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# BRAINSEG – Brain Structures Segmentation Pipeline Using Open Source Tools

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## Abstract

Structure segmentation is often the first step in the diagnosis and treatment of various diseases. Because of the variations in the various brain structures and overlapping structures, segmenting brain structures is a very crucial step. Though a lot of research had been done in this area, still it is a challenging field. Using prior knowledge about the spatial relationships among structures, called as atlases, the structures with dissimilarities can be segmented efficiently. Multiple atlases prove a better one when compared to single atlas, especially when there are dissimilarities in the structures. In this paper, we proposed a pipeline for segmenting brain structures using open source tools. We test our pipeline for segmenting brain structures in MRI using the publicly available data provided by MIDAS.

**Index Terms:** Brain structure segmentation, Multi Atlas, Pipeline, Patch, MRI

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## 1. Introduction

Segmenting brain tissues/ structures is the primary step in diagnosis and treatment of various brain related disorders. The MRI scan gives clear and exhaustive images of soft tissue. Bones can't be visualize using MRI because bone tissue doesn't comprise much water. Due to this, MRI, fMRI are widely used in tissue and structure segmentation. Tissue segmentation can be done using intensity thresholding. But segmenting brain structures are complicated as a structure can be comprised of more than one tissue type. Various tools and techniques are available for segmenting brain structures. Based on object boundary, shape and homogeneity of an image, Balafar et. al., 2010<sup>[1]</sup> classify the segmentation techniques as shown in the figure 1.

Abo Eleneen and Gamil Abdel Azim, 2013, proposed a method that use fisher information measure and intensity contrast to segment medical images<sup>[2]</sup>. An optimal region growing threshold which combines local

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search procedure with thresholding region growing was proposed by Afifi et. al.,2015<sup>[3]</sup>. A review on segmentation techniques has been discussed by Ritu Agarwal and Manisha Sharma, 2014<sup>[4]</sup>. R. Neela and R. Kalaimagal, 2014, presented a review on intensity and model based segmentation methods for MRI<sup>[5]</sup>. K. Santle Camilus and V. K. Govindan, 2012, presented a review on graph based segmentation<sup>[6]</sup>. Atlas based segmentation is one of the recent techniques<sup>[7]</sup>. Atlas is a set of intensity image and its segmented image. Each atlas contains the probability of a class at a given pixel, intensity distribution given at that label, about the distribution of the class of its neighbor. Out of all proposed techniques, segmenting structures using atlases gives good result. Since there are large anatomical variations in the structures, using multiple atlases rather than single atlas gives superior results. The accuracy of the result largely depends on the selection of atlases. In this paper, we develop a pipeline using publicly available tools to segment the subcortical brain structures from MRI scan. We evaluate the performance of our pipeline using the dataset provided in the MICCAI (Medical Image Computing and Computer Assisted Intervention) 2012 Challenge on Segmentation: Algorithms, Theory and Applications. This dataset has data from 15 young patients and segmented into 207 structures.

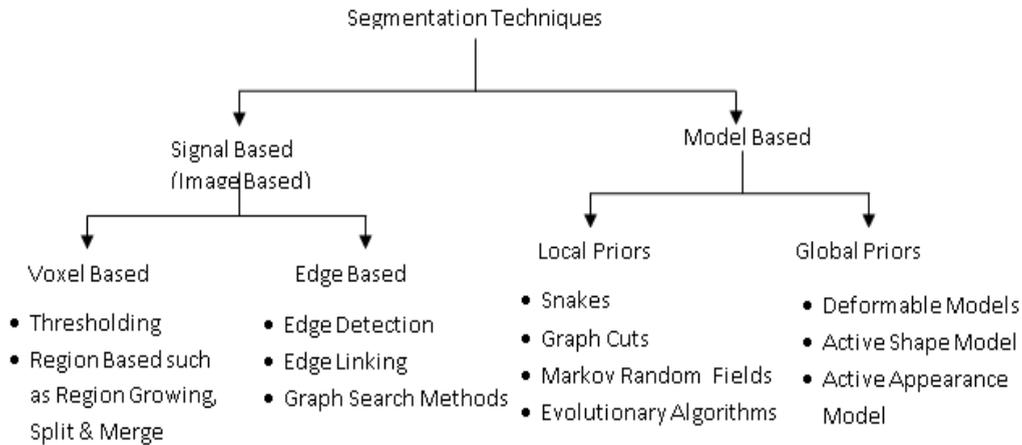


Fig. 1. Classification of segmentation techniques

## 2. Materials and Methods

In our pipeline we use pre-labeled MRI images called atlases to segment the subcortical structures and the segmentation pipeline is shown in figure 2. In multi atlas segmentation, there are two phases. In the first phase, a non-linear registration between atlas intensity image and the test image is done and the labels from the corresponding atlas label images are propagated to the test image. This yields a set of segmented images for the given test image. In the second phase, for each voxel in the test image, the corresponding labels from all segmented images are combined together to produce final segmentation. First the intensity inhomogeneity is corrected for all the test images and atlas. Next all images are rigidly registered with a template for further processing. Next preprocessing step removes the skull and extra cerebral tissues. A set of atlas images are selected from the atlas set using mutual information measure. After than each atlas image is non-rigidly registered with the test image and the labels from the atlas images are transferred to the test image. Then all segmented images are fused together to form the final segmentation. For preprocessing we use publicly available tools and to measure the similarity between atlases we use mutual information and for measuring the similarity between patches in label fusion step we use patch distance.

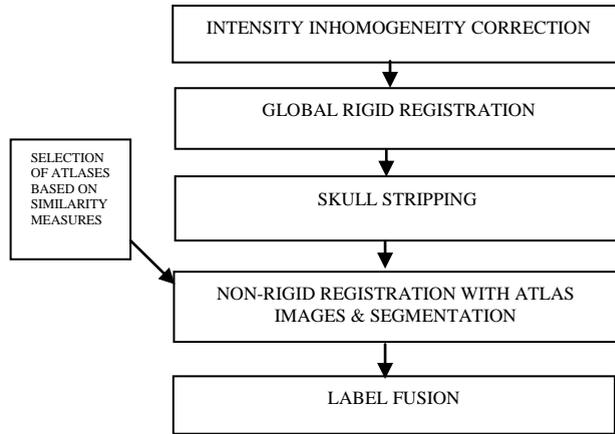


Fig. 2. Pipeline for segmenting brain structures

### 2.1. Intensity Inhomogeneity Correction Using ANTs's *N4BiasFieldCorrection*

The intensity inhomogeneity is caused mainly due to the RF coil imperfections. This artifact, results in the variations of intensities in the same tissues. These variations affect the segmentation results. Various methods are proposed for intensity inhomogeneity correction<sup>[8-10]</sup>. N4 is a bias correction algorithm and is a variation of N3 algorithm described by Tustison et. al.,2012<sup>[10]</sup>. Using *N4BiasCorrection* command<sup>[11]</sup>, the intensity inhomogeneity of MRI scan can be corrected.

- `N4BiasFieldCorrection -i inputfile.nii.gz -o outputfile.nii.gz`

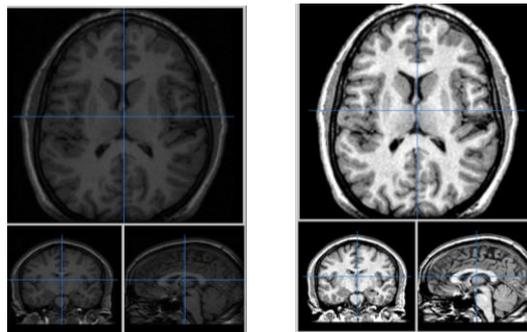


Fig. 3. (a) Before bias correction; (b) After bias correction

### 2.2. Global Rigid Registration with MNI Template Space Using 3DSlicer's *BRAINS Tool*

Registration is an important preprocessing step in the analysis of images. It is a process of finding geometric transformation so that two images are perfectly aligned. Depending on the nature of transformation, the registration can be classified into rigid, affine, projective, curved and non-rigid<sup>[12]</sup>. Before further processing, we need to align all images in the same image space. This is also called as spatial normalization, ie. registration of MRI scans of brain images to a common space such as Talairach space<sup>[13]</sup> or the MNI space<sup>[14]</sup>. Here, we use 3D Slicer's Brains tool for doing global registration. We align all images in the MNI work space.

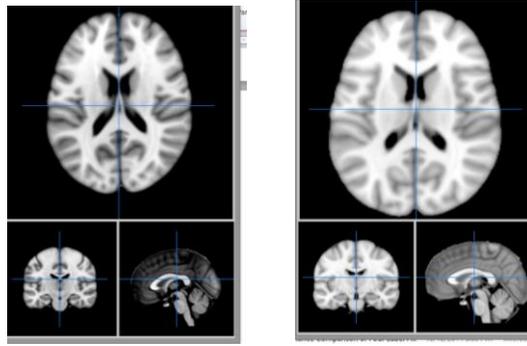


Fig. 4. (a) MNI Template image T1- fixed; (b) Output image after global rigid registration

### 2.3. Skull Stripping Using the Tool ROBEX

Skull Stripping removes non-brain tissue in MR brain images. Many Skull Stripping methods have been proposed<sup>[15-19]</sup>. Skull stripping improves the performance of the registration and segmenting process. We use the ROBEX tool proposed by<sup>[20]</sup> and downloaded from<sup>[21]</sup>.

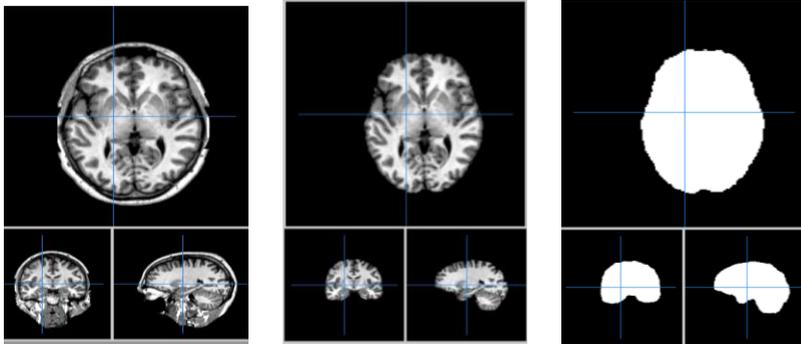


Fig. 5. (a) Input image before masking; (b) After Masking ; (c) Image mask

### 2.4. Non-Rigid Registration of Subject Image with template Image Using ANTs's ANT and WarpImageTransform tool

There are enormous researches in the segmentation of brain structures. Several studies have shown that applying prior knowledge in the process of segmentation gives a better performance<sup>[22-24]</sup>. Especially using multiple atlases gives greater accuracy when there are large variations in the structures<sup>[25]</sup>. To transfer labels from the atlas images, target image should be geometrically aligned [non-rigid/rigid] with all atlases and a deformation field should be calculated. Using this, labels from the atlas images are propagated to the target image. In our experiment, we select 10 atlas images. Mutual information between each atlas and test image pair is calculated and the top 10 atlas images are selected. Using ANTs tool, we non-rigidly aligned all the atlas images with the target image and labels are propagated from the atlas image to the target image.

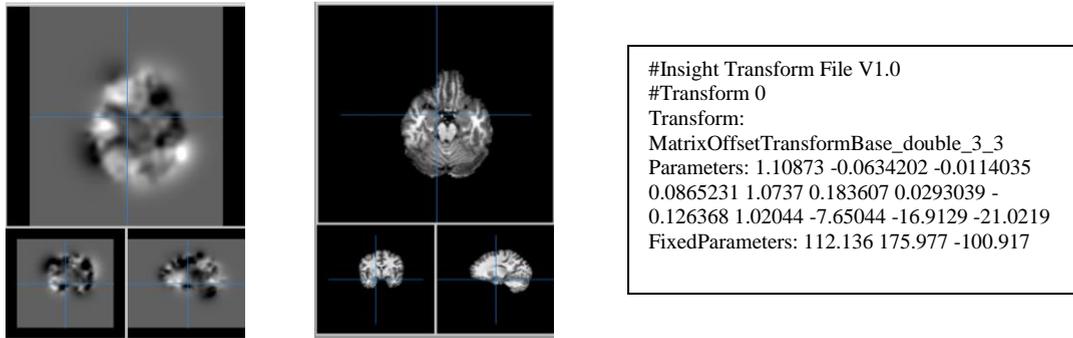


Fig. 6. (a) Warped image; (b) Final Registered image; (c) Deformation Field

### 2.5. Label Fusion Using Patch Differences

For each voxel in the test image,  $TX_i$ , we have to select an optimal label from a label set ( $L_{i1}, L_{i2}, \dots, L_{in}$ ).  $N$  refers number of atlases and  $M$  refers to the number of voxels in the test image. Various methods have proposed for the final label fusion step<sup>[26-30]</sup>. To measure the similarity between patches, we calculate spatial distance that considers both neighbouring voxels in addition to the center voxel. We use this similarity measure to calculate local weight ( $WLX_i$ ). The similarity between the atlas and the target image is used to calculate the global weight ( $WGi$ ). Larger weights will be assigned to the atlas where the similarity is greater. Then using both weights (Local + Global), using majority voting, the labels for each voxel in test image will be assigned.

$$TX_i = \underset{\text{label } l}{\operatorname{argmax}} \sum_{i=1}^n WLX_i + WGi$$

label 1

(1)

## 3. Results and Discussion

All the test and atlas images we used in our paper are downloaded from MIDAS digital archive system<sup>[31]</sup>. All data are already intensity homogeneity corrected. Preprocessing has to be done for all subject and atlas scans. Intensity inhomogeneities were corrected using ANTs N4BiasFieldCorrection, then skull stripping were performed using ROBEX. Top 10 atlases are selected by measuring the similarities with the test image. Here, we use mutual information as the similarity measure. The test image is registered with each atlas image using ANTs tool. Labels are propagated from the atlas images using “warpimagemultitransform”. This step gives a set of segmented images for the test image. Finally the labels from these segmented images are fused together using patch differences described in the previous section, which gives a final segmentation. The bias field correction takes about 20 seconds for each image. The global registration takes 2 seconds for each image. For skull stripping, each image takes 12 seconds, non-rigid registration and label propagation takes about 40 minutes for each image atlas pair. Atlas selection takes about 20 seconds. Finally the label fusion takes 1 ½ hours. All these operations were performed using shell scripting and the sample commands are given below:

```

>n4biasfieldcorrection -d 3 -i h: \data\training\1003_3.nii -o h:\newdata\bias_1003_3.nii.gz -s 4
>BRAINSfit -- fixedVolume h:\newdata\bias_1003_3.nii.gz -- movingVolume mnitemplate.nii.gz --
outputTransform h: \newdata\rigid_1003_3.nii.gz -- transformType Rigid --histogramMatch
>robex h: \newdata\rigid_1003_3.nii.gz h: \results\skullstrip\1003_3_robex.nii.gz h:
\results\skullstrip\1003_3_robex_mask.nii.gz
        
```

```

>ants 3 -m PR [h:\results\skullstrip\1003_3_robex.nii.gz,h:\results\skullstrip\1007_3_robex.nii.gz ,1,4] -i
50x50x0 -t Elast [1.0] -o h:\register\skull_prnew_seg37.nii.gz
>warpimagemultitransform 3 h:\results\skullstrip\1007_3_robex.nii.gz h: \register\skull_prnew_total37.nii.gz
-R h: \results\skullstrip\1003_3_robex.nii.gz h: \register\skull_prnew_seg37warp.nii.gz h:
\register\skull_prnew_seg37affine.txt --use-NN
>warpimagemultitransform 3 h: \data\training\1007_3_glm.nii h: \register\skull_prnew_glm37.nii.gz -R h:
\results\skullstrip\1003_3_robex.nii.gz h: \register\skull_prnew_seg37warp.nii.gz h:
\register\skull_prnew_seg37affine.txt --use-NN

```

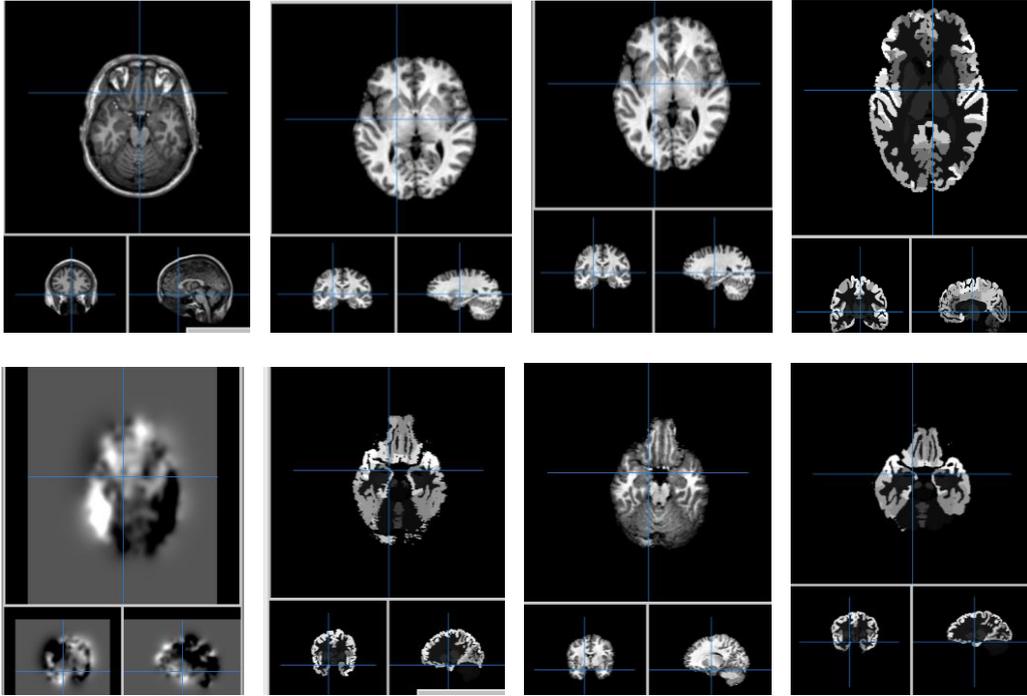


Fig. 7. (a) Test Image; (b) Test image after skull stripping ; (c) An atlas - intensity image ; (d) An atlas – labeled image; (e) Test image ‘a’ after registered with atlas ‘c’; (f) Segmentation of test image ‘a’ ; (g) Test image ‘a’ after label propagation – for one set of atlas; (h) Final segmentation of test image after fusion.

To measure the efficiency of our pipeline, we use Dice co-efficient, Jaccard co-efficient and kappa statistics<sup>[32,33]</sup>. We compare the segmented image with the golden standard image. Our pipeline for the test image (Fig 5a) gives DICE = 0.954800, JACCARD = 0.913332 and KAPPA= 0.945296. Our experiment was conducted for 15 test images. The same test image gives DICE= 0.824501, JACCARD = 0.902120 and KAPPA= 0.932134 for simple majority voting method and gives DICE= 0.924500, JACCARD= 0.945255 and KAPPA= 0.89344 for weighted majority voting.

#### 4. Conclusions

We have presented a pipeline for segmenting brain structures using open source tools. We compared our pipeline with simple majority voting and weighted majority voting. For all the operations, only non-rigid registration and fusion steps consumes more time. For doing each set of registration, 30 to 40 minutes are

needed. To do final fusion, the algorithm takes 1 ½ hours. The time taken to compare our result with the golden standard is 49332 milliseconds.

Table 1. Performance comparison of various algorithms

MEASURES	BRAINSEG	MV	WMV
DICE	0.9548	0.824501	0.9245
JACCARD	0.913332	0.90212	0.945255
KAPPA	0.945296	0.932134	0.89344

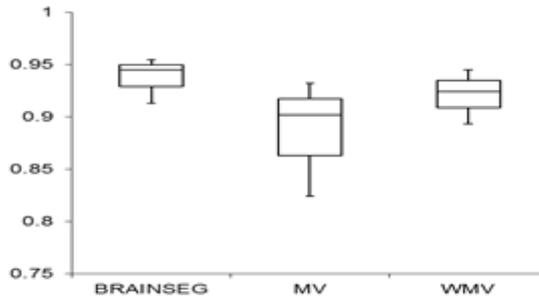


Fig. 8. Comparison of BRAINSEG with MV & WMV

Table 2. Comparison of our segmentation pipeline for different number of atlases.

Atlases	Total	Jaccard	Dice	Volume sim.	False negative	False positive
10	0.895681	0.822509	0.902612	-0.0154748	0.104319	0.09035
7	0.880107	0.802049	0.890152	-0.0228275	0.119893	0.099571
5	0.85359	0.772619	0.871726	-0.0424947	0.14641	0.10935
4	0.817069	0.729576	0.843647	-0.0650567	0.182931	0.127988

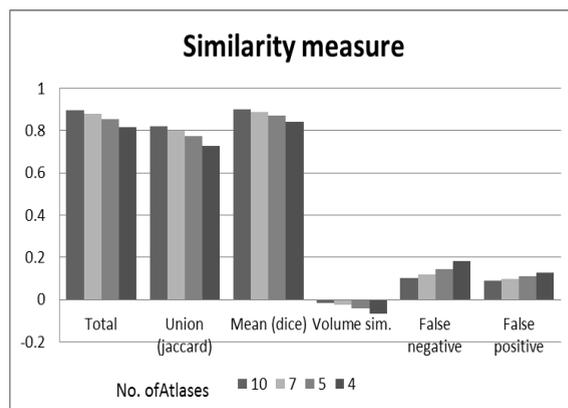


Fig. 9. Comparison for number of atlases

Figure 8 and Table 1 shows the performance of simple majority voting, weighted majority voting and our pipeline for a single test image. Figure 9 and Table 2 shows the segmentation performance of our pipeline for a various number of atlases and for the same test image. For 10 atlases, it gives a maximum accuracy. When compare to majority voting and weighted majority voting methods, our pipeline gives better accuracy. We can use various similarity measures to select the top 10 atlases such as normalized mutual information, normalized correlation coefficient, etc. Various patch comparison methods using graphs, trees, etc. can be used. These are the future directions of our research.

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