A Magnetic Resonance Imaging Simulation Framework of the Developing Fetal Brain

Hélène Lajous[1,2], Tom Hilbert[1,3,4], Christopher W. Roy[1], Sébastien Tourbier[1], Priscille de Dumast[1,2], Yasser Alemán-Gómez[1], Thomas Yu[4], Patric Hagmann[1], Mériam Koob[1], Vincent Dunet[1], Tobias Kober[1,3,4], Matthias Stuber[1,2], and Meritxell Bach Cuadra[1,2,4]

[1]Department of Radiology, Lausanne University Hospital and University of Lausanne, Lausanne, Switzerland, [2]CIBM Center for Biomedical Imaging, Lausanne, Switzerland, [3]Advanced Clinical Imaging Technology (ACIT), Siemens Healthcare, Lausanne, Switzerland, [4]Signal Processing Laboratory 5 (LTS5), Ecole Polytechnique Fédérale de Lausanne (EPFL), Lausanne, Switzerland

Synopsis

Accurate characterization of in utero human brain maturation is critical. However, the limited number of exploitable magnetic resonance acquisitions not corrupted by motion in this cohort of sensitive subjects hinders the validation of advanced image processing techniques. Numerical simulations can mitigate these limitations by providing a controlled environment with a known ground truth. We present a flexible framework that simulates magnetic resonance acquisitions of the fetal brain in a realistic setup including stochastic motion. From simulated images comparable to clinical acquisitions, we assess the accuracy and robustness of super-resolution fetal brain magnetic resonance imaging with respect to noise and motion.

Introduction

There is a growing awareness of the importance of processes occurring during early brain development on health later in life [1,2]. Magnetic Resonance Imaging (MRI) is a powerful tool for depicting brain tissue contrast and therefore has the potential to investigate equivocal neurological patterns in utero. Before birth, fast 2D spin echo sequences are typically used to minimize the effects of unpredictable fetal motion during the acquisition. Access to large-scale data, usually corrupted by stochastic movements of the fetus, remains relatively scarce, hampering the development and evaluation of advanced image processing methods. Numerical phantoms provide a controlled environment where the ground truth is known to meet a variety of challenges related to the acquisition process for accurate, robust and reproducible research [3,4]. In this context, we have developed a simulation framework for Half-Fourier Acquisition Single-shot Turbo spin Echo (HASTE). Since motion correction is crucial in fetal MRI, the potential of this new tool is highlighted by an application example: the assessment of super-resolution (SR) reconstruction techniques that combine orthogonal series of 2D thick slices into an isotropic 3D high-resolution volume of the fetal brain with reduced intensity artefacts and motion sensitivity [5–9].

Methods

Figure 1 provides an overview of the simulation pipeline of HASTE acquisitions implemented using MATLAB (MathWorks, R2019a). Segmented high-resolution anatomical images from a normative spatiotemporal MRI atlas [10] are used as a model of the normal fetal brain. Segmented brain tissues are labeled as gray matter, white matter or cerebrospinal fluid, and are assigned corresponding T1 and T2 relaxation times at 1.5T [11–15]. The extended phase graph (EPG) simulation [16] allows for computing the decay of the transverse magnetization over time in every voxel of the anatomical images from the reference T1 and T2 maps and from simulated intensity non-uniformities [17], according to the HASTE sequence pulse design. The Fourier transform of the resulting 4D matrix is used to sample the actual k-space of the simulated HASTE images as described in Figure 2. While intra-slice motion is neglected, inter-slice random rigid movements of the fetus are implemented during k-space sampling according to motion estimation from clinical data [18]. Three levels of motion are defined: low, moderate and strong, that are characterized by less than 5%, 10% and 20% of corrupted slices respectively, and an amplitude of translation in every direction of [-1, 1]mm, [-2, 2]mm and [-2, 2]mm and of rotation of [-2, 2]°, [-4, 4]° and [-4, 4]° respectively. Complex Gaussian noise is added to simulate thermal noise during the acquisition. The final simulated HASTE images are reconstructed by 2D inverse Fourier transform. HASTE acquisitions of the fetal brain are simulated in three orthogonal orientations with a shift of ± 1.6 mm in-plane for acquisitions in the same orientation. The acquisition parameters comply with the clinical protocol set up at our local hospital for fetal brain examination. A case study on SR is presented using a previously reported reconstruction pipeline [8,19]. The quality of SR reconstruction is evaluated based on the normalized root mean squared error (NRMSE), the local structural similarity (SSIM) index [20] and its mean (MSSIM) over the image compared to a 3D 1.1-mm isotropic HASTE simulation uncorrupted by noise or movement. Six realizations are simulated for each SNR. The impact of low, respectively moderate movements of the fetus on the quality of SR reconstruction is studied using a reference series without motion, respectively with low motion amplitude.

Results

Figure 3 compares simulated motion-corrupted HASTE images of the fetal brain at 26, 30 and 32 weeks of gestational age to clinical acquisitions. Figure 4 shows the NRMSE and the MSSIM between SR reconstructions from various numbers of low-resolution series and a 3D isotropic high-resolution reference. The NRMSE decreases when increasing the number of series used for SR reconstruction. Noisier images lead to a slight decrease in the MSSIM, which in turn increases with the number of series. The quality of SR reconstructions from simulated data with an SNR similar to that observed in clinical acquisitions is the same as for SR reconstructions from simulated data with twice as much signal. The addition of motion-corrupted low-resolution series to reconstruct a SR volume of the fetal brain does not increase the MSSIM. In the case of moderate motion, the MSSIM is smaller than in the case of low motion. Figure 5 illustrates the improved sharpness in a region-of-interest of SR reconstruction when increasing the number of motion-corrupted series at an SNR similar to that of clinical acquisitions.

Discussion and Conclusion

We developed a new framework for fetal brain MRI simulations and explored its potential for evaluation and optimization of SR reconstruction techniques. This powerful tool simulates HASTE images comparable to real clinical acquisitions. Its flexibility in the choice of the sequence parameters but also other settings such as the gestational age makes it possible to simulate MR images of the fetal brain throughout the growth of the fetus with various SNR and amplitude of fetal movements. The controlled environment implemented demonstrates that the SR reconstruction algorithm used is robust to noise and motion. Such a numerical phantom provides a valuable framework for reproducibility studies and validation of advanced image processing techniques.

Acknowledgements

This work was supported by the Swiss National Science Foundation through grants 141283 and 182602, the Centre d'Imagerie BioMédicale (CIBM) of the UNIL, UNIGE, HUG, CHUV and EPFL, and the Leenaards and Jeantet Foundations.

References

1. Kwon EJ, Kim YJ. What is fetal programming?: a lifetime health is under the control of in utero health. Obstet Gynecol Sci. 2017;60(6):506-519. doi:10/gf5fj6

2. O'Donnell KJ, Meaney MJ. Fetal origins of mental health: The developmental origins of health and disease hypothesis. Am J Psychiatry. 2017;174(4):319-328. doi:10/f92t6n

3. Wissmann L, Santelli C, Segars WP, Kozerke S. MRXCAT: Realistic numerical phantoms for cardiovascular magnetic resonance. J Cardiovasc Magn Reson. 2014;16:63. doi:10/gf6bpx

4. Roy CW, Marini D, Segars WP, Seed M, Macgowan CK. Fetal XCMR: a numerical phantom for fetal cardiovascular magnetic resonance imaging. Journal of Cardiovascular Magnetic Resonance. 2019;21(1):29. doi:10/gf33j3

5. Rousseau F, Kim K, Studholme C, Koob M, Dietemann JL. On super-resolution for fetal brain MRI. International Conference on Medical Image Computing and Computer-Assisted Intervention. 2010;13(Pt 2):355-362. doi:10/bns47p

6. Gholipour A, Estroff JA, Warfield SK. Robust super-resolution volume reconstruction from slice acquisitions: application to fetal brain MRI. IEEE Transactions on Medical Imaging. 2010;29(10):1739-1758. doi:10/b2xmdp

7. Kuklisova-Murgasova M, Quaghebeur G, Rutherford MA, Hajnal JV, Schnabel JA. Reconstruction of fetal brain MRI with intensity matching and complete outlier removal. Medical Image Analysis. 2012;16(8):1550-1564. doi:10/f4hxwz

8. Tourbier S, Bresson X, Hagmann P, Thiran J-P, Meuli R, Cuadra MB. An efficient total variation algorithm for super-resolution in fetal brain MRI with adaptive regularization. NeuroImage. 2015;118:584-597. doi:10/f7p5zx

9. Kainz B, Steinberger M, Wein W, et al. Fast volume reconstruction from motion corrupted stacks of 2D slices. IEEE Transactions on Medical Imaging. 2015;34(9):1901-1913. doi:10/f3svr5

10. Gholipour A, Rollins CK, Velasco-Annis C, et al. A normative spatiotemporal MRI atlas of the fetal brain for automatic segmentation and analysis of early brain growth. Sci Rep. 2017;7(1):476. doi:10/gf39sn

11. Hagmann CF, De Vita E, Bainbridge A, et al. T2 at MR imaging is an objective quantitative measure of cerebral white matter signal intensity abnormality in preterm infants at term-equivalent age. Radiology. 2009;252(1):209-217. doi:10/bqkd9r

12. Blazejewska AI, Seshamani S, McKown SK, et al. 3D in utero quantification of T2* relaxation times in human fetal brain tissues for age optimized structural and functional MRI. Magn Reson Med. 2017;78(3):909-916. doi:10/gf2n9z

13. Vasylechko S, Malamateniou C, Nunes RG, et al. T2* relaxometry of fetal brain at 1.5 Tesla using a motion tolerant method. Magnetic Resonance in Medicine. 2015;73(5):1795-1802. doi:10/gf2pbh

14. Nossin-Manor R, Card D, Morris D, et al. Quantitative MRI in the very preterm brain: Assessing tissue organization and myelination using magnetization transfer, diffusion tensor and T1 imaging. Neuroimage. 2013;64:505-516. doi:10/f4jgtg

15. Yarnykh VL, Prihod'ko IY, Savelov AA, Korostyshevskaya AM. Quantitative assessment of normal fetal brain myelination using fast macromolecular proton fraction mapping. American Journal of Neuroradiology. 2018;39(7):1341-1348. doi:10/gdv9nf

16. Weigel M. Extended phase graphs: Dephasing, RF pulses, and echoes - pure and simple. Journal of Magnetic Resonance Imaging. 2015;41(2):266-295. doi:10/gghctd

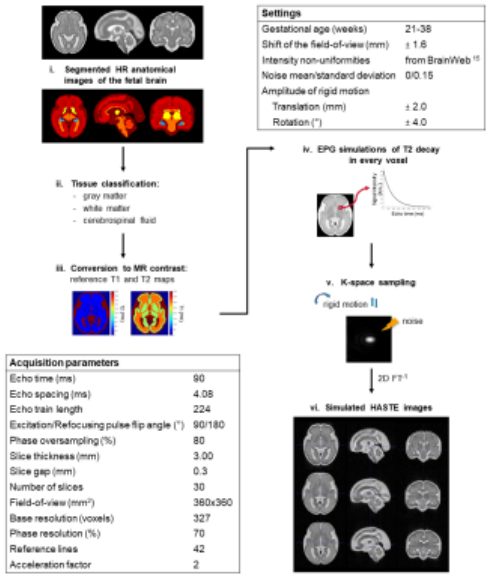
17. BrainWeb: Simulated brain database. https://brainweb.bic.mni.mcgill.ca/brainweb/

18. Oubel E, Koob M, Studholme C, Dietemann J-L, Rousseau F. Reconstruction of scattered data in fetal diffusion MRI. Medical image analysis. 2012;16(1):28-37. doi:10/fhbqtj

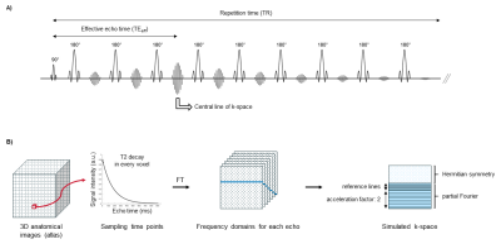
19. Tourbier S, Bresson X, Hagmann P, Meuli R, Bach Cuadra M. Sebastientourbier/Mialsuperresolutiontoolkit: MIAL Super-Resolution Toolkit v1.0. Zenodo; 2019. doi:10.5281/zenodo.2598448

20. Wang Z, Bovik A, Sheikh H, Simoncelli E. Image quality assessment: From error visibility to structural similarity. IEEE Transactions on Image Processing. 2004;13:600-612. doi:10/c7sr27

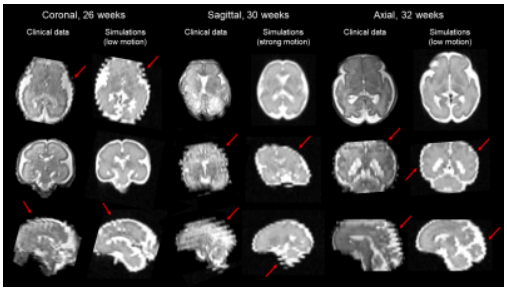
Figures



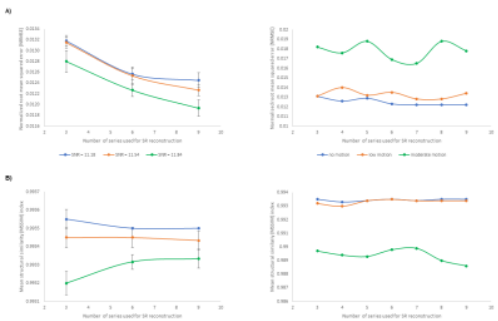
Simulation pipeline of HASTE acquisitions from segmented high-resolution anatomical images of the fetal brain. This framework offers a great flexibility in the choice of the sequence parameters but also other settings such as the age of the fetus, the SNR of the acquisitions, and the amplitude of fetal motion.



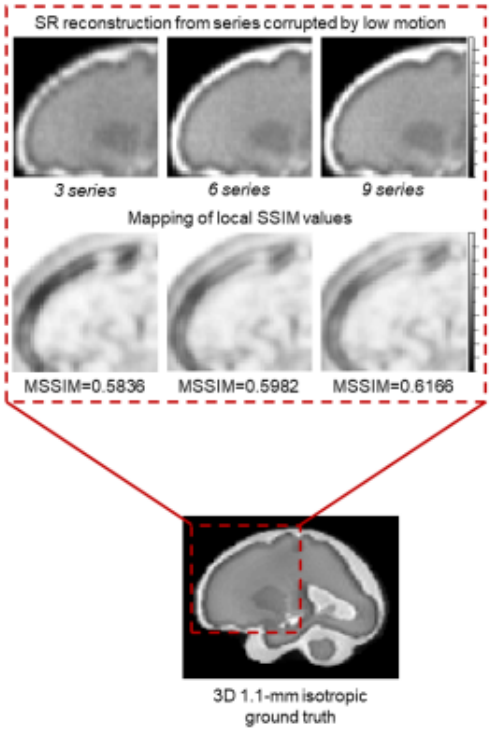
A) Pulse diagram of the HASTE sequence. B) K-space sampling of simulated HASTE images from the decay of the transverse magnetization in every voxel of the anatomical images. For each echo, at most one line from the Fourier domain of the corresponding image is used to fill k-space of the simulated HASTE acquisition, with the central line corresponding to the effective echo time (TE_{eff}). Hermitian symmetry is used to fill the unsampled part of k-space.



Visual inspection and comparison between simulated HASTE images and clinical acquisitions at three different gestational ages (26, 30 and 32 weeks). Various levels of fetal movement can be observed. Arrows point out typical out-of-plane motion patterns.



A) NRMSE and B) MSSIM between SR reconstructions from various numbers of static low-resolution series simulated with different SNR (11.54 leading to similar appearance as in clinical acquisitions) (left), respectively SR reconstructions from various numbers of low-resolution series with different amplitudes of movement (right), and a simulated static 3D 1.1-mm isotropic HASTE ground truth.



Appreciation of sharpness and tissue contrast enhancement in SR reconstructions from higher numbers of simulated orthogonal low-resolution HASTE images corrupted by low motion in comparison with a 3D high-resolution HASTE ground truth. The frontal cortex looks smoother and the putamen area sharper in the SR reconstruction from 9 series compared to the SR reconstruction from 3 series. The mapping of local SSIM values and the computation of the MSSIM over the corresponding region-of-interest support these observations.