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Diffusion Tensor Imaging for the Differentiation of Microangiopathy, Infarction and Perfusion-Diffusion Mismatch Lesions[1]

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Purpose: This study was designed to evaluate the usefulness of diffusion tensor imaging (DTI) and the DTI indices for differentiating between microangiopathy lesions, acute infarction lesions and perfusion-diffusion mismatch areas.

Materials and Methods: DTI was performed in 35 patients with the use of a 1.5 Tesla MRI system. The MRI parameters were as follows: a spin echo EPI sequence with a b-value = 1000 s/mm^2, 25 diffusion directions, a repetition time of 8400 msec, an echo time of 75 msec, a matrix size of 128 × 128, a FOV of 22 cm and a 4 mm slice thickness. From the diffusion tensor images, the apparent diffusion coefficient (ADC), fractional anisotropy (FA), volume ratio (VR), relative anisotropy (RA), anisotropy index (AI), exponential ADC (eADC) and magnitude diffusion coefficient (MDC) were measured for the contra-lateral normal area (28 cases), the microangiopathy lesions (10 cases), the infarction lesions (17 cases) and the perfusion-diffusion mismatch area (8 cases).

Results: As compared to the normal area, the microangiopathy lesions showed increased ADC and MDC values and decreased FA, VR, RA, AI and eADC values. The infarction lesions showed increased VR, RA and eADC values, a normal FA, a decreased AI and decreased ADC and MDC values. The mismatch area showed a similar pattern as that for the microangiopathy lesions; however, the differences were not prominent, with an increase of the ADC and MDC values and a decrease of FA, VR, RA, AI and eADC values.

Conclusion: The DTI indices could have a role in making the differential diagnosis of microangiopathy, acute infarction and perfusion-diffusion mismatch lesions.

Index words : Brain
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Diffusion weighted imaging (DWI) is a unique method for observing the mobility of water in tissue, and it is used as a principal method for diagnosing acute infarction. Diffusion tensor imaging (DTI) is used to investigate fiber connectivity and evaluating brain development by mapping water diffusion. DTI describes the magnitude, degree and orientation of diffusion anisotropy, and this modality is considered to be a robust method to characterize disease with high sensitivity. The theoretical background and clinical applications of the DTI and DTI indices, as well as the DTI method and tractography for examining the white matter (WM), have been well explained in previous reports (1–4).

Microangiopathy is common finding when performing clinical MRI, but microangiopathy cannot be differentiated from acute infarction without performing DWI. A perfusion-diffusion mismatch area is unrecognizable without a perfusion study.

The purpose of this study was to evaluate the use of DTI and to determine the differences and the usefulness of the various DTI indices for making the differential diagnosis of microangiopathy, acute infarction and the perfusion-diffusion mismatch areas.

Materials and Methods

DTI was performed in 35 patients with the use of a 1.5 Tesla MRI system with an 8-channel head coil (Signa Excite HD, GE Medical Systems, Milwaukee, WI, USA). The MRI parameters were as follows: a spin echo EPI sequence with a b-value = 1000 s/mm^2, 25 diffusion directions, a repetition time of 8400 msec, an echo time of 75 msec, a matrix size of 128 × 128, a FOV of 22 cm and a 4 mm slice thickness. The apparent diffusion coefficient (ADC, × 10^{-3} mm^2/sec), the fractional anisotropy (FA), volume ratio (VR), the relative anisotropy (RA), the anisotropy index (AI), the exponential ADC (eADC) and the magnitude diffusion coefficient (MDC) were measured by placement of region-of-interest (ROI) circles on the contra-lateral normal area (28 cases), the microangiopathy lesions (10 cases), the acute infarction lesions (17 cases) and the perfusion-diffusion mismatch area (8 cases) on the diffusion tensor images and using the vendor-supplied software (Functool 2; GE Medical Systems, Fremont, CA, USA) (Figs. 1, 2).

T-tests were used to assess the significance of the differences of the values of the DTI indices. A p value < 0.05 was considered to be statistically significant.

Results

The ADC values were 0.79 for the normal area, 1.16 for the microangiopathy lesions, 0.48 for the infarction lesions and 0.84 for the mismatch area. The FA values were 0.36 for the normal area, 0.21 for the microangiopathy lesions, 0.36 for the infarction lesions and 0.31 for the mismatch area. The VR values were 0.16 for the normal area, 0.05 for the microangiopathy lesions, 0.19 for the infarction lesions and 0.12 for the mismatch area. The RA values were 0.31 for the normal area, 0.18 for the microangiopathy lesions, 0.32 for the infarction lesions and 0.27 for the mismatch area. The AI values were 0.07 for the normal area, 0.04 for the microangiopathy lesions, 0.03 for the infarction lesions and 0.06 for the mismatch area. The eADC values were 0.46 for the normal area, 0.32 for the microangiopathy lesions, 0.64 for the infarction lesions and 0.44 for the mismatch areas. The MDC values were 0.83 for the normal area, 1.17 for the microangiopathy lesions, 0.50 for the infarction lesions and 0.87 for the mismatch area (Tables 1–4).

As compared with the contra-lateral normal area, based on the use of the *t*-test, significant differences were determined for all the abnormalities for the ADC, FA, VR, RA, AI, eADC and MDC ($p=0.000$, $p=0.001$, $p=0.004$, $p=0.002$, $p=0.035$, $p=0.000$ and $p=0.000$, respectively). The differences between the microangiopathy lesions and the infarction lesions were significant for the ADC, FA, VR, RA, eADC and MDC ($p=0.000$, $p=0.001$, $p=0.001$, $p=0.001$, $p=0.000$ and $p=0.000$, respectively; only the AI was not significant, $p=0.524$). The differences between the microangiopathy lesions and the mismatch area were significant for the ADC, FA, VR, RA, eADC and MDC ($p=0.000$, $p=0.020$, $p=0.039$, $p=0.020$, $p=0.000$ and $p=0.000$, respectively; only the AI was not significant, $p=0.300$). The differences between the infarction lesions and the mismatch area were significant for the ADC, eADC and MDC (all $p=0.000$) and those for the FA, VR, RA and AI were not significant ($p=0.337$, $p=0.132$, $p=0.308$ and $p=0.265$, respectively).

Discussion

The DTI indices that are classified as isotropy indices include the ADC, Trace and eADC, and indices that are classified as anisotropy indices including FA, RA and VR (5). DTI is considered to have an important role for

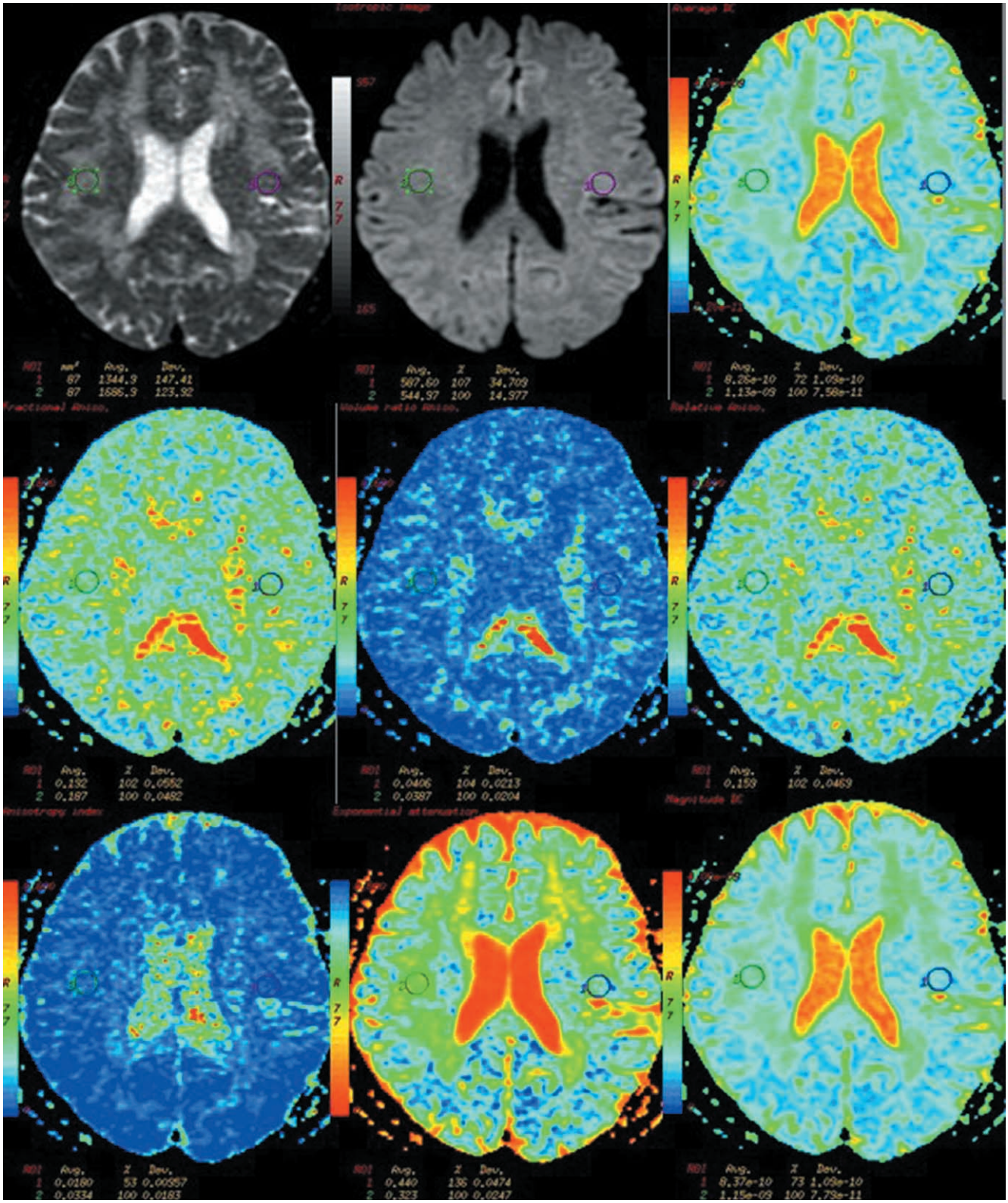

Fig. 1. The MR images of a 60-year-old woman, who suffered from hypertension and cognitive dysfunction, showed marked microangiopathy at the deep white matter. The diffusion tensor images were processed and they were used to measure the values of several indices at the contra-lateral normal area (left circle) and the area of microangiopathy (right circle).
B_0 image (top line, left), Isotropic image (top line, middle), Apparent diffusion coefficient (top line, right), Fractional anisotropy (middle line, left), Volume ratios (middle line, middle), Relative anisotropy (middle line, right), Anisotropy index (bottom line, left), Exponential ADC (bottom line, middle). Magnitude diffusion coefficient (bottom line, left)

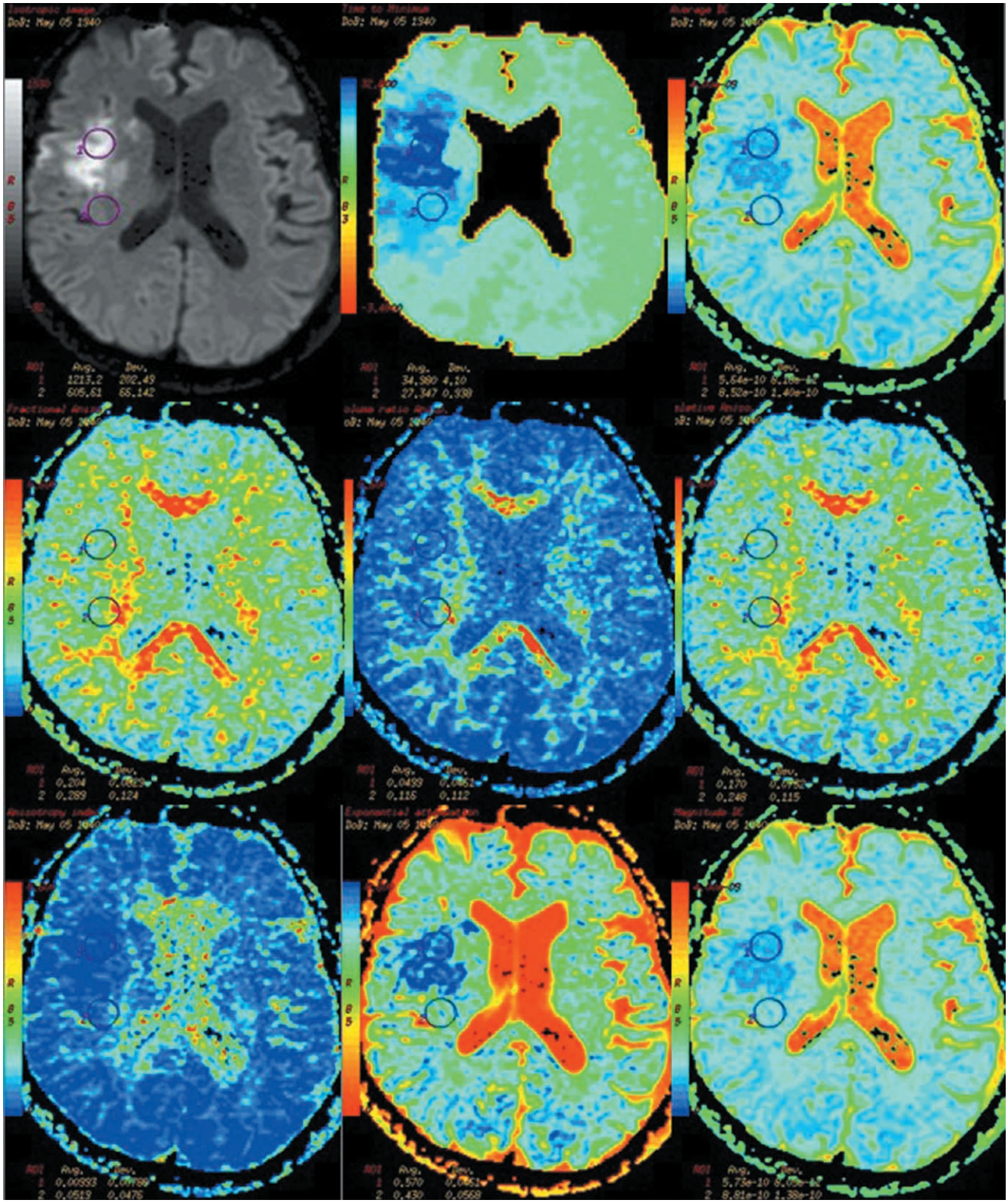

Fig. 2. A 67-year-old man who suffered from a right middle cerebral artery (MCA) infarction was evaluated at two hours after the attack. A perfusion-diffusion mismatch area was noted on the perfusion study (b) and the values of the DTI indices were measured at the infarction site (anterior circle) and the perfusion-diffusion mismatch area (posterior circle).
Isotropic image (top line, left), Perfusion study (the time to peak image, top line, middle), Apparent diffusion coefficient (top line, right), Fractional anisotropy (middle line, left), Volume ratios (middle line, middle), Relative anisotropy (middle line, right), Anisotropy index (bottom line, left), Exponential ADC (bottom line, middle), Magnitude diffusion coefficient (bottom line, left)

diagnosing disease, predicting the prognosis and planning the treatment of ischemic brain injury (6). The combination of DTI and functional MRI (fMRI) provides new insights into structure-function relationships (7); DTI allows visualization of the WM tracts and it is beneficial for the surgical planning of brain tumors (8).

DWI and anisotropy have been introduced for evaluating patients after a stroke (9). The isotropic maps are appropriate to detect hyper-acute stroke and the anisotropic images are useful to differentiate hyper-acute stroke from acute stroke (10). DTI makes it possible to distinguish the acute ischemic changes from the chronic ischemic changes. The ADC is increased for a chronic ischemic lesion (11) and vasogenic edema (10, 12, 13), and the ADC is decreased for acute ischemia (9) and cytotoxic edema (10, 13). The ADC values are useful to predict the viability of tissue and the outcome of stroke (14, 15). In previous studies, the measured ADC values in the thalamus and splenium were 0.72 and 0.62, respectively, and the measured ADC values in the ischemic WM and gray matter (GM) were 0.54 and 0.46, respectively (3, 16). The measured ADC value of the normal brain was 0.86, and the measured ADC values were 0.56, 0.73 and 0.87 for a WM infarction and 0.71, 0.78 and 1.21 for infarcted GM at 4.5 hours, 51 hours and 85 days, respectively (5). The ADC value of an acute infarct is reduced by 30–50% within 30 minutes of the onset (17), it initially decreases, it becomes normalized after seven to nine days and then it increases in the chronic phase (18). In our cases, the ADC was 0.79 in the normal brain and the ADC decreased by 39% to 0.48 for an acute infarction, and the ADC increased for microangiopathy to 1.15 and for a mismatch area to 0.84, which is a similar pattern of value changes as that for vasogenic edema or chronic infarction. In Wallerian degeneration, the ADC (0.96) was not different as compared to that of the normal brain (19). However, the ADC values were increased at the area of Wallerian degeneration of the corpus callosum, as seen on the serial diffusion tensor images (11). Secondary degeneration of

Table 1. The Values of the DTI Indices in the Contra-Lateral Normal Area (Males:Females, 16:12; Mean Age: 61Years)

Number	ADC	FA	VR	RA	AI	eADC	MDC
1	0.79	0.35	0.15	0.30	0.062	0.46	0.83
2	0.77	0.26	0.08	0.22	0.030	0.47	0.79
3	0.75	0.38	0.15	0.33	0.062	0.47	0.79
4	0.81	0.38	0.18	0.34	0.080	0.45	0.86
5	0.80	0.34	0.14	0.29	0.054	0.46	0.83
6	0.64	0.29	0.09	0.24	0.026	0.53	0.66
7	0.71	0.47	0.19	0.36	0.069	0.50	0.76
8	0.85	0.33	0.13	0.28	0.061	0.43	0.88
9	0.75	0.38	0.19	0.34	0.068	0.48	0.79
10	0.78	0.32	0.11	0.26	0.054	0.46	0.82
11	0.70	0.50	0.30	0.46	0.107	0.50	0.78
12	0.71	0.36	0.15	0.31	0.051	0.49	0.75
13	0.83	0.37	0.15	0.31	0.070	0.44	0.87
14	0.79	0.56	0.37	0.53	0.179	0.46	0.90
15	0.72	0.41	0.19	0.36	0.074	0.49	0.76
16	1.09	0.32	0.13	0.28	0.104	0.34	1.13
17	0.76	0.37	0.18	0.33	0.057	0.48	0.80
18	0.83	0.24	0.07	0.20	0.031	0.44	0.85
19	0.83	0.28	0.10	0.24	0.045	0.44	0.86
20	0.76	0.49	0.31	0.45	0.127	0.47	0.84
21	0.79	0.37	0.16	0.32	0.065	0.45	0.83
22	0.79	0.33	0.14	0.28	0.052	0.46	0.82
23	0.88	0.30	0.13	0.27	0.064	0.42	0.92
24	0.81	0.25	0.07	0.21	0.030	0.45	0.83
25	0.78	0.30	0.11	0.25	0.046	0.46	0.81
26	0.74	0.36	0.14	0.31	0.056	0.48	0.78
27	0.78	0.27	0.09	0.23	0.036	0.46	0.81
28	0.76	0.37	0.16	0.33	0.062	0.47	0.80
Mean	0.79	0.36	0.16	0.31	0.065	0.46	0.83
SD	0.08	0.08	0.07	0.08	0.032	0.03	0.08

ADC, apparent diffusion coefficient; FA, fractional anisotropy; VR; volume ratio; RA, relative anisotropy; AI, anisotropy index; eADC, exponential ADC; MDC, magnitude diffusion coefficient

the fiber tract proximal and distal to a primary lesion can be detected on ADC images (20). The diffusion tensor images reflect the pathological changes of the demyelinating process. The plaque centers of acute multiple sclerosis showed an increased ADC (1.36–2.11) as compared with the rim, the normal-appearing WM and the chronic lesions (21).

The eADC has been introduced to remove the contributions of the T2 signal intensity. The eADC is an index that has the advantages of DWI and ADC maps, and it can depict ischemic infarction with a pure diffusion effect. The eADC is increased for an acute infarct, it is normalized in 8–10 days and it is decreased for a chronic infarct; a hypointense signal reflects cellular lysis and the loss of cellular integrity (22). In our cases, the eADC was 0.46 for the normal brain, and the eADC increased for infarction lesions (0.64) and it decreased for the microangiopathy lesions (0.32) and the mismatch area (0.44).

The early changes of diffusion anisotropy reflect the cellular changes in acute ischemia and they may provide a potential marker to predict the clinical outcome (5). Decreased anisotropy has been correlated with a motor deficit after stroke and diffusion anisotropy allows physicians to evaluate the prognosis of ischemic stroke (19). The diffusion anisotropy values are more

Table 2. The Values of the DTI Indices for the Microangiopathy Lesions (Males:Females, 4:6,; Mean Age: 62 Years)

Number	ADC	FA	VR	RA	AI	eADC	MDC
1	1.28	0.17	0.04	0.14	0.037	0.28	1.30
2	1.12	0.18	0.04	0.15	0.030	0.33	1.13
3	1.34	0.19	0.04	0.16	0.044	0.26	1.35
4	1.19	0.19	0.04	0.16	0.039	0.31	1.20
5	1.25	0.18	0.03	0.15	0.036	0.29	1.27
6	1.06	0.31	0.10	0.26	0.078	0.35	1.10
7	1.30	0.19	0.04	0.16	0.041	0.27	1.31
8	1.10	0.21	0.05	0.18	0.044	0.34	1.12
9	0.85	0.33	0.13	0.29	0.062	0.43	0.88
10	1.06	0.17	0.03	0.14	0.023	0.35	1.07
Mean	1.15	0.21	0.05	0.18	0.043	0.32	1.17
SD	0.15	0.06	0.03	0.05	0.016	0.05	0.14

ADC, apparent diffusion coefficient; FA, fractional anisotropy; VR; volume ratio; RA, relative anisotropy; AI, anisotropy index; eADC, exponential ADC; MDC, magnitude diffusion coefficient

Table 3. The Values of the DTI Indices for Infarction Lesions (Males:Females, 12:5; Mean Age: 58 Years)

Number	ADC	FA	VR	RA	AI	eADC	MDC
1	0.45	0.57	0.44	0.54	0.064	0.64	0.51
2	0.51	0.31	0.14	0.27	0.021	0.61	0.53
3	0.57	0.25	0.08	0.21	0.018	0.57	0.59
4	0.28	0.45	0.30	0.41	0.014	0.76	0.30
5	0.46	0.30	0.10	0.25	0.013	0.64	0.47
6	0.52	0.28	0.11	0.23	0.020	0.60	0.54
7	1.02	0.51	0.29	0.46	0.221	0.36	1.13
8	0.42	0.30	0.12	0.26	0.010	0.66	0.43
9	0.34	0.31	0.13	0.27	0.007	0.72	0.35
10	0.45	0.25	0.08	0.22	0.008	0.66	0.46
11	0.35	0.43	0.30	0.40	0.020	0.78	0.38
12	0.49	0.36	0.16	0.31	0.021	0.62	0.51
13	0.46	0.20	0.05	0.17	0.007	0.64	0.47
14	0.39	0.24	0.08	0.20	0.006	0.68	0.40
15	0.26	0.60	0.52	0.60	0.019	0.78	0.30
16	0.55	0.21	0.06	0.18	0.010	0.58	0.56
17	0.58	0.52	0.30	0.48	0.071	0.56	0.63
Mean	0.48	0.36	0.19	0.32	0.032	0.64	0.50
SD	0.17	0.13	0.14	0.13	0.052	0.10	0.19

ADC, apparent diffusion coefficient; FA, fractional anisotropy; VR; volume ratio; RA, relative anisotropy; AI, anisotropy index; eADC, exponential ADC; MDC, magnitude diffusion coefficient

Table 4. The Values of the DTI Indices for the Perfusion-Diffusion Mismatch Area (Males:Females, 4:4; Mean Age: 58 Years)

Number	ADC	FA	VR	RA	AI	eADC	MDC
1	0.73	0.42	0.22	0.38	0.078	0.48	0.79
2	0.81	0.35	0.16	0.31	0.070	0.45	0.85
3	0.85	0.26	0.09	0.22	0.042	0.43	0.88
4	0.89	0.22	0.06	0.18	0.029	0.41	0.91
5	0.73	0.27	0.08	0.22	0.030	0.48	0.75
6	0.75	0.47	0.25	0.42	0.097	0.48	0.81
7	1.18	0.22	0.06	0.19	0.063	0.34	1.20
8	0.77	0.26	0.08	0.22	0.028	0.47	0.79
Mean	0.84	0.31	0.12	0.27	0.055	0.44	0.87
SD	0.15	0.09	0.07	0.09	0.026	0.05	0.14

ADC, apparent diffusion coefficient; FA, fractional anisotropy; VR; volume ratio; RA, relative anisotropy; AI, anisotropy index; eADC, exponential ADC; MDC, magnitude diffusion coefficient

sensitive than the ADC to observe WM packing and myelination in newborns; further, FA is highly sensitive to micro-structural changes and it is considered a marker of the white matter's integrity (23). The FA decreases with age (24) and it decreases for patients with mild cognitive impairment prior to the development of dementia (25). Anisotropy is decreased in edema (12) and the FA is increased in the acute phase (26) and it is decreased in the chronic phase (11, 26). The FA of the thalamus and splenium have been measured as 0.37 and 0.84, respectively, and the FA of the ischemic WM and GM have been measured as 0.45 and 0.36, respectively (3). FA is hyperacutely elevated at the deep WM in less than seven hours (1.10) and it is reduced at 24 hours (0.85). Reduction of the FA suggests the commencement of tissue damage (16). In our cases, the FA value for infarction was same as that for the normal area (0.36), and the FA value was decreased for microangiopathy lesions (0.21) and the mismatch area (0.31). As determined in previous studies, the FA values for Wallerian degeneration decreased at the corpus callosum (11, 20) and the FA value was 0.39 (normal, 0.45) on the affected side and it was correlated with a motor deficit (19). The plaque centers for acute multiple sclerosis had decreased FA values (0.11-0.18) as compared with the rim, the normal-appearing WM and the chronic lesions (21).

The other DTI indices have not been well studied and the usefulness of the indices for clinical applications has not been evaluated. In our cases, all of the MDC and RA values showed a similar pattern with that of the ADC and FA, respectively. The VR and eADC also showed a similar pattern as that of the FA values, except for an increased VR (0.19, normal: 0.16) and eADC (0.64, normal: 0.46) for infarction lesions. The AI was decreased for all the abnormalities and it was most prominent for infarction lesions (0.032, normal: 0.065). As compared with the contra-lateral normal area, the abnormal areas showed significant differences in all the DTI values and the differences between microangiopathy and the infarction lesions and between the microangiopathy lesions and the mismatch area were significant for all the DTI values except for the AI. The differences between the infarction lesions and the mismatch area were only significant for the ADC, eADC and MDC.

In summary, the microangiopathy lesions showed increased ADC and MDC values, and decreased FA, VR, RA, AI and eADC values. The acute infarction lesions showed increased VR, RA and eADC values, normal FA values, a decreased AI value and decreased ADC and MDC values. The mismatch area showed a similar pattern as that of the microangiopathy lesions; however, any differences were not prominent, with a moderate increase of ADC and MDC values and a moderate decrease of the FA, VR, RA, AI and eADC values.

In conclusion, we suggest that the DTI indices could have a role in making the differential diagnosis of microangiopathy, infarction and perfusion-diffusion mismatch lesions.

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뇌의 미세혈관 병증, 경색, 관류-확산 불일치 병변의 감별을 위한 Diffusion Tensor Imaging[1]

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목적: 뇌의 미세혈관 병증, 경색, 관류-확산 불일치 병변의 감별에 있어서 여러 가지 확산 텐서 영상들의 임상적용 가능성을 평가하는 것이다.

대상과 방법: 1.5 테슬라 자기공명영상 장치를 이용하여 35명의 환자에서 확산텐서 영상을 얻었다. 자기공명영상은 spin echo EPI sequence를 확산 계수 1000 s/mm^2, 확산경사 방향 25, 반복시간 8400 msec, 에코시간 75 msec, 화소수 128 × 128, 영상크기 22 cm, 절편두께 4 mm로 하였다. 이들 영상에서 반대측 정상 부위(28예), 미세혈관 병증(10예), 뇌경색(17예), 관류-확산 불일치 병변 부위(8예)에서 apparent diffusion coefficient (ADC), fractional anisotropy (FA), volume ratio (VR), relative anisotropy (RA), anisotropy index (AI), exponential ADC (eADC), magnitude diffusion coefficient (MDC)를 측정하여 비교하였다.

결과: 정상부위보다 미세혈관 병증 부위는 ADC와 MDC의 증가를 보였고, FA, VR, RA, AI, eADC의 감소를 보였다. 뇌경색 부위는 VR, RA, eADC는 증가하고, 정상 FA를 보였으며, AI, ADC, MDC는 감소하였다. 관류-확산 불일치 병변 부위는 미세혈관 병증 부위와 비슷하게 ADC와 MDC는 증가하고, FA, VR, RA, AI, eADC는 감소하였으나, 차이는 현저하지 않았다.

결론: 여러 가지 확산 텐서 영상들은 뇌의 미세혈관 병증, 경색, 관류-확산 불일치 병변의 감별 진단에 도움을 줄 수 있다.