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Quantitative Assessment of MRI Features in Patients with Relapsing-Remitting Multiple Sclerosis

Babak Shekarchi[1], Samaneh Fartook Zadeh[2]*, Azim Mehvar[3] and Mohamad Sabahi[4]

[1]Department of Radiology AJA University of Medical Sciences, Tehran Iran.
[2]Department of Cardiology AJA University of Medical Sciences, Tehran Iran.
[3]Department of Pediatric AJA University of Medical Sciences, Tehran Iran.
[4]Control and Intelligent Processing Center of Excellence, School of Electrical and Computer Engineering, University of Tehran Iran.

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Relapsing-remitting multiple sclerosis (RRMS) is a chronic inflammatory demyelinating disease of the central nervous system. Magnetic Resonance Imaging (MRI) has a remarkable role in the assessment of the disease. The aim of the study is to evaluate MRI features and also to determine linear correlation between them. Nineteen RRMS patients (5 males, 14 females) have been included in this study. Neurological examination using EDSS scores was performed for all patients. Each patient underwent T1, T2, Flair and DWI imaging. Twenty different features were evaluated in the research. Four features obtained directly from images, contain: DWI lesion size, number of DWI lesion, T2 lesion size and number of T2 lesion. In addition, EDSS is considered as one of the features. The volume of the lesion is presented as feature of lesion volume which is obtained by suitable software. In this paper we proposed a new method to calculate the rest of MRI features. The method uses histogram analysis of mean parenchymal diffusivity (MPD) map to calculate some features. The obtained features from the method contain: moment 2 to moment 6 (m2-m6), kurtosis, skewness, peak position (PP), peak height (PH), entropy (ENT), MPD-value, white matter fraction (WMF), gray matter fraction (GMF) and brain parenchymal fraction (BPF). Statistical results show EDSS has significant linear correlation with DWI lesion size, number of DWI lesion size, T2 lesion size and PP ($P<0.05$, $R=[0.5\text{-}0.6]$). All moments, m2-m6, kurtosis, skewness and PH have significant linear correlation together ($P<0.05$, $R=[0.8\text{-}1]$). According to the results, ENT has negative significant correlation with m2-m6, kurtosis, skewness, PH ($P<0.05$, $R=[-0.8\text{-}(-0.6)]$) but has positive significant correlation with MPD-value and BPF ($P<0.05$, $R=0.5$). MPD-value has negative linear correlation with m2-m6, lesion volume and PH ($P<0.05$, $R=[-0.8\text{-}(-0.5)]$). The proposed method and features could be helpful in the analysis of treatment planning protocol and will be beneficial in the study of treatment effects.

Key words: Histogram analysis, MRI features, DWI, RRMS, MS lesion.

One of the most common progressive diseases of central nervous system (CNS) is multiple sclerosis (MS) which is a chronic inflammatory demyelinating disease[1,2]. Myelin sheath is the fast transmission responsible of signals between neurons. Because of the damage of the myelin, MS changes the structure and morphology of the brain. Loss of myelin or demyelination will disrupt the signal transmission of the nervous system. The demyelination causes malfunction of body, such as sever muscle weakness, blurred vision and cognitive difficulties[3]. MS patients are classified in four clinical types[4,5]: relapsing-remitting MS (RRMS), secondary-progressive MS (SPMS), primary-progressive MS (PPMS), relapsing-progressive (RPMS). Each type of MS affects the patients in unique ways. For quantifying

* To whom all correspondence should be addressed.
Tel.: +989123715287;
E-mail : sami.fartook@yahoo.com

disability in MS, expanded disability status scale (EDSS) is commonly used[6].

Magnetic Resonance Imaging (MRI)isan important technique of medical imaging that is a helpful evaluation method of MS. A variety of MRI protocols for improving the performance are used, including MRI-PD weighted (PD-W), MRI-T1 weighted (T1-W), MRI-T2 weighted (T2-W), MRI-diffusion weighted imaging (DWI) and fluid-attenuated inversion recovery (Flair)[7].DWI is a MRI technique that measures tissue water diffusion and also provides information on tissue structure[8]. DWI is a useful technique in discrimination of various pathologies like tumor, ischemia and infection [9]. Microstructures and microdynamic process influence diffusion of water molecules. Moreover, apparent diffusion coefficient (ADC) maps can be derived quantitatively[10]. The water diffusion of MS plaques is restricted and also normal appearing white matter (NAWM) is practically affected in MS patients[11]. In this research we study MRI features that are obtained from different MRI images of the MS patients. We propose a new method to calculate some MRI features that would be effective in the analysis of the treatment effects. In addition, the correlations of the features will be presented to understand their relationships.

MATERIALS AND METHOD

Patients

nineteen patients (5 males, 14 females) with MS have been included in this study. All were diagnosed as RRMS patients. The patients aged between 16 and 45 years (mean 30.8+8.8). Neurological examination was assessed using expanded disability status scale (EDSS) and ranged from 0.5 to 3 (mean 1.320.61).The procedure was approved by our institution review board.

MRI examination protocol

MR images of all the patients were acquired on a same scanner (1.5T General Electric Signa LX, Milwaukee, WI, USA) at Athari MRI Center, Tehran, Iran. For each patient, a T2-W image, T1-W, Flair and DWI image were acquired. T1-W and Flair (TR/TE/TI 10000/120/2500ms) images and also T2-W and DWI (TR/TE/TI 8800/125/2500ms) were obtained as axial plane. DWI (B_{1000}) and T2-W (B_0) images are obtained by Echo Planar Imaging (EPI) with the following parameters: matrix size 128128, FOV 2424, slice thickness 5mm, slice gap 0, number of slice 28 and scan time 1.16min. T1-W and Flair are acquired with the following parameters: matrix size 256192, FOV 2424, slice thickness 4mm, slice gap 0.5mm, number of slice 31 and scan time 4.5min.

MRI Analysis

In this study we investigated some MRI features which are extracted from MRI images, including DWI, T2, T1 and Flair images. Some of the features are obtained using proposed method and others are obtained by an expert and special software. Then linear relationships of the features are evaluated and significant relations are revealed. The proposed method calculates some features using DWI and T2 images. Figure1 shows block diagram of the proposed method.

Segmentation

In the first part of the proposed method T2-W images are segmented to white matter (WM), gray matter (GM) and cerebrospinal fluid (CSF) components. The segmentation procedure is implemented by Statistical Parametric Mapping (SPM) software package (http.//www.fil.ion.ucl.ac.uk/spm/). Then fraction of these components are calculated and used as MRI features[12]. Fractions of WM (WMF), GM (GMF) and brain parenchyma (BPF) are calculated as follows: WMF=WM/(WM+GM+CSF), GMF=GM/(WM+GM+CSF), BPF=(WM+GM)/(WM+GM+CSF). The results of the segmentation are presented in the figure2.

Parenchymal mask

In order to restrict the processing on brain parenchyma area, those voxels that belong to CSF and skull should be removed. The brain parenchyma area is segmented by implementation of thresholding method on BPF map. Appling a threshold value for segmentation of an imageobject is a controversial subject[7,13]. We chose here a threshold value of 0.1 to segment brain parenchyma area in BPF map as brain parenchymal mask (BPM). The obtained result is also represented in figure2.

Registration and mean diffusivity

To obtain mean diffusivity map (MDM) of the whole brain, following calculation should be performed.

$$MDM=-\ln (rDWI/T2)/b \quad ...(1)$$

where b=1000s/mm^2. This equation is based on voxel-by-voxel analysis. So, first of all DWI image should be registered to T2-W image where rDWI is registered DWI image. The registration procedure was implemented by SPM software package and also mutual information function and trilinear method were used as objective function and interpolation method, respectively. Then, the previously created BPM is multiplied to the MDM to create mean parenchymal diffusivity (MPD) map. To obtain only those voxel within parenchyma tissue, the resulting MPDshould be eroded (eMPD) using a circular structuring element by one voxel. The obtained results are presented in Fig. 3.

Histogram analysis

Histogram analysis of the eroded mean parenchymal diffusivity (eMPD) is then performed for each patient using the bin width of 1% of the maximum mean parenchyma diffusivity. The normalized histogram of the eMPD map of theRRMS patient is shown in figure4.

Features of peak height (PH), peak position (PP), MPD-value, entropy (ENT), kurtosis,moment 2-6 and skewness are obtained using histogram analysis. In statistics, kurtosis[14] is width of peak measure of the histogram and is commonly defined as:

$$\text{Kurtosis}=\sum_{i=1}^{N}(x_i-\bar{x})^4/((N-1)\sigma^4) \quad ...(2)$$

whereN is number of bins. x_i, $\bar{x}$ and σ are the ith value, mean and standard deviation of the histogram, respectively.In statistics, skewness[14] is an asymmetry measure of the histogram and is commonly defined as:

$$\text{Skewness}=\sum_{i=1}^{N}(x_i-\bar{x})^3/((N-1)\sigma^3) \quad ...(3)$$

Moments about the mean are central moments. The kth central moment[14] of a random variable X is defined as:

$$M_k=E(X-E(X))^k \quad ...(4)$$

where E is mathematical expectation operator. Here, we chose 2th moment to 6th moment. Another important feature which we used in this work is ENT. The ENT is calculated as:

$$\text{ENT}=\sum_i(-p_i)(\log p_i) \quad ...(5)$$

where p_i isthe probability of intensity i and is calculated as follows:

$$Pi=\text{num.voxels (i)/num.voxels (entire image)} \quad ...(6)$$

The feature of ENT is a measure of disorganization of the histogram that any abnormality such as MS lesions can influence it[12]. The obtained features from the proposed method are described above. In addition to the described features, in this study we used other important features which contain: EDSS, DWI lesion size, number of DWI lesions, T2-W lesion size, and number of T2-W lesions that are determined by an expert. Lesion volume is another feature that is determined by SPM software package. The lesion volume shows the MS lesions volume of the Flair image that is registered to T1-W image.

Statistical analysis

Linear correlation was used to investigate existence of linear relationship between the features without any complicated model to our data. Linear correlation quantifies the linear relationship of two features that ranges from -1 to +1. Values close to +1 represent a positive linear relationship and values close to -1 represent a negative linear relationship and values equal to or close to 0 propose there is no linear relation. P-value gives significance of correlation coefficient and p-value<0.05 is statistically significant.

Table 1. MRI features in RRMS patients. Values are presented as: mean (S.D.)

# of DWI Lesion 13.6(10.2)	Skewness 3.3(0.4)	MPD-value8.7(3) $\times 10^{-4}$(mm^2/s)	m2 5.4(1.5) $\times 10^{-4}$
DWI lesion size 45.6(56.3)	Kurtosis 13.9(2.9)	ENT 4.1(0.3)	m3 4.5(2.4)10^{-5}
# of T2 Lesion 49.4(21.5)	BPF 0.68(0.1)	EDSS 1.32(0.6)	m4 4.9(3.6)10^{-6}
T2 Lesion Size 123.3(131.8)	GMF 0.37(0.1)	PH 0.12(0.03)	m5 5.7(5.3)10^{-7}
Lesion volume 1.5(0.7)(ml)	WMF 0.31(0.1)	PP 42.6(8.6)	m6 7.1(7.9)10^{-8}

RESULTS

In this study twenty MRI features from 19 RRMS patients were assessed using statistical analysis. The obtained MRI features are reported in table1. According to the results, feature of DWI lesion size has significant linear correlation with EDSS, number of DWI lesion and T2 lesion size (P<0.05, R=0.6). Number of DWI lesion has significant correlation with EDSS (P<0.05, R=0.6). T2 lesion size has significant correlation with EDSS and WMF (P<0.05, R=0.5). EDSS is linearly correlated with PP (P=0.02, R=0.5). T2 lesion size has significant correlation with WMF (P=0.04, R=0.5). All moments, m2-m6, kurtosis, skewness and PH that are obtained from histogram analysis of mean parenchymal diffusivity map, have significant linear correlation together (P<0.05, R=[0.8-1]). The results show that ENT has negative linear correlation with all moments, m2-m6, kurtosis, skewness and PH (P<0.05,R=[-0.8-(-0.6)]). MPD-value has negative linear correlation with all moments, m2-m6, lesion

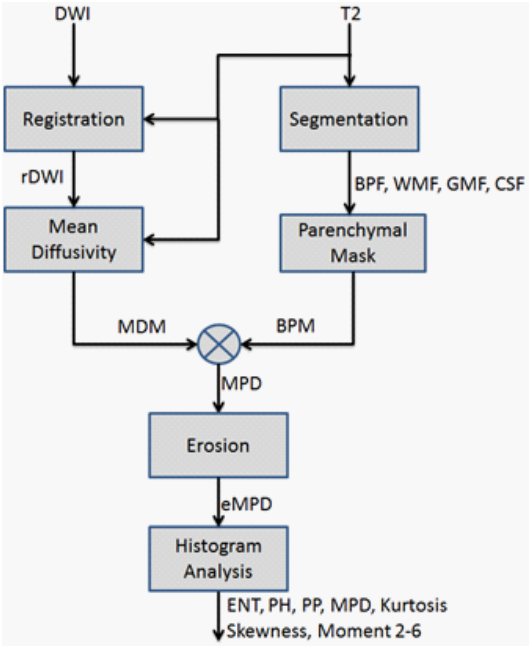

Fig. 1. Block diagram of the proposed method

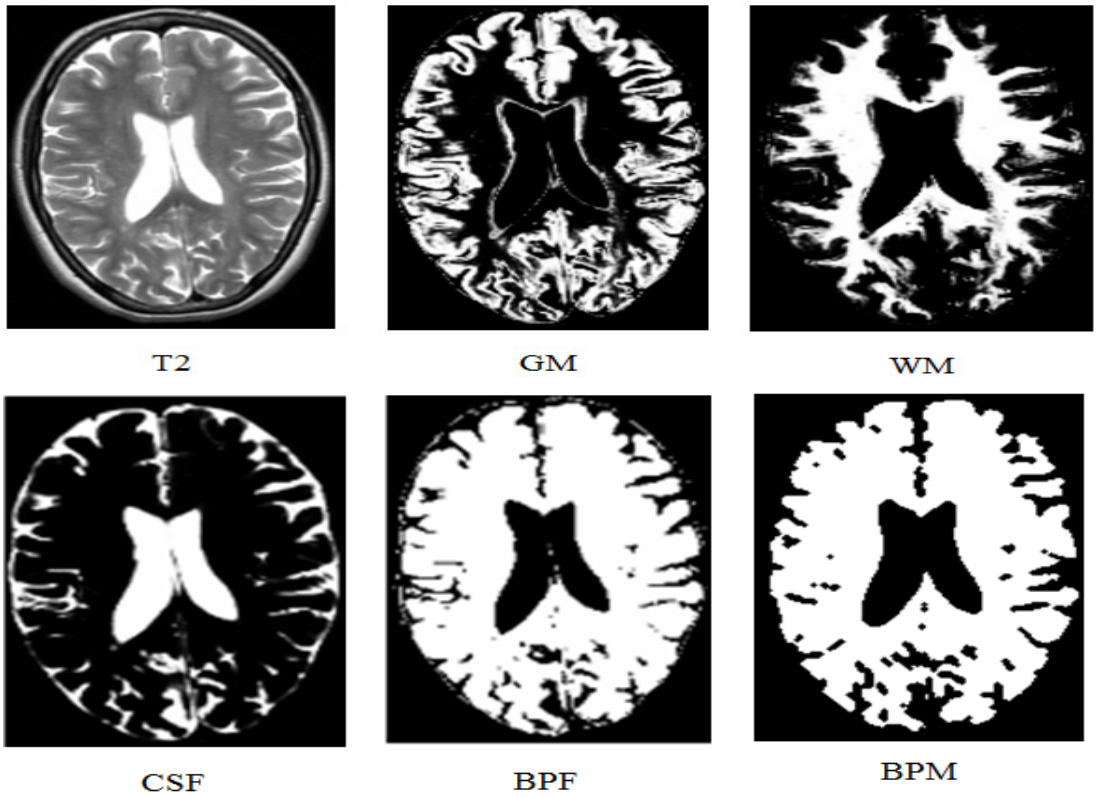

Fig. 2. Segmentation results and Brain Parenchymal Mask (BPM)

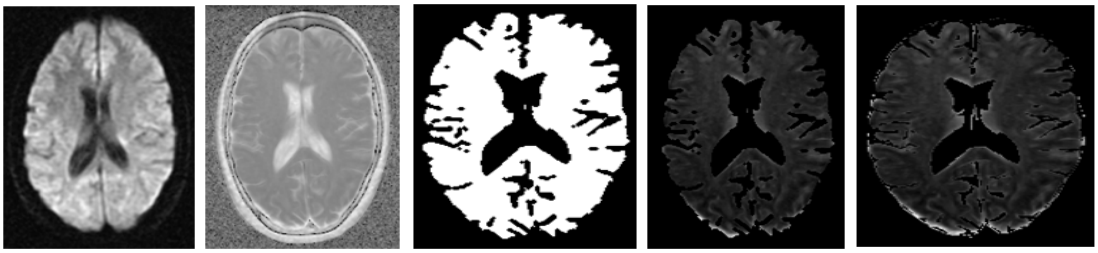

Fig. 3. Registration result and mean diffusivity maps. rDWI is registered DWI to T2 image. BPM is applied to MDM to crate MPD

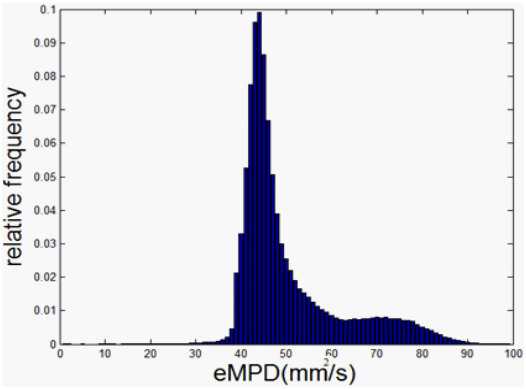

Fig. 4. Normalized histogram of the eMPD map of the RRMS patient

volume and PH (P<0.05, R=[-0.8-(-0.5)]) but has positive linear correlation with ENT (P=0.03, R=0.5). PP shows linear correlation with m2, m3, m4, kurtosis, skewness and PH (R<0.05, R=[0.5-0.6]).According to results, BPF has linear correlation with WMF, GMF and ENT (P<0.05, R=[0.5-0.7]).All of the possible relationships were investigated between different features but just the mentioned relations had significant correlation and others were not significant.

CONCLUSION

In this study, we investigated MRI images of RRMS patients. First of all, twenty MRI features were extracted. Some of the features were obtained using the proposed method and others were directly obtained from MRI images. Then, existence of linear correlation between the features was assessed. The results showed significant positive or negative correlation between some features. The results of our study make prominent the validity of histogram based features when compared to other MRI features of RRMS patients as well as their relationship together. In addition the results highlight the correlation of EDSS with T2, diffusion weighted images of MS lesions and peak position of the histogram. The proposed histogram based method provides further knowledge to the visual assessment of the images. The proposed method and features could be clinically helpful in analysis of treatment effect and also in follow up of disease activity.

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