NeoBrainS12 Challenge: Adaptive neonatal MRI brain segmentation with myelinated white matter class and automated extraction of ventricles I-IV

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Abstract. The measurement of white matter structure and features of the cortical surface in the neonatal brain can help define biomarkers that predict the risk of adverse neurological outcome. The measurement of these structures relies upon accurate automated segmentation routines, but these are often confounded by neonatal-specific imaging difficulties including poor contrast, low resolution, partial volume effects and the presence of significant natural and pathological anatomical variability. In this work we develop and evaluate an adaptive multi-modal maximum a posteriori expectation-maximisation segmentation algorithm as part of the MICCAI 2012 neonatal MRI segmentation challenge.

1 Introduction

Fundamental to performing volumetric and morphometric studies of the infant brain is the ability to classify different brain tissues. In contrast to adults, the segmentation of the neonatal brain is complicated due to a combination of: low-signal-to noise ratio; increased voxel partial volume (PV) as a result of adapting the resolution to the smaller neonatal head; and the existence of both natural and pathological intensity variability.

As a result of the crucial role of segmentation, a number of authors have produced techniques specifically for neonatal MRI, primarily by adapting and enhancing well-established techniques in the adult brain [1, 2].

Here we extend and develop an adaptive segmentation pipeline specifically for preterm neonates based on [3] incorporating a *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) and implicit correction of PV containing voxels[1]. Key extensions of this algorithm are the inclusion of a myelinated white matter class and the ability to separate the ventricle system from the remainder of the cerebrospinal fluid (CSF) space.

[1] Software used in this work is available on the NiftySeg website niftyseg.sf.org

The proposed pipeline is expected to be robust because of both the inclusion of manually defined tissue priors, providing both spatial tissue class labels and priors on the model parameters, thus constraining the space of solutions of the algorithm [3]. The other model components also contribute to the overall algorithm stability: the MRF introduces spatial smoothness; the bias field correction compensates for intensity non-uniformity and the partial volume correction helps ameliorate misclassification due to the neonate specific grey/white matter intensity inversion.

2 Methods

In order to simplify the segmentation process we carry out two preprocessing steps - brain masking and construction of spatial tissue priors.

In order to extract the brain, we generate a template mask from the example manual segmentations provided as part of the challenge: the two examples for each of the 30 week and 40 week cases are registered [4] and the brain mask defined as those pixels not labelled as background[2]. A masked brain can be obtained alongside the corresponding registration of the example T2-weighted data with each case to be segmented.

To construct the tissue class priors we make further use of the registered example manual segmentations. To improve the capture range of the (registered) manual segmentation priors, the manual segmentations are smoothed with a Gaussian kernel of width 8 voxels. Eight classes are thus defined for white matter, cortical grey matter, extra-ventricular CSF, deep grey matter structures, cerebellum, brainstem, myelinated white matter and ventricular space (see Figure 1). In addition we are able to define semi-conjugate priors on the model parameters from the manual segmentation T2 weighted tissue intensities.

The segmentation protocol then proceeds using the following pipeline:

1. tissue intensity priors are registered to the individual subject using affine and non-rigid free-form deformations [4][2], the registration result is then used to define the subject-specific brain mask and the spatial priors.
2. segmentation of six major tissue classes is carried out using a MAP-EM strategy (white matter, cortical grey matter, subcortical grey matter, total CSF space, cerebellum and brainstem) using the manual segmentation priors. This algorithm includes intensity non-uniformity correction, spatial smoothness introduced via a Markov Random Field and estimation of an outlier class enabling the rejection of intensity clusters that have a large Mahalanobis distance from the estimated model, thus reducing their influence in the parameter estimation [5].
3. explicit white-matter partial volume correction is carried out and the white matter prior adjusted as in [3]. Briefly, the method downweights the prior probability of white matter (wm_{prior}) in the presence of high grey matter

[2] Registration software used in this work is publicly available at: *http://sourceforge.net/projects/niftyreg/*.

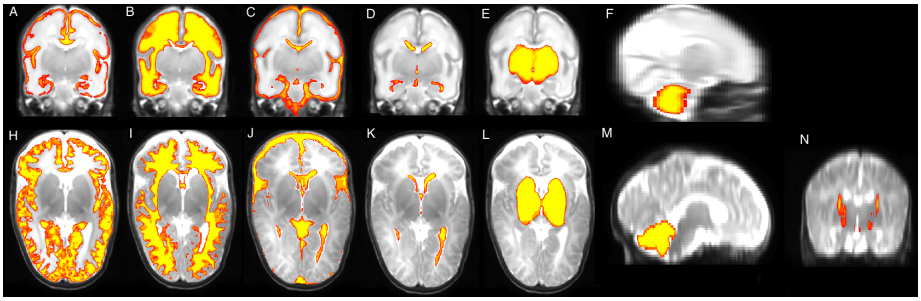

Fig. 1. Example priors for top row (A-F): 30 week and bottom row (H-N): 40 week infants for: cortical grey matter, white matter, total CSF space, ventricular space, deer grey matter structures, cerebellum and myelinated white matter (myelinated white matter class not shown for 30week prior). Brainstem prior not shown.

or CSF probability (p_{gm} and p_{csf}) estimated from the segmentation step in 2 using the update: $wm^*_{prior} = wm_{prior}(1 - \sqrt{p_{csf}p_{gm}})$.

4. segmentation of the six major classes in step 2 is repeated including the adjusted white matter prior of step 3 yielding a final probabilistic segmentation.
5. a two class segmentation of the CSF space is obtained by segmentation of the CSF space from step 4 into ventricular and extra-ventricular components using priors obtained from the manual segmentation data.
6. a second two class segmentation of the sub cortical grey matter is obtained by segmentation of the DGM space from step 4 into a grey matter and myelinated white matter component.

This pipeline generates a probabilistic segmentation from which integer class labels can be formed by taking the most likely value within each voxel. If the voxel with the highest probability from step 4 is CSF or deep grey matter, this is further separated into ventricular/extra-ventricular or deep grey matter/myelinated white matter respectively using the results of steps 5 and 6.

3 Results

Figure 1 shows example anatomical priors formed from the provided manual segmentations. The example priors are overlaid on the anatomical template image used to guide the registration of the priors to the subject specific space. The 30 week priors in the top row of Figure 1 and the corresponding 40 week priors on the bottom row are each formed from the two provided example manual segmentations for each type of data and thus form a limited prior representation of the population to be segmented.

Figure 2 shows example segmentations from each of the three sets for 30 week (top row) and 40 week cases (middle and bottom rows). Although in general the registration appears accurate, there remains some white matter partial volume in the CSF space (images B,I,P) which would require a more aggressive correction than that proposed here. In addition, the paucity of myelinated white matter

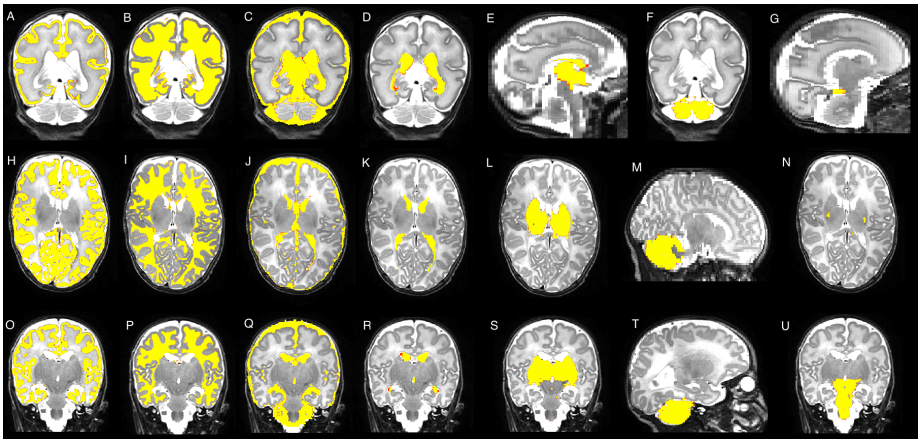

Fig. 2. Example segmentations for the first case in each dataset for top row (30 week infant (coronal)), middle row (40 week infant (axial)), bottom row (40 week infant (coronal)). Classes shown are: cortical grey matter, unmyelinated white matter, total CSF space, ventricular space, deep grey matter structures, cerebellum and myelinated white matter (**G** and **N**) or brainstem (**U**).

and difficulties associated with the definition make this class difficult to assess. Nonetheless, an estimate of the myelinating or myelinated white matter may be segmented using the tissue class priors built from the manual segmentation in Figure 1.

Results of the segmentation challenge are summarised in Table 1. Briefly the algorithm appears to perform well on the cortical grey matter, deep grey, white matter and cerebellar tissue structures, but performs poorly specifically on the myelinated white matter class. This is likely the result of the low number of voxels present in this tissue type and the absence of complementary information from the T1-weighted segmentation that was used in the manual segmentation. Ventricles, in general, are well-extracted from the ventricular space with the exception of set 3 case 3.

4 Discussion & Conclusion

This work has extended a tool for the accurate segmentation of neonatal MRI at both 30 and 40 weeks gestational age. The algorithm is fully automatic and extended beyond [3] specifically for this challenge to include additional tissue classes for the ventricular space and myelinated white matter. Algorithm runtime is about 15minutes per subject on a tired 2008 iMac including the CPU-based registration steps.

The algorithm relies explicitly on accurate tissue prior information; this has been derived from the manual segmentations provided as training data and represents and upper bound on the possible Dice scores obtained, thus the accuracy of the algorithm is limited by the extent to which the two priors represent the population to be segmented. In addition, our technique segments only the T2-

Set	Subject	CGM	DGM	UWM	MWM	BS	CB	Vent	EV-CSF	WMT	CSF
1	1	0.85	0.89	0.88	0.2	0.8	0.89	0.78	0.7	0.87	0.71
1	2	0.77	0.88	0.86	0.25	0.82	0.9	0.78	0.66	0.86	0.67
1	3	0.88	0.9	0.88	0.21	0.83	0.9	0.87	0.77	0.87	0.79
2	1	0.69	0.84	0.88	0.21	0.7	0.88	0.85	0.77	0.88	0.78
2	2	0.73	0.82	0.91	0.08	0.72	0.86	0.85	0.73	0.91	0.76
2	3	0.72	0.85	0.89	0.18	0.78	0.88	0.89	0.78	0.89	0.81
3	1	0.74	0.88	0.86	0.04	0.71	0.92	0.8	0.64	0.85	0.68
3	2	0.71	0.85	0.81	0.1	0.75	0.92	0.72	0.52	0.81	0.56
3	3	0.74	0.82	0.85	0.11	0.74	0.91	0.6	0.57	0.84	0.59

Table 1. Dice overlap results for comparison with manual segmentation for three subjects and three datasets for the proposed algorithm. Labels are as follows: CGM=cortical grey matter, DGM=basal ganglia and thalami, UWM=unmyelinated white matter, MWM=myelinated white matter, BS=brainstem, CB=cerebellum, Vent=ventricular space, EV-CSF=extra-ventricular CSF, WMT=total white matter (UWM+MWM) and CSF=total CSF space (Vent+EV-CSF).

weighted data since this was used to guide the manual segmentations which form the priors. If both T1- and T2-weighted manual segmentations are available, the information could be combined to allow a multi-model segmentation which is implicit in the MAP-EM framework. The priors must also be accurately aligned with the subject data; non-rigid registration may be required because of the diversity in head shape and pathology in this population, thus the accuracy of this step can a limiting factor, although the MAP-EM procedure is much more tolerant of misalignment than techniques relying on label propagation. Segmentation accuracy is also limited by the voxel resolution; highly anisotropic voxels result in discontinuous through-plane tissue type which can cause problems when using a MRF to enforce spatial consistency, this effect could be mitigated by the inclusion of high-resolution T1 data. The T1 data could also be used to provide improved estimation of the myelinated white matter class since T1 hyper-intensity associated with the myelination process is often highly visible.

The original algorithm in [3] was developed for the inclusion of diverse pathological cases such as ventriculomegaly and included a strategy for relaxation of the anatomical priors. This step was not included in this work since the given data was considered normal. If infants with abnormality are included, this prior relaxation strategy could be used to guide the segmentation towards the specific anatomy.

In summary we have presented a segmentation tool developed specifically for very preterm neonatal brain MRI at both 30 and 40 weeks gestation age. Accurate segmentation techniques and challenge-style studies will facilitate volumetric biomarker studies of novel neuroprotective agents.

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