SEGMENTATION OF SUBCORTICAL STRUCTURES IN BRAIN MRI USING GRAPH-CUTS AND SUBJECT-SPECIFIC A-PRIORI INFORMATION

Robin Wolz, Paul Aljabar, Daniel Rueckert
Department of Computing
Imperial College London
London, UK

Rolf A. Heckemann, Alexander Hammers
MRC Clinical Sciences Centre
Imperial College London
London, UK

ABSTRACT

We propose a general framework for segmentation of subcortical structures in magnetic resonance brain images based on multi-atlas label propagation and graph cuts. The label maps obtained from multi-atlas segmentation are used to build a subject-specific probabilistic atlas of a structure of interest. From this atlas and an intensity model estimated from the unseen image, a Markov random field-based energy function is defined and via graph cuts. Compared to a previously proposed approach, our method does not rely on manual training of the intensity model and is applied to six subcortical structures. We used this approach to segment the hippocampus on 60 images from the Alzheimer’s Disease Neuroimaging Initiative (ADNI) and achieved an average overlap (Dice) of 0.86 with a manually delineated reference.

Index Terms— structural MR images, atlas-based segmentation, graph cuts, subcortical structures, MRF

1. INTRODUCTION

The accurate and robust segmentation of subcortical brain structures in magnetic resonance (MR) images is an increasingly important step in many clinical applications, like assisting in the diagnosis of schizophrenia or Alzheimer’s disease.

Although much research has been published in this area [1, 2, 3, 4, 5], no method has established itself in routine clinical use. One well-validated approach relies on combining the segmentations obtained from non-rigidly aligning multiple manually labeled atlases with the target image [3]. The final label at each voxel is determined by applying vote-rule decision fusion. This method makes no use of the target intensity information. Considering such information, however, potentially results in further improvements to the quality of multi-atlas segmentation.

Combining prior knowledge of the intensity and spatial distribution of an object of interest in the contextual framework of a Markov random field (MRF) is an established technique for brain segmentation (e.g., [1, 6, 4]). In these approaches spatial information in form of a probabilistic atlas and an estimation of the probability distribution of the target structure’s intensities are used to formulate an energy function. Since Boykov et al. [7] proposed graph cuts as a generic method for finding the global optimum for labelling tasks in computer vision, it has been widely used for optimization in this area. Recently, two brain segmentation methods based on MRFs and graph cuts have been introduced: Song et al. [8] proposed a method for tissue class segmentation of 2D MR images. Their spatial prior is defined as a probabilistic atlas that is affinely registered to the target image. The intensity distributions of white matter (WM), gray matter (GM), and cerebrospinal fluid (CSF) are modelled using Gaussian distributions. Another promising approach, proposed by van der Lijn et al. [9] for segmenting the hippocampus, can be considered an extension of the multi-atlas segmentation approach of [3] and tackles the previously described problem as follows: instead of directly fusing the individual segmentations obtained from registering multiple atlases to the target image, they are used to build a probabilistic atlas which is combined with statistical intensity models for foreground and background to formulate an energy function to be minimized.

A limitation of this method is the reliance on a strictly controlled training of its statistical intensity model where a Gaussian distribution for the hippocampus and a Parzen estimate of the background distribution are defined on the manually labeled atlas images. This approach requires the use of identical MR sequences for the atlas (training images) and target (subject images).

In this paper we propose a generalized framework for the segmentation of subcortical brain structures in MR images which overcomes these problems: We directly estimate the Gaussian distribution for the foreground from the target image. Furthermore we use a spatially varying mixture of Gaussians (MOG) for the background in order to better model the different background parts surrounding a structure of interest.

We have extended the method to six subcortical structures and evaluated it on 60 images from the Alzheimer’s Disease Neuroimaging Initiative (ADNI) trial.
2. METHOD

The task of segmenting an image $I$ into structures of interest can be described as assigning a label $f_p \in \mathcal{L}$ to each voxel $p \in I$. A MRF-based energy function can be formulated as

$$E(f) = \sum_{p \in I} D_p(f_p) + \sum_{\{p,q\} \in N} V_{p,q}(f_p, f_q),$$

where $N$ is a neighborhood of voxels and $f$ is the labeling of $I$ [7]. The data term $D_p(f_p)$ measures the disagreement between a prior probabilistic model and the observed data. $V_{p,q}(f_p, f_q)$ is a smoothness term penalizing discontinuities in $N$. To optimize Eq. (1) with graph cuts, a graph $G = < V, E >$ with a node $v \in V$ for each voxel $p$ is defined on image $I$. Its edges $e \in E$ consist of connections between each node $v$ and two terminal nodes $s,t$ as well as connections defined between neighboring voxels. The terminals $s$ and $t$ represent the two labels describing foreground and background. By determining an s-t cut on $G$, the desired segmentation can be obtained [7]. The data term in the MRF model defines the weights of the edges connecting each node with both terminals and the smoothness term encodes the edge weights of neighboring nodes.

This segmentation based on graph cuts leads to a binary segmentation into foreground and background. To segment multiple structures, we can apply the algorithm for each structure $S_i$ independently and then consolidate the individual segmentations in a final step.

2.1. Estimation of a subject-specific data term

The weights of the edges connecting each node with the terminals are determined from a spatial prior and a model of the intensity distribution of the structure of interest. To estimate the corresponding parameters as accurately as possible, we derive both models from the unseen target image.

2.1.1. Spatial prior

Various authors have used prior spatial knowledge in the shape of a probabilistic atlas for MRF-based brain segmentation (e.g. [6, 4, 8, 9]). While most of these approaches rely on affinely aligning a fixed probabilistic atlas for tissue classes (WM, GM and CSF) or subcortical structures, van der Lijn et al. [9] use the propagated labels from multi-atlas segmentation [3] to build a subject-specific probabilistic atlas directly in the coordinate system of the unseen image. The assumption is that building an atlas from multiple registrations compensates for errors in the constituent atlases and registrations. We implemented a similar approach using a non-rigid registration method [10] to align all $N$ atlases with the target image. By applying the resulting transformations $T_j$ to each label set $f_j$, each atlas is warped to the target image’s coordinate frame.

$$P_A(f_i) = \frac{1}{N} \sum_{j=1,\ldots,N} \left\{ \begin{array}{ll} 1, & f_i = f_j^T \vspace{0.5em} \end{array} \right. \text{else}$$

$P_A$ defines the spatial prior contribution to the data term in the graph cuts model.

2.1.2. Intensity model

The intensity prior for tissue classes or specific structures is usually modelled by a Gaussian probability distribution. The main challenge is the accurate and robust estimation of its parameters. In [6], van Leemput et al. describe an expectation-maximization based method to successively improve an initial estimate of the parameters. For the hippocampal segmentation proposed in [9], the parameters of the Gaussian distribution are estimated a priori from manually labeled training images, which restricts the application of the method to images acquired using identical MR sequences as the training images. To arrive at a more generally applicable method, we directly estimate the parameters of the Gaussian distribution of the structures of interest from the unseen target image. It is estimated from all those voxels which at least 95% of the atlases assign to this particular structure. The intensity component of the source link weight for a given voxel $p$ and structure $f_i$ is denoted by $P_s$ and is estimated from the intensity distribution model, i.e. $P_s(p, f_i) = P(y_p|f_i)$.

For many subcortical structures, the background does not consist of a single homogeneous area. Therefore, it is meaningful to describe its intensity distribution by a multivariate model instead of a single Gaussian distribution. Van der Lijn et al. [9] proposed a Parzen window estimated from a manually outlined area around the hippocampus on training images. To enable a more robust approach that does not rely on manual training and to allow for a more detailed description by using different models for different parts of the background, we propose a spatially varying mixture of Gaussians (MOG) model. The MOG model is defined by the general Gaussian distributions of the three tissue classes based on the method described in [6] and the more precise distributions of the defined regions of interest based on the target specific atlas described above. When segmenting a particular structure $i$ with label $f_i$, the Gaussian intensity distributions of all other structures $j \neq i$ and of the tissue classes $T_k, k = 1, \ldots, 3$ are combined to estimate the likelihood of the voxel belonging to the background. This is carried out using spatial priors for the structures (obtained as described above) and for the tissue classes (obtained from previously generated and non-rigidly aligned probabilistic atlases). The likelihood of a voxel being in the background with respect to structure $i$ is estimated by:

$$P(y_p|f_{i\text{,back}}) = (1 - \gamma_{\text{struct}}) \sum_{k=1,\ldots,3} \gamma_k P(y_p|T_k) + \gamma_{\text{struct}} \sum_{j=1,\ldots,N, j \neq i} \gamma_j P(y_p|f_i).$$
where $\gamma_k$ is the tissue spatial prior, $\gamma_j = P_A(f_j)$ is the structure spatial prior and $\gamma_{\text{struct}} = \sum_{j=1,..,N} \gamma_j$. Eq. 3 provides the intensity component of the edge weight from voxel $p$ to the sink node $t$ for the current structure, denoted by $P_l(p, f_i)$, i.e. $P_l(p, f_i) = P(y_p|f_i, \text{back})$

The intensity and spatial contributions, $P_x$, $x \in s, t$ and $P_A$, are combined to give the data term that defines the edge weights connecting each node to the source $s$ and sink $t$. It is defined as the log-likelihood:

$$D_p(f_i) = -\alpha \ln P_x(p, f_i) - (1 - \alpha) \ln P_A(f_i)$$  \hspace{1cm} (4)

The parameter $\alpha$ governs the influence of $P_A$ and $P_x$ on the final segmentation result.

2.1.3. Spatially varying weighting of $P_A$ and $P_x$

Most subcortical structures have boundaries that are defined by varying amounts of tissue contrast on T1-weighted MR images. Thus, a high weighting of $P_x$ is not meaningful everywhere. To account for this variation, we propose a spatially adaptive parameter $\alpha$. We segmented the 30 atlas images twice in a leave-one-out fashion, with $\alpha = 0.2$ and $\alpha = 0.8$ to examine the influence of $P_x$. We then transformed all segmentation results to a standard space and built a confidence map that encodes for each voxel the number of times only one choice of $\alpha$ gave the correct label. Positive and negative values for this number are used in cases where a high and a low $\alpha$, respectively, performed better. During the segmentation of an unseen image this confidence map is warped to its coordinate frame and used to modify the initial value of $\alpha$ for each voxel independently.

2.2. Smoothness term

Following [8], a smoothness term based on intensity $y$ as well as the intervening contour probabilistic map $B$ (derived from the gradient image) are used to define the weights of edges connecting two neighboring voxels $p$ and $q$:

$$V_{p,q}(f_p, f_q) = c \left( 1 + \ln \left( 1 + \frac{1}{2} \left( \frac{|y_p - y_q|}{\sigma} \right)^2 \right) \right)^{-1}$$

$$+ \left( 1 - c \right) \left( 1 - \max_{x \in M_{p,q}} (B_x) \right)$$  \hspace{1cm} (5)

where $M_{p,q}$ is a line joining $p$ and $q$, and $\sigma$ is the robust scale of image $I$ [8]. The parameter $c$ controls the influence of the boundary- and intensity based part.

3. DATA AND RESULTS

We evaluated our method on 60 T1 weighted 1.5T MR images from different subjects in the Alzheimer’s Disease Neuroimaging Initiative (ADNI) database\(^1\). The subjects in this study are classified into three groups: Alzheimer’s patients (AD), patients showing mild cognitive impairment (MCI) and control subjects (controls). We randomly chose 20 subjects from each group. For each image a manual hippocampal segmentation was provided by ADNI.

We used two different sets of atlases for the segmentation. The first set consisted of 30 ADNI images with corresponding hippocampus labels. The subjects were different from those used for evaluation, and had been classified as AD, MCI, and controls (10 each). The second set of atlases consists of 30 images of healthy subjects that had been manually segmented into 67 structures [3]. We applied our method to the following structures of this atlas and used the results for visual inspection: hippocampus, amygdala, putamen, thalamus, nucleus accumbens and caudate nucleus.

3.1. Comparison with manually labeled data

Our method shows a clear improvement in segmentation accuracy compared with standard multi-atlas segmentation. Table 1 and Fig. 1 show the overlap (similarity index (SI) or Dice coefficient) for the segmentation of the hippocampus for standard multi-atlas segmentation and the proposed method. The difference is significant ($p < 0.001$ on Student’s two-tailed paired t-test).

<table>
<thead>
<tr>
<th></th>
<th>multi-atlas</th>
<th>proposed method</th>
</tr>
</thead>
<tbody>
<tr>
<td>SI overlap</td>
<td>0.842 ± 0.030 [0.739-0.984]</td>
<td>0.860 ± 0.024 [0.787-0.897]</td>
</tr>
</tbody>
</table>

Table 1. Average SI overlap for hippocampus segmentation.

The improvements with our method are similar to those reported in [9], but eschew the need for manual training of the intensity models.

![Fig. 1. SI for the hippocampus in 60 test cases with multi-atlas segmentation and the difference with the proposed method](image)

To show the importance of an intensity model independent of the MR sequence, we applied our method using a previously trained intensity model. We evaluated the intensity distribution of the manually delineated hippocampi and the three tissue classes on 10 MR images which were acquired on the same scanner. The average SI overlap for hippocampus segmentations with this trained model on 30 images that have

\(^1\)(www.loni.ucla.edu/ADNI)
been acquired with an MR protocol different to the training images are on average 0.851 compared to 0.848 for standard multi-atlas segmentation and 0.867 for our proposed method.

3.2. Visual inspection

Visual inspection of the segmentation results obtained from our second atlas set confirm the results described above and show improved segmentation results compared with standard multi-atlas segmentation. (examples in Fig. 2).

![Fig. 2](image)

Fig. 2. Transverse sections showing segmentation outlines superimposed on MR image. (a): Proposed method – thalamus (blue), putamen (yellow) and caudate (white). (b): Multi-atlas method: hippocampus (green) and amygdala (red). (c): Same structures with proposed method, showing improved segmentation with reduced amount of false-positive labelling compared to (b).

4. CONCLUSION

We propose a method for subcortical brain segmentation in MR images based on subject-specific a priori information of spatial extent and intensity distribution of structures of interest. Label maps obtained from multi-atlas segmentation are used to generate a subject-specific probabilistic atlas. This atlas is paired with intensity models for both the foreground and the background to formulate an MRF-based energy function. In contrast to a previously proposed method, our algorithm does not rely on manual training of the intensity models. Therefore, this method is more generally applicable as it is not tied to a specific MR sequence. A Gaussian distribution for the foreground model is directly estimated from the target image, while the background model is described by a mixture of Gaussians estimated from a tissue class segmentation, our subject-specific atlas and non-rigidly aligned atlases for tissue probabilities. We introduced a spatially varying weighting between the intensity model and the spatial prior based on a previously learned confidence map. We evaluated the proposed method on pathological image data from the ADNI study and were able to increase the SI overlap for the segmentation of the hippocampus significantly from 0.842 with standard multi-atlas segmentation to 0.860. In future work, we are planning to reduce the computational expense of the method. A useful approach may be to register an unseen image to a standard space only instead of registering multiple atlases to it. In this standard space, a subject-specific atlas could be assembled by choosing suitable manually labeled images from a database. By incorporating an appropriate criterion for choosing suitable atlases, which could be based on previously learned features, it may be possible to substitute the beneficial, but computationally expensive deformation of multiple atlases to the target space.

5. REFERENCES