# Quantitative T2 Relaxometry in Fetal Brain: Validation Using Modified FaBiaN Fetal Brain MRI Simulator

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**Abstract.** With development of fast imaging techniques and powerful motion correcting reconstruction techniques, high resolution 3D fetal brain images with a high level of anatomical detail are possible to acquire. A quantitative framework has been proposed that leverages fast imaging techniques and motion correcting reconstruction techniques to build quantitative T2 maps of the fetal brain. This study proposes a simulated phantom that modifies the FaBiaN fetal MRI simulated phantom to enable validation of this quantitative framework. We found that the slice-to-volume reconstruction (SVR) algorithm preserves quantitative T2 measurements and, therefore the proposed pipeline is suitable for reconstruction of quantitative T2 maps of fetal brain tissue.

**Keywords:** Fetal brain MRI · Relaxometry · Slice to volume registration

## 1 Introduction

The fetal period is characterised by rapid growth and, in the fetal brain, myelination, generation of synapses, movement of cells and changes in water result in observable changes in tissue properties. In addition, changes due to pathology may impacts fetal and post-natal development [14]. Relaxometry describes tissue relaxation properties in MRI [4] and therefore presents an opportunity to study fetal brain development and pathology. Traditional quantitative MRI methods, though, have been highly susceptible to motion, while requiring long scan times [13,20]. In the fetal setting, this presents a challenge, as relaxometry measurements will be corrupted by fetal motion and maternal breathing.

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**Related Work:** Clinical fetal imaging relies on rapid sequences such as Single-shot turbo spin-echo (TSE) to avoid in-plane motion [9] and advances in motion correction have allowed for high quality 3D imaging of fetal brains [6] and other fetal anatomy [18,19]. Recently, echo planar imaging (EPI) has been leveraged to obtain T2* measurements in fetal brain [3,20] and other fetal tissues [1,15]. However, due to a lack of ground truth the quantitative fetal MRI measurements are difficult to validate. A recently developed simulated fetal brain MRI phantom, known as the Fetal Brain magnetic resonance Acquisition Numerical phantom (FaBiAN) [8], can facilitate such validation. This phantom integrates accurate simulations of signals from Siemens' Half-Fourier Acquisition Single-shot Turbo spin Echo (HASTE) sequence, also called Single-Shot Fast Spin Echo (SS-FSE for GE Healthcare), with different levels of fetal motion to simulate realistic fetal brain scans based on spatiotemporal fetal brain atlas [5].

**Contributions:** We propose a new framework to measure T2 relaxation time in the fetal brain by combining Single-shot TSE acquisition with varying echo times (TE) and SVR [6], using the SVR toolkit (SVRTK)[1]. We build on our previous work [2], in which we successfully validated our T2 measurement against a gold standard multi-echo spin-echo (MESE) sequence by scanning a phantom made up of a spherical flask of agar gel and five vials of MnCl2. However, a validation of such measurement for the motion corrupted fetal data has not been carried out thus far. To address this gap we propose a modified FaBiAN simulator which accurately models fetal acquisition of the Philip's system, on which we performed our fetal brain T2 measurements using five real fetal MRI datasets. Subsequently, we simulate realistic motion corrupted fetal data and quantify the measurement errors in reconstructed T2 maps to validate the SVR step in the T2 relaxometry framework for the fetal brain. Finally, we present measurements of T2 on five real fetal subjects using the validated framework.

## 2 Methodology

### 2.1 Quantitative T2 Measurement Framework for Fetal MRI

The proposed T2 relaxometry framework, validated against a gold-standard method for a static phantom in our previous work [2], is summarised in Fig. 1. The steps of this framework are:

1. Stacks are acquired in three approximately orthogonal views for three different TE = 80, 180 and 400 ms (a total of nine stacks) and denoised using a shearlet-based algorithm [7]. A selected stack, used in the reconstruction of the template volume, is manually brain-masked.
2. The fetal brain MRI for each TE is reconstructed separately using SVR with default parameters [6] on the three stacks of each TE. The reconstructed TE = 180 ms volume was used as a template for the reconstruction of the other

[1] https://github.com/SVRTK/SVRTK.

volumes to maximise the consistency of the volumes for different echo times. The TE = 80 and 400 ms volumes were further registered to the TE = 180 ms volume, and the entire set is registered to the fetal atlas for the given gestational age [17].

3. Using a pre-calculated dictionary of slice corrected SS-FSE signals, the T2 value for each voxel is found as the dictionary entry with a minimum scalar product with normalised measured signal.

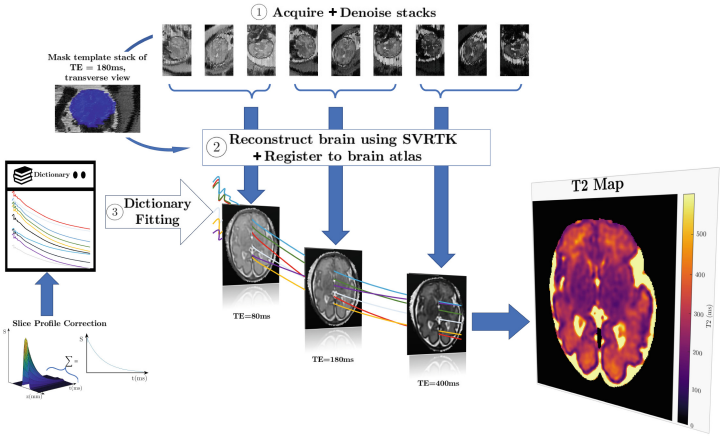


**Fig. 1.** The quantitative T2 measurement framework for fetal brain MRI.

This framework was applied to real fetal MRI data to obtain measurements of T2 in the fetal brain. To validate that the SVR step of the proposed framework preserves T2 measurements, we modified the FaBiAN phantom to generate simulated motion-corrupted fetal data from a simulated ground truth quantitative T2 maps of fetal brain, and applied the framework to measure the reconstruction error in the simulated T2 maps.

### 2.2 Overview of the FaBiAN Phantom

The FaBiAN phantom uses high resolution 3D fetal atlas segmentations [5] at 0.8 mm isotropic as the reference for its simulations. These segmentations are split into three tissue classes: white matter (WM), grey matter (GM) and cerebrospinal-fluid (CSF) with corresponding T1 and T2 values chosen by the authors [8]. The reference 3D segmentation map is then upsampled (using nearest-neighbour or NN) in the slice-select direction as a Gaussian slice profile is applied to the signals.

Signals are generated at each point on the upsampled reference map based on the tissue class of the given point resulting in a large matrix of signals for

each point of the reference maps. Slices are then sampled based on the sampling scheme. Five percent of the slices were initially chosen, randomly, to have motion applied to them and before these slices are sampled, the upsampled reference map is translated and rotated to simulate motion and the signal matrix is updated with the signals based on the transformed reference map.

The slices are sampled by multiplying a Gaussian profile with the signals at the point of the given slice and summing across the slice-select direction to obtain the 2D slice. This is then transformed into a 2D k-space representation of the slice using MATLAB's fast Fourier transform and this k-space is sampled based on HASTE (Siemen's) or SSTSE (GE Healthcare) and any acceleration factors. This is then inverse Fourier transformed to obtain the 2D slice and the this is done for all the slices to obtain the final 3D motion corrupted image.

The modifications proposed in this study reflect the Philip's specific implementation as well as address the computational limitations imposed in this study. The original simulation had up to "16 CPU workers with 20 GB of RAM each" [8], while this study has access to a total of 64 GB of RAM (and the final modifications suggested in this study allow for the simulations to be ran on a machine with 16 GB of RAM). Further information on implementation of the FaBiAN phantom is given in the publication [8] written by the developers of the phantom.

### 2.3 The Fetal Brain Model

This study uses the normative spatiotemporal magnetic resonance atlas [5] in our simulations and reference T1 and T2 values identical to the original FaBiAN phantom [8]. Our initial real fetal brain T2 measurements [2] confirmed that these values (232 ms for WM and 162 for GM) are realistic and there are no literature T1 values for fetal brains at the time of this study.

### 2.4 Modelling Fetal Motion

Fetal motion was modelled in the FaBiAN phantom using motion randomly sampled from an uniform distribution at 3 different levels with each level corresponding to an amplitude of 3D translation and 3D rotation in any direction in 3D space. The developers of the FaBiAN phantom took clinical advise to inform their model of fetal motion [8] and, as such, this study closely follows their motion models while proposing slight modifications.

This study applies the light motion and moderate motion amplitudes from the FaBiAN phantom, which are defined as $[-1, 1]$ mm and $[-3, 3]$ mm maximum translation in any direction in 3D space, and $[-2, 2]^\circ$ and $[-5, 5]^\circ$ maximum rotation along an axis represented by an arbitrary 3D vector in 3D space [8]. These are for each incidence of motion. However in this study, the translation displacements and rotation angles were obtained using a normal distribution with the amplitudes representing $3 \times \sigma$ of the normal distribution. The rotation axes were chosen by an uniform distribution, as in the original FaBiAN phantom.

In a similar manner to the FaBiAN phantom, this study also translates and rotates the fetal atlas before sampling the slice and uses this transformed atlas as the new reference. However, in this study there is a 10% (for light motion) or 12.5% (for moderate motion) chance of a transformation being made to the atlas before sampling. The slices during the sampling of which a transformation is applied is not pre-selected (as these slices are randomly pre-selected in the original FaBiAN phantom).

In addition, transformations in the FaBiAN phantom were interpolated using nearest neighbour interpolation [8]. In contrast, we are using linear interpolation on individual tissue classes and max-voting to transform the segmentations in order to preserve image quality. We implement interleaved slice order with four packages, according to our Philips acquisition slice order, (i.e. 1,5,9... then 2,6,10..., then 3,7,11,... and finally 4,8,12,...) instead of the Siemens' interleaved scheme.

### 2.5 Modelling Signals with Slice Profiles

Although pure T2 relaxation can be modelled as a simple exponential decay, in practice the use of non-180° refocusing pulses, and slice selective pulses in general, leads to signals deviating from this relationship and, thus we use the EPG formalism [11,12,21] to model this extra complexity.

In addition, signals are influenced by the varying flip angles along the slice profile as the slice profile is not an ideal square. To model these flip angles, refocusing and excitation pulses from the Philip's scanners are utilised and the overall signal for the given T2 entry of the dictionary is modelled by integrating the signal along each point on the slice profile [10].

We proposed an optimised simulation of MRI signals in individual slices, which deviates from the original FaBiaN implementation. First, the slice position is calculated based on the slice index and resolution in the slice direction. A generous window is applied in the slice direction (approximately 6× the slice width) to fully capture the entire slice profile and any off-centre signal. All the T1 and T2 values in this window of the reference map are obtained. This is then upsampled based on the number of points (experimentally set to 62) on the slice profile being simulated. The signals are then modelled at each of these points based on the flip angle profile and local T1 and T2 values, and the final signal decay (a signal as a function of time) is calculated by summing along the slice profile direction, resulting in 2D + t slice object. The entire unsampled k-space for this slice is then obtained through a Fourier transform of this profile across each time point.

### 2.6 Sampling K-Space

For Single-shot TSE images, slightly more than half of the k-space is sampled to speed up acquisition (controlled by partial Fourier factor parameter) and the rest of the k-space is zero-filled. We propose to manipulate the TE by changing

the partial Fourier factor, such that the centre of k-space is sampled at the given TE.

To further speed up acquisition, Philips uses SENSE to reduce acquired field of view (similarly to GRAPPA in the Siemens [8]) and this study simulates a pseudo SENSE (factor 2) reconstruction by sampling two lines of k-space for each echo. Complex noise is added to k-space before inverse Fourier transforming to image space to get the final slice image. We do not model any field inhomogeneities in these simulations.

### 2.7 Modelling the Signals for the Dictionary

The dictionary signals were modelled both in this and our previous work [2] in a similar manner to that described in Sect. 2.5. Except the T2 was constant for across all slice points (as the dictionary has no spatial information and, therefore it cannot be known how T2 might vary across the slice), based on the T2 entry of the dictionary for which the signal is being modelled. As such, partial volume is not modelled but the effect on the signal due to a finite signal profile is modelled. The T1 value for the entire dictionary is kept constant at $T1 = 3000$ ms. In addition, the resolution of the dictionary across the T2 values is 1ms and the range of T2s in the dictionary are from 25–3000 ms (as upon experimentation, T2 in the range of 0–25 ms was not required to be measured and these dictionary entries produced unreliable results due to the rapid decay).

### 2.8 Simulated Experiments

We apply the quantitative T2 measurement framework (Sect. 2.1, [2]) to reconstruct reference fetal brain MRI T2 maps (Sect. 2.3) from the simulated fetal data generated using our modified FaBiaN simulator. The simulated data contains three stacks with orthogonal orientation per TE, with in-plane resolution 1.25 mm, slice thickness 2.5 mm and slice spacing 1.25 mm (overlapping slices). We achieve TE = 80, 180 and 400 ms by using partial fourier factors 0.6, 0.8 and 0.96 respectively.

We consider five different settings in our experiments:

1. We do not model any fetal motion or partial volume (PV) along the slice profile. This ideal scenario allows us to exclude the SVR step as it presents artifacts only created through k-space sampling and not due to the slice-profile effects and therefore does not require any motion correction or super-resolution (SR) reconstruction.
2. We model PV along the slice profile but model no motion and do not implement any SR or SVR reconstruction.
3. We model PV along the slice profile but model no motion. We apply SR reconstruction and only global rigid stack alignment by using a single SVR iteration.
4. We model the entire motion simulation (with PV and motion) with light motion and apply SVR to reconstruct the T2 maps.

5. We model the entire motion simulation (with PV and motion) with moderate motion and apply SVR to reconstruct the T2 maps.

These experiments are done for fetal phantoms with gestational ages 21, 27, 29, 31, 35 weeks from the spatiotemporal atlas to simulate the same ages as those scanned in the quantitative framework.

### 2.9 Fetal Brain Measurements

The quantitative fetal scans were acquired on a Philip's INGENIA 1.5T scanner in clinical sessions with consent to research. Five subjects were imaged, with fetal anomalies as commented by radiologists. Single-shot TSE images were acquired with in-plane resolution 1.25 mm, slice thickness 2.5 mm and slice spacing 1.25 mm, and TE = 80, 180 and 400 ms (as described in Fig. 1) in three diverse views per TE (resulting in nine stacks per subject). Due to the tight fit of the FOV and the maternal body, the views were not perfectly orthogonal to avoid wrap artefacts. However, the views were sufficiently diverse to allow for successful SVR. The scan calibration was performed only once to ensure consistency. The T2 maps were reconstructed according the pipeline presented in Sect. 2.1.

## 3 Results

### 3.1 Simulated Fetal MRI

Figure 2 presents different views for an example of images generated from the simulation of motion for GA = 29 weeks. These demonstrate a distinct difference in the levels of motion.

### 3.2 Reconstruction of T2 Maps from Simulated Fetal Data

**Quantitative Evaluation:** Figure 3 presents the errors between original and reconstructed phantom T2 maps across all gestational ages. The box and whisker plots show median and inter-quartile range (IQR) of the errors in ms, and demonstrate the trend of the errors across five different experiments. The plot demonstrates small median errors in white matter (–2.7 ms, –3.8 ms, –1.5 ms, –2.0 ms and –2.5 ms for the experiments 1–5, respectively), suggesting a minimal bias in the measurement. The IQR of the errors stay consistent in the WM. In experiment 1 the quartiles range from –12 ms to 6 ms, whereas in experiment 5 these range from –13 to 7 ms. However, these ranges are still relatively small (less then 10%) compared to the nominal WM T2 of 232 ms. However, in the grey matter errors are larger, resulting from significant partial volume effects affecting the thin fetal cortex. Median errors show positive bias, consistent with shorter cortical T2 being mixed with longer T2 of white matter and cerebro-spinal fluid (CSF). Notably, the SR reconstruction diminishes the bias and reduces the spread of errors in the cortex, especially in the scenario of PV and no motion with SR reconstruction, or experiment 3, in comparison

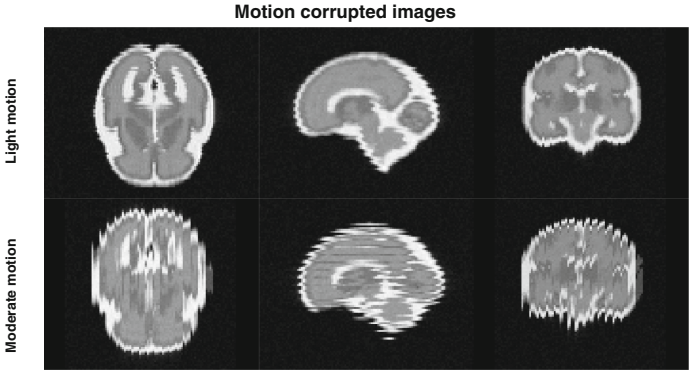


**Fig. 2.** The result of the motion artifacts simulated based on fetal motion and the slice and k-space sampling mentioned above.

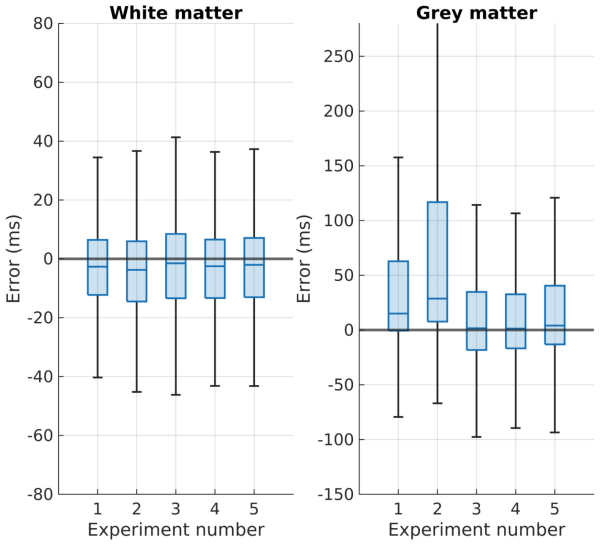


**Fig. 3.** Boxplots summarising the errors in ms of all the experiments (1–5) given above and amalgamated across all the simulations across all gestational ages.

to experiment 2 (PV, no motion, no SR reconstruction). While in experiment 1, the Quartiles range from 0ms to 63 ms, in experiment 3 the Quartiles range from –18 ms to 35 ms with the lowest median error of 1.6 ms. Moderate motion introduced marginally greater error in cortex in terms of bias and spread, however this was lower than experiment 2, which models partial volume but has no SR or SVR reconstruction.

**Qualitative Evaluation:** Example reconstructed T2 maps for each experiment are presented in Fig. 4. We can observe that SR reconstruction (experiments 3–5) results in better delineation of the cortex. In particular in experiment 3 with

no motion, it can be seen that the cortex has been most accurately recovered by SR. The percentage error maps demonstrate, that the errors are dominated by partial volume effects, especially on the boundary with CSF.

### 3.3 Fetal Measurements

Table 1 presents average T2 measurements for different brain tissue types obtained from quantitative MRI scans of five fetal subjects. We observe that T2 values are consistently higher for fetuses in comparison to neonates. Fetal T2 values are also consistently higher in comparison to fetal T2* values across all tissue types. The values in Table 1 were obtained as an average across all fetal subjects.

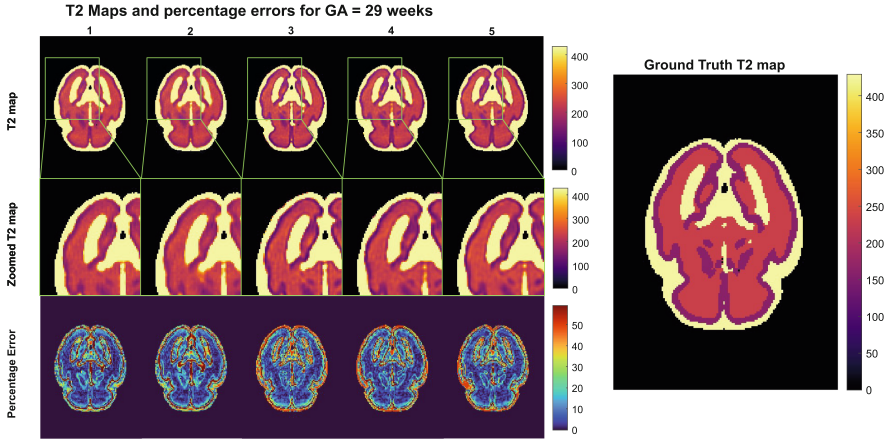


**Fig. 4.** The T2 maps (top row), highlight of the separation of cortex and white matter (middle row) and absolute percentage difference bottom row and the ground truth T2 map is given on the right. The T2 values were obtained based on the scheme described in [8]

**Table 1.** Table comparing values of fetal T2 of this study to neonatal T2 and to fetal T2* in literature. The full table including the mean values over each ROI ($\pm\sigma$ over the ROI) for each subject is given in the Supplementary material.

| Tissue | Average Fetal T2 (ms) $\pm\sigma$ (ms) | Neonatal T2 (ms) $\pm\sigma$ (ms) Using JSR [16] on 3T | Literature T2* (ms) $\pm\sigma$ (ms) Vasylechko [20] 1.5T | Literature T2* (ms) $\pm\sigma$ (ms) Blazejewska [3] 1.5T |
|---|---|---|---|---|
| Cortex | $199 \pm 33$ | $133 \pm 29$ | – | $163 \pm 30$ |
| DGM | $201 \pm 26$ | $132 \pm 45$ | Thalamus: $154 \pm 24$ | – |
| WM | $283 \pm 39$ | $218 \pm 50$ | FWM: $234 \pm 38$ | FWM: $259 \pm 34$ |
| Subplate | $292 \pm 43$ | – | – | $268 \pm 17$ |

## 4 Discussion

In this work we validated a framework for quantitative T2 measurement of fetal brain MRI [2] using a modified FaBiaN fetal brain MRI simulator. The results suggest that our proposed framework is accurate, with errors primarily driven by partial volume effects on tissue boundaries. We have shown that the SVR step preserves the T2 values. The median errors are very close to 0ms, proving that no bias is being introduced by the reconstructions. Inter-quartile ranges are within 10ms for WM showing good accuracy in homogeneous areas. The inter-quartile ranges are higher within the cortex, especially in positive direction, which is consistent with partial volume on boundaries with CSF. In addition, the reconstruction process recovers crucial structural details such as cortex which is particularly affected by the partial volume in the images that were not reconstructed using super-resolution technique.

The limitations of our modified phantom include lack of clinical validation, and further analysis of the individual elements of SVR pipeline. Currently, our phantom is specific to the acquisition parameters of our fetal MRI sequences, and we have not modelled the field inhomogeneities or signal drop-out due to in-plane motion. These present potential future works to further improve the physics of the simulation. At the time of this study, there are no other measurements of fetal T2 for comparison of the values obtained in this paper. Therefore, comparative studies may present a direction of future work.

## 5 Conclusion

We proposed a framework for quantitative T2 measurement of fetal brain MRI. We also presented initial measured T2 values for different fetal brain tissues. Our validation using a proposed modified FaBiaN simulator suggest feasibility of the our framework to study fetal brain and pathology.

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