Mixture Segmentation of Multispectral MR Brain Images for Multiple Sclerosis

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ABSTRACT

We present a fully automatic mixture model-based tissue classification of multispectral (T_1- and T_2-weighted) magnetic resonance (MR) brain images. Unlike the conventional hard classification with a unique label for each voxel, our method models a mixture to estimate the partial volumes (PV) of multiple tissue types within a voxel. A new Markov random field (MRF) model is proposed to reflect the spatial information of tissue mixtures. A mixture classification algorithm is performed by the maximum *a posterior* (MAP) criterion, where the expectation maximization (EM) algorithm is utilized to estimate model parameters. The algorithm interleaves segmentation with parameter estimation and improves classification in an iterative manner. The presented method is evaluated by clinical MR image datasets for quantification of brain volumes and multiple sclerosis (MS).

Keywords: Magnetic Resonance, segmentation, partial volume, multispectral, Markov random field.

1. INTRODUCTION

Automatic image segmentation is the key step in medical imaging for quantifying the shape and volume of different types of tissues. Efficient quantitative analysis will facilitate diagnosis and therapy in clinical applications, such as three-dimensional (3-D) visualization, image guided surgery, and computer aided detection.

Magnetic resonance (MR) imaging technique has been widely used in the studies of brain disorders, e.g. multiple sclerosis (MS). MS is the most common inflammatory demyelinating disease of the central nervous system [1, 2]. For treatment of MS, classification of lesions and segmentation of brain volumes into different tissue types, i.e., white matter (WM), gray matter (GM), and cerebral spinal fluid (CSF) are necessary to provide an objective evaluation of MS burden for drug treatment assessment.

Current advanced MR imaging techniques provide efficient acquisition of multispectral images as T_1-, T_2-weighted, and fluid attenuated inversion recovery (FLAIR) images. These images are well spatially registered over the 3-D space. Therefore, multispectral MR images shall provide valuable mutual information for image analysis [3, 4]. In MR brain images, there exist artifacts, such as noise and partial volume (PV) effect, where voxels contain a mixture of multiple tissues. Thus, classification of voxels exclusively into one unique class is not practical [5, 6, 7].

In this paper, we present a fully automatic approach for modeling the PV effect and noise artifact in the classification of brain tissues for PV effect minimization. The objective of this paper is to investigate the mixture model-based tissue classification algorithm through clinical image datasets for quantification of brain volumes and MS burden.

This paper is organized as follows. Section 2 describes our method for automatic image segmentation, including mixture tissue model and parameter estimation. The method is validated in Section 3 on clinical MR images for segmenting lesions and quantifying brain tissues. Finally, Section 4 presents discussions and conclusions of our approach.

2. METHODS

2.1. Image Segmentation Scheme

MR images were acquired using a 1.5T Phillips Edge whole-body scanner with the body coil as the transmitter and a birdcage head coil as the receiver. The protocols for collecting T_1-weighted and T_2-weighted are shown in Table 1. The field-of-view (FOV) of MR images is 24 cm, resulting 256x256 matrix size in two-dimension (2-D) and 1.5 mm slice thickness. A FLAIR image with CSF saturation was also acquired with the same location and FOV in the session. FLAIR images were acquired to differentiate lesions. The total MRI scanning time can be limited to 40 minutes.

TABLE I. MR IMAGE PROTOCOLS

Image Type	Sequence	FOV (cm)	T_E (ms)	T_R (ms)	Flip angle
T_1	3D SPGR	24	5	30	30°
T_2	3D EXPRESS	24	95	4000	30°

We first applied the Karhunen- Loeve (K-L) Wiener filter for restoration of blurred and noisy images, where MR imaging noise can be assumed as white Gaussion. Because the slice thickness with 1.5 mm is larger than the 2-D pixel size with 0.9375 x 0.9375 mm^2, a Fourier domain interpolation with zero padding was performed in order to construct the isotropic voxels. This step will be necessary for neighborhood selection in the following segmentation model. We further stripped away the skull and scalp of the brain images and extracted the corresponding intra-cranial volume (ICV) from the T_2-weighted images. The flowchart of our segmentation scheme is shown in Fig. 1.

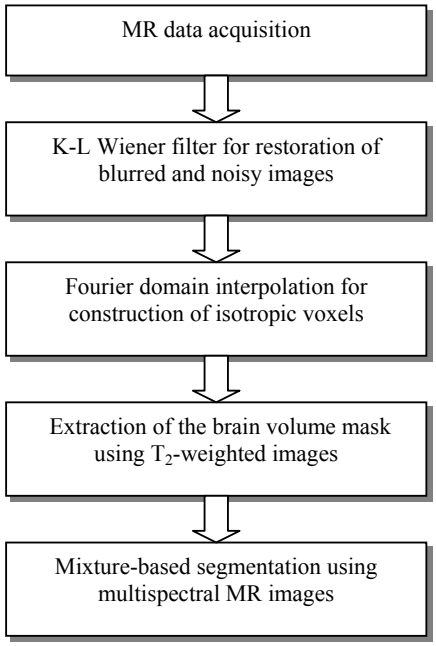

Fig. 1 Flowchart of the mixture-based segmentation scheme.

2.2. Mixture Model-based Tissue Classification

Given the *l* element of multispectral images $Y = \{Y_{il}\}$, *i = 1, 2, ..., I,* over the total number of voxels in the acquired image, let *M* be a set of vectors $M = \{m_1, ..., m_2, ..., m_I\}$, where m_{ik} reflects the fraction of tissue type *k* inside voxel *i*. Each y_{il} follows a random process as

$$y_{il} = \sum_{k=1}^{K} m_{ik}\,\mu_{kl} + n_{il} \qquad (1)$$

where μ_{kl} denotes the mean of class *k*; m_{ik} is the probability of voxel *i* belonging to class *k*; and n_{il} is the Gaussian noise with zero mean and a covariance matrix of Σ_k with diagonal value of σ_{kl} only. Let Φ be a parameter set $\{\mu_{kl}, \sigma_{kl}\}$ associated with the tissue type k.

According to the maximum *a posterior* (MAP) principle, we have

$$P(M,\Phi \mid Y) \propto P(Y \mid M,\Phi)P(M)P(\Phi) \qquad (2)$$

where we assume the mixture *M* and the parameter Φ are conditionally independent.

Given the mixture M and the parameter Φ, the multivariate likelihood function of Y follows a Gaussian distribution. That is,

$$P(Y \mid M,\Phi) = \prod_{i=1}^{I}(\frac{1}{2\pi})^{\frac{L}{2}} \mid \Sigma_k \mid^{\frac{1}{2}} \exp[-\frac{1}{2}(y_i - \mu^T m_i)^T \Sigma_k^{-1}(y_i - \mu^T m_i)] \qquad (3)$$

A Markov random field (MRF) model-based prior [8, 9] is usually constructed to reflect the neighborhood information. In this study, we define the prior distribution of mixture *M* as,

$$P(m_i \mid N_i) = \frac{1}{\alpha}\exp(-\beta\sum_{N_i}\kappa_j \parallel m_i - m_j \parallel) \qquad (4)$$

where N_i denotes the neighborhood of voxel *I*; α is a normalization constant, β is a adjustable parameter controlling the degree of the penalty, and κ_j is a scaling factor. A first-order neighborhood selection is chosen as shown in Fig. 2.

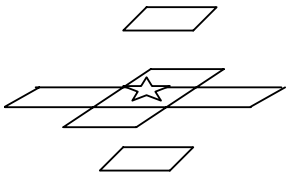

Fig. 2. A description of neighborhood selection in 3-D view. The current voxel is marked by an asterisk.

The expectation maximization (EM) algorithm seeks a solution for the model parameter via the complete sampling density in an iterative manner. The model parameter can be estimated as

$$\mu_{kl}^{(n+1)} = \frac{\sum_i x_{ikl}^{(n)}}{\sum_i m_{ik}} \qquad (5)$$

$$\sigma_{kl}^{(n+1)} = \frac{1}{I}\sum_i \frac{(x_{ikl}^2)^{(n)} - 2m_{ik}\mu_{kl}^{(n+1)}x_{ikl}^{(n)} + (m_{ik}\mu_{kl}^{(n+1)})^2}{m_{ik}} \qquad (6)$$

where x_{ikl} is the contribution of tissue type *k* to the observation of y_{il} and

$$x_{ikl}^{(n)} = m_{ik}\mu_{kl}^{(n)} + \frac{m_{ik}\sigma_{kl}^{(n)}}{\sum_{j=1}^{k} m_{ij}\sigma_{jl}^{(n)}} \cdot (y_{il} - \sum_{j=1}^{K} m_{ij}\mu_{jl}^{(n)}) \quad (7)$$

$$x_{ikl}^{2(n)} = x_{ikl}^{(n)2} + m_{ik}\sigma_{kl}^{(n)} \frac{\sum_{j\neq k}^{K} m_{ij}\sigma_{jl}^{(n)}}{\sum_{j=1}^{K} m_{ij}\sigma_{jl}^{(n)}} \quad (8)$$

3. RESULTS

In order to evaluate the repeatability of our algorithm, two healthy volunteers (age 33), one male and one female, were recruited for validation. For each volunteer, two scans were performed within one-week period. We assumed that the skull and brain volume of healthy volunteers remain the same in a time period and multispectral images are spatially registered. We define the WMF as the fraction of WM relative to ICV, the GMF as the fraction of GM relative to ICV, and the total atrophy (TA) as the fraction of total CSF to ICV. Repeatability was further assessed by the ratio between standard deviation (stdev) and mean of the corresponding measurements. Fig. 3 shows the repeatability test of volunteer studies. The TA measurement can be achieved at a high repeatability which is less than 0.5%. Taking an average of all measurements together, the average repeatability is 1.4%.

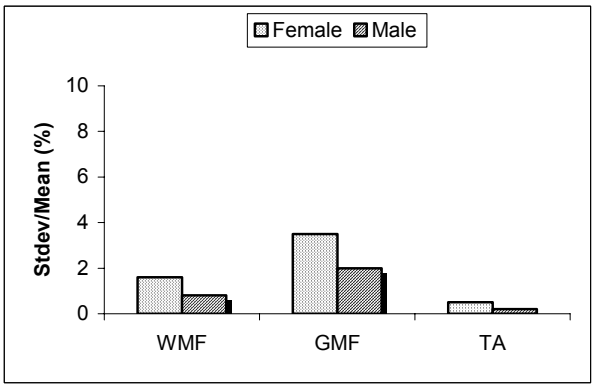

Fig. 3. Repeatability test of volumetric analysis on volunteer studies.

In addition, we also recruited six MS patients (age range 37-54 years old), those were clinically described as relapsing remitting and secondary progressive MS patients. Each patient was scanned twice within a half-year interval, resulting in a total of sixteen datasets. Fig. 3 shows one slice of the T_1-, T_2-weighted, FLAIR images (top), the PV mixture segmentation of WM, GM, and CSF (middle), and the detected lesions (bottom). Table II lists the PV-based quantitative measurements (cm^3) of WM, GM, and CSF. The method was implemented on a HP workstation xw6000/2.4GHz. It took two minutes in average for processing one image size with 256x256x100.

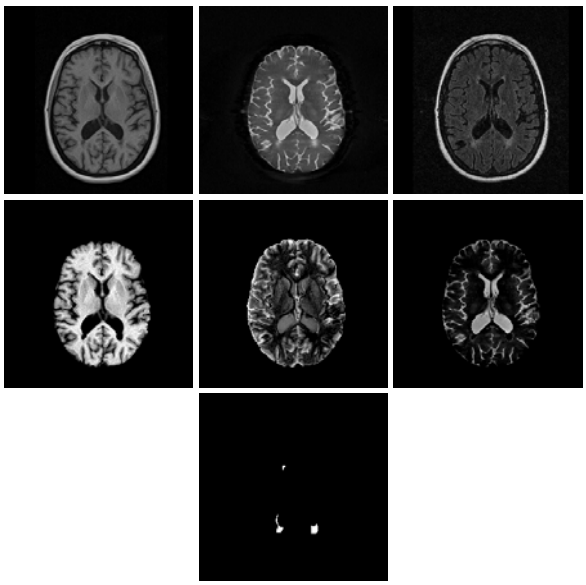

Fig. 4. One slice of the T_1-, T_2-weighted, FLAIR images (top), the PV mixture segmentation of WM, GM, and CSF (middle), and the detected lesions (bottom).

TABLE II. QUANTITATIVE MEASUREMENTS (CM^3) OF WM, GM, AND CSF.

Subjects	Age/Sex	WM	GM	CSF	Lesion
1 (baseline)	41/F	776.1	675.7	117.2	0.8
1 (half year)	41/F	766.6	696.2	95.8	1.1
2 (baseline)	54/F	862.2	686.3	156.9	1.3
2 (half year)	54/F	833.8	707.7	181.3	5.2
3 (baseline)	37/F	797.8	695.8	123.6	3.3
3 (half year)	37/F	825.8	691.1	110.9	3.4
4 (baseline)	43/M	671.5	671.7	63.8	1.5
4 (half year)	43/M	631.7	707.9	102.8	1.1
5 (baseline)	53/F	780.9	575.4	158.1	0.1
5 (half year)	53/F	771.9	568.6	202.9	0.9
6 (baseline)	53/F	740.0	549.5	89.5	12.2
6 (half year)	53/F	713.4	527.4	77.5	15.5

4. DISCUSSION AND CONCLUSIONS

We have developed a fully automatic mixture model-based mixture classification algorithm for segmenting MS lesions and quantifying brain tissues. An initial model parameter estimation is necessary to achieve a robust parameter estimation through the EM algorithm. In this study, we applied a fully automated fast self-adaptive online vector quantization segmentation for estimating the initial model parameters [10].

The performance of algorithm was evaluated by clinical multispectral MR brain image datasets. For healthy volunteer, TA measurement shows high repeatability with less than 0.5%. The average repeatability of all measurements can be achieved at 1.4%. It is noted that some of this variance in repeatability study may be due to the MR scanner. Nevertheless, our results

show high repeatability in volumetric analysis. This indicated that this method is feasible towards quantitative analysis of MS burden. Further research on improving the analysis with inclusion of in-homogeneity correction is under progress [11].

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