Registration of 3D Fetal Brain US and MRI

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Abstract. We propose a novel method for registration of 3D fetal brain ultrasound and a reconstructed magnetic resonance fetal brain volumes. The reconstructed MR volume is first segmented using a probabilistic atlas and an ultrasound-like image volume is simulated from the segmentation of the MR image. This ultrasound-like image volume is then affinely aligned with real ultrasound volumes of 27 fetal brains using a robust block-matching approach which can deal with intensity artefacts and missing features in ultrasound images. We show that this approach results in good overlap of four small structures. The average of the co-aligned US images shows good correlation with anatomy of the fetal brain as seen in the MR reconstruction.

Keywords: Fetal 3D ultrasound, ultrasound and MR registration, fetal ultrasound template, block matching.

1 Introduction

Fetal ultrasound (US) is the imaging modality of choice for assessing fetal development in clinical practice. Recently, fetal brain magnetic resonance imaging (MRI) has become an important modality for assessing fetal brain development thanks to development of fast-spin-echo sequences for acquisition of 2D slices which can deal with unpredictable and fast fetal motion. Emerging volumetric fetal brain MRI reconstruction and segmentation techniques can now support quantitative studies of fetal brain development [1]. Recent advances in US technology allow 3D acquisitions of the fetal brain which can potentially facilitate volumetric assessment of fetal brain. US, compared to MRI, has a well demonstrated safety, a lower cost and causes less stress to the patients. Models of fetal brain anatomy constructed from fetal brain MRI can facilitate development of image analysis methods for fetal 3D ultrasound and their validation.

In this we paper we propose a method for 3D alignment of fetal brain MRI to US, which is one of the important tools with potential to facilitate automatic image analysis of 3D brain fetal US. Registration of brain MRI and US was

previously proposed for image guided neurosurgery in adults to non-rigidly correct for brain-shift during surgery [2] as well as for rigid alignment of adult or neonatal brain [3]. The major challenge in aligning MR and US images is that there does not exist a simple intensity mapping between the two modalities, as they visualize complementary features. While MRI offers good contrast between soft tissues, especially white matter (WM), grey matter (GM) and cerebro-spinal fluid (CSF), US depicts surfaces of the structures with superior spatial resolution compared to MRI, while the WM-GM boundary does not appear in US at all. Roche et al. [3] suggested to estimate a non-linear relationship between MR and US image intensities and used a generalized correlation ratio as a similarity measure. Arbel et al. [2] proposed to perform segmentation of the brain MRI followed by simulation of an US-like image which is then registered with the US image using local normalized cross-correlation (NCC) as a similarity measure. As the relationship of MR and US intensities in fetal brain is difficult to describe, we propose to simulate US-like image from the segmented MRI, similar to [2]. Features of fetal brain visible in 3D US in relation to the anatomy have been described in the clinical literature [4]. We can therefore build on this knowledge and convert a segmentation of the anatomical structures in fetal brain MRI to into features which appear in fetal US (Sec. 2). US images are corrupted by intensity artefacts, such as shadows and attenuation. Compared to cranial sonography in adults and neonates, where radiographer can position the probe next to the opening in the skull, such artefacts are significantly more pronounced in US of the fetal head, due to difficulties with positioning of the probe and interference with maternal tissues. Additionally, partly calcified and not completely fused fetal skull causes uneven loss of signal strength. Wein et.al. [5] suggested to estimate the attenuation from knowledge of physical properties of the scanned organ, however, these are not well described for fetal head and brain. Therefore in this paper we propose to apply a robust block-matching strategy [6] with local CC as a similarity measure (Sec. 3) to overcome the limitations of a global similarity measure [3] and gradient descent optimisation [2] in presence of significant intensity artefacts in fetal brain US. The method has been applied to align 27 3D US images at gestational ages (GA) 18 to 22 weeks with an MRI of a single subject of GA 23 weeks (Sec. 4). In spite of a relatively significant GA difference between subjects we achieved good volume overlaps for four small structures. The estimated transformations were used to coalign the US images with the MRI template. The average of the coaligned US images depicts the near-complete anatomy of the fetal brain as visible in 3D US.

2 Construction of US-Like Template Image from MRI

2.1 Reconstruction of Fetal Brain MRI

We constructed the US-like template from MRI of a single fetus. As US depicts structures of small scale compared to spatial resolution of MRI (e.g. septi pellicidi), it was essential to perform a high quality reconstruction of the MRI. To achieve this, the fetal brain volume was reconstructed from stacks of thin

Fig. 1. Overview of the segmentation of the MR template and conversion into US-like image

slices (2.5mm) using a super-resolution approach [7]. High signal to noise ratio was achieved by carefully choosing the point-spread-function (PSF) to match the real acquisition. The PSF was approximated by a 3D Gaussian with full width at half maximum (FWHM) equal to slice thickness in through-plane direction to approximate the slice selection profile (truncated sinc function) and $1.2\times$ resolution for in-plane direction to approximate the sinc function. The reconstructed volume is presented in Fig. 3a.

2.2 Segmentation of Brain Structures in MRI

The reconstructed MR volume of a single fetus with GA 23 weeks was segmented and converted to the US-like image, see overview in Fig. 1. First, we performed an automatic segmentation using the EM algorithm [8] into six brain structures - WM, cortex, CSF, deep grey matter (DGM), brainstem and cerebellum. As there are no fetal probabilistic atlases publicly available at present, we used a spatio-temporal neonatal probabilistic atlas [9]. The youngest time-point in this atlas is 29 weeks GA. The difference in shape and cortical folding for these GA requires a flexible non-rigid registration and for this we used non-rigid B-spline registration with final control point spacing 2.5mm and normalized mutual information. We found that registration of a blurry probabilistic template with such resolution is unstable, but subject-to-subject registration across such age-range produces good results for the kind of structures we are interested in. We therefore first segmented the brain MR volume of another fetus with GA 28 weeks. This image was then registered with the MR template (23 weeks GA). The segmentation of the older fetus was then used as a prior during EM segmentation of the younger. The cortex prior was slightly blurred before segmentation to account for cortical folding of the older subject. Though the cortex-WM separation still had some errors this was not an issue as their boundary is not visible in US and these two tissues were joined together. At this gestation, the cerebellum does not appear as one homogeneous structure in US, but high fluid content of cerebellar hemispheres gives it appearance of two dark cysts surrounded by bright tissue [10], see Fig. 3. The cerebellar cysts were therefore manually excluded from the automatic segmentation of the cerebellum.

2.3 Segmentation of Non-brain Structures in MRI

Some of the most echogenic landmarks in fetal US depict the non-brain structures, especially the skull, choroid plexus, septi pellucidi and membrane of the falx in brain midline (see Fig. 3). We therefore performed semi-automatic or manual segmentation of these four structures in the MR template.

Segmentation of the skull in MRI is a difficult task as it appears dark and often borders other tissues also appearing dark on T2w MRI. Additionally, the fetal skull is rather thin compared to the resolution during acquisition, making it difficult to delineate due to the partial volume effect. The skull was therefore estimated from the brain mask created by joining automatic segmentations of five brain tissues and CSF. A distance transform from this brain mask was calculated, and it was visually determined that the voxels with distance up to 2mm can be labeled as the skull. The segmentation of the skull was then manually corrected.

In fetal brain US, the brain tissue (with exception of the corpus callosum) is clearly divided into a right and left hemisphere. This however is only partially visible in MRI due to insufficient resolution and partial volume effects along the midline. We therefore artificially separated the WM segmentation into two parts (by removing the voxels closer than 1.5mm to the WM surface) and calculated distance transforms from these two WM cores. All the brain structures (except for WM) were separated into right or left by removing voxels with the roughly same distance from the two WM cores (the midline voxels). The midline was then added as another structure to simulate the falx visible on fetal brain US. Additional two structures which are significant landmarks on fetal brain US - choroid plexus and septum pellucidum - were segmented manually.

The segmentation pipeline described here included manual steps, however this template will be used for inter-subject registration and therefore does not need to be repeatedly segmented. Additionally, it can be used for atlas-based segmentation of MRI of new subjects.

2.4 Converting the Segmentation into US-Like Image

US B-mode images are created by reflections of tissue surfaces with difference in acoustic impedance and speckle patterns produced by interference of tissue microstructure with the sound waves. These intensity patterns are further affected by intensity attenuation (or signal loss along the beam direction) and shadows, which occur when beam is fully reflected by a strong reflector. In this work we assume that the fetal brain US is mainly composed of echogenicity of the tissues and neglect the reflections at the tissue boundaries and intensity artefacts. The visibility of brain surface is also due to a presence of a highly echogenic thin tissue layer [4] not visible in MRI. We therefore convert the segmentation to artefact-free US-like image in which each region of interest is assigned uniform intensity representing the average echogenicity of this region. We did not include a model of speckle in the US-like image, as it is not useful for guiding inter-subject alignment. The US-like image is then registered with real US images using a method robust to the artefacts and missing features (Sec. 3).

The segmented anatomical structures were assigned a visually determined intensity value in order from brightest to darkest: 1. skull, 2. choroid plexus, septi pellucidi and midline, 3. brain surface, 4. cerebellum, 5. DGM and brainstem, 6. cerebral hemispheres. As we use local NCC as similarity measure, the exact value of tissue intensity is not important, but the correctness of the order of brightness is essential. The US-like image is shown in Fig. 2c.

3 Alignment of MRI and US

The block-matching algorithm [6] iteratively estimates the alignment T between two images by alternating between two stages. In the first stage, for each block in the source image b_S^i , the most similar (homologous) block b_T^j is found in the corresponding exploration neighborhood (determined by the latest estimate of the transformation T) in the target image. We use NCC to find the most similar blocks, as the construction of US-like image from MRI effectively changes our registration problem from multi-modal to mono-modal. NCC is calculated independently for each pair of blocks, ensuring low sensitivity to intensity artefacts. The centroids of the pairs of the homologous blocks define a displacement field which is regularized in the second stage. All the blocks with variance smaller than a pre-defined threshold are excluded in the first stage so that only blocks carrying features are used for estimation of the transformation T , thus improving robustness towards missing features.

In the second stage, the rigid or affine transformation is estimated from the displacement field using least trimmed squared regression (LTS) [11]. The LTS estimator reduces the influence of outliers by minimizing the sum of a given number (h) of smallest squared residuals. A residual error is obtained as the difference between the displacement d_i at centroid C_S^i and the one obtained by applying the estimated transformation to it. Such robust estimation of transformation is essential to remove influence of displacements for the source blocks which have no corresponding target block due to missing features in US images.

$$T^* = \underset{T}{\operatorname{argmin}} \sum_1^h \|(C_S^i + d(i)) - T[C_S^i]\|^2$$

4 Results

The proposed registration method was applied to 27 US volumes of the fetal head, with GA 18-22 weeks. Images were acquired with a Philips HD9 or iU22 machine using a 3D transabdominal probe with mechanical steer. The images were first consistently re-oriented and scaled to a similar size using a scaling factor derived from the age of the subject. The block-matching algorithm was then used to align the US-like image derived from the MR template with each US image. We determined the rigid alignment first followed by the affine alignment. The block-matching was applied in two resolution levels (isotropic voxel size

Fig. 2. A 2D view of 3D US of three fetuses before (a) and after (b) alignment with the MR template. After alignment the view shows transventricular plane in all three cases. Compare to US-like image (c). Note that the difference in cortical folding in the area around hippocampus stems from differences in GA.

2mm and 1mm). We used blocks of $3 \times 3 \times 3$ voxels and neighbourhoods with 7 voxels in each direction. The variance threshold used to exclude blocks was $0.04 \times$ intensity range. The LTS transformation was estimated using 75% of the displacements. Figs. 2a,b show US images before and after alignment with the US-like image (Fig. 2c).

In each of the 27 ultrasound images, four small structures - choroid plexus (CP), cavum septi pellucidi (CSP), posterior ventricular cavity (VC) and cerebellar hemisphere (CH) - were manually delineated by a clinical expert. All these structures were also delineated in the MR template. The average volume (Dice) overlaps for these four structures are presented in Table 1 (fourth row). We achieved average volume overlaps around 0.5 which we consider very good, as the residual differences in brain shape between subjects and ages are still expected to be significant after global affine alignment. In all cases, all four structures were overlapping after alignment and therefore none of the registrations failed. To further illustrate the quality of alignment, Fig. 3c presents the average of all 27 US volumes aligned using the inverse of the estimated transformations.

To demonstrate that converting MRI to US-like image is essential we compared our proposed method with two recognized approaches which can perform multimodal registration of original MRI with US images: 1. Registration using normalized mutual information using IRTK¹; 2. Block-matching method using correlation ratio (CR). In the second method the similarity measure had to be changed compared to our proposed approach because NCC is not suitable for multimodal registration and CR is a suitable multimodal similarity measure to be used in conjunction with block-matching [6]. CR can be implemented as a statistical measure or the functional relationship between intensities of the target and source image can be defined by a parametric model. Due to the small size of the blocks in our approach we consider affine relationship of the intensities a reasonable assumption. In this case CR is equivalent to squared NCC. In the first multimodal approach the average volume overlaps were much smaller

¹ <http://www.doc.ic.ac.uk/~dr/software/>

Table 1. Average volume overlaps and their standard deviations after registration of the source image (second column) to US images. The last column shows number of failed cases.

Registration	Similarity	Source	CP	VC	CH	CSP	failed
Gradient descent	NMI	MRI	0.18 ± 0.24	0.12 ± 0.20	0.12 ± 0.16	0.13 ± 0.16	14
block-matching	CR	MRI	0.47 ± 0.15	0.41 ± 0.18	0.48 ± 0.16	0.37 ± 0.15	0
block-matching	CR	US-like	0.56 ± 0.12	0.39 ± 0.15	0.54 ± 0.13	0.40 ± 0.10	0
block-matching	NCC	US-like	0.57 ± 0.10	0.42 ± 0.14	0.56 ± 0.09	0.43 ± 0.10	0

Fig. 3. Axial, coronal and sagittal view of (a) brain MRI of a single fetus used as a template; (b) brain 3D US of a single fetus after alignment with MR template; (c) average of the 27 fetal brain 3D US aligned with the MR template. Highlighted structures: Choroid plexus (CP), septi pellucidi (SP), falx (mid), deep grey matter (DGM), cerebellum (cer), posterior ventricular cavity (vent), skull.

and in a number of the cases the registration failed on the criterion that at least three out of four segmented structures have non-zero overlap (see Table 1, first row). In the multimodal block-matching approach none of the registrations failed but average overlaps were significantly smaller (see Table 1, second row). This demonstrates that US-like image offers better correspondences with US images than original MRI. The third experiments demonstrates, that the more constrained NCC yields better performance for the block-matching of the US-like image with real US images than the less constrained CR (see Table 1, third row).

5 Discussion and Conclusion

In this paper we have presented a novel method for affine registration of fetal brain MR and US volumes. The method succeeded in all 27 cases and we achieved good volume overlaps for four small structures. The average of the co-aligned US volumes revealed near-complete anatomy of the fetal brain. The results suggest that 3D US in conjunction with MR prior has potential for development of new medical image analysis tools for assessment fetal brain development.

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