

2.2 Analysis

The obtained stack of TSE images of each subject at five different orientations was used as input dataset for a slice-to-volume (SVR) registration model by Uus et al. to generate motion-corrected fetal brain reconstructions (see Fig. 2) [21]. In parallel, a set of images (see Fig. 1) acquired at three to five different TEs were obtained from the single-shot multi-echo gradient echo sequences for both fetal brain and placentas of each subject. For the T2* fitting, 3D masks were obtained with open-source software either fully manually (placenta) or using manual refinement after automatic brain extraction was performed (brain). Quality of the segmentations was assessed by an expert radiographer (KC).

T2* values were obtained by fitting the signal intensity of each voxel within the placenta or brain as a function of echo time. Fitting was performed using a non-linear least squares regression in python of the following mono-exponential decay model:

$$S = M_0 \cdot e^{\frac{-TE_i}{T2^*}} \tag{1}$$

where M_0 is the proton density and TE_i contains the different echo times with $i \in [0, 5]$. M_0 was initialized with the voxel intensity at the first echo time and T2* initialization was in the range of 0–300 ms. Bounds range was 0–10000 for M_0, 0–500 ms for the T2* values in the placenta and 0–1000 ms for the fetal brain.

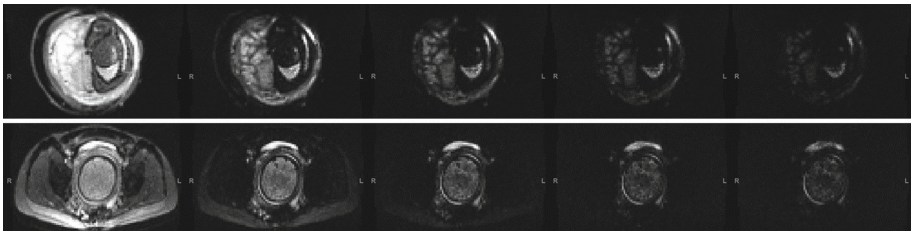

Fig. 1. Example of a placenta slice (top row) and fetal brain slice (bottom row) from 3D multi-echo gradient echo data across different TE (from left to right: 44 ms, 117.92 ms, 191.84 ms, 265.76 ms and 339.68 ms).

3 Results

Seven of the eight subjects tolerated the entire scan well, one woman was not comfortable and abandoned the scan after 10 min. T2w data is thus available for all but for that case, where not enough data was acquired for the SVR reconstruction. T2* scans were added in four of the eight subjects. Anatomical data from one of the cases is illustrated in Fig. 2, displaying a coronal and a sagittal view through the uterus as well as a resulting SVR result from the fetal brain.

Example multi-echo images from the placenta and brain with their corresponding T2* maps are shown in Fig. 3. Obtained T2* maps obtained have the capability to capture the differences in T2* between different regions of the fetal brain and highlight placental lobularity.

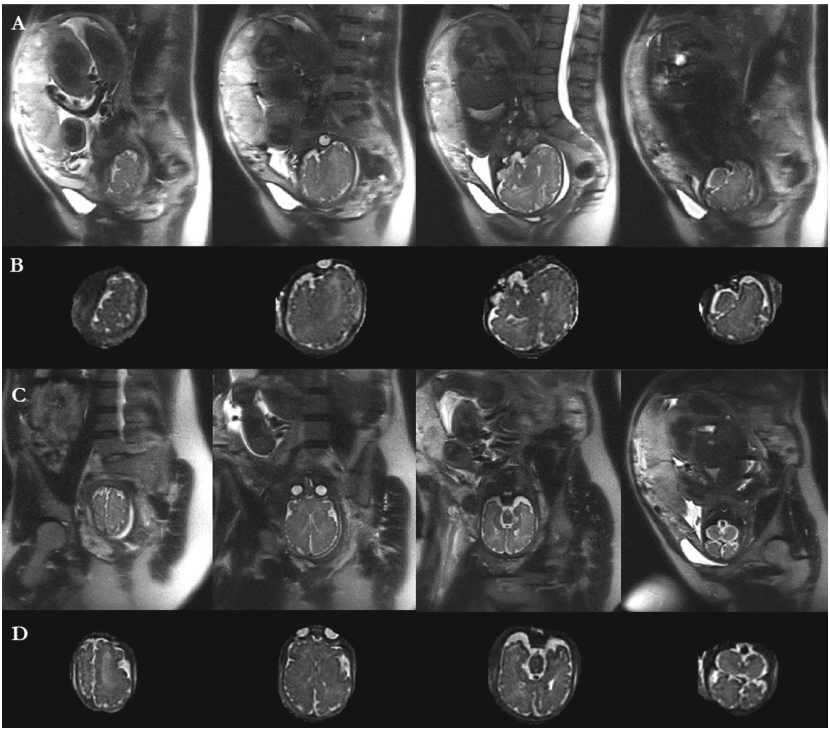

Fig. 2. Sagittal and coronal views of a structural T2-weighted TSE image at 37 weeks gestational age together with its corresponding SVR reconstruction of the fetal brain. A) Sagittal slices across the uterus; B) Sagittal slices of the fetal brain SVR; C) Coronal slices across the uterus together with D) the fetal brain SVR.

Figure 4 shows example data and the achieved fitted mono-exponential decay curves in the regions of interest (ROI) indicated. Two voxels in different regions of both placenta and fetal brain were selected and their intensities across TEs plotted. In the placenta, signal in the intervillous space is higher and decays slower than in the septa. Similar behaviour can be seen in the fetal brain fitting, where the voxel selected in the white matter region has higher values across the TEs than the one situated around the basal ganglia.

Mean T2* values across the fetal brain and placenta were calculated for each subject, together with brain and placenta volumes. Figure 5 shows these quantitative results in red over gestational age, superimposed over results from 3T (yellow) and 1.5T (violet) to allow cross-field strength comparison. Placental volume (A) shows a weak positive correlation with gestational age, independent of field strength. A clear negative correlation between mean placental T2* and gestational age can be observed on all field strength, with the absolute values of T2* increasing with field strength for similar gestational age (B). Mean T2* values obtained for the placenta are around 211 ms at around 21 weeks gestational age, dropping

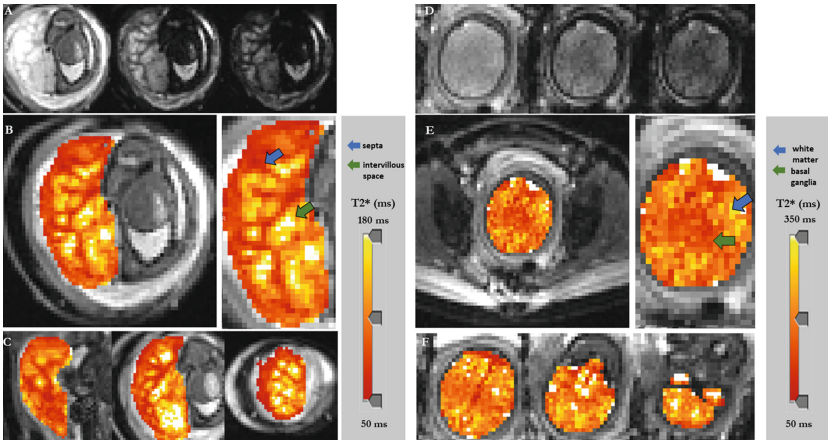

Fig. 3. Placenta and fetal brain gradient-echo images at 37 weeks gestational age over 3 echo times (from left to right: 44 ms, 117.92 ms, 191.84 ms) and their T2* maps over different axial slices. A) Slice of the placenta gradient-echo images over 3 TE; B) T2* map of the placenta overlaid on first echo time image in A and a zoom in with blue and green arrows pointing to the septa and intervillous space, respectively; C) Different placental T2* map slices over different axial views; D) Slice of the fetal brain gradient-echo images over 3 TE; E) T2* map of the fetal brain overlaid on first echo time image in B and a zoom in with blue and green arrows pointing to white matter and basal ganglia, respectively; F) Different fetal brain T2* map slices over different axial views; (Color figure online)

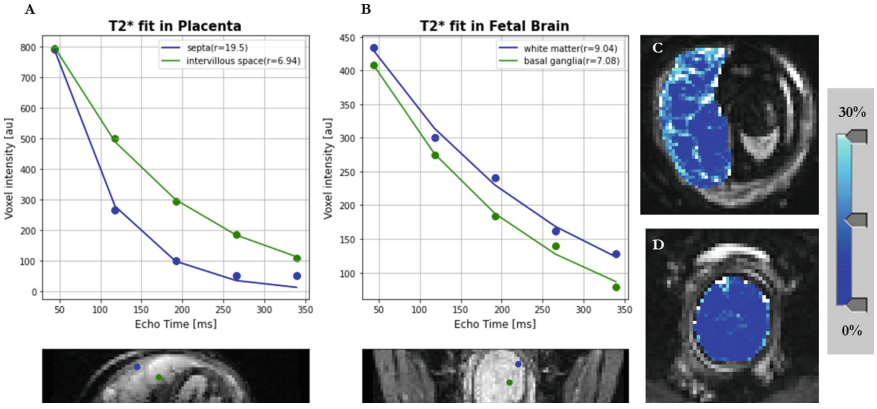

Fig. 4. T2* fitting in brain and placenta at 37 weeks gestational age examples with residual maps overlaid with the second echo image. A) T2* fitting for septa in blue and intervillous space in green on top with chosen voxels position on the bottom; B) T2* fitting for white matter in blue and basal ganglia in green on top with chosen voxels position on the bottom; C) Placenta residual map; D) Fetal Brain residual map with colormap on the right side. (Color figure online)

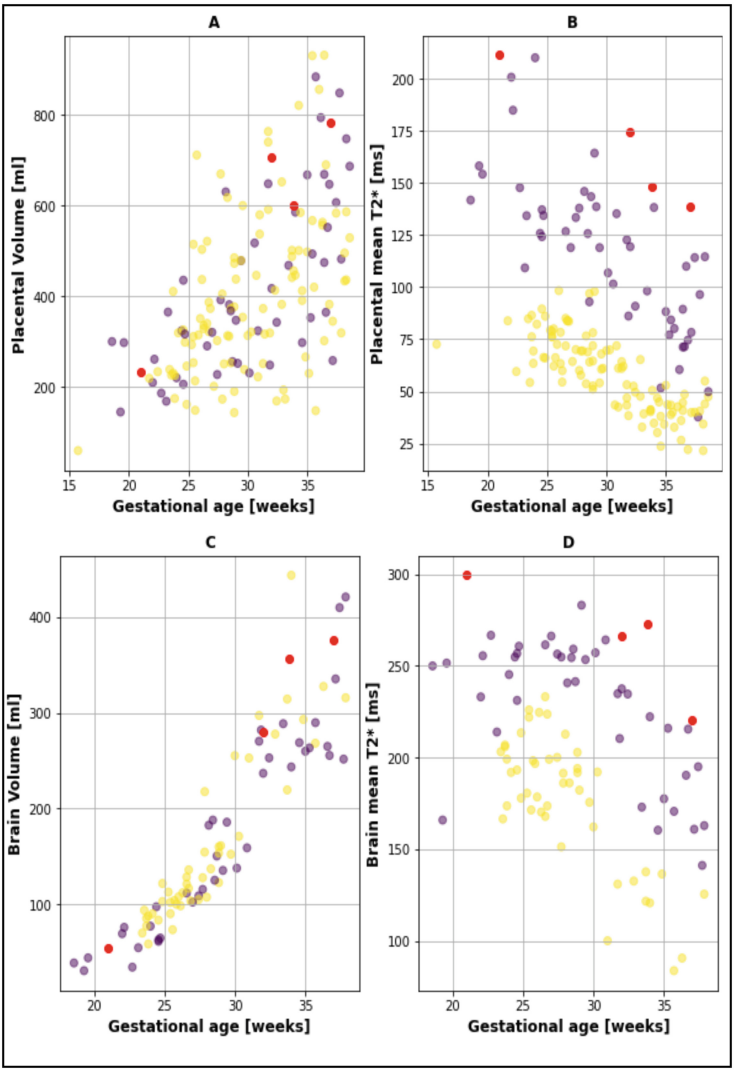

Fig. 5. Quantitative results over gestational age. A) Placental volume from T2* scan, B) Placental mean T2*, C) Fetal brain volume from T2* scan and D) Mean fetal brain T2* over gestational age. Red dots refer to data acquired at 0.55T, purple at 1.5T and yellow at 3T. (Color figure online)

to 107 ms at 37 weeks. A strong positive correlation can be observed between fetal brain volume and gestational age, again independent of field strength (C). Finally, a negative correlation between brain T2* and gestational age can be observed, with the data at the highest field strength (in yellow) again displaying the lowest

overall values for the same gestational age and the data from low field (in red) on average with the highest values (D).

4 Discussion and Conclusions

The included dataset will be made available from the corresponding author upon reasonable academic request in accordance with the rules of ethical approval (REC 21/LO/0742). The analysis code is already available at Github Link. This work provides the important initial evidence of the feasibility of a short, clinically acceptable under 15 min anatomical and quantitative T2* analysis for low-field fetal MRI on a contemporary clinical low-field MRI.

It adds to the previous work by Gowland et al. in their purpose-built scanner [4,6–8], demonstrating the data quality achievable on a clinical scanner at this field strength. Despite its lower SNR, low-field MRI is known to be less susceptible to geometric distortion related to B0 inhomogeneities, translated here in achieving high quality data without using image based shimming techniques. Further studies will include B0 maps to quantitatively illustrate this. Wider bore diameters together with shorter length carry the potential to contribute to help with comfort and claustrophobia together with the possibility to scan pregnant women with higher BMI > 30.

Further studies will need to be performed to provide quantitative evidence for this. We show both anatomical data, suitable for high resolution reconstruction and T2* measurements in the brain and placenta. The achieved resolution for these functional scans allows robust identification of different brain and placental regions (Fig. 4, Fig. 3).

The achieved T2* maps are of good quality. Quantitative T2* results in this study are among the first reported, to the best of our knowledge, in an 0.55T scanner for fetal and placenta imaging. Matched T2* decay with gestational age with previously published studies, can be seen in both ROIs [1,11,18,22]. In agreement to previous work, Fig. 5 shows a clear decay in mean T2* values of the placenta with gestational age [11,12,18].

Following the same trend, fetal brain mean T2* also appears to decay with gestational age as previously reported by Vasylechko et al. [22]. The recorded fetal brain volume from these T2* scans is well in line with the volumes as obtained in other studies [2,3,13]. In addition, results obtained for total brain volume are aligned with the ones reported by Chang et al. over gestational age using Ultrasound fetal data [2].

While observing a decrease in T2* over gestational age, similar to all previous studies at 1.5T and 3T, the T2* values in this study are higher for same gestational age (211.19 ms at around 21 weeks gestational age compared to 120 ms on 1.5T and 75 at 3T) than previously reported on 1.5T or 3T, as expected [9,17]. These observed overall higher T2* times are in line with the general increase in T2* observed with decreasing field strength [14]. Figure 5 illustrates these trends for both placenta and brain in 0.55T, 1.5T and 3T.

The demonstrated higher T2* in the intervillous space, particularly close to the centers of the lobules and overall granularity illustrated is in agreement with

previously published results [12]. The intervillous space receives inflowing maternal blood from the spiral arteries which continues along the villi to exchange oxygen and nutrients with the fetal blood. The oxygen-rich blood in this area, with increasing decay due to fetal uptake towards the borders of the lobules, is in line with the observed pattern. The vasculature in the septa on the other hand, carrying deoxygenated blood back to the maternal circulation corresponds well to the lower signal intensity. Notably, here at low field, the overall longer T2* times allow us to observe smaller differences in these low-signal regions even in later gestation (see Fig. 3 for a scan at 37 weeks).

Similar findings can be demonstrated in the fetal brain, where the basal ganglia show lower T2* than white matter in line with previous studies [22]. However, the reasons behind differences observed in the fetal brain remain unclear. Some studies suggest increased T2* is related to changes in myelin and iron concentration [22]. The observed higher T2* (see Fig. 5) in turn allows single-shot acquisitions with higher resolution, contributing to motion robustness and decreased loss in SNR compared to multi-shot sequences [20].

Obtained residual maps (see Fig. 4) show lower and more homogeneous results for the fetal brain than the placenta, where some anatomical relationship can be appreciated especially around the septa.

This preliminary study has, however, some limitations. The data set used included only a total of eight subjects with only four of them containing multi-echo EPI data. Although the results are in agreement with already published results in the field, a larger dataset with a wider spread across gestational age and including different placental and fetal brain pathologies is needed to further validate these results.

Another major limitation is fetal brain T2* were reported for the whole volume instead of differentiating between regions which might contribute to a better understanding of the clinical value of the parameter. Finally, although motion was assessed visually, no motion correction was applied in the multi-echo data, causing potential inconsistencies.

Future work will focus on including further modalities such as diffusion MRI, T1 relaxometry and perfusion MRI to study the developing placenta and fetus in even more detail. Moreover, taking advantage of low-field scanner properties, we will aim to include women with higher BMI to study the suitability of the proposed protocol to achieve good image quality in this challenging cohort. Finally, future studies will include a larger dataset, and explore the effect of motion correction on the present results.

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