DOMAIN GENERALIZATION IN FETAL BRAIN MRI SEGMENTATION WITH MULTI-RECONSTRUCTION AUGMENTATION

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ABSTRACT
Quantitative analysis of in utero human brain development is crucial for abnormal characterization. Magnetic resonance imaging (MRI) segmentation is therefore an asset for quantitative analysis. However, the development of automated segmentation methods is hampered by the scarce availability of fetal brain MRI annotated datasets and the limited variability within these cohorts. In this context, we propose to leverage the power of fetal brain MRI super-resolution (SR) reconstruction methods to generate multiple reconstructions of a single subject with different parameters, thus as an efficient tuning-free data augmentation strategy. Overall, the latter significantly improves the generalization of segmentation methods over SR pipelines.

Index Terms— Magnetic resonance imaging (MRI), Super-resolution (SR) reconstruction, Automated fetal brain tissue segmentation, Data augmentation, Domain adaptation

1. INTRODUCTION

Human brain undergoes most significant changes in utero. During the prenatal period, disruption of maturation processes may lead to abnormal development resulting in severe conditions such as congenital diseases, developmental delay or cognitive impairment later in life [1, 2]. Magnetic resonance imaging (MRI) is a complementary imaging modality for prenatal diagnosis as it has proven its clinical value for the assessment of intracranial structures [3, 4, 5]. Structural T2-weighted (T2w) MRI offers a good soft-tissue contrast to monitor the fetal brain growth and tissue maturation. Being very sensitive to the stochastic fetal motion, fast 2D acquisition schemes are used in order to minimize intra-slice motion [6]. The downside effect of such acquisition stands in the strong anisotropy of the resulting low-resolution (LR) images with remaining inter-slice motion.

In the last decades, super-resolution (SR) algorithms have offered the possibility to reconstruct a single high-resolution (HR) motion-free isotropic volume from a set of LR orthogonal acquisitions [7, 8, 9]. Such SR reconstruction methods leverage the redundancy in LR images to estimate inter-slice inter-series motion. Subsequently, a HR image is restored by solving an inverse problem in which a regularization function is considered with varying weight. As previously discussed in [10], different reconstruction translates into a substantial variation in the reconstructed image appearance (Fig. 2).

Although SR-reconstructed volumes allow the analysis of 3D imaging biomarkers [11, 12], yet morphometric and volumetric measures remain restricted as they strongly rely on the MR image tissue segmentation. Manual annotations are time-consuming and prone to inter-rater reliability, hence, automatic segmentation methods are a key asset for further quantitative analysis [13, 14]. However, automatic fetal brain MRI segmentation remains challenging as it is subject to many domain shifts, amongst which the SR pipeline. Indeed, the many different intensity-based operations and regularization performed during SR reconstruction induce an inter-SR method data distribution shift that is for the segmentation method to overcome.

Recent works [10, 15] evidence the need for domain adaptation strategies to fit the SR domain gap in fetal brain MRI segmentation. While [10] uses noisy registration-based labelling between same-subject different-SR method volumes, [15] takes advantage of synthetic fetal brain MRI to increase the training sample size in the SR target domain. More generally, domain-adaptation strategies for MRI segmentation have been proposed [16, 17]. Nevertheless, such methods are all data-driven, hence adjustment to the target task requires optimization efforts. Moreover, while these methods specifically aim to integrate non-linear intensity changes, these are not specifically addressing the real SR domain shift.

In this paper, we propose for the first time to exploit in-SR domain multi-reconstruction, i.e. reconstructions of the same brain obtained with different regularization weight, as an intensity-based data augmentation for intracranial tissue segmentation of fetal brain MRI. In that manner, we hypothesize that the intensity variability of the training samples of a segmentation model is increased, without increasing the need for manual annotation. We will show also the domain generalization power of our original multi-reconstruction approach on a pure out-of-SR domain dataset.
2. MATERIALS

2.1. Clinical MR exams
Forty (40) clinical fetal brain MR exams from 21 to 35 weeks of gestational age (GA) (mean ± standard deviation (SD): 28.4±4.2) were retrospectively collected from our institution. Acquisitions were either performed at 1.5T (N = 37) or 3T (N = 3), respectively resulting to 1.125mm and 0.5469mm in-plane isotropic, and 3.3mm and 3mm through-plane resolution.

2.2. In-SR domain dataset – CHUV-set
All clinical exams (Section 2.1) were SR-reconstructed into subject’s space with the MIALSRTK pipeline (default regularization weight, i.e. \( \lambda = 0.75 \)) [9]. Volumes were aligned into a common reference space and resampled to 1.1 \( \times \) 1.1 \( \times \) 1.1mm\(^3\). Following the FeTA annotation guidelines [13], the extra-axial cerebrospinal fluid spaces (CSF), the cortical gray matter (cGM), the white matter (WM), the ventricular system, the cerebellum, the deep gray matter (dGM) and the brainstem were manually annotated.

2.3. Out-of-SR domain pure testing set – FeTA-KCL
Forty (40) clinical fetal brain images from the FeTA dataset are used as out-of-domain pure testing set [13, 18]. Subjects were aged from 21.2 to 34.8 weeks of GA (27.1 ± 3.9). They were reconstructed with SIMPLE-IRTK\(^1\) [7, 13]. SR volumes were resampled to an isotropic resolution of 0.8mm. Tissue annotations of the CSF, the cGM, the WM, the ventricles, the cerebellum, the dGM and the brainstem were manually refined and completed with the additional corpus callosum (CC) label [18]. For the remainder of this study, CC and WM tissue classes are merged in order to match the tissue distribution available in CHUV-set (see Section 2.2).

\(^1\)Simplified version of the Image Registration Toolkit, Ixico Ltd. licence

3. METHODOLOGY

Our experiment design is shown in Fig. 1 including datasets (A and B), the methods development (C) and their assessment (D). We propose a single-pipeline multi-reconstruction approach as data augmentation for fetal brain MRI segmentation. To strengthen the generalization of our findings, we assess our multi-reconstruction approach with two different SR pipelines, namely NiftyMIC [8] and MIALSRTK [9]. First, we assess our single-pipeline multi-reconstruction method in a pure data augmentation set up (Task (a)). Second, we further evaluate our augmentation approach in an out-of-domain experiment (Task (b)).

3.1. SR reconstruction-based data augmentation
SR reconstructions. All clinical MR exams presented in Section 2.1 are reconstructed through two different SR pipelines, such that we have the following two new independent HR Multi-SR datasets:

Multi-MIALSRTK Subjects are reconstructed through the MIALSRTK [9] pipeline with the following regularization weights \( \lambda \in \{0.1, 0.75, 1.5, 3.0\} \);

Multi-NiftyMIC Subjects are reconstructed through the NiftyMIC [8] pipeline with the regularization weights \( \alpha \in \{0.01, 0.02, 0.05, 0.1\} \).

Fig. 2 shows a representative patch of a 32 weeks of GA fetal brain multi-reconstructed through MIALSRTK and NiftyMIC SR pipelines. High \( \lambda \) (respectively low \( \alpha \)) offers a better tissue contrast, although the overall image appears more noisy. Conversely, low \( \lambda \) (respectively high \( \alpha \)) increase the overall smoothness of the image. Thus, variations of the regularization weight echo texture changes in the SR-reconstructed images.

Weak labelling. All reconstructed brains of Multi-MIALSRTK and Multi-NiftyMIC have a tissue labelmap in the space of their CHUV-set reconstruction. Through a rigid registration-based approach, manual annotations are propagated to the
newly generated Multi-SR sets.

Training configurations. We define three configurations based on their training data (Table 1, Fig. 1(C)). Baseline is trained on the 30 training subjects from CHUV-set, and MIALSRTK-augmented, respectively NiftyMIC-augmented, is trained on the 120 Multi-MIALSRTK, respectively Multi-NiftyMIC, reconstructed volumes of the same 30 fetal brains.

Table 1: Summary of training configurations.

| Training set | Baseline | MIALSRTK-augmented | NiftyMIC-augmented |
|--------------|----------|---------------------|--------------------|
| # subjects   | CHUV-set | 30                  | 30                 |
|              | Multi-MIALSRTK | 120                | 120                |
| # volumes    | Manual   | Weak                | Weak               |
|              | 30       | 120                 | 120                |

3.2. Evaluation

We compare our multi-reconstruction approach in:

(a) Data augmentation task. In this in-domain experiment, we compare the performances of Baseline and MIALSRTK-augmented on the 10 left-out subjects from CHUV-set.

(b) Domain generalization task. We evaluate the performances of Baseline, MIALSRTK-augmented and NiftyMIC-augmented on the 40 out-of-domain FeTA-KCL images.

The performances of SR-augmented and Baseline are evaluated with the Dice similarity coefficient (DSC) [19] and the average symmetric surface distance (ASSD) [20] between the ground truth (GT) manual annotations and the predicted segmentation. A paired Wilcoxon rank-sum test is performed between SR-augmented configurations and Baseline. p-values are adjusted for multiple comparisons using Bonferroni correction in the statistical analysis of individual fetal brain tissues. Statistical significance level is set to $p < 0.05$.

3.3. Model and training strategy

From the MONAI framework [21], we use the popular 3D U-Net architecture that performed remarkably on fetal brain MRI tissue segmentation in the 2021 MICCAI FeTA challenge [14]. Spatial (flipping, rotation, resampling) and intensity-based (bias field, gaussian noise) transformations are randomly applied. Lastly, image patch intensities are normalized. We adopt a 5-folds cross-validation (CV). Networks are trained for 100 epochs minimizing a dice focal loss function, where both terms equally contribute. All configurations adopt the same training strategy.

At test-time, we proceed to an ensemble evaluation of all 5 CV networks predictions on 50% overlapping patches selected through a sliding window approach.

4. RESULTS

4.1. Data augmentation

Table 2 (a) reports the DSC and ASSD performances for both tasks. Overall, the performance of the segmentation algorithm is significantly enhanced when each fetal brain is multi-reconstructed through the same pipeline as the target (testing) images, even though the weak labelling process incurred. The benefit of MIALSRTK-augmented is further statistically significant for all tissue classes.

4.2. Domain generalization

SR-augmented qualitatively enhances the segmentation accuracy compared to Baseline, especially in the infratentorial structures, i.e. the brainstem, the cerebellum and the $4^{th}$ ventricle (Fig. 3, circles). Additionally, the WM tract of the CC are better captured with our multi-reconstruction approach, and even more than compared to the GT (Fig. 3, arrows).

Quantitative results (Table 2 (b)) show, from 10 in-domain subjects to 40 out-of-domain subjects, a performance loss of both Baseline and MIALSRTK-augmented configurations. Nevertheless, while Baseline shows a loss of 0.07 and 0.94, respectively in DSC and ASSD MIALSRTK-augmented only drops of 0.04 and 0.58. Our multi-reconstruction approach hence seems more robust to the inter-SR method domain shift. Regardless of the SR method of the training data, our multi-reconstruction augmentation strategy significantly improves the segmentation performance on out-of-SR domain images, both in DSC and ASSD. On a tissue-wise analysis, SR-augmented configurations are always significantly better performing than Baseline. The benefit of our multi-reconstruction approach is even more pronounced in the small structures such as the ventricles, the cerebellum, the dGM and the brainstem where the gain in DSC is greater.
Table 2: DSC and ASSD (mean ± SD) of the different training configurations in data augmentation (a) and domain generalization (b) tasks. The best scores between SR-augmented configurations and Baseline are shown in bold. Arrows indicates whether the metric is better maximized (↑) or minimized (↓). The corresponding p-values (paired Wilcoxon rank sum test) are adjusted for multiple comparisons using Bonferroni correction. Statistical significance (*) is p < 0.05.

|                | DSC (↑) | ASSD (↓) |
|----------------|---------|----------|
| **(a) Data augmentation** |         |          |
| Baseline       | 0.84 ± 0.02 | 0.70 ± 0.07 |
| MIALSRTK-augmented | 0.87 ± 0.01(*) | 0.56 ± 0.05(*) |
| NiftyMIC-augmented | 0.84 ± 0.02 | 1.03 ± 0.80(*) |
| **(b) Domain generalization** |         |          |
| Baseline       | 0.84 ± 0.02 | 0.70 ± 0.07 |
| MIALSRTK-augmented | 0.87 ± 0.01(*) | 0.56 ± 0.05(*) |
| NiftyMIC-augmented | 0.87 ± 0.01(*) | 1.03 ± 0.80(*) |

Fig. 3: Sagittal view of a 27.8 weeks-old (top) and coronal view of the 33.1 weeks-old (bottom) fetal brain tissue segmentation obtained in the different configurations studied. White arrows and circles show representative areas where our multi-reconstruction approach improves the segmentation accuracy.

Fig. 4: Mean DSC (plain) and ASSD (dashed) performance in the domain generalization task as a function of GA in weeks. The steepest improvement appears in the cerebellum (0.67 for the Baseline vs. 0.79 and 0.86 for MIALSRTK- and NiftyMIC-augmented). From a GA-based analysis (Fig. 4), we observe that Baseline overall performs worse on young and old (< 25 and > 30 weeks of GA) fetuses. On the contrary, although a similar trend is noticeable for SR-augmented methods, it is substantially less pronounced. Consequently, in this inter-domain segmentation task, SR-augmented configurations seem to better benefit the endpoint of the GA range studied.

5. CONCLUSION

We have demonstrated that having single-pipeline multi-reconstruction of fetal brain MR exams (i) is an efficient intensity-based data augmentation strategy and (ii) reduces the performance drop in target image domain shift in segmentation task. Our multi-reconstruction approach, combined to conventional data augmentation strategies, increases the representation of fetal brain MRI variability in the training phase of supervised segmentation method. Although we did not investigate multi-pipeline multi-reconstruction augmentation, one can expect an even stronger benefit of our method. In its batch processing approach, our multi-reconstruction strategy is an out-of-the-box easy to adapt method. Future work will investigate this multi-reconstruction augmentation at inference in order to increase the prediction robustness.
6. COMPLIANCE WITH ETHICAL STANDARDS

The local ethics committee of the Canton of Vaud, Switzerland (CER-VD 2021-00124) approved the retrospective collection and analysis of MRI data and the prospective studies for the collection and analysis of the MRI data in presence of a signed form of either general or specific consent.

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