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Comparison of visual and automatic quantitative measurement results on 3D volumetric mri in multiple sclerosis patients

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Abstract

Multiple sclerosis (MS) is a chronic, demyelinating disease in which magnetic resonance imaging (MRI) is frequently used in the diagnosis and treatment process. Atrophy and plaque counting in the brain can be measured quantitatively with 3-dimensional (3D) MRI examinations. This study aims to determine the results of automatic, quantitative measurements of 3D volumetric MRIs in relapsing-remitting MS (RRMS) patients, to compare the consistency with the visual, semi-quantitative evaluation results made by the radiologists. 46 patients who were diagnosed with RRMS between 01/03/2018 and 31/12/2020 in the neurology outpatient clinic of our hospital, were clinically stable in their follow-up, had at least two 3D MRIs without artifacts constituted the study group. A neuroradiologist, a radiologist experienced in neuroradiology, and VolBrain software evaluated the patients' brain volumes, plaque numbers, and differences in follow-up MRIs. The mean age of 21 female and 25 male patients was 40.4 ± 8.8 years; the mean total brain volume was 1127 ± 137.63 mm3. A high level of agreement was found between the radiologists in terms of whole-brain volume differences between the two MRIs, which was not statistically significant (95.7%; K = -0.002; p = 0.88). There was no agreement between VolBrain and radiologists (K = -0.043; p = 0.333). Regarding the plaque number analysis; a high level and statistically significant agreement among radiologists (87%; K = 0.665; p <0.001); low-moderate level of agreement (56.5 / 60.9%; K = 0.182 / 0.282; p = 0.047 / 0.003) between VolBrain and radiologists was found. While there was no significant agreement in volume measurements between the VolBrain software and radiologists, varying degrees of the agreement were detected in the plaque counts. Software that can make an automatic, quantitative, and rapid evaluation of MS disease is still being developed.

Keywords: Multiple sclerosis, MRI, volumetric, atrophy, plaque

Introduction

Multiple sclerosis (MS); is a chronic disease characterized by demyelination, inflammation, and neurodegeneration [1]. Relapsing-remitting MS (RRMS) is the most common MS subtype. The disease shows a progressive course over time with relapse and recovery periods [2]. In this MS subtype, radiological imaging is of particular importance. Revealing evidence of active diseases, such as a new MS plaque and/or contrast enhancement on magnetic resonance imaging (MRI) during episodes is important for the diagnosis and treatment process [3].

On the other hand, it is known that diffuse demyelination and axonal damage in MS patients permanently cause both regional and general brain volume loss. The relationship between brain atrophy and clinical parameters in MS patients has been the subject of many studies in recent years [4]. However, many new methods have been developed to measure more accurately brain volume with MRI. Many automatic and semi-automatic software can calculate the brain volume in mm3 thanks to the 3-dimensional (3D) brain MR imaging performed with 1-millimeter thick sections [5]. This study aims to determine the automatic, quantitative measurement results of 3D volumetric MRIs acquired in the follow-up of RRMS patients; to compare the consistency with the visual, semi-quantitative evaluation made by the radiologists.

Material and Methods

61 patients who were diagnosed with RRMS in our hospital's neurology outpatient clinic between 01/03/2018 and 31/12/2020 and who were clinically stable in their follow-up were included

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in the study. 12 patients who do not have at least two consecutive brain MRIs in the MS protocol in the specified date range and 3 patients who could not be further analyzed due to the presence of artifacts in their images were excluded from the study. This study has been approved by the institutional ethics committee.

MRI images of the patients were obtained with a 1.5T MRI device (Magnetom AERA, Siemens, Erlangen, German). MRI was performed in all patients with the routine thin-slice MS protocol used in our radiology clinic. Along with the multiplanar PSIR, T1A, T2A sequences; FLAIR, precontrast, and postcontrast T1W images were obtained with a 1 mm slice thickness covering the whole brain. 3D T1A and 3D FLAIR images were then converted from standard Dicom format to NIfTI format and anonymized with appropriate software (dcm2nii, https://www.nitrc.org/plugins/mwiki /index.php/dcm2nii: MainPage) [6]. Radiological analysis was performed by a free, automated, online MRI brain volumetry software (VolBrain, https://volbrain.upv.es/) [7]. Brain volumes were measured with VolBrain 1.0 interface, and plaque numbers were counted with LesionBrain 1.0 interface (Figure-1).

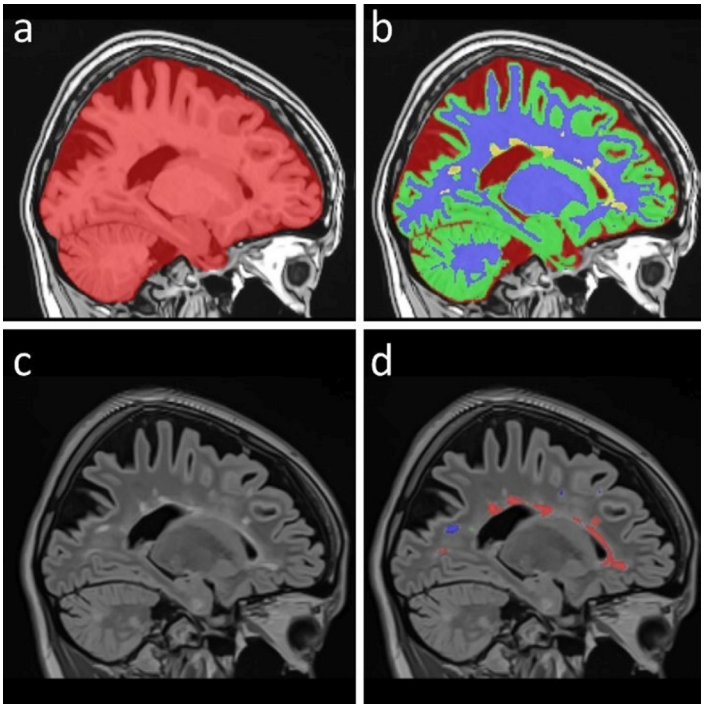

Figure 1. Analysis of 3D MR images with VolBrain software. Intracranial cavity extraction from 3D T1W images (a), gray/white matter discrimination (b), 3D FLAIR image (c), and detection of MS plaques (d).

A neuroradiologist and a radiologist with 22 years of experience in neuroradiology separately evaluated images of all patients. Changes in cerebral volume, cerebellar volume, and several plaques were analyzed. Results were categorized into stable, increased, and decreased groups. On the other hand, cut-off values were chosen as "0.5%" for volume changes and "3" for plaque number changes to further categorize the VolBrain outcomes [8]. Differences smaller than these values were included in the stable category. The compatibility of the results of the two radiologists and the software was evaluated statistically.

SPSS 22 package program was used for statistical analysis. The numerical variables in the study were mean, median, standard deviation, the smallest-largest value; categorical variables were presented as numbers, percentages. Interobserver agreement of two radiologists and VolBrain program in detecting changes in plaque numbers and volumes were evaluated with Kappa test. Statistical significance was accepted for p values of < 0.05.

Results

A total of 46 RRMS patients were enrolled. Twenty-one of the patients were female (45.6%) and 25 were male (54.4%). The mean age of the patients was 40.4 ± 8.8 years; the average time between MRI scans was calculated as 10 ± 3 months. The mean total brain volume of women was 1117.3 ± 137.2 mm3 whereas 1140 ± 140.4 mm3 in men. No statistically significant difference was found between total brain volumes according to gender ($p = 0.583$). There was a low level of negative correlation between patient age and total brain volume, but this relationship was not statistically significant ($r = -0.020$; $p = 0.897$).

According to the automatic brain volumetry results, there was more than a 0.5% decrease in difference in the cerebral volume of 22 patients, in the cerebellar volume of 18 patients, and the total brain volume of 22 patients. Regarding all patients, an average of 0.88% reduction in total brain volume was found. The cerebral, cerebellar, and total brain volume averages of the patients in both brain MRIs and the differences between them are summarized in (Table 1.) In the visual analysis of radiologists, the first radiologist found a decrease in the cerebral volume of 1 patient, and the second radiologist found a decrease in the cerebellar volume of 1 patient. Both radiologists detected a decrease in total brain volume in one patient each. In the evaluation of interobserver agreement, a 95.7% agreement was found between both radiologists in the whole brain volume. An agreement varying between 50-60.9% was observed between the automatic measurement software and the radiologists. However, these results were not statistically significant due to the small sample size ($K < 0$; $p > 0.05$). The consistency between the volumetric analysis results of the radiologists and the automated volumetry software is presented in (Table 2.)

The plaque number analysis with automated volumetry software has shown an average of 35.02 plaques in the first, and an average of 35.13 plaques in the second MRI in the whole brain. A mean of 11.21% increase in the total number of plaques was found in all patients (Table 3). A total number of plaques has increased in the follow-up of 7 patients and a decrease was observed in the follow-up of 14. In the infratentorial area, no plaque was detected in any patient in both MRIs in the cerebellum, one plaque was detected in the medulla in 3 patients each. The radiologists visually evaluated the total number of plaques in the whole brain. The first radiologist detected an increase in the number of plaques in 7 patients and a decrease in 3 patients; the second radiologist found an increase in the number of plaques in 8 patients and a decrease in 4 patients. There was 87% agreement between both radiologists. 56.5% and 60.9% agreement were found between VolBrain software and radiologists. In the plaque category; a statistically significant and high level of agreement was found among radiologists ($K = 0.665$ $p < 0.001$); a low-medium level of agreement was found between the VolBrain software and radiologists ($K = 0.182 / 0.282$; $p = 0.047 / 0.003$). The agreement between the radiologists and the automatic volumetry software in the plaque number analysis is presented in (Table 3.)

Table 1. Automated Whole Brain Volumetry Results

	1st MRI		2nd MRI		Difference (%)
Volume (cm³)	**Average**	**Standart deviation**	**Average**	**Standart deviation**	
Cerebrum	999.87	127.28	987.57	118.07	0.96
Cerebellum	127.78	15.18	127.62	15.10	0.08
Whole Brain	1127.65	137.63	1115.19	128.14	0.88

Table 2. The consistency between analysis results of the radiologists and the automated volumetry software

	Cerebral volume % K (p)	Cerebellar volume % K (p)	Whole brain volume % K (p)	Plaque number % K (p)
R1-R2	97.83 0 (-)	97.83 0 (-)	95.65 -0.022 (0.88)	86.96 0.665 (<0.001)
R1-Vb	50.00 -0.043 (0.333)	60.87 0 (-)	50.00 -0.043 (0.333)	56.52 0.182 (0.047)
R2-Vb	52.17 0 (-)	58.70 -0.043 (0.418)	50.00 -0.043 (0.333)	60.87 0.282 (0.003)

R: radiologist; Vb: volBrain

Tablo 3. Automated plaque count results

Average plaque number	1st MRI	2nd MRI	Difference (%)
Periventricular	10.54	11.35	15.44
Juxtacortical	16.35	15.15	38.00
Deep White Matter	8.07	8.59	16.97
Cerebellum	0.00	0.00	0
Medulla	0.07	0.04	<0.1
Supratentorial	34.96	35.09	11.24
Infratentorial	0.07	0.04	<0.1
Whole brain	35.02	35.13	11.21

Discussion

Neuroradiological imaging is essential in patients with multiple sclerosis. Brain atrophy and the number of plaques are interpreted by comparing them with previous examinations in each new MRI, and the findings obtained to make a significant contribution to the management of the disease. In-vivo quantitative measurement of brain atrophy is an independent marker of the clinical course of the disease [4-9]. However, the lack of a standard measurement method affects the results. On the other hand, changes in plaque count are also associated with disease activity. In this study, it was investigated whether there was a difference between experienced radiologists in the field of neuroradiology and an automated volumetry software (VolBrain) in the measurement of the changes in the number of plaques and brain volumes during the follow-up of RRMS patients. According to our findings, while no significant difference was found between radiologists, significant differences were detected between the VolBrain software and radiologists.

Multiple sclerosis disease causes significant volume losses in the gray and white matter of the cerebrum and cerebellum as the disease progresses. This loss is directly related to the clinical process of the patient. Although automatic volumetry software facilitates these measurements, differences may occur between different software and between radiologists and software results [7]. At this point, problems such as the quality of the obtained MRI images, artifacts, and standardization of the acquisition technique come to the fore. Hannoun et al. found that differences occur in the thalamus and whole-brain segmentation with the measurements made from post-contrast sequences [10]. In the multicenter study of Sitter et al, it was found that white matter lesions and general brain atrophy in MS affect gray matter volumetry results; thus, significant volume differences occur between software [11]. Guo et al. emphasized the importance of performing MRI with the same device for the consistency of automatic volumetry results [12]. In our study, all MRI acquisitions were performed with the same MRI device, and no significant difference was found between radiologists in cerebral, cerebellar, and all brain volumes; besides, a statistically significant difference was found between the radiologists and the automated measurement software. However, it is noteworthy that the volume differences between MRIs were more than 10% in only three patients. De Stefani et al. found that there is an average volume loss of more than 0.5% per year in MS patients [8]. The 10-month average interval between two MRI scans in our study might have caused relatively smaller volume changes than radiologists can visually analyze. Brune et al. support our claim by their comment: the annual difference in brain atrophy is smaller than the neuroradiologists can detect [13].

In multiple sclerosis disease, plaques can be seen in any part of the central nervous system. Detection of plaques with MRI is among the McDonald criteria used in the diagnosis of the disease [14]. There are many studies in the literature showing the correlation between MS plaques and clinical parameters and cognitive outcomes

[15–17]. In our study, differences were detected between the automatic plaque count results and radiologists. Very few plaques could be detected by automatic measurement, specifically in the infratentorial area. Significant differences were found between radiologists and software in terms of plaque number changes. Brune et al. stated that the results of automatic measurement software have a 62.5% accuracy in the evaluation of plate numbers when compared with the gold-standard neuroradiologists [13]. In our study, an average of 58.7% agreement was found between VolBrain and radiologists, similarly. In the study of Yablonskiy et al., it was mentioned that the gray/white matter contrast ratio in MS differs with iron accumulation and/or cellular damage [18]. This may result in differences in automated measurement results and thus inaccuracies in plaque counts. Also, the inclusion of all T2 hyperintense lesions non-specifically in the plaque count and the exclusion of T1 hypointense chronic MS plaques are other problems that such software has not yet overcome [19].

VolBrain software can measure intracranial cavity, white/gray matter and CSF volumes, cerebrum, cerebellum and brainstem volumes, lateral ventricles, and subcortical gray matter volumes automatically. MS plaques in periventricular, subcortical, deep white matter regions, cerebellum, and medulla were counted. However, patient images must be downloaded, converted to the appropriate file format, anonymized, and must be uploaded to the software's website to make these measurements. After these steps, an average of 10-30 minutes of additional time is required for the system to generate reports. These requirements make it difficult to use the system, especially in outpatient clinics and radiology report rooms where workflow is intense. However, such software can be used more easily if it is integrated into hospital information systems.

There are some limitations related to this study. Firstly, we didn't standardize factors such as the acquisition time of MRIs, drugs and treatments used, and fluid intake which all have small differences in brain volume [20-21]. Secondly, the relatively short time interval between MRI scans has resulted in small volume differences in the brain. Both issues may have affected the volume differences detected with the VolBrain software. Third, we didn't compare the volBrain software with any other software. It can be compared with one / more different automated measurement software and the accuracy rate can be compared with them. Also, the software we use has technical issues that may cause errors in plaque count, as stated above. All of these can affect the plaque count and agreement of results with radiologists.

Conclusion

Automated, quantitative, and rapid evaluation of brain MRIs in MS disease is an ongoing issue. Reports provided by the software still need verification from a radiologist or neurologist. Large-scale validation studies and improvements are required for the use of such software in daily practice.

Conflict of interests
The authors have no conflicts of interest to declare

Financial Disclosure
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Ethical approval
Ethical approval for this study was obtained from Izmir Bozyaka Education and Research Hospital by the Ethics Committee. (Decision number:01, date:27/11/2020).

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