Diffeomorphic Construction of a Normative Spatiotemporal Fetal Brain MRI Template

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Purpose

The recent advances in volumetric fetal brain MRI [1,2] hold out the potential for the analysis of early brain growth through the development of digital MRI atlases of the fetal brain. Probabilistic spatiotemporal atlases of the fetal brain have been recently developed through manual or automatic segmentation of fetal brain tissue and pairwise registration utilizing affine or regular grid of control points non-rigid transformation models [3,4].While probabilistic templates encode the anatomic variability in the probability maps, deformable templates encode the anatomic variability in deformation fields, therefore deformable templates are expected to effectively capture the anatomic variations through deformable registration. Large deformations that are required to capture the significant anatomic variability between subjects at different gestation age and maturation levels are usually not elements of a vector space; instead they belong to the high-dimensional group of diffeomorphisms [5]. It is therefore crucial to develop a diffeomorphic spatiotemporal template construction method for fetal brain MRI. Therefore, as compared to the recent work that has focused on probabilistic atlas construction, our purpose is to develop a diffeormorphic deformable spatiotemporal template for the fetal brain.

Methods

We build our method over the elegant large diffeomorphic deformable mapping approach formulated in [5,6]. Our method integrates kernel regression in time (age) [7] with symmetric spatial normalization based on viscous fluid model [6]. Given a collection of M images $I_i(x)$:$\mathrm{R}^3\rightarrow\mathrm{R}$ acquired at the corresponding ages t_i from individuals in the population, the problem is formulated as finding a set of transformations h_i: $\mathrm{R}^3\rightarrow\mathrm{R}^3$ and a template $I(x,t)$:$\mathrm{R}^4\rightarrow\mathrm{R}$ that is a weighted minimum distance representation of the population anatomy at any age t. The problem is formulated as:

$$(1)\qquad (\hat{h}_i,\hat{I}(t)) = \arg\min_{h_i,I} \frac{1}{\sum_{i=1}^{M} K(t-t_i)} \sum_{i=1}^{M} K(t-t_i)[(I_i\circ h_i - I(t))^2 + \|Lv_i\|^2], \quad \textit{where} \quad (2)\ \frac{d}{ds}h_i(x,s) = v_i(h_i(x,s),s)\ ;\ s\in[0,1]$$

where $K(.)$ is the Gaussian kernel; Equation (1) involves two terms that minimize the difference in image intensities and the Sobolev norm of velocity fields v_i; and Equation (2) shows the Lagrangian ODEs that define the model of deformation flow with the simulated time variable s. To solve this optimization problem we use a numerical approach [6]. The algorithm starts with an initial estimation of I by weighted averaging of rigidly registered images I_i. Symmetric normalization is performed between I and every I_i in each iteration and the average deformation is computed by kernel-weighted average of deformation fields. The algorithm typically converges in 7-10 iterations. The ANTS software tool [6] was used for implementation.

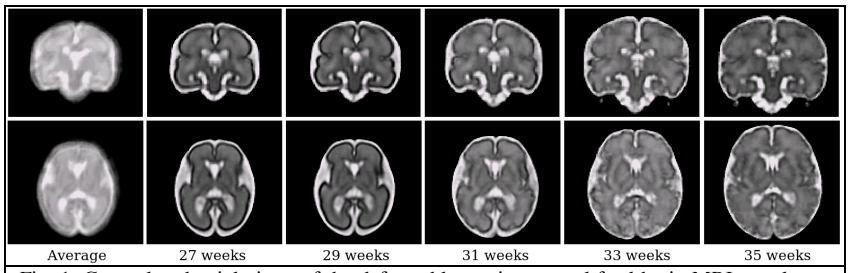

Fig. 1: Coronal and axial views of the deformable spatiotemporal fetal brain MRI template at five gestation ages (27, 29, 31, 33, and 35 weeks) which shows sharp representation of the anatomy as compared to simple averaging of the MR images of all 40 subjects (on left).

Data

Fetal MRI was obtained for 40 healthy fetuses from 26.14 to 35.86 weeks GA (30.50±3.05). The criteria for choosing healthy fetuses in this study involved excluding pregnant women with multiple gestations, congenital infection, or any maternal contraindication to MRI, and excluding fetuses with brain dysgenesis or other systemic anomalies by ultrasound, as well as those with chromosomal abnormalities by amniocentesis. Imaging was performed on a 1.5T Philips scanner and a 32-channel phased-array cardiac coil. Multi-planar single-shot turbo spin echo MRI was performed with TE/TR of 120 ms/12500 ms, 0.625 signal averages, 2-mm slice thickness and no inter-slice gap. No maternal sedation was used.

Results

Volumetric brain MRI was reconstructed for all fetuses with isotropic resolution of 1mm in 3D using motion-corrected super-resolution volume reconstruction [2]. The images were preprocessed with intensity non-uniformity correction and were rigidly registered. The processed images were then used for spatiotemporal template construction. Fig. 1 shows coronal and axial slices of the spatiotemporal template at five gestation ages. As compared to the average of images on the left the template shows sharp anatomic boundaries at any age. Fig. 2 shows the growth trajectory of the intracranial volume (in milliliter) based on the individual data (asterisks), a linear fit (dashed line; ICV=25GA-478, R^2=0.92), and the spatiotemporal template (solid line). Red dots show the confidence interval of the linear fit. The template closely follows the growth pattern. Fig. 3 shows 3D visualization of the segmented cortex, white matter, brainstem, and the cerebellum on the spatiotemporal template.

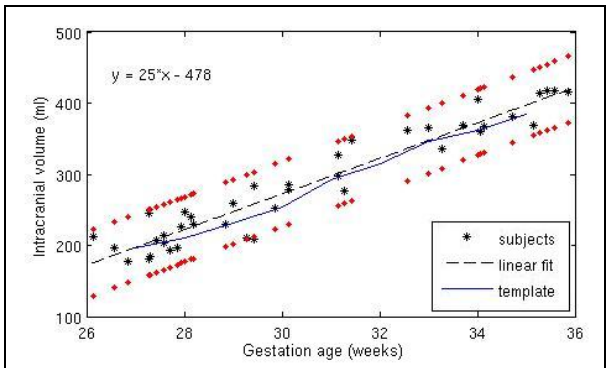

Fig. 2: Intracranial volume of subjects (black asterisks); and the estimated values through linear growth model (dashed line), and the values obtained from the spatiotemporal template (solid line).

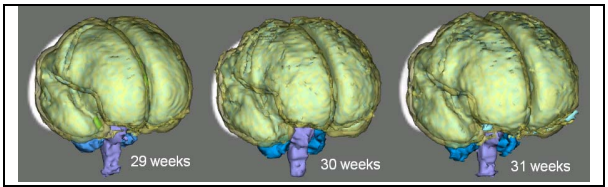

Fig. 2: Marching cubes surface model rendering of the segmented cortex, white matter, brainstem, and cerebellum on the template.

Discussion

The developed deformable spatiotemporal MRI template can be used as a reference for registration, segmentation, shape analysis, and the analysis of cortical folding in normal vs. abnormal brains based on in-vivo fetal MRI.

References

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