ADC Measurements in Various Patterns of Multiple Sclerosis Lesions

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Objective: *To determine the difference of mean apparent diffusion coefficients (ADC) among different patterns of focal multiple sclerosis (MS) lesions, to compare mean lesion ADC between 2 clinical subgroups and to correlate mean lesion ADC with disability.*
Material and Method: *Thirty seven patients (26 with relapsing-remitting multiple sclerosis (MS) and 11 with secondary-progressive MS) underwent both conventional and diffusion-weighted MR imaging of the brain. After creating ADC maps, region identification was done by using b = 0 images and T2-weighted images. ADC values were measured for MS lesions and (NAWM).*
Results: *A total of 288 lesions were identified on the images. The mean ADC for the lesions was significantly higher than that of NAWM. Hypointense T1 lesions (n = 221) had a significantly higher mean ADC than isointense T1 lesions (n = 67) in both nonenhancing lesions (n = 250) and enhancing lesions (n = 38). The enhanced rim of ring-enhancing lesions (n = 18) had lower ADC than the central nonenhanced portions. Confluent lesions (n = 62) had a substantially higher mean ADC than discrete lesion (n = 226). Mean lesion ADC of secondary progressive MS was significantly higher than relapsing remitting MS. No correlation between mean lesion ADC and (EDSS) score was found.*
Conclusion: *Quantitative diffusion-weighted imaging is useful to elucidate the heterogeneous pathological substrate of MS in different patterns of MS lesions, to differentiate 2 major clinical subgroups.*

Keywords: *Multiple sclerosis, Echo-planar diffusion-weighted imaging, Apparent diffusion coefficient (ADC), Normal appearing white matter (NAWM), Expanded disability status scale (EDSS)*

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MR imaging plays a very important role in diagnosing multiple sclerosis (MS) and provides surrogate markers for therapeutic efficacy[1]. But the lesion load, as determined on conventional T2-weighted images, has not correlated strongly with clinical disability[2]. Moreover, this sequence has not delineated subtle abnormalities within normal appearing white matter (NAWM) which is known to be damaged in MS and may represent the occult disease burden[3]. Gadolinium(Gd)-enhancement[4] has been used in an attempt to characterize "activity" of focal MS lesions however, information on tissue damage still cannot be provided.

Several recent studies have suggested that hypointensity on T1-weighted images relates to axonal destruction and can be used as a marker of irreversible disease[5-7]. However, the definition of hypointense areas is highly subjective due to variability of MR sequences. Quantitative MRI techniques have been used in an attempt to increase the specificity in characterizing the heterogeneous pathological substrate of MS.

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Diffusion-weighted imaging (DWI) is a quantifiable MRI technique that is very sensitive to molecular water mobility. DWI uses strong magnetic field gradient pulses to amplify the dephasing effects of normal molecular motion, resulting in attenuation of the MR signal[8]. Measurement of water diffusion can be easily calculated as apparent diffusion coefficient (ADC) values. Pathologic processes that modify the integrity of CNS structures lead to changes in ADC. Initial studies using diffusion gradients applied in one direction, reported increased ADC in MS lesions compared to NAWM, but these studies were limited by the smaller sample size and by motion artifacts in the images[9,10]. A following study confirmed elevated ADC in lesions and hypothesized that this elevation was related to an increase in extracellular space from disruption of the axons[11]. Another study, using navigated spin-echo DWI to reverse motion artifact, reported quantitative information on acute edematous and chronic lesions[12].

The purpose of the present study was to determine if there are quantitative ADC differences among focal MS lesions that show different patterns on T1-weighted and Gd-enhanced MR images, to compare mean lesional ADC between 2 different clinical subgroups and to correlate mean lesional ADC with clinical disability.

Material and Method

Subjects

Thirty-seven patients with clinically defined multiple sclerosis[13] who underwent MRI at UCSD medical center from January 2001 to December 2003, were studied. There were 26 patients with relapsing-remitting disease (RRMS), and 11 with secondary-progressive disease (SPMS). Patients with RRMS consisted of 18 females and 8 males, 18-59 years old (mean = 38.27 years), who had an Expanded Disability Status Scale (EDSS) scores between 0.0 and 6.5 (mean, 2.73). Patients with SPMS (7 females and 4 males, mean age 37.9 years, range 16-60 years) had EDSS scores between 6 and 9 (mean, 7.5).

MRI Protocols

Brain MRI was performed on patients using a 1.5 Tesla MR system. The MR protocol included the following sequences: Sagittal and axial T1-weighted spin-echo (TR/TE = 450/15, 5-mm thick sections, 256 x 192 matrix, 24-cm field of view [FOV]); axial fast spin-echo T2-weighted (TR/TEeff = 3786/96, echo train length = 8, 5-mm thick sections with 2.5-mm spacing, 196 x 512 matrix, 24-cm FOV); axial fluid-attenuated inversion-recovery (FLAIR) images (TR/TE /TI = 9000/105/2500, 5-mm thick sections with 2.5-mm spacing, 256 x 154 matrix, 22-cm FOV); and sagittal FLAIR (TR/TE/TI = 8500/105/2500, 3-mm thick sections with 1-mm spacing, 256 x 196 matrix, 22-cm FOV). A multislice single-shot spin-echo echo-planar diffusion-weighted imaging sequence (TR/TE = 4521/110, 5-mm thick sections with 1.5-mm spacing, 128 x 96 matrix, 24-cm FOV) was also employed. The diffusion gradients were sequentially applied in the x, y and z axis directions with 3 different *b* values (0, 500, 1000 s/mm^2). In each region of interest (ROI), the ADCs in the x, y and z directions were calculated using the Stejskal and Taner equation by linear fitting of the logarithm of the SI (ln SI) versus *b* value. Diffusion trace maps were computed from the isotropic diffusion image and the baseline image on a pixel-by-pixel basis. Finally, gadolinium dimeglumine (0.1 mmol/kg) was injected intravenously and axial and coronal T1-weighted images with fat suppression technique (TR/TE = 774/14, 5-mm thick sections, 256 x 144 matrix, 22-cm FOV) were obtained immediately after injection.

Lesion Identification and the Region of Interest Selection

Lesions were identified on T2-weighted FSE and FLAIR images. First, lesions were classified as discrete or confluent. Using the T1-weighted images, all lesions were classified further as either hypointense or isointense compared to signal intensity of surrounding white matter. Then, using postcontrast T1-weighted images, lesions were defined as enhancing or non-enhancing lesions, and if enhancing, as ring or nodular enhancing pattern. All lesions were classified by two neuroradiologists through consensus agreement.

After lesion identification on T2-weighted and FLAIR images, the lesions were outlined on the diffusion-weighted images (b = 0) so that the regions of interest (ROI) on ADC maps were aligned precisely with the lesions on T2-weighted images. The mean ADC values (average of the ADC in three orthogonal directions or diffusion trace) were obtained. Sizes of the ROIs were chosen to be appropriate for each lesion. To avoid partial volume artifacts, lesions near cortical sulci or ventricular outline were excluded. Also, ROIs were not placed in areas of potential susceptibility artifacts, such as near the aerated sinuses or skull base. To avoid including normal tissue or other regions of abnormal tissue in the ROI analysis, the slices above and below the selected slices were carefully reviewed.

For nonenhancing lesions and nodular enhancing lesions, the ROIs were drawn to include the entire lesion. For ring enhancing lesions, two separate ROIs were drawn in the central nonenhancing part and the enhancing rim. In addition, ROIs of uniform size (40 mm^2) were manually positioned in different white matter areas (frontal, parietal, temporal, occipital and cerebellum). All ROIs were chosen by one observer who was blinded to clinical subgroup information and EDSS scores.

Reliability of MRI Measurements

The same individual, blinded to clinical data, re-measured the ADCs of all patients and controls at least 3 weeks after the initial analysis.

Average intraclass correlation coefficient to determine intraobserver reliability were 0.82 to 0.90 for the ADC of MS lesions, 0.78 to 0. 90 for the ADC of NAWM of patients.

Statistical Method

The authors used Mean (SD) and 95% CI to describe ADC values of different lesion patterns and NAWM. Mann-Whitney U test was used to compare mean ADC of smaller sample size of enhancing lesions. Paired-t test was used to compare different portion of ring enhancing lesions. Spearman's rank correlation test was used to measure correlations between mean lesion ADC and EDSS score. The statistical tests were

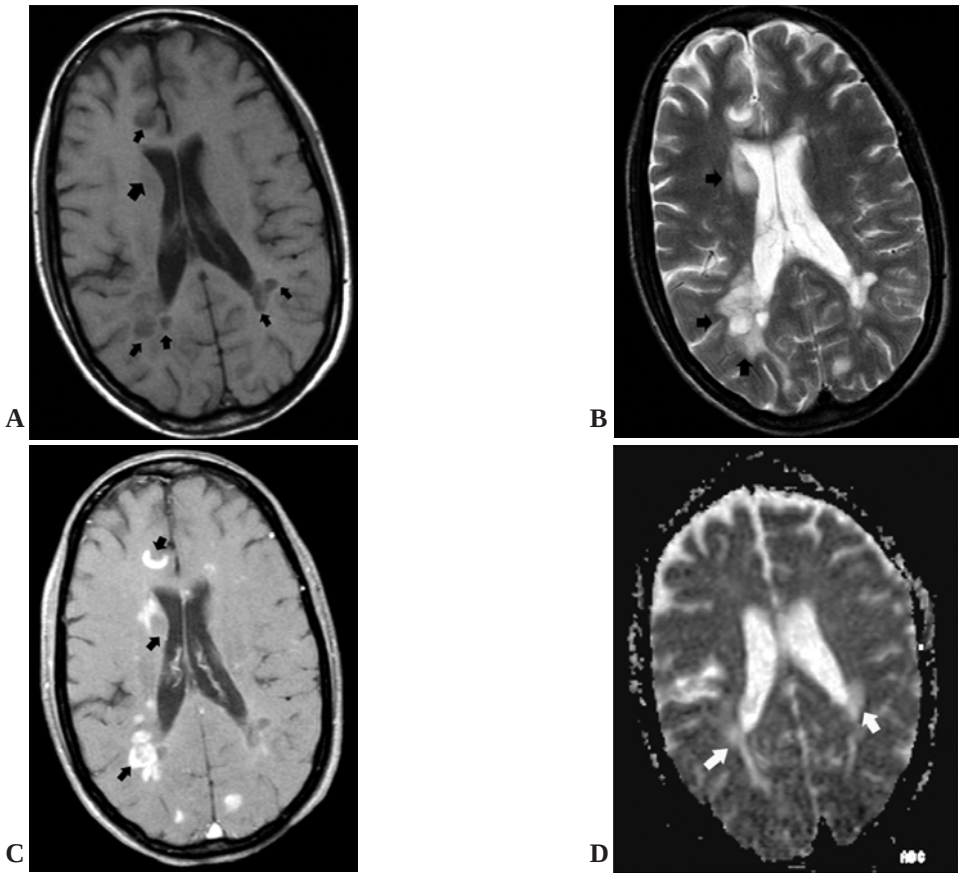


Fig. 1 Various patterns of focal MS lesions (same patient)
A. Axial unenhanced T1-weighted image demonstrates multiple small hypointense lesions (small arrows) and one isointense lesion (large arrow)
B. Axial T2-weighted image reveals a large confluent lesions around posterior body, a smaller one close to anterior body of RT lateral ventricle (long arrows) and multiple small discrete lesions (short arrows)
C. Enhanced T1-weighted with fat suppression shows multiple ring enhancing lesions (short arrows) and nodular enhancing lesions (long arrows)
D. DWI, ADC mapping image shows hyperintensity due to increased ADC of the lesions (arrows)

performed at a significance level of 0.05 by using STATA software package (version 8.0).

Results

1. ADC of Various Patterns of MS Lesions

A total of 288 focal MS lesions were identified on T2-weighted images from 37 patients. Ten of the 37 patients had enhancing lesions, for a combined total of 38 enhancing lesions; eight lesions were classified as isointense and 30 as hypointense to white matter on axial unenhanced T1-weighted images. Of the 38 enhancing lesions, 18 were ring - enhancing lesions with both an enhancing rim and a central nonenhancing portion, and the other 20 lesions showed nodular enhancement. Of the 250 nonenhancing lesions, 59 were isointense and 191 were entirely hypointense to white matter on unenhanced T1-weighted images (Fig. 1, 2).

Of the 288 lesions, 226 were discrete lesions and 62 were confluent lesions. The mean ADC was calculated in the lesions and in every area of measured normal appearing white matter in MS patients.

The tables present the overall appearance of MS lesions and their ADC values including comparisons (Table 1, 2).

Non-enhancing Lesion Analysis

The mean ADC values of these lesions were different according to their signal intensity on unenhanced T1-weighted images. Mean ADC of hypointense nonenhancing lesions (141.31 $\pm$ 23.28 x 10^{-5} mm^2/sec) was significantly higher than isointense nonenhancing lesions (102.37 $\pm$ 6.47 x 10^{-5} mm^2/sec) with a mean difference, 38.94 (95%CI: 32.99, 44.99; $p < 0.0001$).

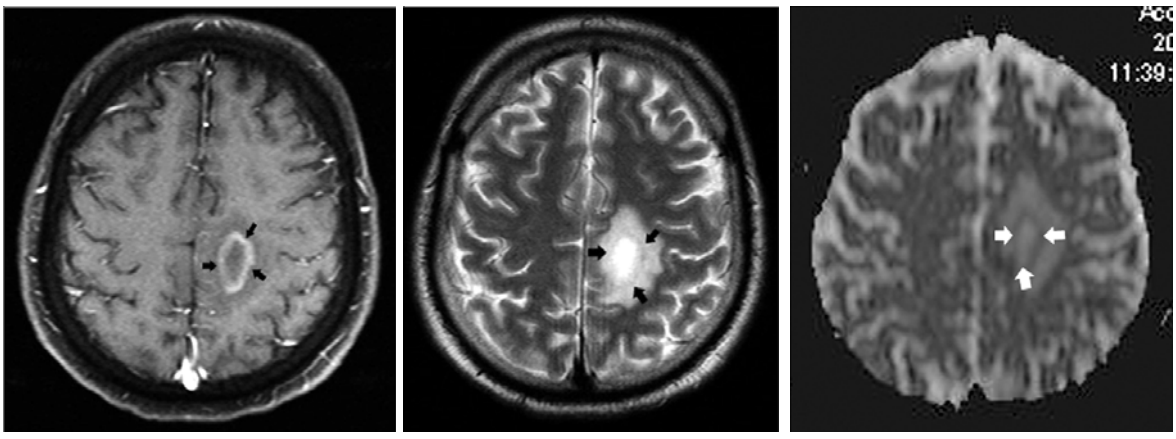
Enhancing Lesion Analysis

Hypointense enhancing lesions had higher diffusion than isointense enhancing lesions. Mean ADC of nodular hypointense enhancing lesions 131.42 $\pm$ 3.23 x 10 mm/sec) was less than the ring hypointense enhancing lesions (167.48 $\pm$ 37.30 x 10 mm/sec) with mean difference, 36.06 (95%CI: -2.75, 29.67; $p = 0.05$) if using the central non-enhancing part as reference.

ADC of enhancing rim (ER) (111.12 $\pm$ 29.33 x 10^{-5} mm^2/sec) was relatively decreased (Fig. 2), compared to the central nonenhancing portion (153.61 $\pm$ 42.26 x 10^{-5} mm^2/sec) of ring enhancing lesions with mean difference, 42.49 (95%CI: 30.89, 54.08; $p < 0.0001$).

Discrete vs Confluent Lesion Analysis

Mean ADC values of confluent lesions (147.95 $\pm$ 26.59 x 10^{-5} mm^2/sec) were substantially higher than discrete lesions (125.68 $\pm$ 24.82 x 10^{-5} mm^2/sec) with mean difference, 22.27 (95%CI: 15.17, 29.39; $p < 0.0001$).



A **B** **C**

Fig. 2 Ring enhancing masslike lesion
A. Axial enhanced T1-weighted image shows a large ring enhancing lesion (short arrows) with surrounding hypointense edematous area (long arrows)
B. Axial T2-weighted image demonstrates more hyperintensity of the lesion (short arrow), compared with perilesional edema (long arrow) and visible faint hypointense ring (double arrows)
C. DWI, ADC mapping image reveals dark ring (short arrows) due to relatively restricted diffusion surrounding by increased diffusion of central nonenhanced portion (c) and outer edematous area (long arrows)

Table 1. Lesion appearance on T1-weighted images and mean ADC measurements

Lesion Appearance	No.	ADC (10^{-5} mm^2/sec)		
		Mean	SD	95%CI for the mean ADC
Nonenhancing lesions	250			
Isointense	59	102.37	6.47	100.70, 104.01
Hypointense	191	141.31	23.28	137.98, 144.63
Enhancing lesions	38			
Hypointense on T1	(30)			
Ring enhancement	14	117.96 (ER), 167.48 (CNE)	28.55, 37.30	101.48, 134.45 (ER) 145.90, 189.01 (CNE)
Nodular enhancement	16	131.42	12.91	124.54, 138.30
Isointense on T1	(8)			
Ring enhancement	4	87.20 (ER), 105.10 (CNE)	19.03, 7.43	56.93, 117.48 (ER) 93.28, 116.92 (CNE)
Nodular enhancement	4	101.08	9.61	85.77, 118.38
Discrete lesions	226	125.68	24.82	122.42, 128.93
Confluent lesions	62	147.96	26.59	141.34, 154.58
NAWM	133	85.71	2.90	85.22, 86.20

Note: CNE = central non-enhancing part, ER = enhancing rim, NAWM = normal appearing white matter, 95%CI = 95% confidence interval

Table 2. Summary of mean apparent diffusion coefficient (ADC) measurement comparisions among various patterns of MS lesions

Comparison of Mean ADC measurements			*p*-value
Lesion pattern	Result	Lesion pattern	
Hypointense nonenhancing	>	Isointense nonenhancing	<0.0001
Nodular hypointense enhancing*	<	Ring hypointense enhancing*	<0.05
Enhancing rim**	<	Central nonenhancing part**	<0.0001
Confluent	>	Discrete	<0.0001
All MS lesion patterns	>	NAWM	<0.0001

Note: * using the central non-enhancing part as reference, ** part of ring enhancing lesion, NAWM = normal appearing white matter

2. ADC of MS Lesions and NAWM

The mean ADC of all MS lesions in 37 patients ($128.66 \pm 15.99 \times 10^{-5}$ mm^2/sec) was significantly elevated, compared to mean ADC of NAWM ($85.71 \pm 2.90 \times 10^{-5}$ mm^2/sec) with mean difference, 42.95 (95%CI: 37.75, 86.67; $p < 0.0001$).

3. ADC in Clinical Subgroups

Twenty-six patients were classified clinically as RRMS, and eleven patients had SPMS. The ADC of MS lesions in SPMS ($139.74 \pm 16.90 \times 10^{-5}$ mm^2/sec) was significantly elevated compared with RRMS ($124.06 \pm 14.09 \times 10^{-5}$ mm^2/sec) with mean difference, 15.68 (95%CI: 4.77, 26.60; $p < 0.0061$).

4. Correlation between Mean ADC of Lesions and EDSS Score

No correlation between mean ADC of lesions and EDSS score was found (r = 0.29; not significant).

Discussion

The heterogeneous pathologic substrate among different multiple sclerosis subgroups and the axonal loss associated with disease progression add to the complexity of this disease. Therefore, quantitative data in multiple sclerosis is critical in understanding the natural history of the disease and in monitoring therapeutic effects[14]. Diffusion-weighted imaging (DWI) potentially may improve the understanding of the irreversible tissue damage associated with MS inflammation. With DWI, one can quantify the extent of structural changes occurring in T2-visible lesions and in the tissue that appears normal on conventional MRI images[15].

In the present study, the authors measured ADC values of MS lesions and different areas of NAWM using echo-planar DWI sequences to elucidate the nature of this clinically and pathologically heterogeneous disease. The authors found increased water diffusivity (elevated ADC) in all MS lesions, both nonenhancing and enhancing lesions compared to NAWM from the patients. These results confirm the findings in earlier studies[10,12]. An increase in the extracellular space caused by edema and demyelination has been proposed as the pathophysiological mechanism for the increased lesional ADC[9]. In the acute phase of disease, the expanded extracellular volume is due to astrocytic proliferation, perivascular inflammation and demyelination, all representing stigmata of the initial step in plaque formation. In chronic MS, the more pronounced increase in diffusivity represents axonal loss and tissue destruction[16].

When the authors classified the lesions based on their appearance on unenhanced T1-weighted images, it was found that the mean ADC of hypointense lesions was higher than isointense lesions in both nonenhancing and enhancing lesions. Hypointense T1 lesions, the so-called black holes, have been related to the degree of matrix destruction and loss of axons in MS[6,7]. Cellular infiltrates with edema, but relative preservation of axons, have been shown in isointense T1 lesions on pathologic examination[17]. The authors also found that the very hypointense lesions on T1-weighted images had higher ADC values than the less hypointense lesions. This apparent inverse relationship of ADC values with signal intensity on T1W images suggests that ADC is a valid quantitative parameter. The present findings concur with previous reports[12,16] and are consistent with the concept that high diffusion values are associated with tissue destruction in MS. The highest lesional ADC values in the present study were observed in enhancing lesions and nonenhancing lesions. This may indicate that hypointensities on T1-weighted images not only represent tissue destruction from demyelination and axonal loss in the late stages of disease, but it may also be associated with acute edematous lesions. Hypointensity in acute lesions may be the result of expansion of extracellular space by edema and the inflammatory process that is reversible at follow up from remyelination[6]. Since enhancement within lesions can persist for 4-6 weeks, longitudinal follow up of diffusion changes in active lesions may be more sensitive and useful to evaluate treatment response in therapeutic trials. Moreover, previous histologic studies have shown scarring and inflammation with variable myelin loss, ranging from mild to severe in nonenhancing lesions[18], which may be the cause of variable hypointensity on T1-weighted images. Some hypointense T1 lesions in the present study were low signal on FLAIR images, which has been associated with severe clinical disability[19]. However, the hypointensity on T1-images is rather subjective by visual evaluation only, whereas DWI provides quantitative information. The pathologic significance of changes in brain ADC in MS must be validated by direct comparison with histology.

For the two different patterns of enhancing lesions (Fig. 1, 2), the authors found lower mean ADC in nodular enhancing lesions than in ring enhancing lesions (central nonenhancing portion), and the difference was more striking in hypointense enhancing lesions. The 95%CI and *p*-value did not reach a statistically significant level, which may be explained by the small sample size of enhancing lesions in the present study. Nonetheless, the data was close to significance.

Previous published data has shown significantly increased magnetization transfer ratio (MTR) in nodular enhancing lesions compared to ring enhancing lesions[20]. On histopathological studies, the elevated MTR correlated with prominent inflammation but only mild demyelination of the nodular enhancing lesions[18,19]. The present finding of lower ADC in nodular enhancing lesions was also in line with a previous report[14] that showed less parenchymal destruction and less demyelination in these lesions. For ring enhancing lesions, the ADC values of the enhancing rim was significantly decreased compared to the central nonenhancing portion, which is concordant with previous reports[14,17]. However, the ADC of the rim remained slightly higher than normal appearing white matter. The rim was bordered by the markedly increased ADC of the nonenhancing portion centrally

and the edematous white matter on the outside. Histopathologically, the enhancing rim corresponds to a layer of macrophage accumulation, several millimeters thick, positioned at the edge of active plaques[21]. The ring enhancing lesions also showed complete central myelin loss with peripheral inflammation[18]. The authors noticed that the standard deviation of the mean ADC of ring enhancing lesions was higher than that of nodular enhancing lesions, which likely relates to more tissue heterogeneity of ring enhancing lesions, as was previously reported by Roychowdhury et al[22].

The present data disclosed significantly higher mean ADC values in the confluent lesions compared to the discrete lesions. To the best of the authors knowledge, this difference in diffusivity has not been reported before. Although the precise histopathologic basis for increased diffusivity is not known, a few possible explanations come to mind. First, the confluent lesions always occur in MS patients who have had long disease duration, and the confluent pattern often develops from progression of many discrete lesions that are likely associated with severe axonal destruction. Second, preliminary studies have reported more prominent confluent lesions in SPMS[23], which correlates with more aggressive tissue destruction. In addition, more than 50% of RRMS move on to a secondary-progressive phase that is associated with a poorer prognosis and less response to treatment[24]. So, it follows that the increase in ADC values of confluent lesions is probably related to more severe axonal destruction.

Furthermore, the authors may be able to tell acute or chronic stage of confluent lesions in the future longitudinal study by using DWI. One previous study has found DWI may add to the diagnostic power of MRI in the setting of demyelinating disorders from acute disseminated encephalomyelopathy (ADEM) by identifying areas of acute and chronic demyelination, even in the absence of contrast enhancement[25].

Finally, the authors did not find any correlation between mean lesional ADC and EDSS score, an association that seems logical but has not been consistently shown in the literature[12,16]. Possible explanations for this inconsistency could be different numbers of patients in clinical subgroups, different types or phases of MS and variable disease duration. Moreover, because of the strong emphasis on ambulation in the middle range of the scale, the EDSS is insensitive to changes in other neurologic functions of patients with moderate to severe disability[1].

Conclusion

The authors have demonstrated differences in measured mean ADC values among MS lesions that differ in appearance on T1-weighted and Gd-enhanced MR images. Quantitative DWI was able to elucidate the heterogeneous pathologic substrate of MS lesions and distinguish the two major subgroups. Finally, these data provide some new challenging information to be validated further with more advanced techniques or aggregated MRI quantification, hopefully leading to better patient management and assisting new therapeutic trials.

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การวัดเชิงปริมาณของการแพร่กระจายของโมเลกุลน้ำในรอยโรคมัลติเปิลสเคลอโรซิสรูปแบบต่าง ๆ โดยเทคนิคเอ็คโค่ พลาน่า ของดิฟฟิวชั่น เอ็มอาร์ไอ

วรินทร์ธร พุทธรักษ์, วาณีรัตน์ กาฬสีห์, วัลลภ เหล่าไพบูลย์, มาลินี เหล่าไพบูลย์, John R Hesselink

วัตถุประสงค์: *เพื่อพิจารณาความแตกต่างของค่าเฉลี่ยของการแพร่กระจายของน้ำในรอยโรคมัลติเปิลสเคลอโรซิสรูปแบบต่าง ๆ และเปรียบเทียบค่าเฉลี่ยดังกล่าวในรอยโรคของกลุ่มผู้ป่วยอาการย่อยที่แตกต่างกัน และหาความสัมพันธ์ระหว่างค่าเฉลี่ยดังกล่าวกับระดับความรุนแรงของภาวะพิการของผู้ป่วย*

วัสดุและวิธีการ: *การศึกษาในผู้ป่วยมัลติเปิลสเคอโรซิสจำนวน 37 คน ที่ได้รับการตรวจเอ็มอาร์ไอปกติ และดิฟฟิวชั่นเอ็มอาร์ไอ โดยหลังจากได้ภาพสำหรับการวัดการแพร่กระจายของโมเลกุลน้ำแล้ว ก็ทำการวัดเชิงปริมาณในรอยโรคที่ปรากฏในตำแหน่งเดียวกับภาพดิฟฟิวชั่นที่ใช้ค่าสัมประสิทธิ์เท่ากับศูนย์ ภาพเทคนิค T2-weighted รวมทั้งทำการวัดในตำแหน่งของเนื้อสมองปกติที่อยู่รอบ ๆ โพรงสมอง*

ผลการศึกษา: *ในจำนวน 288 รอยโรคที่ปรากฏในภาพเอ็มอาร์ไอสมอง พบว่า ค่าเฉลี่ยการแพร่กระจายของโมเลกุลน้ำในรอยโรคนั้นมากกว่าเนื้อสมองปกติที่อยู่รอบ ๆ โพรงสมองอย่างมีนัยสำคัญ และพบว่ารอยโรคที่เห็นเป็นสีดำในภาพเทคนิค T1-weighted นั้นก็มีค่าเฉลี่ยของการแพร่กระจายของน้ำมากกว่ารอยโรคที่มีสีคล้ายเนื้อสมอง นอกจากนั้นบริเวณวงแหวนรอบนอกที่ขาวขึ้นหลังการฉีดสารเพิ่มความทึบนั้นมีการแพร่กระจายของน้ำต่ำกว่าบริเวณตรงกลางที่ไม่เปลี่ยนแปลงหลังการฉีดสารทึบรังสี ส่วนรอยโรคที่เป็นปื้นขนาดใหญ่นั้นมีค่าการแพร่กระจายมากกว่าในรอยโรคที่มีขนาดเล็กขอบเขตชัด และค่าเฉลี่ยการแพร่กระจายของน้ำในรอยโรคของกลุ่มผู้ป่วยที่มีอาการมากขึ้นเร็วหลังการเป็นซ้ำนั้นมีมากกว่า และพบว่าไม่มีความสัมพันธ์กันระหว่างค่าเฉลี่ยการแพร่กระจายของน้ำในรอยโรคกับระดับความรุนแรงของความพิการของผู้ป่วย*

สรุป: *เทคนิคเอ็คโค่ พลาน่า ของดิฟฟิวชั่น เอ็มอาร์ไอมีประโยชน์ช่วยบ่งบอกและย้ำถึงความสลับซับซ้อนของการเกิดพยาธิสภาพในโรคมัลติเปิลสเคลอโรซิสในระดับโมเลกุล โดยดูได้จากความแตกต่างของค่าเฉลี่ยของการแพร่กระจายของน้ำในรอยโรคลักษณะต่าง ๆ และผู้ป่วยกลุ่มอาการย่อยต่าง ๆ*