Automatic Cortical Segmentation for Developing Neonates with the Correction of Mislabeled Partial Volumes (MLPVs)

H. Xue[1,2], L. Srinivasan[1], S. Jiang[1], S. J. Counsell[1], M. A. Rutherford[1], D. Edwards[3], D. Rueckert[2], and J. Hajnal[1]

[1]Robert Steiner MRI Unit Imaging Sciences Department, MRC Clinical Sciences Centre, Hammersmith Hospital, Imperial College London, London, London, United Kingdom, [2]Visual Information Processing, Department of Computing, Imperial College London, London, London, United Kingdom, [3]Department of Paediatrics, MRC Clinical Sciences Centre, Hammersmith Hospital, Imperial College London, London, London, United Kingdom

Introduction Analysis of brain structure and particularly the cortex from MR images of neonatal brains is of great interest both for developmental neurobiology and for detecting subtle neurological disorders. However, methods developed for use with images of adult brain can fail because immature tissues display different patterns of relative signal strengths and signal heterogeneity. We have identified a specific problem for cortical delineation caused by unmyelinated white matter which results in inverted gray-white matter contrast. In consequence partial voluming between gray matter and cerebrospinal fluid (CSF) can lead to signals that mimic white matter resulting in **mislabeled partial volumes (MLPVs).** We have developed a fully automatic algorithm to detect and successfully eliminate MLPVs for improved cortical segmentation and have tested this on 25 newborn infants with the gestational ages (GA) at scan ranging from ~27 to 45 weeks.

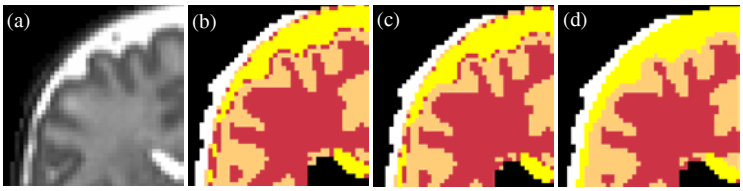

Fig. 1. An illustration of the EM scheme with the MLPV removal. (a) A neonatal T2w image; (b) Partial volume voxels on the csf-gray matter and csf-non-brain boundaries are incorrectly classified by the original EM method; (c) The segmentation results after the 4-th iteration of three-step EM method with MLPV suppression (d) The final results after 14 iterations (CSF = yellow, WM = red, GM = beige, non-brain = white)

Mislabeled Partial Volumes For new-born neonates, non-myelinated white matter (WM) has higher signal intensity than gray matter (GM) in T2w images. Because the cerebrospinal fluid (CSF) has the highest intensity in T2w images and the image resolution of MRI is limited, many voxels between CSF and GM will have similar intensities to the white matter which is brighter than GM and darker than CSF. These voxels can be incorrectly classified as white matter by intensity-based segmentation approaches (Fig. 1(b)). The same mislabeled partial volume problem exists for neonatal T1w images. In this case, CSF is the darkest and gray matter is the brightest; thus intermediate voxels between CSF and gray matter will have intensities similar to white matter. In adult brain white matter is fully myelinated and on T1w/T2w images has the highest/lowest intensity, so that the MLPV problem does not exist.

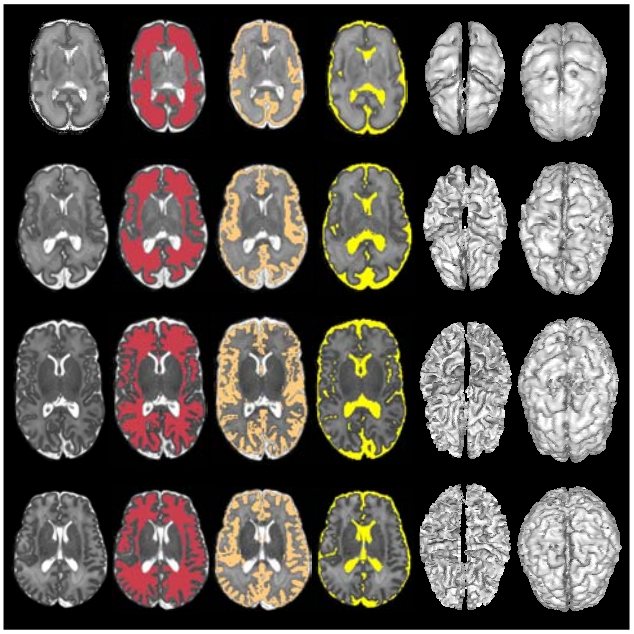

Fig. 2. 3D automatic brain segmentation results. From top to bottom, gestational ages at scan are 29.9, 34, 39.9 and 44 weeks. From left to right: segmented white matter, cortical gray matter and CSF respectively all overlaid on transverse slices from T2w scans. The corpus callosum has been masked off by label propagation. Last two columns show 3D renderings of inner and outer cortical surfaces directly from the segmentation.

Segmentation Method The algorithm we developed addresses the difficulties of segmenting the developing neonatal cortex. First label propagation using non-rigid image registration is used to propagate an atlas segmentation of the deep gray matter structure and the corpus callosum so these could be excluded from further analysis. A Gaussian mixture model (GMM) is then used to describe the tissue-class-specific intensity probability density function (PDF). The expectation-maximization (EM) procedure [1] is used to find optimal parameters for the GMM. To remove the MLPVs, we developed a knowledge based approach to extend the two-step EM algorithm with a MLPV removal step. As the white matter MLPVs may appear on the csf-gray matter boundary for neonatal T1w and T2w images, if a voxel is classified as white matter and within its neighborhood there are CSF and gray matter voxels simultaneously, this voxel is likely to be a partial volume voxel. The same detection rule can be used for white matter and gray matter MLPVs on the CSF-non-brain tissue boundary in neonatal T2w images. We exploit a so-called first-order neighborhood system, i.e., only the six nearest neighbors on the 3D image grid are used. All suspected MLPVs detected after every EM step are suppressed by adjusting the prior probabilities to favor accurate tissue classes. If a voxel x is likely to be incorrectly classified as white matter the prior probability of WM should be decreased. Because the sum of prior probabilities of all tissue classes should always be one, the accurate tissue classes (here CSF and GM) are favored by increasing their prior probabilities. Fig. 1(c-d) indicates the segmentation results after the MLPV removal step is integrated into the EM algorithm. The more iterations are preformed, the less misclassification is left in the result. Finally all MLPVs are removed and the algorithm stops. A further problem is signal heterogeneity of the partially myelinated white matter, which can lead to regional over- or under-segmentation if only a global model is used for tissue classification. We therefore subdivide the brain for regional analysis after an initial global EM segmentation. Specifically, a spatial clustering is performed on gray and white matter voxels and the obtained clustering centers are used to define a voronoi tessellation on the brain space. The segmentation step is independently performed on every voronoi region, which is initialized by the output of the global segmentation. The final segmentation of every local region is refined by switching the GMM to a non-parametric PDF estimator. The kernel density estimation method is used to refine the class PDF which forms the basis of a final tissue classification.

Results We applied our method to 25 subjects selected by GA at scan from ~27 to 45 weeks (mean GA 36.1 ± 4.7). MR images were acquired on a 3T Philips Intera system (Best, Holland) using a standard 6 channel head array coil. The preterm infants were sedated with chloral hydrate and a trained neonatologist was present throughout scanning. The MR sequence parameters were as follows: T2w fast spin echo pseudo volumes: TR 1712 /TE 160ms, FOV 220, matrix 224×224, flip angle 90°, voxel size of $0.86 \times 0.86 \times 1$mm with the 50% slice overlapping. To quantitatively validate the segmentation, a human rater manually segmented three orthogonal slices for every subject. The overlap rate between the automatic and manual segmentation is quantified by the Dice similarity coefficient (DSC) [2].The mean DSC is 0.758 ± 0.037 for gray matter and 0.794 ± 0.078 for white matter after the EM scheme with integrated MLPV removal step. Compared to the results without MLPVs correction, improvements of 3.7% and 7.4% are obtained. More 3D brain segmentation results are shown in Fig. 2.

Conclusion Our method addresses the MLPV problem in segmenting brain MR images for developing neonates and clearly improves the segmentation of cortical gray matter and non-myelinated white matter. The algorithm has been tested for 25 newborn infants from very premature to term equivalent gestational ages. Comparison to the manual established gold-standard shows overall good-to-excellent performance by the algorithm.

References [1] V. Leemput, et al., IEEE TMI:18, 897–908, 1996. [2] L. R. Dice, Ecology:26(3), 297–302, 1945.

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