Automated ROI Extraction of Placental and Fetal Regions for 30 minutes of EPI BOLD Acquisition with Different Maternal Oxygenation Episodes

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Purpose: Blood-oxygen-level-dependent (BOLD) magnetic resonance imaging (MRI) with oxygen exposure is a non-invasive technique used to directly estimate changes in oxygenation in specific organs. Changes in the BOLD-MRI signal during hyperoxia in the placenta and fetal organs have been previously shown [1,2]. In these studies, regions of interest (ROIs) were chosen manually in each time frame to mitigate fetal and maternal movements. In this work, we propose a registration pipeline to automate ROI extraction in placenta and fetal body. Different registration pipelines have been evaluated, using manual ROI delineation as gold standard.

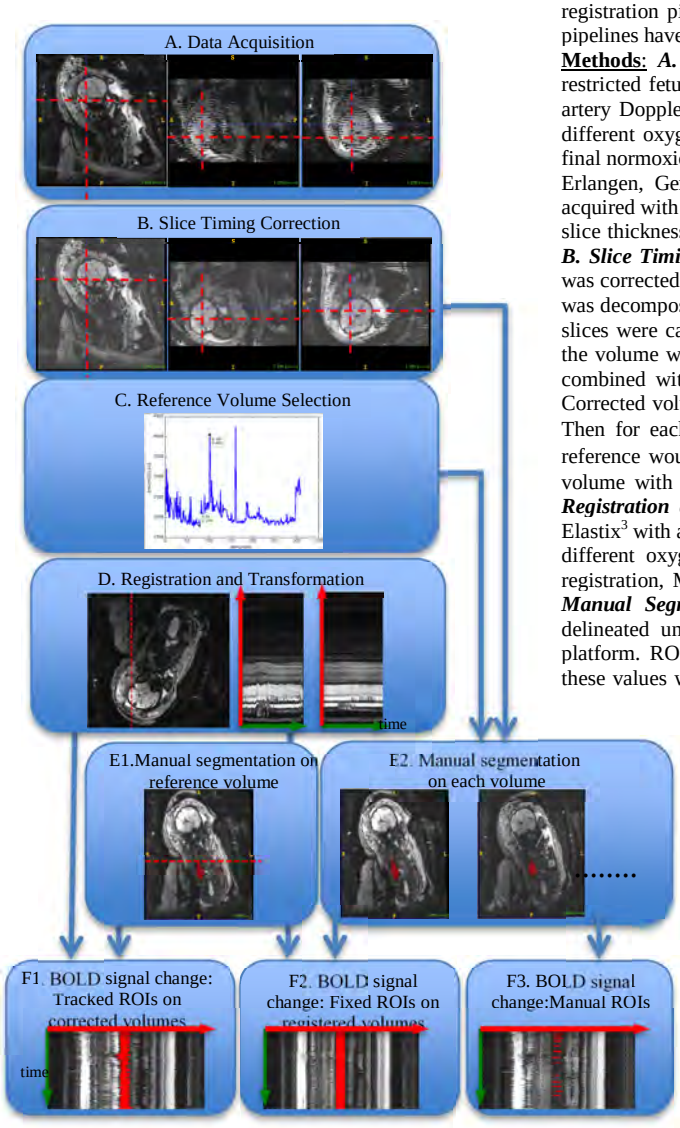

Figure 1: Different BOLD signal intensity change measurement workflows

Methods: ***A. Data Acquisition*:** In this IRB approved study, 32 week gestational age growth restricted fetus with estimated weight at 8th percentile and diminished diastolic flow on umbilical artery Doppler was scanned. The study was designed as three consecutive 10 minute episodes of different oxygen supply: initial normoxic episode (21% O2), hyperoxic episode (15 l/min), and a final normoxic episode. The experiment was performed on a 3T Skyra scanner (Siemens Healthcare, Erlangen, Germany) using an 18-channel body and 12-channel spine receive arrays. Data was acquired with single shot gradient echo EPI: TR 5820 ms, TE 32 ms, FA 90°, 70 slices (interleaved), slice thickness 3 mm matrix 110x110, FOV 330x330mm. A total of 308 3D frames were acquired. ***B. Slice Timing Correction:*** Since 3D frames were acquired with interleaved slices, each volume was corrected before estimating the motion correction of the whole 4D sequence. First, each volume was decomposed into two different volumes with even and odd slices, in these two volumes missing slices were calculated by linear interpolation. The volume with odd components was registered to the volume with even components. After the registration, odd slices in the registered volume were combined with the previous even slices to create the corrected volume. ***C. Reference Volume:*** Corrected volumes were compared one-to-one by computing their mean squared difference (MSD). Then for each volume, ΣMSD has been calculated. In order to demonstrate how the choice of reference would affect the registration, one volume with the lowest ΣMSD (volume 79), and one volume with the highest ΣMSD (volume 102) were chosen from the first normoxic episode. ***D. Registration and Transformation:*** All volumes were registered to the reference volumes using Elastix[3] with a B-spline transformation. As the local tissue signal intensity changes along time due to different oxygenation episodes, mutual information[4] was used as similarity metric. Before the registration, MRI bias correction (N4 ITK MRI bias correction) was applied to each volume. ***E. Manual Segmentation:*** Regions of interest in the placenta and fetal organs were manually delineated under the supervision of an experienced radiologist using the ITK-SNAP software platform. ROIs were manually segmented in fifteen volumes throughout the time sequence, and these values were used as gold standard. ***F. BOLD Signal Change:*** To obtain the accurate BOLD signal curves, four methods were compared, with and without image registration. a) No registration: ROIs in reference volume 79 were used in the whole unregistered sequence. b) Registration: For each reference volume (79 and 102) ROIs were segmented and applied to the whole registered sequence; c) ROI tracking: Manually delineated ROIs on reference volume 79 where warped to every volume using the transformation obtained by registration. Mean BOLD intensity curves of the ROI were extracted with MATLAB (The MathWorks Inc, Natick,MA, USA). **Results:** ¨Figure 1 shows our workflow with the intermediate results for slice timing correction (B), registration (D) and manual segmentation (E). The result of registration (reference volume 79) is demonstrated with the time profile at the location indicated by a red dash line (Figure 1D). The map of ROI is demonstrated with the time profile at the location indicated by a red dash line (Figure 1E1) for each pipeline (F). Figure 2 shows the normalized BOLD signal intensity change calculated in the placental and the fetal liver ROIs. Signal intensity measurements on a fixed ROI without registration and registration to the volume with highest ΣMSD (volume 102) show lowest registration performance for both organs compared to manual segmentation. For both placenta and liver, it is shown that the best approach is ROI tracking. However, the results of the registration to the volume with least ΣMSD are also comparable with ROI tracking. **Conclusion and Discussion**: In this study, non-rigid registration was applied to the whole uterus and promising results were obtained for BOLD signal intensity analysis both in placenta and the fetal organs. On the other hand, this approach can create undesired features in different tissue types with different rigidity or stiffness such as bones. For more specific analysis in the fetal organs, the presented registration algorithm could be improved by adding a regularization or penalty term to the registration, or by applying tissue-dependent filtering of the deformation field[5]. Note that, this study is an on-going study and more clinical cases are being collected.

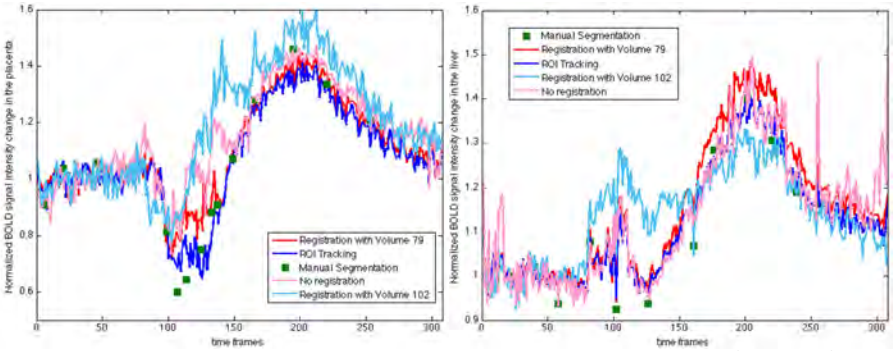

Figure 2: Normalized BOLD signal intensity changes calculated in the placental (left) and the fetal liver regions (right)

References: **1**. Sørensen, Anne, et al., Prenatal diagnosis 33.2 (2013): 141-145. **2**. Sørensen, A., et al. Ultrasound in Obstetrics & Gynecology 42.3 (2013): 310-314. **3**. Klein, Stefan, et al. Medical Imaging, IEEE Transactions on 29.1 (2010): 196-205 **4**. K. K. Wong, et al., J. Magn. Reson. Imag., vol. 27, pp. 529–537, 2008. **5**. Staring, Marinus, PhD thesis, Utrecht University, The Netherlands, 2008. **Acknowledgements:** We would like to thank Dr. Clare Tempany, Dr. Arvind Palanisamy and Dr. Carmen Carreira. This project is supported by the Comunidad de Madrid, the Madrid MIT M+Vision Consortium and NIH R01 EB017337.