Quantitative morphometry analysis of the fetal brain using clinical MR imaging

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Motivation: In vivo fetal magnetic resonance imaging provides a unique approach for the study of early human brain development [1]. In utero cerebral morphometry could potentially be used as a marker of the cerebral maturation and help to distinguish between normal and abnormal development in ambiguous situations. However, this quantitative approach is a major challenge because of the movement of the fetus inside the amniotic cavity, the poor spatial resolution provided by very fast MRI sequences and the partial volume effect. Extensive efforts are made to deal with the reconstruction of high-resolution 3D fetal volumes based on several acquisitions with lower resolution [2,3,4]. Frameworks were developed for the segmentation of specific regions of the fetal brain such as posterior fossa, brainstem or germinal matrix [5,6], or for the entire brain tissue [7,8], applying the Expectation-Maximization Markov Random Field (EM-MRF) framework. However, many of these previous works focused on the young fetus (i.e. before 24 weeks) and use anatomical atlas priors to segment the different tissue or regions. As most of the gyral development takes place after the 24th week, a comprehensive and clinically meaningful study of the fetal brain should not dismiss the third trimester of gestation. To cope with the rapidly changing appearance of the developing brain, some authors proposed a dynamic atlas [8]. To our opinion, this approach however faces a risk of circularity: each brain will be analyzed / deformed using the template of its biological age, potentially biasing the effective developmental delay. Here, we expand our previous work [9] to propose post-processing pipeline without prior that allow a comprehensive set of morphometric measurement devoted to clinical application. **Data set & Methods:** Prenatal MR imaging was performed with a 1-T system (GE Medical Systems, Milwaukee) using single shot fast spin echo (ssFSE) sequences (TR 7000 ms, TE 180 ms, FOV 40 x 40 cm, slice thickness 5.4mm, in plane spatial resolution 1.09mm). For each fetus, 6 axial volumes shifted by 1 mm were acquired under mother's sedation (about 1min per volume). First, each volume is segmented semi-automatically using region-growing algorithms to extract fetal brain from surrounding maternal tissues. Inhomogeneity intensity correction [10] and linear intensity normalization are then performed. Brain tissues (CSF, GM and WM) are then segmented based on the low-resolution volumes as presented in [9]. A high-resolution image with isotropic voxel size of 1.09 mm is created as proposed in [2] and using B-splines for the scattered data interpolation [11]. Basal ganglia segmentation is performed using a levet set implementation on the high-resolution volume [12]. The resulting white matter image is then binarized and given as an input in FreeSurfer software (http://surfer.nmr.mgh.harvard.edu) to provide topologically accurate three-dimensional reconstructions of the fetal brain according to the local intensity gradient. **Results:** Fig. 1 depicts an example of the tissue segmentation. An example of 3D cortical surface reconstruction is shown in Fig. 2. All cortical surfaces are carefully checked overlaid on their corresponding high-resolution images by experienced raters using the same principles as generally accepted in adult imaging studies; manual corrections are performed when needed. In Table 1, we show a variety of measurements for 3 fetuses aged from 29 to 31.5 weeks. An acceptable degree of variance is observed between the different volumes found for each low-resolution volumes of the same fetus. The overall results show an increase of the white and gray matter volumes with age, while CSF volume seems to show a different trajectory. The cortical surface analysis shows an increase in the total cortical area with age. Using the global Gyrification Index, measured as the ratio between the total cortical surface and the surface of an outer hull, we do not evidence any consistent direction of changes with age. When measuring the curvature of the cortical surface, the average mean curvature is not drastically modified while we observe an increase in the percentage of cortical surface showing positive curvature values. **Discussion:** We hereby demonstrate the feasibility of quantitative studies of the fetal brain during the third trimester of gestation based on clinically acquired images. As our reconstruction's and segmentation's pipeline do not use any prior, our method can potentially answer clinically relevant question such as the true *developmental age* of the fetus without being biased by its *biological age*.

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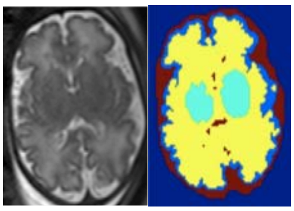

Fig. 1. Tissue classification

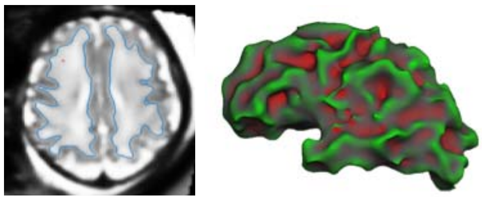

Fig. 2. Surface extraction

	WM		Basal		Cortical GM		CSF		ICV		Cortical Area	Global GI	Mean curvature	% Positive curvature
GA (SA)	Mean	Var	Mean	Var	Mean	Var	Mean	Var	Mean	Var				
29	873,681	8,184 (9%)	6,021	538 (9%)	65,645	2541 (4%)	43,635	3484 (8%)	203,540	6423 (3%)	21,116	1.16	-0.0883	26.94%
29.4	129,477	4,870 (4%)	8,068	1138 (14%)	61,418	5871 (10%)	76,882	2132 (3%)	270,701	2112 (1%)	25,411	1.12	-0.0966	26.45%
31.5	157,192	12,130 (8%)	12,428	2634 (21%)	68,790	13,972 (20%)	54,670	3152 (6%)	294,431	2879 (1%)	32,679	1.19	-0.0864	33.61%