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Original Article

The evaluation of the optic nerve in multiple sclerosis using MRI histogram analysis

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Abstract

Aim: Comparison of optic nerve with healthy subjects by MRI histogram analysis in patients with multiple sclerosis (MS).

Material and Methods: A total of 78 patients with age range of 39 ms (18-54), 27 females, 12 males and 39 healthy age range (19-54), 26 females and 13 males (control group) were included in the study. The right optic nerve in the MS and control group was included in the study. ROI was placed on the optic nerve from the images and numerical data were obtained by histogram analysis. Numerical data were loaded into MATLAB program.

Results: Mean, standard deviation, minimum, maximum, median, variance and entropy values were significantly higher in MS patients than control group($p<0.05$). In MS patients, changes in tissue histology were detected in the optic nerve compared to healthy individuals by mri histogram analysis without a visual change in the optic nerve.

Conclusion: We think that the diagnosis of optic neuritis, which has an important role in disability in MS patients, will improve the quality of life of patients with early diagnosis and treatment by MRI histogram analysis of the optic nerve.

Keywords: Multiple sclerosis; histogram analysis; MRI; optic nerve

INTRODUCTION

Multiple sclerosis (MS) is an autoimmune and chronic neurodegenerative disease characterized by inflammation in the central nervous system, demyelination and axonal degeneration (1). Vision disorders are one of the most common symptoms of MS. It may also be one of the main symptoms of optic neuritis in MS patients. From a radiological perspective, conventional and non-conventional MRI techniques are often used in the diagnosis of optic neuritis. Contrast agents are used for diagnosis in conventional MRI (2,3).

Histogram analysis is now a widely used tissue analysis method and has also been a popular method in clinical practice in recent years. It is usually used as a guide for diagnosis in interstitial lung disease patients, definition of prognostic factors, characterization of tumors and radiotherapy treatment (4).

Tissue analysis is a method that usually evaluates signalsand gives information regarding the location and density of the pixels and gray matter. Additionally, each pixel in a digital image corresponds to a density level for different tones of gray. Objects shown in an image characterizing the main structure of a tissue are actually mathematical parameters calculated using pixel distribution (4,5).

Entropy is one of the commonly used parameters in tissue analysis measurement methods. It is a tissue analysis method that characterizes tissue heterogeneity by calculating tissue density or the distribution of irregular tissues within an area or volume. It is a parameter that indicates irregularities in tissues. This method was successfully applied to the classification of pathological tissues in liver, thyroid, breasts, kidneys, prostate, heart, brain and lungs (4,6,7).

Thanks to the histogram analysis, which is a sub-group of artificial intelligence in today's medical community, the present study aims to affect the optic nerve in multiple sclerosis without using contrast agent in MRI.

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MATERIAL and METHODS

The present study was retrospectively designed, and an ethical approval(session :2019/21 ,decision no:02) was obtained from our hospital.

A total of 78 patients with age range of 39 ms (18-54), 27 females, 12 males and 39 healthy age range (19-54), 26 females and 13 males (control group) were included in the study. Patients who suffered from Behçet's disease, diabetes mellitus, glaucoma, who underwent an ophthalmic surgery and who had orbital mass were excluded from the study. Patients' unilateral optic nerves were included in the study. In addition, right optic nerves were examined in patient and control group for better standardization. The examination was performed by a radiologist usingROI from coronal T2 weighted sequences on the optic nerve in brain MRI images(Workstation: 27 inch iMac computer, Apple Inc. Cupertino, 88 California, USA).

Image Evaluation and Analysis

ROI placement (Figure 1)on the optic nerve (surface area: 11.5-13mm2) for histogram analysis. The images were enlarged as much as possible, and a line drawing tool was used to make boundaries clear. In addition, total 115-120 pixel images in ROI were transferred to an XML (ExtensibleMarkum Language) file. MATLAB version 2009b (MatrixLaboratory, MathworksInc, Natick, ABD) was used for histogram analysis on XML files. Mean, standard deviation (SD), minimum, maximum, median, variance, entropy (irregularity), uniformity (inhomogeneity), size L%, M% and U%, skewness and kurtosis parameters were analyzed in the histogram analysis.

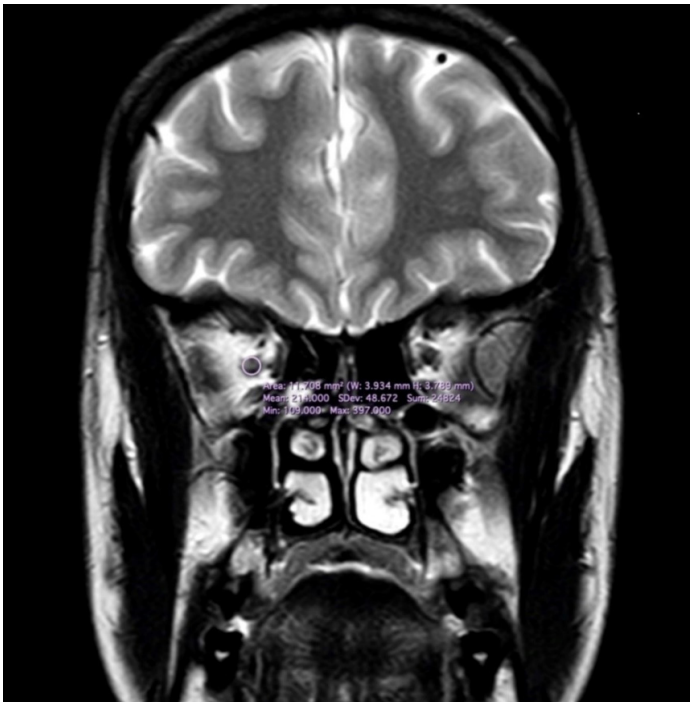

Figure 1. Optic nerve ROI placement in coronal T2-weighted MR images

A chi-square and student's T test were used to compare patient and control group. Additionally, ROC analysis was used to find threshold values, and the level of diagnostic efficacy of these parameters in differentiating optic nerves in MS patients and normal individuals was determined.

MRI Examination

The MRI examinations were performed using 1.5T MRI with a cranial coil (Philips Ingenia 1.5T, Eindhoven 2015, the Netherlands); T2-weighted images in the coronal plane (repetition time [milliseconds]/time echo [milliseconds]: 4833/100, field of view: 220 × 183 mm and matrix 356 × 209 mm) were obtained using 5-mm slice thickness. A 1-mm intersection gap and 24 coronal sections were obtained as well.

RESULTS

Mean, standard deviation, minimum, maximum, median, variance and entropy values in MS patients were found to be significantly higher compared to the control group($p<0.05$)Table 1. A ROC curve analysis was performed for mean value, and the area under the curve (AUC) was 0.808. When the threshold value is selected as 252.95, differentiation can be performed with a sensitivity of 74.4% and a specificity of 71.8% (Figure 2).

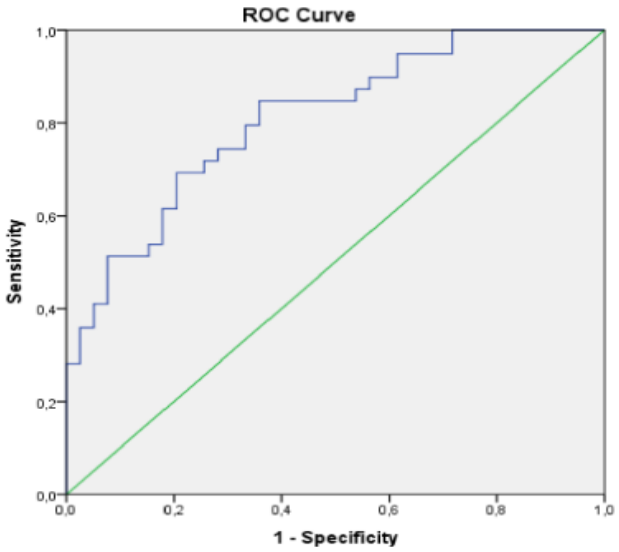

Figure 2. ROC analysis of mean

AUC values for other parameters are given in Table 2. When the threshold value for SD is selected as 61.53,differentiation can be performed with a sensitivity and specificity of 74.4%. Similarly, when the threshold value for the maximum is selected as 413.50, differentiation can be performed with a sensitivity of 71.8% and a specificity of 76.9%. Finally, when the threshold value for the variance is selected as 3785.92,differentiation can be performed with a sensitivity and specificity of 74.4%.Sensitivity and specificity values for other threshold values such as entropy, minimum and median parameters were not found to be statistically significant.

Table 1. The analysis of histogram parameters of the normal and Multiple sclerosis (MS)side *Statistically significant difference, p<0.05

	MS(n=39) mean±SD	Control(n=39) mean±SD	p
Mean*	317.92±139.87	232.20±40.78	0.000
Standart Deviation*	71.24±31.90	47.73±16.41	0.000
Minimum*	170.28±111.64	126.38±54.13	0.030
Maximum*	499.44±219.03	363.79±73.84	0.000
Median*	314.92±138.24	232.16±39.61	0.001
Variance*	6067.25±7213.48	2540.84±1712.29	0.004
Entropy*	6.23±0.15	6.12±0.18	0.004
Size%L	14.95±3.31	15.56±3.08	0.407
Size%U	15.67±2.63	14.61±2.80	0.088
Size%M	69.36±4.56	69.82±4.86	0.668
Kurtosis	3.02±0.74	3.32±1.17	0.181
Skewness	0.14±0.55	0.09±0.56	0.721
Uniformity	0.25±0.07	0.25±0.07	0.813

Table 2. The statistically significant histogram analysis parameters in patients with multiple sclerosis, area under the curve, threshold value, sensitivity and specificity values

	AUC	Threshold	Sensitivity	Specificity
Mean	0.808	252.95	74.4	71.8
Standard Deviation	0.786	61.53	74.4	74.4
Minimum	0.614	124.00	.641	56.4
Maximum	0.805	413.50	71.8	76.9
Median	0.789	251.50	71.8	66.7
Variance	0.786	3785.92	74.4	74.4
Entropy	0.674	6.17	71.8	56.4

DISCUSSION

In today's scientific community, histogram analysis is considered as a popular sub-group of artificial intelligence applications. In this respect, it can be stated that the present study is the first study to have benefited from histogram analysis on optic nerves in MS patients.

Tissue analysis is critical in cases where changes cannot be detected through analyzing an image. For instance, tissues of an anatomical structure may undergo some changes, which can be detected through the statistical analysis of pixel distribution in an image of these issues instead of a visual analysis (7). Many studies in the existing literature use MRI images for histogram analysis due to its high resolution (7). Therefore, the present study also benefits from MRI images for histogram analysis.

The fields of application for histogram analysis in neuroradiology are the differentiation of brain tumors and normal parenchyma, typology and classification of tumors, diagnosis of focal cortical dysplasia and hippocampal sclerosis in epilepsy, MS, acute ischemic stroke, Alzheimer and migraine (8-11).

Mathias et al. applied tissue analysis on spinal MRI in order to measure pathological changes in spinal cord in MS patients, and detected tissue differences between normal individuals and MS patients before spinal cord atrophy was visually detected (12).

J. Zang et al. performed tissue analysis on MS lesion, normal white matter and normal-appearing white matter in MS patients and healthy individuals, and indicated some changes in histological tissue before a visual lesion appeared on white matter in a brain MRI(13).

O Yu et al. differentiated active and non-active plaques without using any contrast agent in a MRI tissue analysis. It is a significant development for MS, which is a chronic disease, to detect active plaques without using any contrast agents (14).

Optic neuritis is the first clinical symptom in nearly 20% of MS patients, and thus it is a crucial symptom in terms of classifying MS patients' disability levels (15). In general, conventional and non-conventional MRI is used in the diagnosis of optic neuritis in patients, and contrast agents are often used in conventional MRI. The use of contrast agents is an invasive method for patients. Hongjan Liu et al. performed an MRI histogram analysis on optic neuritis patients and healthy individuals, and detected significant differences in the optic nerve between patients and healthy individuals without using contrast agent (1,7,16,17). The present study, similarly, detected optic nerve changes in MS patients and healthy individuals using MRI histogram analysis without any contrast agents.

The common point of the above-mentioned studies in the literature is the use of histogram analysis for the diagnosis of pathological tissues without needing any other visual pathology. In a similar vein, the present study also indicated that tissue density in MS patients' optic nerves differed from those in healthy individuals thanks to the histogram analysis although optic nerves were not considered as visually pathological. In other words, it was proven without using any visual pathology that the optic nerve was affected.

LIMITATIONS

Since our study was retrospective, we did not know about optic neuritis clinic.

CONCLUSION

It can be concluded in the present study that early diagnosis of optic neuritis, which plays a vital role in disabilities in MS patients, through an MRI histogram analysis on the optic nerve and starting an immediate treatment will definitely improve MS patients' life quality.

Competing interests: The authors declare that they have no competing interest.
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