Brain Extraction Methods for Neonates

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Abstract

Brain extraction is a very important preprocessing step for neuroimage analysis. Many automatic brain extraction tools have been developed during the past decade, however, most of them have been designed for adult brains. Since the morphology and shape are quite different between brains of adults and neonates, this makes them less suitable for neonatal brain extraction. In this paper, we introduce three methods which are specifically tailored for newborns and compare them against three state-of-the-art skull-stripping tools. The results show that our methods yield more accurate outcomes than these tools.

1 Introduction

Brain extraction is a very important preprocessing step for neuroimage analysis. The performance of brain extraction algorithms directly affects postprocessing steps such as image registration, brain volume calculation and tissue-type classification. To date, numerous automatic brain extraction tools have been developed, most of which are specifically designed for adult brain MR images. However, brain morphologies between neonates and adults are quite different. Tissues such as skull and cerebro-spinal fluid (CSF) form a clear dark gap surrounding brain tissues in T1-weighted MR images of the adult brain, which can be easily used as a feature for brain extraction. However, this gap is missing in neonatal brains, and consequently existing tools designed for adult brains cannot produce satisfactory results when applied to neonatal images.

In this work we introduce three methods specifically tailored for neonatal brains, all of which are based on brain mask propagation using B-spline FFD non-rigid registration [2]. We also evaluate the performance of three popular existing tools: Brain Extraction Tool (BET) [5], Brain Surface Extractor (BSE) [4], and Hybrid Watershed Algorithm (HWA) [3]. All results are then compared against manual segmentations, as a gold standard.

2 Materials

Due to the limited availability of manual segmentations, three cases were selected from a database of eight newborn subjects, all of which were acquired using a volumetric 3D magnetization prepared T1-weighted gradient echo pulse sequence (MPRAGE) on a 3T scanner with flip angle = 18°, TR=minimum, TE=minimum, TI=450ms, FOV=256×256×128mm, voxel resolution = 1×1×1mm.To remove the effects of intensity inhomogeneities, all images were preprocessed using N4ITK [6].

3 Methods

We first briefly describe the three state-of-the-art brain extraction methods that are designed for adult brains.

BET is included in FMRIB Software Library (current version 4.1). It performs an intensity-based estimation of brain/non-brain threshold to determine centre of gravity of the brain and then uses triangular tessellation to evolve and fit the brain's surface by the application of a set of locally adaptive model forces. The default setting and the following parameters are used for our experiments: "-R/-S/-B"; "-f" = 0.1-0.5.

BSE is included in BrainSuite (current version 09). It uses an anisotropic diffusion filter after which a Marr-Hildreth operator employing low-pass filter is applied to detect edges, morphological analysis is then applied to extract brain from the edge map. The default setting and the following parameters are used: "-n" = 1-5, "-d" = 10-20, "-s" = 0.5-0.9.

HWA is included in FreeSurfer (current version 5.0). It combines both watershed algorithms, which provides initial brain volume estimation, and deformable surface models, which smoothly fit around the brain. A statistical atlas is used to help to correct the brain extraction. The default setting and the following parameters are used: "-atlas", "-less", "-more".

We have designed three specifically tailored methods suitable for neonatal brain extraction, which are described as following:

Manual Segmentation Propagation (MSP): the target image is first affinely registered to 10 neonatal subjects whose manual segmentations are available. The best matched subject is chosen based on similarity measure and further aligned to the target using non-rigid registration based on B-spline free form deformation. The manual segmentation is then propagated to the target image. For validation purposes, CSF is removed by intensity thresholding since CSF appears dark compared to other brain tissues. Finally, a two-voxel-size opening operation is used to remove small regions that either completely detached or not sufficiently connected to the main brain part.

Brain Atlas Propagation (BAP): the target image is registered to a neonatal brain T1-template (gestational age 42wks), which is available to public (www.brain-development.org), using affine and non-rigid registration. Next, the obtained transformation is used to propagate the brain-mask atlas, which already aligned to and comes together with the T1-template, to the target image. Similarly as in MSP, CSF is then removed and an erosion-dilation clean up is applied.

Expectation-Maximization Segmentation (EMS): instead of propagating the whole brain-mask atlas, the transformation obtained in BAP is applied to align tissue-type atlases (brainstem, cerebellum, cortex, cerebellum, CSF and deep gray matter) to the target image. These aligned atlases serve as spatial priors, and a standard EM segmentation [1] is performed

during which the intensity distribution of each tissue is modelled as a Gaussian distribution while the background is modelled as a mixture of four Gaussian distributions. A posterior probability map, or soft segmentation, for background and each tissue is generated as output. Then for each voxel of the target image, if it has the highest probability of belonging to any of the brain tissues, that voxel is identified as brain. Finally, thresholding and clean up is again performed as in BAP and MSP.

For MSP, BAP and EMS, a multi-resolution approach is used for the non-rigid registration, with B-spline control points spacing = 16mm, 8mm, 4mm, 2mm for each level. Intermediate results are reported.

4 Results

As a measure of volume overlap, the mean Dice's coefficients over three cases are calculated to evaluate the performance of all methods. The Dice's coefficient is defined as $2|A \bigcap B| / (|A| + |B|)$, where A and B are algorithm output and gold standard, respectively. In order to differentiate between the error types, False Discovery Rate (FDR) = $N_{FP}/(N_{FP} + N_{TP})$ and False Negative Rate (FNR) = $N_{FN}/(N_{FN} + N_{TP})$ are also calculated, where N_{FP}, N_{TP}, N_{FN} refers to number of false positive, true positive, false negative voxels respectively. Intuitively, FDR corresponds to non-brain which the algorithm fails to remove, and FNR can be interpreted as brain removed falsely by the algorithm. The run time for each method on a typical PC (Intel(R) Core(TM) i7 2.93GH, 6GB RAM) is also recorded.

Table 1 summarizes the results of all methods. Due to space constraints, only the default setting and parameters which provide the best results for BET, BSW, HWA are shown. Figures 1 and 2 show the comparison of all methods, the parameters that provide the highest Dice coefficient within each method is used.

5 Discussion

Due to the significant morphological differences between adult and neonatal brains, it is found that the established brain extraction tools cannot achieve reasonably accurate results on neonatal images. BET has a tendency to cut off larger parts of the brain, while HWA leaves a substantial part of skull unremoved. BSE produces the best result among the three established tools if parameters are carefully chosen, but is still not performing as well as when applied on adult images [4].

The results achieved by our three methods are much closer to the gold standard. BAP and MSP yield similarly accurate results when B-spline control point spacing is properly tuned, with a slightly lower Dice's score for EMS. However, it should be noted that EMS achieves the lowest false negative rates, therefore it removes the smallest part of true brain by error among all methods. For post-processing, although application dependent, cutting off part of the brain is generally a more severe problem than leaving some residual non-brain tissues.

Another finding is that for MSP, the Dice's coefficient increases for increasing free form deformation mesh resolution, while for atlas propagation (both BAP and EMS), the best result is achieved when the CP spacing is reduced to 4mm, further decreasing will not improve results any more, which we attribute to the fuzziness of the atlas.

In conclusion, we have introduced three automatic methods specifically tailored to neonatal brain extraction. The results show that they all outperform existing major brain extraction

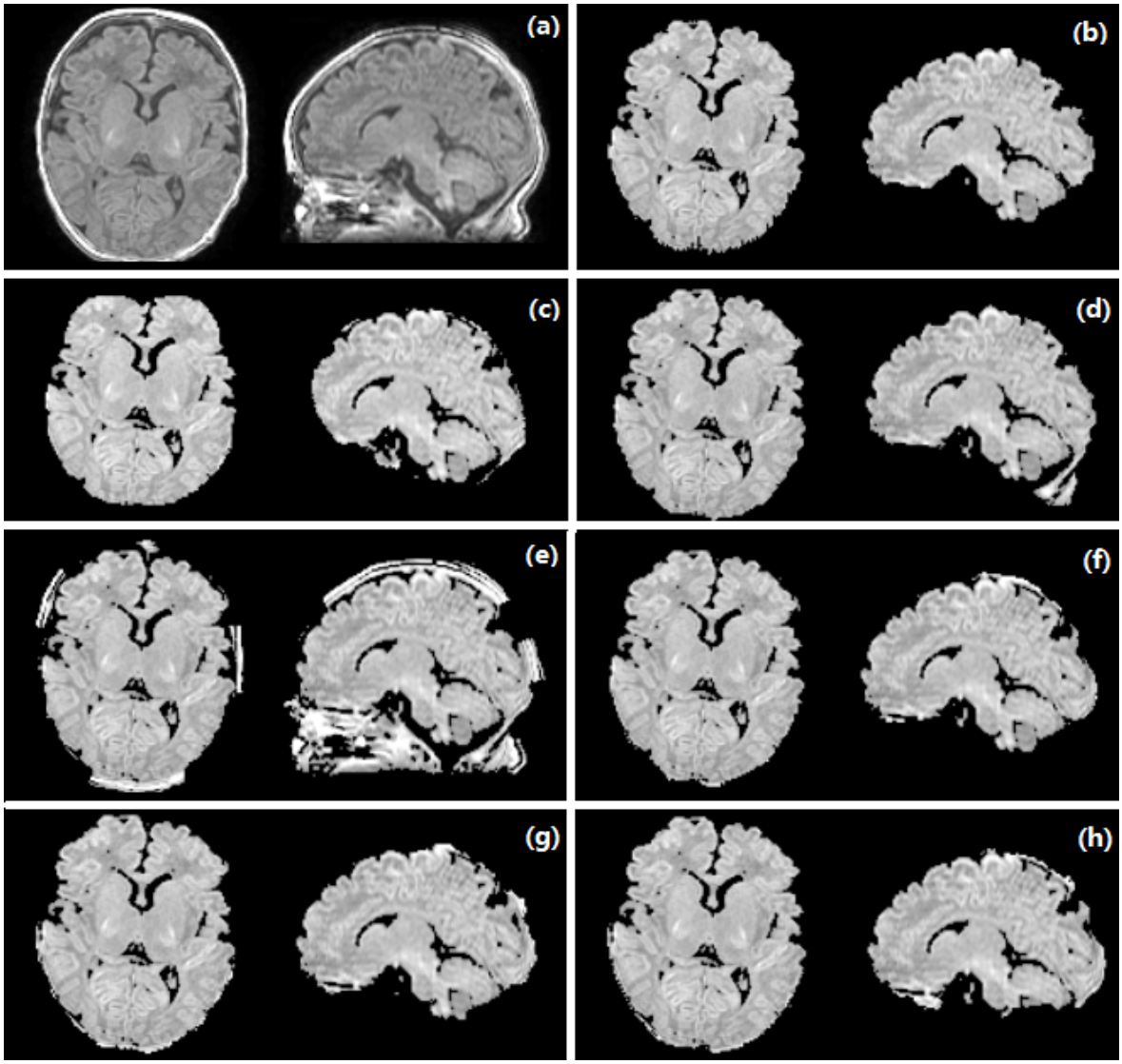
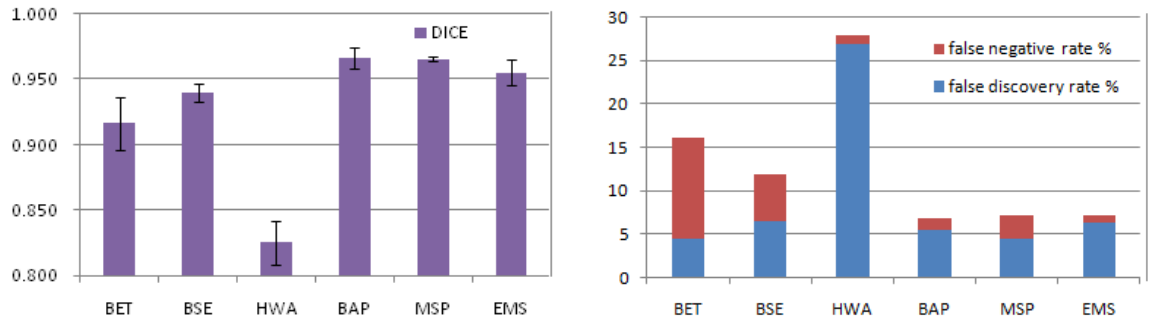


Figure 1: Visual demonstration of brain extraction results. (a) original image (b) manual segmentation (c) BET (d) BSE (e) HWA (f) BAP (g) MSP (h) EMS



(a) (b)

Figure 2: Comparison of 6 methods (a) DICE's coefficients (b) error type analysis

Method	Parameters	DICE	FDR %	FNR %	Time
BET	default	.925(.011)	13.69(1.90)	0.17(0.16)	15sec
	-B -f .4	.916(.020)	4.44(1.15)	11.72(5.26)	2min
BSE	default	.911(.003)	14.68(1.24)	2.24(1.17)	30sec
	-n4 -d20 -s0.7 -p	.939(.007)	6.44(1.83)	5.51(1.59)	1min
HWA	default	.809(.041)	29.42(9.05)	0.40(0.34)	1min
	-less	.825(.017)	26.97(6.08)	1.01(0.38)	2min
BAP	16 mm	.963(.007)	5.94(0.85)	1.31(0.57)	10min
	8 mm	.965(.007)	5.48(1.11)	1.29(0.44)	30min
	4 mm	.966(.008)	5.54(1.16)	1.21(0.46)	2hr
	2 mm	.965(.008)	5.74(1.15)	1.11(0.41)	7hr
MSP	16 mm	.959(.004)	4.26(0.34)	3.83(1.13)	15min
	8 mm	.961(.002)	4.63(0.78)	3.04(1.24)	40min
	4 mm	.964(.002)	4.45(0.71)	2.69(1.11)	3hr
	2 mm	.965(.002)	4.48(0.68)	2.47(1.03)	8hr
EMS	16 mm	.945(.012)	6.35(1.32)	0.75(0.20)	12min
	8 mm	.954(.010)	6.31(1.11)	0.80(0.23)	32min
	4 mm	.955(.010)	6.30(1.09)	0.82(0.27)	2hr
	2 mm	.955(.009)	6.28(1.01)	0.85(0.25)	7hr

Table 1: Comparison of results of 6 methods with different parameters. The numbers in brackets are standard deviations. Parameters for BAP, MSP, EMS stand for B-spline control point spacing.

tools that are based on adult brain morphology. In the future, we will further investigate the methods we introduced for applications to a larger neonatal brain database.

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