Outlier Rejection for Adaptive Neonatal Segmentation

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Introduction: Preterm birth (below 32 weeks gestation) is associated with significant cognitive and neuromotor impairments, the frequency and severity of which increase with decreasing gestational age [1]. Much research has been focused on the development of biomarkers of neurological injury in an attempt to identify babies at increased risk of adverse neurodevelopmental outcomes. Fundamental to performing volumetric and morphometric studies is the ability to classify different brain tissues. In contrast with adults, neonatal brain MRI is complex to segment due to lack of contrast, partial volume (PV) effect, the existence of hypo- and hyper-intensities, substantial natural and pathological anatomical variability and the characteristic reversal of white/grey matter intensities in both T1 and T2 MRI. Recent developments in neonatal brain segmentation have used template atlases [2] to mitigate the low SNR and CNR of the image, which is problematic in pathological cases, as their anatomy may be markedly different from the one derived from a normal population atlas. Furthermore, the presence of white matter (WM) and grey matter (GM) hypo- and hyper-intensities introduces intensity outliers that lead to an overestimation of the segmentation model parameters. We propose a new segmentation pipeline incorporating a novel *Maximum a Posteriori* Expectation-Maximization (MAP-EM) based probabilistic segmentation technique that includes intensity non-uniformity (INU) correction, spatial dependence via a Markov Random Field (MRF), a robust outlier rejection technique that ignores unexpected intensity clusters and an *a priori* relaxation scheme that enables the adaptation of normal population priors to pathological cases.

Methods: The segmentation model used here can be summarized by $\hat{\Phi}_y = \arg\max_{\Phi} f(y \mid \Phi_y) g(\Phi_y) + \lambda$, where $f(y \mid \Phi_y)$ is the data term, $g(\Phi_y)$ is the *a priori* term over the model parameters and λ is the term that enables the outlier rejection component as described in [3]. The first term (data driven term) can be described as a combination of a multivariate normal distribution, a spatial smoothness term and an atlas term. The multivariate normal distribution is characterized by mean and covariance matrix per class, corrected by a INU component, modeled as a linear combination of smoothly varying basis functions [4]. The spatial smoothness term is introduced as Markov Random Field (MRF) which assumes that the probability that a voxel belongs to a certain tissue type depends on its first-order neighbors [4]. The atlas term is an modeled as a sample from a population atlas by assuming a Dirichlet distribution [5]. The second term (*a priori* term) of the segmentation model enforces an *a priori* knowledge over the parameter distribution, thus constraining the space of solutions to a predefined space and providing increased robustness in the case of strong INU, large amount of WM and GM hypo- and hyper-intensities or large anatomical variability. Finally, the third term (outlier rejection component), similar to the one presented in [3], is introduced into the model. This enables the rejection of intensity clusters that have a large Mahalanobis distance from the estimated model (model outliers), thus reducing their influence in the parameter estimation. A skull stripping process is also needed in order to locate the region of interest for the segmentation algorithm. This is done using a label fusion technique similar to the one presented in [6] but based on a locally normalized cross correlation ranked STAPLE algorithm [7]. This technique was used because most brain extraction algorithms developed for adults fail due to both intensity contrast reversal and pathologic abnormalities. Assuming skull stripped images, we model the problem with 6 classes, each one with a corresponding digital atlas prior probability for white matter (WM), cortical grey matter (cGM), deep grey matter (dGM), cerebrospinal fluid (CSF), pons (Pon) and cerebellum (Cer) respectively at every voxel position[8].

Results: The data was acquired on a 1.5T Siemens's Avanto using TR=17*ms*, TE=6*ms* and flip angle of 21°. In total 43 T1-weighted volumes were analyzed with resolution 0.39x0.39x1*mm*. The mean gestational age is 27.1±2.7 weeks (range 23.1-32.3), mean birth-weight 970±373g (range 540-2470g) and mean age at scan 40.4±1.74 (range 35.7-44.3). The male to female ratio is 22/21.
Qualitative analysis: An expert visually inspected all 43 images. In all cases where the datasets passed quality control checks with regards to signal-to-noise ratio and imaging artifacts, the segmentation showed high accuracy, suitable for further volumetric analysis. Quantitative analysis In order to assess the quality of the segmentation, and due to low inter-rater reliability in other structures, the proposed segmentation was compared to manually segmented ventricles. Two subsets were chosen from the full database: one containing 15 neonates with normal anatomy and another containing 4 patients with noticeable anatomical differences (2 cases with ventriculomegaly and 2 with excessive sub-arachnoid CSF). For each dataset, a Dice score was calculated between the proposed method and the manual segmentation. The proposed algorithm was also compared to the Maximum Likelihood Expectation Maximization (ML-EM) algorithm [9]. On the subset containing the 15 normal subjects, the proposed method obtains a Dice score of 0.905±0.033 when compared to 0.725±0.217 for the ML-EM, representing a statistically significant improvement ($p<0.01$) in the accuracy of the segmentation. On the second subset, the Dice scores for the proposed method are 0.93, 0.87, 0.93 and 0.94, and respectively 0.22, 0.15, 0.35, and 0.55 for the ML-EM method, showing a marked improvement in the accuracy of the segmentation in pathological cases. Note that the improvement is due to both the non-adaptive nature of the ML-EM algorithm and the bias introduced by model outliers.

Conclusion: We have presented a segmentation algorithm tailored specifically for neonatal T1 segmentation, using a MAP-EM algorithm with a new prior relaxation strategy combined with a semi-conjugate prior over the intensities and an outlier rejection term to reduce the bias introduced by WM and GM abnormalities. Experiments performed on a clinical cohort also show significant improvements in segmentation accuracy, mainly in pathological cases, when compared to a ML-EM algorithm.

[1] Marlow *et al.,* NEJM 2005; [2] Weisenfeld *et al.*, NeuroImage 2009; [3] Van Leemput *et al.*, TMI 2003; [4] Cardoso *et al.*, Neuroimage 2011; [5] Cardoso *et al.*, MICCAI 2011 [6] Leung *et al.*, Neuroimage 2010; [7] Cardoso *et al.*, MICCAI-MALSF 2011; [8] Kuklisova-Murgasova *et al.,* Neuroimage 2011; [9] Van Leemput *et al.*, TMI 1999

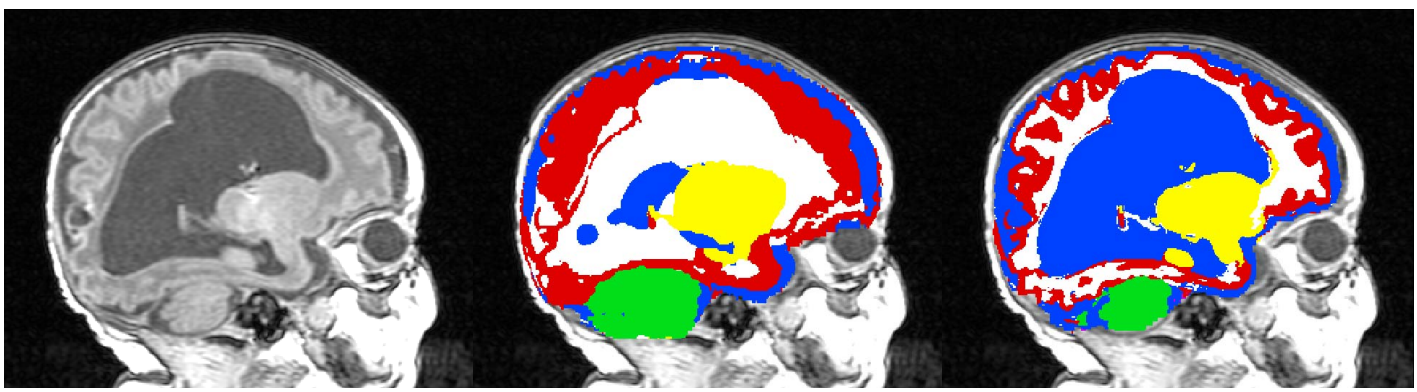

Figure 1 – Example segmentation of a patient with ventriculomegaly. From left to right: T1 image, ML-EM segmentation [9], proposed MAP-EM segmentation. Colours: WM=White, cGM=Red , CSF=Blue, dGM=Yellow, Cerebelum=Green