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# Multimodal spatial-based segmentation framework for white matter lesions in multi-sequence magnetic resonance images

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ABSTRACT

*Objective:* Multi-sequence magnetic resonance (MR) imaging is a frequently used method for characterising and quantifying white matter (WM) lesions in the human brain. The number and size of lesions are commonly determined to assess the diseases in clinical settings. Accurate WM lesion segmentation is very important for disease diagnosis and progression surveillance. The goal of this paper is to present an approach for improving WM lesion segmentation accuracy.
*Methods:* In this paper, we propose a novel method integrating the multi-sequence and spatial information in a Bayesian framework for WM lesion detection from multi-sequence human brain magnetic resonance images (MRIs). The entire framework is based on a three-step approach: First, a multinomial logistic regression (MLR) algorithm is used to assess the conditional probability distributions of intensities in WM lesions and brain tissues from training data. Second, the spatial information previously given by a Markov random field (MRF) prior is integrated with multimodal information in the Bayesian framework to strengthen the spatial constraint. This step is especially effective when WM lesions have intensity values similar to those of other brain tissues. Finally, a post-processing step based on biological knowledge is used to remove some false positives.
*Results:* Our method is validated using two datasets. The experimental results show that our algorithm agrees well with manual expert labelling and indicate that our multimodal spatial-based method offers a significant advantage over other approaches.
*Conclusions:* A three-step approach for combining multimodal and spatial information is proposed for WM lesion segmentation. The advantages of this approach are discussed, and a practical application to two datasets is presented.



## 1. Introduction

Multiple Sclerosis (MS) is a disease of the central nervous system that involves damage to the myelin sheath enveloping neuronal fibres called axons [1,2]. In clinical research, lesions are typically used as a sign for MS diagnosis [3]. Typical lesions are white matter (WM) lesions, which are visible in magnetic resonance imaging (MRI). Consequently, the ability to detect and quantify lesion volumes and activity in brain magnetic resonance (MR) images is very important in diagnosing and assessing these diseases [4]. Compared with manual segmentation performed by radiologists, computer-assisted lesion segmentation has several advantages, such as consistency in lesion detection, the elimination of subjectivity or intra-rater variability and a reduction in costs associated with manual labelling [5].

Numerous automatic lesion segmentation algorithms have been developed over the past two decades. According to [6], these methods can be categorised into two main groups: Supervised and unsupervised segmentation methods. The supervised approaches [7–14] perform WM lesion segmentation by using a *priori* information or knowledge. Such *a priori* information is generally obtained from an atlas or a training dataset provided by neuroradiologists. In contrast, unsupervised methods [15–30] do not require labelled training data to perform the segmentation. Most of these methods use clustering techniques or outlier detection approaches to separate the WM lesion voxels from normal brain tissue voxels.

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Both supervised and unsupervised methods have their own advantages. It is difficult to determine which type of method is more suitable for WM lesion segmentation. The supervised approaches, which use data given by radiologists to train a classifier to perform the segmentation task, are very popular for lesion extraction. In recent years, this type of method has been widely proposed with the development of new machine learning methods. In Ref. [15], Anbeek et al. used the k-nearest neighbour (KNN) method with prior spatial information and a fuzzy inference system claiming a high segmentation accuracy in comparison to its predecessors. A similar classifier combined with a template-driven segmentation was proposed in Ref. [16] where an atlas-based KNN classifier was first used for brain tissue segmentation followed by a thresholding segmentation approach to automatically determine a threshold to identify WM lesions in the FLAIR images. In this approach, the false positive lesions were subsequently removed to ensure that the lesions are within the white matter. A new parametric method of WM lesion segmentation was introduced in Ref. [17]. A training set was applied to build a vector image joint histogram and an explicit model of the feature vectors was then generated and used to train a naive Bayesian classifier. Finally, the testing samples composed of multi-sequence images were classified by the trained naive Bayesian classifier. Support vector machines (SVMs) have also been used for WM lesion segmentation. In Ref. [21], Lao et al. proposed a computer-assistant segmentation method in which an SVM classifier was first trained on manually delineated WM lesions, and then used to perform voxel-wise segmentation.

Although several machine learning algorithms primarily focus on analysing intensity properties in multi-sequence MR images, spatial information also plays a very important role in WM lesion detection [21,31]. In Ref. [31], the authors proposed a quantitative predictive model of tissue outcome that combines regional imaging features available after onset. The remarkable improvement of prediction results obtained in that work indicates the importance of using region information. Therefore, it is necessary to combine multi-sequence and spatial information to improve WM lesion segmentation accuracy. Here, the multi-sequence information denotes the attribute vector, which is composed of different intensity values in multi-MR sequences. In this paper, we propose a novel method integrating multimodal and spatial information in a Bayesian framework for WM lesion detection by using multi-sequence MR images. The entire framework is based on a three-step approach: (1) Learning: a multinomial logistic regression (MLR) algorithm is used to assess the conditional probability distributions of WM lesion and brain tissues from training data; (2) Segmentation: spatial information previously given by a Markov random field (MRF) is integrated with multi-sequence information in a Bayesian framework to improve the accuracy of lesion segmentation. This step is especially effective when the intensity values of some WM lesions and other tissues are similar. (3) Refinement: a post-processing step based on biological information is used to remove some false positives. Our method presents two contributions: (1) We integrate multi-sequence, spatial and biological information together for WM lesion segmentation, which is beneficial due to the inclusion of both the intensity-spatial information available in the multi-sequence MR data and prior biological knowledge from clinical research. (2) The MRF regularisation term is improved by integrating the edge penalty function into a multilevel logistic (MLL) prior, which aims at preserving edges while performing spatial regularisation. Our method is quantitatively evaluated on two datasets. The first dataset contains 50 subjects, and the ground truth of each case is manually generated by an expert radiologist. The second dataset is obtained from the 2008 MICCAI MS lesion segmentation challenge, which contains 20 training cases and 25 testing cases, acquired from the Children's Hospital Boston (CHB) and University of North Carolina (UNC). The segmentation results of these two datasets demonstrate that our method is stable and offers an effective tool for automatic WM matter lesion segmentation.

## 2. Problem description

MRI provides four sequences as potential candidates for WM lesion segmentation, including T1-weighted (T1-w), T2-weighted (T2-w), PD-weighted (PD-w) and fluid-attenuated inversion recovery (FLAIR) images. The intensities of WM lesions in T1-w images are quite similar to those of grey matter (GM). Therefore, WM lesions are hard to distinguish just by using the intensities in T1-w images. In general, WM lesions intensities are brighter than the surrounding white matter (WM) intensities in T2-w, proton density-weighted (PD-w) and FLAIR images. However, the intensities of WM lesions in T2-w and PD-w images are similar to those of cerebrospinal fluid (CSF), making it difficult to distinguish them. Compared with other three modalities, FLAIR sequence is a more highly sensitive sequence for WM lesion detection. However, FLAIR imaging sequence sometimes introduces some bony and flow artifacts into the image. Therefore, FLAIR sequence is usually used to detect WM lesions together with at least two sequences of T1-w, T2-w and PD-w images. By using different MR sequences for lesion segmentation, the intensity feature space is increased and the difference between brain tissues will be more apparent [3]. In this paper, FLAIR, T1-w and T2-w sequences are used to detect WM lesions. Fig. 1 shows an example of these three modalities of MRI for a subject with WM lesions from ACCORD-MIND dataset viewed best as the bright intensities in the FLAIR image.

Based on previous analysis, we can define some notations that will be used throughout this paper. Let $K \equiv \{1, 2, 3, 4\}$ denote a set of four class labels: WM lesion, WM and GM, and CSF; let $S \equiv \{1, \cdots, n\}$ denotes a set of integers indexing $n$ voxels of an image. And let $x_i = \{x_i^{FL}, x_i^{T1}, x_i^{T2}\} \in R^3$ denote multi-sequence

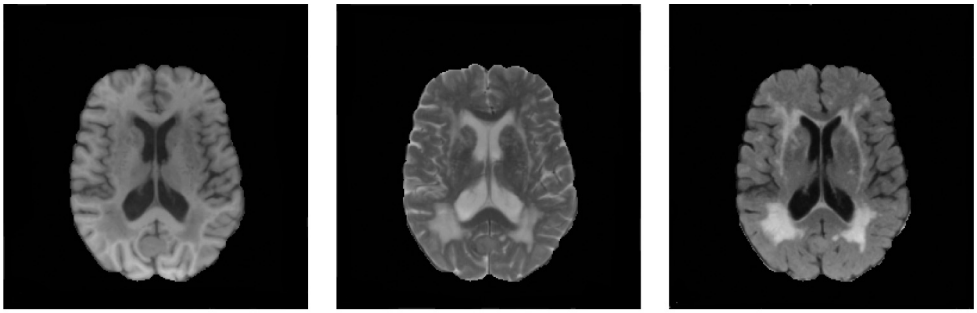


**Fig. 1.** Three different sequences for a selected subject from ACCORD-MIND dataset.