Published in final edited form as:

Proc SPIE Int Soc Opt Eng. 2017 March ; 10137: . doi:10.1117/12.2254610.

Semi-automatic segmentation of the placenta into fetal and maternal compartments using intravoxel incoherent motion MRI

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Abstract

Intravoxel incoherent motion (IVIM) magnetic resonance imaging is an emerging non-invasive technique that has been recently applied to quantify in vivo global placental perfusion. We propose a robust semi-automated method for segmenting the placenta into fetal and maternal compartments from IVIM data, using a multi-label image segmentation algorithm called '*GrowCut*'. Placental IVIM data were acquired on a 1.5T scanner from 16 healthy pregnant women between 21-37 gestational weeks. The voxel-wise perfusion fraction was then estimated after non-rigid image registration. The seed regions of the fetal and maternal compartments were determined using structural T2-weighted reference images, and improved progressively through an iterative process of the GrowCut algorithm to accurately encompass fetal and maternal compartments. We demonstrated that the placental perfusion fraction decreased in both fetal ($-0.010/\text{week}$) and maternal compartments ($-0.013/\text{week}$) while their relative difference ($f_{\text{fetal}} - f_{\text{maternal}}$) gradually increased with advancing gestational age ($+0.003/\text{week}$, $p=0.065$). Our preliminary results show that the proposed method was effective in distinguishing placental compartments using IVIM.

Keywords

DWI; IVIM; placenta; segmentation; GrowCut

1. INTRODUCTION

The placenta is an organ of complex structure that provides nutrients and gases to the fetus during pregnancy. The perfusion of maternal blood in the human placenta, so called *placental perfusion*, has a crucial role for the effective delivery of nutrients and gases to the fetus¹. Any impedance to blood flow through the placenta compromises placental perfusion, and ultimately compromises the provision of necessary nutrients to the growing fetus². Therefore, placental perfusion may be used as an early biomarker of placental dysfunction associated with fetal growth restriction (FGR).

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Diffusion-weighted imaging (DWI) is a promising tool that has recently been explored as a non-invasive quantitative method to quantify placental perfusion during pregnancy without the need for exogenous contrast agents. Specifically, intravoxel incoherent motion (IVIM) analysis has been recently applied to measure placental perfusion^{3–6}. The fraction of moving blood in the total volume of the placenta, called the *perfusion fraction*, can be estimated using IVIM under the assumption that the DWI signal is associated with both water diffusion in tissues and blood diffusion inside capillaries.

Previous studies suggest that the perfusion fraction is heterogeneous throughout the placenta. Moore *et al.* segmented the placenta into two zones: the inner zone (chorionic plate or fetal side) and the outer zone (decidual plate or maternal side)³. They reported an abnormal spatial pattern of the perfusion fraction in FGR. Specifically, placentas from normal pregnancies had a larger perfusion fraction in the outer zone than in the inner zone while placentas in FGR had a smaller perfusion fraction in the outer zone. Although the results were interesting, the placenta was empirically segmented in their study such that the estimation of averaged perfusion fraction in each compartment could have been affected by the investigator/rater subjectivity. Indeed, the intervillous space of the placenta is hard to be separated into fetal and maternal sides with diffusion-weighted imaging given that the placenta is comprised of complex and hierarchical villous branches⁷.

There is a paucity of tools which are available to automatically distinguish placental compartments. The purpose of this study was to develop a semi-automatic method for segmenting the placenta into fetal and maternal compartments from IVIM images, using a multi-label image segmentation algorithm called ‘*GrowCut*’, to allow for the objective comparison of perfusion properties between individual compartments.

2. METHODS

2.1 Image acquisition and preprocessing

DWI data were acquired from sixteen healthy pregnant women between 21–37 weeks of gestation (mean: 29±6). Imaging of the whole uterus from the axial plane of the mother was obtained using a single shot spin echo (SE) echo planar imaging (EPI) sequence with pulsed gradients corresponding to 9 optimally spaced b values {0,25,50,114,243,500,543,800,900} sec/mm² on a 1.5T GE MR scanner. The scanning parameters were as follows: repetition time (TR) 8000 ms, echo time (TE) 53.8 ms, data matrix 96×96, field of view (FOV) 420×420 mm², 40–50 slices with 4 mm thickness and no inter-slice gap. Single shot fast spin echo (SSFE) T2-weighted images were also acquired with the following parameters: TR 1200 ms, TE 160 ms, FOV 420×420 mm², data matrix 256×192, 40–50 slices with 4 mm thickness and no inter-slice gap, along with a chemical fat saturation pulse.

The mask of the whole placenta was manually created by delineating the region of interest (ROI) and ITK-SNAP⁸. After correcting the inhomogeneity of magnetic field, inter-volume motion correction was performed using three-dimensional non-rigid image registration based on free form deformation in Elastix^{9–11}. The 3D interpolation process localized inside the placental mask also enabled the removal of spurious signal loss between slices inside the placental ROI, attributed to instantaneous subject motion.

2.2 Parameter estimation

The IVIM intensity was modeled with the following equation based on the assumption that DWI signals are attributed not only to extra-cellular diffusion but also intra-cellular blood perfusion^{4,12}:

$$S(b) = S_0 \left[(1 - f) \times e^{-bD} + f \times e^{-bD^*} \right]$$

The diffusion coefficient (D) describes the degree of diffusion of water molecules within tissues (in mm²/sec) while the pseudo-diffusion coefficient (D*) is associated with perfusion of blood moving in a large scale. The perfusion fraction (f) represents the fraction of moving blood within the total volume of a voxel, and S₀ describes the signal intensity at zero b-value. Three parameters (D, D*, f) were estimated voxel-wise from a motion-corrected DWI sequence using the Levenberg-Marquardt nonlinear least squares method¹³.

2.3 Placental segmentation

Initial regions of fetal and maternal compartments were manually delineated on the volume of DWI data acquired at b=25 sec/mm² by a clinician-scientist (N.A.) with expertise in placental imaging and anatomy. Using the T2 anatomical image as a reference, the initial fetal compartment was defined as the placental area immediately adjacent to the umbilical cord insertion site on the volume acquired at b=25 sec/mm², and bounded by areas of diffusing signal intensity within the placenta¹⁴, and the remainder of the placenta was given as the initial maternal compartment. A total of 30% of the voxels were randomly sampled from both initial fetal and maternal regions, and exploited as seed voxels from which the regions were iteratively improved using the GrowCut method¹⁵. Based on the cellular automaton model, the state of each voxel was represented with the label L, strength W, and feature vector F given as gradient-free signal intensities S₀. Each voxel was assigned to one of three label types such as 'unlabeled', 'fetal', and 'maternal'. The seed voxels had initially the strength of 0.3 while others had zero strength. Through iterative competition of each voxel with neighborhood, the label of each seed voxel was 'conquered' by a neighbor voxel with higher strength, in other words, changed into that of the neighbor. The state transition was also limited by another rule that the voxel state becomes less vulnerable to the neighborhood as its S₀ intensity is more heterogeneous compared to its neighborhood. Synthetically, the label L and strength W of a seed voxel were transformed into the label L_n and strength g*W_n of neighbor if

$$g(|F - F_n|) \times W_n > W$$

where F_n and W_n are the label and strength of neighbor, and g(·) is a monotonously decreasing function bounded to [0,1],

$$g(|F - F_n|) = 1 - \frac{|F - F_n|}{\max_i |F - F_i|}$$

This cell evolution rule is depicted in Figure 1. Finally, each seed region grew or shrank to encompass either the fetal or maternal compartment until the transitions of voxel state converged. All the above method was implemented using MATLAB and significantly accelerated by embedding C codes compiled as mex files.

3. RESULTS

The overall semi-automatic process for placental segmentation using GrowCut is illustrated in Figure 2; the initial fetal compartment was roughly defined based on the T2 reference image (Fig 2B) and automatically improved using the GrowCut algorithm (Fig 2C). Figure 3 shows that the proposed method was effective in eliminating non-placental structures/tissues from the seed mask. After GrowCut-based placental segmentation, the fetal and maternal compartments occupied $31.5 \pm 7.0\%$ and $68.2 \pm 7.0\%$ of the placenta, respectively.

Figure 4 illustrates the maps of diffusion coefficients and perfusion fraction, which shows how both voxel-wise parameters are distributed over the placenta. The perfusion fraction was estimated to be 0.58 ± 0.11 in the fetal compartment, and 0.56 ± 0.13 in the maternal compartment ($p=0.12$ [paired t-test with two tails]). As reported previously⁴, the perfusion fraction (f) decreased in both fetal ($-0.010/\text{week}$, $R^2=0.27$, $p=0.04$) and maternal compartments ($-0.013/\text{week}$, $R^2=0.31$, $p=0.02$) as gestational age (GA) increased (see Figure 5). The relative difference in perfusion fraction between fetal and maternal compartments ($f=f_{\text{fetal}}-f_{\text{maternal}}$) trended increasing over GA ($+0.003/\text{week}$, $R^2=0.22$, $p=0.06$) as shown in Figure 5. When controlling for GA, the perfusion fraction in the fetal compartment tended to be lower compared to the maternal compartment in $\text{GA} < 30$ weeks (f_{fetal} vs. f_{maternal} : $0.637 \pm 0.106 < 0.645 \pm 0.130$, $p=0.58$) but did not reach statistical significance. However, the perfusion fraction in the fetal compartment was significantly larger than that of maternal compartment in $\text{GA} \geq 30$ weeks ($0.528 \pm 0.096 > 0.500 \pm 0.101$, $p=0.01$).

4. DISCUSSION AND CONCLUSION

We propose a novel semi-automatic method for separating fetal and maternal compartments using in vivo placental IVIM data. The placental segmentation was semi-automatically accomplished; initial seed regions were manually defined based on placental anatomy, and precisely refined using the GrowCut algorithm. Although the results need to be validated on a larger dataset, our preliminary results show that the proposed method is a promising tool to objectively and non-invasively study functional and structural differences in perfusion between fetal and maternal compartments of the placenta in vivo.

Some technical limitations deserve to be mentioned. First, the quality of the segmentation was still affected by how well the initial seed regions of the fetal and maternal compartments were defined. To avoid this problem, a fully-automated method of placental segmentation would need to be developed, which is currently underway. Second, the placental segmentation based on S_0 values is controversial. The S_0 value was exploited as a feature vector of each voxel in the process of GrowCut algorithm, assuming that the feature vector would be considerably distinct between fetal and maternal compartments. However, there is

no physiological evidence supporting that the S_0 value is the best approach to distinguish the fetal and maternal compartments. A variety of attributes of the DWI signals as well as the S_0 value may be jointly considered to create a multi-dimensional feature vector, which may improve the quality of the segmentation.

To the best of our knowledge, the proposed method is the first application of image segmentation techniques to identify fetal and maternal compartments using in vivo placenta DWI data. The proposed semi-automated process for placental segmentation lays an important technical foundation for novel in vivo assessment of placental function, and may provide important, currently unavailable insights into the origins and progression of placental dysfunction in the compromised pregnancy. Ongoing technical improvements are needed in order to validate the accuracy of the image segmentation. The ability for this novel technique to distinguish placental dysfunction in high-risk pregnancies awaits further study.

ACKNOWLEDGMENTS

This neuroimaging research was supported by NHLBI R01 (HL116585-01, C. Limperopoulos) Antecedents of Impaired Brain Development in Fetuses with Heart Disease and Award Numbers UL1TR000075 and KL2TR000076 from the NIH National Center for Advancing Translational Sciences. We thank the research coordinators, the patients and their families.

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Figure 1.

Evolution of cell states through the GrowCut algorithm. The state (L, W, F) of the middle cell was changed into (L_n, gW_n, F_n) by the neighbor with state (L_n, W_n, F_n) according to the evolution rule.

Figure 2.

The semi-automatic process of placental segmentation using GrowCut. (A) T2-weighted image, (B) the initial seed region of the fetal compartment segmented on the T2-weighted image, and (C) finalized fetal compartment after the iterative process of the GrowCut algorithm.

Figure 3.

An example showing the effects of GrowCut on removing non-placental tissues from segmentation. The initial seed region was segmented with included non-placental tissues (B). The non-placental tissues were eliminated from the segmented fetal compartment after running GrowCut (C).

Figure 4.

An example of the (A) diffusion coefficient and corresponding (B) perfusion fraction maps which were estimated voxel-wise. Yellow and blue colors correspond to high and low magnitudes of either the diffusion coefficient or perfusion fraction.

Figure 5.

The change in perfusion fraction over gestational age (A) and the relative difference (Δf) in perfusion fraction between fetal and maternal compartments (B).